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Research article

Roles of empathy in altruistic cooperation in adults with and without autism spectrum disorder

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ABSTRACT

Background: Altruistic cooperation (AC) is essential in human social interactions. Previous studies have investigated AC-related behavior in children with autism spectrum disorder (ASD), revealing that there is considerable individual variability in the behavior. However, this issue is still largely unexplored especially in the adult population.

Aims: To investigate individual differences in AC-related behavior, we conducted the resource allocation task (RAT) and modified version of the ultimatum game (mUG) among adults with and without ASD.

Methods and procedures: The study employed a cross-sectional design, involving 27 adults with ASD (mean age 29.1 ± 4.3 years; three females) and 27 adults with typical development (TD) (mean age 25.8 ± 6.7 years; two females), who completed the RAT and mUG tasks. Beyond clinical characteristics, we assessed three primary psychological metrics: the interpersonal reactivity index (IRI), Barratt impulsiveness scale, and the behavioral inhibition and activation systems.

Outcomes and results: No significant differences were observed in the proportions of participants with high AC when assessed by RAT (p = 0.15) and mUG (p = 0.59) between the TD and ASD groups. Participants with high AC from the RAT demonstrated higher perspective-taking scores on the IRI than those with low AC within both the TD (p = 0.04) and ASD groups (p = 0.03). In the TD group, high AC individuals also scored higher on the IRI's fantasy subscale as per the mUG (p = 0.03); however, this trend was not present in the ASD group.

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Conclusions and implications: The present findings indicate that empathy plays an important role in individual differences in AC-related behavior among adults with and without ASD, although the role could be different depending on the types of AC-related behavior between TD and ASD populations.

1. Introduction

Altruistic cooperation (AC) is an essential element of successful social interactions [1,2]. Human beings cooperate with each other in more complex ways than other primate species [3]. Although individuals with autism spectrum disorder (ASD), which is characterized by difficulties in social interaction and repetitive and restricted behaviors [4–7], often demonstrate alterations in AC-related behavior in clinical settings, there is a considerable individual variability in the behavior. A better understanding of this issue may provide important insights into developing effective individualized interventions for social cognitive impairments in ASD.

Concerning the previous research on AC-related behavior in ASD, most studies focused on pediatric population. For example, Downs (2003) reported that high-functioning children with autism cooperated similarly to typical development (TD) children in a Prisoner's Dilemma game task [8]. Manfredi et al. (2021) showed that children with ASD engaged less frequently in altruistic behavior than those with Down syndrome when another person was not able to achieve their goal [9]. Meanwhile, Paulus et al. (2017) revealed that children with ASD were more tended to display spontaneous assistance in the absence of a helpee than TD children [10]. These inconsistent findings indicate that the mechanisms of AC-related behavior in individuals with ASD is extraordinarily complex and demand further investigation.

Recently, more attention has been given either in research or clinical practice associated with ASD in adulthood [11,12]. Along this line, a number of previous studies examined the various types of social cognition in adults with ASD [13–15]. Yet, few studies have focused on AC-related behavior in adults with ASD. Ikuse et al. (2018) reported that adults with ASD distributed more money in the ultimatum game (UG) than adults with TD; however, they behaved rather consistently, irrespective of conditions where social and non-social stimuli were displayed [16]. A recent study showed that adults with ASD exhibited more generous decisions than those with TD in the social discounting task; there were also considerable individual differences in the behavior [17]. Thus, some autistic adults show alterations in AC-related behavior, whereas others do not. However, this issue remains largely unexplored.

Several factors are known to influence AC-related behavior in adults with TD. In particular, empathy, impulsiveness, and motivational systems have been repeatedly reported to be associated with individual differences in AC-related behaviors in TD subjects. TD adults with high levels of empathy show more prosocial behavior than TD adults with low levels of empathy, implying that alterations in empathy lead to profound alterations in AC-related behavior [18–20]. It has been shown that people who are impulsive in intertemporal choice have low degrees of reciprocal altruism [21,22]. Regarding the motivational systems, previous studies reported that dispositional sensitivities to rewards and punishments partly explained levels of cooperation in public goods games [23].

