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Version 3 of the Alzheimer's Disease Centers' Neuropsychological Test Battery in the Uniform Data Set (UDS)

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DISCLOSURES

Sandra Weintraub is participating in clinical trials of antidementia drugs from Eli Lilly and Company and has no other conflicts of interest to declare.

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Abstract

INTRODUCTION—The neuropsychological battery of the Uniform Data Set (UDSNB) was implemented in 2005 by the National Institute on Aging (NIA) Alzheimer Disease Centers (ADC) program to measure cognitive performance in dementia and mild cognitive impairment due to AD. This paper describes a revision, the UDSNB 3.0.

METHODS—The Neuropsychology Work Group of the NIA Clinical Task Force recommended revisions through a process of due diligence to address shortcomings of the original battery. The UDSNB 3.0 covers episodic memory, processing speed, executive function, language and constructional ability. Data from 3,602 cognitively normal participants in the National Alzheimer Coordinating Center database were analyzed.

RESULTS—Descriptive statistics are presented. Multivariable linear regression analyses demonstrated score differences by age, sex and education and were also used to create a normative calculator available online.

DISCUSSION—The UDSNB 3.0 neuropsychological battery provides a valuable non proprietary resource for conducting research on cognitive aging and dementia.

INTRODUCTION

Since 2005, the University of Washington's National Alzheimer's Coordinating Center (NACC) has collected the Uniform Data Set (UDS) on participants from over 30 past and present US Alzheimer's Disease Centers (ADC). The UDS consists of data collection protocols employed systematically on participants enrolled into the Clinical Cores of each ADC^{1,2}. Participants with clinical diagnoses of normal cognition (NC), mild cognitive impairment (MCI) and dementia of various etiologies including Alzheimer's disease (AD) are recruited, enrolled and followed annually. Consent is obtained at the individual ADCs, as approved by individual Institutional Review Boards (IRBs), and the University of Washington's IRB has approved the sharing of de-identified UDS data. The UDS data, include demographics, medical history, medication use, clinical and neurological exam findings, measures of function and behavior, clinical ratings of dementia severity (e.g., Clinical Dementia Rating, CDR³), and neuropsychological test scores. Systematic guidelines for clinical diagnosis are based on the most up to date published diagnostic research criteria.^{1,4}

All UDS data collection instruments were constructed with the guidance and approval of the Clinical Task Force (CTF), a group originally constituted by the National Institute on Aging (NIA) to develop standardized methods for collecting longitudinal data that would encourage and support collaboration across the ADCs¹⁻⁵. As of December 1, 2016, the NACC database contained data on 34,748 UDS participants from past and present ADCs.

ADCs used the first version of the UDSNB starting in September 2005, and in February 2008, a second version, UDSNB 2.0, was implemented with slight revisions to instructions and data collection forms. Tests in the original version of the battery, used until March 2015, were chosen to capture the continuum of cognitive decline from normal cognition through AD dementia, incorporating relevant domains described in detail previously². An online calculator was developed to aid in scoring⁶.

In 2010, encouraged by recognition of the growing importance of diagnostic biomarkers⁷ and the identification of preclinical stages of AD⁸, the Neuropsychology Work Group, a committee to review the UDSNB 2.0 and make recommendations for future data collection, was convened. This paper describes the rationale and procedures for the development of UDSNB 3.0 and provides normative test scores for a cohort of cognitively normal individuals from the NACC database.

METHODS

Rationale and Procedures for Battery Design and Test Selection

The Clinical Task Force and Neuropsychology Work Group outlined the rationale for change. First, in longitudinal follow up, healthy controls showed practice effects, especially for the memory task, even reciting the story prior to administration on visits subsequent to baseline. UDSNB 2.0 measures were published tests, increasing the potential for multiple exposures either through clinical practice or in ancillary research conducted at the ADCs. Licensing costs and restrictions on sharing these instruments with intramural, extramural and international researchers also created challenges for collaboration. Furthermore, the importance of early detection required instruments that would be sensitive to earlier stages of cognitive decline or even “preclinical” states. Finally, UDSNB 2.0 lacked tests of visuospatial functions and nonverbal memory, both of which can constitute areas of early decline, particularly in those with Lewy Body disease^{9,10} or those with the posterior cortical atrophy variant of Alzheimer’s disease¹¹⁻¹³. Therefore, we created novel tests to address some of the shortcomings of the existing battery, while at the same time having a mechanism for preserving longitudinal continuity with previous data.

The Work Group included members from several ADCs to ensure multicenter representation, and ex-officio members from the NACC and the NIA. The group conducted weekly or monthly conference calls, as needed, and in-person meetings 1–2 times per year to outline a strategy to assess options for change. This included considering different platforms for testing (paper-and pencil vs computer), considering whether or not to change the types of constructs tested with the UDSNB 3.0, and evaluating existing instruments for inclusion into the new battery. Criteria were developed to aid in decision-making. Early on, after reviewing a library of potential tests, the group decided to adopt nonproprietary

measures to allow the ADCs to freely share the battery with collaborators. Also early on, it was decided to postpone computerized testing, as the field was rapidly evolving with increasingly sophisticated technology.

