# The Genetics of Endophenotypes of Neurofunction to Understand Schizophrenia (GENUS) Consortium: A Collaborative Cognitive and Neuroimaging Genetics Project

Gabriëlla A. M. Blokland[1,2,3], Elisabetta C. del Re[4,2,5], Raquelle I. Mesholam-Gately[6,2], Jorge Jovicich[7], Joey W. Trampush[8,9,10], Matcheri S. Keshavan[6,2,11], Lynn E. DeLisi[4,2], James T. R. Walters[13], Jessica A. Turner[14,15], Anil K. Malhotra[8,9,10], Todd Lencz[8,9,10], Martha E. Shenton[5,2], Aristotle N. Voineskos[16,17], Dan Rujescu[18,19], Ina Giegling[18], René S. Kahn[20], Joshua L. Roffman[21,22,23], Daphne J. Holt[2,21,22], Stefan Ehrlich[24,22,2], Zora Kikinis[5,2], Paola Dazzan[25,26], Robin M. Murray[25,26], Marta Di Forti[25,26], Jimmy Lee[27], Kang Sim[27], Max Lam[27], Rick P. F. Wolthusen[24,2,22], Sonja M. C. de Zwarte[20], Esther Walton[24], Donna Cosgrove[28], Sinead Kelly[29,30,31], Nasim Maleki[22,2,23], Lisa Osiecki[1], Marco M. Picchioni[25,26], Elvira Bramon[25,26,33], Manuela Russo[25,26], Anthony S. David[25,26], Valeria Mondelli[25,26], Antje A. T. S. Reinders[25,26], M. Aurora Falcone[25,26], Annette M. Hartmann[18], Bettina Konte[18], Derek W. Morris[34], Michael Gill[35,30], Aiden P. Corvin[35,30], Wiepke Cahn[20], New Fei Ho[27], Jian Jun Liu[36], Richard S. E. Keefe[37], Randy L. Gollub[22,2], Dara S. Manoach[22], Vince D. Calhoun[14,38], S. Charles Schulz[39], Scott R. Sponheim[39], Donald C. Goff[40,21], Stephen L. Buka[41], Sara Cherkerzian[42,43], Heidi W. Thermenos[6,2], Marek Kubicki[5,44,45,1], Paul G. Nestor[4,2,47], Erin W. Dickie[16], Evangelos Vassos[25,26], Simone Ciufolini[25,26], Tiago Reis Marques[25,26], Nicolas A. Crossley[25,26], Shaun M. Purcell[1,2,3,48,49], Jordan W. Smoller[1,2,3], Neeltje E. M. van Haren[20], Timothea Toulopoulou[50,51,52], Gary Donohoe[28,35,30], Jill M. Goldstein[42,53,23,22], Larry J. Seidman[6,2], Robert W. McCarley[4,2], Tracey L. Petryshen[1,2,3]

[1]Psychiatric and Neurodevelopmental Genetics Unit, Center for Genomic Medicine & Department of Psychiatry, Massachusetts General Hospital, Boston, MA, United States
[2]Department of Psychiatry, Harvard Medical School, Boston, MA, United States
[3]Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA, United States
[4]Laboratory of Neuroscience, Clinical Neuroscience Division, Department of Psychiatry, Veterans Affairs Boston Healthcare System, Brockton, MA, United States
[5]Psychiatry Neuroimaging Laboratory, Department of Psychiatry, Brigham and Women's Hospital, Boston, MA, United States
[6]Massachusetts Mental Health Center Public Psychiatry Division, Beth Israel Deaconess Medical Center, Boston, MA, United States
[7]Center for Mind/Brain Sciences (CiMEC), University of Trento, Trento, Italy
[8]Center for Psychiatric Neuroscience, The Feinstein Institute for Medical Research, Division of Northwell Health, Manhasset, NY, United States
[9]Division of Psychiatry Research, The Zucker Hillside Hospital, Division of Northwell Health, Glen Oaks, NY, United States
[10]Hofstra Northwell School of Medicine, Departments of Psychiatry and Molecular Medicine, Hempstead, NY, United States
[11]University of Pittsburgh Medical Center, Pittsburgh, PA, United States
[12]Veterans Affairs Boston Healthcare System, Brockton, MA, United States
[13]Department of Psychological Medicine, Cardiff University, Cardiff, United Kingdom
[14]The Mind Research Network, Albuquerque, NM, United States
[15]Departments of Psychiatry and Psychology, University of New Mexico, Albuquerque, NM, United States
[16]Kimel Family Translational Imaging Genetics Laboratory, Research Imaging Centre, Campbell Family Mental Health Institute, Centre for Addiction and Mental Health, Department of Psychiatry, Faculty of Medicine, University of Toronto, Toronto, ON, Canada
[17]Department of Psychiatry and Institute of Medical Science, University of Toronto, Toronto, ON, Canada
[18]Department of Psychiatry, Psychotherapy and Psychosomatics, University of Halle-Wittenberg, Halle an der Saale, Germany
[19]Department of Psychiatry, Ludwig Maximilians University, Munich, Germany
[20]Brain Centre Rudolf Magnus, Department of Psychiatry, University Medical Centre Utrecht, Utrecht, The Netherlands
[21]Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States
[22]MGH/HST Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, United States
[23]Brain Genomics Lab, Psychiatric Neuroimaging Division, Massachusetts General Hospital, Boston, MA, United

States
[24]Division of Psychological & Social Medicine and Developmental Neurosciences, Faculty of Medicine, Technische Universität Dresden, Dresden, Germany
[25]Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom
[26]National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust, London, United Kingdom
[27]Institute of Mental Health, Woodbridge Hospital, Singapore
[28]The Cognitive Genetics and Cognitive Therapy Group, Department of Psychology, National University of Ireland, Galway, Ireland
[29]Department of Psychiatry, Institute of Molecular Medicine, Trinity College Dublin, St. James Hospital, Dublin, Ireland
[30]Trinity College Institute of Neuroscience, Trinity College, Dublin, Ireland
[31]Laboratory of NeuroImaging, Keck School of Medicine, University of Southern California, Los Angeles, CA, United States
[32]Psychiatric Neuroimaging Division, Massachusetts General Hospital, Boston, MA, United States
[33]Mental Health Neuroscience Research Department, UCL Division of Psychiatry, University College London, United Kingdom
[34]Neuroimaging and Cognitive Genomics (NICOG) Centre, School of Psychology and Discipline of Biochemistry, National University of Ireland, Galway, Ireland
[35]Neuropsychiatric Genetics Group, Department of Psychiatry, Institute of Molecular Medicine, Trinity College Dublin, St. James Hospital, Dublin, Ireland
[36]Genome Institute, Singapore
[37]Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, United States
[38]Department of Electrical and Computer Engineering, University of New Mexico, Albuquerque, NM, United States
[39]Department of Psychiatry, University of Minnesota, Minneapolis, MN, United States
[40]Nathan S. Kline Institute for Psychiatric Research, Department of Psychiatry, New York University Langone Medical Center, New York, NY, United States
[41]Department of Epidemiology, Brown University, Providence, RI, United States
[42]Connors Center for Women's Health and Gender Biology, Division of Women's Health, Departments of Psychiatry and Medicine, Brigham and Women's Hospital, Boston, MA, United States
[43]Department of Psychiatry and Medicine, Harvard Medical School, Boston, MA, United States
[44]Departments of Psychiatry and Radiology, Harvard Medical School, Boston, MA, United States
[45]Department of Radiology, Brigham and Women's Hospital, Boston, MA, United States
[46]Department of Psychiatry, Massachusetts General Hospital, Boston, MA, United States
[47]Laboratory of Applied Neuropsychology, University of Massachusetts, Boston, MA, United States
[48]Laboratory of Sleep and Neuropsychiatric Genetics, Brigham and Women's Hospital, Boston, MA, United States
[49]Division of Psychiatric Genomics, Departments of Psychiatry and Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, United States
[50]Department of Psychology, Bilkent University, Bilkent, Ankara, Turkey
[51]Department of Psychology, The University of Hong Kong, Pokfulam, Hong Kong, SAR, China
[52]Department of Basic and Clinical Neuroscience, Institute of Psychiatry, Psychology, and Neuroscience, King's College London, London, United Kingdom
[53]Departments of Psychiatry and Medicine, Harvard Medical School, Boston, MA, United States