This study aimed to further elucidate AC-related behaviors in adults with ASD. We examined these behaviors in adults both with and without ASD by performing two behavioral economics tasks focused on allocation and acceptance decisions. Whereas most prior research on AC-related behaviors in adults with ASD concentrated on either allocation or acceptance individually [16,17], our study's investigation into both behaviors simultaneously should broaden the scope of these earlier findings. This could contribute to creating targeted interventions for social cognitive deficits in ASD. Specifically, we applied the resource allocation task (RAT) and UG, which were widely used in a variety of settings [24–26]. The current RAT was designed based on the social value orientation (SVO) task in which the participant determines the outcome for himself/herself and a hypothetical other [26,27]. Regarding the UG, we used a modified version of UG (mUG) that included social contextual information concerning intentions behind monetary proposals of others [25,28]. In addition to clinical characteristics, three abovementioned psychological factors (empathy, impulsiveness, and motivational systems) were evaluated.

A very recent study reported that TD adults demonstrated low AC due to alexithymic traits but not autistic traits; thus, authors proposed that alexithymia impairs AC-related behavior by altering empathic abilities across the autism spectrum [29]. Furthermore, alterations in empathy have been repeatedly found to be associated with various types of social cognitive impairments in ASD [30,31]. Therefore, we hypothesized that the proportion of high AC participants, as evaluated by RAT and mUG, would not be lower in the ASD group compared with the TD group. We also predicted that levels of empathy would differ between high and low AC participants in both TD and ASD groups. Additionally, previous studies have demonstrated atypical processes underlying prosocial behaviors in conditions where social contextual factors were added in individuals with ASD [16,32]. Hence, we further hypothesized that psychological measures related to AC-related behavior assessed by mUG would show differences between adults with and without ASD.

2. Methods

2.1. Participants

Initially, we recruited 32 adults with ASD and 32 TD adults for this study, basing our sample size on power analysis and prior ASD social decision-making research [16,33]. However, five individuals from each group ultimately did not participate for various reasons (detailed in Fig. S1). Consequently, we enrolled 27 adults with ASD [age range 20–35 years, mean \pm SD: 29.1 \pm 4.3, including three females (11.1 %)] and 27 TD adults [age range 20–45 years, mean \pm SD: 25.8 \pm 6.7, including two females (7.4 %)] in the study.

We recruited participants with ASD from a database of volunteers who were clinically diagnosed with ASD in Showa University Karasuyama Hospital. The procedure to identify individuals with ASD was similar as in our previous studies [15,17,34]. Sex, current smoking status, and estimated full-scale intelligence quotient (IQ) levels were matched between the groups (smoking status is known to be related to various types of decision making [35]). Cancellations and a limited experimental timeframe (Fig. S1) resulted in the TD group being somewhat younger than the ASD group (Table 1). Due to the higher prevalence of ASD in males, estimated at 2–5 times more common than in females [36], our study enrolled a greater number of male participants compared to females. As expected, the autism spectrum quotient (AQ) [37,38] scores were higher in the ASD group than in the TD group. Additional details regarding the procedures and participants are indicated in the Supplementary Methods.

The study received approval from the institutional review board of Showa University Karasuyama Hospital and the Committee on Medical Ethics of Kyoto University [ethical approval number B-2014-018] and adhered to the World Medical Association's Code of Ethics. After a complete description of the study, written informed consent was obtained from all participants. All ASD participants were adults without intellectual disabilities (age \geq 20 years, IQ > 85), endowing them with adequate decision-making capacity for participation in the study.

2.2. Study design, setting, and procedures

This cross-sectional study took place at Showa University Karasuyama Hospital, Tokyo, Japan. After clinical interviews, the participants performed following behavioral tasks and psychological measures. Details are described in the Supplementary Methods.

