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The Genetics of Endophenotypes of Neurofunction to Understand Schizophrenia (GENUS) consortium: A collaborative cognitive and neuroimaging genetics project

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

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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 individuals at familial high-risk (FHR) for 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 5,199 psychosis patients, 4,877 controls, and 725 FHR individuals. All participants have relevant demographic data and all patients have relevant clinical data. The sex ratio is 56.5% male and 43.5% female. Significant differences exist between diagnostic groups for premorbid and current IQ (both $p < 1 \times 10^{-10}$). Data from a diversity of neuropsychological tests are available for 92% of participants, and 30% have structural MRI scans (half also have diffusion-weighted MRI scans). SNP data are available for 76% of participants. The ancestry composition is 70% European, 20% East Asian, 7% African, and 3% other.

Conclusions—The Consortium is investigating the genetic contribution to brain phenotypes in a schizophrenia sample collection of >10,000 participants. The breadth of data across clinical,

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Contributors

Dr. Blokland, Dr. del Re, and Dr. Petryshen drafted the manuscript. Dr. Blokland performed the statistical analyses. Dr. Petryshen designed the collaborative project. All other authors participated in aspects of the study design (both within and across sites), including subject recruitment and data collection. All authors were responsible for reviewing, editing, and approving the final version of the manuscript.

Conflict of Interest

All authors declare that they have no conflicts of interest with respect to this study.

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genetic, neuropsychological, and MRI modalities provides an important opportunity for elucidating the genetic basis of neural processes underlying schizophrenia.

Keywords

schizophrenia; neuropsychology; cognition; neuroimaging; MRI; genetics

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). 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/ μ L) 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 5,199 patients, 4,877 controls, and 725 FHR participants (unaffected relatives of psychosis patients), totaling 10,801 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 76.4% schizophrenia, 8.9% schizoaffective disorder (SAD), 1.8% schizophreniform disorder (SPD), 6.5% bipolar disorder with psychosis (BD), and 6.3% 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 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 (<1–58 years) and the inclusion of FHR participants, the sample collection has a wide age range (8–86 years). The sex composition is 56.5% male and 43.5% 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 $p < 1 \times 10^{-10}$; 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; 54.7% 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) (29.5% 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 63.8% or 27.6% of patients, respectively, and 21.2% 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 4,892 patients (75.6% schizophrenia, 9.4% SAD, 1.7% SPD, 6.8% BD, 6.5% other psychosis), 4,370 controls, and 720 FHR individuals (9,982 participants or 92.4% 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. Supplementary Table 3 provides detailed information on the specific tests and number of participants. There are substantial differences in the mean premorbid IQ and mean current IQ between diagnostic groups (both $p < 1 \times 10^{-10}$; 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 1,364 patients (74.4% schizophrenia, 7.9% SAD, 3.8% SPD, 5.3% BD, 8.6% other psychosis), 1,520 controls, 379 FHR individuals (3,263 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 1,931 participants, and 9 samples have T2-weighted structural scans from 1,821 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 (69.2%). For 10 samples, only a proportion of participants had been genotyped. Four of the 19 samples had genomic DNA from 978 participants (9.1%), of which 947 (8.8%) 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 (4,099 patients, 3,851 controls, 306 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 $\alpha = 5 \times 10^{-8}$.

The ancestry breakdown based on genotype data is 70.2% European (2,835 patients, 2,703 controls, 264 FHR), 19.5% East Asian (624 patients, 982 controls, 1 FHR), 7.3% African (454 patients, 111 controls, 35 FHR), 2.0% American (predominantly Latino; 138 patients, 28 controls, 3 FHR), and 1.0% other ancestry (53 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, such as the 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, WAIS Digit Symbol Coding) 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 allow 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 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. The rich phenotypic data are expected to provide new insights into neural functions that are disrupted in psychosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

- Adams HH, Hibar DP, Chouraki V, Stein JL, Nyquist PA, Renteria ME, Trompet S, Arias-Vasquez A, Seshadri S, Desrivieres S, Beecham AH, Jahanshad N, Wittfeld K, Van der Lee SJ, Abramovic L, Alhusaini S, Amin N, Andersson M, Arfanakis K, Aribisala BS, Armstrong NJ, Athanasiu L, Axelsson T, Beiser A, Bernard M, Bis JC, Blanken LM, Blanton SH, Bohlken MM, Boks MP, Bralten J, Brickman AM, Carmichael O, Chakravarty MM, Chauhan G, Chen Q, Ching CR, Cuellar-Partida G, Braber AD, Doan NT, Ehrlich S, Filippi I, Ge T, Giddaluru S, Goldman AL, Gottesman RF, Greven CU, Grimm O, Griswold ME, Guadalupe T, Hass J, Haukvik UK, Hilal S, Hofer E, Hoehn D, Holmes AJ, Hoogman M, Janowitz D, Jia T, Kasperaviciute D, Kim S, Klein M, Kraemer B, Lee PH, Liao J, Liewald DC, Lopez LM, Luciano M, Macare C, Marquand A, Matarin M, Mather KA, Mattheisen M, Mazoyer B, McKay DR, McWhirter R, Milaneschi Y, Mirza-Schreiber N, Muetzel RL, Maniega SM, Nho K, Nugent AC, Loohuis LM, Oosterlaan J, Pappmeyer M, Pappa I, Pirpamer L, Pudas S, Putz B, Rajan KB, Ramasamy A, Richards JS, Risacher SL, Roiz-Santianez R, Rommelse N, Rose EJ, Royle NA, Rundek T, Samann PG, Satizabal CL, Schmaal L, Schork AJ, Shen L, Shin J, Shumskaya E, Smith AV, Sprooten E, Strike LT, Teumer A, Thomson R, Tordesillas-Gutierrez D, Toro R, Trabzuni D, Vaidya D, Van der Grond J, Van der Meer D, Van Donkelaar MM, Van Eijk KR, Van Erp TG, Van Rooij D, Walton E, Westlye LT, Whelan CD, Windham BG, Winkler AM, Woldehawariat G, Wolf C, Wolfers T, Xu B, Yanek LR, Yang J, Zijdenbos A, Zwiens MP, Agartz I, Aggarwal NT, Almasy L, Ames D, Amouyel P, Andreassen OA, Arepalli S, Assareh AA, Barral S, Bastin ME, Becker DM, Becker JT, Bennett DA, Blangero J, van Bokhoven H, Boomsma DI, Brodaty H, Brouwer RM, Brunner HG, Buckner RL, Buitelaar JK, Bulayeva KB, Cahn W, Calhoun VD, Cannon DM, Cavalleri GL, Chen C, Cheng CY, Cichon S, Cookson MR, Corvin A, Crespo-Facorro B, Curran JE, Czisch M, Dale AM, Davies GE, De Geus EJ, De Jager PL, de Zubicaray GI, Delanty N, Depondt C, DeStefano AL, Dillman A, Djurovic S, Donohoe G, Drevets WC, Duggirala R, Dyer TD, Erk S, Espeseth T, Evans DA, Fedko IO, Fernandez G, Ferrucci L, Fisher SE, Fleischman DA, Ford I, Foroud TM, Fox PT, Francks C, Fukunaga M, Gibbs JR, Glahn DC, Gollub RL, Goring HH, Grabe HJ, Green RC, Gruber O, Gudnason V, Guelfi S, Hansell NK, Hardy J, Hartman CA, Hashimoto R, Hegenscheid K, Heinz A, Le Hellard S, Hernandez DG, Heslenfeld DJ, Ho BC, Hoekstra PJ, Hoffmann W, Hofman A, Holsboer F, Homuth G, Hosten N, Hottenga JJ, Pol HE, Ikeda M, Ikram MK, Jack CR Jr, Jenkinson M, Johnson R, Jonsson EG, Jukema JW, Kahn RS, Kanai R, Kloszewska I, Knopman DS, Kochunov P, Kwok JB, Lawrie SM, Lemaitre H, Liu X, Longo DL, Longstreth WT Jr, Lopez OL, Lovestone S, Martinez O, Martinot JL, Mattay VS, McDonald C, McIntosh AM, McMahon KL, McMahon FJ, Mecocci P, Melle I, Meyer-Lindenberg A, Mohnke S, Montgomery GW, Morris DW, Mosley TH, Muhleisen TW, Muller-Myhsok B, Nalls MA, Nauck M, Nichols TE, Niessen WJ, Nothen MM, Nyberg L, Ohi K, Olvera RL, Ophoff RA, Pandolfo M, Paus T, Pausova Z, Penninx BW, Pike GB, Potkin SG, Psaty BM, Reppermund S, Rietschel M, Roffman JL, Romanczuk-Seiferth N, Rotter JI, Ryten M, Sacco RL, Sachdev PS, Saykin AJ, Schmidt R, Schofield PR, Sigurdsson S, Simmons A, Singleton A, Sisodiya SM, Smith C, Smoller JW, Soininen H, Srikanth V, Steen VM, Stott DJ, Sussmann JE, Thalamuthu A, Tiemeier H, Toga AW, Traynor BJ, Troncoso J, Turner JA, Tzourio C, Uitterlinden AG, Hernandez MC, Van der Brug M, Van der Lugt A, Van der Wee NJ, Van Duijn CM, Van Haren NE, Van TED, Van Tol MJ, Vardarajan BN, Veltman DJ, Vernooij MW, Volzke H, Walter H, Wardlaw JM, Wassink TH, Weale ME, Weinberger DR, Weiner MW, Wen W, Westman E, White T, Wong TY, Wright CB, Zielke HR, Zonderman AB, Deary IJ, DeCarli C, Schmidt H, Martin NG, De Craen AJ, Wright MJ, Launer LJ, Schumann G, Fornage M, Franke B, Debette S, Medland SE, Ikram MA, Thompson PM. Novel genetic loci underlying human intracranial volume identified through genome-wide association. *Nat Neurosci.* 2016; 19(12):1569–1582. [PubMed: 27694991]
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR). American Psychiatric Press Inc; Washington, DC: 2000.
- Andreasen, NC. Scale for the Assessment of Negative Symptoms (SANS). University of Iowa; Iowa City: 1983.
- Andreasen, NC. Scale for the Assessment of Positive Symptoms (SAPS). University of Iowa; Iowa City: 1984.

