CNS Vital Signs®

CNS Vital Signs Interpretation Guide

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One Key Difference – Measuring Millisecond Precise Cognitive Speed... "CNS Vital Signs is sensitive in detecting cognitive impairment ...uses computerized forms of traditional tests such as Symbol Digit Modalities and Stroop ...are easy to use, require significantly less time to administer, produce instant scoring and can incorporate alternate forms, necessary to minimize learning effect on follow-up. ***...also, the capacity to accurately-automatically quantify "speed factor" via multiple parameters such as reaction time, psychomotor speed, and processing speed, increasing their sensitivity in detecting even subtle changes in information processing speed."*** **

** Cognitive Impairment in Relapsing Remitting and Secondary Progressive Multiple Sclerosis Patients: Efficacy of a Computerized Cognitive Screening Battery; ISRN Neurology, 2014 Mar 13

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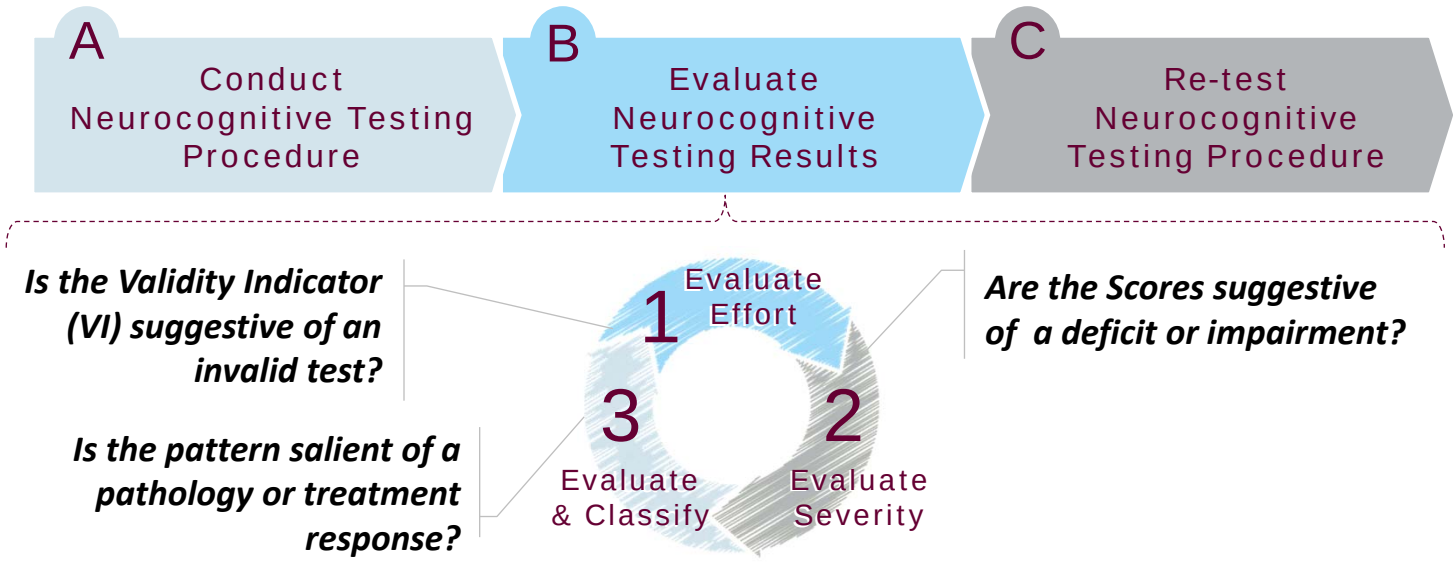
Why CNS Vital Signs Testing Platform?

CNS Vital Signs computerized neuropsychological / neurocognitive tests enables a non-invasive, customizable clinical procedure to efficiently and objectively aid in assessing a broad-spectrum of brain function domain performances under challenge (cognition stress test) and the millisecond precise measurement of important cognitive functions. The testing platform also contains 50+ well recognized, evidence-based rating instruments to help identify clinical symptoms, behaviors, and comorbidities salient to the evaluation and ongoing management of many neurological, psychiatric and other clinical conditions. Serial evaluation of neurocognition can help patients and caregivers navigate problems related to daily living, school or vocational work.



HOW?

A: After medical necessity for neurocognitive testing has been determined practices use CNS VS assessment platform for the evaluation, management and treatment in patient care. It is important to conduct a valid assessment and clinics can refer to and use the Test Administration Guide for optimal results. Testing strategy should be determined using the ten neurocognitive tests and/or the sixty plus evidenced-based rating instruments. For initial baseline evaluations or in complex presentations, a customizable broad-spectrum battery is always an appropriate consideration or starting point.

B: Review the immediately auto-scored report to 1 validate testing effort, 2 evaluate the Domain Dashboard to quickly assess the level of impairment or grade the level of severity based on age matched norms ages 8-90, and 3 Evaluate the Cognitive Domains to help rule-in, rule-out, confirm certain clinical conditions or evaluate treatment results. Feedback to the patient on the testing results may be presented at the clinical encounter or at a subsequent patient visit.

C: If invalid test results were noted then consider re-testing the patient to confirm clinical results. If the test results were valid, then, as part a continuum of care, reschedule testing to track disease progression and measure ongoing status or outcomes.

NOTE: The **Validity Indicator** denotes a guideline for representing the possibility of an invalid test or domain score. "No" means a clinician should evaluate whether the test subject understood the test, put forth their best effort, or has a clinical condition requiring further evaluation.

All assessment results should be considered with other relevant clinical information such as history, physical examination, other psychological or neuropsychological tests, lab results, imaging studies, etc., in accordance with good clinical practice standards. CNS Vital Signs is not a diagnostic. Diagnosis is a clinical exercise that relies on data from many different sources.

CNS Vital Signs Test Report Example **...Current Cognitive Status View**

*...is auto-scored from computerized versions of **VENERABLE NEUROPSYCHOLOGICAL TESTS**. The results measures the **MILLISECOND PRECISE SPEED** and **ACCURACY** of a patient's response. **TOTAL TESTING TIME** depends on the number of tests and rating instruments selected.*

CNS Vital Signs Clinical Report	**Test Date: July 23 2012 10:48:38**
Subject Reference ID: Case Study Example	**Administrator: Technician**
Age: 27	**Language: English (United States)**
Total Test Time: 29:40 (min:secs)	**Version 3,2,0,34**

Patient Profile:	Percentile Range		3	1	> 74	25 - 74	9 - 24	2 - 8	< 2
	Standard Score Range				> 109	90 - 109	80 - 89	70 - 79	< 70
Domain Scores	Subject Score	Standard Score	Percentile	VI**	Above	Average	Low Average	Low	Very Low
Neurocognition Index (NCI)	NA	85	16	Yes			x		
Composite Memory	102	103	58	Yes		x			
Verbal Memory	51	93	32	Yes		x			
Visual Memory	51	110	75	Yes	x				
Psychomotor Speed	174	93	32	Yes		x	2		
Reaction Time*	555	107	68	Yes		x			
Complex Attention*	21	56	1	Yes					x
Cognitive Flexibility	26	63	1	Yes					x
Processing Speed	48	79	8	Yes				x	
Executive Function	34	75	5	Yes				x	
Simple Attention	40	108	70	Yes		x			
Motor Speed	124	105	63	Yes		x			

