

Appendix 1. Description of subtests and calculation of domain scores on CNS Vital Signs

CNS Vital Signs Subtest	Description of subtest	Subtest is included in the following domains:
Verbal Memory	Fifteen words are presented, 1 by 1, on the screen; a new word is presented every 2 seconds. The subject is asked to remember these words. Then, a list of 30 words is presented. The 15 target words are mixed randomly among 15 new/distractor words. When the subject recognizes a word from the original list, he or she presses the space bar. After this trial of 30 words, the subject goes on to do the next 6 tests. At the end of the battery, about 20 minutes later, the 15 target words appear again, mixed with 15 new non-target words.	Verbal memory
Visual Memory	This test is identical to verbal memory only instead of using words this test uses geometric figures.	Visual memory
Finger Tapping Test (FTT)	Subjects are asked to press 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 3 test trials. The test is repeated with the left hand. The score is the average number of taps, right and left.	Psychomotor speed
Symbol Digit Coding (SDC)	Symbol digit coding is based on the symbol digit modalities test, itself a variant of the Wechsler digit symbol substitution test. There is a grid on the subject's screen, which has a series of symbols with empty boxes underneath of them. There is a key at the top of the screen, with each of the symbols and the corresponding numbers to go along with them. Patients are asked to fill in the empty boxes underneath the symbols, in the order in which they appear, with the corresponding number for the symbol (found in the key). Patients are given 90 seconds to correctly fill in as many numbers as possible.	Psychomotor speed, processing speed
Stroop Test	The test has 3 parts. In the first part, the words RED, YELLOW, BLUE, and GREEN (printed in black ink) appear at random on the screen. The subject presses the space bar as soon as he or she sees the word. In the second part, the same words appear on the screen, printed in color. The subject is asked to press the space bar when the color of the word matches what the word says (ie, RED in red ink). In the third part, the subject is asked to press the space bar when the color of the word does not match what the word says (ie, RED in blue ink).	Reaction time, complex attention, cognitive flexibility

Shifting Attention Test (SAT)	<p>Subjects are instructed to match geometric objects either by shape or by color. Three figures appear on the screen, 1 on top and 2 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; the colors are mixed randomly. The subject is asked to match one of the bottom figures to the top figure, based on either shape or color. The rules change at random. The goal is to make as many correct matches as one can in the time 90 seconds.</p>	<p>Complex attention, cognitive flexibility, executive function</p>
Continuous Performance Test (CPT)	<p>The subject is asked to respond to target stimulus "B" but not to any other letter. In 5 minutes, the test presents 200 letters. Forty of the stimuli are targets (the letter "B"), 160 are non-targets (other letters). The stimuli are presented at random, with the target stimulus "blocked" so it appears 8 times during each minute of the test.</p>	<p>Complex attention</p>
Nonverbal Reasoning Test (NVRT)	<p>The reasoning test includes 15 presentations with a 14-second response time. The test runs continuously for about 5 minutes. It consists of a series of puzzles, or visual analogies, similar to those in Raven's Progressive Matrices. The puzzles are progressively more difficult. The subject identifies the correct response from a field of possible answers by selecting a number to match the answer.</p>	<p>Reasoning</p>