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COGNITIVE PROFILES AND HERITABILITY ESTIMATES IN THE OLD ORDER AMISH

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Abstract

Objective—To establish the applicability of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) in the Old Order Amish (OOA). To assess the genetic contribution to the RBANS total score and its cognitive domains using a large family-based sample of OOA.

Methods—RBANS data were collected in 103 OOA individuals from Lancaster County, Pennsylvania, including 85 individuals without psychiatric illness and 18 individuals with current psychiatric diagnoses.

Results—The RBANS total score and all five cognitive domains of in non-psychiatric OOA were within half a standard deviation of the normative data of the general population. The RBANS total score was highly heritable ($h^2=0.51$, $p = 0.019$). OOA with psychiatric diagnoses had numerically lower RBANS total score and domain scores compared to their non-psychiatric participants.

Conclusion—The RBANS appears a suitable cognitive battery for the OOA population, as measurements obtained from the OOA are comparable to normative data in the US population. The heritability estimated from the OOA is in line with heritabilities of other cognitive batteries estimated in other populations. These results support the use of RBANS in cognitive assessment, clinical care, and behavioral genetic studies of neuropsychological functioning in this population.

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INTRODUCTION

Cognitive functions are controlled by complex genetic and environmental contributions. An important condition for using neurocognitive measurements as quantitative phenotypes in genetic research is the demonstration of a significant heritability, i.e., the phenotypic variance is influenced by additive genetic variance. Family studies are commonly used to estimate trait heritabilities and represent a first step towards identifying potential genetic etiologies and thus biological underpinning. The Old Order Amish (OOA) are known for their large family sizes and provide efficient samples for heritability estimation due to the relatedness of the population. The OOA are of European Caucasian ancestry. Most individuals in the population share similar rural upbringing, lifestyle, level of basic academic training and minimal illicit substance use. The many features of relative environmental homogeneity in the OOA offer a rarely available setting to compare heritability across different aspects of cognitive traits.

There are potential challenges for research of cognitive function in the OOA. One is whether standardized batteries developed for general population are applicable, as cultural factor influences cognitive performance¹. In this context, the lack of empirical data on OOA formal cognitive performance is a major gap. In the first step to address this, we opted to use the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)², and tested whether this standard neuropsychological battery may be applicable in this population isolate. The RBANS measures five cognitive indices: visuospatial/constructional skills, immediate memory, delayed memory, language, and attention², has been used extensively in neuropsychiatric research^{2, 3}, and takes 30 minutes to administer. We chose the RBANS primarily because of its brevity, psychometric rigor, and breadth of assessment for cognitive domains. Therefore, the first aim is to demonstrate the equality of the RBANS normative cognition data obtained in the OOA with the norms established in the non-Amish.

A secondary goal of this study was to estimate the heritability of RBANS, as the large pedigree provides large numbers of relative pairs and thus power for heritability analysis. Although heritability of cognitive function has been estimated in other populations, heritability estimation in the OOA has particular advantages. For example, the OOA share a relatively uniform level of formal education. They attend school from grades 1–8, followed by one year of vocational training. This completes their formal education. Cognitive capacity is a factor that determines different terminal education levels attained in the general population. In turn, education impacts cognitive skills. Education level is, therefore, a difficult factor to fully account for in behavioral and genetic studies. Here, there is an interesting population-level control that enables comparison of heritability of cognitive traits with minimized formal education variance.

However, there are also a number of challenges or factors to consider for testing cognition in this population. For instance, the OOA are bilingual, speaking a local German dialect in home and church, but using English for formal education and communication with non-Amish. Therefore, they may have some disadvantage in English language-based cognitive assessments. Another potentially culturally relevant factor is that OOA society mandates avoidance of competitiveness; and performance evaluation oriented activities may be viewed

as worldly^{4, 5}. However, the field of neuropsychological assessment views effort as an integral part of formal measurement^{6, 7}. How a culture that does not explicitly promote performance evaluation may influence cognitive testing presents another interesting challenge. In this context, the RBANS has an embedded measure called the Effort Index (EI)³, which should help address this issue.

