

Addendum 2:

Description of selected neuropsychological and neurophysiological tests

General intellectual function

- The vocabulary test (WAIS-R): consist of 35 words of increasing difficulty that had to be defined or explained. The test give an estimate of verbal and general intellectual ability (1).
- The similarities test (WAIS-R): consist of 14 pairs of words. The task is to say what each pair of words has in common, preferably with the closest denominator. The test measures the ability of verbal concept formation and reasoning skills (1).
- The picture completion test (WAIS-R): consist of 20 cards with pictures. The task is to say what is missing in each picture within a 20-second time limit. The test measures visuoperceptual analysis (1).
- Raven Progressive Matrices: are multiple choice tests of abstract reasoning. In each test item, a candidate is asked to identify the missing segment required to complete a larger pattern. Many items are presented in the form of a 3x3 or 2x2 matrix, giving the test its name (2). investigate the subject's ability to make comparison and to think by analogy, developing a logical method of thought independent of previously acquired materials (3;3).

Memory and learning

- The digit span test (WAIS-R): involves repeating orally presented digits either forwards or backwards. Digits forward measures attention span, while digits backward involves both a memory component and a reversing operation (mental double-tracking). The test score is the total number of digits correctly repeated forward and backward (1) (4).
- Logical Memory/Immediate recall (WAIS): the examiner reads a little selection of about 4 or 5 lines. Afterwards the subject's task is to repeat what the examiner read.
- Memory selection A: Anna Thompson/ of South/ Boston/ employed/ as a scrub woman/ in an office building/ reported/ at the City Hall/ Station/ that she had been held up/ on State Street/ the night before/ and robbed/ of fifteen dollars/. She had four/ little children/ the rent/ was due/, and they had not eaten/ for 2 days/. The officers/ touched by the woman's story/ made up a purse/ for her/.
- Memory selection B: The American/ liner/ New York/ struck a mine/ near Liverpool/ Monday/ evening/. In spite of a blinding/ snowstorm/ and darkness/ the sixty/ passengers, including 18/ women/, were all rescued/, though the boats/ were tossed about/ like corks/ in the heavy sea/. They were brought into port/ the next day/ by a British/ steamer/.(5). The participant is asked to recall as much of the story as he/she can immediately following each presentation (Logical Memory

	I) and as much of each story after a 30-minute delay (Logical Memory II) (6).
Visual Reproduction (WAIS):	consist of 3 cards with simple geometric figures on them. The subject has 10 seconds to look at them and afterwards draw them from memory. Total maximum score on all figures are 14 (5).
The word pairs test:	consist of 15 cards with 1 word on each side forming pairs. After the initial presentation of all the cards, the first word in each pair is shown. The task is to say the associated word within 10 seconds. The test measures association learning and the delayed recall of verbal material (1).
The serial digit learning test (SDL-8):	a string of 8 digits is presented orally, and the task continues until the string is repeated correctly in 2 consecutive trials or until 12 trials are performed. SDL-8 assesses short term memory and learning. Incidental memory is tested by asking the subjects to supply from memory as many as possible of the 9 symbols used in the digit symbol test (WAIS-R) immediately after the completion of the entire matrix (1).
The Benton visual retention test:	consist of 10 cards containing 1 to 3 figures with increasing difficulty. After an exposure of 10 seconds, the task is to reproduce each card by drawing. The number of correct reproductions and errors is recorded. This test involves immediate memory span, visuospatial perception, visuomotor response, and visual and verbal conceptualization (1).
The Kimura recurring figures test:	consist of 160 cards with geometric or irregular nonsense figures. First, 20 different cards are presented. Among the remaining 140 cards, 8 of the initial 20 occurred 7 times mixed with 84 new (one-of-a-kind) figures. False positive responses are subtracted from the correct responses to give the total score. This test is a test of visual memory requiring a recognition response; hence it is independent of drawing skills (1).
Modification of Kimura's test, Recurrent Figures Tests:	viewing for 10 s, eight photographed nonsense shapes, each of which are centered on 6.4 cm square card. Afterwards, three sets of 20 cards, each containing the original eight plus 12 nonsense shapes (seen for the first time) are presented. The 12 additional photographed shapes are each centered on 6.4 cm square cards, as the original eight designs. The total number of original figures recognized correctly and those misidentified are summed separately for all three presentations (7;7).
Rey's Auditory-Verbal Learning (AVL):	The first part, a recall task, consist of five auditive presentations of a series of 15 words and after each presentation, the subject reproduces verbally the words he recalls. The period of time allotted for that is 60 s after the first presentation and 90 s after each of the four subsequent presentations. All the words (ie, correct ones, repetitions, and errors) are recorded within time intervals of 15 s. For the five trials together, the total number of correct words recalled within 30 s and within the whole recall period is calculated, and similarly the total number of errors and repetitions produced within the whole recall period is calculated. For each trial separately, the total number of words reproduced correctly within the whole recall period is also calculated.