The UDSNB 2.0 faced the serious issue of a new battery disrupting the longitudinal follow up of participants tested with the initial battery since 2008. Thus, the decision was made after careful review by the Work Group and the CTF and presentations to the centers, to model the new battery on the old one and to drop or replace existing measures. Digit Symbol from the WAIS-R was dropped while the Trail Making tests and category list generation tests (animals, fruits and vegetables) were retained. In addition, four measures were replaced with similar measures developed previously by several of the centers and tested in published research studies. The section below describes the instruments.

Materials, data recording forms, and a manual for administration and scoring were created and revised with feedback from the centers. After a brief period of pilot data collection with the new instruments to refine the instructions and address any questions about administration and scoring we made additional revisions and conducted a larger pilot study (N=935) that compared the UDSNB 2.0 and 3.0 versions in individuals divided into four groups based on their MMSE scores (26–30, 21–25, 16–20, 10–15) in a “crosswalk” study¹⁴. The pairs of scores for the original and corresponding replacement tests were compared using equipercentile equating, and the analyses provided a crosswalk of equivalent test scores between the original and replacement tests (e.g., a score of 15 on the MoCA is equivalent to a score of 21 on the MMSE). The results of the crosswalk study provided good evidence for relatively reliable equivalence across both measures and that the chosen tests were reasonable replacements for the older tests. Crosswalk scores could also assist in making longitudinal comparisons.

Selection of Tests for the UDS Neuropsychological Battery 3.0

The Work Group recommended replacing the MMSE with the Montreal Cognitive Assessment (MoCA),^{15,16} Logical Memory Immediate and Delayed with the Craft Story 21 Immediate and Delayed Recall¹⁷; Digit Span Forward and Backward with the Number Span Forward and Backward Test; and the Boston Naming Test (BNT) with the Multilingual Naming Test (MINT)¹⁸. Each decision was based on the rationale outlined below.

General Cognitive Measure—The Montreal Cognitive Assessment (MoCA)^{15,16} was selected to replace the MMSE as a measure of overall cognitive impairment. Factors influencing this decision included the fact that the MOCA is more difficult than the MMSE as demonstrated in studies showing lower MoCA than MMSE scores in the same samples¹⁹ and hence more likely to detect subtle cognitive deficits. Furthermore, floor and ceiling effects are less common with the MoCA, which also allows for a broader range of scores in MCI samples than does the MMSE.²⁰ Thus, the MoCA is more appropriate than the MMSE for detecting early cognitive decline. The MoCA has been validated in white²¹ and African American²² groups. A disadvantage of the MoCA is that it can yield lower scores in diverse healthy population-based samples²³. However, an abbreviated version reportedly demonstrated predictive ability with respect to diagnosis of MCI in a low-education,

illiterate sample²⁴. In another study, MoCA was more sensitive to mild cognitive impairment and discriminated MCI from other samples better than the MMSE^{25,26}. MoCA scores have also been shown to correlate with the Activities of Daily Living Questionnaire²⁷ a measure of functional integrity in dementia²⁸. The MoCA has the further advantage of yielding not only a total score (overall measure) but also index scores based on individual items tapping domains of attention, retentive memory, orientation, language, and executive function²⁹.

The MoCA requires about 10 minutes to administer and yields a total score of 30 and the above-mentioned domain index scores. The index scores (not included in the present report) offer the potential to identify early dementia profiles of clinical dementia subtypes such as behavioral variant frontotemporal dementia and primary progressive aphasia. The Memory Index score has been shown to be especially predictive of decline from amnesic MCI to AD dementia.²⁹ The paper-and-pencil version of the MoCA has been translated into multiple languages and dialects within languages³⁰ and is freely available (<http://www.mocatest.org/>). The NACC was given permission to use it for 25 years without royalties or restrictions on sharing the test with collaborators.

Development of Domain-Specific Neuropsychological Tests

1. Episodic Memory Tests—Memory loss is the hallmark symptom of the most common clinical dementia syndrome associated with Alzheimer’s disease.³¹ Early studies of AD dementia emphasized the importance of measures of episodic memory, such as word list learning and story recall, in the evaluation for dementia. The group decided on a story memory test since most ADCs were already using Logical Memory, immediate and delayed recall conditions.

Craft and colleagues had designed multiple forms of a story recall test similar to Logical Memory in a study of the impact of insulin on cognition in mild AD dementia^{17,32}. The complete set of 22 stories had previously been tested for equivalence in a diverse sample of college age adults who were administered all of the stories in counterbalanced order in the laboratory of Andrew Saykin (personal communication) and provided to the Work Group for consideration. Additional data on alternate sets of stories were included in published studies of patients undergoing systemic chemotherapy for treatment of breast cancer as well as individuals with traumatic brain injury and healthy controls^{33–36}. In a pilot study to determine the equivalence of twenty-two stories in middle-aged and older adults the Work Group determined that three stories offered the greatest relationship to Logical Memory and to one another. These three were reviewed by the work group and one was chosen for its content relevance to a diverse population, “Craft Story 21”.

