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Age-related Differences in Cognition across the Adult Lifespan in Autism Spectrum Disorder

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It is largely unknown how age impacts cognition in autism spectrum disorder (ASD). We investigated whether age-related cognitive differences are similar, reduced or increased across the adult lifespan, examined cognitive strengths and weaknesses, and explored whether objective test performance is related to subjective cognitive challenges. Neuropsychological tests assessing visual and verbal memory, generativity, and theory of mind (ToM), and a self-report measure assessing cognitive failures were administered to 236 matched participants with and without ASD, aged 20–79 years (IQ > 80). Group comparisons revealed that individuals with ASD had higher scores on visual memory, lower scores on generativity and ToM, and similar performance on verbal memory. However, ToM impairments were no longer present in older (50+ years) adults with ASD. Across adulthood, individuals with ASD demonstrated similar age-related effects on verbal memory, generativity, and ToM, while age-related differences were reduced on visual memory. Although adults with ASD reported many cognitive failures, those were not associated with neuropsychological test performance. Hence, while some cognitive abilities (visual and verbal memory) and difficulties (generativity and semantic memory) persist across adulthood in ASD, others become less apparent in old age (ToM). Age-related differences characteristic of typical aging are reduced or parallel, but not increased in individuals with ASD, suggesting that ASD may partially protect against an age-related decrease in cognitive functioning. Despite these findings, adults with ASD experience many cognitive daily challenges, which highlights the need for adequate social support and the importance of further research into this topic, including longitudinal studies. ***Autism Res*** *2016, 9: 666–676.*

Keywords: autism spectrum disorder; aging; older adults; cognition; neuropsychology; memory; theory of mind; generativity

Introduction

Typical aging is associated with age-related decline in various cognitive domains, such as episodic memory [e.g., Goh, An, & Resnick, 2012; Nyberg, Lövdén, Riklund, Lindenberger, & Bäckman, 2012], executive functions [EF; e.g., Hasher & Zacks, 1988; Verhaeghen & Cerella, 2002], and advanced theory of mind [ToM; e.g., Charlton, Barrick, Markus, & Morris, 2009; Maylor, Moulson, Muncer, & Taylor, 2002]. Cognitive challenges encountered by typically aging individuals show large overlap with those faced by individuals with autism spectrum disorder (ASD) at younger ages. For example, children and adolescents with ASD, a neurodevelopmental disorder characterized by qualitative impairments in social communication and interaction and restricted, repetitive behavior [American Psychiatric Association, 2013], display difficulties in aspects of episodic memory [Boucher, Mayes, & Bigham, 2012], EF [Brunsdon & Happe, 2014; Hill, 2004], and ToM [Yirmiya, Erel, Shaked, & Solomonica-Levi, 1998]. While ASD is a lifelong condition, it is unknown [Happé & Charlton, 2012; Mukaetova-Ladinska, Perry, Baron, & Povey, 2012] what happens to individuals with ASD when aging processes start to kick in.

Even though some are arguing that having ASD might protect against developing dementia [Oberman & Pascual-Leone, 2014], to our knowledge only two studies actually focused on cognition in older adults. A series of case-studies (67–84 years, $N = 5$) indicated that older adults with ASD still encounter cognitive deficits, although only three were assessed with actual memory and EF tests [James, Mukaetova-Ladinska, Reichelt, Briel, & Scully, 2006]. In the first ASD group study on age-related cognitive differences among older adults (51–83 years, $N = 46$), the effect of age was not homogenous across domains [Geurts & Vissers, 2012; Goh et al., 2012]. The authors postulated three hypotheses regarding age-related patterns. First, age may have a similar effect in individuals with and without ASD

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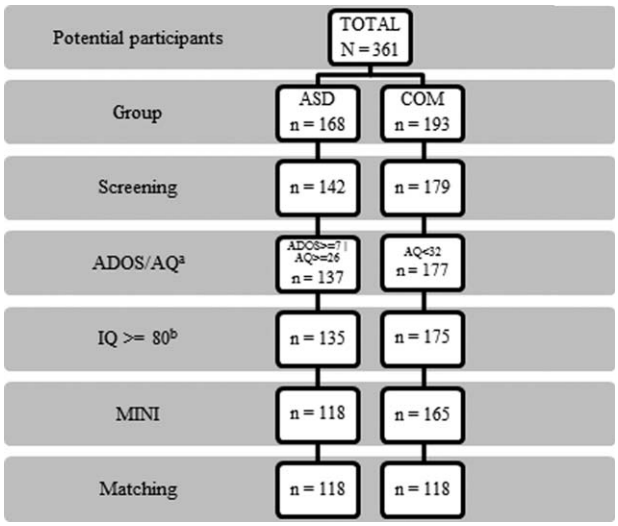

