

Visual memory and sustained attention impairment in youths with autism spectrum disorders

Y.-L. Chien^{1,2}, S. S.-F. Gau^{1,2,3*}, C.-Y. Shang¹, Y.-N. Chiu¹, W.-C. Tsai¹ and Y.-Y. Wu⁴

¹Department of Psychiatry, National Taiwan University Hospital and College of Medicine, Taipei, Taiwan

²Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan

³Department of Psychology, School of Occupational Therapy, Graduate Institute of Brain and Mind Sciences, and Graduate Institute of Epidemiology and Preventive Medicine, National Taiwan University, Taipei, Taiwan

⁴Department of Psychiatry, Chang Gung Memorial Hospital-Linkou Medical Center, Chang Gung University College of Medicine, Tao-Yuan, Taiwan

Background. An uneven neurocognitive profile is a hallmark of autism spectrum disorder (ASD). Studies focusing on the visual memory performance in ASD have shown controversial results. We investigated visual memory and sustained attention in youths with ASD and typically developing (TD) youths.

Method. We recruited 143 pairs of youths with ASD (males 93.7%; mean age 13.1, s.d. 3.5 years) and age- and sex-matched TD youths. The ASD group consisted of 67 youths with autistic disorder (autism) and 76 with Asperger's disorder (AS) based on the DSM-IV criteria. They were assessed using the Cambridge Neuropsychological Test Automated Battery involving the visual memory [spatial recognition memory (SRM), delayed matching to sample (DMS), paired associates learning (PAL)] and sustained attention (rapid visual information processing; RVP).

Results. Youths with ASD performed significantly worse than TD youths on most of the tasks; the significance disappeared in the superior intelligence quotient (IQ) subgroup. The response latency on the tasks did not differ between the ASD and TD groups. Age had significant main effects on SRM, DMS, RVP and part of PAL tasks and had an interaction with diagnosis in DMS and RVP performance. There was no significant difference between autism and AS on visual tasks.

Conclusions. Our findings implied that youths with ASD had a wide range of visual memory and sustained attention impairment that was moderated by age and IQ, which supports temporal and frontal lobe dysfunction in ASD. The lack of difference between autism and AS implies that visual memory and sustained attention cannot distinguish these two ASD subtypes, which supports DSM-5 ASD criteria.

Received 21 July 2014; Revised 30 November 2014; Accepted 17 December 2014; First published online 23 April 2015

Key words: Attention, autism, autism spectrum, neurocognition, visual memory.

Introduction

Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders characterized by deficits in social communication and restricted, repetitive patterns of behavior, interests or activities (American Psychiatric Association, 2013). Beyond the core symptoms, children with ASD have been shown to have deficits in visual short-term memory, an ability to maintain and retrieve visual information (Cowan, 2001). An early study conducted by Boucher & Warrington (1976) demonstrated an impairment in forced-choice recognition of pictures compared with ability- or age-matched controls but normal cued recall

and paired-associate learning in individuals with autism. However, using the delayed-response visual discrimination task, Prior & Chen (1976) found no difference when learning and acquisition were equated. Then, Boucher & Lewis (1992) reported that unfamiliar face recognition was impaired in children with autism, but their ability to recognize buildings was normal, suggesting that impaired face recognition does not result from impaired attention or discrimination. Later on, Minshew & Goldstein (2001) reported worse performance on a list of learning tasks, immediate and delayed recall of a story and of a complex geometric figure and maze learning task by youths with high-functioning autism (HFA), implying that youths with HFA failed to initiate organizing strategies and utilize contextual information. Based on the hypothesis of a fractionably developed visual memory system, Blair *et al.* (2002) reported that adults with autism had selective memory impairments in the recognition of faces and potential agents, but a superior ability in

* Address for correspondence: S. S.-F. Gau, M.D., Ph.D., Department of Psychiatry, National Taiwan University Hospital and College of Medicine, no. 7, Chung-Shan South Road, Taipei 10002, Taiwan.

(Email: gaushufe@ntu.edu.tw)

recognizing buildings or leaves, suggesting a reduced sensitivity to agency cues. A recent study also reported that children with ASD were unable to make use of semantic affordance of the matrix patterns on the Visual Pattern Test in order to construct a global representation for memory (Mammarella *et al.* 2014).

In summary, there are controversial findings on visual memory in ASD. Some studies revealed no impairment of visual discrimination (Prior & Chen, 1976) and equal performance in recognition of buildings but not unfamiliar faces (Boucher & Lewis, 1992). Some showed deficits in the forced-choice recognition of pictures (Boucher & Warrington, 1976), and in the immediate and delayed recall of complex geometric figures (Minshew & Goldstein, 2001) compared with typically developing (TD) youths, and a possible effect of impaired semantic global organization (Mammarella *et al.* 2014). Some even found superior recognition memory of non-agency objects such as leaves and buildings (Blair *et al.* 2002).

The inconsistent findings can be explained by the use of tasks of various targets (e.g. words, faces or pictures) and demands (e.g. forced-choice or free recall, immediate or delayed recall), the degree of depending on verbal ability, and the potential effects of age and intelligence on visual memory. A visual memory task of meaningless shapes that are difficult to label and are independent of language ability can eliminate influences from cognitive functions other than visual memory, such as semantic memory (Salmanian *et al.* 2012). Yet, the evidence for visual memory of meaningless shapes in ASD is too little to draw a conclusion. Ameli *et al.* (1988) found poor memory with meaningless patterns, but normal with meaningful pictures; however, Salmanian *et al.* (2012) reported that the differences between ASD and controls disappeared after adjusting for intelligence quotient (IQ), implying that visual memory of meaningless shapes in ASD could be moderated by general intellectual abilities. Intelligence has been shown also to correlate with visuospatial memory (Miyake *et al.* 2001; Cowan *et al.* 2005) through its effect on strategic choices for memory (Cusack *et al.* 2009). Whether ASD youths with superior IQ benefit from memorizing meaningless patterns is of particular interest. Regarding the age effect, only a few studies have shown a lack of typical adolescent development in visual tasks of rapid enumeration of the elements and global shape recognition (Scherf *et al.* 2008), suggesting that recognition and memory deficits increased from adolescence to adulthood (O'Hearn *et al.* 2014). Whether there existed an age effect on visual memory of meaningless shapes is as yet unclear.