2.3. Behavioral economics tasks

2.3.1. Resource allocation task (RAT)

The current RAT was designed based on the SVO task used in previous studies [26,27]. The task consists of nine decomposed games wherein the participant determines the outcome for himself/herself and a hypothetical other (Fig. 1A). Three different decompositions correspond to three types of SVOs: (1) cooperative orientation, reflecting a preference for joint outcomes; (2) individualistic orientation, reflecting a preference for own outcomes; and (3) competitive orientation, reflecting a preference for a large positive difference between own and other outcomes (Table S1). When participants select six or more consistent choices, they are classified as belonging to one of three types of SVO: cooperative, individualistic, or competitive. In previous studies, cooperative participants have been categorized as the "prosocial" group, whereas individualistic and competitive participants have been categorized as the "proself" group [26,27]. Hence, we regarded a participant who made six or more cooperative choices as a participant with high AC; otherwise, they were regarded as a low AC participant.

2.3.2. Modified version of the ultimatum game (mUG)

The UG is used globally to evaluate AC and perception of fairness [16,39]. In UG, the proposer receives a sum of money and suggests a plan to divide it between him/herself and the responder (participant). The responder selects to either accept or reject this proposal. If the responder accepts, the money will be divided according to the proposal. If the responder declines the proposal, neither player will receive money [33]. However, in real life, people's propensity to engage in cooperative behavior depends on the intentions of the interaction partner [40]. More specifically, people cooperate (accept unfair offers) if the inequity is unintentional. Meanwhile, previous studies developed a modified version of the UG (mUG), which is a two-choice game where one offer is shown together with an alternative offer [25,28]. This version of UG was used to investigate AC-related behavior in developmental studies and research on antisocial personality disorder [25,28].

To assess participants' levels of AC, following prior research [25,28], the current mUG included two conditions that were labeled depending on the alternative offer pitted against an unfair 8/2 offer: (i) 5/5 offer (fair alternative) and (ii) 8/2 offer (no alternative) (Fig. 1B). One coin was equivalent to 10 Japanese yen (approximately 0.10 US dollars). The difference in acceptance rates between the "no alternative" and "fair alternative" conditions were calculated. Higher scores indicate higher levels of AC. In this study, we divided the participants into high or low AC (\geq or < median value in all participants) based on their difference scores. To enhance ecological validity and reduce habituation, a "reversed condition" pitted the 5/5 against the 8/2 offer, although it was not included in the

 Table 1

 Demographic and clinical characteristics of participants.

	TD Group	ASD Group	Statistics	
	(n=27)	(n=27)	\overline{p}	
Age (years, mean \pm SD)	25.8 ± 6.7	29.1 ± 4.3	0.04 ^a	
Male/female	25/2	24/3	0.64 ^b	
Current smoker/non-smoker	3/24	3/24	1.00^{b}	
Estimated full-scale IQ (mean \pm SD)	105.3 ± 9.3	106.6 ± 12.2	0.64 ^a	
AQ (mean \pm SD)	16.1 ± 6.9	33.8 ± 5.5	<0.01 ^a	

Abbreviations: ASD = autism spectrum disorder, AQ = autism spectrum quotient, IQ = intelligence quotient, TD = typical development.

^a Two-sampled *t*-test.

b Two-tailed chi-squared test.

Fig. 1. Behavioral Tasks. (A) The RAT. For each of the choices, the participants were asked to select one that they preferred the most from three decompositions. (B) The mUG. The participants were presented with the two distributions that were available to the proposer. The offer made by the proposer was indicated by a red circle around one of the two options available to the proposer. The participants were asked to accept or reject the offer by selecting "Yes" or "No" using the keyboard.

Abbreviations: $ASD = autism\ spectrum\ disorder,\ mUG = modified\ version\ of\ the\ ultimatum\ game,\ RAT = resource\ allocation\ task,\ TD = typical\ development.$

analysis.

