Measuring attention performance among ADHD versus non ADHD children

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Measuring attention performance among ADHD versus non ADHD children

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Abstract

This study examined the validity of a Continuous Performance Test (MOXO-CPT) among 798 children aged 7-12 years. Receiver Operating Characteristic (ROC) analyses showed that the MOXO-CPT was highly accurate in identifying ADHD children who were previously diagnosed by using DSM-IV-TR criteria. In addition, the test significantly discriminated ADHD children from non-ADHD children.

These findings emphasize the importance of incorporating distracters into CPT and integrating several different attention parameters when measuring attention functions.

In light of the criticism voiced against the low validity of CPT's, a valid CPT would be valuable for theory, research, and clinical work.

Introduction

Attention-deficit hyperactivity disorder (ADHD) is among the most common neurobehavioral disorders of childhood, characterized by inattention, impulsivity and hyperactivity. Using the DSM-IV criteria (APA, 1994), prevalence rates in the United States ranged from 7.4% to 9.9% (Barkley, 2006; CDC, 2010).

In the absence of available biological markers that would support conferring diagnoses, information about the symptoms is usually collected by using interviews based on DSM-IV-TR criteria of ADHD and validated behavioral rating scales (AAP, 2001; APA, 2000; Skounti, Philalithis, & Galanakis, 2007). The subjective nature of these methods makes them vulnerable to clinician and informant biases (Rousseau, Measham, & Bathiche-Suidan, 2008; Serra-Pinheiro, Mattos, &Regalla, 2008; Skounti et al., 2007).

As a result, there has long been interest in developing objective laboratory-based measures that could support the clinical diagnosis of ADHD. One of the most popular laboratory-based tools is the computerized continuous performance test (CPT), which was originally developed as a measure of vigilance (Rosvold, Mirsky, Sarason, Bransome & Beck, 1956). Generally, CPT tasks require the subjects to maintain vigilance and react to the presence (or absence) of a specific stimulus within a set of distracters presented continuously.

The use of the CPT as an objective measure of attention in ADHD has several advantages. It can measure the ability to concentrate on a single task for a certain length of time. In addition, it is considered an objective tool to gather quantifiable information on the changes of attention as a result of a medical or non-medical treatment. Finally, CPT is inexpensive, easy to administer, and some versions include appropriate age norms.

Despite its vast popularity in clinical and empirical settings, many authors have identified concerns about using CPT as a diagnostic tool. One of the major controversies regarding the CPT is related to its low sensitivity and specificity rates (Edwards et al., 2007; McGee, Clark

& Symons, 2000; Riccio, Waldrop, Reynolds, & Lowe, 2001; Skounti et al., 2007). Although some studies (Aaron, Joshi, and Phipps, 2004; Epstein et al., 2003; Seidel & Joschko, 1990) have demonstrated differences in CPT performance between ADHD and normal controls, many others have questioned its ability to consistently discriminate ADHD children from normal controls, psychiatric controls or learning disabilities (Corkum & Siegel, 1993; DeShazo, Grofer, Lyman, Bush, & Hawkins, 2001; Schachar, Logan, Wachsmuth, & Chajczyk, 1988; Trommer, Hoeppner, Lorber, & Armstrong, 1988; Werry, Reeves, & Elkind, 1987).

The CPT was also criticized for its low ecological validity (Barkley, 1991; Pelham et al., 2011; Rapport, Chung, Shore, Denney, & Isaacs, 2000). That is, the CPT ability to simulate the difficulties of ADHD patients in everyday life. Being administrated in laboratory conditions (Barkley, 1991; Gutiérrez-Maldonado, Letosa-Porta , Rus-Calafell, & Peñaloza-Salazar, 2009), CPT are usually free of distracting stimuli, which are thought to impair the cognitive performance of ADHD children (APA, 1994; 2000).

In light of the limitations of the existing CPTs, the American Academy of Pediatrics did not support the use of CPT tests in the diagnostic process of ADHD (AAP, 2001). At the same time, the inaccuracy of the subjective measurement tools of ADHD still calls for a reliable and valid CPT tests (AAP, 2001; Dickerson Mayes, Calhoun, & Crowell, 2001; Skounti et al., 2007).

The current study examined the validity of the MOXO-CPT (Berger & Goldzweig, 2010) in the diagnosis of ADHD in children aged 7-12 years. This study had two objectives: the first one was to assess the MOXO-CPT's ability to measure differences in attention performance among ADHD versus non-ADHD children. The second objective was to evaluate the construct validity of the MOXO-CPT in the diagnosis of ADHD, using the DSM-IV-TR criteria (APA, 2000) as the 'gold standard'.

The term 'MOXO' derives from the world of Japanese martial arts and means a 'moment of lucidity'. It refers to the moments preceding the fight, when the warrior clears his mind from distracting, unwanted thoughts and feelings.

Results of a pilot study with a small group of children (Berger & Goldzweig, 2010) showed that the MOXO-CPT was valid for ADHD diagnosis in children, and was more sensitive to ADHD than other CPT tests, such as the T.O.V.A (Greenberg, 1997) and the Conners CPT (Conners, 2000).

Methods

Participants

Participants in this study were 798 children aged 7 to 12 years, of them 493 boys and 305 girls. The study group included 339 children diagnosed with ADHD (Mean age, 9.27, S.D= 1.65) and the control group included 459 children without ADHD (Mean age =9.71, S.D= 1.64).

The children were divided to six different age categories (7, 8, 9, 10, 11, and12 years). For example, the category of “8 years” included children who were equal or older than 8, but younger than 9.

As can be seen in Table 1, within each age category, the study and control group did not differ in gender distributions.

Participants in the ADHD group were recruited from children referred to the out-patient pediatric clinics of the Neuro-Cognitive Center, based in a tertiary care university hospital. The children were referred through their pediatrician, general practitioner, teacher, psychologist, or directly by the parents.

Inclusion criteria for participants in the ADHD group were:

1. Each child met the criteria for ADHD according to DSM-IV-TR criteria (APA, 2000), as assessed by a certified pediatric neurologist. The diagnostic procedure included an interview with the child and parents, fulfillment of questionnaires, and medical/neurological examination that confirmed ADHD diagnosis.

2. Each child scored above the standard clinical cutoffs for ADHD symptoms on Conners' ADHD/DSM-IV Scales (Conners, 1997a; Conners, 1997b, APA, 2000).