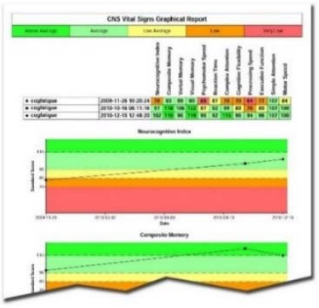
Domain Dashboard: Above average domain scores indicate a standard score (SS) greater than 109 or a Percentile Ra (PR) greater than 74, indicating a high functioning test subject. Average is a SS 90-109 or PR 25-74, indicating normal function. Low Average is a SS 80-89 o 9-24 indicating a slight deficit or impairment. Below Average is a SS 70-79 or PR 2-8, indicating a moderate level of deficit or impairment. Very Low is a less than 70 or a PR less than 2 indicating a deficit and impairment. Reaction times are in milliseconds. An * denotes th raw scores calculations generated from data values of the individual subtests.
VI – Validity Indicator:** Denotes a guideline for representing the possibility of an i or not the test subject understood the test, put forth their best effort, or has a clinical

Verbal Memory Test (VBM)	**Score**	**Standard**	**Percentile**
Correct Hits - Immediate	13	102	55
Correct Passes - Immediate	14	95	37
Correct Hits - Delay	9	85	16
Correct Passes - Delay	15	109	73
Visual Memory Test (VIM)	**Score**	**Standard**	**Percentile**
Correct Hits - Immediate	13	107	68
Correct Passes - Immediate	14	117	87
Correct Hits - Delay	13	111	77
Correct Passes - Delay	11	93	32
Finger Tapping Test (FTT)	**Score**	**Standard**	**Percentile**
Right Taps Average	64	104	61
Left Taps Average	60	105	63
Symbol Digit Coding (SDC)	**Score**	**Standard**	**Percentile**
Correct Responses	50	80	9
Errors*	2	92	30
Stroop Test (ST)	**Score**	**Standard**	**Percentile**
Simple Reaction Time*	231	108	70
Complex Reaction Time Correct*	542	100	50
Stroop Reaction Time Correct*	568	112	79
Stroop Commission Errors*	8	5	1
Shifting Attention Test (SAT)	**Score**	**Standard**	**Percentile**
Correct Responses	47	82	12
Errors*	13	75	5
Correct Reaction Time*	1003	97	42
Continuous Performance Test (CPT)	**Score**	**Standard**	**Percentile**
Correct Responses	40	104	61
Omission Errors*	0	104	61
Commission Errors*	0	108	70
Choice Reaction Time Correct*	400	99	47

The CNS Vital Signs Neurocognitive Assessment Report is designed to present the testing results in a **SUMMARY DOMAIN DASHBOARD** and a **DETAILED REPORT** format immediately following the testing session. The CNS Vital Signs reports are logical and intuitive making the reports interpretation by a qualified health professional relatively straightforward. All assessment results should be considered with other relevant clinical information such as history, physical examination, other psychological or neuropsychological tests, lab results, imaging studies, etc., in accordance with good clinical practice standards.

Serial administered neurocognitive tests can also be presented in a **LONGITUDINAL REPORT** format to track disease progression, outcomes, or treatment effects.

Longitudinal View



Evaluate Effort – Validity Indicator

Besides measuring the individual neurocognitive functioning status of an individual patient, CNS Vital Signs can aid in detection of symptom validity (Validity Indicators) issues like poor effort or secondary gain concerns like academic accommodations, drug or disability seeking, malingering, etc.

Patient Profile:	Percentile Range				> 74	25 - 74	9 - 24	2 - 8	< 2
	Standard Score Range			A	> 109	90 - 109	80 - 89	70 - 79	< 70
Domain Scores	Subject Score	Standard Score	Percentile	VI**	Above	Average	Low Average	Low	Very Low
Neurocognition Index (NCI)	NA	85	16	Yes			x		
Composite Memory	102	103	58	Yes		x			
Verbal Memory	51	93	32	Yes		x			
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Psychomotor Speed	174	93	32	Yes		x			
Reaction Time*	555	107	68	Yes		x			
Complex Attention*	21	56	1	Yes					x
Cognitive Flexibility	26	63	1	Yes					x
Processing Speed	48	79	8	Yes				x	
Executive Function	34	75	5	Yes				x	
Simple Attention	40	108	70	Yes		x			
Motor Speed	124	105	63	Yes		x			

Evaluate Validity: The Validity Indicator (VI) helps identify the possibility of an invalid test. Embedded measures helps evaluate whether the patient is manipulating testing performance for a secondary gain, or they simply did not read the test instructions correctly.

WHY? When analyzing test data, either in research, or in clinical practice, it is important to know whether a test result is valid or not. Clinicians need to know if testing subjects misunderstood the instructions or are generating "dubious results" or a "non-credible response pattern." CNS Vital Signs has developed "validity indicators" for its tests and domains that indicate whether the patient gave poor effort or generated invalid results (feigning, malingering, etc.) Across the span of neurological and psychiatric disorders, it is important to have "valid" tests to get a true evaluation of a patient.

WHAT? The CNS Vital Signs A **Validity Indicator (VI)** is a guideline identifying the possibility of an invalid test or domain score. When reviewing a report, a **"No"** in the VI column suggests the clinician should evaluate whether the test subject understood the test, put forth their best effort, or has a clinical condition requiring further evaluation. The CLINICAL DOMAIN validity indicators are identified as B **'Possibly Invalid'** based on validity data and is indicated on the suspected test(s). ***The* NCI** (Neurocognition Index) ***is invalid if any test or domain is invalid.***

Non Verbal Reasoning Test (NVRT)	Score	Standard	Percentile	B Possibly Invalid
Correct Responses	7	98	45	The **NVRT** measures how well a subject can perceive and understand the meaning of visual or abstract information and recognizing relationships between visual-abstract concepts. The NVRT is comprised of 15 matrices, or visual analogies. The matrices are progressively more difficult. Each is presented for 14.5 seconds. Non-verbal reasoning is the process of perceiving and reaching conclusions through the use of symbols and patterns.
Average Correct Reaction Time*	7208	84	14	
Commission Errors*	8	93	32	
Omission Errors*	0	118	88	

Non-Verbal Reasoning: correct responses >= 4 and Correct > incorrect responses.

NOTE: The CNS Vital Signs batteries can be successfully completed, without assistance, by a normal child with a 4th grade reading level. Likewise, elderly with MMSE scores above 22 can complete the battery. Keep in mind, it is not uncommon for patients to generate an invalid result on one test in the battery due to misreading the instructions or giving-up on the test. ***Proper pretest instruction leads to a better testing experience.***

Evaluate Effort – Validity Indicator

HOW? The Validity Indicator alerts the clinician to the possibility of an invalid test allowing the clinician, examiner or testing technician to question the testing subject: Do the testing results reflect an understanding of the test and the instructions? Did the testing subject put forth their best effort? Did they get a good night's sleep? Does the subject have poor vision and need their glasses? Do the results suggest willful exaggeration, e.g., malingering?

Should a subject test abnormally low triggering an "invalid" test (NO as displayed in the Validity Indicator section of the report) then that would be a reason for retesting the individual, unless your clinical judgment makes you believe that is the best score the patient can achieve. Like any suspicious lab, the test should be re-administered, and it can be done with CNS Vital Signs through the RETEST function.

Before Retesting, the test examiner or technician should reinforce the need for the subject to give a good testing effort and use the "Validity Indicator" as a tool to help with the reinforcement. To RETEST a subject, go to MENU > RETEST SUBJECT > and select the appropriate subject and retest the subject. Upon retest, should a subject test abnormally low again triggering yet another "invalid" test (NO as displayed in the Validity Indicator section of the report) and the clinician believes it was the patient's best effort further evaluation or referrals should be considered.

