

Running Title: Executive Dysfunction in ASD

Disordered Cortical Connectivity Underlies the Executive Function Deficits in
Children with Autism Spectrum Disorders

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ABSTRACT

The present study examined the executive function and cortical connectivity of children with autism spectrum disorders (ASD) and investigated whether the executive function deficits exhibited by these children were differentially affected and associated with the cortical connectivity. The present study compared high-functioning (HFA) and low-functioning (LFA) children with typically developing children (TDC) on their executive functions as measured by the Hong Kong List Learning Test, D2 Test of Concentration, Five Point Test, Children's Color Trail Test, Tower of California Test, and Go/No-Go task and neural connectivity as measured by theta coherence in the distributed fronto-parietal network. Thirty-eight children with ASD (19 HFA and 19 LFA) and 28 TDC children, aged 8 to 17 years, participated voluntarily in the study. The results on executive function showed that the LFA group demonstrated the poorest performance as exhibited by their Executive Composite and individual executive function scores, while the TDC group exhibited the highest. These results have extended the findings of previous studies in demonstrating that HFA and LFA children have significant differences in their degree of executive function deficits. The results on neural connectivity also showed that children with ASD demonstrated a different pattern of electroencephalography (EEG) coherence from TDC children, as demonstrated by the significantly elevated theta coherence in the fronto-parietal network, and that the severity of executive dysfunction between high- and low-functioning children with ASD was found to be associated with the disordered neural connectivity in these children.

What this paper adds?

The present findings have shed light on the neurophysiological underpinnings of the cognitive impairments and behavioral symptoms associated with autism, which will be invaluable for future research into the early identification, assessment, and design of teaching and remedial interventions for young children with autism.

Keywords: EEG coherence; theta; executive dysfunction; autism; children

1. Introduction

Autistic spectrum disorders (ASD) consist of a spectrum of neurodevelopmental disorders that are characterized by disturbances in communication, poor social skills, and restricted/stereotyped behaviors or interests (American Psychiatric Association, 2002). The prevalence of ASD is high, with recent statistics reported by the Centers for Disease Control and Prevention (CDC) at one in 68, making ASD one of the most prevalent childhood developmental disorders. Variability in the degree of language impairment, intellectual ability, and symptom severity was found among individuals with ASD, ranging from severe intellectual disability to isolated cognitive problems, such as stereotypic behavior and difficulty in understanding others feelings (Baron-Cohen, S. 2001; Dennis et al., 1999; Happe, 1999). High-functioning autism is at one end of the ASD spectrum, with less severe signs and symptoms than other forms of autism. Although these children have average intelligence, school and daily activities can still be challenges of great magnitude. One reason for this is that these children may still show many of the key characteristics of the disorder. They often appear rigid and inflexible, show a strong liking for repetitive behavior and elaborate rituals, and have great difficulty understanding abstract uses of language, such as humor. Particularly detrimental are the presence of restricted and repetitive stereotypic behaviors and uncontrollable temper outbursts over trivial changes in the environment. Although the exact cognitive profile and underlying basis of cognitive processing in autism is not well understood, it has been suggested that fundamental to these cognitive and behavioral problems is a deficiency in executive function (Gilotty, Kenworthy, Sirian, Black, & Wagner, 2002; Ozonoff, 1997).

Executive functions refer to a broadly defined cognitive domain that includes a multidimensional set of abilities required to perform complex behaviors for the attainment of a future goal (Donders, 2002; Nyden, Gillber, Hjelmquist, Heiman, 1999) and are thought to be involved in cognitive processes, such as planning, organization, self-monitoring, cognitive flexibility, and the inhibition of inappropriate actions (Ozonoff et al., 2004). Individuals with ASD have been found to exhibit executive dysfunctions, including disorganized actions and strategies typified by decreased initiative, perseveration, difficulties in forming novel concepts, and the lack of inhibition of inappropriate actions (Bennetto, Pennington

& Rogers, 1996; Ozonoff & Jensen, 1999). Neuropsychological studies of executive functions in autism have been inconclusive, however, with some reporting deficits in planning and cognitive flexibility, but not inhibition (Ozonoff & Jensen, 1999), while others have suggested difficulties in response inhibitory control and slow information processing (Schmitz et al., 2006). Some researchers have posited that individuals with ASD may have distinct primary deficits that underlie their executive dysfunctions and have suggested that one of the factors affecting the different cognitive domains of executive functioning in autism is the deficient ability to integrate information across contexts (Klinger, Klinger, & Pohlig, 2000). Specifically, individuals with autism have difficulty learning the relationships between different parts of stimuli, as well as perceiving relationships across multiple experiences, and they tend to compensate for the deficient executive function by memorizing visual details or individual rules from each situation that they encounter (Klinger et al., 2000; Ozonoff et al., 2004). This impaired ability to attend to and integrate information from the environment may explain the reason why children with autism tend to follow routines in precise detail and show great distress over trivial changes in the environment.