3. All children were drug naïve.

Participants in the control group were randomly recruited from pupils in primary schools. Inclusion criteria for participants in the control group were:

1. Each child scored below the clinical cutoff point for ADHD symptoms on Conners' ADHD/DSM-IV Scales (Conners, 1997a; Conners, 1997b).
2. Absence of academic or behavioral problems, as reported by parents and teachers.

Exclusion criteria were intellectual disability, other chronic condition, chronic use of medications, and other primary psychiatric diagnosis (e.g., depression, anxiety, and psychosis).

All participants agreed to participate in the study and their parents gave written informed consent to the study, approved by the Helsinki committee (IRB) of Hadassah-Hebrew University Medical Center (Jerusalem, Israel).

Measures

Measurement of child behavior - The parent and teacher forms of the Conner's ADHD/DSM-IV Scales were used to assess the level of children's ADHD behaviors (Conners, 1997a; Conners, 1997b; APA 2000).

MOXO- CPT Description

This version of the CPT is a computerized performance test as previously described (Berger & Goldzweig, 2010). A set of target and non-target stimuli were shown sequentially in the middle of a computer screen. The child was instructed to respond as quickly as possible to the target stimuli by pressing the keyboard's space bar once, and only once. In addition, the child was instructed to avoid responding to all other stimuli or pressing any other key. While performing the CPT, the children were accompanied by technician who made sure that the children understood the instructions and watched them throughout the test without interfering.

Both target and non-target stimuli were cartoon pictures that did not include any letters or numbers (see Figure 1). These features are significant, given that some children with ADHD also demonstrate learning difficulties (e.g., dyslexia) that may be confounded with CPT performance (Seidman, Biederman, Monuteaux, Doyle, & Faraone, 2001).

The MOXO-CPT duration was 15.2 minutes, contained eight levels, each of them 114 seconds long. Every level included three types of elements: a target stimulus, a non-target stimulus, and a "void" period. First, a stimulus (target/ non-target) was presented for a changing duration of time (3 sec, 1 sec, or 0.5 seconds). Then, the stimulus was followed by a "void" period (blank screen) of the same duration. Prior to the void period, the stimulus (target / non-target) was presented on the screen whether or not the participant responded to it. In other words, pressing the keyboard's space bar did not eliminate the stimulus.

This method of presentation enabled to measure the timing of the response (whether the response occurred during stimulus presentation or during the void period) as well as the accuracy of the press (whether the response occurred at all). Each level included 33 targets stimuli, 20 non-target stimuli, and 53 void periods.

Distracters - In order to simulate everyday environment, the MOXO-CPT contained interfering stimuli that serve as distracters. The distracters included three types of basic elements that characterize the child's environment: a) pure visual distracters (e.g., flying birds, magician's wand), b) pure auditory distracters (e.g., a voice of a gong, squeaking birds), and c) combination of both the visual and auditory distracters. Overall, six different distracters were presented (Figure 2). Every one of the eight levels of the MOXO-CPT included a different set of distracters: two levels (1 and 8) contained only target and non-target stimuli without distracters, two levels (2 and 3) contained pure visual stimuli, two levels (4 and 5) contained pure auditory stimuli, and two levels (6 and 7) contained a combination of visual and auditory stimuli.

While the target stimulus was presented at the center of the screen, the visual distracters appeared at one of the four sides of the display: down, up, left or right. The sequence of distracters and their exact position on the display were predefined for each level. Distracters were displayed for varied durations ranging from for 3.5 to 14.7 seconds, with a constant void interval of 0.5 second between two sequential distracting elements.

The burden of the interfering stimuli increased in the odd number levels. That is, the third, fifth, and seventh levels included higher burden of distracters than the second, fourth and sixth levels, respectively.

Performance indices – The MOXO-CPT included four indices named: Attention, Timing, Impulsivity, and Hyperactivity.

Attention – This parameter included the number of correct responses (pressing the key in response to a target stimulus), which were performed either during the stimulus presentation on the screen or during the void period that followed. Thus, it was possible to evaluate whether the participant responded correctly to the target (was attentive to the target) independently of how fast he was. Knowing how many responses are expected, it was also possible to calculate the number of times the target was presented, but the patient did not respond to it (omission errors).

Timing – This parameter included the number of correct responses (pressing the key in response to a target stimulus) which were performed only while the target stimulus was still presented on the screen. This parameter did not include responses that were performed during the void period (after the stimulus has disappeared).

According to the National Institute of Mental Health (2012), inattention problems in ADHD may be expressed in "difficulties in processing information as quickly and accurately as others". Traditionally, difficulties in timing at a CPT are evaluated by mean response time for correct responses to the target (which is interpreted as a measure of information processing and motor response speed) and by the standard deviation of response time for correct responses to the target (which is interpreted as a measure of variability or consistency) (Greenberg & Waldman, 1993; Halperin, Matier, Bedi, Sharma, & Newcorn, 1992). In these paradigms the stimulus is presented for short and fixed periods of time and the response occurs after the stimulus has disappeared. Given the short, fixed presentation, accurate but slow participants may be mistakenly diagnosed as inattentive. While a group of patients would respond correctly if allowed more time, inattentive patients would not respond at all because they were not alert to the target. Therefore, the measurement of response time per-se, addresses only the ability to respond quickly, but not the ability to respond accurately.

By implanting a void period after each stimulus and using variable presentation durations of the elements, the MOXO-CPT could distinguish accurate responses performed in "good timing" (quick and correct responses to the target performed during stimulus presentation) from accurate but slow responses (correct responses to the target performed after the stimulus presentation; during the void period). These two aspects of timing correspond to the two different problems of ADHD described by the National Institute of Mental Health (2012): responding quickly and responding accurately.

Impulsivity - This parameter included the number of commission errors (responses to a non-target stimulus), performed as the initial response to the non-target stimuli. Usually, commission errors are coded in any case of inappropriate response to the target (e.g., pressing a random key) (Greenberg & Waldman, 1993). In contrast, the MOXO-CPT's impulsivity parameter considered as impulsive behavior only the first pressing on the keyboard's space–bar in response to non-target stimulus. All other non-inhibited responses (e.g., pressing the keyboard more than once) were not coded as impulsive responses (as will describe in the next paragraph).