Previous studies have established the link between spatial attention and spatial working memory (Smyth

& Scholey, 1994; Awh *et al.* 1998; Awh & Jonides, 2001). Visual short-term memory is thought to be the active maintenance of attention to visual stimuli important for ongoing reactions (Chun, 2011), and that it depends not only on actively sustained maintenance of relevant sensory representations of a limited number of visual objects, but also inhibition of distraction (Cowan, 2001; Awh *et al.* 2006). Our previous study demonstrated attention deficits in autism and Asperger's disorder (AS) with different patterns between the two (Chien *et al.* 2014). With regard to the intimate relatedness between visual working memory and visual attention, whether the prior findings of visual memory deficits reflect true deficits as such, or instead, sustained attention deficits remains unclear. In addition, visuospatial abilities were shown to differ between autism and AS in some studies (e.g. Sahyoun *et al.* 2009) but not in others (e.g. Miller & Ozonoff, 2000). Also, whether diagnosis subgrouping within autism spectrum differed in terms of memory of meaningless shapes has not been investigated, either.

This study aimed to investigate visual memory and sustained attention in youths with ASD using tasks with meaningless shapes as compared with TD youths. We examined the moderating effects of age and IQ on visual memory performance and sustained attention, by stratification and by testing of the interaction. We also compared visual memory performance after adjusting for sustained attention. Our hypotheses are that youths with ASD may show visual memory deficits on meaningless shapes and impaired visual sustained attention, and that ASD youths with higher IQ or those older may not show the deficits. Besides, the visual memory impairment remained in ASD youths while sustained attention was controlled.

Method

Participants

The sample consisted of 143 youths with ASD (male 93.7%, aged 13.1, s.d. 3.5 years), and 143 age- and sex-matched TD controls (aged 13.1, s.d. 3.8 years). The diagnoses of autistic disorder (autism) ($n=67$) and AS ($n=76$) were made by board-certificated child psychiatrists based on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria, and validated by the Autism Diagnostic Interview-Revised (ADI-R) interview. Youths with ASD were recruited from out-patient clinics of the National Taiwan University Hospital and Chang Gung Memorial Hospital, and TD controls were recruited from similar school districts of youths with ASD by the assistance of school principals and teachers rather than by advertisement. Subjects with full-scale

IQ (FIQ) scores lower than 80, or with current or lifetime major psychiatric diagnoses according to the Chinese-language Kiddie Schedule for Affective Disorders and Schizophrenia – epidemiological version (K-SADS-E) were excluded from the study.

Diagnostic interview for ASD and other diagnoses

The ADI-R (Lord *et al.* 1994; Gau *et al.* 2011) is a standardized, semi-structured interview with the caregivers of children aged from 18 months to adulthood. It covers most developmental and behavioral aspects of ASD, including reciprocal social interaction, communication, and repetitive behaviors and stereotyped patterns. The ratings were based on an assessment under current conditions and under the most severe state at 4–5 years, as recalled by the caregivers. The Chinese ADI-R was approved by the World Psychological Association in 2007 (Gau *et al.* 2013; Chien *et al.* 2014).

The K-SADS-E is a standard, semi-structured interview scale for the systemic assessment of both past and current mental disorders in children and adolescents. The Chinese K-SADS-E (Gau & Soong, 1999; Gau *et al.* 2005) has been widely used in clinical research to assess DSM-IV psychiatric disorders (e.g. Lin *et al.* 2013; Gau & Huang, 2014).

Neuropsychological tests for assessing visual memory

For fair comparison between age and IQ subgroupings, the neuropsychological tests were administered to all participants in a fixed order, by well-trained psychologists according to the standard protocols at a laboratory specializing in neurocognitive assessments. The following four tasks selected from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (CANTABclipse; UK) were used to test visual memory and sustained attention.

Spatial recognition memory (SRM)

This task assessed recognition memory for spatial locations in a two-choice forced discrimination paradigm (Sahakian *et al.* 1988). In the presentation phase, empty boxes were shown at different locations on the screen, and the participant was required to remember the places where the boxes were presented. The participant then saw five stimuli in succession at different locations each for 3 s. Following a 5-s pause, the participant then viewed two boxes and was required to touch the box located in a place that was previously targeted. The subtest was repeated three more times, each time with five new locations. Two indices are presented:

(1) the percentage of correct responses; and (2) the mean response latency for correct responses.

Delayed matching to sample (DMS)

This task assessed the ability to remember the features of a complex and abstract pattern in a four-choice delayed recognition memory paradigm (Egerhazi *et al.* 2007). In the simultaneous matching condition, the sample pattern remained on screen when four choice patterns appeared. In the delayed condition, a delay of 0, 4 or 12 s was introduced between the appearance of the sample pattern and later the choice patterns. The participant was instructed to touch the pattern that matched the sample, and to repeat the trial until a correct choice was made. After three practice trials, there were 20 counterbalanced test trials in a pseudo-random order, including five simultaneous trials and five trials for each of the three delay intervals. The following indices are reported: (1) the mean latency, that is, the mean time taken to respond with correct responses; (2) the number of correct responses in the simultaneous, three delay conditions, and in total; and (3) the probability of an error after a correct and an error response.

Paired associates learning (PAL)

The PAL test assessed visuo-spatial associative learning, and contained both a delayed response procedure and a conditional learning task (Egerhazi *et al.* 2007). Participants would complete the eight stages in order. For each stage, boxes were displayed and opened in random order. The patterns shown in the boxes were then displayed in the screen center one by one. The participants were told to touch the box where the pattern was originally located with up to 10 trials at each stage. When they got all the correct locations, they would proceed to the next stage. If they could not complete a stage correctly, the test was terminated. Three indices were analysed: (1) total errors; (2) total trials required to locate all the patterns correctly in all stages; (3) first trial memory scores; (4) mean errors and mean trials to success; (5) stages completed on the first trial.

