

Hyperactivity • Impulsivity • Inattention

Objectively measure neural control functions related to the core ADHD symptom domains.



Quotient[®]
ADHD test

Concrete Data to Inform Clinical Decisions

- Use the Quotient[®] ADHD Test at the initial visit to quantify the severity of deficits related to hyperactivity, impulsivity and inattention. Objective evidence streamlines the conversation with the patient.
- Re-assess new patients in 3-6 weeks to evaluate progress toward goals and to help guide treatment planning.
- Test established patients periodically at med check visits to supplement clinical information.

Simple Test Procedure

Trained paraprofessionals can administer the test

- Input demographics, diagnostic information and medications.
- Explain the test to the patient. Run a 30-second practice test. Repeat as needed.
- Start the test.

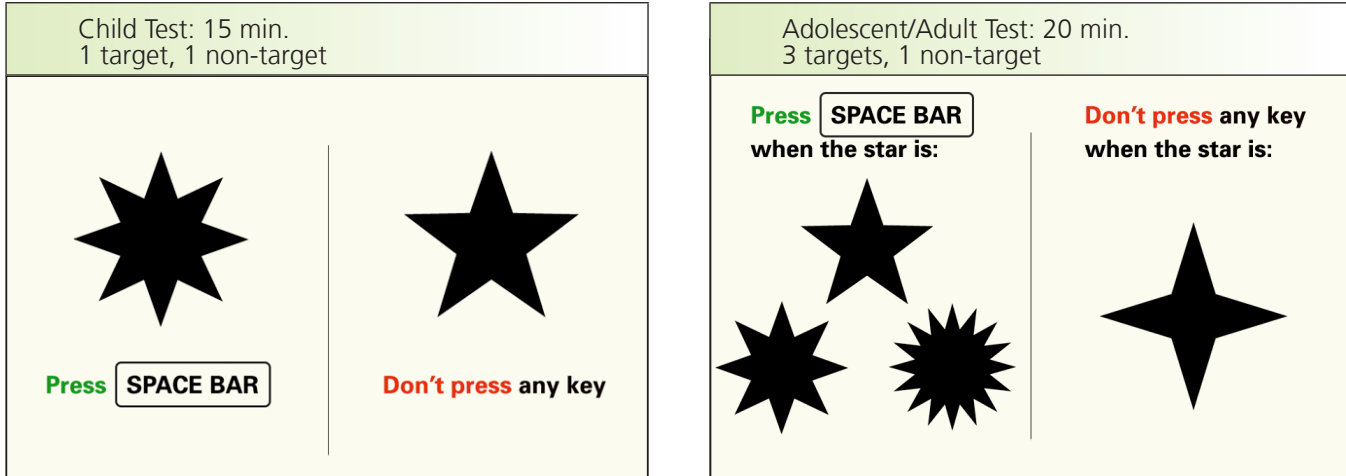


Figure 1. Screen shots of the Child and Older Adolescent/Adult Quotient® ADHD Tests.

The Quotient® ADHD Report

Composite Scores

Quotient ADHD system
 Clinician Name: BioDx Marketing
 Patient Name: Tony BioDx
 Test Date: Jun 23 2008 9:38 am
 Date of Birth: May 24 1996
 Gender: M Age: 12

QUOTIENT™ ADHD SYSTEM INDEX
 The Quotient™ ADHD System Index includes 19 indices, 6 for motion and 13 for attention. The resulting index is the degree of agreement between the Quotient™ ADHD Test results of this patient and patients with ADHD.

Unlikely Possible Probable Likely

QUOTIENT™ ADHD SYSTEM SCALED SCORES
 The Quotient™ ADHD System Scaled Score consists of:
 • Motion Scaled Score - a composite of how this patient's motion compares to the community sample.
 • Attention Scaled Score - a composite of how this patient's attention compares to the community sample.
 • Global Scaled Score - demonstrates the combination of indices for this patient as compared to the community.

