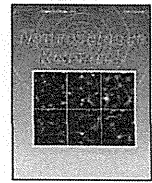


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Visual imagery while reading concrete and abstract Japanese kanji words: An fMRI study



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ABSTRACT

Neuroimaging studies have investigated differences in neural correlates between abstract and concrete concepts but this has not been done with Japanese participants. Concrete words have higher imageability than abstract words, such that they elicit more visual imagery. The present study used functional MRI to investigate brain activity of Japanese participants ($N = 16$) during generation of visual images for written concrete or abstract Japanese kanji words. Concrete words elicited significantly more activation than abstract words in the left middle frontal gyrus (LMFG), bilateral superior frontal gyrus, and left fusiform gyrus (LFG). Psychophysiological interaction (PPI) analyses were performed to assess LMFG and LFG functional connections. LMFG activity was accompanied by increased functional interaction with the left superior parietal lobule (LSPL), and LFG activity was accompanied by increased functional interaction with the LMFG. This finding suggests that the LMFG plays an important role in visual imagery, with interactions between this region and both the LSPL and LFG.

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1. Introduction

Imagery elicited by words involves recalling the sensory qualities of objects. The vividness of the imagery is highly correlated with word concreteness. Paivio (1991) proposed a dual-coding theory such that cognition operates via two neural pathways associated with verbal and imagery-based systems. Concrete words are more easily recalled than abstract words due to their greater imageability. Concrete words are acquired through sensory experiences, in contrast to abstract words, which are acquired through their use in sentences and their relationships with other concepts. Abstract words cannot be learned until a certain representational capacity is developed that permits the utilization of linguistic contexts (Bloom, 2000). Typically, concrete words have a processing advantage over abstract words. A deep dyslexic patient with a left hemisphere injury had a specific impairment for reading abstract words but was able to read concrete words, which indicates that different neural pathways are utilized for processing these two stimulus types (Coltheart et al., 1980).

Functional neuroimaging studies have recently investigated neural substrates for understanding language, specifically focusing on differences between concrete and abstract words (D'Esposito et al., 1997; Mellet et al., 1998; Jessen et al., 2000; Wise et al., 2000; Fiebach and Friederici, 2004; Whatmough et al., 2004; Mestres-Missé et al., 2009). In an fMRI study, participants generating visual imagery while listening to concrete words showed more brain activity in the left inferior temporal area (Brodmann's area; BA37) and in the occipital association cortex (BA19), in contrast to a condition where they simply listened to abstract words (D'Esposito et al., 1997). Visual mental imagery appears to be a function of the visual association cortex, with its generation localized to the left side. In a PET study, listening to concrete word definitions associated with mental images specifically elicited activation of the bilateral inferior temporal gyri as compared to abstract words (Mellet et al., 1998). For the latter, greater activation of the bilateral superior temporal gyri and the anterior part of the right middle temporal gyrus was observed compared to concrete words. In another PET study, activity increased with noun imageability in the left mid-fusiform gyrus (Wise et al., 2000). In an fMRI study, participants made lexical decisions about word and pseudo-word stimuli, and the results showed right hemisphere activation during the processing of abstract language representations (Kiehl et al., 1999). A meta-analysis combined data from 19 neuroimaging studies to

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identify differences in neural representations of abstract and concrete concepts. The comparison of concrete versus abstract concepts showed significant activation differences for the left fusiform gyrus (LFG), left precuneus, left parahippocampal gyrus, and left posterior cingulate. There were also activation differences for the left inferior frontal gyrus, left middle temporal gyrus, and left superior temporal gyrus. These differences indicate that concrete concepts are relatively easy to image with a corresponding engagement of the perceptual system, while abstract concepts appear to engage the verbal system (Wang et al., 2010).

However, no previous study has required participants to generate visual imagery during both concrete and abstract stimulus conditions. Visual images of concrete stimuli are associated with left inferior temporal gyrus activation; however, no comparisons of visual imagery for concrete and abstract stimuli have been conducted (D'Esposito et al., 1997; Mellet et al., 1998). Previous lexical decision task studies demonstrated a correlation between noun imageability and increasing brain activity in the LFG, although such a judgment-based button pressing task does not explicitly reflect the generation of visual imagery (Kiehl et al., 1999; Wise et al., 2000; Fiebach and Friederici, 2004; Whatmough et al., 2004). To investigate possible brain circuit differences for visual imagery across concrete and abstract representations, we developed a visual imagery task that required participants to generate visual images for both abstract and concrete kanji words.

