Grasby, Katrina, Jahanshad, Neda, Painter, Jodie N., Colodro-Conde, Lucía, Bralten, Janita, Hibar, Derrek P., Lind, Penelope A., Pizzagalli, Fabrizio, Ching, Christopher R. K., McMahon, Mary Agnes B., Shatokhina, Natalia, Zsembik, Leo C. P., Thomopoulos, Sophia I., Zhu, Alyssa H., Strike, Lachlan T., Agartz, Ingrid, Alhusaini, Saud, Almeida, Marcio A. A., Alnæs, Dag, Amlien, Inge K., Andersson, Micael, Ard, Tyler, Armstrong, Nicola J., Ashley-Koch, Allison, Atkins, Joshua R., Bernard, Manon, Brouwer, Rachel M., Buimer, Elizabeth E. L., Bülow, Robin, Bürger, Christian, Cannon, Dara M., Chakravarty, Mallar, Chen, Qiang, Cheung, Joshua W., Couvy-Duchesne, Baptiste, Dale, Anders M., Dalvie, Shareefa, de Araujo, Tânia K., de Zubicaray, Greig I., de Zwarte, Sonja M. C., den Braber, Anouk, Doan, Nhat Trung, Dohm, Katharina, Ehrlich, Stefan, Engelbrecht, Hannah-Ruth, Erk, Susanne, Fan, Chun Chieh, Fedko, Iryna O., Foley, Sonya F., Ford, Judith M., Fukunaga, Masaki, Garrett, Melanie E., Ge, Tian, Giddaluru, Sudheer, Goldman, Aaron L., Green, Melissa J., Groenewold, Nynke A., Grotegerd, Dominik, Gurholt, Tiril P., Gutman, Boris A., Hansell, Narelle K., Harris, Mathew A., Harrison, Marc B., Haswell, Courtney C., Hauser, Michael, Herms, Stefan, Heslenfeld, Dirk J., Ho, New Fei, Hoehn, David, Hoffmann, Per, Holleran, Laurena, Hoogman, Martine, Hottenga, Jouke-Jan, Ikeda, Masashi, Janowitz, Deborah, Jansen, Iris E., Jia, Tianye, Jockwitz, Christiane, Kanai, Ryota, Karama, Sherif, Kasperaviciute, Dalia, Kaufmann, Tobias, Kelly, Sinead, Kikuchi, Masataka, Klein, Marieke, Knapp, Michael, Knodt, Annchen R., Krämer, Bernd, Lam, Max, Lancaster, Thomas M., Lee, Phil H., Lett, Tristram A., Lewis, Lindsay B., Lopes-Cendes, Iscia, Luciano, Michelle, Macciardi, Fabio, Marquand, Andre F., Mathias, Samuel R., Melzer,

Tracy R., Milaneschi, Yuri, Mirza-Schreiber, Nazanin, Moreira, Jose C. V., Mühleisen, Thomas W., Müller-Myhsok, Bertram, Najt, Pablo, Nakahara, Soichiro, Nho, Kwangsik, Olde Loohuis, Loes M., Orfanos, Dimitri Papadopoulos, Pearson, John F., Pitcher, Toni L., Pütz, Benno, Quidé, Yann, Ragothaman, Anjanibhargavi, Rashid, Faisal M., Reay, William R., Redlich, Ronny, Reinbold, Céline S., Repple, Jonathan, Richard, Geneviève, Riedel, Brandalyn C., Risacher, Shannon L., Rocha, Cristiane S., Mota, Nina Roth, Salminen, Lauren, Saremi, Arvin, Saykin, Andrew J., Schlag, Fenja, Schmaal, Lianne, Schofield, Peter R., Secolin, Rodrigo, Shapland, Chin Yang, Shen, Li, Shin, Jean, Shumskaya, Elena, Sønderby, Ida E., Sprooten, Emma, Tansey, Katherine E., Teumer, Alexander, Thalamuthu, Anbupalam, Tordesillas-Gutiérrez, Diana, Turner, Jessica A., Uhlmann, Anne, Vallerga, Costanza Ludovica, van der Meer, Dennis, van Donkelaar, Marjolein M. J., van Eijk, Liza, van Erp, Theo G. M., van Haren, Neeltje E. M., van Rooij, Daan, van Tol, Marie-José, Veldink, Jan H., Verhoef, Ellen, Walton, Esther, Wang, Mingyuan, Wang, Yunpeng, Wardlaw, Joanna M., Wen, Wei, Westlye, Lars T., Whelan, Christopher D., Witt, Stephanie H., Wittfeld, Katharina, Wolf, Christiane, Wolfers, Thomas, Wu, Jing Qin, Yasuda, Clarissa L., Zaremba, Dario, Zhang, Zuo, Zwiers, Marcel P., Artiges, Eric, Assareh, Amelia A., Ayesa-Arriola, Rosa, Belger, Aysenil, Brandt, Christine L., Brown, Gregory G., Cichon, Sven, Curran, Joanne E., Davies, Gareth E., Degenhardt, Franziska, Dennis, Michelle F., Dietsche, Bruno, Djurovic, Srdjan, Doherty, Colin P., Espiritu, Ryan, Garijo, Daniel, Gil, Yolanda, Gowland, Penny A., Green, Robert C., Häusler, Alexander N., Heindel, Walter, Ho, Beng-Choon, Hoffmann, Wolfgang U., Holsboer, Florian, Homuth, Georg, Hosten, Norbert, Jack, Clifford R., Jang, MiHyun, Jansen, Andreas, Kimbrel, Nathan A., Kolskår, Knut, Koops, Sanne, Krug, Axel, Lim, Kelvin O., Luykx, Jurjen J., Mathalon, Daniel H., Mather, Karen A., Mattay, Venkata S., Matthews, Sarah, Mayoral Van Son, Jaqueline, McEwen,

Sarah C., Melle, Ingrid, Morris, Derek W., Mueller, Bryon A., Nauck, Matthias, Nordvik, Jan E., Nöthen, Markus M., O'Leary, Daniel S., Opel, Nils, Martinot, Marie-Laure Paillère, Pike, G. Bruce, Preda, Adrian, Quinlan, Erin B., Rasser, Paul E., Ratnakar, Varun, Reppermund, Simone, Steen, Vidar M., Tooney, Paul A., Torres, Fábio R., Veltman, Dick J., Voyvodic, James T., Whelan, Robert, White, Tonya, Yamamori, Hidenaga, Adams, Hieab H. H., Bis, Joshua C., Debette, Stephanie, Decarli, Charles, Fornage, Myriam, Gudnason, Vilmundur, Hofer, Edith, Ikram, M. Arfan, Launer, Lenore, Longstreth, W. T., Lopez, Oscar L., Mazoyer, Bernard, Mosley, Thomas H., Roshchupkin, Gennady V., Satizabal, Claudia L., Schmidt, Reinhold, Seshadri, Sudha, Yang, Qiong, Alvim, Marina K. M., Ames, David, Anderson, Tim J., Andreassen, Ole A., Arias-Vasquez, Alejandro, Bastin, Mark E., Baune, Bernhard T., Beckham, Jean C., Blangero, John, Boomsma, Dorret I., Brodaty, Henry, Brunner, Han G., Buckner, Randy L., Buitelaar, Jan K., Bustillo, Juan R., Cahn, Wiepke, Cairns, Murray J., Calhoun, Vince, Carr, Vaughan J., Caseras, Xavier, Caspers, Svenja, Cavalleri, Gianpiero L., Cendes, Fernando, Corvin, Aiden, Crespo-Facorro, Benedicto, Dalrymple-Alford, John C., Dannlowski, Udo, de Geus, Eco J. C., Deary, Ian J., Delanty, Norman, Depondt, Chantal, Desrivières, Sylvane, Donohoe, Gary, Espeseth, Thomas, Fernández, Guillén, Fisher, Simon E., Flor, Herta, Forstner, Andreas J., Francks, Clyde, Franke, Barbara, Glahn, David C., Gollub, Randy L., Grabe, Hans J., Gruber, Oliver, Håberg, Asta K., Hariri, Ahmad R., Hartman, Catharina A., Hashimoto, Ryota, Heinz, Andreas, Henskens, Frans A., Hillegers, Manon H. J., Hoekstra, Pieter J., Holmes, Avram J., Hong, L. Elliot, Hopkins, William D., Hulshoff Pol, Hilleke E., Jernigan, Terry L., Jönsson, Erik G., Kahn, René S., Kennedy, Martin A., Kircher, Tilo T. J., Kochunov, Peter, Kwok, John B. J., Le Hellard, Stephanie, Loughland, Carmel M., Martin, Nicholas G., Martinot, Jean-Luc, McDonald, Colm, McMahon, Katie L., Meyer-Lindenberg, Andreas, Michie, Patricia T., Morey, Rajendra A., Mowry, Bryan,

Title: The genetic architecture of the human cerebral cortex.

Authors: Katrina L. Grasby[1†*], Neda Jahanshad[2†*], Jodie N. Painter[1‡], Lucía Colodro-Conde[1,3-5‡], Janita Bralten[6,7‡], Derrek P. Hibar[2,8‡], Penelope A. Lind[1,4,9‡], Fabrizio Pizzagalli[2‡], Christopher R.K. Ching[2,10], Mary Agnes B. McMahon[2], Natalia Shatokhina[2], Leo C.P. Zsembik[11], Sophia I. Thomopoulos[2], Alyssa H. Zhu[2], Lachlan T. Strike[12], Ingrid Agartz[13-16], Saud Alhusaini[17,18], Marcio A.A. Almeida[19], Dag Alnæs[13,14], Inge K. Amlien[20], Micael Andersson[21,22], Tyler Ard[23], Nicola J. Armstrong[24], Allison Ashley-Koch[25], Joshua R. Atkins[26,27], Manon Bernard[28], Rachel M. Brouwer[29], Elizabeth E.L. Buimer[29], Robin Bülow[30], Christian Bürger[31], Dara M. Cannon[32], Mallar Chakravarty[33,34], Qiang Chen[35], Joshua W. Cheung[2], Baptiste Couvy-Duchesne[12,36,37], Anders M. Dale[38,39], Shareefa Dalvie [40], Tânia K. de Araujo[41,42], Greig I. de Zubicaray[43], Sonja M.C. de Zwarte[29], Anouk den Braber[44,45], Nhat Trung Doan[13,14], Katharina Dohm[31], Stefan Ehrlich[46], Hannah-Ruth Engelbrecht[47], Susanne Erk[48], Chun Chieh Fan[49], Iryna O. Fedko[44], Sonya F. Foley[50], Judith M. Ford[51], Masaki Fukunaga[52], Melanie E. Garrett[25], Tian Ge[53,54], Sudheer Giddaluru[55], Aaron L. Goldman[35], Melissa J. Green[56,57], Nynke A. Groenewold[40], Dominik Grotegerd[31], Tiril P. Gurholt[13-15], Boris A. Gutman[2,58], Narelle K. Hansell[12], Mathew A. Harris[59,60], Marc B. Harrison[2], Courtney C. Haswell[61,62], Michael Hauser[25], Stefan Herms[63-65], Dirk J. Heslenfeld[66], New Fei Ho[67], David Hoehn[68], Per Hoffmann[63,64,69], Laurena Holleran[70], Martine Hoogman[6,7], Jouke-Jan Hottenga[44], Masashi Ikeda[71], Deborah Janowitz[72], Iris E. Jansen[73,74], Tianye Jia[75-77], Christiane Jockwitz[78-80], Ryota Kanai[81-83], Sherif Karama[33,84,85], Dalia Kasperaviciute[86,87], Tobias Kaufmann[13,14], Sinead Kelly[88,89], Masataka Kikuchi [90], Marieke Klein[6,7,29], Michael Knapp[91], Annchen R. Knodt[92], Bernd Krämer[93,94], Max Lam[67,95], Thomas M. Lancaster[50,96], Phil H. Lee[53,97], Tristram A. Lett[48], Lindsay B. Lewis[85,98], Iscia Lopes-Cendes[41,42], Michelle Luciano[99,100], Fabio Macciardi[101], Andre F. Marquand[7,102], Samuel R. Mathias[103,104], Tracy R. Melzer[105-107], Yuri Milaneschi[108], Nazanin Mirza-Schreiber[68,109], Jose C.V. Moreira[42,110], Thomas W. Mühleisen[63,78,111], Bertram Müller-Myhsok[68,112,113], Pablo Najt[32], Soichiro Nakahara[101,114], Kwangsik Nho[115], Loes M. Olde Loohuis[116], Dimitri Papadopoulos Orfanos[117], John F. Pearson[118,119], Toni L. Pitcher[105-107], Benno Pütz[68], Yann Quidé[56,57], Anjanibhargavi Ragothaman[2], Faisal M. Rashid[2], William R. Reay[26,27], Ronny Redlich[31], Céline S. Reinbold[20,63,64], Jonathan Repple[31], Geneviève Richard[13,14,120,121], Brandalyn C. Riedel[2,115], Shannon L. Risacher[115], Cristiane S. Rocha[41,42], Nina Roth Mota[6,7,122], Lauren Salminen[2], Arvin Saremi[2], Andrew J. Saykin[115,123], Fenja Schlag[124], Lianne Schmaal[125-127], Peter R. Schofield[128,129], Rodrigo Secolin[41,42], Chin Yang Shapland[124], Li Shen[130], Jean Shin[28,131], Elena Shumskaya[6,7,132], Ida E. Sønderby[13,14], Emma Sprooten[7], Katherine E. Tansey[96], Alexander Teumer[133], Anbupalam Thalamuthu[134], Diana Tordesillas-Gutiérrez[135,136], Jessica A. Turner[137,138], Anne Uhlmann[40,139], Costanza Ludovica Vallerga[36], Dennis van der Meer[140,141], Marjolein M.J. van Donkelaar[142], Liza van Eijk[3,12], Theo G.M. van Erp[101], Neeltje E.M. van Haren[29,143], Daan van Rooij[7,102], Marie-José van Tol[144], Jan H. Veldink[145], Ellen Verhoef[124], Esther Walton[137,146,147], Mingyuan Wang[67], Yunpeng Wang[13,14], Joanna M. Wardlaw[59,100,148], Wei Wen[134], Lars T. Westlye[13,14,120], Christopher D. Whelan[2,17], Stephanie H. Witt[149], Katharina Wittfeld[72,150], Christiane Wolf[151], Thomas Wolfers[6], Jing Qin Wu[26], Clarissa L. Yasuda[42,152], Dario Zaremba[31], Zuo Zhang[153], Marcel P. Zwiers[7,102,132], Eric Artiges[154], Amelia A. Assareh[134], Rosa Ayesa-Arriola[136,155], Aysenil Belger[61,156], Christine L. Brandt[13,14], Gregory G. Brown[157,158], Sven Cichon[63,64,78], Joanne E. Curran[19], Gareth E. Davies[159], Franziska Degenhardt[69], Michelle F. Dennis[62], Bruno Dietsche[160], Srdjan Djurovic[161,162], Colin P. Doherty[163-165], Ryan Espiritu[166], Daniel Garijo[166], Yolanda Gil[166], Penny A. Gowland[167], Robert C. Green[168-170], Alexander N.

