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Neural processing associated with comprehension of an indirect reply during a scenario reading task

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Abstract

In daily communication, we often use indirect speech to convey our intention. However, little is known about the brain mechanisms that underlie the comprehension of indirect speech. In this study, we conducted a functional MRI experiment using a scenario reading task to compare the neural activity induced by an indirect reply (a type of indirect speech) and a literal sentence. Participants read a short scenario consisting of three sentences. The first two sentences explained the situation of the protagonists, whereas the third sentence had an indirect, literal, or unconnected meaning. The indirect reply condition primarily activated the bilateral fronto-temporal networks (Brodmann's Areas (BA) 47 and 21) and the dorso-medial prefrontal cortex (dmPFC). In the literal sentence condition, only the left fronto-temporal network (BA 45 and 21) and the dmPFC (posterior region) were activated. In addition, we found greater activation resulting from comprehension of an indirect reply than from literal sentence comprehension in the dmPFC, the left middle frontal area (BA 9), the bilateral inferior frontal area (BA 9/47), and the right middle temporal area (BA 21). Our findings indicate that the right and left fronto-temporal networks play a crucial role in detecting contextual violations, whereas the medial frontal cortex is important for generating inferences to make sense of remarks within a context.

Keywords: Indirect reply, functional MRI, pragmatics, inference, mentalizing

1. **Introduction**

Indirect speech is used to convey non-literal or indirect meanings and improves the efficiency of everyday communication. In the last half century, indirect speech has been studied by philosophers, linguists, and psycholinguists. Grice (1975) proposed an influential theory of conversation (the Cooperative Principle), which has guided research on the comprehension of indirect speech. Consider the following exchange:

Peter: Do you want some coffee?

Mary: Coffee would keep me awake.

In this exchange, Mary does not directly answer Peter's question. Her utterance seems to convey not just literal meanings but also non-literal, implicit meanings. That is, the utterance implies the speaker's intention. In Grice's view, her utterance has violated the "Maxim of Relevance." However, because the listener assumes the speaker is being relevant, the listener will try to infer an intended meaning. Grice called such inferences conversational implicatures. Following Grice's view, Holtgraves (1998, 1999) proposed a model describing the interpretive processes involved in certain types of indirect speech. This model assumes that the listener recognizes when a speaker has violated the "Maxim of Relevance" and generates an inference to understand the statement. The generated inference is based on the listener's belief about why the violation occurred. According to this model, a major motivation for violating the Maxim of Relevance is "face management," the communicative practices that individuals use to mutually

protect one another's "face" or public self (Brown & Levinson, 1987). Holtgraves (1999) also indicated that indirect speech often has a negative connotation, and people generally interpret indirect speech as conveying a negative opinion.

Recently, Pinker, Nowak, and Lee (2008) proposed a three-part theory of indirect speech using game theory, social psychology, and evolutionary psychology. Following the conversation theory of Grice and the politeness theory of Brown and Levinson (1987), Pinker emphasized that indirect speech allows for plausible deniability, permitting a cooperative listener to accept what is said and recognize that an uncooperative listener cannot react negatively to an ambiguous, indirect suggestion. In cases of plausible deniability, a negative message can be conveyed without losing face, thus making indirect speech an important face-saving device in everyday communication. These studies highlight several important features of indirect speech. First, a listener detects the speaker's violation of the Maxim of Relevance to identify that indirect speech is being used. Second, the listener needs to infer the mental states of others (i.e., derive beliefs, intentions, and emotional states) to comprehend the meaning of the indirect speech. Third, indirect speech functions as a face-saving device because it provides plausible deniability. These aspects of indirectness and politeness in speech allow for complex relationships in our daily communication.

Neuropsychological studies in patients have investigated whether the left or right

hemisphere plays a specific role in indirect speech comprehension (Channon, Pellijeff, & Rule, 2005; Foldi, 1987; Happe, 1993; Hirst, LeDoux, & Stein, 1984; Stemmer, Giroux, & Joanette, 1994). For example, Foldi (1987) examined the ability of patients with left and right hemisphere damage to assess their comprehension of indirect requests. Participants viewed two slides and listened to the accompanying verbal exchange. The participant would observe the first speaker ask one of three possible question types (indirect command, direct command, or wh-question). The second speaker would then complete the exchange with one of four response types (pragmatically appropriate, literal, physically veritable, or syntactically similar). After each exchange, the participant was asked to judge whether the response of the second speaker was appropriate. The results showed that patients with right hemisphere damage had a selective difficulty for appreciating indirect commands. They more often preferred literal interpretations to pragmatic interpretations than normal and aphasic, subjects. Hirst, LeDoux, and Stein (1984) also examined the ability of patients with left (anterior aphasics) and right hemisphere damage to comprehend indirect speech. Their material consisted of 40 videotaped episodes with two protagonists. For example, when eating dinner, one of the protagonists might ask, "Can you play tennis?"(direct question); in this example, a simple "yes" or "no" response would be appropriate. Alternatively, the protagonist might ask, "Can you pass the salt?"(indirect request); in this case, the action of passing the salt would be appropriate. Patients with left hemisphere damage

(anterior aphasics) had difficulty comprehending an utterance, "Can you X?" in the form of a direct question but could fully understand the same utterance when the context suggested that it was an indirect request. In contrast, patients with right hemisphere damage had little difficulty understanding direct questions, but they often judged that inappropriate actions (e.g., "picking up a racket and swinging it while eating dinner") were appropriate. Hirst, LeDoux, and Stein (1984) suggested that these patients might have difficulty assessing their scripts of world knowledge and have difficulty with the pragmatic component.

