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People with High Empathy Show Increased Cortical Activity around the Left Medial Parieto-Occipital Sulcus after Watching Social Interaction of On-Screen Characters

（共感性の高い人は画面上のキャラクターの社会的交流場面を観た後に左内側頭頂後頭溝周辺の皮質活動の増強を示す）

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People with High Empathy Show Increased Cortical Activity around the Left Medial Parieto-Occipital Sulcus after Watching Social Interaction of On-Screen Characters

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Abstract

People with high empathy interpret others' mental states in daily social interactions. To investigate their characteristics of social cognitive processing, we compared neuromagnetic activities between 20 males with high empathy and 23 males with low empathy while watching social interactions between two characters. Twenty stories of four-panel comic strips were presented; the first three panels described social interactions, and the last panel described empathic/non-empathic behaviors. People with high empathy exhibited increased cortical activity in the right occipital region, medial part of the bilateral superior frontal gyri, and right posterior insula while watching social interaction scenes, which suggests that they paid attention to others' faces and bodies, and inferred others' mental states. They also exhibited increased cortical activity in the left superior frontal gyrus while watching empathic behaviors. Moreover, they exhibited increased cortical activity in the region around the left medial parieto-occipital sulcus, which is related to self-projection, while passively watching both empathic and non-empathic endings. Taken together, these results suggest that people with high empathy pay attention to others and actively infer others' mental states while watching social interactions, and that they reconstruct others' mental states and intentions through self-projection after watching a sequence of others' behaviors.

Key words: comic strips, empathic ability, magnetoencephalography, self-projection

Introduction

Empathy is important for us to form appropriate interpersonal relationships with others. Elements that comprise empathy are affective and cognitive empathy (Davis 1980; Davis 1983; Baron-Cohen and Wheelwright 2004; Jolliffe and Farrington 2006; Reniers et al. 2011). Affective empathy involves reacting emotionally to the emotions of others, and cognitive empathy involves understanding another person's perspective, thoughts, and intentions (Davis 1980; Davis 1983; Baron-Cohen and Wheelwright 2004).

The ability to empathize differs between individuals, and several self-administered questionnaires, such as Interpersonal Reactivity Index (IRI) (Davis 1980) and the empathy quotient (EQ) (Baron-Cohen et al. 2003), can be used to evaluate these individual differences (for review, see Neumann et al. 2015). Large-scale studies using these questionnaires on healthy individuals have shown that their empathic ability ranges from high to low (Baron-Cohen and Wheelwright 2004; Kim and Lee 2010; Baron-Cohen et al. 2014; Braun et al. 2015). Previous studies have suggested the following behavioral and cognitive characteristics among people with high empathy: i) paying more attention to others (in particular to the others' eyes) (Cowan et al. 2014; Chakrabarti et al. 2017; Hedger et al. 2018) and being good at inferring others' mental state from their eyes (Focquaert et al. 2010), ii) mimicking others' facial expressions (Sonnby-Borgström 2002; Sonnby-Borgström et al. 2003; Rymarczyk et al. 2016), iii) showing activation of the "empathy for pain" system in response to others' physical/social pain (Singer et al. 2004; Saarela et al. 2007; Masten et al. 2011), and iv) preferring a behavior that makes others feel comfortable (Mehrabian 1997; Loudin et al. 2003; Johnson et al. 2014; Lockwood et al. 2014) and considering other peoples' happy faces as a reward (Chakrabarti et al. 2006; Gossen et al. 2014).

People with high empathy make it a priority to interpret the mental state of others; hence, they pay attention to others. To adequately interpret the mental state (in particular, intentions) of others in daily social interaction, one should observe the whole sequence of their behavior, facial expressions, and direction of gaze. Previous studies have investigated brain activity in people when watching others' behavior in daily social interactions using four-panel comic strips; Völlm et al. (2006), Sebastian et al. (2012), and Wang et al. (2015) reported increased activity in the temporal-parietal junction (TPJ), while Brunet et al. (2000), Völlm et al. (2006), Lee et al. (2010), and Wang et al. (2015) reported increased activity in the middle temporal gyrus. These two regions are considered the core components of the mentalizing network (Mar 2011) and suggested to be involved in inferring others' intentions. Therefore, we assumed that people with high empathy would show greater activation in the TPJ and middle temporal gyrus than those with low empathy when watching social interaction. In addition, because people with high empathy are more likely to empathize with others' pain than those with low empathy (Singer et al. 2004; Saarela et al. 2007; Masten et al. 2011), people with high empathy tend to pay greater attention to those who are physically or mentally stressed while watching others' social interactions. Thus, they may demonstrate increased activity in the anterior insula and anterior cingulate gyrus.

Empathic or non-empathic behavior is often observed in social interactions. When the others observe such behavior, instead of simply inferring the intentions, additional processing to comprehend the empathic/non-empathic behavior may happen. Völlm et al. (2006) demonstrated that the medial prefrontal cortex, amygdala, and anterior and posterior cingulate gyrus are activated more strongly during the empathic conditions (inferring the main character's emotional states and selecting the other character's empathic behavior making the main character feel better) than the theory of mind (ToM) conditions (inferring the main character's intention and selecting an appropriate ending as the final behavior of the character). However, Wang et al. (2015) observed no such brain activity in a similar comparative study. Sebastian et al. (2012) also showed higher brain activity in the temporal pole, precuneus, and posterior cingulate gyrus in empathic conditions than in the ToM conditions. The overlapping region was the posterior cingulate gyrus, which showed increased activity under the empathic conditions, between the abovementioned studies. The medial parietal region, including the posterior cingulate gyrus, may support the imagination processes required to infer others' mental state (Mar 2011) and empathize (Bzdok et al. 2012). Thus, we thought that people with high empathy may have higher brain activity in the posterior cingulate gyrus when they watch the empathic/non-empathic behavior than people with low empathy.

To investigate the characteristics of social cognitive processing among people with high empathy, we performed an exploratory study to compare the brain activity between people with high empathy and those with low empathy when watching social interaction scenes. We created 20 stories of four-panel comic strips describing social interaction scenes between two characters (characters A and B). In the first three panels of comic strips, direct or indirect interactions between the two characters were displayed. Character B experienced mental stress (in nine stories) and physical stress (in eight stories), presented his/her needs (in two stories), and displayed a physical disadvantage (in one story). Each story had three endings (displayed in the last panel): 1) character A was empathic to character B (empathic ending), 2) character A was non-empathic (non-empathic ending), and 3) the story had an unpredictable ending. The Japanese version of the EQ (Wakabayashi et al. 2006) was used to extract the subset of people demonstrating high and low empathy. Neuromagnetic activities of these people were measured using magnetoencephalography (MEG) when four-panel comic strips were presented. We proposed the following two hypotheses: 1) people with high empathy would show a greater activity in the TPJ, middle temporal gyrus, anterior insula, and/or anterior cingulate gyrus than those with low empathy while watching social interaction scenes (in the first three panels of the four-panel comic strips) and 2) people with high empathy would show a greater activity in the posterior cingulate gyrus than those with low empathy while watching others' empathic/non-empathic behaviors (in the last panel).

Material and Methods

Participants

To select approximately 20 males with high empathy and 20 with low empathy, 125 healthy males, aged ≥20 years (mean age: 21.9 ± 2.4 years, range: 20–37 years) and who spoke Japanese fluently, were recruited at Kyoto University, and their EQ was determined. The gender was limited to males, considering gender differences in empathic ability (Baron-Cohen and Wheelwright 2004; Kim and Lee 2010; Baron-Cohen et al. 2014; Braun et al. 2015). The enrolled participants had no previous history of mental illnesses or central nervous system diseases. Following the Japanese version of the EQ (Wakabayashi et al. 2006), we evaluated 100 items in total: 40 questions for EQ, 40 items for systemizing quotient (SQ; an evaluation scale that measures the ability to understand laws, including physical and social laws) (Baron-Cohen et al. 2003), and 20 items for filler. The EQ score ranged from 0 to 80; the higher the score is, the higher the empathic ability is. Questions were presented in a random order on a personal computer screen. The participants were asked to answer the questions one by one, and they had a choice to refuse any question that they did not want to answer. A total of 119 participants answered all the questions. The average EQ of 119 participants was 32.9 (standard deviation [SD]: 11.5, range: 11–62; Supplementary Figure 1 [SFig. 1]), which was slightly higher than that observed in Wakabayashi et al.'s study (2006) involving Japanese male university students (mean EQ: 30.6; SD: 9.92; n=616). We sent an email to 29 participants with an EQ score of ≥41 (high EQ) and 35 participants with an EQ score of ≤25 (low EQ) for MEG measurement, and 22 participants with high EQ and 23 participants with low EQ agreed to participate in the MEG measurement. To equalize the age of both groups (high and low EQ), two participants with high EQ, who were over 30 years, were excluded from the analysis. Finally, there were 20 participants in the high EQ group (age range: 20–24 years, mean age: 21.3 years, 19 right-handed, 1 both-handed, mean EQ score: 47.5) and 23 in the low EQ group (age range: 20–25 years, mean age: 21.3 years, 21 right-handed, 1 both-handed, 1 left-handed, mean EQ score; 20.5). Age and SQ scores were not significantly different between the two groups (Table 1). In all participants, MEG was measured approximately 1–7 months after the EQ measurement.

Ethics Statement

This study was approved by the Ethics Committee of Kyoto University Graduate School and the Faculty of Medicine and Kyoto University Hospital. All participants provided written informed consent.

Stimuli

We created 20 stories of four-panel comic strips describing social interaction scenes, in which character A showed empathic or non-empathic behavior toward character B (Fig. 1; Supplementary Table 1). In Panels 1 to 3, direct or indirect interactions between two characters were displayed, and character B experienced mental stress (in nine stories) and physical stress (in eight stories), presented his/her needs (in two stories), and displayed a physical disadvantage (in one story); character A noticed these states. Character A also experienced mental stress (in five stories) and physical stress (in two stories) and presented his/her needs (in ten stories); we portrayed character A's stress or needs to make the participants feel that character A's non-empathic behavior was understandable. Each story had three different endings (an empathic ending, a non-empathic ending, and an unpredictable ending), therefore, three different four-panel comic strips were created from one story, with the first three panels being common. In an empathic ending (Panel 4a), character A either helped or satisfied character B's needs. In a non-empathic ending (Panel 4b), character A gave priority to his/her plans. In both endings, character A's behavior seemed natural in the context and did not violate social norms. There is a possibility that the difference in brain activity between these two endings could reflect expectations rather than empathy-related elements; unlike the low EQ group, the high EQ group may have expected the empathic endings. To address this possibility, we created an unpredictable ending (Panel 4c), in which character A's behavior did not include empathetic/non-empathetic elements. We planned to check the distribution of the contrast for Panels 4a and 4c when the interaction between groups (high EQ/low EQ) and empathic/non-empathic endings (Panels 4a/4b) became significant.

Details regarding the 20 stories and characteristics of the characters are provided in Supplementary Table 1. Because we wanted the participants to watch various social interaction scenes, we varied the relationship between characters A and B (intimacy, combination of genders, and combination of generations) in each story. In 13 stories, the two characters who knew each other interacted directly in Panels 1–3 (an example is shown in Fig. 1A); note that in one story (story #4), one character appeared to the other character only in an "imagination balloon". In contrast, in seven stories, the two characters who did not know each other were in the same place, and they were able to notice each other (an example is shown in Fig. 1B); note that, among these seven stories, direct interaction occurred only in case of empathic endings. Five stories each were created for the following combinations of genders of characters A and B: male/male, male/female, female/male, and female/female. Character A was an adult in all stories, and character B was elderly in six, an adult in seven, and a child in seven stories. The height, hairstyle, and clothes of the characters clearly showed gender and age. The eyes, eyebrows, and mouth of the characters were not drawn to ensure that the participants only pay attention to the characters' behavior; however, the nose was drawn to show the orientation of the characters' faces. Sweat, tears, and sighs were drawn to express the emotions or mental state of the characters. In Panels 1 to 3, there were conversations or speaking to themselves, and the words were described in word balloons. In contrast, in Panel 4, there were no conversations or speaking to themselves, so as to prevent language-related processing. All images from Panels 1 to 4 were in grayscale, with a gray background and black text.

The procedure for creating comic strips was as follows: first, four authors (MH, JM, MF, and AM) created 22 storyboards, referring to the examples by Lee et al. (2010). A professional illustrator drew four-panel comic strips from 22 stories. Ten healthy participants (5 males, 5 females; average age 24.4 years) watched all four-panel comic strips. They rated whether the stories with empathic and non-empathic endings could be easily understood (comprehensibility rating) and the character A's behavior was empathic (empathic rating) on a scale of 1–5 ("very poor" – "good enough"). Because the range of the average score for comprehensibility was 4.6–5.0 for the empathic ending and 4.7–5.0 for the non-empathic ending, we assumed that all stories were easily understood. The range of average score was 3.9–5.0 for the empathic ending and 1.2–2.6 for the non-empathic ending. Therefore, the story in which the empathic ending had the minimum score (the least empathic ending in 22 stories) and the non-empathic ending had the maximum score (the least non-empathic ending in 22 stories) were excluded. Finally, we used 20 stories for MEG measurement; the range of average score for the empathic ending was 4.2–5.0 and that for the non-empathic ending was 1.2–2.4.

In addition, another group of 10 healthy participants (5 males, 5 females; average age 21.8 years) watched the unpredictable ending and answered whether the ending was unpredictable; based on the results, we modified the ending of one of the stories.

Task

For MEG measurement, the participant sat on a recording chair in a magnetically shielded room and watched the images (vertical: 5.6 °, horizontal: 8.0 °) projected by a liquid crystal projector on a screen at a distance of 1.8 m from the face. Each trial (period including presentation of one four-panel comic strip; an example is shown in Fig. 1C) started when the participant pressed a button. A fixation cross appeared for 1.0 seconds, and then each panel of comic strips appeared for 1.5 seconds. To ensure that the participants paid attention to the content of each panel, a two-choice question about the content of the comic strip (e.g., Who was putting the dishes away, a woman/a boy?) was displayed after Panel 4 in half of the trials (60 trials); the participants answered the question with a button press. After the completion of the trial, the participants took a short break and pressed the button when they wanted to proceed to the next trial. There were 20 stories, and each story had three endings (Panels 4a–4c), amounting to 60 four-panel comic strips. These 60 comic strips were presented twice for each participant; therefore, 120 trials (i.e., 120 presentations of comic strips) were conducted (Panels 1–3 were presented 120 times each, and Panels 4a, 4b, and 4c were presented 40 times each). Within the 120 trials, the comic strips were randomly presented; the trials were divided into eight sessions (approximately 3–4 min per session), and the participant took a break between sessions. We confirmed that the participants refreshed themselves at each break and then proceeded to the next session.

The participants were asked to 1) avoid blinking as far as possible when the image appeared on the screen, 2) answer questions as correctly as possible, 3) to blink if required when no image appeared on the screen, and 4) keep the head position as stable as possible during the recording. We did not ask the participants to empathize with the characters or pay attention to specific characters when they watched the stories. Moreover, we did not require the participants to judge whether character A's behavior in Panel 4 was appropriate. Of note, most of the previous studies required participants to infer the mental state of the on-screen characters, which was not required in our study; the participants only had to understand the story to answer the questions.

Before performing the actual MEG measurement, the participants were asked to sit on a recording chair and asked whether they could properly see the images on the screen. Non-magnetic glasses were used if necessary. The participants practiced the task with two mock comic strips, and the actual measurements were taken after they adequately understood the task.

Control of the visual stimuli and measurement of button-press responses were performed using the presentation software (Presentation; Neurobehavioral Systems, CA). There was a delay of 0.0333 seconds between triggering the presentation software and appearance of the actual image on the screen. We considered this delay in the MEG analysis.

MEG measurement

We recorded MEG signals using a 306-channel whole-head neuromagnetometer (Vectorview; Elekta Neuromag, Finland), which has 204 planar gradiometers and 102 magnetometers. Because the hardware was upgraded in the middle of the study period, the measurement settings were different for the first half (10 participants in the high EQ group, 12 participants in the low EQ group) and the second half of the participants (10 participants in the high EQ group, 11 participants in the low EQ group). The recording passband was 0.1–200 Hz for the first half and 0.1–400 Hz for the second half of the participants. The sampling rate was 603 Hz for the first half and 1206 Hz for the second half of the participants. The locations of fiducial points (left and right pre-auricular points and nasion) and head-position-indicator coils attached to the scalp were recorded using a 3D digitizer prior to the MEG recording. The shape of the head was digitized. The head position relative to the MEG sensor array was measured at the beginning of each session, and the height of the chair was adjusted, when necessary, so that the maximum vertical displacement of the head position among sessions was maintained at less than 1 cm. Vertical and horizontal eye movements and blinking were recorded using an electrooculogram.