Most previous studies of visual imagery have used alphabetical letters and words. Japanese kanji words are morphograms. Iwata (1984) proposed that kanji words are processed differently from alphabetical letters, such that kanji are semantic stimuli whereas letters are phonological. Brain activation differences between reading kanji and English words have been examined for native Japanese adults, using fMRI. Reading English showed more activation of the inferior frontal and left angular gyri, due to phonological processing and verbal working memory demands (Buchweitz et al., 2009). Patient with lesions of the lower middle frontal gyrus and adjacent anterior precentral gyrus cannot write kanji due to visual imagery impairments (Sakurai et al., 1997).

We investigated whether visual imagery for kanji stimuli is associated with LFG activation as was found for alphabetical language, and hypothesized that the LMFG might play an important role in such imagery. We expected that the differences of brain activity associated with imagery between concrete and abstract kanji words might reveal regions associated with visual imagery specifically. To examine this, we performed psychophysiological interaction (PPI) analyses to identify the regions connected to the LMFG and LFG.

2. Materials and methods

2.1. Participants

Sixteen right-handed Japanese male adults took part in the study (mean age = 26.1 ± 5.9 years, range: 20–36 years). Only male participants were included to rule out any potential influence of sex differences on the present findings.

None of the participants suffered from psychiatric or neurological disorders or had ever sustained a head injury. On the revised Wechsler Adult Intelligence Scale (WAIS-R), all participants showed full-scale intelligence quotients (FIQs) over 80 (mean FIQ = 110.2 ± 11.7 ; mean verbal IQ (VIQ) = 115.9 ± 13.3 ; mean performance IQ (PIQ) = 100.4 ± 11.5).

The study protocol was approved by the two ethics committee of Hiroshima University and Matsuda Hospital. Written informed consent was obtained from each participant. Participants were paid 1500 yen per hour (about \$17 per hour).

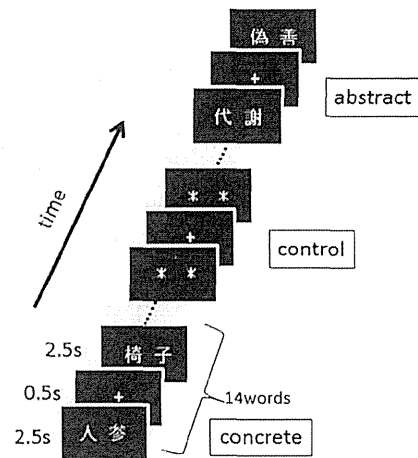


Fig. 1. Stimuli and tasks. Schematic representation of the experimental design. Each word was presented for 2.5 s, with an inter-stimulus interval of 0.5 s. Inter-trial interval (ITI) was 12 s. Concrete, abstract and control blocks were randomly presented five times and each consisted of 14 words, for a total of 70 words.

2.2. Materials

Stimuli consisted of 70 concrete and 70 abstract written kanji words made up of two characters drawn from the Japanese lexicon (Sakuma et al., 2005). The concrete words (e.g., 人参 carrot, 椅子 chair) had high imageability (>5 , mean 5.6 ± 0.4) and the abstract words (e.g., 代謝 metabolism, 偽善 hypocrisy) had low imageability (<4 , mean 3.4 ± 0.3) on a standardized seven-point scale (Ogawa et al., 1974). Concrete words fell into 14 different categories (word lists by semantic principles, 2004; e.g., tools = 17 words, food = 12, clothing = 10, plants = 8, body parts = 6, materials = 4, dwellings = 4, animals = 2, others = 7). The concrete and abstract words were matched for frequency of occurrence in the Asahi newspaper over 14 years (from 1985 to 1998) ($F(69, 69) = 1.0, p = 0.98$) (Amano and Kondo, 2000). The mean number of writing stroke sequences for concrete words was 18.1 ± 5.4 , and that for abstract words was 17.8 ± 5.4 . This was not a significant difference ($p = 0.72$).

Participants were instructed to read silently and generate visual imagery with their eyes open during blocks of concrete and abstract words. Each block consisted of 14 words of either type, each of which was presented for 2.5 s, followed by a 0.5 s fixation period. Inter-trial intervals (ITI) were 12 s in duration and participants just looked at the fixation cross (Fig. 1). We used control blocks to minimize visual satiation. During the control blocks, participants were instructed only to look at the characters "****", which were repeated 14 times in a block and presented for the same duration as the other stimuli. Each block was randomly presented five times throughout a session. Presentation order of the concrete, abstract and control blocks was counterbalanced across participants. Participants practiced with one block on a personal computer before undergoing the experiment in the fMRI scanner. After the fMRI experiment, the participants were asked "How well could you image the words?" Participants provided ratings for all the words they were shown during the MRI scan, using an imageability rating score ranging from 1 = "Never" to 7 = "Extremely Well".

