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# The Computerized Neurocognitive Battery: Validation, Aging Effects, and Heritability Across Cognitive Domains

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Objective: The Computerized Neurocognitive Battery (CNB) enables efficient neurocognitive assessment. The authors aimed to (a) estimate validity and reliability of the battery's Dutch translation, (b) investigate effects of age across cognitive domains, and (c) estimate heritability of the CNB tests. *Method:* A populationrepresentative sample of 1,140 participants (aged 10-86), mainly twin-families, was tested on the CNB, providing measures of speed and accuracy in 14 cognitive domains. In a subsample (246 subjects aged 14-22), IQ data (Wechsler Intelligence Scale for Adults; WAIS) were available. Validity and reliability were assessed by Cronbach's alpha, comparisons of scores between Dutch and U.S. samples, and investigation of how a CNB-based common factor compared to a WAIS-based general factor of intelligence (g). Linear and nonlinear age dependencies covering the life span were modeled through regression. Heritability was estimated from twin data and from entire pedigree data. Results: Internal consistency of all tests was moderate to high (median = 0.86). Effects of gender, age, and education on cognitive performance closely resembled U.S. samples. The CNB-based common factor was completely captured by the WAIS-based g. Some domains, like nonverbal reasoning accuracy, peaked in young adulthood and showed steady decline. Other domains, like language reasoning accuracy, peaked in middle adulthood and were spared decline. CNB-test heritabilities were moderate (median h2 = 31%). Heritability of the CNB common factor was 70%, similar to the WAIS-based g-factor. Conclusion: The CNB can be used to assess specific neurocognitive performance, as well as to obtain a reliable proxy of general intelligence. Effects of aging and heritability differed across cognitive domains.

Keywords: neurocognition, intelligence, heritability, aging, computerized testing

Supplemental materials: http://dx.doi.org/10.1037/neu0000248.supp

Cognitive performance varies greatly among individuals. Possible sources of individual variation are gender, age, and genetic and environmental factors. Studies on cognitive functioning increasingly aim to find the biological basis of cognition in brain substrates or

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genetic variants. These neurobiological and genetic association studies on individual differences in cognition require reliable and well-defined phenotypes obtained in large numbers of participants. Such studies would benefit greatly from the availability of cognitive tests that are optimally suited to explore mechanistic neurobiological and neurodevelopmental models in large samples. Understanding how cognitive functions develop across the life span and how they are influenced by environmental and genetic factors is critical for elucidating healthy and pathological brain function.

As cognitive functions may be differentially sensitive to sources of variation, both basic functions, such as processing speed or attention, and more complex functions, like reasoning or emotion processing, require consideration. Notably, neurocognitive tests based on functional neuroimaging are designed to activate specific brain systems, whereas traditional neuropsychological and intelligence tests may activate multiple brain systems simultaneously, making the latter less suitable in neurobiological studies (Gur, Erwin, & Gur, 1992).

To address the need for an efficient and comprehensive neurocognitive battery, the Brain Behavior Laboratory of the University of Pennsylvania has developed the Web based Computerized Neurocognitive Battery (CNB; Gur et al., 2001; Gur et al., 2012). This battery is the result of an iterative validation process during which tests and test items were selected. Tests aim to target specific brain regions, which was validated in functional brain imaging studies (Roalf et al., 2014). Since its introduction, the CNB has undergone minor revisions including shortening of tests and adding new ones. The current version of the CNB (Gur et al., 2012) yields quantitative performance (accuracy and speed) measures in five neurobehavioral functions: executive-control, memory, complex cognition, social cognition, and sensorimotor speed. More specifically, within these five neurobehavioral functions the battery assesses performance across 14 cognitive domains, which are described in Table 1 and described in Supplementary Material S1.

The need for an efficient and reliable neurocognitive battery extends beyond the English speaking countries for large-scale genetic, developmental and aging studies. For this reason we translated test instructions and test items from English into Dutch. International collaborative studies would benefit from the assurance that cognitive batteries can be deployed universally: cognitive performance and effects such as sex and age should be comparable across countries.

The objectives of this article are first to estimate validity and reliability of the battery's Dutch translation, second to investigate effects of age across cognitive domains, and third to estimate how these cognitive abilities are influenced by environmental and genetic factors. With regard to the validation part of our study, we aim to confirm reliability, validity, and feasibility in home and laboratory settings of the CNB in a large population-based sample of 1140 participants (10-86 years). Here we present indices of reliability based on internal consistency (Cronbach's alpha) and on intercorrelations among the test scores. To confirm validity, we compare mean scores and effects of gender and age in the Dutch to the U.S. population. In addition, we correlate CNB scores to measures of a person's own and parental level of education. We also consider whether the CNB can provide scores comparable to intelligence scores as derived from traditional intelligence tests. If so, this would provide further convergent validity, because, although individual CNB test scores will be difficult to compare to traditional IQ scores, across batteries the sources of between test covariance can be expected to be the same (Johnson, te Nijenhuis, & Bouchard, 2008), genetic sources in particular (Plomin & Kovas, 2005).

Table 1
Cognitive Domains and Test Names, Order of Administration, and Mean Administration Time (in Minutes), Number of Participants
Who Completed the Test, and the Test's Mean Score (and SD), Cronbach's Alpha Coefficients (α) of Accuracy Score (Percentage or Number of Correct Responses) and Speed (Median Response Time, in ms)

