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Decision flexibilities in autism spectrum disorder: an fMRI study of moral dilemmas

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Abstract

People make flexible decisions across a wide range of contexts to resolve social or moral conflicts. Individuals with autism spectrum disorder (ASD) frequently report difficulties in such behaviors, which hinders the flexibility in changing strategies during daily activities or adjustment of perspective during communication. However, the underlying mechanisms of this issue are insufficiently understood. This study aimed to investigate decision flexibility in ASD using a functional magnetic resonance imaging task that involved recognizing and resolving two types of moral dilemmas: cost–benefit analysis (CBA) and mitigating inevitable misconducts (MIM). The CBA session assessed the participants' pitting of result-oriented outcomes against distressful harmful actions, whereas the MIM session assessed their pitting of the extenuation of a criminal sentence against a sympathetic situation of defendants suffering from violence or disease. The behavioral outcome in CBA-related flexibility was significantly lower in the ASD group compared to that of the typical development group. In the corresponding CBA contrast, activation in the left inferior frontal gyrus was lower in the ASD group. Meanwhile, in the MIM-related flexibility, there were no significant group differences in behavioral outcome or brain activity. Our findings add to our understanding of flexible decision-making in ASD.

Key words: autism spectrum disorder; flexibility; functional magnetic resonance imaging; inferior frontal gyrus; moral dilemma

Introduction

Flexibility is a core aspect of human behaviors. An appropriate adjustment of thoughts and behaviors in response to changing environmental demands is not only indispensable for survival but also imperative for harmonious social living (Vlek and Keren, 1992; Barrett and Henzi, 2005; McNally *et al.*, 2012; Welborn *et al.*, 2016). In particular, moral dilemmas (MDs) frequently arise during human socialization (Mobbs *et al.*, 2007; Schneider *et al.*, 2013; Tei *et al.*, 2017, 2019a; Shamay-Tsoory *et al.*, 2019), and their flexible resolution prompts social adaptations (Bartels, 2008; Crockett *et al.*, 2010; Shenhav and Greene, 2010; Berns *et al.*, 2012).

Individuals with autism spectrum disorder (ASD), which is characterized by altered social interaction and atypical, pervasive interests, often report facing difficulties in making flexible or optimal decisions when faced with MDs (Schneider *et al.*, 2013; Fujino *et al.*, 2020a). These difficulties can negatively affect their social functioning (Geurts *et al.*, 2009; Fujino *et al.*, 2019; Hu *et al.*, 2021; Uddin, 2021). Investigations on the underlying mechanisms of decision flexibility can contribute to a better understanding of ASD and may provide helpful knowledge for the development of effective interventions.

Several functional magnetic resonance imaging (fMRI) studies have inspected flexible cognition and behavior in people with ASD

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(Philip et al., 2012; Uddin, 2021). For example, previous studies examining cognitive inflexibility in ASD using various neuropsychological tasks, such as the Wisconsin Card Sorting Test and the intradimensional/extradimensional task, have found that neural networks involving the lateral prefrontal cortex (PFC), parietal cortex and cingulate gyrus were altered in this disorder (Geurts et al., 2009; Dajani and Uddin, 2015). Moreover, recent studies investigating flexible choice behavior using decision-making and reversal learning tasks have shown the alteration of activity in brain regions important for executive function, response planning and change detection (D'Cruz et al., 2016; Uddin, 2021). However, although several studies reported an atypical pattern of moral reasoning in ASD (Moran et al., 2011; Zalla et al., 2011; Buon et al., 2013; Schneider et al., 2013; Bellesi et al., 2018; Dempsey et al., 2020; Hu et al., 2021), our understanding of the neural mechanisms underlying decision inflexibility in MD situations in this disorder is still limited.

