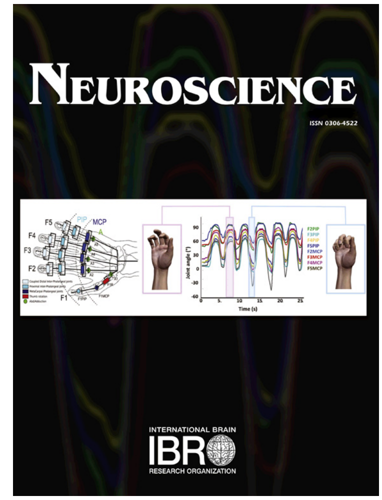

Role of spontaneous brain activity in explicit and implicit aspects of cognitive flexibility under socially conflicting situations: a resting-state fMRI study using fractional amplitude of low-frequency fluctuations

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Title: Role of spontaneous brain activity in explicit and implicit aspects of cognitive flexibility under socially conflicting situations: a resting-state fMRI study using fractional amplitude of low-frequency fluctuations

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Abbreviations: ACC, anterior cingulate cortex; ASD, autism spectrum disorder; CFS, Cognitive Flexibility Scale; DPARSFA, Data Processing Assistant for Resting-state fMRI Advanced Edition; EPI, echo-planar imaging; FA, flip angle; fALFF, fractional amplitude of low-frequency fluctuations; fMRI, functional magnetic resonance imaging; FOV, field of view; FWE, family-wise error; IAT, Implicit Association Test; LPFC, lateral prefrontal cortex; MNI, Montreal Neurological Institute; NEO-PI-R, Revised NEO Personality Inventory; REI, Rational-Experiential Inventory; RS-fMRI, resting-state functional magnetic imaging; SCID I, Structured Clinical Interview for DSM-IV Axis I Disorders; TE, echo time; TR, repetition time; 3D-MPRAGE, 3-dimensional magnetization-prepared rapid gradient-echo

Abstract

We are constantly exposed to socially conflicting situations in everyday life, and cognitive flexibility is essential for adaptively coping with such difficulties. Flexible goal choice and pursuit are not exclusively conscious, and therefore cognitive flexibility involves both explicit and implicit forms of processing. However, it is unclear how individual differences in explicit and implicit aspects of flexibility are associated with neural activity in a resting state. Here, we measured intrinsic fractional amplitude of low-frequency fluctuations (fALFF) by resting-state functional magnetic imaging (RS-fMRI) as an indicator of regional brain spontaneous activity, together with explicit and implicit aspects of cognitive flexibility using the Cognitive Flexibility Scale (CFS) and Implicit Association Test (IAT). Consistent with the dual processing theory, there was a strong association between explicit aspects of flexibility (CFS score) and "rationalism" thinking style and between implicit aspects (IAT effect) and "experientialism." The level of explicit flexibility was also correlated with fALFF values in the left lateral prefrontal cortex, whereas the level of implicit flexibility was correlated with fALFF values in the right cerebellum. Furthermore, the fALFF values in both regions predicted individual preference for flexible decision-making strategy in a vignettes simulation task. These results add to our understanding of the neural mechanisms underlying flexible decision-making for solving social conflicts. More generally, our findings highlight the utility of RS-fMRI combined with both explicit and implicit psychometric measures for better understanding individual differences in social cognition.

Keywords: decision-making; cerebellum; prefrontal cortex; rationalism; experientialism

INTRODUCTION

To support your family, would you prioritize profit and monetary gain despite being treated unfairly? We are constantly exposed to such psychologically, ethically, and socially conflicting situations in everyday life, and cognitive flexibility is necessary for adaptive coping (Milders et al., 2008; Ravizza and Carter, 2008; Wakusawa et al., 2015). The dual processing theory posits two different modes of processing; one is explicit, rational, analytic, and conscious, and the other is implicit, experiential, intuitive, and unconscious (Evans, 2008; Lieberman, 2007). Flexible goal choice and pursuit are not exclusively rational and conscious (Custers and Aarts, 2010), but may also heavily rely on experiential learning and implicit processing. In this line, a recent article argued that individual differences in thinking styles (e.g., rational versus experiential) represent discrete behavioral patterns of flexible adaptation (Kozhevnikov et al., 2014).

To date, task functional magnetic resonance imaging (fMRI) studies have shown that diverse brain regions are involved in flexible decision-making. For example, previous studies on healthy population have shown that frontoparietal network plays a key role in perceptual aspect of flexible behavior (Douw et al., 2016; Kim et al., 2011; Sekutowicz et al., 2016; Smith et al., 2004). In addition, clinical studies reported that patients with psychiatric disorders [e.g., autism spectrum disorder (ASD), obsessive-compulsive disorder] showed altered activation in brain regions, such as lateral prefrontal cortex (LPFC), inferior parietal cortex, ventral striatum, anterior cingulate cortex (ACC), and cerebellum, compared to healthy subjects while performing tasks related to flexibility, which might be associated with their impaired cognitive-behavioral flexibility (Geurts et al., 2009; Gu et al., 2008; Zastrow et al., 2009). However, it is unclear how individual differences in trait-level explicit and implicit aspects of flexibility are associated with neural activity in a resting state.

Resting-state neuroimaging modalities can provide useful information regarding stable neural characteristics without being confounded by components unique to functional tasks (He et al., 2014; Karoly et al., 2013; Lai and Wu, 2015; Raichle, 2010, Xu et al., 2015). For this reason, intrinsic spontaneous brain activity measured by resting-state fMRI (RS-fMRI) has been widely used in recent years to explore the neural correlates of dispositional traits (Fox and Raichle, 2007; Markett et al., 2013; Wei et al., 2014). Furthermore, individual differences in spontaneous brain activity may reflect distinct experiences and learning histories (Lewis et al., 2009; Vahdat et al., 2011). Thus, we hypothesized that dispositional variation in cognitive flexibility could be explained by regional differences in the intensity of spontaneous brain activity. Here we focused on fractional amplitude of low-frequency fluctuations (fALFF) as an indicator of the intensity of spontaneous brain activity (Zou et al., 2008). The fALFF approach improves the ALFF approach, with better sensitivity and specificity for detecting spontaneous brain activity (Zou et al., 2008). For instance, the fALFF is found to correlate with individual differences in empathy (Cox et al., 2012), Stroop task performance (Takeuchi et al., 2015), and personality traits (e.g., extraversion) (Wei et al., 2014).