*Please address correspondence to: Tracey Petryshen, Psychiatric and Neurodevelopmental Genetics Unit, Center for Genomic Medicine, Massachusetts General Hospital, 185 Cambridge Street, Boston MA 02114, United States; Phone: +1 617 726 4960; Fax: +1 617 726 0831; E-mail: tpetryshen@mgh.harvard.edu

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## Abstract

**Background:** Schizophrenia has a large genetic component, and the pathways from genes to illness manifestation are beginning to be identified. The Genetics of Endophenotypes of Neurofunction to Understand Schizophrenia (GENUS) Consortium aims to clarify the role of genetic variation in brain abnormalities underlying schizophrenia. This article describes the GENUS Consortium sample collection.

**Methods:** We identified existing samples collected for schizophrenia studies consisting of patients, controls, and/or high-risk individuals with a family history of schizophrenia. Samples had single nucleotide polymorphism (SNP) array data or genomic DNA, clinical and demographic data, and neuropsychological and/or brain magnetic resonance imaging (MRI) data. Data were subjected to quality control procedures at a central site.

**Results:** Sixteen research groups contributed data from 5,155 psychosis patients, 4,832 controls, and 725 familial high-risk (FHR) individuals. All participants have relevant demographic data; all patients have relevant clinical data. The sex ratio is 57% male and 43% female. Significant differences exist between diagnostic groups for premorbid and current IQ (both $p<1\times10^{-10}$). Data from a diversity of neuropsychological tests are available for 93% of participants, and 30% have structural MRI scans (half also have diffusion-weighted MRI scans). SNP data are available for 75% of participants. The ancestry composition is 71% European, 19% East Asian, 7% African, and 3% other.

**Conclusions:** The GENUS Consortium is investigating the genetic contribution to brain phenotypes in a schizophrenia sample collection of >10,000 participants. The breadth of data across clinical, genetic, neuropsychological, and MRI modalities provides an excellent opportunity for further elucidating the genetic basis of neural processes underlying schizophrenia.

## Keywords

# 1. Introduction

Clinical presentation of schizophrenia varies among individuals, but in general is characterized by positive (hallucinations, delusions), negative (social withdrawal), and disorganization symptoms, cognitive impairments, altered brain structure and function, and severe deficits in global and social functioning. There is a generalized cognitive impairment, as well as specific deficits across cognitive domains including processing speed, attention, working memory, verbal memory, and executive functioning, that are present as early as the pre-morbid state during childhood and persist through chronic stages of illness (Lewandowski et al., 2011; Seidman and Mirsky, under review). There is consistent evidence from schizophrenia neuroimaging studies for ventricular enlargement, reduced gray matter volume of cortical and subcortical brain regions, and reduced white matter volume and fractional anisotropy of predominantly fronto-temporal tracts (Bora et al., 2011; Haijma et al., 2013; Shenton et al., 2001; van Erp et al., 2016). Unaffected relatives of schizophrenia patients exhibit milder cognitive deficits and brain structural abnormalities (Boos et al., 2007; Keshavan et al., 2010; Thermenos et al., 2013), suggesting these abnormalities are risk factors for the disorder rather than secondary effects. The molecular mechanisms underlying these brain abnormalities are only beginning to be unraveled, which has hindered the identification of rational targets for developing better treatments.

A practical approach for elucidating the disease biology is identifying genes that confer risk and characterizing their function within the brain. It is long known that schizophrenia has a large genetic component, with heritability between 64-81% (Lichtenstein et al., 2009; Sullivan et al., 2003). Genome wide association studies (GWAS) of schizophrenia case/control datasets by the Psychiatric Genomics Consortium (PGC) have identified over 100 chromosomal loci that have genome-wide significant evidence for association (PGC Schizophrenia Working Group, 2014). GWAS results indicate that schizophrenia is a polygenic disorder, for which thousands of common genetic variants with modest individual effects act in aggregate to increase disease liability (Psychosis Endophenotypes International Consortium et al., 2014; Purcell et al., 2009; Ripke et al., 2013). Rare variants further contribute to schizophrenia liability (CNV and Schizophrenia Working Groups of the Psychiatric Genomics Consortium; Psychosis Endophenotypes International Consortium, 2017; Malhotra and Sebat, 2012).

A promising approach to translate these genetic findings into an understanding of the neural processes involved in schizophrenia is to evaluate their relevance to disease endophenotypes (Gottesman and Gould, 2003). In this context, cognitive measures have a moderate to high heritability ($h^2 = 0.2$-$0.7$) (Seidman et al., 2015; Stone and Seidman, 2016), while volumetric and diffusion brain measures are highly heritable ($h^2 = 0.6$-$0.8$) (Blokland et al., 2012; 2016). Common genetic variation (based on SNPs) explains a substantial proportion of this heritability, estimated at $h^2 = 0.3$-$0.4$ for cognitive (Hatzimanolis et al., 2015; Robinson et al., 2015) and brain volume phenotypes (Ge et al., 2015). Moderate to high genetic correlations between schizophrenia and cognitive and brain structural phenotypes ($r_g = 0.5$-$0.8$) suggest a partially shared genetic etiology (Blokland et al., 2016; Bohlken et al., 2016; Lee et al., 2016). Indeed, polygenic risk for schizophrenia is significantly associated with prefrontal inefficiency during working memory performance in patients and controls (Walton et al., 2013a; Walton et al., 2013b), as well as lower cognitive performance among healthy populations (Germine et al., 2016; Hubbard et al., 2016; Lencz et al., 2014; Liebers et al., 2016) and schizophrenia patients (Martin et al., 2015). Specific genetic risk variants have also been associated with altered cognition and brain structure among patients (Donohoe et al., 2010; 2013; Lencz et al., 2010; Martin et al., 2015; Wassink et al., 2012; Yeo et al., 2014) although some studies are negative (van Scheltinga et al., 2013), possibly due to the use of small samples that are prone to inconsistent results. Analyses of large, well-phenotyped samples consisting of both psychosis patients and control individuals will be important for clarifying the role of genetic risk variants in brain abnormalities relevant to illness.