- Auer PL, Lettre G. Rare variant association studies: considerations, challenges and opportunities. *Genome medicine*. 2015; 7(1):16. [PubMed: 25709717]
- Axelrod BN. Validity of the Wechsler Abbreviated Scale of Intelligence and other very short forms of estimating intellectual functioning. *Assessment*. 2002; 9(1):17–23. [PubMed: 11911230]
- Blokland GAM, de Zubicaray GI, McMahon KL, Wright MJ. Genetic and environmental influences on neuroimaging phenotypes: A meta-analytical perspective on twin imaging studies. *Twin research and human genetics: the official journal of the International Society for Twin Studies*. 2012; 15(3): 351–371. [PubMed: 22856370]
- Blokland GAM, Mesholam-Gately RI, Touloupoulou T, del Re EC, Lam M, DeLisi LE, Donohoe G, Walters JTR, Seidman LJ, Petryshen TP. GENUS Consortium. Heritability of neuropsychological measures in schizophrenia and non-psychiatric populations: A systematic review and meta-analysis. *Schizophrenia bulletin*. 2016
- Bohlken MM, Brouwer RM, Mandl RC, Kahn RS, Hulshoff Pol HE. Genetic variation in schizophrenia liability is shared with intellectual ability and brain structure. *Schizophrenia bulletin*. 2016; 42(5):1167–1175. [PubMed: 27056715]
- Boos HB, Aleman A, Cahn W, Hulshoff Pol HE, Kahn RS. Brain volumes in relatives of patients with schizophrenia: a meta-analysis. *Arch Gen Psychiatry*. 2007; 64(3):297–304. [PubMed: 17339518]
- Bora E, Fornito A, Radua J, Walterfang M, Seal M, Wood SJ, Yucel M, Velakoulis D, Pantelis C. Neuroanatomical abnormalities in schizophrenia: a multimodal voxelwise meta-analysis and meta-regression analysis. *Schizophrenia research*. 2011; 127(1–3):46–57. [PubMed: 21300524]
- CNV and Schizophrenia Working Groups of the Psychiatric Genomics Consortium; Psychosis Endophenotypes International Consortium. Contribution of copy number variants to schizophrenia from a genome-wide study of 41,321 subjects. *Nature genetics*. 2017; 49(1):27–35. [PubMed: 27869829]
- Davies G, Armstrong N, Bis JC, Bressler J, Chouraki V, Giddaluru S, Hofer E, Ibrahim-Verbaas CA, Kirin M, Lahti J, van der Lee SJ, Le Hellard S, Liu T, Marioni RE, Oldmeadow C, Postmus I, Smith AV, Smith JA, Thalamuthu A, Thomson R, Vitart V, Wang J, Yu L, Zgaga L, Zhao W, Boxall R, Harris SE, Hill WD, Liewald DC, Luciano M, Adams H, Ames D, Amin N, Amouyel P, Assareh AA, Au R, Becker JT, Beiser A, Berr C, Bertram L, Boerwinkle E, Buckley BM, Campbell H, Corley J, De Jager PL, Dufouil C, Eriksson JG, Espeseth T, Faul JD, Ford I, Generation S, Gottesman RF, Griswold ME, Gudnason V, Harris TB, Heiss G, Hofman A, Holliday EG, Huffman J, Kardina SL, Kochan N, Knopman DS, Kwok JB, Lambert JC, Lee T, Li G, Li SC, Loitfelder M, Lopez OL, Lundervold AJ, Lundqvist A, Mather KA, Mirza SS, Nyberg L, Oostra BA, Palotie A, Papenberg G, Pattie A, Petrovic K, Polasek O, Psaty BM, Redmond P, Reppermund S, Rotter JI, Schmidt H, Schuur M, Schofield PW, Scott RJ, Steen VM, Stott DJ, van Swieten JC, Taylor KD, Trollor J, Trompet S, Uitterlinden AG, Weinstein G, Widen E, Windham BG, Jukema JW, Wright AF, Wright MJ, Yang Q, Amieva H, Attia JR, Bennett DA, Brodaty H, de Craen AJ, Hayward C, Ikram MA, Lindenberg U, Nilsson LG, Porteous DJ, Raikonen K, Reinvang I, Rudan I, Sachdev PS, Schmidt R, Schofield PR, Srikanth V, Starr JM, Turner ST, Weir DR, Wilson JF, van Duijn C, Launer L, Fitzpatrick AL, Seshadri S, Mosley TH Jr, Deary IJ. Genetic contributions to variation in general cognitive function: A meta-analysis of genome-wide association studies in the CHARGE consortium (N=53949). *Molecular psychiatry*. 2015; 20(2): 183–192. [PubMed: 25644384]
- Donohoe G, Morris DW, Corvin A. The psychosis susceptibility gene ZNF804A: associations, functions, and phenotypes. *Schizophrenia bulletin*. 2010; 36(5):904–909. [PubMed: 20688871]
- Donohoe G, Walters J, Hargreaves A, Rose EJ, Morris DW, Fahey C, Bellini S, Cummins E, Giegling I, Hartmann AM, Moller HJ, Muglia P, Owen MJ, Gill M, O'Donovan MC, Tropea D, Rujescu D, Corvin A. Neuropsychological effects of the CSMD1 genome-wide associated schizophrenia risk variant rs10503253. *Genes, brain, and behavior*. 2013; 12(2):203–209.
- Eum S, Hill SK, Rubin LH, Carnahan RM, Reilly JL, Ivleva EI, Keedy SK, Tamminga CA, Pearson GD, Clementz BA, Gershon ES, Keshavan MS, Keefe RS, Sweeney JA, Bishop JR. Cognitive burden of anticholinergic medications in psychotic disorders. *Schizophrenia research*. 2017
- Fedorov A, Beichel R, Kalpathy-Cramer J, Finet J, Fillion-Robin JC, Pujol S, Bauer C, Jennings D, Fennessy F, Sonka M, Buatti J, Aylward S, Miller JV, Pieper S, Kikinis R. 3D Slicer as an image

