



TITLE:

# Resting-state functional connectivity predicts recovery from visually induced motion sickness

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1        1    **RESEARCH ARTICLES**

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## 1 Abstract

2 Movies depicting certain types of motion often provoke uncomfortable symptoms similar  
3 to motion sickness, termed visually induced motion sickness (VIMS). VIMS generally  
4 evolves slowly during the viewing of a motion stimulus and, when the stimulus is  
5 removed, the recovery proceeds over time. Recent human neuroimaging studies have  
6 provided new insights into the neural bases of the evolution of VIMS. In contrast, no  
7 study has investigated the neural correlates of the recovery from VIMS. Study of the  
8 recovery process is critical for the development of a way to promote recovery and could  
9 provide further clues for understanding the mechanisms of VIMS. We thus investigated  
10 brain activity during the recovery from VIMS with functional connectivity magnetic  
11 resonance imaging. We found enhanced recovery-related functional connectivity patterns  
12 involving brain areas such as the insular, cingulate, and visual cortical regions, which  
13 have been suggested to play important roles in the emergence of VIMS. These regions  
14 also constituted large interactive networks. Furthermore, the increase in functional  
15 connectivity was correlated with the subjective awareness of recovery for the following  
16 five pairs of brain regions: insula–superior temporal gyrus, claustrum–left and right  
17 inferior parietal lobules, claustrum–superior temporal gyrus, and superior frontal gyrus–  
18 lentiform nucleus. Considering the previous findings on the functions of these regions  
19 and the present results, it is suggested that the increase in FC may reflect brain processes  
20 such as enhanced interoceptive awareness to one’s own bodily state, a neuroplastic  
21 change in visual processing circuits, and/or the maintenance of visual spatial memory.

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1        1    **Introduction**

2        2    First-person perspective images, such as movies captured by action cameras or drones,  
3        3    have recently become popular. Such movies are so realistic that viewers can feel as if they  
4        4    themselves are moving inside the image space. However, the rich image experience is  
5        5    associated with a side effect, termed visually induced motion sickness (VIMS), which  
6        6    involves unpleasant motion sickness (MS)-like symptoms caused by movies depicting  
7        7    certain types of movement. The symptoms are classified into three types: (1) oculomotor  
8        8    (eyestrain, difficulty focusing, headache), (2) nausea (stomach awareness, increased  
9        9    salivation, burping), and (3) disorientation (dizziness, vertigo, drowsiness) (Shupak &  
10       10   Gordon, 2006; Kennedy *et al.*, 2010). These symptoms can last for more than an hour  
11       11   (Kennedy *et al.*, 1993a; Ujike *et al.*, 2008).

12       12        VIMS generally emerges and evolves slowly during exposure to a motion stimulus,  
13       13        and, when the stimulus is removed, the individual slowly recovers from the MS symptoms  
14       14        over time. For the emergence and evolutionary phase of VIMS, several neuroimaging  
15       15        studies have revealed the underlying brain response (Napadow *et al.*, 2013; Miyazaki *et*  
16       16        *al.*, 2015; Farmer *et al.*, 2015; Toschi *et al.*, 2017). Napadow *et al.* (2013) measured the  
17       17        functional magnetic resonance imaging (fMRI) activity of female participants during the  
18       18        presentation of translating black/white stripes for a long enough period to induce VIMS,  
19       19        finding that nausea was associated with a broad network of brain areas including the  
20       20        insula, cingulate cortex, and limbic regions, which are known to process stress, emotion,  
21       21        and interoception. In addition, Miyazaki *et al.* (2015) measured fMRI visual cortical  
22       22        activities during the evolutionary phase of VIMS, which was provoked by the presentation  
23       23        of live-action images containing translational and rotational global motion components.  
24       24        The results showed that the activities of the middle temporal (MT+) area were  
25       25        desynchronised between the left and right hemispheres when participants had MS. The  
26       26        MT+ area has been suggested to interact with the parieto-insular vestibular cortex (PIVC),  
27       27        the centre of vestibular sensation, in the processing of self-motion stimuli that can induce  
28       28        VIMS (Brandt *et al.*, 1998; Kleinschmidt *et al.*, 2002; Smith *et al.*, 2012; Frank *et al.*,  
29       29        2014, 2016). Taking these results together, the insular, cingulate, visual, vestibular  
30       30        cortical, and limbic regions are likely involved in the evolution of VIMS.

31       31        These findings seem to be consistent with several hypotheses concerning the  
32       32        incidence and evolution of MS. The modulation of the MT+ activities could be related to



1 the eye movement hypothesis (Ebenholtz, 1992; Ebenholtz *et al.*, 1994). This hypothesis  
2 proposes that exposure to a specific motion environment could induce abnormal eye  
3 movements that would stimulate the MS-related nuclei in the brainstem. The MT+ has  
4 been suggested to be intimately involved in eye movement control (Corbetta *et al.*, 1998;  
5 Dieterich *et al.*, 1998, 2003; Konen *et al.*, 2005) and therefore might also be associated  
6 with the incidence of MS. In addition, the involvement of PIVC may be related to the  
7 postural instability theory (Ricchio & Stoffregen, 1991), indicating the importance of  
8 postural sway, which would be processed by the PIVC. Additionally, both visual and  
9 vestibular signals could be ascribed to the sensory conflict hypothesis (Reason & Brand,  
10 1975; Reason, 1978; Oman, 1990), which proposes that mismatches between multiple  
11 sensory inputs such as visual and vestibular signals could lead to MS. Thus, recent  
12 neuroimaging studies have provided information on neural correlates of the emergence  
13 of VIMS in relation to its existing theories.

14 What happens during recovery from VIMS? Study of the recovery process from  
15 VIMS is critical for developing ways to promote recovery from the unpleasant symptoms  
16 of VIMS and could also provide clues for further investigation of its mechanisms. The  
17 brain processes related to the recovery phase of VIMS are still unclear but previous  
18 studies of unpleasant events similar to MS, such as fatigue or stress, may provide some  
19 hints. For example, Peltier *et al.* (2005) reported a fatigue-related reduction in functional  
20 connectivity, which was originally defined as a ‘temporal correlation between spatially  
21 remote neurophysiological events’ (Friston *et al.*, 1993), and functional connectivity has  
22 since been widely studied to elucidate functionally coordinated behaviour between brain  
23 regions. They measured fMRI time-series in the rest phase after participants completed a  
24 muscle fatigue task and found decreased functional connectivity between the motor  
25 cortices of the left and right hemispheres. In another example, van Marle *et al.* (2010)  
26 measured resting-state fMRI activity soon after female participants experienced  
27 psychological stress induced by viewing a strongly aversive movie. They reported  
28 increased functional coupling of the amygdala with the dorsal anterior cingulate cortex,  
29 anterior insula, and dorsorostral pontine region, indicating the extended state of  
30 hypervigilance that promotes sustained salience and mnemonic processing. These  
31 examples suggest that, during recovery, brain reorganisation could occur in functional  
32 brain networks related to the negative effects.

1 We therefore conjectured that such brain reorganisation would also occur during the  
2 recovery from VIMS. To test this prediction, we investigated resting-state fMRI activities  
3 during the recovery phase of VIMS. Specifically, we predicted that the functional  
4 connectivity of brain regions such as the insula, cingulate, visual, and/or vestibular  
5 cortical regions would be selectively changed because these regions have been linked to  
6 the emergence and evolutionary phase of VIMS.

## 7

## 8 **Methods**

9 The present study analysed resting-state data obtained in our previous study (Miyazaki *et*  
10 *al.*, 2015), which provides details of the experiment and the task data.

## 11

## 12 **Participants**

13 Participants were 14 volunteers (12 men and 2 women, including 4 authors; mean age,  
14 34.9 years; range, 25–48 years) with normal or corrected-to-normal vision. All  
15 participants had no history of neurologic or psychiatric disorder and provided written  
16 informed consent. All experimental procedures were approved by the Human Studies  
17 Committee of the Graduate School of Human and Environmental Studies at Kyoto  
18 University and the Department of Neurosurgery at Meiji University of Oriental Medicine.

19 Participants were classified into two groups: the VIMS group ( $n = 6$ , all men including  
20 2 authors; mean age  $\pm$  SD,  $34.7 \pm 8.0$  years) who experienced VIMS in the experimental  
21 session; and the healthy group ( $n = 6$ , 2 women and 4 men including 2 authors; mean age  
22  $\pm$  SD,  $33.3 \pm 7.2$  years) who did not experience VIMS. A possible concern is that the  
23 recruitment of some authors as participants would affect our results. We thus conducted  
24 three types of statistical analyses to address this possibility: a sub-analysis excluding the  
25 author participants, an analysis calculating the interclass correlation and design effect of  
26 authorship, and a linear mixed-effects model using authorship as one of the factors. None  
27 of the analyses suggested substantial effects of authorship.

28 The VIMS or healthy classification was performed using a self-reported VIMS (yes or  
29 no) by asking, ‘Did you get motion sick during the experimental session?’. Two of the  
30 participants in the VIMS group were subsequently excluded from the analysis of the  
31 recovery process because they had not recovered from the VIMS according to the  
32 Simulator Sickness Questionnaire (SSQ) score (Kennedy *et al.*, 1993b). Briefly, the SSQ

1 was developed as a standard measure for evaluating the severity of simulator sickness and  
 2 has also been used to measure VIMS symptoms. However, several studies (Stanney *et al.*,  
 3 1998; Stoffregen *et al.*, 2019; Walter *et al.*, 2019) have indicated that the SSQ could  
 4 deviate from self-reports. Such a discrepancy was not observed in the present study. The  
 5 SSQ scores of the VIMS group markedly increased immediately after the VIMS-inducing  
 6 stimulus and decreased to a normal level during the subsequent rest (recovery) phase  
 7 (except for the abovementioned 2 participants), whereas the SSQ scores of the healthy  
 8 group did not change throughout the experimental session (see Figure 4 in Miyazaki *et*  
 9 *al.* [2015]), suggesting that the SSQ scores show a similar trend to the self-reports.

### 11 **Visual stimuli**

12 In the experiment, two types of visual stimuli—a global motion stimulus and a local  
 13 one—were presented. The global motion stimulus was a 6-min-long live-action movie  
 14 containing first-person-perspective, global visual motion. This stimulus content could  
 15 induce VIMS in viewers. In contrast, the local motion stimulus was a 6-min-long live-  
 16 action movie consisting of 8 by 8 patches (total, 64), which reduced the global motion  
 17 stimulus to one-eighth vertically and horizontally. This stimulus was a control and did not  
 18 induce VIMS in viewers because the stimulus contained no global motion component that  
 19 could trigger VIMS. The stimulus was based on Wall and Smith (2008).

20 These stimuli were projected onto a screen located over the participant's forehead  
 21 using a DLP projector (LVP-HC3800; Mitsubishi, Japan). The spatial resolution was 1080  
 22 × 720 pixels, and the refresh rate was 60 Hz. The participant was supine and viewed the  
 23 stimuli through a planar mirror located 25 cm from the eyes. See Miyazaki *et al.* (2015)  
 24 for details.

### 26 **Experimental procedure**

27 The experimental procedure is shown in Figure 1. Before and after the presentation of the  
 28 two aforementioned stimuli, three rest phases (Rest-1, Rest-2, and Rest-3) were arranged.  
 29 Each rest phase was 5 min long and comprised presentation of a grey background with a  
 30 fixation point at the centre. Before the experimental session, participants were instructed  
 31 to relax with their eyes open during the rest phases, and participants were allowed to leave  
 32 the experiment at any time if they could not continue the session. Throughout the session,

1 participants lay supine on the MRI scanner table without firm restriction of their head or  
2 body so as to minimise undesired effects such as pain and distraction. After the first rest  
3 phase (Rest-1), participants viewed the local motion stimulus; none experienced VIMS.  
4 Next, the participants experienced the second rest phase (Rest-2) and then viewed the  
5 global motion stimulus; 8 of the 14 participants experienced VIMS, as described above.  
6 The third rest phase (Rest-3) followed. The order of the stimulus presentations (the local  
7 motion stimulus followed by the global one) was not balanced to avoid a carryover effect  
8 from the global to the local motion period because our preliminary experiment had  
9 indicated that, when the global stimulus precedes the local one, the VIMS symptoms can  
10 be prolonged and overlap the subsequent local stimulus presentation.

11 To rate the degree of VIMS symptoms, participants answered the Simulator Sickness  
12 Questionnaire (SSQ) (Kennedy *et al.*, 1993b) 6 times in total, that is, before and after  
13 each stimulus presentation and each rest phase. The SSQ was developed as a metric of  
14 simulator sickness, and this metric consists of 16 questions on symptoms such as  
15 headache and nausea, based on four grades. The SSQ has generally also been used as a  
16 metric for VIMS. The question items of the SSQ were presented to participants through  
17 images, and the questions were answered by use of a response pad with four buttons (HH-  
18 1x4L; Current Design Inc., Philadelphia, PA). A decrease in the SSQ scores between  
19 before and after the rest phases, which would reflect recovery from VIMS, was analysed  
20 because the aim of the present study was to investigate the recovery phase of VIMS at  
21 rest.

22  
23 (Please place Figure 1 around here)

## 24 25 **MRI data acquisition**

26 Functional MR images were acquired using a clinical 3-T MR scanner (Trio TIM;  
27 Siemens, Germany) and a 20-channel phased-array head coil with a T2\*-weighted  
28 gradient-echo echo planar sequence (repetition time [TR] = 2000 ms; echo time [TE] =  
29 30 ms; flip angle [FA] = 90°; voxel size [VS] = 3 mm × 3 mm × 4 mm; field of view  
30 [FOV] = 192 mm × 192 mm; 37 slices; axial orientation parallel to the AC-PC plane;  
31 interleaved acquisition). The functional images were continuously scanned from 10 s  
32 before Rest-1 to the end of Rest-3, taking about 35 min. For anatomical registration, brain

1 structural images were acquired using a 3D magnetisation-prepared rapid gradient-echo  
2 T1-weighted sequence with the following parameters: TR = 1800 ms, TE = 3.03 ms,  
3 inversion time = 650 ms, FA = 9°, VS = 0.8 mm × 0.8 mm × 0.8 mm, FOV = 205 mm ×  
4 205 mm, 176 slices, axial orientation parallel to the AC-PC plane, interleaved acquisition.  
5

## 6 **Behavioural data analyses**

### 7 *Visually induced motion sickness*

8 After the experimental session, participants self-reported whether or not they experienced  
9 VIMS while viewing the global motion stimulus and were provisionally classified into  
10 the VIMS or healthy group based on the self-report as mentioned above. To objectively  
11 test the validity of this grouping criterion based on the self-reports, SSQ scores, which  
12 are a metric for MS symptoms, were statistically tested to determine whether the scores  
13 of the VIMS group selectively increased after the global motion stimulus. Details of this  
14 analysis are provided in Miyazaki *et al.* (2015).  
15

### 16 *Recovery from visually induced motion sickness*

17 Next, to verify that the VIMS group participants recovered during Rest-3, the differences  
18 in the SSQ scores between before and after each rest phase were computed, and the  
19 differences were statistically tested to determine whether the score of the VIMS group  
20 became significantly larger only for Rest-3, reflecting the recovery from VIMS, and  
21 whether the scores of the other rest phases did not change. To facilitate interpretation of  
22 the results, we examined not only the SSQ Total Score, but also the other three subscales:  
23 Oculomotor, Nausea, and Disorientation. This analysis was performed using R software  
24 (R Core Team, 2017) (see also Miyazaki *et al.*, 2015). A linear mixed-effects model  
25 analysis was performed with the *lmer* function of the lme4 package (Bates *et al.*, 2014).  
26 This model had a within-participants fixed effect PHASE (Rest-1 *vs.* Rest-2 *vs.* Rest-3),  
27 a between-participants fixed effect GROUP (VIMS *vs.* healthy participant groups), an  
28 interaction of PHASE and GROUP, and a random effect of each individual participant.  
29 This analysis was conducted separately for the four scales of the SSQ (Total Score,  
30 Nausea, Oculomotor, and Disorientation).  
31

32 When the PHASE × GROUP interaction was statistically significant, for the *post hoc*  
analysis, the simple effect of PHASE was tested separately for the VIMS and healthy

1 groups. Specifically, the differences in scores between the levels of PHASE (i.e., three  
 2 ways of Rest-1 vs. Rest-2; Rest-2 vs. Rest-3; and Rest-1 vs. Rest-3) were tested by means  
 3 of the functions *testInteractions* and *testFactors* of the *phia* package (De Rosario-  
 4 Martinez, 2015) separately for each participant's group. In contrast, when the interaction  
 5 was not significant, the main effect of PHASE was reported instead. The significance  
 6 level for all statistical analyses was set to 0.05, with correction by the Bonferroni method  
 7 for multiple comparisons involving the four scales of the SSQ, the two participant groups,  
 8 and the repetition of the *post hoc* tests.

## 10 **fMRI data analyses**

### 11 *Preprocessing*

12 All fMRI data were preprocessed using AFNI software (Cox, 1996) as follows: (1) slice  
 13 timing correction; (2) head motion correction; (3) extraction of 5-min-long time-series  
 14 signals (150 fMRI volumes) acquired during each rest phase; (4) transformation to the  
 15 standard Talairach space for group analysis; (5) smoothing with the Gaussian kernel of  
 16 an isotropic 9-mm FWHM; (6) band-pass filtering with a cutoff of 0.01–0.1 Hz; and (7)  
 17 removal of fMRI volumes whose motion or its derivatives exceeded 0.2 mm (i.e., motion  
 18 'scrubbing') to reduce the effect of head movement on fMRI data, in addition to the  
 19 removal of outlier volumes where the ratio of the number of outlier voxels exceeded 0.1.

### 21 *Brain connectedness mapping*

22 After the preprocessing, connectedness maps were made by use of the AFNI *3dTCorrMap*  
 23 function. Connectedness is the average of the Pearson correlation coefficients between a  
 24 specific voxel time-series and the other in the brain mask (Gotts *et al.*, 2012). The Pearson  
 25 correlation coefficient is a real number ranging from  $-1$  to  $+1$ , and this value was  
 26 converted to a Fisher's  $Z$  value with the *3dTCorrMap* function for the following analyses.  
 27 The  $Z$  values were compared between the VIMS and healthy groups within the Talairach  
 28 space by using the AFNI *3dLME* function. For the mapping of the results of this  
 29 comparison, the voxel-wise  $P$  value was set to 0.0001. The false-positive rate for the  
 30 clustering was estimated by use of the *3dClustSim* function, in which the threshold  $\alpha$  for  
 31 the cluster size was set to 0.10; this relatively loose threshold was used because this was  
 32 a first screening procedure to restrict candidates. The conventional 0.05 threshold was



1 used in the second screening based on functional connectivity described below. Based on  
2 this mapping, the regions whose connectedness changed significantly during the recovery  
3 phase of VIMS were detected. Specifically, the regions were determined according to the  
4 following criteria: the connectedness was changed only for the VIMS group selectively  
5 during Rest-3 when the VIMS participants experienced VIMS, whereas that of the healthy  
6 group did not change for all rest phases (interaction contrast calculated using the *3dLME*  
7 function: absolute intergroup difference in  $Z_{\text{Rest-3}} - 0.5 \times Z_{\text{Rest-1}} - 0.5 \times Z_{\text{Rest-2}}$ : the VIMS  
8 group – the healthy group  $> 3.891$ , which corresponds to  $P < 0.0001$ ).

9 Through these steps, 12 brain regions were identified with significant changes in  
10 connectedness during recovery from VIMS (described below). In each region, the mean  
11 time-series averaged across voxels within the region was calculated and used as a seed  
12 for the functional connectivity analysis in the following section.

