## Cognitive performance across the lifespan and domains

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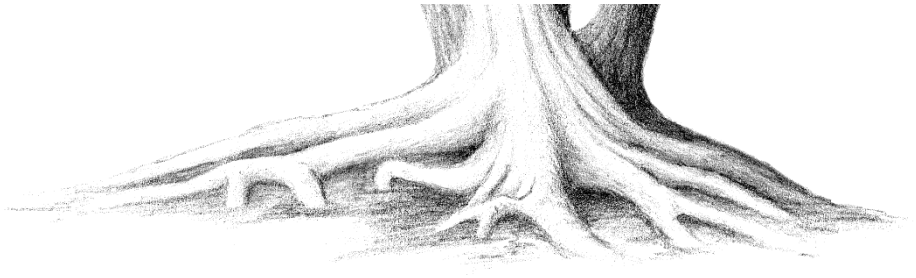
# Chapter 2

## Sample description and procedure in studies on the Computerized Neurocognitive Battery in the Dutch population



The Computerized Neurocognitive Battery (CNB), developed by The Brain and Behavior Laboratory of the University of Pennsylvania, was translated into Dutch by the Department of Biological Psychology, Vrije Universiteit Amsterdam. A large data collection project with the Dutch CNB took place between 2010 and 2013. Initially, the CNB was tested in a group of 30 students (pilot phase) and next in a group of over 1100 participants from the Netherlands Twin Register (NTR).

## Characteristics of participating families in the CNB study

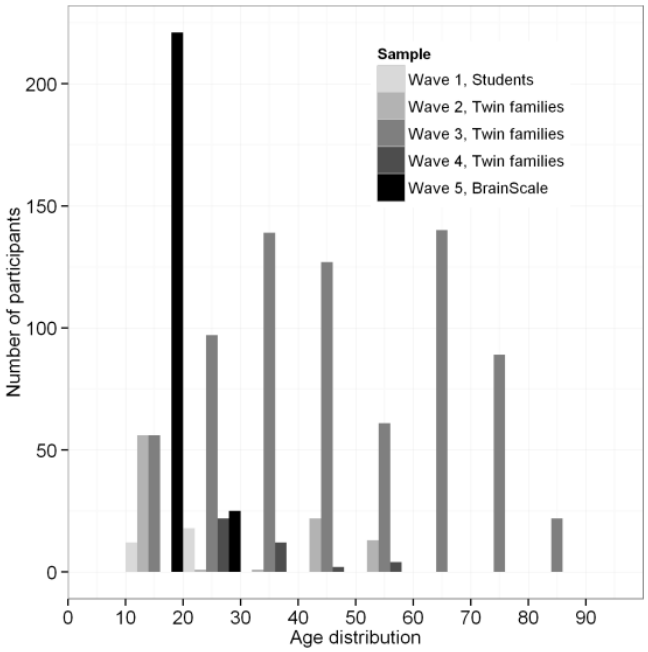
The complete sample with data from the neuropsychological testing project was tested in 5 different waves. During the pilot phase (wave 1), 30 undergraduate students participated in data collection in the lab. Students signed up themselves, and received study credits for participation.

Families from the NTR in the second and third wave were recruited based on living area (provinces near Amsterdam) and age. In the second wave, twin pairs around age 14 and 15 were selected, and their parents and siblings were allowed to participate as well during these home visits (in total 93 participants from 26 families). The third wave recruited elderly participants of the NTR, preferably with available genotype data in the database, and again all family members were invited to participate (in total 731 participants from 276 families).

A fourth wave consisted of a group of 20 twin pairs from an MRI study in twin pairs discordant for obsessive compulsive symptoms (den Braber et al., 2013b) who took part in cognitive testing while they were in the Amsterdam Medical Center for the appointment.