Although the exact cognitive profile and the underlying basis of executive dysfunction are uncertain, results from previous studies that reported structural, physiologic, and functional abnormalities in the frontal region of individuals with ASD (Harrison, Demaree, Shenal, & Everhart, 1998; Mundy, 2003; Ozonoff et al., 2004; Rumsey & Ernst, 2000) have widely suggested that the frontal cortex is one of the major brain regions implicated in the cognitive impairments and repetitive stereotypic behaviors commonly observed in the disorder (Schroeter, Zysset, Wahl, & von Cramon, 2004). For example, results from neurobiological studies have revealed abnormal neurobiological processes in the frontal lobes that underlie the cognitive deficits in ASD (Mundy, 2003; Ozonoff et al., 2004; Schmitz et al., 2006). Functional imaging studies have also found altered patterns of activation and glucose metabolism in various areas of the frontal lobes in individuals with ASD during neuropsychological tasks of executive function (Hazlett, et al., 2004; Harmony, Alba, Marroquin, & Gonzalez-Frankenberger, 2009; Schmitz, et al., 2006). In addition to the frontal lobe, increasing evidence also shows that effective executive functioning involves the integrated action of multiple brain areas of the fronto-parietal network (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-associated tasks (Klingberg, & Roland, 1998). Given that executive function relies on the frontal cortex and its distributed network to the parietal regions (Babiloni et al., 2004; Osaka et al., 2004), it has been postulated that abnormalities in this neural connectivity may account for the unusual cognitive processing and resultant behavioral symptoms of ASD (Fletcher & Henson, 2001; Rippon, Brock, Brown, & Boucher, 2007). Indeed, diffusion tensor imaging (DTI) studies of cortical connectivity have shown reduced myelin integrity in the ventromedial prefrontal cortex and at the temporo-parietal junctions in individuals with ASD (Barnea-Goraly et al., 2004; Lewis & Elman, 2008). In addition, evidence for disordered neural connectivity in ASD was also found in functional MRI studies that demonstrated that the inhibitory deficit in ASD is associated with decreased synchronization between activated brain areas in the inhibition networks in these individuals (Kana, Keller, Minshew, & Just, 2007). Similarly, electrophysiological studies in children with ASD using coherence, a quantitative electroencephalography (EEG) that measures the level of synchrony or cortical connectivity between brain areas in response to cognitive processes (Coben, Clarke, Hudspeth, & Barry, 2008; Rippon et al., 2007; Thatcher, North, & Biver, 2005), have also provided evidence to suggest disordered connectivity across neural systems in these children (Just, Cherkassky, Keller, & Minshew, 2004; Castelli, Frith, Happe, & Frith, 2002; Luna et al., 2002). Based on the documented executive dysfunctions and the reported neural connectivity in ASD, it is probable that executive function deficits in ASD maybe the result of poor orchestration of the fronto-parietal network due to aberrant connectivity that interrupts efficient cognitive processing.

Coherence analysis of the EEG is a useful indicator of cortical connectivity among functional areas in the brain (Barry, Ckarke, McCarthy, & Selikowitz, 2007; Weiss, & Mueller, 2003). EEG coherence is a measure of phase correlation that describes levels of synchronization between neuronal assemblies in terms of the linearity of the relationship between two EEG signals measured at different sites of the scalp and reflects the degree of functional connectivity between neuronal

substrates (Nunez, & Srinivasan, 2006). The examination of the temporal synchronization of neuronal activities during cognitive tasks through the calculation of the coherence between two EEG signals can provide useful information about underlying cortical coupling and connectivity between distinct regions of the brain (Weiss, & Mueller, 2003). For example, greater theta (4–7.5 Hz) coherence was found in the frontal lobe, as well as between the anterior and posterior brain regions, during executive function tasks, including visual planning (Petsche, & Etlinger, 1998), attentional and inhibitory processing (Barry et al., 2007; Harmony et al., 2009) and memory (Chan et al., 2011). Higher theta coherence than that for typical control individuals was also found between the frontal and temporal regions during resting conditions in patients known to have executive dysfunctions (Babiloni et al., 2004; Ford, Mathalon, Whitfield, Faustman, & Roth, 2002) and in high-functioning children with autism (Murias, Webb, Greenson, & Dawson, 2007).

Drawing together the different pieces of evidence linking autism with executive dysfunction and disordered neural connectivity and the fact that cognitive processing is differentially affected in low- and high-functioning individuals with ASD (Cheung, Chan, Sze, Leung, & To, 2010; Dennis et al., 1999), it is reasonable to assume that low-functioning individuals with ASD would have more severe impairments in executive functioning and abnormalities in the neural connectivity of the fronto-parietal network than their high-functioning counterparts. To test this hypothesis, the present study investigated executive functioning and its association to neural connectivity in high- and low-functioning children with ASD and compared them with typically developing children. It was anticipated that (1) high-functioning children with ASD would demonstrate significantly poorer performance than normal children in the different measures of executive functioning, whereas low-functioning children with ASD would show similar deficits in the different executive functions, but to a more severe degree than the high-functioning group; and (2) children with ASD would demonstrate abnormal neural connectivity, as measured by EEG theta coherence in the frontal cortex and its network to the parietal regions of the brain, and the low-functioning group would show greater abnormalities in cortical connectivity than their high-functioning counterparts. Given that theta coherence is critically involved in central executive processes, we also hypothesized that (3) executive function

deficits would be associated with abnormal cortical connectivity, as indexed by theta coherence of the fronto-parietal network, in children with ASD.

2. Methods

2.1. Participants

Forty-eight children with ASD and 30 children with typical development (TDC), aged 8 to 17 years, participated voluntarily in the study. The children with ASD were recruited from the Parents' Association of Pre-School Handicapped Children in Hong Kong or the subject pool of the Neuropsychology Laboratory of The Chinese University of Hong Kong. All children with ASD were diagnosed by pediatricians of the Child Assessment Centres of the Department of Health in Hong Kong based on the criteria in the *Diagnostic and Statistical Manual of Mental Disorders* (4th edition, text revision) (DSM-IV-TR; American Psychiatric Association, 2002) or the Autism Diagnostic Observation Schedule (ADOS) (Lord, Rutter, DiLavore, & Risi, 2002). The diagnosis was later confirmed by a clinical psychologist based on the information collected through a standard clinical interview using the DSM-5 (American Psychiatric Association, 2013) and the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & LeCouteur, 1994). According to the DSM-5 criteria, all of them met the diagnostic criteria of ASD. The TDC children were recruited from local primary schools by sending invitation letters / emails and telephone call to school principals / teachers.

Two children from each group withdrew from the study due to personal reasons. The parents or caregivers of all participated children were interviewed based on a standard interview protocol which covered the aspects of developmental milestones and medical history of the child. Based on the information collected through the interview, 19 high-functioning and 19 low-functioning children with ASD, and 28 children with TDC were selected for analyses. All children included in the analyses for the present study were medication-free and without histories of neurological / psychological problems or abnormal developmental milestones. As many of the neuropsychological measures used in the present study were paper-and-pencil tasks that require adequate motor skills, all children recruited were without physical disabilities or reported motor dysfunction.

Table 1 shows the demographic characteristics of the children. The three groups were matched on age [$F(2, 63) = .25, p > .05$] and had a similar gender

distribution [$\chi^2 = 5.20, p > .05$]. Among the children with ASD, those having a general intelligence quotient (IQ) of 70 and above were classified as high-functioning (HFA), while those with an IQ below 70 were classified as low-functioning (LFA). While the HFA group was matched with the TDC group on IQ ($t(45) = .85, p > .05$), the LFA group had significantly poorer IQ [$t(36) = 9.54, p < .001$], ranging from borderline to mild-grade intellectual disability. No significant difference was found in the severity of autistic features between the HFA and LFA groups as indicated by the ADI-R (Lord et al., 1994) scores on Social Interaction ($t = .00, p > .05$), Communication ($t = .29, p > .05$), and Repetitive/Stereotyped Behavior ($t = -1.01, p > .05$).