With this in mind, the GENUS Consortium aims to improve knowledge of the contribution of genetic variation to schizophrenia brain abnormalities by investigating relevant brain traits in a large, comprehensively phenotyped sample collection. The GENUS Consortium draws upon the efforts of sixteen research groups that have previously collected samples consisting of psychosis patients (predominantly schizophrenia), unaffected controls, and/or unaffected familial high-risk (FHR) individuals assessed for neuropsychological function and/or brain structure, all of which have genome-wide SNP data or genomic DNA. Assembly of these samples into one harmonized collection substantially increases the statistical power compared to the individual samples alone. The large, well-phenotyped GENUS sample collection provides a prime opportunity to investigate the genetic basis of brain abnormalities in psychosis in order to gain insight into the underlying neural mechanisms. The purpose of this article is to describe the design, composition, and data components of the sample collection, while subsequent articles will focus on data analyses.

## 2. Methods

### 2.1. Collection of samples

Research groups that had previously collected samples for the purpose of schizophrenia studies were identified from the psychiatric genetics community and publications. Criteria for inclusion were: availability of SNP genotype data or genomic DNA, as well as demographic, neuropsychological and/or magnetic resonance imaging (MRI) data, and, for patients, clinical data.

### 2.2. Informed consent and ethics approval

The lead principal investigator for each sample verified approval from their institutional ethics committee for sharing human subject data. All research participants provided written informed consent (or legal guardian consent and subject assent). Ethics approval for the GENUS Consortium study at the central site was obtained from the Partners Healthcare (USA) Institutional Review Board. All data were anonymized prior to transfer to the central site.

### 2.3. Clinical and demographic data

For demographic data, all research groups had collected data on age at recruitment, sex, and education level, and most groups had also collected data on socioeconomic status and handedness. Clinical data were available for patients and, for some samples, FHR individuals. All site-specific clinical variables were renamed according to a common variable naming convention. Raw data underwent quality control analyses at the central site for expected value ranges and outliers. To enable comparison across sites, we computed basic descriptives (means and standard deviations for quantitative variables; frequency tables for categorical variables) and plotted histograms to check for unexpected differences in data distributions. Antipsychotic medication dosages, both current and lifetime, where available, were converted to chlorpromazine equivalents based on published dosage equivalence estimates (Gardner et al., 2010; Woods, 2003).

### 2.4. Neuropsychological data

The specific neuropsychological tests ranged across samples, although all research groups administered tests within the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) consensus cognitive battery (Nuechterlein et al., 2008) or tests with similar design and scoring. We therefore focused on MATRICS tests and tests that measure similar cognitive constructs as the MATRICS tests. Additionally, we included visuospatial ability and verbal ability tests, as most groups administered these tests. All site-specific test variables were renamed according to a common variable naming convention. The raw data from each test were checked for errors by calculating descriptive statistics and visualizing data distributions for each study sample. Premorbid IQ was estimated from reading tests (or vocabulary if reading

tests were not available), and current IQ from Wechsler Adult Intelligence Scale (WAIS) subtests (see Supplementary Materials).

*2.5. Neuroimaging data*

For those research groups that acquired MRI scans, we required 1.5 or 3 Tesla field strength, and availability of control scans in order to normalize the imaging data. We imposed no restrictions on the scanner vendor or model. As an initial assessment of quality, a subset of 12 scans from each sample (3 male patients, 3 female patients, 3 male controls, 3 female controls) were visually inspected for consistent artifacts using 3DSlicer (http://www.slicer.org; Fedorov et al., 2012), including partial brain coverage, wrap-around and motion artifacts, and gross signal/contrast inhomogeneity. Further quality control analyses were carried out upon receipt of the full dataset and will be described elsewhere.

*2.6. SNP genotype data*

Each research group provided raw SNP array genotype data, when available, or genomic DNA extracted from whole blood, buffy coat or saliva (≥2 ng/µL) that we genotyped on the Illumina Infinium PsychArray. Although most participants had self-reported ancestry information, we assigned ancestry by merging genotype call data from each sample with the 1000 Genomes Reference Panel (Sudmant et al., 2015; The 1000 Genomes Project Consortium et al., 2015), and applying multidimensional scaling using Plink software (Purcell et al., 2007) to extract ancestry principal components. Model-based clustering (R function 'Mclust') was applied to classify participants into ancestral populations as defined by the 1000 Genomes Reference Panel. Basic quality control analyses of raw genotype data consisted of removing unplaced SNPs and confirming consistency between reported sex and X chromosome genotype.

*2.7. Statistical analyses*

Quantitative demographic data from patient, control, and FHR groups were compared using ANOVA. Chi-square tests compared the relative proportions of males/females, ancestral populations, and handedness across groups. For all statistical tests, an uncorrected alpha of 0.05 was applied.

## 3. Results

*3.1. Central data management*

Sixteen research groups contributed data from 19 samples consisting of 5,155 patients, 4,832 controls, and 725 FHR participants (unaffected relatives of psychosis patients), totaling 10,712 participants. **Table 1** lists the data from each sample that was provided to the central site (Massachusetts General Hospital). Details for each data modality are provided in the sections below. Each research group provided the central site with detailed sample information (see Supplementary Materials), including recruitment (source, target diagnosis, illness stage [e.g. first-episode sample]), inclusion/exclusion criteria (ranges of age, IQ, and years of education; substance and medication use, MRI contraindications), and data modalities, which the central site reviewed and obtained clarification as necessary. Some samples have been previously contributed to other research consortia or the data made available in repositories (see Supplementary Materials).

*3.2. Demographic and clinical characteristics of samples*

**Table 2** shows the demographic and clinical characteristics of the 19 samples. The patient diagnoses consist of 78.9% schizophrenia, 8.8% schizoaffective disorder (SAD), 1.8% schizophreniform disorder (SPD), 6.6% bipolar disorder with psychosis (BD), and 4.0% other psychoses.

Fourteen samples consist of controls and patients with a range of illness durations, except for one sample (GAP) consists of only first-episode patients and controls. Four of these

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14 samples also contain FHR individuals. Two samples consist of FHR and controls, two samples consisted of only patients, and one sample consists of only controls. Given the range of illness duration (0-58 years) and the inclusion of FHR participants, the sample collection has a wide age range (8-86 years). The sex composition is 57% male and 43% female. There are significant differences between the patient, control, and FHR groups in age (younger FHR), sex ratio (more male patients), years of education (fewer in patients), and ancestral population (all $p<1\times10^{-10}$; **Table 2**), but not in handedness. These differences must be adjusted in analyses, or matched subsets selected.

The most common clinical data across the samples are the Positive and Negative Syndrome Scale (PANSS; 54.4% of patients) (Kay et al., 1987; Peralta and Cuesta, 1994), Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984) (41.9% of patients), and Global Assessment of Functioning (GAF; 33.9% of patients) (American Psychiatric Association, 2000).

Current or lifetime average dose of antipsychotic medication (chlorpromazine equivalents) (Gardner et al., 2010; Woods, 2003) is available for 58.2% or 26.0% of patients, respectively, and 20.4% of patients have both dosage estimates. Dosages are similar to other clinical samples (Eum et al., 2017; van Erp et al., 2016), suggesting that this patient collection is representative of and generalizable to the clinical population.