2.3. fMRI procedure

Structural and functional data were collected using a Symphony 1.5T (Siemens, Munich, Germany). A time course series of 292 scans was acquired using T2*-weighted, gradient echo, echo planar imaging (EPI) sequences. The first six volumes of the fMRI run

(pre-task period) were discarded because the magnetization was unsteady, with the remaining 286 volumes being used for statistical analysis. Each volume consisted of 30 slices, with a slice thickness of 4 mm with no gap, and covered the entire cerebral and cerebellar cortices. The time interval between two successive acquisitions of the same image (TR) was 3000 ms, the echo time (TE) was 40 ms, and the flip angle was 90°. The field of view (FOV) was 256 mm, and the matrix size was 64 × 64, giving voxel dimensions of 4 mm × 4 mm × 4 mm. Scan acquisition was synchronized to the onset of each trial. We also acquired anatomic images using a T1-weighted, gradient echo, pulse sequence (TR = 12 ms; TE = 4.5 ms; flip angle = 20°; FOV = 256 mm; voxel dimensions of 1 mm × 1 mm × 1 mm).

2.4. Data analysis

Data were analyzed using statistical parametric mapping (SPM8) software (Wellcome Department of Cognitive Neurology, London, UK). Data were realigned to remove effects of head movements between scans, slice-time corrected, and normalized to a standard template based upon the Montreal Neurological Institute (MNI) reference brain. The normalized functional images were then smoothed with an 8-mm full width at half-maximum (FWHM) Gaussian filter.

Initially, four comparisons were examined for each participant: (1) concrete words versus control, (2) abstract words versus control, (3) concrete words versus abstract words, and (4) abstract words versus concrete words. One-sample *t*-tests were used for comparisons across all contrasts. Activations common to all participants were determined using group analyses, adjusted for VIQ, PIQ and FIQ. Each IQ score was entered into a general linear model as a nuisance covariate. A statistical threshold of uncorrected $p < 0.001$, cluster size (k) > 5 was used.

Psychophysiological interaction (PPI) analysis indicates when the contribution of activity in one brain area to another area changes significantly with the experimental or psychological context (Friston et al., 1997). To undertake PPI analysis, a design matrix is established, which typically contains three columns of variables as follows: (1) a psychological variable that reflects the experimental paradigm, (2) a time-series variable representing the time course of the source region. The source region was an 8-mm sphere with a center defined by the peak coordinates of the foregoing analysis, and (3) an interaction variable that represents the interaction between (1) and (2). The regression coefficient for the interaction term gives a measure of PPI. A significant effect for PPI in the present study context means that the correlation (or covariance) between the source and seed regions during the concrete word condition is significantly different from that observed during the abstract word condition. In this regard, PPI analysis assesses functional connectivity differences between regions of interest. To perform PPI analysis, the first eigenvariate time series of the 8-mm sphere was extracted from the former analyses. The effect of the interaction term was studied using the contrast [1 0 0], where the first column represents the interaction term. Then, the individual images were taken to the second level to perform a random effects analysis using a one-sample *t*-test. We designated the LFG as a region of interest because of its involvement with concreteness in previous studies (Wise et al., 2000). Another region of interest was the LMFG, which plays an important role in writing Japanese and visual imagery of kanji words (Sakurai et al., 1997). The functional connections between the LFG [8-mm sphere centered ($x = -24, y = -34, z = -22$)] and LMFG [8-mm sphere centered ($x = -38, y = 42, z = 36$)] and other regions were assessed. A statistical threshold of uncorrected $p < 0.005$, cluster size (k) > 10 was used.

3. Results

3.1. Behavioral data

Imageability rating scores collected from the participants after the fMRI experiment were significantly higher for concrete (mean 6.2 ± 0.9) than abstract words (mean 3.1 ± 1.2) ($p < 0.001$). These results are consistent with the imageability differences for these words described by Ogawa et al. (1974).