							Acc	curacy		Speed			
Cognitive domain	Test name	Test label	Order	Duration	N	M	SD	Cronbach's α	M	SD	Cronbach's α		
Executive control													
Abstraction/flexibility	Penn Conditional Exclusion Test <sup>a</sup>	CET	9	4.9	1,125	1.9	.8	d	2813.3	1392.6	d		
Attention	Penn Continuous Performance Test <sup>a</sup>	CPT	3	5.3	1,125	54.8	5.4	.86	487.7	49.1	.82		
Working memory	Letter-N-Back Test <sup>a</sup>	LNB	6	9.2	1,114	18.8	1.8	.77	537.7	118.0	.80		
Memory													
Verbal memory	Penn Word Memory Test <sup>b</sup>												
	Immediate	CPW-i	5	3.1	1,125		2.8	.62	1564.5	368.2			
	Delayed	CPW-d	8	1.1	1,124	35.0	3.3	.64	1541.7	376.6	.91		
Face memory	Penn Facial Memory Test												
	Immediate	CPF-i	4	3.9	1,123			.56	1992.7	544.2	.92		
	Delayed	CPF-d	7	1.5	1,121	32.1	3.5	.57	1834.2	489.7	.89		
Spatial memory	Visual Object Learning Test <sup>a</sup>												
	Immediate	VOLT-i	13	2.7	1,117			.48	1973.8		.87		
	Delayed	VOLT-d	17	.5	1,115	15.4	2.4	.48	1811.5	519.7	.86		
Complex cognition													
Nonverbal reasoning	Penn Matrix Reasoning Test	MAT	12	7.8	1,129	13.9	5.2	.90	10806.0		.88		
Language reasoning	Penn Verbal Reasoning Test <sup>a,b</sup>	VRT	14	1.8	1,123			.53		3332.5	.74		
Spatial ability	Variable Penn Line Orientation Test <sup>a</sup>	LOT	16	5.5	1,119	12.9	3.7	.79	10506.8	3861.8	.97		
Social cognition													
Emotion identification	Penn Emotion Identification Test	EI	2	2.3	1,132	32.1	3.5	.62	2273.4	685.7	.92		
Emotion differentiation	Measured Emotion Differentiation Test	EDT	10	3.4	1,131	28.0	3.5	.69	3721.0	1369.1	.94		
Age differentiation	Age Differentiation Test	ADT	15	3.0	1,122	26.8	3.9	.74	3238.4	1493.5	.94		
Sensorimotor	-												
Sensorimotor speed	Motor Praxis Test	MP	1	1.8	1,130	20.0	.4	.93	793.2	221.3	.95		
Motor speed	Penn Computerized Finger-Tapping Test <sup>a</sup>	TAP	11	3.5	С	с	с	с	110.6	15.1	.96		

Note. N = number of participants; M = mean score; SD = standard deviation.

<sup>&</sup>lt;sup>a</sup> Short test version. <sup>b</sup> Different items for children. <sup>c</sup> No accuracy score available for TAP. <sup>d</sup> Not amenable for calculating.

Once we have established that the CNB provides reliable and valid measures of cognition, we can explore the etiology of individual differences in these cognitive phenotypes. These extend beyond sex- and linear age effects: therefore our second aim is to estimate nonlinear effects of age across the life span. Many cognitive functions improve as children mature, but with different trajectories for different functions: a well-known example is the late development of executive functions compared to memory (Gur et al., 2012). However, later in life cognitive abilities start to decrease again, especially in the domains of processing speed, memory, and executive functioning, although there is currently little agreement on the time of onset of this decline (Salthouse, 2009; Schaie, 2005; Deary et al., 2009). Cognitive aging is most often studied in a small age range (i.e., only elderly), usually including only one or a few cognitive functions. Here we will explore the patterns of development across cognitive domains and covering the life span.

Our third and final aim regards environmental and genetic effects on the cognitive tests. Initial studies on a subset of the tests show heritability estimates between 10 and 70% (Calkins et al., 2010; Greenwood et al., 2007; Gur et al., 2007) in the U.S. population. These estimates are based on selected samples of schizophrenia patients. We will extend these findings by estimating heritability for all accuracy and speed scores in an unselected sample, which facilitates generalization to the general population. We will also estimate heritability of the common variance among the CNB test scores. Because indicators of common variance among psychometric IQ tests (i.e., general factors of intelligence) are the most heritable among the indicators of intelligence, with an estimated heritability coefficient of 50% to 80% (Jensen, 1998; Plomin, 2012), we expect a high heritability. If so in our analyses, this would further confirm validity.

Heritability was estimated using two approaches, both based on the resemblance in cognitive performance among family members as a function of their genetic relatedness. Half of our sample consisted of twins; the other half of parents, siblings, and children of twins and siblings. The first approach is based on information from the mono- and dizygotic twin pairs, who are of the same age by definition, and estimate the extent to which their resemblance is due to shared genes, or common environmental influences shared by offspring growing up in the same family. In the second approach we extend the analyses to data from the entire pedigree, that is, all family members, where cross-generation resemblance is analyzed simultaneously with the resemblance in twin pairs. These pedigree-based analyses provide information on genetic stability across generations.

#### Method

#### **Participants**

Participants were mainly recruited by the Netherlands Twin Register (NTR), which is a population-based register that recruits twins and other multiples, their parents, siblings, spouses, and offspring (Boomsma et al., 2006; Willemsen et al., 2013; van Beijsterveldt et al., 2013). In total there were 1,140 participants, mainly (n = 1,110) from 431 families who were recruited from all regions in the Netherlands. The other 30 subjects were university students. Most participants (621) were part of a twin pair or triplet.

Twin pairs were monozygotic (54 male, 100 female pairs) or dizygotic (42 male, 60 female, 71 opposite sex pairs). The rest of the sample consisted of siblings (150), parents of twins (279), partners of twins and siblings (51), and offspring of twins and siblings (9). The age range was from 10 to 86 (M = 37.73, SD = 20.86). The figure in Supplementary Material S2 depicts the age distribution of these 472 males (41.4%) and 668 females. On average, participants had 12.92 years of education (SD = 3.29). The average number of years of education in their parents was 12.34 (similar to the average in the Dutch population, UNESCO Institute for Statistics, 2013).

#### **Procedure**

Studies and procedures were approved by the Medical Ethics Review Committee of the VU Medical Center Amsterdam and the Central Committee on Research Involving Human Subjects. Participants were approached by mail. When they (and possibly other family members) were willing to participate, a structured telephone call followed. This phone call had the purpose of informing participants and of asking about exclusion criteria. Exclusion criteria were epilepsy or paralysis, and physical problems that would influence test performance (like a broken arm or severe vision problems).