Among the brain areas related to flexible decision-making, the LPFC has been consistently reported to play vital roles in deliberate reasoning by interpreting incoming information during explicit reinforced leaning, capacities crucial for cognitive flexibility (Fujino et al., 2016; Koechlin et al., 2003; Oaksford, 2015; Tanji et al., 2007). In contrast, the ventral striatum is considered essential for implicit leaning by trial and error (Ito et al., 2015; Wilkinson et al., 2014). In addition, cerebellar activity has been observed repeatedly during implicit social emotional learning tasks, suggesting that the role of the cerebellum in implicit processing may not be limited to perceptual domains but also extend to cognitive/social domains (Lam et al., 2013; Van Overwalle et al., 2014). Based on the close association of cognitive flexibility with such learned processing capacities (Kehagia et al., 2010), we predicted that explicit aspects of flexibility would be associated with spontaneous brain activity in areas important for explicit learning, whereas implicit aspects of flexibility would be associated with activity in areas important for implicit learning.

In this study, we first estimated individual explicit aspects of flexibility using the self-report Cognitive Flexibility Scale (CFS; Martin and Rubin, 1995) and implicit aspects by the Implicit Association Test (IAT; Greenwald et al., 1998). Subsequently, we identified brain regions where spontaneous brain activity (fALFF values) was associated with dispositional variation in explicit or implicit aspects of flexibility. We also assessed the relationships between these two types of flexibility and individual differences in thinking style and personality traits. Finally, to confirm that the identified spontaneous brain activity patterns influence practical flexible decision-making, we applied a vignettes simulation task involving realistic socially conflicting situations (Brady and Wheeler, 1996), and performed regression analyses between task scores and regional brain activity measures.

We found that the level of explicit flexibility was associated with the rationalism thinking style and fALFF values in the left lateral prefrontal cortex, whereas the level of implicit flexibility was associated with experientialism and fALFF values in the right cerebellum. Furthermore, the fALFF values in both regions predicted individual preference for flexible decision-making strategy in a vignettes simulation task. These results add to our understanding of the neural mechanisms underlying flexible decision-making for solving social conflicts.

EXPERIMENTAL PROCEDURES

Participants

Twenty-two volunteers recruited from among undergraduate and graduate students participated in this study [mean age: 21.4 ± 1.2 (*S.D.*) years; 6 females; 20 right-handed]. The sample size was determined based on previous fMRI studies of individual differences in attitudes or behavior that used IAT (Berlingeri et al., 2016; Suslow et al., 2010; Yi et al., 2014). No volunteer met criteria for any psychiatric disorder according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I), and none had a history of head trauma, neurological illness, serious medical or surgical illness, or substance abuse. Predicted IQ was 104.1 ± 8.3 as estimated using the Japanese Version of the National Adult Reading Test short form (Matsuoka and Kim, 2006).

This study was approved by the Committee on Medical Ethics of Kyoto University and conducted in accordance with The Code of Ethics of the World Medical Association. After a complete description of the study, written informed consent was obtained from each participant.

Explicit and implicit aspects of flexibility

Cognitive Flexibility Scale (CFS)

As stated in the Introduction, we were interested in the role of cognitive flexibility particularly within a social context. Thus, we used the CFS, one of the most widely used questionnaires for assessing individual flexible choice tendencies in response to social conflict (Martin and Rubin, 1995; Oshiro et al., 2016). A large number of previous studies have used CFS to assess cognitive flexibility (Cranmer and Martin, 2015; Curran and Andersen, 2017), and its usefulness for assessing impairment of this ability in various psychiatric disorders such as ASD and anxiety disorders has also been reported (Lee and Orsillo, 2014; Okuda et al., 2017). The CFS is a self-report scale consisting of 12 items, each rated on a 6-point Likert scale. The scale evaluates participants' awareness that there are alternative ways of behaving and their willingness and perceived ability to be flexible. Item responses are summed to an overall score ranging from 12 to 72, with higher scores indicating greater cognitive flexibility.

Implicit Association Test (IAT)

We applied the Implicit Association Test (IAT; Greenwald et al., 1998) to measure implicit aspects of flexibility (Fig. 1). The IAT is a widely validated approach to measuring individual differences in implicit aspects of personality and social cognition (Lane et al., 2007; Suslow et al., 2010, 2017). The IAT comprises a series of response time tasks that require participants to classify word stimuli that appear at the lower portion of a computer screen into corresponding categories and paired attributes appearing in the upper left or right. The basic assumption of the IAT is that past learning experiences can be represented by the facilitation of information processing of associated concepts as measured by rate of processing and response time (Greenwald et al., 1998). Response times are expected to be shorter when paired target category and attribute labels match a person's automatic associations. Conversely, response times are expected to be longer when paired target category and attribute labels contradict automatic associations.

To estimate individual differences in implicit aspects of flexibility under socially conflicting situation, the present IAT evaluated the extent to which participants associated fairness vs. unfairness (target categories) with profit vs. loss (attribute categories). In social circumstances, we often have to make difficult moral tradeoffs to maximize social welfare. It is well established that people are intrinsically averse to unfairness/inequality (in particular disadvantage type) (Fehr and Schmidt, 1999; Haruno and Frith, 2010). However, successfully navigating social life often requires self-regulation in the face of perceived unfairness (Crocket, 2009). For example, it is often necessary to accept unfair offers to maximize profit/welfare for oneself as well as others (Crockett et al., 2008; Reilly, 1998; Takahashi et al., 2012). Therefore, socially flexible individuals who have developed, through social complexity, sophisticated strategies that balance competition and cooperation to achieve "deep pragmatism" (higher social and reproductive success) are predicted to have formed a relatively weak automatic association between unfairness and negative valence. In other words, individuals who cannot easily separate themselves from moral percepts and have low tolerance of unfairness would tend to show much slower response times in the incongruent condition (i.e., fairness/loss for one response key, unfairness/profit for the other response key) compared to the congruent condition (i.e., unfairness/loss for one response key; fairness/profit for the other response).