High scaled scores are associated with the scores that patients with ADHD receive.

High Motion	Inattention	Global Scaled Score
8.214	7.521	8.114

Related Definitions
 • Patients with ADHD = Individuals who have met the DSM-IV criteria for the diagnosis of ADHD in a clinical setting and received a Quotient assessment.
 • Community Sample = Individuals representing a cross-sectional sample of the general community (irrespective of diagnostic status) and who received a Quotient assessment.

DISCLAIMER
 The test interpretation should be used as part of a comprehensive diagnostic process and not as a substitute for the diagnostic process itself.

Motion Analysis

Quotient ADHD system
 Clinician Name: BioDx Marketing
 Patient Name: Tony BioDx
 Test Date: Jun 23 2008 9:38 am
 Date of Birth: May 24 1996
 Gender: M Age: 12.08 Grade: 6

MOTION ANALYSIS
 Motion Capture by Corresponding Reflector Location

Measures

Measure	Reflector Location
Immobility Duration: (m/seconds) The average amount of time spent sitting path.	Head
Reversions: (number) The number of position changes.	Head
Displacements: (meters) The total distance moved by the marker.	Head
Area: (coordinates) (square) The total area covered by the marker's path.	Head
Spatial Complexity: (scale score) The complexity of the movement path. Lower values indicate linear or back and forth movement; higher values indicate more complex movement.	Head
Temporal Scaling: (scale score) The pattern of movement in time. Lower value indicate lack of movement; higher values indicate increased movement.	Head

Attention Task

Quotient ADHD system
 Clinician Name: BioDx Marketing
 Patient Name: Tony BioDx
 Test Date: Jun 23 2008 9:38 am
 Date of Birth: May 24 1996
 Gender: M Age: 12.08 Grade: 6

ATTENTION ANALYSES
 Patient's Response to Targets and Non-Targets

Patient's Response Results

Measure	Results	Reference Range (16-84 Percentile)
Accuracy: (percent) The percentage of correct responses.	83.3	72.2 - 95.0
Omission Errors: (percent) The percentage of missed targets (a measure of inattention).	10.2	0.4 - 13.8
Commission Errors: (percent) The percentage of incorrect responses to non-targets (a measure of impulsivity).	23.4	7.7 - 45.7
Latency: (m/seconds) The average amount of time to respond correctly (speed).	508	366 - 532
Variability: (m/seconds) The variation in response time to the correct target.	137	89 - 183
C.O.V.: (number) A normalized measure of response time variation.	27	20 - 39

Attention State Analysis

Quotient ADHD system
 Clinician Name: BioDx Marketing
 Patient Name: Tony BioDx
 Test Date: Jun 23 2008 9:38 am
 Date of Birth: May 24 1996
 Gender: M Age: 12.08 Grade: 6