Recently, Martin-Rodriguez and Leon-Carrion (2010) used a meta-analysis to review 26 studies comparing the performance of patients with acquired brain injury (ABI) and healthy controls in four tasks widely used to study the Theory of Mind (ToM): a first-order belief task, a second-order belief task, an indirect speech task, and a social faux pas task. In this meta-analysis, the number of correct responses in each task was used as a performance indicator for both the patients and the healthy controls. For the effect sizes (ES) measure, Cohen's d was used to standardize the mean differences in ToM performance between the ABI patients and the healthy controls. To explain part of the heterogeneity between the results of the studies, moderator variables (demographic, task-related, and clinical moderator variables) were coded. Using these moderator variables, authors performed four independent meta-regression analyses (first order ToM tasks, second order ToM tasks, understanding indirect speech, and faux pas). The results of

these meta-regression analyses showed that demographic variables (differences in age, gender and education level between samples) did not significantly affect effect sizes. With respect to clinical moderator variables, studies with patients with frontal lobe lesions reported higher ESs only in faux pas tasks, and the proportion of patients with lesions in the right hemisphere was positively associated with ESs in indirect speech and faux pas tasks. Thus, these neuropsychological studies and meta-analyses suggest that the right hemisphere plays a crucial role in indirect speech comprehension.

Neuroimaging studies that attempt to identify the neural basis of understanding indirect speech have not yet been attempted; however, the manner in which people comprehend non-literal meanings, such as irony (Eviatar & Just, 2006; Rapp, et al., 2010; Uchiyama, et al., 2006; Wakusawa, et al., 2007; Wang, Lee, Sigman, & Dapretto, 2006, 2007), humor (Bartolo, Benuzzi, Nocetti, Baraldi, & Nichelli, 2006; Brunet, Sarfati, Hardy-Bayle, & Decety, 2000; Goel & Dolan, 2001), metaphor comprehension (Bottini, et al., 1994; Rapp, Leube, Erb, Grodd, & Kircher, 2004, 2007), and idiom comprehension (Boulenger, Hauk, & Pulvermuller, 2009; Lauro, Tettamanti, Cappa, & Papagno, 2008; Zempleni, Haverkort, Renken, & Stowe, 2007), has been the focus of many neuroimaging studies. Some of these neuroimaging studies may provide insight into the brain regions that mediate the comprehension of indirect speech. In particular, irony and indirect speech involve similar processes. In both processes, what the

speaker says does not necessarily correspond to what he/she intends. To understand these non-literal statements, the listener has to infer the speaker's mental state. This mentalizing process (second-order ToM processing) is critical for the comprehension of indirect speech and irony. Rapp et al. (2010) reviewed thirteen studies of patients with brain lesions and five studies that used fMRI to investigate irony comprehension. On the basis of these studies, the authors highlighted three regions involved in irony comprehension: the medial prefrontal cortex (Shamay-Tsoory, Tomer, & Aharon-Peretz, 2005; Wakusawa, et al., 2007), the left hemisphere language regions (Shamay-Tsoory & Aharon-Peretz, 2007; H. Uchiyama, et al., 2006; Wang, et al., 2006; Zaidel, Kasher, Soroker, & Batori, 2002), and their right hemisphere homologues (Eviatar & Just, 2006; R. L. Mitchell & Crow, 2005). The authors also suggested that the medial prefrontal region is a key region for ToM processing, the right hemisphere language region is involved in irony detection, and the left hemisphere language region is involved in irony comprehension.

The neuropsychological and neuroimaging studies described above suggest that the detection and comprehension processing of pragmatic speech are associated with regions that play a role in mentalizing and semantic processes, especially the medial frontal cortex and the bilateral fronto-temporal networks. To evaluate these neural substrates, we conducted an fMRI experiment using a scenario reading task. There are some types of indirect speech (e.g., request,

question, and reply). For example, an indirect request (“Can you open the window?") is an utterance that conveys the information regarding the listener’s ability to open the window, which prompts a specific action. In contrast, an indirect reply is an utterance that flouts the Maxim of Relevance (Grice, 1975) and that expresses the speaker’s intention. In this study, we focused on the comprehension of an indirect reply and evaluated the neural activity associated with the comprehension processing. As with previous studies, we predicted that neural activity would be increased in the medial frontal cortex, which is associated with mentalizing processes. Additionally, we predicted that neural activity would be increased in the right and left inferior frontal areas which have been implicated in the detection and comprehension of non-literal or indirect meanings.

2. **Methods**

2.1. Participants

Fifteen graduate and undergraduate students (eleven men and four women; mean age = 25.2 years) participated in this experiment. All of the participants had no history of mental disorders, were native Japanese speakers, and were right-handed. Handedness was assessed using the Edinburgh Handedness Survey (Oldfield, 1971). The experiment was approved by the Ethics Committee of Hokkaido University Graduate School of Medicine and performed in accordance

with the Declaration of Helsinki. All of the participants gave their written informed consent prior to participation.

