The neural correlates of the metacognitive function of other perspective: a multiple regression analysis study

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Perspective taking is defined as the social cognitive function of imagining the world or imagining oneself from another's viewpoint. Previously, we reported that behavioral activation increased the dorsal medial prefrontal cortex (dmPFC) activation during other perspective self-referential processing for positive words in subthreshold depression, but did not report whether metacognitive function was related to the dmPFC activation. Therefore, we sought to test the relationship between the dmPFC activation during other perspective self-referential processing for positive words and an individual's metacognitive evaluation of other perspective. Thirty-four healthy individuals underwent functional MRI scans during a referential task with two viewpoints (self/other) and two emotional valences (positive/negative). Neural activation during other perspective self-referential processing for positive words was correlated with the metacognitive function of participants measured by the Interpersonal Reactivity Index (IRI). We found a positive correlation between the score in perspective taking of the IRI and activation in the dmPFC during other perspective self-referential processing for positive words. The present findings showed that self-report questionnaires assessing participants' metacognitive evaluation of other perspective were correlated with dmPFC activation during positive metacognition of other perspective task. However, we did not conduct a behavioral activation intervention in the present study. The present students were healthy. The IRI is a subjective measure of multidimensional trait empathy. It is necessary to develop an objective measurement for the metacognitive function of other perspective in the near future. ***NeuroReport*** **28:671–676 Copyright © 2017 The Author(s). Published by Wolters Kluwer Health, Inc.**

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Introduction

Perspective taking is defined as the social cognitive function of imagining the world or imagining oneself from another's viewpoint [1]. Perspective taking is understanding oneself from another individual's perspective (i.e. the metacognitive function of taking the 'other perspective'; e.g. 'Linda thinks I am calm'). Individuals with depression show impairments in positive self-referential processing taken from the other perspective [2] and such altered self-referential processing may lead to the maintenance of depressive symptoms [3]. In addition, a previous meta-analysis of neuroimaging studies has reported that self-referential tasks in healthy individuals have consistently activated the ventromedial prefrontal cortex (vmPFC) and the dorsal medial prefrontal cortex (dmPFC) [4]. Moreover, Esslen *et al.* [5] reported that prereflective aspects of the self were implemented to a greater degree in the vmPFC, whereas reflective aspects of the self were implemented in the dmPFC. Also, previous neuroimaging studies have shown that individuals with depression consistently show abnormal activation of the amygdala, insula, orbitofrontal cortex, vmPFC, and dmPFC [6]. Healthy individuals show increased dmPFC activation during positive self-referential processing, whereas individuals with depression show decreased dmPFC activation during positive self-referential processing [7]. Furthermore, our previous study has indicated that behavioral activation (BA) increased activation in the dmPFC, which is associated with other perspective self-referential processing for positive words and that it is also correlated with an improvement in depressive symptoms [8]. Also, several previous neuroimaging studies have suggested that dmPFC activation might reflect the metacognitive function [9,10]. Furthermore, Lutz *et al.* [10] indicated that individual's metacognitive awareness for inner experiences was correlated with dmPFC activation during metacognitive tasks. For these reasons, we

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assumed that increased positive metacognitive function of other perspective, which is associated with dmPFC activation, would lead to improvements in depressive symptoms. However, we did not examine whether the metacognitive functions of other perspective itself were related to the dmPFC activation. To date, little is known about the relationship between an individual's metacognitive evaluation of other perspective and dmPFC activation during metacognitive tasks. Therefore, we examined the relationship between self-report questionnaires of an individual's metacognitive evaluation of other perspective and dmPFC activation during metacognitive tasks. In the present study, self-report questionnaires for participants' metacognitive evaluation of other perspective were measured using the perspective taking of the Interpersonal Reactivity Index (IRI) [11,12]. The perspective taking of the IRI evaluates the tendency for an individual to take the 'psychological point of view of others' [13]. In previous studies, Beitel *et al.* [14] and Birnie *et al.* [15] reported a positive correlation between the perspective taking of the IRI and the Mindful Attention Awareness Scale (MAAS) [16], which assesses one's metacognitive function. On the basis of these results, we chose to use the perspective taking of the IRI as a measure of an individual's metacognitive function of other perspective. We hypothesized that there would be a positive correlation between the scores in perspective taking of the IRI and activation in the dmPFC during other perspective self-referential processing for positive words. Therefore, the aim of the present study was to examine the relationship between dmPFC activation of other perspective self-referential processing for positive words and the variability of the perspective taking of the IRI.