computing platform for the Quantitative Imaging Network. *Magnetic resonance imaging*. 2012; 30(9):1323–1341. [PubMed: 22770690]

Fennema-Notestine C, Gamst AC, Quinn BT, Pacheco J, Jernigan TL, Thal L, Buckner R, Killiany R, Blacker D, Dale AM, Fischl B, Dickerson B, Gollub RL. Feasibility of multi-site clinical structural neuroimaging studies of aging using legacy data. *Neuroinformatics*. 2007; 5(4):235–245. [PubMed: 17999200]

Franke B, Stein JL, Ripke S, Anttila V, Hibar DP, van Hulzen KJ, Arias-Vasquez A, Smoller JW, Nichols TE, Neale MC, McIntosh AM, Lee P, McMahon FJ, Meyer-Lindenberg A, Mattheisen M, Andreassen OA, Gruber O, Sachdev PS, Roiz-Santanez R, Saykin AJ, Ehrlich S, Mather KA, Turner JA, Schwarz E, Thalamuthu A, Yao Y, Ho YY, Martin NG, Wright MJ, O'Donovan MC, Thompson PM, Neale BM, Medland SE, Sullivan PF. Schizophrenia Working Group of the Psychiatric Genomics C, Psychosis Endophenotypes International C, Wellcome Trust Case Control C, Enigma C. Genetic influences on schizophrenia and subcortical brain volumes: large-scale proof of concept. *Nat Neurosci*. 2016; 19(3):420–431. [PubMed: 26854805]

Gardner DM, Murphy AL, O'Donnell H, Centorrino F, Baldessarini RJ. International consensus study of antipsychotic dosing. *The American journal of psychiatry*. 2010; 167(6):686–693. [PubMed: 20360319]

Ge T, Nichols TE, Lee PH, Holmes AJ, Roffman JL, Buckner RL, Sabuncu MR, Smoller JW. Massively expedited genome-wide heritability analysis (MEGHA). *Proc Natl Acad Sci U S A*. 2015; 112(8):2479–2484. [PubMed: 25675487]

Germine L, Robinson EB, Smoller JW, Calkins ME, Moore TM, Hakonarson H, Daly MJ, Lee PH, Holmes AJ, Buckner RL, Gur RC, Gur RE. Association between polygenic risk for schizophrenia, neurocognition and social cognition across development. *Translational psychiatry*. 2016; 6(10):e924. [PubMed: 27754483]

Goldstein JM, Cherkerzian S, Tsuang MT, Petryshen TL. Sex differences in the genetic risk for schizophrenia: history of the evidence for sex-specific and sex-dependent effects. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*. 2013; 162B(7):698–710.

Gottesman II, Gould TD. The endophenotype concept in psychiatry: Etymology and strategic intentions. *The American journal of psychiatry*. 2003; 160(4):636–645. [PubMed: 12668349]

Hajima SV, Van Haren N, Cahn W, Koolschijn PC, Hulshoff Pol HE, Kahn RS. Brain volumes in schizophrenia: a meta-analysis in over 18 000 subjects. *Schizophrenia bulletin*. 2013; 39(5):1129–1138. [PubMed: 23042112]

Han X, Jovicich J, Salat D, van der Kouwe A, Quinn B, Czanner S, Busa E, Pacheco J, Albert M, Killiany R, Maguire P, Rosas D, Makris N, Dale A, Dickerson B, Fischl B. Reliability of MRI-derived measurements of human cerebral cortical thickness: the effects of field strength, scanner upgrade and manufacturer. *NeuroImage*. 2006; 32(1):180–194. [PubMed: 16651008]

Hatzimanolis A, Bhatnagar P, Moes A, Wang R, Roussos P, Bitsios P, Stefanis CN, Pulver AE, Arking DE, Smyrnis N, Stefanis NC, Avramopoulos D. Common genetic variation and schizophrenia polygenic risk influence neurocognitive performance in young adulthood. *Am J Med Genet B Neuropsychiatr Genet*. 2015; 168B(5):392–401. [PubMed: 25963331]

Hibar DP, Stein JL, Renteria ME, Arias-Vasquez A, Desrivieres S, Jahanshad N, Toro R, Wittfeld K, Abramovic L, Andersson M, Aribisala BS, Armstrong NJ, Bernard M, Bohlken MM, Boks MP, Bralten J, Brown AA, Chakravarty MM, Chen Q, Ching CR, Cuellar-Partida G, den Braber A, Giddaluru S, Goldman AL, Grimm O, Guadalupe T, Hass J, Woldehawariat G, Holmes AJ, Hoogman M, Janowitz D, Jia T, Kim S, Klein M, Kraemer B, Lee PH, Olde Loohuis LM, Luciano M, Macare C, Mather KA, Mattheisen M, Milanesechi Y, Nho K, Papmeyer M, Ramasamy A, Risacher SL, Roiz-Santanez R, Rose EJ, Salami A, Samann PG, Schmaal L, Schork AJ, Shin J, Strike LT, Teumer A, van Donkelaar MM, van Eijk KR, Walters RK, Westlye LT, Whelan CD, Winkler AM, Zwiers MP, Alhusaini S, Athanasiu L, Ehrlich S, Hakobjan MM, Hartberg CB, Haukvik UK, Heister AJ, Hoehn D, Kasperaviciute D, Liewald DC, Lopez LM, Makkinje RR, Matarin M, Naber MA, McKay DR, Needham M, Nugent AC, Putz B, Royle NA, Shen L, Sprooten E, Trabzuni D, van der Marel SS, van Hulzen KJ, Walton E, Wolf C, Almasy L, Ames D, Arepalli S, Assareh AA, Bastin ME, Brodaty H, Bulayeva KB, Carless MA, Cichon S, Corvin A, Curran JE, Czisch M, de Zubicaray GI, Dillman A, Duggirala R, Dyer TD, Erk S, Fedko IO, Ferrucci L, Foroud TM, Fox PT, Fukunaga M, Gibbs JR, Goring HH, Green RC, Guelfi S, Hansell