2.2. Stimulus materials

The experimental design consisted of three conditions (indirect reply, literal sentence, and unconnected sentence) and a baseline condition in which only fixation crosses were presented. For the indirect reply condition, scenarios were created on the basis of a previous study by Holtgraves (1999). In the Holtgraves (1999) experiments, there were three situation types: opinions ("What did you think of my presentation?" - "It's hard to give a good presentation."), disclosures ("Did you get a raise yet?" - "The economy is still bad."), and request refusals ("Can you work my shift this Friday?" - "I'm having a party Friday."). For the present experiment, we prepared eight of each of the three situation types in the same way. Each scenario consisted of a short dialogue involving two people: an initial remark spoken by the first person to a second person and a reply by the second person to the initial remark. In the indirect reply scenarios, the reply was a violation of the relevance maxim, and it was therefore likely to be interpreted as conveying a negative opinion, negative disclosure or request refusal. In the literal scenarios, the context of the scenario supported a literal reading of the reply and thus made an indirect interpretation unlikely (e.g.,"What do you think of my oil painting?" - "Your painting is very good."). In the unconnected scenarios, the reply was not related to the initial remark (e.g.,

"What did you think of my English pronunciation?" - "Your marriage partner is not good."). To eliminate the influence of repetition effects, we did not use the same sentences or the same names. Prior to the fMRI experiment, we conducted a preliminary experiment. All of the materials were presented to twelve participants who were not recruited for the main study. These participants rated their acceptability of the materials. As a result of the preliminary experiment, we selected 20 scenarios for each condition, and we used 16 scenarios (six opinions, five disclosures, and five request refusals) for the fMRI experiment. The remaining four scenarios were used for training.

2.3. Procedures

2.3.1. Tasks

All participants completed a scenario reading task. The scenarios consisted of two parts. The first part explained the context of the dialogue and gave an initial remark spoken by one person to a second person. In the second part, the second person replied to the initial remark (target stimulus). When the target stimulus was presented, the participant responded by pressing one of three buttons of a response box suitable for MRI experiments. The participant indicated whether the stimulus had a positive connotation, a negative connotation, or was meaningless. In addition to the task conditions, a baseline condition was included to minimize habituation. For the baseline condition, fixation crosses were presented in place of the context of the dialogue. After

presenting another fixation, three fixation crosses were presented in place of the target stimulus, and the participant indicated whether the stimulus was meaningless by pressing one of three buttons.

2.3.2. Presentation of the stimuli and behavioral responses

The MRI scanning phase consisted of four sessions (118 functional image volumes per session with four initial volumes to avoid transient non saturation effects). During each scanning session, participants were presented with 16 stimuli: four indirect reply scenarios, four literal scenarios, four unconnected scenarios and four baseline stimuli. In each session, the order of these 16 stimuli was randomized. Each participant completed four sessions, and the order of the sessions was counterbalanced across subjects. Each stimulus was displayed at the center of a rear projection screen. Participants viewed the screen through a mirror system mounted on a head coil. Participants were tested individually and reaction times and judgments were recorded. The first stimuli (two sentences) were presented simultaneously for 8 s and immediately followed by the fixation cross for 2 s. The final stimulus was presented for 4 s and immediately followed by the fixation cross for 8 s. The presentation of the stimuli and the recording of the participants' responses were controlled with E-prime (Psychology Software Tools, Inc.). All of the participants completed the experiments within 30 minutes.

2.4. fMRI data acquisition

A whole-body, 1.5-T Signa Echo-Speed scanner (General Electric, Inc.) was used to acquire two sets of images from 22 axial slices: high-resolution, T1-weighted anatomical images and gradient-echo, echo-planar T2*-weighted images with blood oxygenation level-dependent (BOLD) contrast. The parameters of the sequence were as follows: TR = 3,000 ms, TE = 40 ms, flip angle = 90°, FOV = 240 x 240 mm, matrix = 64 x 64, slice thickness = 4 mm, and slice gap = 0.8 mm. A total of 472 scans were acquired per participant (118 volumes x four sessions).

2.5. fMRI data analysis

The data were analyzed using statistical parametric mapping (SPM5, Welcome Department of Cognitive Neurology, London, UK: http://www.fil.ion.ucl.ac.uk/spm; Friston et al., 1995). After correcting for differences in slice timing within each image volume, all functional volumes were realigned to the first volume of each participant to correct for head motion. The volumes were subsequently coregistered with each participant's anatomical image, spatially normalized to the Montreal Neurological Institute (MNI) brain template and smoothed using an 8-mm, full-width-at-half-maximum Gaussian kernel. We used an event-related design to minimize habituation and learning effects. Each stimulus onset of the target stimulus was convolved with a canonical hemodynamic response function. For each subject, parameter estimates were assessed with least squares regression analysis, and contrast images were computed for each experimental condition relative to the baseline condition.

For the group analysis, a random-effect analysis was conducted following a general linear model in which each of the conditions was modeled with the canonical hemodynamic response function. A high-pass filter (1/128 Hz cutoff) was used to remove low-frequency noise. Global scaling was not applied. Statistical parametric maps were generated for each contrast of the t statistic on a voxel-by-voxel basis. The threshold for the SPM{t} was set at $t > 3.79$ (corresponding to uncorrected $p < .001$), and the cluster size larger than ten voxels.

3. **Results**

3.1.Behavioral results

Reaction time was defined as the period between the presentation of the target stimulus and the button press by the participant. The mean reaction time was 2172.7 ms for the indirect reply condition, 1691.4 ms for the literal sentence condition, 1684.3 ms for the unconnected sentence condition, and 709.0 ms for the baseline condition. A one-way ANOVA revealed a significant main effect of reaction time ($F (3, 59) = 33.34$, $p < .0001$), and Tukey-Kramer post hoc tests revealed significant differences in reaction time among the four types of stimuli ($HSD (3) = 2.65$, $p < .05$). The mean reaction time for the indirect reply condition was significantly longer than for the other three conditions, and there were no significant differences between the literal sentence condition and the unconnected sentence condition. The mean rate of correct responses

was 92.1% for the indirect reply condition, 94.6% for the literal sentence condition, 93.3% for the unconnected sentence condition, and 98.3% for the baseline condition. There was no significant difference in the rate of correct responses (F (3, 59) = 1.198, p = .318). The participants performed all conditions satisfactorily.

