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DOI
10.1016/j.psychres.2023.115063

Publication date
2023

Document Version
Final published version

Published in
Psychiatry Research

License
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Psychiatry Research 321 (2023) 115063

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

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ARTICLE INFO

Keywords:
Aging
Cognition
Autism

ABSTRACT

Longitudinal studies on cognitive aging in autism are scarce, and largely underpowered, yet essential to obtain more conclusive results on cognitive changes in autism during adulthood. In the largest longitudinal study on cognition thus far, we aimed to get more insight into cognitive aging in autism. As pre-registered, we computed reliable change indices (RCIs) and multilevel models to estimate cognitive changes in 128 autistic, and 112 non-autistic adults (range: 24–85 yrs.) over two to three timepoints (average interval: 3.5 yrs.). Participants were tested on 15 outcome measures, covering verbal memory, visual (working) memory, prospective memory, theory of mind, fluency, response speed, inhibition, planning, and switching. RCIs showed no significant differences between groups (autism/no-autism) in changes over time. Using multilevel models, most tasks showed sensitivity to cross-sectional age-related effects, and/or longitudinal changes, with worse performance at older age, and later timepoints. However, effects were not significantly different between the autism and no-autism group. This lack of group differences was substantiated by additional Bayesian analyses. In sum, the current study provides evidence for parallel (similar) cognitive aging in autism. Specifically, autistic individuals diagnosed in adulthood, without intellectual disability, do not seem at risk for accelerated cognitive decline.

1. Introduction

Autism can be described as a developmental difference, shaping the lives of autistic individuals from the first to the final stages of life. However, research on the entire lifespan of autistic individuals is scarce. On cognitive aging, specifically, longitudinal studies are needed to elaborate on the inconsistent findings in cross-sectional studies thus far. Some might argue that autistic individuals are more vulnerable for cognitive aging (Bowler, 2007; Braden et al., 2017; Geurts and Vissers, 2012), supported by epidemiological data indicating increased risks for certain neurodegenerative disorders (Bishop-Fitzpatrick and Kind, 2017; Croen et al., 2015; Geurts, McQuaid, et al., 2020; Hand et al., 2019; Rydzewska et al., 2018; Vivanti et al., 2021) – and by higher rates of self-reported cognitive difficulties in adults with autism (Geurts, Pol, et al., 2020; Klein et al., 2022; Lever and Geurts, 2016). However, though not consistent, most cognitive research tends to observe a gentler pattern in which cross-sectional age-related differences between autistic and non-autistic individuals are minimal or even advantageous towards autistic individuals (Ambery et al., 2006; Geurts and Vissers, 2012; Lever and Geurts, 2016; Roestorf et al., 2019; Tse et al., 2019; Zivrali Yarar et al., 2020). Longitudinal studies are warranted to determine whether autistic adults are indeed not particularly at risk for increased impact of cognitive aging or whether previous cross-sectional results are clouded by cohort effects.

Cohort effects could have affected previous cross-sectional conclusions, especially in studies where age of diagnosis, and age of cognitive assessment were related. Even though numerous reasons for late diagnoses are possible, if an individual with autism is diagnosed at, or after retirement age, this *could* imply that their autism affected their school, studies, or work differently compared to those diagnosed at younger ages. Possibly, certain genetic and/or environmental factors in these individuals allowed them to compensate for aspects that they might have struggled with throughout life. Such compensatory mechanisms show parallels to cognitive reserve, which is known to mitigate the effects of neural decline (Cabeza et al., 2018; Stern et al., 2019). For instance, individuals with high educational attainment are known to show less, or late cognitive decline (Habib et al., 2007). Although speculative, compensatory mechanisms in late-diagnosed autistic

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https://doi.org/10.1016/j.psychres.2023.115063
Received 1 November 2022; Received in revised form 10 January 2023; Accepted 14 January 2023
Available online 18 January 2023

individuals could have caused cross-sectional conclusions on cognitive aging in autism to be too optimistic.

Longitudinal data on autistic cognitive aging is scarce. In the first longitudinal study that measured the development of IQ and language over a 40-year follow-up period, most individuals ($n = 45$, 75%) showed improvements or stable performances from childhood (2–13 years) to middle adulthood (29–64 years; Howlin and Magiati, 2017). However, those individuals who failed to progress in early language development, showed severe impairments in middle adulthood ($n = 15$, 23%). Two studies covering middle- and late adulthood show contrasting results. In one study (Roestorf et al., 2019) they observed no age-related changes on general intelligence, memory, and language in both younger (18–49 yrs.) and older (50–79 yrs.) autistic ($n = 33$) and non-autistic ($n = 18$) adults over a two-year time period. Yet in another study (Pagni et al., 2022) they observed more extensive cognitive decline in short-term memory, but not long-term memory, in a sample of 23 autistic and 22 non-autistic middle-aged adults (40–64 yrs.) over a two-to-three year time period. However, both studies (Roestdorf et al., 2019; Pagni et al., 2022) failed to detect general changes over time (i.e., in both groups). Furthermore, modest sample sizes limited the generalizability of these results. As such, more extensive longitudinal studies are needed to obtain conclusive results on cognitive aging in autism.

Next to these longitudinal studies on autism, we could build on studies describing cognitive aging in other developmental conditions, such as schizophrenia, and Attention Deficit/Hyperactivity Disorder (ADHD). Considering that schizophrenia, and ADHD show large diagnostic overlap with autism, and parallels in cognitive development to autism (Antshel et al., 2016; Jutla et al., 2022), one might argue that cognitive ageing might occur similarly across these developmental conditions. In a review by Rund (2018) it was concluded that schizophrenia is mostly *neurodevelopmental* in nature, not *neurodegenerative*. Longitudinal data indicated that in schizophrenia, cognitive functions are relatively stable throughout adulthood, yet more extensive brain changes seem present - hypothetically related to medication use. In ADHD, aging research is complicated by the interrelationships between the core aspects of ADHD and the characteristics of cognitive aging. Some ADHD symptoms might be expressed differently after childhood (hyperactivity), whilst others might co-occur with old-age disease (inattention/impulsivity) (Moffitt et al., 2015). To date, it is therefore unclear whether ADHD is an actual risk factor for dementia, or merely a "phenotypic mimic" (Callahan et al., 2017). In sum, studying cognitive aging in developmental conditions is complicated, as brain and cognitive changes can be misaligned and, developmental changes in (late) adulthood complicate the study of developmental differences. However, in line with preliminary evidence on cognitive aging in autism, neither a diagnosis of ADHD nor schizophrenia seems to be an obvious risk factor for accelerated cognitive decline.