Hyperactivity - This parameter included all types of commission responses that are not coded as impulsive responses. Several examples are: 1. Multiple responses- pressing the keyboard's space bar more than once (in response to target/ non-target), which is commonly interpreted as a measure of motor hyper-responsivity (Greenberg & Waldman, 1993). The MOXO-CPT considered as multiple responses only the second press and above (the first response would be considered as correct response with good timing, as correct response with poor timing, or as impulsive response, depends on the type of element appearing on the screen). 2. Random key pressing - pressing any keyboard button other than the space bar. By separating commission errors due to impulsive behavior from commission errors due to motor hyper-responsivity, it was possible to identify the multiple sources of response inhibition problems. Thus, the MOXO- CPT was able to differentiate impulsive responses from hyperactive responses.

Data Analyses

All analyses were conducted with Matlab version R2011b. In order to compare the performance of ADHD children and non-ADHD children, independent samples T-tests were performed, for each one of the four MOXO-CPT parameters. The diagnostic value of the MOXO-CPT was assessed by calculating the areas under the receiver operating characteristic (ROC) curves, which were used to assess the best cutoff points to distinguish between ADHD and non-ADHD children.

Results

Differentiating Between ADHD and non-ADHD children

Differences between the study and the control group in the four parameters of performance in the MOXO-CPT (attention, timing, hyperactivity, and impulsivity) were examined by two tailed T-test analyses for independent samples. In addition, differences between the groups were measured by comparing the total score of the MOXO-CPT, which takes into account all four parameters (Table 2). Results of the analyses revealed that in all age categories, significant differences were found between ADHD and non-ADHD children. As can be seen in table 2, ADHD children received significantly lower scores in the Attention and Timing parameters than normal controls. That is, ADHD children were less attended to the stimuli and performed less reactions on accurate time. Furthermore, ADHD children received significantly higher scores in the Hyperactivity and Impulsivity parameters than normal controls. Thus, ADHD children produced more Hyperactive and Impulsive responses as compared to non-ADHD children. Finally, ADHD children received higher total scores in the MOXO-CPT as compared to non-ADHD children. That is, ADHD children's general performance in the MOXO-CPT was worse than their unaffected peers of the same age. It should also be noted that using the total score of the MOXO-CPT produced the highest difference between ADHD and non-ADHD performance, as compared to any single parameter.

Diagnostic Utility of the MOXO-CPT

Since inclusion criteria required that each participating child (in the ADHD group) met the criteria for ADHD diagnosis according to DSM-IV-TR (APA, 2000), the sensitivity and specificity of the MOXO-CPT were calculated using these criteria. Results of ROC analyses are presented in table 3. The table shows the cut-off points, sensitivity and specificity rates of the MOXO-CPT, based on the total scores of the MOXO-CPT (taking into account all four parameters). Different sensitivity and specificity rates could be used for different purposes of the test (e.g., screening, diagnosis). However, we have used the optimal value which represents the maximized classification accuracy with the highest sensitivity and specificity rates. Results showed that in all age categories, the optimal cut-off points were associated with both high sensitivity and specificity rates (all above 80%).

Figure 3 presents an example of a ROC analysis, in a group of children aged 8-9 years. As can be seen in the figure, the total score of the MOXO-CPT produced the highest sensitivity and specificity rates, as compared to any single parameter.

Discussion

The current study investigated the diagnostic utility of the MOXO-CPT (Berger & Goldzweig, 2010) for the assessment of ADHD in a sample of children aged 7-12 years. Results showed that the MOXO-CPT significantly discriminated between children with ADHD and their unaffected peers of the same age. As measured by the MOXO-CPT, children with ADHD were more inattentive, more impulsive and more hyperactive than normal controls of the same age. In addition, they had more difficulties in responding on accurate timing. The largest difference between ADHD and non-ADHD children was revealed in the total score of the test. Moreover, the total score of the MOXO-CPT yielded the highest sensitivity and specificity rates, as compared to any single parameter. Given the complexity of ADHD etiology and clinical manifestation, it is little wonder that the total score of the MOXO-CPT was superior to any single parameter in identifying ADHD. This finding emphasizes the importance of integrating several different attention parameters in measuring attention functions.

Results of the ROC analyses showed that the MOXO-CPT was highly accurate in identifying participants with ADHD, based on the DSM-IV-TR (APA, 2000) criteria. For all ages, optimal cutoff values were associated with both high sensitivity and specificity rates (above 80%).

Selection of a threshold for a screening test is best achieved according to the needs of the specific setting in which it is to be used. 'Optimal' cutoff values vary depending on the risk-benefit ratio between false positive and false negative test results and the base rate of the target disorder in the population at hand. Important information may be lost when defining sensitivity and specificity in relation to a single cutoff value of a continuous variable (Sox, 1986). The discussion regarding which are the best criteria for diagnosis is beyond the scope of this study.

The literature has long been debating the reliability and validity of using CPT tests for case identification and diagnosis of ADHD (Dickerson et al., 2001; Skounti et al., 2007). Low validity of CPT tests may not only lead to inaccurate diagnosis but could also prevent effective intervention and might further complicate the symptoms in the long term (Sonuga-Barke, Koerting, Smith, McCann, &Thompson, 2011).

The MOXO-CPT has several advantages that may make it preferable for use in clinical and diagnostic settings. Due to the presence of distracters, the MOXO-CPT could be construed as more ecologically valid. It also allows monitoring the impact of distracting stimuli on the attention performance of ADHD children.

In addition, the tests' indices of ADHD symptoms are more accurately defined. Thus, the test could distinguish hyperactive behavior from impulsive behavior. Moreover, the timing ability was re-conceptualized, so the test could measure two different types of problems: difficulties to sustain attention and difficulties in responding on accurate timing. The findings of this study are therefore of great value since they offer a sensitive, objective assessment tool in assessing ADHD symptomatology.

Several limitations of this study should be considered. The first limitation results from the study's sampling method. Participation in the study was based on a voluntary agreement of children and their parents. This self-selected sampling strategy tends to be biased towards favoring more cooperative and motivated individuals. Therefore, it is not possible to determine whether this sample also represents other children that were not recruited and whether cooperation is confounded with ADHD variables. This limitation is typical to most clinic-based ADHD studies around the world (Gau et al., 2010; Lee & Ausley, 2006). Moreover, the clinics from which ADHD children were recruited were based in tertiary care hospital. This population has heterogeneous background characteristics including those correlates of ADHD. On the other hand, the fact that the control group was recruited from a random population supports our findings by showing that the test is able to identify the ADHD children from a random population sample.