CNS Vital Signs Embedded Indicators of Valid Effort

Clinical Domains	TEST VALIDITY INDICATORS
Composite Memory	Both Verbal and Visual Memory are Valid.
Verbal Memory	Verbal Memory raw score > 30.
Visual Memory	Visual Memory raw score > 30.
Psychomotor Speed	Both FTT and SDC are Valid
Reaction Time	Stroop: Simple RT < Complex RT < Stroop RT
Complex Attention	Valid Stroop, CPT, and SAT. Correct > incorrect response in all tests.
Cognitive Flexibility	Valid Stroop and SAT. Correct > incorrect responses in all tests.
Processing Speed	SDC: Correct Responses >= 20 AND Correct Responses > Errors
Executive Function	SAT: errors < correct responses.
Non-Verbal Reasoning	NVR: correct responses >= 4 and Correct > incorrect responses.
Social Acuity	POET: correct responses > 3. Correct > incorrect responses
Sustained Attention	4PCPT: Part 2 > 2 correct; part 3 > 5 correct; part 4 > 5 correct. Correct > incorrect responses in all parts.
Working Memory	
Simple Attention	CPT: if >= 10 years old, CPT is valid if Correct Responses - Commission Errors* >= 30, if < 10 years old CPT is valid if Correct Responses - Commission Errors* >= 25
Motor Speed	FTT: total taps >= 40

FTT - Finger Tapping Test; SAT – Shifting Attention Test; SDC – Symbol Digit Coding Test; RT – Reaction Time; CPT – Continuous Performance Test; POET – Perception of Emotions Test; NVR – Non-verbal Reasoning; 4PCPT – Four Part CPT

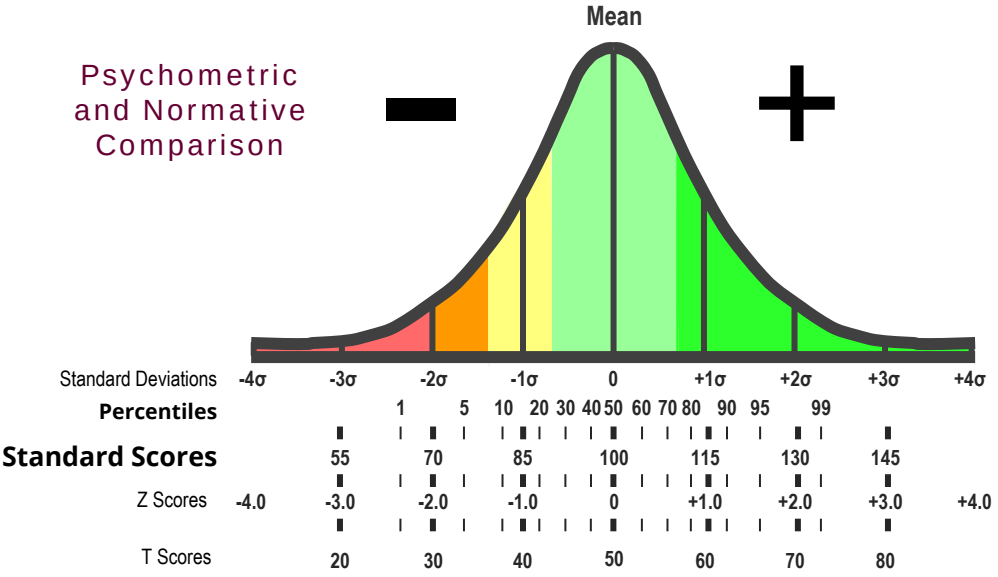
The "Validity Indicator" scoring algorithm is based on research presented (Detecting Invalidity In Neurocognitive Tests) at International Society for CNS Clinical Trials and Methodology (ISCTM) in 2009. The poster is available on the CNS Vital Signs website.

Evaluate Severity – Impairment Status

Evaluate Severity: The scores help identify cognitive deficits and their level of impairment.

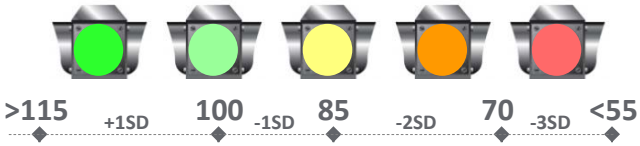
Assess even slight cognitive impairment (millisecond precision) providing immediate clinical insight into a patient's cognitive deficits and level of impairment. This gives patients, family members and caregivers knowledge of cognitive domains that underpin the ability to conduct activities of daily living. CNS Vital Signs grades ***severity of impairment*** based on an age-matched normative comparison database. Most neuropsychiatric and neurodegenerative conditions are multifactorial in nature. Effective evaluation of neurocognitive and behavioral issues can provide a standardized and efficient method of collecting valid and important neuropsychiatric clinical endpoints. These neuropsychiatric clinical endpoints can systematically document a patient's clinical course. Altogether, CNS Vital Signs computerized testing can facilitate a more complete assessment and provide a basis for patient and family feedback.

The CNS Vital Signs STANDARD SCORES and PERCENTILE RANKS are auto-scored using an algorithm based on a normative data set of 1600+ subjects, ranging from Ages 8 – 90. In the age-matched normative sample subjects were: (1) in good health, (2) had no past or present psychiatric or neurological disorders, head injury, or learning disabilities, and the (3) Sample subjects were free of any centrally acting medications. The CNS Vital Signs normative data is presented in ten age groups: less than 10 years old, 10–14, 15–19; in deciles to 79, and finally, 80 years or older. The standard scores are normalized with a mean of 100 and standard deviation of 15. Percentile Ranks is a mathematical transformation of the standard score and an index of how the subject scored compared to other subjects of the same age on a scale of 1 to 99. NORMAL AGING affects performance on all CNS Vital Signs tests. A patient's standard scores are based on data from normal controls that are the same age. EDUCATION and SPECIAL SKILLS may also affect test performance; therefore, concern should be taken for patients that are very intelligent or well educated yet their scores are below average. Like any laboratory test, an abnormal result should be the occasion for further evaluation. As with any neuropsychological tests, results can be affected by motivation or effort level and the Validity Indicator will help identify those patients.



	Standard Scores	Percentile Scores	
Above:	> 110	> 74	High Function and High Capacity
Average:	90 - 110	25 - 74	Normal Function and Normal Capacity
Low Average:	80 - 90	9 - 24	Slight Deficit and Slight Impairment
Low:	70 - 79	2 - 8	Moderate Deficit and Impairment Possible
Very Low:	< 70	< 2	Deficit and Impairment Likely

Evaluate Severity



Neurocognitive Domain Dashboard

Patient Profile:	Percentile Range				> 74	25 - 74	9 - 24	2 - 8	< 2
	Standard Score Range				> 109	90 - 109	80 - 89	70 - 79	< 70
Domain Scores	Subject Score	Standard Score	Percentile	VI**	Above: Above Expected Level	Average: At Expected Level	Low Average: Borderline	Low: Below Expected Level	Very Low: Well Below Expected Level
Neurocognition Index (NCI)	NA	85	16	Yes			x		
Composite Memory	102	103	58	Yes		x			
Verbal Memory	51	93	32	Yes		x			
Visual Memory	51	110	75	Yes	x				
Psychomotor Speed	174	93	32	Yes		x			
Reaction Time*	555	107	68	Yes		x			
Complex Attention*	21	56	1	Yes					x
Cognitive Flexibility	26	63	1	Yes					x
Processing Speed	48	79	8	Yes				x	
Executive Function	34	75	5	Yes				x	
Simple Attention	40	108	70	Yes		x			
Motor Speed	124	105	63	Yes		x			