MRI acquisition

T1-weighted magnetic resonance (MR) images of the participants' heads were acquired to obtain anatomical information with the 0.2-T Signa Profile System (General Electric Medical System, WI).

Impression rating of stimuli by MEG participants

After the MEG recording was completed, the participants performed the impression rating of the four-panel comic strips in another room. They rated the comprehensibility and empathy on a scale from 1 to 5 ("very poor" – "good enough") for both the empathic and non-empathic endings (impression ratings of unpredictable endings were not performed to keep the experiment time as short as possible). The total number of comic strips that were rated was 40 (20 each for empathic and non-empathic endings).

Analysis of behavioral data

The correct answer rate and mean reaction time for the questions during the MEG measurement were calculated for each participant. For 20 stories, the comprehensibility and empathy for the empathic and non-empathic endings were rated separately (acquired after MEG measurement) for each participant. The correct answer rate, reaction time, comprehensibility, and empathic rating were compared using the Mann-Whitney U test to examine whether there was a difference between the high and low EQ groups. The significance level was set at $P < 0.05$. SPSS statistics Ver. 25 was used for the statistical analysis.

MEG analysis

Step 1. Preprocessing

Step 1-1. External noise reduction and head movement compensation using Maxfilter. Signal space separation with temporal extension (Taulu and Simola 2006) was applied using Maxfilter (Elekta Neuromag) to reduce external noise from the raw MEG signal and to compensate for the displacement of the head position among sessions.

Step 1-2. Cleaning signals and extracting epochs using the MNE. The MEG signal after applying Maxfilter (calculated in Step 1-1) was analyzed using the MEG/EEG analysis software MNE (https://www.martinos.org/mne/stable/index.html) (Gramfort et al. 2014). First, artifacts derived from vertical and horizontal eye movements were reduced using independent component analysis. Then, a bandpass filter of 0.5–30 Hz was applied. To extract the brain magnetic responses evoked by the comic strip presentation, the continuous signal was epoched from −0.2 seconds to 1.5 seconds after the on-screen presentation of each panel. The baseline period was set from −0.2 to 0 seconds. The epoched signals were resampled at 500 Hz to match the sampling rates of the first and second half of the participants.

Step 1-3. Signal averaging. Averaging was performed for each panel after rejecting epochs with artifacts, such as blinking or excessive muscle activity. The average numbers were 82–120 for Panels 1–3 (each panel was presented 120 times) and 22–40 for Panels 4a, 4b, and 4c (each panel was presented 40 times). These averaged magnetic responses were used for the current source estimation.

Step 1-4. Calculation of root-mean-square signals. The root-mean-square (RMS) signals of regional planar gradiometer sensors were created from the averaged magnetic responses (calculated in Step 1-3) to show the time course of the responses in each head region (frontal, temporal, parietal, or occipital region), reflecting strong neural activities in that region. These RMS signals were used for display purposes and not used for the current source estimation.

Step 1-5. Calculation of the noise covariance. The noise covariance between sensors was calculated for each participant using the signals during the baseline periods in all epochs (calculated in Step 1-2). This was used for the current source estimation.

Step 2. Source modeling

Statistical Parametric Mapping 12 (SPM12; http://www.fil.ion.ucl.ac.uk/spm/) was used to deform the template surface, and Brainstorm (http://neuroimage.usc.edu/brainstorm/) was used for the current source estimation (Tadel et al. 2011).

Step 2-1. Creating a cortical sheet that fitted well into the cortical gray matter of the participant. This step was based on the idea of "canonical source reconstruction" proposed by Mattout et al. (2007). Brainstorm provided a template surface with 15002 vertices representing the mid-point between the white matter and cortex envelopes of the ICBM152 template brain (ICBM152_2016c) with anatomical labels by Desikan et al. (2006). It was deformed to fit the participant's cortical gray matter using the following procedure. First, the participant's MR images were imported with SPM12, and the anterior commissure position was determined. The normalization field was calculated using SPM12 according to the standard normalization procedure. Then, the template surface was deformed to fit the participant's cortical gray matter through inverse normalization. This "personalized" cortical surface (i.e. the inverse-normalized template surface) was superimposed on the MR images of each participant and was visually inspected to confirm the fitting. The shape of the personalized cortical surface appeared similar to that of the actual cortical gray matter, but the size of the surface was slightly larger. To improve the fitting, the personalized cortical surface was made smaller by an average of 3%. The inner skull surface, which was considered the head layer of the ICBM152 template brain, was also deformed through the same inverse normalization.

Step 2-2. Importing MR images and personalized surfaces with Brainstorm. The MR images and personalized cortical surfaces of each participant were imported using Brainstorm. The locations of the fiducial points (left and right pre-auricular points and nasion) were defined on the participant's MR images. We ensured that the personalized cortical surface fitted the participant's MR images in the Brainstorm participant coordinate system.

Step 2-3. Calculation of forwarding model. The averaged magnetic responses for each panel (calculated in Step 1-3) were imported using Brainstorm. The overlapping sphere model (Huang et al. 1999) was used as the conductor model of the participant's brain. A dipole was placed at each vertex of the personalized cortical surface, resulting in 7501 dipoles in the right and left hemispheres, respectively (15002 dipoles in total). Each dipole was oriented normal to the local cortical surface. The forward model was calculated based on the abovementioned assumptions.

Step 2-4. Current source estimation. Standardized low-resolution brain electromagnetic tomography (sLORETA) (Pascual-Marqui 2002) was used for current source estimation. The noise covariance between sensors (calculated in Step 1-5) was included in the estimation (Engemann et al. 2015). The sLORETA value was calculated for each dipole on the personalized cortical surface; because the estimated current density was normalized at each dipole, the sLORETA value had an arbitrary unit. The estimated current had a direction, which was indicated by a positive (toward the cortical surface) or negative (toward the white matter) sLORETA value. The sLORETA values were calculated for 15002 vertices (dipoles) at each sampling point (851 sampling points) in each condition (Panels 1 to 3, 4a, 4b, and 4c) per participant.

Step 2-5. Export the results of the current source estimation. The results of the current source estimation were exported to Gifti files for processing using SPM12. These Gifti files contained the sLORETA values and coordinates of 15002 vertices (dipoles). The time of interest was 0–1300 ms. The time range was divided into 25 bins: every 20 ms in 0–200 ms (10 bins), every 50 ms in 200–600 ms (8 bins), and every 100 ms in 600–1300 ms (7 bins). The sLORETA values with signs at each vertex (dipole) in a certain time bin were averaged. Because the current sources were estimated from a participant-specific cortical surface, the coordinates of each vertex (dipole) were different among participants. However, when exporting the coordinates of each vertex (dipole), the participant-specific coordinates were replaced by the MNI coordinates of the original template surface (ICBM152 template brain). Therefore, the coordinate values in the Gifti files for all participants were identical. Finally, we obtained sLORETA values (with signs) for six conditions and 25-time bins (150 Gifti files in total) per participant.

Step 2-6. Calculation of "grand-mean" source waveforms in the high and low EQ groups. To show precise temporal characteristics of source activities between −200 ms and 1300 ms in the high and low EQ groups, the sLORETA values for each panel (calculated in Step 2-4) were averaged within the high EQ (n=20) and low EQ (n=23) groups. These waveforms were used only for display purposes and not for statistical analysis.

Step 3. Statistical analysis with SPM12

The Gifti files (created in Step 2–5) containing sLORETA values with signs were imported using SPM12 and analyzed using a general linear model for each time bin. Note that the signed sLORETA values were used for statistical analysis.

Step 3-1. Comparison between the high and low EQ groups of each panel. To evaluate the differences between the high and low EQ groups for each panel, groups (a between-participant factor: 2 levels; high EQ and low EQ groups) and panels (a within-participant factor: 6 levels; Panels 1–3, 4a, 4b, and 4c) were included in the model. The measurements were assumed to be independent of the groups but dependent on the panels. The variance was assumed to be unequal between both the groups and panels. The group differences for each panel were calculated as F values; in addition, the corresponding p-values were calculated.

Step 3-2. Interaction between groups and empathic/non-empathic endings. To evaluate the interaction between groups and empathic/non-empathic endings (Panels 4a and 4b), we included the following factors in the model: participants, groups, panels, and the interaction (groups * panels). The measurements were assumed to be independent of participants and groups but dependent on the panels. The variance was assumed to be equal among the participants and unequal among groups and panels. The interaction between groups and empathic/non-empathic endings were calculated as F values, and the corresponding p-values were calculated.

Step 3-3. Condition differences between empathic and non-empathic endings. The factors included in the model were the same as in Step 3-2. The F values of the condition difference between empathic and non-empathic endings; in addition, the corresponding p-values were calculated.

Step 3-4. Adjusting the alpha level. Testing all 15002 vertices (dipoles) creates a serious multiple comparison problem; therefore, the alpha level of each test should be adjusted to keep the family-wise error rate (FWER) <0.05. Barnes et al. (2011) proposed a method to estimate the number of separable (independent) sources in the brain using MEG measurements. According to them, the alpha level can be divided by the number of separable sources to keep the FWER below the nominal level. We estimated the number of separable sources for each participant according to Barnes et al.'s (2011) method (average: 2306; range: 2121–2388); accordingly, the alpha level for each vertex (dipole) was set at 0.05 / 2306=0.0000217. The p-values calculated at Step 3-1, 3-2, and 3-3 were considered statistically significant if they were <0.0000217.

Results

Behavioral data

Response to questions during MEG measurement. No significant differences were found between the high and low EQ groups in the correct answer rate and reaction time for the questions during the MEG measurement (Table 1).

Impression rating of comic strips after completing MEG measurements. The MEG participants performed impression ratings of comic strips with empathic and non-empathic endings (Panels 4a and 4b) after MEG measurements. No significant group differences were observed in comprehensibility ratings (Table 1 and SFig. 2). In contrast, significant group differences were found in empathic ratings (Table 1; the mean score of each participant is shown in SFig. 2). The mean score for the empathic ending was significantly higher in the high EQ group than in the low EQ group (4.85 *vs*. 4.65; p=0.003), whereas the mean score for the non-empathic ending was significantly lower in the high EQ group than in the low EQ group (1.56 *vs.* 1.85; p <0.001).

MEG signals and source activities

Magnetic field activity at the sensor level. The upper parts of Figs. 2 and 3 show the regional RMS signals, which display the time course of the magnetic field activity in each head region (RMS signals of all regions and panels are shown in SFigs. 3 and 4). Distinct activities were identified in the occipital region at 80–100 ms (Fig. 2), occipital and temporal regions at 120–140 ms (Fig. 2), and temporal and parietal regions at 200–250 ms and 350–400 ms (Fig. 3) after the onset of the panel presentation. The distribution of these activities was almost bilaterally symmetrical.

Current source activities. The lower parts of Figs. 2 and 3 represent current source activities of the time bins when the distinct activities were identified at the sensor level (Fig. 2A: 80–100 ms, Fig. 2B: 120–140 ms, Fig. 3A: 200–250 ms, and Fig. 3B: 350–400 ms); the source activities of Panels 3 and 4c have been omitted because of space limitations. The source activities were localized in the bilateral medial occipital lobes at 80–100 ms (Fig. 2A) and in the bilateral lateral occipital cortices around the preoccipital notch at 120–140 ms (Fig. 2B). The source activities were broadly distributed in the bilateral parietal lobes and the left lateral temporal lobe at 200–250 ms (Fig. 3A) and in the bilateral temporal, parietal, and occipital lobes at 350–400 ms (Fig. 3B). The high EQ group generally showed larger current source activities than the low EQ group.

Brain regions showing significant group differences

Group differences in Panels 1–3. The upper part of Fig. 4 shows the brain regions that displayed significant group differences in Panel 1 or 2; Table 2 shows a summary of the regions. No significant differences were found in Panel 3. The lower part of Fig. 4 shows the sLORETA values (signed values: the sign represents the current direction) and intensities (absolute values) at the representative dipoles. In Panel 1, the source waveforms (i.e., temporal changes in the sLORETA values) around the right occipital areas at approximately 100–200 ms after the onset of the panel presentation were different between the high and low EQ groups, with the high EQ group generally exhibiting a higher intensity; significant group differences were found in the right lateral occipital cortex (100–120 ms: dipole #1, 100–140 ms: dipole #2, 180–200 ms: dipole #3) and right fusiform gyrus (180–200 ms: dipole #4). In Panel 2, the high EQ group demonstrated higher intensity in the bilateral superior frontal gyri (medial part: dipoles #5 and #6) 500 ms after the onset of the panel presentation than the low EQ group, and a significant group difference was found at 900–1000 ms. In addition, significantly higher intensity was observed in the right insula (in the posterior part: dipole #7) at 1100–1300 ms in the high EQ group than in the low EQ group.

Fig. 5, showing the F values of all panels at the representative dipoles, displays significant group differences in Panels 1 and 2 (the dipole indices in Fig. 5 are the same as in Fig. 4). The F values for the right lateral occipital cortex (dipoles #1, #2, and #3) and right fusiform gyrus (dipole #4) reached the statistical threshold only in Panel 1, and those for the right and left superior frontal gyrus (dipoles #5 and #6) and right insula (dipole #7) reached the statistical threshold only in Panel 2.

Group differences in the empathic and/or non-empathic endings. The upper part of Fig. 6 shows the brain regions that displayed significant group differences for the empathic (Panel 4a) and/or non-empathic endings (Panel 4b). Table 2 summarizes these regions. In Panel 4a, significantly higher intensity was observed in the left superior frontal gyrus (dipole #1) at 200–250 ms in the high EQ group than in the low EQ group. In addition, the high EQ group showed higher intensity than the low EQ group around the medial part of the left parieto-occipital sulcus (the precuneus, cuneus, lingual gyrus, and isthmus-cingulate cortex) after approximately 200 ms from the onset of the panel presentation; significant group differences were found after 450 ms at the left precuneus (dipole 2: 450–500 ms), left lingual gyrus (450–600 ms: dipole #3, 800–900 ms: dipole #5), and left isthmus-cingulate cortex (500–700 ms: dipole #4). In Panel 4b, the high EQ group also showed higher intensity than the low EQ group around the medial part of the left parieto-occipital sulcus after approximately 200 ms from the onset of the panel presentation; significant group differences were found after 450 ms at the left precuneus (450–500 ms: dipole #6, 550–600 ms: dipole #8), left cuneus (550–600 ms: dipole #7), and left isthmus-cingulate cortex (550–700 ms: dipole #4). In the high EQ group, the source waveforms for Panels 4a and 4b had a prolonged component around the medial part of the left parieto-occipital sulcus, starting at approximately 200–300 ms and becoming salient after 400 ms. In contrast, no such components were found in Panels 1–3 of the high EQ group or any of the panels of the low EQ group.

Fig. 7, showing the F values of all panels at the representative dipoles, displays significant group differences in Panels 4a and/or 4b (the dipole indices of Fig. 7 are the same as Fig. 6). The F values for the left superior frontal gyrus (dipole #1) and left lingual gyrus (dipoles #3 and #5) reached the statistical threshold only in Panel 4a. The F values for the left precuneus (dipoles #2, #6, and #8) and left cuneus (dipole #7) reached the statistical threshold in either Panel 4a or 4b; the other F values, which did not reach the statistical threshold, were close to the threshold. The F values for the left isthmus-cingulate cortex (dipole #4) reached the statistical threshold in both Panels 4a and 4b.

Group differences for an unpredictable ending. Table 2 shows a summary of the brain regions that displayed significant group differences for the unpredictable ending (Panel 4c). SFig. 5 illustrates the regions and F values for all panels at the representative dipoles. In Panel 4c, significant group differences were found at relatively long latencies in the left lateral occipital cortex (500–550 ms), left isthmus-cingulate cortex (800–900 ms), left fusiform gyrus (900–1000 ms), left lingual gyrus (900–1000 ms), and left rostral middle frontal gyrus (1000–1100 ms).

Interaction between groups and empathic/non-empathic endings

No significant interaction between groups (high EQ/low EQ) and empathic/non-empathic endings (Panels 4a/4b) was found in any time bins.

Condition differences between empathic and non-empathic endings

Table 3 shows the brain regions that displayed significant condition differences between empathic (Panel 4a) and non-empathic endings (Panel 4b); the significant dipoles were concentrated at the left lateral temporal areas (particularly around the left middle temporal gyrus) at 350–550 ms (SFig. 6). SFig. 7 shows the F values for all condition contrasts at the representative dipoles displaying significant condition differences between Panels 4a and 4b (the dipole indices shown in SFig. 7 are the same as in SFig. 6).