3.2.Imaging results

A main effect of the indirect reply condition relative to the baseline condition identified activation in the left middle frontal gyrus (MFG; BA 6/9), the dmPFC (BA 6/8/9/10), the bilateral inferior frontal gyri (IFG; BA 47), the right middle temporal gyrus (MTG; BA 21), the left anterior cingulate cortex (ACC; BA 32), the caudate, and the cuneus (Table 2 and Figure 1). In the literal sentence condition relative to the baseline condition, the left frontal cortex was activated in rostrolateral sections of the superior (BA 8), middle (BA 11), medial (BA 6) and IFG (BA 45). The left MTG (BA 21), the caudate and the declive were also activated. A main effect of the unconnected sentence condition relative to the baseline condition was identified activation in the bilateral IFG (BA 45/47), the left MFG (BA 8/11) and the right MTG (BA 21).

The primary goal of this study was to identify the different neural substrates involved in the comprehension of an indirect reply and a literal sentence. We analyzed the differences between the indirect reply condition and the literal sentence condition directly. As shown in Figure 2 and Table 4, the contrast between these two conditions showed greater activation in the

dmPFC (BA 8/9), the left MFG (BA 9), the bilateral IFG (BA 9/47), the left precuneus (BA 23/31), and the right MTG (BA 21).

A parametric modulation analysis was performed to ensure that this activation was not the result of differences in difficulty among the conditions. For each stimulus, we examined the correlation between the reaction time and the amplitude of the cortical activations. The reaction time for each trial was entered into the model as a parameter and used to estimate the parametric modulation of this effect. The behavioral results showed that the mean reaction time was significantly longer for the indirect reply condition when compared with the other three conditions. If there were differences in difficulty among the conditions, the results of the parametric modulation analysis should show a significant positive correlation between the reaction time and the amplitude of the cortical responses. In the indirect reply condition, however, a significant correlation ($p < .001$, uncorrected) was observed only in the left precuneus (Table 3).

4. **Discussion**

The present study was designed to identify the different neural substrates involved in understanding the indirect reply and literal sentence conditions. A main effect of the indirect reply condition was identified in the bilateral IFG, the MTG (Brodmann's Areas (BA) 47 and

21) and the dmPFC. In the literal sentence condition, only the left IFG and MTG (BA 45 and 21) and the dmPFC (posterior region) were activated. We also found greater activation for comprehension of an indirect reply than for a literal sentence comprehension in the dmPFC, the left MFG (BA 9), the bilateral IFG (BA 9 and 47), and the right MTG (BA 21). Our results support the hypothesis that comprehension of an indirect reply increases activation in the dmPFC, a region associated with mentalizing processes, and in the bilateral IFG and the MTG, regions associated with the detection of non literal or indirect meanings.

The results of the parametric modulation analysis showed a significant positive correlation only in the left precuneus for the indirect reply condition. This finding indicates that the activation in the dmPFC and the bilateral IFG and the MTG (BA 47 and 21) was not the result of differences in difficulty among the conditions.

4.1.Comprehension of an indirect reply and IFG activation

The present study showed that the ventral portion of the IFG (BA 47) was activated bilaterally by both the indirect reply and the unconnected sentence condition. In contrast, only the left IFG (BA 45) was activated in the literal sentence condition. In both the indirect reply and unconnected sentence conditions, the reply was a violation of the relevance maxim and was not related to the initial remark. This violation was thought to be the cause of the activation in Brodmann's Area 47. Brodmann's Area 47, the lower portion of the inferior frontal gyrus (pars

orbitals), is selectively involved in processing the semantic aspects of a sentence, rather than syntactic processing (Bookheimer, 2002; Dapretto & Bookheimer, 1999; Uchiyama, et al., 2008). Previous functional neuroimaging studies have reported an increased BOLD response in the IFG during the following: sentence and discourse comprehension (bilateral IFG; Dapretto & Bookheimer, 1999; Kuperberg, et al., 2006; Rodd, et al., 2005; Zempleni, Haverkort, et al., 2007), detection of semantic anomalies(left IFG; Hagoort, Hald, Bastiaansen, & Petersson, 2004; Ni, et al., 2000), following presentation of an ambiguous statement (bilateral IFG; Rodd, et al., 2005; Zempleni, Renken, et al., 2007), or during the construction of a situation model (bilateral IFG; Ferstl, Rinck, & von Cramon, 2005; Menenti, Petersson, Scheeringa, & Hagoort, 2009). On the basis of these previous studies, our results suggest that semantic processing at the sentence level is related to bilateral IFG activation (BA 47).