ATTENTION ANALYSES CONTINUED
 Attention States During Testing

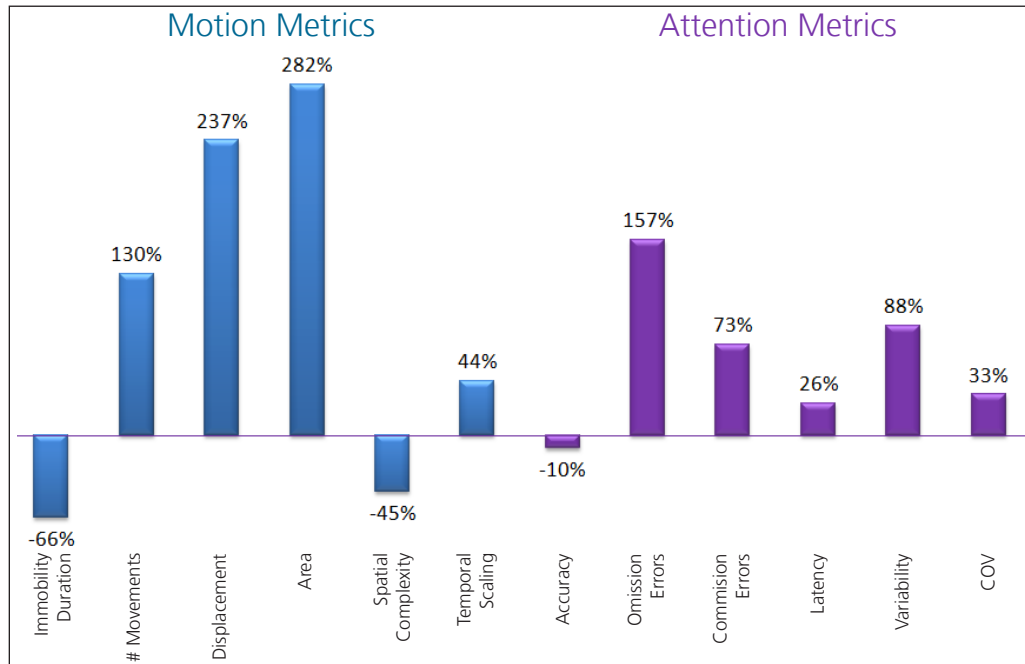
Attention State Results

Measure	Results	Reference Range (16-84 Percentile)	Age Percentile (N = 24 Age Percentiles)
Number of Shifts: (number) A measure of how many times a change in behavioral states occurs over the course of a test.	23	5 - 18	2
Attentive: (percent) Percent of all recorded blocks in which subjects performed with very high level of accuracy.	33.0	10.0 - 90.0	34
Impulsive: (percent) Percent of blocks when subjects performed better than chance but made a significant number of commission errors.	33.3	6.7 - 53.3	43
Disengaged: (percent) Percent of blocks when subjects performed better than chance but missed a significant number of targets.	26.7	0.0 - 16.7	1
Random: (percent) Percent of blocks in which subjects performed no better than predicted by random chance.	3.3	0.0 - 20.0	45
Minimal: (percent) Percent of blocks when subjects performed no better than predicted by random chance and made few responses.	3.3	0.0 - 3.3	18
Contrary: (percent) Percent of blocks when subjects performed worse than predicted by random chance.	0.0	0.0 - 0.0	99

Generate the report in minutes

- Upload the raw data from the Quotient® ADHD System via the secure internet portal.
- Download the report from any computer connected to the internet.
- Discuss the results with the parent or patient. Concrete data makes the conversation more efficient.

Differences in Micro-motion and Attention Metrics in ADHD vs. Controls²



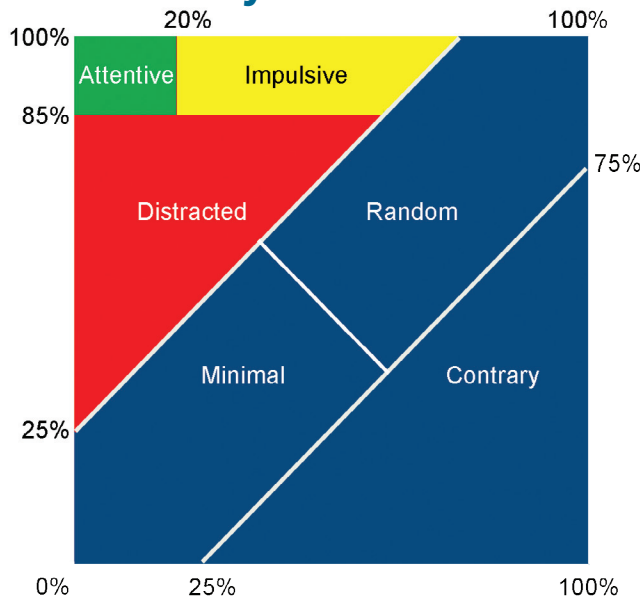
Methods

- 18 boys (9.3±2.4 yrs) with ADHD
- 11 controls (8.3 ± 1.8 yrs)
- The Quotient® ADHD System measures micro-motion of the head 50 times per second using an infrared Motion Tracking System.