4

1 2 3

SD = Standard Deviation from the MEAN

CNS Vital Signs presents testing results in Subject (raw), Standard Scores, and Percentile Ranks. Results obtained from a CNS Vital Signs assessment can be used to evaluate or monitor a patient's condition and the subsequent treatment and management of that patient. Below, is a description of each domain category:

1 ***Subject Scores*** are *computed from raw score calculations using the data values of individual subtests and are simply the number of correct responses, incorrect responses, and reaction times. Reaction times are in milliseconds. An ASTERISK (*) denotes that "lower score is better" e.g., timing, otherwise higher scores are better.*

2 ***Standard Scores*** *are normalized from raw scores and present an age matched score relative to other people in a normative sample. CNS Vital Signs standardized have a mean of 100 and a standard deviation is 15. Higher scores are always better. The schema where the mean is 100 and the standard deviation is 15 is similar to the presentation of IQ scores where the mean for normal is 100.*

3 ***Percentile Scores*** *is a mathematical transformation of the standard score and an index of how the subject scored compared to other subjects of the same age on a scale of 1 to 99. If an individual obtained a score at the 52nd percentile (50th percentile is average), this would mean that their performance would be equal to 52% of his same-aged peers in the general population. Higher scores are always better.*

Severity Classification Grade:

	Standard Scores	Percentile Scores	
Above:	> 110	> 74	High Function and High Capacity
Average:	90 - 110	25 - 74	Normal Function and Normal Capacity
Low Average:	80 - 90	9 - 24	Slight Deficit and Slight Impairment
Low:	70 - 79	2 - 8	Moderate Deficit and Impairment Possible
Very Low:	< 70	< 2	Deficit and Impairment Likely

Quick View Age-Matched Normative Scores 4

Variation in neurocognitive scores can be multifactorial in nature.

The brain develops and ages… ***based on genetics and external environmental challenges e.g., maternal health, education, exercise, diet, life experiences, socioeconomic status, health status, attitudinal and emotional factors, physical / medical comorbidities, treatments, etc.***

Why Computerized Neuropsychological Testing?

"Neurocognitive disorders—*are characterized by decline from a previously attained level of cognitive functioning* (or by peer group standardized normative comparison)… *Objective assessments are essential*… *The move to evaluate neurocognitive disorders as early as possible emerged from the recognition of a long predementia stage in neurodegenerative diseases, improvements in early detection, and the increasing emphasis on early intervention to prevent or postpone dementia… In fact, because mild neurocognitive disorder needs to be distinguished from both normal cognitive ageing and major neurocognitive disorder (or dementia), even greater reliance on neuropsychological assessment is called for..*

Evaluation criteria: ***Evidence of modest cognitive decline from a previous level of performance in one or more cognitive domains…**"***


REVIEWS

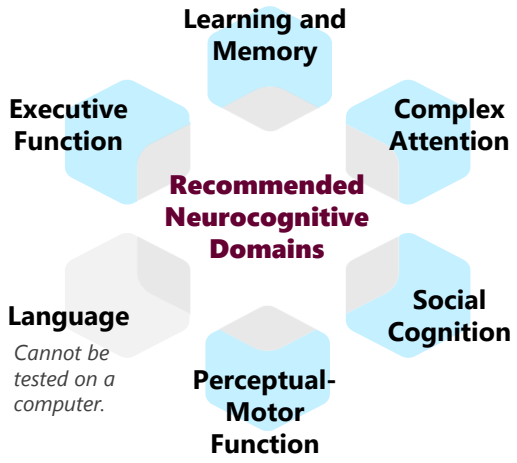
Classifying neurocognitive disorders: the DSM-5 approach

Perminder S. Sachdev, Deborah Blacker, Dan G. Blazer, Mary Ganguli, Dilip V. Jeste, Jane S. Paulsen and Ronald C. Petersen

Abstract | Neurocognitive disorders—including delirium, mild cognitive impairment and dementia—are characterized by decline from a previously attained level of cognitive function. These disorders ha

** Adapted From: Perminder S. Sachdev, Deborah Blacker, Dan G. Blazer, Mary Ganguli, Dilip V. Jeste, Jane S. Paulsen & Ronald C. Petersen: Classifying neurocognitive disorders: the DSM-5 approach: Nature Reviews Neurology volume 10, pages 634–642 (2014)

DSM-5 Neurocognitive Disorder, Five Key Cognitive Domains Tested by CNS VS



Evaluate Pattern: Impairment pattern helps identify pathologies and possible comorbidities.

CNS Vital Signs cognitive testing procedure provides valid and reliable clinical endpoints to help in the evaluation and management of patients. Many conditions at the group level are associated with cognitive impairments. Attention should be paid to the nature (speed and accuracy) and response pattern as well as errors. Patient's scoring well below average in one domain or below average in two domain areas, might well be impaired and should be evaluated further. The first step in evaluating such a patient is to repeat the test under more favorable circumstances. Like any laboratory test, repetitive results outside of normal should be investigated. If the scores are low the second time, a targeted work-up may be necessary.

Lifespan Testing:

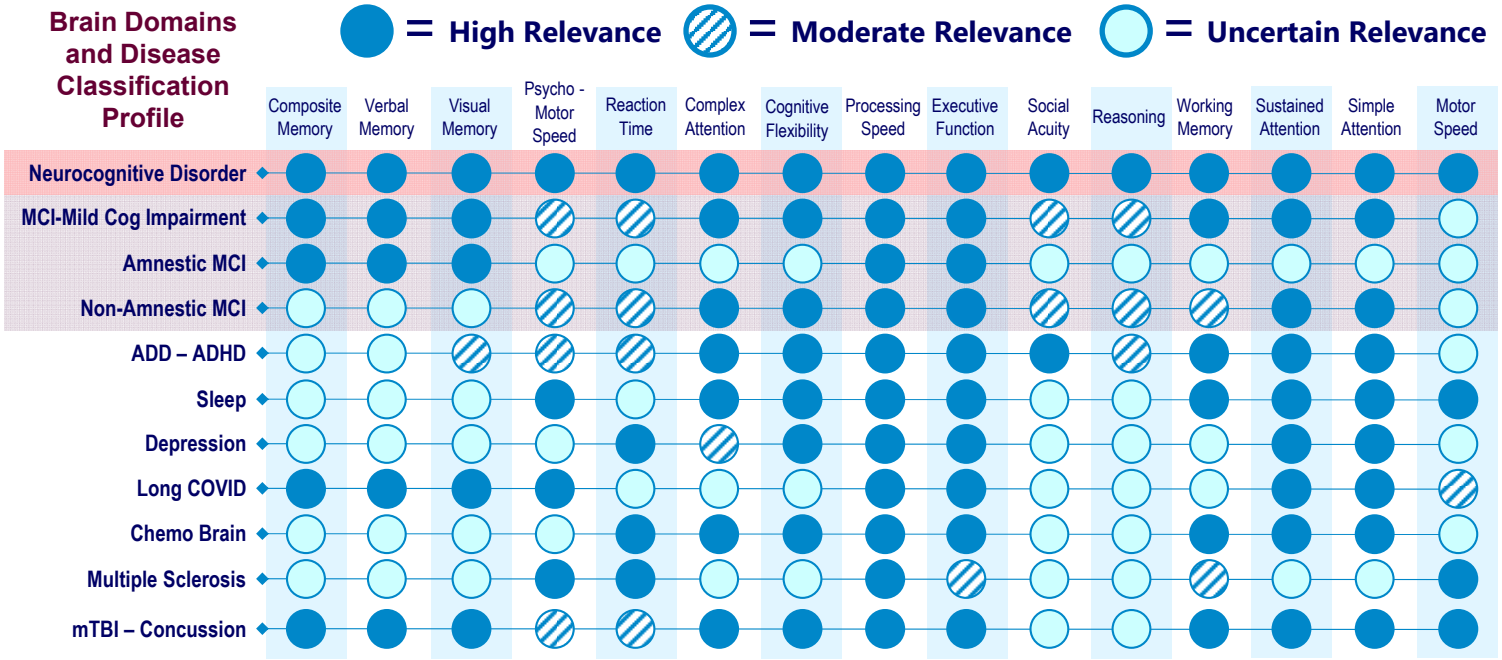
CNS Vital Signs represents an advancement in early detection due to its lifespan (ages 8 to 90) collection of normative data. It is ideal to support the increasing emphasis on early intervention to prevent or postpone dementia and other progressive neuro-psych conditions.