The current study investigates longitudinal cognitive aging in a sample of autistic ($n = 128$) and non-autistic adults ($n = 112$) between 24 and 85 years, extending our previous cross-sectional work (Lever and Geurts, 2016; Torenvliet et al., 2021). A comprehensive cognitive test battery ($k = 15$) is administered in three waves in two, overlapping, cohorts. Using reliable change indices (RCIs), frequentist multilevel regression, and Bayesian statistics cognitive changes are assessed. We expect that older participants perform worse compared to younger participants (cross-sectional age effect), and that performance declines over time (longitudinal interval effect) on nearly all cognitive tasks. Also, the possibility that older individuals decline faster than younger participants over time (age*interval interaction) is assessed. Most importantly, we expect a parallel aging pattern between autistic and non-autistic adults, hence, we hypothesize that reliable change rates are similar across groups, and that cross-sectional age, and longitudinal interval effects are similar for autistic and non-autistic individuals.

2. Methods

2.1. Design

We used a multistage overlapping cohort design, with two cohorts included at different timepoints (see Geurts et al., 2021). Data collection included four waves; at Wave 2 no cognitive data was obtained, and is thus not part of this study. The first cohort was included at Wave 1, had the second cognitive measurement at Wave 3, and some had a third measurement at Wave 4. The second cohort was included at Wave 3 and had the second measurement at Wave 4. Three measures were added at Wave 3; for these measures data are only available in Wave 3 and 4, see Fig. 1.

2.2. Participants

Participants ($n = 464$; n_{autism}=207 and $n_{no\text{-}autism}$=257) between 24 and 85 years were eligible for the current study. Autistic individuals were included if 1) they had a registered diagnosis according to the DSM (American Psychiatric Association, 2013) criteria, and 2) they scored above the Autism Diagnostic Observation Schedule [−2] cut-off (ADOS [−2], Bastiaansen et al., 2011; Bildt et al., 2013; Lord et al., 2012), or the Autism-spectrum Quotient (AQ, Baron-Cohen et al., 2001).[1] Exclusion criteria for both groups were 1) a history of neurological disorders (e.g., epilepsy, stroke, multiple sclerosis), schizophrenia or having experienced more than one psychotic episode, 2) Wechsler Adult Intelligence Scale-IV (WAIS-IV; Wechsler, 2003) IQ <70 or Mini Mental State Examination (MMSE; Folstein et al., 1975) < 18,[2] 3) current alcohol or drugs dependency as indicated by the administration of the MINI International Neuropsychiatric Interview (MINI; Sheehan et al., 1997; Van Vliet et al., 2000). For the no-autism group four additional exclusion criteria were: 1B) a history of autism or AD(H)D, 2B) first-degree relatives (i.e., parents, children, siblings) with autism or AD(H)D, 3B) AQ > 32, 4B) ADHD-SR symptoms in childhood ≥ 7 and/or adulthood ≥ 6. Exclusion criteria were checked at each timepoint.

2.3. Materials

Eleven cognitive tests with 15 outcome variables were administered, see Table 1 for a brief description and references. This test battery includes measures which are either particularly sensitive to cognitive decline, such as memory and processing speed (Salthouse, 2019) and/or thought to be different in autistic adults, such as verbal fluency, and Theory of Mind (Torenvliet et al., 2021). Raw test scores were converted to *z*-scores, using baseline test scores (T1) of all participants in the no-autism group to compute means and standard deviations ($n = 257$). After recoding, higher *z*-scores indicated better performance.

Next to the cognitive variables, we administered the Cognitive Failures Questionnaire (CFQ; Broadbent et al., 1982) measuring self-reported cognitive functioning, the AQ measuring autism-related traits (Baron-Cohen et al., 2001), WAIS III/IV matrix reasoning and vocabulary subtests as a proxy for IQ (Wechsler, 1997a, 2003), and the MMSE (Folstein et al., 1975) measuring global cognitive impairments. All these measures have sufficient (AQ; Baron-Cohen et al., 2001) to good (CFQ; Broadbent et al., 1982, WAIS; Wechsler 1997a, 2003, MMSE; Folstein et al., 1975) psychometric properties, and have been used widely in autism and/or aging research.

[1] In Cohort 1, 25% (N=13) of the followed-up autistic participants scored below the ADOS cut-off (total < 7), in Cohort 2, 20.5% (N=15) scored below the ADOS-2 cut-off (total < 9). These participants all scored above the AQ cut-off. Rates are very similar to our results at T1, which were not changed by including only ADOS+ participants (see Lever et al., 2016; Torenvliet et al., 2021). Therefore, results are reported as pre-registered.

[2] None of our participants scored below 25 on the MMSE.

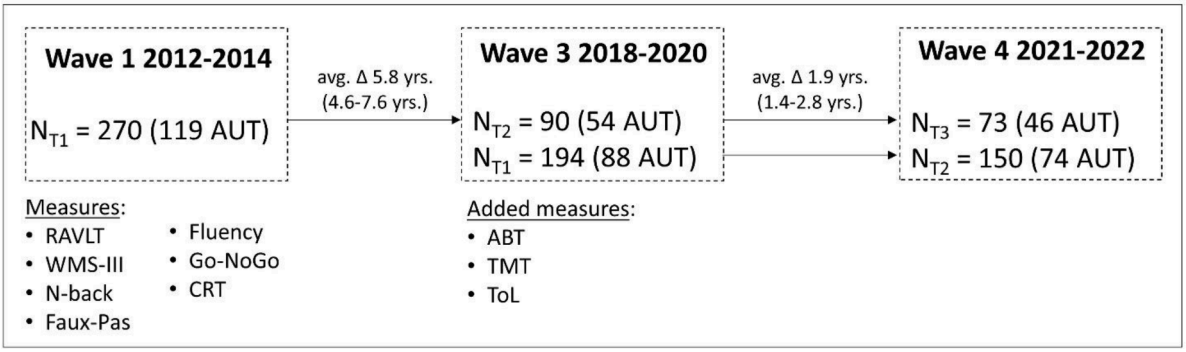

Fig. 1. Illustrative display of the study design.
Note. AUT, autism; avg., average; yrs., years; RAVLT, Rey Auditory Verbal Learning Test; WMS-III, Wechsler Memory Scale 3rd edition; CRT, choice response task; ABT, Amsterdam Breakfast Task; TMT, trail making test; ToL, tower of London.