3.2. Image data

Group analyses (see Table 1)

- (1) The comparison of concrete words versus control showed significant activation of the left supplementary motor area (Brodmann's area; BA6), left inferior temporal gyrus, left insula, pars triangularis of the left inferior frontal gyrus (BA45), left precentral gyrus and left superior parietal lobule (LSPL) (Fig. 2A upper side). The LMFG was included in the left inferior frontal gyrus cluster.
- (2) The comparison of abstract words versus control showed significant activation of the left supplementary motor area (BA6), left inferior temporal gyrus, pars triangularis of the left inferior frontal gyrus (BA45), left middle occipital gyrus, right inferior occipital gyrus and the LSPL (Fig. 2A lower side). The LMFG was included in the left inferior frontal gyrus cluster.
- (3) The comparison of concrete versus abstract words showed significant activation of the LMFG (BA9), left middle temporal gyrus (BA19), LFG, left precuneus, left cerebellum and right superior frontal gyrus (Fig. 2B).
- (4) The comparison of abstract versus concrete words showed significant activation of the supramarginal gyrus and pars triangularis of the inferior frontal gyrus (BA45).

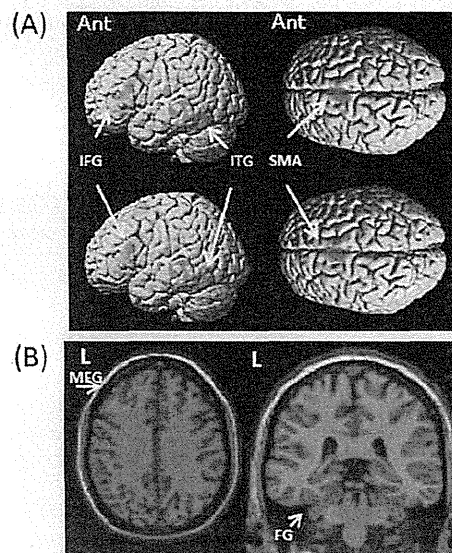


Fig. 2. (A) The upper side shows brain areas activated by concrete words relative to control (marked in red). The lower side shows brain areas activated by abstract words relative to control (marked in red). A statistical threshold of uncorrected $p < 0.001$, cluster size (k) > 5 was used. Ant; anterior, left side; right side; superior view, IFG; inferior frontal gyrus, ITG; inferior temporal gyrus, SMA; supplementary motor area. (B) The left side shows the LMFG [$x = -38, y = 42, z = 36$] and the right side shows the LFG [$x = -24, y = -34, z = -22$] significantly activated by concrete words relative to abstract words (marked in red). MFG: middle temporal gyrus; FG: fusiform gyrus. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1
Significant areas of activation for each comparison.

	Region	Cluster extent	L/R	MNI coordinates			z-Score	
				x	y	z		
Concrete versus control	Supplementary motor area	779	L	-6	4	60	4.86	
	Supplementary motor area	17	R	14	4	68	3.84	
	Pars triangularis of inferior frontal gyrus	563	L	-40	36	10	4.28	
	Pars triangularis of inferior frontal gyrus	22	R	56	22	22	3.74	
	Insula	296	L	-28	28	-6	3.84	
	Insula	22	R	36	32	0	3.65	
	Putamen	7	L	-20	6	4	3.22	
	Putamen	15	R	30	6	0	3.74	
	Precentral gyrus	41	L	-40	-6	50	3.74	
	Precentral gyrus	6	L	-36	-8	66	3.49	
	Superior parietal lobule	47	L	-22	-62	44	4.08	
	Inferior temporal gyrus	525	L	-50	-56	-14	4.73	
	Inferior occipital gyrus	16	L	-24	-88	-8	3.42	
	Abstract versus control	Supplementary motor area	1028	L	-4	16	52	5.13
Pars triangularis of inferior frontal gyrus		848	L	-46	20	24	4.36	
Pars triangularis of inferior frontal gyrus		29	R	56	28	20	3.81	
Precentral gyrus		74	L	-44	-2	48	3.55	
Pars orbitalis of frontal inferior gyrus		28	L	-46	42	-12	3.32	
Superior parietal lobule		45	L	-30	-60	48	4.05	
Inferior temporal gyrus		558	L	-48	-54	-14	5.03	
Middle occipital gyrus		199	L	-26	-86	-2	3.87	
Inferior occipital gyrus		51	R	38	-82	-4	3.50	
Middle frontal gyrus		74	L	-38	42	36	4.33	
Superior frontal gyrus		8	L	-24	38	50	3.61	
Concrete versus abstract	Superior frontal gyrus	35	R	26	4	68	3.41	
	Precuneus	5	L	-6	-64	60	3.46	
	Fusiform	6	L	-24	-34	-22	3.44	
	Middle temporal gyrus	9	L	-50	-64	12	5.08	
	Cerebellum4.5	7	L	-12	-38	-16	3.30	
	Abstract versus concrete	Pars triangularis of inferior frontal gyrus	8	L	-52	22	6	3.25
		Supramarginal gyrus	7	L	-46	-40	28	3.42

Activated region volumes are given in voxels. MNI coordinates (x, y, z) refers to the center of activation within each region (R, right; L, left).