Testing took place at the VU Laboratory (n=358), at the participants' home (n=536), or in the laboratory of the University Medical Center Utrecht (n=246). In all settings, test conditions were controlled to prevent disturbance or distractions. Prior to the start of the testing, the administrator fully explained the procedure, after which written informed consent was obtained. Participants of 12 years of age and older signed themselves. For children up to 16 years parents needed to sign as well. Following the CNB protocol from the Brain Behavior Laboratory, participants were asked to complete a reading test (Swagerman et al., in press). For none of the participants did the reading test indicate that they were unable to complete the CNB. Participants received a gift voucher and compensation for their traveling costs. All participants received feedback on their performance, in the form of a graph in which their score was ranked with participants of the same age.

Standardized procedures were followed for both the home and laboratory test location. The participant sat at a desk, with the test administrator behind him or her. Macbooks were used for administration with identical mouse and screen settings. All participants were instructed to use only the mouse and spacebar for responses (laptop mousepad was disabled).

Prior to the start of each test, the administrator read the test instructions out loud to the participant, after which the participant was provided with practice trials (except for the memory tests and the Conditional Exclusion Test). The practice trials had to be completed successfully in order to start the test. During the cognitive assessment, the experimenters kept track of whether test scores were valid, based on the participant's apparent motivation or interruption of the test session. Automated test score validation occurred upon upload to the Pennsylvania web servers that host the CNB (Gur et al., 2012). Completion of the battery lasted on average 1.5 hr (ranging between approximately 50 min and 3 hr), including optional breaks at three designated points.

A subsample of adolescent participants (n = 246, 14-22 years old), took part in the Brainscale study on development of brain and

cognition (van <u>Soelen et al., 2012</u>). These participants completed a shortened version of the Wechsler Intelligence Scale for Adults (WAIS; <u>Wechsler, 1997</u>) on the same day as they were assessed on the CNB.

#### Measures

In addition to the CNB, participants were asked about, or filled out a questionnaire on lifestyle (drinking, smoking, exercise behavior), height, weight, and medication use.

Cognitive battery. The Dutch translation of the current CNB includes a total of 17 tests, yielding measures of performance (accuracy and speed) in 14 cognitive domains (Table 1; Supplementary Material S1). All test instructions and test items were translated from English into Dutch, and back-translated by a professional translator. In addition, the frequency of the words in the A and B versions of the Word Memory Test and Verbal Reasoning Test were compared, to ensure that both versions were of equal difficulty.

Accuracy was defined as the percentage or number of correct responses on a test. Measures of speed were derived from the median response time in milliseconds of correct responses, and were multiplied by -1. Hence for both accuracy and speed, higher scores denote better performance. The Finger tapping test (TAP) did not provide accuracy scores: the score reflected the number of taps one can produce within 10 seconds over 6 attempts. TAP score thus constitutes a speed score, where a relatively high score denotes relatively fast motor speed.

**Psychometric IQ.** The shortened WAIS included two verbal and two performance tests, which were, in order of assessment, Vocabulary (verbal), Block Design (nonverbal), Similarities (verbal), and Matrix Reasoning (nonverbal). Using normative tables per age group, raw test scores were transformed into standardized scale scores (Wechsler, 1997). Then a correction for the number of excluded subtests was applied (2 out of 6 verbal and 2 out of 5 nonverbal tests) to obtain total (TIQ), verbal (VIQ), and performance IQ (PIQ).

Years of education. Participants were asked how many years of education they and their parents had completed. Repeating a school year did not count as an extra year. In case the same type of education was repeated at a higher level (e.g., economics degree at college level followed by university level), only the number of years at the highest level was counted. Parental education was defined as the mean number of years of paternal and maternal education, or of one of them if the other was unknown.

#### **Statistical Analyses**

Validity and reliability. Excluding test scores of children under  $13 \ (n=4)$  and scores that were judged invalid (0.8%), we calculated in SPSS 21.0 for each test the average accuracy score, average speed score, average duration, and the Cronbachs's alpha coefficient of internal consistency (not possible for the Conditional Exclusion Test). Further, correlations among accuracy scores, correlations among speed scores, and per test the correlation between accuracy score and speed score were calculated (all while correcting for effects of gender and age). Accuracy and speed scores were skewed. In addition, the data had to be considered as clustered since the study involved family members. Statistical analyses (other than

the genetic analyses) thus required correction of the standard errors of the parameters. This was accomplished by analyzing the data in the statistical program R (version 3.1.1, R Core Team, 2014) using packages lavaan (Rosseel, 2012) and lavaan.survey (Oberski, 2014), by including family number as cluster variable (each student received a unique family number), and by opting for robust sandwich estimation. This procedure allowed for the analysis of clustered, nonnormally distributed, but continuous outcome variables.

Following <u>Gur et al. (2010)</u> we obtained gender differences on all cognitive measures, and correlations between performance scores and education as well as parental education. Because own educational level is meaningful only after the typical age that maximal academic training can be achieved, we restricted these analyses to a subsample over age 30 (n = 632, M = 14.2, sd = 3.4).

In the literature, the variance that is common to IQ subtest scores is usually described by the latent variable referred to as general intelligence or simply *g* (Jensen, 1998; Spearman, 1904). A strong correlation between the common variance in CNB test performance and general intelligence (as derived from traditional batteries) would imply that once performance measures on the CNB are aggregated, a CNB sum score would be similar to a traditional TIQ score. TIQ can be considered to constitute the most accurate proxy of general intelligence (after the *g*-factor score). The WAIS VIQ, PIQ, and TIQ scores that were available in the subsample therefore provided the opportunity to test this using the following approach.