4.2.Comprehension of an indirect reply and right hemisphere activation

Both the left and right IFG (BA 47) and the MTG (BA 21) were activated in the indirect reply condition, but only the left IFG (BA 45) and the MTG (BA 21) were activated in the literal sentence condition. Although the left hemisphere is viewed as being language dominant, a number of fMRI studies have reported increased activation in right hemispheric brain regions during language comprehension. Activation of the right hemisphere seems to occur when the task demands are increased and higher level language processing is required, such as during the

comprehension of semantically ambiguous sentences or pragmatic speech (Bottini, et al., 1994; Eviatar & Just, 2006; Robertson, et al., 2000; Rodd, Davis, & Johnsrude, 2005; St George, Kutas, Martinez, & Sereno, 1999; Xu, Kemeny, Park, Frattali, & Braun, 2005; Zempleni, Renken, Hoeks, Hoogduin, & Stowe, 2007). Moreover, some studies have shown that regions in the right hemisphere are sensitive to discourse coherence (Caplan & Dapretto, 2001; Kuperberg, Lakshmanan, Caplan, & Holcomb, 2006). Kuperberg, Lakshmanan, Caplan, and Holcomb (2006) investigated causal inferencing across three types of sentence scenarios: highly causally related, moderately related, or unrelated. They found that, when compared with moderately related sentences, the right IFG (BA 47) showed stronger responses to sentences that were unrelated to the preceding two-sentence contexts. These findings suggest that the right IFG may play an initial role in the detection of incoherence within discourse. In our study, the indirect reply was out of context and elicited higher activation in the bilateral IFG and the MTG (BA 47 and 21).The literal sentence, however, was consistent with the prior context and elicited higher activation only in the left IFG and the MTG (BA 45 and BA 21, respectively). In the unconnected sentence conditions, we observed bilateral IFG (BA 47) activation but not dmPFC activation. The target stimuli in the unconnected condition were completely inconsistent with the prior context, and they neither matched the situation nor conveyed any related meaning. It was easier, therefore, to detect the contextual violation in the unconnected sentence condition

than in the indirect reply condition. Accordingly, the mean reaction time for the unconnected sentence condition was shorter than for the indirect reply condition. This result suggests that participants stopped attempting to understand the meaning after detecting a contextual violation.

Moreover, some previous studies have proposed models for the impact of emotional information on the activation pattern (Borod, Andelman, Obler, Tweedy, & Welkowitz, 1992; Davidson, Ekman, Saron, Senulis, & Friesen, 1990; Ross & Monnot, 2011). However, our results showed that the bilateral frontal regions (especially the ventral portion of the IFG, BA 47) were activated by both the indirect reply and the unconnected sentence condition. In the unconnected sentence condition, the stimulus was meaningless and was not affected by emotional valence. That is, the activation pattern cannot be explained only by the involvement of an emotional factor. In consideration of these results, we conclude that bilateral IFG and MTG (BA 47 and BA 21, respectively) activation may reflect semantic processing related to the detection of contextual violations. These results are congruent with previous neuropsychological studies in which patients with right hemisphere damage had difficulty assessing their scripts of world knowledge and had difficulty with the pragmatic component.

4.3.Comprehension of an indirect reply and activation in the dmPFC

We found greater activation for the comprehension of an indirect reply than for literal sentence comprehension in the dmPFC and the bilateral IFG, and the MTG (Table 4 and Figure 2). Many

studies have implicated the dmPFC in higher cognitive functions, including mentalizing, self-knowledge, social knowledge, action monitoring, and outcome monitoring (Amodio & Frith, 2006; Gallagher & Frith, 2003). Furthermore, several neuroimaging studies have suggested that the dmPFC may play a role in comprehending stories that include a ToM component (Bird, Castelli, Malik, Frith, & Husain, 2004; Ferstl & von Cramon, 2001, 2002), and that include the discourse coherence (Ferstl & von Cramon, 2001; Kuperberg et al., 2006; Ferstl, Neumann, Bogler, & von Cramon, 2008). Ferstl and Cramon (2002) showed that the dmPFC establishes a pragmatic connection between the presented sentences and is thus important for coherence processes related to language comprehension. Other studies have indicated that the medial frontal cortex is involved in higher level language comprehension, and activation in the medial frontal cortex has been associated with several aspects of pragmatic comprehension, including plausibility judgment (Bottini, et al., 1994), reasoning (Goel, Gold, Kapur, & Houle, 1997), coherence judgment (Ferstl & von Cramon, 2002), metaphor comprehension (Shibata, Abe, Terao, & Miyamoto, 2007a,b), and self-referential processing (Gusnard, Akbudak, Shulman, & Raichle, 2001). In the present study, the indirect reply was out of context, whereas the literal sentence was consistent with the prior context. Thus, to understand these inconsistent statements, the participant was required to infer why the speaker was using non literal and indirect statements and establish a pragmatic connection between the

presented remarks. In accordance with these ideas, our results found an involvement of the dmPFC in mentalizing processes, such as determining the speaker's mental state and generating inferences to make sense of the remarks within the context.

Our experiment also required the participants to respond by pressing one of three buttons to indicate whether the stimulus had a positive connotation, a negative connotation, or was meaningless. These judgment processes may reflect activation in the dmPFC. In the indirect reply condition, activation in the medial frontal cortex covered a large area from the anterior to the posterior region. In contrast, in the literal sentence condition, activation in the medial frontal cortex was localized to the posterior region. Previous studies have shown strong evidence for a different role for the anterior region in comparison to the posterior medial frontal cortex (Grezes, Frith, & Passingham, 2004; Tamir & Mitchell, 2010; Walter, et al., 2004). Amodio and Frith (2006) used a meta-analysis to review previous research that reported selective activation in the medial frontal cortex during tasks associated with action monitoring, outcome monitoring, self-knowledge, person perception, and mentalizing. They reported that the posterior region is involved in the continuous internal monitoring of action while the anterior region is involved in self-knowledge, person perception, and mentalizing tasks. In accordance with their study, activation in the medial frontal cortex (posterior region) due to literal sentence comprehension might be related to action monitoring processes (e.g., judging whether the stimulus had a

positive connotation, a negative connotation, or was meaningless). In contrast, activation in the medial frontal cortex (anterior region) due to comprehension of an indirect reply might be related to coherence processes that establish a pragmatic connection between the presented sentences and the mentalizing process.