2.2. Procedure

All children participated with informed parental consent. The participants were also asked for their verbal assent to take part in the study. Figure 1 presents the flow of selection process of the participants. Forty-eight children with ASD and 30 typically developing children participated voluntarily in the study. All children were assessed individually in a neuropsychological assessment session and an EEG recording session. The sequence of the neuropsychological assessment and EEG recording for the children was counterbalanced to avoid an order effect. The entire assessment session took approximately 2 hours, with a 10-minute break between the neuropsychological assessment and the EEG recording sessions. During the assessment session, the parent/caregiver accompanying the child was interviewed based on a standard interview protocol and the ADI-R. All assessments and interview were administered by well-trained research assistants. Children who did not meet the inclusion criteria, had positive history of neurological or other psychiatric disorders or were on any medication were excluded for subsequent analyses. In the neuropsychological assessment, a neuropsychological battery consisting of the Wechsler Intelligence Scale for Children-Third Edition, short form (WISC-III short form; Kaufman, Kaufman, Balgopal, & McLean, 1996), and executive functioning tasks, including the Hong Kong List Learning Test (HKLLT 2nd ed.; Chan, 2006), D2 Test of Concentration (D2; Brickenkamp, 1981), Five Point Test (5-point; Regard, Strauss, & Knapp, 1982), Children's Color Trails Test (CCTT; Williams et al., 1995), and Tower of California Test (ToC; Mattson, Goodman, Caine, Delis, & Riley, 1999), was administered to each participant

individually. These tasks were carefully chosen to provide effective measures on the different cognitive domains of executive function, including, memory, attention, cognitive flexibility, inhibitory control, generativity, planning and organization, in children with ASD. For non-verbal children for whom the WISC-III short form could not be used, the Stanford-Binet Intelligence Scale – Fourth Edition (SB-FE) (Thorndike, Hagen, & Sattler, 1986) was administered. The IQ scores obtained from the two intelligence tests were used as a means to classify children with ASD into high-functioning (i.e., $IQ \geq 70$) or low-functioning (i.e., $IQ < 70$) subgroups. In the EEG recording session, five minutes of continuous EEG signals in the eye-open resting condition were recorded by trained research assistants in a sound-attenuated room that allowed for clean EEG acquisition. The experimental procedure was approved by the NTEC-CUHK Clinical Research Ethics Committee and the HKIED Human Research Ethics Committee.

2.3. Measures

2.3.1. Wechsler Intelligence Scale for Children-Third Edition (WISC-III) Short Form. The WISC-III short form (Kaufman et al., 1996) was used in the study to assess general intelligence. The test comprises the two verbal subtests of Similarities and Arithmetic and the two performance subtests of Picture-Completion and Block Design from the original WISC-III. The short form yields an IQ score with a mean of 100 and a standard deviation of 15.

2.3.2. Stanford-Binet Intelligence Scale – Fourth Edition (SB-FE). The SB-FE (Thorndike et al., 1986) assesses verbal reasoning, abstract/visual reasoning, quantitative reasoning, and short-term memory and yields an IQ score with a mean of 100 and a standard deviation of 16.

2.3.3. Hong Kong List Learning Test (HKLLT). The HKLLT (2nd ed.; Chan, 2006) is primarily a memory test that also measures the frontal lobe functions of learning strategies and organization (Cheung et al., 2010). The test consists of a randomly organized list of 16 two-word Chinese characters presented once during each of three learning trials. Children in the present study 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, which reflects the ability to acquire new verbal information that is associated with frontal lobe function. A recognition test consisting of the 16 target words and 16 distracters was

presented after a 30-minute delayed recall trial. The children were required to discriminate whether the words had been previously presented. A discrimination score that assessed memory retrieval ability 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. Higher total learning and discrimination scores indicate better frontal-lobe related memory function.

2.3.4. D2 Test of Concentration (D2). This test (Brickenkamp, 1981) measures inhibition, concentration and error judgment, which are representative features of executive function. It is a letter cancellation task printed on a piece of paper with different letters with a different number of dashes above and below the letters. The children were asked to cancel all letter d's with 2 dashes. There were a total of 14 lines, and for each line, the time allowed was 20 seconds. The number of omissions and wrong cancellations were recorded to give performances on inhibition, concentration and error judgment. Lower rate of omissions indicates better inhibitory control.

2.3.5. Five Point Test (5-point). This test (Regard et al., 1982) measures figural fluency in terms of the production of novel designs under time constraints. It provides implication on the ability of generativity and cognitive flexibility. Children in the present study were asked to create as many original shapes by connecting five points with straight lines within five minutes. This test is a non-verbal analog to verbal fluency tasks and was used in the present study because it is a good measure of frontal lobe pathology. Higher number of novel designs generated indicates better cognitive flexibility.

2.3.6. Children's Color Trail Test (CCTT). The CCTT (Williams et al., 1995) is an altered version of the Trail Making Test in the Halstead-Reitan Battery (Reitan & Wolfson, 1993). It is specifically designed to be a culture-free test for children. The second trial of the test measures the frontal lobe functions, including speed of attention and mental flexibility. This is a paper-based test, with duplicates of each number from 1 to 15 embedded within pink and yellow circles. The children were required to connect the circles in ascending order, alternating between pink and yellow colors, as quickly as possible. The completion time in seconds for the second trial was recorded, where shorter duration indicates better attention and cognitive flexibility.

2.3.7. The Tower of California Test (ToC). The ToC (Mattson et al., 1999) is a

modification of the Tower of Hanoi (Borys, Spitz, & Dorans, 1982) and Tower of London (Morris, Ahmed, Syed, & Toone, 1993; Shallice, 1982) tests and was administered in the present study to assess spatial planning, inhibitory control and cognitive flexibility (Delis, Kaplan, & Kramer, 2001). It consists of nine items that involve moving discs on three colored, vertical pegs to match a target arrangement while adhering to the rules. The score was calculated as the number of items successfully completed, where higher score indicates better planning, inhibitory control and flexibility.