Häusler[171,172], Walter Heindel[173], Beng-Choon Ho[174], Wolfgang U. Hoffmann[133,150], Florian Holsboer[68,175], Georg Homuth[176], Norbert Hosten[177], Clifford R. Jack Jr.[178], MiHyun Jang[166], Andreas Jansen[160,179], Nathan A. Kimbrel[62,180], Knut Kolskår[13,14,120,121], Sanne Koops[29], Axel Krug[160], Kelvin O. Lim[181], Jurjen J. Luykx[29,182,183], Daniel H. Mathalon[184,185], Karen A. Mather[128,134], Venkata S. Mattay[35,186,187], Sarah Matthews[146], Jaqueline Mayoral Van Son[136,155], Sarah C. McEwen[188,189], Ingrid Melle[13,14], Derek W. Morris[32], Bryon A. Mueller[181], Matthias Nauck[190,191], Jan E. Nordvik[121], Markus M. Nöthen[69], Daniel S. O'Leary[174], Nils Opel[31], Marie-Laure Paillère Martinot[154,192], G. Bruce Pike[193], Adrian Preda[194], Erin B. Quinlan[153], Paul E. Rasser[27,195-197], Varun Ratnakar[166], Simone Reppermund[134,198], Vidar M. Steen[162,199], Paul A. Tooney[26,197], Fábio R. Torres[41,42], Dick J. Veltman[108], James T. Voyvodic[61], Robert Whelan[200], Tonya White[143,201], Hidenaga Yamamori[202], Hieab H.H. Adams[203-205], Joshua C. Bis[206], Stephanie Debette[207,208], Charles Decarli[209], Myriam Fornage[210], Vilmundur Gudnason[211,212], Edith Hofer[213,214], M. Arfan Ikram[203], Lenore Launer[215], W. T. Longstreth[216], Oscar L. Lopez[203,217], Bernard Mazoyer[218], Thomas H. Mosley [219], Gennady V. Roshchupkin[203,204,217], Claudia L. Satizabal[220-222], Reinhold Schmidt[213], Sudha Seshadri[220,222,223], Qiong Yang[224], The Alzheimer's Disease Neuroimaging Initiative#, CHARGE consortium#, EPIGEN consortium#, IMAGEN consortium#, SYS consortium#, The Parkinson's Progression Markers Initiative#, Marina K.M. Alvim[42,152], David Ames[225,226], Tim J. Anderson[105-107,227], Ole A. Andreassen[13,14], Alejandro Arias-Vasquez[6,7,122], Mark E. Bastin[59,100], Bernhard T. Baune[31,228,229], Jean C. Beckham[180,230], John Blangero[19], Dorret I. Boomsma[44], Henry Brodaty[134,231], Han G. Brunner[6,7,232], Randy L. Buckner[233-235], Jan K. Buitelaar[7,102,236], Juan R. Bustillo[237], Wiepke Cahn[238], Murray J. Cairns[26,27,239], Vince Calhoun[240], Vaughan J. Carr[56,57,241], Xavier Caseras[96], Svenja Caspers[78,80,242], Gianpiero L. Cavalleri[243,244], Fernando Cendes[42,152], Aiden Corvin[245], Benedicto Crespo-Facorro[136,155,246], John C. Dalrymple-Alford[106,107,247], Udo Dannlowski[31], Eco J.C. de Geus[44], Ian J. Deary[99,100], Norman Delanty[17,165], Chantal Depondt[248], Sylvane Desrivières[77,153], Gary Donohoe[70], Thomas Espeseth[13,120], Guillén Fernández[7,102], Simon E. Fisher[7,124], Herta Flor[249], Andreas J. Forstner[63,64,69,250,251], Clyde Francks[7,124], Barbara Franke[6,7,122], David C. Glahn[104,252], Randy L. Gollub[97,234,235], Hans J. Grabe[72,150], Oliver Gruber[93], Asta K. Håberg[253,254], Ahmad R. Hariri[92], Catharina A. Hartman[255], Ryota Hashimoto[202,256,257], Andreas Heinz[258], Frans A. Henskens[195,259], Manon H.J. Hillegers[143,260], Pieter J. Hoekstra[261], Avram J. Holmes[234,262], L. Elliot Hong[263], William D. Hopkins[264], Hilleke E. Hulshoff Pol[29], Terry L. Jernigan[39,49,157,265], Erik G. Jönsson[14,16], René S. Kahn[29,266], Martin A. Kennedy[119], Tilo T.J. Kircher[160], Peter Kochunov[263], John B.J. Kwok[128,129,267], Stephanie Le Hellard[162,199], Carmel M. Loughland[195,268], Nicholas G. Martin[37], Jean-Luc Martinot[154], Colm McDonald[32], Katie L. McMahon[269], Andreas Meyer-Lindenberg[270], Patricia T. Michie[271], Rajendra A. Morey[61,62], Bryan Mowry[12,272], Lars Nyberg[21,22,273], Jaap Oosterlaan[274-276], Roel A. Ophoff[116], Christos Pantelis[228,229,277], Tomas Paus[278-280], Zdenka Pausova[28,281], Brenda W.J.H. Penninx[108], Tinca J.C. Polderman[73], Danielle Posthuma[73,282], Marcella Rietschel[149], Joshua L. Roffman[234], Laura M. Rowland[263], Perminder S. Sachdev[134,283], Philipp G. Sämann[68], Ulrich Schall[27,197], Gunter Schumann[75,77,153,284,285], Rodney J. Scott[26,286], Kang Sim[287], Sanjay M. Sisodiya[86,288], Jordan W. Smoller[53,234,289], Iris E. Sommer[144,260,261,290], Beate St Pourcain[7,124,146], Dan J. Stein[291,292], Arthur W. Toga[23], Julian N. Trollor[134,198], Nic J.A. Van der Wee[293], Dennis van 't Ent[44], Henry Völzke[133], Henrik Walter[48], Bernd Weber[171,172], Daniel R. Weinberger[35,294], Margaret J. Wright[12,295], Juan Zhou[296], Jason L. Stein[11§*], Paul M. Thompson[2§*], Sarah E. Medland[1,3,9§*] on behalf of the Enhancing NeuroImaging Genetics through Meta-Analysis Consortium - Genetics working group

Affiliations:
[1]*Psychiatric Genetics, QIMR Berghofer Medical Research Institute, Brisbane, Australia.*
[2]*Imaging Genetics Center, Mark and Mary Stevens Neuroimaging and Informatics Institute, Keck School of Medicine of USC, University of Southern California, Los Angeles, USA.*
[3]*School of Psychology, University of Queensland, Brisbane, Australia.*
[4]*School of Biomedical Sciences, Queensland University of Technology, Brisbane, Australia.*
[5]*Faculty of Psychology, University of Murcia, Murcia, Spain.*
[6]*Department of Human Genetics, Radboud university medical center, Nijmegen, The Netherlands.*
[7]*Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen, The Netherlands.*
[8]*Personalized Healthcare, Genentech, Inc., South San Francisco, USA.*
[9]*Faculty of Medicine, University of Queensland, Brisbane, Australia.*
[10]*Graduate Interdepartmental Program in Neuroscience, University of California Los Angeles, Los Angeles, USA.*
[11]*Department of Genetics & UNC Neuroscience Center, University of North Carolina at Chapel Hill, Chapel Hill, USA.*
[12]*Queensland Brain Institute, University of Queensland, St Lucia, Australia.*
[13]*NORMENT - K.G. Jebsen Centre for Psychosis Research, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway.*
[14]*NORMENT - K.G. Jebsen Centre for Psychosis Research, Institute of Clinical Medicine, University of Oslo, Oslo, Norway.*
[15]*Department of Psychiatric Research, Diakonhjemmet Hospital, Oslo, Norway.*
[16]*Centre for Psychiatric Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden.*
[17]*Department of Molecular and Cellular Therapeutics, Royal College of Surgeons in Ireland, Dublin, Ireland.*
[18]*Neurology Department, Yale School of Medicine, New Haven, USA.*
[19]*Department of Human Genetics and South Texas Diabetes and Obesity Institute, University of Texas Rio Grande Valley School of Medicine, Brownsville, USA.*
[20]*Centre for Lifespan Changes in Brain and Cognition, Department of Psychology, University of Oslo, Oslo, Norway.*
[21]*Department of Integrative Medical Biology, Umeå University, Umeå, Sweden.*
[22]*Umeå Center for Functional Brain Imaging, Umeå University, Umeå, Sweden.*
[23]*Laboratory of Neuro Imaging, Mark and Mary Stevens Neuroimaging and Informatics Institute, Keck School of Medicine of the University of Southern California, Los Angeles, USA.*
[24]*Mathematics and Statistics, Murdoch University, Murdoch, Australia.*
[25]*Duke Molecular Physiology Institute, Duke University Medical Center, Durham, USA.*
[26]*School of Biomedical Sciences and Pharmacy, University of Newcastle, Callaghan, Australia.*
[27]*Priority Centre for Brain and Mental Health Research, University of Newcastle, Callaghan, Australia.*
[28]*The Hospital for Sick Children, University of Toronto, Toronto, Canada.*
[29]*Department of Psychiatry, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.*
[30]*Institute for Radiology and Neuroradiology, University Medicine, Ernst-Moritz-Arndt University, Greifswald, Germany.*

[31]*Department of Psychiatry, University of Münster, Münster, Germany*.
[32]*Centre for Neuroimaging & Cognitive Genomics, National University of Ireland Galway, Galway, Ireland*.
[33]*Douglas Mental Health University Institute, McGill University, Montreal, Canada*.
[34]*Departments of Psychiatry and Biological and Biomedical Engineering, McGill University, Montreal, Canada*.
[35]*Lieber Institute for Brain Development, Baltimore, USA*.
[36]*Institute for Molecular Bioscience, The University of Queensland, Brisbane, Australia*.
[37]*Genetic Epidemiology, QIMR Berghofer Medical Research Institute, Brisbane, Australia*.
[38]*Department of Neurosciences, University of California, San Diego, La Jolla, USA*.
[39]*Department of Radiology, University of California San Diego, San Diego, USA*.
[40]*Department of Psychiatry and Mental Health, University of Cape Town, Cape Town, South Africa*.
[41]*Department of Medical Genetics and Genomic Medicine, School of Medical Sciences, University of Campinas - UNICAMP, Campinas, Brazil*.
[42]*BRAINN - Brazilian Institute of Neuroscience and Neurotechnology, Campinas, Brazil*.
[43]*Faculty of Health, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia*.
[44]*Department of Biological Psychology, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*.
[45]*Alzheimer Center Amsterdam, Department of Neurology, Amsterdam Neuroscience, Vrije Universiteit Amsterdam, Amsterdam UMC, Amsterdam, The Netherlands*.
[46]*Division of Psychological & Social Medicine and Developmental Neurosciences, Faculty of Medicine, Technische Universität Dresden, Dresden, Germany*.
[47]*Division of Human Genetics, Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa*.
[48]*Division of Mind and Brain Research, Department of Psychiatry and Psychotherapy, Campus Charité Mitte, Charité - Universitätsmedizin Berlin corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany*.
[49]*Department of Cognitive Science, University of California San Diego, San Diego, USA*.
[50]*Cardiff University Brain Research Imaging Centre, Cardiff University, Cardiff, UK*.
[51]*San Francisco Veterans Administration Medical Center, San Francisco, USA*.
[52]*Division of Cerebral Integration, National Institute for Physiological Sciences, Okazaki, Japan*.
[53]*Psychiatric and Neurodevelopmental Genetics Unit, Center for Genomic Medicine, Massachusetts General Hospital, Boston, USA*.
[54]*Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Boston, USA*.
[55]*NORMENT - K.G. Jebsen Centre for Psychosis Research, Department of Clinical Science, University of Bergen, Bergen, Norway*.
[56]*School of Psychiatry, University of New South Wales, Sydney, Australia*.
[57]*Neuroscience Research Australia, Sydney, New South Wales, Australia*.
[58]*Department of Biomedical Engineering, Illinois Institute of Technology, Chicago, USA*.
[59]*Centre for Clinical Brain Sciences and Edinburgh Imaging, University of Edinburgh, Edinburgh, UK*.
[60]*Division of Psychiatry, University of Edinburgh, Edinburgh, UK*.

[61]*Duke UNC Brain Imaging and Analysis Center, Duke University Medical Center, Durham, USA*.
[62]*Mental Illness Research Education and Clinical Center for Post Deployment Mental Health, Durham VA Medical Center, Durham, USA*.
[63]*Department of Biomedicine, University of Basel, Basel, Switzerland*.
[64]*Institute of Medical Genetics and Pathology, University Hospital Basel, Basel, Switzerland*.
[65]*Department of Genomics, Life & Brain Research Center, University of Bonn, Bonn, Germany*.
[66]*Department of Cognitive and Clinical Neuropsychology, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*.
[67]*Research Division, Institute of Mental Health, Singapore, Singapore*.
[68]*Max Planck Institute of Psychiatry, Munich, Germany*.
[69]*Institute of Human Genetics, University of Bonn, School of Medicine & University Hospital Bonn, Bonn, Germany*.
[70]*Centre for Neuroimaging & Cognitive Genomics, School of Psychology, National University of Ireland Galway, Galway, Ireland*.
[71]*Department of Psychiatry, Fujita Health University School of Medicine, Toyoake, Japan*.
[72]*Department of Psychiatry and Psychotherapy, University Medicine Greifswald, Greifswald, Germany*.
[73]*Complex Trait Genetics, Center for Neurogenomics and Cognitive Research, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*.
[74]*Department of Neurology, Alzheimer Center, Amsterdam Neuroscience, Vrije Universiteit Medical Center, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*.
[75]*Institute of Science and Technology for Brain-Inspired Intelligence, Fudan University, Shanghai, China*.
[76]*Key Laboratory of Computational Neuroscience and Brain-Inspired Intelligence (Fudan University), Ministry of Education, Shanghai, China*.
[77]*Centre for Population Neuroscience and Precision Medicine (PONS), Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK*.
[78]*Institute of Neuroscience and Medicine (INM-1), Research Centre Jülich, Jülich, Germany*.
[79]*Department of Psychiatry, Psychotherapy and Psychosomatics, Medical Faculty, RWTH Aachen University, Aachen, Germany*.
[80]*JARA-BRAIN, Jülich-Aachen Research Alliance, Jülich, Germany*.
[81]*Department of Neuroinformatics, Araya, Inc., Tokyo, Japan*.
[82]*Sackler Centre for Consciousness Science, School of Psychology, University of Sussex, Falmer, UK*.
[83]*Earth-Life Science Institute, Tokyo Institute of Technology, Tokyo, Japan*.
[84]*Department of Psychiatry, McGill University, Montreal, Canada*.
[85]*McConnell Brain Imaging Center, Montreal Neurological Institute, Montreal, Canada*.
[86]*Department of Clinical and Experimental Epilepsy, UCL Queen Square Institute of Neurology, London, UK*.
[87]*Genomics England, Queen Mary University of London, London, UK*.
[88]*Public Psychiatry Division, Massachusetts Mental Health Center, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA*.
[89]*Psychiatry Neuroimaging Laboratory, Department of Psychiatry, Brigham and Women's Hospital, Harvard Medical School, Boston, USA*.

[90]*Department of Genome Informatics, Graduate School of Medicine, Osaka University, Suita, Japan*.
[91]*Department of Medical Biometry, Informatics and Epidemiology, University Hospital Bonn, Germany*.
[92]*Department of Psychology and Neuroscience, Duke University, Durham, USA*.
[93]*Section for Experimental Psychopathology and Neuroimaging, Department of General Psychiatry, Heidelberg University Hospital, Heidelberg, Germany*.
[94]*Centre for Translational Research in Systems Neuroscience and Psychiatry, Department of Psychiatry & Psychotherapy, University Medical Center Göttingen, Göttingen, Germany*.
[95]*Human Genetics, Genome Institute of Singapore, Singapore, Singapore*.
[96]*MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, UK*.
[97]*Department of Psychiatry, Harvard Medical School, Boston, USA*.
[98]*McGill Centre for Integrative Neuroscience, McGill University, Montreal, Canada*.
[99]*Department of Psychology, University of Edinburgh, Edinburgh, UK*.
[100]*Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK*.
[101]*Department of Psychiatry and Human Behavior, School of Medicine University of California, Irvine, Irvine, USA*.
[102]*Department of Cognitive Neuroscience, Radboud university medical center, Nijmegen, The Netherlands*.
[103]*Department of Psychiatry, Yale University School of Medicine, New Haven, USA*.
[104]*Olin Neuropsychiatric Research Center, Institute of Living, Hartford Hospital, Hartford, USA*.
[105]*Department of Medicine, University of Otago, Christchurch, Christchurch, New Zealand*.
[106]*New Zealand Brain Research Institute, Christchurch, New Zealand*.
[107]*Brain Research New Zealand - Rangahau Roro Aotearoa, Christchurch, New Zealand*.
[108]*Department of Psychiatry, Amsterdam Public Health and Amsterdam Neuroscience, Amsterdam UMC/Vrije Universiteit & GGZ inGeest, Amsterdam, Netherlands*.
[109]*Institute of Neurogenomics, Helmholtz Zentrum München, German Research Centre for Environmental Health, Neuherberg, Germany*.
[110]*IC - Institute of Computing, Campinas, Brazil*.
[111]*Cécile and Oskar Vogt Institute of Brain Research, Medical Faculty, Heinrich Heine University, Düsseldorf, Germany*.
[112]*Munich Cluster for Systems Neurology (SyNergy), Munich, Germany*.
[113]*Institute of Translational Medicine, Liverpool, UK*.
[114]*Drug Discovery Research, Astellas Pharmaceuticals, 21 Miyukigaoka, Tsukuba, Ibaraki 305-8585, Japan*.
[115]*Department of Radiology and Imaging Sciences, Indiana University School of Medicine, Indianapolis, USA*.
[116]*Center for Neurobehavioral Genetics, University of California Los Angeles, Los Angeles, USA*.
[117]*NeuroSpin, CEA, Université Paris-Saclay, Gif-sur-Yvette, France*.
[118]*Biostatistics and Computational Biology Unit, University of Otago, Christchurch, Christchurch, New Zealand*.
[119]*Department of Pathology and Biomedical Science, University of Otago, Christchurch, Christchurch, New Zealand*.
[120]*Department of Psychology, University of Oslo, Oslo, Norway*.

[121]*Sunnaas Rehabilitation Hospital HT, Nesodden, Norway*.
[122]*Department of Psychiatry, Radboud university medical center, Nijmegen, The Netherlands*.
[123]*Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, USA*.
[124]*Language and Genetics Department, Max Planck Institute for Psycholinguistics, Nijmegen, The Netherlands*.
[125]*Orygen, The National Centre of Excellence for Youth Mental Health, Melbourne, Australia*.
[126]*The Centre for Youth Mental Health, University of Melbourne, Melbourne, Australia*.
[127]*Department of Psychiatry, Vrije Universiteit University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*.
[128]*Neuroscience Research Australia, Sydney, Australia*.
[129]*School of Medical Sciences, University of New South Wales, Sydney, Australia*.
[130]*Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, USA*.
[131]*Population Neuroscience & Developmental Neuroimaging, Bloorview Research Institute, University of Toronto, East York, Canada*.
[132]*Donders Centre for Cognitive Neuroimaging, Radboud University, Nijmegen, The Netherlands*.
[133]*Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany*.
[134]*Centre for Healthy Brain Ageing, University of New South Wales, Sydney, Australia*.
[135]*Neuroimaging Unit, Technological Facilities, Valdecilla Biomedical Research Institute IDIVAL, Santander, Spain*.
[136]*Centro Investigacion Biomedica en Red Salud Mental, Santander, Spain*.
[137]*Department of Psychology, Georgia State University, Atlanta, USA*.
[138]*Mind Research Network, Albuquerque, USA*.
[139]*Department of Psychiatry, University of Vermont, Burlington, USA*.
[140]*NORMENT, Division of Mental Health and Addiction, Oslo University Hospital & Institute of Clinical Medicine, University of Oslo, Oslo, Norway*.
[141]*School of Mental Health and Neuroscience, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands*.
[142]*Max Planck Institute for Psycholinguistics, Nijmegen, The Netherlands*.
[143]*Department of Child and Adolescent Psychiatry/Psychology, Erasmus Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands*.
[144]*Cognitive Neuroscience Center, Department of Biomedical Sciences of Cells and Systems, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands*.
[145]*Department of Neurology, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands*.
[146]*MRC Integrative Epidemiology Unit, Department of Population Health Sciences, Bristol Medical School, Bristol, UK*.
[147]*Department of Psychology, University of Bath, Bath, UK*.
[148]*UK Dementia Research Institute, The University of Edinburgh, Edinburgh, UK*.
[149]*Department of Genetic Epidemiology in Psychiatry, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany*.
[150]*German Center for Neurodegenerative Diseases Rostock/Greifswald, Greifswald, Germany*.
[151]*Department of Psychiatry, Psychosomatics and Psychotherapy, University of Würzburg, Würzburg, Germany*.