Rapid visual information processing (RVP)

The RVP task, a 4-min visual continuous performance task modified from Wesnes and Warburton's task (1984), is designed to assess sustained attention capacity (Sahakian *et al.* 1989). Digits (ranging from 2 to 9) appeared one at a time (100 digits/min) in the screen center in a random order. Participants were asked to press a response pad when they detected any one of three number sequences (3–5–7, 2–4–6 or

4–6–8). The following indices are presented: (1) total misses (occasions the participant failed to respond); (2) probability of hits (correct response, h), i.e. total hits divided by the sum of total hits and total misses; (3) total correct rejections (stimuli that were correctly rejected); (4) probability of false alarms (the participant responding incorrectly, f), i.e. total false alarms divided by the sum of total false alarms and total correct rejections (Tanner & Swets, 1954; CANTABeclipse™: Test Administration Guide version 3); (5) A' (calculated as $0.5 + [(h - f) + (h - f)^2] / [4 \times h \times (1 - f)]$), a signal detection measure of sensitivity to the target, regardless of response tendency (Sahgal, 1987); and (6) mean latency (mean time taken to respond in correct responses). Sensitivity (A') refers to how hard or easy it is to detect from background events that a target stimulus is present. This index of target sensitivity is considered to represent attentiveness (Stanislaw & Todorov, 1999).

Procedure

The research ethics committee of the university hospital approved this study prior to its implementation (200903062R; ClinicalTrials.gov number, NCT00916851). Written informed consent was obtained from both the participants and their parents after the procedures were fully explained. All of the participants and their parents were interviewed using the Chinese-language K-SADS-E for the child's DSM-IV psychiatric diagnoses. A total of 20 of the ASD youths (14.0%) were currently being treated with methylphenidate under the co-morbid diagnosis of attention-deficit/hyperactivity disorder (ADHD). The participants then performed the CANTAB tasks in the hospitals. The medications, if any, were discontinued at least 24 h before the task.

Statistical analysis

The data analysis was carried out using SAS 9.2 software (USA). The PROC MIXED procedure (Demidenko, 2004; Littell *et al.* 2006) was used to conduct the linear multi-level model with random and fixed effects to compare the CANTAB performance while controlling for sex, age and FIQ. The comparison groups were treated as fixed effects, since the pairing samples were matched by sex and age; individual differences were treated as random effects. Cohen's d was calculated to estimate the effect size: small (0.2–0.3), medium (0.5–0.8) and large (>0.8). Analysis of covariance was used to compare the autism, AS and TD groups adjusting for sex, age, FIQ and/or sensitivity index RVP A' . We used the Bonferroni correction method to adjust p values in a *post-hoc* analysis for multiple comparisons. To

examine the performance in individuals with superior IQ, we compared 42 youths with ASD and 60 TD youths who had a FIQ higher than one standard deviation ($FIQ > 115$).

To test the age effect, we performed linear regression analysis first to treat age as a continuous variable. Next, we divided the sample into three age groups, i.e. <12, 12–14 and >14 years at the time of testing, roughly corresponding to childhood, early adolescence and late adolescence, based on the evidence that cortical thinning during the 12–14 years period predicted visuospatial functioning (Squeglia *et al.* 2013) and that processing speed begins to level off at age 15 years (Kail & Ferrer, 2007). We then investigated the main effects of age and diagnosis (ASD and TD) groups, as well as their interaction (age \times diagnosis). Significance was set at a $p < 0.05$ level.

Ethical Standards

All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Results

Sample characteristics

The demographics and IQ profiles for the whole sample, the ADI-R subscores of the most severe condition at around 4–5 years old, and the current conditions are presented in Table 1. Youths with ASD had lower verbal IQ, performance IQ and FIQ than the TD youths. There were no significant differences in the distribution of sex, age and IQ profiles between autism and AS (see online Supplementary Table S1).

Group comparison between ASD and TD

The ASD group had significantly fewer correct responses on SRM and DMS (all delay conditions), fewer hits and correct rejections but more misses on RVP, and more errors on DMS and PAL, with medium effect sizes (Cohen's $d = -0.32$ to -0.61 , 0.30 to 0.63) (see online Supplementary Table S3). There was no significant group difference regarding correct responses on DMS (simultaneous), stages completed on PAL and false alarm on RVP. In general, there was no group difference in the mean latency of responses on SRM, DMS (delay) and RVP, except for a shorter reaction time on DMS (simultaneous). The two groups were not different in the control task Big/Little Circle (see online Supplementary Table S2).

Table 1. Demographic data of youths with ASD and TD youths

	ASD (<i>n</i> = 143)	TD (<i>n</i> = 143)	<i>F</i>	<i>p</i>
Male, <i>n</i> (%)	134 (93.7)	134 (93.7)		
Age, years	13.1 (3.5)	13.1 (3.8)	1.46	0.229
Age range, years	8–25	8–25		
IQ profiles				
Verbal IQ	106.3 (17.2)	112.3 (9.7)	13.36	0.000
Performance IQ	106.1 (18.2)	111.6 (13.3)	8.37	0.004
Full-scale IQ	106.5 (17.2)	112.9 (10.7)	14.53	0.000
ADI-R (current)				
A: Social reciprocal interaction	9.22 (4.36)			
B: Communication (verbal)	9.65 (3.83)			
B: Communication (non-verbal)	4.80 (2.60)			
C: Restricted interests/stereotyped behaviors	5.22 (2.47)			
ADI-R (severe)				
A: Social reciprocal interaction	18.57 (6.32)			
B: Communication (verbal)	13.93 (4.15)			
B: Communication (non-verbal)	7.12 (2.85)			
C: Restricted interests/stereotyped behaviors	7.17 (2.57)			

Data are given as mean (standard deviation) unless otherwise indicated.

ASD, Autism spectrum disorder; TD, typically developing; IQ, intelligence quotient; ADI-R, Autism Diagnostic Interview-Revised.

The significance of group comparison remained after adjusting for sex and age (Table 2) as well as further adjusting for FIQ (Table 2) except for the mean latency of correct response on DMS (simultaneous). When sustained attention deficit (RVP A') was further controlled, visual memory impairment on SRM (correct response), DMS (number of total correct, probability of an error following a correct response) and PAL (all indices) remained significant (see online Supplementary Table S4). The effect sizes were medium to large on SRM, DMS (delay) and PAL (Cohen's $d = 0.5$ – 0.64), with the highest one on PAL [first trial memory scores (Cohen's $d = -0.64$) and mean trial to success (Cohen's $d = 0.63$)].