2.3.8. Go/No-Go Task. This is a computerized task that measured impulse control in the present study (Kana et al., 2007). Children were required to press a key as quickly as possible when a black ball (Go stimulus) appeared on the computer screen and to inhibit their responses when a red ball (No-Go stimulus) appeared. The total testing time was 6 minutes, and the stimuli were displayed one at a time in the center of the computer screen for 500 ms in random order at a ratio of 4:1 (192 black balls: 48 red balls), followed by 1000 ms of blank intervals. The total commission errors on “No-Go” trials measured inhibition. Lower commission errors indicate better inhibitory control.

2.4. EEG

2.4.1. 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 referenced to linked ears, was used to collect EEG data at a sampling rate of 256 Hz with a low pass filter of 40 Hz and high pass filter of 1 Hz. Impedance at each electrode site was kept below 10 k Ω . A resting EEG was collected in the eyes-open condition for 5 minutes. The children were asked to focus on a figure (e.g., a car) displayed on a computer screen, and body movements were time-marked by a research assistant for off-line analyses. The EEG data were stored and later displayed on a computer for selection and analysis. Artifact-free EEG data were selected based on both computer selection (reject levels were set at ± 150 μ V) and visual examination for eye movements and muscle artifacts using the NeuroGuide (version 2.1.8) software program. A minimum of one minute of artifact-free data were selected (John et al., 1988 for discussion of the qEEG method), and 2-sec epochs selected from the continuous live trace were spectrally

processed to the different frequency domains using the fast Fourier Transformation (FFT) to compute coherence values. Theta coherence measures (4 – 7.5 Hz) were used in the present study.

2.4.2. EEG Coherence Measures. Theta coherence (4–7.5 Hz), an index that measures temporal synchronization of EEG activity between two brain regions underneath the electrodes and reflects the functional connectivity between the two regions, were computed from EEG signals collected from the 19 electrode positions (Fp1, Fp2, F3, F4, F7, F8, Fz, T3, T4, T5, T6, C3, C4, Cz, P3, P4, Pz, O1, and O2). Based on Sauseng's (2005) paradigm on central executive processes, two short-range coherence measures of the anterior and posterior cortical regions were computed to dissociate from the long-range fronto-parietal cortical connection. The short-range coherence measure of the anterior network was computed by averaging the signals from the electrode sites FP1, FP2, F3, Fz and F4, and the short-range coherence measure of the posterior network was computed by averaging the signals from electrode sites P3, Pz, P4, O1 and O2. Long-range coherence was defined as any electrode pairs that were separated by at least one electrode in between, and the long-range coherence measure to examine the fronto-parietal network was computed by averaging the signals from electrode sites F3, Fz, F4, P3, Pz and P4. Each coherence value was transformed using Fisher's Z-transform.

2.5. Data Analysis

Executive functioning of TDC and the HFA and LFA children were compared and examined for differences. To reduce the number of statistical comparisons, one Executive Composite score was computed from the seven individual measures of executive function, including the HKLLT, D2, 5-Point, CCTT, ToC and Go/NoGo tasks. The raw scores on the different executive function measures were converted to Z scores, using the grand mean and standard deviation of the executive measures derived from the normative data. The Z scores from the different executive function measures were then averaged to yield the Executive Composite score. Higher scores indicated poorer executive functioning. The Executive Composite score and the seven scores from the individual executive functions of the HFA and LFA groups of children with ASD and TDC children were compared using an analysis of variance (ANOVA). Where significant group differences were found, *post hoc* comparisons were performed to identify the significant pairwise differences. The EEG theta coherence measures of the three groups were compared

on the two short-range (anterior, posterior) and one long-range (fronto-parietal) coherence measures also using a repeated-measures ANOVA, with *connection* (anterior, posterior, fronto-parietal) as within-subject and *group* (TDC, HFA, LFA) as between-subject factors, and post-hoc comparisons were made using *F*-tests. The relationship between executive functioning, EEG coherence and immune function were examined using Pearson's correlation. Given that specific hypotheses were tested and that the number of participants were relatively small, we did not adjust the alpha level to maintain a reasonable balance between the risks of Type I and Type II errors.

3. Results

3.1. Executive Functioning

The two groups of children with ASD were compared with TDC children on the Executive Composite score and the 7 scores from the HKLLT, D2, 5-point, CCTT, ToC and Go/No-Go using analysis of variance (ANOVA), followed by *post hoc t*-tests to examine pairwise differences. To control for inflated type 1 errors as a result of multiple *post hoc* comparisons, a Bonferroni correction, with the adjusted alpha level of $p=.007$, was employed. The results indicated that the three groups of children showed significantly different Executive Composite [$F(2, 63) = 47.91, p < .001$] scores, HKLLT Total Learning [$F(2, 63) = 45.15, p < .001$] and Discrimination [$F(2, 63) = 48.08, p < .001$] scores, as well as the D2 Concentration Performance [$F(2, 63) = 38.62, p < .001$] scores. The LFA group demonstrated the poorest performance, while the TDC group exhibited the highest (Table 2). It should be noted that the significantly lower scores on the HKLLT Discrimination and D2 Concentration Performance of both groups of children with ASD were largely related to their higher false alarm rates on the HKLLT [$F(2, 63) = 13.38, p < .001$] and commission errors [$F(2, 63) = 6.53, p = .003$] on the D2. While the HFA group ($M = 1.94, SD = 3.7$) showed a higher false alarm rate on the HKLLT ($M = 1.94, SD = 3.7$) and greater commission errors on D2 ($M = 13.78, SD = 24.93$) than the TDC group ($M = .25, SD = .44; M = 3.46, SD = 5.42$, respectively), the LFA group performed worst and exhibited a significantly higher false alarm rate ($M = 5.33, SD = 4.7$) and commission errors ($M = 107.46, SD = 269.43$) than both TC and HFA children. Increased commission errors and false alarm rates have been commonly observed in individuals with ASD, suggesting that they were more

vulnerable to interference generated from irrelevant information. In addition, it was found that the HFA group showed comparable performance to the TDC group on the 5-point Unique Design ($t = .28$, $p = .78$), CCTT-2 Time ($t = -1.82$, $p = .08$), and ToC Achievement ($t = 1.69$, $p = .10$) scores. Again, the LFA group performed significantly poorer than both the HFA and TDC groups on these tasks [F values ranging from 19.66 to 28.75, $p < .001$]. No significant difference, however, was found among the three groups of children on the Go/No-Go total commission errors [$F(2, 63) = 3.02$, $p = .06$], which might be due to the large variability within the HFA and LFA groups (Table 2).