[152]*Department of Neurology, FCM, UNICAMP, Campinas, Brazil.*
[153]*Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.*
[154]*INSERM Unit 1000 - Neuroimaging & Psychiatry, Paris Saclay University,Gif sur Yvette, France.*
[155]*Department of Psychiatry, University Hospital Marqués de Valdecilla, School of Medicine, University of Cantabria–IDIVAL, Santander, Spain.*
[156]*Department of Psychiatry and Frank Porter Graham Child Development Institute, University of North Carolina at Chapel Hill, Chapel Hill, USA.*
[157]*Department of Psychiatry, University of California San Diego, San Diego, USA.*
[158]*VA San Diego Healthcare System, San Diego, USA.*
[159]*Avera Institute for Human Genetics, Sioux Falls, USA.*
[160]*Department of Psychiatry and Psychotherapy, Philipps-University Marburg, Marburg, Germany.*
[161]*Department of Medical Genetics, Oslo University Hospital, Oslo, Norway.*
[162]*NORMENT, Department of Clinical Science, University of Bergen, Bergen, Norway.*
[163]*Department of Neurology, St James's Hospital, Dublin, Ireland.*
[164]*Academic Unit of Neurology, TBSI, Dublin, Ireland.*
[165]*Future Neuro, Royal College of Surgeons in Ireland, Dublin, Ireland.*
[166]*Information Sciences Institute, University of Southern California, Los Angeles, USA.*
[167]*Sir Peter Mansfield Imaging Centre, University of Nottingham, Nottingham, UK.*
[168]*Brigham and Women's Hospital, Boston, USA.*
[169]*The Broad Institute, Boston, USA.*
[170]*Harvard Medical School, Boston, USA.*
[171]*Center for Economics and Neuroscience, University of Bonn, Bonn, Germany.*
[172]*Institute of Experimental Epileptology and Cognition Research, University Hospital Bonn, Germany.*
[173]*Department of Clinical Radiology, University of Münster, Münster, Germany.*
[174]*Department of Psychiatry, University of Iowa College of Medicine, Iowa City, USA.*
[175]*HMNC Holding GmbH, Munich, Germany.*
[176]*University Medicine Greifswald, Interfaculty Institute for Genetics and Functional Genomics, Department of Functional Genomics, Greifswald, Germany.*
[177]*Institute of Diagnostic Radiology and Neuroradiology, Greifswald, Germany.*
[178]*Dept of Radiology, Mayo Clinic, Rochester, USA.*
[179]*Core-Unit Brainimaging, Faculty of Medicine, University of Marburg, Marburg, Germany.*
[180]*Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, USA.*
[181]*Department of Psychiatry, University of Minnesota, Minneapolis, USA.*
[182]*Department of Translational Neuroscience, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.*
[183]*GGNet Mental Health, Apeldoorn, The Netherlands.*
[184]*Department of Psychiatry and Weill Institute for Neurosciences, University of California San Francisco, San Francisco, USA.*
[185]*Mental Health Service 116d, Veterans Affairs San Francisco Healthcare System, San Francisco, USA.*
[186]*Department of Neurology, Johns Hopkins University, Baltimore, USA.*

[187]*Department of Radiology, Johns Hopkins University, Baltimore, USA.*
[188]*Pacific Brain Health Center, Santa Monica, USA.*
[189]*John Wayne Cancer Institute, Santa Monica, USA.*
[190]*Institute of Clinical Chemistry and Laboratory Medicine, University Medicine Greifswald, Greifswald, Germany.*
[191]*German Centre for Cardiovascular Research, Greifswald, Germany.*
[192]*Child and adolescent psychiatry department, APHP Pitié Salpêtrière hospital, Paris, France.*
[193]*Radiology and Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary, Calgary, Canada.*
[194]*School of Medicine, University of California Irvine, Irvine, USA.*
[195]*School of Medicine and Public Health, University of Newcastle, Callaghan, Australia.*
[196]*Priority Centre for Stroke and Brain Injury, University of Newcastle, Callaghan, Australia.*
[197]*Hunter Medical Research Institute, Newcastle, Australia.*
[198]*Department of Developmental Disability Neuropsychiatry, University of New South Wales, Sydney, Australia.*
[199]*Dr. Einar Martens Research Group for Biological Psychiatry, Center for Medical Genetics and Molecular Medicine, Haukeland University Hospital, Bergen, Norway.*
[200]*School of Psychology, Trinity College Dublin, Dublin, Ireland.*
[201]*Department of Radiology, Erasmus University Medical Centre, Rotterdam, The Netherlands.*
[202]*Department of Psychiatry, Osaka University Graduate School of Medicine, Suita, Japan.*
[203]*Department of Epidemiology, Erasmus MC Medical Center, Rotterdam, The Netherlands.*
[204]*Department of Radiology and Nuclear Medicine, Erasmus MC Medical Center, Rotterdam, The Netherlands.*
[205]*Department of Clinical Genetics, Erasmus MC Medical Center, Rotterdam, The Netherlands.*
[206]*Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, USA.*
[207]*Inserm, Bordeaux Population Health Research Center, team VINTAGE, UMR 1219, University of Bordeaux, Bordeaux, France.*
[208]*Department of Neurology, CHU de Bordeaux, Bordeaux, France.*
[209]*Department of Neurology, University of California, Davis, Sacramento, USA.*
[210]*Institute of Molecular Medicine, University of Texas Health Science Center at Houston, Houston, USA.*
[211]*Icelandic Heart Association, Kopavogur, Iceland.*
[212]*Faculty of Medicine, University of Iceland, Reykjavik, Iceland.*
[213]*Clinical Division of Neurogeriatrics, Department of Neurology, Medical University of Graz, Graz, Austria.*
[214]*Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, Graz, Austria.*
[215]*Laboratory of Epidemiology and Population Sciences, Intramural Research Program, National Institute on Aging, Bethesda, USA.*
[216]*Departments of Neurology and Epidemiology, University of Washington, Seattle, USA.*
[217]*Medical Informatics, Erasmus MC Medical Center, Rotterdam, The Netherlands.*
[218]*Neurodegeneratives Diseases Institute UMR 5293, CNRS, CEA, University of Bordeaux, Bordeaux, France.*
[219]*MIND Center, University of Mississippi Medical Center, Jackson, USA.*

[220]*Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, University of Texas Health Sciences Center, San Antonio, USA.*
[221]*Department of Epidemiology & Biostatistics, University of Texas Health Sciences Center, San Antonio, USA.*
[222]*Department of Neurology, Boston University School of Medicine, Boston, USA.*
[223]*Framingham Heart Study and Department of Neurology, Boston University School of Medicine, Boston, USA.*
[224]*Department of Biostatistics, Boston University School of Public Health, Boston, USA.*
[225]*Academic Unit for Psychiatry of Old Age, University of Melbourne, Melbourne, Australia.*
[226]*National Ageing Research Institute, Melbourne, Australia.*
[227]*Department of Neurology, Canterbury District Health Board, Christchurch, New Zealand.*
[228]*Department of Psychiatry, Melbourne Medical School, The University of Melbourne, Melbourne, Australia.*
[229]*Florey Institute of Neuroscience and Mental Health, University of Melbourne, Parkville, Australia.*
[230]*VA Mid-Atlantic Mental Illness Research Education and Clinical Center for Post Deployment Mental Health, Durham, VA Healthcare System, Durham, USA.*
[231]*Dementia Centre for Research Collaboration, University of New South Wales, Sydney, Australia.*
[232]*Department of Clinical Genetics and School for Oncology & Developmental Biology (GROW), Maastricht University Medical Center, Maastricht, The Netherlands.*
[233]*Department of Psychology and Center for Brain Science, Harvard University, Boston, USA.*
[234]*Department of Psychiatry, Massachusetts General Hospital, Boston, USA.*
[235]*Department of Radiology, Massachusetts General Hospital, Boston, USA.*
[236]*Karakter Child and Adolescent Psychiatry University Center, Nijmegen, The Netherlands.*
[237]*Department of Psychiatry, University of New Mexico, Albuquerque, USA.*
[238]*Department of Psychiatry, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.*
[239]*Schizophrenia Research Institute, Randwick, Australia.*
[240]*Tri-institutional Center for Translational Research in Neuroimaging and Data Science (TReNDS), Georgia State University, Georgia Institute of Technology, Emory University, Atlanta, USA.*
[241]*Department of Psychiatry, Monash University, Clayton, Australia.*
[242]*Institute for Anatomy I, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany.*
[243]*Molecular and Cellular Therapeutics, The Royal College of Surgeons In Ireland, Dublin, Ireland.*
[244]*The SFI FutureNeuro Research Centre, Dublin, Ireland.*
[245]*Department of Psychiatry, Trinity College Dublin, Dublin, Ireland.*
[246]*Hospital Universitario Virgen Del Rocio, IBiS, Universidad De Sevilla, Sevilla, Spain.*
[247]*School of Psychology, Speech and Hearing, University of Canterbury, Christchurch, New Zealand.*
[248]*Department of Neurology, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium.*
[249]*Department of Cognitive and Clinical Neuroscience, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany.*
[250]*Department of Psychiatry (UPK), University of Basel, Basel, Switzerland.*
[251]*Centre for Human Genetics, University of Marburg, Marburg, Germany.*

[252]*Tommy Fuss Center for Neuropsychiatric Disease Research, Boston Children's Hospital and Department of Psychiatry, Harvard Medical School, Boston, USA.*
[253]*Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway.*
[254]*Department of Radiology and Nuclear medicine, St. Olavs University Hospital, Trondheim, Norway.*
[255]*University of Groningen, University Medical Center Groningen, Department of Psychiatry, Groningen, The Netherlands.*
[256]*Molecular Research Center for Children's Mental Development, United Graduate School of Child Development, Osaka University, Suita, Japan.*
[257]*Department of Pathology of Mental Diseases, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan.*
[258]*Department of Psychiatry and Psychotherapy, Charité Campus Mitte, Charité - Universitätsmedizin Berlin, Berlin, Germany.*
[259]*Health Behaviour Research Group, University of Newcastle, Callaghan, Australia.*
[260]*Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.*
[261]*Department of Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.*
[262]*Department of Psychology, Yale University, New Haven, USA.*
[263]*Maryland Psychiatry Research Center, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, USA.*
[264]*Department of Comparative Medicine, The University of Texas MD Anderson Cancer Center, Bastrop, USA.*
[265]*Center for Human Development, University of California San Diego, La Jolla, USA.*
[266]*Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, USA.*
[267]*Neurogenetics and Epigenetics, Brain and Mind Centre, The University of Sydney, Sydney, Australia.*
[268]*Hunter New England Mental Health Service, Newcastle, Australia.*
[269]*Herston Imaging Research Facility, School of Clinical Sciences, Queensland University of Technology, Brisbane, Australia.*
[270]*Department of Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany.*
[271]*School of Psychology, University of Newcastle, Callaghan, Australia.*
[272]*Queensland Centre for Mental Health Research, The University of Queensland, Brisbane, Australia.*
[273]*Department of Radiation Sciences, Umeå University, Umeå, Sweden.*
[274]*Emma Children's Hospital Academic Medical Center, Amsterdam, The Netherlands.*
[275]*Department of Pediatrics, Vrije Universiteit Medical Center, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands.*
[276]*Clinical Neuropsychology section, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands.*
[277]*NorthWestern Mental Health, Sunshine Hospital, St Albans, Australia.*
[278]*Bloorview Research Institute, University of Toronto, Toronto, Canada.*
[279]*Departments of Psychology and Psychiatry, University of Toronto, Toronto, Canada.*
[280]*Centre for Developing Brain, Child Mind Institute, New York City, USA.*

[281]*Department of Physiology, University of Toronto, Toronto, Canada*.
[282]*Department of Clinical Genetics, Vrije Universiteit Medical Centre, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands*.
[283]*Neuropsychiatric Institute, The Prince of Wales Hospital, Sydney, Australia*.
[284]*PONS Research Group, Department of Psychiatry and Psychotherapie, Charité Campus Mitte, Humboldt University Berlin, Berlin, Germany*.
[285]*Leibniz Institute for Neurobiology, Magdeburg, Germany*.
[286]*Division of Molecular Medicine, John Hunter Hospital, New Lambton Heights, Australia*.
[287]*General Psychiatry, Institute of Mental Health, Singapore, Singapore*.
[288]*Chalfont Centre for Epilepsy, Chalfont-St-Peter, UK*.
[289]*Stanley Center for Psychiatric Research, Broad Institute, Boston, USA*.
[290]*Department of Medical and Biological Psychology, University of Bergen, Bergen, Norway*.
[291]*Department of Psychiatry and Neuroscience Institute, University of Cape Town, Cape Town, South Africa*.
[292]*MRC Unit on Risk & Resilience in Mental Disorders, University of Cape Town, Cape Town, South Africa*.
[293]*Department of Psychiatry, Leiden University Medical Center, Leiden, The Netherlands*.
[294]*Psychiatry, Neurology, Neuroscience, Genetics, Johns Hopkins University, Baltimore, USA*.
[295]*Centre for Advanced Imaging, University of Queensland, Brisbane, Australia*.
[296]*Center for Cognitive Neuroscience, Neuroscience and behavioral disorders program, Duke-National University of Singapore Medical School, Singapore, Singapore*.

Abstract: The cerebral cortex underlies our complex cognitive capabilities, yet we know little about the specific genetic loci influencing human cortical structure. To identify genetic variants impacting cortical structure, we conducted a genome-wide association meta-analysis of brain MRI data from 51,665 individuals. We analyzed the surface area and average thickness of the whole cortex and 34 regions with known functional specializations. We identified 237 significant loci and found significant enrichment for loci influencing total surface area within regulatory elements active during prenatal cortical development, supporting the radial unit hypothesis. Loci impacting regional surface area cluster near genes in Wnt signaling pathways, which influence progenitor expansion and areal identity. Variation in cortical structure is genetically correlated with cognitive function, Parkinson's disease, insomnia, depression, neuroticism, and ADHD.

One Sentence Summary: Common genetic variation is associated with inter-individual variation in the structure of the human cortex, both globally and within specific regions, and is shared with genetic risk factors for some neuropsychiatric disorders.

Main Text: The human cerebral cortex is the outer grey matter layer of the brain, which is implicated in multiple aspects of higher cognitive function. Its distinct folding pattern is characterized by convex (*gyral*) and concave (*sulcal*) regions. Computational brain mapping approaches use the consistent folding patterns across individual cortices to label brain regions (*1*). During fetal development excitatory neurons, the predominant neuronal cell-type in the cortex, are generated from neural progenitor cells in the developing germinal zone (*2*). The radial unit hypothesis (*3*) posits that the expansion of cortical surface area (SA) is driven by the proliferation of these neural progenitor cells, whereas thickness (TH) is determined by the number of their neurogenic divisions. Variation in global and regional measures of cortical SA and TH have been reliably associated with neuropsychiatric disorders and psychological traits (*4*) (table S1). Twin and family-based brain imaging studies indicate that SA and TH measurements are highly heritable and are influenced by largely different genetic factors (*5-7*). Despite extensive studies of genes impacting cortical structure in model organisms, our current understanding of the genetic variation impacting human cortical size and patterning is limited to rare, highly penetrant variants (*8, 9*). These variants often disrupt cortical development, leading to altered postnatal structure. However, little is known about how common genetic variants impact human cortical SA and TH.

To identify genetic loci associated with variation in the human cortex we conducted genome-wide association meta-analyses of cortical SA and TH measures in 51,665 individuals from 60 cohorts from around the world, who were primarily of European descent (~94%; tables S2–S4). Cortical measures were extracted from structural brain MRI scans in 34 regions defined by the commonly used Desikan-Killiany atlas, which establishes coarse partitions of the cortex. The regional boundaries are based on gyral anatomy labeled from between the depths of the sulci (*10, 11*). We analyzed two global measures, total SA and average TH, and SA and TH for the 34 regions averaged across both hemispheres, yielding 70 distinct phenotypes (Fig. 1A; table S1).

Within each cohort genome-wide association (GWAS) for each of the 70 phenotypes was conducted using an additive model. To identify genetic influences specific to each region, the primary GWAS of regional measures included the global measure of SA or TH as a covariate. To estimate the multiple testing burden associated with analyzing 70 phenotypes we used matrix spectral decomposition (*12*), which yielded 60 independent traits, and a multiple-testing significance threshold of $P \leq 8.3 \times 10^{-10}$.

The principal meta-analysis comprised results from 33,992 participants of European ancestry (23,909 from 49 cohorts participating in ENIGMA and 10,083 from the UK Biobank). We sought replication for loci reaching genome-wide significance ($P \leq 5 \times 10^{-8}$) in an additional ENIGMA cohort (777 participants) and with the CHARGE consortium (*13*) (13,952 participants). In addition, we meta-analyzed eight cohorts of non-European ancestry (2,944 participants) to examine the generalization of these effects across ancestries. High genetic correlations were observed between the meta-analyzed ENIGMA European cohorts and the UK Biobank cohort using LD-score regression (total SA $r_G = 1.00$, *Z*-score $P_{rG} = 2.7 \times 10^{-27}$, average TH $r_G = 0.91$, *Z*-score $P_{rG} = 1.7 \times 10^{-19}$, indicating consistent genetic architecture between the 49 ENIGMA cohorts and data collected from a single scanner at the primary UK Biobank imaging site.