Regarding the activation in dmPFC, it is undeniable that negative emotion affected the activation of the region. However, some studies have indicated that not only negative emotions but also positive emotions selectively affected the activation of these regions (Lewis et al., 2006; Fossati et al., 2003). That is, the activation of the region cannot be explained only by the involvement of an emotional factor. On the basis of these findings, we conclude that dmPFC activation may reflect cognitive processes involved in comprehending indirect reply.

4.4.Limitations of the method

One serious limitation of this study is the task effect of our stimulus materials. In our experiment, all of the target stimuli in the indirect reply condition were expressed as having a negative connotation, whereas all of the target stimuli in the literal sentence condition were expressed as having a positive connotation. The participant judged whether the stimulus had a positive connotation or a negative connotation. Some studies reported that the evaluation of the emotional state influenced the activation pattern (Ferstl, Rinck, & von Cramon, 2005).These

results suggest that an individual's emotional state may affect activation pattern. Further studies are needed to clarify the relationship between emotional factors and the activation pattern. In particular, it is necessary to conduct well-designed experiments to evaluate how emotional processes interact with cognitive processes.

Furthermore, in this study we evaluated neural activity associated with the comprehension of an indirect reply; we did not focus on the other types of indirect speech (e.g., request or question). Further research on comprehension processing of the other types of indirect speech would clarify the neural mechanisms associated with the comprehension of pragmatic speech.

4.5.Summary and Conclusions

In this study we present the first neuroimaging data recorded during the comprehension of an indirect reply. This study also supports previous patient-based neuropsychological studies, suggesting that pragmatic comprehension is associated with certain brain regions that are involved in mentalizing and semantic processing, such as the dmPFC and the bilateral frontal lobe. These findings integrate and extend upon previous behavioral and neuropsychological studies. On the basis of our data, we conclude that the right and left IFG and the MTG play a crucial role in detecting contextual violations, whereas the dmPFC is important for generating

inferences to make sense of remarks within a context.