Scoring of Logical Memory allows several acceptable responses for each item recalled. Following the protocol from Craft and colleagues³², items were scored in a similar manner to Logical Memory (“paraphrase score”) but another score was also calculated (“verbatim score”), allocating a point for each item recalled exactly as delivered in the story. The verbatim score (not included in the present report) was intended to serve as potentially more sensitive than the paraphrase score in detecting very early memory decline.

Finally, we introduced a novel measure of nonverbal memory, a function not previously included in the UDSNB 2.0. Following the copy of the Benson Complex³⁷ figure (see below under Visuospatial Test) delayed figure reproduction was tested.

2. Language Tests—The 32-item Multilingual Naming Test (MINT)^{18,38} was selected to replace the short BNT. The MINT was originally developed to test naming in four languages, English, Spanish, Hebrew, and Mandarin Chinese, taking care to equate the level of difficulty of items across languages. The BNT was developed in New England and designed for American English speakers and contains items that either have no equivalent word or different frequencies of usage in other languages. The MINT is sensitive to naming impairment in Alzheimer’s disease¹⁸.

Word fluency is measured with semantic and letter word list generation tests. The former were part of UDSNB 2.0, while two letter generation tasks were added (“F” and “L”) for UDSNB 3.0. Each task requires 60 seconds and correct items are totaled. Note is made of errors and rule violations.

3. Visuospatial Tests—The UDSNB 2.0 did not contain a visuospatial test. Visuospatial symptoms emerge in later stages of amnesic dementia due to AD but also may appear early in the clinical syndromes of posterior cortical atrophy and dementia associated with cortical Lewy Body disease. The Benson Complex Figure³⁷ was added as a test of constructional ability (Copy condition). Figural elements are scored for presence and placement. Reproduction is tested after a delay to measure retentive memory (see above under Episodic Memory). Comparison between patients with clinical dementia of the Alzheimer type and frontotemporal dementia showed distinctive profiles of performance and associations with frontal and parietal cortical atrophy regions in the groups.^{37,39}

5. Immediate Attention, Working Memory, Executive Attention Tests—Immediate attention span is commonly tested with Digit Span.⁴⁰ For studies requiring multiple forms to reduce practice effects, a series of number sets was randomly generated to provide alternatives to the digit span test (Joel Kramer lab, personal communication). The number spans for the UDS task were randomly generated with the restriction that no digit would be adjacent to a digit that was one higher or one lower (e.g., a ‘7’ would not be succeeded or preceded by a 6 or 8). Every attempt was also made to exclude sequences that contained area codes. The number span is the longest list recalled. The total number of trials administered up to failure on two trials at one length is also recorded. Backward span is a measure of working memory. The Trail Making Tests were retained from the UDSNB 2.0 to measure processing speed (Part A) and executive attention (Part B).

Study Sample

This report is based on analyses UDS data submitted to NACC by the ADCs between March 15, 2015, and November 30, 2016. The sample was restricted to individuals who received the UDSNB3.0 and at that visit had a clinical diagnosis of normal cognition and a global CDR score of 0. If a participant had received UDSNB 3.0 more than once, data were included from only the first administration. Although some participants’ scores on the

UDSNB 3.0 appeared to be outside the range of normal scores (e.g., MoCA score of 9), we chose not to remove any participants from the descriptive analyses because normalcy was not defined by the tests. Therefore, we describe the full range of scores in those with a clinical diagnosis of normal cognition and a global CDR=0.

Data, Analyses, Normative Calculator—First we describe the demographics of the sample (age, education, and sex). The mean, median, 25th and 75th percentiles, and ranges of scores for the overall sample are presented. Histograms are provided for each of the tests to illustrate the distribution of scores in the overall sample. The mean scores and standard deviations for each test are provided by age divided into five groups (<60 years, 60–69 years, 70–79 years, 80–89 years, 90 years) and education, divided into four groups (12 years, 13–15 years, 16 years, 17 years). Unadjusted linear regression analyses tested for differences by age or education group. Finally, we ran linear regression models to estimate the effect of age (continuous), sex, and education (continuous) on each neuropsychological measure. Adjusted linear regression models were first run with either age, gender, or education predicting the neuropsychological test score (data not shown), and then multivariable models were run with all three demographics included in the model.

We developed a calculator for the UDSNB 3.0 tests based on previously published methods used to produce the calculator for UDSNB 2.0 tests⁶. While our descriptive analyses focused on all participants meeting our eligibility criteria, for the normative calculator, we excluded a handful of participants who performed five standard deviations outside of the mean on any particular test to improve the distribution of residuals and better satisfy model assumptions. This restriction resulted in excluding the following participants from the regression analyses: five participants from the analysis of the MoCA, four participants from the analysis of the Benson Complex Figure Copy, sixteen participants from the analysis of the Trail Making Part A, and five participants from the analysis of the MINT.