#### 13 *ROI-based functional connectivity analysis*

14 As stated above, the mean time-series averaged across voxels within the brain regions  
15 showing significant changes in connectedness during recovery from VIMS were used as  
16 seeds to examine functional connectivity throughout the entire brain. Then, using the  
17 same method as in the analysis of connectedness, functional connectivity intensity was  
18 compared between the VIMS and healthy groups. After adjustment to the false-positive  
19 rate for clustering, the result was mapped in Talairach space (voxel-wise  $P$  value = 0.0001,  
20  $\alpha = 0.05$ ), through which the brain regions with changes in functional connectivity during  
21 recovery from VIMS that fulfilled the following criteria were identified: (i) functional  
22 connectivity in Rest-3 following the onset of VIMS changed only in the VIMS group  
23 (interaction contrast calculated using the *3dLME* function: absolute intergroup difference  
24 in  $Z_{\text{Rest-3}} - 0.5 \times Z_{\text{Rest-1}} - 0.5 \times Z_{\text{Rest-2}}$ : the VIMS group – the healthy group  $> 3.891$ , which  
25 corresponds to  $P < 0.0001$ ) and (ii) neither group had a change in functional connectivity  
26 during other rest phases (the VIMS group,  $|Z_{\text{Rest-2}} - Z_{\text{Rest-1}}| < 1.96$ , which corresponds to  
27  $P > 0.05$ ; the healthy group,  $|Z_{\text{Rest-3}} - 0.5 \times Z_{\text{Rest-1}} - 0.5 \times Z_{\text{Rest-2}}| < 1.96$ ;  $|Z_{\text{Rest-2}} - Z_{\text{Rest-1}}|$   
28  $< 1.96$ ).

29 This functional connectivity analysis extracted 19 pairs of brain regions, and changes  
30 in each functional connectivity were analysed using R software (R Core Team, 2017) and  
31 a linear mixed-effects model (the same model used in the analysis of the SSQ scores)  
32

1 consisting of a within-participants fixed effect (PHASE; Rest-1 vs. Rest-2 vs. Rest-3), a  
2 between-participants fixed effect (GROUP; VIMS vs. the healthy group), an interaction  
3 of PHASE and GROUP, and a random effect of each individual participant.

4 Because the PHASE  $\times$  GROUP interactions for all region pairs were statistically  
5 significant, a *post hoc* test was performed to analyse the simple main effect of PHASE in  
6 the VIMS and healthy groups separately. Specifically, the differences in connectivity  
7 between Rest-1 and Rest-2, Rest-2 and Rest-3, and Rest-1 and Rest-3 were tested in each  
8 group. The Bonferroni method was used to correct multiple comparisons for functional  
9 connectivities in the 19 pairs of brain regions, the two participant groups, and repeated  
10 *post hoc* tests of the three PHASE combinations.

### 11 12 *Correlation analysis*

13 Correlation analysis was performed to clarify whether a change in the SSQ Total Score  
14 (i.e., subjective awareness of recovery) could be predicted from the change in functional  
15 connectivity. Because exceptionally large changes in SSQ Total Scores were observed in  
16 some participants, the Spearman's rank correlation coefficient, a nonparametric statistic  
17 that is seldom affected by such variation, was used to analyse the 19 pairs of brain regions  
18 separately. Because of the multiple comparisons, *P* values were subjected to Bonferroni  
19 correction.

### 20 21 *Global network analyses*

22 To analyse the functional network of the brain regions showing recovery-related increases  
23 in connectedness, a multivariate analysis was performed. First, for each participant and  
24 for each rest phase, a partial correlation coefficient of the fMRI time-series was computed  
25 for each pair of the 12 brain regions, resulting in a  $12 \times 12$  matrix. The partial correlation  
26 matrix was then converted into a distance matrix, where the distance was defined by 1  
27 minus the absolute partial correlation coefficient. Second, for each rest phase, within-  
28 group averaged distance matrices were computed for VIMS and healthy groups. The  
29 distance matrices of the first phase (Rest-1) and second phase (Rest-2) were further  
30 averaged as a control for the recovery phase (Rest-3). Third, the columns and rows of the  
31 distance matrices were reordered to place similar brain regions closer, using the *seriation*  
32 function with the 'HC' option in the *seriation* package (Hahsler *et al.*, 2008) of R software.



1 Finally, dendrograms, which are hierarchical clustering trees, were derived from the  
 2 distance matrices using the *pvclust* package (Suzuki & Shimodaira, 2019) of R software,  
 3 which provided *P* values of each cluster through multiscale bootstrap resampling.  
 4 Independently of the above analyses, statistically independent brain networks were  
 5 extracted by a dictionary learning framework. The procedure and the results are detailed  
 6 in the Supplementary Materials.

## 7

## 8 Results

### 9 Behavioural results

10 Details of the results for VIMS symptoms induced in the experiment are provided in  
 11 Miyazaki *et al.* (2015). In brief, 8 of the 14 participants experienced VIMS due to the  
 12 global motion stimulus, and the remaining 6 did not (Figs. 3 and 4 of Miyazaki *et al.*  
 13 [2015]). These results were confirmed by statistical analysis of the SSQ scores (Table 1  
 14 of Miyazaki *et al.* [2015]). Participants were divided into VIMS (*n* = 8) and healthy (*n* =  
 15 6) groups based on the presence and absence of VIMS, respectively. However, 2 of the 8  
 16 participants in the VIMS group did not recover from the VIMS even after the  
 17 experimental session, and this was reflected in their SSQ scores, which did not decrease  
 18 even after Rest-3. Because the aim of this study was to analyse the recovery phase of  
 19 VIMS, these 2 participants were excluded from the subsequent analyses.

20 To verify that the participants in the VIMS group had recovered from VIMS during  
 21 Rest-3, a linear mixed-effects model analysis of the SSQ score was performed before and  
 22 after each rest phase (Table 1 and Fig. 2). SSQ Total Scores decreased during Rest-3 only  
 23 in the VIMS group. The interaction of PHASE and GROUP was statistically significant  
 24 ( $\chi^2(2) = 13.30, P = 0.005$ , Bonferroni corrected). A *post hoc* test of the simple main effect  
 25 of PHASE showed that SSQ scores decreased significantly during Rest-3 only in the  
 26 VIMS group (the VIMS group: Rest-1 vs. Rest-2:  $\chi^2(2) = 0.03, P > 1$ ; Rest-2 vs. Rest-3:  
 27  $\chi^2(2) = 15.04, P = 0.001$ ; Rest-1 vs. Rest-3:  $\chi^2(2) = 16.41, P = 0.0007$ ; the healthy group:  
 28 Rest-1 vs. Rest-2:  $\chi^2(2) = 4.72, P = 0.417$ ; Rest-2 vs. Rest-3:  $\chi^2(2) = 0.07, P > 1$ ; Rest-1  
 29 vs. Rest-3:  $\chi^2(2) = 5.98, P = 0.203$ , Bonferroni corrected), verifying that the participants  
 30 in the VIMS group recovered from the VIMS during Rest-3.

31 Among the three SSQ subscales, the Disorientation score was similar to the Total  
 32 Score (PHASE  $\times$  GROUP interaction:  $\chi^2(2) = 19.16, P = 0.0002$ ; *post hoc* test: the VIMS

1 group: Rest-1 vs. Rest-2:  $\chi^2(2) = 0.02, P > 1$ ; Rest-2 vs. Rest-3:  $\chi^2(2) = 18.52, P = 0.0002$ ;  
 2 Rest-1 vs. Rest-3:  $\chi^2(2) = 19.87, P = 0.0001$ ; the healthy group: Rest-1 vs. Rest-2:  $\chi^2(2) =$   
 3  $0.53, P > 1$ ; Rest-2 vs. Rest-3:  $\chi^2(2) < 0.01, P > 1$ ; Rest-1 vs. Rest-3:  $\chi^2(2) = 0.52, P > 1,$   
 4 Bonferroni corrected). As for Nausea and Oculomotor, the PHASE  $\times$  GROUP interactions  
 5 were not significant (Nausea,  $\chi^2(2) = 7.74, P = 0.084$ ; Oculomotor,  $\chi^2(2) = 5.48, P =$   
 6  $0.259$ ; Bonferroni corrected), and the main effect of PHASE was also not significant  
 7 (Nausea,  $\chi^2(2) = 4.28, P = 0.539$ ; Oculomotor,  $\chi^2(2) = 4.62, P = 0.444$ ; Bonferroni  
 8 corrected).

9  
 10 (Please place Figure 2 and Table 1 around here)

### 11 12 **Brain connectedness mapping**

13 To test our hypothesis that the recovery phase of VIMS induces changes in functional  
 14 connectivity in some brain regions, we examined the substantial changes in functional  
 15 connectivity by calculating connectedness, which is the mean correlation coefficient of a  
 16 specific voxel time-series to other voxel time-series (Gotts *et al.*, 2012), and then by  
 17 mapping the results in Talairach space. As anticipated, the map revealed 12 brain regions  
 18 with significant increases in connectedness during Rest-3 in the VIMS group (Table 2 and  
 19 Fig. 3). The 12 regions included the primary visual cortex in the occipital cortex (the left  
 20 and right lingual gyrus; Fig. 3k and g, respectively) and the left and right insula (Fig. 3c  
 21 and d) and cingulate regions (the right anterior cingulate and left cingulate gyrus; Fig. 3b  
 22 and h, respectively). In addition, the left superior frontal gyrus (Fig. 3j) and the right  
 23 inferior frontal gyrus (Fig. 3l) were included in the 12 brain regions. Furthermore,  
 24 connectedness significantly increased in the cerebellum (left cerebellar tonsil; Fig. 3e)  
 25 and the subcortical region (left and right thalamus and the right claustrum; Fig. 3a, i, and  
 26 f, respectively) during the recovery phase of VIMS. In contrast, no brain region had a  
 27 significant decrease in connectedness during the recovery phase.

28  
 29 (Please place Figure 3 and Table 2 around here)

### 30 31 **ROI-based functional connectivity analyses**

32 For the 12 ROIs with increased connectedness, the question arose as to whether functional

1 connectivity had increased in a broad area or in only specific regions. To address this  
2 question, the entire brain was screened for functional connectivity using the 12 ROIs as  
3 seeds. It was found that 8 of the 12 seed regions showed increases in functional  
4 connectivity with specific regions during only Rest-3 (recovery phase) for the VIMS  
5 group. These regions were the left thalamus, left and right insula, left cerebellar tonsil,  
6 right claustrum, left cingulate gyrus, left superior frontal gyrus, and left inferior frontal  
7 gyrus. Each of these regions had selective increases in functional connectivity with  
8 several other regions, resulting in the following 19 region pairs: left thalamus–right insula,  
9 left thalamus–right inferior parietal lobule, left thalamus–right declive, left insula–left  
10 thalamus, left insula–left inferior parietal lobule, right insula–left superior temporal gyrus,  
11 right insula–left inferior temporal gyrus, left cerebellar tonsil–left parahippocampal gyrus,  
12 right claustrum–left cingulate gyrus, right claustrum–right inferior parietal lobule, right  
13 claustrum–left inferior frontal gyrus, right claustrum–left superior temporal gyrus, right  
14 claustrum–left inferior parietal lobule, left cingulate gyrus–right insula, left superior  
15 frontal gyrus–left medial frontal gyrus, left superior frontal gyrus–left middle temporal  
16 gyrus, left superior frontal gyrus–left lentiform nucleus, and right inferior frontal gyrus–  
17 left inferior frontal gyrus (Table 3). The locations of the 19 pairs are shown in the left  
18 panels of Figure 4 and Supplementary Figure 1. The other 4 of the 12 seed regions had  
19 no selective changes in functional connectivity.

20 The phase (Rest-1, -2, and -3) × group (Healthy and VIMS) interaction effect can be  
21 clearly seen in the right panels of Figure 4 and Supplementary Figure 1. The functional  
22 connectivity of the VIMS group (yellow solid line) remained comparable in Rest-1 and  
23 Rest-2 but increased in Rest-3 (recovery phase), whereas that of the healthy group (white  
24 broken line) did not show an increase in any phase. These results were statistically  
25 confirmed by a linear mixed-effects model analysis. The interaction effects of resting  
26 phases (PHASE: Rest-1, Rest-2, and Rest-3) and participants' group (GROUP: VIMS and  
27 healthy) were statistically significant for all 19 pairs (Table 3). We thus analysed the  
28 simple effect of PHASE separately for the VIMS and healthy groups. The statistical  
29 results for the VIMS and healthy groups are shown in Tables 4 and 5, respectively. The  
30 selective increases in functional connectivity for the VIMS group during Rest-3 (recovery  
31 phase) were statistically significant for almost all pairs and the effect sizes (Cohen's *d*)  
32 were relatively large (Table 4). For example, for the right insula–left thalamus pair (#6 in

1 Tables 4 and 5), the simple effect of the Rest-3 PHASE was statistically significant for  
2 only the VIMS group (Rest-2 vs. Rest-3:  $\chi^2(2) = 53.99$ ,  $P = 2 \times 10^{-11}$ , Cohen's  $d = 3.00$ ;  
3 Rest-1 vs. Rest-3:  $\chi^2(2) = 38.05$ ,  $P = 8 \times 10^{-8}$ , Cohen's  $d = 2.52$ , Bonferroni corrected)  
4 (#6 in Table 4), whereas this effect was not found for the other control conditions (VIMS  
5 group: Rest-1 vs. Rest-2:  $\chi^2(2) = 1.39$ ,  $P > 1$ , Cohen's  $d = 0.48$ ; healthy group: Rest-1 vs.  
6 Rest-2:  $\chi^2(2) = 0.13$ ,  $P > 1$ , Cohen's  $d = 0.15$ ; Rest-2 vs. Rest-3:  $\chi^2(2) = 0.88$ ,  $P > 1$ ,  
7 Cohen's  $d = 0.38$ ; Rest-1 vs. Rest-3:  $\chi^2(2) = 1.70$ ,  $P > 1$ , Cohen's  $d = 0.53$ , Bonferroni  
8 corrected) (#6 in Tables 4 and 5). Similar selective changes in functional connectivity  
9 were observed in the other 18 region pairs (see Tables 3, 4, and 5). However, as an  
10 exception, the functional connectivity between the left superior frontal gyrus and left  
11 middle temporal gyrus showed a tendency toward an increase in the second vs. third rest  
12 phases in the VIMS group (#17 in Table 4).

13  
14 (Please place Figure 4 and Tables 3, 4, and 5 around here)

### 15 16 **Correlation analyses**

17 To determine whether the increases in functional connectivity were associated with  
18 subjective recovery from VIMS, we conducted correlation analyses between the change  
19 in functional connectivity and that in the SSQ Total Scores for the 19 pairs of brain regions  
20 (Fig. 5). The following 5 pairs showed statistically significant negative correlations,  
21 indicating regions in which greater increases in functional connectivity were associated  
22 with greater recovery from VIMS: the right insula–left superior temporal gyrus  
23 (Spearman's rank correlation  $\rho = -0.83$ ,  $P = 0.017$ , Fig. 5a), right claustrum–right inferior  
24 parietal lobule ( $\rho = -0.83$ ,  $P = 0.016$ , Fig. 5b), right claustrum–left superior temporal  
25 gyrus ( $\rho = -0.92$ ,  $P = 0.0004$ , Fig. 5c), right claustrum–left inferior parietal lobule ( $\rho =$   
26  $-0.80$ ,  $P = 0.038$ , Fig. 5d), and left superior frontal gyrus–left lentiform nucleus ( $\rho =$   
27  $-0.80$ ,  $P = 0.038$ , Fig. 5e; all Bonferroni corrected). The correlation was not statistically  
28 significant in the remaining 14 pairs: the left thalamus–right insula ( $\rho = -0.64$ ,  $P = 0.469$ ),  
29 left thalamus–right inferior parietal lobule ( $\rho = -0.63$ ,  $P = 0.510$ ), left thalamus–right  
30 declive ( $\rho = -0.71$ ,  $P = 0.181$ ), left insula–left thalamus ( $\rho = -0.73$ ,  $P = 0.137$ ), left insula–  
31 left inferior parietal lobule ( $\rho = -0.62$ ,  $P = 0.576$ ), right insula–left thalamus ( $\rho = -0.67$ ,  
32  $P = 0.330$ ), right insula–left inferior temporal gyrus ( $\rho = -0.61$ ,  $P = 0.647$ ), left cerebellar

1 tonsil–left parahippocampal gyrus ( $\rho = -0.71, P = 0.181$ ), right claustrum–left cingulate  
2 gyrus ( $\rho = -0.75, P = 0.095$ ), right claustrum–left inferior frontal gyrus ( $\rho = -0.74, P =$   
3  $0.115$ ), left cingulate gyrus–right insula ( $\rho = -0.70, P = 0.212$ ), left superior frontal gyrus–  
4 left medial frontal gyrus ( $\rho = -0.63, P = 0.510$ ), left superior frontal gyrus–left middle  
5 temporal gyrus ( $\rho = -0.58, P = 0.932$ ), and right inferior frontal gyrus–left inferior frontal  
6 gyrus ( $\rho = -0.61, P = 0.698$ ; all Bonferroni corrected).

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15 8 (Please place Figure 5 around here)

### 16 17 18 19 20 10 **Global network analyses**

21 The above connectedness map shows the 12 brain regions with recovery-selective  
22 increases in connectedness (Fig. 3 and Table 2). To explore the possibility that these  
23 regions constituted larger functional networks, we conducted a multivariate analysis in  
24 which the network of these regions was analysed based on distance matrices representing  
25 dissimilarity among the fMRI time-series in each pair of these regions (Supplementary  
26 Figure 2), from which hierarchical clustering dendrograms were derived. Figure 6  
27 compares the results of the VIMS group (a, c) with those of the healthy group (b, d). As  
28 clearly shown in Fig. 6, the 12 brain regions of the VIMS group showed more global  
29 network structures for both recovery (Rest-3) and non-recovery (the average of Rest-1  
30 and Rest-2) phases, in contrast to the healthy group, for which there was only a  
31 statistically significant cluster (marked with asterisks) of the left and right lingual gyri.  
32 Notably, the statistically significant clusters of the VIMS group (marked with asterisks)  
33 comprised the brain regions with recovery-selective increases in ROI-based functional  
34 connectivity (marked with underlines) and the regions with correlation with the SSQ  
35 (marked with italics), corroborating the above analyses (Figs. 4 and 5). During the  
36 recovery phase (Rest-3), the left thalamus additionally participated in the visual cortical  
37 cluster, and this cluster was combined with the other cluster of the left/right insular and  
38 cingulate areas in a higher level. Interestingly, during the phases before sickness  
39 developed, the VIMS group already showed a distinct cluster composed of the left  
40 cingulate gyrus and right thalamus in conjunction with the visual cortical cluster. Some  
41 of these networks were also independently confirmed by dictionary learning-based  
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1 connectivity mapping (Supplementary Figure 3).

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3 (Please place Figure 6 around here)

## 4 **Discussion**

5 Here, we investigated resting-state fMRI functional connectivity during the recovery  
6 phase of VIMS. The analysis showed increased functional connectivity in some brain  
7 areas, including the insula, cingulate, and visual cortical regions. These regions were also  
8 found to constitute large interactive networks. Furthermore, some of the connectivity  
9 increases were strongly correlated with the subjective awareness of recovery from VIMS  
10 (decrease in subjective SSQ scores) for the following five pairs of brain regions: the  
11 insula–superior temporal gyrus, claustrum–left inferior parietal lobule, claustrum–right  
12 inferior parietal lobule, claustrum–superior temporal gyrus, and superior frontal gyrus–  
13 lentiform nucleus. These brain regions included key areas related to the emergence and  
14 evolution of VIMS. The insula had increased connectivity with the cingulate gyrus during  
15 recovery from VIMS (Supplementary Figure 1k). The insular and cingulate regions have  
16 also exhibited a correlated activation during a higher nausea state (Napadow *et al.*, 2013).  
17 Additionally, the insula showed a significant correlation between sympathovagal balance  
18 and connectivity with a middle temporal region (MT+/V5) during a visually induced  
19 nausea sensation (Toschi *et al.*, 2017), which is a visual motion-sensitive area. Moreover,  
20 the middle temporal region has exhibited decreased inter-hemispheric synchronisation  
21 during VIMS (Miyazaki *et al.*, 2015). Here, this key area had increased connectivity with  
22 the superior frontal region during recovery from VIMS (Supplementary Figure 1m). In  
23 addition to these key brain areas, several regions detected in our analysis of the recovery  
24 from VIMS, such as the inferior frontal gyrus (Supplementary Figure 1j and 1n),  
25 cerebellar tonsil (Supplementary Figure 1h), and declive (Supplementary Figure 1c), have  
26 been linked to the evolution of VIMS (Farmer *et al.*, 2015). These results thus conformed  
27 with our initial expectations that key brain regions related to the emergence and evolution  
28 of VIMS could also be involved in the recovery. Further studies are required to verify this  
29 speculation because the present work is a correlational study that cannot establish a causal  
30 relationship.