Methods

Participants

In the present study, we recruited new, healthy individuals who had not participated in our previous study [8]. Participants were recruited from Hiroshima University by screening with the Japanese version of the Beck Depression Inventory-II [17] and the Japanese version of the Composite International Diagnostic Interview [18]. The inclusion criterion was a Beck Depression Inventory-II score of less than 10. The exclusion criteria were major depressive episode within the past year, a lifetime history of bipolar disorder, current psychopharmacological or psychological treatment, and the presence of significant suicidality. Thirty-four healthy individuals (mean age = 18.6 years, SD = 0.5; 21 men, 13 women) participated in the fMRI study. One participant was excluded from the fMRI analyses because of excessive movement artifacts (e.g. > 4 mm). In total, data of 33 participants (mean age = 18.6 years, SD = 0.5; 21 men, 12 women) were analyzed (Table 1). The ethics committee of Hiroshima University approved the study protocol. Before the study, written informed consent was obtained from all participants.

Table 1 Mean scores and SDs of BDI-II, IRI

	Mean (SD)
BDI-II	3.6 (2.6)
IRI perspective taking	17.7 (3.5)

BDI-II, Beck Depression Inventory-II; IRI, Interpersonal Reactivity Index.

Evaluation

Neural activation during other perspective self-referential processing was measured using an fMRI task. Also, self-report questionnaires for participants' metacognitive function of other perspective were assessed using the perspective taking of the IRI. The IRI is a widely used multidimensional measure of trait empathy. It consists of four subscales: perspective taking, personal distress, empathic concern, and fantasy [12]. Perspective taking evaluates the tendency for an individual to adopt the 'psychological point of view of others'. Personal distress is self-oriented and associated with aversive emotional responses in the observer. Empathic concern is other-oriented and related to feelings of compassion and sympathy for the observed individual. Fantasy examines the participants' abilities to transpose themselves into fictional situations. Each subscale contains seven items and is measured on a five-point Likert scale ranging from 0 ('Does not describe me well') to 4 ('Describes me very well'). For each subscale, a minimum score of 0 or a maximum score of 28 is possible.

Experimental design

Thirty-four healthy individuals underwent fMRI scans while they completed the referential task. Before scanning, participants completed the IRI and chose their second closest friend of the same sex to be used as the 'other' during the experiment. The fMRI task [8,19] included five judgment conditions: other perspective self-judgment condition (OS), other perspective other-judgment condition (OO), self-perspective self-judgment condition (SS), self-perspective other-judgment condition (SO), and a control judgment (i.e. word recognition) condition (Cont). In OS condition trials, participants judged the presented positive (OS-P) or negative (OS-N) trait words using his or her friend's viewpoint as applicable to one's own self. In OO condition trials, participants judged the presented positive (OO-P) or negative (OO-N) trait words using his or her friend's viewpoint as applicable to his or her friend. In SS condition trials, participants judged positive (SS-P) or negative (SS-N) trait words using the self viewpoint, applicable to one's own self. In SO condition trials, participants judged positive (SO-P) or negative (SO-N) trait words using the self viewpoint as applicable to his or her friend. Finally, in control (Cont) condition trials, participants judged positive (Cont-P) or negative (Cont-N) words as to whether or not they could understand their meanings. Participants performed each condition eight times and each condition included four blocks. At the onset of each block, a fixation cross was displayed for 1000 ms, followed by an instruction cue presented for 3000 ms. Each block consisted of five trials that included a fixation cross displayed for 1000 ms, followed by an adjective displayed for 3000 ms and the participant's response. A fixation point was displayed between blocks for 4000 ms as an intermission, and then the instruction cue for the next block was presented. The duration of each block was 28 s. To control for order effects, blocks within a run were presented in a pseudorandom order, with no two consecutive blocks featuring the same instructions. The total time for the task was 1120 s. Details of the fMRI task have been described in our previous paper [8].