Discussion

The present study compared neuromagnetic activities between the high and low EQ groups when watching social interaction scenes, including empathic/non-empathic endings. The main findings were as follows: 1) both the high and low EQ groups regarded the empathic behaviors in those stories as empathic and the non-empathetic behaviors as non-empathic, but the high EQ group felt a stronger impression than the low EQ group, 2) when the social interaction scenes were presented, the high EQ group showed a significantly stronger cortical activity than the low EQ group at the right occipital region before 200 ms and at the medial part of the bilateral superior frontal gyri and right posterior insula after 900 ms, 3) in comparison to the low EQ group, the high EQ group showed significantly stronger cortical activity for empathic endings at the left superior frontal gyrus at 200–250 ms and for both the empathic or non-empathic endings around the medial part of the left parieto-occipital sulcus after 450 ms, 4) no significant interaction was observed between the high and low EQ groups and empathic/non-empathic endings, and 5) significant condition differences were observed between empathic and non-empathic endings in the left lateral temporal areas (in particular around the left middle temporal gyrus) at 350–550 ms.

Behavioral data in the high and low EQ groups

The high EQ (score of ≥41) and low EQ (score of ≤25) groups comprised healthy males aged 20–25 years who were undergraduate or graduate students at Kyoto University. Both groups correctly answered >95% of the questions after comic strip presentation during MEG measurement. In empathic ratings, both groups regarded the empathic behaviors in those stories as empathic and the non-empathic behaviors as non-empathic, but the high EQ group felt a stronger impression than the low EQ group. Even though there were no differences in background factors (age, gender, and education) between the high and low EQ groups, the high EQ group sharply distinguished empathic behavior from non-empathic behaviors, thereby reflecting their empathic abilities, which were measurable using the EQ. This finding is consistent with the finding that people with high cognitive empathy are more likely to evaluate as bad behavior against other people's antisocial behavior (Yoder and Decety 2014).

Group differences in Panels 1–3

Our primary objective was to compare brain activity between the high and low EQ groups when watching social interaction scenes. To achieve this objective, we presented 20 social interaction scenes between two characters in the form of four-panel comic strips.

In Panel 1, the high EQ group showed increased cortical activity in the right lateral occipital cortex and the right fusiform gyrus at around 100–200 ms. Because attention to visual stimuli can enhance P1 (100–130 ms) and N1 (170–190 ms) components of visual evoked potentials arising from the occipitotemporal region (Clark and Hillyard 1996; for review, see Hillyard and Anllo-Vento 1998), the high EQ group may have paid more attention to Panel 1 than the low EQ group. Although it is unknown what the high EQ group paid attention to in Panel 1, considering previously reported functions of the right occipital area, we assume that the high EQ group may have paid attention to the characters' faces and bodies. The activated region in the right lateral occipital cortex (showing a significant group difference at 180–200 ms) was located close to the cortical areas for face (Pitcher et al. 2011) and body (Downing et al. 2001) perception. Moreover, the activated region in the right fusiform gyrus corresponded to the area that gets activated for both face and face-like objects at 165 ms (Hadjikhani et al. 2009). Our findings suggest that people with high empathy pay more attention to people's faces and bodies when watching social interaction (this notion is supported by Chakrabarti et al. [2017] and Hedger et al. [2018]).

In Panel 2, the high EQ group showed increased cortical activity in the medial part of the bilateral superior frontal gyri at 900–1000 ms and the right posterior insula at 1100–1300 ms. The medial part of the superior frontal gyrus is involved in inferring others' mental states (Frith and Frith 2006). Moreover, the activated region in this study corresponded to the area that is specifically more activated when participants watch scenes in which the social interaction takes place (Walter et al. 2004; Völlm et al. 2006; Arioli and Canessa 2019) or may take place (e.g., a person preparing a romantic dinner) (Walter et al. 2004). Thus, people with high empathy may prioritize inferring the mental states of others in the context of social interaction. Although previous studies have found increased activities in the anterior insular cortex and anterior cingulate gyrus in people with high empathy when watching others' physical/social pain (Singer et al. 2004; Saarela et al. 2007; Masten et al. 2011), we found significant group differences in increased activities in the right posterior insula rather than in the anterior insula. The posterior insula is involved in the processing of directly experienced pain (Lamm et al. 2011). One possibility could be that the region involved when empathizing with others' stress might have extended to the posterior insula in people with high empathy.

The regions showing group differences in Panels 1 and 2 did not display group differences in the other panels. It is interesting that even though all panels displayed human character(s) and most of the panels displayed social interaction (direct or indirect) and characters' physical/mental stress, the high EQ group showed increased activity in the brain regions involved in face and body perception only in Panel 1 and those involved in watching or anticipating social interaction and pain processing only in Panel 2. Because Panel 1 was the first image describing the character(s), the high EQ group may have paid more attention to the character(s) in Panel 1. In Panel 2, the other character appeared in 17 out of 20 stories, and the physical/mental stress of character(s) were displayed in 13 out of 20 stories. Panel 2 may be central to the direct interaction or possibility of direct interaction between the two characters and depicting the physical/mental stress of the characters; thus, the inference of the mental state of both characters and pain-related processing may have occurred mainly during Panel 2 in the high EQ group.

Although previous studies have suggested that the TPJ and/or middle temporal gyrus are involved in inferring others' intentions (Brunet et al. 2000; Völlm et al. 2006; Wang et al. 2015; Lee et al. 2010; Sebastian et al. 2012) and that these regions show greater activity when people with high empathy infer others' mental state from their eyes (Focquaert et al. 2010), the present study did not find significant group differences between the high and low EQ groups in these regions. According to Arioli and Canessa's (2019) meta-analysis, the TPJ is more active while inferring an individuals' mental state than processing social interactions. The present study did not require the participants to infer the characters' mental states; therefore, they were asked to passively watch social interactions (this is different from the previous studies; see, Brunet et al. 2000; Völlm et al. 2006; Wang et al. 2015; Lee et al. 2010; Sebastian et al. 2012). It could be a reason why the present study did not show group difference in the TPJ. According to the same meta-analysis (Arioli and Canessa 2019), the posterior part of the middle temporal gyrus (including the posterior superior temporal sulcus) is more active in processing social interactions than in making inferences on an individual's mental state. The authors suggested that this region is involved in decoding visuomotor information of others' actions. The high EQ group may have processed such visuomotor information more actively than the low EQ group, but there was no sign of such differences in the present study. On the other hand, the present study found condition differences (between the empathic and non-empathic endings) in the middle part of the left middle temporal gyrus; differences in the stories with empathic and non-empathic endings may have affected the cortical activity in this region.

Group differences in the empathic and/or non-empathic endings

Our secondary objective was to compare the brain activity between the high and low EQ groups when they watch the empathic/non-empathic behavior of others. For this objective, we created four-panel comic strips with three types of endings: one character showed empathic behavior toward the other character (empathic ending: Panel 4a) and one character showed a non-empathic behavior toward the other character (non-empathic ending: Panel 4b) or an unpredictable ending (Panel 4c). Because we wanted to compare the brain activity while passively watching others' empathic/non-empathic behavior between the high and low EQ groups, the participants were not required to empathize with the characters or judge whether the characters' behavior in Panel 4 was appropriate or not.

In Panel 4a, the high EQ group showed increased cortical activity in the left superior frontal gyrus at 200–250 ms. The left superior frontal gyrus (dorsal premotor area) is involved in observing the hand action of others (Filimon et al. 2007). One character offered a helping hand to the other character in most stories with the empathic endings; the high EQ group may have paid attention to the hand action of the character. Alternatively, the high EQ group may have mentally simulated empathic behavior of the character because the dorsal premotor area is also shown to be involved in motor imagery (for review, see Hardwick et al. 2018).

In Panels 4a and 4b, the high EQ group showed increased cortical activity in the region around the medial part of the left parieto-occipital sulcus after 450 ms. The source waveforms of the high EQ group in Panels 4a and 4b in this region had a prolonged component that started at approximately 200–300 ms and became salient after 400 ms, but no such components were found in Panels 1–3 of the high EQ group or in any panels of the low EQ group. The prolonged components elicited by Panels 4a and 4b were similar in shape and distribution, even though Panels 4a and 4b had different stimuli and gave different impressions to the participants. In addition, neither significant condition differences between Panels 4a and 4b nor significant interaction between the groups (high EQ and low EQ) and endings (Panels 4a and 4b) were found in this region. Moreover, this prolonged component in the high EQ group is likely to reflect complex processing rather than the processing of single-panel visual information because cortical activities in Panels 1–3 in this region appeared to cease approximately by 500 ms. These findings suggest that this component is elicited only when participants in the high EQ group had just seen the end of each story, regardless of whether it depicted an empathic or non-empathic behavior (note that similar waveforms were observed in Panel 4c in the high EQ group).

It was interesting to review the function of the region around the medial part of the left parieto-occipital sulcus. The left precuneus and left lingual gyrus are involved in mind-wandering and spontaneous thought processes (Fox et al. 2015). The precuneus is also involved in episodic memory retrieval (Cavanna and Trimble 2006). The left isthmus-cingulate cortex (i.e., retrosplenial cortex) is involved in complex cognitive functions such as remembering (Silson et al. 2019), spatial navigation (Shine et al. 2016), perspective taking (Sulpizio et al. 2016), and self-referential processing (Summerfield et al. 2009) (for review, see Vann et al. 2009; Chrastil, 2018). Moreover, the precuneus and retrosplenial cortex (the areas surrounding the parieto-occipital sulcus) are the core regions related to self-projection (Buckner and Carroll 2007; Spreng et al. 2009; Chrastil 2018). Self-projection is the ability to shift one's perspective from the present moment to a simulated time, place, or person (Buckner and Carroll, 2007). Therefore, the prolonged component, which was observed only in the high EQ group, can be considered to have arisen from this region. One possible reason why the region related to self-projection was activated in the high EQ group was that participants in the high EQ group reviewed the outline of the story recalling the contents of Panels 1–3 and inferred the mental state and intention behind the others' behavior, although they were not asked to do so. In other words, people with high empathy may reconstruct the mental state and intention of others through self-projection when they have finished watching a sequence presenting others' behaviors in social interaction. Previous studies (Völlm et al. 2006; Sebastian et al. 2012) suggest that the posterior cingulate gyrus is one of the regions involved in inferring the intention behind others' complex behavior (such as social interaction) rather than simple behavior. Because the posterior cingulate is close to the precuneus and the retrosplenial cortex, brain activity related to self-projection may have already been captured in these studies. One may assume that the cortical activity around the medial part of the left parieto-occipital sulcus in the high EQ group may have been recruited to answer the questions related to Panel 4. However, this cortical activity is not a prerequisite for answering the questions because the correct answer rate was comparable in the high and low EQ groups, although the low EQ group did not show such cortical activity.

Limitation

The present study has some limitations. First, only male participants were included, and all were Japanese, of a specific age group, and had similar educational backgrounds, which could affect the generalizability of the findings. Second, there may be unmeasured differences in background factors between the high and low EQ groups, although there were no differences in age, gender, or educational background. Third, the empathic ability was measured only using the EQ. Several batteries can measure empathic ability (e.g., IRI), but what EQ captures and what other batteries capture may be slightly different. Fourth, measured neuromagnetic signals may not reflect a part of cortical activity because MEG is not good at detecting a radially oriented current (Ahlfors et al. 2010). Finally, we did not ask the participants to complete a questionnaire after the MEG recordings about their thoughts while watching the comic strips. Therefore, no behavioral clues could be obtained to understand the participants' thoughts while watching the comic strips.

Conclusion

When social interaction scenes were presented, the high EQ group showed increased cortical activity in the right occipital region within 200 ms after the onset of the panel presentation and in the medial part of the bilateral superior frontal gyri and right posterior insula after 900 ms. These findings suggest that people with high empathy paid attention to others' faces and bodies and infer the mental state (including stress) of others in the context of social interaction. The high EQ group also showed increased cortical activity in the left superior frontal gyrus (dorsal premotor area) at 200–250 ms when stories with the empathic endings were presented, which suggests that people with high empathy paid attention to the character's hand action and/or mentally simulated the empathic behavior of others. Moreover, the high EQ group showed increased cortical activity in the region around the medial part of the left parieto-occipital sulcus after 450 ms when they passively watched both the empathic and non-empathic endings, which suggests enhancement in the cortical activity related to self-projection. These results suggest that people with high empathy pay attention to others and actively infer others' mental states while watching social interactions and that they reconstruct others' mental states and intentions through self-projection after watching a sequence of others' behaviors.

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Notes

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Author Contributions

M.H., J.M., M.F., and A.M. designed the study; M.H., J.M., and K.T. acquired the data; M.H., J.M. analyzed the behavioral and the MEG data; M.H., J.M., and A.M. wrote the manuscript; M.M., T.M., and H.F. supervised the project and provided critical feedback to the manuscript.

References

Ahlfors SP, Han J, Belliveau JW, Hämäläinen MS. 2010. Sensitivity of MEG and EEG to source orientation. *Brain Topogr.* 23:227-232.

Arioli M, Canessa N. 2019. Neural processing of social interaction: Coordinate-based meta-analytic evidence from human neuroimaging studies. *Hum Brain Mapp*. 40:3712-3737.

Barnes GR, Litvak V, Brookes MJ, Friston KJ. 2011. Controlling false positive rates in mass-multivariate tests for electromagnetic responses. *Neuroimage.* 56:1072-1081.

Baron-Cohen S, Cassidy S, Auyeung B, Allison C, Achoukhi M, Robertson S, Pohl A, Lai MC. 2014. Attenuation of typical sex differences in 800 adults with autism vs. 3,900 controls. *PLoS One*. 9:e102251.

Baron-Cohen S, Richler J, Bisarya D, Gurunathan N, Wheelwright S. 2003. The systemizing quotient: an investigation of adults with Asperger syndrome or high-functioning autism, and normal sex differences. *Philos Trans R Soc Lond B Biol Sci.* 358:361-374.

Baron-Cohen S, Wheelwright S. 2004. The empathy quotient: an investigation of adults with Asperger syndrome or high functioning autism, and normal sex differences. *J Autism Dev Disord*. 34:163-175.

Braun S, Rosseel Y, Kempenaers C, Loas, G, Linkowski P. 2015. SELF-REPORT OF EMPATHY: A SHORTENED FRENCH ADAPTATION OF THE INTERPERSONAL REACTIVITY INDEX (IRI) USING TWO LARGE BELGIAN SAMPLES. *Psychol Rep*. 117:735-753.

Brunet E, Sarfati Y, Hardy-Baylé MC, Decety J. 2000. A PET investigation of the attribution of intentions with a nonverbal task. *Neuroimage*. 11:157-166.

Buckner RL, Carroll DC. 2007. Self-projection and the brain. *Trends Cogn Sci*. 11:49-57.

Bzdok D, Schilbach L, Vogeley K, Schneider K, Laird AR, Langner R, Eickhoff SB. 2012. Parsing the neural correlates of moral cognition: ALE meta-analysis on morality, theory of mind, and empathy. *Brain Struct Funct.* 217:783-796.

Cavanna AE, Trimble MR. 2006. The precuneus: a review of its functional anatomy and behavioural correlates. *Brain.* 129:564-583.

Chakrabarti B, Bullmore E, Baron-Cohen S. 2006. Empathizing with basic emotions: common and discrete neural substrates. *Soc Neurosci.* 1:364-384.

Chakrabarti B, Haffey A, Canzano L, Taylor CP, McSorley E. 2017. Individual differences in responsivity to social rewards: Insights from two eye-tracking tasks. *PLoS One.* 12:e0185146.

Chrastil ER. 2018. Heterogeneity in human retrosplenial cortex: A review of function and connectivity. *Behav Neurosci.* 132:317-338.

Clark VP, Hillyard SA. 1996. Spatial selective attention affects early extrastriate but not striate components of the visual evoked potential. *J Cogn Neurosci.* 8:387-402.

Cowan DG, Vanman EJ, Nielsen M. 2014. Motivated empathy: the mechanics of the empathic gaze. *Cogn Emot.* 28:522-530.

Davis MH. 1980. A multidimensional approach to individual differences in empathy. *JSAS Catalog of Selected Documents in Psychology*. 10:85.

Davis MH. 1983. Measuring individual differences in empathy: Evidence for multidimensional approach. *J Pers Soc Psychol.* 44:113-126.

Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, Buckner RL, Dale AM, Maguire RP, Hyman BT, Albert MS, Killiany RJ. 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage.* 31:968-980.

Downing PE, Jiang Y, Shuman M, Kanwisher N. 2001. A cortical area selective for visual processing of the human body. *Science.* 293:2470-2473.

Engemann D, Strohmeier D, Larson E, Gramfort A. 2015. Mind the noise covariance when localizing brain sources with m/EEG. *2015 International Workshop on Pattern Recognition in NeuroImaging.* 9-12.