### 3.3. Neuropsychological measures

All 19 samples have neuropsychological data from 4,865 patients (78.2% schizophrenia, 9.3% SAD, 1.7% SPD, 6.9% BD, 4.0% other psychosis), 4,368 controls, and 723 FHR individuals (9,956 participants or 93% of sample; **Table 1**). The most common tests administered across the samples are shown in **Table 3**, with highest overlap across samples for Digit Symbol Coding, Verbal Fluency, and Word List Learning. **<span style="color:red">Supplementary Table 3</span>** <span style="color:red">provides detailed information on the specific tests and number of participants.</span> There are substantial differences in the mean premorbid IQ and mean current IQ between diagnostic groups (both $p<1\times10^{-10}$; **Table 2**). The mean premorbid and current IQ of controls and FHR individuals are higher than the population mean of 100, as previously reported by other psychosis studies (Hill et al., 2013; Seidman et al., 2015). However, the difference of ~10 IQ points between the GENUS patients and controls is consistent with the literature (Khandaker et al., 2011; Woodberry et al., 2008). Among the controls, current IQ is notably higher than premorbid IQ. The high current IQ is predominantly driven by samples that used few (2-4) WAIS subtests, which may overestimate current IQ compared to samples that used many subtests (i.e., full-scale IQ) (Axelrod, 2002). The higher current IQ may also be due to a ceiling effect, where the reading tests used to estimate premorbid IQ have a lower maximum score (~130) than WAIS subtests used to estimate current IQ (maximum 160).

### 3.4. Neuroimaging data

Thirteen samples have T1-weighted structural MRI scans from 1,343 patients (78.6% schizophrenia, 8.0% SAD, 3.9% SPD, 5.4% BD, 4.2% other psychosis), 1,502 controls, 370 FHR individuals (3,215 participants or 30% of sample; **Table 1**). Quality evaluation of a subset of scans from each sample discounted systematic gross errors and indicated that all datasets are high quality. In addition to the T1-weighted acquisitions, 10 samples have diffusion-weighted MRI scans from 1,946 participants, and 9 samples have T2-weighted structural scans from 1,836 participants. **Table 4** lists the scanners and primary scan parameters for each sample. Full scan acquisition parameters are provided in the Supplementary Materials.

### 3.5. SNP genotype data

As detailed in the Supplementary Materials, 15 of the 19 samples had previously acquired raw SNP genotype data from 7,478 participants (66.4%). For 10 samples, only a proportion of participants had been genotyped. Four of the 19 samples had genomic DNA from

978 participants (8.7%), of which 947 (8.4%) participants had sufficient DNA quality and quantity for genotyping on the Illumina Infinium PsychArray at the central site. **Table 1** lists the SNP arrays used for each sample. **Supplementary Table 1** lists the number of genotyped participants in each sample and **Supplementary Table 2** provides the demographic and clinical characteristics. Of the total 8,425 participants with genotype data, 164 participants were excluded during quality control analyses due to low (<98%) genotype call rate, resulting in 8,261 participants with genotype data suitable for imputation (4,102 patients, 3,850 controls, 309 FHR). Further quality control and imputation procedures will be described elsewhere. The mean call rate across the cleaned dataset is 99.8% (range 99.3%-99.9%). The sample collection has 80% power to detect a genetic variant that explains 0.5% of the variance of a phenotype at a genome-wide significant alpha = $5\times10^{-8}$.

The ancestry breakdown based on genotype data is 70.7% European (2910 patients, 2758 controls, 287 FHR), 19.1% East Asian (624 patients, 982 controls, 1 FHR), 7.2% African (456 patients, 114 controls, 36 FHR), 2.0% American (predominantly Latino; 138 patients, 29 controls, 3 FHR), and 1.0% other ancestry (54 patients, 27 controls, 3 FHR).

## 4. Discussion

This article provides a general description of the GENUS Consortium and its sample collection, which is the largest known dataset of psychosis patients, controls, and FHR individuals with data spanning genetics, clinical, cognitive and, for a subset, structural MRI and diffusion imaging. This dataset enables large-scale investigations of brain-based phenotypes. Due to data sharing restrictions of many of the individual samples, the full dataset is currently only available to external researchers through collaboration with GENUS Consortium members. The extent of data and large size of the GENUS dataset, as well as the breadth of expertise of the GENUS Consortium members, provide a host of opportunities for analyses. For example, examining sex differences in disease-related phenotypes is an important but often overlooked aspect of psychiatric studies (Goldstein et al., 2013) that can be addressed with this large, well-phenotyped sample collection.

The GENUS Consortium differs in several aspects from other large-scale efforts investigating the genetic architecture of cognition and neuroanatomy relevant to psychosis (e.g., COGENT, ENIGMA, B-SNIP, Brain Genomics Superstruct Project, Philadelphia Neurodevelopmental Cohort) (Franke et al., 2016; Germine et al., 2016; Holmes et al., 2015; Lee et al., 2016; Lencz et al., 2014; Tamminga et al., 2013). A key difference is that many other studies do not have data for both cognition and brain structure modalities from the same participants. Bridging multiple brain phenotype modalities, as in the GENUS sample collection, is important for heterogeneous disorders such as schizophrenia that are defined by diverse symptoms and abnormalities whose relationships are mostly unknown. Another difference is the GENUS subject-level data are stored at the central site, allowing for stringent quality control and site comparability analyses, and the option for mega-analyses across the entire dataset, whereas some other studies are limited to meta-analysis of results generated by each site separately.

A major strength of the GENUS sample collection is the existence of extensive data across patients, controls, and FHR individuals that enable analyses of genetic effects in multiple diagnostic groups. While informative genetic findings are emerging from large healthy cohorts, this is currently lacking in psychosis cohorts, and it remains unclear whether genetic factors influencing brain structure and function in healthy cohorts have the same effect in psychiatric patients. The GENUS Consortium analyses will initially focus on relating schizophrenia genetic risk variants identified by prior GWAS with the cognitive and brain structural phenotypes available in this sample collection. While the ENIGMA Consortium did not detect significant effects of schizophrenia genetic risk variants on subcortical volumes in mixed diagnosis and healthy individuals (Franke et al., 2016), a study of cortical thickness and surface area reported

that a substantial proportion (30-45%) of the heritability is explained by schizophrenia genetic risk variants (Lee et al., 2016). This suggests that some brain structural measures may be more genetically related to schizophrenia than others, or that genetic relationships differ in diseased and healthy brain. In addition, GWAS of cognitive performance and brain regional volumes have detected novel genetic associations (Adams et al., 2016; Davies et al., 2015; Hibar et al., 2015; Trampush et al., 2017) that could be further investigated in the GENUS sample collection.

Regarding genetic analyses, the GENUS sample collection is best suited for characterizing SNPs, polygenic factors, and pathways identified by GWAS (e.g., PGC GWAS mega-analyses)PGC Schizophrenia Working Group (2014) for effects on brain-based phenotypes, or replicating findings from other genetic studies of cognition or brain structure. Due to the small effect sizes of common genetic variants, our dataset is not well powered for GWAS discovery. SNP-based heritability approaches (e.g., GCTA) require approximately 4000 subjects for 80% power to estimate heritability as low as 20% (Visscher et al., 2014), a reasonable assumption for cognitive and brain volume traits (Franke et al., 2016; Trampush et al., 2017); therefore, some of our phenotypes (e.g. letter-number span tests, Table 3; WAIS Digit Symbol Coding, Table S3) are suitable for this approach. Rare variant association studies require enormous samples for adequate statistical power (Auer and Lettre, 2015; Zuk et al., 2014), therefore our dataset is not sufficient on its own for such analyses. The availability of multiple phenotypes enables a breadth of analyses, with the caveat that significance thresholds must be adjusted for multiple testing, although accounting for correlations between phenotypes or other data reduction methods could reduce the multiple testing burden, allowing for more lenient thresholds. The statistical power of our dataset could also be maximized by merging phenotypes into one phenotype, such as Spearman's 'g', in which data from many neuropsychological tests are used to derive a single measure of general cognitive ability (Spearman, 1904)."