RESULTS

The sample included 3,602 cognitively normal participants over age 60 receiving the UDSNB 3.0 (Table 1). The majority of the sample (65%) were women and were between 70 and 89 years of age (67%) and highly educated (69%). These analyses did not divide the sample by race since most participants in the sample were white (83%), with an additional 14% African American and 3% other race, reflecting the overall distribution of these groups within the ADCs receiving the UDS.

Means, 25th, 50th and 75th percentile, and score ranges for each test in the overall sample are reported in Table 2. Histograms demonstrate whether the distribution of test scores were approximately normal (Supplemental File 1). Tests with an approximately normal distribution of scores included Craft Story Immediate and Delayed (paraphrase and verbatim), Number Span Forward and Backward (total correct trials and longest span), the letter list generation task (F&L words), and the Benson Complex Figure Recall. Scores on the MoCA, MINT, and copy condition of the Benson Complex Figure Copy were highly skewed due to ceiling effects. However, the MoCA appears to be less affected by ceiling effects than the MMSE.²

Table 3 shows the means and standard deviations (SD) by each measure across the five age groups, and Table 4 shows means and SD for the four education groups. In the multivariable regression analyses (Table 5), women performed statistically significantly ($p < 0.01$) better than men on the Craft Story Immediate and Delayed, Verbal Fluency Phonemic Test, and Vegetables List Generation, but worse on the Benson Copy Figure Recall, Number Span Forward, and MINT (Table 5). Women and men performed similarly, without statistically significant differences, on the Benson Complex Figure Copy, Number Span Backward, Animal List Generation, and Trail Making Parts A and B. Increasing age was associated with worse scores and increasing years of education was associated with better scores on all of the tests ($p < 0.01$).

For the data to be useful in characterizing research participants, a calculator was created to indicate the level of performance on each measure. The calculator uses the intercepts, regression coefficients, and root mean square errors (RMSE) resulting from the regression analyses described above to calculate unadjusted and adjusted z-scores for individuals of a particular sex, age, and/or education level. The RMSE is the square root of the average squared differences between the observed score and the predicted score, which we substitute as an estimate for a population standard deviation. The adjusted z-scores are calculated for each test adjusting for a single demographic characteristic (i.e., sex, age, or education) and adjusting for all three of these demographics. One can enter an individual's demographics and raw test scores, and the calculator uses the resulting z-scores to calculate percentile estimates that indicate the individual's level of impairment on any given test (e.g., Low Average, or Severely Impaired). Two new variables were also added to this calculator to improve the precision of percentile estimates for Trail Making Part A and Part B. These two tests are terminated if the subjects cannot complete within a specified time length (150 seconds and 300 seconds for A and B, respectively), resulting in the same score regardless of how many lines are correctly connected. We added connections-per-second (correct lines connected divided by the time to completion) for both Part A and B. These two new variables provide more accurate Z-scores and percentiles for the Trail Making tests.

The normative calculator for the UDSNB 3.0 tests can be found on NACC's website (http://www.alz.washington.edu/WEB/UDS3_NormsCalculator.xlsx).

DISCUSSION

This paper reports the results from a study to develop normative data for the Version 3.0 revision of the Uniform Data Set Neuropsychological Battery. The complete UDS contains not only neuropsychological battery but also demographic, medical, family history, neurological, biomarker, psychiatric, and functional data and available post mortem diagnosis on Clinical Core participants who have been followed longitudinally. Earlier versions have been collected since 2005 and stored in the database of the National Alzheimer Coordinating Center at the University of Washington. All the data are available for sharing with researchers and therefore provide a rich source for generating hypotheses and investigating cognitive aging and dementia in a well-defined cohort.

The current revision of the neuropsychological battery provides an updated set of tests, targeting predominantly the symptoms of the most typical, amnesic, presentation of Alzheimer's disease. The tests are nonproprietary and have the potential to increase sensitivity over former measures to very early symptoms of cognitive decline in older individuals with different levels of education. The new measures are similar to the old measures but have also enriched the standard data collection with novel scores to enhance available data using a relatively brief battery. The normative calculator provides a convenient tool to characterize the level of performance on the measures of the UDSNB 3.0 battery. The battery and the calculator are available on line (https://www.alz.washington.edu/WEB/npsych_means.html) (http://www.alz.washington.edu/NONMEMBER/UDS/DOCS/VER3/UDS3_npsych_worksheets_C2.pdf)

There are some limitations to the study reported above. Although the ADCs encourage the participation of a diverse sample with respect to gender, education and race, there was an over-representation of individuals who were white, female, and highly educated. Thus, the findings are most relevant to research settings where these demographics are representative of the research volunteers. It will be important to expand the normative data for under represented groups and also for population-based samples. Another limitation is that the battery focuses on the spectrum from healthy cognition to dementia of the Alzheimer type and does not explicitly target symptoms associated with other forms of dementia. The Clinical Task Force has introduced additional data collection modules, however, including specialized tests of symptoms related to frontotemporal dementia. Plans are under way to further expand clinical symptom assessment in other dementia syndromes. The availability of the UDSNB 3.0 at no cost to researchers will aid in encouraging more consistent and systematic data collection in disparate studies of cognitive aging and dementia.