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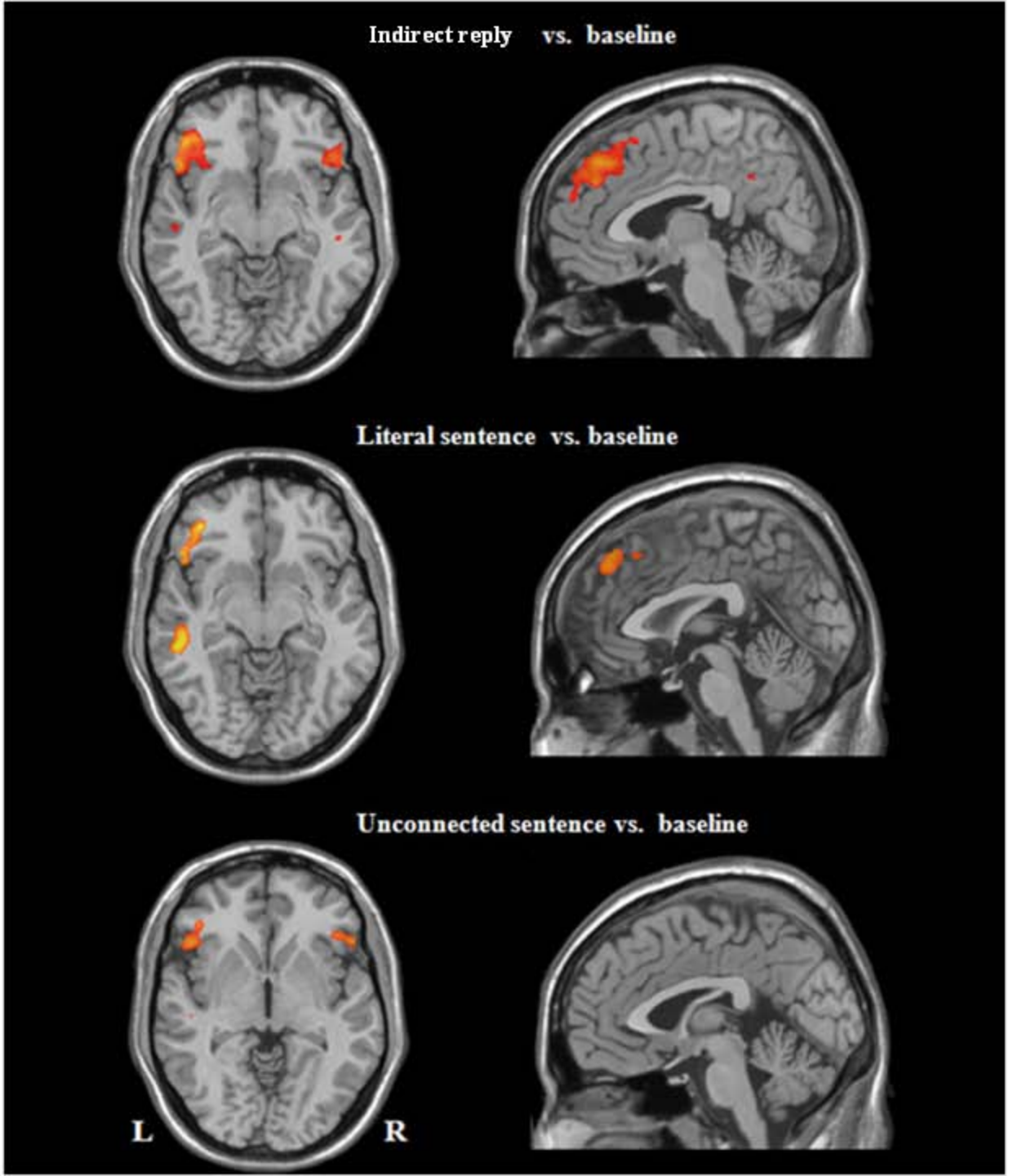
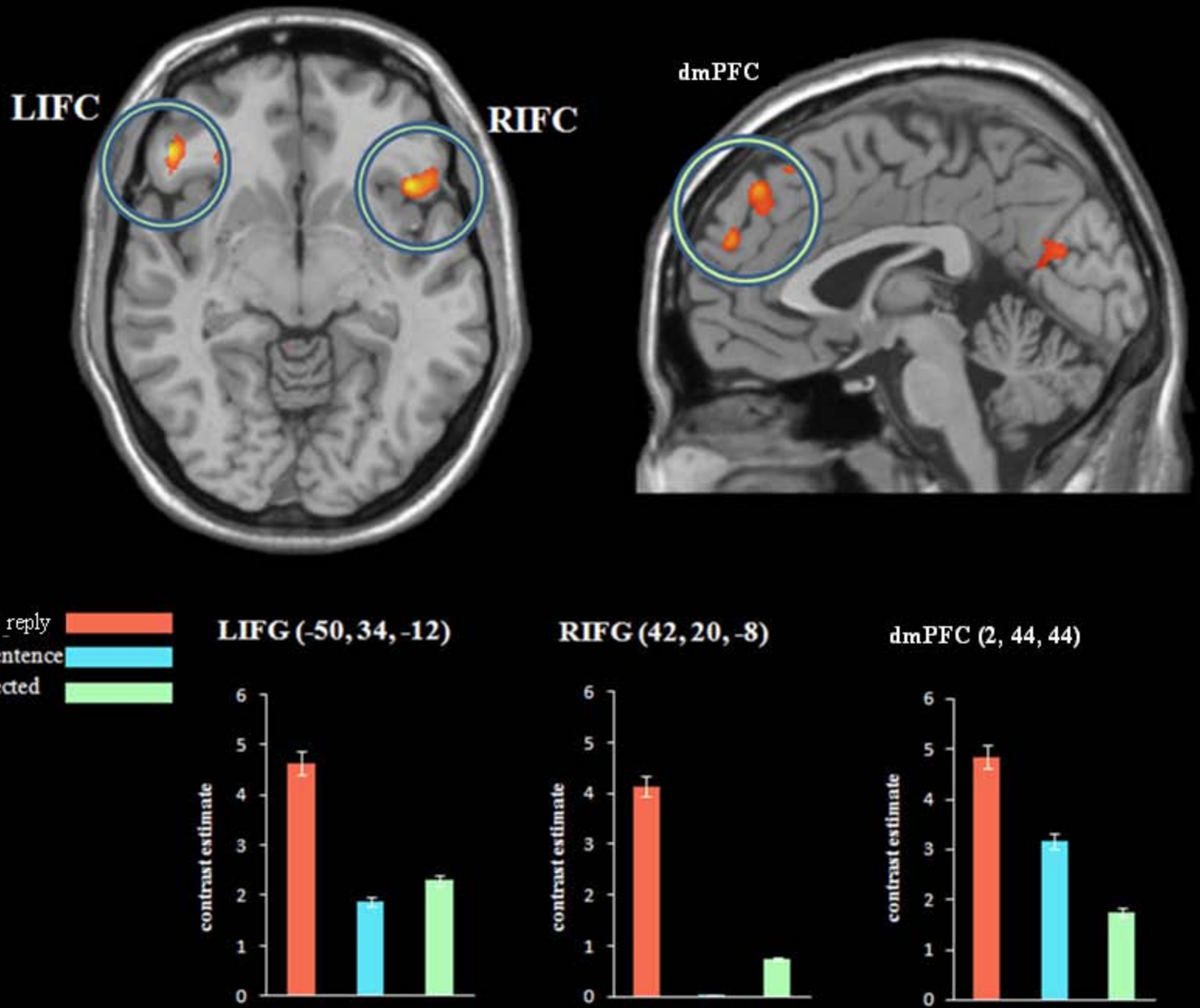
Figure legends

Figure 1. Summary of imaging results. Top row: The main effect of indirect reply versus baseline condition. Middle row: The main effect of literal sentence versus baseline condition. Bottom row: The main effect of unconnected sentence versus baseline condition. A random-effects analysis was performed ($p < .001$, uncorrected).

Figure 2. The panel shows the activation of the contrast in the indirect reply condition versus the literal sentence condition. Parameter estimate graphs of indirect reply (pink), literal sentence (blue), and unconnected sentence (green) conditions are presented as the mean of 15 participants. Error bars indicate the standard error of the mean.