Filimon F, Nelson JD, Hagler DJ, Sereno MI. 2007. Human cortical representations for reaching: mirror neurons for execution, observation, and imagery. *Neuroimage*. 37:1315-1328.

Focquaert F, Steven-Wheeler MS, Vanneste S, Doron KW, Platek SM. 2010. Mindreading in individuals with an empathizing versus systemizing cognitive style: An fMRI study. *Brain Res Bull*. 83:214-222.

Fox KC, Spreng RN, Ellamil M, Andrews-Hanna JR, Christoff K. 2015. The wandering brain: meta-analysis of functional neuroimaging studies of mind-wandering and related spontaneous thought processes. *Neuroimage.* 111:611-621.

Frith CD, Frith U. 2006. The neural basis of mentalizing. *Neuron.* 50:531-534.

Gossen A, Groppe SE, Winkler L, Kohls G, Herrington J, Schultz RT, Gründer, G, Spreckelmeyer, KN. 2014. Neural evidence for an association between social proficiency and sensitivity to social reward. *Soc Cogn Affect Neurosci.* 9:661-670.

Gramfort A, Luessi M, Larson E, Engemann DA, Strohmeier D, Brodbeck C, Parkkonen L, Hämäläinen MS. 2014. MNE software for processing MEG and EEG data. *Neuroimage.* 86:446-460.

Hadjikhani N, Kveraga K, Naik P, Ahlfors SP. 2009. Early (M170) activation of face-specific cortex by face-like objects. *Neuroreport.* 20:403-407.

Hardwick RM, Caspers S, Eickhoff SB, Swinnen SP. 2018. Neural correlates of action: Comparing meta-analyses of imagery, observation, and execution. *Neurosci Biobehav Rev*. 94:31-44.

Hedger N, Haffey A, McSorley E, Chakrabarti B. 2018. Empathy modulates the temporal structure of social attention. *Proc R Soc B*. 285:20181716.

Hillyard SA, Anllo-Vento L. 1998. Event-related brain potentials in the study of visual selective attention. *Proc Natl Acad Sci USA.* 95:781-787.

Huang MX, Mosher JC, Leahy RM. 1999. A sensor-weighted overlapping-sphere head model and exhaustive head model comparison for MEG. *Phys Med Biol.* 44:423-440.

Johnson MM, Caron KM, Mikolajewski AJ, Shirtcliff EA, Eckel LA, Taylor J. 2014. Psychopathic traits, empathy, and aggression are differentially related to cortisol awakening response. *J Psychopathol Behav Assess.* 36:380-388.

Jolliffe D, Farrington DP. 2006. Development and validation of the Basic Empathy Scale. *J Adolesc.* 29:589-611.

Kim J, Lee SJ. 2010. Reliability and validity of the korean version of the empathy quotient scale. *Psychiatry Investig.* 7:24-30.

Lamm C, Decety J, Singer T. 2011. Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage.* 54:2492-2502.

Lee SJ, Kang DH, Kim CW, Gu BM, Park JY, Choi CH, Shin NY, Lee JM, Kwon JS. 2010. Multi-level comparison of empathy in schizophrenia: an fMRI study of a cartoon task. *Psychiatry Res*. 181:121-129.

Lockwood PL, Seara-Cardoso A, Viding E. 2014. Emotion regulation moderates the association between empathy and prosocial behavior. *PLoS One.* 9:e96555.

Loudin JL, Loukas A, Robinson S. 2003. Relational aggression in college students: examining the roles of social anxiety and empathy. *Aggress Behav.* 29:430-439.

Mar RA. 2011. The neural bases of social cognition and story comprehension. *Annu Rev Psychol.* 62:103-134.

Masten CL, Morelli SA, Eisenberger NI. 2011. An fMRI investigation of empathy for 'social pain' and subsequent prosocial behavior. *Neuroimage.* 55:381-388.

Mattout J, Henson RN, Friston KJ. 2007. Canonical source reconstruction for MEG. *Comput Intell Neurosci.* 2007:67613.

Mehrabian A. 1997. Relations among personality scales of aggression, violence, and empathy: Validational evidence bearing on the Risk of Eruptive Violence Scale. *Aggress Behav.* 23:433-445.

Neumann DL, Chan RCK, Boyle GJ, Wang Y, Westbury HR. 2015. Measures of empathy: Self-report, behavioral, and neuroscientific approaches, in Boyle, G.J., Saklofske, D.H., Matthews, G. (Eds.), *Measures of personality and social psychological constructs*. pp. 257-289. Elsevier Academic Press.

Pascual-Marqui RD. 2002. Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details. *Methods Find Exp Clin Pharmacol.* 24 Suppl D:5-12.

Pitcher D, Walsh V, Duchaine B. 2011. The role of the occipital face area in the cortical face perception network. *Exp Brain Res.* 209:481-493.

Reniers RL, Corcoran R, Drake R, Shryane NM, Völlm BA. 2011. The QCAE: a Questionnaire of Cognitive and Affective Empathy. *J Pers Assess.* 93:84-95.

Rymarczyk K, Żurawski Ł, Jankowiak-Siuda K, Szatkowska I. 2016. Emotional Empathy and Facial Mimicry for Static and Dynamic Facial Expressions of Fear and Disgust. *Front Psychol.* 7:1853.

Saarela MV, Hlushchuk Y, Williams AC, Schürmann M, Kalso E, Hari R. 2007. The compassionate brain: humans detect intensity of pain from another's face. *Cereb Cortex.* 17:230-237.

Sebastian CL, Fontaine NM, Bird G, Blakemore SJ, Brito SA, McCrory EJ, Viding E. 2012. Neural processing associated with cognitive and affective Theory of Mind in adolescents and adults. *Soc Cogn Affect Neurosci.* 7:53-63.

Shine JP, Valdés-Herrera JP, Hegarty M, Wolbers T. 2016. The Human Retrosplenial Cortex and Thalamus Code Head Direction in a Global Reference Frame. *J Neurosci.* 36:6371-6381.

Silson EH, Gilmore AW, Kalinowski SE, Steel A, Kidder A, Martin A, Baker CI. 2019. A Posterior-Anterior Distinction between Scene Perception and Scene Construction in Human Medial Parietal Cortex. *J Neurosci.* 39:705-717.

Singer T, Seymour B, O'Doherty J, Kaube H, Dolan RJ, Frith CD. 2004. Empathy for pain involves the affective but not sensory components of pain. *Science.* 303:1157-1162.

Sonnby-Borgström M. 2002. Automatic mimicry reactions as related to differences in emotional empathy. *Scand J Psychol.* 43:433-443.

Sonnby-Borgström M, Jönsson P, Svensson O. 2003. Emotional empathy as related to mimicry reactions at different levels of information processing. *J Nonverbal Behav.* 27:3-23.

Spreng RN, Mar RA, Kim AS. 2009. The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: a quantitative meta-analysis. *J Cogn Neurosci.* 21:489-510.

Sulpizio V, Committeri G, Lambrey S, Berthoz A, Galati G. 2016. Role of the human retrosplenial cortex/parieto-occipital sulcus in perspective priming. *Neuroimage.* 125:108-119.

Summerfield JJ, Hassabis D, Maguire EA. 2009. Cortical midline involvement in autobiographical memory. *Neuroimage.* 44:1188-1200.

Tadel F, Baillet S, Mosher JC, Pantazis D, Leahy RM. 2011. Brainstorm: a user-friendly application for MEG/EEG analysis. *Comput Intell Neurosci.* 2011:879716.

Taulu S, Simola J., 2006. Spatiotemporal signal space separation method for rejecting nearby interference in MEG measurements. *Phys Med Biol.* 51:1759-1768.

Vann SD, Aggleton JP, Maguire EA. 2009. What does the retrosplenial cortex do? *Nat Rev Neurosci.* 10:792-802.

Völlm BA, Taylor AN, Richardson P, Corcoran R, Stirling J, McKie S, Deakin JF, Elliott R. 2006. Neuronal correlates of theory of mind and empathy: a functional magnetic resonance imaging study in a nonverbal task. *Neuroimage.* 29:90-98.

Wakabayashi A, Baron-Cohen S, Wheelwright S. 2006. Individual and gender differences in Empathizing and Systemizing: measurement of individual differences by the Empathy Quotient (EQ) and the Systemizing Quotient (SQ). *Shinrigaku Kenkyu.* 77:271-277.

Walter H, Adenzato M, Ciaramidaro A, Enrici I, Pia L, Bara BG. 2004. Understanding intentions in social interaction: the role of the anterior paracingulate cortex. *J Cogn Neurosci.* 16:1854-1863.

Wang Y, Liu WH, Li Z, Wei XH, Jiang XQ, Neumann DL, Shum DH, Cheung EF, Chan RC. 2015. Dimensional schizotypy and social cognition: an fMRI imaging study. *Front Behav Neurosci.* 9:133.

Yoder KJ, Decety J. 2014. Spatiotemporal neural dynamics of moral judgment: a high-density ERP study. *Neuropsychologia.* 60:39-45.

Table 1. Demographic characteristics of the high and low EQ groups.

	High EQ group (n=20)			Low EQ group (n=23)			U test
	Mean	Range	SD	Mean	Range	SD	p-value
Age	21.3	20–24	1.3	21.3	20–25	1.3	0.889
EQ score	47.5	41–56	5.3	20.5	11–25	4.0	<0.001***
SQ score	33.0	11–55	14.5	27.0	7–56	12.6	0.184
Response to questions during MEG sessions							
Correct answer rate (%)	97.7	90.0–100	2.7	96.6	88.3–100	3.2	0.190
Reaction time (s)	2.02	1.41–3.62	0.47	2.04	1.33–3.04	0.42	0.480
Impression rating of comic strips (after completing MEG sessions)							
Comprehensibility							
empathic ending	4.99	4.90–5.00	0.03	4.94	4.35–5.00	0.15	0.107
non-empathic ending	4.97	4.80–5.00	0.06	4.88	4.15–5.00	0.24	0.248
Empathic rating							
empathic ending	4.85	4.30–5.00	0.16	4.65	4.20–4.95	0.23	0.003**
non-empathic ending	1.56	1.05–2.05	0.25	1.85	1.15–2.20	0.24	<0.001***

Note: EQ, empathy quotient; SQ, systemizing quotient **p<0.01 and ***p<0.001.

Table 2. Regions of significant group difference (high vs. low EQ) in Panels 1, 2, 4a, 4b, and 4c.

condition	time	anatomical label	hemi	MNI coordinates			max F value	number of vertices
				x	y	z		
Panel 1	100–120 ms	lateral occipital cortex	R	31	−95	−14	23.9	4
	120–140 ms	lateral occipital cortex	R	25	−91	−16	20.1	2
	180–200 ms	fusiform gyrus	R	33	−74	−10	21.5	4
		lingual gyrus	R	23	−79	−6	21.5	3
		lateral occipital cortex	R	50	−73	−15	21.3	6
Panel 2	900–1000 ms	superior frontal gyrus	L	−5	50	28	20.6	9
		superior frontal gyrus	R	5	54	19	20.1	2
	1100–1200 ms	insula	R	34	−3	−5	20.1	1
	1200–1300 ms	insula	R	34	−3	−5	19.1	1
Panel 4a	200–250 ms	superior frontal gyrus	L	−27	−3	67	21.8	1
	450–500 ms	lingual gyrus	L	−12	−54	1	19.1	1
		precuneus	L	−15	−52	37	19.0	1
	500–550 ms	lingual gyrus	L	−12	−54	1	24.0	1
		isthmus-cingulate cortex	L	−13	−53	7	20.7	1
	550–600 ms	isthmus-cingulate cortex	L	−13	−53	7	20.6	1
		lingual gyrus	L	−12	−54	1	20.3	1
	600–700 ms	isthmus-cingulate cortex	L	−13	−53	7	18.8	1
	800–900 ms	lingual gyrus	L	−18	−47	−11	18.8	1
Panel 4b	450–500 ms	precuneus	L	−12	−72	37	20.8	4
	550–600 ms	precuneus	L	−13	−61	22	23.4	10
		isthmus-cingulate cortex	L	−13	−53	7	23.2	2
		cuneus	L	−16	−65	18	21.8	4
	600–700 ms	isthmus-cingulate cortex	L	−13	−53	7	20.1	1

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	500–550 ms	lateral occipital cortex	L	−12	−105	−7	19.5	1
	800–900 ms	isthmus-cingulate cortex	L	−13	−53	7	19.0	1
Panel 4c	900–1000 ms	fusiform gyrus	L	−30	−57	−11	22.5	5
		lingual gyrus	L	−31	−53	−5	21.1	4
	1000–1100 ms	rostral middle frontal gyrus	L	−39	23	22	19.1	2

Note: max F value shows the maximum F value among the significant vertices of each anatomical label. hemi=hemisphere; L/R = left/right.

Table 3. Regions of significant condition difference in Panels 4a and 4b.

time	anatomical label	hemi	MNI coordinates x	y	z	max F value	number of vertices
60–80 ms	rostral middle frontal gyrus	L	−28	52	28	23.9	13
80–100 ms	rostral middle frontal gyrus	L	−33	50	27	19.9	2
350–400 ms	middle temporal gyrus	L	−66	−22	−23	21.6	5
400–450 ms	middle temporal gyrus	L	−66	−22	−23	32.9	23
	inferior temporal gyrus	L	−56	−23	−20	24.0	4
	superior temporal gyrus	L	−54	−17	−8	23.0	3
	precentral gyrus	R	26	−8	47	20.9	1
	lingual gyrus	L	−27	−63	−5	20.8	1
450–500 ms	middle temporal gyrus	L	−66	−22	−23	38.2	28
	superior temporal gyrus	L	−54	−17	−8	33.0	16
	inferior temporal gyrus	L	−56	−23	−20	25.9	5
	transverse temporal cortex	L	−45	−26	13	24.7	5
	insula	L	−34	−23	21	24.2	6
	supramarginal gyrus	L	−48	−31	17	24.2	18
	postcentral gyrus	L	−41	−21	17	20.5	1
500–550 ms	middle temporal gyrus	L	−56	−18	−15	30.7	22
	superior temporal gyrus	L	−54	−17	−8	30.3	16
	transverse temporal cortex	L	−49	−23	11	25.5	6
	postcentral gyrus	L	−41	−21	17	23.8	2
	inferior temporal gyrus	L	−56	−23	−20	23.6	4
	precentral gyrus	R	54	−4	51	22.2	2
	supramarginal gyrus	L	−46	−24	22	21.5	4
	insula	L	−37	−24	20	20.3	4
	posterior cingulate cortex	L	−11	−16	38	19.5	1

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600–700 ms	superior temporal gyrus	L	−36	10	−27	21.1	3
	lateral orbitofrontal cortex	L	−35	19	−24	20.7	1
	insula	L	−33	4	−21	20.1	1
	temporal pole	L	−34	7	−28	19.9	1
	inferior temporal gyrus	L	−38	5	−37	19.6	1
	middle temporal gyrus	L	−53	9	−36	19.2	1

Note: max F value shows the maximum F value among the significant vertices of each anatomical label. hemi=hemisphere; L/R = left/right.