3.2. EEG coherence measures

Maps showing the mean absolute and relative theta power are presented in Fig. 2. A visual examination showed that the theta power measures were higher across multiple electrode sites during eye-open resting in the children with ASD, in particular the LFA group, than in the TDC. Repeated-measures ANOVA results showed a significant *connection* (anterior, posterior, and fronto-parietal) by *group* (TDC, HFA, LFA) interaction effect [$F(4, 126) = 9.48$, $p < .001$] and demonstrated a significant between-group difference in theta coherence measures [$F(2, 63) = 12.49$, $p < .001$]. *Post hoc* tests (Fig. 3) indicated that no significant difference was found in the short-range anterior connection [$F(2, 63) = .67$, $p = 5.15$] between the TDC ($M = 1.18$, $SD = .11$), the HFA ($M = 1.17$, $SD = .09$), and LFA ($M = 1.21$, $SD = .12$) children during the eyes-open resting condition. Conversely, autistic children, regardless of functioning level, demonstrated significantly elevated theta coherence compared with TDC in the posterior [$F(2, 63) = 31.75$, $p < .001$] and long-range fronto-parietal [$F(2, 63) = 6.35$, $p = .003$] connections. *Post hoc* statistics also showed that the short-range coherence in the posterior region of the TDC group ($M = .92$, $SD = .10$) showed significantly lower theta coherence in the posterior region, but no significant difference was found between the HFA ($M = 1.12$, $SD = .10$) and LFA ($M = 1.12$, $SD = .09$) groups ($t = .29$, $p > .05$). In addition, it was indicated that the long-range fronto-parietal connection of the LFA group ($M = .70$, $SD = .11$) was significantly higher ($t = -2.69$, $p < .01$) than the HFA ($M = .63$, $SD = .09$) and the TDC ($M = .63$, $SD = .09$) ($t = -2.43$, $p < .01$) children; and that the HFA group, in turn, was significantly higher ($t = -2.17$, $p < .05$) than the TDC group ($M = .59$, $SD = .09$).

3.3. Association between Executive Function and EEG Coherence

To explore whether the executive function deficit of autistic children was related to neural connectivity, in particular the long-range fronto-parietal connection, we examined the relationship between executive function and the different coherence measures using Pearson's correlation (Table 3). The results showed that executive function was significantly associated with the EEG theta coherence. Specifically, the Executive Composite score was significantly correlated with the short-range coherence of the posterior region ($r = .38, p = .002$) and the long-range fronto-parietal coherence ($r = .36, p = .003$) in the combined TDC, HFA and LFA groups. Further ASD subgroup analysis has also shown that the executive composite score was significantly correlated with the long-range fronto-parietal coherence ($r = .32, p = .04$) in the autistic children, but no correlation was found in the short-range posterior coherence ($r = -.11, p = .53$). Furthermore, no significant association was found between the executive function and any of the coherence measures in the subgroup analysis of the TDC control group.

4. Discussion

The main purpose of the present study was to examine the executive dysfunctions of a group of high- and low-functioning children with ASD and determine whether the executive function deficits exhibited by these children were associated with disordered neural connectivity. The present study has extended the findings of previous studies on high-functioning children with ASD (Gilotty et al., 2002; Ozonoff, 1997) in demonstrating that high- and low-functioning children with ASD had significant differences in their degree of executive function deficits. The results on neural connectivity also showed that autistic children demonstrated a different pattern of neural connectivity, as indicated by the significantly elevated theta coherence in the fronto-parietal network, and that the executive dysfunctions differentially affected in the high- and low-functioning children with ASD were associated with the disordered neural connectivity in these children.

The present findings supported our hypothesis that executive functions are differentially affected among individuals with ASD, where low-functioning children performed significantly poorer than high-functioning children, as shown in their Executive Composite and individual executive function scores. These results are consistent with findings from a previous study, which reported that

individuals with ASD who have intellectual disability (low-functioning) showed significantly more developmental abnormalities than those with normal intelligence (high-functioning) (Burack & Volkmar, 1992). While the HFA children in our study performed comparably to normal children on the 5-point, CCTT, and ToC tests, both the HFA and LFA groups were relatively unimpaired in commission errors on the Go/No-Go task, suggesting that they performed within the normal range in cognitive functions, such as mental flexibility, planning and inhibition. These results are in line with some previous findings that children with frontal lobe damage performed relatively normally on some cognitive tests but showed disorganized strategies and actions when the cognitive tasks were mentally effortful or when the information was meaningful or in vast amount (Mangeot, Armstrong, Colvin, Yeates & Taylor, 2002; Ozonoff & Strayer, 2001).

As some researchers have noted, executive functions are a broadly defined cognitive domain involving the “on-line” coordination of a multidimensional set of abilities to perform complex behaviors (Denckla, 2002). It is possible that standardized neuropsychological assessments measuring very specific areas of cognitive processes may not be sensitive enough to detect executive dysfunctions in everyday activities that involve a combination of different executive functions (Donders, 2002). This may explain why children with ASD in the present study were relatively unimpaired in terms of simple commission errors on the Go/No-Go task, which was a continuous performance task but showed impaired performance in intrusion errors and false alarms on the HKLLT and D2, which were list learning and visual cancellation tasks involving complex and multiple executive functions (Stuss et al., 1994). These results support the notion that a comprehensive battery with multiple neuropsychological measures of the same construct, but with varying complexity, is necessary to delineate the specificity of executive dysfunctions in children with ASD (Welsh, Pennington, Ozonoff, Rouse, & McCabe, 1990).

