Objective Measures of Attention-Deficit/Hyperactivity Disorder: A Pilot Study

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ABSTRACT: **Background:** Most aspects of attention-deficit/hyperactivity disorder diagnosis rely on subjective judgment. Computerized continuous performance tests are designed to improve the validity of the process but are controversial due to low odds ratios. There is a need to find more definitive measures of assessment.

Objectives: To test the validity and reliability of a new tool, a computerized continuous performance functions test, which includes a multi-task approach designed to achieve a higher odds ratio of assessment.

Methods: We applied this test to 58 children aged 6–12 years: 45 were diagnosed as ADHD and 13 non-ADHD children served as a control group.

Results: The CPF test was able to differentiate between non-ADHD and ADHD children. CPF test results were more accurate than other continuous performance tests. The results were statistically significant in all test parameters, confirming the test's validity and reliability.

Conclusions: The CPF test includes a combination of tasks based on an algorithm designed to test several domains of attention. In this pilot study the CPF test was found to be a valid and reliable tool for the diagnosis of ADHD in children. This test might increase the diagnostic utility of computerized tests. The research points to the need for developing a more definitive process for ADHD diagnosis.

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Attention-deficit/hyperactivity disorder is among the most prevalent chronic health conditions affecting school-age children [1,2]. Extensive research has helped characterize biological and genetic components involved in ADHD [3,4]. Several different types of attention domains were recognized; moreover, the individual child's performance can lead to different "subtypes" of ADHD, a fact that complicates the diagnostic procedure [2,5]. It was expected that genetic studies would become part of the diagnostic procedure. Geneticists and neuroscientists are now "well aware that genes do not control behaviors directly, that almost all behavioral traits emerge from complex interactions between multiple genes and environments, and that the brain bases of both personality and psychopathology are distributed across complex neural networks and are usually not caused by single loci" [6]. Therefore, the diagnosis of ADHD is still mainly characterized by a structured interview based on DSM-IV-TR clinical criteria, together with behavior rating scales [7,8]. This process is subjective and might be easily biased [9]. There has long been interest in developing laboratory parameters that could support the diagnosis [10]. The interest stems from the potential advantages that objective laboratory measures might have over more traditional measures [10]. This was the rationale for the invention of computerized continuous performance tests. But the clinical utility of different CPTs was found to be low and is the subject of much controversy due to inconsistent validity results [9,11,12]. Most studies do not provide support for the validity of the CPT as an attention measure, and they failed to demonstrate the discriminant validity of any CPT score regardless of the behavior rating scales used [9,13]. Most researchers concluded that the data supporting the validity of CPT are limited and there is a need for further validity studies [9,12,14]. The American Academy of Pediatrics concluded that CPTs are not useful in ADHD assessments [9].

In this pilot study we introduce a computerized test designed to diagnose ADHD. The test is termed a Continuous Performance Functions test since it includes a combination of tasks and is based on an algorithm testing several domains of attention in order to increase its diagnostic utility. The aim of this pilot study was to test the validity and reliability of the CPF test in the diagnosis of ADHD in children, compared to the 'gold standard'.

SUBJECTS AND METHODS

The study was conducted in an outpatient clinic of a neuropediatric unit in a tertiary care university hospital. The study

ADHD = attention-deficit/hyperactivity disorder
CPF = continuous performance functions

CPT = continuous performance tests

population comprised 58 children aged 6–12 years; 13 of them served as a control group: 7 (54%) boys and 6 (46%) girls with a mean age of 10.50 years (standard deviation 1.81). These children were healthy and did not show any symptoms or signs of ADHD, according to their parents' rating scales and reports. The study group included 45 children: 32 (71%) boys and 13 (29%) girls with a mean age of 9.86 years (SD 1.89). ADHD diagnosis was established by a certified pediatric neurologist based on DSM-IV-TR criteria [7] after an interview with the child and parents; a neurologic examination, the completion of DSM-based questionnaires by parents and teachers, and neuropsychologic evaluation confirmed the diagnosis. The children in the study group also completed a CPT: either TOVA or Conners [15,16]. All 58 children completed the CPF test while not under the influence of any medication. All the children in the study were drug naïve.