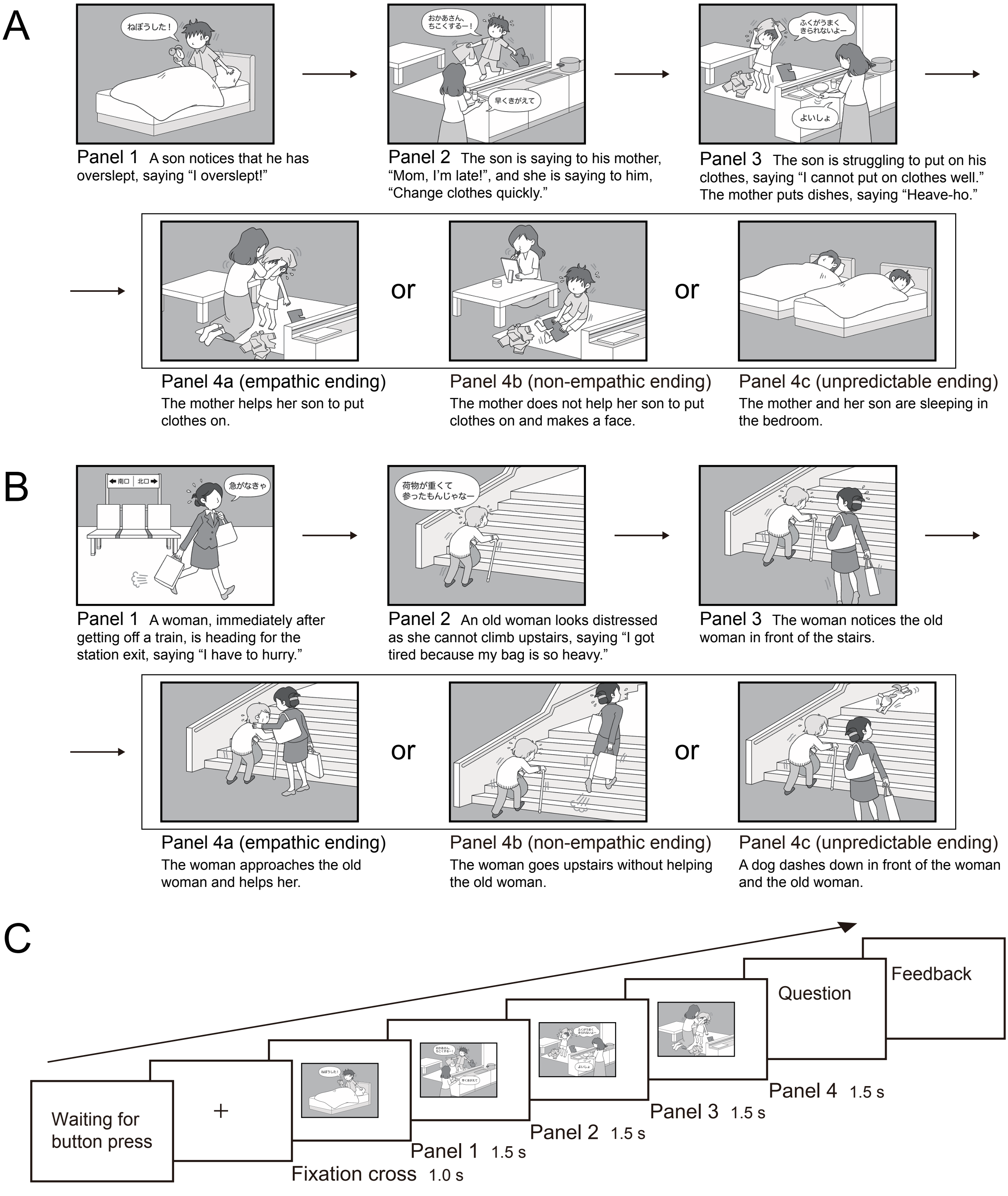


Figure 1. Stimuli and tasks. (A) and (B): Examples of four-panel comic strips (A: story No. 1; B: story No. 11) are shown. The first three panels are common, and the three types of the fourth panels represent different endings: a) empathic, b) non-empathic, and c) unpredictable ending. (C): Sequence of the tasks. The fixation cross was displayed for 1.0 s after the participant pressed a button at his timing, and then each panel was displayed for 1.5 s on the screen. A two-choice question (e.g., “Who was putting the dishes away, a woman/ a boy?”) was displayed after the disappearance of the fourth panel in half of the trials, and the participant answered the question by button press. Feedback was given as to whether the participant’s answer was correct or not. The background of the screen is white, and the texts and the fixation cross are in black in this figure, but the colors were reversed during the actual measurements.

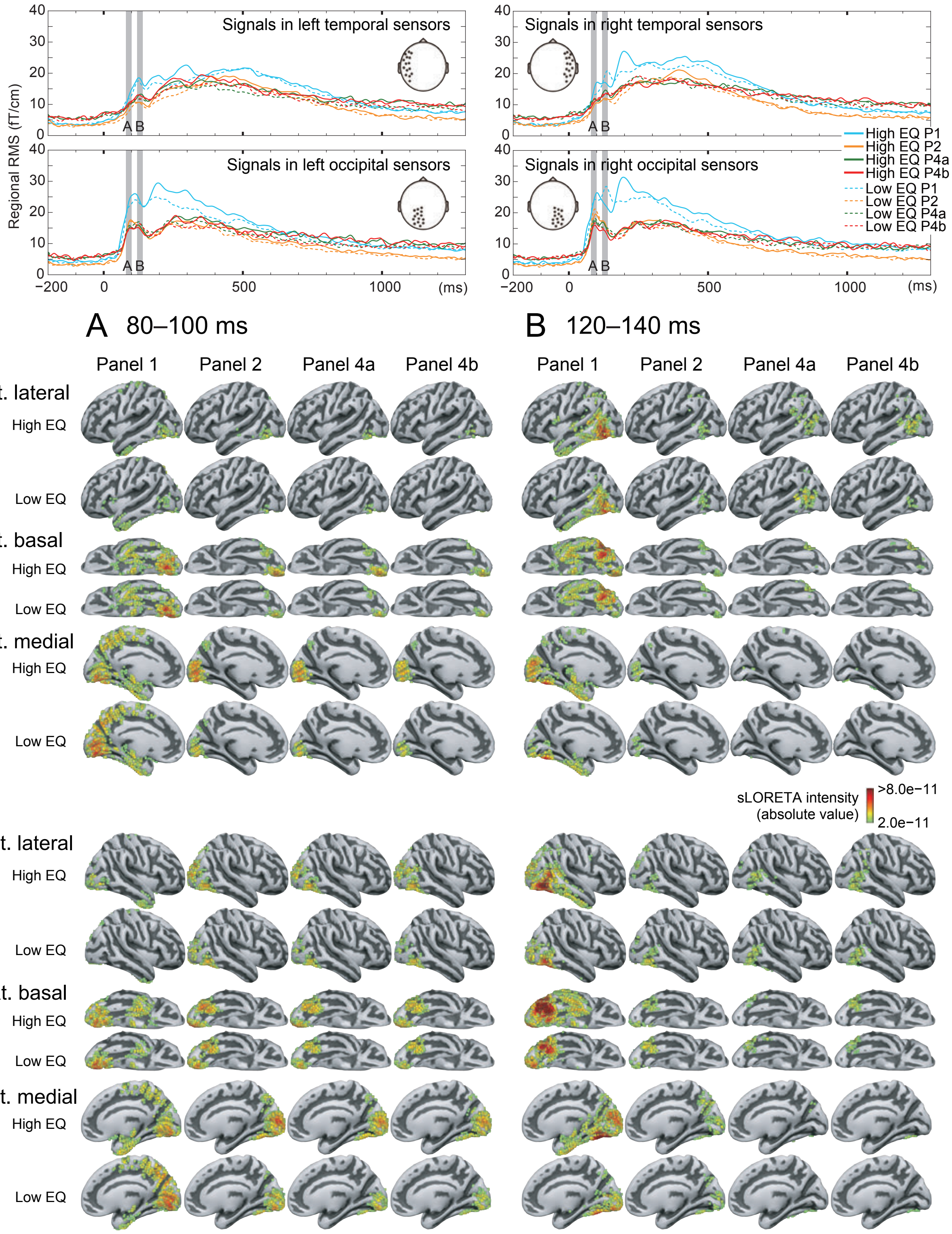


Figure 2. Top: Regional root-mean-square signals in temporal and occipital sensors in Panels 1 (light blue), 2 (orange), 4a (green), and 4b (red) from −200 to 1300 ms. Time "0 ms" means the onset of the panel presentation. Solid and dot lines indicate the high and low EQ groups, respectively. We selected two peaks at 80–100 ms (A) and 120–140 ms (B). All other waveforms are shown in SFig. 3 and SFig. 4. Middle and bottom: Mean source activities at 80–100 ms (A) and 120–140 ms (B) in Panels 1, 2, 4a, and 4b. The color of each cube on the smoothed cortex represents an sLORETA intensity (absolute value) of the dipole at that position. Note that the cubes are hidden if the intensity does not reach an arbitrary threshold (2.0e−11). Lt: left; Rt: right.

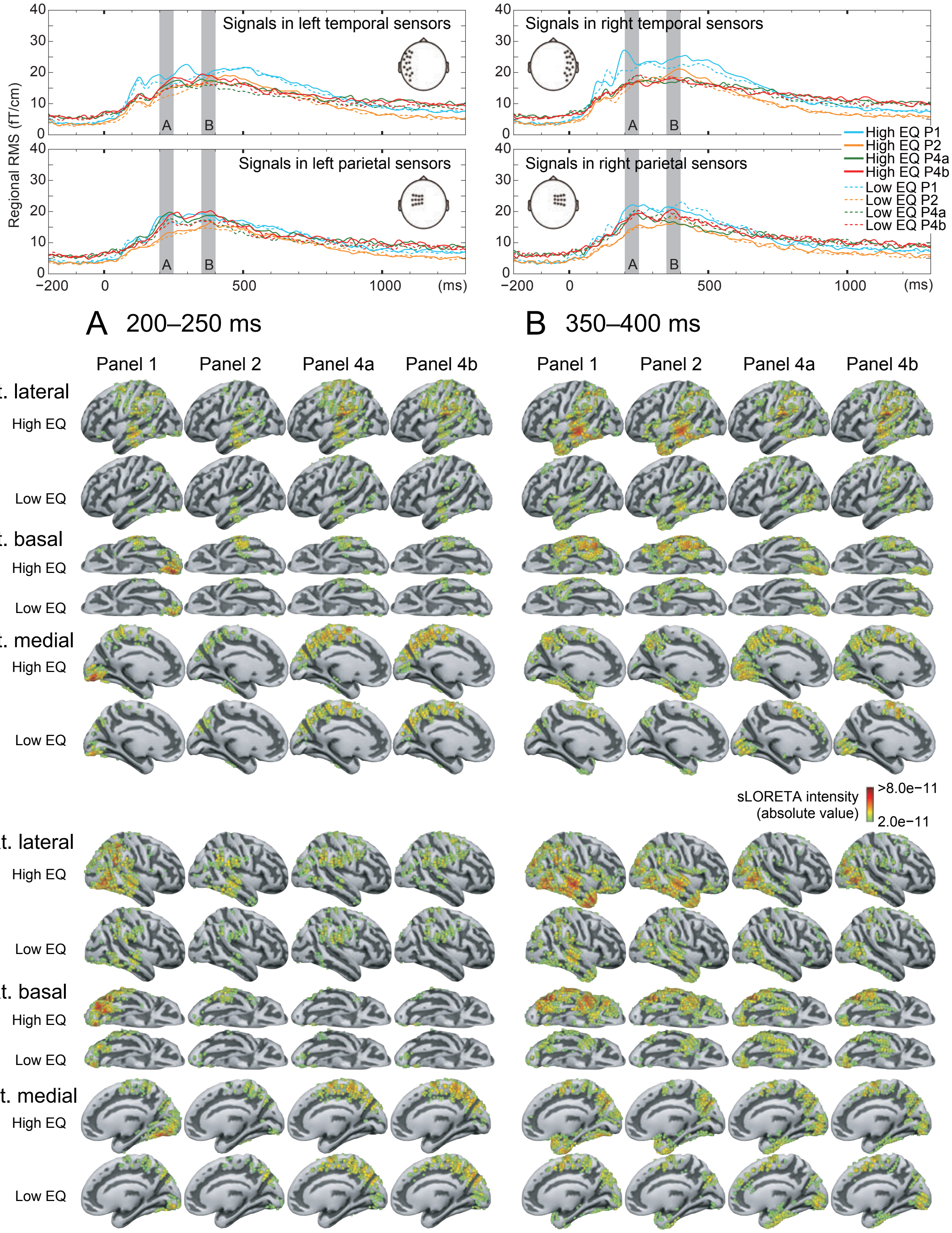


Figure 3. Top: Regional root-mean-square signals in temporal and parietal sensors in Panels 1 (light blue), 2 (orange), 4a (green), and 4b (red) from −200 to 1300 ms. Solid and dotted lines indicate the high and low EQ groups, respectively. We selected two peaks at 200–250 ms (A) and 350–400 ms (B). All other waveforms are shown in Sfig. 3 and Sfig. 4. Middle and bottom: Mean source activities at 200–250 ms (A) and 350–400 ms (B) in Panels 1, 2, 4a, and 4b. The color of each cube on the smoothed cortex represents an sLORETA intensity (absolute value) of the dipole at that position. Note that the cubes are hidden if the intensity does not reach an arbitrary threshold (2.0e−11). Lt: left; Rt: right.

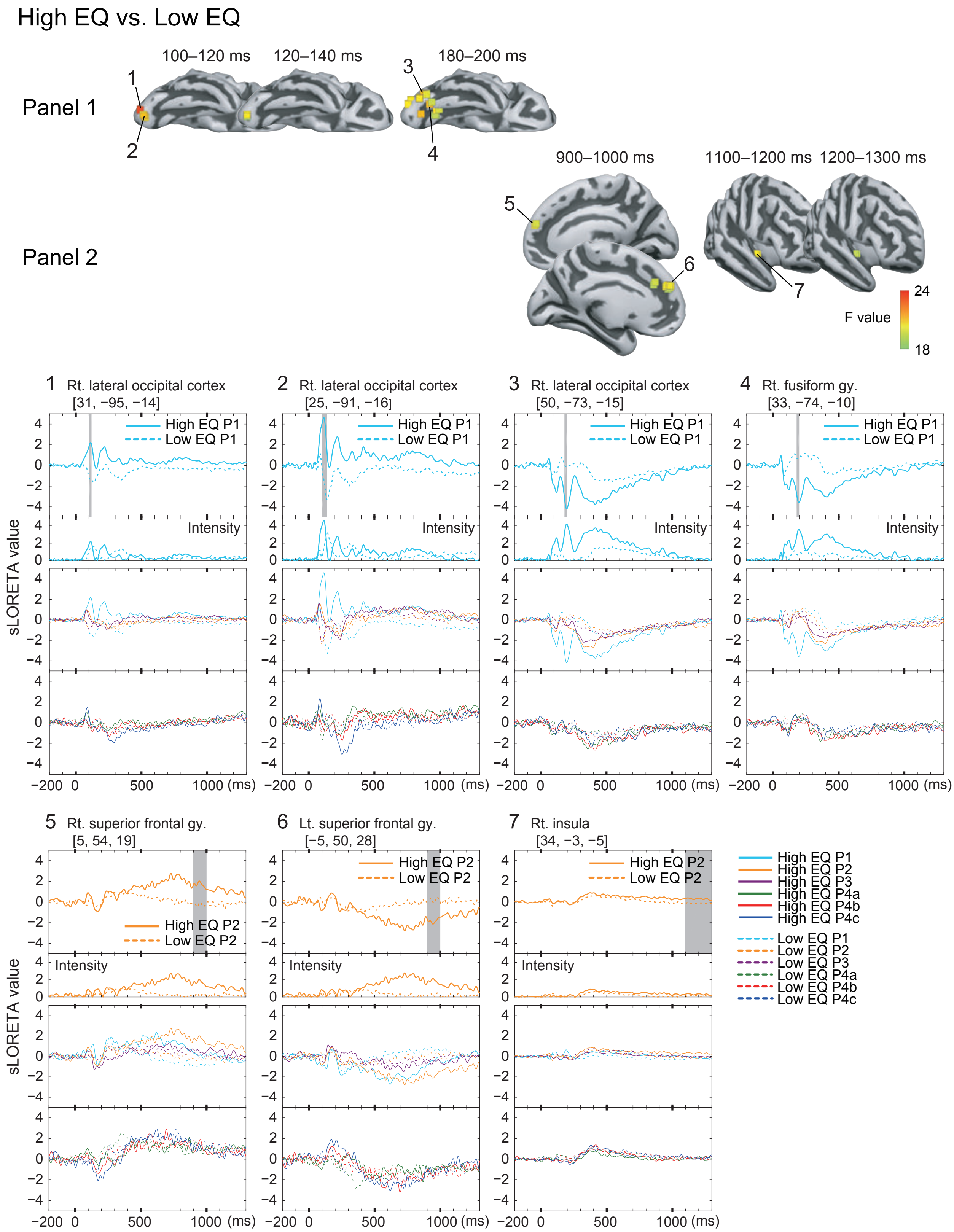


Figure 4. Group differences in Panel 1 or 2. Top: Brain regions that show significant group differences ($p<0.0000217$, which corresponds to FWE corrected $p<0.05$) in Panel 1 or 2. The color of each cube on the smoothed cortex represents the F value of the dipole at that position. Middle and bottom: Source waveforms at the representative regions (dipoles); the shaded area shows a significant time window at that dipole. The upper first and second panels show the mean sLORETA values and its intensities in conditions showing significant differences, respectively. The third and fourth panels show the mean sLORETA values of Panels 1–3 and 4a–4c, respectively. The sign of the sLORETA value represents the current direction: a positive value means that the current direction is toward the cortical surface, and a negative value means that the current direction is toward white matter. All sLORETA values and their intensities are shown multiplied by 1.0e11. Line colors represent conditions (Panels), and line styles represent groups (high and low EQ). An anatomical label of the dipole position is shown with MNI coordinates. Lt: left; Rt: right; gy: gyrus.