Figure 1. Diagram of the inclusion process. ASD, autism spectrum disorder; COM, comparison group; ADOS, Autism Diagnostic Observation Schedule; AQ, Autism-spectrum Quotient; IQ, estimated intelligence quotient; MINI, Mini International Neuropsychiatric Interview. Neuropsychological and questionnaire data was obtained from all participants except for Faux Pas (ASD: $n = 117$; COM: $n = 116$) and CFQ (ASD: $n = 116$). [a]Due to low sensitivity of the ADOS when administered to intellectually able adults [Bastiaansen, Thioux, et al., 2011], we required ASD participants to exceed the threshold on either the ADOS or AQ. Only five participants of those scoring below the ADOS cutoff (<7; $n = 35$) did not exceed the AQ cutoff (<26). The majority met the ADOS threshold ($n = 88$). [b]None of the participants was excluded based on the Mini Mental State Examination (i.e., no scores <26 were observed).

(parallel development hypothesis), which was observed for verbal memory. Second, ASD may have a detrimental effect (double jeopardy hypothesis), resulting in a steeper age-related decrease in cognitive functioning, as was observed for visual memory. Third, ASD may "protect" against age-related differences (safeguard hypothesis), as a reduced pattern was observed for generativity. The relatively small sample size of the study, and lack of using a standardized diagnostic instrument to verify already existing ASD diagnoses, warrants replication [Geurts & Vissers, 2012].

The current study was designed to test the three hypotheses by determining whether these earlier findings for episodic memory (visual and verbal) and generativity (fluency) can be replicated, but also by focusing on ToM. ToM is a highly relevant cognitive domain for ASD, which was ignored in the previous study. Besides using standardized assessment and including a much larger, independent, age-comparable group (50–79 years, $n = 113$), we extended the age range (20–79 years, $N = 236$) to study cognition not only in old age, but also across the adult lifespan. Please note that recently, in another ASD group study exploring age-related differences over the adult lifespan (20–61 years) in relational memory, a safeguard pattern on a specific aspect of relational memory was found [Ring, Gaigg, & Bowler, in press]. Finally, as elderly with ASD experienced more cognitive challenges in everyday life than typical older individuals [van Heijst & Geurts, 2014], we explored whether subjective cognitive failures are related to objective test performance.

We expected decreased performance in the ASD group compared to age-, gender-, and IQ-matched controls on phonemic [e.g., Bramham et al., 2009; Geurts & Vissers, 2012; Rumsey & Hamburger, 1988] and semantic [Spek, Schatorjé, Scholte, & van Berckelaer-Onnes, 2009] fluency, and advanced ToM [Chung, Barch, & Strube, 2014], but not on visual and verbal memory [Boucher et al., 2012; Geurts & Vissers, 2012]. We hypothesized age-related effects in ASD to be (a) increased on visual memory, (b) parallel on verbal memory, (c) reduced on phonemic and semantic fluency, and (d) reduced on ToM, given that ToM abilities decline in typical aging [e.g., Duval, Piolino, Bejanin, Eustache, & Desgranges, 2011] and social abilities seem to improve with age in adults with ASD [Bastiaansen, Thioux et al., 2011].

Methods

Participants

Individuals with ASD between 20 and 79 years were recruited through several mental health institutions across the Netherlands, and by means of advertisements on client organization websites. We applied the following exclusion criteria: (a) no prior clinical ASD diagnosis according to DSM-IV [American Psychiatric Association, 2000] criteria; (b) history of neurological disorders (e.g., epilepsy, stroke, cerebral contusion) or schizophrenia, or having experienced more than one psychosis; (c) Autism Diagnostic Observation Schedule < 7 [ADOS; Lord et al., 2000] and Autism-spectrum Quotient < 26 [AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001]; (d) IQ < 80 or Mini Mental State Examination < 26 [MMSE; Folstein, Folstein, & McHugh, 1975]; (e) current alcohol or drugs dependency. Based on these criteria, we excluded 50 of the initial 168 individuals with ASD (see Fig. 1) and included the remaining 118 participants.

Individuals without ASD (i.e., comparison group [COM]) were recruited by means of advertisements on the university website and on social media, and within the researchers' social environment. The following exclusion criteria were applied: (a) clinical diagnosis of ASD or Attention Deficit Hyperactivity disorder (ADHD); (b) history of neurological disorders or schizophrenia, or having ever experienced a psychosis; (c)

Table 1. Means (Standard Deviations) of the Demographic and Clinical Scores of the ASD and COM Group for Both the Whole Sample and a Subset of Participants over 50 Years.