Evaluate and Classify Neurocognitive Disorders

An overarching goal in examining clinical disorders in relationship to neuropsychological functioning is trying to classify patterns of deficits associated with the disorder. CNS Vital Signs aids clinicians by providing objective, valid, reliable, and efficient measure of a broad-spectrum of cognitive or brain domains associated with identification of most neuro-psych conditions as well as effects from cancer and its treatments, infectious diseases e.g., Lyme, AIDS-HIV, metabolic e.g., diabetes, occupational, forensic, genetic phenotype, cardiovascular, neurotoxicity, human performance, and more.

Personalized and Precise Cognitive Profile: No single cognitive profile characterizes all patients with a neuro-psych condition. In other words, medical conditions are many times clinically heterogeneous disorders influenced by diverse clinical and risk factors. Patients may not fit into any one domain pattern and may present with widely differing co-occurring comorbidities including varying cognitive profiles. ***That is why a broad-spectrum battery greatly assists in the evaluation and management of patients.*** Like most neuropsychological or psychological tests, clinicians will recognize, over time, which domains reveal the clinical conditions of their patients. The profiles below may help clinicians evaluate test results. The profile patterns below are based on a review of published literature and data.

Relevant Domains Described in the Literature



Brain Injury & Stroke Brain injury and Stroke domain score performance may vary depending on several factors that include type of blow to the head, site of the blow, location and seriousness of stroke and the patient's individual history.

Epilepsy Neurocognitive Function is dependent on the type of epilepsy and medication effect. Note: Cognitive function is more frequently impaired in people with epilepsy than in the general population, and the degree of cognitive impairment varies according to the epilepsy syndrome. Behavioral disorders are also more frequent in people with epilepsy than in individuals who do not have epilepsy. Behavioral disturbance is observed more frequently in people with drug-resistant epilepsy, frequent seizures, and/or associated neurological or mental abnormalities. In children and adolescents, some data suggests a close link between behavior/cognition and some specific epilepsy syndromes. Optimal management requires a careful balance between, on the one hand, the desire to reach early and maximal seizure control and, on the other, the need to avoid tolerability problems related to cognitive and behavioral impairments.

Chronic Pain Neurocognitive Function is dependent on medication effect and pain pathology. CNS VS is ideal for measuring a baseline status and treatment outcomes.

Brain Fog Brain fog isn't a medical condition. It's a term used for certain symptoms that can affect your patient's mental clarity or ability. Brain Fog patient complaints can help document the potential for possible cognitive impairment and establish medical necessity.

Evaluate and Classify Neurocognitive Disorders

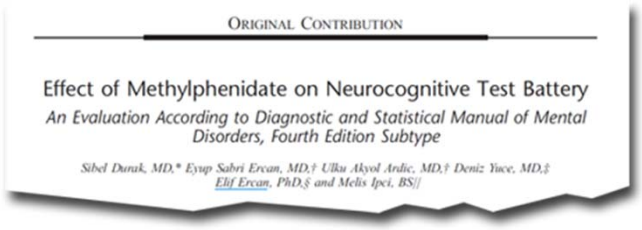
Evaluating ADHD, managing and treatment planning can vary based on many intrinsic and extrinsic factors:

"*Over the past century, the syndrome currently referred to as attention-deficit hyperactivity disorder (AD/HD) has been conceptualized in relation to varying cognitive problems including attention, reward response, executive functioning, and other cognitive processes. More recently, it has become clear that whereas ADHD is associated at the group level with a range of cognitive impairments, no single cognitive dysfunction characterizes all children with ADHD. In other words, ADHD is not a one-size-fits-all phenomenon. Patients with this syndrome do not fit into any one category and present with widely differing co-occurring disorders—including varying cognitive profiles.*"

Source: Cognitive Impairments With ADHD, Psychiatric Times. Vol. 26 No. 3, 2009

CNS Vital Signs aids in the objective, valid, reliable and personalized assessment of cognitive disfunction and treatment improvement in ADHD. CNS VS also provides important evidence-based ADHD rating scales to measure and track symptoms, behaviors and co- occurring conditions.

Objective Psychometric Measures to Evaluate Treatment Response and Outcomes


ORIGINAL CONTRIBUTION

Effect of Methylphenidate on Neurocognitive Test Battery

An Evaluation According to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Subtype

Sibel Durak, MD,* Eyup Sabri Ercan, MD,† Ulku Akyol Ardic, MD,† Deniz Yuce, MD,‡ Elif Ercan, PhD,§ and Melis Ipci, BS||

Adapted From:
Effect of Methylphenidate on Neurocognitive Test Battery;
Journal of Clinical Psychopharmacology;
Volume 34, Number 4, August 2014

...Findings revealed controls scored better than ADHD subjects and ADHD subjects scored better on MPH than with no drug

Evaluate the neuropsychological characteristics of PI - predominantly inattentive, R – restrictive, and CB - combined (inattentive & hyperactive) AD/HD subtypes...

Comparisons of CNSVS Domain Scores Between the AD/HD Groups Before MPH Medication Administration