Across the 70 cortical phenotypes we identified 369 loci that were genome-wide significant in the principal meta-analysis ($P \leq 5 \times 10^{-8}$; Fig. 1B; table S5). Of these, 190 have not been previously associated with either intracranial volume or cortical SA, TH, or volume (*13-18*). Twenty five of these were insertions or deletions (INDELs). Fourteen INDELs had a proxy single nucleotide polymorphism (SNP) available in the European replication data; no proxies were available for nine INDELs and one SNP. Of the 360 loci for which the SNP or a proxy was available, 307 (SA: 241, TH: 66) remained genome-wide significant when the replication data were included in the meta-analysis, with 237 passing multiple testing correction ($P \leq 8.3 \times 10^{-10}$; SA: 187, TH: 50). Of the 307 loci, 292 were available in the meta-analysis of non-European cohorts. The 95% confidence intervals around the non-European meta-analysis effect sizes included those from the European meta-analysis for 238 of these loci. Of the 292 loci available in the non-European cohorts, 279 had effects in the same direction in both the European and non-European meta-analyses, and 136 became more significant when the whole sample was meta-analyzed (table S5; fig. S1). Variability in effects across ancestry may be due to differences in allele frequency; however, the power for these comparisons is limited and further comparisons with larger non-European cohorts will help clarify the generalizability of these effects (table S5). We examined gene-based effects (allowing for a 50 kb window around genes), and found significant associations for 313 genes across the 70 cortical phenotypes (table S6). The meta-analytic results are summarized as Manhattan, QQ, Forest, and LocusZoom plots (figs. S2–S5).

Genetics of total SA and average TH

Common variants explained 34% (*SE* = 3%) of the variation in total SA and 26% (*SE* = 2%) in average TH. These estimates account for more than a third of the heritability estimated from the QTIM twin sample (91% for total SA and 64% for average TH; table S7), indicating that more genetic variants, including rare variants, are yet to be identified. To examine the extent to which our results could predict SA and TH, we derived polygenic scores (PRS) from the principal meta-analysis results. These scores significantly predicted SA and TH in an independent sample of 5,095 European participants, explaining between 2–3% of the trait variance (given a PRS threshold of $P \leq 0.01$ $R^2_{SA} = 0.029$, linear regression coefficient *t*-test $P = 6.54 \times 10^{-50}$; $R^2_{TH} = 0.022$, *t*-test $P = 3.34 \times 10^{-33}$; table S8).

We observed a significant negative genetic correlation between total SA and average TH ($r_G = -0.32$, *SE* = 0.05, *Z*-score $P_{rG} = 6.5 \times 10^{-12}$; Fig. 2A), which persisted after excluding the

chromosome 17 inversion region known to influence brain size (*14*) (r_G = -0.31, *SE* = 0.05, *Z*-score P_{rG} = 3.3 x 10^{-12}). Genetic correlations could indicate causal relationships between traits, pleiotropy, or a genetic mediator influencing both traits. Latent causal variable (LCV) analysis, which tests for causality using genome-wide data (*19*), showed no evidence of causation (LCV genetic causality proportion gcp = 0.06, *t*-test $P_{gcp=0}$ = 0.729). The negative correlation suggests that genetic influences have opposing effects on SA and TH, which may result from pleiotropic effects or genetic effects on a mediating trait that, for example, might constrain total cortical volume. The absence of causality and the small magnitude of this correlation is consistent with the radial unit hypothesis (*3*), whereby different developmental mechanisms promote SA expansion and increases in TH.

As expected, total SA showed a positive genetic correlation with intracranial volume (ICV); this correlation remained after controlling for height demonstrating that this relationship is not solely driven by body size (Fig. 2A; table S8). The global cortical measures did not show significant genetic correlations with the volumes of major subcortical structures (Fig. 2A) except for total SA and the hippocampus, consistent with their shared telencephalic developmental origin.

To identify if common variation associated with cortical structure relate to gene regulation within a given tissue type, developmental time period, or cell-type, we performed partitioned heritability analyses (*20*) using sets of gene regulatory annotations from adult and fetal brain tissues (*21, 22*). Total SA and average TH showed the strongest enrichment of heritability within genomic regions of active gene regulation (promoters and enhancers) in brain tissue and *in vitro* neural models derived from stem cell differentiation (Fig. 2B; fig. S6A). To examine temporally specific regulatory elements, we selected those active regulatory elements specifically present in either mid-fetal brain or adult cortex. Total SA showed significant enrichment of heritability only within mid-fetal specific active regulatory elements, whereas average TH showed significant enrichment only within adult specific active regulatory elements (Fig. 2C, fig S6B). Stronger enrichment was found in regions of the fetal cortex with more accessible chromatin in the neural progenitor-enriched germinal zone than in the neuron-enriched cortical plate (fig. S6C), similar to a previous analysis for intracranial volume (*21*). We then performed an additional partitioned heritability enrichment analysis using regulatory elements associated with cell-type specific gene expression derived from a large single-cell RNA-seq study of the human fetal brain (*23*). This analysis revealed significant enrichment of total SA heritability in all progenitor cell-types including those in active phases of mitosis as well as three different classes of progenitor cells including outer radial glia cells, a cell-type associated with expansion of cortical surface area in human evolution (*2*) (Fig 2D, fig S6D). We also identified significant enrichments in upper layer excitatory neurons, oligodendrocyte progenitor cells, and microglia. These findings suggest that total SA is influenced by common genetic variants that may alter gene regulatory activity in neural progenitor cells during fetal development, supporting the radial unit hypothesis (*3*). In contrast, the strongest evidence of enrichment for average TH was found in active regulatory elements in the adult brain samples, which may reflect processes occurring after mid-fetal development, such as myelination, branching, or pruning (*24*).

We conducted pathway analyses to determine if there was enrichment of association near genes in known biological pathways (*25*). We found 91 significant gene-sets for total SA and four for average TH (table S9). Gene-sets associated with total SA included chromatin binding, a process

guiding neurodevelopmental fate decisions (*26*) (table S9, fig. S7A). In addition, consistent with the partitioned heritability analyses implicating neural progenitor cells in total SA, gene ontology terms relevant to cell-cycle also showed significant enrichment in these analyses.

Loci influencing total SA and average TH

Seventeen of the 255 replicated loci were associated with total SA; 12 survived correction for multiple testing (Fig. 2E, table S5). Eight loci influencing total SA have been previously associated with ICV (*14*). These include rs79600142 (principal meta-analysis P_{MA} = 2.3 x 10^{-32}; replication P_{rep} = 3.5 x 10^{-43}; *P*-values reported from all meta-analytic results were for *Z*-scores from fixed-effect meta-analyses), in the highly pleiotropic chromosome 17q21.31 inversion region, which has been associated with Parkinson's disease (*27*), educational attainment (*28*), and neuroticism (*29*). On 10q24.33, rs1628768 (*Z*-score P_{MA} = 1.7 x 10^{-13}; P_{rep} = 1.0 x 10^{-17}) was shown by our bioinformatic annotations (*30*) to be an expression quantitative trait locus (eQTL) influencing expression levels of the *INA* gene, and of the schizophrenia candidate genes (*31*) *AS3MT*, *NT5C2* and *WBP1L* (linear regression coefficient *t*-test false discovery rate (FDR) corrected *P*-value for the association of rs1628768 with expression data from surrounding genes $FDR_{CommonMind\ Consortium(CMC)}$ < 1.0 x 10^{-2}; tables S11–S12). This region has been associated with schizophrenia, however, rs1628768 is in low linkage disequilibrium (LD) with the schizophrenia-associated SNP rs11191419 (r^2 = 0.15; (*32*)). The 6q21 locus influencing total SA is intronic to *FOXO3* (which also showed a significant gene-based association with total SA, table S6). The major allele of the lead variant rs2802295 is associated with larger total SA (*Z*-score P_{MA} = 2.5 x 10^{-10}; P_{rep} = 2.5 x 10^{-13}) and is in complete LD with rs2490272, a SNP previously associated with higher general cognitive function (*33*).

One locus not previously associated with ICV was rs11171739 (*Z*-score P_{MA} = 8.4 x 10^{-10}; P_{rep} = 8.1 x 10^{-11}) on 12q13.2. This SNP is in high LD with SNPs associated with educational attainment (*28*), and is an eQTL for *RPS26* in fetal (*34*) and adult cortex (*30*)(*t*-test of Pearson's *r* FDR_{FETAL} = 2.0 x 10^{-24}, empirical *t*-test of Pearson's *r* $FDR_{Genotype\text{-}Tissue\ Expression(GTEx)}$ = 3.3 x 10^{-40}; tables S11–S12). On 3p24.1, rs12630663 (*Z*-score P_{MA} = 1.3 x 10^{-8}; P_{rep} = 1.4 x 10^{-8}) is of interest due to its proximity (~200kb) to *EOMES* (also known as *TBR2*), which is expressed specifically in intermediate progenitor cells in the developing fetal cortex (*35*). rs12630663 is located in a chromosomal region with chromatin accessibility specific to the germinal zone in the human fetal cortex (*21*). Putatively causal SNPs in this region (table S13) show significant chromatin interactions with the *EOMES* promoter (*36*). The region also contains numerous regulatory elements that when excised via CRISPR/Cas9 in differentiating neural progenitor cells significantly reduced *EOMES* expression (*21*). A rare homozygous chromosomal translocation in the region separating the regulatory elements from *EOMES* (fig. S8) silences *EOMES* expression and causes microcephaly (*37*), demonstrating that rare and common non-coding variation can have similar phenotypic consequences, but to different degrees.

The two replicated loci associated with average TH, neither of which have been previously identified, survived correction for multiple testing (Fig. 2E; table S5). On 3p22.1, rs533577 (*Z*-score P_{MA} = 8.4 x 10^{-11}; P_{rep} = 3.7 x 10^{-12}) is a fetal cortex eQTL (*t*-test FDR_{FETAL}= 1.8 x 10^{-4}) for *RPSA,* encoding a 40S ribosomal protein with a potential role as a laminin receptor (*38*). Laminins are major constituents of extracellular matrix, and have critical roles in neurogenesis, neuronal differentiation and migration (*39*). On 2q11.2, rs11692435 (*Z*-score P_{MA} = 3.2 x 10^{-10};

P_{rep} = 4.5 x 10^{-10}) encodes a missense variant (p.A143V) predicted to impact ACTR1B protein function (*40*), and is an *ACTR1B* eQTL in fetal cortex (*t*-test FDR_{FETAL} = 3.9 x 10^{-2}) (tables S11–S12). *ACTR1B* is a subunit of the dynactin complex involved in microtubule remodeling, which is important for neuronal migration (*41*).

Genetics of regional SA and TH

The amount of phenotypic variance explained by common variants was higher for SA (8–31%) than TH (5–21%) for each of the specific cortical regions (Fig. 3A–B; table S7). To focus on region specific influences we controlled for global measures in the regional GWAS, which reduced the covariance between the regional measures (tables S14–S15). Similar to the genetic correlation between global SA and TH, when significant, genetic correlations between regional SA and TH within the same region were moderate and negative (tables S14–S15). This suggests that genetic variants contributing to the expansion of SA in a specific region tend to also contribute to thinner TH in that region.

Genetic correlations between regions were calculated separately for SA and TH. Most genetic correlations between regions did not survive multiple testing correction. For SA significant positive genetic correlations were generally found between physically adjacent regions and negative correlations between more distal regions (Fig. 3A). This pattern mirrored the phenotypic correlations between regions and was also observed for TH (Fig. 3A–B). Consistent with this, hierarchical clustering of the genetic correlations resulted in a general grouping by physical proximity (fig. S9). These positive genetic correlations were strongest between SA of regions surrounding the major, early forming sulci (e.g., pericalcarine, lingual, cuneus, and lateral occipital regions surrounding the calcarine sulcus), which may potentially reflect genetic effects acting on the development of the sulci (*11*).

To further investigate biological pathways influencing areal (regional) identity, we aggregated association statistics using multivariate GWAS analyses (*42*) separately for regional SA and TH. These analyses identify variants shared across regions and those within specific regions while accounting for the phenotypic correlations between regions. Pathway analyses of the multivariate SA results showed significant enrichment for 903 gene sets (table S10), many of which are involved in Wnt signaling, with the canonical Wnt signaling pathway showing the strongest enrichment (*Z*-score, *P* = 8.8 x 10^{-11}). Wnt proteins regulate neural progenitor fate decisions (*43, 44*) and are expressed in spatially specific manners influencing areal identity (*45*). Pathway analyses of the multivariate TH results did not yield any findings that survived multiple testing correction.

Loci influencing regional SA and TH

A total of 224 loci were nominally associated with regional SA and 64 with regional TH; of these 175 SA and 48 TH loci survived multiple testing correction (table S5). As shown in Fig. 1B, most loci were associated with a single cortical region. Of the loci influencing regional measures, few were also associated with global measures. Those that were showed effects in the same direction, implying that the significant regional loci were not due to collider bias (*46*) (fig. S10).

The strongest regional association was observed on chromosome 15q14 with the precentral SA (rs1080066, *Z*-score P_{MA} = 1.8 x 10^{-137}; P_{rep} = 4.6 x 10^{-189}; variance explained = 1.03%; Fig. 4A). Across 12 traits we observed 48 independent significant associations from 21 LD blocks (r^2 threshold ≤ 0.02; see Fig. 4B, table S5). As we observed strong association with the SA of both pre- and post-central gyri (Fig. 4C), we localized the association within the central sulcus in 5,993 unrelated individuals from the UK Biobank. The most significant association between rs1080066 and sulcal depth was observed around the *pli de passage fronto-pariétal moyen* (linear regression coefficient *t*-test *P* = 7.9 x 10^{-21}), a region associated with hand fine-motor function in humans (*47*), which shows distinct depth patterns across different species of primates (*48*) (Fig. 4D). rs1080066 is a fetal cortex eQTL for a downstream gene *EIF2AK4* (*t*-test FDR_{FETAL} = 4.8 x 10^{-2}) encoding the GCN2 protein, which is a negative regulator of synaptic plasticity, memory and neuritogenesis (*49*). The functional data also highlight *THBS1* via chromatin interaction between the rs1080066 region and the promoter in neural progenitor cells and an eQTL effect in whole blood (*Z*-score $FDR_{BIOSgenelevel}$ = 6.1 x 10^{-6}). *THBS1* has roles in synaptogenesis and the maintenance of synaptic integrity (*50*).

Consistent with enrichment in the pathway analyses, a number of other loci were located in regions with functional links to genes involved in Wnt signaling (fig. S7B), including 1p13.2, where rs2999158 (lingual SA, *Z*-score P_{MA} = 1.9 x 10^{-11}, P_{rep} = 3.0 x 10^{-11}; pericalcarine SA, *Z*-score P_{MA} = 1.9 x 10^{-11}; P_{rep} = 9.9 x 10^{-16}) is an eQTL for *ST7L* and *WNT2B* (*t*-test FDR_{CMC} < 1.0 x 10^{-2}) in adult cortex (tables S11–S12). On 14q23.1, we observed 22 significant loci (table S5) from five LD blocks. Our strongest association here was for the precuneus SA (rs73313052: *Z*-score P_{MA} = 1.1 x 10^{-24}; P_{rep} = 2.2 x 10^{-35}). These loci are located near *DACT1* and *DAAM1*, both involved in synapse formation and critical members of the Wnt signaling cascade (*51, 52*). rs73313052 and high LD proxies are eQTLs for *DAAM1 (t*-test FDR_{CMC} < 1.0 x 10^{-2}) in adult cortex (tables S11–S12).

Several of our regional associations occur near genes with known roles in brain development. For example, on chromosome 1p22.2, rs1413536 (associated with the inferior parietal SA: *Z*-score P_{MA} = 1.6 x 10^{-10}; P_{rep} = 3.1 x 10^{-14}) is an eQTL in adult cortex for *LMO4* (*t*-test FDR_{CMC} < 1.0 x 10^{-2}), with chromatin interactions between the region housing both this SNP and rs59373415 (which is associated with the precuneus SA: *Z*-score P_{MA} = 1.6 x 10^{-10}, P_{rep} = 5.3 x 10^{-12}) and the *LMO4* promoter in neural progenitor cells (table S11–S12). *Lmo4* is one of the few genes already known to be involved in areal identity specification in the mammalian brain (*53*).

Genetic relationships with other traits

To examine shared genetic effects between cortical structure and other traits, we performed genetic correlation analyses with GWAS summary statistics from 23 selected traits. We observed significant positive genetic correlations between total SA and general cognitive function (*54*), educational attainment (*28*), and Parkinson's disease (*27*), indicating that allelic influences resulting in larger total SA are in part shared with those influencing greater cognitive capabilities as well as an increased risk for Parkinson's disease. For total SA, significant negative genetic correlations were detected with insomnia (*55*), attention deficit hyperactivity disorder (ADHD; *56*), depressive symptoms (*57*), major depressive disorder (*58*), and neuroticism (*29*) (Fig. 5A; table S16), again indicating that allelic influences resulting in smaller total SA are in part shared with those influencing an increased risk for these disorders and traits. To map the magnitude of

these effects across the brain, we calculated the genetic correlations across the cortical regions without correction for the global measures (Fig. 5B). Genetic correlations with average TH did not survive multiple testing correction, perhaps due to the weaker genetic associations detected in the TH analyses. At the regional level, significant genetic correlations were observed between educational attainment and cortical thickness in the inferior parietal, precentral and rostral anterior cingulate regions (rG = -0.22, 0.16 and -0.16; Z-score PrG = 2.0 x 10-6, 6.8 x 10-5 and 8.0 x 10-5 respectively). Significant genetic correlations were also observed between precentral thickness and general cognitive function (rG = 0.19, Z-score PrG = 8.8 x 10-7) as well as between the posterior cingulate thickness and subjective well-being (rG = 0.25, Z-score PrG = 3.4 x 10-5). To confirm these correlations were not driven by the presence of cases within the meta-analysis, genetic correlations were recalculated from a meta-analysis of GWAS from population-based cohorts and GWAS of controls from the case-control cohorts (N = 28,503). All genetic correlations remained significant with the exception of the genetic correlation between total SA and depressive symptoms (table S17).