Four items were selected as the to-be-sorted stimuli for each of the concepts. Stimuli from the fairness and unfairness categories were, respectively *honesty, equality, neutrality, conscientiousness*, and *deviation, difference, irregularity, violation*. Stimuli from the categories profit/loss were *acquirement, benefit, positive, winning*, and *debt, waste, negative, cost*, respectively. The present IAT comprised seven blocks according to the standard procedures (Greenwald et al., 1998): (block 1) 20 practice trials with target categories only; (block 2) 20 practice trials with attribute categories only; (block 3) 20 practice trials for a congruent block with both target and attribute categories; (block 4) 40 test trials for a congruent block with both target and attribute categories; (block 5) 20 practice trials with target categories only in reversed positions; (block 6) 20 practice trials for an incongruent block with both reversed target categories and the attribute categories; and (block 7) 40 test trials for an incongruent block with both reversed target categories and the attribute categories. Participants were told they would be making a series of category judgments. On each trial, a stimulus word was displayed in the center of a computer screen. Category labels were displayed on the left and right sides of the window. Participants used the letter a on the left side and the letter l on the right side of the keyboard for their responses. They were told to be as accurate as possible, while also going as quickly as possible. An incorrect response led to a feedback of red "×." An inter-trial interval of 300 ms was used. The IAT was conducted using E-Prime software (Psychology Software Tools, Inc., Pittsburgh, PA, USA).

Computation of the IAT effect as Greenwald's D score was conducted based on the improved scoring algorithm (Greenwald et al., 2003; Lane et al., 2007). No subjects showed latencies less than 300 ms in more than 10% of trials. Trials with latencies greater than 10000 ms were deleted. Each error latency was replaced by the mean + twice the *S.D.* of correct latencies within the same block. The mean latency in the trials of block 3 was subtracted from that of block 6. Similarly, the mean latency in the trials of block 4 was subtracted from that of block 7. Then, each difference score was divided by its associated trial *S.D.* of response latencies. The IAT effect (as measured by D score) was computed as the average of these two scores. Thus, a lower IAT effect implies greater implicit flexibility.

Thinking styles and personality traits

Rational-Experiential Inventory (REI)

We used the Rational-Experiential Inventory (REI; Naito et al., 2004; Pacini and Epstein, 1999) to measure individual differences in thinking styles. The REI reliably measures an individual's preference for two styles of thinking: need for cognition (rationalism) and faith in intuition (experientialism). There are 40 questions with 5-point response scales (20 each for rationalism and experientialism). All scores are averaged to provide variables ranging from 1 to 5, with a higher score reflecting a greater tendency to endorse the construct measured.

Revised NEO Personality Inventory (NEO-PI-R)

We administered the Japanese version of the Revised NEO Personality Inventory (NEO-PI-R) (Costa and MacCrae, 1992; Shimonaka et al., 1998), one of the most widely used questionnaires for assessing broad personality traits. This self-report questionnaire comprises 240 items and contains five dimensional scales (neuroticism, extraversion, openness, agreeableness, and conscientiousness) that correspond to a five-factor personality trait model. Participants are asked to respond to each item by designating answers from 0 (strongly disagree) to 4 (strongly agree). NEO-PI-R results are presented as T scores with a mean of 50 and standard deviation (*S.D.*) of 10. Higher scores indicate higher levels of the particular trait.

Way of response in socially conflicting situations

To further examine flexibility, we applied a simulation (vignettes) task rather than additional psychological questionnaires. This vignettes task was developed by Brady and Wheeler (1996), and involves socially conflicting situations that may happen in natural settings outside the laboratory. Brady and Wheeler (1996) categorized responses as “utilitarian” or “formalist,” a well-known response contrast in socially conflicting situations. Utilitarian refers to the tendency to assess ethical situations flexibly prioritizing their consequences for people (result-oriented), while formalist represents the human tendency to assess ethical situations in terms of their consistent conformity to patterns, rules, or some other formal feature.

This task simultaneously monitors two forms of response to the vignettes: (1) the preference for a particular kind of solution and (2) the preference for reasoning in support of that solution. Participants are asked to read and simulate the seven vignettes about conflicting situation in daily life as a protagonist (the authors first adopted eight vignettes that elicited the greatest variation in responses during pilot studies, but one vignette concerning capital punishment was later dropped from analysis because the utilitarian−formalist distinction was unclear). Each vignette was followed by four statements, each representing a different way of thinking about/responding to the situation. Subjects were asked to rate each of the four statements on a scale of 1 to 7 according to extent the statement fits their way of thinking/behavioral response. These four statements represent possible individual decision types in a form of a 2 × 2 matrix [(A) utilitarian solution/utilitarian reasoning, (B) utilitarian solution/formalist reasoning, (C) formalist solution/utilitarian reasoning, (D) formalist solution/formalistic reasoning].

Higher scores indicate stronger preference for a specific option. Based on the previous study (Brady and Wheeler, 1996), we computed each participant's total tendency toward a particular solution-rationale combination by calculating the average of the participant's responses to each combination for all seven vignettes. The following vignette is an example of this task.

"You work for a state auditor's office which has a policy against accepting gifts from anyone with whom the state may have business. Your birthday is in one week, and a very good friend of your father's has just dropped by with a pair of fine leather gloves and a birthday card. This person also works for a construction firm which has built city facilities in the past . . ."

(A) Both the person and your father might be upset if you do not accept the gift.

(B) One should respect another's good intentions.

(C) The general welfare of the public is best served if you and other state employees remain independent of outside influences.