Inclusion criteria were: children aged 6–12 years, diagnosed as ADHD and otherwise healthy. Exclusion criteria were: mental retardation, a chronic condition other than ADHD, chronic use of medications, and children diagnosed with depression, anxiety or psychosis. Since we work in a tertiary care center in Jerusalem our population is extremely variable and multicultural and includes a spectrum of families with regard to potentially confounding factors correlated with the diagnosis of ADHD.

Ethical approval was obtained from the Internal Review Board (Helsinki Committee) of Hadassah-Hebrew University Medical Center. The study was registered in the NIH (NCT00646464 – ClinicalTrials.gov). All children agreed to participate in the study and all parents signed an informed consent form.

CPF TEST DESCRIPTION

The system includes software only, compatible with any computer with an internet browser and flash player installed (developed by Neurotech Solutions Ltd, Kfar Mordechai, Israel). A set of target and non-target stimuli (other than letters or numbers) was shown in the middle of the computer screen. The child was instructed to respond (as quickly as possible) to the "target" stimuli by pressing the keyboard's space bar only, and only once. The child was instructed to avoid responding to all other stimuli or pressing any other key. The CPF test is based on an algorithm designed to test several domains of attention by including a multi-task approach. The test contains 8 levels, each one 114 seconds long. Every level consists of the same measurable elements (target and non-target) shown in the same sequence. At each sub-level, the duration of each element presentation changes in the same manner (3 sec, 1 sec, 0.5 sec). Every level has a different set of disturbances: two levels (first and last) contain only target and non-target stimuli without further disturbances. Two levels contain visual disturbances, two levels contain audio disturbances, and two levels contain a combination of both visual and audio disturbances. In each set of two levels, there are low and high grades of disturbances. Between each two disturbances, there is a 0.5 second gap ("void time"). Since the CPF test measures reaction time with millisecond precision it can demonstrate children who are "slow but accurate responders." There are several age-appropriate difficulty levels, so the test can be applied to different age groups. The duration of the study is 15.2 minutes.

SD = standard deviation

ANALYSIS

The user's actions/inactions are measured and analyzed according to the elements shown on the screen. The system counts the number of times the spacebar is pressed or not pressed at each level in relation to the shown elements. It also registers the time lapse from appearance of the element until the spacebar is pressed and if other computer keys (not the spacebar) are pressed. In order to find a performance pattern the system can also compare the grades and presses among the different levels.

OUTPUT

After the test was over a conclusion panel (report) was shown. The report automatically presented a list of measurements, as table and graphs, based on the individual's performance pattern [Figures 1 and 2]. In this study, four parameters were evaluated:

- Attention (A): counting response to target stimuli = "good press" which measured sustained attention.
- Hyperactivity (H): number of times that the child presses any key (if more than once) = press commission, which measured response inhibition.
- Impulsivity (I): counting "bad press" = a response to non-target stimuli, measured distractability.

