Supporting Information

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SI Materials and Methods

Thematically Organized Psychosis Study Subjects. The Thematically Organized Psychosis (TOP) Study was launched in 2004 as a collaborative study involving the University of Oslo and all of the hospitals in the Oslo region, and it was funded by the University of Oslo, Regional Health Authorities, and the Research Council of Norway.

The clinical participants were recruited continuously from psychiatric units (outpatient and inpatient) in four major hospitals in Oslo. Trained psychiatrists and clinical psychologists carried out clinical assessments. Diagnosis was based on the Structured Clinical Interview from *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition Axis I disorders (1). Diagnostic reliability was found satisfactory, with overall agreement with *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition diagnostic categories of 82% with $\kappa = 0.77$ (95% confidence interval = 0.60–0.94) (2). Information from follow-up visits was used to secure correct diagnoses.

The healthy control participants were randomly selected from national statistical records from the same catchment area and contacted by letter to invite them to participate. The study is part of the TOP Research initiative and was approved by the Regional Committee for Medical Research Ethics, the Norwegian Data Inspectorate, and the Health Authority. All participants gave written informed consent.

Exclusion criteria for all groups were hospitalized head injury, neurological disorder, mental retardation (IQ below 70), and age outside the age range of 18–65 y. The healthy control sample was screened with an interview about severe mental illness and the Primary Care Evaluation of Mental Disorders (3), and subjects were excluded if they or any of their close relatives had a lifetime history of a severe psychiatric disorder (schizophrenia, bipolar disorder, or major depression with psychotic features), if they had an unstable medical condition known to interfere with brain function (including hypothyroidism, uncontrolled hypertension, and diabetes), or if they had a substance abuse or dependency in the last 3 mo. All cases and controls were Caucasians (subject ethnicity determined during the clinical interviews). About 90% of patients and about 86% of controls were ethnically Norwegian (i.e., the patient and both parents were born in Norway; the remaining subjects had one parent born in another northwestern European country).

Alzheimer's Disease Neuroimaging Initiative Subjects. Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (http://www.loni.ucla.edu/ADNI). The ADNI was launched in 2003 by the National Institute on Aging, the National Institute of Biomedical Imaging and Bioengineering, the Food and Drug Administration, private pharmaceutical companies, and nonprofit organizations as a $60 million, 5-y public–private partnership. The primary goal of ADNI has been to test whether serial MRI, PET, other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment and early Alzheimer's disease (AD). Determination of sensitive and specific markers of very early AD progression is intended to aid researchers and clinicians in developing new treatments and monitoring their effectiveness as well as lessening the time and cost of clinical trials.

The principle investigator of this initiative is Michael W. Weiner (Veterans Affairs Medical Center and University of California, San Francisco, CA). ADNI is the result of efforts of many coinvestigators from a broad range of academic institutions and private corporations, and subjects have been recruited from over 50 sites across the United States and Canada. The initial goal of ADNI was to recruit 800 adults (ages 55–90 y) to participate in the research (~200 cognitively normal older individuals to be followed for 3 y, 400 people with mild cognitive impairment to be followed for 3 y, and 200 people with early AD to be followed for 2 y). Up to date information is at http://www.adni-info.org.

MR Image Processing. All scans were first corrected for scanner- and site-specific spatial distortions based on information provided for each system by the scanners' manufacturers (4). The two 3D T1-weighted scans were then rigid body-registered to each other (motion-corrected) and subsequently averaged together to increase the signal to noise ratio. Next, subcortical and cortical segmentations were performed for each subject (5). The FreeSurfer 3.0.2 software package (http://surfer.nmr.mgh.harvard.edu) was used to create a 3D model of the cortical surface for cortical surface area measurements. This model was done by using both intensity and continuity information from the entire 3D MR volume in segmentation and deformation procedures to construct representations of the gray/white matter boundary and pial surface (5–7).