We selected all CNB accuracy scores, those on the Motor Praxis test excluded, because WAIS scores are based on accuracy scores rather than speed scores, and concern cognitive abilities and knowledge rather than motor skills. Next, we forced a confirmatory oblique 2-factor model on the (WAIS and CNB accuracy) data, in which the CNB scores loaded on one latent factor (labeled g-CNB in Figure 1) and the WAIS VIQ and PIQ scores on the other (labeled g-WAIS). As WAIS IQ scores are already age corrected, we added linear and (mean-centered) quadratic age terms as predictors of the CNB scores to make them comparable to the WAIS. The correlation between the two latent factors was considered to indicate the strength to which the common variance among the CNB accuracy test scores relates to general intelligence as assessed by the WAIS. A high correlation would indicate that the CNB can provide a valid and reliable estimation of general intelligence. To be able to confirm this, we obtained factor scores on the g-CNB and correlated these with WAIS TIQ scores. This correlation was interpreted as a measure of both reliability and cross-validity.

**Analyses of aging effects.** Relations between test performance scores and age were analyzed according to a model in which the scores on a particular test were regressed on age (across the age range in the data: 13–86 years old) and on (mean centered) age squared.

**Heritability analyses.** To estimate heritability, data of monozygotic (MZ) twins who are (nearly) genetically identical and dizygotic (DZ) twin pairs who share on average half of their segregating genes were analyzed first (Boomsma, Busjahn, & Peltonen, 2002). Because MZ and DZ twins differ in their genetic similarity, genetic effects are suggested for a trait if the MZ correlation is higher than the DZ correlation. Effects of common environment shared by twins are suggested to also contribute to twin resemblance when the DZ correlation is larger than half the MZ correlation. Modeling of twin data was performed in OpenMx (Boker et al., 2011) by raw-data maximum likelihood. All speed scores were log-transformed prior to analysis to reduce skewness (to the right toward slow response times)

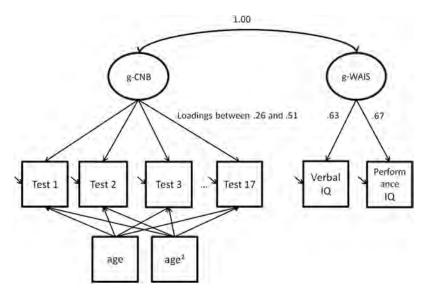


Figure 1. Oblique two-factor model of overlap in variance of Computerized Neurocognitive Battery (CNB) tests and Weschsler Intelligence Scale for Adults (WAIS) Verbal and Performance IQ scales. Circles represent the two latent variables that describe common variance among CNB tests (labeled g-CNB) and common variance among WAIS subtests (labeled g-WAIS). Squares represent the observed CNB test scores and WAIS Verbal and Performance IQ scores. Double-headed arrows between two variables represent correlations and single-headed arrows between two variables represent standardized regression effects (factor loadings included). Any other single-headed arrows represent residuals.

and heteroscedasticity (more variance with older age). First, in a saturated model, means, variances, and twin correlations were estimated for monozygotic (MZ) and dizygotic (DZ) twin pairs. Next, parameters representing the influence of additive genetic factors (A), common environment shared by twins (C) and unique environment (E, including measurement error) were estimated (Plomin, Defries, Knopik, & Neiderhiser, 2013). The model included gender, age, and (mean centered) age<sup>2</sup> as moderators of the mean scores. Second, heritability was estimated in Mendel (Lange, Westlake, & Spence, 1976; Lange et al., 2013), analyzing the entire pedigree structure including twins. The approach implemented in Mendel takes the entire pedigree information to estimate variance components and allows for the inclusion of all relatives. The effect of common environment (C) was estimated for twins and their nontwin siblings growing up in the same household up to age 22 (mean age when children move out of their parents' house, Statistics Netherlands, 2014). Heritability analyses were performed for the 15 accuracy and 17 speed outcomes. As 98% of all participants had perfect accuracy on the Motor praxis test, for the sensorimotor domain only speed was examined. In addition, heritability was estimated for both the factor score on the g-CNB and WAIS TIQ scores.

#### Results

#### Validity

Internal consistencies and intercorrelations. Table 1 includes general information about the cognitive tests and domains, mean duration, mean accuracy and speed score, and Cronbach's alpha coefficient. These coefficients of internal consistency were high for speed (median = 0.92) and moderate to high for accuracy

(median = 0.62). Table 2 summarizes the intercorrelations among the performance scores. When intercorrelations were estimated without correcting for gender and age, results are similar but generally a little stronger. As expected, correlations among accuracy scores were all positive (although the magnitudes ranged considerably, mostly small to moderate). Intercorrelations among speed scores were for the majority positive with magnitudes ranging from small to large. Correlations between accuracy score and speed of each test varied considerably, ranging from negative and large (-0.73, nonverbal reasoning) to positive and moderate (0.26, verbal memory) with a median of 0.07.

Some tests were thus characterized by a tendency of better accuracy being accompanied by faster response time, whereas others were characterized by a tradeoff, where better accuracy was accompanied by slower response time (the nonverbal reasoning test in particular).

**Gender differences.** Figure 2 depicts the mean gender differences on the performance measures. We found that females tended to score more accurate on all social cognition tests as well as the face and word memory tests (negative effects in Table 3) whereas males showed higher scores in the language reasoning, spatial ability and spatial memory (delayed) tests (positive effects in Table 3). Regarding speed, males were faster on the motor speed and spatial ability tests, and females on the verbal memory (delayed), emotion identification, and age differentiation tests.

**Education and parental education.** Figure 3 provides the correlations between cognitive performance and education. The correlations between years of education and accuracy were all positive, ranging from small (0.16, age differentiation) to moderate (0.49, language reasoning). Those with speed ranged from moderately negative -0.17 (nonverbal reasoning) to moderately pos-

SWAGERMAN ET AL. 58

Intercorrelations Between Accuracy (Upper Triangle) and Speed (Lower Triangle) and Cross Correlations Between Accuracy and Speed (on Diagonal, Underscored