The second part, a recognition task, consists in the presentation of a 1-min story containing those 15 words in a logical context. As the subject is listening to the tape recorder, he orally repeats the words recognized. The total number of correct and faulty recognitions is recorded (8).

Short Term Memory (Paired-associates):

consist of five pairs of high (real) association (> 90% associative value) alphabetic trigrams and five pairs of low (nonsense) association (< 10% associative value) trigrams, selected from the list compiled by Archer (1960). The trigram pairs are presented individually using a slide projector at a rate of 1 per 5s. Once all five pairs have been shown, the first member of each pair is shown in a random order and the subject is required to write down the matching member. This sequence is repeated until all five trigrams are recalled correctly. The procedure is the same for both real and nonsense trigrams. The number of trigrams correctly recalled on the first trial and the number of trials to criterion are recorded for both real and nonsense trigrams (9).

Long Term Memory:

this test is a continuation of the paired-associate test described above. Without prior warning, the subjects are asked to recall the real and nonsense trigrams they had learned earlier (approx. 1.5 h before). The first members of each trigram pair are presented in the order they were last seen in the short term memory test. Number of trigrams correctly recalled is recorded (9).

Sternberg Task:

a set of two, three, four or five randomly selected digits from 0-9 is presented orally to the subject and he is asked to remember it. A digit is then displayed on the response box to which the subject is required to respond with the YES button if the digit is included in the memory or positive set or the NO button if the digit is not (negative set). A total of 48 presentations are made in which each type of digit set (i.e. two, three, four or five digits) is represented twice and each individual set is tested six times, three each for positive and negative responses. Mean reaction time is calculated for each type of digit set (9).

Iconic Memory:

pairs of letters are presented to the central foveal or peripheral portion of the visual field, and the cue card is a black triangle positioned in the place of one of the letter pairs. After dark adaptation, subjects are instructed to fixate a red spot which remains on for 400 ms, after which the stimulus card is presented for 150, 300 or 450 ms, to be replaced by the cue card for a further 150 ms. Three trials are presented in each position for each stimulus speed, for a total of 27 trials. The number of letters correctly recalled is recorded (9).

Tests for perceptual-motor speed and reaction time

The trailmaking test:

in part A, the task is to connect consecutively numbered circles by drawing lines between them, while part B requires an alternation between 2 sequences, with numbered and lettered

Digit Symbol Test(WAIS-R):	circles, respectively. The time taken to complete the test and the number of errors are recorded. This test involves attention, motor speed, visual scanning, and visuomotor tracing (1). is a symbol substitution task. Based on a printed key the subject is asked to combine 9 symbols with the corresponding 9 digits. The WAIS-R raw score is the number of correctly placed symbols in 90 seconds. The position after 90 seconds is marked, but the whole worksheet is completed. The test measures motor speed, visuomotor coordination, visual scanning, and sustained attention under time pressure (1).
Symbol-digit Substitution (NES):	the test is a psychomotor task. It is a computerized modification of the Digit Symbol Test from the Wechsler Adult Intelligence Scale-R (WAIS-R). In this task, 5 sets of 9 symbols matched with nine numbers at the top of the screen in one panel are presented sequentially. The subject is presented a scrambled symbol array without numbers at the bottom of the screen. The subject has to manually enter the correct number to be paired with the symbols at the bottom. The number of incorrect pairs and the latency for each pair are recorded. There is one practice session. The pairing of symbols with numbers is varied between sets to avoid learning effects. Score: Latency to complete task elements. Time: 4 min (10).
The simple reaction-time test (NES 2):	the task is to press a button as fast as possible when a large square appears on the computer screen. Individual reaction-time latencies are recorded. This test measures visuomotor speed and attention (1).
The continuous performance test (NES 2):	Different letters are flashed on the computer screen for about 50 ms at a frequency of one per second for 5 min. The subject is required to push a button with the index finger of the preferred hand each time the letter "S" is projected on the screen. This test measures sustained visual attention and reaction time (11).
Simple reaction time:	the subject is required to grasp a falling steel pole as quickly as possible following a visual cue from the pole. The task is repeated seven times. Each subject's score is the average reaction time for five of the seven trials, excluding maximum and minimum reaction times (4).
Choice reaction time:	Choice reaction time tasks require distinct responses for each possible class of stimulus. For example, the observer may be asked to press one button if a red light appears and a different button if a green light appears (2).