Indirect reply vs. baseline
Literal sentence vs. baseline
Unconnected sentence vs. baseline
L
R


LIFC
RIFC
dmPFC
Indirect reply
Literal sentence
Unconnected
LIFG (-50, 34, -12)
RIFG (42, 20, -8)
dmPFC (2, 44, 44)
contrast estimate
0
1
2
3
4
5
6

Tables

Table 1 Example scenario

Sentence condition	Scenario
	Taro has given a 10 minutes presentation in his class. Taro asked his friend Jiro, "What did you think of my presentation?"
Indirect reply	Target: "It's hard to give a good presentation."
	Yoko is taking a painting class and has finished her painting. Yoko asked her friend Ai, "What do you think of my oil painting?"
Literal sentence	Target: "Your painting is very good."
	Ichiro is attending English conversation classes. Ichiro asked his friend Kazuo, "What did you think of my English pronunciation?
Unconnected	Target: "Your marriage partner is not good."

Table 2

Brain regions showing significant BOLD signal increases during each sentence conditions.

Region of activation	Left/Right	Brodmann area	Cluster size	Voxel t-value	Z value	MNI cordinates		
						X	Y	Z
Indirect reply condition								
Middle Frontal	L	6/9	1176	5.20	5.20	-50	18	38
Medial Frontal	L	6/8	24	4.10	4.10	-14	2	64
Medial Frontal	L	8	649	4.07	4.07	-4	38	44
Medial Frontal		9		5.73	4.05	0	42	34
Medial Frontal	L	10	61	4.04	4.04	-10	56	22
Inferior Frontal	L	47		6.21	4.24	-46	36	-8
Inferior Frontal	R	47	289	5.20	5.20	50	24	-4
Precentral	L	44		7.44	4.66	-56	16	10
Middle Temporal	R	21	52	5.12	3.78	50	8	-28
Precuneus	L	31	30	5.42	3.92	-8	-52	34
Caudate	L		44	5.18	3.81	-8	16	8
Anterior Cingulate	L	32	16	4.68	3.57	-8	40	12
Cuneus	L	23	14	4.47	3.46	-8	-74	8
Literal sentence condition								
Superior Frontal	L	8		4.22	3.33	-6	30	52
Middle Frontal	L	11		6.31	4.27	-38	40	-12
Medial Frontal	L	6/8	196	5.06	3.76	-4	44	40
Inferior Frontal	L	45	634	7.62	4.72	-52	22	20
Inferior Frontal	L			6.45	4.33	-56	20	2
Middle Temporal	L	21	199	6.88	4.48	-54	-36	-8
Middle Temporal	L	21		4.34	3.40	-66	-40	-8
Caudate	L	44	14	4.83	3.65	-10	18	10
Declive	R		28	4.99	3.72	12	-78	-20
Unconnected sentence condition								
Inferior Frontal	R	47	87	8.37	4.93	54	24	0
Inferior Frontal	L	47	434	6.14	4.21	-46	22	-14
Inferior Frontal	L	45		5.23	3.83	-52	16	4
Middle Frontal	L	8	36	5.19	3.81	-48	20	42
Middle Frontal	L	11		4.78	3.62	-36	38	-12
Middle Temporal	L	21	10	4.13	3.28	-52	-24	-10

This table presents the results of the 2nd level random effects group analysis. The Voxel T-values represent the value for local maxima at $p < .001$ (uncorrected, $t > 3.79$). The cluster size refers to the total number of voxels included in the cluster (minimum of 10 voxels).

Table 3

Brain regions showing significant BOLD signal increases relating to response times.

Region of activation	Left/Right	Brodmann area	Cluster size	Voxel t-value	Z value	MNI cordinates		
						X	Y	Z
Indirect reply condition								
Precuneus	L	7	22	6.26	4.26	-24	-60	46
Caudate	R		47	5.10	3.71	22	-16	24
Middle Frontal	R	46	12	4.50	3.43	46	26	20
Literal sentence condition								
Precuneus	L	7	12	8.25	4.80	-18	-64	44
Caudate	R		33	5.88	4.04	20	-8	26
Middle Frontal	R	46	14	5.20	3.76	46	28	20
Unconnected sentence condition								
Precuneus	L	7	14	5.98	4.08	-18	-64	44
Caudate	R		43	6.16	4.14	22	-12	24

The z values in the parametoric analyses with the reaction times are shown ($p < .001$, uncorrected)

Table 4

Brain regions showing significant BOLD signal increases during Indirect reply versus Literal sentence.

Region of activation	Left/Right	Brodmann area	Cluster size	Voxel t-value	Z value	MNI cordinates		
						X	Y	Z
Indirect reply vs. Literal sentence								
Medial Frontal	R	8	26	5.12	3.78	2	44	44
Medial Frontal		9		3.95	3.19	0	40	36
Medial Frontal	R	9	20	4.74	3.60	4	54	26
Middle Frontal	L	9	16	5.11	3.78	-40	12	36
Inferior Frontal	L	47	121	8.04	4.84	-50	34	-12
Inferior Frontal	R	47	74	6.26	4.25	42	20	-8
Inferior Frontal	R	9	12	4.10	3.27	54	18	26
Precuneus	L	31	78	4.77	3.62	-2	-72	22
Precuneus	L	23		4.05	3.35	-2	-62	16
Middle Temporal	R	21	16	5.22	3.83	50	8	-30

This table presents the results of the 2nd level random effects group analysis. The Voxel T-values represent the value for local maxima at $p < .001$ (uncorrected). The cluster size refers to the total number of voxels included in the cluster (minimum of 10 voxels).