	All			50+		
	ASD ($n = 118$)	COM ($n = 118$)	Statistics	ASD ($n = 57$)	COM ($n = 56$)	Statistics
Gender	83 M/35 F	83 M/35 F		44 M/13 F	43 M/13 F	
Education[a]	0/1/0/3/35/53/26	0/0/1/3/19/59/36	Fisher's test, $P = 0.08$	0/0/0/1/18/22/16	0/0/1/3/9/29/14	Fisher's test, $P = 0.17$
Diagnosis[b]	18/60/35/5			12/30/15/0		
Age	47.6 (14.9) range 20–79	47.7 (15.4) range 20–77	$F(1, 235) = 0.00$, $P = 0.98$, $\eta_p^2 = 0.00$	60.8 (6.9) range 50–79	61.5 (7.2) range 50–77	$F(1, 112) = 0.28$, $P = 0.60$, $\eta_p^2 = 0.00$
IQ	114.8 (16.9) range 84–155	114.3 (15.3) range 80–149	$F(1, 235) = 0.06$, $P = 0.81$, $\eta_p^2 = 0.00$	116.8 (16.4) range 84–153	116.1 (15.3) range 80–149	$F(1, 112) = 0.05$, $P = 0.83$, $\eta_p^2 = 0.00$
MMSE	29.1 (1.0) range 26–30	29.1 (1.0) range 26–30	$F(1, 235) = 0.07$, $P = 0.79$, $\eta_p^2 = 0.00$	29.1 (0.8) range 27–30	29.0 (1.1) range 26–30	$F(1, 112) = 0.34$, $P = 0.56$, $\eta_p^2 = 0.00$
AQ	33.7 (8.3) range 8–49	12.4 (5.5) range 2–26	$F(1, 234)^c = 542.40$, $P < 0.001$, $\eta_p^2 = 0.70$	34.9 (8.0) range 8–48	13.4 (5.0) range 4–25	$F(1, 111)^c = 290.85$, $P < 0.001$, $\eta_p^2 = 0.73$
ADOS[d]	8.6 (3.1) range 1–19			8.3 (3.0) range 3–18		

Note. ASD, autism spectrum disorder; COM, comparison group; M, male; F, female; IQ, estimated intelligence quotient; MMSE, Mini Mental State Examination; AQ, Autism-spectrum Quotient; ADOS, Autism Diagnostic Observation Schedule.

[a] The numbers between brackets indicate the educational level based on the Verhage Coding System [1964], ranging from 1 (primary education not finished) to 7 (university degree).

[b] The numbers between brackets indicate a diagnosis of Autism/Asperger/Pervasive Developmental Disorder Not Otherwise Specified/ASD.

[c] One ASD participant did not complete the AQ (but met the ADOS criterion and, hence, was included).

[d] Of the final sample, 30 participants scored below the ADOS cutoff (<7). Excluding these participants from the analyses did not alter the pattern of results (see eTables 2 and 3 in the Supporting Information).

ASD or schizophrenia in close family members (i.e., parents, children, brothers, and sisters); (d) AQ > 32; (e) IQ < 80 or MMSE < 26; and (f) current alcohol or drugs dependency. We excluded 26 of the initial 193 individuals without ASD. Of the remaining 167 participants, 118 were selected based on gender, age (within seven years, mean difference = 0.05, SD = 2.2), and IQ (within 22 points, mean difference = −0.5, SD = 10.0) to match the 118 ASD participants on these variables (Table 1).

Individuals were approximately evenly distributed across the age range per 10-year-bin (i.e., *n* ranges from 38 [19–29 years] to 51 [50–59 years]), even though there were fewer participants in the oldest bin (i.e., 70–79 years, $n = 16$). Information about clinical diagnoses, medical conditions, and family members were obtained by means of self-report.

Materials

ASD assessment. The ADOS module 4 [de Bildt & de Jonge, 2008; Lord et al., 2000] is the most commonly used, instrument to assess the current presence of ASD symptoms within the domains of communication, reciprocal social interaction, imagination, and restricted and repetitive behavior, during a standardized, semi-structured observation. Exceeding a specific cutoff (i.e., 7) on the combined communication/social interaction domain, is indicative of an ASD [Bastiaansen, Meffert et al., 2011]. The AQ [Baron-Cohen et al., 2001; Hoekstra, Bartels, Cath, & Boomsma, 2008] is a valid and reliable self-reported questionnaire for the assessment of autistic traits consisting of 50 items. We employed a threshold of 26 for the ASD group and a threshold of 32 for the COM group, as suggested for, respectively a referred clinical sample and the general population [Baron-Cohen et al., 2001; Woodbury-Smith, Robinson, Wheelwright, & Baron-Cohen, 2005]. Due to low sensitivity of the ADOS when administered to intellectually able adults [Bastiaansen et al., 2011], we required ASD participants to exceed the threshold on either the ADOS or AQ, but the majority did meet the ADOS criterion ($n = 88$; 74.6%).

Screening instruments. We administered the Vocabulary and Matrix Reasoning subtests of the Wechsler Adult Intelligence Scale third edition [WAIS-III; Uterwijk, 2000; Wechsler, 1997a] to estimate IQ; the MMSE [Folstein et al., 1975; Kok & Verhey, 2002; Molloy, Alemayehu, & Roberts, 1991] to screen individuals for pathological cognitive impairment; the Mini International Neuropsychiatric Interview Plus [MINI-Plus; Sheehan et al., 1998; van Vliet, Leroy, & van Megen, 2000] to assess the presence or absence of alcohol dependence, substance dependence, and psychoses.