Another limitation of the study is the exclusion of ADHD children with severe comorbidities. Since ADHD is associated with many psychiatric disorders (Gentile, Atiq, & Gillig, 2006) this exclusion limits the generalization of our results.

Future research should explore the psychometric properties of the MOXO-CPT in other age groups, in samples with comorbid features, and in different sub-types of ADHD.

Despite its shortcomings, this study suggests important information about using CPT in clinical and empirical settings, and may be a first step towards a more accurate and objective diagnostic process of ADHD.

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Abstract

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These findings emphasize the importance of incorporating distracters into CPT and integrating several different attention parameters when measuring attention functions.

In light of the criticism voiced against the low validity of CPT's, a valid CPT would be valuable for theory, research, and clinical work.

Introduction

Attention-deficit hyperactivity disorder (ADHD) is among the most common neurobehavioral disorders of childhood, characterized by inattention, impulsivity and hyperactivity. Using the DSM-IV criteria (APA, 1994), prevalence rates in the United States ranged from 7.4% to 9.9% (Barkley, 2006; CDC, 2010).

In the absence of available biological markers that would support conferring diagnoses, information about the symptoms is usually collected by using interviews based on DSM-IV-TR criteria of ADHD and validated behavioral rating scales (AAP, 2001; APA, 2000; Skounti, Philalithis, & Galanakis, 2007). The subjective nature of these methods makes them vulnerable to clinician and informant biases (Rousseau, Measham, & Bathiche-Suidan, 2008; Serra-Pinheiro, Mattos, &Regalla, 2008; Skounti et al., 2007).

As a result, there has long been interest in developing objective laboratory-based measures that could support the clinical diagnosis of ADHD. One of the most popular laboratory-based tools is the computerized continuous performance test (CPT), which was originally developed as a measure of vigilance (Rosvold, Mirsky, Sarason, Bransome & Beck, 1956). Generally, CPT tasks require the subjects to maintain vigilance and react to the presence (or absence) of a specific stimulus within a set of distracters presented continuously.

The use of the CPT as an objective measure of attention in ADHD has several advantages. It can measure the ability to concentrate on a single task for a certain length of time. In addition, it is considered an objective tool to gather quantifiable information on the changes of attention as a result of a medical or non-medical treatment. Finally, CPT is inexpensive, easy to administer, and some versions include appropriate age norms.

Despite its vast popularity in clinical and empirical settings, many authors have identified concerns about using CPT as a diagnostic tool. One of the major controversies regarding the CPT is related to its low sensitivity and specificity rates (Edwards et al., 2007; McGee, Clark

& Symons, 2000; Riccio, Waldrop, Reynolds, & Lowe, 2001; Skounti et al., 2007). Although some studies (Aaron, Joshi, and Phipps, 2004; Epstein et al., 2003; Seidel & Joschko, 1990) have demonstrated differences in CPT performance between ADHD and normal controls, many others have questioned its ability to consistently discriminate ADHD children from normal controls, psychiatric controls or learning disabilities (Corkum & Siegel, 1993; DeShazo, Grofer, Lyman, Bush, & Hawkins, 2001; Schachar, Logan, Wachsmuth, & Chajczyk, 1988; Trommer, Hoeppner, Lorber, & Armstrong, 1988; Werry, Reeves, & Elkind, 1987).

The CPT was also criticized for its low ecological validity (Barkley, 1991; Pelham et al., 2011; Rapport, Chung, Shore, Denney, & Isaacs, 2000). That is, the CPT ability to simulate the difficulties of ADHD patients in everyday life. Being administrated in laboratory conditions (Barkley, 1991; Gutiérrez-Maldonado, Letosa-Porta , Rus-Calafell, & Peñaloza-Salazar, 2009), CPT are usually free of distracting stimuli, which are thought to impair the cognitive performance of ADHD children (APA, 1994; 2000).

In light of the limitations of the existing CPTs, the American Academy of Pediatrics did not support the use of CPT tests in the diagnostic process of ADHD (AAP, 2001). At the same time, the inaccuracy of the subjective measurement tools of ADHD still calls for a reliable and valid CPT tests (AAP, 2001; Dickerson Mayes, Calhoun, & Crowell, 2001; Skounti et al., 2007).

The current study examined the validity of the MOXO-CPT (Berger & Goldzweig, 2010) in the diagnosis of ADHD in children aged 7-12 years. This study had two objectives: the first one was to assess the MOXO-CPT's ability to measure differences in attention performance among ADHD versus non-ADHD children. The second objective was to evaluate the construct validity of the MOXO-CPT in the diagnosis of ADHD, using the DSM-IV-TR criteria (APA, 2000) as the 'gold standard'.

The term 'MOXO' derives from the world of Japanese martial arts and means a 'moment of lucidity'. It refers to the moments preceding the fight, when the warrior clears his mind from distracting, unwanted thoughts and feelings.

Results of a pilot study with a small group of children (Berger & Goldzweig, 2010) showed that the MOXO-CPT was valid for ADHD diagnosis in children, and was more sensitive to ADHD than other CPT tests, such as the T.O.V.A (Greenberg, 1997) and the Conners CPT (Conners, 2000).

Methods

Participants

Participants in this study were 798 children aged 7 to 12 years, of them 493 boys and 305 girls. The study group included 339 children diagnosed with ADHD (Mean age, 9.27, S.D= 1.65) and the control group included 459 children without ADHD (Mean age =9.71, S.D= 1.64).

The children were divided to six different age categories (7, 8, 9, 10, 11, and12 years). For example, the category of “8 years” included children who were equal or older than 8, but younger than 9.

As can be seen in Table 1, within each age category, the study and control group did not differ in gender distributions.

Participants in the ADHD group were recruited from children referred to the out-patient pediatric clinics of the Neuro-Cognitive Center, based in a tertiary care university hospital. The children were referred through their pediatrician, general practitioner, teacher, psychologist, or directly by the parents.

Inclusion criteria for participants in the ADHD group were:

1. Each child met the criteria for ADHD according to DSM-IV-TR criteria (APA, 2000), as assessed by a certified pediatric neurologist. The diagnostic procedure included an interview with the child and parents, fulfillment of questionnaires, and medical/neurological examination that confirmed ADHD diagnosis.

2. Each child scored above the standard clinical cutoffs for ADHD symptoms on Conners' ADHD/DSM-IV Scales (Conners, 1997a; Conners, 1997b, APA, 2000).