NK, Hartman CA, Hegenscheid K, Heinz A, Hernandez DG, Heslenfeld DJ, Hoekstra PJ, Holsboer F, Homuth G, Hottenga JJ, Ikeda M, Jack CR Jr, Jenkinson M, Johnson R, Kanai R, Keil M, Kent JW Jr, Kochunov P, Kwok JB, Lawrie SM, Liu X, Longo DL, McMahon KL, Meisenzahl E, Melle I, Mohnke S, Montgomery GW, Mostert JC, Muhleisen TW, Nalls MA, Nichols TE, Nilsson LG, Nothen MM, Ohi K, Olvera RL, Perez-Iglesias R, Pike GB, Potkin SG, Reinvang I, Reppermund S, Rietschel M, Romanczuk-Seiferth N, Rosen GD, Rujescu D, Schnell K, Schofield PR, Smith C, Steen VM, Sussmann JE, Thalamuthu A, Toga AW, Traynor BJ, Troncoso J, Turner JA, Valdes Hernandez MC, van 't Ent D, van der Brug M, van der Wee NJ, van Tol MJ, Veltman DJ, Wassink TH, Westman E, Zielke RH, Zonderman AB, Ashbrook DG, Hager R, Lu L, McMahon FJ, Morris DW, Williams RW, Brunner HG, Buckner RL, Buitelaar JK, Cahn W, Calhoun VD, Cavalleri GL, Crespo-Facorro B, Dale AM, Davies GE, Delanty N, Depondt C, Djurovic S, Drevets WC, Espeseth T, Gollub RL, Ho BC, Hoffmann W, Hosten N, Kahn RS, Le Hellard S, Meyer-Lindenberg A, Muller-Myhsok B, Nauck M, Nyberg L, Pandolfo M, Penninx BW, Roffman JL, Sisodiya SM, Smoller JW, van Bokhoven H, van Haren NE, Volzke H, Walter H, Weiner MW, Wen W, White T, Agartz I, Andreassen OA, Blangero J, Boomsma DI, Brouwer RM, Cannon DM, Cookson MR, de Geus EJ, Deary IJ, Donohoe G, Fernandez G, Fisher SE, Francks C, Glahn DC, Grabe HJ, Gruber O, Hardy J, Hashimoto R, Hulshoff Pol HE, Jonsson EG, Kloszewska I, Lovestone S, Mattay VS, Mecocci P, McDonald C, McIntosh AM, Ophoff RA, Paus T, Pausova Z, Ryten M, Sachdev PS, Saykin AJ, Simmons A, Singleton A, Soininen H, Wardlaw JM, Weale ME, Weinberger DR, Adams HH, Launer LJ, Seiler S, Schmidt R, Chauhan G, Satizabal CL, Becker JT, Yanek L, van der Lee SJ, Ebling M, Fischl B, Longstreth WT Jr, Greve D, Schmidt H, Nyquist P, Vinke LN, van Duijn CM, Xue L, Mazoyer B, Bis JC, Gudnason V, Seshadri S, Ikram MA, Wright MJ, Schumann G, Franke B, Thompson PM, Medland SE, Martin NG. Alzheimer's Disease Neuroimaging I, Consortium C, Epigen Imagen Sys. Common genetic variants influence human subcortical brain structures. *Nature*. 2015; 520(7546):224–229. [PubMed: 25607358]

Hill SK, Reilly JL, Keefe RS, Gold JM, Bishop JR, Gershon ES, Tamminga CA, Pearlson GD, Keshavan MS, Sweeney JA. Neuropsychological impairments in schizophrenia and psychotic bipolar disorder: Findings from the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) study. *The American journal of psychiatry*. 2013; 170(11):1275–1284. [PubMed: 23771174]

Holmes AJ, Hollinshead MO, O'Keefe TM, Petrov VI, Fariello GR, Wald LL, Fischl B, Rosen BR, Mair RW, Roffman JL, Smoller JW, Buckner RL. Brain Genomics Superstruct Project initial data release with structural, functional, and behavioral measures. *Scientific data*. 2015; 2:150031. [PubMed: 26175908]

Hubbard L, Tansey KE, Rai D, Jones P, Ripke S, Chambert KD, Moran JL, McCarroll SA, Linden DE, Owen MJ, O'Donovan MC, Walters JT, Zammit S. Evidence of common genetic overlap between schizophrenia and cognition. *Schizophrenia bulletin*. 2016; 42(3):832–842. [PubMed: 26678674]

Kay SR, Fiszbein A, Opler LA. The Positive And Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia bulletin*. 1987; 13(2):261–276. [PubMed: 3616518]

Keshavan MS, Kulkarni S, Bhojraj T, Francis A, Diwadkar V, Montrose DM, Seidman LJ, Sweeney J. Premorbid cognitive deficits in young relatives of schizophrenia patients. *Front Hum Neurosci*. 2010; 3:62. [PubMed: 20300465]

Khandaker GM, Barnett JH, White IR, Jones PB. A quantitative meta-analysis of population-based studies of premorbid intelligence and schizophrenia. *Schizophrenia research*. 2011; 132(2–3):220–227. [PubMed: 21764562]

Lee PH, Baker JT, Holmes AJ, Jahanshad N, Ge T, Jung JY, Cruz Y, Manoach DS, Hibar DP, Faskowitz J, McMahon KL, de Zubicaray GI, Martin NH, Wright MJ, Öngür D, Buckner R, Roffman J, Thompson PM, Smoller JW. Partitioning heritability analysis reveals a shared genetic basis of brain anatomy and schizophrenia. *Molecular psychiatry*. 2016; 21(12):1680–1689. [PubMed: 27725656]

Lencz T, Knowles E, Davies G, Guha S, Liewald DC, Starr JM, Djurovic S, Melle I, Sundet K, Christoforou A, Reinvang I, Mukherjee S, DeRosse P, Lundervold A, Steen VM, John M, Espeseth T, Raikkonen K, Widen E, Palotie A, Eriksson JG, Giegling I, Konte B, Ikeda M, Roussos P, Giakoumaki S, Burdick KE, Payton A, Ollier W, Horan M, Donohoe G, Morris D, Corvin A, Gill M, Pendleton N, Iwata N, Darvasi A, Bitsios P, Rujescu D, Lahti J, Hellard SL, Keller MC,

Andreassen OA, Deary IJ, Glahn DC, Malhotra AK. Molecular genetic evidence for overlap between general cognitive ability and risk for schizophrenia: A report from the Cognitive Genomics consortium (COGENT). *Molecular psychiatry*. 2014; 19(2):168–174. [PubMed: 24342994]

Lencz T, Szeszko PR, DeRosse P, Burdick KE, Bromet EJ, Bilder RM, Malhotra AK. A schizophrenia risk gene, ZNF804A, influences neuroanatomical and neurocognitive phenotypes.