Baseline Measurements	PI Mean (SD)	R Mean (SD)	CB Mean (SD)	Control Mean (SD)	*P*	Pairwise Comparisons
Neurocognition Index	87.62 (14.66)	90.71 (11.77)	90.25 (11.14)	96.91 (10.87)	<0.001*	(PI=R=CB) < control
Composite Memory	84.56 (21.86)	87.97 (19.5)	91.89 (20.92)	96.73 (18.82)	0.01	PI < control
Psychomotor speed	92.96 (10.49)	94.12 (10.87)	93.63 (12.54)	99.77 (16.58)	<0.001	(PI=R=CB) < control
Reaction time	78.54 (21.63)	83.15 (18.42)	81.86 (16.49)	83.26 (28.57)	0.65*	
Complex attention	91.38 (24.6)	94.92 (16.81)	90.77 (18.41)	102.15 (12.45)	<0.001*	(PI=R=CB) < control
Cognitive flexibility	90.84 (16.15)	93.32 (15.51)	91.15 (14.1)	102.82 (15.28)	<0.001	(PI=R=CB) < control
Symbol Digit Coding (*Processing Speed Domain*)						
Correct responses	41.24 (12.73)	41.82 (13.8)	40.23 (12.36)	48.18 (11.77)	<0.001	(PI=R=CB) < control
Errors	0.92 (1.18)	1.09 (1.26)	1 (2.28)	3.6 (5.53)	<0.001*	(PI=R=CB) < control
Shifting Attention Test (*Executive Function Domain*)						
Correct responses	34.44 (10.09)	35.43 (11.33)	34.07 (9.95)	42.23 (9.98)	<0.001	(PI=R=CB) < control
Errors	15.34 (7.83)	15.71 (9.41)	17.52 (8.02)	11.55 (6.06)	<0.001*	(PI=R=CB) > control
Correct reaction time	1290.6 (133.52)	1224.91(236.4)	1233.39 (175)	1188.6 (222.75)	0.01*	CB > control
CPT (*Simple Attention Domain*)						
CPT Correct	38.54 (2.61)	37.84 (5.25)	38.3 (2.71)	39.19 (1.14)	<0.001*	R > control
Omission	1.46 (2.61)	1.61 (2.15)	1.7 (2.71)	0.81 (1.14)	<0.001*	CB > control
Commission errors	3.42 (4.65)	11.59 (66.7)	3.99 (4.02)	1.71 (1.68)	<0.001*	R > control, CB > control
Choice RT correct	506.84 (79.92)	490.2 (100.28)	515.36 (81.96)	470.5 (68.55)	<0.001	PI < control

*The Welch ANOVA test was used for comparisons between diagnostic groups, and post hoc comparisons were performed with Tamhane's T2 test. All other comparisons were performed with the ANOVA test, and post hoc tests were performed with the Tukey test.

Comparisons After MPH Administration

PI Mean (SD)	R Mean (SD)	CB Mean (SD)
95.53 (11.96)	98.66 (11.62)	97.38 (10)
81.27 (22.57)	85.59 (20.44)	85.9 (17.7)
98.88 (9.77)	99.8 (11.09)	99.73 (10.52)
88.25 (19.19)	89.88 (17.98)	86.43 (17.92)
105.51 (16.27)	108.53 (17.14)	107.58 (12.63)
104.77 (15.63)	108.42 (14.14	106.58 (13.74)

...Study included 360 children and adolescents (277 boys, 83 girls) between 7 and 15 years of age who had been diagnosed with ADHD at the Department of Child and Adolescent Psychiatry using K-SADS-PL and DSM-IV

...Subjects were grouped according to ADHD subtypes as PI (n = 51), R (n = 65), and CB (n = 165). Seventy-nine healthy children were recruited into the study as the control group

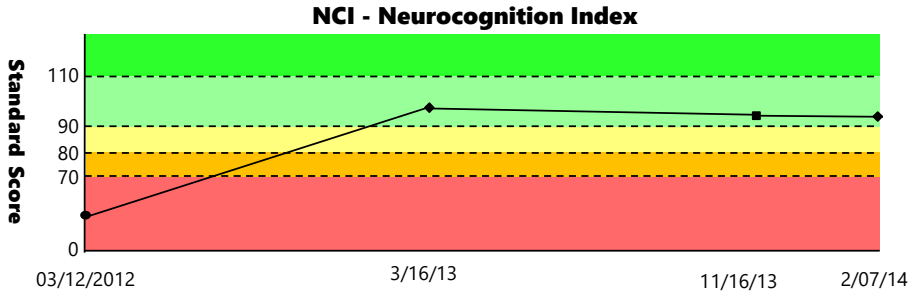
*** Attention-deficit/hyperactivity disorder (ADHD); Søren Dalsgaard; Eur Child Adolesc Psychiatry (2013) 22 (Suppl 1):S43–S48

****** RESTRICTIVE (DSM-V):*** If criterion A1 (inattention) is met, but no more than two symptoms from criterion A2 (hyperactivity / impulsivity) have been present for the past 6 months.

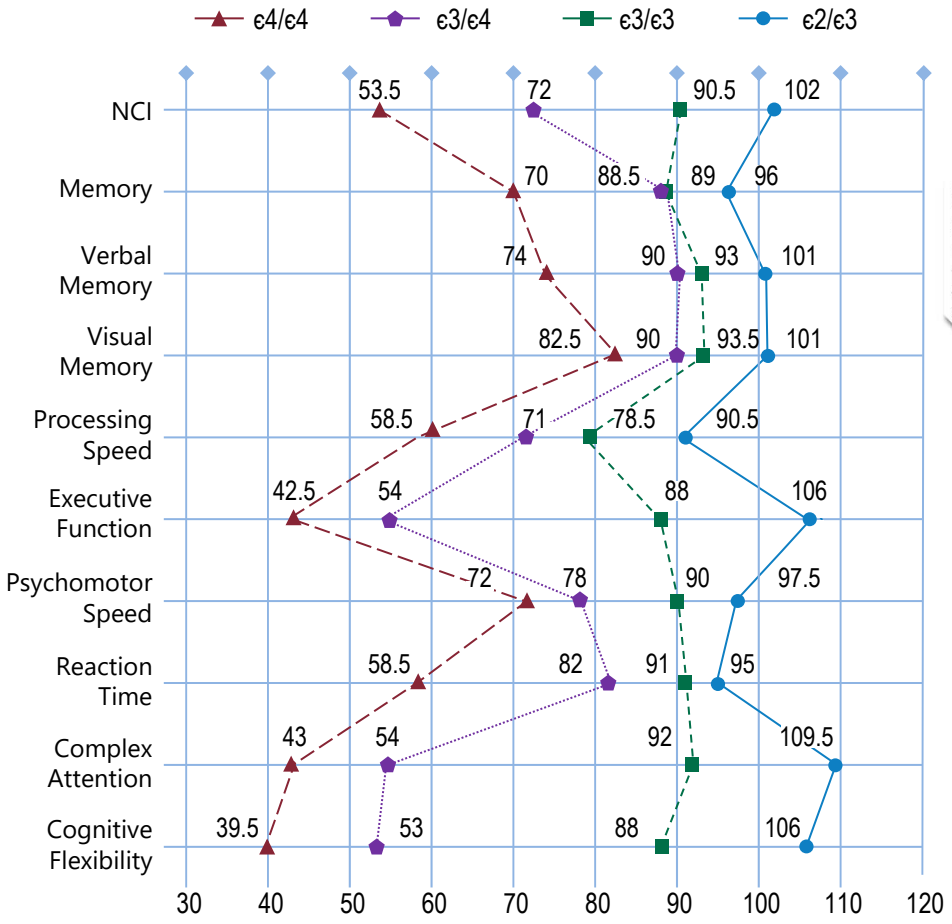
Amnestic MCI Baseline: 60-Year-Old Male Initial MMSE 25*

Patient Profile:	Percentile Range				> 74	25 - 74	9 - 24	2 - 8	< 2
	Standard Score Range				> 109	90 - 109	80 - 89	70 - 79	< 70
Domain Scores	Subject Score	Standard Score	Percentile	VI**	Above	Average	Low Average	Low	Very Low
Neurocognition Index (NCI)	NA	53	1	No					X
Composite Memory	72	60	1	Yes					X
Verbal Memory	36	57	1	Yes					X
Visual Memory	36	75	5	Yes				X	
Psychomotor Speed	178	116	86	Yes	X				
Reaction Time*	710	99	47	Yes		X			
Complex Attention*	118	-104	1	No					X
Cognitive Flexibility	27	92	30	Yes		X			
Processing Speed	47	105	63	Yes		X			
Executive Function	29	92	30	Yes		X			
Simple Visual Attention	-66	-874	1	No					X
Motor Speed	130	121	92	Yes	X				

Amnestic MCI Longitudinal View: 60-Year-Old Male



CNS VS Correlation to Alzheimer's ApoE Polymorphisms



Average **Standard Scores** for cognitive functions in particular groups of *ApoE* gene polymorphisms.