MRI acquisition

MRI scanning was performed using a Verio 3.0 T device (Siemens AG, Munich, Germany). A time-course series of 536 scans were acquired with T2*-weighted, gradient echo, echo-planar imaging sequences. Each volume consisted of 38 slices, with a slice thickness of 3.8 mm with no gap. The repetition time was 2000 ms, the echo time was 25 ms, and the flip angle was 80°. The field-of-view was 240 mm and the voxel size was $3.8 \times 3.8 \times 3.8\ mm^3$. After functional scanning, structural scans were acquired using a T1-weight gradient echo pulse sequence (repetition time = 2300 ms, echo time = 2.98 ms, flip angle = 9°, field-of-view = 256 mm, voxel size = $1 \times 1 \times 1\ mm^3$), which facilitated localization.

fMRI data analysis

Image processing and statistical analyses were carried out using Statistical Parametric Mapping (SPM8) software (Welcome Department of Cognitive Neurology, London, UK). The first five volumes of the fMRI run were discarded to allow for T1 stabilization. All of the remaining volumes were slice timing corrected, realigned to the mean volume to correct for head motion, spatially normalized using the Montreal Neurological Institute (MNI) T1 template, and smoothed with a 6 mm full-width, half-maximum Gaussian filter. A whole-brain voxel-by-voxel multiple linear regression model was used at the individual participant level. Each condition was modeled using a box-car function convolved with a canonical hemodynamic response function. The realignment parameters were also included in the models as covariates of no interest. To evaluate brain activation related to OS-P, we created one contrast ('OS-P minus Cont-P') in the first-level analysis for each participant. This contrast was subjected to group analysis using a random-effects model. First, a one-sample *t*-test was performed for all participants to assess the overall effect of OS-P. Second, to identify activation in cortical regions associated with the perspective taking of the IRI, we carried out a multiple regression analysis on OS-P with brain activation as the dependent variable and the score in perspective taking of the IRI as the independent variable. According to our previous study [8], BA increased the dmPFC activation during OS-P and it correlated with improved depressive symptoms. Therefore, we were only interested in the activity involved in OS-P. The other referential condition was excluded from analyses. The statistical threshold of P value of less than 0.05 family-wise error (FWE) corrected for the whole brain was used, with the exception of a priori hypothesized regions corrected for a small volume (search volume is a priori region of interest masks). We used the dmPFC as the a priori region of interest (ROI) on the basis of our previous work [8]. We carried out an ROI analysis using the data of a previous functional brain imaging study of other perspective self-referential processing to validate our hypothesis. The ROI was defined on the basis of a functional brain imaging study by Ruby and Decety [20] that we used it in our previous study [8] (6 mm radius sphere, center at MNI coordinates $x=4$, $y=50$, $z=40$). Brain activations were reported if they exceeded P value of less than 0.001 (uncorrected) at the single voxel level and P value of less than 0.05 (FWE corrected for the whole brain or FWE small volume corrected within the dmPFC ROI) at the cluster level.

Results

fMRI data

Brain regions showing activity associated with OS-P

We first investigated the brain regions in which neural activity was correlated with OS-P. Consistent with our previous study [8], the left medial prefrontal cortex (BA8) showed significant activation in OS-P. The other region that showed significant activation was the left caudate nucleus.