Neuropsychopharmacology: official publication of the American College of Neuropsychopharmacology. 2010; 35(11):2284–2291. [PubMed: 20664580]

Lewandowski KE, Cohen BM, Öngür D. Evolution of neuropsychological dysfunction during the course of schizophrenia and bipolar disorder. *Psychological medicine*. 2011; 41(2):225–241. [PubMed: 20836900]

Lichtenstein P, Yip BH, Bjork C, Pawitan Y, Cannon TD, Sullivan PF, Hultman CM. Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study. *Lancet*. 2009; 373(9659):234–239. [PubMed: 19150704]

Liebers DT, Pirooznia M, Seiffudin F, Musliner KL, Zandi PP, Goes FS. Polygenic risk of schizophrenia and cognition in a population-based survey of older adults. *Schizophrenia bulletin*. 2016; 42(4):984–991. [PubMed: 26873889]

Malhotra D, Sebat J. CNVs: harbingers of a rare variant revolution in psychiatric genetics. *Cell*. 2012; 148(6):1223–1241. [PubMed: 22424231]

Martin AK, Robinson G, Reutens D, Mowry B. Common genetic risk variants are associated with positive symptoms and decision-making ability in patients with schizophrenia. *Psychiatry research*. 2015; 229(1–2):606–608. [PubMed: 26070766]

Nuechterlein KH, Green MF, Kern RS, Baade LE, Barch DM, Cohen JD, Essock S, Fenton WS, Frese FJ 3rd, Gold JM, Goldberg T, Heaton RK, Keefe RS, Kraemer H, Mesholam-Gately R, Seidman LJ, Stover E, Weinberger DR, Young AS, Zalcman S, Marder SR. The MATRICS Consensus Cognitive Battery, part 1: Test selection, reliability, and validity. *The American journal of psychiatry*. 2008; 165(2):203–213. [PubMed: 18172019]

Peralta V, Cuesta MJ. Psychometric properties of the positive and negative syndrome scale (PANSS) in schizophrenia. *Psychiatry research*. 1994; 53(1):31–40. [PubMed: 7991730]

PGC Schizophrenia Working Group. Biological insights from 108 schizophrenia-associated genetic loci. *Nature*. 2014; 511(7510):421–427. [PubMed: 25056061]

Bramon E, Pirinen M, Strange A, Lin K, Freeman C, Bellenguez C, Su Z, Band G, Pearson R, Vukcevic D, Langford C, Deloukas P, Hunt S, Gray E, Dronov S, Potter SC, Tashakkori-Ghanbaria A, Edkins S, Bumpstead SJ, Arranz MJ, Bakker S, Bender S, Bruggeman R, Cahn W, Chandler D, Collier DA, Crespo-Facorro B, Dazzan P, de Haan L, Di Forti M, Dragovic M, Giegling I, Hall J, Iyegbe C, Jablensky A, Kahn RS, Kalaydjieva L, Kravaviti E, Lawrie S, Linszen DH, Mata I, McDonald C, McIntosh A, Myin-Germeys I, Ophoff RA, Pariante CM, Paunio T, Picchioni M, Ripke S, Rujescu D, Sauer H, Shaikh M, Sussmann J, Suvisaari J, Tosato S, Touloupoulou T, Van Os J, Walshe M, Weisbrod M, Whalley H, Wiersma D, Blackwell JM, Brown MA, Casas JP, Corvin A, Duncanson A, Jankowski JA, Markus HS, Mathew CG, Palmer CN, Plomin R, Rautanen A, Sawcer SJ, Trembath RC, Wood NW, Barroso I, Peltonen L, Lewis CM, Murray RM, Donnelly P, Powell J, Spencer CC. Psychosis Endophenotypes International Consortium, Wellcome Trust Case-Control Consortium; Psychiatric Genomics C. A genome-wide association analysis of a broad psychosis phenotype identifies three loci for further investigation. *Biological Psychiatry*. 2014; 75(5):386–397. [PubMed: 23871474]

Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MA, Bender D, Maller J, Sklar P, de Bakker PI, Daly MJ, Sham PC. PLINK: a tool set for whole-genome association and population-based linkage analyses. *American journal of human genetics*. 2007; 81(3):559–575. [PubMed: 17701901]

Purcell SM, Wray NR, Stone JL, Visscher PM, O'Donovan MC, Sullivan PF, Sklar P. Common polygenic variation contributes to risk of schizophrenia and bipolar disorder. *Nature*. 2009; 460(7256):748–752. [PubMed: 19571811]

Ripke S, O'Dushlaine C, Chambert K, Moran JL, Kahler AK, Akterin S, Bergen SE, Collins AL, Crowley JJ, Fromer M, Kim Y, Lee SH, Magnusson PK, Sanchez N, Stahl EA, Williams S, Wray NR, Xia K, Bettella F, Borglum AD, Bulik-Sullivan BK, Cormican P, Craddock N, de Leeuw C,

Durmishi N, Gill M, Golimbet V, Hamshere ML, Holmans P, Hougaard DM, Kendler KS, Lin K, Morris DW, Mors O, Mortensen PB, Neale BM, O'Neill FA, Owen MJ, Milovancevic MP, Posthuma D, Powell J, Richards AL, Riley BP, Ruderfer D, Rujescu D, Sigurdsson E, Silagadze T, Smit AB, Stefansson H, Steinberg S, Suvisaari J, Tosato S, Verhage M, Walters JT, Levinson DF, Gejman PV, Kendler KS, Laurent C, Mowry BJ, O'Donovan MC, Owen MJ, Pulver AE, Riley BP, Schwab SG, Wildenauer DB, Dudbridge F, Holmans P, Shi J, Albus M, Alexander M, Campion D, Cohen D, Dikeos D, Duan J, Eichhammer P, Godard S, Hansen M, Lerer FB, Liang KY, Maier W, Mallet J, Nertney DA, Nestadt G, Norton N, O'Neill FA, Papadimitriou GN, Ribble R, Sanders AR, Silverman JM, Walsh D, Williams NM, Wormley B, Arranz MJ, Bakker S, Bender S, Bramon E, Collier D, Crespo-Facorro B, Hall J, Iyegbe C, Jablensky A, Kahn RS, Kalaydjieva L, Lawrie S, Lewis CM, Lin K, Linszen DH, Mata I, McIntosh A, Murray RM, Ophoff RA, Powell J, Rujescu D, Van Os J, Walshe M, Weisbrod M, Wiersma D, Donnelly P, Barroso I, Blackwell JM, Bramon E, Brown MA, Casas JP, Corvin AP, Deloukas P, Duncanson A, Jankowski J, Markus HS, Mathew CG, Palmer CN, Plomin R, Rautanen A, Sawcer SJ, Trembath RC, Viswanathan AC, Wood NW, Spencer CC, Band G, Bellenguez C, Freeman C, Hellenthal G, Giannoulidou E, Pirinen M, Pearson RD, Strange A, Su Z, Vukcevic D, Donnelly P, Langford C, Hunt SE, Edkins S, Gwilliam R, Blackburn H, Bumpstead SJ, Dronov S, Gillman M, Gray E, Hammond N, Jayakumar A, McCann OT, Liddle J, Potter SC, Ravindrarajah R, Ricketts M, Tashakkori-Ghanbaria A, Waller MJ, Weston P, Widaa S, Whittaker P, Barroso I, Deloukas P, Mathew CG, Blackwell JM, Brown MA, Corvin AP, McCarthy MI, Spencer CC, Bramon E, Corvin AP, O'Donovan MC, Stefansson K, Scolnick E, Purcell S, McCarroll SA, Sklar P, Hultman CM, Sullivan PF, Wellcome Trust Case Control C, Psychosis Endophenotypes International C, Multicenter Genetic Studies of Schizophrenia C. Genome-wide association analysis identifies 13 new risk loci for schizophrenia. *Nature genetics*. 2013; 45(10):1150–1159. [PubMed: 23974872]

Robinson EB, Kirby A, Ruparel K, Yang J, McGrath L, Anttila V, Neale BM, Merikangas K, Lehner T, Sleiman PM, Daly MJ, Gur R, Gur R, Hakonarson H. The genetic architecture of pediatric cognitive abilities in the Philadelphia Neurodevelopmental Cohort. *Mol Psychiatry*. 2015; 20(4): 454–458. [PubMed: 25023143]