Continuous maps of cortical surface area were obtained by computing the area of each triangle of a standardized tessellation mapped to each subject's native space using a spherical atlas registration procedure (5). This mapping provides point by point estimates of the relative areal expansion or compression of each location in atlas space. Cortical maps were smoothed with a full-width, half-maximum Gaussian kernel of 30 mm and mapped into a standardized spherical atlas space using a nonrigid, high-dimensional spherical averaging method to align cortical folding patterns (5). This procedure provides accurate matching of morphologically homologous cortical locations across subjects on the basis of each individual's anatomy and minimizes metric distortion. The maps produced are not restricted to the voxel resolution of the original images and thus, capable of detecting submillimeter differences between groups (8).

Statistics. Occipital cortical area measurements had modest skew (0.40) and kurtosis (0.15), and they deviated significantly from a normal distribution based on a Shapiro–Wilk test ($P = 0.003$) but not a Kolmogorov–Smirnov test ($P = 0.06$). A normal probability plot of occipital area measurements revealed no obvious outliers, and the data were not transformed for the genome-wide association study (GWAS).

Before computing genetic relatedness between subjects, SNPs were pruned based on linkage disequilibrium ($R^2 > 0.5$, 50-SNP window, 5-SNP slide increment) to remove redundant markers that might skew population substructure estimates, leaving 198,585 SNPs. The smartpca software (9) was used to find the top four eigenvectors that explained the most variance in these genotypes, and the associated eigenvalues were included as covariates in a follow-up GWAS along with sex, age, and diagnosis. Next, λ_{GC} was estimated again, and genomic control was performed. The SEs of β-coefficient estimates for the interaction term were multiplied by $\lambda_{GC}^{0.5}$ and then used to calculate adjusted χ^2 statistics (β^2/SE_{GC}^2) with one degree of freedom and corresponding P values.

Differential Gene Expression Analysis. The differential search tool on the Allen Human Brain Atlas website (http://human.brain-

map.org/) was used to identify genes with significantly higher expression in occipital cortex (target structure) compared with whole cerebral cortex (contrast structure) (10); 37,022 probes (93% of 21,245 genes with an Entrez gene ID had at least two unique probes) were tested for higher expression in the target relative to the contrast structure in two adult male subjects (H0351.2001 and H0351.2002) using a two-sample *t* test with False Discovery Rate correction. Probes were sorted by *P* value, and two probes for *GPCPD1* were ranked 35th (A_23_P91350) and 207th (A_23_P353704) of 37,022 gene probes. Genes with at least two significant probes of the top 207 probes were kept for additional analysis, and only 11 genes with this level of support were more significant than *GPCPD1*. The cortical expression pattern for the most significant *GPCPD1* probe (A_23_P91350) was visualized on an MRI reconstruction of two adult male brains using the Allen Brain Explorer 2 application.

1. First M, Spitzer R (1995) *Structured Clinical Interview for DSM-IV Axis I Disorders: Patient Edition (SCID-P), Version 2* (New York State Psychiatric Institute, Biometrics Research, New York).
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10. Allen Human Brain Atlas (2011) *Allen Institute for Brain Science, Seattle, WA*. Available at http://human.brain-map.org. Accessed March 25, 2011.

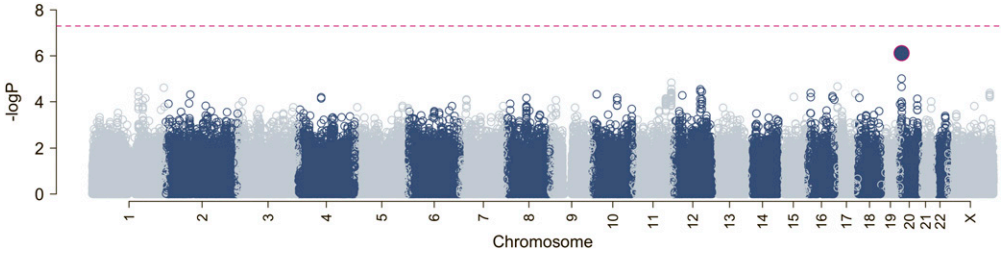

Fig. S1. Manhattan plot of genomic inflation adjusted *P* values from occipital cortical area scaling GWAS in TOP.