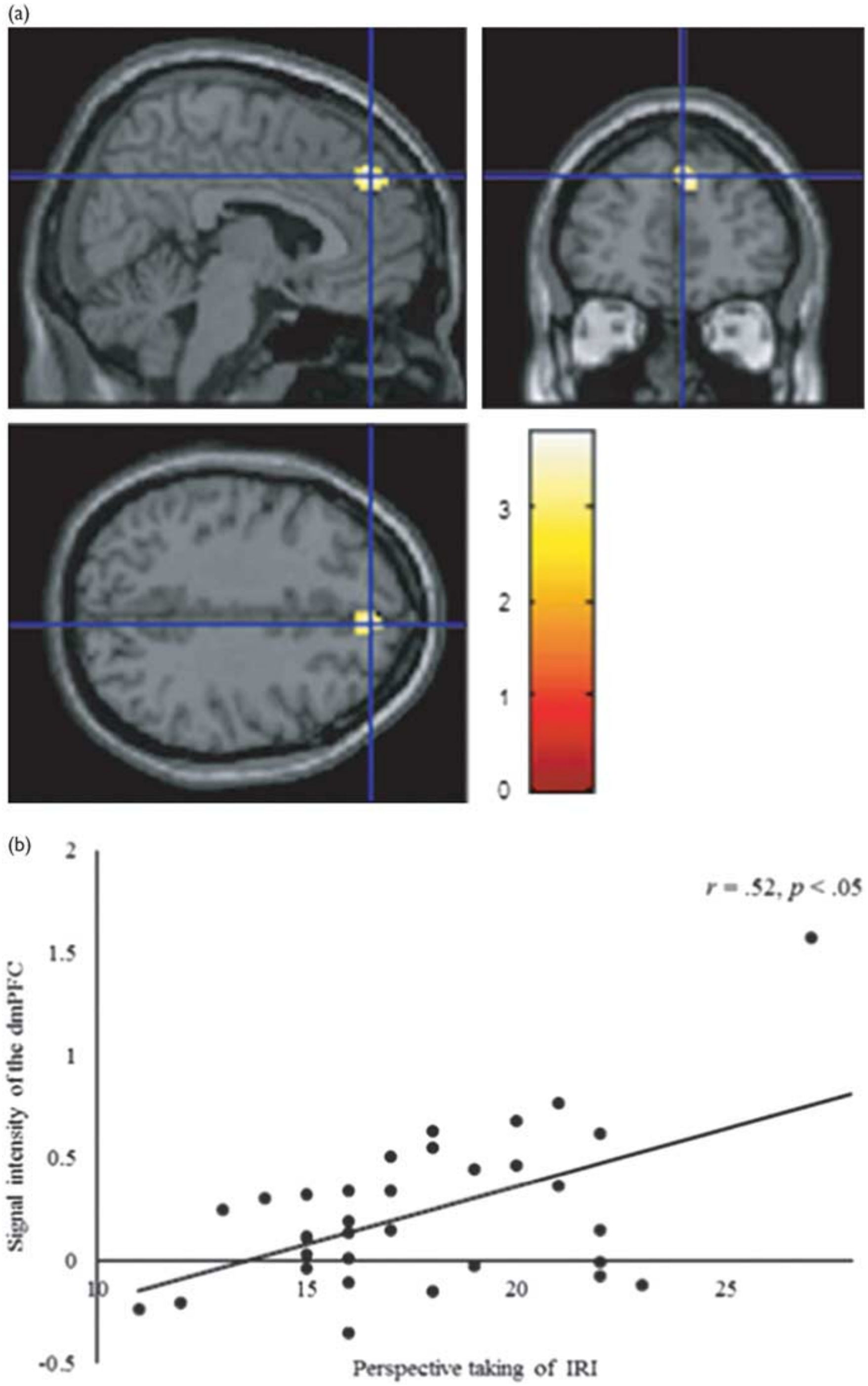
Multiple regression analysis

We carried out multiple regression analyses between the brain activation during OS-P and the perspective taking score of the IRI. However, there were no areas that fulfilled the whole-brain correction criteria. In addition, we carried out ROI analyses on the basis of our hypothesis. The scores in perspective taking of the IRI showed a significant positive correlation with activation in the right dmPFC ($x=6$, $y=46$, $z=38$, $t=3.79$, cluster size = 37, cluster level FWE small volume corrected $P=0.021$) during OS-P (Fig. 1a and b).