Segall JM, Turner JA, van Erp TG, White T, Bockholt HJ, Gollub RL, Ho BC, Magnotta V, Jung RE, McCarley RW, Schulz SC, Lauriello J, Clark VP, Voyvodic JT, Diaz MT, Calhoun VD. Voxel-based morphometric multisite collaborative study on schizophrenia. *Schizophrenia bulletin*. 2009; 35(1):82–95. [PubMed: 18997157]

Seidman LJ, Helleman G, Nuechterlein KH, Greenwood TA, Braff DL, Cadenhead KS, Calkins ME, Freedman R, Gur RE, Gur RC, Lazzaroni LC, Light GA, Olincy A, Radant AD, Siever LJ, Silverman JM, Sprock J, Stone WS, Sugar C, Swerdlow NR, Tsuang DW, Tsuang MT, Turetsky BI, Green MF. Factor structure and heritability of endophenotypes in schizophrenia: Findings from the Consortium on the Genetics of Schizophrenia (COGS-1). *Schizophrenia research*. 2015; 163(1–3):73–79. [PubMed: 25682549]

Shenton ME, Dickey CC, Frumin M, McCarley RW. A review of MRI findings in schizophrenia. *Schizophrenia research*. 2001; 49(1–2):1–52.

Spearman C. General intelligence objectively determined and measured. *Am J Psychol*. 1904; 15:201–293.

Stone, WS., Seidman, LJ. Neuropsychological and structural neuroimaging endophenotypes in schizophrenia. In: Cicchetti, D., editor. *Developmental Psychopathology*. 3. John Wiley & Sons, Inc; Hoboken, New Jersey: 2016. p. 931-965.

Sudmant PH, Rausch T, Gardner EJ, Handsaker RE, Abyzov A, Huddleston J, Zhang Y, Ye K, Jun G, Hsi-Yang Fritz M, Konkel MK, Malhotra A, Stutz AM, Shi X, Paolo Casale F, Chen J, Hormozdiari F, Dayama G, Chen K, Malig M, Chaisson MJ, Walter K, Meiers S, Kashin S, Garrison E, Auton A, Lam HY, Jasmine Mu X, Alkan C, Antaki D, Bae T, Cerveira E, Chines P, Chong Z, Clarke L, Dal E, Ding L, Emery S, Fan X, Gujral M, Kahveci F, Kidd JM, Kong Y, Lameijer EW, McCarthy S, Flicek P, Gibbs RA, Marth G, Mason CE, Menelaou A, Muzny DM, Nelson BJ, Noor A, Parrish NF, Pendleton M, Quitadamo A, Raeder B, Schadt EE, Romanovitch M, Schlattl A, Sebra R, Shabalina AA, Untergasser A, Walker JA, Wang M, Yu F, Zhang C, Zhang J, Zheng-Bradley X, Zhou W, Zichner T, Sebati J, Batzer MA, McCarroll SA, Mills RE, Gerstein MB, Bashir A, Stegle O, Devine SE, Lee C, Eichler EE, Korb J. Genomes Project C. *An*

- integrated map of structural variation in 2,504 human genomes. *Nature*. 2015; 526(7571):75–81. [PubMed: 26432246]
- Sullivan PF, Kendler KS, Neale MC. Schizophrenia as a complex trait: evidence from a meta-analysis of twin studies. *Arch Gen Psychiatry*. 2003; 60(12):1187–1192. [PubMed: 14662550]
- Tamminga CA, Ivleva EI, Keshavan MS, Pearlson GD, Clementz BA, Witte B, Morris DW, Bishop J, Thaker GK, Sweeney JA. Clinical phenotypes of psychosis in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP). *The American journal of psychiatry*. 2013; 170(11):1263–1274. [PubMed: 23846857]
- Auton A, Brooks LD, Durbin RM, Garrison EP, Kang HM, Korbel JO, Marchini JL, McCarthy S, McVean GA, Abecasis GR. The 1000 Genomes Project Consortium. A global reference for human genetic variation. *Nature*. 2015; 526(7571):68–74. [PubMed: 26432245]
- Thermenos HW, Keshavan MS, Juelich RJ, Molokotos E, Whitfield-Gabrieli S, Brent BK, Makris N, Seidman LJ. A review of neuroimaging studies of young relatives of individuals with schizophrenia: a developmental perspective from schizotaxia to schizophrenia. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*. 2013; 162B(7):604–635.
- Touloupoulou T, Goldberg TE, Mesa IR, Picchioni M, Rijdsdijk F, Stahl D, Cherny SS, Sham P, Faraone SV, Tsuang M, Weinberger DR, Seidman LJ, Murray RM. Impaired intellect and memory: A missing link between genetic risk and schizophrenia? *Arch Gen Psychiatry*. 2010; 67(9):905–913. [PubMed: 20819984]
- Trampush JW, Yang ML, Yu J, Knowles E, Davies G, Liewald DC, Starr JM, Djurovic S, Melle I, Sundet K, Christoforou A, Reinvang I, DeRosse P, Lundervold AJ, Steen VM, Espeseth T, Raikkonen K, Widen E, Palotie A, Eriksson JG, Giegling I, Konte B, Roussos P, Giakoumaki S, Burdick KE, Payton A, Ollier W, Horan M, Chiba-Falek O, Attix DK, Need AC, Cirulli ET, Voineskos AN, Stefanis NC, Avramopoulos D, Hatzimanolis A, Arking DE, Smyrnis N, Bilder RM, Freimer NA, Cannon TD, London E, Poldrack RA, Sabb FW, Congdon E, Conley ED, Scult MA, Dickinson D, Straub RE, Donohoe G, Morris D, Corvin A, Gill M, Hariri AR, Weinberger DR, Pendleton N, Bitsios P, Rujescu D, Lahti J, Le Hellard S, Keller MC, Andreassen OA, Deary IJ, Glahn DC, Malhotra AK, Lencz T. GWAS meta-analysis reveals novel loci and genetic correlates for general cognitive function: a report from the COGENT consortium. *Molecular psychiatry*. 2017; 22(3):336–345. [PubMed: 28093568]
- van Erp TG, Hibar DP, Rasmussen JM, Glahn DC, Pearlson GD, Andreassen OA, Agartz I, Westlye LT, Haukvik UK, Dale AM, Melle I, Hartberg CB, Gruber O, Kraemer B, Zilles D, Donohoe G, Kelly S, McDonald C, Morris DW, Cannon DM, Corvin A, Machielsen MW, Koenders L, de Haan LA, Veltman DJ, Satterthwaite TD, Wolf DH, Gur RC, Gur RE, Potkin SG, Mathalon DH, Mueller BA, Preda A, Macciardi F, Ehrlich S, Walton E, Hass J, Calhoun VD, Bockholt HJ, Sponheim SR, Shoemaker JM, van Haren NE, Pol HE, Ophoff RA, Kahn RS, Roiz-Santianez R, Crespo-Facorro B, Wang L, Alpert KI, Jonsson EG, Dimitrova R, Bois C, Whalley HC, McIntosh AM, Lawrie SM, Hashimoto R, Thompson PM, Turner JA. Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. *Molecular psychiatry*. 2016; 21(4):547–553. [PubMed: 26033243]
- van Erp TG, Preda A, Nguyen D, Faziola L, Turner J, Bustillo J, Belger A, Lim KO, McEwen S, Voyvodic J, Mathalon DH, Ford J, Potkin SG, Fbirm. Converting positive and negative symptom scores between PANSS and SAPS/SANS. *Schizophrenia research*. 2014; 152(1):289–294. [PubMed: 24332632]
- van Scheltinga AF, Bakker SC, van Haren NE, Derks EM, Buizer-Voskamp JE, Cahn W, Ripke S, Ophoff RA, Kahn RS. Psychiatric Genome-Wide Association Study C. Schizophrenia genetic variants are not associated with intelligence. *Psychological medicine*. 2013; 43(12):2563–2570. [PubMed: 23410598]
- Visscher PM, Hemani G, Vinkhuyzen AA, Chen GB, Lee SH, Wray NR, Goddard ME, Yang J. Statistical power to detect genetic (co)variance of complex traits using SNP data in unrelated samples. *PLoS genetics*. 2014; 10(4):e1004269. [PubMed: 24721987]
- Walton E, Geisler D, Lee PH, Hass J, Turner JA, Liu J, Sponheim SR, White T, Wassink TH, Roessner V, Gollub RL, Calhoun VD, Ehrlich S. Prefrontal Inefficiency Is Associated With Polygenic Risk for Schizophrenia. *Schizophrenia bulletin*. 2013a