Table 1
Overview of cognitive outcome variables.

Task	Outcome	Additional information (score range)	Test-retest reliability
RAVLT[a]	Verbal Recall I	Immediate recall trial 1–5 (0–75)	0.80
	Verbal Recall II	Delayed recall (0–15)	0.83
WMS-III[b]	Visual Recall I	Immediate recall (0–104)	unavailable
	Visual Recall II	Delayed recall (0–104)	unavailable
ABT[c]	Event Based PM	Total correct (0–3)	unavailable
	Time Based PM	Total correct (0–3)	unavailable
N-back[d]	Working memory	Accuracy difference score (−1.0–1.0)	unavailable
Faux-Pas[e]	Theory of Mind	Total score (0–38)	unavailable
DAT[f]	Letter Fluency	Nr. of correct words	0.80
GIT[g]	Category Fluency	Nr. of correct words	0.92
Go-NoGo[h]	Inhibition	(Accuracy NoGo/mean RT Go)*100	unavailable
ToL[i]	Planning	Total Move Score (# excess moves)	unavailable
TMT[j]	Set-shifting	Total Time B/Total Time A	unavailable
CRT[k]	Response speed	Mean reaction time	unavailable
	Response variability	Standard deviation reaction time	unavailable

Note. RAVLT, Rey Auditory Verbal Learning Test; WMS-III, Wechsler Memory Scale; ABT, Amsterdam Breakfast Task; GIT, Groninger Intelligentie Test; ToL, Tower of London; TMT, Trail Making Test; CRT, Choice Response Task; Nr., Number.
[a] Saan and Deelman (1986).
[b] Wechsler (1997b).
[c] in house development (based on Altgassen et al., 2019).
[d] in house development (see Lever et al., 2015).
[e] Baron-Cohen et al. (1999), Spek et al. (2010).
[f] Schmand et al. (2010).
[g] Mulder et al. (2006).
[h] in house development (see Torenvliet et al., 2023, preprint).
[i] Shallice, 1982. ToL completion time was recorded, and limited to 120 s per trial. After 120 s, the trial was ended and the maximum number of moves (20) was administered for this trial.
[j] in house development (based on Reitan and Wolfson, 1985).
[k] in house development (see Lever et al., 2015).

2.4. Procedure

The screening procedure and corresponding materials are described in the study protocol paper, see Geurts et al. (2021). Cognitive tasks were administered during 2–2.5 h testing sessions in counterbalanced order. All participants received monetary compensation (€30,-) for their participation, and (partial) reimbursement of their travelling costs. The set-up and results of this study were discussed with our older/autistic think tank, and approved by the ethical review board of the Department of Psychology of the University of Amsterdam (2011-PN-1952; 2018-BC-9285).

2.5. Analyses

Our pre-registered analyses plan (https://aspredicted.org/VVZ_MHZ) consists of five parts. First, attrition analyses were performed. We investigated differences between those who participated at follow-up and those who did not in group (autism/no-autism), cohort, and sex-ratio across groups, and differences in baseline age, IQ, AQ score, CFQ score, and MMSE score for both groups (autism/no-autism) separately.

Second, reliable change indices (RCIs) were estimated to assess the extent of change from T1 to T2 in two ways. In method 1, RCIs on all outcomes were calculated based on average difference scores (Frerichs and Tuokko, 2005)[3]:

$$RCI_{SE} = \frac{x_2 - x_1 - (m_2 - m_1)}{se_{diff}},\ se_{diff} = \frac{1}{n-1}\sum_i (z_i - \overline{z_i})^2$$

Chi-squared tests assessed group differences (autism vs. non autism, and improvement vs. stable vs. decline), using Holm-corrected p-values ($k = 15$). In method 2, RCIs were calculated with previously observed test-retest reliabilities (i.e., independent of the current sample); commonly used in clinical practice (Jacobson and Truax, 1991)[4]:

$$RCI_{Rxx} = \frac{x_2 - x_1 - (m_2 - m_1)}{se_{diff}},\ se_{diff} = \sqrt{2s_e^2},\ S_e = s_1\sqrt{1 - r_{xx}}$$

These were calculated for outcomes with the most comparable available samples, namely RAVLT recall I and II, and both fluency tasks (see Table 1). Holm corrected chi-squared tests assessed group differences (k=4). Both methods were assessed separately in the two cohorts (Wave 1–3, and Wave 3–4), with a 1.645 cut-off for reliable change (90% CI; Duff, 2012). Method 2 was expected to be more sensitive than method 1, as test-retest reliabilities are based on shorter intervals, and larger samples, resulting in smaller se_{diff}.

Third, multilevel regression analyses (R-package lme4; Bates et al., 2015; R Version 3.6.1) were performed to identify the effects of age and interval. Outcome variables were the z-scores on each cognitive measure. Interval effects were estimated in each individual (random intercepts and slopes). In Model 1, effects of interval (between timepoints) were estimated to assess longitudinal changes across groups on each

[3] m2, m1, and se_{diff} were estimated in the no-autism group from Cohort 2 (n=76).
[4] S_1 were estimated in the no-autism group at T1, and r_{xx} were the reported test re-test reliabilities, see Table 1.

outcome. In Model 2, age (centered) and the age*interval interaction were added to assess cross-sectional age effects, and whether the effects of interval were different for individuals of younger/older baseline age. Model 2 describes the interval effect only for the sample mean age (e.g., 50 yrs.). Therefore, longitudinal effects (interval) were obtained from Model 1 (Goh et al., 2012). In Model 3, group was added Model 1 to assess group differences in longitudinal change. In Model 4, group was added to Model 2 to assess group differences in cross-sectional age effects and/or age*interval interactions. In addition (not pre-registered), we conducted Bayesian analyses to quantify the evidence for multilevel models without an interval*group, and age*interval*group interaction, i.e., testing the null hypothesis of no differential aging effect. Bayes factors (BF_{01}) were computed based on BIC values (Wagenmakers, 2007). $BF_{01} > 3$ indicated substantial evidence in favor of the null model (Jarosz and Wiley, 2014).

Fourth, simple regression analyses were performed to predict which factors could explain individual differences in changes over time. Individual beta coefficients extracted from Model 1 (interval only) were used as outcome variables, with sex, baseline CFQ and baseline IQ as predictors in each group. All regression analyses were Holm corrected ($k = 15$).