Neuropsychological tests. *Visual memory*. Visual Reproduction is a valid and reliable subtest of the Wechsler Memory Scale third edition [WMS-III; Wechsler, 1997b], used to assess visual memory. In five consecutive trials, participants had 10 sec to memorize a geometrical figure and reproduce it immediately thereafter and after a 30-min delay period. Moreover, participants had to recognize the originally learned figures among 48 geometrical figures. Dependent variables are the sum of correctly recalled elements during immediate and delayed recall, and the sum of correctly recognized learned and rejected new figures (i.e., recognition).

Verbal memory. The Rey Auditory Verbal Learning Task [RAVLT; Rey, 1964; van den Burg, Saan, & Deelman, 1985] is a commonly used, valid, and reliable instrument [Saan & Deelman, 1986] to assess verbal memory. Participants learned and recalled a list of 15 unrelated words in five consecutive trials and, after a 20-min interval, recalled the list again and recognized the words among a list of 15 old and 15 new words. Dependent variables are the sum of correctly recalled words during the five learning trials (i.e., immediate recall) and after 20 minutes (i.e., delayed recall), and sum of correctly recognized old and rejected new words (i.e., recognition).

Generativity and semantic memory. In verbal fluency measures phonological and/or semantic cues are given to recall information from semantic memory [Goh et al., 2012]. Therefore, fluency measures are often used to assess both generativity (as EF measure) and semantic memory [Schmand, Groenink, & Van den Dungen, 2008]. Phonemic fluency was evaluated with the Controlled Oral Word Association Test [COWAT; Benton & Hamsher, 1989; Schmand et al., 2008], which has good internal consistency [Schmand et al., 2008]. Participants named as many words as possible starting with a provided letter in three trials of 1 min each (D,A,T), but were not allowed to name proper nouns, numbers, and serial words starting with the same prefix. Semantic fluency was assessed with the Word Naming subtest of the Groninger Intelligence Test [GIT; Luteijn & Barelds, 2004], which has good reliability and sufficient internal consistency [Mulder, Dekker, & Dekker, 2006]. Participants named as many words as possible belonging to a specific category in two trials of 1 min each (animals, professions). Dependent variables are the total number of correctly named words.

ToM. An abbreviated version of the Faux Pas test [Spek, Scholte, & Van Berckelaer-Onnes, 2010; Stone, Baron-Cohen, & Knight, 1998] was used to assess advanced ToM. Five stories containing a faux pas, which is a socially unintended inappropriate response [Baron-Cohen, O'Riordan, Stone, Jones, & Plaisted, 1999], and four stories without faux pas were read with the participants and questions about the faux pas were asked, together with two control questions to assure the stories were properly understood. Dependent variable is the sum of correctly answered questions on all stories minus the control questions.

Data collected through WMS-III and Faux Pas were coded by two raters (see eAppendix 1 in the Supporting Information).

Self-report questionnaire. The Cognitive Failures Questionnaire [CFQ; Broadbent, Cooper, FitzGerald, & Parkes, 1982; Merckelbach, Muris, Nijman, & de Jong, 1996] is a valid and reliable [Vom Hofe, Mainemarre, & Vannier, 1998] 25-item self-report questionnaire used to assess the experience of memory errors, committing blunders, and distractibility in everyday situations. CFQ total score is the dependent variable.

Procedure

Participants were informed about the study purposes and procedure and written informed consent was obtained. They filled out the AQ and CFQ and were tested in two sessions, in which (a) ASD assessment and screening took place; (b) neuropsychological tests were administered in counterbalanced order (additional experimental tests and questionnaires were administered, but will be discussed elsewhere). Participants received compensation for their travel expenses; most COM participants also received additional compensation (max. €20). Data was collected between March 2012 and July 2014. The study was approved by the institutional review board of the University of Amsterdam (2011-PN-1952).

Statistical Analyses

First, to compare the two groups on several cognitive domains, we ran three MANOVAs for visual memory, verbal memory, and generativity and semantic memory, and two ANOVAs for ToM and CFQ, each with Group (ASD, COM) as between-subject factor. Second, to investigate the effect of age, we ran linear multiple regression analyses for each domain with (centered) Age, Group, and Age × Group as predictors. If there was an Age × Group interaction, we ran follow-up regression analyses for each group separately. Third, to determine whether our results are comparable to Geurts and Vissers [2012], we reran the above mentioned analyses on a subgroup of participants, including individuals of 50 years or older. Fourth, to explore whether cognitive performance was associated with self-reported cognitive failures, we ran, per group,

Table 2. Group Means, Standard Deviations, and Statistics of the CFQ and of each Neuropsychological Test for Both the Whole Group and a Subset of Participants over 50 Years.