There are considerable challenges to combining data acquired by many research groups. The heterogeneity in the data collected and the protocols used by each group requires careful harmonization of the data to maximize comparability between the samples and minimize confounds. Our harmonization approaches will be described in greater detail in subsequent data-based articles. Briefly, we are applying methods that use controls from each sample to standardize the data (i.e., generate Z scores), as has been reported for neuropsychological data (Toulopoulou et al., 2010) and structural MRI data (Segall et al., 2009; Wilke et al., 2014). Further, variability in multi-site imaging data due to different scanner models and field strengths, acquisition protocols, and image segmentation methods (Han et al., 2006) can be minimized by processing all scans using a consistent segmentation routine, which enables detection of subtle effects (Fennema-Notestine et al., 2007), including gray matter loss in schizophrenia datasets (Segall et al., 2009). Regarding clinical data, positive and negative symptom data can be converted between the PANSS and SANS/SAPS, the most common clinical scales in our dataset, using regression-based equations (van Erp et al., 2014). As for the limited medication dosage information of our dataset, this can be addressed partially by confirming findings from the full cohort in the subset with medication data to rule out medication confounds. We are harmonizing the genotype data from various SNP arrays by imputing genotypes based on a reference panel to generate a common set of SNPs across all samples, an accepted approach in the field (PGC Schizophrenia Working Group, 2014). Although heterogeneous data collected by multiple sites is not ideal, the large volume of available legacy data with deep phenotypic and genotype information warrants maximizing its use by generating one merged dataset that has far greater statistical power than the individual samples.

In summary, the GENUS Consortium sample collection is a valuable resource that builds upon previous efforts by individual research groups and complements other psychosis datasets. This high-powered sample collection integrates measures of brain structure, cognition, and genetics for studying the biological basis of psychosis through original analyses and

<span style="color:red">collaborative replication studies. There will be the opportunity for multiple publications from these data, including articles focusing on harmonization and genetic analyses of the cognitive data and imaging data, and publications that incorporate multi-modal data.</span> The rich phenotypic data are expected to provide new insights into neural functions that are disrupted in psychosis.

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**Table 1. Description of the GENUS Consortium Sample Collection.**

| Acronym | Sample | Site | GWAS Array | Neuropsychological data | | | | | T1-weighted structural MRI data | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Patients (N) | Controls (N) | FHR (N) | Male (%) | Eur (%) | Patients (N) | Controls (N) | FHR (N) | Male (%) | Eur (%) |
| CAMH | Centre for Addiction and Mental Health | Toronto, Canada | Illumina OmniExpress | 90 | 107 | 0 | 54.8 | 76.1 | 89 | 115 | 0 | 55.4 | 76.5 |
| CATIE | Clinical Antipsychotic Trials of Intervention Effectiveness | Multi-site, USA | Affymetrix 500K; Perlegen's custom 164K chip | 741 | 0 | 0 | 73.6 | 54.7 | --- | --- | --- | --- | --- |
| CIDAR/VA | Boston Center for Intervention Development and Applied Research / VA Healthcare System | Boston, USA | Illumina OmniExpress | 76 | 107 | 6 | 68.8 | 60.0 | 69 | 102 | 6 | 67.8 | 58.8 |
| COGS-UK | Cognition and Genetics in Schizophrenia & Bipolar Disorder | Cardiff, UK | Illumina Infinium OmniExpressExome-8 | 843 | 0 | 0 | 58.8 | 97.4 | --- | --- | --- | --- | --- |
| GAP | Genetics and Psychosis First – Episode Study | London, UK | Illumina HumanCore-24 Exome BeadChip | 164 | 160 | 0 | 59.6 | 46.8 | 132 | 94 | 0 | 56.2 | 35.0 |
| IMH-SIGNRP | Institute of Mental Health – Singapore Imaging Genetics and Neuropsychological Research in Psychosis | Singapore | Illumina Human OmniZhongHua-8; Illumina Human1M-Duo; Affymetrix 6.0 | 150 | 58 | 0 | 55.8 | 0 | 224 | 72 | 0 | 61.8 | 0 |
| IMH-STCRP | Institute of Mental Health – Singapore Translational and Clinical Research in Psychosis | Singapore | Illumina HumanOmniZhongHua-8 BeadChip | 420 | 1,012 | 0 | 52.9 | 0 | --- | --- | --- | --- | --- |
| KCL-MFS | King's College London – Maudsley Family Study | London, UK | Affymetrix 6.0 | 183 | 120 | 278 | 48.0 | 95.1 | --- | --- | --- | --- | --- |
| KCL-MTS | King's College London – Maudsley Twin Study | London, UK | Affymetrix 6.0 | 126 | 297 | 47 | 42.8 | 100 | 63 | 75 | 23 | 60.1 | 94.5 |
| L&R | Language and Risk in Schizophrenia | Boston, USA | Illumina Infinium PsychArray* | 0 | 31 | 44 | 34.7 | 74.7 | 0 | 33 | 51 | 33.3 | 77.4 |
| MCIC | Mind Clinical Imaging Consortium | Multi-site, USA | Illumina HumanOmni1-Quad BeadChip | 112 | 95 | 0 | 72.0 | 75.3 | 118 | 97 | 0 | 70.2 | 75.5 |
| MGH | Massachusetts General Hospital | Boston, USA | Illumina Infinium PsychArray* | 433 | 0 | 0 | 72.3 | 68.7 | 61 | 123 | 0 | 64.8 | 73.1 |
| NEFS | New England Family Study | Boston, USA | Illumina Infinium PsychArray* | 83 | 151 | 33 | 44.6 | 86.2 | 72 | 155 | 20 | 54.6 | 89.9 |
| PAGES | Phenomics and Genomics Sample | Munich, Germany | Illumina OmniExpress; Illumina HumanHap300 | 210 | 1,341 | 0 | 50.0 | 99.6 | --- | --- | --- | --- | --- |
| PHRS | Pittsburgh High Risk Study | Pittsburgh, USA | Illumina Infinium PsychArray* | 0 | 53 | 80 | 45.1 | 51.1 | 0 | 46 | 70 | 44.0 | 54.3 |
| TCD/NUIG | Trinity College Dublin / National University of Ireland, Galway | Multi-site, Ireland | Affymetrix 6.0; Illumina HumanCore Exome | 904 | 330 | 0 | 60.3 | 99.9 | 175 | 312 | 0 | 58.8 | 99.8 |
| UMCU-SZ1 | University Medical Center Utrecht – Schizophrenia Study 1 | Utrecht, Netherlands | Illumina HumanHap550; Illumina Infinium OmniExpressExome-8 | 197 | 143 | 0 | 68.3 | 98.6 | 159 | 157 | 0 | 69.3 | 99.1 |
| UMCU-SZ2 | University Medical Center Utrecht – Schizophrenia Study 2 | Utrecht, Netherlands | Illumina HumanHap550; Affymetrix 6.0; Illumina Infinium OmniExpressExome-8 | 233 | 144 | 235 | 58.8 | 97.5 | 184 | 131 | 212 | 59.0 | 93.6 |
| ZHH | Zucker Hillside Hospital | New York, USA | Illumina OmniExpress | 0 | 219 | 0 | 49.3 | 100 | --- | --- | --- | --- | --- |
| TOTAL | | | | 4,865 | 4,368 | 723 | 56.3 | 72.2 | 1,346 | 1,512 | 382 | 58.1 | 71.3 |

Data in this table are based on the total GENUS sample collection; data for the subset with genotype data are provided in Supplementary Table 1.
All samples with T1 MRI scans also have diffusion-weighted MRI scans except the PHRS, UMCU-SZ1, and UMCU-SZ2 samples.
Population ancestry determined from genetic data (where available) or self report.
Eur = European-derived ancestry; FHR = familial high-risk.
*Samples genotyped at the central GENUS site.