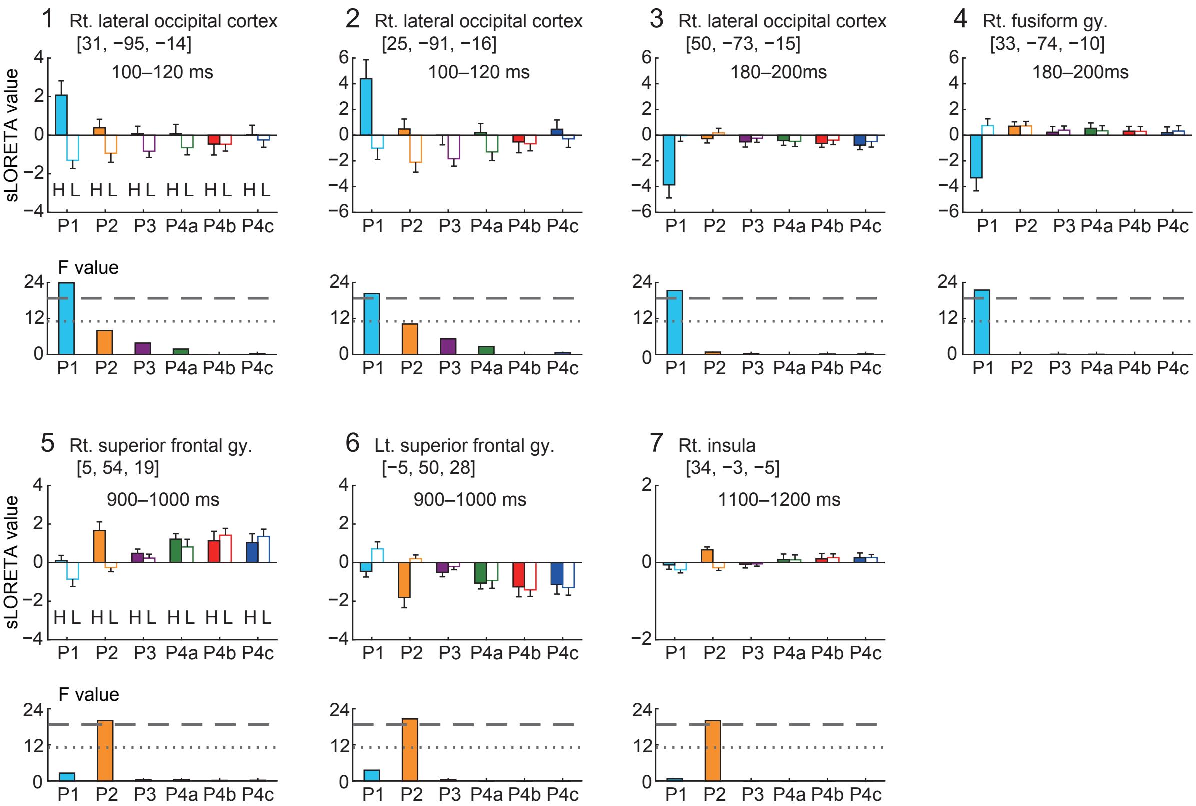


Figure 5. F values for group contrasts of all conditions at the representative regions 1–7 in Fig. 4 (the brain regions that show significant group differences in Panel 1 or 2). The upper panel shows the mean dipole amplitudes in the selected region and time window, and error bars represent the standard error of mean. As in Fig. 4, the sLORETA value is signed, which represents the current direction. Bar colors represent conditions (Panels), and bar styles (filled or open) represent groups (high and low EQ). The lower panel shows all F values of group contrasts. Dashed and dotted lines indicate corrected (p=0.0000217, corresponding F value=18.75) and uncorrected (p=0.001, corresponding F value=11.09) significance levels, respectively. Lt: left; Rt: right; gy: gyrus; H: high EQ group; L: low EQ group.

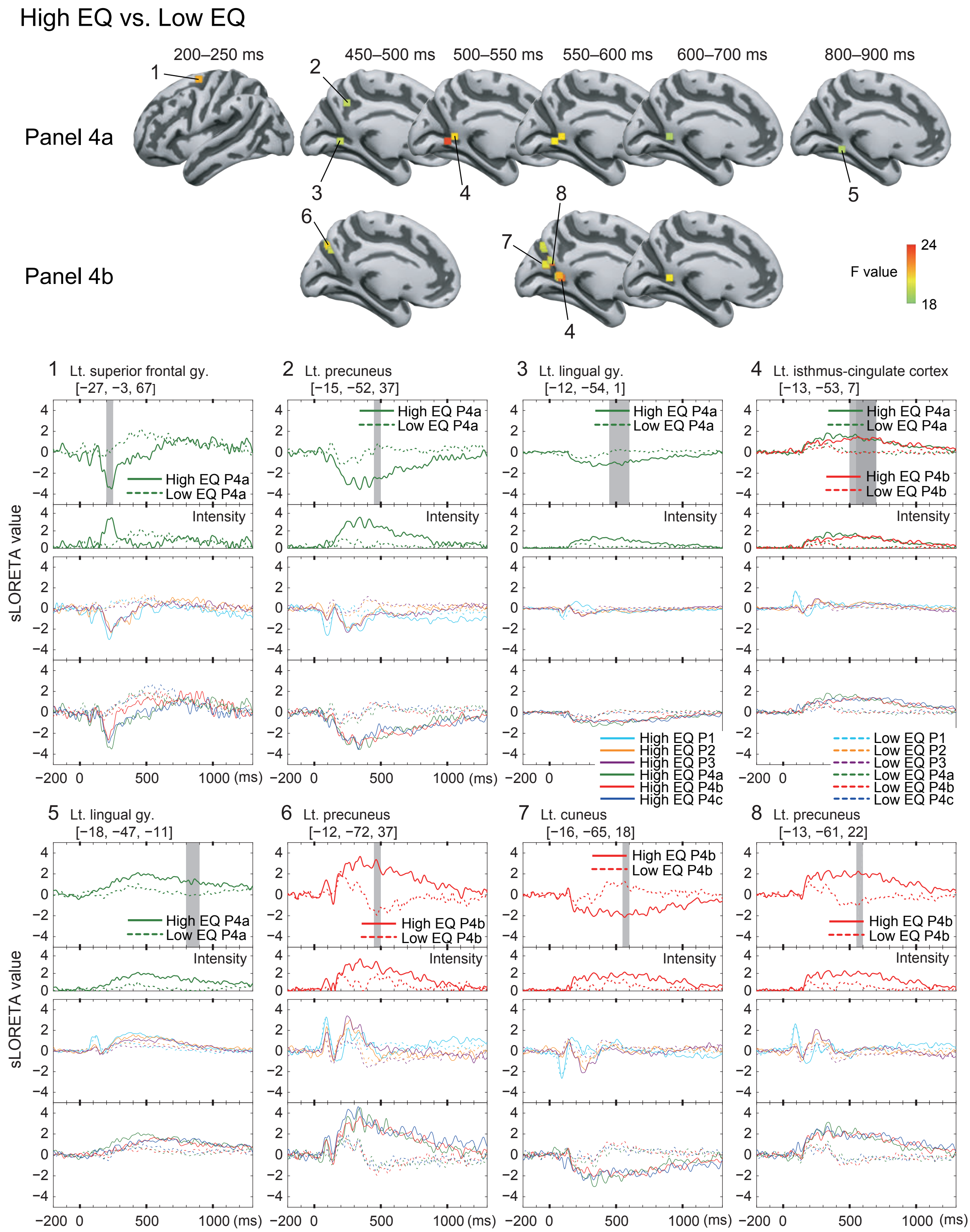


Figure 6. Group differences in Panels 4a and/or 4b. Top: Brain regions that show significant group differences (p<0.0000217) in Panels 4a and/or 4b. The color of each cube on the smoothed cortex represents the F value of the dipole at that position. Middle and bottom: Source waveforms at the representative regions (dipoles); the shaded area shows a significant time window at that dipole (group contrasts of Panels 4a and 4b were simultaneously significant at 550–600 ms and 600–700 ms time windows in region 4 (left isthmus-cingulate cortex), so 550–700 ms time window is marked in dark gray). The upper first and second panels show the mean sLORETA values and their intensities for conditions showing significant differences, respectively. The third and fourth panels show the mean sLORETA values of Panels 1–3 and 4a–4c, respectively. All sLORETA values and its intensities are shown multiplied by 1.0e11. Lt: left; Rt: right; gy: gyrus.

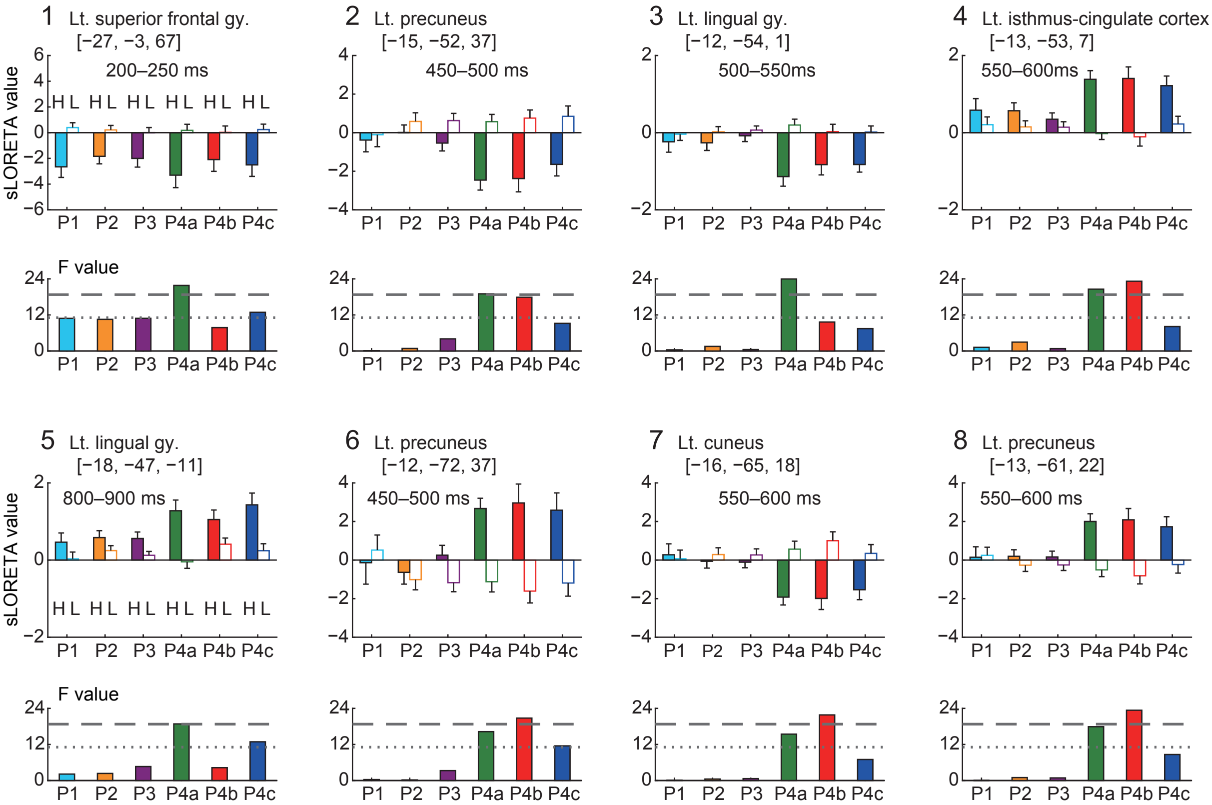
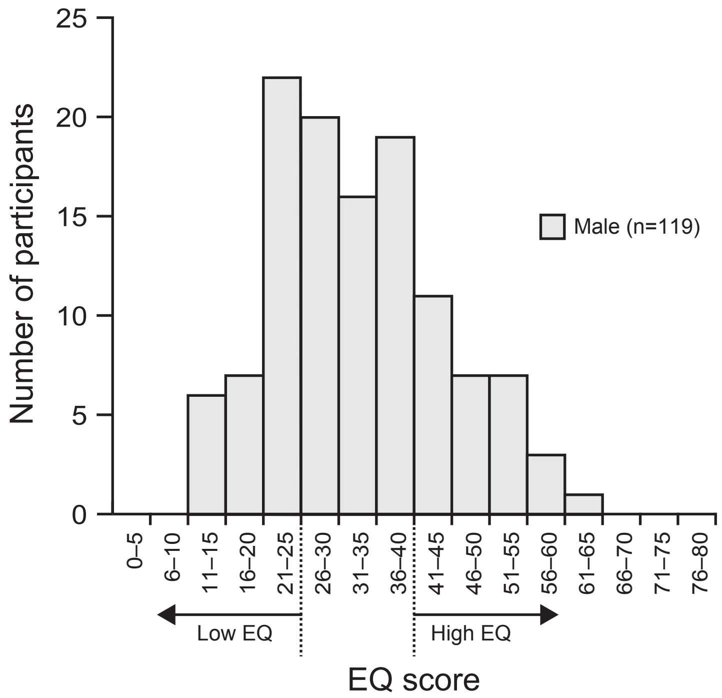
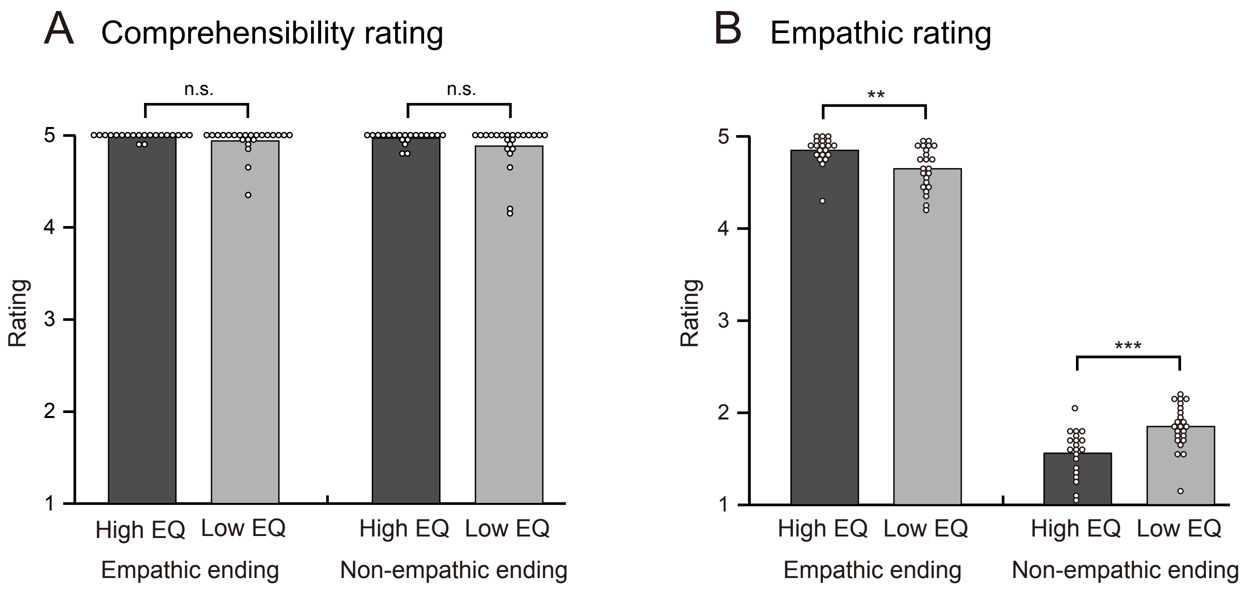