	Exec	Executive contro	ntrol			Me	Memory			Comp	Complex cognition	tion	Soc	Social cognition	tion	Sensorimoto	motor
Cognitive domain (test name)	CET	CPT	LNB	CPW-i	CPW-d	CPF-i	CPF-d	VOLT-i	VOLT-d	MAT	VRT	LOT	EI	EDT	ADT	MP	TAP
Abstraction/flexibility (CET)	.12	.18	.12	.16	.15	.10	80.	.12	.13	.23	.17	.18	.18	.12	.10		
Attention (CPT)	.17	.21	.20	.16	.22	.21	.16	.11	.14	.27	.24	.21	.16	.19	.16		
Working memory (LNB)	.14	.50	.18	.16	.20	.15	.16	.10	.11	.25	.25	.12	.13	.16	.11		
Verbal Memory—immediate (CPW-i)	.24	.35	.20	.26	.58	.23	.21	.22	.18	.25	.22	14	.15	.20	14		
Delayed (CPW-d)	.25	.34	.20	.78	<u>.16</u>	.28	.26	.17	.20	.27	.25	.20	.12	.24	.12		
Face Memory—immediate (CPF-i)	.24	.25	.12	.52	.53	.14	.62	.21	.22	.22	.22	.18	.26	.20	.18		
Delayed (CPF-d)	.22	.27	.13	.52	.62	.74	.07	.20	.21	.23	.22	.19	.25	.21	.21		
Spatial Memory—immediate (VOLT-i)	.28	.21	90:	.51	.57	.55	.55	03	.52	.26	.22	.16	.12	.15	.12		
Delayed (VOLT-d)	.21	.21	80:	.43	.53	.48	.54	.65	<u>06</u>	.26	.21	.21	.10	.19	.15		
Nonverbal reasoning (MAT)	.25	.01	90:	01	.05	.14	.16	.15	.19	73	.42	.33	.20	.33	.24		
Language reasoning (VRT)	.24	.17	.15	.18	.21	.26	.22	.25	.27	.31	03	.24	.19	.27	.19		
Spatial ability (LOT)	.27	.21	Π.	.35	.38	.39	.41	4. 4	.45	.28	.33	15	.12	.31	.27		
Emotion Identification (EI)	.22	.28	.18	.49	.43	.48	.47	.36	.28	.10	.24	.33	.14	.24	.22		
Emotion Differentiation (EDT)	.35	.23	.16	.36	.38	.48	.47	4. 4	.34	.28	.35	.45	.47	07	.46		
Age Differentiation (ADT)	.27	.17	Π.	.26	.32	.46	.48	.46	.38	.30	.29	.45	.36	.62	03		
Sensorimotor speed (MP)	.15	.27	.18	.50	.40	.25	.27	.24	.17	01	90:	.24	.43	.21	.13		
Motor speed (TAP)	.07	.24	.14	.32	.28	.17	.18	.13	.14	10	.01	.21	.18	.15	90.	.30	
Note. Correlations are corrected for age and sex.	and sex																

itive 0.39 (verbal memory. Their medians were moderate and positive (accuracy 0.29; speed 0.20).

Correlations between mean parental education and cognitive accuracy were also positive and also ranged from small (0.05, sensorimotor speed) to moderate (0.28 nonverbal reasoning). Correlations with parental education and speed ranged from negative and small (-0.02, nonverbal reasoning) to positive and moderate 0.31 (sensorimotor speed). Both medians were positive but small (accuracy 0.14; speed 0.04).

Relation to psychometric intelligence. The mean IQ scores in the subsample of 246 participants who completed the shortened WAIS were comparable to the population average of 100 (SD =15): VIQ 102.44 (SD = 13.76), PIQ 106.15 (SD = 14.25), TIQ 103.80 (SD = 12.74). The tests that correlated highest with IQ were Word Memory and Verbal- and Matrix Reasoning (see Supplementary Material S3).

Fitting the oblique two-factor model (see Figure 1) showed that the latent g-CNB factor and the common g-WAIS factor had to be considered to represent the same construct, because the estimated correlation between the two factors equaled 1.0, denoting a perfect relation. That overall performance on the CNB compares well to cognitive performance as assessed by the traditional WAIS IQ test battery was confirmed by the high correlation between the factor scores on the g-CNB and WAIS Total IQ, which was 0.82.

In conclusion, the results imply that, corrected for age effects, overall performance on the CNB compares well to general intelligence as assessed by a psychometric intelligence test battery. This would suggest that one does not need an intelligence battery in addition to the CNB in order to obtain estimates of general intelligence (next to performance measures of specific neurocognitive functioning). In the interest of possible future assessment of intelligence via the CNB, Supplementary Material S3 includes a description of how to calculate IQ scores based on CNB test scores.

#### **Analyses of Aging Effects**

The correlations between cognitive performance and age (see Supplementary Figure S4 for illustration) ranged in magnitudes from positively small (0.15, language reasoning) to negatively moderate (-0.35, emotion identification) for accuracy. Associations with speed were all negative, and ranged from small (-0.03, language reasoning)to moderate (-0.53, spatial memory delayed). The contributions of linear and quadratic age effects are detailed in Table 3. Examples of the curvilinear age dependencies are visualized in Figure 4 (see Supplementary Figures S5 for all CNB tests).

In general, the results clearly indicate that test performance tends to decline as a nonlinear function of age, but also that the pattern of decline differs across the cognitive domains. Often, cognitive performance peaked during childhood or adolescence after which performance gradually declined with a steeper slope after this peak: this was seen for many of the speed measures, and accuracy on nonverbal reasoning, attention, and most memory tests. However, for other domains, like language reasoning (accuracy), performance increased into middle adulthood and was followed by limited decline.