**Table 2. Clinical and demographic characteristics of the GENUS Consortium Sample Collection.**

| | Patients | | Controls | | Familial High Risk | | *Statistic* | *df* | *p* |
|---|---|---|---|---|---|---|---|---|---|
| | **N** | **Mean ± SD (Range)** | **N** | **Mean ± SD (Range)** | **N** | **Mean ± SD (Range)** | | | |
| **Age (years)** | 5,152 | 39.3±12.1 (13-82) | 4,832 | 39.2±15.7 (8-86) | 725 | 34.9±16.0 (10-85) | F = 31.3 | 2, 10706 | $<1\times10^{-10}$ |
| **Education Level (years)** | 4,646 | 12.3±2.6 (1-24) | 3,985 | 13.3±2.6 (4-26) | 721 | 13.1±3.2 (3-24) | F = 158.9 | 2, 9349 | $<1\times10^{-10}$ |
| **Premorbid IQ** | 3,130 | 97.0±15.5 (44-145) | 1,352 | 107.2±10.6 (62-145) | 83 | 105.1±16.0 (45-134) | F = 248.9 | 2, 4562 | $<1\times10^{-10}$ |
| **Current IQ** | 1,897 | 93.8±18.1 (47-155) | 2,779 | 113.4±14.9 (67-161) | 602 | 105.1±15.6 (58-152) | F = 823.4 | 2, 5275 | $<1\times10^{-10}$ |
| **Illness Duration (years)** | 4,057 | 14.5±11.4 (<1-58) | --- | --- | --- | --- | --- | --- | --- |
| **Age at Onset (years)** | 4,074 | 24.5±8.2 (3-66) | --- | --- | --- | --- | --- | --- | --- |
| **Global Assessment of Functioning** | 1,780 | 59.8±15.9 (11-100) | --- | --- | --- | --- | --- | --- | --- |
| **PANSS Positive symptoms** | 2,868 | 16.4±7.3 (7-47) | --- | --- | --- | --- | --- | --- | --- |
| **PANSS Negative Symptoms** | 2,865 | 16.7±7.1 (6-43) | --- | --- | --- | --- | --- | --- | --- |
| **PANSS General Symptoms** | 2,874 | 32.0±11.5 (0-78) | --- | --- | --- | --- | --- | --- | --- |
| **SAPS Positive Symptoms** | 1,983 | 8.1±13.0 (0-121) | --- | --- | --- | --- | --- | --- | --- |
| **SANS Negative Symptoms** | 2,202 | 13.9±17.7 (0-103) | --- | --- | --- | --- | --- | --- | --- |
| **Antipsychotic dose – current CPZEQ** | 3,130 | 389.9±410.7 (0-5,000) | --- | --- | --- | --- | --- | --- | --- |
| **Antipsychotic dose – lifetime average CPZEQ** | 1,404 | 338.0±365.9 (0-3,125) | --- | --- | --- | --- | --- | --- | --- |
| | **N** | **%** | **N** | **%** | **N** | **%** | | | |
| **Sex (male / female; % male)** | 3,384 / 1,770 | 65.6 | 2,394 / 2,438 | 49.5 | 317 / 408 | 43.7 | $\chi^2 = 319.1$ | 2 | $<1\times10^{-10}$ |
| **Antipsychotic medication exposure** | | | | | | | | | |
|     **Atypical** | 2,067 | 48.0 | --- | --- | --- | --- | --- | --- | --- |
|     **Typical** | 409 | 9.5 | --- | --- | --- | --- | --- | --- | --- |
|     **Both Typical and Atypical** | 545 | 12.7 | --- | --- | --- | --- | --- | --- | --- |
|     **Naïve / None** | 471 | 10.9 | --- | --- | --- | --- | --- | --- | --- |
|     **Unknown Class** | 422 | 9.0 | --- | --- | --- | --- | --- | --- | --- |
|     **No information** | 391 | 9.8 | --- | --- | --- | --- | --- | --- | --- |
| **Diagnosis** | | | | | | | | | |
|     **Schizophrenia** | 4,066 | 78.9 | --- | --- | --- | --- | --- | --- | --- |
|     **Schizoaffective Disorder** | 454 | 8.8 | --- | --- | --- | --- | --- | --- | --- |
|     **Schizophreniform Disorder** | 93 | 1.8 | --- | --- | --- | --- | --- | --- | --- |
|     **Bipolar Psychosis** | 338 | 6.6 | --- | --- | --- | --- | --- | --- | --- |
|     **Other Psychosis** | 204 | 4.0 | --- | --- | --- | --- | --- | --- | --- |
| **Ancestral Population** | | | | | | | $\chi^2 = 567.6$ | 12 | $<1\times10^{-10}$ |
|     **European** | 3,397 | 71.7 | 635 | 70.3 | 3,697 | 76.5 | --- | --- | --- |
|     **East Asian** | 1,109 | 13.5 | 3 | 23.0 | 697 | 12.3 | --- | --- | --- |
|     **African** | 152 | 9.8 | 54 | 3.2 | 507 | 6.8 | --- | --- | --- |
|     **American (Predominantly Latino)** | 30 | 2.7 | 3 | 0.6 | 140 | 1.3 | --- | --- | --- |
|     **South Asian** | 35 | 1.0 | 7 | 0.7 | 49 | 0.9 | --- | --- | --- |
|     **Mixed** | 8 | 0.4 | 0 | 0.2 | 18 | 0.2 | --- | --- | --- |
|     **No information** | 101 | 0.9 | 23 | 2.1 | 46 | 2.1 | | | |
| **Handedness (right / other; % right-handed)** | 2,254 / 272 | 89.2 | 2,313 / 271 | 89.5 | 609 / 68 | 89.9 | $\chi^2 = 0.32$ | 2 | 0.85 |

Data in this table are based on the total GENUS sample collection; data for the subset with genotype data are provided in Supplementary Table 2.