Figure 1. CPF test results of a child from the control (non-ADHD) group

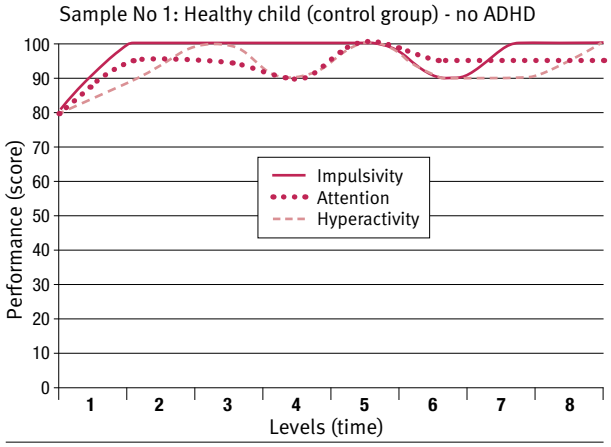
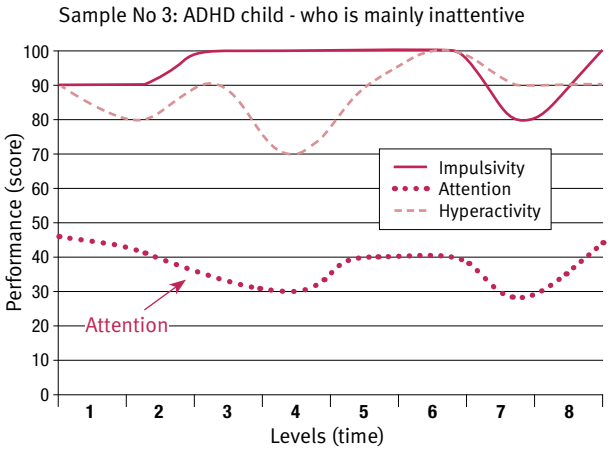


Figure 2. CPF test results of a child from the study (ADHD) group who is mainly inattentive



- Reaction time (RT) = counting the time lapse from every element appearance until spacebar pressing. In each parameter the child could react in a different way when visual, auditory, spatial and integrated attention was needed, since each of the eight levels had a different set of disturbances.

STATISTICAL ANALYSIS

SPSS 14 Program, release 14.02.2 (17 March 2006), was used for all statistical analyses. First, we calculated the percentages of true positives (ADHD indication) for each of the CPTs, with 95% confidence interval for each of the percentages. Then, an overall comparison was performed between the CPF test indexes comparing study and control groups by means of MANOVA. Later, the univariate ANOVA was calculated to determine the exact sources of differences between the groups. Logistic regression was performed to determine the ability of the CPF test indexes to differentiate between the groups.

RESULTS

One objective of this study was to test the reliability of the CPF test analysis among children aged 6–12 years. Table 1 presents the percentages of "true positive" (ADHD indication) among the 45 study group children. True positive was found for 75% using TOVA [15] (false negative 25%), for 52% using the Conners CPT [16] (false negative 36%), and for 64% using both together (false negatives 46% with a confidence interval of 21–50%). The true positive percent for the CPF test was 100%. Therefore, the TOVA/Conners tests showed a relatively low sensitivity by diagnosing only 29 children (64%) in the study group as ADHD. These results are compatible with the results reported in the medical literature [9,11,13]. Another objective was to test the validity of the CPF test diagnosis by comparing the test performance of the study (ADHD) group to that of the control group. Four indexes were calculated for the CPF test results: Attention (A), Hyperactivity (H), Impulsivity (I) and Reaction Time (RT). Table 2 compares the performance between the study and control groups. The MANOVA resulted in an overall difference between the groups. All the univariate analyses (A, H, I, RT) were found to be significant, meaning that there was a significant difference between the groups in every index. The logistic regression model based on all the indexes was significant [chi-square(4)=41.1, $P < 0{,}0001$; Cox & Snell R square=0.507]. One subject from the control group was classified as belonging to the research group, and two subjects from the research group as belonging to the control group. Thus, the overall correct classification percentages were 94.8%. These results demonstrated that the CPF test differentiated between non-ADHD and ADHD children. Figure 1 presents the test results of a child from the control (non-ADHD) group. Figure 2 shows the results of a child from the study (ADHD) group who was mainly inattentive.