When comparing the autism, AS and TD groups (see online Supplementary Table S5), we found there was no significant group difference between autism and AS (Bonferroni adjusted $p > 0.05$, Cohen's $d = -0.19$ to 0.28). Both two ASD groups performed worse than the TD group on all tasks except similar correct rejection and target sensitivity (A') on RVP (Bonferroni adjusted $p > 0.05$).

Task difficulty effect in DMS

The data showed a task difficulty effect in different intervals of delay DMS (0, 4 and 12 s) relative to simultaneous DMS ($F_{3,1107} = 112.9$, $p < 0.0001$) (Fig. 1). A significant diagnosis \times interval interaction

showed that the ASD–TD difference enlarged as the interval of delay DMS tasks increased from 0, 4 to 12 s.

The interactions between diagnosis and each delay interval (0 s *v.* simultaneous, 4 s *v.* simultaneous, 12 s *v.* simultaneous), after controlling for sex, age and FIQ, showed significant diagnosis \times delay intervals in 4 s delay DMS ($F_{1,825} = 6.25$, $p = 0.013$) and 12 s delay DMS ($F_{1,825} = 19.11$, $p < 0.0001$) relative to simultaneous DMS (Table 3).

Comparison in the subsample with superior FIQ

In the subsample with FIQ higher than 115 (42 ASD and 60 TD youths), there was no significant difference between ASD and TD youths in the correct responses, total trials or total errors on DMS, PAL and RVP, but there were fewer correct responses on SRM with a marginal significance (see online Supplementary Table S2).

Age effects on visual memory performance

When age was treated as a continuous variable, performance on the DMS and RVP significantly improved with age from childhood to adolescence in both groups. However, improvement in SRM and PAL performance was noted in the TD group only, but not in the ASD group.

Table 2. Comparison of performance on visual memory tasks between youths with ASD and TD youths, adjusting for sex, age and/or FIQ

	Adjusted for sex and age		Adjusted for sex, age and FIQ		ASD × age		Cohen's <i>d</i>
	<i>F</i>	<i>p</i> ^a	<i>F</i>	<i>p</i> ^a	<i>β</i> (s.e.)	<i>p</i> ^a	
Spatial recognition memory							
Percentage of correct responses	15.74	0.000	17.31	<0.0001*	0.15 (0.08)	0.054	−0.61
Delayed matching to sample							
Probability of an error following a correct response	12.92	0.001	14.85	0.000*	−0.01 (0.00)	0.042	0.50
Probability of an error following an error response	4.67	0.033	5.72	0.018	−0.01 (0.01)	0.106	0.30
Correct responses							
Total	14.99	0.000	17.28	<0.0001*	0.32 (0.13)	0.015	−0.52
All delays	13.57	0.000	15.97	0.000*	0.33 (0.13)	0.008	−0.52
Simultaneous	2.07	0.153	2.32	0.130	−0.01 (0.02)	0.615	−0.16
Delay 0 s	4.63	0.033	5.28	0.023	0.07 (0.05)	0.151	−0.32
Delay 4 s	8.39	0.004	10.99	0.001*	0.11 (0.05)	0.016	−0.41
Delay 12 s	10.52	0.002	12.44	0.001*	0.15 (0.06)	0.016	−0.50
Paired associates learning							
First trial memory scores	18.5	<0.0001	18.74	<0.0001*	0.04 (0.13)	0.750	−0.64
Mean errors to success	15.58	0.000	15.38	0.000*	−0.04 (0.03)	0.211	0.58
Mean trials to success	19.98	<0.0001	19.86	<0.0001*	−0.02 (0.01)	0.129	0.63
Stages completed on first trial	19.18	<0.0001	19.71	<0.0001*	0.04 (0.04)	0.780	−0.59
Total errors	16.18	<0.0001	16.06	0.000*	−0.23 (0.24)	0.334	0.59
Total trials	16.71	<0.0001	16.81	<0.0001*	−0.11 (0.08)	0.182	0.59
Rapid visual information processing							
A'	10.00	0.002	10.26	0.002*	0.00 (0.00)	0.070	−0.34
Probability of false alarm	0.09	0.766	0.08	0.771	0.00 (0.00)	0.667	0.06
Probability of hit	12.43	0.001	12.65	0.001*	0.01 (0.01)	0.013	−0.40
Total correct rejections	8.07	0.005	8.42	0.004	0.68 (0.39)	0.084	−0.32
Total false alarm	0.08	0.780	0.07	0.785	0.10 (0.25)	0.688	0.06
Total hits	12.41	0.001	12.63	0.001*	0.35 (0.14)	0.014	−0.40
Total misses	12.33	0.001	12.55	0.001*	−0.36 (0.14)	0.012	0.40

ASD, Autism spectrum disorder; TD, typically developing; FIQ, full-scale intelligence quotient; *β*, regression coefficient estimate; s.e., standard error.

^aUncorrected *p* values.

*Significant after Bonferroni correction (*p* = 0.0023).

We further divided our sample into childhood, early adolescence and late adolescence subgroups and found that age subgroups had significant main effects on SRM, RVP and DMS (except for A' and total correct responses in simultaneous matching), showing the older the youths, the better the performance (Table 4). In PAL, the late adolescence subgroup had higher memory scores and more stages completed in the first trial, and required fewer trials to succeed. Furthermore, an age × diagnosis interaction was significant in DMS and RVP, but not in SRM, and PAL. Significant age × diagnosis interactions were found in the correct responses to delay matching, and the probability of an error following a correct response of DMS,

and in the probability of hit, total hits and total misses of RVP (Table 2).