In addition to the executive dysfunctions, the results from the EEG measurements also showed that the children with ASD in the present study had higher levels of theta coherence than typically developing children in the posterior area, and between the frontal and parietal regions of the brain. The increased theta coherence in the posterior region found in the autistic children is in line with findings from prior studies that suggested the abnormal modulation of increased activation of the posterior sensory cortical regions may underlie the often reported

overwhelming sensory overload and high anxiety level associated with autism (Frith, 2003). More interestingly, among the two groups of children with ASD, the results showed that the significantly elevated theta coherence in the fronto-parietal network was more pronounced in LFA children relative to their HFA counterparts. This finding is consistent with previous studies that reported greater increase of EEG coherence of the slow bands in patients with more severe cognitive impairments (Comi et al., 1998; Mann, Maier, Franke, Roschke, & Gansicke, 1997; Newton et al., 1994). Our findings that elevated long-range theta coherence in the fronto-parietal network was significantly associated with poorer executive functioning is in line with prior studies documenting the contribution of the distributed fronto-parietal network in the executive control of cognitive processing (Belmonte et al., 2004; Courchesne & Pierce, 2005; Rippon et al., 2007).

It is worth noting that our findings of increased fronto-parietal coherence in children with ASD are in contrast to previous studies, which demonstrated reduced long-range coherences that suggested a pattern of underconnectivity between different brain regions in individuals with ASD (Coben et al., 2008; Isler et al., 2010; Murias et al., 2007). It is possible that the discrepancy of the findings could be attributed to the different age cohorts participating in the different studies (e.g., 5.5 – 8.5 years old in Isler's study, 6-11 years old in Coben's study, 18-38 years old in Murias's study versus 8-17 years old in present study); different experimental tasks adopted (a light flashing task in Isler's study and an eyes-close resting condition in Coben's and Murias's study versus an eyes-open resting condition in present study); the region of interest targeted (occipital region in Isler's study versus fronto-parietal regions in present study); and the frequency band selected for analysis (long-range alpha coherence in Murias's study versus theta coherence in present study). Specifically, in Murias's study, adults with ASD showed a global reduction of the alpha coherence in the frontal networks while their theta coherence was enhanced in the frontal and temporal brain regions during resting condition. These results suggest that EEG coherence of the different frequency band can have opposite direction of coupling. Additionally, although it is true that higher coherence is usually indicative of increased neural connectivity (Nunez & Srinivasan, 2006), some have suggested that the higher theta coherence may in fact be associated with disordered connectivity of distributed neural networks (Chan et al., 2011). Our finding of the significant association between the

long-range theta coherence and executive performance in children with ASD, where the higher the fronto-parietal theta coherence, the poorer the executive performance, might reflect differences in the neural-bases underlying cognitive processes in children with ASD. During the eyes-open resting condition, EEG data were collected while the child was asked to focus on a figure of a car displayed on a computer screen. What appeared to be a simple task of sustained attention to the TDC group might have indeed been mentally effortful to the autistic children, who are known to have problems in attentional and inhibitory controls. Viewed from this perspective, our findings appear to suggest that rather than indicative of a pattern of overconnectivity, the increased coherence between brain areas in the children with ASD may in fact be a neural manifestation of widely aberrant connectivity (Noonan, Haist, & Muller, 2009) and a reflection of a constant effort (Monk et al., 2009) of these children to control their behaviors. This interpretation is in line with the previous neuroimaging and neuropsychological studies that reported increased task-free functional connectivity in individuals with ASD (Mizuno, Villalobos, Davies, Dahl, & Muller, 2006; Monk et al., 2009; Noonan et al., 2009; Shih et al., 2010).

In sum, the present findings extended those of previous studies in demonstrating that executive function deficits varied with the level of general intellectual functioning in children with ASD, where lower-functioning children showed more extensive executive function deficits and performed significantly poorer than their higher-functioning counterparts on different measures of executive functions. More interestingly, the difference in severity of executive dysfunction between high- and low-functioning children with ASD was found to be associated with the underlying neurophysiology in these children. While findings from the present study raised some interesting questions with respect to the relationship between executive dysfunction and disordered cortical connectivity in children with ASD, it should be noted that the study is limited in its generalization of the findings to individuals with ASD by the relatively small sample size, the large within-group variations in both executive function and EEG coherence measures, and the restricted age range. Further study is warranted to extend the application to individuals with ASD from a larger sample of autistic individuals stratified into different age groups or to other clinical populations in which executive dysfunction is a major symptom.

5. Conclusion

The present study examined whether the executive dysfunctions in children with ASD are associated with the disordered neural connectivity in these children. It was found that the children with autism performed significantly less well in executive functioning tasks than typically developing children, and that the deficient executive functions was differentially affected in the high- and low-functioning children with ASD. In addition, our findings support the model of disrupted functional connectivity as a neuropathological explanation of ASD, where the executive dysfunctions in the autistic children were closely related to the extent of disordered neural connectivity of their brains, indexed by EEG theta coherence of the distributed fronto-parietal network. The results of this study will help shed light on the neurophysiological underpinnings of the cognitive impairments and behavioral symptoms associated with autism, which is invaluable for designing teaching and remedial intervention for young children with autism.

Conflict of interest

The authors declare no conflict of interest.

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Figure 1

Flow of participants through each stage of the experiment.

ASD = Children with Autistic Spectrum Disorders; TDC = Typically Developing Children