3.3. PPI analyses

LMFG activity during the concrete-specific component (concrete image–abstract image) was accompanied by increased functional interaction with the LSPL [$x = -32$, $y = -46$, $z = 56$, size = 35, z-score = 3.08], left inferior occipital lobe, and left supplementary motor area (Fig. 3). There was decreased functional interaction with the right middle frontal gyrus, left insula, and right middle temporal gyrus.

LFG activity was accompanied by increased functional interaction with the LMFG [$x = -26$, $y = 2$, $z = 34$, size = 76, z-score = 4.09], right middle occipital lobe, left pars triangularis of the inferior

frontal gyrus and right FG. There was decreased functional interaction with the bilateral precuneus and right middle temporal gyrus.

4. Discussion

We investigated neural activity associated with visual imagery during the reading of concrete and abstract kanji words. Comparisons of concrete versus abstract words showed significant differences in activity of the LMFG, bilateral superior frontal gyri, and LFG. PPI analyses showed that LMFG activity was accompanied by increased functional interaction with the LSPL, and that activity in the LFG was accompanied by increased functional interaction with the LMFG. This finding shows that the LMFG plays an important role in visual imagery processing.

A novel feature of this study was the use of PPI analysis to investigate LMFG and LFG connectivity. The LMFG had not been previously mentioned in studies using alphabetic concrete and abstract words although this region shows significant activation during scene imagery ($-34\ 46\ 26$; in Talairach coordinates; de Borst et al., 2012). These coordinates are situated near our LMFG results ($-38\ 42\ 36$ in MNI coordinates versus $-38\ 42\ 31$ in Talairach coordinates), which were converted from MNI to Talairach coordinate space using formulas provided by Matthew Brett (<http://www.mrcctu.cam.ac.uk/Imaging/mmspace.html>). The LMFG belongs to the dorsolateral prefrontal cortex region, which underlies working memory functions that can be subdivided into four sub-components: The central executive, visuospatial sketch pad, phonological loop and episodic buffer. The visuospatial sketch pad holds and manipulates visual images (Baddeley et al., 2011). In an fMRI study, LMFG activation was associated with internally generating instances of a category (e.g., US states). This finding suggests the existence of a left frontal neural network for accessing the mental lexicon (Hugdahl et al., 1999). As we hypothesized,

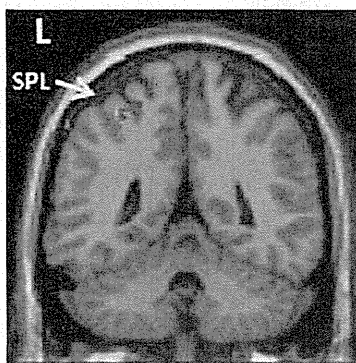


Fig. 3. PPI analyses were performed to assess the functional connections of the LMFG [8-mm sphere centered ($x = -38$, $y = -42$, $z = 36$)]. The left superior parietal lobule (SPL) showed significant activation. A statistical threshold of uncorrected $p < 0.005$, cluster size (k) > 10 was used.

the LMFG was important for visual imagery associated with kanji words.

The LSPL was activated in the concrete versus control and abstract versus control comparisons, suggesting that this region plays an important role in formation of word concept visual images. The LSPL is important for mental imagery (Kosslyn et al., 2001), particularly for mental rotation of images (Richter et al., 2000). The LSPL responds to increases in noun and verb imageability (Bedny and Thompson-Schill, 2006) and is also included in the orthographic pathway for kanji words, which starts from the left inferior temporal gyrus and runs to the premotor area (Sakurai et al., 2007). Visual imagery involves two visual pathways. One is the dorsal visual pathway, which runs from the primary visual cortex to the posterior parietal lobe and processes spatial information such as object location and motion. The other is the ventral visual pathway, which runs from the primary visual cortex to the inferior temporal gyrus and processes subjective surface information such as object shape and color (Kosslyn et al., 2001). Previous imaging studies have focused on the distinctions between the ventral “what” (e.g., faces or objects) and the dorsal “where” (e.g., spatial layout) cortical processing streams in visual perception (Ungerleider and Haxby, 1994).