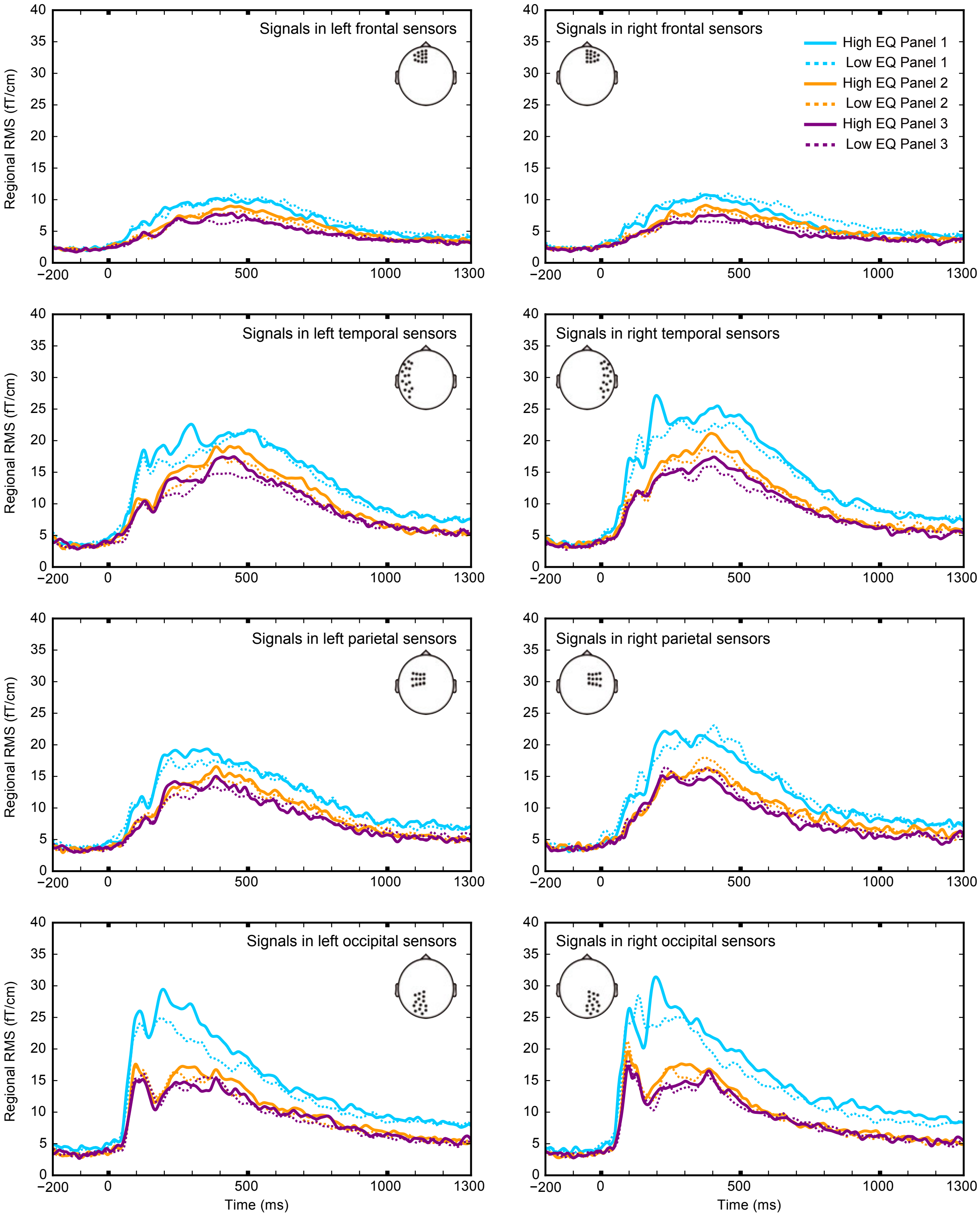
Figure 7. F values for group contrasts of all conditions at the representative regions 1–8 in Fig. 6 (the brain regions that show significant group differences in Panels 4a and/or 4b). The upper panel shows the mean sLORETA values in the selected region and time window, and error bars represent the standard error of mean. Bar colors represent conditions (Panels), and bar styles (filled or open) represent groups (high and low EQ). The lower panel shows all F values for group contrasts. Dashed and dotted lines indicate corrected (p=0.0000217, corresponding F value=18.75) and uncorrected (p=0.001, corresponding F value=11.09) significance levels, respectively. Lt: left; Rt: right; gy: gyrus; H: high EQ group; L: low EQ group.



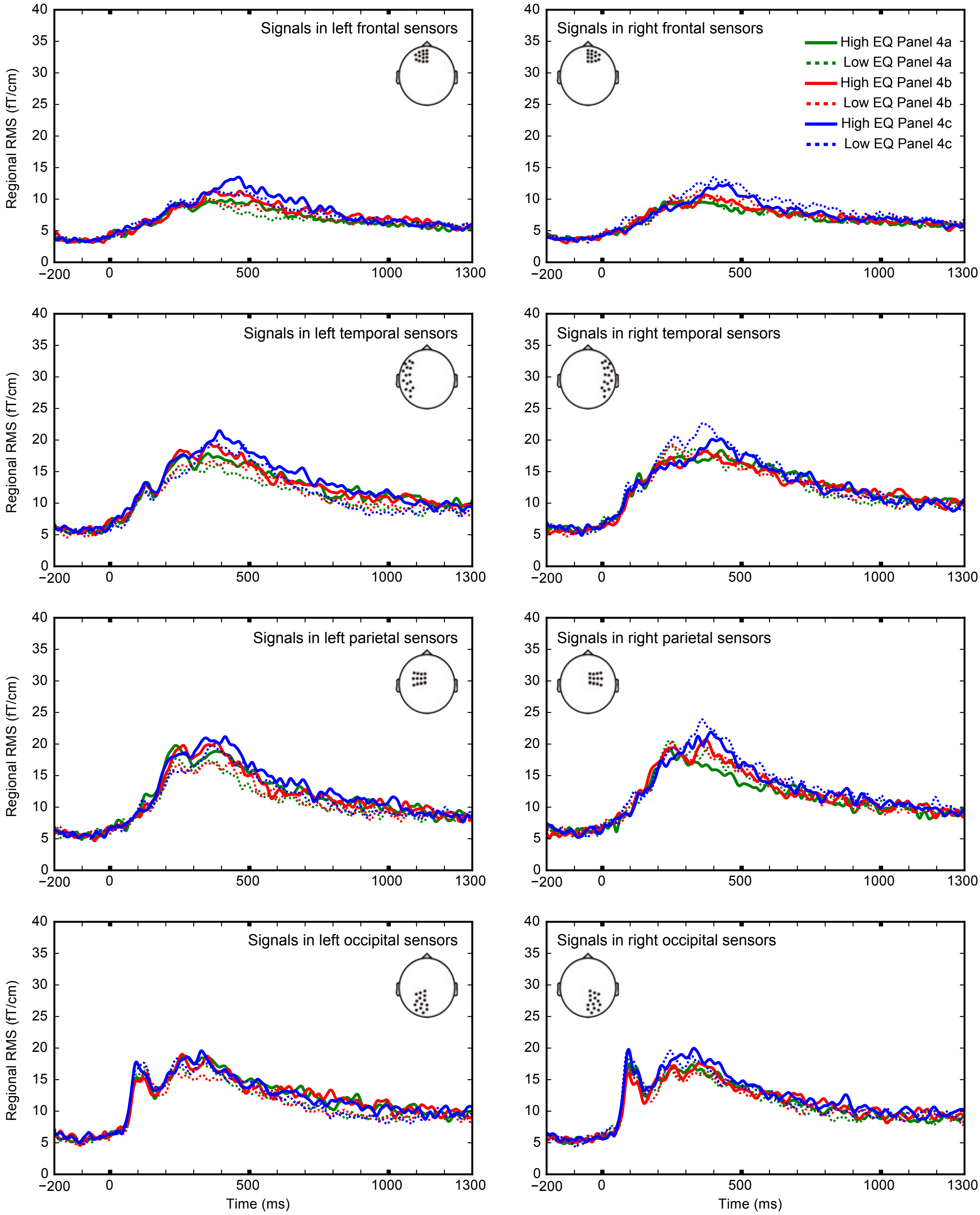
Supplementary Figure 1. Histogram of EQ scores (n=119). Participants with 41 points or more were regarded as high EQ group and participants with 25 points or less as low EQ group.



Supplementary Figure 2. Group comparisons for comic strips' comprehensibility (A) and empathic rating (B) of empathic and non-empathic endings. A five rating in the comprehensibility rating indicates that participants feel that they can easily understand the story, while a one rating indicates that they feel that they cannot understand it at all. A five rating in the empathic rating indicates that participants feel that the character sufficiently cares about the other character's feelings, while a one rating indicates that they feel that the character does not care at all. Dark and light gray bars indicate mean values of high EQ group (n=20) and low EQ group (n=23), respectively. Each circle shows the mean value of each participant. n.s.: not significant, **$p<0.01$ and ***$p<0.001$, Mann-Whitney U test.

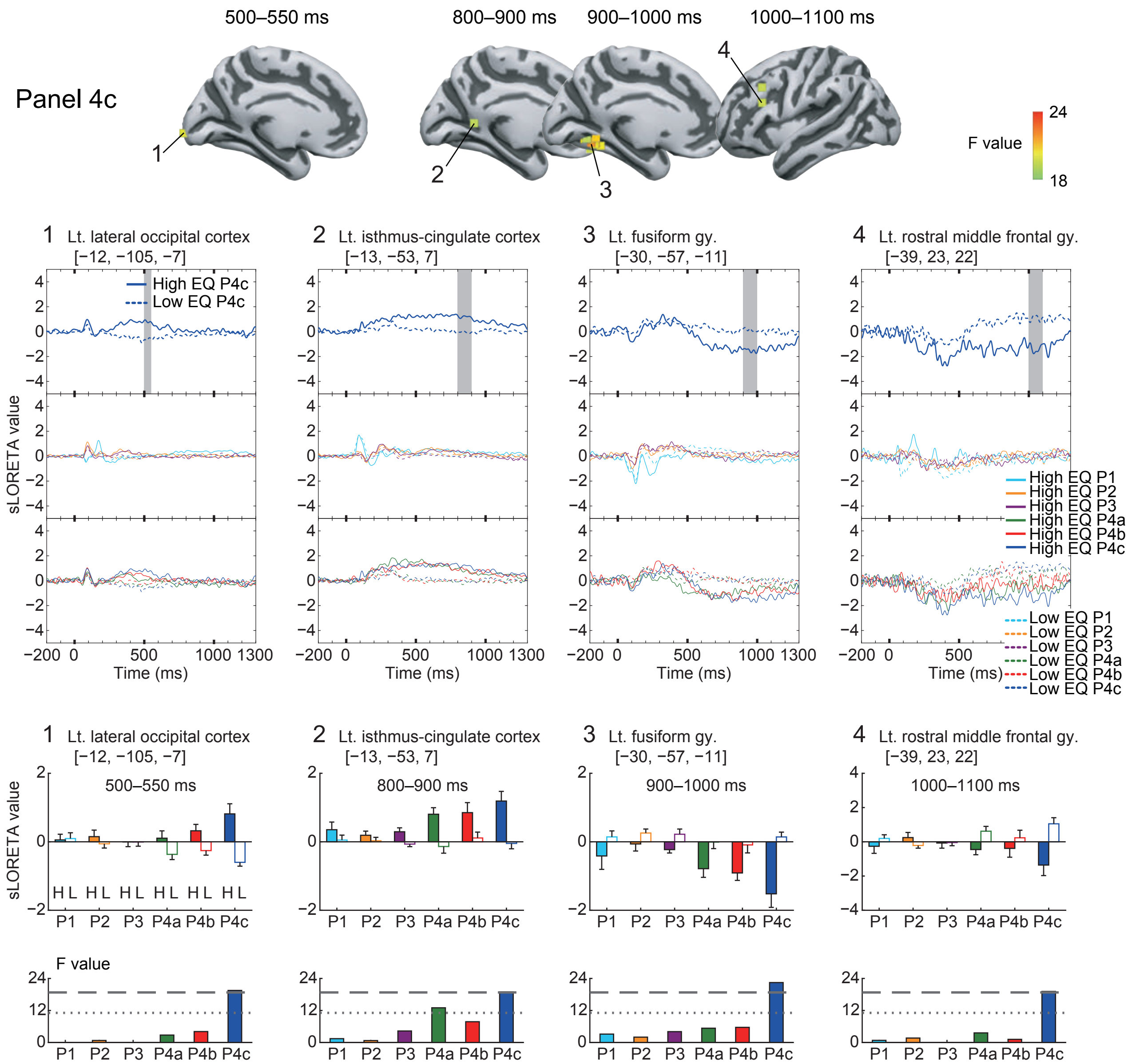


Supplementary Figure 3. Regional root-mean-square signals of planar gradiometers from −200 ms to 1300 ms. Time “0 ms” means the onset of the panel presentation. Light blue, orange, and purple lines represent Panels 1, 2, and 3, respectively. Solid and dot lines represent high and low EQ groups, respectively. Black dots in a head shape show the approximate sensor locations.

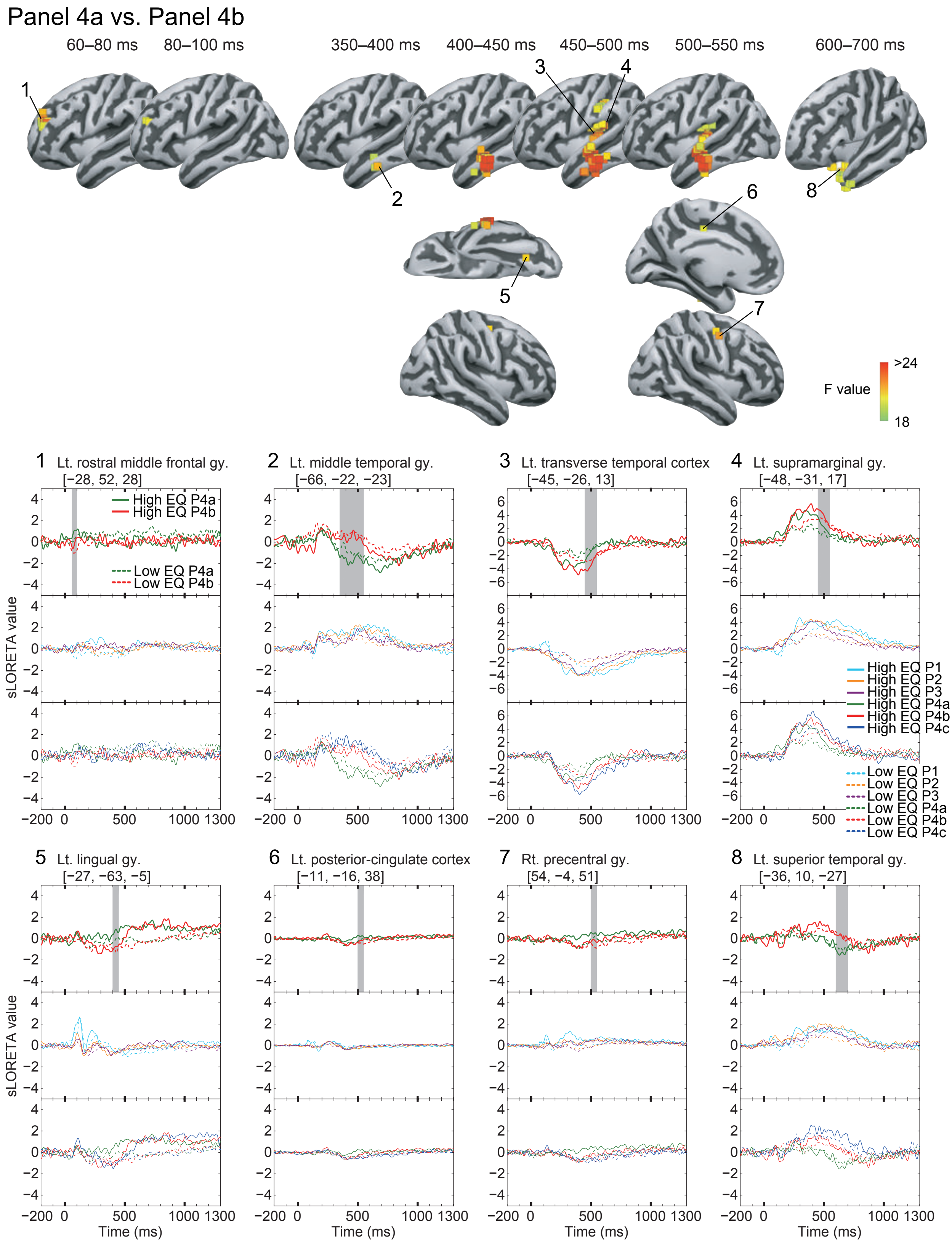


Supplementary Figure 4. Regional root-mean-square signals of planar gradiometers from −200 ms to 1300 ms. Time "0 ms" means the onset of the panel presentation. Green, red, and blue lines represent Panels 4a, 4b, and 4c, respectively. Solid and dot lines represent high and low EQ groups, respectively. Black dots in a head shape show the approximate sensor locations.