Fifth, sensitivity analyses for parts three and four were performed, only including participants of Cohort 2, because intervals, and sample sizes were expected to be more similar between the two groups (autism vs. no-autism) within this cohort.

3. Results

At the first follow up (T2), the total sample consisted of 240 participants (n_{autism}=128, $n_{no\text{-}autism}$=112), and at the second follow up (T3) 73 participants (n_{autism}=46, $n_{no\text{-}autism}$=27) were included. Cohort 1 consisted of 90 participants; Cohort 2 consisted of 150 participants (see Fig. 1). Autistic and non-autistic participants were equally divided between the cohorts. Characteristics of the total sample are described in Table 2. Education differed significantly between groups, with more people with practical education in the autism group than in the no-autism group. MMSE score (global cognitive functioning) and estimated IQ did not differ significantly, yet AQ score (autism characteristics), and CFQ score (self-reported cognitive difficulties) were significantly higher in the autism group, and the average time interval (T1-T2, and T1-T3) was significantly longer in the autism group. Assessing the two cohorts seperately reduced the variance in intervals, yet they were still significantly longer in the autism group (see Tables S1A, and B).

3.1. Attrition analyses

Reasons for drop-out were mostly that no consent was given to be contacted for future research[5] (only in Cohort 1; $n = 121$, n_{autism}=31) or that participants were not willing to participate when contacted ($n = 64$, n_{autism}=35). Sixteen (n_{autism} =12) participants could not be contacted, three passed away (n_{autism} =2), 20 (n_{autism} =9) were excluded at T2 for various reasons.

Drop-out rates were significantly higher in the no-autism group compared to the autism group ($n_{dropout\ autism}$=80 [38%], $n_{dropout\ no\text{-}autism}$=144 [56%], $\chi^2[464] = 14.28$, $p<.01$) and higher in Cohort 1 than in Cohort 2 ($n_{dropout\ C1}$=180 [67%], $n_{dropout\ C2}$=44 [23%], $\chi^2[464] = 87.05$, $p<.01$). No significant difference in sex ratio was observed. In the autism group, no significant differences between the drop-out and followed-up group were observed on baseline age, IQ, AQ score, CFQ score, or MMSE score (all p's>0.10). In the no-autism group, those who were younger at baseline (age: $\mu_{dropout}$=46.6, $\mu_{follow\text{-}up}$=55.3, $t[463] = -4.48$, $p <0.01$), and those with lower estimated IQ participated less in the follow-up study (IQ: $\mu_{dropout}$=110.9, $\mu_{follow\text{-}up}$=115.4, $t[463] = -2.17$, p=.03). Other differences were not significant (p's>0.25).

[5] At the first stage of cohort 1, the study was not yet conceptualized as longitudinal, thus, some participants were not informed about future research.

Table 2
Descriptive statistics of the autism and no-autism group.

Descriptive	Autism (n = 128)	No-autism (n = 112)		
Cohort (1/2, 1%)	54/74, 42%	36/76, 32%	χ^2=2.57	
Sex (M/F, M%)	84/44, 65%	72/40, 64%	χ^2=0.03	
Education[a]	35/49/43	16/53/43	χ^2=6.32*	
	Mean (SD), min-max	Mean (SD), min-max	t-value	Cohen's d
Age T1 (yrs.)	52.2 (14.2), 24.3–79.3	55.4 (14.1), 30.4–85.3	−1.73	-0.23
Time T1-T2 (yrs.)	3.5 (2.0), 1.6–7.0	3.0 (1.8), 1.4–7.6	2.44*	.26
Time T1-T3 (yrs.)	8.1 (0.7), 7.1–9.4	7.6 (0.7), 6.7–9.0	4.05**	.71
IQ[b]	114.7 (15.5), 84–153	115.4 (16.0), 73–155	−0.33	-0.04
MMSE[c]	29.0 (1.1), 25–30	29.1 (1), 26–30	0.06	<0.01
AQ[d]	34.9 (7.3), 8–48	13.0 (5.8), 2–28	25.88**	3.32
CFQ[e]	47.0 (14.6), 15–80	30.1 (10.0), 8–53	10.54**	1.35

Note. M, male; F, female; **=p<.01; *=p<.05.

[a] Level of education was determined by the Verhage Coding System, between slashes: junior secondary or practical education / senior secondary education or vocational college / university degree.

[b] IQ was estimated at baseline by using two subtests (matrix reasoning and vocabulary) of the Wechsler Intelligence Scale-III or IV (WAIS-III, WAIS-IV; Wechsler, 1997, 2003).

[c] Mini Mental State Examination (MMSE; Folstein et al., 1975) measured global cognitive impairments at baseline. Individuals scoring below 25 were excluded ($n = 0$).

[d] Autism Quotient (AQ) measured self-reported autism characteristics. In the autism group, 9% ($N = 12$) scored below the AQ cut-off. These participants all scored above the ADOS or ADOS-2 cut-off.

[e] Cognitive failures questionnaire (CFQ) measured self-reported cognitive functioning.

3.2. Reliable change indices

RCIs based on method 1 (average difference scores) showed no significant differences in reliable changes between the autism, and no-autism group, in neither cohort (all uncor. p's>0.15, see Fig. 2a, Table S2A). Across groups, percentages of individuals who reliably declined ranged from 0–22% in Cohort 1, and 0–7% in Cohort 2, percentages of individuals who improved ranged from 0–18% in Cohort 1, and from 0–10% in Cohort 2. Rates of decline were highest on visual/verbal memory I and II, and both fluency tasks. Rates of improvement were highest on theory of mind, and inhibition. RCIs based on method 2 (test-retest reliabilities from previous studies) led to higher change rates than using average difference scores. Across groups, percentages of individuals who declined ranged from 15–34% in Cohort 1, and 1–13% in Cohort 2, percentages of individuals who improved ranged from 0–9% in Cohort 1, and 1–22% in Cohort 2. No significant differences in reliable changes were observed between the autism, and no-autism group, in neither cohort (see Fig. 2b, Table S2B).

In sum, most of the expected decline over time was observed in Cohort 1 and based on test-retest reliabilities. The majority of individuals performed consistently over time. Changes over time did not significantly differ between autistic and non-autistic individuals.