We found that concrete words produced increased LFG activation as compared with abstract words, with PPI analyses revealing that the LFG had connectivity with the LMFG. Our LFG activation ($-24-34-22$; in MNI coordinate) was more anterior than that observed in previous alphabetic studies (D’Esposito et al., 1997; Wise et al., 2000; Whatmough et al., 2004; Wang et al., 2010). However, learning of new concrete words selectively evokes greater activation of the ventral anterior fusiform gyrus ($-24-40-24$; in MNI coordinate) than abstract words because this process is driven by imageability, activation that is situated quite close to the LFG activation we observed. This may suggest that visual imagery activated the anterior FG.

Our results revealed that the LMFG had connectivity with the LSPL and LFG. A combined examination using fMRI and electroencephalography investigated the spectro-temporal properties of nodes, particularly of the frontal cortex, during visual imagery of complex scenes (de Borst et al., 2012). The results showed early activation of the mesial superior frontal gyrus, right middle frontal gyrus, and premotor cortex in both the fMRI and EEG data. Later on during imagery, the ventro-temporal cortex and parietal cortex were activated. Frontal regions integrate the “what” and “where” content of thoughts into one visually imagined scene (de Borst et al., 2012). The dorsolateral prefrontal cortex, including the LMFG, receives spatial information from the parietal lobe (Tovée and Cohen-Tovée, 1996), with the dorsolateral prefrontal cortex receiving activation associated with higher visual processing of objects from the inferior temporal cortex (Tovée and Cohen-Tovée, 1996). The ventral “what” and dorsal “where” cortical processing streams receive feedback projections from the prefrontal cortex during working memory tasks (Tovée and Cohen-Tovée, 1996). We propose that the interaction between the LMFG and LFG/LSPL reflects the finding that concrete words have higher imageability than abstract words and therefore elicit more visual imagery. And concrete words likely require more central executive processing resources to image than abstract words.

We found that the comparison of abstract versus concrete words showed significant activation of the left pars triangularis of the inferior frontal gyrus (BA45), consistent with the findings of Wang et al. (2010). This region belongs to Broca’s area and is involved with language perception and processing, with these areas also activated by inner speech (Indefrey and Levelt, 2004). The inferior frontal gyrus has an anatomical connection with the inferior temporal gyrus, and plays roles in grapheme-to-phoneme conversion and semantic knowledge (Wang et al., 2010). Abstract words are acquired after

learning to utilize linguistic contexts (Bloom, 2000) and require more semantic knowledge than concrete words.

Our results revealed that both concrete and abstract words activated regions of the left pars triangularis of the inferior frontal gyrus (BA45), left inferior temporal gyrus, LSPL and left supplementary motor area (BA6). We suggest that kanji words commonly activate two visual pathways in the language and premotor areas. However, visual imagery was associated with different degrees of brain activity in the LMFG across the concrete and abstract word conditions.

There are sex differences on language and visuospatial fMRI tasks, such that males show more left lateralization during phonological tasks and greater bilateral activity during visuospatial tasks, whereas females show greater bilateral activity during phonological tasks and are more right lateralized during visuospatial tasks (Clements et al., 2006). We studied a small sample of males and so it is difficult to generalize our results to females. Visual imagery was more difficult to produce while looking at kanji words than while looking at nothing, and the imagery duration was shorter than that used in a previous study (de Borst et al., 2012). Further studies using larger numbers of participants are needed to more fully elucidate the neural mechanisms underlying visual imagery.

5. Conclusions

LMFG activity was associated with visual imagery for kanji words. Imagery associated with concrete kanji words elicited significantly more activation of the left middle frontal gyrus (LMFG), bilateral superior frontal lobe and left fusiform gyrus (LFG) than found for abstract kanji words. We suggest that the interaction observed between the LMFG and LFG/LSPL reflects the higher imageability of concrete as compared to abstract words, such that more visual imagery is elicited by such stimuli.

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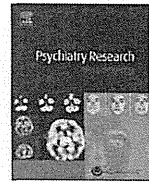
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Brief report

Distinctive spontaneous regional neural activity in patients with somatoform pain disorder: A preliminary resting-state fMRI study



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ABSTRACT

This resting-state functional magnetic resonance imaging study found that nine patients with somatoform pain disorder exhibited atypical precentral gyrus activation compared with 20 healthy controls. The role of the precentral gyrus in pain-related processing is discussed.