Recognizing the potential of cognitive genetics research in this population isolate and also the opportunity to improve mental health care in this historically underserved group, we set out in this pilot study to accomplish two aims: to develop normative data; and to use the power of this population to calculate heritability for basic cognitive functioning.

METHODS

Participants

We administered the RBANS in 103 OOA individuals from Lancaster County, Pennsylvania. Initial recruitment was done via phone calls and mailings to OOA who had participated in previous studies. All were screened via psychiatric questionnaire, 18 of whom were found to have psychiatric disease and assessed by the Structured Clinical Interview for DSM-IV (SCID). All participants have an 8th grade education. All OOA members are the offspring of about three hundred founders and the degree of shared genetic variance between any two individuals can be calculated from the OOA genealogical records kept at the National Institute of Health Anabaptist Genealogy Database⁸⁻¹⁰. The 103 individuals were from 17 nuclear families although they could be further linked to a single pedigree with eight generations. Exclusion criteria included history of head injury with cognitive sequelae or loss of consciousness for over five minutes, major medical and neurological conditions, substance abuse or addiction (except tobacco use), reported learning difficulty, and absence of completing 8th grade education. The sample included 85 healthy OOA participants (53 females and 32 males) without psychiatric diagnosis and 18 OOA (13 females and 5 males) with DSM-IV Axis I diagnoses. The percentage of individuals with psychiatric condition in this sample (17.5%) is comparable to the rate of mental illnesses in the general population (e.g., 18.6% in the U.S. in the 2012 survey) (SAMHSA 2013). The diagnoses of the 18 members of the OOA include major depressive (n=8), bipolar (n=7); schizophrenia spectrum (n=2), and generalized anxiety (n=1) disorder. This sample provided us the means to estimate heritability of RBANS score, as well as to compare differences in RBANS scores between participants with vs. without psychiatric conditions. Patients with severe mental illnesses were required to be evaluated for capacity to understand and sign consent. All participants gave written informed consents approved by the University of Maryland IRB.

RBANS

Administering the RBANS according to the protocol manual, the test consisted of Line Orientation and Figure Copy for the Visuospatial/Constructional Index; List Learning and Story Memory for the Immediate Memory Index; List Recall, List Recognition, Story Recall, and Figure Recall for the Delayed Memory Index; Picture Naming and Semantic Fluency for the Language Index; and the Digit Span and Coding for the Attention Index.

The performance in the OOA was compared with the US normative RBANS data. The US normative RBANS data was based on a representative sample of the US population proportionate to US demographic variables as recorded in the 1995 US Bureau of the Census. Specifically, the standardization sample for RBANS consisted of 540 adults equally divided into six age groups (20–39, 40–49, 50–59, 60–69, 70–79, and 80–89). Sex proportions were basically commensurate with US Census data. In terms of race/ethnicity, each age group in the sample contained analogous proportions of Hispanics, African-Americans, Whites, and other racial/ethnic groups in line with US Census data. Educational level of the sample group was stratified according to three levels (less than high school, equal to high school, and greater than high school) based on the number of years completed. For the purpose of the RBANS standardization sample, researchers divided the United States into four geographic regions in line with US Census data as follows: Northeast, North Central; South, and West; census proportions by geographic region was respectively: 20.2%, 23.6%, 35.6%, and 20.5% the four regions while the standardization sample percentages for the northeast, north central, south, and west regions (Randolph, 1998).

Statistics

The RBANS included age-based norms from raw scores to obtain standard scores with means set at 100 and standard deviation at 15 for the total score and all cognitive domain index scores. One-sample t-tests were used to determine the differences between performance in OOA healthy controls and the norms from the non-Amish general population (mean=100, SD=15). However, the statistical significance of this comparison would be sensitive to sample size. Another way to compare the norms of two populations is to follow the convention of statistical similarity when scores were within one-half of a standard deviation of the mean ($SD \pm 7.5$)¹¹. Therefore, a score within 92.5–107.5 in OOA would be considered similar to the norm of the general population and above or below would be considered statistically different from the norm, as long as the ranges of standard deviations of the scores are also similar between the two populations. The RBANS Effort Index was calculated where a compromised motivation in performances is indicated if the score is above 2³.