			All				50+			
Domain	Measure	Dependent variable	ASD	COM	*F*	η_p^2	ASD	COM	*F*	η_p^2
General cognition	CFQ	CFQ total score	46.0 (15.3)	29.1 (10.6)	96.47**	0.29	47.2 (13.1)	30.3 (11.1)	54.30**	0.33
Visual memory[a]	WMS-III	Immediate recall score	90.6 (11.4)	87.5 (11.7)	4.17*/**	0.02	88.53 (10.4)	82.0 (12.3)	9.30**	0.08
		Delayed recall score	77.1 (20.0)	79.8 (21.8)	0.01	0.00	71.7 (20.3)	66.8 (24.6)	1.35	0.01
		Recognition score	45.0 (2.6)	45.3 (2.5)	0.56	0.00	44.8 (2.4)	44.2 (2.4)	1.88	0.02
Verbal memory[b]	RAVLT	Immediate recall score	47.9 (11.1)	49.2 (10.3)	0.94	0.00	45.5 (9.9)	44.3 (10.3)	0.54	0.00
		Delayed recall score	10.4 (3.4)	10.4 (3.1)	0.00	0.00	9.9 (3.0)	8.9 (3.1)	3.41	0.03
		Recognition score	29.2 (1.3)	29.1 (1.4)	0.17	0.00	29.1 (1.2)	28.5 (1.9)	3.17	0.03
Generativity and semantic memory[c]	DAT	Nr of correct words	39.9 (11.2)	43.4 (10.9)	5.82*/**	0.02	38.3 (10.7)	43.0 (11.3)	5.12*/**	0.04
	GIT	Nr of correct words	44.3 (11.2)	47.7 (10.2)	6.12*/**	0.03	42.2 (10.6)	46.8 (11.4)	4.48*	0.04
Theory of mind	Faux Pas	Faux pas score	27.1 (4.9)	29.4 (6.2)	10.27**	0.04	26.7 (4.9)	27.8 (6.0)	1.02	0.01

Note. ASD, autism spectrum disorder; COM, comparison group; CFQ, Cognitive Failure Questionnaire; WMS-III, Wechsler Memory Scale third edition; RAVLT, Rey Auditory Verbal Learning Task; DAT, Dutch Version of the Controlled Word Association Task; GIT, Groninger Intelligentie Test.

[a] MANOVA overall test for all participants: $F(3, 232) = 4.41$, $P = 0.005$, $\eta_p^2 = 0.05$. While removing the outliers did not change the results of WMS delayed recall and recognition, it altered the results of immediate recall, $F(1, 231) = 7.32$, $P = 0.007$, $\eta_p^2 = 0.03$. The scores of the ASD and COM group were now significantly different. Removing the outliers on the other variables did not change the pattern of findings. MANOVA overall test for subset 50+: $F(3, 109) = 3.76$, $P = 0.01$, $\eta_p^2 = 0.09$.

[b] MANOVA overall test for all participants: $F(3, 232) = 1.43$, $P = 0.24$, $\eta_p^2 = 0.02$. MANOVA overall test for subset 50+: $F(3, 111) = 2.47$, $P = 0.07$, $\eta_p^2 = 0.06$.

[c] MANOVA overall test for all participants: $F(2, 233) = 3.98$, $P = 0.02$, $\eta_p^2 = 0.03$. Removing outliers strengthened the effects, $F(2, 231) = 5.54$, $P = 0.004$, $\eta_p^2 = 0.05$. MANOVA overall test for subset 50+: $F(2, 110) = 3.22$, $P = 0.04$, $\eta_p^2 = 0.06$. Removing outliers strengthened the effect of phonemic fluency, $F(1, 109) = 4.18$, $P = 0.02$, $\eta_p^2 = 0.07$. The scores of the ASD and COM group were now significantly different.

*$P < 0.05$. **$P < 0.01$.

Spearman correlations between CFQ and each dependent measure.

As normality assumptions were violated for almost all dependent variables and transformation did not normalize the data, data were analyzed with both parametric and nonparametric tests. As both analyses yielded analogous results, we only report parametric tests. Unless removing outliers (i.e., data points more than three SD from each group mean) changed the pattern of results, analyses are reported including outliers. To reduce the probability of Type I errors, alpha was set at 0.01 for the group comparisons and regression analyses. An alpha level of 0.05 was employed for the exploratory analyses.

Results

Group Comparisons

The ASD group reported many more cognitive failures on the CFQ than the COM group, but group differences were absent on most neuropsychological tests (Table 2). However, groups differed significantly on ToM, and, after removing outliers[1], on visual memory immediate recall, and generativity. These findings are discussed below.

Visual memory. ASD participants yielded higher scores on immediate recall of the WMS-III Visual Reproduction subtest than COM participants, suggesting that visual memory is a cognitive strength of adults with ASD.