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Research in Context

Systematic Review

The first version of the UDSNB was based on a review of the literature (e.g., Ovid and PubMed) for cognitive domains and specific constructs sensitive to age-related decline and Alzheimer's disease and the review was updated with information about newer instruments for screening and constructs not previously included in the original version. Some tests incorporated into the UDSNB 3.0 were copyrighted and permission was given to the National Alzheimer Coordinating Center, University of Washington, from the authors to use the tests in the battery.

Interpretation

The UDSNB 3.0 is a valuable nonproprietary resource for researchers.

Future Directions

Data continue to be accumulated and can be reanalyzed on a larger, more demographically diverse sample. Clinical groups of cognitively normal and cognitive impaired individuals will be compared in future publications. Data are also available to researchers via requests to the National Alzheimer Coordinating Center.

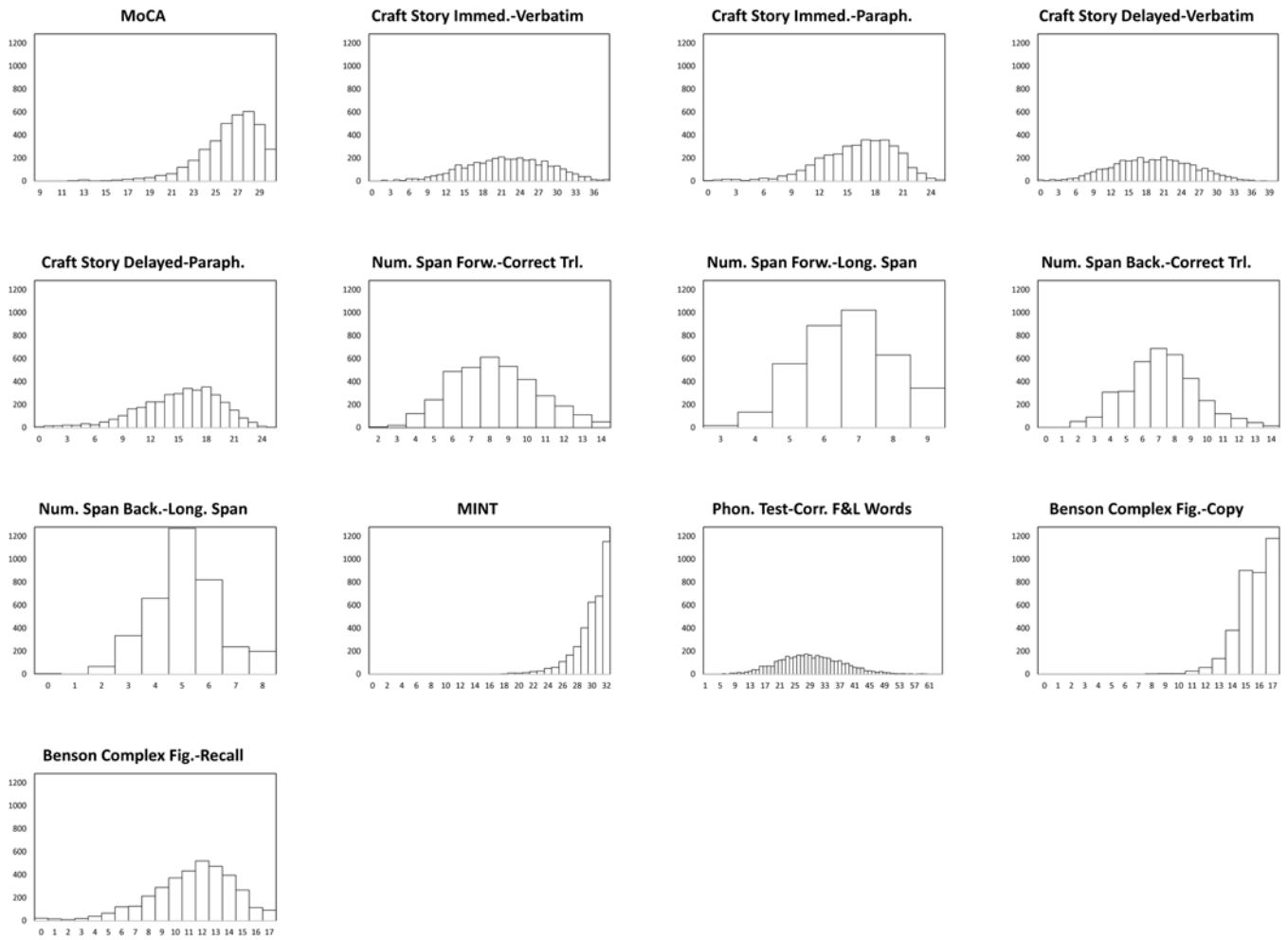


Figure 1.0. Histograms showing score distributions for each measure on the UDSNB 3.0. From these graphs, many of the measures have a normal or near normal distribution, with the exception of the MoCA total score, the score for the copy of the Benson Complex Figure, and the total score for the MINT.