Discussion

As one of few studies investigating visual memory in youths with ASD, and with probably the largest sample, we found that youths with ASD performed worse than TD youths on all the visual memory tasks, i.e. SRM, DMS, PAL and the visual attention task, RVP, without significant difference between autism and AS. Besides, the significant ASD–TD difference disappeared in the subsample with superior IQ. We also found that both ASD and TD youths had improved performance with

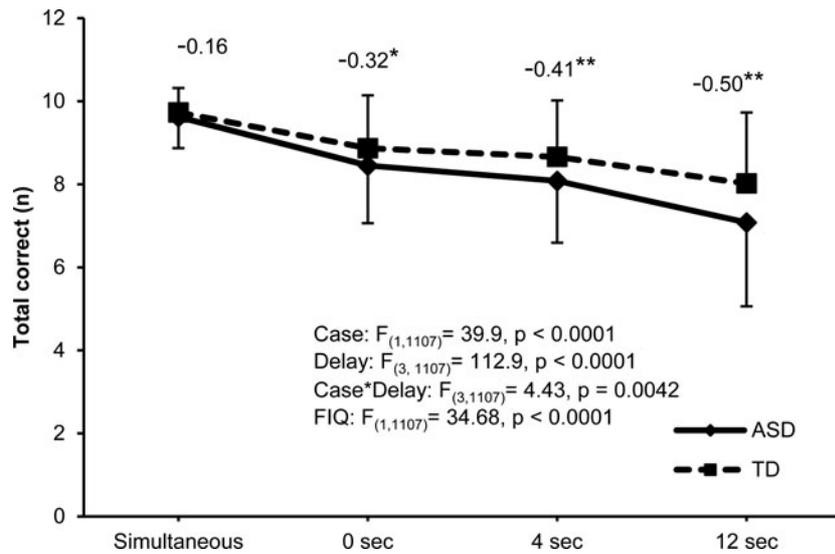


Fig. 1. Total correct numbers in delayed matching to sample simultaneous and delay conditions: diagnosis group effect (case), delay conditions (simultaneous, 0 s, 4 s and 12 s) and their interaction after controlling for full-scale intelligence quotient (FIQ). Values are effect sizes (Cohen's *d*). Standard deviations are represented by vertical bars. ASD, Autism spectrum disorder; TD, typically developing.

Table 3. Final model integrating the main effects of diagnostic group and different levels of task demand on the number of correct responses, controlling for confounding variables^a

	β (95% CI)	<i>F</i>	<i>p</i>
ASD <i>v.</i> TD controls	0.02 (-0.30 to 0.34)	0.02	0.902
0 s <i>v.</i> simultaneous	-1.49 (-2.08 to -0.90)	24.78	<0.0001
4 s <i>v.</i> simultaneous	-2.02 (-2.61 to -1.44)	45.63	<0.0001
12 s <i>v.</i> simultaneous	-3.38 (-3.97 to -2.79)	127.44	<0.0001
ASD × (0 s <i>v.</i> simultaneous)	0.32 (-0.06 to 0.69)	2.74	0.098
ASD × (4 s <i>v.</i> simultaneous)	0.48 (0.10 to 0.85)	6.25	0.013
ASD × (12 s <i>v.</i> simultaneous)	0.84 (0.46 to 1.21)	19.11	<0.0001

β , Regression coefficient estimate; CI, confidence interval; ASD, autism spectrum disorders; TD, typically developing
^aVariables included sex, age and full-scale intelligence quotient.

age in DMS and RVP while only TD youths improved in SRM and PAL. Further interaction analyses showed that the slope of improving visual memory with regard to DMS and RVP tasks was greater in TD youths than in ASD youths. In DMS, the longer the delay was, the greater the group difference, with the gap wider among older youths with ASD.

Consistent with previous studies testing memory of meaningless shapes (Ameli *et al.* 1988; Steele *et al.* 2007; Salmanian *et al.* 2012), we found a significant visual memory impairment in youths with ASD. These findings were in accordance with some earlier studies that demonstrated visual memory impairment in tasks such as recognition of pictures (Boucher & Warrington, 1976), delayed recall of complex geometric figures (Minschew & Goldstein, 2001), or semantic global organization of visual matrix patterns (Mammarella *et al.* 2014), but not others (Prior & Chen, 1976). Hence, our findings provide strong evidence to extend our knowledge that individuals with ASD demonstrate visual memory impairment across different tasks, with more consistent memory deficits relative to meaningless shapes than other tasks.

Compared with the finding of Salmanian *et al.* (2012) that visual memory deficits in youths with ASD lost statistical significance after controlling for IQ, our data showed that the significance did not change after controlling for IQ. However, in the subsample of superior IQ, the performance of ASD youths did not differ from that of TD youths, indicating that IQ is an important moderating factor but not a confounding factor for the association between ASD and visual memory impairment. Although individuals with ASD had preserved visuospatial function and non-agency objects recognition (Blair *et al.* 2002), they, except for those with superior IQ showing no difference, still had deficits in recalling abstract geometric figures or locations, reflecting a core deficit in visual memory. On the other hand, youths with ASD, as expected,

Table 4. Effects of age groups on visual memory performance (age as a categorical variable by the general linear model)

	Age group		Diagnosis		Age group × diagnosis	
	<i>F</i>	<i>p</i> ^a	<i>F</i>	<i>p</i> ^a	<i>F</i>	<i>p</i> ^a
Spatial recognition memory						
Number of correct responses	6.02	0.003	28.5	<0.0001	1.64	0.196
Delayed matching to sample						
Probability of an error following a correct response	19.32	<0.0001	24.11	<0.0001	3.43	0.034
Probability of an error following an error response	8.33	0.000	8.93	0.003	2.62	0.075
Total correct	22.33	<0.0001	27.05	<0.0001	4.46	0.013
Simultaneous	2.65	0.073	1.93	0.166	0.39	0.675
All delays	21.5	<0.0001	26.84	<0.0001	4.79	0.009
Delay 0 s	11.68	<0.0001	9.62	0.002	1.79	0.169
Delay 4 s	22.08	<0.0001	17.85	<0.0001	2.86	0.059
Delay 12 s	10.36	<0.0001	23.16	<0.0001	4.48	0.012
Paired associates learning						
First trial memory scores	5.48	0.005	29.11	<0.0001	1.44	0.238
Stages completed on first trial	1.8	0.167	23.61	<0.0001	1.17	0.313
Mean errors to success	3.2	0.043	28.68	<0.0001	0.79	0.457
Mean trials to success	6.94	0.001	27.27	<0.0001	1.55	0.214
Total errors	2.12	0.122	24.53	<0.0001	1.19	0.306
Total trials	2.91	0.056	25.3	<0.0001	0.71	0.492
Rapid visual information processing						
A' target sensitivity	76.1	<0.0001	17.15	<0.0001	2.5	0.084
Total correct rejections	77.44	<0.0001	15.03	0.000	2.97	0.053
Total false alarms	12.58	<0.0001	0.42	0.515	0.46	0.629
Total hits	68	<0.0001	21.41	<0.0001	3.58	0.029
Total misses	67.96	<0.0001	21.36	<0.0001	3.72	0.026

^aUncorrected *p* values.

showed significant sustained attention deficits compared with TD youths (Chien *et al.* 2014). The novel finding that visual memory deficits of meaningless shapes mostly remained when the effect of sustained attention impairment was regressed out warrants further investigation. This echoes the argument that impaired face recognition itself does not result from impaired attention (Boucher & Lewis, 1992). Although there is a close link between visual memory and attention (e.g. Awh *et al.* 2006), attention deficits may moderate, rather than mediate, visual memory performance in ASD.