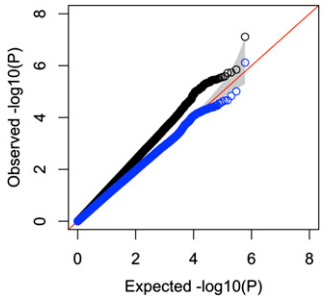

Fig. S2. Quantile–quantile plot of *P* values from occipital cortical area scaling GWAS in TOP before (black) and after (blue) adjustment for genomic inflation (λ_{GC} = 1.23).

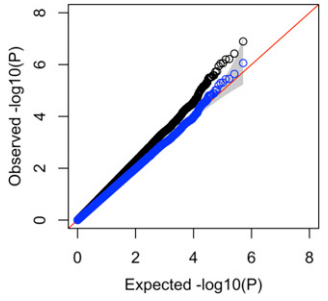

Fig. S3. Quantile–quantile plot of *P* values from occipital cortical area scaling GWAS in ADNI before (black) and after (blue) adjustment for genomic inflation (λ_{GC} = 1.19).

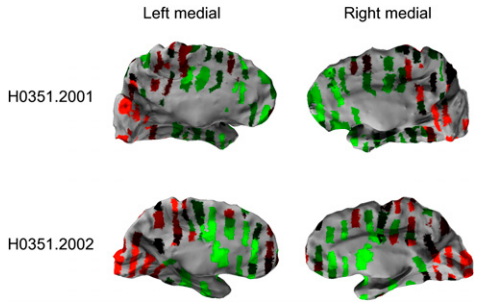

Fig. S4. *GPCPD1* expression pattern across the medial cortical surface in two adult male brains based on microarray data from the Allen Human Brain Atlas (1); *z* scores range from −1.5 (green) to +1.5 (red).

1. Allen Human Brain Atlas (2011) *Allen Institute for Brain Science, Seattle, WA*. Available at http://human.brain-map.org. Accessed March 25, 2011.

Table S1. rs238295 association with scaling of regional cortical surface area in three studies

		TOP			*ADNI*			*PING*			
Hemi	Region	β	SE_{GC}*	P_{GC}*	β	SE_{GC}*	P_{GC}*	β	SE_{GC}*	P_{GC}*	P_{meta}
R	Pericalc.	0.0036	0.0011	0.0016	0.0028	0.0011	0.0039	0.0031	0.0015	0.0207	4.4×10^{-6}
L	Lateral occipital	0.0071	0.0020	0.0003	0.0031	0.0021	0.0707	0.0048	0.0035	0.0836	8.6×10^{-5}
L	Pericalc.	0.0031	0.0011	0.0054	0.0015	0.0011	0.0760	0.0025	0.0013	0.0258	4.1×10^{-4}
R	Lingual	0.0034	0.0014	0.0131	0.0035	0.0015	0.0090	0.0022	0.0021	0.1570	4.1×10^{-4}
R	Lateral occipital	0.0047	0.0019	0.0155	0.0039	0.0017	0.0111	0.0026	0.0032	0.2062	7.2×10^{-4}
L	Inferior parietal	−0.0058	0.0022	0.0092	−0.0033	0.0019	0.0427	−0.0013	0.0033	0.3479	3.6×10^{-3}
L	Superior temporal	−0.0041	0.0015	0.0055	−0.0004	0.0015	0.3944	−0.0028	0.0018	0.0603	8.2×10^{-3}
L	Lingual	0.0036	0.0015	0.0171	0.0007	0.0015	0.3135	0.0026	0.0022	0.1242	1.9×10^{-2}
L	Middle temporal	−0.0011	0.0015	0.4780	−0.0033	0.0014	0.0090	−0.0015	0.0019	0.2153	2.0×10^{-2}
L	Transverse temporal	−0.0008	0.0003	0.0169	−0.0002	0.0003	0.2455	−0.0003	0.0005	0.2494	2.3×10^{-2}

*SEs (SE_{GC}) and *P* values (two-tailed for TOP; one-tailed for ADNI and PING) were corrected for genomic inflation based on the median χ^2 (one degree of freedom) statistic inflation measured in the three datasets (TOP λ_{GC} = 1.23, ADNI λ_{GC} = 1.19, and PING λ_{GC} = 1.00). Hemi, hemisphere; Pericalc, pericalcarine.

Other Supporting Information Files

SI Appendix