31 In our experiment, the 2 female participants did not experience motion sick and were



1 included in the healthy group. This result is somewhat inconsistent with the view that  
2 women are more susceptible to MS than men (Munafò *et al.*, 2017). This may be simply  
3 due to the small sample size and/or the difference in experimental stimuli. The type of  
4 visual motion stimuli has been reported to affect the sex difference in MS incidence: the  
5 translational motion stimulus induced a sex difference in MS incidence, whereas the  
6 rotational one did not (Klosterhalfen *et al.*, 2006; Koslucher *et al.*, 2015; Munafò *et al.*,  
7 2017). It thus seems that our global motion stimulus, which included a rotational  
8 component caused by camera rotation, might have difficulty inducing a sex difference.

9 A closer look at the changes in functional connectivity along the resting phases (Rest-  
10 1, Rest-2, and Rest-3) (Fig. 4) suggests two different groups that might have distinct roles  
11 among the five pairs of brain regions. For the first group, the right insula–superior  
12 temporal gyrus (Fig. 4a) and the superior frontal gyrus–lentiform nucleus (Fig. 4e),  
13 functional connectivity remained roughly comparable in the healthy and VIMS groups  
14 before the VIMS (Rest-1 and Rest-2) but increased only in the VIMS group during the  
15 recovery from VIMS (Rest-3), indicating temporary reorganisations of neural circuitry  
16 triggered by the experience of unusual motion environments. In contrast, for the second  
17 group, the claustrum–inferior parietal lobule (Fig. 4b and 4d), functional connectivity was  
18 weaker in the VIMS group than in the healthy group before the onset of VIMS but became  
19 comparable in the two groups during the recovery from VIMS. A similar intrinsic  
20 difference between the groups was also observed in the dendrogram (Fig. 6c vs. Fig. 6d).  
21 These results imply that VIMS group participants might have weaker connectivities  
22 between specific brain regions, possibly reflecting VMIS susceptibility and/or tolerance.  
23 It would be interesting to address MS susceptibility and/or tolerance in a future study with  
24 a larger sample size.

25 The main limitations of this study include its small sample size and its correlational  
26 nature. However, this is the first study to elucidate the brain process in the recovery phase  
27 of VIMS. Thus, it would be interesting to discuss possible reasons why the functional  
28 connectivity between the brain regions increased during the recovery from VIMS. Here,  
29 we propose three possibilities and discuss them in relation to the current understanding  
30 of VIMS and related hypotheses. The first possibility is that the changes in functional  
31 connectivity observed during the recovery phase could be related to interoceptive  
32 awareness (perception of one’s own bodily state) because interoceptive awareness is

1 expected to increase to alleviate the symptoms of VIMS, such as dizziness, eye pain, and  
 2 nausea. In this regard, it is interesting that connectivities, including those of insular and  
 3 cingulate regions, were increased in our study. The insular cortex, the likely centre of the  
 4 neural basis of interoception, is also regarded as the limbic sensory cortex (Craig, 2002;  
 5 Craig & Craig, 2009) because this brain site might be involved in the homeostatic  
 6 regulation of the brain stem. In addition, the cingulate gyrus is also known as the limbic  
 7 motor cortex and might contribute to interoception together with the insular cortex (Craig,  
 8 2002; Craig & Craig, 2009). Indeed, according to Napadow *et al.* (2013), the cingulate  
 9 cortex is coactivated with the insular cortex when the perception of nausea is triggered  
 10 by visual stimuli. The claustrum, which had functional connectivity with multiple brain  
 11 regions in this study, has been reported to be involved in the processing of conscious  
 12 perception, suggesting its association with interoceptive perception (Crick & Koch, 2005).  
 13 Therefore, the strengthened brain networks centring on the insula and claustrum in this  
 14 study might reflect the internal perception of a poor physical state triggered by VIMS.  
 15 Similarly, after observing the strengthening of the amygdala network (including the  
 16 insular cortex) immediately after the induction of psychological stress by visual stimuli,  
 17 van Marle *et al.* (2009) suggested that the strengthened amygdala network might reflect  
 18 negative hypervigilance.

19 The second possibility is that the changes in functional connectivity observed during  
 20 the recovery phase of VIMS could reflect plastic changes in neural circuits related to  
 21 visual processing, such as visual attention and eye movement control. In this regard, we  
 22 note that visual processing regions, including the middle temporal gyrus, which is a visual  
 23 motion-sensitive area, exhibited significantly increased functional connectivity during the  
 24 recovery phase of VIMS in our study. Indeed, the middle temporal gyrus had strong  
 25 connectivity with the superior frontal gyrus (Supplementary Figure 1m and #17 in Tables  
 26 3, 4, and 5). Interestingly, similar results were reported in previous neuroimaging studies  
 27 of visual or motor learning (Albert *et al.*, 2009a, b; Lewis *et al.*, 2009; Stevens *et al.*,  
 28 2009, 2015). Stevens *et al.* (2009) showed that functional connectivities between the  
 29 neural network in the occipital face and scene areas and frontal cortex were increased  
 30 during the rest phase immediately after a visual face and scene recognition task and that  
 31 subsequent memory retrieval performance was predicted by the extent of the changes in  
 32 the functional connectivity. This suggests that a functional connectivity increase during a



1 rest phase after a task might reflect the neuroplastic change needed to improve the efficacy  
 2 of task processing. In addition to this change in connectivity between occipital visual and  
 3 frontal regions, brain areas showing increased functional connectivity in this study (the  
 4 insula–superior temporal gyrus [Figure 4A], insula–inferior temporal gyrus  
 5 [Supplementary Figure 1g], cingulate gyrus–insula [Supplementary Figure 1k], superior  
 6 frontal gyrus–medial frontal gyrus [Supplementary Figure 1l], and left and right inferior  
 7 frontal gyrus [Supplementary Figure 1n]) were coactivated when regulating visual  
 8 attention or eye movement in previous fMRI studies (Corbetta *et al.*, 1998; Dieterich *et*  
 9 *al.*, 1998, 2003; Konen *et al.*, 2005). As for the increased connectivity of the claustrum to  
 10 multiple brain regions in this study, this area is related to visual and multisensory attention  
 11 and was reported to be activated at the same time as the inferior parietal lobule and interior  
 12 frontal gyrus (Vohn *et al.*, 2007), both of which were detected in this study. Attention is  
 13 closely associated with eye movement (Corbetta *et al.*, 1998), and eye movement has  
 14 been proposed to cause MS, including VIMS, in the eye movement hypothesis  
 15 (Ebenholtz, 1992; Ebenholtz *et al.*, 1994). The eye movement hypothesis posits that MS  
 16 is caused by abnormal eye movement induced in a certain type of motion environment.  
 17 Given this prior knowledge and our results, the increase in functional connectivity  
 18 observed during the recovery from VIMS might reflect a plastic change in neural circuits  
 19 related to visual processing, such as visual attention and/or eye movement control.

20 Another putative neuronal circuit of VIMS is the vestibular cortex, which is  
 21 concerned with balance sensation. Previous neuroimaging studies employing visual and  
 22 vestibular stimuli suggested a close cooperation between the motion-sensitive visual  
 23 cortices and vestibular cortex for self-motion perception (Brandt *et al.*, 1998;  
 24 Kleinschmidt *et al.*, 2002; Smith *et al.*, 2012; Frank *et al.*, 2014, 2016). In addition, we  
 25 observed significant changes in functional connectivity in the higher-order visual areas  
 26 of the inferior and middle temporal gyri during recovery from VIMS (Supplementary  
 27 Figure 1g and 1m; Tables 3, 4, and 5). However, no change in connectivity was seen in  
 28 the PIVC, known as the centre of the neural basis of vestibular sensation. This might have  
 29 been because visual inputs could be the only trigger of VIMS and because the visual  
 30 system could be the sole centre of brain dynamics during the recovery phase.

31 Finally, the third possibility is that the increased functional connectivity in these brain  
 32 regions during recovery from VIMS might reflect the maintenance of spatial memory. We

1 found increased connectivity between the cerebellar tonsil and parahippocampal gyrus  
 2 (Supplementary Figure 1h). The parahippocampal gyrus has been suggested to be the  
 3 centre of visual spatial information processing (Epstein *et al.*, 1998; Epstein, 2008) and  
 4 is presumably related to the recognition and memorisation of the space where one exists.  
 5 Previous resting-state fMRI studies of memory maintenance reported a significant  
 6 increase in functional connectivity between the brain regions involved in memory  
 7 processing after memory tasks (Tambini *et al.*, 2010; Gordon *et al.*, 2014). For example,  
 8 in Tambini *et al.* (2010), the resting-state connectivity between the hippocampus and  
 9 lateral occipital complex increased after associative memory tasks, which enabled the  
 10 prediction of subsequent memory performance. Therefore, the increased connectivity in  
 11 these regions might reflect novel spatial experiences in memory processing in the present  
 12 participants with VIMS.

13 If change in functional connectivity is related to the neuroplastic changes and/or  
 14 memory processing described above, then our findings might provide some insight into  
 15 the neural process underlying the sensory conflict hypothesis (Reason & Brand, 1975;  
 16 Reason, 1978; Oman, 1990). This hypothesis suggests that a conflict or mismatch among  
 17 multiple sensory inputs, including visual and vestibular inputs, would cause MS.  
 18 Interestingly, this hypothesis also indicates that a conflict not only among sensory inputs,  
 19 but also between a sensory input and an empirically acquired sensory memory (so-called  
 20 ‘neural store’) would cause MS. From this perspective, individuals with MS such as  
 21 VIMS can develop adaptation, and tolerance increases when similar stimuli are repeated  
 22 because of the reduced conflict between a sensory input and the ‘neural store’, which is  
 23 the memory or plasticity acquired from the repeated sensory experience (Reason & Brand,  
 24 1975; Reason, 1978; Oman, 1990). Although the ‘neural store’ has been just a concept,  
 25 the actual brain network associated with this concept may have been revealed by our  
 26 findings. If so, these findings can advance our understanding of the neural mechanisms  
 27 underlying the development of MS and adaptation to it.

## 29 **Competing Interests**

30 The authors declare that they have no conflict of interest related to this publication.

## 32 **Author Contributions**

- 1 1 J.M.: Conceptualisation, Formal analysis, Investigation, Writing - Original Draft, Writing  
2  
3 2 - Review & Editing.  
4  
5 3 H.Y.: Project Administration, Supervision, Conceptualisation, Methodology, Writing -  
6  
7 4 Original Draft, Writing - Review & Editing, Funding acquisition.  
8  
9 5 Y.I.: Supervision, Writing - Review.  
10  
11 6 H.Y., T.Y.: Methodology, Software support, Writing - Review.  
12  
13 7 T.M., M.U., T.H.: Methodology, Imaging, Writing - Review.  
14

15 8

## 16 9 **Data Accessibility**

- 17  
18 10 Data in this study are available upon request. Please contact the corresponding author for  
19  
20 11 access.  
21

22 12

## 23 13 **Abbreviations**

- 24  
25 14 VIMS, visually induced motion sickness; MS, motion sickness; MRI, magnetic resonance  
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27 15 imaging; fMRI, functional magnetic resonance imaging; SSQ, Simulator Sickness  
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29 16 Questionnaire, ROI, region of interest; MT+, middle temporal complex.  
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1 **Table Captions**

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5 **Table 1. Statistical analysis of the degree of recovery in the subjective score of the**  
6 **Simulator Sickness Questionnaire (SSQ) (decrease in the SSQ between the post- and**  
7 **pre-rest phases)**

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12 This analysis was performed using a linear mixed-effects model with a within-participants  
13 fixed effect PHASE (Rest-1 vs. Rest-2 vs. Rest-3), a between-participants fixed effect  
14 GROUP (VIMS vs. the healthy participant group), an interaction of PHASE × GROUP,  
15 and a random effect of each individual participant. If there was a PHASE × GROUP  
16 interaction, *post hoc* analysis was conducted on the simple effect of PHASE. For the effect  
17 size of the interaction and the simple effect, *f*-squared and Cohen's *d* were computed,  
18 respectively. If there was no interaction, the main effect of PHASE was tested. The *P*  
19 values of the interaction were Bonferroni corrected for the number of scales of the SSQ,  
20 whereas those of the *post hoc* analyses were corrected for the number of the SSQ scales,  
21 participant groups, and comparison repetitions.  
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32 **Table 2. Brain regions whose connectedness increased significantly during the**  
33 **recovery phase from visually induced motion sickness**

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21 Connectedness was computed using the AFNI software *3dTCorrMap* function separately  
22 for the 12 participants. These data were then transformed to the standard Talairach space.  
23 In this standard space, the connectedness was compared by use of the AFNI *3dLME*  
24 function, and the brain regions whose connectedness changed significantly during the  
25 recovery from VIMS were detected. Voxel-wise threshold  $P < 0.0001$  and cluster level  
26 threshold  $\alpha < 0.10$  were used.

28 **Table 3. Brain region pairs whose functional connectivity increased during the**  
29 **recovery phase of visually induced motion sickness (VIMS) and the GROUP ×**  
30 **PHASE interaction effect**

31  
32 A seed-based functional connectivity analysis revealed 19 brain region pairs whose

1 connectivities increased during the recovery from VIMS. The increases in connectivity  
2 were statistically tested with a linear mixed-effects model. The linear mixed-effects model  
3 had a within-participants fixed effect PHASE (Rest-1 vs. Rest-2 vs. Rest-3), a between-  
4 participants fixed effect GROUP (VIMS vs. the healthy participant group), interaction of  
5 PHASE  $\times$  GROUP, and a random effect of each individual participant. For the effect size  
6 of the PHASE  $\times$  GROUP interaction, *f*-squared was computed. The *P* values of the  
7 interaction were Bonferroni corrected for the number of brain region pairs. The  
8 numbering of the 19 pairs corresponds to that in Figure 4 and Supplementary Figure 1.

9  
10 **Table 4. Statistical analysis of the functional connectivity of brain region pairs for**  
11 **the visually induced motion sickness (VIMS) group**

12  
13 The linear mixed-effects model had a within-participants fixed effect PHASE (Rest-1 vs.  
14 Rest-2 vs. Rest-3), a between-participants fixed effect GROUP (VIMS vs. the healthy  
15 participant group), the interaction of PHASE  $\times$  GROUP, and a random effect of each  
16 individual participant. Because there was a PHASE  $\times$  GROUP interaction for all 19 brain  
17 pairs (Table 3), a *post hoc* test was conducted on the simple effect of PHASE. For the  
18 effect size of the simple effect, Cohen's *d* was computed. The *P* values of the *post hoc*  
19 tests were Bonferroni corrected for the number of brain region pairs, participant groups,  
20 and comparison repetitions. The numbering of the 19 pairs corresponds to that in Figure  
21 4 and Supplementary Figure 1.

22  
23 **Table 5. Statistical analysis of the functional connectivity of brain region pairs for**  
24 **the healthy group**

25  
26 The description is the same as that of Table 4 but for the healthy participant group.

27  
28 **Supplementary Table 1. Statistical analysis of the effect of head movement on**  
29 **functional connectivity**

30  
31 The effect of head motion (maximum framewise displacement [FD]) on functional  
32 connectivity was statistically assessed by using a linear mixed-effects model, in which a  
33 within-participants fixed effect of FD and interactions of FD  $\times$  PHASE and FD  $\times$



1        1    GROUP were included, in addition to the fixed effects of PHASE, GROUP, and PHASE  
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3        2    × GROUP and a random effect of each individual participant. If the head movement-  
4  
5        3    related interactions (i.e., FD × PHASE and FD × GROUP) were statistically significant,  
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7        4    the statistics for FD were omitted because it was difficult to determine the effect.  
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1 **Figure Captions**

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5 **Figure 1. Schematic diagram showing the time course of the experimental session**

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9 After the first rest phase (Rest-1), the local motion stimulus was presented as a control.  
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11 After the second rest phase (Rest-2), the global motion stimulus, which can induce  
12  
13 visually induced motion sickness (VIMS), was presented. Finally, the third rest phase  
14  
15 (Rest-3) comprised the recovery from VIMS.  
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18 **Figure 2. Time course of the change in the Total Score (TS) of the Simulator Sickness**  
19  
20 **Questionnaire (SSQ)**

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23 The vertical axis shows the change in the TS (post-score minus pre-score) of the SSQ.  
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25 The horizontal axis shows the experimental phase (Rest-1, Rest-2, and Rest-3). The  
26  
27 visually induced motion sickness (VIMS) group's participants experienced motion  
28  
29 sickness soon before the third rest phase (Rest-3), and recovery from symptoms occurred  
30  
31 during Rest-3. Accordingly, the score of the VIMS group (solid line) significantly  
32  
33 decreased before and after Rest-3, whereas the score of the healthy group participants  
34  
35 (broken line), who did not experience VIMS, did not change as much.  
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38 **Figure 3. Twelve brain regions whose connectedness significantly increased during**  
39  
40 **the recovery phase from visually induced motion sickness (VIMS)**

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43 Each row is as follows: a, left thalamus; b, anterior cingulate; c, left insula; d, right insula;  
44  
45 e, cerebellar tonsil; f, claustrum; g, right lingual gyrus; h, cingulate gyrus; i, right  
46  
47 thalamus; j, left superior frontal gyrus; k, left lingual gyrus; and l, inferior frontal gyrus.  
48  
49 Each column shows, from left to right, axial, sagittal, and coronal brain images. The  
50  
51 following thresholds were set: voxel-wise threshold  $P < 0.0001$ , cluster level threshold  $\alpha$   
52  
53  $< 0.10$ .  
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56 **Figure 4. Brain regions whose functional connectivity with the seed regions**  
57  
58 **increased in the recovery phase from visually induced motion sickness (VIMS)**

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3 2 Each column shows, from left to right, axial, sagittal, and coronal brain images, and the  
4 3 change in the functional connectivity (Z scores averaged within the participants' groups)  
5 4 of each experimental phase, separately for VIMS and healthy groups, respectively (error  
6 5 bars are standard errors). Each panel is the result for the following brain regions (the brain  
7 6 region in brackets is the corresponding seed): a–left superior temporal gyrus (right insula),  
8 7 b–right inferior parietal lobule (right claustrum), c–left superior temporal gyrus (right  
9 8 claustrum), d–left inferior parietal lobule (right claustrum); and e–left lentiform nucleus  
10 9 (left superior frontal gyrus). For this mapping, we used the following thresholds: voxel-  
11 10 wise threshold  $P < 0.0001$ , cluster level threshold  $\alpha < 0.05$ . The numbering of brain region  
12 11 pairs corresponds to that in Tables 3, 4, and 5.

13 **Figure 5. Correlation plots between the change in the Total Score (TS) of the**  
14 **Simulator Sickness Questionnaire (SSQ) and the change in functional connectivity**

15  
16 16 The vertical axis is the change in the TS of the SSQ: Rest-3 minus the average of Rest-1  
17 17 and Rest-2; the greater the recovery in VIMS symptoms, the greater the decrease in this  
18 18 score. The horizontal axis is the change in functional connectivity: Rest-3 minus the  
19 19 average of Rest-1 and Rest-2. In the graphs,  $\rho$  indicates Spearman's rank correlation  
20 20 coefficient, with the corresponding  $P$  value shown below. The  $P$  values were Bonferroni  
21 21 corrected for multiple comparisons among the 19 brain region pairs. Abbreviations: IPL,  
22 22 inferior parietal lobule; L, left; R, right; SFG, superior frontal gyrus; STG, superior  
23 23 temporal gyrus.