Generativity and semantic memory. COM participants named more correct words starting with a given letter (phonemic fluency) and words belonging to a

[1]There were 5 outliers on the visual memory test (3 ASD, 2 COM), 5 on verbal memory (3 ASD, 2 COM), 2 on phonemic and semantic fluency (ASD), 2 on ToM (COM).

Table 3. Standardized Beta Coefficients and *P* Values of the Regression Models with Age, Group, and Age × Group as Factors for all 236 Participants.

	WMS-III						RAVLT											
	IR[a]		DR[b]		REC[c]		IR[d]		DR[e]		REC[f]		DAT[g]		GIT[h]		FP[i]	
	β	*P*	*B*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*
Age	−0.48	<0.001***	−0.47	<0.001***	−0.49	<0.001***	−0.46	<0.001***	−09.42	<0.001***	−0.37	<0.001***	−0.05	0.58	−0.06	0.47	−0.26	0.003**
Group	0.13	0.03*	0.01	0.92	−0.05	0.42	−0.06	0.29	0.00	0.99	0.03	0.68	−0.16	0.02*	−0.16	0.01*	−0.21	0.001**
Age × Group	0.21	0.01*	0.09	0.30	0.23	0.007**	0.14	0.09	0.16	0.07	0.18	0.04*	−0.03	0.74	−0.13	0.15	0.13	0.15

Note. WMS-III, Wechsler memory scale third edition; RAVLT, Rey auditory verbal learning task; IR, immediate recall; DR, delayed recall; REC, recognition; DAT, Dutch version of the Controlled Word Association Task; GIT, Groninger Intelligentie test; FP, Faux Pas. Removing the outliers strengthened the already found effects, but did not change the pattern of findings.

[a] $R^2 = 0.15$, $F(3, 232) = 13.88$, $P < 0.001$. [b] $R^2 = 0.17$, $F(3, 232) = 15.56$, $P < 0.001$. [c] $R^2 = 0.14$, $F(3, 232) = 12.18$, $P < 0.001$. [d] $R^2 = 0.15$, $F(3, 232) = 13.14$, $P < 0.001$. [e] $R^2 = 0.11$, $F(3, 232) = 9.73$, $P < 0.001$. [f] $R^2 = 0.08$, $F(3, 232) = 6.58$, $P < 0.0001$. [g] $R^2 = 0.03$, $F(3, 232) = 2.36$, $P = 0.07$. [h] $R^2 = 0.06$, $F(3, 232) = 4.73$, $P = 0.003$. [i] $R^2 = 0.08$, $F(3, 229) = 6.69$, $P < 0.001$.

*$P < 0.05$. **$P < 0.01$. ***$P < 0.001$.

given category (semantic fluency) than ASD participants, indicating difficulties for adults with ASD in this domain.

ToM. COM participants had better Faux Pas performance than ASD participants. Hence, adults with ASD showed ToM problems.

Age-related Differences

Age had a significant effect on all domains, except generativity. As most regression analyses did not reveal any Age × Group interaction (Table 3), age seemed to have a similar effect in the ASD and COM group. Yet, we observed an interaction for visual memory recognition and a borderline significant interaction for visual memory immediate recall. These findings are discussed below.

Visual memory. While age did not explain a relevant proportion of variance in the ASD group, $F(1, 116) = 2.58$, $P = 0.11$, $R^2 = 0.02$, it did in the COM group, $F(1, 116) = 39.76$, $P < 0.001$, $R^2 = 0.26$. Inspection of the beta coefficients revealed a steeper decrease in performance in the COM group ($\beta = -0.51$) compared to the ASD group ($\beta = -0.15$). These results indicate that recognition in adults with ASD did not significantly differ over age, whereas performance of adults without ASD deteriorated with increasing age. Similar results were found for immediate recall. Age explained a small amount of variance in the ASD group, $F(1, 116) = 3.90$, $P = 0.05$, $R^2 = 0.03$, but a considerable amount in the COM group, $F(1, 116) = 36.19$, $P < 0.001$, $R^2 = 0.24$. Again, inspection of the beta coefficients revealed a steeper decrease in performance in the COM group ($\beta = -0.49$) compared to the ASD group ($\beta = -0.18$).

Older Adults

Selection of 50+ participants yielded a subset of 57 ASD and 56 COM participants between 50 and 79 years. The two groups did not differ on gender, age, IQ, MMSE score, or educational level (Table 1). Group comparisons revealed that, similarly to the whole group analyses, elderly with ASD reported more cognitive failures, had higher scores on visual memory immediate recall, and had lower scores on phonemic fluency, compared to COM participants. In contrast, older individuals with ASD had no longer reduced ToM scores compared to the COM group (Table 2). The impact of age was similar among groups on all investigated domains (Table 4), including visual memory, which is in contrast to the overall analyses.

Table 4. Standardized Beta Coefficients and *P* Values of the Regression Models with Age, Group, and Age × Group as Factors for the Subset of 50+ Participants ($n = 113$).