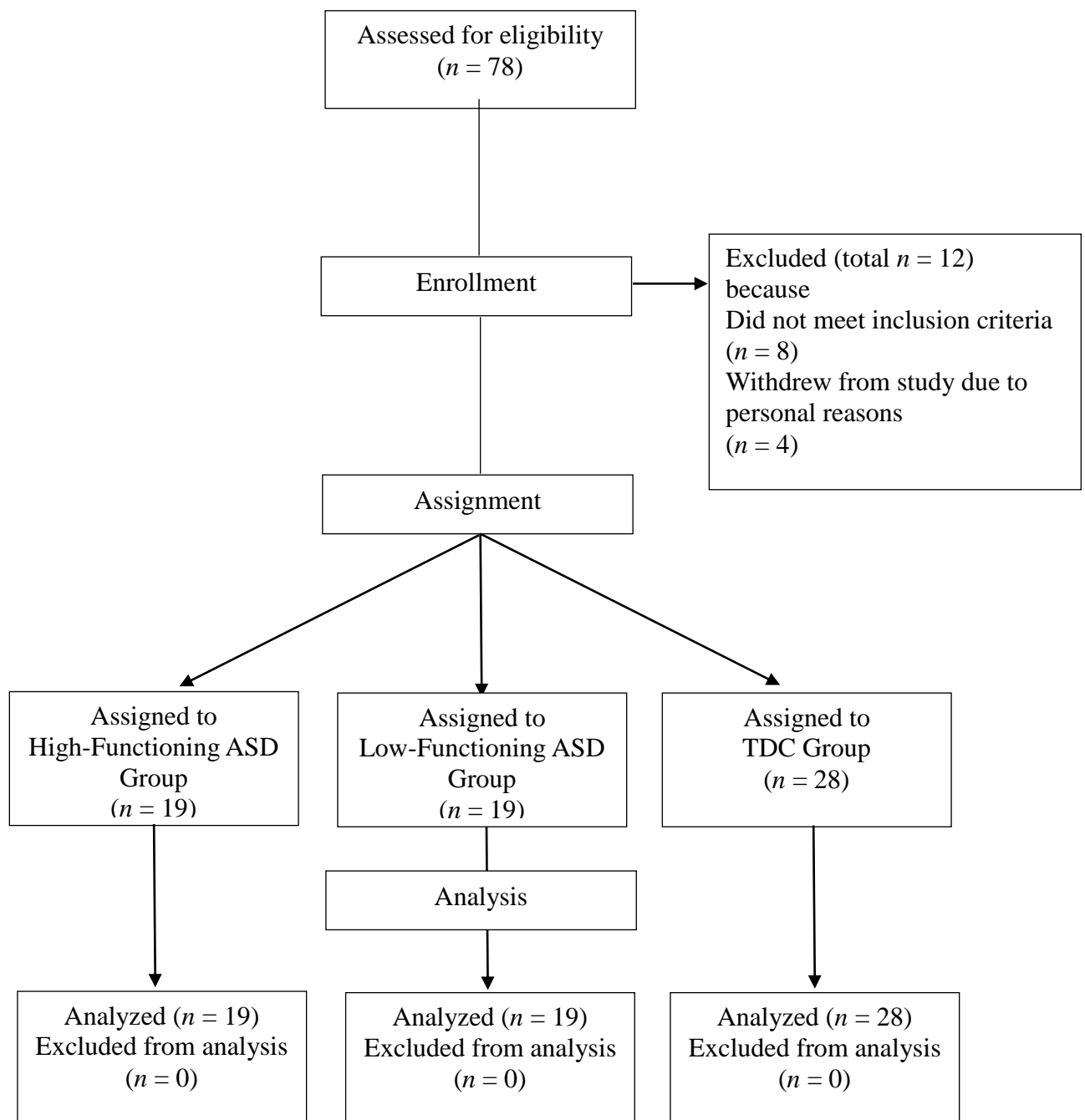


Figure 2

Mean values of absolute and relative theta power in Typically Developing (TDC), High-Functioning (HFA) and Low-Functioning (LFA) Children with Autistic Spectrum Disorders (ASD).

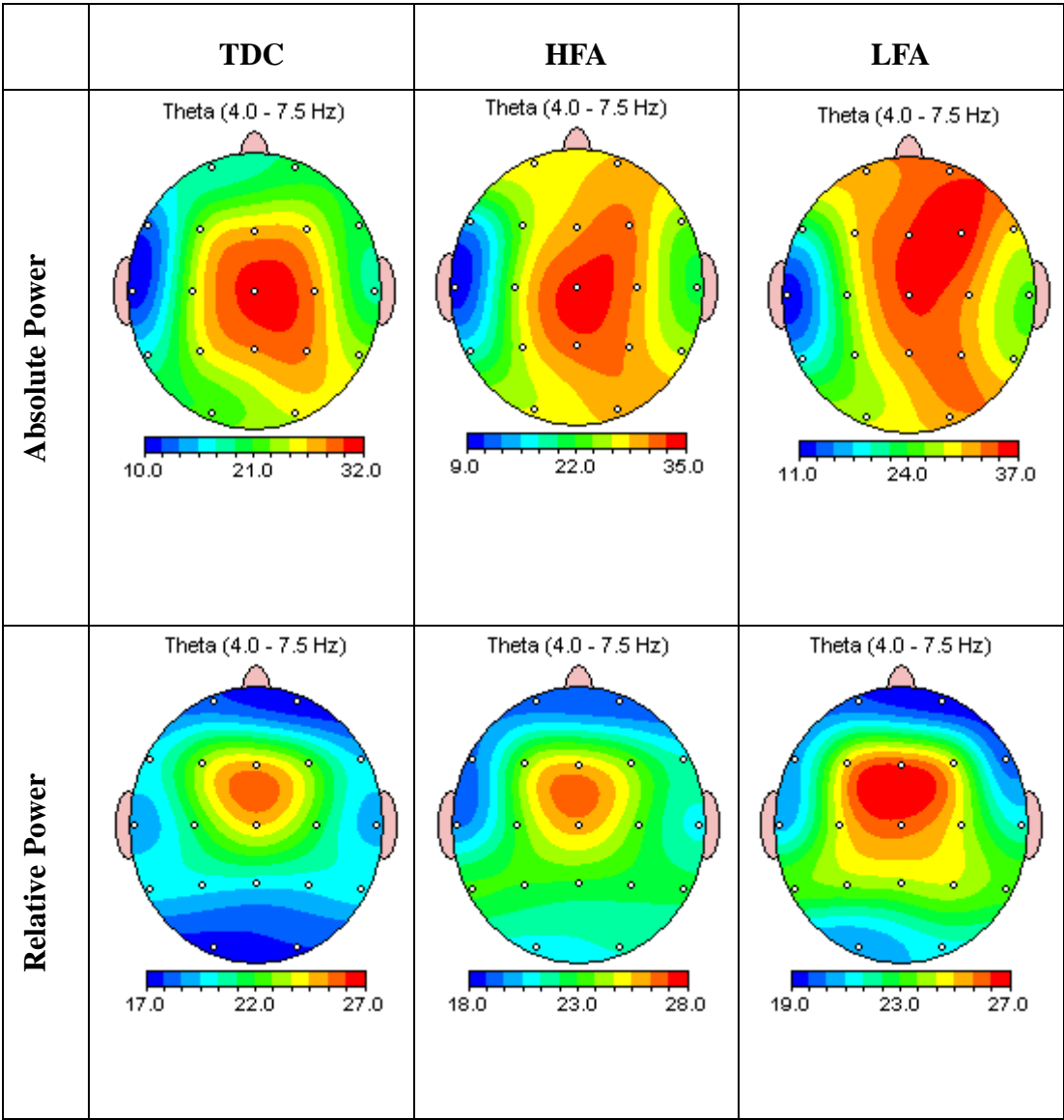


Figure 3

Mean (Fisher-Z) coherence of Children in the Typically Developing (TDC), High- (HFA) and Low- (LFA) functioning ASD Groups. Both HFA and LFA children demonstrated significantly higher mean coherence values for fronto-parietal long-range and posterior short-range connections than that of the TDC group.