24  
25 **Figure 6. Hierarchical clustering trees of the 12 brain regions showing recovery-**  
26 **selective increases in connectedness**

27  
28 (a) The dendrogram of the VIMS group for the recovery phase (Rest-3), which was  
29 29 derived from the distance matrix (Supplementary Fig. 2a), whose elements indicate 1  
30 30 minus absolute partial correlation between each pair of the 12 regions. Statistically  
31 31 significant clusters are marked with an asterisk ( $P < 0.05$ ) or plus ( $P < 0.1$ ). Brain regions  
32 32 showing recovery-selective increases in the ROI-based functional connectivity and

1 correlations with SSQ are underlined and in italics, respectively. (b) The same as (a) but  
2 for the healthy group. (c) The same as (a) but for the control phase (the average of Rest-  
3 1 and Rest-2). (d) The same as (c) but for the healthy group. Abbreviations: L, left; R,  
4 right; LG, lingual gyrus; SFG, superior frontal gyrus; IFG, inferior frontal gyrus.  
5

6 **Supplementary Figure 1. Brain regions whose functional connectivity with the seed**  
7 **regions increased in the recovery phase from visually induced motion sickness**  
8 **(VIMS)**

9  
10 Each column shows, from left to right, axial, sagittal, and coronal brain images, and the  
11 change in functional connectivity (Z scores averaged within the participants' groups) of  
12 each experimental phase, separately for VIMS and healthy groups, respectively (error  
13 bars are standard errors). Each panel is the result for the following brain regions (the brain  
14 region in brackets is the corresponding seed): a–right insula (right thalamus), b–right  
15 inferior parietal lobule (right thalamus), c–right declive (right thalamus), d–left thalamus  
16 (left insula), e–right inferior parietal lobule (left insula), f–left thalamus (right insula), g–  
17 left inferior temporal gyrus (right insula), h–left parahippocampal gyrus (left cerebellar  
18 tonsil), i–left cingulate gyrus (right claustrum), j–left inferior frontal gyrus (right  
19 claustrum), k–right insula (left cingulate gyrus), l–left medial frontal gyrus (left superior  
20 frontal gyrus), m–left middle temporal gyrus (left superior frontal gyrus), and n–left  
21 inferior frontal gyrus (right inferior frontal gyrus). For this mapping, we used the  
22 following thresholds: voxel-wise threshold  $P < 0.0001$ , cluster level threshold  $\alpha < 0.05$ .  
23 The numbering of brain region pairs corresponds to that in Tables 3, 4, and 5.  
24

25 **Supplementary Figure 2. Distance matrices of the 12 brain regions showing**  
26 **recovery-selective increases in connectedness**

27  
28 (a) The distance matrix of the VIMS group for the recovery phase (Rest-3), whose  
29 elements indicate 1 minus absolute partial correlation between each pair of the 12 regions.  
30 Brain regions showing recovery-selective increases in the ROI-based functional  
31 connectivity and correlations with SSQ are underlined and in italics, respectively. (b) The  
32 same as (a) but for the healthy group. (c) The same as (a) but for the control phase (the

1 average of Rest-1 and Rest-2). (d) The same as (c) but for the healthy group.  
2  
3 Abbreviations: L, left; R, right; LG, lingual gyrus; SFG, superior frontal gyrus; IFG,  
4  
5 inferior frontal gyrus.  
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9 **Supplementary Figure 3. Statistically independent brain networks related to**  
10 **recovery from visually induced motion sickness (VIMS)**  
11  
12

13 (a) The within-participant averaged distance matrix for the recovery phase of the VIMS  
14 group. Each element represents a cross-correlation coefficient between each pair of the  
15 22 regions determined by a dictionary learning technique. This analysis derived 22  
16 regions of interest (ROIs). (b) The top 10% connections derived from the distance matrix.  
17 The connections are overlaid on a glass brain. Yellow circles and red lines denote the  
18 derived regions and connections, respectively. The connections are as follows: R Posterior  
19 Cingulate–L Lingual Gyrus, L Lingual Gyrus–R MOG, L Lingual Gyrus–L MTG, L  
20 Lingual Gyrus–R MOG, L Lingual Gyrus–L MOG, R Superior Occipital Gyrus–R MOG,  
21 R Culmen–R Parahippocampal Gyrus, R Culmen–R Cuneus, R Culmen–L Cuneus, R  
22 Culmen–R MOG, R Culmen–L MOG, R Parahippocampal Gyrus–L Cuneus, R  
23 Parahippocampal Gyrus–L Posterior Cingulate, R Cuneus–L Cuneus, R Cuneus–L  
24 Precuneus, L Cuneus–R MOG, R MOG–L MTG, L MOG–R MOG, L MOG–R MOG, L  
25 MTG–R MOG, L MTG–L MOG, and R MOG–R MOG. Abbreviations: L, left; R, right;  
26 MTG, middle temporal gyrus; MOG, middle occipital gyrus.  
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**Table 1. Statistical analysis of the degree of recovery in the subjective score of the Simulator Sickness Questionnaire (SSQ) (decrease in the SSQ between the post- and pre-rest phases)**

Scale	GROUP × PHASE interaction		Simple effect of PHASE						
	Statistics <i>P</i> value ( $\chi^2$ )	Effect size $f^2$	VIMS			Healthy			
			Coefficient Estimate ± SE	Statistics <i>P</i> value ( $\chi^2$ )	Effect size Cohen's <i>d</i>	Coefficient Estimate ± SE	Statistics <i>P</i> value ( $\chi^2$ )	Effect size Cohen's <i>d</i>	
<b>Total score</b>	.005 (13.30)	0.45	Rest-1 vs. Rest-2	46.75 ± 11.45	> 1 (0.03)	0.07	-4.99 ± 2.29	.417 (4.72)	0.89
			Rest-2 vs. Rest-3	-41.76 ± 10.77	.001 (15.04)	1.58	-0.62 ± 2.29	> 1 (0.07)	0.11
			Rest-1 vs. Rest-3	-43.63 ± 10.77	0.0007 (16.41)	1.65	-5.61 ± 2.29	.203 (5.98)	1.00
<b>Disorientation</b>	.0002 (19.16)	0.72	Rest-1 vs. Rest-2	-2.32 ± 15.09	> 1 (0.02)	0.06	-2.32 ± 3.19	> 1 (0.53)	0.30
			Rest-2 vs. Rest-3	-64.96 ± 15.09	0.0002 (18.52)	1.76	2.32 ± 3.19	> 1 (< 0.01)	0.30
			Rest-1 vs. Rest-3	-67.28 ± 15.09	0.0001 (19.87)	1.82	-5.92 ± 3.19	> 1 (0.52)	< 0.01
<b>Main effect of PHASE</b>									
				<b>Coefficient</b> Estimate ± SE		<b>Statistics</b> <i>P</i> value ( $\chi^2$ )		<b>Effect size</b> Cohen's <i>d</i>	
<b>Nausea</b>	.084 (7.74)	0.24		-7.16 ± 3.46		.539 (4.28)		0.6	
<b>Oculomotor</b>	.259 (5.48)	0.16		-4.21 ± 1.96		.444 (4.62)		0.62	

This analysis was performed using a linear mixed-effects model with a within-participants fixed effect PHASE (Rest-1 vs. Rest-2 vs. Rest-3), a between-participants fixed effect GROUP (VIMS vs. the healthy participant group), an interaction of PHASE × GROUP, and a random effect of each individual participant. If there was a PHASE × GROUP interaction, post hoc analysis was conducted on the simple effect of PHASE. For the effect size of the interaction and the simple effect, f-squared and Cohen's *d* were computed, respectively. If there was no interaction, the main effect of PHASE was tested. The *P* values of the interaction were Bonferroni corrected for the number of scales of the SSQ, whereas those of the post hoc analyses were

**Table 2. Brain regions whose connectedness increased significantly during the recovery phase from visually induced motion sickness**

	Cluster label	Hemisphere	Voxel	Talairach coordinate			Broadman area	Cluster level $\alpha$
				x	y	z		
1	Thalamus	Left	131	+4.5	+19.5	+8.5	—	$\ll 0.01$
2	Anterior Cingulate	Right	49	-22.5	-43.5	+8.5	9, 10	$\ll 0.01$
3	Insula	Left	41	+40.5	-10.5	+5.5	13, 44	$\ll 0.01$
4	Insula	Right	25	-31.5	-13.5	+8.5	13	$< 0.01$
5	Cerebellar Tonsil	Left	21	+13.5	+43.5	-39.5	-	$< 0.01$
6	Clastrum	Right	16	-25.5	+19.5	+17.5	13	$< 0.01$
7	Lingual Gyrus	Right	11	-4.5	+91.5	-3.5	17, 18	$< 0.03$
8	Cingulate Gyrus	Left	10	+1.5	-19.5	+35.5	6, 32	$< 0.03$
9	Thalamus	Right	7	-22.5	+31.5	+8.5	30	$< 0.06$
10	Superior Frontal Gyrus	Left	7	+25.5	-40.5	+14.5	9, 10, 32	$< 0.06$
11	Lingual Gyrus	Left	6	+13.5	+94.5	-12.5	17, 18	$< 0.07$
12	Inferior Frontal Gyrus	Right	6	-28.5	-10.5	+26.5	-	$< 0.07$

Connectedness was computed using the AFNI software 3dTCorrMap function separately for the 12 participants. These data were then transformed to the standard Talairach space. In this standard space, the connectedness was compared by use of the AFNI 3dLME function, and the brain regions whose connectedness changed significantly during the recovery from VIMS were detected. Voxel-wise threshold  $P < 0.0001$ , cluster level threshold  $\alpha < 0.10$  were used.



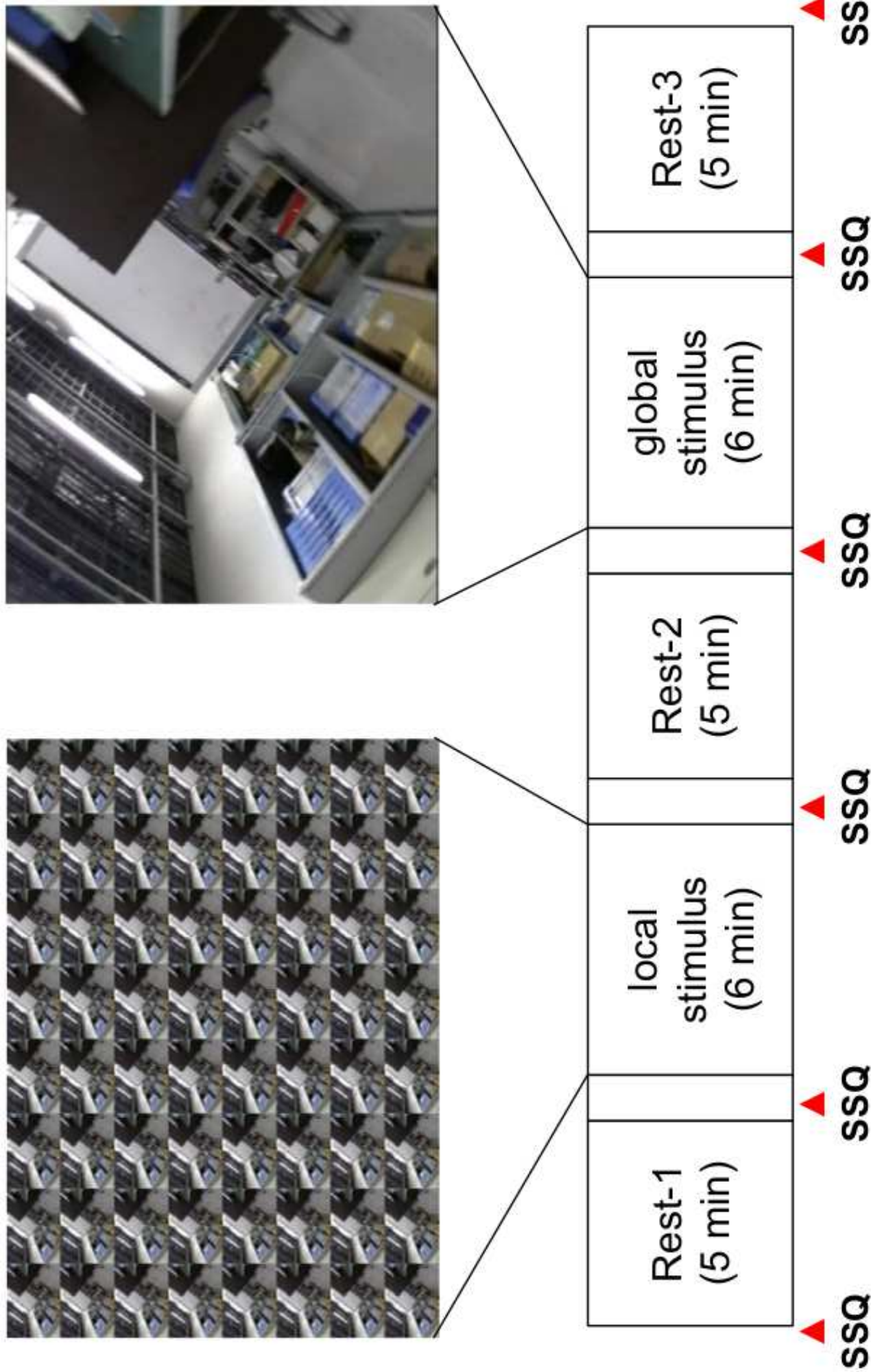


			Rest-1 vs. Rest-2			Rest-2 vs. Rest-3			Rest-1 vs. Rest-3			
			Coefficient	Test statistics	Effect size	Coefficient	Test statistics	Effect size	Coefficient	Test statistics	Effect size	
			Estimate ± SE	<i>P</i> value ( $\chi^2$ )	Cohen's <i>d</i>	Estimate ± SE	<i>P</i> value ( $\chi^2$ )	Cohen's <i>d</i>	Estimate ± SE	<i>P</i> value ( $\chi^2$ )	Cohen's <i>d</i>	
L Thalamus	1	Insula	Right	-0.07 ± 0.07	> 1 (1.05)	0.42	0.34 ± 0.07	5×10 <sup>-5</sup> (25.70)	2.07	0.27 ± 0.07	.006 (16.37)	1.65
	2	Inferior Parietal Lobule	Right	-0.04 ± 0.06	> 1 (0.44)	0.27	0.30 ± 0.06	4×10 <sup>-5</sup> (25.94)	2.08	0.26 ± 0.06	.001 (19.61)	1.81
	3	Declive	Right	-0.03 ± 0.04	> 1 (0.82)	0.37	0.27 ± 0.04	3×10 <sup>-12</sup> (57.83)	3.10	0.24 ± 0.04	2×10 <sup>-9</sup> (44.86)	2.73
L Insula	4	Thalamus	Left	0.02 ± 0.05	> 1 (0.10)	0.13	0.27 ± 0.05	2×10 <sup>-6</sup> (32.17)	2.32	0.29 ± 0.05	2×10 <sup>-7</sup> (35.93)	2.45
	5	Inferior Parietal Lobule	Right	-0.04 ± 0.07	> 1 (0.35)	0.24	0.43 ± 0.07	8×10 <sup>-8</sup> (38.05)	2.52	0.39 ± 0.07	3×10 <sup>-6</sup> (31.12)	2.28
R Insula	6	Thalamus	Left	-0.06 ± 0.05	> 1 (1.39)	0.48	0.40 ± 0.05	2×10 <sup>-11</sup> (53.99)	3.00	0.34 ± 0.05	8×10 <sup>-8</sup> (38.05)	2.52
	7	Superior Temporal Gyrus	Left	0.11 ± 0.08	> 1 (2.13)	0.60	0.30 ± 0.08	.010 (15.40)	1.60	0.41 ± 0.08	.0003 (29.00)	2.20
	8	Inferior Temporal Gyrus	Left	0.11 ± 0.07	> 1 (2.79)	0.68	0.26 ± 0.07	.016 (14.53)	1.56	0.38 ± 0.07	5×10 <sup>-6</sup> (30.05)	2.24
L Cerebellar Tonsil	9	Parahippocampal Gyrus	Left	-0.003 ± 0.08	> 1 (0.001)	0.01	0.32 ± 0.08	.008 (15.92)	1.63	0.32 ± 0.08	.009 (15.65)	1.62
	10	Cingulate Gyrus	Left	-0.01 ± 0.06	> 1 (0.05)	0.09	0.33 ± 0.06	3×10 <sup>-6</sup> (31.22)	2.28	0.32 ± 0.06	9×10 <sup>-6</sup> (28.86)	2.19
R Claustrum	11	Inferior Parietal Lobule	Right	-0.06 ± 0.07	> 1 (0.64)	0.33	0.33 ± 0.07	.0002 (22.58)	1.94	0.27 ± 0.07	.009 (15.60)	1.61
	12	Inferior Frontal Gyrus	Left	-0.004 ± 0.05	> 1 (0.01)	0.03	0.29 ± 0.05	5×10 <sup>-6</sup> (30.03)	2.24	0.28 ± 0.05	8×10 <sup>-6</sup> (29.17)	2.21
	13	Superior Temporal Gyrus	Left	0.11 ± 0.07	> 1 (2.30)	0.62	0.27 ± 0.07	.019 (14.19)	1.54	0.38 ± 0.07	1×10 <sup>-5</sup> (27.91)	2.16
L Cingulate Gyrus	14	Inferior Parietal Lobule	Left	0.01 ± 0.06	> 1 (0.01)	0.04	0.26 ± 0.06	.002 (18.80)	1.77	0.27 ± 0.06	.001 (19.67)	1.81
	15	Insula	Right	-0.002 ± 0.07	> 1 (0.002)	0.02	0.35 ± 0.07	1×10 <sup>-5</sup> (28.37)	2.17	0.34 ± 0.07	1×10 <sup>-5</sup> (27.97)	2.16
L Superior Frontal Gyrus	16	Medial Frontal Gyrus	Left	0.04 ± 0.06	> 1 (0.51)	0.29	0.26 ± 0.06	.0003 (22.06)	1.92	0.31 ± 0.06	7×10 <sup>-6</sup> (29.29)	2.21
	17	Middle Temporal Gyrus	Left	0.06 ± 0.07	> 1 (0.68)	0.34	0.25 ± 0.07	.090 (11.26)	1.37	0.31 ± 0.07	.003 (17.45)	1.71
	18	Lentiform Nucleus	Left	0.10 ± 0.07	> 1 (1.71)	0.53	0.27 ± 0.07	.026 (13.60)	1.51	0.37 ± 0.07	7×10 <sup>-5</sup> (24.96)	2.04
R Inferior Frontal Gyrus	19	Inferior Frontal Gyrus	Left	0.001 ± 0.05	> 1 (0.0004)	0.01	0.24 ± 0.05	2×10 <sup>-5</sup> (27.66)	2.15	0.24 ± 0.05	1×10 <sup>-5</sup> (27.87)	2.16

The linear mixed-effects model had a within-participants fixed effect PHASE (Rest-1 vs. Rest-2 vs. Rest-3), a between-participants fixed effect GROUP (VIMS vs. the healthy participant group), the interaction of PHASE × GROUP, and a random effect of each individual participant. Because there was a PHASE × GROUP interaction for all 19 brain pairs (Table 3), a post hoc test was conducted on the simple effect of PHASE. For the effect size of the simple effect, Cohen's *d* was computed. The *P* values of the post hoc tests were Bonferroni corrected for the number of brain region pairs, participant groups, and comparison repetitions. The numbering of the 19 pairs corresponds to that in Figure 4 and Supplementary Figure 1.