Table 1

Sample Distribution by Gender, Age, and Education

Age	Education	Male	Female	Total
<60 yrs	12	13	23	36
	13–15	23	48	71
	16	34	69	103
	17+	44	76	120
	Missing	6	6	12
60–69 yrs	12	32	65	97
	13–15	47	142	189
	16	102	164	266
	17+	158	293	451
	Missing	3	7	10
70–79 yrs	12	45	130	175
	13–15	61	159	220
	16	110	201	311
	17+	274	407	681
	Missing	1	7	8
80–89 yrs	12	27	77	104
	13–15	26	103	129
	16	59	112	171
	17+	151	177	328
	Missing	1	1	2
90 yrs	12	4	27	31
	13–15	6	11	17
	16	10	15	25
	17+	19	26	45
	Missing	0	0	0
Grand total		1256	2346	3602

As of December 2016

Table 2
 Summary Statistics for Clinically Cognitively Normal Uniform Data Set Participants

UDS Version 3 Neuropsychological Test ^a	Domain	Max. score	N	Mean (SD)	Sample's scores			Range
					Q ₂₅	Q ₅₀	Q ₇₅	
Montreal Cognitive Assessment (MoCA) – total score	Dementia severity	30	3581	26.3 (2.8)	25, 27, 28	9–30		
Craft Story 21 Recall Immed. Verbatim – total units	Memory	44	3552	21.9 (6.6)	17, 22, 27	0–38		
Craft Story 21 Recall Immed. Paraphrase – total units	Memory	25	3552	16.1 (4.1)	14, 17, 19	0–25		
Craft Story 21 Recall Delay. Verbatim – total units	Memory	44	3550	19.1 (6.7)	14, 19, 24	0–40		
Craft Story 21 Recall Delay. Paraphrase – total units	Memory	25	3550	15.1 (4.3)	12, 16, 18	0–25		
Benson Complex Figure Copy – total score	Visuospatial	17	3584	15.6 (1.4)	15, 16, 17	0–17		
Benson Complex Figure Recall – total score	Visuospatial	17	3576	11.2 (3.1)	9, 12, 13	0–17		
Number Span Test Forward – total correct trials	Attention	14	3591	8.3 (2.3)	7, 8, 10	2–14		
Number Span Test Forward – longest span	Attention	9	3591	6.7 (1.3)	6, 7, 8	3–9		
Number Span Test Backward – total correct trials	Attention	14	3590	7.2 (2.2)	6, 7, 9	0–14		
Number Span Test Backward – longest span	Attention	8	3590	5.1 (1.3)	4, 5, 6	0–8		
Multilingual Naming Test (MINT) – total score	Lang.-Naming	32	3564	30.0 (2.4)	29, 31, 32	0–32		
Phonemic Test – F-words total in 60 seconds	Lang.-Verbal fluency	40	3589	15.1 (4.7)	12, 15, 18	1–35		
Phonemic Test – L-words total in 60 seconds	Lang.-Verbal fluency	40	3574	14.2 (4.5)	11, 14, 17	0–35		
Phonemic Test – total F- and L-words	Lang.-Verbal fluency	80	3572	29.2 (8.6)	23, 29, 35	1–64		
Animals list generation– total in 60 seconds	Lang.-Category fluency	77	3596	21.4 (5.7)	17, 21, 25	0–49		
Vegetables list generation– total in 60 seconds	Lang.-Category fluency	77	3590	15.1 (4.3)	12, 15, 18	1–35		
Trail Making Test Part A – time in seconds	Processing speed	150	3583	30.9 (13.4)	22, 28, 36	9–150		
Trail Making Test Part B – time in seconds	Executive function	300	3561	82.2 (46.3)	54, 70, 95	13–300		

Abbreviations: UDS = Uniform Data Set; Max = maximum; Lang = Language; Immed = Immediate; Delay = Delayed As of December 2016

^aHigher scores indicate better scores except for the Trail Making Test Parts A and B