The final group consisted of participants of the BrainScale study (wave 5). The group of twins and siblings in the BrainScale project were acquired throughout the Netherlands in a combined research project between the NTR and the Brain Center Rudolf Magnus from the University Medical Center Utrecht. These participants were selected from the NTR in 2005 when the first data collection started, and were currently participating in the third wave of data collection in this project. In total this sample consisted of 176 twins and 70 siblings (in total 139 females, 107 males, mean age 17.45, $SD = 1.32$). A detailed description of the sample and data collection during the third assessment can be found in Chapter 3.

**Figure 1.** Number of participants per age cohort in the different waves of data collection.




In total, neuropsychological data of 1140 participants were collected. The final sample was comprised of 668 female and 472 male participants between the ages of 10 and 86 (mean age = 37.73, *SD* = 20.86). A graphical indication of the age distribution is given in Figure 1. The twin-family part of the sample consisted of 1110 participants from 431 NTR families. The majority of this sample was part of a twin pair (618). The rest of the sample were parents of twins (126 fathers, 160 mothers), siblings of twins (144), spouses of twins (43) and siblings (10), and children of twins (6) and siblings (3).

## Procedure

These studies were approved by the Medical Ethics Review Committee of the Vrije Universiteit Medical Center Amsterdam and the Central Committee on Research Involving Human Subjects (wave 5), and research procedures were performed in accordance with the Declaration of Helsinki. Examples of letters, brochures and documents can be found in the Appendices (1 to 5).

## Invitation

All participants were sent an invitation letter including a brochure (Appendix 1 and 2) with detailed information about the study and procedures. Besides general information about the study purpose and procedure, it stated that participants would receive gift vouchers, and were compensated for travel expenses. Further, a summary of their results on the computerized tests would be mailed to them afterwards as a token of appreciation (Appendix 4).

Following this letter, participants were contacted by phone to inquire whether they had received the letter and were willing to participate. A telephone protocol was used that specified for each moment of contact: the date and time, what was discussed, whether each participant of a family was willing to participate, when to call back (if necessary), the reason for not participating (if applicable), the confirmed date of the appointment, and the date of sending the confirmation letter including study materials. Participants were provided the option to choose whether they preferred a home visit or an appointment at the Vrije Universiteit Amsterdam (VU) laboratory, except for participants of the MRI study which was always taking place in the hospital. When families agreed to participate, each individual was sent a confirmation of the appointment and consent forms (Appendix 3). Consent forms were signed by parents as well as children when the child was younger than 18.

## Procedures

The data collection took place at the participants' home (536), the VU laboratory (318), the Amsterdam Medical Center (40), and the University Medical Center Utrecht (246). Depending on the wave of data collection, experimental procedures varied slightly. Measurements and instruments are described below.

The experimental procedure would always start with an explanation. Next, basic information about medication use and education was gathered. After participation, adults were asked to fill in the latest survey of the Adult NTR at home and all NTR participants were asked to collect buccal epithelium for DNA isolation.

In the first wave (the university students) and the second wave (young twins and their parents and siblings) the procedure started with the reading test. Then participants completed the Computerized Neurocognitive Battery (CNB). During the first and second designated breakpoint of the CNB, blood pressure was measured. During the third breakpoint a standardized interview was administered which included questions about education or occupation, sleep, smoking, drinking, exercise, time spent walking and biking, menstruation and general health (Appendix 5). The procedure took on average 2 hours per person.

After the first two waves, a few measurements were added to the procedure. First, cardiac autonomous nervous system (ANS) activity was recorded by a non-invasive device. Electrodes of the VU University Ambulatory Monitoring System were placed on the back and chest (VU-AMS, de Geus, Willemsen, Klaver, & Van Doornen, 1995; Willemsen, de Geus, Klaver, Van Doornen, & Carroll, 1996). This recording provides measurements of for example heart rate (interbeat interval and variability), heart rate variability, T-wave amplitude and pre-ejection period. During a 5-minute measurement, participants watched a calming movie of a beach during which a baseline recording of autonomous nervous system activity was made. Also an additional measurement of blood pressure was taken during this resting baseline. Measurements of length and weight were taken, and hip and waist circumference were measured.