Our study, being the first study to address the age effect on memory of meaningless shapes, demonstrated a clear age effect in the improvement of performance from childhood to adolescence, implying that visual memory and sustained attention is a function of age. The significant age and diagnosis interaction in DMS and RVP performance suggests that despite improving visual memory and sustained attention with age in both

ASD and TD youths, the magnitude of improvement was greater in TD youths. Our finding is in line with O'Hearn *et al.* (2014), who showed that immediate memory deficits (of recognizing faces and cars) in autism become more robust and general from childhood (only faces) to adulthood (both faces and cars), suggesting a developmental plateau in visual object processing. The lesser involvement of memory of meaningless shapes in the ability to translate information from a visual to a phonological form (inner speech) was demonstrated in TD youths with a significant age effect (e.g. Palmer, 2000). Other factors, such as the maturation of neurological networks integrating complex cognitive processes for visual coding, may account for the age-related changes (Pickering, 2001). Developmental changes in processing strategies and speed, and attentional capacity are also likely to influence visual memory performance and contribute to the lesser improvement in ASD (Cowan & Alloway, 1997). Moreover, our findings of more deficits among older

youths with ASD on DMS and RVP, but not in spatial working memory (SRM and PAL), highlight the different trajectories of neurocognitive development in ASD. In other words, youths with ASD still have the potential to improve their spatial working memory, just like TD youths. These findings strengthen the argument that the visual memory system is developmentally fractionable (Blair *et al.* 2002).

DMS and PAL are supposed to be sensitive to changes in medial temporal lobe functioning with some input from the frontal lobes to DMS (Sahakian *et al.* 1988; Moscovitch, 1994; Robbins *et al.* 1994), while SRM and RVP are sensitive to frontal dysfunction (and to parietal dysfunction as well in RVP) (Robbins *et al.* 1998). Our findings lend indirect evidence to support temporal and frontal lobe dysfunction in ASD, which has been documented using both functional (e.g. Castelli *et al.* 2002; Luna *et al.* 2002) and structural magnetic resonance imaging (e.g. Rojas *et al.* 2006; Bonilha *et al.* 2008; Ke *et al.* 2008). Furthermore, adolescence is a critical period for frontal lobe development (Begley, 2000; Giedd, 2008); youths with autism revealed abnormal white matter development in the temporal, parietal and occipital lobes, but not the frontal lobe (Hua *et al.* 2013). Our findings of a lack of age and diagnosis interaction on SRM and PAL, the tasks involving spatial working memory and being related to frontal lobe functioning (Luna *et al.* 2002), correspond to this regional brain growth hypothesis (Hua *et al.* 2013). However, the older ASD youths performed worse on the other two tasks not involving spatial memory (DMS and RVP), supporting a previous argument of slowed development in the temporal and parietal lobes during adolescence (Luna *et al.* 2002). Given their lesser improvement with age, deviated performance on DMS and RVP could potentially serve as trait markers for ASD.

Our data also revealed that the magnitude of group difference increased as memory loading increased on DMS. Similar findings have been reported in ADHD (Shang & Gau, 2011). However, our finding is considered novel since no study has provided such data in ASD. Moreover, elder ASD youths performed worse during longer delay conditions (4 and 12 s), rather than the 0 s delay condition, implying that individuals with ASD, like TD youths, may potentially improve with age on tasks with lower memory loading. Our results collectively implied that visual memory and attention impairment in youths with ASD is indeed moderated by age and memory loading, as well as the involvement of spatial working memory. This may explain the controversial findings in previous studies, and therefore needs to be considered in future investigations.

Differing from early impressions (e.g. Sahyoun *et al.* 2009), our findings of no significant difference between

autism and AS are in line with evidence showing equivalent cognitive abilities between AS and HFA (e.g. Ozonoff *et al.* 2000). Visual memory deficits of meaningless shapes may be inherent to ASD psychopathology, independent of diagnostic subgroups.

Several limitations should be considered when interpreting our results. First, the sample was male-predominant (93.7%) with a wide age range (8–25 years) and normal intelligence, so the findings may not be generalized to the entire ASD population. Therefore, we cautiously adjusted for sex and age in the statistical analysis. Although the normal IQ in our sample is assumed to lead the comparison towards the null and may underestimate the group difference, visual memory and sustained attention still significantly differed between the two groups after adjusting for IQ. Our samples do not match on IQ because of an intention to test the moderating effect of IQ and the concern about over-matching that is under debate (e.g. Lundervold *et al.* 2012). Second, the comparison may be biased when the task does not interest them. In this study, youths with ASD showed comparable performance on several tasks (e.g. stages completed in PAL, simultaneous matching in DMS) and mean latency of responses relative to TD youths, reflecting that they performed the tasks as seriously as TD youths. Nevertheless, the study used a matched design with a relatively large sample, the diagnosis of autism and AS was confirmed by a standardized diagnostic assessment, the ADI-R, and the potential correlates were assessed comprehensively. The results showed that youths with ASD, particularly older youths, had visual memory and sustained attention impairment across tasks.

For most ASD youths with visual memory impairment, special tutoring may be needed to split the tasks, or to present the visual materials simultaneously for their learning. Since the impairment is highly age-dependent, diagnosis \times age interaction and age-stratified analyses should be regularly examined in future studies on the developmental neurobiology of ASD. Future longitudinal studies are warranted to explore the neural substrate of visual memory and sustained attention deficits and to trace the trajectory of different neurocognitive functions.