Heritability (h^2) was estimated by the maximum likelihood variance decomposition method in SOLAR-Eclipse (<http://www.mdbbrain.org/solareclipse/>), defined as the proportion of the total phenotypic variance (σ_p^2) that is explained by additive genetic factors (σ_g^2) in related individuals. The covariance matrix, Ω , is given by $\Omega = 2 \cdot \Phi \cdot \sigma_g^2 + I \cdot \sigma_e^2$, where σ_g^2 is the portion of the variance that is due to additive genetic factors, Φ is the kinship matrix, σ_e^2 is the variance due to unique environmental effects and measurement error, and I is an identity matrix. The variance parameters are estimated by comparing the observed phenotypic covariance matrix with the covariance matrix predicted by kinship. Age and sex were covariates in all heritability calculations. Significance of the heritability is tested by comparing the likelihood of the model in which σ_g^2 is constrained to zero with that of a model in which σ_g^2 is estimated.

RESULTS

Normative performance in OOA individuals

The non-psychiatric OOA individuals were 12 to 89 years old (mean and standard deviation: 47.9 ± 17.8). The total score and all five indices in the non-psychiatric OOA ($n=85$) were within the 92.5–107.5 score range and all standard deviations were similar or narrower than the general population norm of 15 (Table 1), although there were differences across cognition domains. The visuospatial/constructional index was the only measure slightly above (101.6) the non-Amish population norm of 100. Two other indices, delayed memory (97.5) and attention (96.9), were also fairly close to the non-Amish norms. The lowest OOA scores were in immediate memory (93.3) and language (92.5), although all of which were still within the bounds of the *a priori* 92.5–107.5 normative score range. There were no significant male vs. female differences in RBANS total and indices. Finally, none of the 103 participants had effort index score at 2 or above, and effort scores in OOA subjects tended to be considerably lower than the norm in the general population (Table 1), thus providing no evidence for lower motivation in RBANS cognitive testing performance among the OOA. Tables 3 and 4 respectively provide RBANS index scores based on age and gender.

Heritability estimate for RBANS

RBANS total score was significantly heritable in the OOA ($h^2=0.51 \pm 0.27$, $p=0.019$) (Table 2). Within the five indices, delay memory and language were significantly heritable ($h^2 = 0.63 \pm 0.22$ and 0.67 ± 0.26 ; $p=0.002$ and 0.014 , respectively). Heritability values for immediate memory, visuospatial/constructional index and attention did not differ significantly from zero.

RBANS performance in psychiatric patients

A comparison of the OOA healthy controls' RBANS scores with OOA psychiatric patients offer another means to understand the applicability of RBANS in this population, as many psychiatric conditions are associated with impaired cognition. Given the small number of psychiatric patients ($n=18$), these patients were combined in this exploratory analysis (Table 1). OOA psychiatric patients were not statistically different from healthy controls in age ($t=-0.99$, $p=0.33$) or sex ratio ($\chi^2=0.63$, $p=0.43$). Psychiatric patients had lower scores compared with non-psychiatric controls in total and domain scores, with effect sizes ranging from 0.32 to 1.08, although these differences achieved statistical significance only for language.

DISCUSSION

We found that the RBANS total score and domain scores measured in healthy OOA controls were comparable with the normative data collected in the general population. This was despite the large perceived and actual disparities in lifestyle, education system, and occupations. Three of the indices, visuospatial/constructional, delayed memory, and attention were especially similar, suggesting comparable levels of normative capacity in these cognitive domains. For heritability, the RBANS was overall significantly heritable ($h^2=0.51$), suggesting that it is substantially influenced by additive genetic factors. To the

best of our knowledge, ours is the first assessment of the heritability of RBANS in any population. Overall, the data suggest RBANS to be an efficient battery for future neuropsychiatric research in OOA.