The mUG featured 24 trials, eight per scenario, with pseudorandomized order and a 1.5-s fixation cross between trials. Participants indicated choices within 5 s, and responses were shown for 1 s. To preclude learning or reputation biases and simulate a realistic context, following previous studies [12,33], we introduced a new proposer for each trial, telling participants they were responding to prior submissions by volunteers (in truth, they interacted with a preprogrammed computer). In line with previous studies [41,42], participants were informed that at the end of the task, the computer would randomly select three trials and compute their earnings, and these payments would supplement their final compensation (we debriefed participants on the purpose of the experiment after the task and provided a set maximum participation fee). Further information is detailed in the Supplementary Methods, Table S2, and Fig. S2.

Participants practiced on a shorter version of the present task at least once and were corrected or instructed on any misunderstanding about how to perform the task. We performed the experiment using E-Prime software (Psychology Software Tools, Inc., Pittsburgh, PA, USA).

2.4. Psychological measures

2.4.1. Interpersonal reactivity index (IRI)

The Japanese version of the interpersonal reactivity index (IRI) [43–45] was used to evaluate empathic abilities. The IRI comprises four 7-item subscales that measure different empathy dimensions. The perspective-taking subscale gauges the propensity to spontaneously adopt others' viewpoints. The fantasy subscale evaluates the ability to transpose the feelings of fictional characters onto oneself. Empathic concern reflects compassion for others, and personal distress measures feelings of discomfort and anxiety from observing others' negative experiences. Higher subscale scores indicate greater empathy.

The IRI has been widely used to assess empathy in TD adults [20,46,47] and has been found effective for evaluating adults with ASD [48,49]. The internal reliability (standardized alpha) of its four subscales ranges between 0.70 and 0.78 [43,44]. Test-retest reliability for the subscales is reported between 0.61 and 0.81 [43,44]. This study's Cronbach's alpha coefficients are detailed in Table S3.

2.4.2. Barratt impulsiveness scale, 11th version (BIS-11)

The Barratt impulsiveness scale-11 (BIS-11) is a widely used tool for assessing impulsiveness [50]. It consists of 30 items, each rated on a 4-point Likert scale. Our study utilized the Japanese version [51], where higher scores indicate increased impulsiveness.

The BIS-11 is commonly employed to evaluate impulsiveness in TD adults [51,52] and has been utilized in studying adults with ASD [53]. The overall BIS-11's Cronbach's alpha coefficient is reported at 0.79 [51], and its test-retest reliability (one-way ANOVA intraclass coefficient) is 0.71 [51]. The Cronbach's alpha coefficients for this study are detailed in Table S3.

2.4.3. Behavioral inhibition and behavioral activation systems (BIS/BAS)

The BIS/BAS scale, a self-report questionnaire, evaluates two motivational systems: the BIS, sensitive to negative cues and punishment, and the BAS, attuned to positive cues and rewards [54,55]. Higher BIS scores (7 items) reflect greater sensitivity to negative outcomes and a tendency to avoid such actions. Higher BAS scores (13 items) signify an increased responsiveness to desirable outcomes, promoting engagement in goal-directed activities [54]. This study incorporated the BIS scores and total BAS subscale scores for analysis, following prior research [56,57], and utilized the Japanese versions of these scales [55].

The BIS/BAS is commonly employed to evaluate motivational systems in TD adults [55,56] and has been utilized in studying adults with ASD [58,59]. The Cronbach's alpha coefficients for BIS and BAS were reported to be 0.80 and 0.81, respectively [55]. Test-retest correlations for BIS and BAS subscales were reported to be from 0.59 to 0.69 [60]. The current study's Cronbach's alpha coefficients are detailed in Table S3.