Manual dexterity and visuomotor coordination

The hand-eye coordination test (NES 2):

the task is to trace over a sine wave pattern on a screen using a joystick in the dominant hand. A cursor moves horizontally at a constant velocity while the subject controls the vertical motion. The deviations in the vertical distance from the set line are recorded. The mean of 2 test trails is used. This test measures visuomotor accuracy and motor coordination ability (1).

Hand-eye coordination:

Aiming and Tracing. Both are paper-pencil tests which require a seated subject to aim a center point or trace a (spiral) pathway with a pencil. Fifty seconds is allowed for the completion of

each of Aiming and Tracing tests. The test score (error) is a function of the distance plotted from a center and the number of times the edges of a concentric circle is touched with the pencil used for the aiming (4).

The grooved pegboard (Kløve/Matthews Motor Steadiness Battery):

consist of a small board with 5x5 holes with randomly oriented slots and small pegs with a ridge along 1 side. The pegs must be turned into position in order for them to fit correctly in the holes. The completion time is recorded. The test measures manual dexterity and complex motor coordination. The completion time in seconds is recorded for each hand (1).

The static steadiness test (Kløve/Matthews Motor Steadiness Battery):

consist of a metal plate with 9 holes with decreasing diameters from 13 to 2.5 mm. The task is to hold an electric pen in each hole for 15 seconds without touching the metal plate. The measures obtained are the number of touches and touch time. The summation scores for all 9 holes are used. The test measures intentional tremor (1).

The Lafayette rotary visual pursuit:

consist of a rotating light situated under a horizontal glass plate. The light traces out a circular path 2 cm wide. The subject tracks the rotating light in a clockwise direction with a photo-sensitive stylus, keeping the stylus within the lit area of the path. The total time the stylus stays within the lit area is recorded automatically. Three trials of one minute duration are presented at speeds of 15 rpm, 30 rpm, and 15 rpm, respectively. Is a eye/hand co-ordination task (9).

Intentional Hand Steadiness Test (IHST):

this test requires the subject to insert and hold a metal stylus in a series of six increasingly smaller holes in a metal stand for 15-s intervals. The stylus is connected to a monitor, and the subject's arm is not braced or supported during the task. The test is performed once using the subject's dominant hand and once using the nondominant hand. The test is a measure of static tremor/control. Scores: number of hits and latency (or duration of touches) for each hole and each hand. Time: 4 min (12).

Hand steadiness:

consist of two 17.5 cm x 5.75 cm plates bolted onto a single Perspex back and held vertical at an adjustable height by a retort stand. Each plate independently forms an electric circuit when hit or touched by a stylus. The subject is required to hold the stylus in a 5 mm diameter hole between the two plates with his arm outstretched keeping it as steady as possible for 1 min. The number and duration of touches on upper and lower plates are recorded independently for the three consecutive 20s periods (9).

The One-hole Test:

this test independently assesses component task elements such as the time it takes to grasp, move, position, and reach while transferring small pins from a large target to a small target hole. Scores: the four response times to grasp, move, position, and reach as well as the number of pins. Time: 7 min. (12).

Visuospatial ability

The block design test (WAIS-R):

uses 4 or 9 cubes colored red on 2 sides, white on 2 sides and red or white on 2 sides. The task is to construct 9 geometric designs with increasing levels of difficult. Bonuses are given for

fast performance. The test measures abilities in visuospatial organization, planning, and construction (1).

Attentional maintenance

Paced Auditory Serial Addition Test (PASAT):

presenting 50 Arabic numbers during each of two interstimulus intervals, 2.4 and 2.0 s. The longer 2.4 s interstimulus interval is presented first, followed by the 2.0 s interval. The total number of correct additions of each of the two adjacent numbers is converted to percentage for each of the two interstimulus intervals (7).

Vigilance:

the subject is required to perform a 5-choice reaction task in which any one of five lights will be illuminated and his task is to switch each light off. As soon as he does so, another light will be illuminated. On 10% of occasions two lights come on. The subject has to acknowledge this by depressing a central button. The test continues for 20 min. Several performance measures are taken every 5 min during the test: average reaction time (after 64 responses), the number of double light presentations correctly noted, the number of single lights presented and correctly noted and the number of single presentations missed. The number of gaps, or occasions when reaction time exceeded twice the previous mean reaction time is also displayed (9).