Participants in wave 4 (opposite-sex twins) and wave 5 (BrainScale twins and siblings) also had an MRI scan of the brain. When their co-twin was in the scanner, participants in wave 4 would follow the same CNB testing protocol as participants from the first and second wave (thus without ANS recording). The procedure of wave 5 will be described in detail in Chapter 3.

## Instruments and measurements

### Behavioral data

#### *Questionnaire*

Participants from the NTR were asked to fill in the most recent survey ('survey 8'). This questionnaire contains questions on emotional and behavior problems (ASR), well-being, lifestyle, exercise behavior, sedentary behavior, and family functioning (Willemsen et al., 2013).

#### *Interview*

In addition to the CNB, participants were asked about, or filled out a questionnaire on lifestyle (e.g., drinking, smoking, exercise behavior).

#### *Education*

Prior to the CNB administration participants were asked about their own educational background, as well as that of their parents. Level of education was defined as the sum of years involved in elementary, secondary and higher education if the educational curriculum (per year) was completed.

### *Medication*

In the confirmation letter, participants were asked to show, or bring with them to the appointment, packages of medication they (recently) used. The brand and substance name, frequency and reason for using the medication were registered.

## Physical examination

### *Length and weight; hip and waist circumference*

Measurements of length and weight were obtained by measurement at the day of testing (wave 3, 4 and 5). Before measurement, participants were asked to take off their shoes. In wave 3 and 4, hip and waist circumference were measured with a tape-measure.

### *Blood pressure and heart rate*

Blood pressure and heart rate were measured in a sitting position with an Omron automatic blood pressure monitoring device. The cuff was attached to the non-dominant arm. Depending on the wave of data collection, measurements were taken once (wave 5), twice (wave 1, 2 and 4), or three times including a baseline measurement (wave 3).

## Neuropsychological assessment

### *Computerized Neurocognitive Battery (CNB)*

The CNB (Computerized Neurocognitive Battery) is a Dutch translation of the current web-based CNB (Gur et al., 2012). It includes a total of 17 tests, resulting in measures of performance accuracy (the percentage or number of correct responses) and response time in five global cognitive functions. These functions, their corresponding test and which cognitive domain they specifically measure are given in Table 1. For more detailed descriptions of these tests we refer to Gur et al., (2010, 2012) and the Supplementary materials of Chapter 5.

Prior to the administration of each of the CNB's tests, instructions were read out loud to the participant by the administrator, after which participants were provided with practice trials (memory tests and the Conditional Exclusion Test excluded). Practice trials had to be completed successfully before the actual trials started. The administrators kept track of whether the participant's test scores were valid or not, for example based on the participant's (lack of) motivation, the presence of distracters, or computer issues. On top of this, automated test score validation occurred upon upload to the Pennsylvania web servers that host the CNB. At the Pennsylvania web servers automated scores were generated for a number of variables describing the performance on the various subtests in great

detail. The main outcome variables extracted from these scores, reflecting overall accuracy and speed of test performance, are listed in Table 2, including the mean score (and SD) for the participants from wave 1-4.

### *Reading ability*

The participants were instructed to read out loud, within one minute, as many words as possible from a card with 116 words. The list was adapted from the "Three Minutes Reading Task", which is frequently used in the Dutch educational system (Cito, 1995).

**Table 1.** Overview of global cognitive functions, corresponding tests and the cognitive domain they measure

| Cognitive function | Test name | Cognitive domain measured |
|---|---|---|
| *Executive-control* | Continuous Performance Test | attention |
| | Letter N-Back Test | working memory |
| | Conditional Exclusion Test | abstraction & mental flexibility |
| *Episodic memory* | Face Memory Test | face memory |
| | Word Memory Test | verbal memory |
| | Visual Object Learning Test | spatial memory |
| *Complex cognition* | Matrix Reasoning Test | nonverbal reasoning |
| | Verbal Reasoning Test | language reasoning |
| | Line Orientation Test | spatial ability |
| *Social cognition* | Emotion Identification Test | emotion identification |
| | Emotion Differentiation Test | emotion differentiation |
| | Age Differentiation Test | age differentiation |
| *Sensorimotor speed* | Motor Praxis Test | sensorimotor speed |
| | Finger Tapping Test | motor speed |