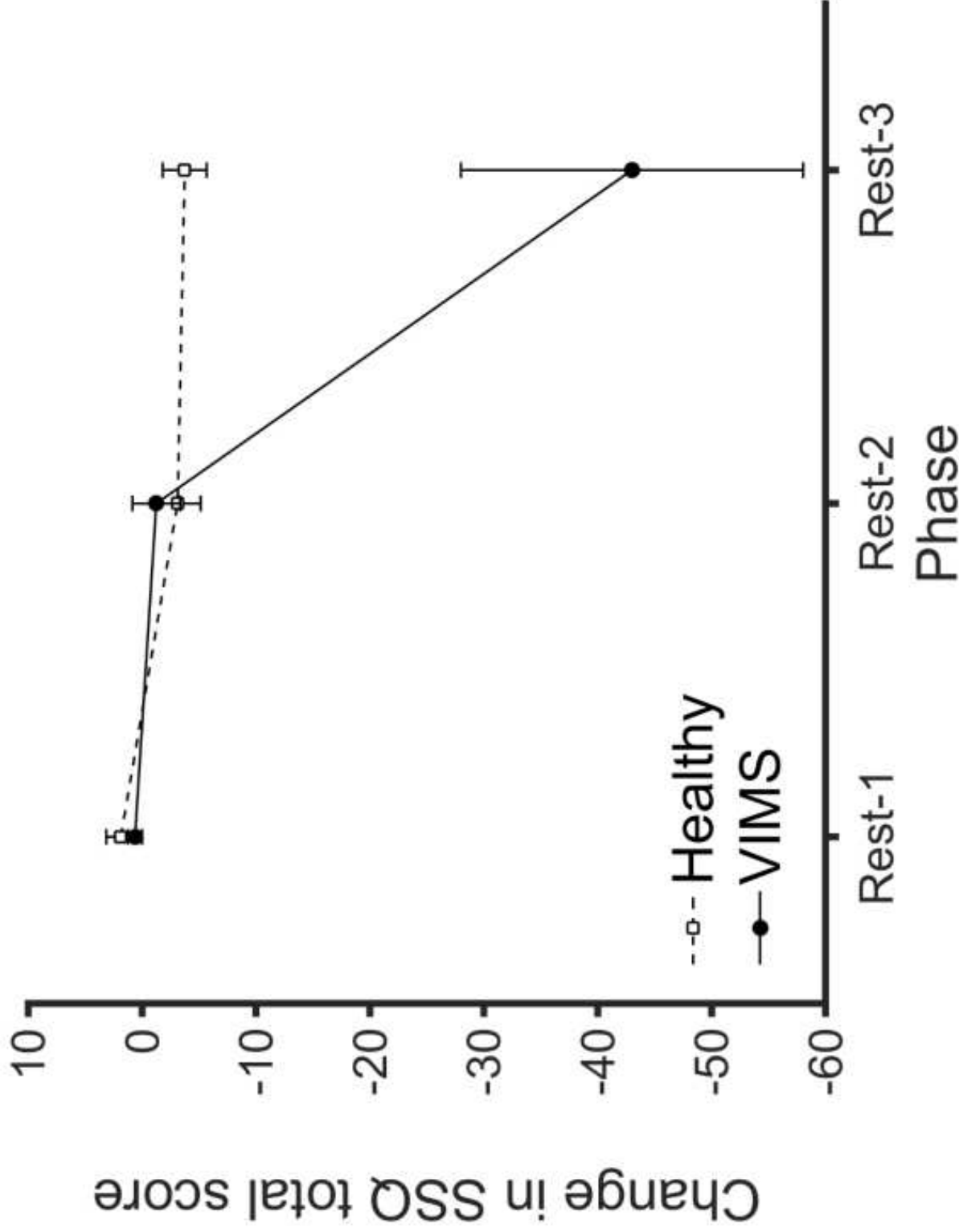
			Rest-1 vs. Rest-2			Rest-2 vs. Rest-3			Rest-1 vs. Rest-3			
			Coefficient Estimate ± SE	Test statistics P value ( $\chi^2$ )	Effect size Cohen's <i>d</i>	Coefficient Estimate ± SE	Test statistics P value ( $\chi^2$ )	Effect size Cohen's <i>d</i>	Coefficient Estimate ± SE	Test statistics P value ( $\chi^2$ )	Effect size Cohen's <i>d</i>	
L Thalamus	1	Insula	Right	-0.01 ± 0.05	> 1 (0.07)	0.11	-0.06 ± 0.05	> 1 (1.25)	0.46	-0.07 ± 0.05	> 1 (1.92)	0.57
	2	Inferior Parietal Lobule	Right	-0.06 ± 0.07	> 1 (0.66)	0.33	-0.05 ± 0.07	> 1 (0.49)	0.29	-0.11 ± 0.07	> 1 (2.30)	0.62
	3	Declive	Right	-0.04 ± 0.06	> 1 (0.59)	0.31	-0.05 ± 0.06	> 1 (0.82)	0.37	-0.10 ± 0.06	> 1 (2.79)	0.68
L Insula	4	Thalamus	Left	-0.07 ± 0.07	> 1 (1.13)	0.43	-0.06 ± 0.07	> 1 (0.90)	0.39	-0.14 ± 0.07	> 1 (4.05)	0.82
	5	Inferior Parietal Lobule	Right	-0.11 ± 0.07	> 1 (2.30)	0.62	-0.04 ± 0.07	> 1 (0.24)	0.20	-0.07 ± 0.07	> 1 (1.05)	0.42
R Insula	6	Thalamus	Left	-0.02 ± 0.05	> 1 (0.13)	0.15	-0.04 ± 0.05	> 1 (0.88)	0.38	-0.06 ± 0.05	> 1 (1.70)	0.53
	7	Superior Temporal Gyrus	Left	0.02 ± 0.06	> 1 (0.08)	0.11	-0.09 ± 0.06	> 1 (2.25)	0.61	-0.07 ± 0.06	> 1 (1.50)	0.50
	8	Inferior Temporal Gyrus	Left	-0.05 ± 0.05	> 1 (1.03)	0.41	-0.04 ± 0.05	> 1 (0.45)	0.27	-0.09 ± 0.05	> 1 (2.84)	0.69
L Cerebellar Tonsil	9	Parahippocampal Gyrus	Left	-0.05 ± 0.07	> 1 (0.45)	0.27	-0.10 ± 0.07	> 1 (2.12)	0.59	-0.15 ± 0.07	> 1 (4.51)	0.87
	10	Cingulate Gyrus	Left	-0.03 ± 0.05	> 1 (0.41)	0.26	-0.06 ± 0.05	> 1 (1.29)	0.46	-0.09 ± 0.05	> 1 (3.15)	0.72
R Claustrum	11	Inferior Parietal Lobule	Right	0.01 ± 0.06	> 1 (0.06)	0.10	-0.12 ± 0.06	> 1 (4.20)	0.84	-0.11 ± 0.06	> 1 (3.26)	0.74
	12	Inferior Frontal Gyrus	Left	-0.08 ± 0.06	> 1 (1.63)	0.52	-0.03 ± 0.06	> 1 (0.25)	0.20	-0.11 ± 0.06	> 1 (3.14)	0.72
	13	Superior Temporal Gyrus	Left	-0.08 ± 0.04	> 1 (4.84)	0.90	-0.04 ± 0.04	> 1 (1.06)	0.42	-0.11 ± 0.04	.142 (10.43)	1.32
L Cingulate Gyrus	14	Inferior Parietal Lobule	Left	-0.07 ± 0.05	> 1 (2.00)	0.58	-0.04 ± 0.05	> 1 (0.46)	0.27	-0.11 ± 0.05	> 1 (4.34)	0.85
	15	Insula	Right	-0.06 ± 0.04	> 1 (2.55)	0.65	-0.06 ± 0.04	> 1 (2.69)	0.67	-0.12 ± 0.04	.137 (10.49)	1.32
L Superior Frontal Gyrus	16	Medial Frontal Gyrus	Left	0.003 ± 0.03	> 1 (0.02)	0.06	-0.08 ± 0.03	.313 (8.97)	1.22	-0.08 ± 0.03	.502 (8.11)	1.16
	17	Middle Temporal Gyrus	Left	-0.06 ± 0.05	> 1 (1.33)	0.47	-0.06 ± 0.05	> 1 (0.70)	0.53	-0.12 ± 0.05	> 1 (6.04)	1.00
	18	Lentiform Nucleus	Left	-0.04 ± 0.06	> 1 (0.50)	0.29	-0.07 ± 0.06	> 1 (1.15)	0.44	-0.11 ± 0.06	> 1 (3.18)	0.73
R Inferior Frontal Gyrus	19	Inferior Frontal Gyrus	Left	-0.02 ± 0.05	> 1 (0.14)	0.15	-0.07 ± 0.05	> 1 (1.70)	0.53	-0.09 ± 0.05	> 1 (2.81)	0.68

The description is the same as that of Table 4 but for the healthy participant group.



**Figure 1. Schematic diagram showing the time course of the experimental session**

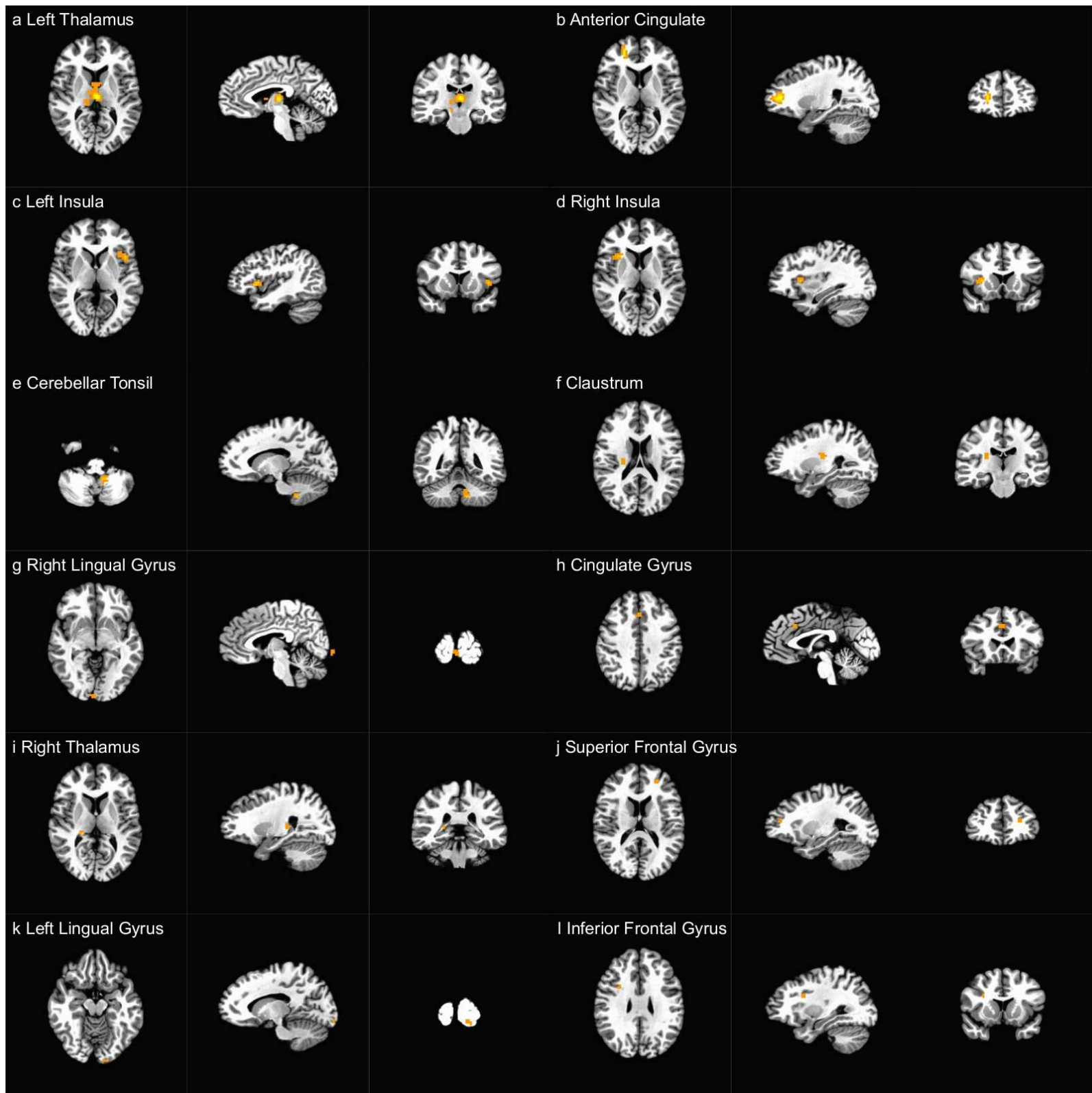
After the first rest phase (Rest-1), the local motion stimulus was presented as a control. After the second rest phase (Rest-2), the global motion stimulus, which can induce visually induced motion sickness (VIMS), was presented. Finally, the third rest phase (Rest-3) comprised the recovery from VIMS.



**Figure 2. Time course of the change in the Total Score (TS) of the Simulator Sickness Questionnaire (SSQ)**

The vertical axis shows the change in the TS (post-score minus pre-score) of the SSQ. The horizontal axis shows the experimental phase (Rest-1, Rest-2, and Rest-3). The visually induced motion sickness (VIMS) group's participants experienced motion sickness soon before the third rest phase (Rest-3), and recovery from symptoms occurred during Rest-3. Accordingly, the score of the VIMS group (solid line) significantly decreased before and after Rest-3, whereas the score of the healthy group participants (broken line), who did not experience VIMS, did not change as much.

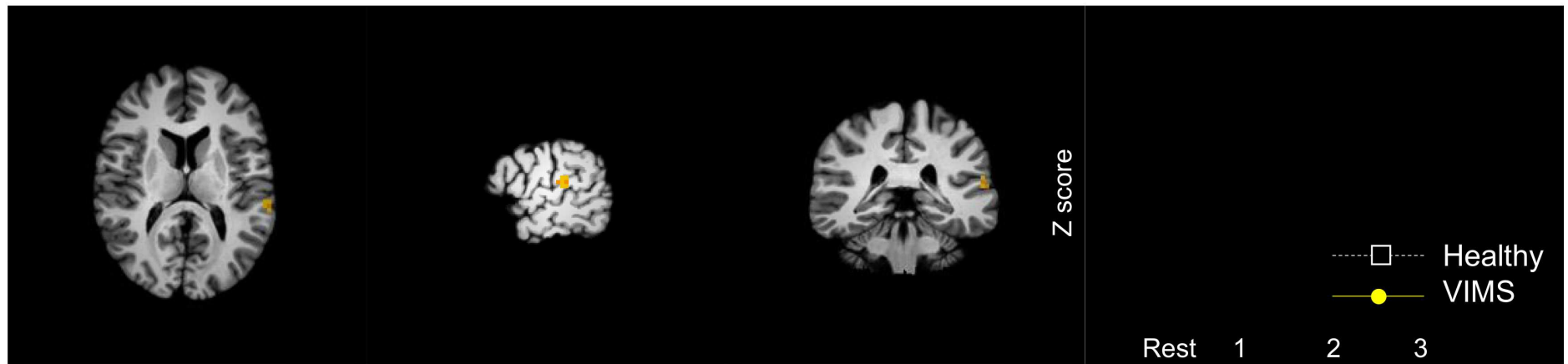




**Figure 3. Twelve brain regions whose connectedness significantly increased during the recovery phase from visually induced motion sickness (VIMS)**

Each row is as follows: a, left thalamus; b, anterior cingulate; c, left insula; d, right insula; e, cerebellar tonsil; f, claustrum; g, right lingual gyrus; h, cingulate gyrus; i, right thalamus; j, left superior frontal gyrus; k, left lingual gyrus; and l, inferior frontal gyrus. Each column shows, from left to right, axial, sagittal, and coronal brain images. The following thresholds were set: voxel-wise threshold  $P < 0.0001$ , cluster level threshold  $\alpha < 0.10$ .

## a 7. L Superior Temporal Gyrus (seed: R Insula)



**Figure 4. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

Each column shows, from left to right, axial, sagittal, and coronal brain images, and the change in the functional connectivity (Z scores averaged within the participants' groups) of each experimental phase, separately for VIMS and healthy groups, respectively (error bars are standard errors). Each panel is the result for the following brain regions (the brain region in brackets is the corresponding seed): a–left superior temporal gyrus (right insula), b–right inferior parietal lobule (right claustrum), c–left superior temporal gyrus (right claustrum), d–left inferior parietal lobule (right claustrum); and e–left lentiform nucleus (left superior frontal gyrus). For this mapping, we used the following thresholds: voxel-wise threshold  $P < 0.0001$ , cluster level threshold  $\alpha < 0.05$ . The numbering of brain region pairs corresponds to that in Tables 3, 4, and 5.

b 11. R Inferior Parietal Lobule (seed: R Claustrum)

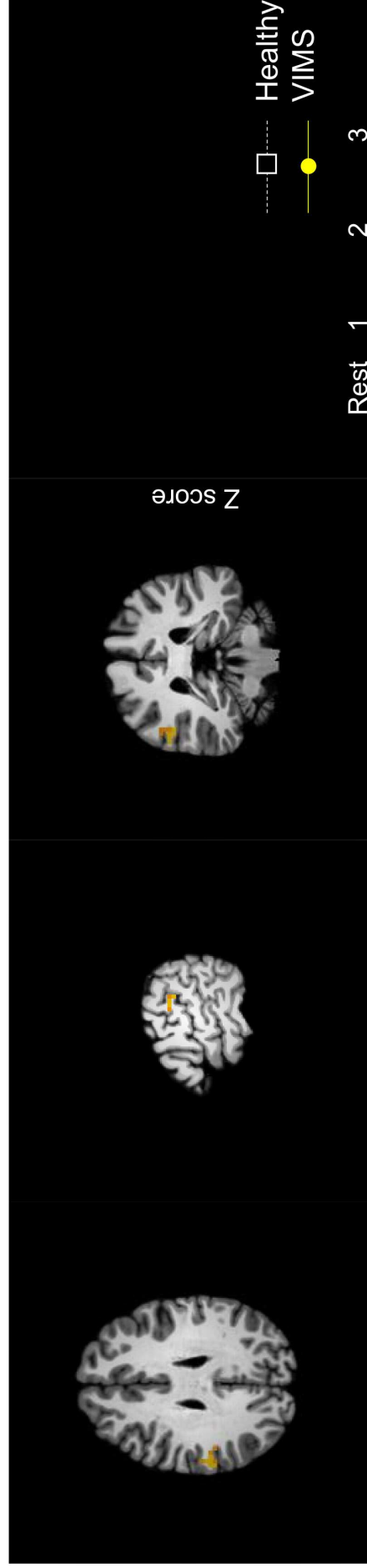


Figure 4. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)

The same as Figure 4a but for right inferior parietal lobule.



c 13. L Superior Temporal Gyrus (seed: R Claustrum)

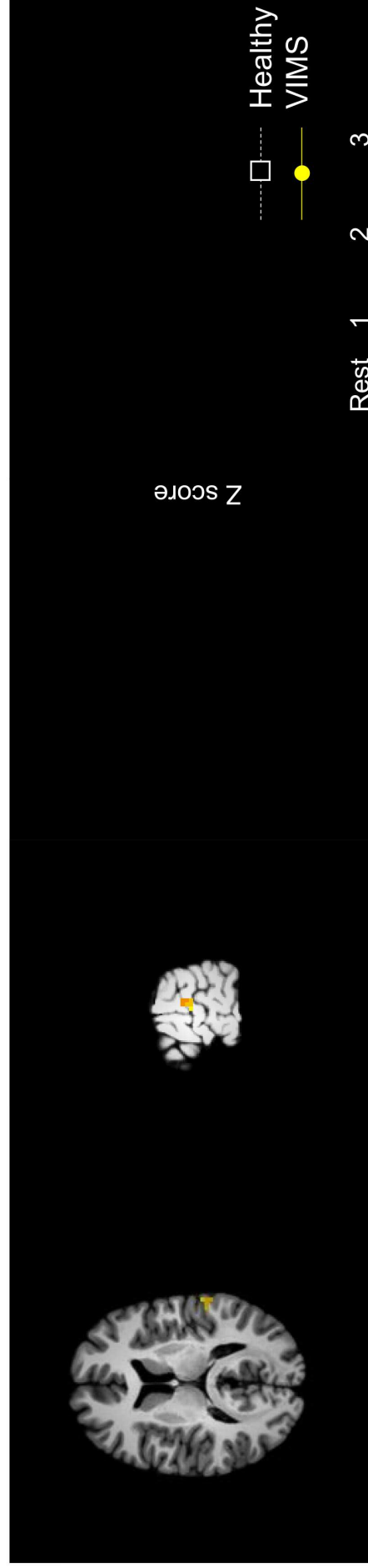


Figure 4. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)

The same as Figure 4a but for left superior temporal gyrus.

d 14. L Inferior Parietal Lobule (seed: R Claustrum)