Table 3

Mean neuropsychological test scores by age group

UDS Version 3 Neuropsychological Test ^a	Mean (SD)				
	<60 years	60–69 years	70–79 years	80–89 years	90 years
Montreal Cognitive Assessment – total score	27.5 (2.1)	26.9 (2.4)	26.3 (2.7)	25.3 (3.0)	23.8 (3.5)
Craft Story 21 Recall Immed. Verbat. – total units	23.1 (6.8)	23.2 (6.4)	22.0 (6.5)	20.0 (6.6)	17.8 (6.4)
Craft Story 21 Recall Immed. Paraph. – total units	16.9 (4.1)	16.9 (3.9)	16.2 (4.0)	15.0 (4.2)	13.3 (4.4)
Craft Story 21 Recall Delay. Verbat. – total units	20.9 (7.0)	20.4 (6.4)	19.2 (6.6)	16.9 (6.6)	15.1 (5.8)
Craft Story 21 Recall Delay. Paraph. – total units	16.3 (4.4)	15.9 (4.0)	15.2 (4.1)	13.6 (4.5)	12.1 (4.3)
Benson Complex Figure Copy – total score	15.7 (1.2)	15.8 (1.2)	15.6 (1.3)	15.4 (1.6)	15.5 (1.5)
Benson Complex Figure Recall – total score	12.6 (2.4)	11.9 (2.8)	11.2 (3.0)	10.1 (3.3)	9.4 (3.6)
Number Span Test Forward – total correct trials	8.7 (2.4)	8.4 (2.3)	8.3 (2.3)	8.0 (2.3)	7.6 (2.1)
Number Span Test Forward – longest span	6.9 (1.3)	6.7 (1.3)	6.7 (1.3)	6.5 (1.3)	6.3 (1.3)
Number Span Test Backward – total correct trials	7.8 (2.3)	7.4 (2.2)	7.1 (2.2)	6.8 (2.2)	6.4 (2.4)
Number Span Test Backward – longest span	5.4 (1.3)	5.2 (1.3)	5.1 (1.3)	4.9 (1.3)	4.7 (1.4)
Multilingual Naming Test (MINT) – total score	30.1 (2.0)	30.3 (2.0)	30.1 (2.2)	29.6 (2.6)	28.4 (3.4)
Phonemic Test – F-words total in 60 seconds	16.3 (4.4)	15.5 (4.6)	14.9 (4.7)	14.6 (4.8)	13.6 (5.0)
Phonemic Test – L-words total in 60 seconds	15.3 (4.3)	14.8 (4.4)	14.0 (4.4)	13.7 (4.5)	12.5 (4.7)
Phonemic Test – total F- and L-words	31.3 (8.3)	30.0 (8.4)	28.8 (8.5)	28.2 (8.6)	26.1 (9.1)
Animals list generation – total in 60 seconds	23.6 (5.3)	22.7 (5.5)	21.2 (5.4)	19.5 (5.6)	17.0 (5.4)
Vegetables list generation – total in 60 seconds	16.3 (4.1)	16.0 (4.3)	15.0 (4.2)	14.0 (4.3)	12.4 (4.1)
Trail Making Test Part A – time in seconds	22.3 (8.4)	27.3 (9.6)	31.0 (10.8)	36.2 (13.3)	42.0 (14.3)
Trail Making Test Part B – time in seconds	55.4 (27.2)	70.1 (33.8)	82.7 (41.4)	102.0 (55.2)	140.6 (75.3)

Abbreviations: UDS = Uniform Data Set; SD = standard deviation; Immed. = Immediate; Delay. = Delayed; Verbat = Verbatim; Paraph = Paraphrase

^aHigher scores indicate better scores except for the Trail Making Test Parts A and B; higher scores indicate slower time to completion

Table 4

Mean neuropsychological test scores by education group

UDS Version 3 Neuropsychological Test ^a	Mean (SD)			
	12 years	13–15 years	16 years	17+ years
Montreal Cognitive Assessment (MoCA) – total score	24.1 (3.7)	25.7 (2.9)	26.6 (2.4)	26.9 (2.2)
Craft Story 21 Recall Immed. Verbatim – total units	19.6 (7.1)	21.2 (6.5)	22.0 (6.5)	22.8 (6.4)
Craft Story 21 Recall Immed. Paraphrase – total units	14.5 (4.7)	15.6 (4.0)	16.3 (4.1)	16.7 (3.8)
Craft Story 21 Recall Delay. Verbatim – total units	16.6 (7.1)	18.3 (6.8)	19.2 (6.6)	20.0 (6.4)
Craft Story 21 Recall Delay. Paraphrase – total units	13.2 (5.0)	14.4 (4.4)	15.3 (4.3)	15.8 (4.0)
Benson Complex Figure Copy – total score	15.2 (1.5)	15.5 (1.4)	15.7 (1.3)	15.8 (1.2)
Benson Complex Figure Recall – total score	10.2 (3.6)	11.0 (3.2)	11.4 (3.1)	11.5 (2.9)
Number Span Test Forward – total correct trials	7.4 (2.2)	7.9 (2.2)	8.4 (2.2)	8.6 (2.3)
Number Span Test Forward – longest span	6.2 (1.3)	6.5 (1.3)	6.8 (1.3)	6.9 (1.3)
Number Span Test Backward – total correct trials	6.1 (2.3)	6.7 (2.2)	7.3 (2.2)	7.5 (2.2)
Number Span Test Backward – longest span	4.5 (1.4)	4.9 (1.3)	5.2 (1.3)	5.3 (1.3)
Multilingual Naming Test (MINT) – total score	28.5 (2.9)	29.4 (2.4)	30.2 (2.0)	30.5 (2.0)
Phonemic Test – F-words total in 60 seconds	12.8 (4.7)	13.9 (4.4)	15.2 (4.6)	16.1 (4.5)
Phonemic Test – L-words total in 60 seconds	11.9 (4.5)	13.0 (4.4)	14.3 (4.1)	15.2 (4.3)
Phonemic Test – total F- and L-words	24.7 (8.6)	26.7 (8.3)	29.4 (8.1)	31.2 (8.2)
Animals list generation– total in 60 seconds	18.5 (5.4)	19.9 (5.3)	21.3 (5.1)	22.8 (5.7)
Vegetables list generation– total in 60 seconds	13.5 (4.0)	14.7 (4.0)	15.1 (4.1)	15.7 (4.5)
Trail Making Test Part A – time in seconds	35.1 (14.4)	32.1 (12.3)	29.7 (11.0)	29.2 (10.9)
Trail Making Test Part B – time in seconds	112.7 (69.8)	91.4 (51.5)	76.1 (36.4)	73.9 (35.9)