Supplementary material

For supplementary material accompanying this paper visit <http://dx.doi.org/10.1017/S0033291714003201>

Acknowledgements

This work was supported by the National Science Council (NSC98-3112-B-002-004, NSC 99-3112-B-002-036, NSC99-2627-B-002-015, NSC100-2627-B-002-014

and NSC101-2627-B-002-002) and the National Taiwan University-AIM for Top University: Excellent Research Project (10R81918-03, 101R892103, 102R892103). The authors thank all the participants in this study.

Declaration of Interest

None.

References

- Ameli R, Courchesne E, Lincoln A, Kaufman AS, Grillon C** (1988). Visual memory processes in high-functioning individuals with autism. *Journal of Autism and Developmental Disorders* **18**, 601–615.
- American Psychiatric Association** (2013). *Diagnostic and Statistical Manual of Mental Disorders*, 5th edn. American Psychiatric Association: Arlington: VA.
- Awh E, Jonides J** (2001). Overlapping mechanisms of attention and spatial working memory. *Trends in Cognitive Sciences* **5**, 119–126.
- Awh E, Jonides J, Reuter-Lorenz PA** (1998). Rehearsal in spatial working memory. *Journal of Experimental Psychology: Human Perception and Performance* **24**, 780–790.
- Awh E, Vogel EK, Oh SH** (2006). Interactions between attention and working memory. *Neuroscience* **139**, 201–208.
- Begley S** (2000). Getting inside a teen brain. Hormones aren't the only reason adolescents act crazy. Their gray matter differs from children's and adults'. *Newsweek* **135**, 58–59.
- Blair RJ, Frith U, Smith N, Abell F, Cipolotti L** (2002). Fractionation of visual memory: agency detection and its impairment in autism. *Neuropsychologia* **40**, 108–118.
- Bonilha L, Cendes F, Rorden C, Eckert M, Dalgalarondo P, Li LM, Steiner CE** (2008). Gray and white matter imbalance – typical structural abnormality underlying classic autism? *Brain Development* **30**, 396–401.
- Boucher J, Lewis V** (1992). Unfamiliar face recognition in relatively able autistic children. *Journal of Child Psychology and Psychiatry* **33**, 843–859.
- Boucher J, Warrington EK** (1976). Memory deficits in early infantile autism: some similarities to the amnesic syndrome. *British Journal of Psychology* **67**, 73–87.
- Castelli F, Frith C, Happé F, Frith U** (2002). Autism, Asperger syndrome and brain mechanisms for the attribution of mental states to animated shapes. *Brain* **125**, 1839–1849.
- Chien YL, Gau SS, Chiu YN, Tsai WC, Shang CY, Wu YY** (2014). Impaired sustained attention, focused attention, and vigilance in youths with autistic disorder and Asperger's disorder. *Research in Autism Spectrum Disorders* **8**, 881–889.
- Chun MM** (2011). Visual working memory as visual attention sustained internally over time. *Neuropsychologia* **49**, 1407–1409.
- Cowan N** (2001). The magical number 4 in short-term memory: a reconsideration of mental storage capacity. *Behavioral and Brain Sciences* **24**, 87–114; discussion 114–185.
- Cowan N, Alloway T** (1997). Development of working memory. In *The Development of Memory in Childhood* (ed. N. Cowan), pp. 314–329. Psychology Press: Hove, UK.
- Cowan N, Elliott EM, Scott Saults J, Morey CC, Mattox S, Hismjatullina A, Conway AR** (2005). On the capacity of attention: its estimation and its role in working memory and cognitive aptitudes. *Cognitive Psychology* **51**, 42–100.
- Cusack R, Lehmann M, Veldsman M, Mitchell DJ** (2009). Encoding strategy and not visual working memory capacity correlates with intelligence. *Psychonomic Bulletin and Review* **16**, 641–647.
- Demidenko E** (2004). *Mixed Models: Theory and Applications*. John Wiley: New York.
- Egerhazi A, Berecz R, Bartok E, Degrell I** (2007). Automated Neuropsychological Test Battery (CANTAB) in mild cognitive impairment and in Alzheimer's disease. *Progress in Neuropsychopharmacology and Biological Psychiatry* **31**, 746–751.
- Gau S-F, Soong W-T** (1999). Psychiatric comorbidity of adolescents with sleep terrors or sleepwalking: a case-control study. *Australian and New Zealand Journal of Psychiatry* **33**, 734–739.
- Gau SSF, Chong MY, Chen THH, Cheng ATA** (2005). A 3-year panel study of mental disorders among adolescents in Taiwan. *American Journal of Psychiatry* **162**, 1344–1350.
- Gau SS, Liu LT, Wu YY, Chiu YN, Tsai WC** (2013). Psychometric properties of the Chinese version of the social responsiveness scale. *Research in Autism Spectrum Disorders* **7**, 349–360.
- Gau SS-F, Huang W-L** (2014). Rapid visual information processing as a cognitive endophenotype of attention deficit hyperactivity disorder. *Psychological Medicine* **44**, 435–446.
- Gau SS-F, Lee C-M, Lai M-C, Chiu Y-N, Huang Y-F, Kao J-D, Wu Y-Y** (2011). Psychometric properties of the Chinese version of the Social Communication Questionnaire. *Research in Autism Spectrum Disorders* **5**, 809–818.
- Giedd JN** (2008). The teen brain: insights from neuroimaging. *Journal of Adolescent Health* **42**, 335–343.
- Hua X, Thompson PM, Leow AD, Madsen SK, Caplan R, Alger JR, O'Neill J, Joshi K, Smalley SL, Toga AW, Levitt JG** (2013). Brain growth rate abnormalities visualized in adolescents with autism. *Human Brain Mapping* **34**, 425–436.
- Kail RV, Ferrer E** (2007). Processing speed in childhood and adolescence: longitudinal models for examining developmental change. *Child Development* **78**, 1760–1770.
- Ke X, Hong S, Tang T, Zou B, Li H, Hang Y, Zhou Z, Ruan Z, Lu Z, Tao G, Liu Y** (2008). Voxel-based morphometry study on brain structure in children with high-functioning autism. *Neuroreport* **19**, 921–925.
- Lin YJ, Chen WJ, Gau SS** (2013). Neuropsychological functions among adolescents with persistent, subsyndromal and remitted attention deficit hyperactivity disorder. *Psychological Medicine* **27**, 1–13.
- Littell RC, Milliken GA, Stroup WW, Wolfinger RD, Schabenberger O** (2006). *SAS for Mixed Models*, 2nd edn. SAS Institute Inc.: Cary, NC.
- Lord C, Rutter M, Le Couteur A** (1994). Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders* **24**, 659–685.
- Luna B, Minshew NJ, Garver KE, Lazar NA, Thulborn KR, Eddy WF, Sweeney JA** (2002). Neocortical system