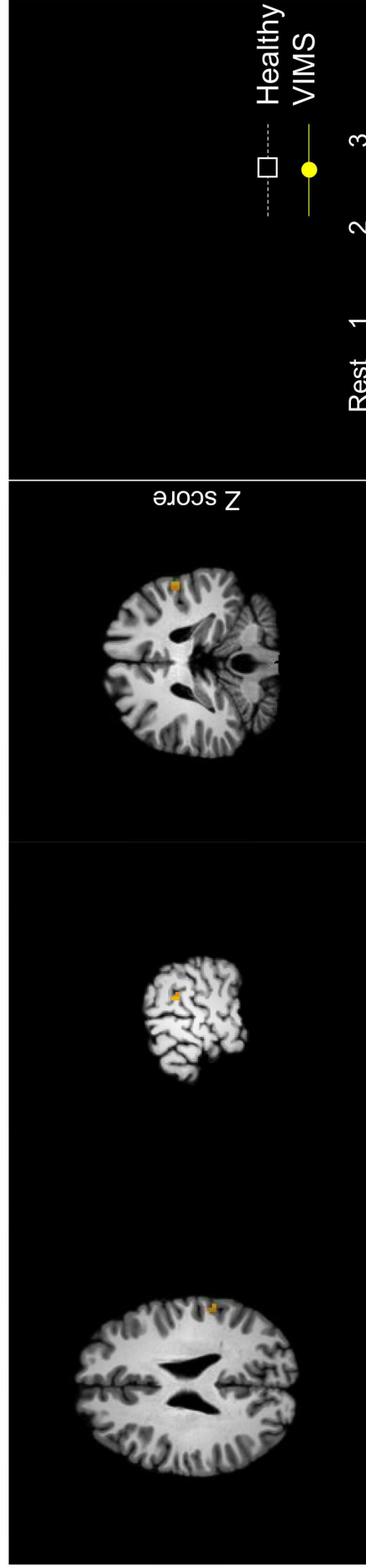
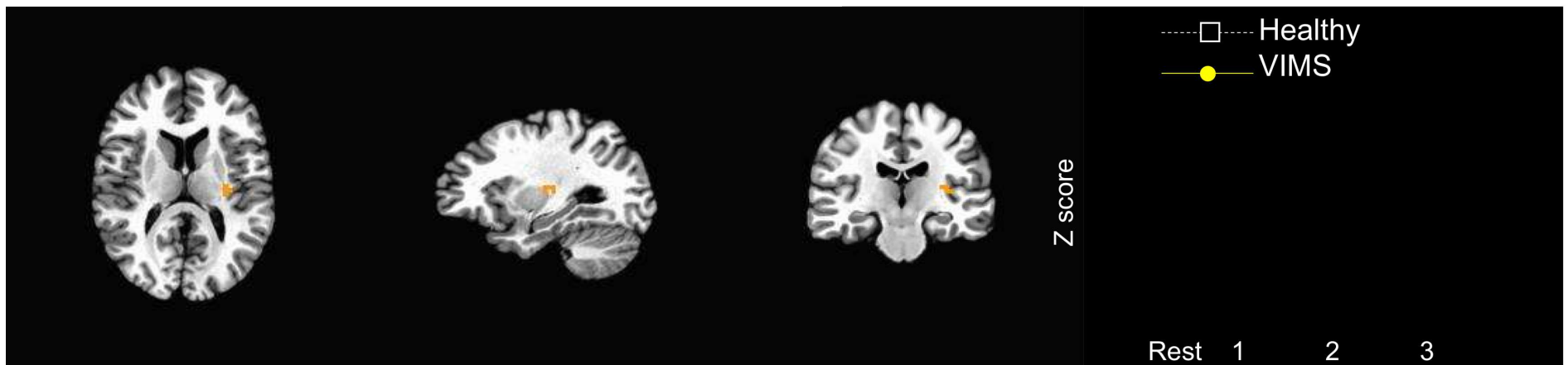


Figure 4. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)

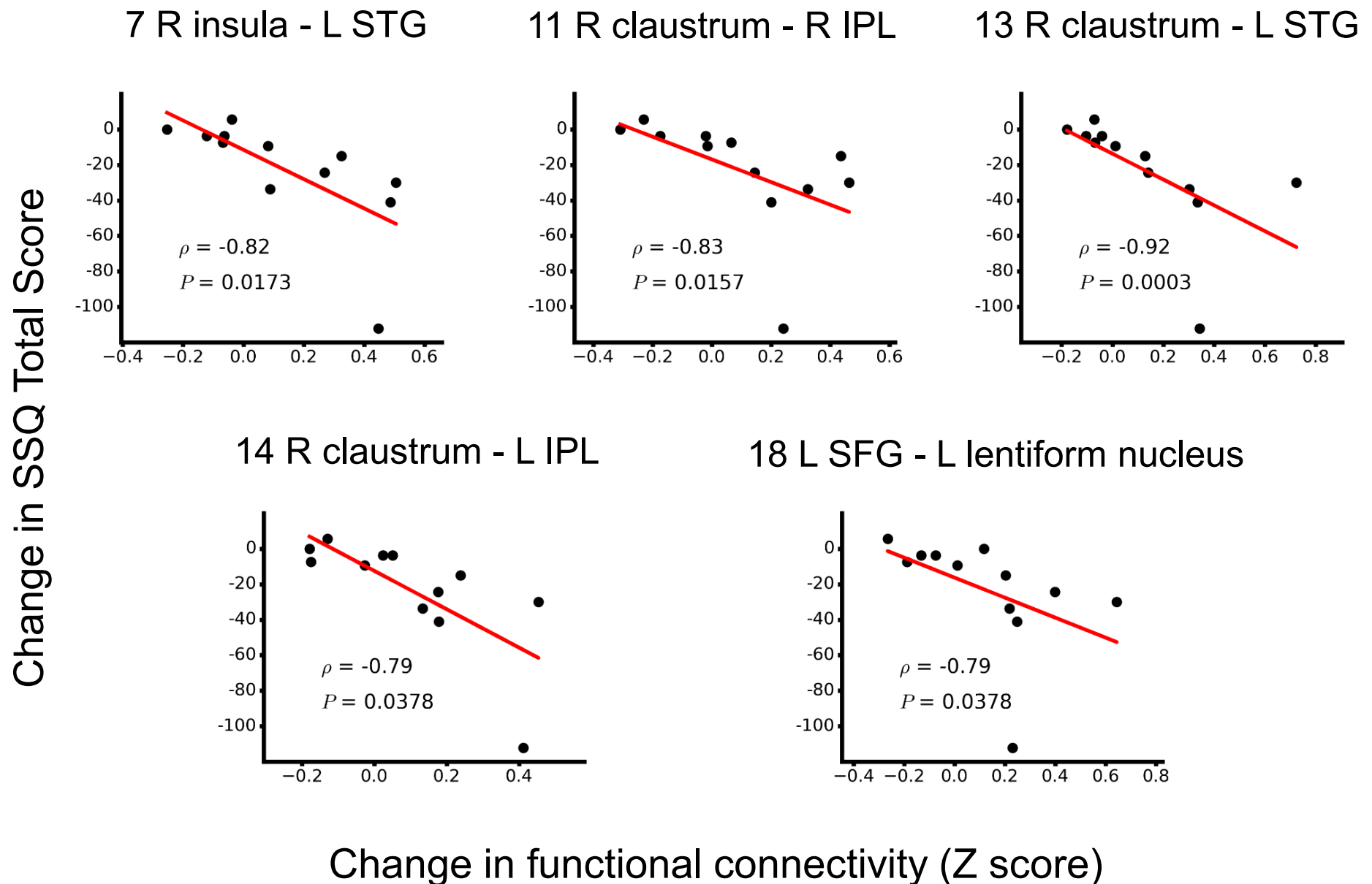
The same as Figure 4a but for left inferior parietal lobule.

## e 18. L Lentiform Nucleus (seed: L Superior Frontal Gyrus)



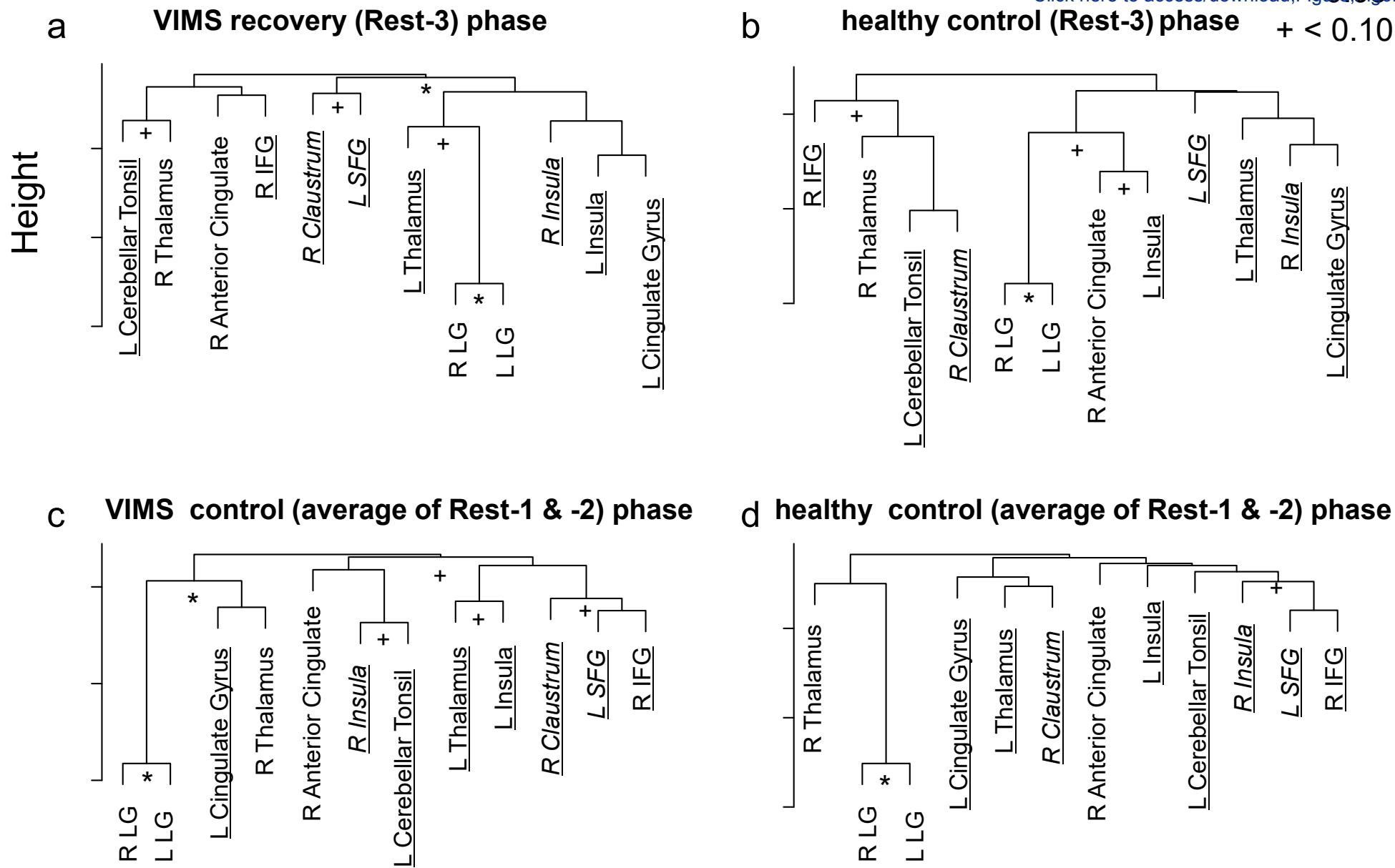
**Figure 4. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Figure 4a but for left lentiform nucleus.



**Figure 5. Correlation plots between the change in the Total Score (TS) of the Simulator Sickness Questionnaire (SSQ) and the change in functional connectivity**

The vertical axis is the change in the TS of the SSQ: Rest-3 minus the average of Rest-1 and Rest-2; the more VIMS symptoms recovered, the more this score decreases. The horizontal axis is the change in functional connectivity: Rest-3 minus the average of Rest-1 and Rest-2. In the graphs,  $\rho$  indicates Spearman's rank correlation coefficient, with the corresponding  $P$  value shown below. The  $P$  values were Bonferroni corrected for multiple comparisons among the 19 brain region pairs. Abbreviations: IPL, inferior parietal lobule; L, left; R, right; SFG, superior frontal gyrus; STG, superior temporal gyrus.



**Figure 6. Hierarchical clustering trees of the 12 brain regions showing recovery-selective increases in connectedness**

(a) The dendrogram of the VIMS group for the recovery phase (Rest-3), which was derived from the distance matrix (Supplementary Fig. 2a), whose elements indicate 1 minus absolute partial correlation between each pair of the 12 regions. Statistically significant clusters are marked with an asterisk ( $P < 0.05$ ) or plus ( $P < 0.1$ ). Brain regions showing recovery-selective increases in the ROI-based functional connectivity and correlations with SSQ are underlined and in italics, respectively. (b) The same as (a) but for the healthy group. (c) The same as (a) but for the control phase (the average of Rest-1 and Rest-2). (d) The same as (c) but for the healthy group. Abbreviations: L, left; R, right; LG, lingual gyrus; SFG, superior frontal gyrus; IFG, inferior frontal gyrus.

## +Supplementary Materials

### **Resting-state functional connectivity predicts recovery from visually induced motion sickness**

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## Statistical assessment of the effects of head motion on functional connectivity

To clarify whether head motion affects functional connectivity, we statistically assessed the effect of head movement on functional connectivity. As a measure of head movement, the framewise displacement (FD) (Power et al. 2012) was computed. Then, the maximum value of FD during each rest phase was derived, and the effect of this maximum FD on the functional connectivity of 19 brain region pairs (listed in Tables 3–5) was tested with a linear mixed-effects model analysis. The linear mixed-effects model had fixed effects of the maximum FD (hereafter “FD”) in addition to PHASE (Rest-1, -2, and -3) and GROUP (VIMS and healthy group) and three interactions of FD  $\times$  PHASE, FD  $\times$  GROUP, and PHASE  $\times$  GROUP, as well as a random intercept for participants. A standard model selection technique was conducted using the *step* function in the lmerTest package (Kuznetsova *et al.* 2017) of R software. The *step* function statistically tests fixed effects based on the Satterthwaite method and removes ineffective terms from the model.

All 19 brain regions again showed a significant PHASE  $\times$  GROUP interaction, confirming our results in the main text. The results for the effect of FD are shown in Supplementary Table 1, in which *P* values were not adjusted. For 15 brain region pairs among the 19 pairs, three head motion-related terms (that is the fixed effect of FD and the interactions of FD  $\times$  PHASE and FD  $\times$  GROUP) were not statistically significant, suggesting no effect of head motion on functional connectivity. A statistically significant FD  $\times$  GROUP interaction was obtained for the remaining four pairs: the right claustrum–right inferior parietal lobule, right claustrum–left superior temporal gyrus, right claustrum–left inferior parietal lobule, and left superior frontal gyrus–left medial frontal gyrus. The PHASE  $\times$  GROUP interaction was again statistically significant, even when the FD  $\times$  GROUP interaction term and the simple effect of FD were included in the model as covariants. The *post hoc* interaction analyses essentially showed the same results for the VIMS group as those obtained with the original model without the covariants. For the healthy group, a slightly different result was obtained. There were simple effects of PHASE not found by the original model for two of the four pairs: the right claustrum–right inferior parietal lobule and the left superior frontal gyrus–left medial frontal gyrus. For these pairs, recovery-selective decreases in functional connectivity were shown for Rest-3 compared with Rest-2.

## Extraction of independent brain networks with dictionary learning

To complement our main results, we performed a separate network analysis that extracted statistically independent resting networks related to the recovery from VIMS. A dictionary learning technique (Mensch et al. 2016) was applied for the fMRI data of the individuals in the VIMS group, using the *nilearn* module of Python (<https://nilearn.github.io/>). First, after preprocessing of the fMRI data as described in the main text, the data during the recovery phase were subjected to dictionary learning (*DictLearn* and *RegionExtractor* methods with the number of components = 15 and



minimum region size = 100 voxels), revealing 22 sparse regions of brain activities. Second, for each pair of the 22 brain regions, cross-correlation coefficients of fMRI time-series were computed, leading to a  $22 \times 22$  matrix. Finally, this matrix was subjected to a connectome analysis using the *plot\_connectome* function (edge threshold = 90%) in *nilearn*.

The result is shown in Supplementary Figure 3. Multiple brain regions critical for VIMS dynamics were found. The connectome map (Supplementary Figure 3b) shows visual processing regions, including the middle temporal gyrus and lingual gyrus, which were also found in the connectedness/functional connectivity approach used in the main text. These visual regions have been reported to have connectivity changes in the evolutionary phase of VIMS (Miyazaki *et al.* 2015; Toschi *et al.* 2017). In addition, the cingulate region, which has been indicated to play key roles in the interoceptive process, such as self-awareness to one's own unpleasant bodily state, during/after VIMS, was detected in this analysis as well as that of the main text (Tables 2–5). Interestingly, the parahippocampal gyrus was again extracted in this analysis. The parahippocampal region is a core area for spatial memory processing (Epstein *et al.* 1998; Epstein, 2008), and memory processing has been suggested to be involved in an adaptation to motion sickness including VIMS (Reason & Brand 1975; Reason 1978; Oman 1990). This result thus suggests that such an adaptive process might underlie the recovery from VIMS. Altogether, this analysis corroborates our results reported in the main text.

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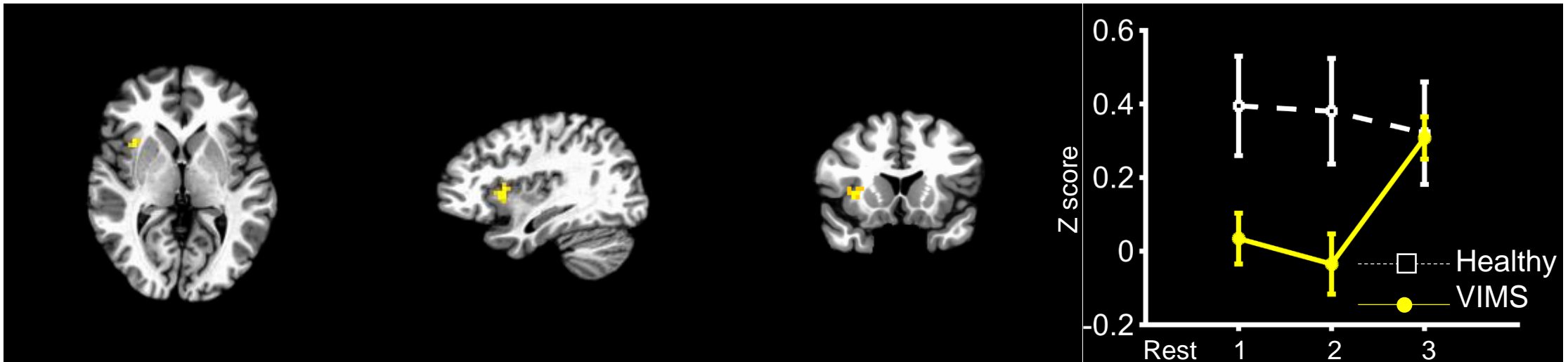
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Supplementary Table 1. Statistical analysis of the effect of head movement on functional connectivity

Seed region	Paired region	Hemisphere	Test statistics		
			FD	FD × GROUP	FD × PHASE
L Thalamus	1 Insula	Right	.739 (.113)	.501 (.722)	.578 (.318)
	2 Inferior Parietal Lobule	Right	.359 (.871)	.739 (.113)	.819 (.203)
	3 Declive	Right	.963 (.002)	.760 (.280)	.896 (.017)
L Insula	4 Thalamus	Left	.929 (.008)	.241 (1.44)	.888 (.120)
	5 Inferior Parietal Lobule	Right	.438 (.621)	.890 (.020)	.941 (.061)
R Insula	6 Thalamus	Left	.671 (.185)	.754 (.100)	.622 (.490)
	7 Superior Temporal Gyrus	Left	.459 (.563)	.191 (1.80)	.396 (.974)
	8 Inferior Temporal Gyrus	Left	.312 (1.06)	.082 (.3.26)	.661 (.424)
L Cerebellar Tonsil	9 Parahippocampal Gyrus	Left	.248 (1.40)	.086 (2.85)	.285 (1.19)
	10 Cingulate Gyrus	Left	.151 (2.19)	.362 (.860)	.624 (.485)
R Claustrum	11 Inferior Parietal Lobule	Right	-	.008 (8.22)	.596 (.533)
	12 Inferior Frontal Gyrus	Left	.633 (.233)	.162 (2.04)	.550 (.368)
	13 Superior Temporal Gyrus	Left	-	.030 (5.26)	.793 (.235)
	14 Inferior Parietal Lobule	Left	-	.046 (4.37)	.733 (.316)
L Cingulate Gyrus	15 Insula	Right	.542 (.381)	.671 (4.08)	.973 (.001)
	16 Medial Frontal Gyrus	Left	-	.022 (6.11)	.367 (1.07)
L Superior Frontal Gyrus	17 Middle Temporal Gyrus	Left	.88 (3.28)	.525 (.420)	.744 (.301)
	18 Lentiform Nucleus	Left	.130 (2.47)	.227 (1.54)	.518 (.683)
R Inferior Frontal Gyrus	19 Inferior Frontal Gyrus	Left	.485 (.502)	.364 (.857)	.418 (.921)

The effect of head motion (maximum framewise displacement [FD]) on functional connectivity was statistically assessed by using a linear mixed-effects model, in which a within-participants fixed effect of FD and interactions of FD × PHASE and FD × GROUP were included, in addition to the fixed effects of PHASE, GROUP, and PHASE × GROUP and a random effect of each individual participant. If the head movement-related interactions (i.e., FD × PHASE and FD × GROUP) were statistically significant, the statistics for FD were omitted because it was difficult to determine the effect.