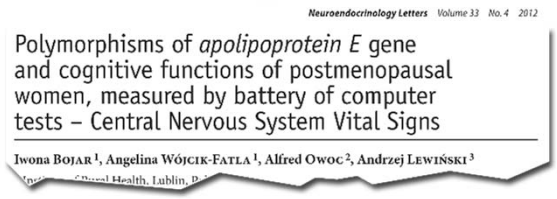
Joe, a 60-year-old male is presenting with memory and concentration concerns and was given CNS Vital Signs Clinical Battery and scored below average compared to his peers in 6 of 11 cognitive domains. His lowest scores were in domains sensitive to amnestic (memory related) MCI.

After considering the H&P, lab results, patient and informant memory questionnaire, sleep scales and the cognitive test results; Joe was referred for a sleep study. Later he was prescribed CPAP and appropriate therapy.

CNS Vital Signs allowed a fine characterization of Joe's clinical course, including apparent variation due to compliance with therapy. Patient and wife were positively influenced by revelation of objective cognitive testing performance, which proved useful in demonstrating probable effects of compliance.

Adopted from: Schmechel et al. International Congress Alzheimer's Disease Paris 2011

Correlation to Biological Markers



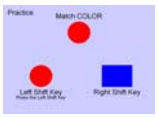
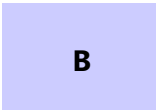
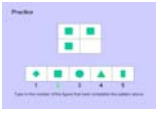
...Study included 107 postmenopausal women between the ages of 52 and 65 (mean 56.6 ± 3.5)

...Subjects were qualified as "normal" with MOCA scores between 26 and 30

...Findings revealed ApoE polymorphisms correlated to levels of cognitive function where as expected ε3/ε4, or ε4/ε4 scored poorly while ε2/ε3 groups scored much better.

Adapted from: Bojar, Iwona & Wójcik-Fatla, Angelina & Owoc, Alfred & Lewiński, Andrzej. (2012). Polymorphisms of apolipoprotein E gene and cognitive functions of postmenopausal women, measured by battery of computer tests - Central Nervous System Vital Signs. Neuro endocrinology letters. 33. 385-92.

10 Normed Neurocognitive Tests

Verbal Memory (VBM) *Approx. 3 Minutes*		■ Learning Words ■ Memory for Words ■ Word Recognition ■ Immediate and Delayed Recall	VBM measures recognition memory for WORDS. Fifteen words are presented, one by one, on the screen every two seconds. For immediate recognition (learning phase), the participant must identify those words nested among fifteen new words. Then, after six more tests, there is a delayed recognition memory trial. ***Subjects respond using the SPACE BAR.***
Visual Memory (VIM) *Approx. 3 Minutes*		■ Learning Shapes ■ Memory for Shapes ■ Shapes Recognition ■ Immediate and Delayed Recall	VIM measures recognition memory for ABSTRACT FIGURES or SHAPES. Fifteen geometric figures are presented, one by one, on the screen. For immediate recognition (learning phase), the participant must identify those figures nested among fifteen new figures. Then, after five more tests, there is a delayed recognition memory trial. ***Subjects respond using the SPACE BAR.***
Finger Tapping (FTT) *Approx. 2 Minutes*		■ Motor Speed ■ Fine Motor Control	FTT test has ***subjects respond by pressing the SPACE BAR*** with their right index finger as many times as they can in 10 seconds. They do this once for practice, and then there are three test trials. The test is repeated with the left hand.
Symbol Digit Coding (SDC) *Approx. 4 Minutes*		■ Complex Information Processing Accuracy ■ Complex Attention ■ Visual-Perceptual Speed ■ Information Processing Speed	SDC test consists of serial presentations of screens, each of which contains a bank of eight symbols above and eight empty boxes below. ***The participant types in the number on the NUMBER ROW that corresponds to the symbol that is highlighted.*** Only the digits from 2 through 9 are used; this is to avoid the confusion between "1" and "I" on the keyboard. ***The computer program does not allow a person to use a numerical pad*** preventing a distinct advantage for those who are skilled at using the numerical pad or for those that are right- versus left-handed.
Stroop Test (ST) *Approx. 4 - 5 Minutes*		■ Simple Reaction Time ■ Complex Reaction Time ■ Stroop Reaction Time ■ Inhibition / Disinhibition ■ Frontal or Executive Skills	Stroop test has three parts. In the first part, the words RED, YELLOW, BLUE, and GREEN (printed in black) appear at random on the screen, and the participant presses the space bar as soon as the test subject sees the word. In the second part, the words RED, YELLOW, BLUE, and GREEN appear on the screen, printed in color. The participant is asked to press the space bar when the color of the word matches what the word says. In the third part, the words RED, YELLOW, BLUE, and GREEN appear on the screen, printed in color. ***The participant is asked to press the SPACE BAR*** when the color of the word does not match what the word says.
Shifting Attention (SAT) *Approx. 2.5 Minutes*		■ Executive Function ■ Shifting Sets: Rules, Categories, & Rapid Decision Making ■ Reaction Time	SAT test is a measure of ability to shift from one instruction set to another quickly and accurately. Participants are instructed to match geometric objects either by shape or by color. Three figures appear on the screen, one on top and two on the bottom. The top figure is either a square or a circle. The bottom figures are a square and a circle. The figures are either red or blue (mixed randomly). The participant is asked to match one of the bottom figures to the top figure. The rules change at random (i.e., match the figures by shape, for another, by color) and ***subject responds by pressing the two SHIFT KEYS.***
Continuous Performance (CPT) *Approx. 5 Minutes*		■ Sustained Attention ■ Choice Reaction Time ■ Impulsivity	CPT test is a measure of vigilance or sustained attention or attention over time. The test subject is asked to respond to the target stimulus "B" but not to any other letter. The stimuli are presented at random. ***Subject responds by pressing the SPACE BAR.***
Perception of Emotions (POET) *Approx. 2 Minutes*		■ Social Cognition or Emotional Acuity ■ Choice Reaction Time	The POET measures how well a subject can perceive and identify specific emotions. "Social cognition" or "emotional acuity" has been defined as "the way in which people make sense of other people and themselves". It is the ability to perceive and understand social information. The reaction times in POET are much longer than in the other tests, indicating the complexity of central processes governing emotional acuity. ***Subjects respond using the SPACE BAR.***
Non-Verbal Reasoning (NVRT) *Approx. 3.5 Minutes*		■ Reasoning ■ Reasoning Recognition Speed	The NVRT measures how well a subject can perceive and understand the meaning of visual or abstract information and recognizing relationships between visual-abstract concepts. The NVRT is comprised of 15 matrices, or visual analogies. The matrices are progressively more difficult. Non-verbal or visual-abstract reasoning is the process of perceiving issues and reaching conclusions using symbols or generalizations rather than concrete information. ***Subjects respond using the SPACE BAR.***
4-Part Continuous Performance (FPCPT) *Approx. 7 Minutes*		■ Sustained Attention ■ Working Memory	The 4PCPT test is a four-part test that measures a subject's working memory and sustained attention. PART ONE - is a simple reaction time test, PART TWO - is a variant of the continuous performance test, the reaction times that are generated are "choice reaction times". PART THREE - is a "one back" CPT. The subject must respond to a figure only if the figure immediately preceding was the same. PART FOUR - is a "two-back" CPT. It is a difficult task and is used to measure working memory. Parts two, three, and four of the tests are used to calculate sustained attention domain. ***Subjects respond using the SPACE BAR.***

