Research in Autism Spectrum Disorders 5 (2011) 237–245

Contents lists available at ScienceDirect

Research in Autism Spectrum Disorders

Journal homepage: http://ees.elsevier.com/RASD/default.asp

Disordered connectivity associated with memory deficits in children with autism spectrum disorders

Agnes S. Chan [a,b,*], Yvonne M.Y. Han [b], Sophia L. Sze [a,b], Mei-chun Cheung [c], Winnie Wing-man Leung [b], Raymond C.K. Chan [d,e], Cho Yee To [f]

[a] *Integrative Neuropsychological Rehabilitation Center, The Chinese University of Hong Kong, Hong Kong, China*
[b] *Neuropsychology Laboratory, Department of Psychology, The Chinese University of Hong Kong, Hong Kong, China*
[c] *Institute of Textiles and Clothing, The Hong Kong Polytechnic University, Hong Kong, China*
[d] *Neuropsychology and Applied Cognitive Neuroscience Laboratory, Institute of Psychology, Chinese Academy of Sciences, Beijing, China*
[e] *Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China*
[f] *Faculty of Education, The University of Michigan, Ann Arbor, USA*

ARTICLE INFO

Article history:
Received 26 March 2010
Accepted 8 April 2010

Keywords:
Autism
EEG
Coherence
Memory
Theta
Children

ABSTRACT

The present study examined the memory performance and cortical connectivity of children with ASD, and investigated whether the memory deficits exhibited by these children were associated with the cortical connectivity. Twenty-one children with ASD and 21 children with normal development (NC), aged 5–14 years, participated in the study. Each child was administered a neuropsychological battery that included the Test of Non-verbal Intelligence (TONI-III), Digit Span test (DS), Rey-Osterrieth Complex Figure Test (Rey-O), and Hong Kong List Learning Test (HKLLT); and an EEG recording session when performing the visual encoding Object Recognition (OR) task. Six neuropsychological measures from the test battery and six EEG coherence measures in the theta band were compared between the children with ASD and normal children. Results indicated that children with ASD performed at comparable levels with normal children in the DS and Rey-O, but were significantly poorer in HKLLT and OR. They also exhibited significantly elevated long-range coherences in the fronto-posterior connections involving the left hemisphere (left anterior–left posterior; left anterior–right posterior). Pearson correlation showed significant negative associations between the anterior–posterior EEG coherences and memory performance.

1. Introduction

Autistic spectrum disorders (ASD) is a neurodevelopmental disorder characterized by disturbances in communication, poor social skills, and an abnormal repertoire of stereotyped behaviors (American Psychiatric Association, 2000). Abnormalities were also found in the higher cortical function of memory in individuals with ASD, where some show severely impaired memory while others fall into the other extreme with 'savant' memory (Mottron, Belleville, Stip, & Morasse, 1998; O'Connor & Hermelin, 1989). While the exact memory profile and the underlying basis of memory processing in autism are uncertain, it has been suggested that the memory deficits in individuals with ASD is associated with deficient executive control in utilizing effective strategies to monitor, organize and maintain information (Cheung, Chan, Sze, Leung, & To, 2010),

---

[*] Corresponding author at: Department of Psychology, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China. Tel.: +852 2609 6654; fax: +852 2603 5019.
E-mail address: aschan@psy.cuhk.edu.hk (A.S. Chan).

1750-9467/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.rasd.2010.04.005

resulting in the impairment being more severe when the memory tasks are mentally effortful or when the information is meaningful, semantically related or in vast amount (Minshew & Goldstein, 1993, 1998, 2001; Minshew, Goldstein, & Siegel, 1997; Toichi & Kamio, 2002, 2003; Williams, Goldstein, & Minshew, 2006).

It is widely accepted that the executive control of memory processing is mediated by the frontal cortex (Buckner, Kelley, & Petersen, 1999; Demb et al., 1995; Fletcher, Shallice, & Dolan, 1998; Sowell, Thompson, Holmes, Jernigan, & Toga, 1999). Increasing evidence shows that it also involves the integrated action of multiple brain areas (Osaka et al., 2004; Sauseng, Klimesch, Schabus, & Doppelmayr, 2005). For example, brain imaging studies have shown that the fronto-parietal network is involved in visuospatial working memory (McEvoy, Pellouchoud, Smith, & Gevins, 2001; Oliveri et al., 2001), and the frontal and parietal regions have been found to have increased regional blood flow during non-verbal paired-associates tasks (Klingberg & Roland, 1998). Increased activations between anterior and posterior brain areas have also been found during memory (Volf & Razumnikova, 1999; Weiss, Muller, & Rappelsberger, 2000) and working memory (Sauseng et al., 2005) tasks.

Given that the executive control of memory processing relies on the frontal cortex and its distributed network to the posterior cortical regions (Fletcher & Henson, 2001; Nyberg et al., 2003; Rugg, Otten, & Henson, 2002; Sauseng et al., 2005; Weiss et al., 2000), it has been postulated that abnormalities in this neural connectivity may underlie the memory deficits in ASD (Rippon, Brock, Brown, & Boucher, 2007). Indeed, diffusion tensor imaging (DTI) studies of individuals with ASD have found reduced myelin integrity in the ventromedial prefrontal cortex and at the temporoparietal junctions (Barnea-Goraly et al., 2004; Lewis & Elman, 2008). In addition, functional imaging studies also found reduced synchronization between activated brain areas on tests of working memory (Koshino et al., 2008; Luna et al., 2002; Silk et al., 2006) in individuals with ASD. Based on the reported memory deficits and the documented disordered connectivity in the autistic brain, it is conceivable that memory deficits in ASD may be associated with disordered connectivity between the fronto-posterior network in these individuals.