3.3. Multilevel modeling

To analyze the effects of cross-sectional age, and changes over time in a continuous manner, we performed multilevel regression analyses on

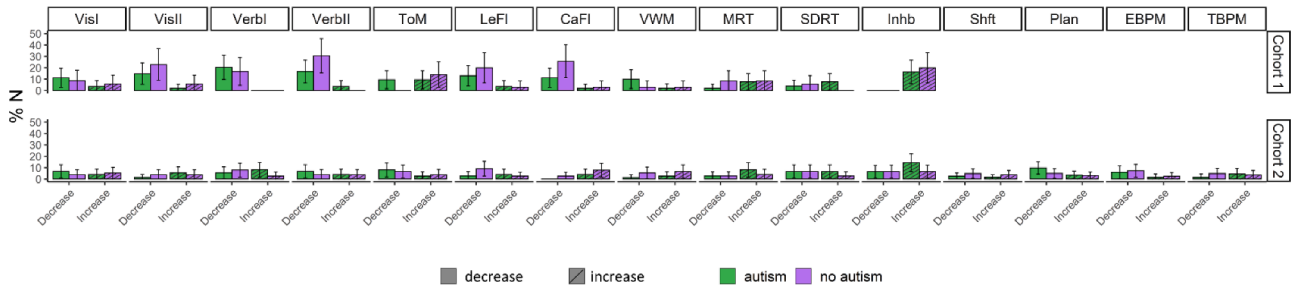

Fig. 2a. Percentage of cognitive increases and decreases per cognitive outcome, group, and cohort reflected by Reliable Change Indices (RCI's) based on average difference scores.

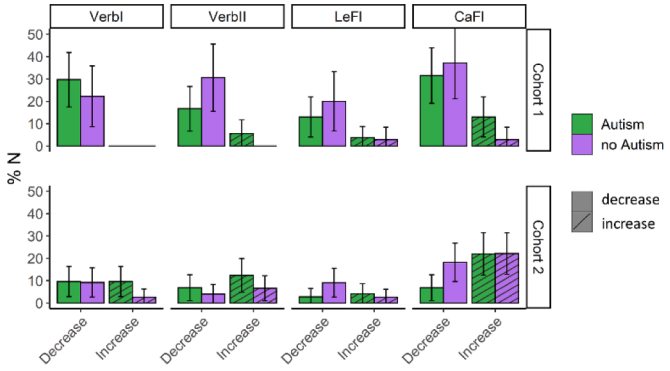

Fig. 2b. Percentage of cognitive increases and decreases per cognitive outcome, group, and cohort reflected by Reliable Change Indices (RCI's) based on Test-Retest Reliabilities.

Note. Error bars reflect 95% confidence intervals. Group differences were all non-significant. For figural clarity, those who remained stable are omitted. VisI, visual recall I; VisII, visual recall II; VerbI, verbal recall I; VerbII, verbal recall II; ToM, theory of mind; LeFl, letter fluency; CaFl, category fluency; VWM, visual working memory; MRT, mean reaction time; SDRT, reaction time variability; Inhb, inhibition; Shft, set shifting; Plan, planning; EBPM, event-based prospective memory; TBPM, time-based prospective memory.

all 15 outcomes. As the models allowed intercepts and slopes to vary between participants, we first assessed the added value of these parameters. Random intercepts significantly improved all models, yet random slopes did not, except for response speed, and visual recall I, and II. As random slopes could not be reliably estimated for some models and the models hardly improved when adding random slopes, subsequent planned analyses on these slopes were omitted, including analyses on the predictive value of sex, baseline IQ, and baseline CFQ. Removing random slopes did not change the parameters of the fixed factors.

Model 1 (interval only) showed a significant effect of interval for category fluency, response speed, inhibition, and event-based prospective memory. Participants generally declined in performance over time, but improved in performance on event-based prospective memory. Model 2 (interval, age, and their interaction) showed that, baseline age effects (cross-sectional) were present in visual/verbal memory, category fluency, response speed, response variability, and both event-/time-based prospective memory. Older individuals generally scored worse than younger individuals at baseline. A significant age*interval interaction was observed on letter fluency, and set shifting. Those older at baseline declined significantly more over time compared to those younger at baseline. Models 1 and 2 are summarized in Fig. 3a; statistical details can be found in Table S3A.

Model 3 (interval, group, and their interaction) showed no significant interval*group interactions. Hence, no significant group differences in longitudinal change were observed. Model 4[6] (interval, age, group, and their interactions) showed no significant age*group interactions, and no significant age*interval*group interactions meaning that individuals with and without autism showed no significant difference in age-related effects (cross-sectional) or age-related changes over time (longitudinal). Models 3 and 4 are summarized in Fig. 3b; statistical details are provided in Table S3B. A graphical display of the group, age, and interval effects is provided in Fig. 4.

In sum, multilevel models showed clear age-related effects, and modest effects of interval. None of the cross-sectional age effects or longitudinal changes over time were significantly different between autistic, and non-autistic individuals.

3.4. Bayesian analyses

BIC Bayes Factors indicated substantial to very strong evidence in favor of the models without group interactions (all $BF_{01} > 28$, see Table S3c, and Fig. S1), substantiating the absence of significant group differences in the effect of interval, and age*interval.

3.5. Sensitivity analyses

Learning effects (i.e., improvement in performance over time) might have obscured previous interval effects, and possibly also interval*group interactions, because (1) we did not observe interval effects for some age-sensitive measures (e.g., visual/verbal recall), and (2) intervals for cohort 2 were shorter than intended due to COVID restrictions. Therefore, we extended the pre-registered sensitivity analyses to analyze the data from both cohorts separately, instead of only for cohort 2.

Multilevel results of the separate cohorts showed better fit of the interval-only models (higher marginal R^2) as compared to the combined cohort models. With time, individuals from cohort 1 significantly declined in performance on verbal recall I and II, category fluency, and response speed, whereas individuals from cohort 2 significantly improved on verbal recall I and II, visual working memory, and event-based prospective memory. In cohort 2, significant declines were still observed on inhibition and processing speed. Both cohorts showed no significant interval*group interactions. The significant interval*age interaction on letter fluency and set shifting remained significant in cohort 1 and 2, respectively, and showed the same pattern as in the combined cohort. Age*group interactions, and age*interval*group interactions were all not significant. Statistical details can be found in Table S4A and S4B, and Fig. S2, B and C (cohort 1), and Table S5A and S5B and Fig. S3A, B and C (cohort 2). Of note, BIC bayes factors in the separate cohorts yielded similar results as compared to the combined

[6] As the data were previously analysed in a cross-sectional manner (Lever and Geurts, 2016; Torenvliet et al., 2021), cross-sectional effects are only briefly noted.