	WMS-III						RAVLT											
	IR[a]		DR[b]		REC[c]		IR[d]		DR[e]		REC[f]		DAT[g]		GIT[h]		FP[i]	
	β	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*
Age	−0.34	0.007**	−0.26	0.04*	−0.38	0.003**	−.41	.002**	−.34	.009**	−.20	.129	−.20	.12	−.22	.08	−.22	.10
Group	0.27	0.003**	0.09	0.30	0.11	0.21	0.04	0.63	0.16	0.08	0.16	0.09	−0.24	0.009**	−0.245	0.007**	−0.10	0.28
Age × Group	0.13	0.28	−0.07	0.58	0.08	0.54	0.16	0.21	0.12	0.35	0.10	0.45	−0.07	0.59	−0.11	0.40	0.05	0.69

Note. WMS-III, Wechsler Memory Scale third edition; RAVLT, Rey Auditory Verbal Learning Task; IR, immediate recall; DR, delayed recall; REC, recognition; DAT, Dutch version of the Controlled Word Association Task; GIT, Groninger Intelligentie Test; FP, Faux Pas. Removing the outliers did not change the pattern of findings.

[a] $R^2 = 0.15$, $F(3, 109) = 6.27$, $P < 0.001$. [b] $R^2 = 0.11$, $F(3, 109) = 4.47$, $P = 0.005$. [c] $R^2 = 0.13$, $F(3, 109) = 5.20$, $P = 0.002$. [d] $R^2 = 0.11$, $F(3, 109) = 4.30$, $P = 0.007$. [e] $R^2 = 0.10$, $F(3, 109) = 4.09$, $P = 0.009$. [f] $R^2 = 0.05$, $F(3, 109) = 1.90$, $P = 0.134$. [g] $R^2 = 0.09$, $F(3, 109) = 3.60$, $P = 0.016$. [h] $R^2 = 0.10$, $F(3, 109) = 4.16$, $P = 0.008$. [i] $R^2 = 0.08$, $F(3, 108) = 1.65$, $P = 0.182$.

*$P < 0.05$. **$P < 0.01$.

Exploratory Analyses

Subjective experience of cognitive failures was not associated with actual test performance in either the ASD or the COM group (all $ps > 0.1$, Spearman's rho ranged from −0.11 to 0.16).

Discussion

In the current study, we investigated age-related differences in cognition across a large sample of individuals with ASD. While changes with age have largely been examined within the general population, alterations faced by adults with ASD when growing old have hardly received any attention. Albeit cross-sectional age-related cognitive decline might be similar or reduced in older adults with ASD, an earlier study indicated it might also be increased, suggesting that ASD and aging can be two factors that jeopardize each other [Geurts & Vissers, 2012]. However, in the present study, we did not find any evidence for this alarming hypothesis, as we observed similar or reduced age-related differences across the adult lifespan in ASD. Hence, for some cognitive domains having an ASD diagnosis might be a protective factor to typically observed age-related decrease in functioning.

Young individuals with ASD demonstrate relatively intact abilities in visual and verbal memory and difficulties in generativity [Boucher et al., 2012; Hill, 2004]. As expected, similar strengths and weaknesses were observed from young to late adulthood [Boucher et al., 2012; Bowler, Limoges, & Mottron, 2009; Bramham et al., 2009; Geurts & Vissers, 2012; Rumsey & Hamburger, 1988], with adults with ASD even outperforming their non-ASD counterparts on visual memory. This latest finding would fit with the idea of individuals with ASD having enhanced visual functioning [Samson, Mottron, Soulieres, & Zeffiro, 2012]. Also ToM, a major difficulty in childhood and adolescence, was impaired when considering the whole age range [Chung et al., 2014]. ToM deficits were, however, no longer observed in older adults with ASD (50+) compared to the older adults without ASD. This result was neither explained by ToM enhancement nor by reduced age-related deterioration in ASD, as predicted. Although age seemed to have a smaller impact in ASD, the difference with non-ASD was too small to detect a differential age-related pattern. Nevertheless, we hypothesize that individuals with ASD continue to be actively involved in trying to understand social situations and other people's thoughts as they know it is difficult for them, leading to similar performance in old age compared to typically aging adults.

While performance declined with increasing age on verbal memory, generativity was not negatively affected by age. This pattern was similar in the two groups (i.e., parallel pattern). Large studies among typically developing adults generally report age-related deterioration on phonemic and semantic fluency [Tombaugh, Kozak, & Rees, 1999], but age effects might be masked in individuals with high verbal intelligence or high educational level [Bolla, Lindgren, Bonaccorsy, & Bleecker, 1990; Tombaugh et al., 1999]. Finally, we found a differential pattern for visual memory: Adults without ASD showed an age-related decrease in performance, whereas adults with ASD did not. Hence, the impact of age was reduced in ASD. A similar effect was reported in a recent study on relational memory processes, in which the role of age seemed to be less pronounced in adults with ASD (age range 20–61 years) on object order recognition [Ring et al., in press]. Furthermore, another recent study suggested that individuals with ASD, in contrast to for example individuals developing dementia, have hyperplastic brains that protect them against cognitive decline [Oberman & Pascual-Leone, 2014]. Indeed, based on a database analysis of Harvard Clinical and Translational Science Center records, individuals with ASD seem to suffer less frequently from Alzheimer's dementia than a general or schizophrenia population [Oberman & Pascual-Leone, 2014]. Although an intriguing finding, it can result from a report bias. Moreover, having a hyperplastic brain may explain general reduced age-related deterioration in ASD, but does not clarify why this advantage would only be restricted to visual memory.