The cognitive categories at the lower limits of the established norms were immediate memory and language. The RBANS language domain aims to assess participant's basic verbal functions and skills using two simple tasks: Picture Naming which asks the participant to name 10 familiar objects and Semantic Fluency which asks to name as many words of a restricted category (fruits/vegetables) as possible in one minute. In talking to many participants after the test was completed, virtually all mentioned not being exposed to certain objects and words such as "cannon" or "trumpet." Attempting to amend this confound would be an arduous yet worthy psychometric undertaking involving development of word frequency tables in order to arrive at culturally equivalent OOA objects/words for this subtest. This would provide items less alien to the OOA. Similarly, the RBANS immediate memory score is heavily relied on language as the score is based on the List Learning and the Story Memory tasks, which require verbalization of words and prose followed by verbal recalls. Therefore, we speculate that the lower performance in language and immediate memory shared the similar disadvantage of English not being the primary spoken language in the OOA. However, we may not want to over-emphasize the differences because many OOA speak near fluent English and these two cognitive domains are still within half a standard deviation of the general norms despite the large differences in education and lifestyle between the OOA and non-Amish.

The highest heritabilities for RBANS domains were observed for delayed memory and language. To the best of our knowledge, the heritability of RBANS has not been assessed in any population, although heritability of delayed memory and language has been measured in other populations using other instruments. In at least three studies, delayed recall also has the highest heritability ($h^2=0.60$ to 0.74) across memory, executive function, and attention domains in different cognitive batteries¹²⁻¹⁴, suggesting similar high heritability in delayed memory between OOA and non-Amish.

The second domain that showed strong heritability is language. Not many neuropsychological batteries include language as a cognitive domain, but language in general has been intensely studied in its heritability. Although language is a particularly complex domain for separating genetic from environmental impacts, the estimated heritability of 0.62 in the OOA is consistent with heritability of language-related phenotypes from across over 100 published literatures¹⁵. For example, language disorders have a heritability ranged from 0.45 to close to 1.0¹⁶⁻¹⁸; language and speech factors of young children showed heritability at 0.34 to 0.56 range¹⁹; and genetic influence of reading performance were at 0.38 to 0.57²⁰. At the other extreme, the lowest heritability among the RBANS domains was attention ($h^2 = 0.01$). This finding is intriguing because of its consistency with low heritability in attention ($h^2=0.09$) in the non-Amish population¹⁴. The reasons for the low heritability in attention as measured by these instruments are unclear.

As our sample included a small group of individuals with psychiatric illness, we compared RBANS scores between subjects with and without psychiatric illnesses. These analyses

revealed reduced RBANS scores across all cognitive domains in individuals with psychiatric illnesses, with scores ranging from 74 to 93. In the general population, patients with schizophrenia showed RBANS scores at the low end of this range^{21–24}; while patients with major depression tended to be at the high end of this range²⁵. Therefore, the data suggest that RBANS appropriately captures cognitive deficits associated with psychiatric illnesses in OOA.

To date, formal cognitive battery norms have not been published in the Amish communities. Earlier findings assumed that distinct cultural outlier groups have a unique set of experiences^{4, 5, 26} with ramifications for validity in formal assessment^{1, 27, 28}. Therefore, to develop appropriate assessment for cognitive functioning in the OOA, it is important to first establish comparability with the general population normative data. To this end, we found that RBANS represents a reasonable choice for the OOA based on their normative data and heritability. Interestingly, one personality assessment battery, the Minnesota Multiphasic Personality Inventory – 2nd Edition (MMPI-2), has been studied²⁹. Findings suggested the MMPI-2 was a useful tool in detecting psychopathology in the Amish. Knabb and Vogt (2011) conducted a similar study using the Millon Clinical Multiaxial Inventory-3rd Edition (MCMI-III) in Amish inpatient, outpatient, and non-clinical samples, and found that this instrument identified mental health conditions at a rate analogous to non-Amish. Together, these data are supportive of the use of these established clinical and psychological batteries normed in the general population to be used in the OOA³⁰.

The potential motivation factor for cognitive testing is an interesting one. As a culture, the OOA strive for humility and uniformity. However, the OOA imbue putting forth one's best effort in every endeavor. Consistent with this, we saw no evidence of compromised motivation on the Effort Index, suggesting that we do not have a significant motivational issue in assessing cognitive performance using standardized tools in the OOA.