Prior fMRI research in people with typical development (TD) has investigated the neural mechanisms of flexible decision-making in two types of MD situations involving (i) cost–benefit analysis (CBA; Greene, 2007) and (ii) mitigating inevitable misconducts (MIM: Yamada et al., 2012). For example, a CBA study assessed the participants' pitting of result-oriented outcomes (well-being maximizing) against distressful harmful actions (i.e. collective gain *vs* personal loss/distress dilemma), and CBA-induced decisions were associated with the activation of diverse brain regions, including lateral PFC, medial PFC and temporoparietal junction (TPJ; Tei et al., 2017). Meanwhile, another MIM study assessed the participants' pitting of the extenuation of a criminal sentence against a sympathetic situation of defendants suffering from violence or disease (i.e. compassionate exculpation *vs* respectful punishment of moral transgression), and the MIM-induced decisions were associated with activity in brain regions including lateral PFC, precuneus and TPJ (Yamada et al., 2012). Both CBA and MIM bear essential roles in socially adaptive behaviors requiring situation-sensitive balancing between exploration and exploitation trade-offs (e.g. Addicott et al., 2021) and in social–affective/empathic engagement (Crone and Dahl, 2012). Therefore, understanding how individuals with ASD behave under these MD situations can potentially reveal new insights into the practical implications of their social cognition.

The current study aimed to investigate decision flexibility in people with ASD. In this endeavor, we used an fMRI task that involved recognizing and resolving two types of MDs (CBA and MIM). We predicted that participants with ASD would show reduced flexibility in both CBA and MIM contexts, as compared to TD participants. We also predicted that unique brain activation patterns would emerge in the respective decision flexibility in CBA and MIM contexts.

Methods

Participants

Twenty-five adults with ASD and 29 with TD were enrolled in this study. The sample size was determined on the basis of previous fMRI studies on moral decision-making by individuals with ASD (e.g. Schneider et al., 2013; Hu et al., 2021). We enrolled only male participants because of potential gender differences in moral decision-making (De Dreu and Kret, 2016; Rosen et al., 2016). Participants with ASD were recruited from a database of volunteers who had received a clinical diagnosis of ASD in the outpatient units of the Showa University Karasuyama Hospital. The diagnostic procedure to identify individuals with ASD was the same as in our previous studies (Fujino et al., 2017; Tei et al., 2018, 2019b). Further details regarding participants are described in Supplementary Methods.

The intelligence quotient (IQ) scores of all ASD participants had been evaluated before the study using either the Wechsler Adult Intelligence Scale—Third Edition or the WAIS-Revised. The IQ scores of the TD participants were estimated using a Japanese version of the National Adult Reading Test, based on previous studies (Matsuoka et al., 2006; Kubota et al., 2020; Fujino et al., 2020b). In addition, all participants completed the Japanese version of the Autism Spectrum Quotient (AQ) test that includes items covering both social and non-social aspects of behavior and cognition (Baron-Cohen et al., 2001; Wakabayashi et al., 2006).

Three participants with ASD and one TD participant were excluded from the analysis (please see Supplementary Methods for details). Thus, data from 22 participants with ASD and 28 TD participants were analyzed (age: 20–46 years). Participants' demographic data are shown in Table 1. The TD and ASD groups were matched for age, handedness, education, estimated IQ level and current smoking status. Smoking status is reportedly associated with various types of decision-making (Critchley and Capewell, 2003; Lejuez et al., 2003; Fujino et al., 2020a). As shown in Table 1, the AQ scores were significantly higher in the ASD group compared to those in the TD group.

This study was approved by the Committee on Medical Ethics of Kyoto University and the institutional review board of Showa University Karasuyama Hospital and was 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 all participants.

fMRI task

During fMRI scanning, we asked participants to confront with a series of everyday MDs, which were designed so that participants would feel that conducting the action in these MD vignettes was morally wrong, but potentially acceptable or permissible

Table 1. Demographic and clinical characteristics of the participants

	TD Group ($n = 28$)	ASD Group ($n = 22$)	Statistics P
Age (years) [min–max]	29.4 ± 6.9 [20–43]	30.4 ± 6.2 [21–46]	0.59[a]
Handedness right/left	25/3	21/1	0.42[b]
Current smoker/non-smoker	2/26	3/19	0.45[b]
Education (years) [min–max]	14.5 ± 1.9 [12–18]	15.0 ± 2.0 [12–18]	0.41[a]
Estimated full-scale IQ [min–max]	105.9 ± 7.9 [87–118]	104.7 ± 13.2 [79–133]	0.73[a]
AQ [min–max]	16.2 ± 6.6 [5–30]	33.3 ± 5.2 [22–46]	< 0.01[a]

[a]Two-sample *t*-test.
[b]Two-tailed chi-squared test.