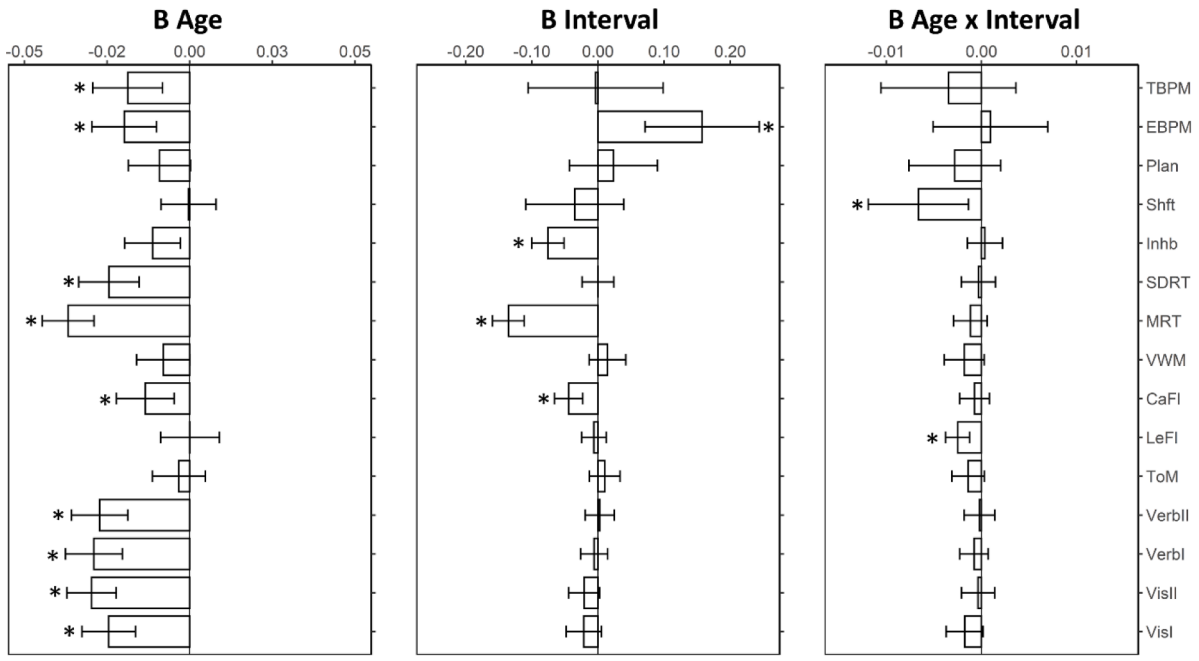

Fig. 3a. Effects of age, interval, and their interactions on each cognitive outcome measure obtained from the multilevel models independent of group.

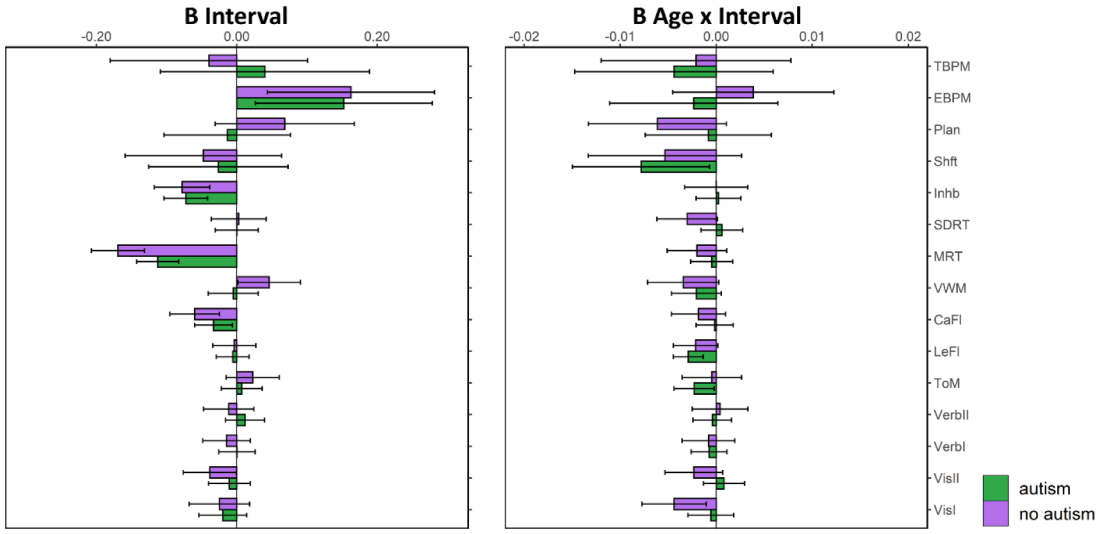

Fig. 3b. Effects of interval, and age and interval interactions per group.
Note. Left-sided bars indicate a decline with age, or interval (negative betas), whereas right-sided bars indicate an improvement with age, or interval (positive betas). *=Holm corrected p-value ⟨.05. In 3b all Holm corrected p-values were ⟩.05. B, standardized beta; VisI, visual recall I; VisII, visual recall II; VerbI, verbal recall I; VerbII, verbal recall II; ToM, theory of mind; LeFl, letter fluency; CaFl, category fluency; VWM, visual working memory; MRT, mean reaction time; SDRT, reaction time variability; Inhb, inhibition; Shft, set shifting; Plan, planning; EBPM, event-based prospective memory; TBPM, time-based prospective memory.

cohorts.

In sum, sensitivity analyses showed that splitting the cohorts was useful for inspecting some contrasting patterns between our two cohorts (improvement vs. decline), especially for verbal recall. Both in improvement and decline over time, autistic individuals seemed to change similarly to non-autistic individuals.

4. Discussion

The current study provides evidence against accelerated cognitive decline in autistic adults. Although nearly all cognitive measures seemed sensitive to either cross-sectional age-related effects or longitudinal age-related changes, none of the models indicated significant evidence for accelerated or protective aging in autistic adults. Bayesian analyses confirmed that evidence was robustly in favor of the null hypotheses that specified no differences in age-related decline between those with- and without autism. When comparing clinically relevant changes over time, group differences were minimal, and if anything, autistic individuals seemed to decline less over time. Given that this is the first larger-scale cognitive study that assesses cognitive aging in autism longitudinally, and aging effects were generally modest, these conclusions have to be interpreted with care. However, it seems that in autism, age-related *longitudinal changes* are similar to previously observed parallel age-related *cross-sectional effects*.