The Symbol Digit Modalities Test (SDMT):

assess higher executive function, concentration and attention. Participants complete a 10-digit trial, then they have 1 min by stopwatch, for the main symbol-digit exchange task. The number of correct is recorded and errors deducted to give an individual score (13).

The Switching Task:

a computer-presented task that requires the subjects to press a “same” or “different” button when confronted with a pattern comparison, semantic letter comparison, or semantic graphical comparison, presented in apparent random order. The order actually follows a complete Latin square procedure, balanced for residual effects. This test modifies the traditional design by inserting extra trials to achieve greater stability of the estimates of switching between tasks and to avoid the ability of subjects to predict the next task. These additions provide a total of 8 repetitions for the 6 switching combinations and between 10 to 16 repetitions for the control conditions. Score: switching time and the number correctly chosen. Time: 4 min (10).

Visuographic abilities

Bender Gestalt Test (BGT), scored by the Pascal-Suttell method:

consist of nine geometric figures drawn in black. These figures are presented to the examinee one at a time; then, the examinee is asked to copy the figure on a blank sheet of paper. The average amount of time to complete the test is five to ten minutes (14).

A modification of the BGT:

to screen for hand-tremor, only figs. 4 and 7 is employed, to detect tremors in hands. A set of figures is exhibited to the examinee, instructing him to reproduce the same figures on a blank piece of paper. The tremor status of the reproduced figures

is read blindly by one of the experimenters unaware of the neurological status of the subjects (4).

Motor skills

Finger Tapping Test:

is a motor-speed task performed with a simple counter. The subject is required to press a button with the index finger as many times as possible within 30 s, first with the preferred hand, then the non-preferred hand, and finally with both hands alternately tapping two buttons. The number of buttons pushed in each trial and the number of errors in alternating tapping are recorded (11).

Verbal skills

NES Vocabulary:

the NES computerized test is a modification of the Armed Forces Qualifying Test (AFQT). Twenty-five words are presented by computer and the subject is asked to select, from a set of four words, the synonym for the word originally presented. This negative control test is not expected to vary with Hg exposure and is a stable measure of CNS function indicating a level of test-taking ability. Score: Number correct. Time: 4 min (10).

Inhibitory control

Stroop Interference Test:

is a demonstration of interference in the reaction time of a task. When a word such as blue, green, red, etc. is printed in a color differing from the color expressed by the word's semantic meaning (e.g. the word "red" printed in blue ink), a delay occurs in the processing of the word's color, leading to slower test reaction times and an increase in mistakes. There are different variations of this test; "Reading Color Names", where participants are required to repeat the written meaning of words with differing colored fonts.

"Naming Colored Words", in which participants are asked to verbally identify the color of each printed color name. Stroop identified a large increase on the time taken by participants to complete the NCW (Naming Colored Words) tasks, an effect still pronounced despite continued practice at each task. This interference is thought to have been caused by the automation of reading, where the mind automatically determines the semantic meaning of the word, and then must override this first impression with the identification of the color of the word, a process which is not automatized (2).

Symptom distress

SCL-90-R:

a self-report checklist. The perceived distress associated with each of the 90 items of the SCL-90-R is rated by each subject on a five-point scale ranging from not at all to extremely. Ratings are categorized into nine symptom dimensions: somatisation, obsessive-compulsive, interpersonal-sensitivity, depression, anxiety, hostility, phobia, paranoid ideation, psychoticism. A general stress index (GSI) is determined by dividing the total rating of all items by 90 (7).

Sensorimotor performance

Grip strength:

grip strength for both hands is determined using a hand dynamometer. Subjects squeeze the handle as hard as they can for 5 sec. The maximum force for three 5-sec trials is recorded (4).

Equilibrium duration test:

subjects are asked to stand erect with one leg bent at the knee, both eyes shut, and arms outstretched. A stopwatch is used to record the duration of the period that the subjects are able to maintain the stance before returning the second foot to the ground. The test is performed three times and the mean endurance time is calculated (4).

Color card reading test:

subject performance on the Colour card reading test is assessed in terms of word reading speed and reading fluency. The colour card has five colour strips (red, blue, yellow, black, and white), printed on a gray board and set in a 10x10 matrix, each colour strip appearing 20 times. The instructions stress the need for both speed and accuracy. The experimenter has a coded copy of each card with the correct response and records any errors (4).