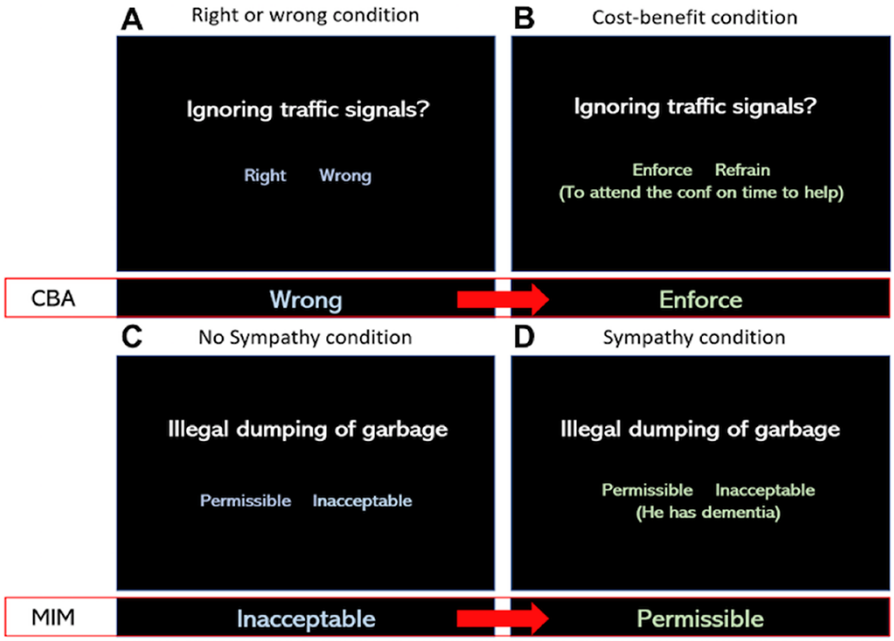

Fig. 1. Experimental design. In the CBA session, participants were instructed to press a button to either (i) evaluate whether these actions are R/W (A) or (ii) judge whether to enforce result-oriented actions to prioritize social benefits and welfare (B). Likewise, regarding the MIM session, participants made decisions on whether to (i) permit social norm/rule violation in no sympathy-evoking situations (C) or (ii) permit these identical violations in sympathy-evoking situations (D).

(Greene *et al.*, 2004; Barbey and Grafman, 2011). The application of MD concerning CBA and MIM to investigate to explore flexibility is a well-established approach that examines participants' frequency in tilting decisions from deontological mindsets (moral rule-based) into more situation-adjusted, flexible mindsets (Greene *et al.*, 2004; Yamada *et al.*, 2012; Tei *et al.*, 2017).

The MD task consisted of two consecutive sessions applying CBA-related MD and MIM-related MD. Regarding CBA, based on our previous fMRI study on moral flexibility (Tei *et al.*, 2017), participants were instructed to press a button to either (i) evaluate whether these actions are right or wrong (R/W condition, Figure 1A) or (ii) judge whether to enforce result-oriented actions to prioritize social benefits and welfare (cost–benefit: C/B condition, Figure 1B). Likewise, regarding MIM, based on a previous moral study (Yamada *et al.*, 2012), participants made decisions on whether to (i) permit social norm/rule violation in no sympathy-evoking situations (NS condition, Figure 1C) or (ii) permit these identical violations in sympathy-evoking situations (SP condition, Figure 1D). For example, in CBA, they were confronted with the outline of vignettes, such as 'Ignoring traffic signals', and the enforcing action resulted in well-being maximization (e.g. to attend the conference on time and help in running the conference). In MIM, the outline described as 'Illegal dumping of garbage' and sympathy-evoking situations were labeled inevitable circumstances (e.g. the person has dementia).