Cortical connectivity between brain regions in response to cognitive processes can be estimated using coherence measures in the electroencephalograpy (EEG) (Murias, Webb, Greenson, & Dawson, 2007; Rippon et al., 2007). EEG coherence measures the level of synchronization between two brain areas in terms of EEG signals recorded at different sites of the scalp (Nunez & Srinivasan, 2006; Srinivasan, Nunez, & Silberstein, 1998). A high level of synchronization between two brain areas is indicated by high EEG coherence; a low level of synchronization is suggested by low coherence (Murias et al., 2007). In addition to the level of synchronicity, different EEG frequencies have been shown to correlate with different cognitive processes (Rippon et al., 2007). Greater long-range coherence in the theta band between the anterior and posterior brain region was found to be associated with increased working memory demands (Sarnthein, Petsche, Rappelsberger, Shaw, & von Stein, 1998) and successful encoding and storage of episodic information (Doppelmayr, Klimesch, Schwaiger, Stadler, & Rohm, 2000; Klimesch, 1999; Volf & Razumnikova, 1999; Weiss & Rappelsberger, 2000). Higher theta coherence was also found between frontal and parietal regions during memory tasks that involved manipulation rather than simple retrieval and maintenance of information (Sauseng et al., 2005). Thus, effective memory processing depends on the timely activation of cortical areas. In light of the documented abnormalities in cortical connectivity in individuals with ASD, we postulated that these individuals would show altered patterns of EEG coherence during memory tasks. As long-range anterior–posterior theta coherence is critically involved in memory processes, we hypothesized that the memory deficit in individuals with ASD would be associated with theta coherence between the frontal and posterior brain regions.

The purpose of the present study was thus to examine the association between memory performance and fronto-posterior theta coherence in individuals with ASD. Most previous studies were done on adults with ASD, and the situation for children was not well known. We therefore examined children with ASD to extend previous knowledge into the pediatric population. We hypothesized that children with ASD would perform significantly poorer than normal children in memory tasks, and show abnormal fronto-posterior theta coherence compared with normal children under the memory task condition. We further hypothesized that the abnormality in theta coherence would be associated with the memory performance in these children.

2. Materials and methods

2.1. Participants

Twenty-one children with ASD and 21 children with normal development (NC), aged 5–14 years, participated in the study. NC children were recruited from local primary schools, and had no history of delay in developmental milestones, neurological or psychiatric disorders as reported by their parents. Children with ASD were recruited either from the Parents' Association of Pre-School Handicapped Children in Hong Kong, or from the database of the Neuropsychology Laboratory of The Chinese University of Hong Kong. All children with ASD were diagnosed by pediatricians of the government Child Assessment Centres in Hong Kong, with the diagnosis confirmed by two clinical psychologists based on the Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.; DSM-IV-TR; American Psychiatric Association, 2000). Of the 21 children with ASD, 16 met the diagnosis of autistic disorder, and five met the criteria of pervasive developmental disorder not otherwise specified (PDD-NOS). Children comorbid with other developmental or neurological disorders (e.g., ADHD, epilepsy, oppositional defiant disorder, specific learning disorder) were excluded. The Childhood

Table 1
Demographic characteristics of the normal controls (NC) and children with autistic spectrum disorder (ASD).

Variable	NC ($n = 21$)	ASD ($n = 21$)
Mean age, years	9.85 (2.15)	10.27 (2.26)
Gender, male/female	14/7	19/2
TONI-III, deviation quotient	106.0 (14.59)	101.86 (16.09)
CARS, total score	–	31.94 (3.29)

Note. Standard deviations are in parentheses. CARS = Childhood Autism Rating Scale; TONI-III = Deviation quotient of the Test of Non-verbal Intelligence, 3rd edition. The dash indicates that the CARS was not administered to normal controls.

Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1986) was administered to estimate the severity of autistic features. Table 1 shows the demographic characteristics of the children. Both groups were matched on age, $t = -.61$, $p > .05$, and general intelligence as measured by the Test of Non-verbal Intelligence, 3rd edition (TONI-III; Brown, Sherbenou, & Johnsen, 1992) ($t = .87$, $p > .05$).

2.2. Procedures and materials

All children participated with informed parental consent. In the neuropsychological assessment session, each child was individually administered a neuropsychological battery which consisted of the TONI-III (Brown et al., 1992) and memory tasks including the Digit Span Test (DS; Hong Kong Education Department & Hong Kong Psychological Society, 1981), Hong Kong List Learning Test (HKLLT 2nd ed.; Chan, 2006), and Rey-Osterrieth Complex Figure Test (Rey-O; Bernstein & Waber, 1996). In the EEG recording session, EEG data were recorded while the child performed the Object Recognition (OR) task. The sequence of the neuropsychological assessment and EEG recording was counter-balanced to avoid order effect. The experimental procedure was approved by the Clinical Research Ethics Committee of The Chinese University of Hong Kong.