**Table 2.** Overview of main output variables (wave 1-4)

| Task or measure used | Main output phenotype | N | Mean ± SD |
|---|---|---|---|
| Cognition | | | |
| Reading ability (1 minute) | Total correct words | 892 | 94.13 ± 14.72 |
| CNB, Cognitive domain | | | |
| Attention | True positive responses (#) | 886 | 1.78 ± 0.80 |
| | Median RT (ms) | 886 | 2923.23 ± 1486.68 |
| Abstraction and mental flexibility | Correct categories (#) | 884 | 54.82 ± 5.64 |
| | Median RT (ms) | 884 | 486.55 ± 50.92 |
| Working memory | True positive responses (#) | 877 | 18.66 ± 1.97 |
| | Median RT (ms) | 876 | 542.73 ± 121.65 |
| Face Memory | Total correct (#) | 882 | 31.45 ± 3.54 |
| | Median RT (ms) | 882 | 2013.87 ± 555.49 |
| Face Memory -delayed | Total correct (#) | 880 | 31.97 ± 3.57 |
| | Median RT (ms) | 880 | 1869.45 ± 503.48 |
| Verbal memory | Total correct (#) | 884 | 36.16 ± 2.93 |
| | Median RT (ms) | 884 | 1611.63 ± 390.10 |
| Verbal memory - delayed | Total correct (#) | 883 | 34.80 ± 3.36 |
| | Median RT (ms) | 883 | 1587.70 ± 396.61 |
| Spatial memory | Total correct (#) | 875 | 15.84 ± 2.32 |
| | Median RT (ms) | 875 | 2048.73 ± 569.66 |
| Spatial memory - delayed | Total correct (#) | 872 | 15.25 ± 2.36 |
| | Median RT (ms) | 872 | 1885.24 ± 537.35 |
| Nonverbal reasoning | Total correct (#) | 887 | 13.06 ± 5.21 |
| | Median RT (ms) | 886 | 10861.37 ±7341.78 |
| Language reasoning | Percentage correct (%) | 878 | 69.89 ± 21.07 |
| | Median RT (ms) | 877 | 8399.40 ± 3339.09 |
| Spatial ability | Total correct (#) | 877 | 12.66 ± 3.76 |
| | Median RT (ms) | 877 | 10707.51 ± 4101.30 |
| Emotion Identification | Total correct (#) | 891 | 31.71 ± 3.52 |
| | Median RT (ms) | 891 | 2353.91 ± 725.51 |
| Emotion Differentiation | Total correct (#) | 889 | 27.71 ± 3.58 |
| | Median RT (ms) | 889 | 3862.67 ± 1445.49 |
| Age Differentiation | Total correct (#) | 879 | 26.57 ± 4.03 |
| | Median RT (ms) | 879 | 3424.03 ± 1579.68 |
| Sensorimotor speed | Total correct (#) | 888 | 19.94 ± 0.41 |
| | Median RT (ms) | 888 | 822.75 ± ± 235.47 |
| Motor speed | Total taps in 1 minute (#) | 882 | 109.66 ± 15.75 |
| Physical examination | | | |
| Height | Centimeters | 769 | 172.91 ± 9.82 |
| Weight | Kilogram | 769 | 76.06 ± 14.99 |
| Diastolic blood pressure | mmHG | 890 | 76.46 ± 11.28 |
| Systolic blood pressure | mmHG | 890 | 129.00 ± 18.10 |
| Heart rate | Beats per minute | 890 | 67.30 ± 10.35 |
| Hip circumference | Centimeters | 770 | 100.20 ± 0.62 |
| Waist circumference | Centimeters | 770 | 83.72 ± 14.03 |

*Note: Median RT refers to the median response time per individual for all correct responses on a test. Mean RT refers to the mean of RT medians across individuals*