- Walton E, Turner J, Gollub RL, Manoach DS, Yendiki A, Ho BC, Sponheim SR, Calhoun VD, Ehrlich S. Cumulative genetic risk and prefrontal activity in patients with schizophrenia. *Schizophrenia bulletin*. 2013b; 39(3):703–711. [PubMed: 22267534]
- Wassink TH, Epping EA, Rudd D, Axelsen M, Ziebell S, Fleming FW, Monson E, Ho BC, Andreasen NC. Influence of ZNF804a on brain structure volumes and symptom severity in individuals with schizophrenia. *Arch Gen Psychiatry*. 2012; 69(9):885–892. [PubMed: 22945618]
- Wilke M, Rose DF, Holland SK, Leach JL. Multidimensional morphometric 3D MRI analyses for detecting brain abnormalities in children: impact of control population. *Human brain mapping*. 2014; 35(7):3199–3215. [PubMed: 25050423]
- Woodberry KA, Giuliano AJ, Seidman LJ. Premorbid IQ in schizophrenia: a meta-analytic review. *The American journal of psychiatry*. 2008; 165(5):579–587. [PubMed: 18413704]
- Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. *J Clin Psychiatry*. 2003; 64(6):663–667. [PubMed: 12823080]
- Yeo RA, Gangestad SW, Walton E, Ehrlich S, Pommy J, Turner JA, Liu J, Mayer AR, Schulz SC, Ho BC, Bustillo JR, Wassink TH, Sponheim SR, Morrow EM, Calhoun VD. Genetic influences on cognitive endophenotypes in schizophrenia. *Schizophrenia research*. 2014; 156(1):71–75. [PubMed: 24768440]
- Zuk O, Schaffner SF, Samocha K, Do R, Hechter E, Kathiresan S, Daly MJ, Neale BM, Sunyaev SR, Lander ES. Searching for missing heritability: designing rare variant association studies. *Proc Natl Acad Sci U S A*. 2014; 111(4):E455–464. [PubMed: 24443550]

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 (%)	Patients (N)	Controls (N)	FHR (N)	Male (%)	Eur (%)
CAMH	Centre for Addiction and Mental Health	Toronto, Canada	123	144	0	56.2	76.1	89	115	0	55.4	76.5	---	---	---	---	---
CATIE	Clinical Antipsychotic Trials of Intervention Effectiveness	Multi-site, USA	741	0	0	73.6	54.7	---	---	---	---	---	---	---	---	---	---
CIDAR/VA	Boston Center for Intervention Development and Applied Research/VA Healthcare System	Boston, USA	76	107	6	68.8	60.0	68	101	6	68.0	59.4	---	---	---	---	---
COGS-UK	Cognition and Genetics in Schizophrenia & Bipolar Disorder	Cardiff, UK	835	0	0	58.8	97.3	---	---	---	---	---	---	---	---	---	---
GAP	Genetics and Psychosis First – Episode Study	London, UK	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	150	63	0	55.9	0	243	81	0	62.4	0	---	---	---	---	---
IMH-STCRP	Institute of Mental Health – Singapore Translational and Clinical Research in Psychosis	Singapore	420	1,012	0	52.9	0	---	---	---	---	---	---	---	---	---	---
KCL-MFS	King’s College London – Maudsley Family Study	London, UK	183	120	278	48.0	95.1	---	---	---	---	---	---	---	---	---	---
KCL-MTS	King’s College London – Maudsley Twin Study	London, UK	127	297	47	42.9	100	63	75	23	60.3	94.5	---	---	---	---	---
L&R	Language and Risk in Schizophrenia	Boston, USA	0	31	44	34.7	74.7	0	33	51	33.3	71.4	---	---	---	---	---
MCIC	Mind Clinical Imaging Consortium	Multi-site, USA	112	95	0	72.0	75.3	118	97	0	71.2	76.7	---	---	---	---	---
MGH	Massachusetts General Hospital	Boston, USA	434	0	0	72.4	68.8	61	123	0	65.2	73.2	---	---	---	---	---
NEFS	New England Family Study	Boston, USA	83	151	33	44.6	86.2	72	155	20	44.5	85.8	---	---	---	---	---
PAGES	Phenomics and Genomics Sample	Munich, Germany	210	1,341	0	50.0	99.6	---	---	---	---	---	---	---	---	---	---
PHRS	Pittsburgh High Risk Study	Pittsburgh, USA	0	53	77	45.4	41.0	0	46	67	44.3	55.8	---	---	---	---	---
TC/D/NUIG	Trinity College Dublin/National University of Ireland, Galway	Multi-site, Ireland	904	290	0	60.9	99.9	175	312	0	56.9	99.8	---	---	---	---	---

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 (%)
UMCU-SZ1	University Medical Center Utrecht – Schizophrenia Study 1	Utrecht, Netherlands	Illumina HumanHap550; Illumina Infinium OmniExpressExome-8	97	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				4,892	4,370	720	56.5	72.2	1,364	1,520	379	57.4	65.0