A limitation of the study included a modest sample size overall and a very small sample of psychiatric patients, limiting our ability to examine constellations of cognitive deficits within individual psychiatric diagnoses. While the RBANS is a useful screening test, the measurement at the level of specific cognitive domains is not very precise as the subtests involve a limited number of items. Thus, conclusions regarding differential heritability across domains should be regarded with caution. The relatively small sample size also limits generalizability of the findings to the total OOA population. The 103 individuals were also comprised a disproportionate amount of men and women (37 and 66, respectively). Replicating the findings using a larger, more demographically balanced sample would be desirable. While the current data are preliminary, they represent the first normative inquiry on a standard cognitive battery in the OOA. There are an estimated 1.6 – 2.4 million Amish population in North American and Europe⁴ and the scope of research with this population is ever increasing. The availability of norms for a standard neuropsychological battery in healthy Old Order Amish should provide support to the neuropsychiatric research and clinical service in the OOA.

A second, potential limitation of this study is that the reported heritability measurements may be impacted by shared familial factors. The small sample size and high degrees of both

shared familial and environmental factors among them make it difficult to formally distinguish the genetic and environmental causes of family resemblance. We believe it to be a minor limitation, as it is the difference in the environmental factors such the diet or socio-economic status that can mistakenly increase the heritability estimates.

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References

1. Cherner M, Suarez P, Lazzaretto D, Fortuny LA, Mindt MR, Dawes S, Marcotte T, Grant I, Heaton R. group H. Demographically corrected norms for the Brief Visuospatial Memory Test-revised and Hopkins Verbal Learning Test-revised in monolingual Spanish speakers from the U.S.-Mexico border region. *Arch Clin Neuropsychol*. 2007; 22(3):343–353. [PubMed: 17293078]
2. Randolph C, Tierney MC, Mohr E, Chase TN. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): preliminary clinical validity. *J Clin Exp Neuropsychol*. 1998; 20(3):310–319. [PubMed: 9845158]
3. Silverberg ND, Wertheimer JC, Fichtenberg NL. An effort index for the Repeatable Battery For The Assessment Of Neuropsychological Status (RBANS). *Clin Neuropsychol*. 2007; 21(5):841–854. [PubMed: 17676548]
4. Kraybill, DB. Concise encyclopedia of OOA, Brethren, Hutterites, and Mennonites. Baltimore: Johns Hopkins University PRes; 2010.
5. Kraybill, DB.; Nolt, SM.; Weaver-Zercher, DL. The OOA way: Patient faith in a perilous world. San Francisco, CA: Wiley-Jossey-Bass; 2010.
6. Green P, Rohling ML, Lees-Haley PR, Allen LM 3rd. Effort has a greater effect on test scores than severe brain injury in compensation claimants. *Brain Inj*. 2001; 15(12):1045–1060. [PubMed: 11712951]
7. Heilbronner RL, Sweet JJ, Morgan JE, Larrabee GJ, Millis SR, Conference P. American Academy of Clinical Neuropsychology Consensus Conference Statement on the neuropsychological assessment of effort, response bias, and malingering. *Clin Neuropsychol*. 2009; 23(7):1093–1129. [PubMed: 19735055]
8. Agarwala RBLG, Hopkins KA, Francomano CA, Schaffer AA. Software for Constructing and Verifying Pedigrees Within Large Genealogies and an Application to the Old Order Amish of Lancaster County. *Genome Research*. 1998; 8:211–221. [PubMed: 9521925]
9. Lee W-JPTI, O'Connell JR, Agarwala R, Schaffer AA. PedHunter 2.0 and its Usage to Characterize the Founder Structure of the Old Order Amish of Lancaster County. *BMC Medical Genetics*. 2010; 11:68. [PubMed: 20433770]
10. Mitchell BDLW-J, Tolea M, Shields K, Ashtorab Z, Madger LS, Ryan KA, Pollin TI, McArdle PF, Shuldiner AR, Schaffer AA. Living the Good Life? Mortality and Hospital Utilization Patters in the Lancaster County Amish. *PLoS ONE*. 2012; 7:e51560. [PubMed: 23284714]
11. Farivar SS, Liu H, Hays RD. Half standard deviation estimate of the minimally important difference in HRQOL scores? *Expert Rev Pharmacoecon Outcomes Res*. 2004; 4(5):515–523. [PubMed: 19807545]
12. Lee JH, Flaquer A, Stern Y, Tycko B, Mayeux R. Genetic influences on memory performance in familial Alzheimer disease. *Neurology*. 2004; 62(3):414–421. [PubMed: 14872023]
13. Greenwood PM, Parasuraman R. Normal genetic variation, cognition, and aging. *Behav Cogn Neurosci Rev*. 2003; 2(4):278–306. [PubMed: 15006290]
14. Greenwood TA, Beeri MS, Schmeidler J, Valerio D, Raventos H, Mora-Villalobos L, Camacho K, Carrion-Baralt JR, Angelo G, Almasy L, Sano M, Silverman JM. Heritability of cognitive