CPZEQ = chlorpromazine 100 mg equivalent; df = degrees of freedom; PANSS = Positive and Negative Syndrome Scale; SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms; SD = Standard Deviation

**Table 3. Core neuropsychological tests available for GENUS Consortium samples.**

| | Attention / Processing Speed | | | Attention / Vigilance | | Working Memory – verbal | | Working Memory – non-verbal | | Verbal Learning & Memory | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Sample* | *Digit Symbol Coding* | *TMT-A\** | *Verbal Fluency* | *CPT-IP\** | *Other* | *Letter-Number Span* | *Other* | *Spatial Span* | *Other* | *Word List Learning* | *Story Recall* | *Other* |
| **CAMH** | RBANS | x* | RBANS Semantic/ COWAT | | | UMD* | RBANS Digit Span | | | RBANS | RBANS | |
| **CATIE** | | | Category Instances/ COWAT | x* | | UMD* | | | SDRT | HVLT | | |
| **CIDAR-VA** | BACS* | x* | MCCB* | x* | ACPT | UMD* | | WMS-III* | | HVLT-R* | WMS-III or CMS | |
| **COGS-UK** | BACS* | x* | MCCB* | x* | | UMD* | | WMS-III* | | HVLT-R* | | |
| **GAP** | WAIS-III | x* | Semantic/ COWAT | | | | WAIS-III Digit Span | WMS-III* | CANTAB SWM | | WMS-III | |
| **IMH-SIGNRP** | BACS* | | BACS Category Instances / COWAT | | | | BACS Digit Sequencing | | | BACS | | |
| **IMH-STCRP** | BACS* | | BACS Category Instances | x* | | | BACS Digit Sequencing | | | BACS | | |
| **KCL-MFS** | WAIS-R | x* | | | CANTAB RVIP | | WAIS-R/ WMS-R Digit Span / Arithmetic | | CANTAB SWM | | WMS-R | WMS-R VerbPA |
| **KCL-MTS** | WAIS-III-UK | x* | Semantic/ COWAT | | CANTAB RVIP | WAIS-III-UK | WAIS-III-UK Digit Span / Arithmetic | WMS-R-UK VisMem Span | CANTAB SWM | | WMS-R-UK | WMS-R-UK VerbPA |
| **L&R** | BACS* | x* | MCCB* | x* | ACPT | UMD* | | WMS-III* | | HVLT-R* | WMS-III | |
| **MCIC** | | x* | D-KEFS Semantic/ Phonemic | | | WAIS-III | | | | HVLT-R* | WMS-III | |
| **MGH** | WAIS-III | | Semantic/ COWAT | x* | | WAIS-III | WAIS-III Digit Span / Arithmetic | | | CVLT | | |
| **NEFS** | WAIS-R | | COWAT | | ACPT | | WAIS-R Digit Span | | | CVLT or CVLT-II | WMS-R or WMS-III | |
| **PAGES** | WAIS-R-DE | x* | Semantic/ Phonemic | | 3-7 CPT | | WAIS-R-DE Digit Span / Arithmetic | | n-back | VLMT | WMS-R-DE | WMS-R-DE VerbPA |
| **PHRS** | | | MAE Semantic/ Phonemic | x* | A-X CPT | | | | Cogtest SWM | Cogtest | | |
| **TCD/NUIG** | | x* | COWAT | x* | 1-9 CPT | WMS-III | | | CANTAB SWM / n-back | CVLT-SF | WMS-III | |
| **UMCU-SZ1** | | | MAE Semantic/ Phonemic | | H-Q CPT | | | | | CVLT-I-NL | | |
| **UMCU-SZ2** | WAIS-III-NL | | | | H-Q CPT | | WAIS-III-NL Arithmetic | | | AVLT | | |
| **ZHH** | BACS* | x* | MCCB* / COWAT | x* | | UMD* | WAIS-R Digit Span | WMS-III* | n-back | HVLT-R* | | |
| **N patients** | 3,488 | 1,549 | 3,956 | 2,337 | 703 | 2,895 | 1,866 | 1,097 | 1,644 | 3,488 | 1,452 | 388 |
| **N controls** | 3,535 | 1,116 | 2,826 | 1,410 | 1,025 | 1,080 | 3,248 | 610 | 904 | 2,519 | 1,017 | 705 |
| **N FHR** | 396 | 196 | 280 | 119 | 381 | 79 | 347 | 76 | 89 | 384 | 82 | 177 |
| **N total** | 7,419 | 2,861 | 7,062 | 3,866 | 2,109 | 4,054 | 5,461 | 1,783 | 2,637 | 6,391 | 2,551 | 1,270 |

## Table 3. Core neuropsychological tests available for GENUS Consortium samples. --- Continued

| Sample | Visual Learning & Memory | | Reasoning / Problem Solving | | | Visuo-spatial Ability | | Verbal Ability | |
|---|---|---|---|---|---|---|---|---|---|
| | BVMT-R* | Other | TMT-B | WCST | Other | Block Design | Other | Vocabulary | Other |
| CAMH | | RBANS Figure Recall | x | | Stroop | | RBANS JOLO / Figure Copy | | |
| CATIE | | | | 64-C | WISC-III Mazes | | | | |
| CIDAR-VA | BVMT-R* | | | 64-C | NAB Mazes* | WASI | | WASI | D-KEFS Proverbs |
| COGS-UK | BVMT-R* | | | | NAB Mazes* | | | | |
| GAP | | WMS-III VisRep | x | | CANTAB SOC | WAIS-III | WAIS-III MR | | WAIS-III INF |
| IMH-SIGNRP | | | | | BACS TOL | | | | |
| IMH-STCRP | | | | 64-P | BACS TOL | | WASI MR / Benton JOLO | | |
| KCL-MFS | | WMS-R VisRep | x | | CANTAB IDED | WAIS-R | WAIS-R OA / PA / PC | WAIS-R | WAIS-R COM / INF / SIM |
| KCL-MTS | | WMS-R-UK VisRep / VisPA | x | | CANTAB IDED | WAIS-III-UK | WAIS-III-UK OA / PA / PC | WAIS-III-UK | WAIS-III-UK COM / INF / SIM |
| L&R | BVMT-R* | | | 64-C | NAB Mazes* | WASI | | WASI | D-KEFS Proverbs |
| MCIC | | BVRT / WMS-III Faces | x | | TOL | WAIS-III | | WAIS-III | WAIS-III SIM |
| MGH | | | | 128-C / 64-C | | WAIS-III | WAIS-III MR / OA / PA / PC | WAIS-III | WAIS-III COM / INF / SIM |
| NEFS | | WMS-III Faces / Rey CFT Recall | | 128-P | Stroop | WAIS-R | WAIS-R PA / Rey CFT Copy | WAIS-R | WAIS-R COM / INF; RAN |
| PAGES | | WMS-R-DE FigMem / VisRep / VisPA | x | 128-C | TOL-DE | WAIS-R-DE | WAIS-R-DE OA / PA / PC | WAIS-R-DE | WAIS-R-DE COM / INF / SIM |
| PHRS | | CNB VOLT | | 128-P | Cogtest Go-No-Go | | | | |
| TCD/NUIG | | WMS-III Faces / CANTAB PAL | x | | CANTAB IDED / SART | WAIS-III-R-UK | WAIS-III-R-UK MR | WAIS-III-R-UK | WAIS-III-R-UK SIM |
| UMCU-SZ1 | | | | | Stroop | WAIS-III-R-NL | WAIS-III-R-NL PA | WAIS-III-R-NL | WAIS-III-R-NL COM |
| UMCU-SZ2 | | | | | NAB Mazes* / RST | WAIS-III-NL | | | WAIS-III-NL INF |
| ZHH | BVMT-R* | | x | 128-P | NAB Mazes* / Stroop | | | | |
| N patients | 897 | 1,604 | 836 | 1,376 | 3,555 | 2,260 | 1,615 | 1,754 | 2,048 |
| N controls | 328 | 1,628 | 1,408 | 835 | 2,781 | 2,744 | 3,131 | 2,425 | 2,617 |
| N FHR | 48 | 317 | 145 | 134 | 350 | 522 | 33 | 285 | 567 |
| N total | 1,273 | 3,549 | 2,389 | 2,345 | 6,686 | 5,526 | 4,779 | 4,464 | 5,232 |

*MATRICS test.