2.5. Statistical analyses

The scores of the behavioral economics tasks and psychological measures were compared between the groups using two-sampled t tests and chi-squared tests for categorical variables. We also compared the clinical variables (age, IQ, and AQ) and psychological measures (IRI, BIS-11, and BIS/BAS) between the high and low AC participants as determined based on the results of behavioral economics tasks (RAT and mUG), using two-sampled t tests in the TD and ASD groups, respectively. As the number of women and smokers were low in the study population, sex and smoking status were not included in the analyses.

We also conducted separate multiple logistic regression analyses [dependent variables: RAT (low AC vs. high AC) and mUG (low AC vs. high AC)] in all participants (TD and ASD groups) based on the previous studies [61,62]. Age, IQ, AQ, IRI, BIS-11, and BIS/BAS were included as independent variables in the backward elimination model. Probabilities of 0.05 and 0.10 were used as entry and removal criteria, respectively (SPSS's default values) [63].

Statistical analyses were performed using SPSS 24 (IBM, Armonk, NY, USA). Results were considered statistically significant at p < 0.05 (two-tailed).

3. Results

The results of the behavioral tasks and psychological measures are presented in Table 2.

3.1. RAT

In the RAT, no significant difference was observed in the proportion of participants preferring cooperative choices (high AC) between the TD (55.6 %) and ASD (74.1 %) groups (p=0.15). In both groups, high AC participants scored higher on the IRI perspective-taking subscale compared to low AC participants (TD: low AC 18.7 ± 3.1 , high AC 21.7 ± 3.8 , p=0.04; ASD: low AC 13.7 ± 4.5 , high AC 17.6 ± 3.6 , p=0.03, Fig. 2). There were no significant differences in other clinical variables and psychological measures between high and low AC participants within both TD and ASD groups. Further details are available in Table S4.

3.2. mUG

No significant differences were observed in the proportion of high AC participants as assessed by the mUG between the TD (55.6 %) and ASD (48.1 %) groups (p = 0.59). In the TD group, high AC participants scored higher on the fantasy subscale of the IRI compared to low AC participants, while this observation was not seen in the ASD group (TD: low AC 18.1 ± 2.4 , high AC 21.1 ± 3.9 , p = 0.03; ASD: low AC 19.8 ± 4.5 , high AC 17.2 ± 3.5 , p = 0.10, Fig. 3). No significant differences in other clinical variables and psychological measures were found between high and low AC participants in both groups. Further information is provided in Table S5.

3.3. Multiple logistic regression analysis

Multiple logistic regression analysis showed that higher AQ and IRI perspective-taking subscale scores were significantly associated with higher AC in the RAT (Table 3). According to mUG, there were no significant variables influencing higher AC as evaluated by mUG.

Table 2Results of behavioral tasks and psychological measures.

	TD Group	ASD Group	Statistics	
	(n = 27)	(n=27)	\overline{p}	
Behavioral economics tasks				
RAT (low AC/high AC)	12/15	7/20	0.15 ^b	
mUG (low AC/high AC)	12/15	14/13	0.59 ^b	
Psychological measures				
IRI Perspective taking (mean \pm SD)	20.3 ± 3.8	16.6 ± 4.1	<0.01 ^a	
Fantasy (mean \pm SD)	19.7 ± 3.6	18.5 ± 4.2	0.25^{a}	
Empathic concern (mean \pm SD)	20.4 ± 2.6	18.9 ± 4.1	0.10^{a}	
Personal distress (mean \pm SD)	15.3 ± 4.0	21.3 ± 4.1	<0.01 ^a	
BIS-11 (mean \pm SD)	63.9 ± 10.4	69.4 ± 10.5	0.06^{a}	
BIS/BAS BIS (mean \pm SD)	18.9 ± 4.6	24.3 ± 3.8	<0.01 ^a	
BAS (mean \pm SD)	41.5 ± 5.1	36.4 ± 7.6	<0.01 ^a	

Abbreviations: ASD = autism spectrum disorder, BIS-11 = Barratt impulsiveness scale, 11th version, BIS/BAS = behavioral inhibition system/behavioral activation system, IRI = interpersonal reactivity index, mUG = modified ultimatum game, RAT = resource allocation task, TD = typical development.