2.3. Measures

Test of Non-verbal Intelligence. The TONI-III (Brown et al., 1992) assessed non-verbal intelligence. This test consists of 45 matrix reasoning questions, giving a raw score that ranged from 0 to 45, which was then converted to a deviation quotient based on the norms provided in the test manual.

Digit span forward (DS). This test was used to assess working memory in the present study. It is a subtest on the Hong Kong version of the Wechsler Intelligence Scale for Children (HKWISC; Hong Kong Education Department & Hong Kong Psychological Society, 1981), and consists of a list of nine random numerals read aloud in sequence by the examiner at the rate of one numeral per second, starting from two numerals up to nine numerals in a total of eight trials. Participants were asked to repeat the numerals after the examiner, in sequence, after each trial. The score was the number of correct trials recalled by the participant.

Hong Kong List Learning Test. The HKLLT (Chan, 2006; Chan & Kwok, 1999) is a verbal learning test. A randomly organized list of 16 Chinese words was presented once during each of three learning trials. Participants were asked to recall the words immediately after each learning trial. The total number of correctly recalled words during the three learning trials gave the Total Learning score. A recognition test consisting of the 16 target words and 16 distracters was presented after a 30-min delayed recall trial. The children were required to discriminate whether the words have been previously learnt. A Discrimination score that assessed memory performance of the children was calculated based on the number of correct hits (i.e., the correct identification of targets) and false alarms (i.e., the false positive) at the recognition trial.

Object recognition task (OR). This test was developed by the authors and consisted of 24 line drawings taken from the Snodgrass and Vanderwart's object database (1980), modified and validated by Rossion and Pourtois (2004). The line drawings were placed in an array of six by four layouts displayed on a computer screen for 3 min. Participants were required to memorize the items for a later recognition task consisting of 12 targets mixed with 12 distractors. Correct identification of the memorized objects was indicated by correct hits (CH). Incorrect identification of distractors was indicated by false alarms (FA), a commonly used neuropsychological measure of intrusion (Cornoldi & Mammerella, 2006). The maximum possible score for CH and FA was 12. A discrimination score (DS) calculated as $[(\mathrm{CH} - \mathrm{FA})/12 \times 100]$ was derived to represent memory performance of the children.

Rey-Osterrieth Complex Figure Test (Rey-O). The Rey-O (Bernstein & Waber, 1996) Immediate Recall score assessed working memory in the study. The child was first asked to copy a complicated figure. The figure was then taken away and the child had to draw as accurately as possible the figure from memory, giving the Immediate Recall score (Rey-O IR) that ranged from 0 to 36.

EEG recording. Each child was tested individually in a sound- and light-attenuated room using the DEYMED Diagnostic TruScan 32 Biofeedback Device. An electrode cap with 19 electrodes, based on the International 10–20 System (Jasper, 1958) referenced to linked ears, was used to collect EEG data at a sampling rate of 256 Hz with a low pass filter of 30 Hz and high pass filter of 1 Hz. Impedance at each electrode site was kept at 10 kΩ or below. EEG was recorded in a task condition when the child performed the OR test. Throughout the session, body movements were time-marked by a research assistant for off-line analyses. EEG data was stored and later displayed on computer for selection and analysis. Movements and muscle artifacts in the EEG were visually examined and removed. One minute of artifact-free data were selected (John, Prichep, Fridman, & Easton, 1988 for discussion of qEEG method) and spectrally processed through fast Fourier Transformation (FFT) using the Neuroguide (version 2.1.8) software to compute coherence values. Theta coherence measures (4–7.5 Hz) were used in the present study.

Coherence measures. Coherence is an index that measures temporal synchronization of the EEG activity of two brain regions underneath the electrodes and reflects the functional connectivity between the two regions. 171 coherence values were computed among the 19 electrode positions (Fp1, Fp2, F3, F4, F7, F8, Fz, T3, T4, T5, T6, C3, C4, Cz, P3, P4, Pz, O1 and O2). Two short-range and four long-range coherence measures of the anterior and posterior cortical regions were computed to examine the frontal and posterior cortical connections in memory processing. Short-range coherence measures of the anterior region (FP1–F7, FP1–F3, F3–F7, FP2–F8, FP2–F4, F4–F8) as well as the posterior region (T5–O1, P3–O1, T5–P3; T6–O2, P4–O2, T6–P4) were respectively averaged to give the two short-range coherence values (i.e., anterior, posterior). Fronto-posterior long-range coherence measures were computed to give two mean *intra-hemispheric* (left: FP1–T5, FP1–P3, FP1–O1, F7–T5, F7–P3, F7–O1, F3–T5, F3–P3, F3–O1; right: FP2–T6, FP2–P4, FP2–O2, F8–T6, F8–P4, F8–O2, F4–T6, F4–P4, F4–O2), and two mean *inter-hemispheric* (left to right: FP1–T6, FP1–P4, FP1–O2, F7–T6, F7–P4, F7–O2, F3–T6, F3–P4, F3–O2; right to left: FP2–T5, FP2–P3, FP2–O1, F8–T5, F8–P3, F8–O1, F4–T5, F4–P3 and F4–O1) long-range coherence measures. Long-range coherence was defined as any electrode pairs that were separated by at least one electrode in between (i.e., the distance between the electrodes must be greater than 10 cm).