In this MD task, we applied a block design (24 s each) that included 10 blocks of CBA-related vignettes (R/W and C/B; 5 blocks each) and another 10 blocks of MIM-related vignettes (SP and NS; 5 blocks each). Each block included four trials (6 s each), where participants viewed short phrases representing each vignette. Specifically, all participants had to make a judgment within 5.5 s while each moral vignette was presented (Figure 1). Subsequently, participants' actual responses were displayed (0.5 s). Cases in which participants could not make a judgment within 5.5 s of the presentation of the judgment screen were considered as missed trials. Overall, participants were presented with a total of 80 vignettes. A fixation cross was displayed between blocks for 14 s. To avoid a confounding effect, R/W, C/B, SP and NS conditions were displayed in a pseudo-random order, that is, the same order of questions for each participant. Subsequently, we examined brain regions comparing C/B against R/W, as well as SP against NS conditions.

Acquisition and pre-processing of fMRI data

All participants underwent MRI scans on a 3 T whole-body scanner equipped with an 8-channel phased-array head coil (Verio, Siemens, Erlangen, Germany). Image processing was carried out using SPM12 (Wellcome Trust Center for Neuroimaging, London, UK) in MATLAB (MathWorks, Natick, MA, USA). Please see Supplementary Methods for details.

Statistical analyses

Behavioral data

We estimated participants' flexibility levels by computing the switching rate of decisions in CBA and MIM sessions (switching was defined as follows: CBA, judging the actions as wrong but choosing to enforce the action in the same vignette; MIM, judging the violation as not permissible in a non-sympathy-evoking circumstance, but permissible in a sympathy-evoking circumstance). Statistical analyses were performed using SPSS 24 (IBM, Armonk, NY, USA). Results were considered statistically significant at $P < 0.05$ (two-tailed).

fMRI data

After pre-processing, we fitted a general linear model to the fMRI data. In the first-level analyses, the design matrix contained four task-related regressors (R/W, C/B, SP and NS) as regressors

of interest. To minimize motion-related artifacts, six movement parameters (three displacements and three rotations) were also included as additional regressors of no interest. Data were high-pass filtered at 128 s. CBA/MIM-related activation was identified using the contrast of C/B *vs* R/W and SP *vs* NS conditions, respectively. The comparison produced a contrast image for each participant, and these contrast images were used for second-level fMRI analyses.

In second-level analyses, we used a random-effects model to make inferences at the population level. First, CBA/MIM-related activation was computed using one-sample *t*-tests separately for the TD and ASD groups. Next, to compare differences in neural activity between the TD and ASD groups, two-sample *t*-tests were performed. Based on previous fMRI studies of decision-making under MDs (Yamada *et al.*, 2012; Tei *et al.*, 2017), we focused on the following regions of interest (ROIs): the inferior frontal gyrus (IFG), the middle frontal gyrus (MFG), the medial PFC, the insula, the amygdala, the anterior cingulate cortex, the precuneus and the TPJ. All anatomical masks of these ROIs (except for the TPJ) were taken from the Automated Anatomical Labeling atlas (Tzourio-Mazoyer *et al.*, 2002) using the WFU PickAtlas toolbox (Maldjian *et al.*, 2003). On the basis of previous studies (Tei *et al.*, 2014, 2017), we applied a standard 10-mm sphere mask for the TPJ ROI [x–y–z Talairach coordinates (±50, –55, 25)]. We defined an activity as significant if it survived family-wise error (FWE) correction for multiple comparisons, with a cluster level of $P < 0.05$ for each ROI (at voxel-level uncorrected $P < 0.001$). With respect to brain regions outside these ROIs, we reported activations thresholded at a voxel-level $P < 0.05$ (FWE corrected) with a minimum cluster extent of 100 contiguous voxels after whole-brain correction for multiple comparisons, based on the previous studies (e.g. Li *et al.*, 2017; Tomasi and Volkow, 2019).

Results

Behavioral data

Overall, the participants [$N = 50$ (TD 28 and ASD 22)] performed the MD task well, missing an average of only 1.07 ± 1.21 (mean ± s.d., TD) and 1.05 ± 1.70 trials (ASD; please see the Methods section for details). There were no significant differences between the groups in the number of missed trials ($P = 0.95$).