Conclusions

- Six motion parameters are reported along with graphs.
- This study demonstrated that the precision of infrared technology and laboratory quantification of micro-motion along with attention had significant power to discriminate children with ADHD from normal controls.

Attention State Analysis in Children with ADHD⁵



Definitions for Attention States

Attentive Good level of accuracy (>85%) with limited errors of omission or commission

Impulsive Good level of accuracy (>85%) with significant errors of commission

Distracted Fair level of accuracy (>50%) with significant errors of omission

Disengaged Accuracy no better than chance (<50%) with patient responding in a disengaged manner

- **Random:** patient performed no better than random chance
- **Minimal:** patient performed no better than random chance **and** made few responses to presented targets
- **Contrary:** performed worse than random chance

Study Overview

- 60 boys (10.6 ± 1.1 years) with combined type ADHD
- 8 healthy controls (11.3 ± 2.0 years)

Results

- Attention state shifts are more robust indicators of ADHD vs. non-ADHD than standard attention metrics.
 - Attention state shifts are more significantly affected by methylphenidate than standard attention metrics.
 - Effect size measures the difference between the mean of two groups divided by their pooled SD. Convention in the social sciences defines an effect size as follows:
 - 0.2 - 0.3 is "small",
 - 0.4 - 0.5 is "medium"
 - 0.8 or greater is "large"
- Ideally, a diagnostic test should have effect sizes substantially greater than 1.

	ADHD	Normal	Effect Size	On Meds	Effect Size
Attention Analysis					
Commission Errors	27.9%	11.6%	0.89	13.6%	1.91
Omission Errors	13.1%	1.2%	0.87	5.0%	1.11
Latency	537 ms	619 ms	1.06	500 ms	1.28
Variability	179 ms	134 ms	0.84	123 ms	2.10
Attention State Analysis					
# Attention Shifts	12.8	5.4	1.67	7.0	2.14
% Attentive	42.6%	82.4%	1.37	75.4%	2.45
% Impulsive	32.7%	14.8%	0.97	18.1%	1.41
% Distracted	11.0%	1.9%	0.75	2.3%	1.47
% Disengaged	13.6%	0.9%	0.62	4.2%	1.03

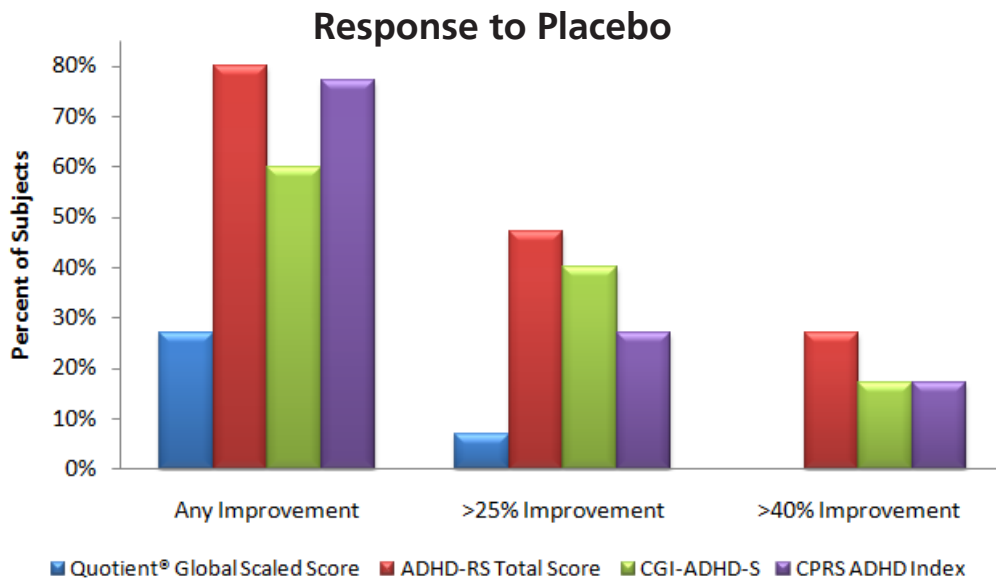
Evaluate the dose and medication for the individual patient