2.4. Data analyses

The neuropsychological memory performance of ASD and NC children were compared on each of the six scores from the DS, HKLLT, OR, and Rey-O using independent *t*-tests. EEG theta coherence measures of the two groups were compared on the two short-range (anterior, posterior), two *intra-hemispheric* long-range (left to left, right to right), and two *inter-hemispheric* long-range (left to right, right to left) coherence measures also using independent *t*-tests. The relationship between the six memory performance scores and the six EEG coherence measures were examined using Pearson correlation. Since the number of participants was relatively small and the comparisons were planned, the alpha level was not adjusted in order to maintain a reasonable balance between the risks of Type I and Type II errors.

3. Results

3.1. Neuropsychological measures on memory performance

Independent *t*-tests indicated no significant difference between the ASD and NC groups on DS ($t = 1.88$, $p = n.s.$) and Rey-O IR ($t = 1.61$, $p = n.s.$). However, the ASD group showed significantly poorer performance than NC children on the HKLLT Total Learning ($t = 3.78$, $p < .01$) and Discrimination ($t = 3.41$, $p < .01$) scores as well as the OR ($t = 4.3$, $p < .01$) (Table 2). It should be noted that there were greater variations in the ASD than NC group in the HKLLT and OR scores, and the significantly lower scores of the ASD group were largely related to their higher false alarm rates on the HKLLT ($t = -2.61$, $p < .05$) and OR ($t = -3.64$, $p < .01$).

Table 2
Mean performance and standard deviation on the memory performance of children in the NC and ASD groups.

Measures	NC ($n = 21$) *M* (SD)	ASD ($n = 21$) *M* (SD)	*t*-Value
DS			
Forward	12.31 (1.7)	10.85 (2.23)	1.88
HKLLT			
Total Learning	29.0 (7.33)	20.05 (8.0)	3.78**
Discrimination Score (%)	89.88 (12.88)	66.67 (28.39)	3.41**
Correct Hit	14.67 (1.98)	13.33 (2.37)	1.98
False Alarm	.29 (.46)	2.67 (4.15)	−2.61*
Rey-O			
Immediate Recall	13.90 (5.78)	10.87 (6.15)	1.61
OR			
Discrimination Score (%)	85.32 (10.83)	48.02 (38.27)	4.30**
Correct Hit	10.29 (1.27)	7.86 (3.12)	3.30**
False Alarm	.05 (.22)	2.10 (2.57)	−3.64**

** $p < .01$.
* $p < .05$.

Table 3
Mean (SD) of short- and long-range coherence of normal controls (NC) and children with autistic spectrum disorder (ASD) during object recognition task.

Measures	NC ($n = 21$) M (SD)	ASD ($n = 21$) M (SD)	t-Value
Short-range			
Anterior	43.2 (5.79)	44.38 (5.08)	−0.70
Posterior	44.7 (8.1)	46.05 (7.47)	−0.56
Long-range			
Intra-hemisphere			
Left	6.36 (2.62)	11.53 (5.29)	-4.02^{**}
Right	13.63 (5.02)	15.3 (5.37)	−1.04
Inter-hemisphere			
Left to right	5.17 (2.34)	7.51 (2.85)	-2.91^{**}
Right to left	6.92 (3.79)	8.87 (3.75)	−1.67

** $p < .001$.

3.2. EEG coherence measures

Children with ASD generally showed elevated coherence in most indices (Table 3). Specifically, they demonstrated significantly elevated fronto-posterior long-range coherences at the left *intra-hemispheric* (left anterior–left posterior) ($t = -4.02$, $p < .01$), and left-to-right *inter-hemisphere* (left anterior–right posterior) ($t = -2.91$, $p < .01$) connections (Fig. 1). They tended to show elevated long-range coherence particularly in the left hemisphere (Fig. 2a). This was in contrast to the pattern observed in NC children, whose coherences were higher in the right than in the left hemisphere. Between-group comparison of the laterality index of the coherence measures, computed as [(left − right)/(left + right)], showed that NC children were significantly more right-lateralized than children with ASD in the anterior–posterior ($t = -2.40$, $p = .024$) connection (Fig. 2b).

3.3. Association between memory performance and EEG coherence measures

Given that both the memory performances and the coherence measures were significantly different between the ASD and NC groups, we examined the relationship between memory performance and coherence using Pearson correlation (Table 4).