#### **Heritability Analyses**

Overall, twin correlations (Supplementary Table S6) of monozygotic twin pairs were larger than of dizygotic twin pairs,

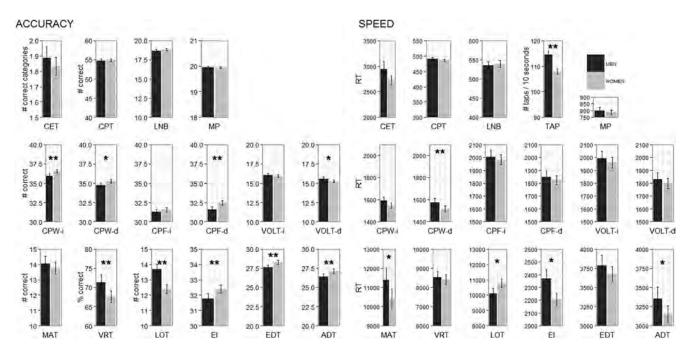


Figure 2. Mean scores (and their 95% confidence intervals) of cognitive test scores in men (dark grey) and women (light grey). See Table 1 for abbreviations of cognitive tests. No accuracy score available for the Finger Tapping Test (TAP). CET = Penn Conditional Exclusion Test; CPT = Penn Continuous Performance Test; LNB = Letter-N-Back Test; MP = Motor Praxis Test; TAP = Penn Computerized Finger-Tapping Test; CPW-i = Penn Word Memory Test-Immediate; CPW-d = Penn Word Memory Test-Delayed; CPF-i = Penn Facial Memory Test-Immediate; CPF-d = Penn Facial Memory Test-Delayed; VOLT-i = Visual Object Learning Test-Immediate; VOLT-d = Visual Object Learning Test-Delayed; MAT = Penn Matrix Reasoning Test; VRT = Penn Verbal Reasoning Test; LOT = Variable Penn Line Orientation Test; EI = Penn Emotion Identification Test; EDT = Measured Emotion Differentiation Test; ADT = Age Differentiation Test. \* p < .05. \*\* p < .01.

suggesting effects of genetic influences on individual differences in test performance.

Genetic modeling of twin data (see Table 4) showed moderate heritability for the majority of the tests. For accuracy, heritability ranged from 0 (ADT) to 52% (nonverbal reasoning, median of 31%). For speed measures, heritability ranged from 15 (working memory) to 49% (face memory delayed, median of 33%). For nearly all cognitive domains, influences of the common environment (C) were absent or small (between 0 and 24%), mostly seen in the social cognition domain.

Heritability estimates based on all available pedigree information were highly similar: between 13 and 49% of the total variance in speed and accuracy could be attributed to genetic factors. These results imply that expression of genes that influence cognitive performance are stable over generations.

Individual differences in the factor scores on the latent variable *g*-CNB were 70% heritable, without any evidence for C, whether based on twin data or on all available family data. This was close to the heritability of Total IQ on the WAIS: 75%.

#### Discussion

The aim of this article was threefold: the first was to establish reliability and validity of the Dutch translation of the Computerized Neurocognitive Battery (CNB). The second was to explore

how cognitive domains, as measured by the CNB, develop across the life span. The third was to estimate how these cognitive abilities are influenced by environmental and genetic factors. We conclude, based on a nonselected sample consisting of family members, that the CNB is a reliable and valid instrument in the Dutch population, with comparable scores to the U.S. studies. As part of the validation objective in our analyses, we report high Cronbach's alpha's across all tests. These indices of internal consistency are slightly lower than those reported by Gur et al. (2010), but this is likely due to the use of shortened tests. Intercorrelations among cognitive tests were of small to moderate magnitude, but of similar magnitude in the Netherlands and the United States without correcting for effects of age and gender. The Dutch and U.S. samples further show similar mean accuracy scores. The Dutch sample demonstrated somewhat longer response times than the U.S. sample, which probably reflects the fact that the age range of the Dutch sample was broader and included more elderly (see also below).

Another part of the validation of the CNB concerned exploration of the role of two well-known covariates of cognitive performance: gender and age. Compared to the results from the U.S. sample, we found effects that were overall similar, although small differences can be noticed. For example, in the Dutch study males and females performed about equally well on tests measuring attention and

60 SWAGERMAN ET AL.

Table 3
Standardized Effect Size (or Correlation) of Univariate Modeling of Effects of Age, Sex, Education (in Years, in Participants Over 30 Years of Age) and Mean Parental Education (in Years) on Accuracy and Speed

	Ag (in ye		Age (in ye		Sex (female males	es 0,	Educa (in year		Paren educat (in ye	tion
Cognitive domain (test name)	Accuracy	Speed	Accuracy	Speed	Accuracy	Speed	Accuracy	Speed	Accuracy	Speed
Executive control										
Abstraction/flexibility (Conditional Exclusion Test)	32**	40**	10**	15**	.04	08	.29**	.13**	.20**	.15**
Attention (Continuous Performance Test)	.10*	10**	44**	32**	01	04	.39**	.16**	.07*	.04
Working memory (Letter-N-Back Test)	$17^{**}$	26**	24**	02	05	.02	.25**	.08	.16**	.07
Memory										
Verbal memory—immediate (Word Memory Test)	12**	38**	10*	35**	11**	06	.27**	.39**	.15**	.24**
Verbal memory—delayed	21**	42**	21**	28**	$07^{*}$	08**	.36**	.33**	.17**	.22**
Face memory—immediate (Facial Memory Test)	.01	12**	32**	26**	04	02	.28**	.19**	.09*	.07
Face memory—delayed	13**	26**	$27^{**}$	21**		03	.32**	.17**	.15**	.12**
Spatial memory—immediate (Object Learning Test)	24**	48**	08*	15**	.03	03	.29**	.23**	.14**	.28**
Spatial memory—delayed	21**	53**	06	13**	.07*	03	.25**	.20**	.16**	.28**
Complex cognition										
Nonverbal reasoning (Matrix Reasoning Test)	30**		26**	.11	.03	$07^{*}$	.44**	$17^{**}$		02
Language reasoning (Verbal Reasoning Test)	.15**	03	$29^{**}$	04	.09**	02	.49**	.01	.12**	01
Spatial ability (Line Orientation Test)	15**	36**	15**	30**	.17**	.09**	.29**	.20**	.10**	.21**
Social Cognition										
Emotion identification (Emotion Identification Test)	35**	44**		28**	09**	12**	.22**	.27**	.20**	.19**
Emotion differentiation (Emotion Differentiation Test)	15**	$47^{**}$	21**	19**	09**	04	.29**	.21**	.16**	.24**
Age differentiation (Age Differentiation Test)	11**	51**	21**	13**	09**	$07^{*}$	.16**	.14**	.12**	.26**
Sensorimotor										
Sensorimotor speed (Motor Praxis Test)	10**	52**	23**	24**	.03	03	.19**	.35**	.05	.31**
Motor speed (Computerized Finger-Tapping Test)		21**		31**		.22**		.28**		.25**

<sup>\*</sup> Significant at  $\alpha = .05$ . \*\* Significant at  $\alpha = .01$ .

working memory, whereas Gur et al. (2010, Figure 3) reported lower attention scores for males and higher working memory for females. However, generalizing across all CNB tests, standardized effect sizes were distributed around zero, which suggests the absence of an overall gender effect. This fits with findings from the literature on intelligence: whenever gender differences are found (also in the Dutch population, e.g., van der Sluis et al., 2008), they are usually test specific and small, and the consensus is that there is no evidence for any gender difference in overall cognitive performance (Hyde, 2014).

