**Appendix 1: Cognitive Tests**

**Mental Status –** The Mini Mental State Examination (MMSE) concentrates only on the cognitive aspects of mental functions. It has eleven questions, easy to administer and is practical to use serially and routinely 1. The MMS is divided into two sections. First section requires vocal responses only and covers orientation, memory, and attention; with a maximum score of 21. Second section tests the ability to name, follow verbal and written commands, with a maximum score is nine. Because of the reading and writing involved in Part II, patients with severely impaired vision may have some extra difficulty that can usually be eased by large writing and allowed for in the scoring.

**Verbal learning and memory**—The California Verbal Learning Test-II (CVLT-II) 2 as described by Delis *et al.* measures verbal learning and memory by immediate and delayed recall and recognition of two sixteen-word lists. As administered to HANDLS participants, List A consists of three trials, followed by list B with one trial. After testing with list B, short-delay short free recall and cued recall of list A are tested. After ~ 30 min delay, long-delay free recall, cued recall and yes/no-recognition attempts of list A conclude the test.

**Non-verbal memory**—The Benton Visual Retention Test 3 consists of ten designs and their reproduction by participants, as accurately as possible. It measures visual memory, perception and visuo-constructional abilities. It is an untimed test scored by the examiner with a reliability range of 0·74 to 0·84 4.

**Working** **memory**—The Digit Span subscale of the Wechsler Adult Intelligence Scale consists of forward and backward test measurements 5. In both tests, seven pairs of increasing, random number sequences, are presented verbally at a rate of one per second. In Digits Forward, the subject repeats the same number sequence after the examiner. In Digits Backward the participant is asked to repeat the number sequence in reverse order. The test is discontinued when the subject fails both the forward and backward trial of any given sequence string. Digits Forward and Backward are measured by the number of correct trials. This is used as a valid test of attention, working memory and concentration.

**Attention and cognitive flexibility**—The Trail Making Test 6 is administered in two timed-parts, lasting 5 to 10 min each. Trails A is administered first, where subjects connect, in ascending order, randomly numbered circles on a page by drawing lines. In Trails B, subjects connect alternating numbered and lettered circles, in ascending order the same way as Trails A. Following of the correct sequence is required to complete each test. Cognitive task burden in Trails B is greater than Trails A. The Trails Making Test, therefore, provides a composite measure of attention, visuomotor tracking, and cognitive flexibility.

**Visuospatial ability**—The Card Rotations Test measures two-dimension visuospatial ability with the help of different card shapes 7. Ten rows of eight cards each are compared with a sample card shape to determine if each card is rotated or flipped over. The completion is marked by identifying two sets of ten card rows in 3 min each. The score is the difference between cards marked correctly vs. incorrectly.

**Perceptual speed**—The Identical Pictures Test includes three components of perceptual speed: perceptual fluency, decision-making speed and immediate perceptual memory. In this timed test, sample objects are matched with an identical picture in the adjacent row of test objects 7. The score is the number of correct answers, minus a fraction of the number of incorrect answers.

**Semantic fluency**—The Semantic Fluency Test is used to assess spontaneous generation of words from specific categories in a preset amount of time 4. In HANDLS, participants were asked to name as many animals as possible within 60s. Then, the total number of unique animals named is aggregated to generate a categorical animal fluency score.

1. Folstein Mf Fau - Folstein SE, Folstein Se Fau - McHugh PR, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician.

2. Delis D KJ, Kaplan E et al. CVLT-II. New York: The Psychological Corporation. 2000.

3. AL B. Benton Visual Retention Test, 5th ed. San Antonio, TX: The Psychological Corporation. 1992.

4. Strauss E SESO. A Compendium of Neuropsychological Tests: Administration, Norms and Commentary, 3rd ed. New York: Oxford University Press. 2006.

5. D W. Wechsler Adult Intelligence Scale – Revised. New York: The Psychological Corporation. 1981.

6. RM R. Trail Making Test: Manual for administration and scoring. Tucson, AZ: Reitan Neuropsychology Laboratory. 1992.

7. Ekstrom RB FJ, Harman HH et al. . Kit of Factor-Referenced Cognitive Tests, revised ed. Princeton, NJ: Educational Testing Service. 1976.