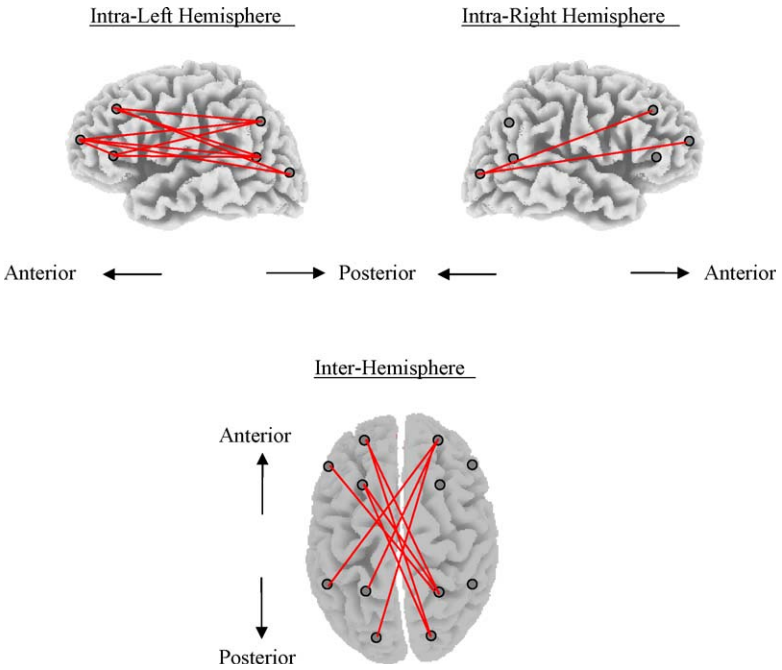

Fig. 1. Topographic maps demonstrating the between-subject differences in intra- and inter-hemispheric theta coherence during encoding of object recognition task. Red lines linking the electrode pairs (grey dots) signify significantly higher coherences in children with autistic spectrum disorder (ASD) than those in normal controls (NC), $p < .05$. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

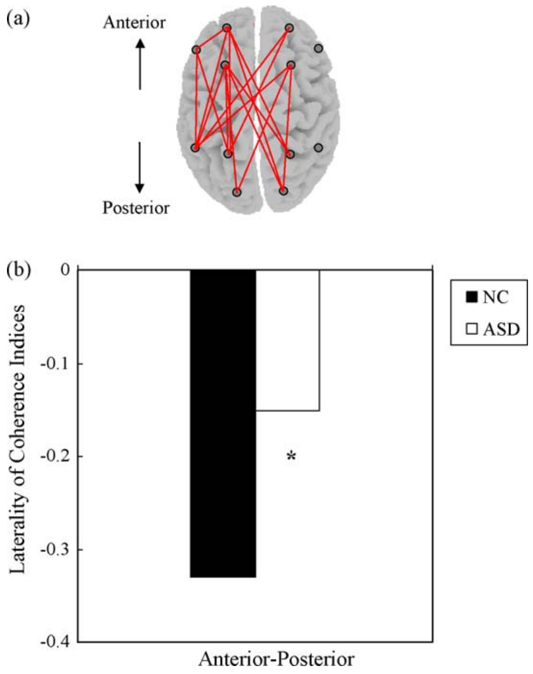

Fig. 2. (a) Coherences depicted in red represent significantly higher values in the ASD group than the normal controls (NC). (b) Laterality of coherence indices at the anterior–posterior region of the ASD and NC groups during object recognition task. Laterality is measured as [(left − right)/(left + right)], where negative value indicates higher coherence at the right hemisphere, and vice versa. $^{*}p < .05$. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

Results on the combined-group analysis showed that the left anterior (LA)–right posterior (RP) coherence measure was most strongly and negatively correlated with memory performance [HKLLT Total Learning ($r = -.53$, $p < .01$); HKLLT Discrimination ($r = -.44$, $p < .01$); OR ($r = -.47$, $p < .01$)]. In addition, the left anterior (LA)–left posterior (LP) coherence measure also significantly and negatively correlated with memory performance [HKLLT Total Learning ($r = -.31$, $p < .05$); OR ($r = -.38$, $p < .01$)]. To exclude the possibility that the correlations reflected only basic group differences, subgroup analyses were also performed for children with ASD ($n = 21$) and NC children ($n = 21$) (Table 4). Consistent with the combined-group analysis, significant and negative correlations were found in the ASD group between memory performance and the *inter-hemispheric* long-range LA–RP coherence [HKLLT Total Learning ($r = -.43$, $p < .05$) and OR ($r = -.43$, $p < .05$)]. Although the significant association between memory performance and the long-range *intra-hemispheric* LA–LP coherence disappeared, this was possibly due to the lower power as a result of the smaller number of participants in the subgroup analysis. No significant correlation was found between the neurophysiological and neuropsychological measures in the NC group.

Table 4

Correlations between long-range coherence and mean memory performance on neuropsychological tests for the whole group ($n = 42$), the ASD ($n = 21$) and NC ($n = 21$) subgroups.

Neuropsychological tests	Long-range coherence	
	Intra-hemisphere, left	Inter-hemisphere, left to right
Whole group ($n = 42$)		
HKLLT – Total Learning	−.31[*]	−.53[**]
HKLLT – Discrimination Score	−.29	−.44[**]
OR – Discrimination Score	−.38[**]	−.47[**]
ASD subgroup ($n = 21$)		
HKLLT – Total Learning	−.14	−.43[*]
HKLLT – Discrimination Score	−.10	−.40
OR – Discrimination Score	−.13	−.43[*]
NC subgroup ($n = 21$)		
HKLLT – Total Learning	.14	−.37
HKLLT – Discrimination Score	.21	−.11
OR – Discrimination Score	.01	−.03

[**] $p < .01$.

[*] $p < .05$.

4. Discussion and conclusions

The present study examined the memory performance and cortical connectivity of children with ASD, and investigated whether the memory deficits exhibited by these children were associated with the cortical connectivity, indicated by EEG coherence during performance of a memory task. Children with ASD performed significantly poorer than normal children on memory tasks as shown by their lower scores on different HKLLT and OR measures. Children with ASD also showed a different pattern of EEG coherence as indicated by the greater left-sided involvement in long-range coherences compared with normal children. It was further found that the higher the EEG long-range coherences in the LA–RP and LA–LP connections, the greater the memory deficit.