Figure 2 shows the mean switching rate of the CBA and MIM sessions in both groups. The switching rate of the CBA session was significantly lower in the ASD group than in the TD group (TD 0.36 ± 0.29, ASD 0.22 ± 0.18, $P = 0.03$, Figure 2A), whereas there were no significant differences in the switching rate of the MIM session between the groups (TD 0.57 ± 0.20, ASD 0.50 ± 0.23, $P = 0.21$, Figure 2B).

fMRI data

ROI analyses

In CBA contrast (C/B > R/W), several brain regions, including the bilateral IFG, bilateral MFG, right medial PFC, bilateral precuneus and bilateral TPJ, were activated in the TD group (Figure 3A, Supplementary Table S1). Meanwhile, the bilateral MFG and bilateral precuneus were activated in the ASD group (Figure 3B, Supplementary Table S1). Two-sample *t*-tests revealed that activation in the left IFG was lower in the ASD group compared to that in the TD group (Figure 4, Supplementary Table S1). We did not find significant differences in any other brain regions between the groups. In MIM contrast (SP > NS), the left MFG and bilateral TPJ were activated in the TD group (Figure 5A, Supplementary Table S1). Meanwhile, the bilateral MFG, bilateral precuneus and bilateral TPJ were activated in the ASD group (Figure 5B, Supplementary Table S1). We did not find significant differences in brain activation between the groups (Supplementary Table S1).

Brain regions outside the ROIs

Outside the ROIs, we found significant brain activation in the right cuneus and left inferior occipital gyrus in CBA contrast (C/B > R/W) in the TD group. No significant brain activation was observed in the ASD group. We did not find any significant differences in brain activation in this contrast between the groups. In MIM contrast (SP > NS), no significant brain activation was observed in the TD or ASD groups. Again, we did not find any significant differences in brain activation between the groups. Please see Supplementary Table S2 for further details.

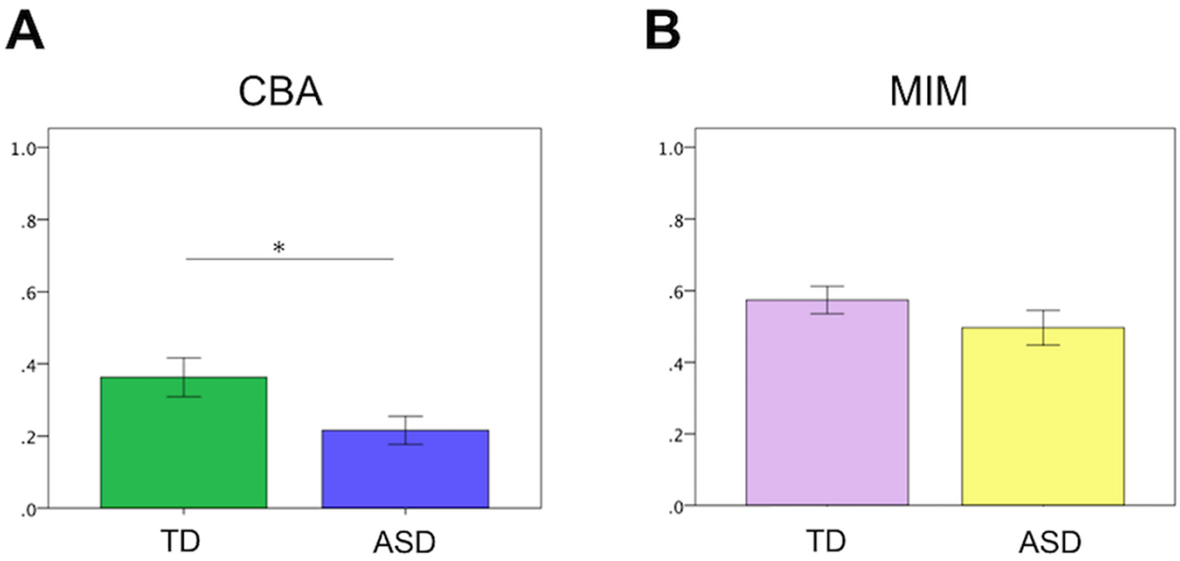

Fig. 2. Switching rate of decisions in CBA and MIM sessions. In the CBA session, the switching rate was significantly lower in the ASD group than in the TD group (A), whereas, in the MIM session, there were no significant differences in the switching rate between the groups (B). The error bars indicate ± standard errors. *$P < 0.05$.