Regarding age effects, the broader age range of the Dutch sample is a likely explanation of the finding that correlations with age tended to be stronger in this sample compared to the U.S. sample (Gur et al., 2010). Yet, the overall picture was the same: Older age is associated with slower as well as less accurate performance, although across cognitive domains the associations with age vary considerably in strength. CNB results are well in line with previous findings from research into cognitive aging (Salthouse, 2009). These findings have shown that the relation between age and cognitive performance is quadratic: (Young) adults often outperform children and adolescents as well as older adults and elderly. Further, they indicate that the shape and rate of cognitive decline tend to differ across domains, and cognitive decline is particularly strong for measures of cognitive speed. In the current sample, cognitive decline in accuracy performance was relatively strong in the domain of attention and nonverbal reasoning. In contrast, decline in verbal reasoning was relatively spared, as the onset was late and the decline progressed at a fairly slow pace.

These observations also fit with the differences in growth curves as derived from traditional psychometric tests. Crystalized cognitive abilities (typically measured by verbal knowledge IQ tests) continue to increase with age, whereas fluid abilities (typically measured by nonverbal cognitive processing tests) show a peak in adulthood followed by decline (Christensen, 2001; Baltes, 1987). It should be noted that our analyses are cross-sectional. This has the disadvantage that they cannot control for cohort effects like the Flynn effect. On the other hand, cross-sectional studies have the advantage that they are not influenced by retest-effects on test scores (Salthouse, 2009; Hofer & Sliwinski, 2001).

Returning to the validation part of our study, convergent validity was indicated by the association of individual test scores with general indices of educational attainment (here operationalized as years of own education and years of parental education), similar to the U.S. population. Positive correlations between cognitive performance and own and parental educational attainment were apparent, although the strengths varied considerably across measures and domains. This held for accuracy measures as well as speed measures. This reiterates the general finding that cognitive performance and educational attainment are associated (Deary & Johnson, 2010), but not equally strong for all measures (Ardila, Ostrosky-Solis, Rosselli, & Gomez, 2000).

We further demonstrated convergent validity of the CNB by the strong relation between the common variance across CNB tests and general intelligence as assessed by the WAIS using a latent factor approach. It should be noted, however, that overall scores on the CNB can never fully predict the total IQ score of the WAIS because observed scores will always be affected by measurement error. Nevertheless the high correlation between the CNB factor scores and WAIS TIQ (0.82) suggests that global measures of

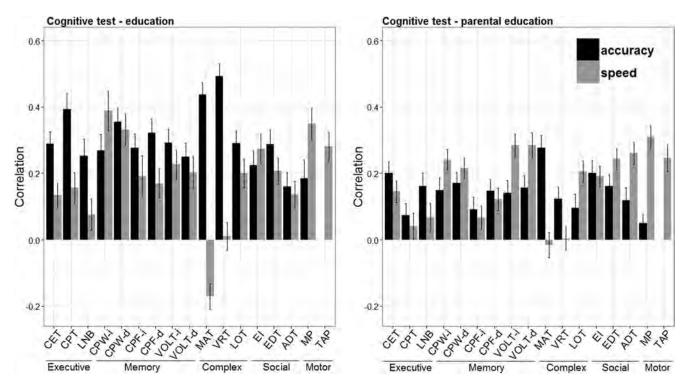


Figure 3. Correlations (and their 95% confidence intervals) of the cognitive tests with participants' own level of education and their parents' level of education. Correlations with accuracy scores are given in black and with speed scores in gray. See Table 1 for abbreviations of cognitive tests. No accuracy score available for the Finger Tapping Test (TAP). CET = Penn Conditional Exclusion Test; CPT = Penn Continuous Performance Test; LNB = Letter-N-Back Test; MP = Motor Praxis Test; TAP = Penn Computerized Finger-Tapping Test; CPW-i = Penn Word Memory Test-Immediate; CPW-d = Penn Word Memory Test-Delayed; CPF-i = Penn Facial Memory Test-Immediate; CPF-d = Penn Facial Memory Test-Delayed; VOLT-i = Visual Object Learning Test-Immediate; VOLT-d = Visual Object Learning Test-Delayed; MAT = Penn Matrix Reasoning Test; VRT = Penn Verbal Reasoning Test; LOT = Variable Penn Line Orientation Test; EI = Penn Emotion Identification Test; EDT = Measured Emotion Differentiation Test; ADT = Age Differentiation Test.

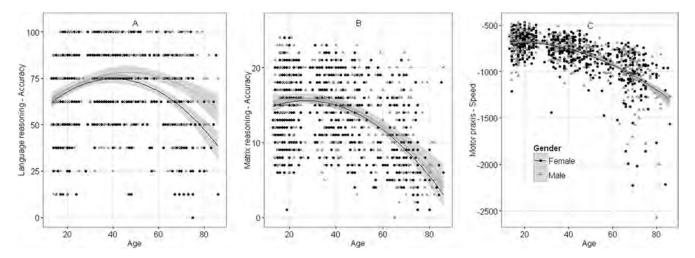


Figure 4. The curvilinear relation between cognitive test scores and age, including 95% confidence intervals. Females are given in black (●), males in gray (▲). A: Language reasoning accuracy. B: Nonverbal reasoning accuracy. C: Sensorimotor speed. Note that cognitive decline is more pronounced in B and C than A.