Our findings on the memory performance of children with ASD are consistent with findings from previous studies that suggested that the memory profile of individuals with ASD were similar to those in patients with frontal-lobe dysfunctions (Alexander, Stuss, & Fansabedian, 2003; Baldo & Shimamura, 2002; Cheung et al., 2010), in that our children with ASD were found to be vulnerable to interference as indicated by increased false alarm responses, a function of inhibitory control mediated by the frontal lobes. Our findings are also consistent with previous studies that suggested that the memory impairment in individuals with ASD would be more severe when the memory tasks are mentally effortful or when the information is meaningful or in vast amount (Cheung et al., 2010; Minshew & Goldstein, 1993, 1998, 2001; Minshew et al., 1997; Toichi & Kamio, 2002, 2003; Williams et al., 2006). In our study, children with ASD performed comparably to normal children on the relatively simple tasks of Digit Span and Rey-O, which required simple sustained attention and working memory. But in more complex tasks requiring multiple executive functions, such as learning and recall in HKLLT and OR, these children showed impaired performance and produced more false alarms than normal children.

In terms of EEG measurements, our findings showed that children with ASD had significantly elevated coherence, particularly on the left hemisphere, during performance of memory tasks. This finding is supported by some neuroimaging and neuropsychological studies reporting greater abnormality found in the left side of the brain and behavioral manifestation similar to patients with left hemisphere disorders. Our finding that children with ASD demonstrated elevated coherence at long-range connections in the inter-hemispheric anterior–posterior regions also provided converging evidence in support of the contribution of the anterior–posterior brain circuit in memory processing in EEG studies (Rippon et al., 2007; Sauseng et al., 2005; Weiss et al., 2000). This notion was also supported by neuroimaging findings that reported left and right prefrontal cortex activation during encoding and retrieval of verbalized matter together with increased activation in the bilateral inferior parietal cortex (Klingberg & Roland, 1998). These researchers also found that the prefrontal activation appeared only in effortful retrieval but not in tasks with near-perfect performance. This may explain why normal children who scored high on OR in our study demonstrated substantially lower coherence in frontal regions than ASD children. Further evidence was provided by Rugg et al. (2002) reporting the involvement of the prefrontal-parietal loop in effective memory encoding and retrieval.

Apart from showing that children with ASD were impaired in memory performance and exhibited abnormal EEG coherence in long-range anterior–posterior connections, the present study has extended previous knowledge in demonstrating an association between memory impairment and abnormal EEG coherence in children with ASD. We found a strong negative association between coherence and memory performance in children with ASD, where the higher the anterior–posterior coherence, the poorer the memory performance. This is consistent with previous findings on adults with ASD, where DTI studies show reduced myelin integrity in the prefrontal and temporoparietal junctions (Barnea-Goraly et al., 2004; Lewis & Elman, 2008); and fMRI studies show reduced synchronization in brain regions under working memory tasks conditions (Koshino et al., 2008; Luna et al., 2002; Silk et al., 2006). However, this is in contrast to a previous coherence study on normal individuals (Sauseng et al., 2005) which found a positive linear association between coherence and memory functioning. This inconsistent finding might reflect differences in the neural-bases underlying memory processing in normal individuals and patients with ASD. Alternatively, our findings may also suggest that coherence substantially exceeding an optimal level might overwhelm the cortical synchronicity and interrupt the efficiency of memory processing, such that the hyper-coherence in children with ASD in our study manifested impaired memory performance. Viewed from this perspective, our finding seems to suggest that the association between memory functioning and anterior–posterior coherence may form of an inverted U-shaped curve with an optimal coherence level, under or above which would result in non-optimal memory functioning. However, further studies are needed to verify this speculation, especially studies on other patient populations with memory problems related to the frontal lobes.

While findings in the present study have shed new light on the association between neuropsychological performance and neurophysiological activities in children with ASD, the following limitations should be noted. First, the use of only a visual encoding task in eliciting coherence data may pose another limitation. Considering the greater right-lateralized coherence in normal children during visual encoding while children with ASD showed more bilateral involvement, it would be informative to also examine whether, if coherence data when performing a verbal memory task were also collected, there would be a leftward shift of coherence in normal children and whether the bilateral hyper-coherence would still be seen in children with ASD. Second, the generalization of the findings to the entire patient population with ASD may be limited due to the relatively small sample size which also posed a constraint on the balance between Type I and Type II errors, and the over-representation of high-functioning children with ASD. Future studies recruiting a larger sample, with a broader age range, and including lower-functioning individuals with ASD would help extend current knowledge to a wider population. Finally, the present study recruited Chinese children with ASD. It would be interesting to conduct cross-cultural studies to investigate whether there are any cultural differences in memory functioning in individuals with ASD.

Acknowledgements

This research was supported by the research grant CUHK 440407 from the Hong Kong Research Grants Council. We thank the Parents' Association of Pre-School Handicapped Children in Hong Kong for their assistance in recruiting participants. The authors would like to thank all the parents and children who participated in this study. Special thanks are due to Ms. Pinky Ho and Ms. Siu-won Kwok for their assistance in recruiting subjects; and to Ms. Debbie Yan and Maggie Ng, for their assistance in data collection.