If replicated, these findings can have valuable contributions to the autism field. Even on cognitive domains where autistic adults generally

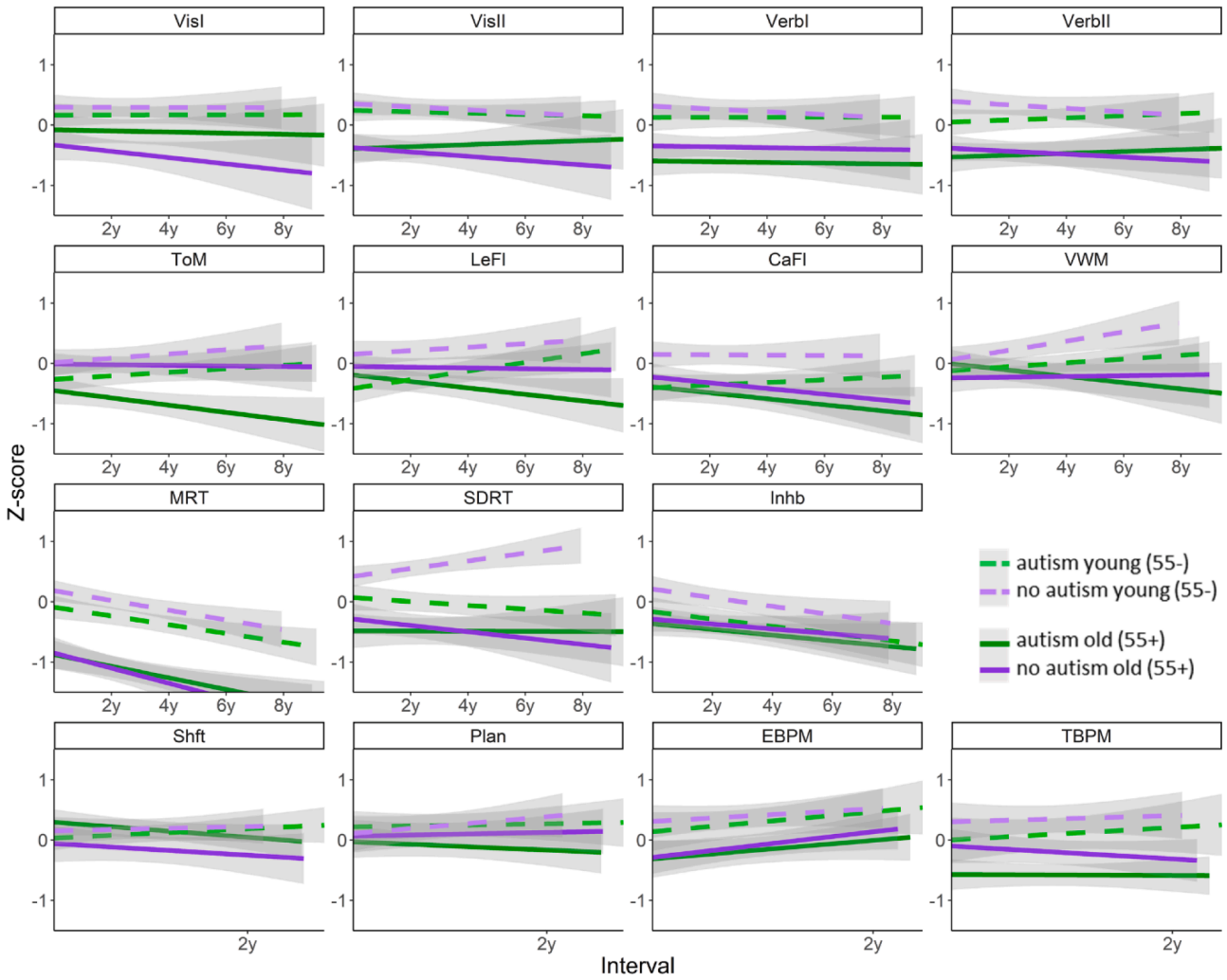

Fig. 4. Graphical display of the effects of interval, age, group, and their interactions of the combined cohorts.
Note. Age was categorized only for visual purposes, in all analyses age was added as a continuous predictor. Intervals were shorter (max. 2.5 years) for outcomes in the bottom row (Shft, Plan, EBPM, TPBM) as these tasks were not administered at Wave 1. VisI, visual recall I; VisII, visual recall II; VerbI, verbal recall I; VerbII, verbal recall II; ToM, theory of mind; LeFl, letter fluency; CaFl, category fluency; VWM, visual working memory; MRT, mean reaction time; SDRT, reaction time variability; Inhb, inhibition; Shft, set shifting; Plan, planning; EBPM, event-based prospective memory; TBPM, time-based prospective memory.

seem to experience more difficulties compared to non-autistic adults (fluency, theory of mind), and on tasks where longitudinal changes were most prominent across groups (response speed, fluency, inhibition, verbal memory) no significant differences in cognitive change between those with, and without an autism diagnosis were observed. Thus, differences in development in various cognitive domains observed in the first stages of life of autistic individuals do not seem to persist or retrace in later stages of life. Therefore, autism seems to show parallels to schizophrenia, being best described by differences in *neurodevelopment*, not *neurodegeneration* (Rund, 2018).

However, disregarding accelerated cognitive decline in autism might contrast with the reported increased risk of old-age disease. It remains puzzling why in autism increased rates of, for instance, dementia, and Parkinson's disease are reported in epidemiological studies (Bishop--Fitzpatrick and Kind, 2017; Croen et al., 2015; Geurts, McQuaid, et al., 2020; Hand et al., 2019; Rydzewska et al., 2018; Vivanti et al., 2021), without observing differences in cognitive decline. However, neurodegenerative disorders are, like developmental conditions, hard to classify correctly and heterogeneous in nature, with misdiagnoses of Alzheimer's Disease (AD) occurring up to 30% (Magnin, 2021). Like in ADHD (Callahan et al., 2017), it is therefore unclear whether autism is indeed a risk factor for old-age disease, or more likely to be a phenotypic mimic. Thus, it could be that autistic people resemble or report characteristics that are typical in old-age disease without the same biological mechanisms underlying these characteristics. Moreover, based on the aforementioned epidemiological studies it is unclear whether most autistic individuals might show altered cognitive aging, or if only a subgroup of autistic individuals is particularly vulnerable for cognitive decline. Consistent with the very first longitudinal study of cognitive aging in autism, in which they observed cognitive decline only for 23% of autistic individuals (Howlin et al., 2014), the current study seems to indicate that an increased risk of late life (cognitive) disease might be true for a subgroup of autistic individuals, whereas generally accelerated aging in autism may be less likely.