Table 1. True positive CPT results in the study group

		Confidence interval 95%	
Test	**ADHD indication**	**Lower limit**	**Upper limit**
Conners	13 (52%)	31%	73%
TOVA	12 (75%)	51%	99%
Conners+TOVA	29 (64%)	50%	79%
CPF test	45 (100%)		

DISCUSSION

Since ADHD children may experience significant functional problems, early recognition and management can redirect the educational, medical and psychosocial development of most children [9,17,18]. Several different "involved" genes were recognized as well as different types of attention domains – visual, auditory, spatial, integrated, sustained, covert and overt, among others [3-5]. In the absence of an

Table 2. Means and SDs of CPF test indexes for each study group

	Study group			Control group			ANOVA	
	N	**Mean**	**STD**	**N**	**Mean**	**STD**	**F(1,56)**	***P***
Attention	45.00	207.89	38.99	13.00	244.23	17.78	10.55	‹ 0.0020
Hyperactivity	45.00	15.20	19.19	13.00	1.54	1.90	6.49	‹ 0.0136
Impulsivity	45.00	18.22	15.76	13.00	7.23	3.70	6.15	‹ 0.0161
Reaction Time	45.00	0.53	0.08	13.00	0.42	0.04	19.13	‹ 0.0001

*MANOVA: F(6,47) = 4.70, $P < 0.001$*MANOVA F(4,53) = 5.88, $P < 0.001$

available "biological marker" that would support a diagnostic test, clinicians are asked to continue to use clinical criteria and rating scales [2,9]. The major difficulty is that judgment and experience are needed to appreciate what is "usual" for an individual child. The impact of subjectivity on symptom assessment is considerable [19]. That is the reason for the quest for objective laboratory parameters of ADHD, which hold the promise to be cost effective, are relatively free of bias, provide immediate information, are easily administered, rely only on the individual being evaluated, and can be administered in a variety of settings [10]. This explains why CPT, although not recommended by the American Academy of Pediatrics, was reported to be the most popular clinic-based computerized tool to diagnose ADHD [20].

Studies of the CPT's validity had mixed results [9,11]. These tests measure the number of correctly detected stimuli as well as response time [9,11,15,16]. The diagnosis is based mainly on visual performance and usually ignores other measures of attention [9,14,15]. This might explain why the available tests suffer from relatively high false negative errors and low overall utility. As much as one-third of the children who fulfill DSM-IV-TR criteria for ADHD can escape detection when tested by CPT [9,11]. This study tried to overcome the technical barriers by using a test that was developed while taking into consideration the recommendations of previous studies. Therefore, the CPF test includes a multi-task approach designed to objectively assess several domains of attention and is intended for clinical use. All this would have failed had the test not been valid and reliable in differentiating between children with and without ADHD. Therefore, the main objective of this study was to test this ability.

The results of this pilot study showed that the CPF test is valid for the diagnosis of ADHD in a population of children aged 6–12. The differences in performance in all tested parameters between the study and control groups were statistically significant.

The CPF test also proved to be reliable for ADHD diagnosis, and more sensitive than CPT in this small group of children. In this pilot study, the CPT had a relatively high false negative rate of 36%, which concurs with the results of previous studies [9,11,13].

This study has several limitations: there is a clear dichotomy between the selected ADHD and control group. This is because the study objective was to test validity and reliability of an unknown diagnostic tool. This also explains the fact that the ADHD group was without severe comorbid features. We assume that this should be the first but not last step towards a robust validation of the CPF test. We also assume that if the differences are significant in a relatively small group, it might be significant in larger cohorts, but this point requires further research. There is a need to retest the results of this study in larger cohorts, build a solid normal range of performance in the general population to better discriminate between ADHD and the comorbidities associated with the disorder, and test validity and reliability among other populations (adolescents, adults, preschoolers and children with and without different comorbidities).

This study might be a helpful step towards more accurate and objective diagnosis since it points to the need for additional information on the reliability and validity of ADHD diagnostic methods. Further research is needed to develop better modalities of assessment that can be applied practically in the primary care setting to reach a more definitive process of ADHD diagnosis.

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