Screening for dementia

Hasegawa's dementia screening scale:

The 11 elements include 5 primitive questions about date, name of the place, age, birth place, and time; 2 intelligence questions about the year of the end of World War II and the name of the prime minister; 1 series involving calculations, i.e., subtract 7 from 100, then 7 from 93; Digit span, i.e., name numbers in reverse, e.g., 6-8-2, 3-5-2-9; immediate visual memory, i.e., identify five items (coin, toothbrush, watch, comb, and spoon) and recall them. There are scoring norms for normal, borderline, predementia, and dementia (4).

Personality tests

Cattell:

a factorially based test exploring 16 personality factors for defining neurotic personality or emotional disturbances such as erethism and anxiety (3); Warmth, Reasoning, Emotional Stability, Dominance, Liveliness, Rule-Consciousness, Social Boldness, Sensitivity, Vigilance, Abstractedness, Privatness, Apprehension, Openness to Change, Self-Reliance, Perfectionism, and Tension (2).

The Profile of Mood States (POMS):

has six subscales that measure continuums from composed-anxious, agreeable-hostile, elated-depressed, confident-unsure, energetic-tired and clearheaded-confused factors. Participants rate the 72 stimulus words for their mood in the previous week (13).

Freiburger Persönlichkeitsinventar (FPI):

consists of 9 scales and 3 summary dimensions (extra/introversion, neuroticism/emotional lability, and masculinity)(15).

Eysenck Personality Inventory (EPI):

score for neuroticism; defined as an enduring tendency to experience negative emotional states. Individuals who score high on neuroticism are

more likely than the average to experience such feelings as anxiety, anger, guilt, and depression. They respond more poorly to environmental stress, and are more likely to interpret ordinary situations as threatening, and minor frustrations as hopelessly difficult. They are often self-conscious and shy, and they may have trouble controlling urges and delaying gratification. Neuroticism is related to emotional intelligence, which involves emotional regulation, motivation, and interpersonal skills. It is also considered to be a predisposition for traditional *neuroses*, such as phobias and other anxiety disorders (2).

Beck Depression Inventory (BDI):

a self-rating scale for depression. Subjects are asked to rate 21 items from 0 to 3 according to how they feel at the present time. Each of the different scores contains a one-sentence description to guide the rater (6).

Critical flicker fusion:

is determined with a Flicker Fusion System, using two lamps flickering coincidentally. Eight trials are presented to both eyes at the same time. The CFF frequency is assessed four times by descending and four times by ascending manually the flicker frequencies and the subject express his first awareness of appearance or disappearance of flicker, respectively. The mean CFF threshold is calculated using the frequencies determined with the eight trials (8).

Colour discrimination:

the 28-Hue test of Roth. The test is applied to each eye (left first) separately under daylight conditions with standard illumination. The subjects wear their reading glasses when necessary. Subjects with confirmed congenital colour discrimination defects and one-eyed subjects are excluded (8).

Hand tremor:

the frequency spectrum of hand-tremor amplitude is investigated under four different conditions (rest position, wrist loading with 2 kg, a pointer directed to a target, and wrist loading plus pointer). The hand-tremor pattern is recorded using an accelerometer fixed on the dorsal side of the hand and connected to a FM tape recorder through a precision sound-level meter. The tremor signals are subsequently analyzed with a real-time spectrum analyzer permitting the determination of peak frequencies, acceleration amplitudes, moments, displacements, and velocities (8).

Hand tremor:

this test is used to measure tremor activity in the hand. Subjects are first required to hold a Tremor Pen in their dominant hand exactly as an ordinary pen is held. The pen is held horizontal to the ground, at the waist and parallel to the body for 10 s. Hand vibrations are recorded and displayed real-time in a time-axis plot on the computer screen. This is repeated with the subject's nondominant hand. Scores: tremor intensity, center frequency, dispersion of power, harmonic index, and tremor index for each hand. Time: 12 min. (12).

Cognitive skills

The California Verbal Learning

Test (CVLT): provides information about the subject's use of learning strategies and their effectiveness and level of interaction between verbal memory and conceptual ability. Each of the 16 items in each CVLT list belongs to one of four categories of "shopping list" items: for example, the first – "Monday's" list – contains four names of fruits, of herbs and spices, of articles of clothing, and of tools. The CVLT provides for two recall trials on both the short-term delay (immediately after the interference trial, the "Tuesday shopping list") and the long-term (20 min) delay. The first of the two recall trials is "free" recall in which the subject is requested to "tell me all" remembered items. The second recall trial utilizes the item categories as cues, asking the subject for items in each of the categories (fruits, then herbs and spices, etc.). From the Monday to the Tuesday list there is a overlap of categories, as the latter list, too, includes four fruits and four herbs or spices, with the remaining eight items split between kinds of fish and kitchen equipment (16).

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