We performed bidirectional Mendelian randomization (MR; *59*) and LCV (*19*) analyses to investigate potential causal relationships underlying the observed genetic correlations with total SA. Both methods provided evidence of a causal effect of total SA on general cognitive function (inverse variance weighted MR $b_{MR\text{-}IVW}$ = 0.15, SE = 0.01, *Z*-score $P = 4.6 \times 10^{-8}$; LCV gcp = 0.40, 95% CIs [0.23–0.57], *t*-test $P_{gcp=0} = 1.4 \times 10^{-9}$) and educational attainment ($b_{MR\text{-}IVW}$ = 0.12, SE = 0.01, *Z*-score $P = 2.1 \times 10^{-21}$; gcp = 0.49, 95% CIs [0.26–0.72], *t*-test $P_{gcp=0} = 8.0 \times 10^{-9}$) (table S18–S19). The MR analyses also indicated association in the reverse direction for both general cognitive function and education years (table S18); however, this was not supported by the LCV analyses (table S19). There was limited to no support for a causal relationship in either direction between total SA and the six other traits that showed significant genetic correlations (table S18–S19). Taken together these findings suggest that the previously reported phenotypic relationships between cortical surface area and general cognitive function (*60, 61*) may in part reflect underlying causal processes.

Discussion

Here we present a large-scale collaborative investigation of the effects of common genetic variation on human cortical structure using data from 51,665 individuals from 60 cohorts. Current knowledge of genes impacting cortical structure has been derived largely from creating mutations in model systems, such as the mouse, and observing impacts on brain structure (*8*). Given the differences between mouse and human cortical structures (*62*), this study provides an important genome-wide insight into human variation and genes impacting a characteristically human phenotype. Previous studies have identified rare variants that have large effects on cortical structure in humans (*8*), and this study adds to the catalog of the type of variation that impacts human cortical structure.

We show that the genetic architecture of the cortex is highly polygenic and that variants often have a specific effect on individual cortical regions. This suggests that there are distinct genes involved in the development of specific cortical areas and raises the possibility of developmental and regional specificity in eQTL effects. We also find that rare variants and common variants in similar locations in the genome can lead to similar effects on brain structure, though to different degrees. For example, a balanced chromosomal translocation near *EOMES* leads to microcephaly

in a region abutting a common variant signal associated with small changes in cortical surface area (fig. S8).

We provide evidence that genetic variation impacting gene regulation in progenitor cell-types, present in fetal development, impacts adult cortical surface area. This is consistent with the radial unit hypothesis, which states that an increase in proliferative divisions of neural progenitor cells leads to an expansion of the pool of progenitors resulting in increases in neuronal production and cortical surface area (*3, 62*). Notably, we see an enrichment of heritability in cortical surface area within regulatory elements that influence outer radial glia cells, this cell-type is considerably more prevalent in gyrencephalic species such as humans and has been hypothesized to account for the increased progenitor pool size in humans (*2*).

We also find that Wnt signaling genes influence areal expansion in humans, as previously reported in model organisms such as mice (*45*). Cortical thickness was associated with loci near genes implicated in cell differentiation, migration, adhesion, and myelination. Consequently, molecular studies in the appropriate tissues, such as neural progenitor cells and their differentiated neurons, will be critical to map the involvement of specific genes.

We demonstrate that genetic variation associated with brain structure also impacts general cognitive function, Parkinson's disease, depression, neuroticism, ADHD, and insomnia. This implies that genetic variants impacting brain structure also impact brain function. While most of the structural differences in the cortex observed in these disorders have been reported for thickness, our results show significant genetic correlations in surface area. This might suggest the phenotypic differences observed in cortical thickness (table S1) partially reflect environmental influences, effects of illness or of treatment. We find evidence that brain structure is an important phenotype along the causal pathway leading from genetic variation to differences in general cognitive function and educational attainment.

In summary, this work identifies genome-wide significant loci associated with cortical surface area and thickness and provides a deeper understanding of the genetic architecture of the human cerebral cortex and its patterning.

Materials and Methods Summary:

Participants

Participants were genotyped individuals with cortical MRI data, from 60 cohorts. Participants in all cohorts in this study gave written informed consent and each site obtained approval from local research ethics committees or Institutional Review Boards. Ethics approval for the meta-analysis was granted by the QIMR Berghofer Medical Research Institute Human Research Ethics Committee (approval: *P2204*).

Imaging

Measures of cortical SA and TH were derived from *in vivo* whole brain T1-weighted MRI scans using FreeSurfer MRI processing software (*1*). SA and TH were quantified for each subject across the whole cortex and within 34 distinct gyral-defined regions according to the Desikan-Killiany atlas averaged across both hemispheres (*10*).

Genetic association analyses

Within each cohort, GWAS were conducted on each of the 70 imaging phenotypes. After quality control, these data were meta-analyzed using METAL (*63*). Initially the GWAS from European cohorts were meta-analyzed together, yielding the principal results that were used in all subsequent analyses. We sought replication of the genome-wide significant loci with data from the CHARGE consortium. To examine generalization of effects, the GWAS from the non-European cohorts were meta-analyzed together, and finally we meta-analyzed the European with the non-European results. Polygenic scores were derived from the principal meta-analysis and used to predict the amount of variance explained by the association of common genetic variants with the cortical SA and TH in an independent sample.

SNP heritability and tests for genetic correlations and causation

Heritability explained by common genetic variants (SNP heritability) was estimated using LD score regression (*64*). Genetic correlations between cortical regions were estimated using cross-trait LD score regression (*65*). To examine genetic relationships with other traits, we estimated genetic correlations using cross-trait LD score regression; to determine if these correlations were causal we used Mendelian randomization (*59*) and latent causal variable analyses (*19*).

Partitioned heritability

Partitioned heritability analysis was used to estimate the percentage of heritability explained by annotated regions of the genome (*66*). Heritability enrichment was first estimated in active regulatory elements across tissues and cell types (*21, 22*). Secondly, heritability enrichment was estimated in mid-fetal specific active regulatory elements and adult cortext specific active regulatory elements. Thirdly, heritability enrichment was estimated in regulatory elements of cell-type specific genes in fetal brain (*23*).

Functional follow-up

The principal meta-analytic results were followed up with gene-based association analysis using MAGMA (*67*). A multivariate analysis of the regional association results was conducted using TATES (*42*). Pathway analyses were conducted on the global measures and the results from the multivariate analyses using DEPICT to identify enrichment of association in known genetic functional pathways (*25*). To identify putatively causal variants we performed fine-mapping with CAVIAR (*68*). Potential functional impact was investigated using FUMA (*30*), which annotates the SNP location, nearby enhancers or promoters, chromatin state, associated eQTLs, and the potential for functional effects through predicted effects.

References and Notes:

1. B. Fischl, FreeSurfer. *Neuroimage* **62**, 774-781 (2012).
2. J. H. Lui, D. V. Hansen, A. R. Kriegstein, Development and evolution of the human neocortex. *Cell* **146**, 18-36 (2011).
3. P. Rakic, Specification of cerebral cortical areas. *Science* **241**, 170-176 (1988).
4. P. M. Thompson *et al.*, ENIGMA and global neuroscience: a decade of large-scale studies of the brain in health and disease across more than 40 countries. . *PsyArXiv*, (2019).
5. M. S. Panizzon *et al.*, Distinct genetic influences on cortical surface area and cortical thickness. *Cereb Cortex* **19**, 2728-2735 (2009).

6. A. M. Winkler *et al.*, Cortical thickness or grey matter volume? The importance of selecting the phenotype for imaging genetics studies. *Neuroimage* **53**, 1135-1146 (2010).
7. L. T. Strike *et al.*, Genetic complexity of cortical structure: differences in genetic and environmental factors influencing cortical surface area and thickness. *Cereb Cortex*, (2018).
8. B. I. Bae, D. Jayaraman, C. A. Walsh, Genetic changes shaping the human brain. *Dev Cell* **32**, 423-434 (2015).
9. D. W. Meechan, T. M. Maynard, E. S. Tucker, A. S. LaMantia, Three phases of DiGeorge/22q11 deletion syndrome pathogenesis during brain development: patterning, proliferation, and mitochondrial functions of 22q11 genes. *Int J Dev Neurosci* **29**, 283-294 (2011).
10. R. S. Desikan *et al.*, An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage* **31**, 968-980 (2006).
11. See supplementary materials.
12. D. R. Nyholt, A simple correction for multiple testing for single-nucleotide polymorphisms in linkage disequilibrium with each other. *Am J Hum Genet* **74**, 765-769 (2004).
13. E. Hofer *et al.*, Genetic determinants of cortical structure (thickness, surface area and volumes) among disease free adults in the CHARGE consortium. *bioRxiv*, 409649 (2019).
14. H. H. Adams *et al.*, Novel genetic loci underlying human intracranial volume identified through genome-wide association. *Nat Neurosci* **19**, 1569-1582 (2016).
15. L. T. Elliott *et al.*, Genome-wide association studies of brain imaging phenotypes in UK Biobank. *Nature* **562**, 210-216 (2018).
16. M. A. Ikram *et al.*, Common variants at 6q22 and 17q21 are associated with intracranial volume. *Nat Genet* **44**, 539-544 (2012).
17. D. P. Hibar *et al.*, Common genetic variants influence human subcortical brain structures. *Nature* **520**, 224-229 (2015).
18. J. L. Stein *et al.*, Identification of common variants associated with human hippocampal and intracranial volumes. *Nat Genet* **44**, 552-561 (2012).
19. L. J. O'Connor, A. L. Price, Distinguishing genetic correlation from causation across 52 diseases and complex traits. *bioRxiv*, 205435 (2017).
20. H. K. Finucane *et al.*, Heritability enrichment of specifically expressed genes identifies disease-relevant tissues and cell types. *Nat Genet* **50**, 621-629 (2018).
21. L. de la Torre-Ubieta *et al.*, The dynamic landscape of open chromatin during human cortical neurogenesis. *Cell* **172**, 289-304.e218 (2018).
22. Roadmap Epigenomics Consortium *et al.*, Integrative analysis of 111 reference human epigenomes. *Nature* **518**, 317-330 (2015).
23. D. Polioudakis *et al.*, A Single-Cell Transcriptomic Atlas of Human Neocortical Development during Mid-gestation. *Neuron* **103**, 785-801 e788 (2019).
24. J. C. Silbereis, S. Pochareddy, Y. Zhu, M. Li, N. Sestan, The cellular and molecular landscapes of the developing human central nervous system. *Neuron* **89**, 248-268 (2016).
25. T. H. Pers *et al.*, Biological interpretation of genome-wide association studies using predicted gene functions. *Nat Commun* **6**, 5890 (2015).
26. J. L. Ronan, W. Wu, G. R. Crabtree, From neural development to cognition: unexpected roles for chromatin. *Nat Rev Genet* **14**, 347-359 (2013).
27. M. A. Nalls *et al.*, Parkinson's disease genetics: identifying novel risk loci, providing causal insights and improving estimates of heritable risk. *bioRxiv*, 388165 (2018).
28. J. J. Lee *et al.*, Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. *Nat Genet* **50**, 1112-1121 (2018).
29. M. Nagel *et al.*, Meta-analysis of genome-wide association studies for neuroticism in 449,484 individuals identifies novel genetic loci and pathways. *Nat Genet* **50**, 920-927 (2018).
30. K. Watanabe, E. Taskesen, A. van Bochoven, D. Posthuma, Functional mapping and annotation of genetic associations with FUMA. *Nat Commun* **8**, 1826 (2017).
31. R. R. R. Duarte *et al.*, Genome-wide significant schizophrenia risk variation on chromosome 10q24 is associated with altered cis-regulation of BORCS7, AS3MT, and NT5C2 in the human brain. *Am J Med Genet B Neuropsychiatr Genet* **171**, 806-814 (2016).
32. Schizophrenia Psychiatric Genome-Wide Association Study Consortium, Biological insights from 108 schizophrenia-associated genetic loci. *Nature* **511**, 421-427 (2014).

33. S. Sniekers *et al.*, Genome-wide association meta-analysis of 78,308 individuals identifies new loci and genes influencing human intelligence. *Nat Genet* **49**, 1107-1112 (2017).
34. H. E. O'Brien *et al.*, Expression quantitative trait loci in the developing human brain and their enrichment in neuropsychiatric disorders. *Genome Biology* **19**, 194 (2018).
35. C. Englund *et al.*, Pax6, Tbr2, and Tbr1 are expressed sequentially by radial glia, intermediate progenitor cells, and postmitotic neurons in developing neocortex. *J Neurosci* **25**, 247-251 (2005).
36. H. Won *et al.*, Chromosome conformation elucidates regulatory relationships in developing human brain. *Nature* **538**, 523-527 (2016).
37. L. Baala *et al.*, Homozygous silencing of T-box transcription factor EOMES leads to microcephaly with polymicrogyria and corpus callosum agenesis. *Nat Genet* **39**, 454-456 (2007).
38. V. DiGiacomo, D. Meruelo, Looking into laminin receptor: critical discussion regarding the non-integrin 37/67-kDa laminin receptor/RPSA protein. *Biol Rev Camb Philos Soc* **91**, 288-310 (2016).
39. V. Solozobova, N. Wyvekens, J. Pruszak, Lessons from the embryonic neural stem cell niche for neural lineage differentiation of pluripotent stem cells. *Stem Cell Rev* **8**, 813-829 (2012).
40. C. Chelala, A. Khan, N. R. Lemoine, SNPnexus: a web database for functional annotation of newly discovered and public domain single nucleotide polymorphisms. *Bioinformatics* **25**, 655-661 (2009).
41. Y. Itoh, A balancing Akt: How to fine-tune neuronal migration speed. *Neurogenesis* **3**, e1256854 (2016).
42. S. van der Sluis, D. Posthuma, C. V. Dolan, TATES: efficient multivariate genotype-phenotype analysis for genome-wide association studies. *PLoS Genet* **9**, e1003235 (2013).
43. A. Chenn, C. A. Walsh, Regulation of cerebral cortical size by control of cell cycle exit in neural precursors. *Science* **297**, 365-369 (2002).
44. R. N. Munji, Y. Choe, G. Li, J. A. Siegenthaler, S. J. Pleasure, Wnt signaling regulates neuronal differentiation of cortical intermediate progenitors. *J Neurosci* **31**, 1676-1687 (2011).
45. S. J. Harrison-Uy, S. J. Pleasure, Wnt signaling and forebrain development. *CSH Perspect Biol* **4**, a008094 (2012).
46. H. Aschard, B. J. Vilhjalmsson, A. D. Joshi, A. L. Price, P. Kraft, Adjusting for heritable covariates can bias effect estimates in genome-wide association studies. *Am J Hum Genet* **96**, 329-339 (2015).
47. M. D. Cykowski *et al.*, The central sulcus: an observer-independent characterization of sulcal landmarks and depth asymmetry. *Cereb Cortex* **18**, 1999-2009 (2008).
48. W. D. Hopkins *et al.*, Evolution of the central sulcus morphology in primates. *Brain Behav Evol* **84**, 19-30 (2014).
49. M. Roffe, G. N. Hajj, H. F. Azevedo, V. S. Alves, B. A. Castilho, IMPACT is a developmentally regulated protein in neurons that opposes the eukaryotic initiation factor 2alpha kinase GCN2 in the modulation of neurite outgrowth. *J Biol Chem* **288**, 10860-10869 (2013).
50. A. R. Jayakumar *et al.*, Decreased astrocytic thrombospondin-1 secretion after chronic ammonia treatment reduces the level of synaptic proteins: in vitro and in vivo studies. *J Neurochem* **131**, 333-347 (2014).
51. R. Habas, Y. Kato, X. He, Wnt/Frizzled activation of Rho regulates vertebrate gastrulation and requires a novel Formin homology protein Daam1. *Cell* **107**, 843-854 (2001).
52. N. D. Okerlund *et al.*, Dact1 is a postsynaptic protein required for dendrite, spine, and excitatory synapse development in the mouse forebrain. *J Neurosci* **30**, 4362-4368 (2010).
53. Z. Huang *et al.*, Transcription factor Lmo4 defines the shape of functional areas in developing cortices and regulates sensorimotor control. *Dev Biol* **327**, 132-142 (2009).
54. J. E. Savage *et al.*, Genome-wide association meta-analysis in 269,867 individuals identifies new genetic and functional links to intelligence. *Nat Genet* **50**, 912-919 (2018).
55. P. R. Jansen *et al.*, Genome-wide analysis of insomnia in 1,331,010 individuals identifies new risk loci and functional pathways. *Nat Genet* **51**, 394-403 (2019).
56. D. Demontis *et al.*, Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. *Nat Genet* **51**, 63-75 (2019).
57. A. Okbay *et al.*, Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nat Genet* **48**, 624-633 (2016).
58. D. M. Howard *et al.*, Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions. *Nat Neurosci* **22**, 343-352 (2019).
59. G. Hemani *et al.*, The MR-Base platform supports systematic causal inference across the human phenome. *Elife* **7**, (2018).
60. M. A. McDaniel, Big-brained people are smarter: A meta-analysis of the relationship between in vivo brain volume and intelligence. *Intelligence* **33**, 337-346 (2005).