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1. Introduction

Somatoform pain disorder (SPD) is characterized by pain at one or more sites that is at least to some degree medically unexplained, with such pain critically linked to psychological and psychosocial problems, according to the DSM-IV (APA, 1994). Various neuroimaging studies have examined potential mechanisms involved in the pathophysiology of SPD (Stoeter et al., 2007; Yoshino et al., 2013). However, only a few studies have examined resting-state abnormalities (Otti et al., 2013a, 2013b).

We investigated regional intensity of spontaneous blood oxygenation level-dependent fluctuations using the regional homogeneity (ReHo) method (Zang et al., 2004). Our study was designed to isolate distinctive resting-state activity in patients with SPD.

2. Methods

2.1. Participants

The participants were nine patients with SPD (four women, mean age = 39.0 ± 5.1 years), diagnosed according to DSM-IV-TR criteria, and 20 control

subjects (13 women, 42.4 ± 6.8 years). All participants were right-handed Japanese. The SPD patients and healthy controls did not significantly differ with regards to gender and age (see Supplementary materials, Table 1). For clinical information, see Supplementary materials, Table 2. Patients were recruited from outpatient sources at the Hiroshima University Hospital. The Structured Clinical Interview for DSM-IV (SCID-IV) (Spitzer et al., 1992) was used to confirm participants' diagnostic status. Exclusion criteria included neurological illness, severe physical disease, organic brain disorder, and use of opioid medication. Any analgesic which could alter pain perception was discontinued 24 h prior to the fMRI scanning. Control participants endorsed no chronic pain problems and had no history of psychiatric disorders. All participants gave their written informed consent before participation, according to a protocol approved by the Hiroshima University ethics committee.

2.2. Clinical assessments

The Short-Form McGill Pain Questionnaire (SF-MPQ) was used to assess pain characteristics (Melzack, 1987). The SF-MPQ consists of 15 descriptors (11 sensory, 4 affective) and a visual analog scale (VAS).

The Beck Depression Inventory-Second Edition (BDI-II) was used to measure depressive symptom (Beck et al., 1996).

2.3. fMRI acquisition and functional imaging data analysis

For Siemens 1.5 T MRI scanning parameters, see Yoshino et al. (2013). A time course series of 120 scans was acquired. Image preprocessing was carried out using Statistical Parametric Mapping (SPM8) software (Wellcome Department of Cognitive Neurology, London, UK). Slice timing and head movement corrections were conducted. The images were then spatially normalized to the Montreal Neurological Institute (MNI) functional template (resampling voxel size = 3 mm × 3 mm × 3 mm).

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After preprocessing in SPM8, linear trend was removed and ReHo analysis was carried out using the R-fMRI data analysis toolkit (REST, <http://restfmri.net/forum/>), version 1.6. The ReHo analysis procedure was carried out according to the method of Zang et al. (2004), and is described in more detail in the supplementary materials. Group-level analyses of the ReHo maps were performed using SPM8 to conduct one-sample *t* tests to detect activity in each group separately, SPD and healthy control) and two-sample *t* tests (to detect between group differences). In these analyses, we conducted a Monte Carlo simulation to determine the combined threshold corresponding to a threshold of $p < 0.05$ (corrected), using the AlphaSim tool from the program Analysis for Functional Neuroimaging (AFNI) (see also Supplementary material). We set the significant group difference at the threshold of a voxel-wise $p < 0.001$ (uncorrected) and at a minimum cluster size of 44 voxels. The spatial coordinates provided by SPM8, which are in MNI brain space, were converted to spatial coordinates of the Anatomical Automatic Labeling (AAL) atlas using the MarsBar SPM Toolbox (<http://www.sourceforge.net/projects/marsbar>).

To analyze how ReHo differences between patients and controls co-varied with inter-individual variability in pain perception intensity, we examined the non-parametric Spearman correlations between mean ReHo data for the cluster and SF-MPQ scores in patients. Effect sizes were extracted using MarsBar. The threshold for statistical significance was set at $p < 0.05$.

3. Results

3.1. Neuroimaging data

Regional brain activities for both groups are shown in Fig. 1A and B. The major regions of the DMN, such as the medial temporal lobe and posterior cingulate cortex, exhibited significantly higher ReHo values during the resting-state for both groups.