Table 4

Variance Components Explained by Additive Genetic Effects (Heritability) Based on Twins, and Based on All Family Members,
Including 95% Confidence Intervals (CI)

		Twin	S	All family r	nembers
Cognitive domain (test name)		Heritability	CI	Heritability	CI
Executive control					
Abstraction/flexibility (Conditional Exclusion Test)	Accuracy	12	0-26	13	03-23
	Speed	41	0-53	38	28-48
Attention (Continuous Performance Test)	Accuracy	42	19-56	38	26-49
	Speed	30	0-51	40	32-48
Working memory (Letter-N-Back Test)	Accuracy	23	0-41	22	07-37
	Speed	15	0-47	31	20-41
Memory	_				
Face memory (Word Memory Test)	Accuracy	31	0-49	34	22-46
	Speed	43	21-56	36	25-47
Delayed	Accuracy	35	0-48	31	22-41
·	Speed	49	17-60	43	32-54
Verbal memory (Facial Memory Test)	Accuracy	27	1-40	26	13-39
	Speed	41	12-53	44	34-53
Delayed	Accuracy	16	0-32	18	03-33
·	Speed	36	0-49	36	26-45
Spatial memory (Object Learning Test)	Accuracy	30	0-44	31	21-40
The state of the s	Speed	33	0–46	33	24-42
Delayed	Accuracy	31	1-44	30	20-39
<b>,</b>	Speed	35	1-48	33	23-43
Complex cognition	1				
Nonverbal reasoning (Matrix Reasoning Test)	Accuracy	52	15-63	40	30-51
g ( , , g ,	Speed	46	1-57	34	23-45
Language reasoning (Verbal Reasoning Test)	Accuracy	29	0–42	37	26–48
	Speed	31	0–49	31	22–39
Spatial ability (Line Orientation Test)	Accuracy	46	25–57	49	42–56
Spatial activity (2010 Citemation 1988)	Speed	34	0-51	30	20-41
Social cognition	Speed	٥.	0 01		20 .1
Emotion identification (Emotion Identification Test)	Accuracy	27	0-48	14	00-29
Zinotton rasimiration (Zinotton rasimiration rasi)	Speed	30	0–50	37	27–46
Emotion differentiation (Emotion Differentiation Test)	Accuracy	4	0-34	17	05-30
Emotion differentiation (Emotion Emicronidation Test)	Speed	23	0-50	35	25–45
Age differentiation (Age Differentiation Test)	Accuracy	0	0-37	22	12–33
rigo differentiation (rigo Differentiation Test)	Speed	40	11–52	32	21–42
Sensorimotor	Бреса	10	11 32	52	21 72
Sensorimotor speed (Motor Praxis Test)	Speed	19	0-53	45	35-55
Motor speed (Computerized Finger-Tapping Test)	Speed	38	14–51	31	19–43
General intelligence	Бреси	50	17 51	J1	17 73
g-CNB (measured by latent factor of CNB accuracy scores)		70	52-77	68	61–75
Total IQ (measured by WAIS)		75 75	61–84	_	01-73

Note. g-CNB = general factor of intelligence, Computerized Neurocognitive Battery; CNB = Computerized Neurocognitive Battery; WAIS = Wechsler Intelligence Scale for Adults.

CNB performance can be used as a good proxy of the universally used total WAIS IQ.

The CNB is a valuable instrument not only for research, but also for clinical purposes. Clinical neuropsychological examinations regularly include intelligence and cognitive testing, because cognitive dysfunction is often a characteristic of psychiatric disorders (Millan et al., 2012). A well-known example is attention-deficit/ hyperactivity disorder, but impairments in attention, memory or planning are also frequently seen in patients with schizophrenia or mood- and anxiety disorders (Heinrichs & Zakzanis, 1998; Marvel & Paradiso, 2004; Castaneda, Tuulio-Henriksson, Marttunen, Suvisaari, & Lönnqvist, 2008). Traditional neuropsychological tests are often designed to obtain a diagnosis on whether cognitive functioning is abnormal. The CNB has a similar clinical utility, because it provides quantitative measures of functioning, and

yields a patients' profile of strengths and weaknesses. It may in addition shorten the clinical cognitive assessment, as obtaining global measures from the CNB makes the use of an additional psychometric intelligence test unnecessary. This reduces administration time as well as the burden for patients or participants.

Finally, the heritability analyses showed moderate estimates with wide ranges for both accuracy (1–52%) and speed (14–50%) and are in line with the studies in the U.S. samples (Calkins et al., 2010; Greenwood et al., 2007; Gur et al., 2007). In addition, estimates based on twin data closely resembled those based on family data, demonstrating that heritability estimates do not necessarily have to be based on twin data, even though twins form a perfectly controlled design because of equal environmental factors like age and prenatal environment. Furthermore, family pedigree analyses enable the study of cross-generation resemblance. From

our analyses on cognitive performance, it can be concluded that family members resemble each other mostly because of shared genetic factors, and only to a small extent due to shared environment. The relatively large component of unshared environmental factors is in agreement with other studies on specific neurocognitive traits like attention or working memory (Polderman et al., 2007; Kremen et al., 2007). Similar to heritability estimates of general intelligence (Haworth et al., 2010), the variance common to subtests showed a high heritability of 70%. This is higher than the heritability coefficients of the variance in single CNB test scores, which is in agreement with the common finding that (intelligence) subtests demonstrate lower heritability coefficients than factors of general intelligence (Kan, Wicherts, Dolan, & van der Maas, 2013). Heritability of test scores (compared to g) may first be reduced due to measurement error. Second, genetic effects that influence specific cognitive performance tend to accumulate as a function of the tests' specificity, with aggregated measures showing the highest heritability. As genetic effects on specific cognitive abilities become blurred in general outcome measures like g, we advise future studies to focus on the specific cognitive functions, rather than general cognitive performance measures. In sum, our findings are in line with results from both research into specific neurocognitive functioning and general intelligence, providing vast evidence for the validity of the CNB.

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Received April 30, 2015
Revision received August 31, 2015
Accepted September 25, 2015