3. All children were drug naïve.

Participants in the control group were randomly recruited from pupils in primary schools. Inclusion criteria for participants in the control group were:

1. Each child scored below the clinical cutoff point for ADHD symptoms on Conners' ADHD/DSM-IV Scales (Conners, 1997a; Conners, 1997b).
2. Absence of academic or behavioral problems, as reported by parents and teachers.

Exclusion criteria were intellectual disability, other chronic condition, chronic use of medications, and other primary psychiatric diagnosis (e.g., depression, anxiety, and psychosis).

All participants agreed to participate in the study and their parents gave written informed consent to the study, approved by the Helsinki committee (IRB) of Hadassah-Hebrew University Medical Center (Jerusalem, Israel).

Measures

Measurement of child behavior - The parent and teacher forms of the Conner's ADHD/DSM-IV Scales were used to assess the level of children's ADHD behaviors (Conners, 1997a; Conners, 1997b; APA 2000).

MOXO- CPT Description

This version of the CPT is a computerized performance test as previously described (Berger & Goldzweig, 2010). A set of target and non-target stimuli were shown sequentially in the middle of a computer screen. The child was instructed to respond as quickly as possible to the target stimuli by pressing the keyboard's space bar once, and only once. In addition, the child was instructed to avoid responding to all other stimuli or pressing any other key. While performing the CPT, the children were accompanied by technician who made sure that the children understood the instructions and watched them throughout the test without interfering.

Both target and non-target stimuli were cartoon pictures that did not include any letters or numbers (see Figure 1). These features are significant, given that some children with ADHD also demonstrate learning difficulties (e.g., dyslexia) that may be confounded with CPT performance (Seidman, Biederman, Monuteaux, Doyle, & Faraone, 2001).

The MOXO-CPT duration was 15.2 minutes, contained eight levels, each of them 114 seconds long. Every level included three types of elements: a target stimulus, a non-target stimulus, and a "void" period. First, a stimulus (target/ non-target) was presented for a changing duration of time (3 sec, 1 sec, or 0.5 seconds). Then, the stimulus was followed by a "void" period (blank screen) of the same duration. Prior to the void period, the stimulus (target / non-target) was presented on the screen whether or not the participant responded to it. In other words, pressing the keyboard's space bar did not eliminate the stimulus.

This method of presentation enabled to measure the timing of the response (whether the response occurred during stimulus presentation or during the void period) as well as the accuracy of the press (whether the response occurred at all). Each level included 33 targets stimuli, 20 non-target stimuli, and 53 void periods.

<u>Distracters</u> - In order to simulate everyday environment, the MOXO-CPT contained interfering stimuli that serve as distracters. The distracters included three types of basic elements that characterize the child's environment: a) pure visual distracters (e.g., flying birds, magician's wand), b) pure auditory distracters (e.g., a voice of a gong, squeaking birds), and c) combination of both the visual and auditory distracters. Overall, six different distracters were presented (Figure 2). Every one of the eight levels of the MOXO-CPT included a different set of distracters: two levels (1 and 8) contained only target and non-target stimuli without distracters, two levels (2 and 3) contained pure visual stimuli, two levels (4 and 5) contained pure auditory stimuli, and two levels (6 and 7) contained a combination of visual and auditory stimuli.

While the target stimulus was presented at the center of the screen, the visual distracters appeared at one of the four sides of the display: down, up, left or right. The sequence of distracters and their exact position on the display were predefined for each level. Distracters were displayed for varied durations ranging from for 3.5 to 14.7 seconds, with a constant void interval of 0.5 second between two sequential distracting elements.

The burden of the interfering stimuli increased in the odd number levels. That is, the third, fifth, and seventh levels included higher burden of distracters than the second, fourth and sixth levels, respectively.

Performance indices – The MOXO-CPT included four indices named: Attention, Timing, Impulsivity, and Hyperactivity.

<u>Attention</u> – This parameter included the number of correct responses (pressing the key in response to a target stimulus), which were performed either during the stimulus presentation on the screen or during the void period that followed. Thus, it was possible to evaluate whether the participant responded correctly to the target (was attentive to the target) independently of how fast he was. Knowing how many responses are expected, it was also

possible to calculate the number of times the target was presented, but the patient did not respond to it (omission errors).

Timing – This parameter included the number of correct responses (pressing the key in response to a target stimulus) which were performed only while the target stimulus was still presented on the screen. This parameter did not include responses that were performed during the void period (after the stimulus has disappeared).

According to the National Institute of Mental Health (2012), inattention problems in ADHD may be expressed in "difficulties in processing information as quickly and accurately as others". Traditionally, difficulties in timing at a CPT are evaluated by mean response time for correct responses to the target (which is interpreted as a measure of information processing and motor response speed) and by the standard deviation of response time for correct responses to the target (which is interpreted as a measure of variability or consistency) (Greenberg & Waldman, 1993; Halperin, Matier, Bedi, Sharma, & Newcorn, 1992). In these paradigms the stimulus is presented for short and fixed periods of time and the response occurs after the stimulus has disappeared. Given the short, fixed presentation, accurate but slow participants may be mistakenly diagnosed as inattentive. While a group of patients would respond correctly if allowed more time, inattentive patients would not respond at all because they were not alert to the target. Therefore, the measurement of response time per-se, addresses only the ability to respond quickly, but not the ability to respond accurately.

By implanting a void period after each stimulus and using variable presentation durations of the elements, the MOXO-CPT could distinguish accurate responses performed in "good timing" (quick and correct responses to the target performed during stimulus presentation) from accurate but slow responses (correct responses to the target performed after the stimulus presentation; during the void period). These two aspects of timing correspond to the two different problems of ADHD described by the National Institute of Mental Health (2012): responding quickly and responding accurately.

Impulsivity - This parameter included the number of commission errors (responses to a non-target stimulus), performed as the initial response to the non-target stimuli. Usually, commission errors are coded in any case of inappropriate response to the target (e.g., pressing a random key) (Greenberg & Waldman, 1993). In contrast, the MOXO-CPT's impulsivity parameter considered as impulsive behavior only the first pressing on the keyboard's space–bar in response to non-target stimulus. All other non-inhibited responses (e.g., pressing the keyboard more than once) were not coded as impulsive responses (as will describe in the next paragraph).