61. E. Vuoksimaa *et al.*, The Genetic Association Between Neocortical Volume and General Cognitive Ability Is Driven by Global Surface Area Rather Than Thickness. *Cereb Cortex* **25**, 2127-2137 (2015).
62. P. Rakic, Evolution of the neocortex: a perspective from developmental biology. *Nat Rev Neurosci* **10**, 724-735 (2009).
63. C. J. Willer, Y. Li, G. R. Abecasis, METAL: fast and efficient meta-analysis of genomewide association scans. *Bioinformatics* **26**, 2190-2191 (2010).
64. B. K. Bulik-Sullivan *et al.*, LD Score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nat Genet* **47**, 291-295 (2015).
65. B. Bulik-Sullivan *et al.*, An atlas of genetic correlations across human diseases and traits. *Nat Genet* **47**, 1236-1241 (2015).
66. H. K. Finucane *et al.*, Partitioning heritability by functional annotation using genome-wide association summary statistics. *Nat Genet* **47**, 1228-1235 (2015).
67. C. A. de Leeuw, J. M. Mooij, T. Heskes, D. Posthuma, MAGMA: generalized gene-set analysis of GWAS data. *PLoS Comput Biol* **11**, e1004219 (2015).
68. F. Hormozdiari, E. Kostem, E. Y. Kang, B. Pasaniuc, E. Eskin, Identifying causal variants at loci with multiple signals of association. *Genetics* **198**, 497-508 (2014).
69. The 1000 Genomes Project Consortium, A global reference for human genetic variation. *Nature* **526**, 68 (2015).
70. S. McCarthy *et al.*, A reference panel of 64,976 haplotypes for genotype imputation. *Nat Genet* **48**, 1279-1283 (2016).
71. S. Purcell *et al.*, PLINK: a tool set for whole-genome association and population-based linkage analyses. *Am J Hum Genet* **81**, 559-575 (2007).
72. C. A. Rietveld *et al.*, GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. *Science* **340**, 1467-1471 (2013).
73. S. Boker *et al.*, OpenMx: An Open Source Extended Structural Equation Modeling Framework. *Psychometrika* **76**, 306-317 (2011).
74. L. Scrucca, M. Fop, T. B. Murphy, A. E. Raftery, mclust 5: Clustering, Classification and Density Estimation Using Gaussian Finite Mixture Models. *R j* **8**, 289-317 (2016).
75. J. J. Tielbeek *et al.*, Genome-wide association studies of a broad spectrum of antisocial behavior. *JAMA Psychiatry* **74**, 1242-1250 (2017).
76. J. Grove *et al.*, Identification of common genetic risk variants for autism spectrum disorder. *Nat Genet* **51**, 431-444 (2019).
77. E. A. Stahl *et al.*, Genome-wide association study identifies 30 loci associated with bipolar disorder. *Nat Genet* **51**, 793-803 (2019).
78. L. Duncan *et al.*, Significant locus and metabolic genetic correlations revealed in genome-wide association study of anorexia nervosa. *Am J Psychiatry* **174**, 850-858 (2017).
79. International Obsessive Compulsive Disorder Foundation Genetics Collaborative (IOCDF-GC) and OCD Collaborative Genetics Association Studies (OCGAS), Revealing the complex genetic architecture of obsessive-compulsive disorder using meta-analysis. *Mol Psychiatry* **23**, 1181-1188 (2018).
80. L. E. Duncan *et al.*, Largest GWAS of PTSD (N=20 070) yields genetic overlap with schizophrenia and sex differences in heritability. *Mol Psychiatry* **23**, 666-673 (2018).
81. A. F. Pardinas *et al.*, Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection. *Nat Genet* **50**, 381-389 (2018).
82. T. Otowa *et al.*, Meta-analysis of genome-wide association studies of anxiety disorders. *Mol Psychiatry* **21**, 1391-1399 (2016).
83. I. Pappa *et al.*, A genome-wide approach to children's aggressive behavior: The EAGLE consortium. *Am J Med Genet B Neuropsychiatr Genet* **171**, 562-572 (2016).
84. I. E. Jansen *et al.*, Genome-wide meta-analysis identifies new loci and functional pathways influencing Alzheimer's disease risk. *Nat Genet* **51**, 404-413 (2019).
85. J. Gao *et al.*, Genome-wide association study of loneliness demonstrates a role for common variation. *Neuropsychopharmacol* **42**, 811-821 (2017).
86. Tobacco and Genetics Consortium, Genome-wide meta-analyses identify multiple loci associated with smoking behavior. *Nat Genet* **42**, 441-447 (2010).
87. International League Against Epilepsy Consortium on Complex Epilepsies, Genetic determinants of common epilepsies: a meta-analysis of genome-wide association studies. *Lancet Neurol* **13**, 893-903 (2014).

88. R. Ferrari *et al.*, Frontotemporal dementia and its subtypes: a genome-wide association study. *Lancet Neurol* **13**, 686-699 (2014).
89. M. Verbanck, C. Y. Chen, B. Neale, R. Do, Detection of widespread horizontal pleiotropy in causal relationships inferred from Mendelian randomization between complex traits and diseases. *Nat Genet* **50**, 693-698 (2018).
90. J. J. Lee, M. McGue, W. G. Iacono, A. M. Michael, C. F. Chabris, The causal influence of brain size on human intelligence: Evidence from within-family phenotypic associations and GWAS modeling. *Intelligence* **75**, 48-58 (2019).
91. H. F. Porter, P. F. O'Reilly, Multivariate simulation framework reveals performance of multi-trait GWAS methods. *Sci Rep* **7**, 38837 (2017).
92. M. Kircher *et al.*, A general framework for estimating the relative pathogenicity of human genetic variants. *Nat Genet* **46**, 310-315 (2014).
93. A. P. Boyle *et al.*, Annotation of functional variation in personal genomes using RegulomeDB. *Genome Res* **22**, 1790-1797 (2012).
94. The GTEx Consortium, Human genomics. The Genotype-Tissue Expression (GTEx) pilot analysis: multitissue gene regulation in humans. *Science* **348**, 648-660 (2015).
95. A. Ramasamy *et al.*, Genetic variability in the regulation of gene expression in ten regions of the human brain. *Nat Neurosci* **17**, 1418-1428 (2014).
96. M. Fromer *et al.*, Gene expression elucidates functional impact of polygenic risk for schizophrenia. *Nat Neurosci* **19**, 1442-1453 (2016).
97. D. Wang *et al.*, Comprehensive functional genomic resource and integrative model for the human brain. *Science* **362**, (2018).
98. P. M. Giusti-Rodriguez, P. F. Sullivan, Using three-dimensional regulatory chromatin interactions from adult and fetal cortex to interpret genetic results for psychiatric disorders and cognitive traits. *bioRxiv*, 406330 (2019).
99. D. V. Zhernakova *et al.*, Identification of context-dependent expression quantitative trait loci in whole blood. *Nat Genet* **49**, 139-145 (2017).
100. L. D. Ward, M. Kellis, HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic Acids Res* **40**, D930-934 (2012).
101. M. Perrot, D. Riviere, J. F. Mangin, Cortical sulci recognition and spatial normalization. *Med Image Anal* **15**, 529-550 (2011).
102. D. Riviere *et al.*, Automatic recognition of cortical sulci of the human brain using a congregation of neural networks. *Med Image Anal* **6**, 77-92 (2002).
103. W. D. Hopkins, O. Coulon, J. Mangin, Observer-independent characterization of sulcal landmarks and depth asymmetry in the central sulcus of the chimpanzee brain. *Neuroscience* **171**, 544-551 (2010).
104. O. Coulon *et al.*, Cortical localization via surface parameterization: a sulcus-based approach. *Neuroimage* **31**, 29-185 (2006).
105. O. Coulon *et al.*, Two new stable anatomical landmarks on the Central Sulcus: definition, automatic detection, and their relationship with primary motor functions of the hand. *Conf Proc IEEE Eng Med Biol Soc* **2011**, 7795-7798 (2011).
106. M. F. Glasser *et al.*, A multi-modal parcellation of human cerebral cortex. *Nature* **536**, 171 (2016).
107. J. D. Power *et al.*, Functional network organization of the human brain. *Neuron* **72**, 665-678 (2011).
108. B. T. T. Yeo *et al.*, The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of neurophysiology* **106**, 1125-1165 (2011).
109. G. W. Bruyn, Atlas of the cerebral sulci. *Clin Neurol Neurosur* **93**, 93 (1991).

Acknowledgments: We thank K. Courtney for making panel A and M. R. Glass for making panel C of the Research Article Summary figure. We thank all cohort participants for making this work possible. We thank the research support staff of all cohorts, including interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, nurses, carers, participating general practitioners, and pharmacists. In addition, ALSPAC are grateful to midwives for their help in recruiting the families who participated in the study and thank L. B. Clauss for help during the quality control process of the ALSPAC neuroimaging data. BETULA thank the Centre for Advanced Study at the Norwegian Academy of Science and Letters in Oslo for hosting collaborative projects and workshops between Norway

and Sweden in 2011–2012 and acknowledge that the image analyses were performed on resources provided by the Swedish National Infrastructure for Computing at HPC2N in Umeå. BONN thank (in alphabetical order) M. Bartling, U. Broicher, L. Ehrmantraut, A. Maaser, B. Mahlow, S. Mentges, K. Raczka, L. Schinabeck, and P. Trautner for their support and help. CARDIFF thank researchers within Cardiff University who contributed to the MBBrains panel. DNS thank the staff of the Laboratory of NeuroGenetics. FBIRN thank L. McMillan for overall study coordination and H. Mangalam, J. Farran, and A. Brenner for administering the University of California, Irvine High-Performance Computing cluster. GIG thank M. Keil, E. Diekhof, T. Melcher, and I. Henseler for assistance in data acquisition. IMpACT acknowledge that in this work samples from the Netherlands node of IMpACT were used and the work was carried out on the Dutch national e-infrastructure with the support of the SURF Cooperative. MCIC thank colleagues who served as mentors, advisors, and supporters during the inception and conduct of the study, including D. Goff, G. Kuperberg, J. Goldstein, M. Shenton, R. McCarley, S. Heckers, C. Wible, R. Mesholam-Gately, and M. Vangel, staff and clinicians at each site responsible for data acquisition including S. Wallace, A. Cousins, R. Mesholam-Gately, S. Stufflebeam, O. Freudenreich, D. Holt, L. Kunkel, F. Fleming, G. He, H. Johnson, R. Pierson, A. Caprihan, P. Somers, C. Portal, K. Norman, D. South, M. Doty, and H. Milner and the expert guidance on image and other types of data acquisition obtained from L. Friedman, S. Posse, J. Jovicich, and T. Wassink. MCIC also acknowledge the many research assistants, students and colleagues who assisted in data curation over the years since data acquisition was completed, including S. Wallace, C. Zyloney, K. Sawlani, J. Fries, A. Scott, D. Wood, R. Wang, W. Courtney, A. Guimaraes, L. Shenkman, M. Kendi, A. T. Karagulle Kendi, R. Muetzel, T. Biehl, and M. Schmidt. MIRECC thank the US military veterans who participated in this research. MPIP thank R. Schirmer, E. Schreiter, R. Borschke, I. Eidner, and A. Olynyik for supporting MR acquisition and data management, the staff of the Center of Applied Genotyping for generating the genotypes of the Munich Antidepressant Response Signature (MARS) cohort, D. P. Auer for initiating the RUD-MR substudy, E. Binder for supporting participation in ENIGMA, and GlaxoSmithKline for providing the genotypes of the Recurrent Unipolar Depression Case-Control Sample. PAFIP acknowledge the IDIVAL Neuroimaging Unit for imaging acquirement and analysis and Valdecilla Biobank for its help in the technical execution of this work. PDNZ are grateful to their colleagues including M. MacAskill, D. Myall, L. Livingston, B. Young, and S. Grenfell, staff at the New Zealand Brain Research Institute and Pacific Radiology Christchurch for study co-ordination and image acquisition, and Ms A. Miller for DNA preparation and banking. QTIM thank the many research assistants, radiographers, and IT support staff for data acquisition and DNA sample preparation. SHIP are grateful to M. Stanke for the opportunity to use his Server Cluster for the SNP imputation as well as to H. Prokisch and T. Meitinger (Helmholtz Zentrum München) for the genotyping of the SHIP-Trend cohort. Sydney MAS acknowledge the genome-wide genotyping was performed by the Ramaciotti Centre, University of New South Wales. Acknowledgements from CHARGE replication cohorts: Austrian Stroke Prevention Family /Austrian Stroke Prevention Family Study thank B. Reinhart for her long-term administrative commitment, E. Hofer for technical assistance in creating the DNA bank, Ing. J. Semmler and A. Harb for DNA sequencing and analyses by TaqMan assays, and I. Poelzl for supervising the quality management processes after ISO9001 at the biobanking and DNA analysis stages. Cardiovascular Health Study thank a full list of principal investigators and institutions that can be found at CHS-NHLBI.org. Framingham Heart Study (CHARGE) especially thank investigators and staff from the Neurology group for their contributions to data

collection. The generation and management of GWAS genotype data for the Rotterdam Study were executed by the Human Genotyping Facility of the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands. Rotterdam Study thank P. Arp, M. Jhamai, M. Verkerk, L. Herrera, M. Peters, and C. Medina-Gomez for their help in creating the GWAS database, and K. Estrada, Y. Aulchenko, and C. Medina-Gomez for the creation and analysis of imputed data. Three-City Dijon thank A. Boland (CNG) for technical help in preparing the DNA samples for analyses. The investigators of the frontotemporal GWAS (Ferrari et al, 2014, Lancet Neurol, PMID 24943344), the consortia members, and their acknowledgments are listed in the Supplementary Materials. **Funding:** This study was supported by U54 EB020403 from the NIH Big Data to Knowledge (BD2K) Initiative, a cross-NIH partnership. Additional support was provided by R01 MH116147, R01 MH1161671, P41 EB015922, RF1 AG051710, RF1 AG041915, R56 AG058854, R01 AG059874, R01 MH117601, the Michael J. Fox Foundation (MJFF; 14848), the Kavli Foundation, and by National Health and Medical Research Council (NHMRC) Project Grant 1158127 (to S.E.M). S.E.M. was funded by an NHMRC Senior Research Fellowship (APP1103623). K.L.G. was supported by APP1173025. L.C.-C. was supported by a QIMR Berghofer Fellowship. J.L.S. was supported by R01MH118349 and R00MH102357. 1000BRAINS thank the Heinz Nixdorf Foundation (Germany) for their generous support of the Heinz Nixdorf Recall Study, which is also supported by the German Federal Ministry of Education and Science (BMBF; FKZ 01EG940) and the German Research Foundation (DFG; ER 155/6-1). This work was further supported by the BMBF through the Integrated Network IntegraMent under the e:Med Program (01ZX1314A to S.Ci), and by the Swiss National Science Foundation (156791 to S.Ci). The Initiative and Networking Fund of the Helmholtz Association supported S.Ca, the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (H2020) supported S.Ci (Human Brain Project SGA1, 720270) and supported S.Ca and S.Ci (Human Brain Project SGA2, 785907). Alzheimer's Disease Neuroimaging Initiative (ADNI1 and ADNI2GO) was supported by NIH (U01 AG024904) and Department of Defense ADNI (W81XWH-12-2-0012). ADNI is funded by the National Institute on Aging (NIA), the National Institute of Biomedical Imaging and Bioengineering, and through generous contributions from: AbbVie; Alzheimer’s Association; Alzheimer’s Drug Discovery Foundation; Araclon Biotech; BioClinica, Inc.; Biogen; Bristol-Myers Squibb Company; CereSpir, Inc.; Cogstate; Eisai Inc.; Elan Pharmaceuticals, Inc.; Eli Lilly and Company; EuroImmun; F. Hoffmann-La Roche Ltd and its affiliated company Genentech, Inc.; Fujirebio; GE Healthcare; IXICO Ltd.; Janssen Alzheimer Immunotherapy Research & Development, LLC.; Johnson & Johnson Pharmaceutical Research & Development LLC.; Lumosity; Lundbeck; Merck & Co., Inc.; Meso Scale Diagnostics, LLC.; NeuroRx Research; Neurotrack Technologies; Novartis Pharmaceuticals Corporation; Pfizer Inc.; Piramal Imaging; Servier; Takeda Pharmaceutical Company; and Transition Therapeutics. The Canadian Institutes of Health Research provided funds to support ADNI clinical sites in Canada. Private sector contributions were facilitated by the Foundation for the National Institutes of Health (www.fnih.org). The grantee organization is the Northern California Institute for Research and Education, and the study was coordinated by the Alzheimer’s Therapeutic Research Institute at the University of Southern California. Samples used in this study were from the National Centralized Repository for Alzheimer's Disease and Related Dementias, which received government support under a cooperative agreement grant (U24 AG21886) awarded by the NIA. Support for data analysis was provided by NLM R01 LM012535 and NIA R03 AG054936 (to K.N.). The UK Medical Research Council (MRC) and

Wellcome (102215/2/13/2) and the University of Bristol provide core support for ALSPAC. A comprehensive list of grants funding is available on the ALSPAC website (http://www.bristol.ac.uk/alspac/external/documents/grant-acknowledgements.pdf). ALSPAC neuroimaging data was specifically funded by RO1 MH085772 (to T.P.). GWAS data was generated by Sample Logistics and Genotyping Facilities at Wellcome Sanger Institute and LabCorp (Laboratory Corporation of America) using support from 23andMe. Data and sample collection by the Australian Schizophrenia Research Bank (ASRB) was supported by the Australian NHMRC, the Pratt Foundation, Ramsay Health Care, and the Viertel Charitable Foundation. The ASRB were also supported by the Schizophrenia Research Institute (Australia), utilizing infrastructure funding from NSW Health and the Macquarie Group Foundation. DNA analysis was supported by the Neurobehavioral Genetics Unit, utilizing funding from NSW Health and the NHMRC Project Grants (1067137, 1147644, 1051672). M.C. was supported by an NHMRC Senior Research Fellowship (1121474). C.P. was supported by a NHMRC Senior Principal Research Fellowship (628386 and 1105825). BETULA was supported by a Wallenberg Scholar grant from the Knut and Alice Wallenberg Foundation and a grant from Torsten and Ragnar Söderbergs Foundation to L.N., HelseVest RHF (911554 to S.L.H.), grants from the Bergen Research Foundation and the University of Bergen to S.L.H., grants from the Dr Einar Martens Fund and the K.G. Jebsen Foundation to S.L.H. and V.M.S., the Research Council of Norway (177458/V 50 to T.E. and 204966/F 20 to L.T.W.). Nijmegen's BIG resource is part of Cognomics, a joint initiative by researchers of the Donders Centre for Cognitive Neuroimaging, the Human Genetics and Cognitive Neuroscience departments of the Radboud University Medical Center, and the Max Planck Institute for Psycholinguistics (funded by the Max Planck Society). Support for the Cognomics Initiative, including phenotyping and genotyping of BIG cohorts, comes from funds of the participating departments and centres and from external national grants: the Biobanking and Biomolecular Resources Research Infrastructure (Netherlands) (BBMRI-NL), the Hersenstichting Nederland, and the Netherlands Organisation for Scientific Research (NWO), including the NWO Brain & Cognition Excellence Program (433-09-229) and the Vici Innovation Program (016-130-669 to B.F.). Additional support was received from the European Union's Seventh Framework Program (FP7) [602805 (Aggressotype), 602450 (IMAGEMEND), and 278948 (TACTICS)], from H2020 [643051 (MiND) and 667302 (CoCA)], and from the Innovative Medicines Initiative 2 Joint Undertaking (H2020/EFPIA) [115916 (PRISM)]. BONN was supported by the Frankfurt Institute for Risk Management and Regulation and B.W. was supported by a Heisenberg Grant of the DFG [WE 4427 (3-2)]. BrainScale was supported by NWO (NWO 51.02.061 to H.E.H.P., NWO 51.02.062 to D.I.B., NWO-NIHC Programs of excellence 433-09-220 to H.E.H.P., NWO-MagW 480-04-004 to D.I.B., and NWO/SPI 56-464-14192 to D.I.B.), FP7 Ideas: European Research Council (ERC-230374 to D.I.B.), and Universiteit Utrecht (High Potential Grant to H.E.H.P.). CARDIFF genotyping was supported by the National Centre for Mental Health. T.M.L. is funded by a Sêr Cyrmu II Fellowship (East Wales European Regional Development Funds (PNU-80762-CU-14) at the Dementia Research Institute, Cardiff University. DNS received support from Duke University as well as NIH (R01DA033369 and R01DA031579). Work from the London cohort of EPIGEN was supported by research grants from the Wellcome Trust (084730 to S.M.S.), University College London (UCL)/University College London Hospitals (UCLH) National Institute for Health Research (NIHR) Biomedical Research Centre/Specialist Biomedical Research Centres (CBRC/SBRC) (114 to S.M.S.), the Comprehensive Local Research Network Flexibility and Sustainability Funding (CEL1300 to S.M.S.), The Big Lottery Fund, the Wolfson