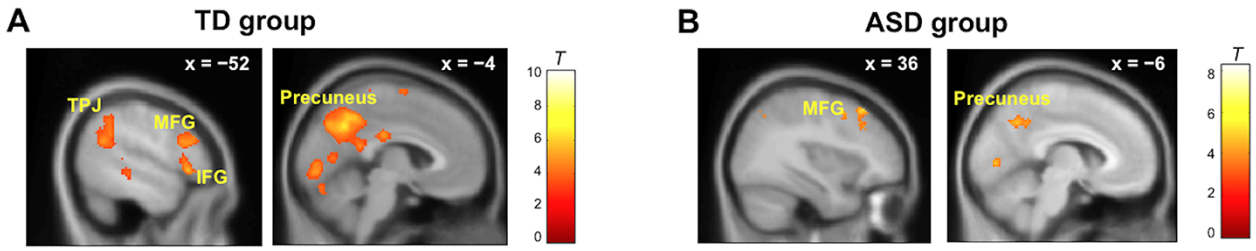

Fig. 3. Brain regions activated in CBA contrast (C/B > R/W). (A) TD group. (B) ASD group. Images were thresholded at an uncorrected *P*-value of 0.001 for visualization purpose.

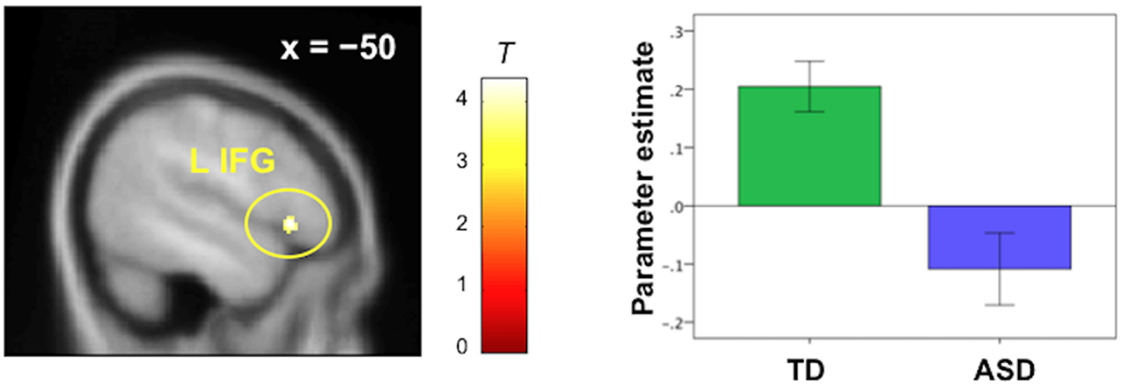

Fig. 4. Difference in brain activation between the TD and ASD groups in CBA contrast (C/B > R/W). In the ASD group, the neural activation in the left IFG was lower compared to that in the TD group during CBA-related decision-making. A statistical threshold was set at cluster-level FWE corrected $P < 0.05$ (at voxel level, uncorrected $P < 0.001$).