Compared with controls, ReHo of SPD patients was significantly higher in the left precentral gyrus (Fig. 1C). There were no regions showing greater activity in controls than in patients.

3.2. ReHo–SF-MPQ correlations

VAS scores were positively correlated with ReHo in the left precentral gyrus ($r = 0.75$, $p = 0.02$).

4. Discussion

This is the first study to use ReHo analysis to examine resting-state brain activity in patients with SPD. These patients showed significant ReHo increases in the left precentral gyrus. Precentral gyrus ReHo differences in patients (compared to controls) resemble activations that have been reported in previous neuroimaging studies of pain-related processing (Seifert and Maihöfner, 2011). Chronic pain disorder is associated with precentral gyrus dysfunction (Riedl et al., 2011). We speculate that atypical activity of this region in patients with SPD may be related to some pathophysiological mechanisms underlying SPD. Tamura et al. (2004) have investigated the effects of transcranial magnetic stimulation (rTMS) of the precentral gyrus on acute pain mediated by A δ -fibers and C-fibers. rTMS of the precentral gyrus has been shown to suppress C-fiber pain processes related to chronic pain conditions. The precentral gyrus appears to an important brain region that could be targeted by treatments for chronic pain.

R-fMRI studies examining SPD have been conducted by Otti et al. (2013a, 2013b), but these measured functional network connectivity (FNC) among pain-associated networks. ReHo has been shown to measure local functional connectivity in the brain during the resting-state (Zang et al., 2004). The different results across these previous FNC studies and the present ReHo analysis may be related to this difference in analytical methodology.

The present study has several limitations. First, the small sample size may limit the robustness of our findings. Secondly, our exclusion criteria did not include all treatments that might influence patients' pain perception, such as antidepressants, although the criteria did include opioids, and a 24 h analgesic-free observation period prior to the fMRI scan was not generally fully effective. Despite these limitations, our results suggest that changes in the left precentral gyrus may be associated with distinctive neural mechanisms underlying SPD.

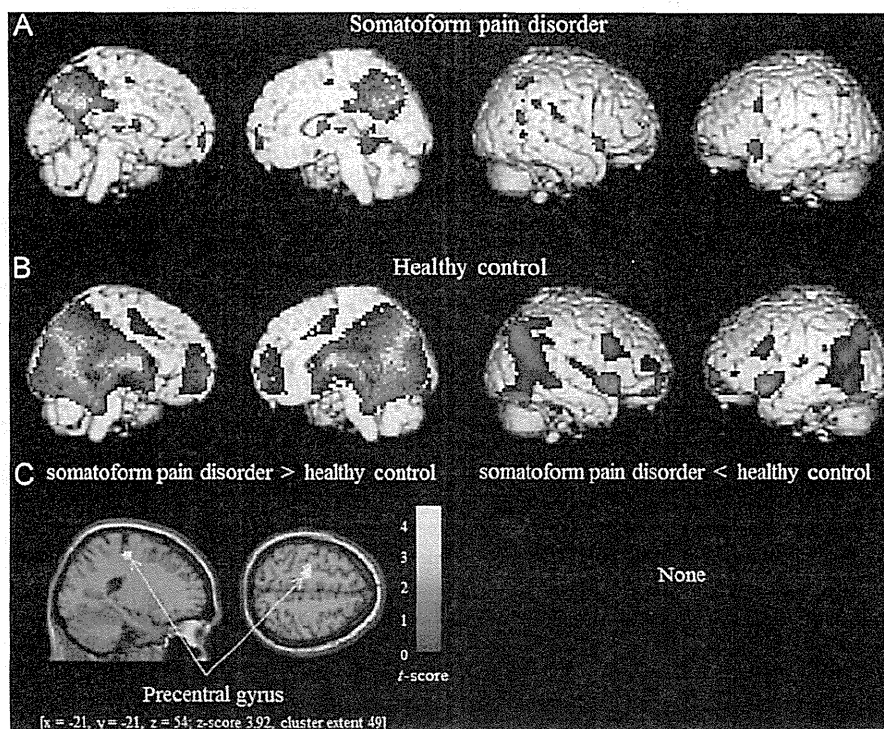


Fig. 1. (A) One sample *t*-test ReHo map for patients with somatoform pain disorder (SPD) and (B) healthy controls (image threshold set at $p < 0.001$). (C) Regions in which increased ReHo was observed in SPD patients (image threshold set at $p < 0.001$, cluster size > 44).

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Appendix A. Supplementary materials

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.psychresns.2013.12.006>.

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