Trust, and the Epilepsy Society. This work was partly undertaken at UCLH/UCL, which received a proportion of funding from the NIHR CBRC/SBRC. FBIRN was supported by the NIH National Center for Research Resources (NCRR) [NIH 1 U24 RR021992 (Function Biomedical Informatics Research Network), NIH 1 U24 RR025736-01 (Biomedical Informatics Research Network Coordinating Center)], the NIH National Center for Research Resources and the National Center for Advancing Translational Sciences (UL1 TR000153), and the NIH through 5R01MH094524, and P20GM103472. This work was supported in part by a Merit Review Award I01CX000497 (J.M.F.) and a Senior Research Career Award (J.M.F.) from the United States Department of Veterans Affairs, Clinical Sciences Research and Development Service. FOR2107 was funded by the DFG (FOR2107 DA1151/5-1 and DA1151/5-2 to U.D.; JA1890/7-1, JA1890/7-2 to A.J.; KI 588/14-1, KI 588/14-2 to T.K.; KR 3822/7-1, KR 3822/7-2 to A.K.; NO246/10-1, NO246/10-2 to M.M.N.). GOBS was supported by the National Institute of Mental Health MH0708143 (to D.C.G.), MH078111 (to J.Bl.), and MH083824 (to D.C.G. and J.Bl.). Brain Genomics Superstruct Project (GSP) was made possible by the resources provided through Shared Instrumentation Grants 1S10RR023043 and 1S10RR023401 and was supported by funding from the Simons Foundation (to R.L.B.), the Howard Hughes Medical Institute (to R.L.B.), NIMH grants R01-MH079799 (to J.W.S.), K24MH094614 (to J.W.S.), K01MH099232 (to A.J.H.), and the Massachusetts General Hospital-University of Southern California Human Connectome Project (U54MH091665). HUBIN was supported by the Swedish Research Council (2006-2992, 2006-986, K2007-62X-15077-04-1, K2008-62P-20597-01-3, 2008-2167, 2008-7573, K2010-62X-15078-07-2, K2012-61X-15078-09-3, 14266-01A,02-03, 2017-949), the regional agreement on medical training and clinical research between Stockholm County Council and the Karolinska Institutet, the Knut and Alice Wallenberg Foundation, and the HUBIN project. HUNT-MRI was funded by the Liaison Committee between the Central Norway Regional Health Authority and the Norwegian University of Science and Technology, and the Norwegian National Advisory Unit for functional MRI. IMAGEN was supported by the European Union's FP6 Integrated Project IMAGEN (LSHM-CT- 2007-037286), the H2020 ERC Advanced Grant STRATIFY (695313), ERANID (PR-ST-0416-10004), BRIDGET (JPND: MR/N027558/1), the FP7 projects IMAGEMEND (602450) and MATRICS (603016), the Innovative Medicine Initiative Project EU-AIMS (115300-2), the Medical Research Foundation and MRC (MR/R00465X/1), the MRC (MR/N000390/1), the Swedish Research Council FORMAS, the NIHR Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, the BMBF (01GS08152, 01EV0711, eMED SysAlc01ZX1311A, Forschungsnetz AERIAL), and the DFG (SM 80/7-1, SM 80/7-2, SFB 940/1). Further support was provided from: ANR (AF12-NEUR0008-01 – WM2NA, and ANR-12-SAMA-0004), the Fondation de France, the Fondation pour la Recherche Médicale, the Mission Interministérielle de Lutte-contre-les-Drogues-et-les-Conduites-Addictives (MILDECA), the Fondation pour la Recherche Médicale (DPA20140629802), the Fondation de l'Avenir, Paris Sud University IDEX 2012,the National Institutes of Health, Science Foundation Ireland (16/ERCD/3797), the NIH (RO1 MH085772-01A1). IMH was supported by the National Healthcare Group, Singapore (SIG/05004; SIG/05028) and the Singapore Bioimaging Consortium (RP C-009/2006) research grants awarded to K.S.; M.La. was supported by an National Medical Research Council Research Training Fellowship (MH095: 003/008-1014) and Singapore Ministry of Health National Medical Research Council Center Grant (NMRC/CG/004/2013). IMpACT was supported by the NWO (433-09-229) and the Vici Innovation Program (016-130-669 to B.F.). Additional support was received from the ERC under

FP7 [602805 (Aggressotype), 602450 (IMAGEMEND), and 278948 (TACTICS)] as well as from H2020 [643051 (MiND), 667302 (CoCA), and 728018 (Eat2beNICE)]. LBC1936 was supported by a Research into Ageing programme grant (to I.J.D.) and the Age UK-funded Disconnected Mind project (http://www.disconnectedmind.ed.ac.uk; to I.J.D. and J.M.W.), with additional funding from the UK MRC (Mr/M01311/1, G1001245/96077, G0701120/79365 to I.J.D., J.M.W. and M.E.B.). The whole genome association part of this study was funded by the Biotechnology and Biological Sciences Research Council (BBSRC; BB/F019394/1). J.M.W. is supported by the Scottish Funding Council through the SINAPSE Collaboration (http://www.sinapse.ac.uk). CCACE (MRC MR/K026992/1) is funded by the BBSRC and MRC. LIBD was supported by direct funding from the NIMH intramural research program of the NIH to the Weinberger Lab and by support from the Lieber Institute for Brain Development and the Maltz Research Laboratories. MCIC was supported primarily by the Department of Energy DE-FG02-99ER62764 through its support of the Mind Research Network (MRN, formerly known as the MIND Institute) and the consortium as well as by the National Association for Research in Schizophrenia and Affective Disorders (NARSAD) Young Investigator Award (to S.Eh.), through the Blowitz-Ridgeway and Essel Foundations and a ZonMw TOP 91211021 (to T.Wh.), a DFG research fellowship (to S.Eh.), the MRN, the NIH through NCRR 5MO1-RR001066 (MGH General Clinical Research Center), NIMH K08 MH068540, the Biomedical Informatics Research Network with NCRR Supplements to P41 RR14075 (MGH), M01 RR 01066 (MGH), NIBIB R01EB006841 (MRN), R01EB005846 (MRN), 2R01 EB000840 (MRN), 1RC1MH089257 (MRN), as well as grant U24 RR021992. Meth-CT was supported by the Medical Research Council, South Africa. MIRECC was supported by NIMH (1R01MH111671) and the US Department of Veterans Affairs (VISN6 MIRECC). MooDS was supported by the BMBF grants [National Genome Research Network Plus (MooDS: Systematic Investigation of the Molecular Causes of Major Mood Disorders and Schizophrenia, http://www.ngfn.de/en/schizophrenie.html); e:Med Programme: Integrated Network IntegraMent (01ZX1314A to M.M.N.; 01ZX1614A to F.D. and M.M.N.)], and was supported by DFG (FOR 1617) as well as Excellence Cluster (EXC 257). MPIP was supported by a grant of the Exzellenz-Stiftung of the Max Planck Society and by the BMBF National Genome Research Network (FKZ 01GS0481). MPRC was supported by the NIH (R01MH116948, R01MH112180, U01MH108148, UG3DA047685, 2R01EB015611, R01DA027680, R01MH085646, P50MH103222, U54 EB020403, and T32MH067533), NSF (IIS-1302755 and MRI-1531491), a State of Maryland contract (M00B6400091), and a Pfizer research grant. MÜNSTER was funded by the DFG (SFB-TRR58, Projects C09 and Z02 to U.D.) and the Interdisciplinary Center for Clinical Research of the medical faculty of Münster (Dan3/012/17 to U.D.). NCNG was supported by the Bergen Research Foundation, the University of Bergen, the Research Council of Norway [FUGE (151904 and 183327), Psykisk Helse (175345), RCN (154313/V50 to I.R. and 177458/V50 to T.E.)], Helse Sørøst RHF (2012086 to T.E.), and Dr Einar Martens Fund. NESDA obtained funding from the NWO (Geestkracht program10-000-1002); the Center for Medical Systems Biology (CSMB, NWO Genomics), BBMRI-NL, VU University's Institutes for Health and Care Research (EMGO+) and Neuroscience Campus Amsterdam, University Medical Center Groningen, Leiden University Medical Center, NIH (R01D0042157-01A, MH081802, Grand Opportunity grants 1RC2 MH089951 and 1RC2 MH089995). Part of the genotyping and analyses were funded by the Genetic Association Information Network (GAIN) of the Foundation for the National Institutes of Health. Computing was supported by BiG Grid, the Dutch e-Science Grid, which is financially supported by NWO. The NeuroIMAGE study was

supported by NIH Grant R01MH62873, NWO Large Investment Grant 1750102007010 (to J.K.B.), ZonMW grant 60-60600-97-193, NWO grants 056-13-015 and 433-09-242, and matching grants from Radboud University Nijmegen Medical Center, University Medical Center Groningen and Accare, and Vrije Universiteit Amsterdam. Further support was received from the FP7 [278948 (TACTICS), 602450 (IMAGEMEND), 602805 (Aggressotype)], and H2020 [667302 (CoCA) and 728018 (Eat2beNICE)]. Netherlands Twin Register (NTR) obtained funding from NWO and ZonMW grants (904-61-090, 985-10-002, 912-10-020, 904-61-193,480-04-004, 463-06-001, 451-04-034, 400-05-717, Addiction-31160008, 016-115-035, 481-08-011, 056-32-010, Middelgroot-911-09-032, OCW_NWO Gravity program –024.001.003, NWO-Groot 480-15-001/674), Center for Medical Systems Biology (CSMB, NWO Genomics), NBIC/BioAssist/RK (2008.024), BBMRI–NL (184.021.007 and 184.033.111); Spinozapremie (NWO- 56-464-14192), KNAW Academy Professor Award (PAH/6635) and University Research Fellow grant to DIB; Amsterdam Public Health research institute (former EMGO+) , Neuroscience Amsterdam research institute (former NCA); the European Science Foundation (EU/QLRT-2001-01254), FP7 (FP7- HEALTH-F4-2007-2013: 01413 (ENGAGE) and 602768 (ACTION)]; the ERC (ERC Advanced, 230374, ERC Starting grant 284167), Rutgers University Cell and DNA Repository (NIMH U24 MH068457-06), the NIH (R01D0042157-01A1, R01MH58799-03, MH081802, DA018673, R01 DK092127-04, Grand Opportunity grants 1RC2 MH089951, and 1RC2 MH089995); the Avera Institute for Human Genetics, Sioux Falls, South Dakota (USA). Part of the genotyping and analyses were funded by the Genetic Association Information Network (GAIN) of the Foundation for the National Institutes of Health. Computing was supported by NWO through 2018/EW/00408559, BiG Grid, the Dutch e-Science Grid and SURFSARA. OATS was supported by the Australian NHMRC/Australian Research Council Strategic Award (401162) and NHMRC Project Grant (1405325). The study was facilitated through Twins Research Australia, a national resource in part supported by a Centre for Research Excellence from the NHMRC. DNA was extracted by Genetic Repositories Australia (NHMRC Grant 401184). Genome-wide genotyping at the Diamantina Institute, University of Queensland, was partly funded by a CSIRO Flagship Collaboration Fund Grant. OSAKA was supported by AMED under JP18dm0307002, JP18dm0207006 (Brain/MINDS) and JSPS KAKENHI J16H05375. PAFIP was supported by the Instituto de Salud Carlos III (PI14/00639 and PI14/00918), MINECO (SAF2010-20840-C02-02 and SAF2013-46292-R) and Fundación Instituto de Investigación Marqués de Valdecilla (NCT0235832 and NCT02534363). PDNZ was supported by the Health Research Council, the Neurological Foundation of New Zealand, Canterbury Medical Research Foundation, University of Otago Research Grant, and Jim and Mary Carney Charitable Trust (Whangarei, New Zealand). PING was supported by the National Institute on Drug Abuse (RC2DA029475) and the U.S. National Institute of Child Health and Human Development (R01HD061414). Parkinson's Progression Markers Initiative (PPMI), a public-private partnership, is funded by the Michael J. Fox Foundation for Parkinson’s Research and funding partners, including AbbVie, Allegran, Avid Radiopharmaceuticals, Biogen Idec, BioLegend, Bristol-Meyers Squibb, Denali Therapeutics, GE Healthcare, Genentech, GSK-GlaxoSmithKline, Eli Lilly & Co., F. Hoffman-La Roche Ltd., Lundbeck Pharmaceuticals, Merck and Company, MSD-Meso Scale Discovery, Pfizer, Piramal, Sanofi Genzyme, Servier, Takeda Pharmaceutical Company, TEVA Pharmaceutical Industries, UCB Pharma SA, and Golub Capital (http://www.ppmi-info.org/about-ppmi/who-we-are/study-sponsors/). QTIM was supported by the National Institute of Child Health and Human Development (R01 HD050735), National Institute of Biomedical Imaging and Bioengineering (Award 1U54EB020403-01,

Subaward 56929223), and NHMRC (Project Grants 496682, 1009064 and Medical Bioinformatics Genomics Proteomics Program 389891). SHIP is part of the Community Medicine Research net of the University of Greifswald, Germany, which is funded by the DFG (01ZZ9603, 01ZZ0103, and 01ZZ0403), the Ministry of Cultural Affairs, the Social Ministry of the Federal State of Mecklenburg-West Pomerania, and the network 'Greifswald Approach to Individualized Medicine (GANI_MED)' funded by the DFG (03IS2061A). Whole-body MR imaging was supported by a joint grant from Siemens Healthineers, Erlangen, Germany and the Federal State of Mecklenburg West Pomerania. Genome-wide data have been supported by the DFO (03ZIK012) and a joint grant from Siemens Healthineers, Erlangen, Germany and the Federal State of Mecklenburg- West Pomerania. The University of Greifswald is a member of the Caché Campus program of the InterSystems GmbH. Sydney MAS was supported by the NHMRC/Australian Research Council Strategic Award (401162) and NHMRC Program Grants (350833, 568969). DNA was extracted by Genetic Repositories Australia (NHMRC Grant 401184). SYS has been funded by the Canadian Institutes of Health Research and the Heart and Stroke Foundation of Canada. Computations were performed on the GPC supercomputer at the SciNet HPC Consortium. SciNet is funded by the Canada Foundation for Innovation under the auspices of Compute Canada; the Government of Ontario; Ontario Research Fund - Research Excellence, and the University of Toronto. TCD-NUIG included data from two sites. NUI Galway data collection was supported by the Health Research Board (HRA_POR/2011/100). Trinity College Dublin was supported by The Science Foundation Ireland Research Investigator project (12.IP.1359 to G.D.). TOP and TOP3T are part of TOP, which is supported by the Research Council of Norway (223273, 213837, 249711, 226971, 262656), the South East Norway Health Authority (2017-112), the Kristian Gerhard Jebsen Stiftelsen (SKGJ-MED-008) and the FP7 [602450 (IMAGEMEND)]. UiO2016 and UiO2017 are part of TOP and STROKEMRI, which is supported by the Norwegian ExtraFoundation for Health and Rehabilitation (2015/FO5146), the Research Council of Norway (249795, 248238), and the South-Eastern Norway Regional Health Authority (2014097, 2015044, 2015073). The UMCU cohort consists of several independent studies, which were supported by ZonMw TOP 40-008-12-98-13009, Geestkracht programme of the ZonMw (10-000-1001), the Stanley Medical Research Institute (Dr. Nolen), the Brain and Behavior Research Foundation (2013-2015 NARSAD Independent Investigator grant 20244 to M.H.J.H.), NWO (2012-2017 VIDI grants 452-11-014 to N.E.M.v.H. and 917-46-370 to H.E.H.P.), and ZonMw (908-02-123 to H.E.H.P.). UNICAMP was supported by FAPESP (São Paulo Research Foundation) 2013/07559-3: The Brazilian Institute of Neuroscience and Neurotechnology (BRAINN). The collection of the chimpanzee brain images were supported by the NIH (NS-42867, NS-73134, and NS-92988). The views expressed in this manuscript are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institutes of Health; or the U.S. Department of Health and Human Services. Infrastructure for the CHARGE Consortium is supported in part by the National Heart, Lung, and Blood Institute (NHLBI; HL105756) and for the neuroCHARGE phenotype working group through the NIA (AG033193). H.H.H.A. was supported by the Netherlands Organization for the Health Research and Development (ZonMw; 916.19.151). Atherosclerosis Risk in Communities Study (ARIC) was a collaborative study supported by the NHLBI (HHSN268201100005C, HSN268201100006C, HSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, HHSN268201100012C, R01HL70825, R01HL087641, R01HL59367, and R01HL086694); the National Human Genome Research Institute (U01HG004402); and the