Alongside observed difficulties in some domains, adults with ASD subjectively experienced many cognitive daily challenges, with a large amount of individuals reporting clinically significant failures (<2SD below normative mean), as revealed by additional exploratory analyses (see eAppendix 2 and eTable 1 in the Supporting Information). Despite these findings, only a few participants performed within the clinical range during testing. Moreover, there is no concordance between subjective cognitive complaints and objective test performance. Hence, even though cognitive performance difficulties in ASD may be clinically insignificant, this discordance warrants further research.

Some may argue that our study suffers from some limitations affecting the interpretation of our findings. First, as the current study was cross-sectional in nature, rather than longitudinal, we cannot yet draw conclusions on how changes in cognition actually develop over time among individuals with ASD. Therefore, conclusions about cross-sectional age-related decline should be interpreted with caution. Second, it can be argued that our sample was intellectually high-functioning with relatively mild ASD characteristics. Most participants were diagnosed in adulthood, which has been associated with relatively mild symptomatology and sufficient cognitive abilities to compensate for ASD-related difficulties [Heijnen-Kohl & van Alphen, 2009]. Nevertheless, all ASD participants already had a formal, clinical diagnosis and before an ASD diagnosis is given, individuals go through thorough assessment by a multidisciplinary team during which developmental history is commonly assessed. Moreover, the majority of participants met ADOS criteria for ASD. Exploratory analyses on only those individuals who exceeded the ADOS threshold, yielded similar results and did not alter the interpretation of our major findings (see eTables 2 and 3 in the Supporting Information). The inclusion of intellectually normal-to-high-functioning individuals was of importance to test whether age-related patterns were comparable to typical developing adults. However, many individuals with ASD have an intellectual disability [Matson & Shoemaker, 2009] and our results may not apply to them. Third, the majority of our ASD participants suffered from a comorbid psychiatric condition, such as depression or anxiety. Although inclusion of those individuals increases the representativeness of the sample, it also may have influenced our findings. Yet, recently, it was shown that comorbidity was not correlated with neuropsychological performance in ASD males [Wilson et al., 2014]. Fourth, although we included a large age range, some age-related differences or changes become apparent only in very old age. As a result, further research including even older individuals may provide more knowledge on the effect of age in ASD. Fifth, we did not replicate some findings of our earlier study [Geurts & Vissers, 2012]. Nevertheless, post-hoc correction for multiple comparisons of the results previously obtained with exploratory regression analyses did reveal similar age-related patterns as found in the current 50+ group. This discrepancy underlines the importance of confirmatory replication studies.

Conclusions

Age-related deterioration in cognitive functioning is characteristic of typical aging. In the current cross-sectional study, we demonstrated that this pattern is parallel or less pronounced in individuals with ASD. We did not find evidence for the hypothesis that age-related differences in cognition are increased in ASD. Cognitive strengths and weaknesses occurring in adulthood are still present in old age, although ToM impairments seem to be less apparent in late adulthood. Taken together, the findings of this cross-sectional study suggest that ASD may indeed be a safeguard for

age-related cognitive decline, but also reveal the crucial role of replication studies. Moreover, the subjectively experienced daily challenges and poor quality of life of older adults with ASD [van Heijst & Geurts, 2014] highlight the importance of research into older adulthood in ASD and the need for more knowledge in order to provide better social and environmental support to improve the life of individuals with ASD across the lifespan. The investigation of cognitive aging in ASD is a completely new and exciting area of research and our study represents a logical initial step providing unique insights into this direction. However, as longitudinal and cross-sectional studies do not always reveal the same age-related patterns [Nyberg et al., 2012], follow-up studies are needed to determine the applicability of these findings on the long term.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

eAppendix 1. Inter-rater concordance
eAppendix 2. Inter-individual differences

eTable 1. Percentages of ASD and COM participants scoring 2SD below or above the normative mean
eTable 2. Group means, standard deviations, and statistics of the CFQ and of each neuropsychological test for the whole group with exclusion of ASD participants that did not meet ADOS criteria ($n = 30$)
eTable 3. Standardized beta coefficients and p values of the regression models with Age, Group, and Age×Group as factors for all participants with exclusion of ASD participants that did not exceed the ADOS threshold ($n = 30$)