Hyperactivity - This parameter included all types of commission responses that are not coded as impulsive responses. Several examples are: 1. Multiple responses- pressing the keyboard's space bar more than once (in response to target/ non-target), which is commonly interpreted as a measure of motor hyper-responsivity (Greenberg & Waldman, 1993). The MOXO-CPT considered as multiple responses only the second press and above (the first response would be considered as correct response with good timing, as correct response with poor timing, or as impulsive response, depends on the type of element appearing on the screen). 2. Random key pressing - pressing any keyboard button other than the space bar. By separating commission errors due to impulsive behavior from commission errors due to motor hyper-responsivity, it was possible to identify the multiple sources of response inhibition problems. Thus, the MOXO- CPT was able to differentiate impulsive responses from hyperactive responses.

Data Analyses

All analyses were conducted with Matlab version R2011b. In order to compare the performance of ADHD children and non-ADHD children, independent samples T-tests were performed, for each one of the four MOXO-CPT parameters. The diagnostic value of the MOXO-CPT was assessed by calculating the areas under the receiver operating characteristic (ROC) curves, which were used to assess the best cutoff points to distinguish between ADHD and non-ADHD children.

Results

Differentiating Between ADHD and non-ADHD children

Differences between the study and the control group in the four parameters of performance in the MOXO-CPT (attention, timing, hyperactivity, and impulsivity) were examined by two tailed T-test analyses for independent samples. In addition, differences between the groups were measured by comparing the total score of the MOXO-CPT, which takes into account all four parameters (Table 2). Results of the analyses revealed that in all age categories, significant differences were found between ADHD and non-ADHD children. As can be seen in table 2, ADHD children received significantly lower scores in the Attention and Timing parameters than normal controls. That is, ADHD children were less attended to the stimuli and performed less reactions on accurate time. Furthermore, ADHD children received significantly higher scores in the Hyperactivity and Impulsivity parameters than normal controls. Thus, ADHD children produced more Hyperactive and Impulsive responses as compared to non-ADHD children. Finally, ADHD children received higher total scores in the MOXO-CPT as compared to non-ADHD children. That is, ADHD children's general performance in the MOXO-CPT was worse than their unaffected peers of the same age. It should also be noted that using the total score of the MOXO-CPT produced the highest difference between ADHD and non-ADHD performance, as compared to any single parameter.

Diagnostic Utility of the MOXO-CPT

Since inclusion criteria required that each participating child (in the ADHD group) met the criteria for ADHD diagnosis according to DSM-IV-TR (APA, 2000), the sensitivity and specificity of the MOXO-CPT were calculated using these criteria. Results of ROC analyses are presented in table 3. The table shows the cut-off points, sensitivity and specificity rates of the MOXO-CPT, based on the total scores of the MOXO-CPT (taking into account all four parameters). Different sensitivity and specificity rates could be used for different purposes of the test (e.g., screening, diagnosis). However, we have used the optimal value which represents the maximized classification accuracy with the highest sensitivity and specificity rates. Results showed that in all age categories, the optimal cut-off points were associated with both high sensitivity and specificity rates (all above 80%).

Figure 3 presents an example of a ROC analysis, in a group of children aged 8-9 years. As can be seen in the figure, the total score of the MOXO-CPT produced the highest sensitivity and specificity rates, as compared to any single parameter.

Discussion

The current study investigated the diagnostic utility of the MOXO-CPT (Berger & Goldzweig, 2010) for the assessment of ADHD in a sample of children aged 7-12 years. Results showed that the MOXO-CPT significantly discriminated between children with ADHD and their unaffected peers of the same age. As measured by the MOXO-CPT, children with ADHD were more inattentive, more impulsive and more hyperactive than normal controls of the same age. In addition, they had more difficulties in responding on accurate timing. The largest difference between ADHD and non-ADHD children was revealed in the total score of the test. Moreover, the total score of the MOXO-CPT yielded the highest sensitivity and specificity rates, as compared to any single parameter. Given the complexity of ADHD etiology and clinical manifestation, it is little wonder that the total score of the MOXO-CPT was superior to any single parameter in identifying ADHD. This finding emphasizes the importance of integrating several different attention parameters in measuring attention functions.

Results of the ROC analyses showed that the MOXO-CPT was highly accurate in identifying participants with ADHD, based on the DSM-IV-TR (APA, 2000) criteria. For all ages, optimal cutoff values were associated with both high sensitivity and specificity rates (above 80%).

Selection of a threshold for a screening test is best achieved according to the needs of the specific setting in which it is to be used. 'Optimal' cutoff values vary depending on the risk-benefit ratio between false positive and false negative test results and the base rate of the target disorder in the population at hand. Important information may be lost when defining sensitivity and specificity in relation to a single cutoff value of a continuous variable (Sox, 1986). The discussion regarding which are the best criteria for diagnosis is beyond the scope of this study.

The literature has long been debating the reliability and validity of using CPT tests for case identification and diagnosis of ADHD (Dickerson et al., 2001; Skounti et al., 2007). Low validity of CPT tests may not only lead to inaccurate diagnosis but could also prevent effective intervention and might further complicate the symptoms in the long term (Sonuga-Barke, Koerting, Smith, McCann, &Thompson, 2011).

The MOXO-CPT has several advantages that may make it preferable for use in clinical and diagnostic settings. Due to the presence of distracters, the MOXO-CPT could be construed as more ecologically valid. It also allows monitoring the impact of distracting stimuli on the attention performance of ADHD children.

In addition, the tests' indices of ADHD symptoms are more accurately defined. Thus, the test could distinguish hyperactive behavior from impulsive behavior. Moreover, the timing ability was re-conceptualized, so the test could measure two different types of problems: difficulties to sustain attention and difficulties in responding on accurate timing. The findings of this study are therefore of great value since they offer a sensitive, objective assessment tool in assessing ADHD symptomatology.

Several limitations of this study should be considered. The first limitation results from the study's sampling method. Participation in the study was based on a voluntary agreement of children and their parents. This self-selected sampling strategy tends to be biased towards favoring more cooperative and motivated individuals. Therefore, it is not possible to determine whether this sample also represents other children that were not recruited and whether cooperation is confounded with ADHD variables. This limitation is typical to most clinic-based ADHD studies around the world (Gau et al., 2010; Lee & Ausley, 2006).

Moreover, the clinics from which ADHD children were recruited were based in tertiary care hospital. This population has heterogeneous background characteristics including those correlates of ADHD. On the other hand, the fact that the control group was recruited from a random population supports our findings by showing that the test is able to identify the ADHD children from a random population sample.