Discussion

The aim of our study was to confirm the relationship between the scores in the metacognitive function of other perspective and increased dmPFC activation associated with OS-P. We found a positive correlation between the scores in the perspective taking of the IRI and activation in the dmPFC during OS-P. The present findings indicated that self-report questionnaires assessing participants' metacognitive evaluation of other perspective were correlated with dmPFC activation during the positive metacognition of other perspective task. The present study is the first to report the relationship between an individual's metacognitive evaluation of other perspective

Fig. 1



(a, b) Correlation between perspective taking of the Interpersonal Reactivity Index (IRI) and hemodynamic responses of other perspective self-judgment condition for positive words. Interindividual variability in perspective taking of the IRI showed a significant positive correlation with the right dorsal medial prefrontal cortex (dmPFC) ($x=6$, $y=46$, $z=38$, $t=3.79$, cluster size = 37, cluster level family-wise error small volume corrected, $P=0.021$) (a). Scatter plots and associated correlation coefficients show the relationship between the interindividual variability in perspective taking of the IRI and increased dmPFC activation during the other perspective self-judgment condition for positive words (b).

and dmPFC activation. Birnie *et al.* [15] reported that mindfulness-based stress reduction therapy (which is one of the cognitive behavior therapy) have increased both score of the MAAS and perspective taking subscale of the IRI, and there was a positive correlation between the scores of the MAAS and the perspective taking of the IRI after the intervention. These results suggest that cognitive behavior therapy may enhance the metacognitive function of being able to take another's perspective. During the course of BA interventions, participants monitor and assess their daily activities and work to change their habitual behaviors, such that pleasant events are increased and depressive symptoms are improved [21,22]. We have previously reported that BA led to increased activation in the dmPFC during other perspective self-referential processing of positive trait words in individuals with subthreshold depression, which might contribute toward an improvement in depressive symptoms and the objective monitoring function [8]. However, in our previous study [8], we did not directly assess the monitoring function with any self-report questionnaires or observer-rated scales. In the present study, participants' metacognitive function of other perspective was assessed using the perspective taking subscale of the IRI, which is a self-report scale. We examined the relationship between dmPFC activation of other perspective self-referential processing for positive words and the variability in perspective taking assessed by the IRI. The location in the dmPFC (MNI coordinates $x=6$, $y=46$, $z=38$) in the present study was different from the location in the study by Lutz *et al.* [10] (MNI coordinates $x=2$, $y=22$, $z=58$). A previous review [23] has suggested that differences in the location of the dmPFC reflect differences in the objects of metacognition, such as the self-image, own body sensations, and feelings. Considering the present finding along with those of our previous study [8], it may be suggested that BA might improve an individual's positive metacognitive functions in terms of the other perspective, which is reflected in neural activity.

There are several limitations to this study. First, our previous study [8] had examined an fMRI task before and after a BA intervention for subthreshold depression. However, we did not conduct a BA intervention in the present study. The present students were healthy. To determine the effect of BA on neural activation during the metacognitive function of other perspective in subthreshold depression, a quantitative evaluation of this metacognitive function before and after a BA intervention in a sample of participants who experience subthreshold depression would be necessary. Second, we assessed the metacognitive function of other perspective using the perspective taking of the IRI. Because the IRI is a subjective multidimensional trait empathy scale, it is necessary to develop an objective measurement for the metacognitive function of other perspective in the near future. Individual metacognitive functions were related to the dmPFC activation during other perspective self-referential processing for positive words, suggesting that the dmPFC activation might be involved in the metacognitive function of other perspective.

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Conceived and designed the experiments: S.Y., Y.O., R.H., R.J., K.T., A.M., S.S., S.Y. Performed the recruitment: Y.O. CIDI managers: Y.O. Performed the CIDI: K.T., S.S., S.Y., Y.N. Performed the fMRI experiments: S.S., S.Y. Contribution to the writing of the manuscripts: S.S., Y.O., G.O., K.T., M.T. All authors have approved the final article.

Conflicts of interest

There are no conflicts of interest.

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