References for all neuropsychological tests are provided in the Supplemental Materials.

Data in this table are based on the total GENUS sample collection (genotyped plus ungenotyped).

Abbreviations: 128-P, 128-C = 128-card paper, computerized version; 64-P, 64-C = 64-card paper, computerized version; ACPT = Auditory CPT; AVLT = Auditory Verbal Learning Test; BACS = Brief Assessment of Cognition in Schizophrenia; BVMT-R= Brief Visuospatial Memory Test-Revised; BVRT = Benton Visual Retention Test; CANTAB = Cambridge Neuropsychological Test Automated Battery; CFT = Complex Figure Test; CMS = Children's Memory Scale; CNB = Computerized Neurocognitive Battery; COWAT = Controlled Oral Word Association Test; CPT(-IP) = Continuous Performance Test (Identical Pairs); CVLT(-SF) = California Verbal Learning Test (Short Form); DE = German version; D-KEFS = Delis–Kaplan Executive Function System; FigMem = Figural Memory; HVLT = Hopkins Verbal Learning Test; IDED = Intra-Extra Dimensional Set Shifting; JOLO = Judgment of Line Orientation; MAE = Multilingual Aphasia Examination; MCCB = MATRICS Consensus Cognitive Battery; NAB = Neuropsychological Assessment Battery; NL = Dutch version; PAL = Paired Associates Learning; RAN = Rapid Automatized Naming; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; RST = Response Shifting Task; RVIP = Rapid Visual Information Processing; SART = Sustained Attention to Response Task; SDRT = Spatial Delayed Response Task; SOC = Stockings of Cambridge; SWM = Spatial Working Memory; TOL = Tower of London; TMT-A, B = Trail Making Test Part A, B; UK = British version; UMD = University of Maryland; VerbPA = Verbal Paired Associates; VisMemSpan = Visual Memory Span; VisPA = Visual Paired Associates; VisRep = Visual Reproduction; VLMT = Verbal Learning and Memory Test; VLT = Verbaler Lern Test; VOLT = Visual Object Learning Test; WAIS = Wechsler Adult Intelligence Scale (Subtests: COM = Comprehension; INF = Information; MR = Matrix Reasoning; OA = Object Assembly; PA = Picture Arrangement; PC = Picture Completion; SIM = Similarities); WASI = Wechsler Abbreviated Scale of Intelligence; WCST = Wisconsin Card Sorting Test; WISC = Wechsler Intelligence Scale for Children; WMS = Wechsler Memory Scale

**Table 4. MRI scan parameters for GENUS Consortium samples.**

| Sample | Magnetic Field Strength | Vendor | Model | T1-weighted sequence | T1 Voxel dimensions (mm) | DW-MRI # diffusion-encoding directions | DW-MRI b-value (s/mm²) | DW-MRI Voxel dimensions (mm) |
|---|---|---|---|---|---|---|---|---|
| **CAMH** | 1.5T | GE | Echospeed | IR-SPGR | 0.78 x 0.78 x 1.5 | 23 | 1000 | 2.6 x 2.6 x 2.6 |
| **CIDAR-VA** | 3T | GE | Signa HDxt Echospeed | IR-SPGR | 1.0 x 1.0 x 1.0 | 51 | 900 | 1.67 x 1.67 x 1.7 |
| | 3T | Siemens | Trio Tim | MP-RAGE | 1.0 x 1.0 x 1.33 | 60 | 700 | 2.0 x 2.0 x 2.0 |
| **GAP** | 3T | GE | Signa HDx | MP-RAGE | 1.01 x 1.01 x 1.2 | 32 | 1300 | 2.4 x 2.4 x 2.4 |
| **IMH-SIGNRP** | 3T | Philips | Intera Achieva | TFE | 0.9 x 0.9 x 0.9 | 15 | 800 | 0.9 x 0.9 x 3.0 |
| **KCL-MTS** | 1.5T | GE | Signa Advantage | SPGR | 0.78 x 0.78 x 1.5 | 64 | 1300 | 2.5 x 2.5 x 2.5 |
| | 1.5T | GE | Signa Advantage | SPGR | 0.78 x 0.78 x 1.5 | 64 | 1300 | 2.5 x 2.5 x 2.5 |
| **L&R** | 3T | Siemens | Trio Tim | MP-RAGE | 1.0 x 1.0 x 1.0 | 60 | 700 | 2.0 x 2.0 x 2.0 |
| **MCIC** | 1.5T | Siemens | Sonata | GRE | 0.7 x 0.7 x 1.5 | 60 | 700 | 2.0 x 2.0 x 2.0 |
| | 3T | Siemens | Trio Tim | MP-RAGE | 0.625 x 0.625 x 1.5 | 12 | 1000 | 2.0 x 2.0 x 2.0 |
| | 1.5T | Siemens | Sonata | GRE | 0.625 x 0.625 x 1.5 | 12 | 1000 | 2.0 x 2.0 x 2.0 |
| **MGH** | 3T | Siemens | Trio Tim | ME-MP-RAGE | 1.2 x 1.2 x 1.2 | 6 | 1000 | 1.375 x 1.375 x 3.0 |
| | 3T | Siemens | Trio Tim | MP-RAGE | 1 x 1 x 1.3 | --- | --- | --- |
| **NEFS** | 1.5T | Siemens | Avanto | MP-RAGE | 1.0 x 1.0 x 1.33 | 60 | 700 | 2.0 x 2.0 x 2.0 |
| | 1.5T | Siemens | Sonata | MP-RAGE | 1.0 x 1.0 x 1.33 | 6 | 600 | 2.0 x 2.0 x 2.0 |
| | 1.5T | Siemens | Sonata | MP-RAGE | 1.0 x 1.0 x 1.5 | --- | --- | --- |
| | 3T | Siemens | Trio Tim | MP-RAGE | 1.0 x 1.0 x 1.33 | 60 | 700 | 2.0 x 2.0 x 2.0 |
| | 1.5T | GE | Genesis Signa | EFGRE | 0.94 x 0.94 x 1.5 | --- | --- | --- |
| **PHRS** | 1.5T | GE | Genesis Signa | SPGR | 1.25 x 1.25 x 1.5 | --- | --- | --- |
| **TCD/NUIG** | 3T | Philips | Intera Achieva | TFE | 0.9 x 0.9 x 0.9 | 15 | 800 | 1.75 x 1.75 x 2.2 |
| | 1.5T | Siemens | Magnetom Symphony | MP-RAGE | 0.45 x 0.45 x 0.9 | --- | --- | --- |
| **UMCU-SZ1** | 1.5T | Philips | NT Intera | FFE | 1.0 x 1.0 x 1.2 | --- | --- | --- |
| **UMCU-SZ2** | 1.5T | Philips | Achieva | FFE | 1.0 x 1.0 x 1.2 | --- | --- | --- |

DW-MRI = Diffusion-Weighted MRI; EFGRE = Enhanced Fast Gradient Echo; FFE = Fast Field Echo; GE = General Electric; GRE = Gradient Recalled Echo; (IR-)SPGR = (Inversion Recovery) Spoiled Gradient Recalled; (ME-)MP-RAGE = (Multi-Echo) Magnetization Prepared Rapid Acquisition Gradient Echo; TFE = Turbo Field Echo