References

Alexander, M. P., Stuss, D. T., & Fansabedian, N. (2003). California Verbal Learning Test: Performance by patients with focal frontal and non-frontal lesions. *Brain, 126*, 1493–1503.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.

Baldo, J. V., & Shimamura, A. P. (2002). Frontal lobes and memory. In A. Baddeley, B. Wilson, & M. Kopelman (Eds.), *Handbook of memory disorders* (2nd ed., pp. 363–379). London: John Wiley & Co.

Barnea-Goraly, N., Kwon, H., Menon, V., Eliez, S., Lotspeich, L., & Reiss, A. L. (2004). White matter structure in autism: Preliminary evidence from diffusion tensor imaging. *Biological Psychiatry, 55*, 323–326.

Bernstein, J. H., & Waber, D. P. (1996). *Developmental scoring system for the Rey-Osterrieth complex figure*. Odessa, FL: Psychological Assessment Resources.

Brown, L., Sherbenou, R. J., & Johnsen, S. K. (1992). *Test of Nonverbal Intelligence: A language-free measure of cognitive ability* (3rd ed.). Austin, TX: PRO-ED.

Buckner, R. L., Kelley, W. M., & Petersen, S. E. (1999). Frontal cortex contributes to human memory formation. *Nature Neuroscience, 2*, 311–314.

Chan, A. S. (2006). *Hong Kong List Learning Test* (2nd ed.). Hong Kong: Department of Psychology and Clinical Psychology Centre, The Chinese University of Hong Kong.

Chan, A. S., & Kwok, I. (1999). *Hong Kong List Learning Test: Manual and Preliminary Norm*. Hong Kong: Department of Psychology, The Chinese University of Hong Kong.

Cheung, M.-c., Chan, A. S., Sze, S. L., Leung, W. W., & To, C. Y. (2010). Verbal memory deficits in relation to organization strategy in high and low-functioning autistic children. *Research in Autism Spectrum Disorders*. doi:10.1016/j.rasd.2010.02.004.

Cornoldi, C., & Mammerella, N. (2006). Intrusion errors in visuospatial working memory performance. *Memory, 14*, 176–188.

Demb, J. B., Desmond, J. E., Wagner, A. D., Vaidya, C. J., Glover, G. H., & Gabrieli, J. D. E. (1995). Semantic encoding and retrieval in the left inferior prefrontal cortex: A functional MRI study of task difficulty and process specificity. *The Journal of Neuroscience, 15*, 5870–5878.

Doppelmayr, M., Klimesch, W., Schwaiger, J., Stadler, W., & Rohm, D. (2000). The time locked theta response reflects interindividual differences in human memory performance. *Neuroscience Letters, 278*, 141–144.

Fletcher, P. C., & Henson, N. A. (2001). Frontal lobes and human memory: Insights from functional neuroimaging. *Brain, 124*, 849–881.

Fletcher, P. C., Shallice, T., & Dolan, R. J. (1998). The functional roles of prefrontal cortex in episodic memory: Encoding. *Brain, 121*, 1239–1248.

Hong Kong Education Department, & Hong Kong Psychological Society. (1981). *The Hong Kong Wechsler Intelligence Scale for Children*. Hong Kong: Government Printer. (in Chinese).

Jasper, H. H. (1958). The 10–20 Electrode System of the International Federation. *Electroencephalography and Clinical Neurophysiology, 10*, 371–375.

John, E. R., Prichep, L. S., Fridman, J., & Easton, P. (1988). Neurometrics: Computer-assisted differential diagnosis of brain dysfunctions. *Science, 239*, 162–169.

Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research Reviews, 29*, 169–195.

Klingberg, T., & Roland, P. E. (1998). Right prefrontal activation during encoding, but not during retrieval, in a non-verbal paired-associates task. *Cerebral Cortex, 8*, 73–79.

Koshino, H., Kana, R. K., Keller, T. A., Cherkassky, V. L., Minshew, N. J., & Just, M. A. (2008). fMRI investigation of working memory for faces in autism: Visual coding and underconnectivity with frontal areas. *Cerbal Cortex, 18*, 289–300.

Lewis, J. D., & Elman, J. L. (2008). Growth-related neural reorganization and the autism phenotype: A test of the hypothesis that altered brain growth leads to altered connectivity. *Developmental Science, 11*, 135–155.

Luna, B., Minshew, N. J., Garver, K. E., Lazar, N. A., Thulborn, K. R., Eddy, W. F., et al. (2002). Neocortical system abnormalities in autism: An fMRI study of spatial working memory. *Neurology, 59*, 834–840.

McEvoy, L. K., Pellouchoud, E., Smith, M. E., & Gevins, A. (2001). Neurophysiological signals of working memory in normal aging. *Cognitive Brain Research, 11*, 363–376.

Minshew, N. J., & Goldstein, G. (1993). Is autism and amnesic disorder? Evidence from the California Verbal Learning Test. *Neuropsychology, 7*, 209–216.

Minshew, N. J., & Goldstein, G. (1998). Autism as a disorder of complex information processing. *Mental Retardation and Developmental Disabilities Research Reviews, 4*, 129–136.

Minshew, N. J., & Goldstein, G. (2001). The pattern of intact and impaired memory functions in autism. *Journal of Child Psychology and Psychiatry, 42*, 1095–1101.