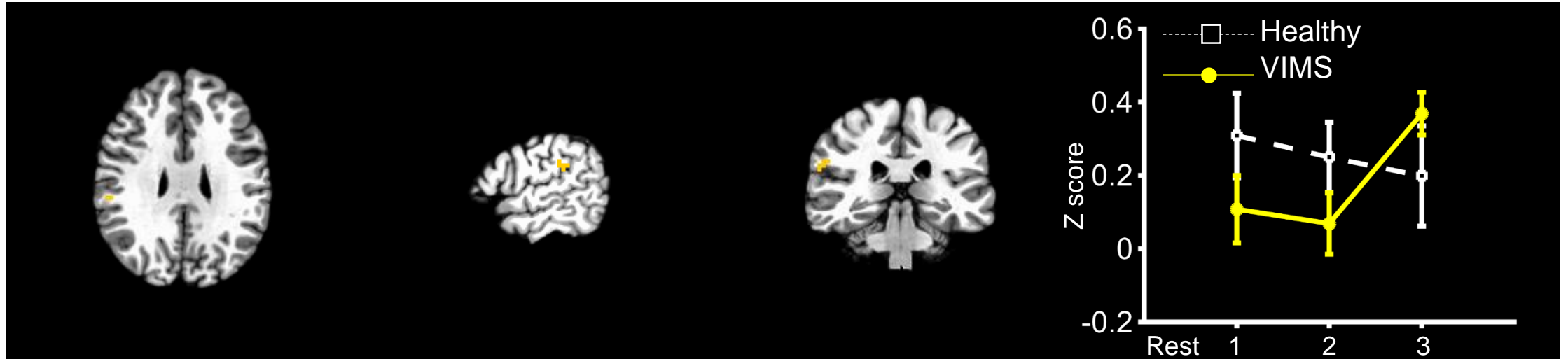
a 1. R Insula (seed: R Thalamus)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

Each column shows, from left to right, axial, sagittal, and coronal brain images, and the change in functional connectivity (Z scores averaged within the participants' groups) of each experimental phase, separately for VIMS and healthy groups, respectively (error bars are standard errors). Each panel is the result for the following brain regions (the brain region in brackets is the corresponding seed): a–right insula (right thalamus), b–right inferior parietal lobule (right thalamus), c–right declive (right thalamus), d–left thalamus (left insula), e–right inferior parietal lobule (left insula), f–left thalamus (right insula), g–left inferior temporal gyrus (right insula), h–left parahippocampal gyrus (left cerebellar tonsil), i–left cingulate gyrus (right claustrum), j–left inferior frontal gyrus (right claustrum), k–right insula (left cingulate gyrus), l–left medial frontal gyrus (left superior frontal gyrus), m–left middle temporal gyrus (left superior frontal gyrus); and n–left inferior frontal gyrus (right inferior frontal gyrus). For this mapping, we used the following thresholds: voxel-wise threshold  $P < 0.0001$ , cluster level threshold  $\alpha < 0.05$ . The numbering of brain region pairs corresponds to that in Tables 3, 4, and 5.

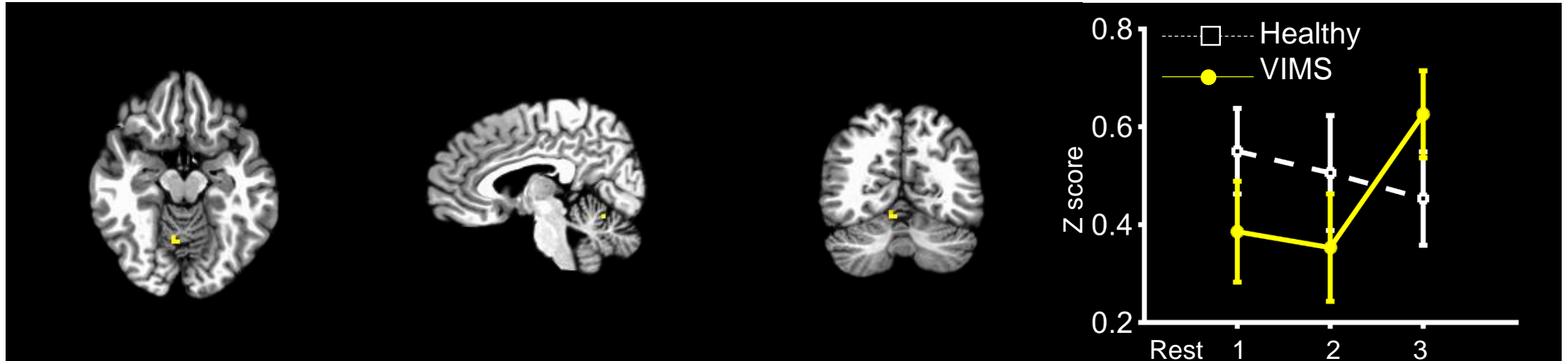
## b 2. R Inferior Parietal Lobule (seed: R Thalamus)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for right inferior parietal lobule.

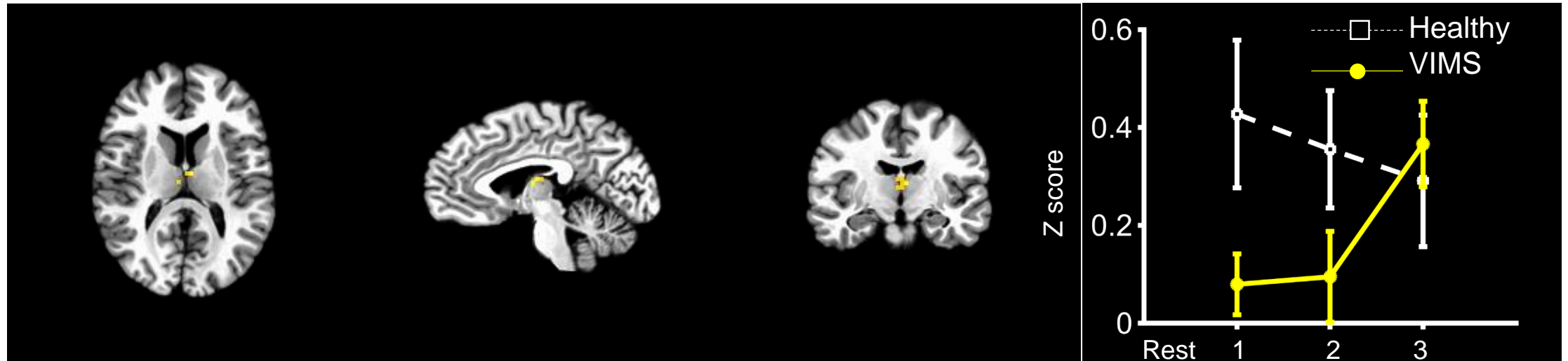
c 3. R Declive (seed: R Thalamus)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for right declive.

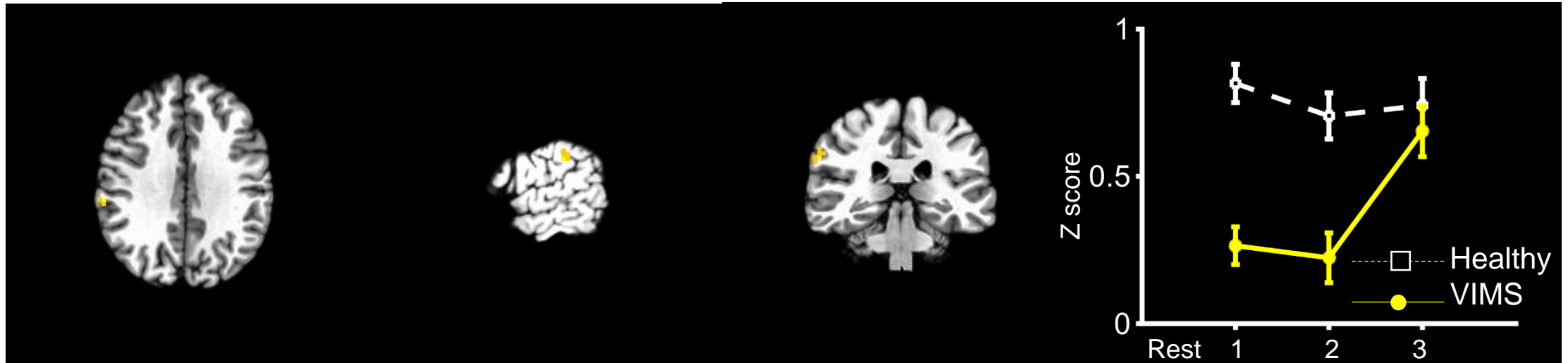
d 4. L Thalamus (seed: L Insula)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left thalamus.

e 5. R Inferior Parietal Lobule (seed: L Insula)

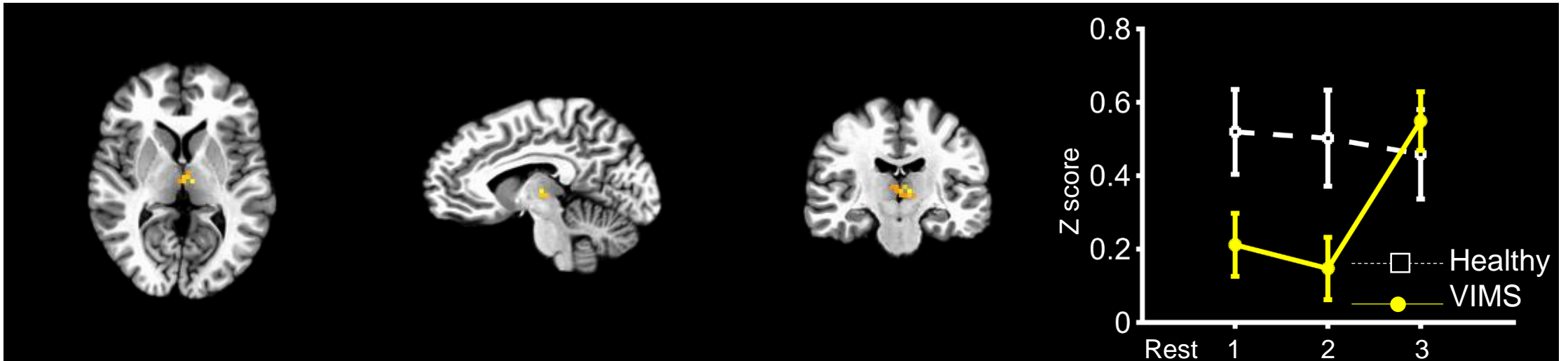


**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for right inferior parietal lobule.



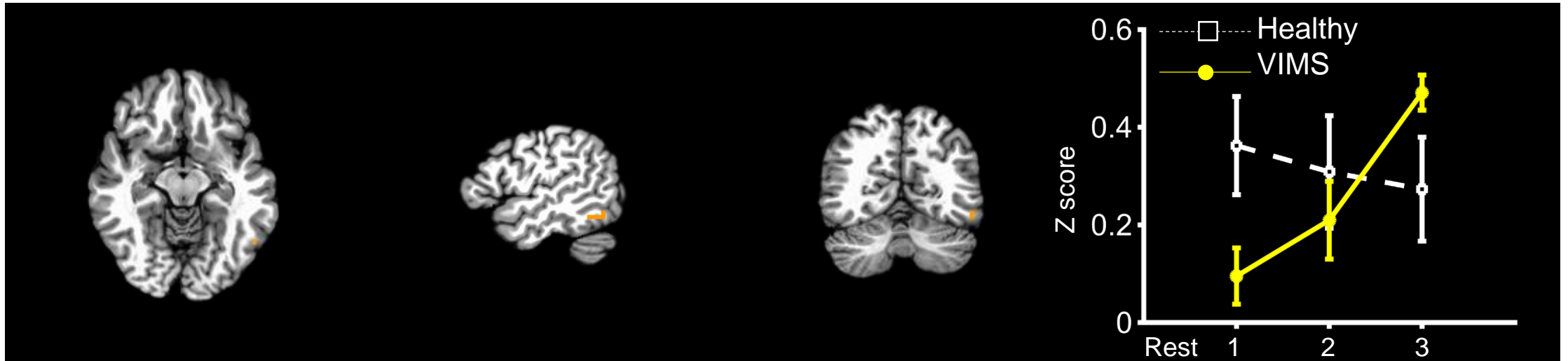
f 6. L Thalamus (seed: R Insula)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left thalamus.

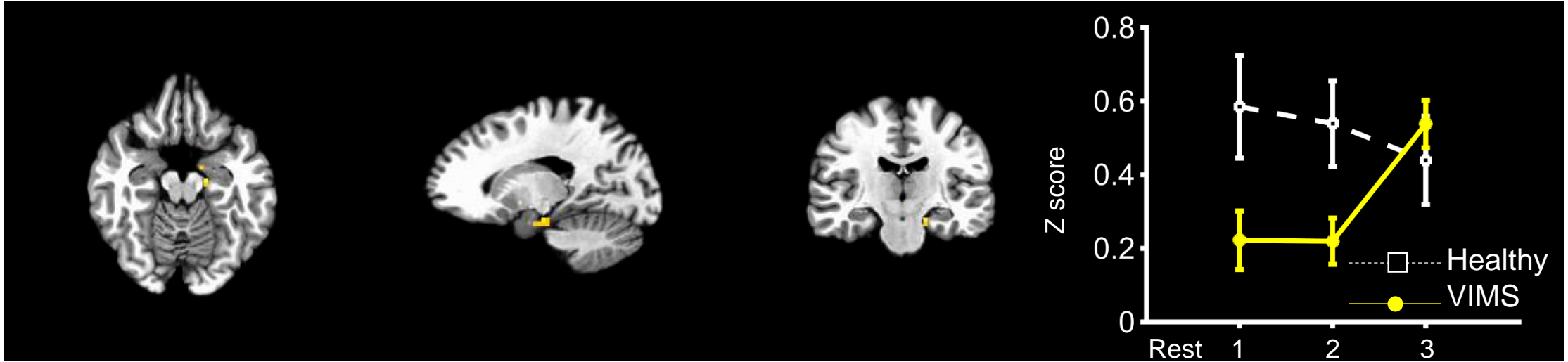
## g 8. L Inferior Temporal Gyrus (seed: R Insula)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left inferior temporal gyrus.

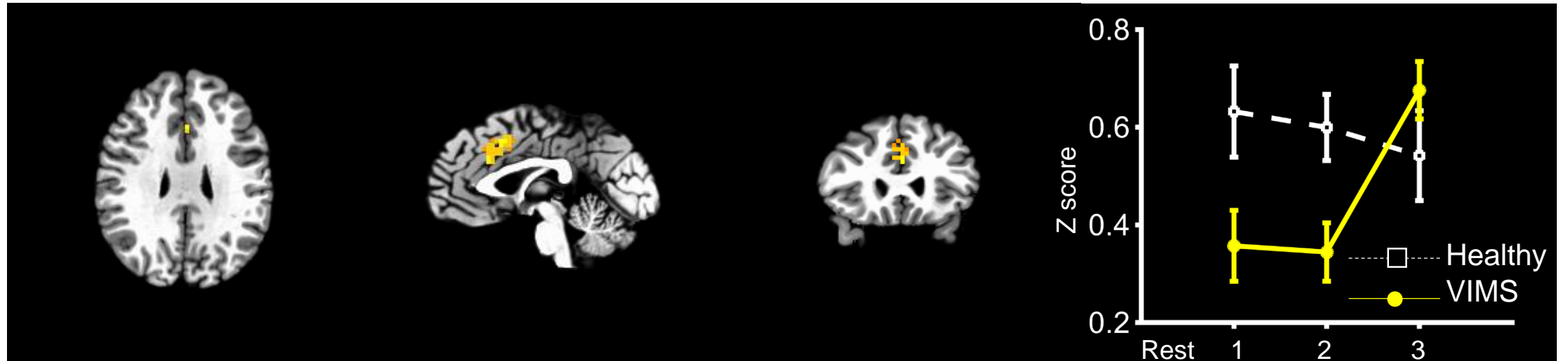
## h 9. L Parahippocampal Gyrus (seed: L Cerebellar Tonsil)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left parahippocampal gyrus.

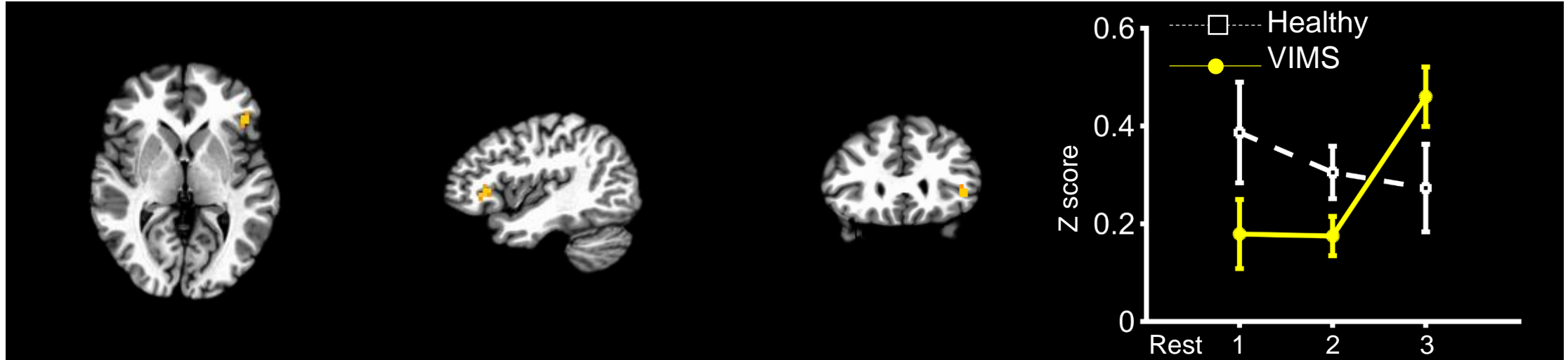
i 10. L Cingulate Gyrus (seed: R Claustrum)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left cingulate gyrus.