- functions in families of successful cognitive aging probands from the Central Valley of Costa Rica. *J Alzheimers Dis.* 2011; 27(4):897–907. [PubMed: 21908911]
15. Stromswold K. The Heritability of Language: A Review and Metaanalysis of Twin, Adoption, and Linkage Studies. *Language.* 2001; 11(4):647–723.
 16. Tomblin JB, Buckwalter PR. Heritability of poor language achievement among twins. *Speech Lang Hear Res.* 1998; 141(1):188–199.
 17. Bishop DV, North T, Donlan C. Genetic basis of specific language impairment: evidence from a twin study. *Dev Med Child Neurol.* 1995; 37(1):66–71.
 18. Bishop DV, Laws G, Adams C, Norbury CF. High heritability of speech and language impairments in 6-year-old twins demonstrated using parent and teacher report. *Behav Genet.* 2006; 36(2):173–184. [PubMed: 16485179]
 19. Hayiou-Thomas ME, Kovas Y, Harlaar N, Bishop DMW, Dale PS, Plomin R. Common genetic etiology for diverse language skills in 4 1/2 year old twins. *Journal of Child Language.* 2006; 33:339–368. [PubMed: 16826830]
 20. Wadsworth S, Corley RP, Hewitt JK, DeFries JC. Colorado Adoption Project. Stability of genetic and environmental influences on reading performance at 7, 12, and 16 years of age in the Colorado Adoption Project. *Behav Genet.* 2001; 31(4):353–359. [PubMed: 11720121]
 21. Gold JM, Queern C, Iannone VN, Buchanan RW. Repeatable battery for the assessment of neuropsychological status as a screening test in schizophrenia I: sensitivity, reliability, and validity. *Am J Psychiatry.* 1999; 156(12):1944–1950. [PubMed: 10588409]
 22. Randolph, C.; Goldberg, TE.; Weinberger, TR. *The neuropsychology of schizophrenia.* 3. New York: Oxford Press; 1993.
 23. Iverson GI, Brooks BL, Haley GMT. Interpretation of the RBANS in Inpatient Psychiatry: Clinical Normative Data and Prevalance of Low Scores for patients with Schizophrenia. *Applied Neuropsychiatry.* 2009; 16:31–41.
 24. Zhang XY, Liang J, Chen da C, Xiu MH, Yang FD, Kosten TA, Kosten TR. Low BDNF is associated with cognitive impairment in chronic patients with schizophrenia. *Psychopharmacology (Berl).* 2012; 222(2):277–284. [PubMed: 22274000]
 25. Baune BT, Miller R, McAfoose J, Johnson M, Quirk F, Mitchell D. The role of cognitive impairment in general functioning in major depression. *Psychiatry Res.* 2010; 176(2–3):183–189. [PubMed: 20138370]
 26. Bush SS, Ruff RM, Troster AI, Barth JT, Koffler SP, Pliskin NH, Reynolds CR, Cilver CH. Symptom validity assessment: Practice issues and medical necessity. NAN policy and planning committee. *Archives of Clinical Neuropsychology.* 2005; 20:419–426. [PubMed: 15896556]
 27. Gasquoine PG, Croyle KL, Cavazos-Gonzalez C, Sandoval O. Language of administration and neuropsychological test performance in neurologically intact Hispanic American bilingual adults. *Arch Clin Neuropsychol.* 2007; 22(8):991–1001. [PubMed: 17900857]
 28. Cates J, Graham L. Psychological assessment of the old order OOA: Unraveling the enigma. *Professional Psychology: Research and Practice.* 2002; 33(2):155–161.
 29. Knabb JJ, Vogt RG, Newgren KP. MMPI-2 characteristics of the Old Order Amish: a comparison of clinical, nonclinical, and United States normative samples. *Psychol Assess.* 2011; 23(4):865–875. [PubMed: 21534692]
 30. Knabb JJ, Vogt RG. Assessing Old Order Amish outpatients with the MCMI-III. *J Pers Assess.* 2011; 93(3):290–299. [PubMed: 21516588]

Mean and SD of RBANS cognitive and effort index scores in non-Amish normative data, OOA non-psychiatric subjects, and OOA subjects with psychiatric diagnoses.