(D) Employees have an obligation to follow state policy.

fMRI data acquisition

All participants underwent a resting state MRI scan. During scanning, participants were instructed to keep their eyes open, stare passively at a fixation cross back-projected onto a screen through a built-in mirror, relax their mind, and not to sleep. Functional images were obtained by a T2*-weighted gradient-echo echo-planar imaging (EPI) sequence using a 3T MRI scanner equipped with a 32-channel phased-array head coil (Verio, Siemens, Erlangen, Germany). The image acquisition parameters were as follows: repetition time (TR) = 2.5 s, echo time (TE) = 29 ms, flip angle (FA) = 90°, field of view (FOV) = 192 × 192 mm, matrix = 64 × 64, and 38 interleaved axial slices of 3-mm thickness without gaps (3-mm cubic voxels). The first two volumes were not saved to allow for signal stabilization and the subsequent 244 volumes were acquired over 10 minutes and 10 seconds. Structural scans were also acquired using T1-weighted 3-dimensional magnetization-prepared rapid gradient-echo (3D-MPRAGE) sequences (TE = 3.51 ms, TR = 2000 ms, TI = 990 ms, FOV = 256 × 256 mm, matrix = 256 × 256, resolution = 1.0 × 1.0 × 1.0 mm^3, and 208 total axial sections without intersection gaps).

fMRI data preprocessing and fALFF calculation

Image processing was carried out using SPM8 (Wellcome Trust Center for Neuroimaging, London, UK) in MATLAB (MathWorks, Natick, MA, USA) and SPM8 extension software DPARSFA (Data Processing Assistant for Resting-state fMRI Advanced Edition, http://rfmri.org/DPARSF) (Yan and Zang, 2010). In brief, for each subject, the skin–skull-stripping procedure was performed using the brain extraction tool from FSL (http://www.fmrib.ox.ac.uk/fsl/) so that these parts were not treated as the outer edge of the brain parenchyma in the processing procedures. Images were manually oriented to the AC-PC line. Functional images were corrected for differences in slice-acquisition timing and were then spatially realigned to correct for head motion. T1-weighted images were co-registered to EPI images and segmented into gray matter, white matter, and cerebrospinal fluid. To reduce the effects of physiological processes and head motion, we regressed out the motion parameters, white matter signal, cerebrospinal fluid signal, and global signal. The global signal is considered to reflect a combination of physiological processes (such as cardiac and respiratory fluctuations) and therefore was treated as a covariate to control for such factors. Although there is an ongoing debate about whether regressing out the global signal is beneficial or affects data detrimentally (Wong et al., 2012), we applied global signal regression because previous studies have also shown that the global signal regression is effective in controlling movement-related artifacts in RS-fMRI data analyses (Klein et al., 2017; Power et al., 2012; Yan et al., 2013). Functional images were spatially normalized to Montreal Neurological Institute (MNI) space (voxel size: 3 × 3 × 3) and then smoothed using a Gaussian kernel with a full width at half maximum of 6 mm in the x, y, and z axes. No participant exhibited head motion of more than 3.0 mm in any direction or 3.0° rotation throughout the resting-state scans.

Subsequently, the fALFF calculation was performed using DPARSFA. Although ALFF appears to be a promising method for detecting spontaneous brain activity, certain cisternal areas have also shown significantly higher ALFF, which is likely to occur because of physiological noise (Zou et al, 2008; Wang et al., 2012). Thus, the fALFF approach was developed to selectively suppress the artifacts from non-specific brain areas, thereby significantly improving the sensitivity and specificity of spontaneous brain activity detection (Zou et al, 2008). Consequently, we focused on fALFF in this study. Based on previous studies (Chyzhyk et al., 2015; Cox et al., 2012; Yu et al., 2017), the fALFF value of each voxel was calculated for each participant. For the time series of each voxel, the sum of the amplitudes within a low-frequency range (0.01–0.1 Hz) was extracted. The fALFF was then computed as the fractional sum of the amplitudes within the low-frequency range divided by the sum of amplitudes across the entire frequency range (Chyzhyk et al., 2015; Cox et al., 2012; Yu et al., 2017). Based on previous studies (Lai and Wu, 2015; Wei et al., 2014), the fALFF of each voxel was divided by the global mean fALFF value to standardize data across participants (the values were also obtained using the DPARSFA toolbox).

Data analyses

Correlations between aspects of flexibility and thinking styles/personality traits

To examine if explicit and implicit aspects of flexibility are associated with specific thinking styles and personality traits, we performed correlational analyses between flexibility scores (CFS scores and IAT effect) and REI scores/T scores of five domains of NEO-PI-R. Correlation analysis was also performed between explicit aspects of flexibility (the CFS scores) and implicit aspects of flexibility (the IAT effect). None of our psychological measures datasets (scores from the CFS, IAT, REI, NEO-PI-R, and vignettes task) statistically violated the assumption of normality (all, $p > 0.05$, Shapiro–Wilk test). Behavioral data were analyzed using SPSS 21 (IBM Corp., Armonk, NY, USA). Results were considered statistically significant at $p < 0.05$ (two-tailed).

Brain regions with fALFF values associated with explicit or implicit aspects of flexibility

To explore the brain regions where the fALFF values were associated with individual differences in explicit and implicit aspects of flexibility (i.e., CFS scores and the IAT effect, respectively) throughout the whole brain, we performed multiple regression analyses separately using a general linear model framework in SPM8 (Worsley and

Friston, 1995). Age and gender were entered into the model as covariates of no interest. Clusters that survived the family-wise error (FWE) correction for multiple comparisons with a cluster-level $p < 0.01$ (height threshold $T = 2.5$) were reported. We interpreted the anatomical location of the clusters by consulting the Talairach Daemon database (http://www.talairach.org), the Anatomic Automatic Labeling toolbox, (Tzourio-Mazoyer et al., 2002) and neuroanatomy atlas textbooks (Duvernoy, 1991; Talairach and Tournoux, 1988).