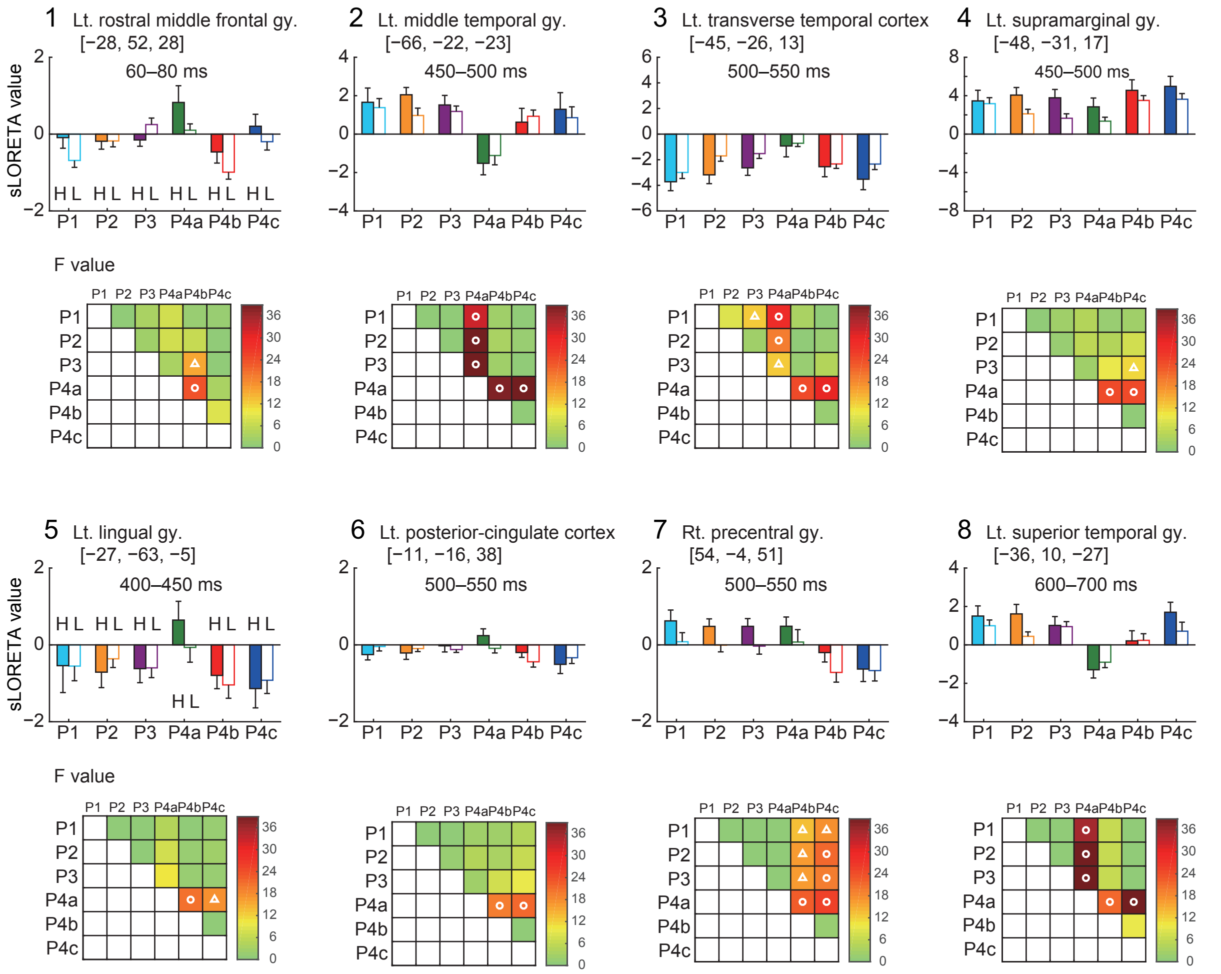
High EQ vs. Low EQ



Supplementary Figure 5. Group differences in Panel 4c. Top: Brain regions that show significant group differences (p<0.0000217) in Panel 4c. The color of each cube on the smoothed cortex represents the F value of the dipole at that position. Middle: Source waveforms at the representative regions (dipoles); the shaded area shows a significant time window at that dipole. The upper panel shows the mean sLORETA values (multiplied by 1.0e11) of conditions showing significant differences, and the middle and lower panels show the mean sLORETA values of Panels 1–3 and Panels 4a–4c, respectively. Bottom: F values for group contrasts of all conditions at the representative regions 1–4. The upper panel shows the mean sLORETA values (multiplied by 1.0e11) in the selected region and time window, and error bars represent the standard error of mean. Bar colors represent conditions (Panels), and bar styles (filled or open) represent groups (high and low EQ). The lower panel shows all F values of group contrasts. Dashed and dotted lines indicate corrected (p=0.0000217, corresponding F value=18.75) and uncorrected (p=0.001, corresponding F value=11.09) significance levels, respectively. Lt: left; Rt: right; gy: gyrus; H: high EQ group; L: low EQ group.



Supplementary Figure 6. Condition differences between Panels 4a and 4b. Top: Brain regions that show significant condition differences (p<0.0000217) between Panels 4a and 4b. The color of each cube on the smoothed cortex represents the F value of the dipole at that position; the shaded area shows a significant time window at that dipole. Middle and bottom: Source waveforms at the representative regions (dipoles). The upper panel shows the mean sLORETA values (multiplied by 1.0e11) of Panels 4a and 4b, and the middle and lower panels show the mean sLORETA values (multiplied by 1.0e11) of Panels 1–3 and Panels 4a–4c, respectively. Note that regions 3 and 4 have different vertical scales from the rest. Lt: left; Rt: right; gy: gyrus.



Supplementary Figure 7. F values for all condition contrasts at the representative regions 1–8 in Supplementary Figure 6 (the brain regions that show significant condition differences between Panels 4a and 4b). The upper panel shows the mean sLORETA values in the selected region and time window, and error bars represent the standard error of mean. Bar colors represent conditions (Panels), and bar styles (filled or open) represent groups (high and low EQ). The lower panel shows all F values of condition contrasts. White circles and triangles indicate corrected (p=0.0000217, corresponding F value=18.90) and uncorrected (p=0.001, corresponding F value=11.15) significance levels, respectively. Lt: left; Rt: right; gy: gyrus; H: high EQ group; L: low EQ group.

Supplementary Table 1. Details of comic strips. Two stories (number 5 and 8) were excluded on the basis of ratings by healthy volunteers.

Story number	Characteristics of A and B		Situation in each panel
No. 1	A: a mother	Panel 1	A son (B) notices that he has overslept.
	B: her son (lower grades)	Panel 2	His mother (A) tells (B) to change clothes quickly.
		Panel 3	(B) tries to put on his clothes in a hurry, but he cannot do it well.
	Panel 4	empathic	(A) helps (B) to put clothes on.
		non-empathic	(A) does not help (B) to put clothes on and makes a face.
		unpredictable	(A) and (B) are sleeping in the bedroom.
No. 2	A: a runner (male)	Panel 1	A runner (B) is running in the scorching sun.
	B: another runner (male) (a friend of A)	Panel 2	Another runner (A), who is a friend of (B), has already been at the resting place. (B) arrives there, and (A) says to (B), “Good job”.
		Panel 3	(B) looks tired. (A) pours a cup of drink.
	Panel 4	empathic	(A) hands the cup to (B).
		non-empathic	(A) does not hand the cup to (B), and (A) drinks it.
		unpredictable	(A) and (B) are training at a gym.

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No. 3	A: a boss (male)		Panel 1	A young staff (B) is working very hard at the desk.
	B: his young staff (male)		Panel 2	(A), the boss of (B), thinks that he will ask (B) to do a task.
			Panel 3	(A) takes many documents and comes closer to (B), then (A) notices that (B) has a lot of work.
		Panel 4	empathic	(A) does not ask (B) to do more tasks, and (A) goes back holding documents.
			non-empathic	(A) puts the documents on (B)'s desk and returns.
			unpredictable	(A) and (B) are cleaning a room.
No. 4	A: a wife		Panel 1	A wife (A) is going to a store for buying a cake.
	B: her husband		Panel 2	On (A)'s way home, she remembers her husband (B) said that he would return at 3 o'clock, and please buy two cakes by that time.
			Panel 3	(A) waits for (B) to come home, but (B) does not come home even though it has been 3 o'clock.
		Panel 4	empathic	(A) puts her and (B)'s cakes in the refrigerator.
			non-empathic	(A) does not wait for (B) to come home and eats her cake.
			unpredictable	A clock on the wall falls, and (A) is surprised.
No. 6	A: a woman (adult)		Panel 1	A woman (B) puts her bicycle in a parking lot.
	B: a woman (adult)		Panel 2	(B) accidentally knocks down other bicycles. A woman (A) comes to put her bicycle there.

(Continues to the next page)

No. 6			Panel 3	(B) begins to pick up the bicycles which fell. (A) puts her bicycle in an empty spot.
		Panel 4	empathic	(A) helps (B) to pick up the bicycles.
			non-empathic	(A) does not help (B) and leaves from there.
			unpredictable	(A) and (B) are playing in a pachinko* parlor.
				* A slot machine
No. 7	A: a man (adult)		Panel 1	A man (A) has just got on a train with heavy bags in both hands.
	B: an old woman		Panel 2	(A) sits in the last vacant seat. He looks tired.
			Panel 3	An old woman (B) with a walking stick looks for a seat and comes closer to (A).
		Panel 4	empathic	(A) gives his place to (B).
			non-empathic	(A) is sitting with facing down and does not offer his place to (B).
			unpredictable	(A) and (B) are crossing each other in front of a restaurant.
No. 9	A: a man (adult)		Panel 1	A man (A) hurries to the station.
	B: an old man		Panel 2	(A) gets in line behind an old man (B) to buy a ticket.
			Panel 3	(B) is in trouble because he does not know how to buy a ticket. (A) is worried about time.
		Panel 4	empathic	(A) approaches (B) and helps him.

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No. 9		Panel 4	non-empathic	(A) moves from behind (B) to another ticket vending machine.
			unpredictable	(A) and (B) pick bread at a bakery.
No. 10	A: a woman (adult)	Panel 1		A woman (A) is sitting on a train seat, and a man (B) comes there to look for a seat.
	B: a man (adult)	Panel 2		(B) sits down near (A).
		Panel 3		(B) suddenly gets a nosebleed, and (A) notices it.
		Panel 4	empathic	(A) hands a tissue to (B).
			non-empathic	(A) goes away from (B).
			unpredictable	(A) is sitting on a train seat and (B) comes there to look for a seat. *This panel is identical to Panel 1.*
No. 11	A: a woman (adult)	Panel 1		A woman (A), immediately after getting off a train, is heading for the station exit in a hurry.
	B: an old woman	Panel 2		An old woman (B) looks distressed as she cannot climb upstairs because her bag is heavy.
		Panel 3		(A) notices (B) in front of the stairs.
		Panel 4	empathic	(A) approaches (B) and helps her.
			non-empathic	(A) goes upstairs without helping (B).
			unpredictable	A dog dashes down in front of (A) and (B).

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No. 12	A: a son (adult)		Panel 1	An old mother (B) is puzzled by her mobile phone.
	B: his old mother		Panel 2	(B) calls her son (A).
			Panel 3	(B) asks (A) to tell her how to send an e-mail with her mobile phone.
		Panel 4	empathic	(A) sits next to (B) and explains how to do it.
			non-empathic	(A) just hands (B) a user’s manual of the mobile phone.
			unpredictable	(A) and (B) are eating udon.
No. 13	A: a grandson (high school)		Panel 1	A grandfather (B) asks his grandson (A) for fishing.
	B: his grandfather		Panel 2	(B) and (A) are fishing at a wharf. (B) experiences a strong fishing bite, but (A) does not experience any bite.
			Panel 3	(B)’s rod is pulled strongly by a big fish and the fish is about to get away. At that time (A) experiences a weak fishing bite.
		Panel 4	empathic	(A) holds (B)’s rod and helps him.
			non-empathic	(A) does not help (B), and instead catches a small fish. (B)’s rod is broken and the big fish goes away.
			unpredictable	(A) and (B) are sitting and waiting for a bite.
No. 14	A: a husband B: his wife		Panel 1	A wife (B) is back home and looks freezing.

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No. 14			Panel 2	Her husband (A) is sitting under a kotatsu* in a living room and puts hot water in a teapot. He does not notice (B)'s coming home. * A traditional heating system in Japan— a table with an electric heater attached to the underside of a frame
			Panel 3	(B) enters the room and gets under the kotatsu. She still looks freezing. (A) notices her coming. (A) puts a warm tea in a cup.
		Panel 4	empathic	(A) gives a cup of tea to (B) first.
			non-empathic	(A) does not offer a cup of tea to (B) and drinks his tea.
			unpredictable	A cat is popping out of the kotatsu.
No. 15	A: a granddaughter (adult)		Panel 1	A granddaughter (A) and her grandmother (B) are eating in a food court.
	B: her grandmother		Panel 2	(A) has finished eating before (B).
			Panel 3	(B) has finished eating. (A) stands up with (A)'s tray to clear the table.
		Panel 4	empathic	(A) carries (A)'s and (B)'s trays together.
			non-empathic	(A) carries only (A)'s tray. (B) staggers to her feet with a walking stick.
			unpredictable	(A) and (B) are eating in the food court. *This panel is similar to Panel 1, but the word balloons are erased.*
No. 16	A: a wife B: her husband		Panel 1	A husband (B) tells his wife (A) that he will change his hairstyle. (A) lightly asks (B) to choose a cooler hairstyle.

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No. 16		Panel 2	(A), waiting for (B), imagines that he looks cool.
		Panel 3	(B)'s hair look afro and he asks (A) whether his new hairstyle is good. (A) realizes that his hairstyle is not as cool as she had imagined.
	Panel 4	empathic	(A) praises (B)'s hairstyle with her thumbs up.
		non-empathic	(A) makes a cross mark with her arms and hands* to tell (B) that his hairstyle is not good. * A Japanese gesture which means "no" or "not good"
		unpredictable	(A) and (B) are in a bookstore. (B)'s hairstyle is the same as in Panel 1.
No. 17	A: a mother	Panel 1	A son (B) is studying very hard for an examination.
	B: her son (elementary school)	Panel 2	(B) takes the examination.
		Panel 3	(B) got 100 marks in the examination. (B) shows the examination paper to his mother (A), who is folding laundry.
	Panel 4	empathic	(A) pats (B)'s head and praises him.
		non-empathic	(A) does not praise (B) and keeps doing the housework.
		unpredictable	(A) and (B) relax under a kotatsu.
No. 18	A: a father	Panel 1	A father (A) heads to the entrance of the zoo hand in hand with his son (B).
	B: his son (preschool)	Panel 2	(A) and (B) go to a lion's cage. (A) and (B) are scared of the lion.

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No. 18			Panel 3	The lion roars at (A) and (B).
		Panel 4	empathic	(A) hugs (B) to make him feel safe.
			non-empathic	(A) runs away from the lion. (B) is left behind.
			unpredictable	(A) heads to the entrance of the zoo hand in hand with (B). *This panel is similar to Panel 1, but the word balloons are erased.*
No. 19	A: a man (adult)		Panel 1	A man (A) is reading a book on a bench. A girl (B) is walking with a balloon.
	B: a girl (lower grades)		Panel 2	(B)'s balloon gets caught in a tree by accident.
			Panel 3	(A) notices that (B) is crying because her balloon is on the tree.
		Panel 4	empathic	(A) stands up and tries to get (B)'s balloon back.
			non-empathic	(A) puts on his earphones and begins to listen to music.
			unpredictable	(A) is reading a book on the bench. (B) is walking with a book. *This panel is similar to Panel 1 with the exception that the balloon is replaced by a book.*
No. 20	A: a woman (adult)		Panel 1	A woman (A) is waiting for a train at the station.
	B: a girl (preschool)		Panel 2	The train is approaching. A girl (B) is walking by (A). (B) is looking for her mother.
			Panel 3	(B) begins to cry, and (A) just notices (B). The train stops, and the door is open.
		Panel 4	empathic	(A) approaches (B) and helps her. The door of the train closes.

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No. 20	Panel 4	non-empathic	(A) leaves (B) and rushes to the train.
		unpredictable	(A) and (B) are sitting on a bench at the station, a little away from each other.
No. 21	A: a father B: his daughter (junior high school)	Panel 1	A daughter (B) shows her father (A) the examination paper with 30 points. (A) scolds (B) and tells her to study hard.
		Panel 2	(B) is studying very hard. (A) comes and sees (B) studying behind her back.
		Panel 3	(B) gets 50 marks at the next examination. (B) shows (A) the examination paper with disappointment.
	Panel 4	empathic	(A) pats (B)'s head and comforts her.
		non-empathic	(A) sighs and turns his back without comforting (B).
		unpredictable	(A) is playing a video game, and (B) is eating cup noodles.
No. 22	A: a mother	Panel 1	A mother (A), holding her daughter's (B), is walking in a hurry.
	B: her daughter (preschool)	Panel 2	(B) stumbles and falls on the way.
		Panel 3	(B) begins to cry and complains of pain.
	Panel 4	empathic	(A) approaches (B) and soothes her.
		non-empathic	(A) still in a hurry pulls (B)'s hand without being concerned about (B)'s complaint.
		unpredictable	(B) goes ahead of (A) and pulls (A)'s hand.