Table 1

	Non-Amish norm (n = 540)	OOA controls (n = 85)	OOA psychiatric cases (n = 18)	Non-Amish vs. OOA controls p-value	OOA control vs. OOA psychiatric cases p-value
Visuospatial/Constructional Index	100 ± 15	101.6 ± 15.9	92.6 ± 19.2	0.367	0.063
Immediate Memory Index	100 ± 15	93.3 ± 12.9	88.1 ± 19.8	0.000	0.275
Delayed Memory Index	100 ± 15	97.5 ± 9.2	92.0 ± 15.2	0.016	0.140
Language Index	100 ± 15	92.5 ± 14.1	76.7 ± 15.0	0.000	0.000
Attention Index	100 ± 15	96.9 ± 13.0	89.8 ± 17.5	0.032	0.104
RBANS Total Score	100 ± 15	94.4 ± 10.9	84.6 ± 16.6	0.000	0.022
Effort Index Score	0.50 ± 1.10	0.12 ± 0.45	0.22 ± 0.65	0.002	0.433

Table 2

Heritability estimate of RBANS and cognitive domain scores. Bolded values are statistically significant. SE: standard error.

Trait	h^2	h^2 SE	p
Visuospatial/Constructional Index	0.40	0.49	0.176
Immediate Memory Index	0.29	0.28	0.141
Delayed Memory Index	0.67	0.26	0.014
Language Index	0.63	0.22	0.002
Attention Index	0.01	0.29	0.486
RBANS Total Score	0.51	0.27	0.020

Table 3

Mean and SD of RBANS index scores of OOA non-psychiatric subjects by age.

	12-19 (n = 2)	20-39 (n = 25)	40-49 (n = 15)	50-59 (n=17)	60-69 (n=14)	70-79 (n=10)	80-89 (n=2)
Visuospatial/Constr. Index	120.5 ± 2.1	97.4 ± 14.2	109.9 ± 10.2	107.4 ± 14.6	104.0 ± 16.1	89.3 ± 19.5	93.5 ± 26.2
Immediate Memory Index	115.0 ± 2.1	94.4 ± 11.3	95.7 ± 10.5	95.5 ± 17.5	83.3 ± 4.9	87.5 ± 10.9	88.0 ± 17.0
Delayed Memory Index	104.0 ± 2.8	96.7 ± 5.6	101.8 ± 7.7	101.0 ± 10.5	85.5 ± 16.8	94.8 ± 12.0	92.0 ± 1.4
Language Index	107.5 ± 2.1	93.2 ± 19.5	94.8 ± 10.9	93.3 ± 12.6	93.5 ± 3.0	86.1 ± 10.7	81.0 ± 2.8
Attention Index	94.5 ± 20.5	93.3 ± 10.9	104.4 ± 10.3	100.8 ± 16.3	90.3 ± 4.5	95.9 ± 13.8	92.5 ± 19.1
RBANS Total Score	111.5 ± 7.8	92.2 ± 8.9	101.2 ± 7.1	99.1 ± 12.7	87.8 ± 8.3	86.4 ± 10.9	86.0 ± 15.6

Table 4

Mean and SD of RBANS index scores of OOA non-psychiatric subjects by gender.

	Visuospatial/Constructional Index	Immediate Memory Index	Delayed Memory Index	Language Index	Attention Index	RBANS Total Score
Male (n=31)	104.7 ± 14.7	90.9 ± 12.9	95.1 ± 11.9	90.5 ± 14.1	95.3 ± 12.5	92.9 ± 11.3
Female (n=54)	99.8 ± 16.4	94.7 ± 12.7	99.0 ± 7.0	93.7 ± 14.1	97.9 ± 13.3	95.2 ± 10.7