Placebo effect confounds subjective rating scales⁶

- Placebo does not produce significant changes in the behavior of school-age children with ADHD.
- Adults who evaluate children with ADHD tend to complete rating scales more positively when they believe the child has been administered medication, even when medication has not actually been administered. Up to 30% of improvement in ADHD rating scales has been attributed to placebo effect.

The Quotient[®] ADHD Test objectively measures response to treatment⁷

- Double-blind design, N=30 (25 boys, 5 girls), age 9.4 ± 2.13 , with ADHD

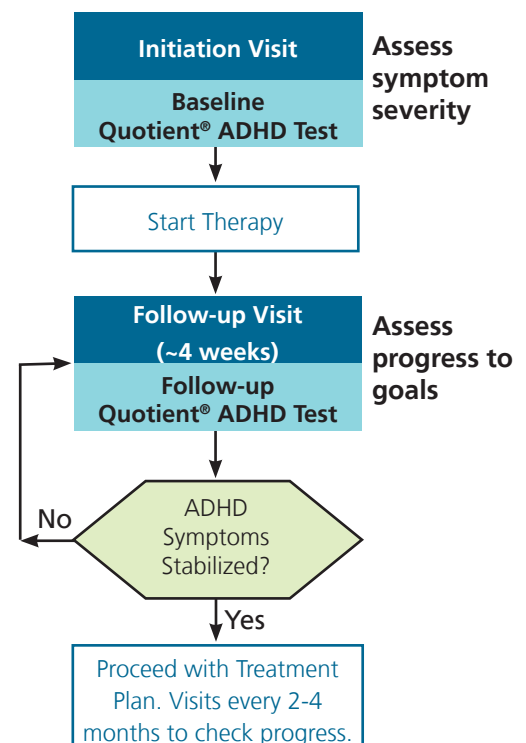


Guidelines and Workflow

Summary of AAP, AACAP and HEDIS Guidelines for Follow-up Care for Children Prescribed ADHD Medication⁸

- Systematic monitoring of dosage and side effects is recommended.⁹
- *Initiation Phase*: Schedule an office visit in the first 30 days to monitor medication tolerance, side effects and progress.¹⁰
- *Continuation and Maintenance Phase*: Schedule office visits at least monthly until symptoms have been stabilized.¹⁰
- Once the dosing is stable, schedule office visits every 2-4 months. "The patient with ADHD should have regular follow-up for medication adjustments to ensure that the medication is still effective, the dose is optimal and the side effects are clinically insignificant."¹⁰

The Quotient[®] ADHD Test aids in the clinical assessment at critical decision points



94.3% Negative Predictive Value (NPV) and 96.2% Specificity¹¹

The Quotient® ADHD Test can help you to rule out ADHD. The combined power of measuring micro-motion and analyzing shifts in attention state makes high specificity and NPV possible.

Specificity	96.2%	True Neg / (False Pos + True Neg)
NPV	94.3%	True Neg / (False Neg + True Neg)
Sensitivity	71.5%	True Pos / (True Pos + False Neg)
PPV	79.2%	True Pos / (True Pos + False Pos)
Agreement	92.0%	(True Pos + True Neg) / Total Subjects

		ADHD Diagnosis	
		ADHD	Non-ADHD
Quotient®	ADHD	True Positive	False Positive
	Non-ADHD	False Negative	True Negative

In a pooled analysis of 853 children between the ages of 6 and 14 who were tested on the Quotient ADHD System (707 typically developing children without ADHD, and 146 children meeting DSM-IV criteria for ADHD), the results of the Quotient® assessment were consistent with the clinical diagnosis in >90% of the cases.