* $p < .05$, ** $p < .001$.

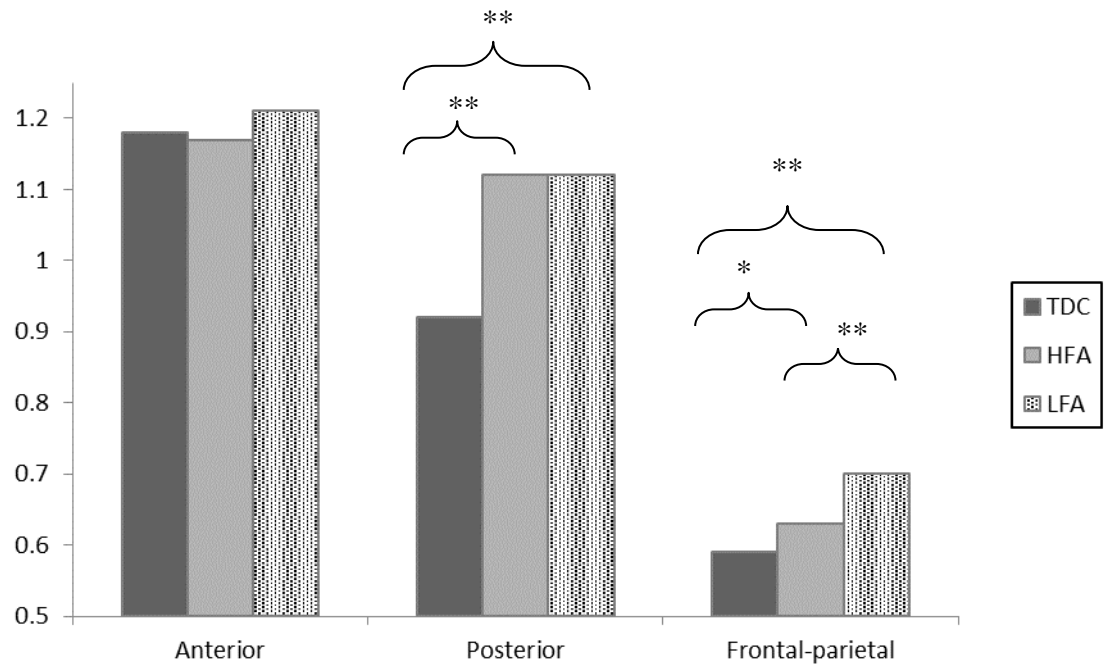


Table 1

Demographic Characteristics of the Children with Typically Developing (TDC), High-Functioning (HFA) and Low-Functioning (LFA) Children with Autistic Spectrum Disorders (ASD)

Variable	TDC (<i>n</i> = 29)	HFA (<i>n</i> = 19)	LFA (<i>n</i> = 19)
Range of Age (in years)	8.33 – 15.91	7.67 – 17.50	7.42 – 15.33
Mean Age (in years)	12.0 (2.33)	11.6 (3.02)	12.1 (2.35)
Gender (male/female)	17/11	15/4	17/2
IQ	109.8 (11.59)	105.2 (21.61)	50.3 (12.73)
ADI-R Social Interaction	----	20.42 (6.25)	20.42 (6.64)
ADI-R Communication	----	11.79 (4.95)	11.32 (5.16)
ADI-R Stereotyped Behavior	----	3.84 (3.45)	4.89 (2.64)

Note. Standard deviations are in parentheses. ADI-R = Autism Diagnostic Interview- revised.

Table 2

Mean Performance and Standard Deviation on the Measures of Executive Functioning Task in the Typically Developing (TDC), High- (HFA) and Low- (LFA) functioning ASD Groups

Measures	TDC (n = 28) M (SD)	HFA(n = 19) M (SD)	LFA (n = 19) M (SD)	F-value	Group Difference		
Executive Composite score	0.30 (0.80)	1.82 (1.31)	4.09 (1.77)	47.91**	TDC<HFA**	TDC<LFA**	HFA<LFA**
<i>Individual test scores</i>							
HKLLT-Total Learning	25.64 (4.75)	18.11 (8.18)	8.05 (5.91)	45.15**	TDC>HFA**	TDC>LFA**	HFA>LFA**
HKLLT-Discrimination %	93.07 (8.31)	70.56 (33.11)	21.92 (30.07)	48.08**	TDC>HFA**	TDC>LFA**	HFA>LFA**
D2-Concentration performance	164.8 (53.72)	118.1 (55.24)	30.26 (44.01)	38.62**	TDC>HFA**	TDC>LFA**	HFA>LFA**
5 Point-Unique design	23.64 (10.86)	22.74 (11.05)	5.95 (6.83)	20.62**		TDC>LFA**	HFA>LFA**
CCTT-Trail2Time2	44.4 (18.86)	73.76 (68.61)	172.4 (109.0)	19.66**		TDC<LFA**	HFA<LFA *
ToC-Achievement	9.57 (2.75)	7.57 (4.59)	2.37 (1.98)	28.75**		TDC>LFA**	HFA>LFA**
Go/NoGo-Commission errors	9.0 (6.09)	10.05 (7.55)	15.18 (11.89)	3.02			

**p<.001, *p<.007

Table 3

Correlation between Executive Function and EEG Coherence of Children in the Typically Developing (TDC), High- (HFA) and Low- (LFA) functioning ASD Groups.

	EEG theta Coherence		
	Anterior (short)	Posterior (short)	Fronto-parietal (Long)
Executive Composite Score			
Whole group (n = 66)	0.15	0.38**	0.36**
ASD subgroup (n = 38)	0.21	-0.11	0.32*
TDC subgroup (n = 28)	0.07	0.08	0.11

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