Minshew, N. J., Goldstein, G., & Siegel, D. J. (1997). Neuropsychologic functioning in autism: Profile of a complex information processing disorder. *Journal of the International Neuropsychological Society, 3*, 303–316.

Mottron, L., Belleville, S., Stip, E., & Morasse, K. (1998). Atypical memory performance in an autistic savant. *Memory, 6*, 593–607.

Murias, M., Webb, S. J., Greenson, J., & Dawson, G. (2007). Resting state cortical connectivity reflected in EEG coherence in individuals with autism. *Biological Psychiatry, 62*, 270–273.

Nunez, P. L., & Srinivasan, R. (2006). Measures of EEG dynamic properties. In P. L. Nunez & R. Srinivasan (Eds.), *Electric fields of the brain: The neurophysics of EEG* (2nd ed., pp. 353–401). New York: Oxford University Press.

Nyberg, L., Marklund, P., Persson, J., Cabeza, R., Forkstam, C., Petersson, K. M., et al. (2003). Common prefrontal activations during working memory, episodic memory, and semantic memory. *Neuropsychologia, 41*, 371–377.

O'Connor, N., & Hermelin, B. (1989). The memory structure of autistic idiot-savant mnemonists. *British Journal of Psychology, 80*, 97–111.

Oliveri, M., Turriziani, P., Carlesimo, G. A., Koch, G., Tomaiuolo, F., Panella, M., et al. (2001). Parieto-frontal interactions in visual-object and visual-spatial working memory: Evidence from transcranial magnetic stimulation. *Cerebral Cortex, 11*, 606–618.

Osaka, N., Osaka, M., Kondo, H., Morishita, M., Fukuyama, H., & Shibasaki, H. (2004). The neural basis of executive function in working memory: An fMRI study based on individual differences. *NeuroImage, 21*, 623–631.

Rippon, G., Brock, J., Brown, C., & Boucher, J. (2007). Disordered connectivity in the autistic brain: Challenges for the "new psychophysiology". *International Journal of Psychophysiology, 63*, 164–172.

Rossion, B., & Pourtois, G. (2004). Revisiting Snodgrass and Vanderwart's object pictorial set: The role of surface detail in basic-level object recognition. *Perception, 33*, 217–236.

Rugg, M. D., Otten, L. J., & Henson, R. N. A. (2002). The neural basis of episodic memory: evidence from functional neuroimaging. *Philosophical Transactions of the Royal Society of London. Series B, Biological sciences, 357*, 1097–1110.

Sarnthein, J., Petsche, H., Rappelsberger, P., Shaw, G. L., & von Stein, A. (1998). Synchronization between prefrontal and posterior association cortex during human working memory. *Proceedings of the National Academy of Sciences of the United States of America, 95*, 7092–7096.

Sauseng, P., Klimesch, W., Schabus, M., & Doppelmayr, M. (2005). Fronto-partietal EEG coherence in theta and upper alpha reflect central executive functions of working memory. *International Journal of Psychophysiology, 57*, 97–103.

Schopler, E., Reichler, R. J., & Renner, B. R. (1986). *The Childhood Autism Rating Scale (CARS)*. New York: Irvington.

Silk, T. J., Rinehar, N., Bradshaw, J. L., Tonge, B., Egan, G., O'Boyle, M. W., et al. (2006). Visuospatial processing and the function of prefrontal-parietal networks in autism spectrum disorders: A functional MRI study. *The American Journal of Psychiatry, 163*, 1440–1443.

Snodgrass, J. G., & Vanderwart, M. (1980). A standardized set of 260 pictures: Norm for name agreement, image agreement, familiarity, and visual complexity. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 6*, 174–215.

Sowell, E. R., Thompson, P. M., Holmes, C. J., Jernigan, T. L., & Toga, A. W. (1999). In vivo evidence for post-adolescent brain maturation in frontal and striatal regions. *Nature Neuroscience, 2*, 859–861.

Srinivasan, R., Nunez, P. L., & Silberstein, R. B. (1998). Spatial filtering and neocortical dynamics: Estimates of EEG coherence. *IEEE Transactions on Biomedical Engineering, 45*, 814–826.

Toichi, M., & Kamio, Y. (2002). Long-term memory and levels-of-processing in autism. *Neuropsychologia, 40*, 964–969.

Toichi, M., & Kamio, Y. (2003). Long-term memory in high-functioning autism: Controversy on episodic memory in autism reconsidered. *Journal of Autism and Developmental Disorders, 33*, 151–161.

Volf, N. V., & Razumnikova, M. (1999). Sex differences in EEG coherence during a verbal memory task in normal adults. *International Journal of Psychophysiology, 34*, 113–122.

Weiss, S., & Rappelsberger, P. (2000). Long-range EEG synchronization during word encoding correlates with successful memory performance. *Cognitive Brain Research, 9*, 299–312.

Weiss, S., Müller, H. M., & Rappelsberger, P. (2000). Theta synchronization predicts efficient memory encoding of concrete and abstract nouns. *Cognitive Neuroscience, 11*, 2357–2361.

Williams, D. L., Goldstein, G., & Minshew, N. J. (2006). The profile of memory function in children with autism. *Neuropsychology, 20*, 21–29.