- abnormalities in autism: an fMRI study of spatial working memory. *Neurology* **59**, 834–840.
- Lundervold AJ, Stickert M, Hysing M, Sørensen L, Gillberg C, Posserud MB** (2012). Attention deficits in children with combined autism and ADHD: a CPT study. *Journal of Attention Disorders*. Published online 31 August 2012. doi:10.1177/1087054712453168.
- Mammarella IC, Giofre D, Caviola S, Cornoldi C, Hamilton C** (2014). Visuospatial working memory in children with autism: the effect of a semantic global organization. *Research in Developmental Disabilities* **35**, 1349–1356.
- Miller JN, Ozonoff S** (2000). The external validity of Asperger disorder: lack of evidence from the domain of neuropsychology. *Journal of Abnormal Psychology* **109**, 227–238.
- Minshew NJ, Goldstein G** (2001). The pattern of intact and impaired memory functions in autism. *Journal of Child Psychology and Psychiatry* **42**, 1095–1101.
- Miyake A, Friedman NP, Rettinger DA, Shah P, Hegarty M** (2001). How are visuospatial working memory, executive functioning, and spatial abilities related? A latent-variable analysis. *Journal of Experimental Psychology: General* **130**, 621–640.
- Moscovitch M** (1994). Cognitive resources and dual-task interference effects at retrieval in normal people: The role of the frontal lobes and medial temporal cortex. *Neuropsychology* **8**, 524–534.
- O'Hearn K, Tanaka J, Lynn A, Fedor J, Minshew N, Luna B** (2014). Developmental plateau in visual object processing from adolescence to adulthood in autism. *Brain and Cognition* **90**, 124–134.
- Ozonoff S, South M, Miller JN** (2000). DSM-IV-defined Asperger syndrome: cognitive, behavioral and early history differentiation from high-functioning autism. *Autism* **4**, 29–46.
- Palmer S** (2000). Working memory: a developmental study of phonological recoding. *Memory* **8**, 179–193.
- Pickering SJ** (2001). The development of visuo-spatial working memory. *Memory* **9**, 423–432.
- Prior MR, Chen CS** (1976). Short-term and serial memory in autistic, retarded, and normal children. *Journal of Autism and Childhood Schizophrenia* **6**, 121–131.
- Robbins TW, James M, Owen AM, Sahakian BJ, Lawrence AD, McInnes L, Rabbitt PM** (1998). A study of performance on tests from the CANTAB battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: implications for theories of executive functioning and cognitive aging. *Journal of the International Neuropsychological Society* **4**, 474–490.
- Robbins TW, James M, Owen AM, Sahakian BJ, McInnes L, Rabbitt P** (1994). Cambridge Neuropsychological Test Automated Battery (CANTAB): a factor analytic study of a large sample of normal elderly volunteers. *Dementia* **5**, 266–281.
- Rojas DC, Peterson E, Winterrowd E, Reite ML, Rogers SJ, Tregellas JR** (2006). Regional gray matter volumetric changes in autism associated with social and repetitive behavior symptoms. *BMC Psychiatry* **6**, 56.
- Sahakian B, Jones G, Levy R, Gray J, Warburton D** (1989). The effects of nicotine on attention, information processing, and short-term memory in patients with dementia of the Alzheimer type. *British Journal of Psychiatry* **154**, 797–800.
- Sahakian BJ, Morris RG, Evenden JL, Heald A, Levy R, Philpot M, Robbins TW** (1988). A comparative study of visuospatial memory and learning in Alzheimer-type dementia and Parkinson's disease. *Brain* **111**, 695–718.
- Sahgal A** (1987). Some limitations of indices derived from signal detection theory: evaluation of an alternative index for measuring bias in memory tasks. *Psychopharmacology (Berlin)* **91**, 517–520.
- Sahyoun CP, Soulières I, Belliveau JW, Mottron L, Mody M** (2009). Cognitive differences in pictorial reasoning between high-functioning autism and Asperger's syndrome. *Journal of Autism and Developmental Disorders* **39**, 1014–1023.
- Salmanian M, Tehrani-Doost M, Ghanbari-Motlagh M, Shahrivar Z** (2012). Visual memory of meaningless shapes in children and adolescents with autism spectrum disorders. *Iran Journal of Psychiatry* **7**, 104–108.
- Scherf KS, Luna B, Kimchi R, Minshew N, Behrmann M** (2008). Missing the big picture: impaired development of global shape processing in autism. *Autism Research* **1**, 114–129.
- Shang CY, Gau SS** (2011). Visual memory as a potential cognitive endophenotype of attention deficit hyperactivity disorder. *Psychological Medicine* **41**, 2603–2614.
- Smyth MM, Scholey KA** (1994). Interference in immediate spatial memory. *Memory and Cognition* **22**, 1–13.
- Squeglia LM, Jacobus J, Sorg SF, Jernigan TL, Tapert SF** (2013). Early adolescent cortical thinning is related to better neuropsychological performance. *Journal of International Neuropsychological Society* **19**, 962–970.
- Stanislaw H, Todorov N** (1999). Calculation of signal detection theory measures. *Behavior Research Methods, Instruments, and Computers* **31**, 137–149.
- Steele SD, Minshew NJ, Luna B, Sweeney JA** (2007). Spatial working memory deficits in autism. *Journal of Autism and Developmental Disorders* **37**, 605–612.
- Tanner WP Jr, Swets JA** (1954). A decision-making theory of visual detection. *Psychological Review* **61**, 401–409.
- Wesnes K, Warburton DM** (1984). Effects of scopolamine and nicotine on human rapid information processing performance. *Psychopharmacology* **82**, 147–150.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.