Another limitation of the study is the exclusion of ADHD children with severe comorbidities. Since ADHD is associated with many psychiatric disorders (Gentile, Atiq, & Gillig, 2006) this exclusion limits the generalization of our results.

Future research should explore the psychometric properties of the MOXO-CPT in other age groups, in samples with comorbid features, and in different sub-types of ADHD.

Despite its shortcomings, this study suggests important information about using CPT in clinical and empirical settings, and may be a first step towards a more accurate and objective diagnostic process of ADHD.

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Table 1: Participants' Background Variables

Age category		ADHD (N=339)	Control (N=459)	
7	N	62	64	
	Male	40 (64.52)	37 (57.81)	χ^2(1, N=798) =1.14, p=0.29
	female	22 (35.48)	30 (42.19)	
8		67	75	
	Male	47 (70.15)	50 (66.67)	χ^2(1, N=798)=0.37, p= 0.55
	female	20 (29.85)	25 (33.33)	
9	N	67	71	
	Male	37 (64.91)	46 (64.69)	χ^2(1, N=798)=0.0004, p=0.98
	female	30 (35.09)	25 (35.31)	
10	N	62	87	
	Male	35 (56.45)	47 (54.02)	χ^2(1, N=798)=0.15, p=0.70
	female	27 (44.55)	40 (45.98)	
11	N	51	87	
	Male	32 (62.74)	55(63.21)	χ^2(1, N=798) =0.01,p=0.94
	female	19 (37.26)	32(27.79)	
12	N	40	74	
	Male	24 (60)	44 (59.46)	χ^2(1, N=798) =0.01,p=0.94
	female	16 (40)	30 (40.54)	

Table 2: Differences between ADHD children and non-ADHD children in MOXO-CPT performance

Age category (Years)	MOXO-CPT parameter	ADHD (N=339)		Control (N=459)		t	df	*p*(2-tailed)
		Mean	(S.D)	Mean	(S.D)			
7	Attention	216.05	(28.44)	248.92	(9.57)	-8.75	124	<0.001
	Timing	138.10	(31.35)	190.17	(22.94)	-10.66	124	<0.001
	Hyperactive	54.81	(43.38)	28.70	(19.04)	4.40	124	<0.001
	Impulsivity	19.32	(11.65)	14.73	(8.72)	2.51	124	0.01
	Total Score	262.38	(78.96)	138.78	(42.23)	11.00	124	<0.001
8	Attention	228.90	(23.07)	251.36	(9.02)	-7.79	140	<0.001
	Timing	148.10	(28.74)	197.32	(23.29)	-11.26	140	<0.001
	Hyperactive	52.54	(37.69)	23.13	(16.37)	6.14	140	<0.001
	Impulsivity	20.13	(18.88)	14.59	(8.61)	2.29	140	0.02
	Total Score	229.04	(67.32)	120.30	(39.20)	11.91	140	<0.001
9	Attention	237.19	(23.88)	253.93	(8.79)	-5.47	136	<0.001
	Timing	167.32	(33.17)	207.89	(23.79)	-8.05	136	<0.001
	Hyperactive	42.65	(30.72)	21.97	(15.90)	4.91	136	<0.001
	Impulsivity	19.35	(12.92)	13.97	(7.91)	2.90	136	0.004
	Total Score	189.71	(55.46)	107.04	(33.24)	10.44	136	<0.001
10	Attention	247.19	(14.68)	256.55	(7.34)	-5.12	147	<0.001
	Timing	184.89	(31.20)	220.14	(20.94)	-8.20	147	<0.001
	Hyperactive	41.37	(31.69)	18.16	(12.39)	6.21	147	<0.001

	Impulsivity	20.61	(14.42)	14.06	(6.37)	3.76	147	<0.001
	Total Score	159.70	(46.35)	85.47	(31.18)	11.69	147	<0.001
11	Attention	247.88	(14.81)	257.24	(6.22)	-5.17	136	<0.001
	Timing	192.67	(28.28)	224.71	(20.45)	-7.69	136	<0.001
	Hyperactive	43	(37.01)	15.48	(12.18)	6.38	136	<0.001
	Impulsivity	19.84	(14.58)	12.85	(6.85)	3.81	136	<0.001
	Total Score	151.29	43.97	75.02	(29.51)	12.18	136	<0.001
12	Attention	249.50	(15.74)	258.44	(4.98)	-4.50	112	<0.001
	Timing	202.73	(26.84)	228.13	(16.90)	-6.19	112	<0.001
	Hyperactive	40.55	(52.15)	13.013	(10.23)	4.40	112	<0.001
	Impulsivity	18.70	(13.26)	12.42	(7.15)	3.29	112	0.001
	Total Score	134.70	(59.01)	66.82	(23.64)	8.71	112	<0.001

Table 3: Psychometric Properties of the MOXO-CPT

Age category (years)		Optimal
7	cutoff	184.60
	Sensitivity	86%
	Specificity	85%
8	cutoff	167.98
	Sensitivity	91%
	Specificity	88%
9	cutoff	144.98
	Sensitivity	90%
	Specificity	85%
10	cutoff	110.88
	Sensitivity	81%
	Specificity	85%
11	cutoff	107.89
	Sensitivity	86%
	Specificity	89%
12	cutoff	91.82
	Sensitivity	85%
	Specificity	85%