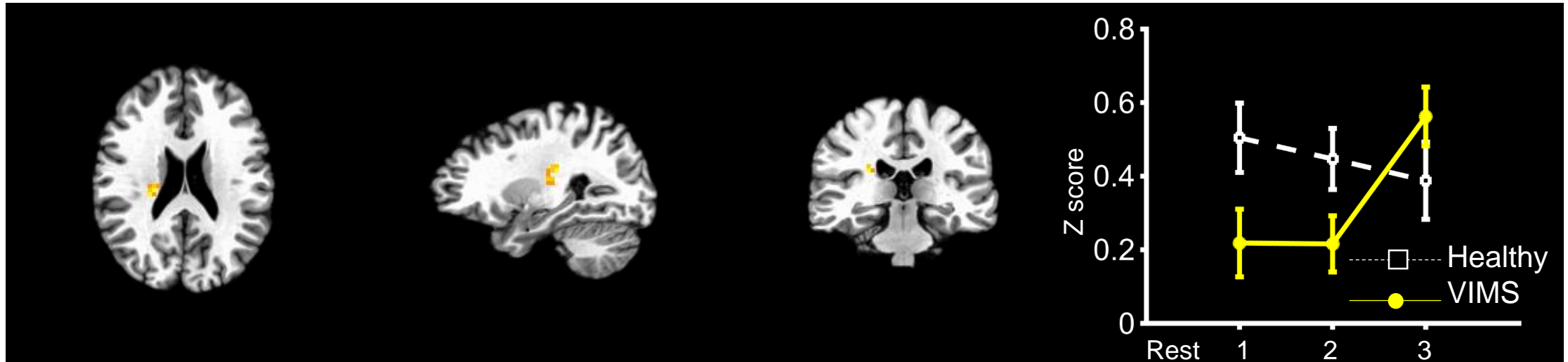
j 12. L Inferior Frontal Gyrus (seed: R Claustrum)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left inferior frontal gyrus.

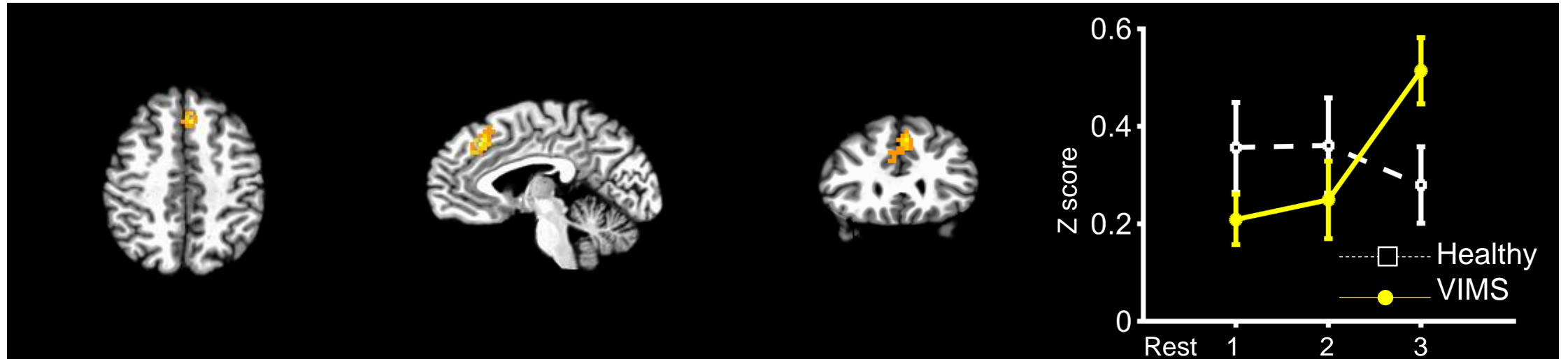
## k 15. R Insula (seed: L Cingulate Gyrus)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for right insula.

## 16. L Medial Frontal Gyrus (seed: L Superior Frontal Gyrus)

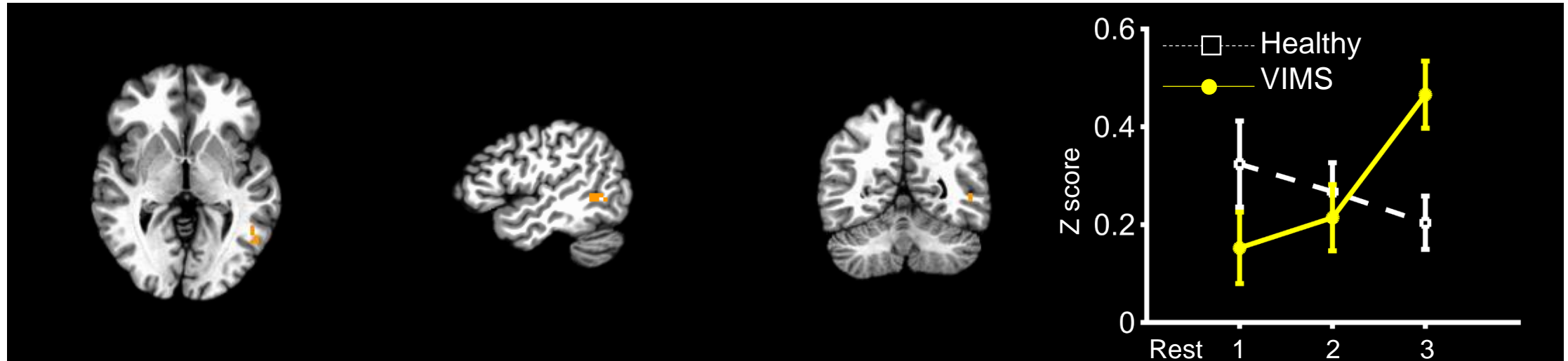


**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left medial frontal gyrus.



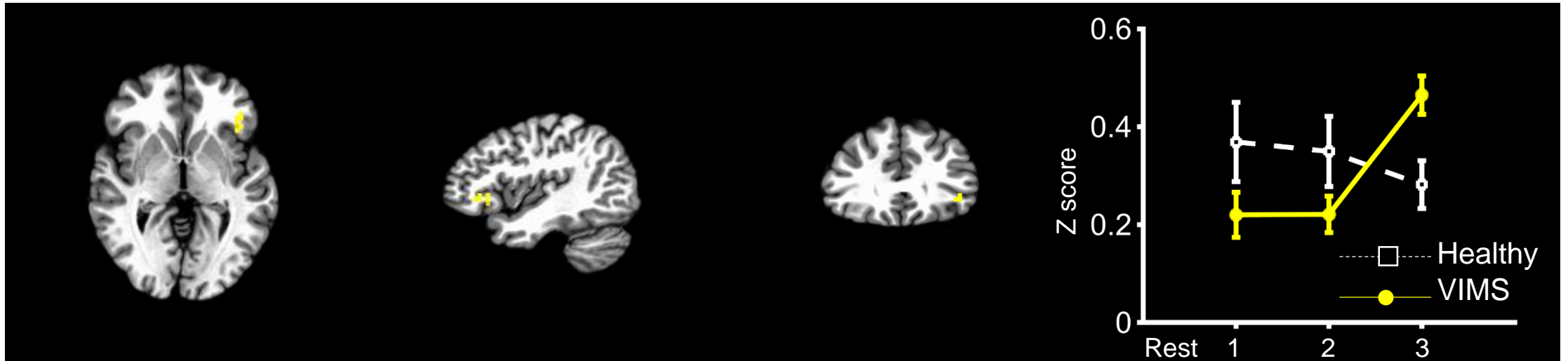
## m 17. L Middle Temporal Gyrus (seed: L Superior Frontal Gyrus)



**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left middle temporal gyrus.

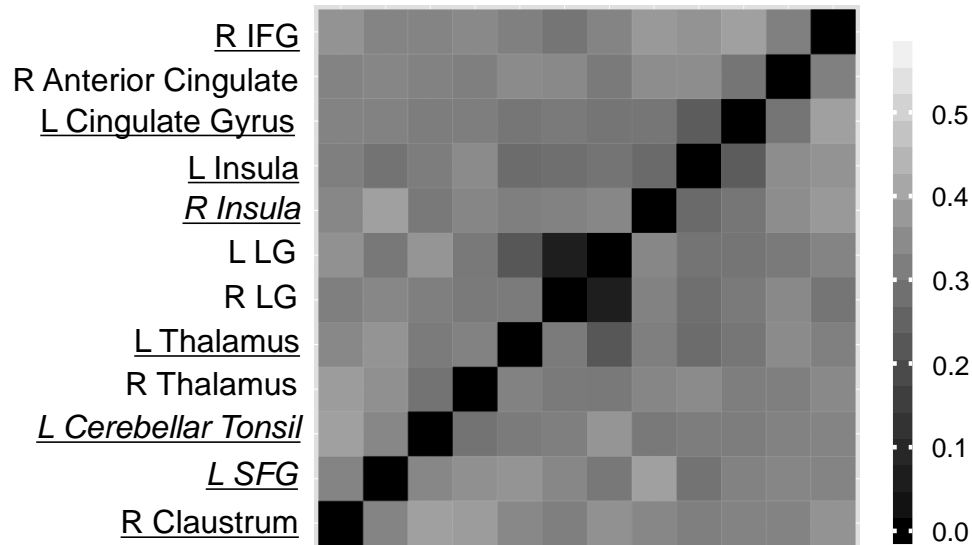
## n 19. L Inferior Frontal Gyrus (seed: R Inferior Frontal Gyrus)



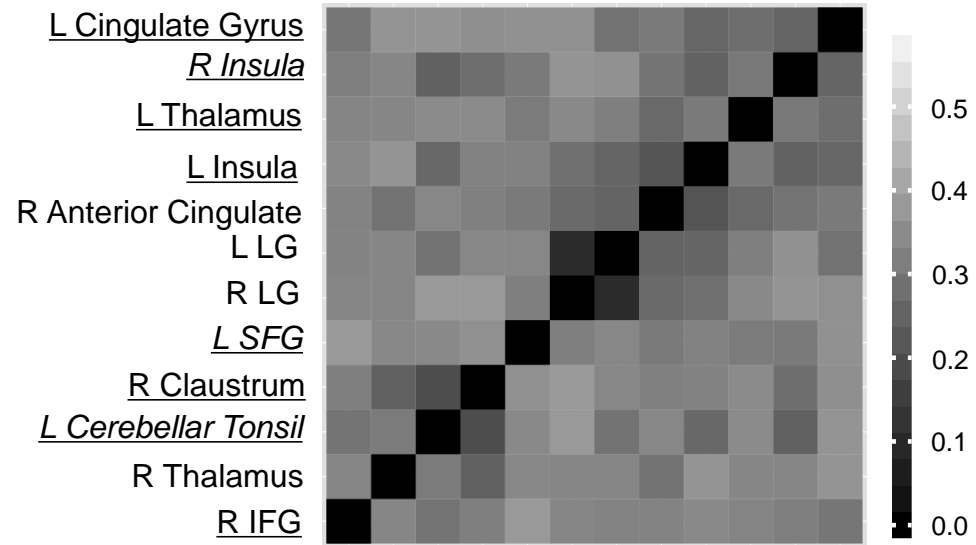
**Supplementary Figure 1. Brain regions whose functional connectivity with the seed regions increased in the recovery phase from visually induced motion sickness (VIMS)**

The same as Supplementary Figure 1a but for left inferior frontal gyrus.

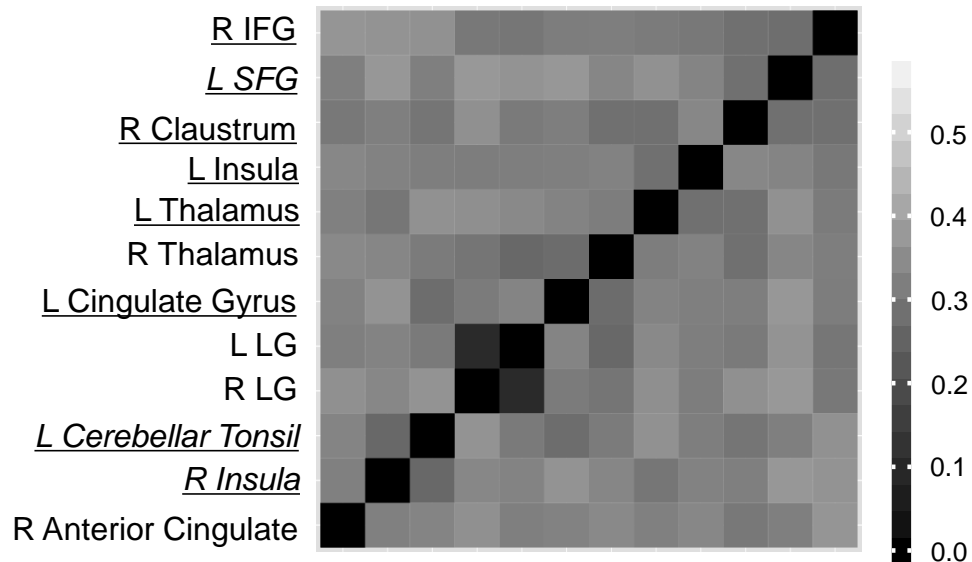
### VIMS recovery (Res-3) phase



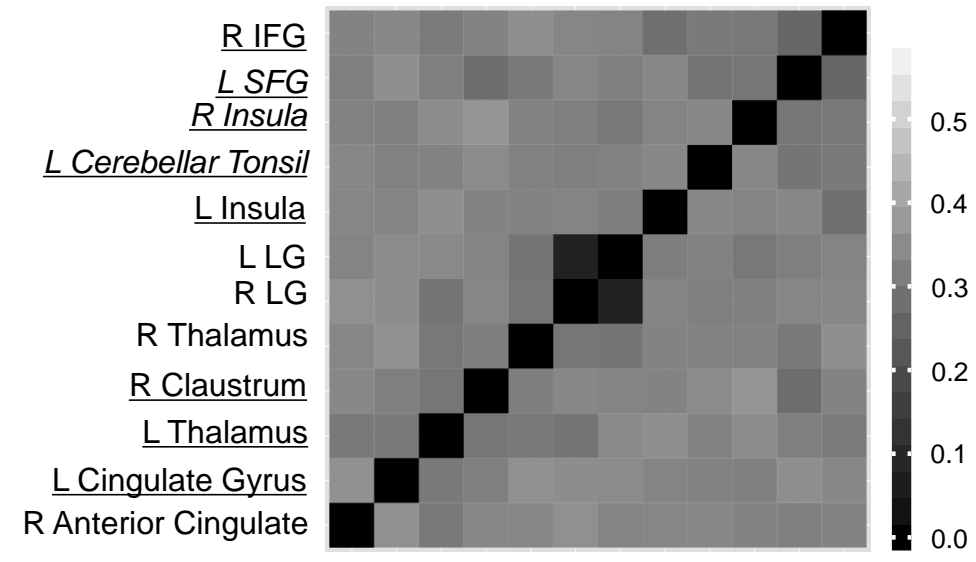
### healthy control (Rest-3) phase



### VIMS control (average of Rest-1 & -2) phase

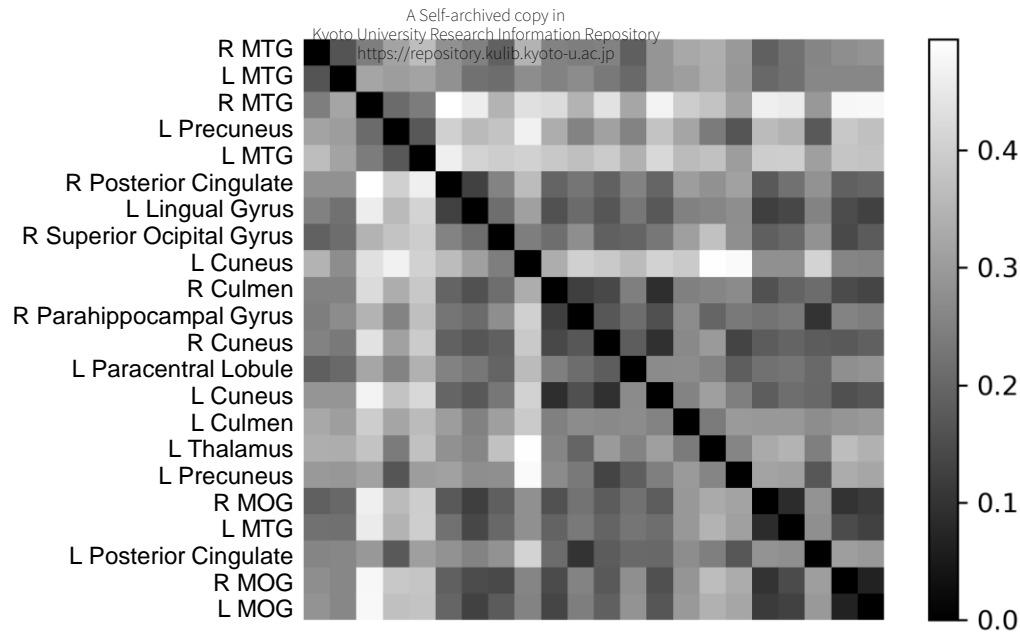


### healthy control (average of Rest-1 & -2) phase

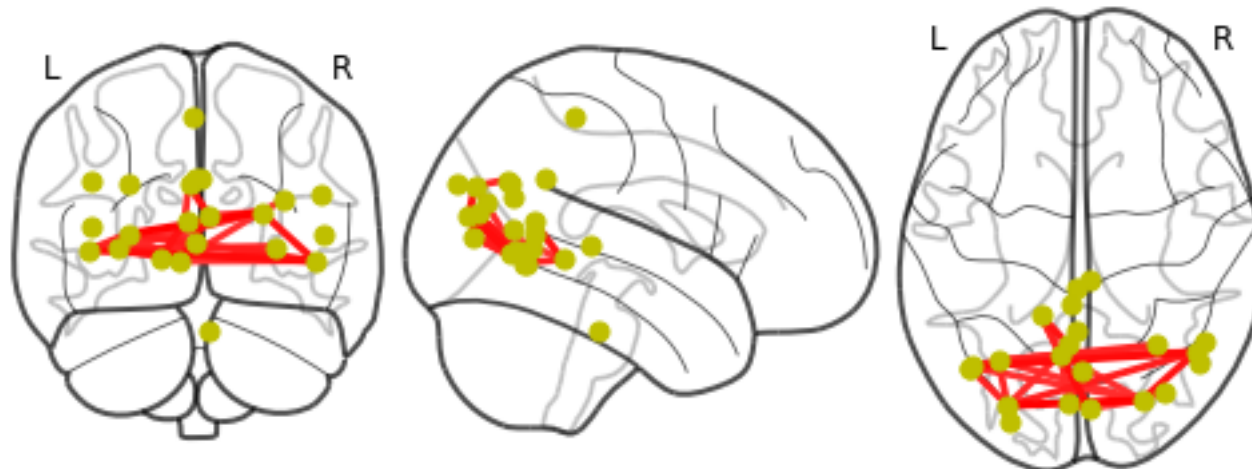


**Supplementary Figure 2. Distance matrices of the 12 brain regions showing recovery-selective increases in connectedness**

(a) The distance matrix of the VIMS group for the recovery phase (Rest-3), whose elements indicate 1 minus absolute partial correlation between each pair of the 12 regions. Brain regions showing recovery-selective increases in the ROI-based functional connectivity and correlations with SSQ are underlined and in italics, respectively. (b) The same as (a) but for the healthy group. (c) The same as (a) but for the control phase (the average of Rest-1 and Rest-2). (d) The same as (c) but for the healthy group. Abbreviations: L, left; R, right; LG, lingual gyrus; SFG, superior frontal gyrus; IFG, inferior frontal gyrus.



b



**Supplementary Figure 3. Statistically independent brain networks related to recovery from visually induced motion sickness (VIMS)**

(a) The within-participant averaged distance matrix for the recovery phase of the VIMS group. Each element represents a cross-correlation coefficient between each pair of the 22 regions determined by a dictionary learning technique. This analysis derived 22 regions of interest (ROIs). (b) The top 10% connections derived from the distance matrix. The connections are overlaid on a glass brain. Yellow circles and red lines denote the derived regions and connections, respectively. The connections are as follows: R Posterior Cingulate - L Lingual Gyrus, L Lingual Gyrus - R MOG, L Lingual Gyrus - L MTG, L Lingual Gyrus - R MOG, L Lingual Gyrus - L MOG, R Superior Occipital Gyrus - R MOG, R Culmen - R Parahippocampal Gyrus, R Culmen - R Cuneus, R Culmen - L Cuneus, R Culmen - R MOG, R Culmen - L MOG, R Parahippocampal Gyrus - L Cuneus, R Parahippocampal Gyrus - L Posterior Cingulate, R Cuneus - L Cuneus, R Cuneus - L Precuneus, L Cuneus - R MOG, R MOG - L MTG, L MOG - R MOG, L MOG - R MOG, L MTG - R MOG, L MTG - L MOG, and R MOG - R MOG. Abbreviations: L, left; R, right; MTG, middle temporal gyrus; MOG, middle occipital gyrus.