CNS Vital Signs Clinical Domain Description

Single Test Domain Multiple Test Domain

Neurocognitive Index (NCI)	**Measure:** An average score derived from the domain scores or a general assessment of the overall neurocognitive status of the patient. **Relevance:** Summary views tend to be most informative when evaluating a population, a condition category, and outcomes.
Composite Memory	**Measure:** How well subject can recognize, remember, and retrieve words and geometric figures. **Relevance:** Remembering a scheduled test, recalling an appointment, taking medications, and attending class.
Verbal Memory	**Measure:** How well subject can recognize, remember, and retrieve words. **Relevance:** Remembering a scheduled test, recalling an appointment, taking medications, and attending class.
Visual Memory	**Measure:** How well subject can recognize, remember and retrieve geometric figures. **Relevance:** Remembering graphic instructions, navigating, operating machines, recalling images, and/or remember a calendar of events.
Psychomotor Speed	**Measure:** How well a subject perceives, attends, responds to visual-perceptual information, and performs motor speed and fine motor coordination. **Relevance:** Ability preform simple motor skills and dexterity through cognitive functions i.e., use of precision instruments or tools, performing mental and physical coordination i.e., driving a car, playing a musical instrument.
Reaction Time*	**Measure:** How quickly the subject can react, in milliseconds, to a simple and increasingly complex direction set. **Relevance:** Driving a car, attending to conversation, tracking and responding to a set of simple instructions, taking longer to decide what response to make.
Complex Attention	**Measure:** Ability to track and respond to a variety of stimuli over lengthy periods of time and/or perform mental tasks requiring vigilance quickly and accurately. **Relevance:** Self-regulation and behavioral control.
Cognitive Flexibility	**Measure:** How well subject is able to adapt to rapidly changing and increasingly complex set of directions and/or to manipulate the information. **Relevance:** Reasoning, switching tasks, decision-making, impulse control, strategy formation, attending to conversation.
Processing Speed	**Measure:** How well a subject recognizes and processes information i.e., perceiving, attending/responding to incoming information, motor speed, fine motor coordination, and visual-perceptual ability. **Relevance:** Ability to recognize and respond/react i.e., fitness-to-drive, occupation issues, possible danger/risk signs or issues with accuracy and detail.
Executive Function	**Measure:** How well a subject recognizes rules, categories, and manages or navigates rapid decision making. **Relevance:** Ability to sequence tasks and manage multiple tasks simultaneously as well as tracking and responding to a set of instructions.
Simple Attention	**Measure:** Ability to track and respond to a single defined stimulus over lengthy periods of time while performing vigilance and response inhibition quickly and accurately. **Relevance:** Self-regulation and simple attention control.
Motor Speed	**Measure:** Ability to perform movements to produce and satisfy an intention towards a manual action and goal. **Relevance:** Preparation and production of simple manual dexterity actions e.g. manipulate and maneuver objects.
Social Acuity	**Measure:** How well a subject can perceive, process, and respond to emotional cues. **Relevance:** Spectrum screen, ability to recognize social cues or read facial expressions. Provides insight into inappropriate behavior, decreased inhibition, insensitivity to social standards, and social behavioral regulation.
Reasoning	**Measure:** How well is subject able to recognize, reason and respond to non-verbal visual-abstract stimuli. **Relevance:** Problem solving skills, ability to forge insights, discern meaning, and ability to perceive relationships.
Sustained Attention	**Measure:** How well a subject can direct and focus cognitive activity on specific stimuli. **Relevance:** How well a subject can focus and complete task or activity, sequence action, and focus during complex thought.
Working Memory	**Measure:** How well a subject can perceive and attend to symbols using short-term memory processes (4PCPT). **Relevance:** Ability to carry out short-term memory tasks that support decision making, problem solving, planning, and execution. Enables "right-now" responses.

Formulas for Calculating the Neurocognitive Domain Scores:

Single Test Domain Multiple Test Domain

BRIEF-CORE Clinical Domains	Domain Score Calculations: 1500+ Norms, Ages 8 to 90
Neurocognition Index - NCI	Average of five domain scores: Composite Memory, Psychomotor Speed, Reaction Time, Complex Attention , and Cognitive Flexibility ; representing a form of a global score of neurocognition
Composite Memory	VBM Correct Hits Immediate + VBM Correct Passes Immediate + VBM Correct Hits Delay + VBM Correct Passes Delay + VIM Correct Hits Immediate + VIM Correct Passes Immediate + VIM Correct Hits Delay + VIM Correct Passes Delay
Verbal Memory	VBM Correct Hits Immediate + VBM Correct Passes Immediate + VBM Correct Hits Delay + VBM Correct Passes Delay
Visual Memory	VIM Correct Hits Immediate + VIM Correct Passes Immediate + VIM Correct Hits Delay + VIM Correct Passes Delay
Psychomotor Speed	FTT Right Taps Average + FTT Left Taps Average + SDC Correct Responses
Reaction Time	(ST Complex Reaction Time Correct + Stroop Reaction Time Correct) / 2
Complex Attention	Stroop Commission Errors + SAT Errors + CPT Commission Errors + CPT Omission Errors
Cognitive Flexibility	SAT Correct Responses - SAT Errors - Stroop Commission Errors
Processing Speed	SDC Correct Responses - SDC Errors
Executive Function	SAT Correct Responses - SAT Errors
Simple Attention	Continuous Performance (CPT) Correct Responses minus CPT Commission Errors
Motor Speed	Finger Tapping Test Right Taps Average + Finger Tapping Test Left Taps Average
Clinical Domains	**Domain Score Calculations: 700+ Norms, Ages 8 to 90**
Working Memory	(4PCPT Part 4 Correct Responses) - (4PCPT Part 4 Incorrect Responses)
Sustained Attention	(4PCPT Part 2 Correct Responses + 4PCPT Part 3 Correct Responses + 4PCPT Part 4 Correct Responses) – (4PCPT Part 2 Incorrect Responses + 4PCPT Part 3 Incorrect Responses + 4PCPT Part 4 Incorrect Responses)
Social Acuity	POET Correct Responses – POET Commission Errors
Reasoning (non-verbal)	NVRT Correct Responses – NVRT Commission Errors

Abbreviations Defined:

VBM – Verbal Memory Test; VIM – Visual Memory Test; SDC – Symbol Digit Coding Test; SAT – Shifting Attention Test; FTT - Finger Tapping Test; ST – Stroop Test; CPT – Continuous Performance Test; 4PCPT – Four Part CPT; POET – Perception of Emotions Test; NVR – Non-verbal Reasoning Test.

Neurocognitive Tests and Domain Scoring Process

The CNS Vital Signs domain scores are derived by summing primary raw scores from one (blue shaded box) or multiple (green shaded box) tests. Domain scores are presented as Subject (raw) Scores, Standard Scores, and Percentile Ranks. Subject Scores are computed from raw score calculations using the data values of individual subtests and are simply the number of correct responses, incorrect responses, commission responses, omission responses and reaction times. The Brief-Core Battery of the seven tests below score eleven Neurocognitive Domains and the Neurocognitive Index. Using all ten tests below score fifteen Neurocognitive Domains and the Neurocognitive Index. All ten tests and rating scales can be custom configured to meet clinical testing or research needs.