^a Two-sampled *t*-test.

b Two-tailed chi-squared test.

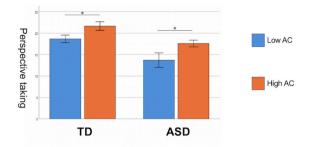


Fig. 2. Results of the RAT. In both TD and ASD groups, high AC participants showed higher scores in the perspective taking subscale of the IRI than low AC participants ($\text{TD}\,p = 0.04$, ASD, p = 0.03). Error bars indicate \pm standard errors. *p < 0.05 Abbreviations: AC = altruistic cooperation, ASD = autism spectrum disorder, IRI = interpersonal reactivity index, RAT = resource allocation task, TD = typical development.

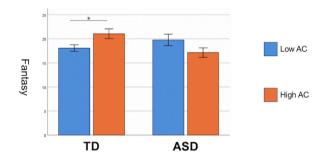


Fig. 3. Results of the mUG. In the TD group, high AC participants showed higher scores in the fantasy subscale of the IRI than low AC participants (p = 0.03), whereas this observation was not seen in the ASD group (p = 0.10). Error bars indicate \pm standard errors. *p < 0.05 Abbreviations: AC = altruistic cooperation, ASD = autism spectrum disorder, IRI = interpersonal reactivity index, mUG = modified version of the ultimatum game, TD = typical development.

Table 3Results of the multiple logistic analysis on the RAT.

	B (SE)	Wald	p	Exp (B)	95%CI
AQ	0.16 (0.06)	8.02	<0.01	1.17	1.05–1.30
IRI Perspective taking	0.35 (0.12)	8.45	<0.01	1.43	1.12–1.81
IRI Personal distress	-0.17 (0.09)	3.39	0.07	0.84	0.70–1.01

Abbreviations: AQ = autism spectrum quotient, IRI = interpersonal reactivity index, RAT = resource allocation task.

4. Discussion

In this study, we used two behavioral economics tasks to assess AC among adults with and without ASD. The results add to our understanding of individual variability in AC-related behavior.

In both the TD and ASD groups, high AC participants based on the RAT showed higher scores in the perspective-taking subscale of the IRI compared with low AC participants. Empathy is a powerful motivator of prosocial behaviors [20,47,64–66]. Specifically, the ability to take another's perspective is reportedly crucial to AC-related behaviors [20,67,68]. For example, Li et al. (2022) revealed that perspective taking was central to the effects of interpersonal traits on altruistic behaviors [46]. A recent examination of TD adults found impairments on RAT due to alexithymic traits; hence alexithymia may impair AC-related behaviors by altering empathic abilities across the autism spectrum [29]. Consistent with those in previous studies, our findings highlight that perspective taking in empathy is key in the individual variation of AC-related behavior in both TD and ASD populations.

In the TD group, high AC participants in the mUG had higher scores on the IRI's fantasy subscale compared to low AC participants. This subscale evaluates the ability to empathize with fictional characters, a crucial aspect of cognitive empathy, similar to perspective-taking [43,44,65]. This result underscores empathy's role in diverse AC-related behaviors, although such a pattern was not observed in the ASD group. Past studies indicate atypical moral reasoning in ASD, despite similar moral task behaviors to TD adults [15,69,70]. For example, while adults with ASD showed comparable judgments of suffering and causality to TD adults, they exhibited nuanced difficulties in assessing intentional action and moral judgments [69]. These findings, along with our results, suggest differences in cognitive processes during AC-related behaviors, particularly regarding the perceived intentions of others, between ASD and TD adults. Future neuroimaging research may further elucidate the mechanisms behind AC-related behavior in adults with ASD.