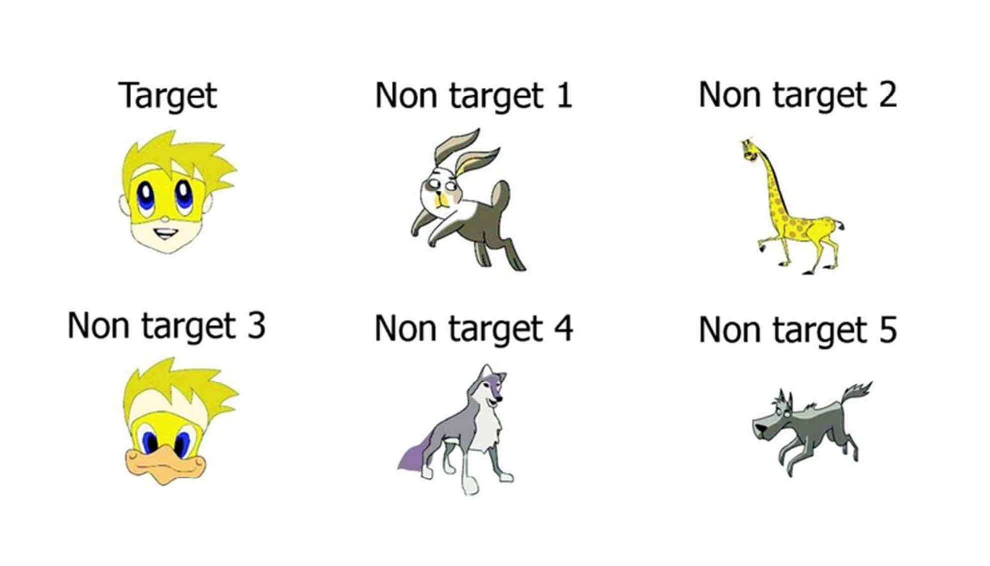

Figure 1
67x38mm (300 x 300 DPI)

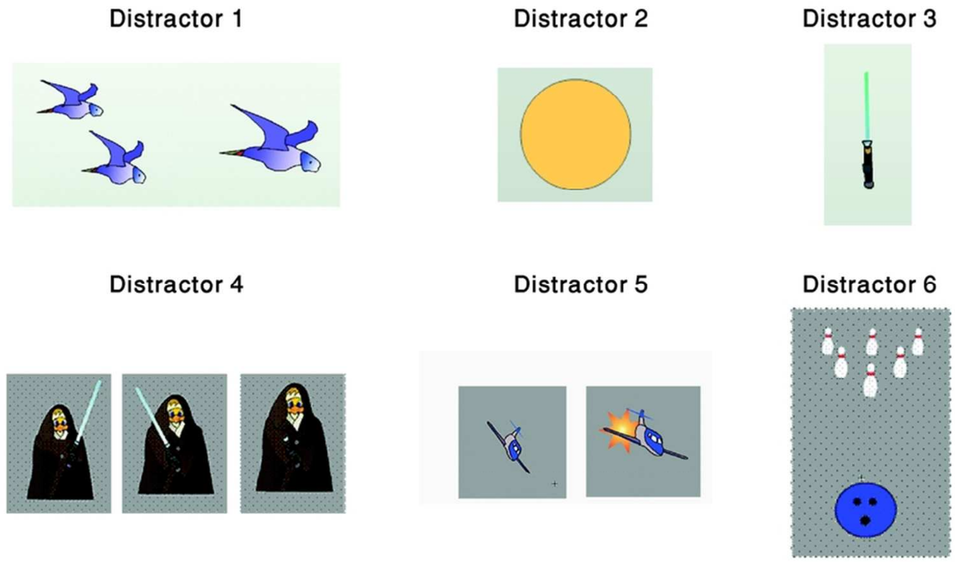

Figure 2
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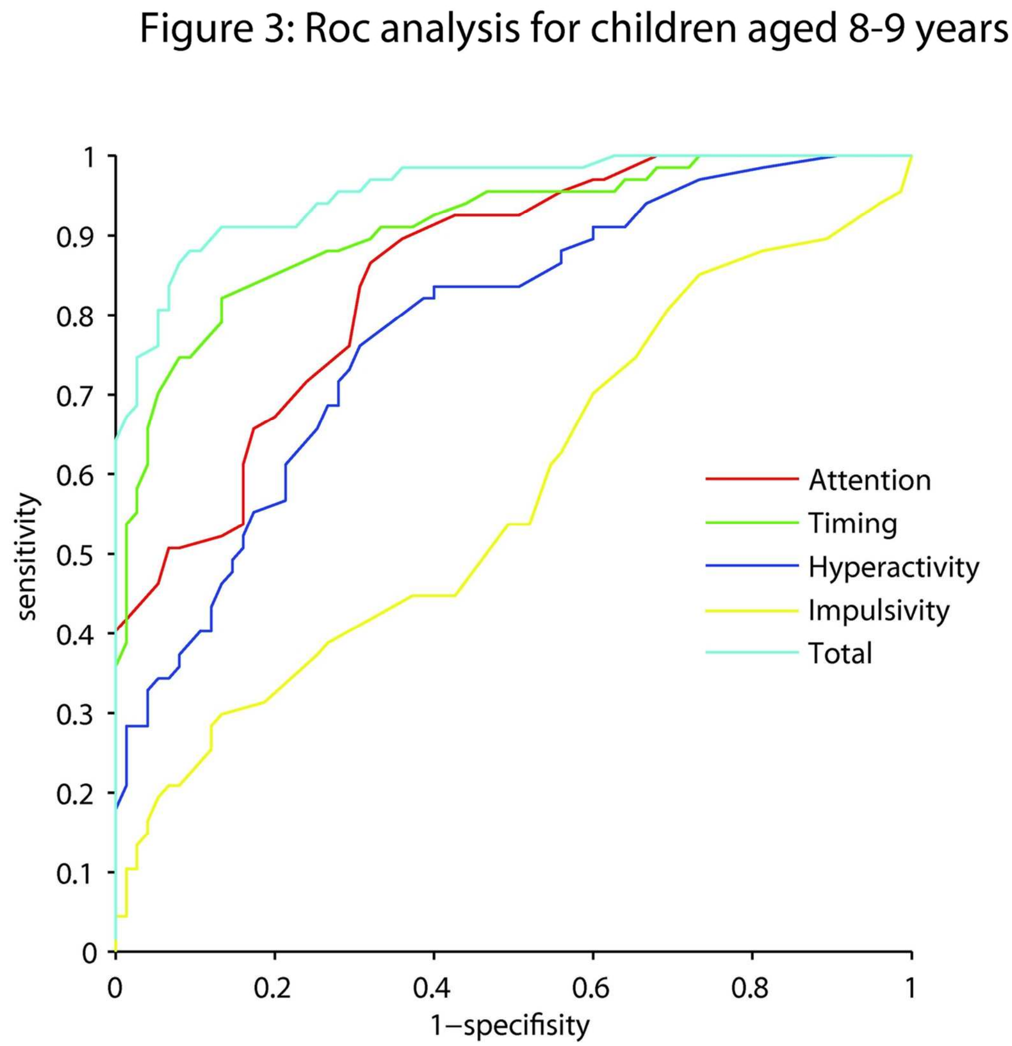

Figure 3
117x122mm (300 x 300 DPI)