Further examination of regional spontaneous brain activities associated with explicit/implicit aspects of flexibility

To confirm that identified regional brain activities practically influence flexible decision-making in socially conflicting situations, we performed regression analyses between the regional fALFF values (independent variables) and the scores measured on the vignettes task (dependent variables). As for the fALFF values, the parameter estimates were extracted as first eigenvariate from the significant clusters using the VOI function in SPM8. Results were considered statistically significant at $p < 0.05$ (two-tailed).

RESULTS

The mean D score (IAT effect) across all subjects was 0.66 ± 0.35 (*S.D.*), which is consistent with the notion that healthy individuals draw an automatic association between unfairness and negative valence. Individual D scores did not correlate with the CFS scores (explicit aspects of flexibility) ($r = 0.16$, $p = 0.49$). There was a strong correlation between individual CFS scores and the level of rationalism ($r = 0.67$, $p < 0.001$) and between the IAT effect and the level of experientialism ($r = -0.56$, $p = 0.006$) (Fig. 2). The CFS scores were positively correlated with conscientiousness ($r = 0.56$, $p = 0.007$), while we did not find any significant correlations between IAT effects and the five factor scores on the NEO-PI-R (Table 1).

Fig. 3 and Table 2 present the brain regions where fALFF values were correlated with CFS scores and IAT effects, respectively. The CFS scores were positively correlated with fALFF values in the left LPFC, including the middle/superior frontal gyrus. On the other hand, the IAT effect was negatively correlated with fALFF values in the right cerebellum (extending into the temporal lobe). In other words, the participants with higher fALFF values in this area showed higher implicit aspects of flexibility. We did not find any significant areas where the fALFF values were negatively correlated with CFS scores or positively correlated with the IAT effect.

Finally, to confirm that these brain activities practically predict the response type in socially conflicting situations, we performed further analyses using the realistic vignettes task. First, we performed simple linear regression analyses between scores for each decision type (A−D) and fALFF values in the left LPFC and right cerebellum. The level of preference for decision type B (utilitarian solution/formalist reasoning) was positively correlated with fALFF values in both the left LPFC ($r = 0.44$, $p = 0.041$) and right cerebellum ($r = 0.48$, $p = 0.023$) (Fig. 4). The preference scores for other decision types (A, C, D) were not significantly correlated with fALFF values in either the left LPFC or right cerebellum (all $p > 0.08$). Thus, we performed a multiple linear regression analysis including the individual preference scores for decision type B (dependent variable) and fALFF values in the left LPFC and right cerebellum (independent variables). The result showed that the fALFF values in both regions were crucial variables for explaining the level of preference for decision type B ($R^2 = 0.51$, left LPFC; standardized coefficient $\beta = 0.53$, $p = 0.004$, right cerebellum; standardized coefficient $\beta = 0.57$, $p = 0.002$).

Additional analyses

To explore the effects of handedness, head motion, and IQ on the results, we performed additional analyses, which did not substantially influence our conclusions. The details of these are as follows.

Handedness

Two participants were left-handed, as determined by the Edinburgh Handedness

Inventory (Oldfield, 1971). However, the slopes of both linear regression lines of correlation after excluding the data of these two participants between the fALFF values in the left LPFC and the CFS scores (r = 0.86, p < 0.001) and between the fALFF values in the right cerebellum and the IAT effect (r = −0.77, p < 0.001) were almost parallel with those of the whole sample (r = 0.86, p < 0.001 and r = −0.74, p < 0.001), respectively (the difference between the slopes: both, p > 0.96, see Fig. 3B and D). In addition, the scores of the Edinburgh Handedness Inventory did not significantly correlate with the fALFF values in the left LPFC or the right cerebellum across participants (both, p > 0.47).

Head motion

Although no participants met our exclusion criteria with respect to head motion (> 3.0 mm in translation or 3.0° of rotation) that were determined based on previous studies using fALFF (e.g., Chyzhyk et al., 2015; Yu et al., 2017), two participants showed relatively high levels of head motion compared with other participants (> 2.0 mm in translation or 2.0° of rotation). However, the slopes of both linear regression lines of correlation after excluding the data of these two participants between the fALFF values in the left LPFC and the CFS scores (r = 0.86, p < 0.001) and between the fALFF values in the right cerebellum and the IAT effect (r = −0.74, p < 0.001) were almost parallel with those of the whole sample (r = 0.86, p < 0.001 and r = −0.74, p < 0.001), respectively (the difference between the slopes: both, p > 0.56, see Fig. 3B and D).

IQ

Although IQ did not significantly correlate with explicit or implicit flexibility (CFS scores or the IAT effect) across participants (both, p > 0.22), previous studies reported that intelligence was an important factor in cognitive flexibility (Colzato et al., 2006). Thus, we also explored the brain regions where the fALFF values were associated with explicit and implicit aspects of flexibility (i.e., CFS scores and the IAT effect, respectively) throughout the whole brain at the same threshold as the main analysis [p < 0.01 (cluster-level FWE corrected, height threshold T = 2.5)], using a general linear model, which included the participants' IQ levels as covariates of no interest (along with age and gender). We also found that the CFS scores were positively correlated with fALFF values in areas including the left LPFC [MNI coordinates (3 local maxima more than 8.0 mm apart): −33, 30, 54 (T = 5.60); −36, 18, 57 (T = 4.81); −6, 30, 51 (T = 4.61), k = 255 voxels] and that the IAT effect was negatively correlated with those in the right cerebellum extending into the temporal lobe [MNI coordinates: 15, −66, −24 (T = 4.72); 36, −57, −12 (T = 4.88); 27, −48, −3 (T = 4.52), k = 160 voxels].

DISCUSSION

To the best of our knowledge, this is the first study to investigate the individual spontaneous neural activity patterns associated with dispositional variation in explicit and implicit aspects of flexibility. By combining psychometric measures of cognitive flexibility (CFS and the IAT) and predominant thinking style (REI) with RS-fMRI, we showed that (1) the level of explicit cognitive flexibility was strongly associated with a rational thinking style and higher spontaneous neural activity (fALFF values) in the LPFC, and (2) the level of implicit flexibility was associated with an experiential thinking style and higher activity in the cerebellum.