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)	5,197	39.3±12.2 (13–82)	4,877	39.2±15.8 (8–86)	725	34.9±16.0 (10–85)	F = 31.2	2, 10796	<1x10 ⁻¹⁰			
Education Level (years)	4,697	12.3±2.6 (1–24)	4,031	13.3±2.6 (4–26)	721	13.1±3.2 (3–24)	F = 163.4	2, 9446	<1x10 ⁻¹⁰			
Premorbid IQ	3,145	97.1±15.5 (44–145)	1,393	107.6±10.7 (62–145)	83	105.1±16.0 (45–134)	F = 263.4	2, 4618	<1x10 ⁻¹⁰			
Current IQ	1,889	93.8±18.1 (47–155)	2,779	113.4±14.9 (67–161)	602	105.1±15.6 (58–152)	F = 817.8	2, 5267	<1x10 ⁻¹⁰			
Illness Duration (years)	4,165	15.1±11.6 (<1–58)	---	---	---	---	---	---	---			
Age at Onset (years)	4,124	23.8±8.6 (1–71)	---	---	---	---	---	---	---			
Global Assessment of Functioning	1,764	59.8±15.9 (11–100)	---	---	---	---	---	---	---			
PANSS Positive symptoms	2,916	16.3±7.3 (7–47)	---	---	---	---	---	---	---			
PANSS Negative Symptoms	2,912	16.7±7.1 (7–43)	---	---	---	---	---	---	---			
PANSS General Symptoms	2,919	32.0±11.8 (0–93)	---	---	---	---	---	---	---			
SAPS Positive Symptoms	1,533	7.9±12.3 (0–121)	---	---	---	---	---	---	---			
SANS Negative Symptoms	983	23.6±20.1 (0–103)	---	---	---	---	---	---	---			
Antipsychotic dose – current CPZEQ	3,315	384.2±406.6 (0–5,000)	---	---	---	---	---	---	---			
Antipsychotic dose – lifetime average CPZEQ	1,433	338.3±365.1 (0–3,125)	---	---	---	---	---	---	---			
Sex (male/female; % male)	3,417/1,781	65.7	2,419/2,458	49.6	317/408	43.7	χ ² = 322.9	2	<1x10 ⁻¹⁰			
Antipsychotic medication exposure												
Atypical	2,100	49.1	---	---	---	---	---	---	---			
Typical	411	9.6	---	---	---	---	---	---	---			
Both Typical and Atypical	544	12.7	---	---	---	---	---	---	---			
Naïve/None	474	11.1	---	---	---	---	---	---	---			
Unknown Class	324	7.6	---	---	---	---	---	---	---			
No information	422	9.9	---	---	---	---	---	---	---			
Diagnosis												
Schizophrenia	3,973	76.4	---	---	---	---	---	---	---			

	Patients		Controls		Familial High Risk		Statistic	df	p
	N	Mean ± SD (Range)	N	Mean ± SD (Range)	N	Mean ± SD (Range)			
Schizoaffective Disorder	465	8.9	---	---	---	---	---	---	---
Schizophreniform Disorder	93	1.8	---	---	---	---	---	---	---
Bipolar Psychosis	338	6.5	---	---	---	---	---	---	---
Other Psychosis	204	3.9	---	---	---	---	---	---	---
Psychosis Unknown Type	126	2.4	---	---	---	---	---	---	---
Ancestral Population							$\chi^2 = 567.6$	12	$< 1 \times 10^{-10}$
European	3,686	71.2	3,396	69.7	632	87.2	---	---	---
East Asian	697	13.5	1,117	22.9	3	0.4	---	---	---
African	510	9.9	152	3.1	57	7.9	---	---	---
American (Predominantly Latino)	140	2.7	30	0.6	3	0.4	---	---	---
South Asian	50	1.0	35	0.7	7	1.0	---	---	---
Mixed	28	0.5	11	0.2	10	1.4	---	---	---
No information	68	1.3	135	2.8	13	1.8	---	---	---
Handedness (right/other, % right-handed)	2,322/260	89.9	2,378/252	90.4	609/59	91.2	$\chi^2 = 1.0$	2	0.60

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.

Sample	Attention/Processing Speed			Attention/Vigilance		Working Memory – verbal		Working Memory – non-verbal		Verbal Learning & Memory		
	Digit Symbol Coding	TMT-A*	Verbal Fluency	CPT/PT*	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		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
MCI-C		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			
TCD/NIJG		x	COWAT	x	1-9 CPT	WMS-III			CANTAB SWM/n-back	CVLT-SF		WMS-III
UMCU-SZI			MAE Semantic/Phonemic		H-Q CPT					CVLT-FNL		
UMCU-SZZ	WAIS-III-NL				H-Q CPT		WAIS-III-NL Arithmetic			AVLT		
ZHH	BACS*	x	MCCB*/COWAT	x		UMD*	WAIS-R Digit Span		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

Sample	Visual Learning & Memory		Reasoning/Problem Solving		Visuo-spatial Ability		Verbal Ability	
	BYMT-R*	Other	WCST	Other	Block Design	Other	Vocabulary	Other
CAMH		RBANS Figure Recall	x	Stroop		RBANS TOLO/Figure Copy		
CATIE			64-C	WISC-III Mazes				
CIDAR-VA	BYMT-R*		64-C	NAB Mazes*	WASI		WASI	D-KEFS Proverbs
COGS-UK	BYMT-R*			NAB Mazes*				
GAP		WMS-III VisRep	x	CANTAB SOC	WASIS-III	WASIS-III MR		WASIS-III INF
IMH-SIGNRP				BACS TOL				
IMH-STCRP			64-P	BACS TOL		WASI MR/Benton JOLO		
KCL-MFS		WMS-R VisRep	x	CANTAB IDED	WASIS-III	WASIS-III MR/OA/PA/PC	WASIS-III	WASIS-III COM/INF/SIM
KCL-MTS		WMS-R-UK VisRep/VisPA	x	CANTAB IDED	WASIS-III-UK	WASIS-III-UK OA/PA/PC	WASIS-III-UK	WASIS-III-UK COM/INF/SIM
L&R	BYMT-R*		64-C	NAB Mazes*	WASI		WASI	D-KEFS Proverbs
MCCIC		BVRT/WMS-III Faces	x	TOL	WASIS-III		WASIS-III	WASIS-III SIM
MGH			128-C/64-C		WASIS-III	WASIS-III MR/OA/PA/PC	WASIS-III	WASIS-III COM/INF/SIM
NEFS		WMS-III Faces/Rey CFT Recall	128-P	Stroop	WASIS-III	WASIS-III PA/Rey CFT Copy	WASIS-III	WASIS-III COM/INF/SIM
PAGES		WMS-R-DE FigMem/VisRep/VisPA	x	TOL-DE	WASIS-III-DE	WASIS-III-DE OA/PA/PC	WASIS-III-DE	WASIS-III-DE COM/INF/SIM
PHRS		CNB VOLT	128-P	Cogtest Go-No-Go				
TCD/NIJG		WMS-III Faces/CANTAB PAL	x	CANTAB IDED/SART	WASIS-III-UK	WASIS-III-UK MR	WASIS-III-UK	WASIS-III-UK SIM
UMCU-SZ1				Stroop	WASIS-III-NL	WASIS-III-R-NL PA	WASIS-III-R-NL	WASIS-III-R-NL COM
UMCU-SZ2				NAB Mazes*/RST	WASIS-III-NL			WASIS-III-NL INF
ZHH	BYMT-R*		128-P	NAB Mazes*/Stroop				
N patients	897	1,604	836	1,376	2,260	1,615	1,754	2,048
N controls	328	1,628	1,408	835	2,744	3,131	2,425	2,617
N FHR	48	317	145	134	522	33	285	567
N total	1,273	3,549	2,389	2,345	6,686	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 Verbal Learning Test; BACS = Brief Assessment of Cognition in Schizophrenia; BYMT-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 = Verbal Learning and Memory Test; WASI = Wechsler Adult Intelligence Scale (Subtests); COM =

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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/mm ²)	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
NEFS	3T	Siemens	Trio Tim	MP-RAGE	1 x 1 x 1.3	---	---	---
	1.5T	Siemens	Avanto	MP-RAGE	1.0 x 1.0 x 1.33	60	700	2.0 x 2.0 x 2.0
PHRS	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	---	---	---
TCDD/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	---	---	---

Sample	Magnetic Field Strength	Vendor	Model	T1-weighted sequence	T1 Voxel dimensions (mm)	DW-MRI # diffusion-encoding directions	DW-MRI b-value (s/mm ²)	DW-MRI Voxel dimensions (mm)
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