No significant differences were observed in the proportion of high AC participants between the TD and ASD groups, as evaluated by RAT and mUG. Additionally, logistic regression analysis using RAT indicated a positive association between higher autistic traits (AQ scores) and AC, suggesting that adults with more pronounced autistic traits exhibit greater AC in the RAT. This finding aligns with prior research showing that adults with ASD often make more altruistic decisions in specific behavioral economics tasks [16,17,33]. Moreover, recent study by Lischke et al. (2022) demonstrates that autistic traits do not necessarily hinder AC-related behavior in TD individuals with varying levels of autistic traits [29]. These findings, coupled with our study's results, reinforce the perspective that autism does not uniformly equate to impairment [42,71–73], suggesting the importance of comprehensive empathic ability assessments in devising effective individualized interventions for social cognitive challenges in ASD.

Clinically, our study underlines the potential of behavioral economics as a robust method for objectively evaluating social behaviors in both ASD and TD individuals [12,42,73]. The results also hint at the usefulness of behavioral economics tools in understanding the diverse patterns of decision-making in ASD. Despite differences in terminology between psychiatry and economics, and the necessity for cautious interpretation, previous studies have shown a link between behavioral economics task outcomes in controlled settings and real-world behaviors [74]. Considering their relative affordability and ease of administration, behavioral economics tools could be instrumental in exploring current symptomatology, developing new mediating markers, and personalizing treatment strategies in ASD.

This study's primary strength lies in its exploration of different types of AC-related behavior, utilizing behavioral economics tasks for both allocation and acceptance within the same sample. This approach expands on previous research that typically focused on either allocation or acceptance in adults with ASD [16,17], potentially informing the development of effective, tailored interventions for social cognitive impairments in ASD.

However, the study has several limitations. First, despite aligning with participant numbers in prior ASD social cognition research [16,33], our sample size was relatively small for observing individual differences. Second, the slightly younger age of the TD group compared to the ASD group necessitates a cautious interpretation of the results. Third, most ASD participants had undergone social skills training at Showa Karasuyama Hospital's daycare center, potentially limiting the representativeness of our findings across the broader ASD community. Fourth, our ASD sample consisted of only individuals with high intellectual functioning (full-scale IQ score >85), which may restrict the generalizability of our results. Finally, the cross-sectional design of this study precludes drawing causal conclusions. To validate and expand upon these findings, future longitudinal studies incorporating a more diverse range of ASD individuals are essential.

In conclusion, the findings of the present study show that empathy plays a key role in individual differences in AC-related behavior among adults with and without ASD, although this role can differ depending on the types of AC-related behavior between TD and ASD populations. Continued research on this area would provide additional clues regarding the development of effective individualized interventions for social cognitive impairments in ASD.

Ethics approval and consent to participate

The study received approval from the institutional review board of Showa University Karasuyama Hospital and the Committee on Medical Ethics of Kyoto University [ethical approval number B-2014-018] and adhered to the World Medical Association's Code of Ethics. After a complete description of the study, written informed consent was obtained from all participants.

Data availability statement

Data included in article/supp. Material/referenced in article.

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CRediT authorship contribution statement

Shoko Okuzumi: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis. Shisei Tei: Writing – review & editing, Project administration, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. Takashi Itahashi: Writing – review & editing, Visualization, Methodology, Investigation, Data curation, Conceptualization. Yuta Y. Aoki: Writing – review & editing, Supervision, Methodology, Investigation, Data curation. Ryu-ichiro Hashimoto: Writing – review & editing, Supervision, Methodology, Investigation, Data curation, Conceptualization. Motoaki Nakamura: Writing – review & editing, Supervision, Methodology, Investigation, Data curation, Conceptualization. Hidehiko Takahashi: Writing – review & editing, Supervision, Investigation, Funding acquisition, Data curation, Conceptualization. Haruhisa

Ohta: Writing – review & editing, Visualization, Resources, Methodology, Investigation, Data curation, Conceptualization. Junya Fujino: Writing – review & editing, Writing – original draft, Project administration, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e36255.

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