Our findings support the notion that both rational and experiential (intuitive) thinking contribute to flexible behavior (Custers and Aarts, 2010; Gigerenzer and Gaissmaier, 2011; McNally et al., 2012). Specifically, rational/explicit decision-making strategies impact conscious flexible behavior, while experiential/implicit strategies impact flexible behavior that operates outside conscious awareness.

The neural results suggest that the level of spontaneous neural activity in the LPFC and the cerebellum could explain individual differences in explicit and implicit aspects of flexibility, respectively. These findings also suggest that explicit and implicit aspects of flexibility may rely predominantly on different brain regions, and that individuals who exhibit greater flexibility have both higher-order rational decision-making capacity, a major function of the LPFC (Coutlee and Huettel, 2012; Hare et al., 2009; Mobbs et al., 2007), as well as more highly developed experiential response capacity for flexible decisions. Indeed, complementary explicit and experiential learning histories are crucial for cognitive flexibility, and the cerebellum may be a major substrate for the latter (De Bartolo et al., 2009; Desmond and Fiez, 1998). Furthermore, cerebellar lobule VI showing the association in this study, has been reported to be involved in diverse dimensions of social cognition, such as mirroring and event/person mentalizing (Van Overwalle et al., 2014). Cerebellar structural/functional abnormalities are found in a substantial proportion of patients with ASD, who often exhibit cognitive inflexibility in a broad range of situations (Fujino et al., 2017; Ito, 2008; Senju et al., 2009). Specifically, implicit understanding of others (e.g., metalizing by visual information) or implicit detection of others' motivations are frequently diminished in ASD (Frith, 2001; Foti et al., 2015). These implicit social skills may be stored in regions associated with implicit memory, and experience-based learning may cultivate implicit/experiential decision-making via neuroplasticity (Gigerenzer and Gaissmaier, 2011; Patterson et al., 2013).

These roles of the LPFC and cerebellum in cognitive flexibility were supported by additional examination using the realistic vignettes task involving socially conflicting situations. That is, spontaneous brain activities in these regions were crucial variables explaining the preference for a specific decision type, utilitarian solution/formalist reasoning (decision type B). Individuals preferring this decision type tend to prioritize value-based choice (result-oriented) to resolve the conflicting situation together with the preference that rationally considered this issue in a manner of a formalist (i.e., rule-based that takes social norm into account) (Brady and Wheeler, 1996). More specifically, both decision types A and B adopt utilitarian solution. However, while decision type A focused solely on utilitarian for solution and rational issue, type B flexibly switch their mind-set between utilitarian and formalist when thinking about these issues, depending on the given conflicting situation. Accordingly, the decision type B is a strategically flexible/adaptive response to maximize profit/welfare of oneself as well as others in socially conflicting situations. The current results support the notion that having well developed explicit and implicit systems may allow individuals to make such flexible decisions (Custers and Aarts, 2010; Koziol et al., 2010).

Among brain regions implicated in previous task fMRI studies of flexible decision-making (e.g., prefrontal cortices, temporoparietal junction, striatum, ACC, cerebellum), spontaneous brain activity distinctively observed in the cerebellum could be due to its effect on long-term adaptive learning. Namely, by confronting conflicting and stressful situations, we gradually obtain cognitive flexibility traits experientially (Kehagia et al., 2010; Spiro, 1988), and thus it requires relatively long time to cultivate our implicit aspects of flexibility. A recent study investigating neural substrates related to motor memory identified brain regions associated with multiple timescales in adaptation: in particular, the activity in the anterior-medial cerebellum, mainly located in the lobule VI identified in this study, was associated with memories for long timescales, while the prefrontal and parietal lobes and the posterior part of the cerebellum were associated with those for short timescales and the activity in the inferior parietal region was associated with those for intermediate timescales (Kim et al., 2015). Our study is in line with the previous findings and supports the notion that the role of the cerebellum in implicit processing is not limited to perceptual domains but also extend to cognitive/social domains.

There are several limitations to this study. First, the sample size was small. Additionally, 6 of the participants were females and 2 were left-handed, which limits the interpretation of the results. Thus, our preliminary findings should be interpreted cautiously and need to be carefully replicated in future research that recruits large number of subjects. In this regard, a recent study has shown that the effect size of the association between individual differences in cognitive abilities and RS-fMRI measures may be very small, and the authors stressed the importance of using a large sample size to increase the reliability of the results (Takeuchi et at., 2015). Although all our psychological measures datasets were normally distributed (all, $p > 0.05$, Shapiro–Wilk test), the small sample size of this study limited the sufficient quantification of individual variability within these measures. In addition, we recruited our study subjects from graduate and undergraduate students to ensure a uniform socioeconomic status, which means that our findings may not be representative of individuals with different backgrounds or from different socioeconomic levels. Second, in this study, we focused on the role of cognitive flexibility in the social context, and thus we used the CFS, which examines individual flexible choice tendencies in response to social conflict. However, cognitive flexibility also plays a role in non-social situations. In this respect, although CFS scores were reported to be significantly associated with other psychometric measures related to cognitive flexibility, such as the cognitive flexibility inventory (Dennis and Vander Wal, 2010) and the coping flexibility scale (Kato, 2012), and recent studies reported a common neural basis underlying social and non-social aspects of cognitive flexibility (Krall et al., 2016; Tei et al., 2017), our findings only contribute a partial explanation for the relationship between cognitive flexibility and spontaneous neural activity. It will be important to apply a variety of psychometric measures related to cognitive flexibility in the future. Third, in this study, we investigated the role of spontaneous brain activity from the point of functional segregation as indicated by fALFF, which has been used as a reliable and sensitive measure in the study of individual differences and personality traits (Kunisato et al., 2011; Takeuchi et al., 2015; Wei et al., 2014). However, the human brain has two basic organizational principles: functional segregation and integration (Cole et al., 2013; Sporns et al., 2000). In line with this notion, previous studies investigated functional connectivity patterns associated with various types of cognitive abilities using task-dependent and resting state fMRI (Caulfield et al., 2016; Cole et al., 2013). In those studies, the roles of the LPFC and cerebellum in functional connectivity were also highlighted (Caulfield et al., 2016; Cole et al., 2013). Future research on a large scale should combine the functional connectivity approach with that of fALFF for more in-depth insight into the neural mechanisms of individual differences in explicit and implicit aspects of cognitive flexibility. Fourth, we used lenient exclusion criteria with respect to head motion (> 3.0 mm in translation or 3.0° of rotation). Thus, our findings need to be carefully replicated using more restricted criteria in future research that recruits large number of subjects.