Abbreviations: UDS = Uniform Data Set; SD = standard deviation; Immed. = Immediate; Delay. = Delayed;

^aHigher scores indicate better scores except for the Trail Making Test Parts A and B

Table 5

Multivariable linear regression coefficients and 95% confidence intervals for sex, age, and education

UDS Version 3 Neuropsychological Test ^a	Female	Age (years)	Education (years)
	Coefficient (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)
Montreal Cognitive Assessment – Total score	0.35 (0.18, 0.52) **	-0.08 (-0.08, -0.07) **	0.33 (0.30, 0.36) **
Craft Story 21 Recall Immediate - Verbatim	0.96 (0.51, 1.40) **	-0.13 (-0.15, -0.11) **	0.41 (0.33, 0.48) **
Craft Story 21 Recall Immediate - Paraphrase	0.60 (0.33, 0.88) **	-0.08 (-0.09, -0.07) **	0.28 (0.23, 0.33) **
Craft Story 21 Recall Delayed - Verbatim	0.78 (0.33, 1.23) **	-0.15 (-0.17, -0.13) **	0.43 (0.35, 0.51) **
Craft Story 21 Recall Delayed - Paraphrase	0.52 (0.23, 0.81) **	-0.10 (-0.11, -0.09) **	0.32 (0.27, 0.37) **
Benson Complex Figure Copy – Total score	0.04 (-0.05, 0.14)	-0.01 (-0.02, -0.01) **	0.07 (0.06, 0.09) **
Benson Complex Figure Recall – Total score	-0.47 (-0.67, -0.26) **	-0.09 (-0.09, -0.08) **	0.16 (0.12, 0.19) **
Number Span Forward – Total correct trials	-0.29 (-0.45, -0.14) **	-0.03 (-0.03, -0.02) **	0.15 (0.13, 0.18) **
Number Span Forward – Longest span	-0.16 (-0.25, -0.07) **	-0.01 (-0.02, -0.01) **	0.08 (0.07, 0.10) **
Number Span Backward – Total correct trials	-0.10 (-0.25, 0.05)	-0.03 (-0.04, -0.03) **	0.17 (0.14, 0.20) **
Number Span Backward – Longest span	-0.06 (-0.15, 0.03)	-0.02 (-0.02, -0.01) **	0.10 (0.08, 0.11) **
Multilingual Naming Test – Total score	-0.81 (-0.96, -0.66) **	-0.03 (-0.04, -0.02) **	0.22 (0.19, 0.25) **
Verbal Fluency Phonemic Test –Total Correct F-words	0.54 (0.22, 0.85) **	-0.05 (-0.07, -0.04) **	0.42 (0.36, 0.47) **
Verbal Fluency Phonemic Test –Total correct L-words	0.63 (0.33, 0.92) **	-0.05 (-0.07, -0.04) **	0.45 (0.40, 0.50) **
Verbal Fluency Phonemic Test – Total correct F and L-words	1.12 (0.55, 1.69) **	-0.09 (-0.12, -0.07) **	0.86 (0.76, 0.96) **
Category Fluency: Animals – Total score	0.35 (-0.02, 0.71)	-0.15 (-0.16, -0.13) **	0.57 (0.50, 0.63) **
Category Fluency: Vegetables – Total score	2.49 (2.22, 2.77) **	-0.08 (-0.10, -0.07) **	0.31 (0.26, 0.36) **
Trail Making Test Part A – Time in seconds	0.03 (-0.72, 0.78)	0.45 (0.41, 0.48) **	-0.73 (-0.86, -0.60) **
Trail Making Test Part A – Correct lines/Time in seconds	-0.00 (-0.02, 0.02)	-0.01 (-0.01, -0.01) **	0.02 (0.01, 0.02) **
Trail Making Test Part B – Time in seconds	1.58 (-1.29, 4.45)	1.64 (1.50, 1.77) **	-4.65 (-5.15, -4.15) **
Trail Making Test Part B – Correct lines/Time in seconds	0.00 (-0.01, 0.01)	-0.01 (-0.01, -0.01) **	0.01 (0.01, 0.01) **

Abbreviations: UDS = Uniform Data Set; CI = Confidence Interval

* Statistically significant at p<0.05;

** statistically significant at p<0.01

^a Higher scores indicate better scores except for the Trail Making Test Parts A and B time in seconds