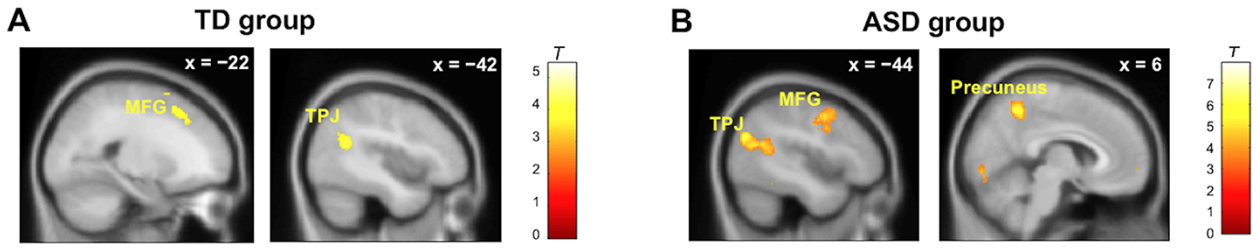

Fig. 5. Brain regions activated in MIM contrast (SP > NS). (A) TD group. (B) ASD group. Images were thresholded at an uncorrected *P*-value of 0.001 for visualization purpose.

Discussion

To the best of our knowledge, this was the first study to investigate decision flexibilities in ASD using an fMRI task involving the resolution of two types of MD in the CBA and MIM contexts. The results have clinical implications and add to the ASD literature on flexibility.

In CBA-related flexibility, the TD participants recruited diverse brain regions including the IFG, MFG, medial PFC, precuneus and TPJ, which are known to be involved in adjustable perspective shifting such as attending to and disengaging from dilemma-induced distress and incentives to resolve and diffuse/control the conflicting situations (Greene *et al.*, 2004; Greene, 2007; Moll and de Oliveira-souza, 2007; Schneider *et al.*, 2013). Our results are consistent with those of previous studies (Berns *et al.*, 2012; Tei *et al.*, 2017) and highlight that these brain areas are crucial in flexible result-oriented moral reasoning via switching or weighing between well-being maximization and personal distress (concerning the situation of others) in the MD situations. These brain areas can subserve modulation of attention to morally and/or socially relevant information (Greene *et al.*, 2004; Yoder *et al.*, 2015).

As predicted, the switching rate in CBA-related flexibility was significantly lower in the ASD group than in the TD group. Previous behavioral studies reported that people with ASD are not only relatively more rule-bound (Geurts *et al.*, 2009; Tei *et al.*, 2019b) but also relatively more 'pure' or 'immaculate' in their response to social/moral transgressions (Shulman *et al.*, 2012; Margoni and Surian, 2016). Additionally, recent studies have shown that ASD participants often tend to over-evaluate moral culpability and negative moral consequences, as compared to TD participants, and the authors proposed that such disproportionate reliance on learned social rules or norms possibly compensates for their less reflexive mentalizing (Zalla *et al.*, 2011; Hu *et al.*, 2021; Uddin, 2021). These findings further suggest that people with ASD might be affected by their personal distress, which could affect CB judgments. However, further research on appropriate measures for personal distress would be required to support this view.

Furthermore, in the corresponding CBA contrast, activation in the left IFG was lower in the ASD group compared to that in the TD group. The lateral PFC, including IFG, plays a key role in various cognitive processes, such as attention, inhibition, switching, working memory and context monitoring (Barbey and Grafman, 2011; Lamm and Majdandžić, 2015; Fujino *et al.*, 2016, 2018; Allaert *et al.*, 2022; Fallon *et al.*, 2020; Qu *et al.*, 2020; Tei *et al.*, 2020). Regarding moral decision-making, this brain area is reported to crucially support utilitarian decisions through cognitive control to override potent emotional responses, maintain goal-directed mindsets and modulate intuitive bias (Mansouri *et al.*, 2017). More specifically, the lateral PFC may incorporate decisions based on adaptive social norms for obligatory, prohibited and permissible courses of action (Barbey and Grafman, 2011), and 'necessary (obligatory or prohibited)' and 'also' 'possible (permissible)' behaviors can be updated based on ones' experiences and social knowledge (Geurts *et al.*, 2009; Fujino *et al.*, 2020a). They may form beliefs, instinct, a sense of values and social cognitions to develop behavior-guiding principles (Satpute and Lieberman, 2006; Evans, 2008), and this processing might be altered or biased in ASD individuals (Dajani and Uddin, 2015).