Notwithstanding these limitations, the current results add to our understanding of the neural mechanisms underlying flexible decision-making for solving social conflicts. More generally, our findings highlight the utility of RS-fMRI combined with both explicit and implicit psychometric measures for better understanding individual differences in social cognition.

Conclusions

In conclusion, the present study demonstrated that strong spontaneous activity in regions implicated in explicit and implicit learning (LPFC and cerebellum, respectively) mediated explicit and implicit aspects of cognitive flexibility for solving social conflicts. Our findings highlight the utility of RS-fMRI combined with psychometric measures of both explicit and implicit forms of cognitive flexibility for better understanding the neural mechanisms underlying flexible decision-making.

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Conflict of interest

All authors declare that they have no conflicts of interest.

Contributors

J.F., S.T., K.F.J., R.K., T.M. and H.T. designed the study and wrote the protocol. J.F., S.T., K.F.J., and R.K. participated in the data acquisition. J.F. and S.T. managed the literature searches and wrote the first draft of the manuscript. J.F. and S.T. performed data processing and statistical analyses. K.F.J., R.K., T.M. and H.T. helped with interpretation of data. All authors contributed to and have approved the final manuscript.

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Table 1. Correlations (r values) between explicit/implicit aspects of cognitive flexibility and thinking styles/personality traits

	Explicit flexibility (CFS)	Implicit flexibility (IAT effect)
Rationalism	0.67 (<0.001)*	–0.11 (0.63)
Experientialism	–0.21 (0.34)	–0.56 (0.006)*
Neuroticism	–0.36 (0.10)	–0.13 (0.57)
Extraversion	0.37 (0.09)	0.21 (0.34)
Openness	0.39 (0.08)	–0.005 (0.98)
Agreeableness	–0.10 (0.65)	0.03 (0.88)
Conscientiousness	0.56 (0.007)*	0.24 (0.29)

*$p < 0.05$

Abbreviations: CFS = Cognitive Flexibility Scale, IAT = Implicit Association Test

Table 2. Regions showing spontaneous brain activity associated with explicit or implicit aspects of flexibility

Brain Region	Coordinates (mm)			T	Cluster
	x	y	z		(voxels)
CFS (positive)					
L superior frontal gyrus	–33	27	54	5.74	290
	–6	30	51	4.83	
L middle frontal gyrus	–36	18	57	5.13	
IAT (negative)					
R cerebellum (lobule VI)	15	–69	–24	4.59	136
R Temporal lobe (fusiform gyrus)	36	–57	–12	5.10	
	27	–48	–3	3.73	

$p < 0.01$ (cluster-level FWE corrected, height threshold $T = 2.5$)

Voxel size is $3 \times 3 \times 3$mm

Three local maxima more than 8.0 mm apart are reported

Coordinates in MNI space

Abbreviations: CFS = Cognitive Flexibility Scale, FWE = family-wise error, IAT = Implicit Association Test, L = left, MNI = Montreal Neurological Institute, R = right

Figure Legends

Fig. 1. The Implicit Association Test (IAT). The IAT comprises a series of response time tasks that require participants to classify word stimuli that appear at the lower portion of a computer screen into corresponding categories and paired attributes appearing in the upper left or right of the screen.

Fig. 2. Correlations of explicit (A) and implicit (B) aspects of flexibility with thinking styles (N = 22). (A) Correlation between CFS scores (explicit cognitive flexibility) and the rationalism thinking style (r = 0.67, p < 0.001). (B) Correlation between the IAT effect (implicit cognitive flexibility) and the experientialism thinking style (r = −0.56, p = 0.006). Dashed lines are 95% confidence interval boundaries.
Abbreviations: CFS = Cognitive Flexibility Scale, IAT = Implicit Association Test

Fig. 3. Regions showing spontaneous brain activity levels associated with explicit or implicit aspects of cognitive flexibility (N =22). A statistical threshold was set at cluster-level FWE corrected p < 0.01. (A) CFS scores were positively correlated with fALFF values in areas including the left LPFC. (B) Slopes of linear regression lines of the correlation between the fALFF values in the left LPFC and CFS scores [whole sample (N =22), r = 0.86, p < 0.001: after excluding the data of left-handed participants (N = 20), r = 0.86, p < 0.001: after excluding the data of participants who showed relatively large head motion (> 2.0 mm in translation or 2.0° of rotation) (N = 20), r = 0.86, p < 0.001]. *Data point of left-handed participant. † Data point of participant who showed relatively large head motion. (C) The IAT effect was negatively correlated with the fALFF values in areas including the right cerebellum. (D) Slopes of linear regression lines of the correlation between the fALFF values in the right cerebellum and the IAT effect [whole sample (N =22), r = −0.74, p < 0.001: after excluding the data of left-handed participants (N = 20), r = −0.77, p < 0.001: after excluding the data of participants who showed relatively large head motion (> 2.0 mm in translation or 2.0° of rotation) (N = 20), r = −0.74, p < 0.001]. *Data point of left-handed participant. † Data point of participant who showed relatively large head motion.