AUC ROC is 0.931 for the Quotient® Global Scaled Score¹¹

The area under the curve of a receiver operator characteristics curve (AUC ROC) is often used to assess classification accuracy for a diagnostic test. AUC of 0.50 reflects random chance and 1.00 gives perfect discrimination between disease and no disease. In a study by Edwards, et. al (2007) of the Connors' CPT II, the strongest measure on the test had an AUC of only 0.644 and most measures did not differ statistically from chance.¹²

Reproducible

>90% Test/Re-test Reliability Aids Assessment for Medication Management¹³

Test/re-test reliability was established for the Quotient® ADHD Test in two studies.

■ Immediate Test/Re-Test



■ Delayed Test/Re-Test



- Correlation coefficients (r) between the baseline tests and repeat tests were high.
- This means that results from re-tests reflect patient performance, not variation in the analytical method.

	Immediate Test/Re-test	Delayed Test/Re-test
N	15	17
Mean age (SD)	9.7 (6.5)	11.9 (6.4)
Boys	9	8
Girls	6	9
Correlation		
Micro-events	0.91	0.84
Accuracy	0.95	0.94
Latency	0.95	0.77

References: **1** Ohashi, K., Vitaliano, G., Polcari, A., Teicher, M.H., 2010. Unraveling the nature of hyperactivity in children with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 67, 388-396. **2** Teicher, M.H., Ito, Y., Glod, C.A., Barber, N.I.. Objective measurement of hyperactivity and attentional problems in ADHD. *J Am Acad Child Adolesc Psychiatry* 1996 35, 334-342. **3** Teicher, M.H., Polcari, A., Foley, M., Valente, E., McGreener, C.E., Chang, W.W., McKay, G., Midha, K.K.. Methylphenidate blood levels and therapeutic response in children with attention-deficit hyperactivity disorder: Effects of different dosing regimens. *J Child Adolesc Psychopharmacol* 2006 16, 416-431. **4** Abikoff, H., Courtney, M., Pelham, W.E., Jr., Koplewicz, H.S. Teachers' ratings of disruptive behaviors: the influence of halo effects. *J Abnorm Child Psychol* 1993 21, 519-533. **5** Novel Strategy for the Analysis of CPT Data Provides New Insight into the Effects of Methylphenidate on Attentional States in Children with ADHD. Teicher, MH, *Journal of Child and Adolescent Psychopharmacology*, 2004; 14 (2) 219-232 **6** Are There Placebo Effects in the Medication Treatment of Children With Attention-Deficit Hyperactivity Disorder? Daniel A. Waschbusch, *Journal of Developmental & Behavioral Pediatrics*, 2009 30(2) 158-168. **7** Does Placebo Response Differ Between Objective and Subjective ADHD Measures in Children with Attention-Deficit/Hyperactivity Disorder? Sumner, CR, Sutton, VS, Teicher, MH and Newcorn, JH. *Postgraduate Medicine*. 2010 122(5), 52-61. **8** The State of Health Care Quality 2009, National Committee for Quality Assurance, Agency for Healthcare Research and Quality, 57-59. **9** Clinical Practice Guideline: Treatment of a School-aged Child with Attention-Deficit/Hyperactivity Disorder. AAP Committee on Quality Improvement. *Pediatrics*. 2001 108(4) 1033-1043. **10** Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, J. Am. Acad. Child Adolesc. Psychiatry, 2007;46(7):894-921. **11**. Data on File. **12** Estimates of the Validity and Utility of the Connors' Continuous Performance Test in the Assessment of Inattentive and/or Hyperactive-Impulsive Behaviors in Children Edwards, MC. *J Abnorm Child Psychol* (2007) 35:393-404 **13** Rate Dependency Revisited: Understanding the Effects of Methylphenidate in Children with Attention Deficit Hyperactivity Disorder. Teicher, MH. *Journal of Child And Adolescent Psychopharmacology*,2003 13(1), p. 41-51.