As rates of age-related disease are known to show steep increases at the final stages of life (70+), patterns of cognitive decline might be different in an older autism cohort. While the current cohort is one of the oldest cohorts described in the autism literature, compared to other aging cohorts, the current cohort is still relatively young. Therefore, more research on old-age trajectories is essential to capture all phases of cognitive aging in autism. The feasibility of including older adults might increase naturally, given the increasing trends in (late) adult autism diagnoses (Russell et al., 2022), and the aging of autistic adults who are currently diagnosed. Of note, based on the current results, old age did

not seem an additional predictor of cognitive decline in autism specifically. Also, research including only older adults (Geurts, et al., 2020; Geurts and Vissers, 2012) does not hint at distinctive age-related differences for autistic people. Therefore, although additional research is needed, we expect similar outcomes for longitudinal autistic cohorts of older age.

The current study is distinctive in covering a wide range of cognitive functions, which nearly all showed either sensitivity to cross-sectional age-related effects or longitudinal age-related changes. However, some measures were less sensitive to longitudinal changes than expected based on cross-sectional findings– i.e., visual (working) memory, and planning. This pattern is consistent with the general aging literature, in which longitudinal age effects are often smaller than cross-sectional patterns (Salthouse, 2003, 2010, 2019). It also highlights the difficulty of longitudinal research in which the repetitive nature of data collection (i.e., learning effects) might cloud age-related decline (Salthouse, 2019). The inclusion of parallel test forms, additional timepoints, and longer intervals between timepoints are key to capture cognitive aging effects more precisely. Acquiring long-term funding seems essential to enable more, and longer time intervals, and reduce rates of attrition.

The partial absence of age-related changes posed a challenge, yet also provided an unexpected advantage. By splitting the cohort by those with generally long intervals (cohort 1, ~5.8 yrs.), and those with shorter intervals (cohort 2, ~1.9 yrs.), we were not only able to detect similar rates of *decline* between autistic- and non-autistic individuals (cohort 1), but we also observed that *learning* seemed to develop at similar pace (cohort 2). In cohort 1, rates of cognitive decline on verbal memory were significant, yet similar across the groups. Oppositely, in cohort 2, we observed significant improvements in verbal memory performance, indicating learning effects, which were also not significantly different between autistic and non-autistic adults. These findings further confirm the hypothesis that individuals with autism are not particularly (in)sensitive to the effects of cognitive aging.

4.1. Strengths & limitations

The study provides a unique insight into cognitive aging in autism in various ways. First, the current study is the first to capture cognitive decline in autism longitudinally in a relatively large sample on a wide range of cognitive abilities. Second, advanced statistical analyses were used to account for heterogeneity within the sample, such as allowing random parameters in the regression models, and investigating the extent of reliable change. Also, additional Bayesian analyses allowed quantifying evidence for the null hypotheses. We also provided scientific rigor by pre-registering our analyses, and adjusting for multiple comparisons.

Some aspects of the current study limit the aforementioned interpretations. First, as the autism group was mainly recruited via clinical institutions, we might have missed individuals from underserved populations. Representative samples remain a persistent issue in autism research (Giwa Onaiwu, 2020; Maddox et al., 2021), and the current study is, unfortunately, no exception as diversity regarding ethnicity and gender identity was limited. Second, educational attainment was relatively high, limiting interpretations to those with practical education. Also, the average IQ was about one standard deviation above the global mean, and we excluded those with an intellectual disability. Given the current knowledge on cognitive reserve (e.g., Cabeza et al., 2018), the current sample might disregard those most vulnerable to cognitive decline. However, the sample's diversity was maximized by accommodating participants (autistic and non-autistic) in their needs, such as providing travel assistance, on-site sessions nearby participants' homes, and sessions at home. Third, attrition rates were relatively high in the first cohort, and in the no-autism group. As this seemed mainly driven by non-autistic adults of younger age (30–45 yrs.), drop-out seemed mainly due to time constraints, and not due to cognitive or physical constraints. Reasons for drop-out (e.g., exclusion based on neurological history or decease) also did not differ between the groups. Therefore, it seems unlikely that differences in attrition have biased our results. Fourth, RCI analyses have to be interpreted with care, as the average interval between timepoints differed significantly between the autistic and non-autistic group. However, as the autistic group had longer average time intervals, one might expect exaggerated group differences in reliable changes (i.e., larger decline in the autism group). As no group differences in reliable changes were observed, the differences in average time intervals do not seem to be of major impact.

5. Conclusions

Based on the current findings, age-related changes in cognition seem similar in autistic- and non-autistic individuals. As this is the first large-scale longitudinal study on cognitive aging in autism, these findings contribute unique knowledge to the autism literature. However, careful interpretation of the current conclusions is essential, and more longitudinal research is key to understand cognitive decline in older autistic adults precisely, and more generally throughout the autistic population.

CRediT authorship contribution statement

C. Torenvliet: Visualization, Formal analysis, Data curation, Conceptualization, Writing – original draft, Writing – review & editing. **A.P. Groenman:** Conceptualization, Writing – original draft, Writing – review & editing. **T.A. Radhoe:** Data curation, Writing – original draft, Writing – review & editing. **J.A. Agelink van Rentergem:** Writing – original draft, Writing – review & editing. **W.J. Van der Putten:** Data curation, Writing – original draft, Writing – review & editing. **H.M. Geurts:** Conceptualization, Funding acquisition, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

None.

Acknowledgements

We would like to thank all our participants for the effort and time they have put into this study, and the clinical institutions and organizations who actively helped recruiting our participants. Furthermore, we would like to thank the students and research assistants involved in the project for their help with the recruitment of participants and data collection. Lastly, we would like to thank our think tank of autistic/older adults for their instrumental contributions to this work.

Funding statement

This study was funded by the VICI Grant (Grant Number: 453–16–006) awarded to HMG by the Netherlands Organization for Scientific Research (NWO).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2023.115063.

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