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Abbreviations: CFS = Cognitive Flexibility Scale, fALFF = fractional amplitude of low-frequency fluctuations, FWE = family-wise error, IAT = Implicit Association Test, LPFC = lateral prefrontal cortex

Fig. 4. Correlations of fALFF values in the left LPFC (A) and right cerebellum (B) with preference for the utilitarian solution/formalist reasoning decision type (type B) in socially conflicting situations (N = 22). (A) Correlation between fALFF values in the left LPFC and preference for decision type B (r = 0.44, p = 0.041). (B) Correlation between fALFF values in the right cerebellum and preference for decision type B (r = 0.48, p = 0.023). Dashed lines are 95% confidence interval boundaries.
Abbreviations: fALFF = fractional amplitude of low-frequency fluctuations, LPFC = lateral prefrontal cortex

Highlights

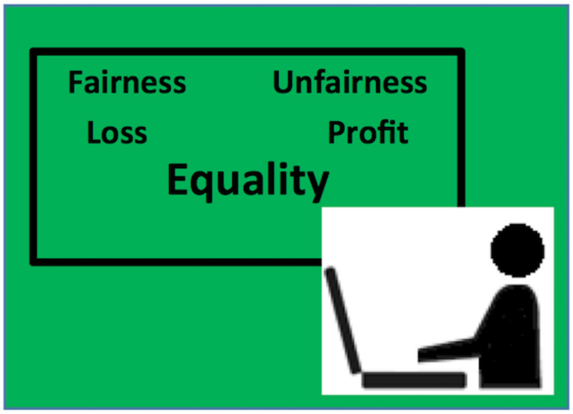
Explicit/implicit aspects of flexibility were assessed by the self-report and IAT.

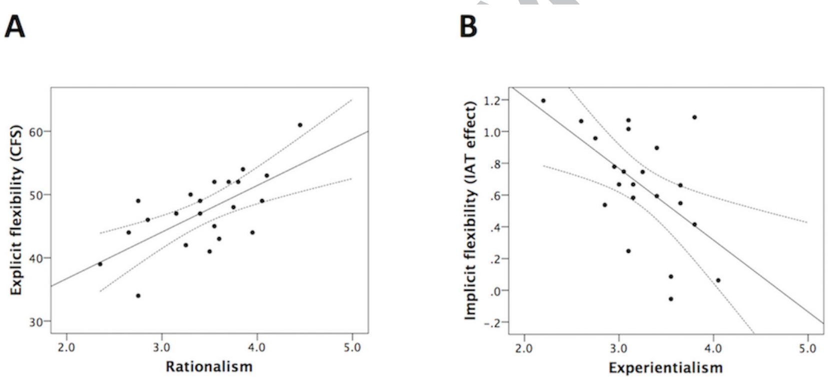
Explicit/implicit flexibility were linked to rationalism/experientialism.

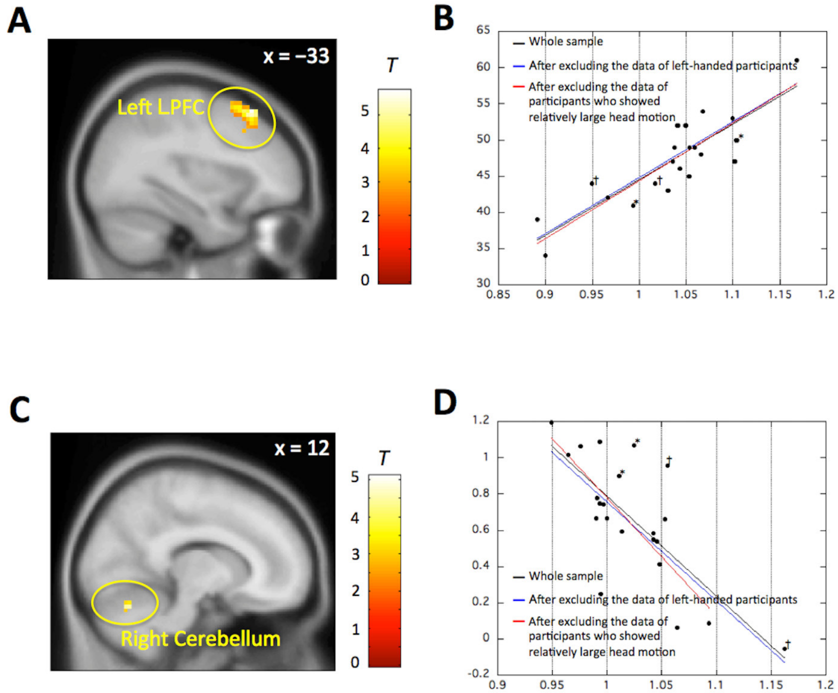
Higher spontaneous brain activity in the LPFC predicted greater explicit flexibility.

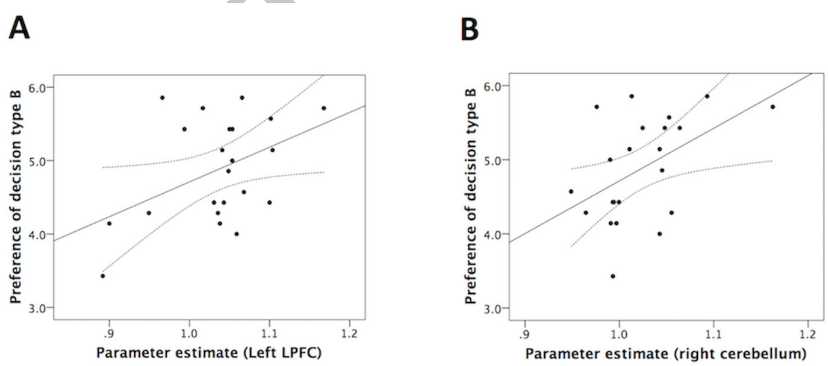
Higher spontaneous activity in the cerebellum predicted greater implicit flexibility.

These brain activities practically influenced socially flexible decision-making**.**


Fairness
Unfairness
Loss
Profit
Equality


A
B
Explicit flexibility (CFS)
Rationalism
Implicit flexibility (IAT effect)
Experientialism


A
x = −33
Left LPFC
T
B
Whole sample
After excluding the data of left-handed participants
After excluding the data of participants who showed relatively large head motion
C
x = 12
Right Cerebellum
D


A
Preference of decision type B
Parameter estimate (Left LPFC)
B
Preference of decision type B
Parameter estimate (right cerebellum)