As for MIM-related flexibility, the MFG and TPJ were activated in the TD group. Activation in these brain areas was commonly observed in both CBA- and MIM-related MD. It is plausible to assume that these brain regions subserve shifting of decision rules/perspectives, mentalizing for people in the MD and contextual understanding and consideration, as well as adjustable attending/disengaging from emotional distress (Crone and Dahl, 2012; Mazefsky, 2015; Tei *et al.*, 2019a, 2021; Fujino *et al.*, 2020b; Park *et al.*, 2021), given that both flexible responses in CBA and MIM were designed to evoke this functioning.

Contrary to our predictions, there were no statistical group differences (ASD/TD) neither in MIM switching rates, nor the brain activity in the MIM contrast. One possible explanation for this finding is that our ASD participants' MIM-related flexibility was relatively intact (compared to CBA-related flexibility). Thus, the potential emotional components of the MIM-related MD, such as affective sharing and emotional identification, might have been somewhat analogous in the ASD and TD groups (e.g. Bird and Viding, 2014). Such an interpretation appears consistent with our brain-imaging findings, i.e. the CBA contrast images showed significant group differences in brain activation in the IFG, whereas the MIM contrast did not show group differences in any brain regions. These results were in line with the abovementioned idea that the potential functional components of the MIM that emerged in the ASD and TD groups were fairly similar. In summary, our results implied that our participants with ASD were relatively intact in terms of MIM-related flexibility but not CBA-related flexibility. Notably, CBA-related flexibility requires the shifting of attention and decision-making rules by illuminating morally and/or socially relevant information, which are areas that individuals with autism frequently report difficulties with (e.g. Shulman *et al.*, 2012; Tei *et al.*, 2019b).

Additionally, it is also possible that our ASD participants were able to make more flexible responses in the 'hypothetical' social dilemma in our laboratory tasks, even though they would behave more inflexibly in their real-world, daily life events (Geurts *et al.*, 2009). While our in-house dilemmas are developed to simulate daily events and participants were requested to imagine themselves as a protagonist in each moral vignette, these dilemmas are still hypothetical. Therefore, it is essential to consider refining the moral reasoning experiments and more sensibly inspect what social contexts lead to atypical responses in people with ASD.

There are several limitations to this study. First, while the sample size was comparable to the previous fMRI studies of moral decision-making on ASD (e.g. Schneider *et al.*, 2013; Hu *et al.*, 2021), it remained relatively small. Second, our sample consisted of only males. Previous studies have shown potential gender differences in moral decision-making (De Dreu and Kret, 2016; Rosen *et al.*, 2016). Thus, our present findings may not be generalized to female subjects. In a similar vein, generalization of the results warrants more exploration of the choice of ROI and whole-brain analyses. It is possible that these limitations restricted significant group differences and/or brain activation patterns in the CBA/MIM contrast images.

Moreover, it is crucial to include adolescents with ASD and the assessment of behavioral/personality features (e.g. empathic traits; Coll *et al.*, 2017) that may provide additional insights. Previous studies have indicated that MIM-related flexibility might be altered in adolescents with ASD (Shulman *et al.*, 2012; Schaller *et al.*, 2019), although this may be attributable to insufficient (immature) mentalizing and sympathy skills, which could be nurtured by social experiences as individuals mature. Meanwhile, recent reviews suggest that people with ASD are on average less biased and more rational/consistent than TD participants when making decisions due to their lower reliance on prior experience and incoming information (Rozenkrantz *et al.*, 2021). However, in light of a reduced cognitive bias, the findings of autism studies involving moral reasoning are rather mixed (e.g. Gleichgerrcht *et al.*, 2013; Schneider *et al.*, 2013). As flexible decision-making in ASD during moral reasoning appears complex, further studies are warranted. In this endeavor, it is crucial to utilize more ecologically valid measures to enhance task variation (Geurts *et al.*, 2009) that allows the assessment of participants' characteristics to understand the effects of different social contexts when making decisions.

Notwithstanding these limitations, the current results add to our understanding of the decision flexibility in ASD. Our findings may be useful in addressing practical implications of their social cognition and behavior.

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Conflict of interest

The authors declared that they had no conflict of interest with respect to their authorship or the publication of this article.

Supplementary data

Supplementary data are available at SCAN online.

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