NIH (HHSN268200625226C). Infrastructure was partly supported by UL1RR025005, a component of the NIH and NIH Roadmap for Medical Research. This project was partially supported by NIH R01 grants HL084099 and NS087541 (to M.Fo.). Austrian Stroke Prevention Family/Austrian Stroke Prevention Family Study databank was supported by the Medical University of Graz and the Steiermärkische Krankenanstaltengesellschaft. The research reported in this article was funded by the Austrian Science Fund (PI904, P20545-P05 and P13180), the Austrian National Bank Anniversary Fund (P15435), and the Austrian Ministry of Science under the aegis of the EU Joint Programme-Neurodegenerative Disease Research (JPND; www.jpnd.eu). Cardiovascular Health Study was supported by NHLBI (HHSN268201200036C, HHSN268200800007C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, U01HL080295, R01HL087652, R01HL105756, R01HL103612, R01HL120393, and R01HL130114), with additional contribution from the National Institute of Neurological Disorders and Stroke. Additional support was provided through R01AG023629, R01AG15928, and R01AG033193 from the NIA. The provision of genotyping data was supported in part by the National Center for Advancing Translational Sciences, CTSI grant UL1TR000124, and the National Institute of Diabetes and Digestive and Kidney Disease Diabetes Research Center grant DK063491 to the Southern California Diabetes Endocrinology Research Center. The Erasmus Rucphen Family Study was supported by the Consortium for Systems Biology, within the framework of the Netherlands Genomics Initiative (NGI)/NWO. ERF as a part of EUROSPAN (European Special Populations Research Network) was supported by the European Commission's 5th Framework Programme (FP5) (QLG2-CT-2002-01254), the FP6 (018947; LSHG-CT-2006-01947), and the FP7 (HEALTH-F4-2007-201413 and 602633). High-throughput analysis of the ERF data was supported by a joint grant from the Netherlands Organisation for Scientific Research and the Russian Foundation for Basic Research (NWO-RFBR 047.017.043). High throughput metabolomics measurements of the ERF study was supported by BBMRI-NL. The Framingham Heart Study was supported by the National Heart, Lung and Blood Institute's Framingham Heart Study (N01-HC-25195 and HHSN268201500001I) and its contract with Affymetrix, Inc. for genotyping services (N02-HL-6-4278). A portion of this research utilized the Linux Cluster for Genetic Analysis (LinGA-II) funded by the Robert Dawson Evans Endowment of the Department of Medicine at Boston University School of Medicine and Boston Medical Center. This study was also supported by grants from the NIA (R01s AG033040, AG033193, AG054076, AG049607, AG008122, AG016495, and U01-AG049505) and the National Institute of Neurological Disorders and Stroke (R01-NS017950). C.Dec. is supported by the Alzheimer's Disease Center (P30 AG 010129). LIFE-Adult: LIFE-Adult is funded by the Leipzig Research Center for Civilization Diseases (LIFE). LIFE is an organizational unit affiliated to the Medical Faculty of the University of Leipzig. LIFE is funded by means of the European Union, by the European Regional Development Fund and by funds of the Free State of Saxony within the framework of the excellence initiative. This work was also funded by the DFG (CRC 1052 "Obesity mechanisms" project A1) and by the Max Planck Society. The Rotterdam Study was funded by Erasmus Medical Center and Erasmus University, Rotterdam, ZonMw, the Research Institute for Diseases in the Elderly (RIDE), the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the European Commission (DG XII), and the Municipality of Rotterdam. The GWAS datasets are supported by NWO Investments (175.010.2005.011, 911-03-012), the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, the Research Institute for Diseases in the Elderly (014-93-015; RIDE2), and the NGI/NWO

Netherlands Consortium for Healthy Aging (050-060-810). This work was performed as part of the CoSTREAM project (www.costream.eu) and received funding from H2020 (667375). Three-City Dijon was conducted under a partnership agreement among the Institut National de la Santé et de la Recherche Médicale (INSERM), the University of Bordeaux, and Sanofi-Aventis. The Fondation pour la Recherche Médicale funded the preparation and initiation of the study. The 3C Study is also supported by the Caisse Nationale Maladie des Travailleurs Salariés, Direction Générale de la Santé, Mutuelle Générale de l'Education Nationale, Institut de la Longévité, Conseils Régionaux of Aquitaine and Bourgogne, Fondation de France, and Ministry of Research–INSERM Programme "Cohortes et collections de données biologiques". S.Deb. received investigator-initiated research funding from the French National Research Agency (ANR) and from the Fondation Leducq. S.Deb. is supported by a starting grant from the European Research Council (SEGWAY), a grant from the Joint Programme of Neurodegenerative Disease research (BRIDGET), from H2020 (643417 and 640643), and by the Initiative of Excellence of Bordeaux University. This work was supported by the National Foundation for Alzheimer's disease and related disorders, the Institut Pasteur de Lille, the labex DISTALZ and the Centre National de Génotypage. Vietnam Era Twin Study of Aging (VETSA) was supported by the US NIH VA San Diego Center of Excellence for Stress and Mental Health R00DA023549, DA-18673, NIA R01 AG018384, R01 AG018386, R01 AG022381, R01 AG022982, R01 DA025109 05, R01 HD050735, K08 AG047903, R03 AG 046413, and R01 HD050735-01A2. **Author Contributions:** †K.L.G. and N.J. contributed to this work as co-first authors. ‡J.N.P., L.C.-C., J.B., D.P.H., P.A.L., and F.P. contributed to this work as co-second authors. §J.L.S., P.M.T., and S.E.M. contributed to this work as co-last authors. #Consortium authors are listed in Supplementary Materials. *N.J., J.L.S., P.M.T., and S.E.M. are corresponding authors: S.E.M. Sarah.Medland@qimrberghofer.edu.au, P.M.T. pthomp@usc.edu, J.L.S. jason_stein@med.unc.edu, N.J. njahansh@usc.edu. Central Analysis and Coordination Group: C.R.K.C., D.P.H., F.P., J.Br., J.L.S., J.N.P., K.L.G., L.C.-C., L.C.P.Z., L.T.S., M.A.B.M., N.J., N.S., P.A.L., P.M.T., S.E.M, S.I.T. Manuscript Writing, Preparation and Revision: A.H.Z., D.P.H., J.Br., J.L.S., J.N.P., K.L.G., L.C.-C., N.J., P.A.L., P.M.T., S.E.M. Project Support: D.Ga., M.A.B.M., M.J., N.S., R.E., V.R., Y.G. Cohort Principal Investigator: A.A.V., A.C., A.H., A.J.F., A.J.H., A.K.H., A.M.D., A.M.-L., A.R.H., A.W.T., B.C.-F., B.F., B.Mo., B.S.P., B.W., B.W.J.H.P., C.A.H., C.Dep., C.F., C.M., C.M.L., C.P., D.Am., D.C.G., D.I.B., D.J.S., D.P., D.R.W., D.v.E., E.G.J., E.J.C.d.G., L.E.H., F.A.H., F.C., G.D., G.F., G.G.B., G.L.C., G.S., H.B., H.E.H.P., H.F., H.G.B., H.J.G., H.V., H.W., I.A., I.E.Som., I.J.D., I.M., J.B.J.K., J.Bl., J.C.Be., J.C.D.-A., J.K.B., J.-L.M., J.L.R., J.N.T., J.O., J.R.B., J.W.S., J.Z., K.L.M., K.S., L.M.R., L.N., L.R., L.T.W., M.E.B., M.H.J.H., M.J.C., M.J.W., M.K.M.A., M.R., N.D., N.J., N.J.A.v.d.W., O.A.A., O.G., P.G.S., P.J.H., P.K., P.M.T., P.S.S., P.T.M., R.A.M., R.A.O., R.H., R.J.S., R.L.B., R.L.G., R.S.K., S.Ca., S.Des., S.E.F., S.L.H., S.M.S., S.R., T.E., T.J.A., T.J.C.P., T.L.J., T.P., T.T.J.K., U.D., V.C., V.J.C., W.C., W.U.H., X.C., Z.P. Imaging Data Collection: A.B., A.d.B., A.F.M., A.J., A.J.H., A.K., A.K.H., A.L.G., A.M.D., A.N.H., A.P., A.R.H., A.R.K., A.U., B.A.M., B.-C.H., B.D., B.F., G.B.P., B.W., B.W.J.H.P., C.B., C.D.W., C.J., C.L.B., C.L.Y., C.M., C.P., C.R.J., C.S.Re., D.Am., D.C.G., D.Gr., D.H.M., D.J., D.J.H., D.J.V., D.M.C., D.P.O., D.R.W., D.S.O., D.T.-G., D.v.E., D.v.R., D.Z., E.A., E.B.Q., E.J.C.d.G., L.E.H., E.Sh., G.B.P., G.D., G.F., G.I.d.Z., G.L.C., G.R., G.S., H.V., H.Y., I.A., I.E.Som., J.A.T., J.E.C., J.E.N., J.K.B., J.-L.M., J.-L.M., J.L.R., J.M.F., J.M.W., J.N.T., J.R., J.T.V., K.D., K.K., K.L.M., K.O.L., K.S., L.M.R., L.R., L.T.W., M.B.H., M.E.B., M.Fu., M.H.J.H., M.Ho., M.-J.v.T., M.J.W., M.-L.P.M., N.E.M.v.H., N.F.H., N.H., N.J.A.v.d.W.,

N.K.H., N.O., O.G., P.A.G., P.E.R., P.G.S., P.K., P.N., P.S.S., R.A.O., R.B., R.H., R.L.B., R.L.G., R.R., R.S.K., R.W., S.A., S.C.M., S.Ca., S.Er., S.Ko., S.M., S.M.S., T.G.M.v.E., T.R.M., T.Wh., T.W.M., U.D., U.S., V.C., V.J.C., V.S.M., W.D.H., W.H., W.W., X.C. Imaging Data Analysis: A.F.M., A.H.Z., A.J.H., A.J.S., A.L.G., A.M.D., A.R., A.R.K., A.S., A.Th., A.U., B.A.G., B.C.R., B.F., B.K., B.S.P., C.B., C.C.F., C.C.H., C.D.W., C.J., C.L.Y., C.R.K.C., C.S.Ro., D.Al., D.C.G., D.Gr., D.H., D.J., D.J.H., D.M.C., D.P.H., D.P.O., D.T.-G., D.v.d.M., D.v.E., D.v.R., D.Z., E.E.L.B., E.Sh., E.Sp., E.W., F.M.R., F.P., F.S., G.I.d.Z., G.R., H.J.G., I.A., I.E.Som., I.K.A., J.A.T., J.B.J.K., J.C.V.M., J.-L.M., J.L.R., J.L.S., J.M.W., J.R., J.Z., K.D., K.L.M., K.N., K.S., K.W., L.B.L., L.H., L.Sa., L.Sc., L.Sh., L.T.S., L.T.W., L.v.E., L.C.P.Z., M.A., M.A.H., M.B.H., M.C., M.E.B., M.Fu., M.Ho., M.J.G., M.-J.v.T., M.J.W., M.Ki., M.La., M.P.Z., M.W., N.E.M.v.H., N.F.H., N.J., N.O., N.T.D., O.G., P.G.S., P.K., P.M.T., P.N., R.B., R.K., R.L.G., R.M.B., R.R., S.A., S.Ca., S.Des., S.Eh., S.Er., S.F.F., S.I.T., S.Ka., S.Ke., S.L.R., S.M.C.d.Z., S.R.M., T.A., T.A.L., T.G., T.G.M.v.E., T.J., T.K., T.L.P., T.P.G., T.R.M., T.Wh., T.Wo., T.W.M., U.D., W.W., X.C., Y.Q., Z.Z. Genetic Data Collection: A.A.A., A.A.-K., A.d.B., A.J.F., A.J.H., A.J.S., A.K.H., A.M.D., A.P., A.R.H., A.R.K., B.-C.H., B.F., B.Mo., B.T.B., B.W., B.W.J.H.P., C.B., C.D.W., C.F., C.M., C.P., C.P.D., C.S.Re., D.C.G., D.H.M., D.R.W., D.W.M., D.Z., E.A., E.B.Q., E.G.J., E.J.C.d.G., L.E.H., F.D., F.M., F.R.T., G.D., G.E.D., G.F., G.H., G.L.C., G.S., H.V., H.Y., I.E.Som., I.L.-C., J.A.T., J.B.J.K., J.Bl., J.E.C., J.E.N., J.-J.H., J.J.L., J.K.B., J.-L.M., J.-L.M., J.L.R., J.M.F., J.Q.W., J.R., J.W.S., K.A.M., K.D., K.O.L., K.S., L.M.R., L.R., L.Sh., M.A.K., M.F.D., M.H.J.H., M.Ha., M.Ho., M.J.C., M.J.W., M.La., M.-L.P.M., M.M.N., M.N., N.A.K., N.E.M.v.H., N.G.M., N.J.A.v.d.W., N.K.H., N.O., O.G., P.A.T., P.H., P.K., P.R.S., P.S.S., R.A.O., R.C.G., R.H., R.L.B., R.R., R.Se., R.S.K., R.W., S.A., S.Ci., S.Dj., S.E.F., S.Eh., S.Er., S.H., S.L.H., S.M.S., T.G.M.v.E., T.J.A., T.K.d.A., T.L.P., T.W.M., U.D., V.C., V.J.C., V.M.S., X.C. Genetic Data Analysis: A.A.-K., A.J.F., A.J.H., A.J.S., A.M.D., A.R.K., A.Te., A.Th., B.C.-D., B.F., B.K., B.M.-M., B.P., B.S.P., B.T.B., C.C.F., C.D.W., C.L.V., C.S.Re., C.S.Ro., C.W., C.Y.S., D.C.G., D.K., D.P.H., D.v.d.M., D.v.E., E.G.J., L.E.H., E.V., E.W., F.M., H.-R.E., I.E.J., I.E.Som., I.E.Søn., I.L.-C., I.O.F., J.Bl., J.Br., J.F.P., J.H.V., J.-J.H., J.L.R., J.L.S., J.N.P., J.Q.W., J.R.A., J.S., J.W.C., J.W.S., K.E.T., K.L.G., K.N., L.C.-C., L.M.O.L., L.Sh., L.C.P.Z., M.A.A.A., M.B., M.E.G., M.Fu., M.Ha., M.I., M.J., M.J.C., M.J.W., M.Ki., M.Kl., M.Kn., M.La., M.Lu., M.M.J.v.D., N.A.G., N.G.M., N.J., N.J.A., N.K.H., N.M.-S., N.R.M., O.G., P.A.L., P.G.S., P.H., P.H.L., P.K., P.M.T., P.R.S., Q.C., R.A.O., R.M.B., R.R., R.Se., S.Da., S.Des., S.E.M., S.Eh., S.G., S.H., S.H.W., S.L.H., S.M.C.d.Z., S.N., S.R.M., T.A.L., T.G., T.G.M.v.E., T.J., T.K.d.A., T.M.L., W.R.R., Y.M., Y.W. CHARGE Study Design: B.Ma., C.Dec., C.L.S., E.H., G.V.R., H.H.H.A., H.J.G., J.C.Bi., L.L., M.A.I., M.Fo., O.L.L., Q.Y., R.Sc., S.Deb., S.S., T.H.M., T.P., V.G., W.T.L. **Competing Interests:** A.M.D. is a Founder of CorTechs Labs, Inc. and has received funding through a Research Agreement between General Electric Healthcare and the University of California, San Diego. The terms of these arrangements have been reviewed by and approved by the University of California, San Diego in accordance with its conflict of interest policies. B.F. has received educational speaking fees from Shire and Medice. B.W.J.H.P. has received (non-related) research funding from Boehringer Ingelheim and Janssen Research. C.D.W. is currently an employee of Biogen. C.R.J. consults for Lilly and serves on an independent data monitoring board for Roche but receives no personal compensation from any commercial entity. C.R.J. receives research support from NIH and the Alexander Family Alzheimer's Disease Research Professorship of the Mayo Clinic. D.H.M. is a consultant for Boehringer Ingelheim, GW/Greenwhich Biosciences, and Aptinyx. D.J.S. has received research grants and/or

consultancy honoraria from Lundbeck and Sun. D.P.H. is currently an employee of Genentech, Inc. and was previously employed by Janssen R&D, LLC. H.B. is on the advisory board for Nutricia Australia. R.S.K. has consulted for Alkermes, Otsuka, Luye Pharma, and Sunovion, and has received speaker fees from Janssen-Cilag and Lundbeck. None of the other authors declare any competing financial interests. H.J.G. has received travel grants and speaker honoraria from Fresenius Medical Care, Neuraxpharm and Janssen Cilag. H.J.G. has received research funding from the German Research Foundation, the German Ministry of Education and Research, the DAMP Foundation, Fresenius Medical Care, the EU Joint Programme Neurodegenerative Disorders and the European Social Fund. L.E.H. has received or is planning to receive research funding or consulting fees from Mitsubishi, Your Energy Systems LLC, Neuralstem, Taisho, Heptares, Pfizer, Sound Pharma, Luye Pharma, Takeda, and Regeneron. N.H. is a stockholder of Siemens AG, Erlangen, Germany. R.B. has received travel grants and speaker honoraria from Bayer Healthcare AG. R.L.B. is a paid consultant for Roche. **Data and Materials Availability:** The meta-analytic results presented in this paper are available to download from the ENIGMA consortium webpage http://enigma.ini.usc.edu/research/download-enigma-gwas-results. Access to cohort data is available either through public repositories or directly from the cohort. Direct requests are required when informed consent or the approved study protocol does not permit deposition into a repository. Requests for data by qualified investigators are subject to scientific and ethical review, to ensure the data will be used for valid scientific research and to ensure compliance with confidentiality, consent, and data protection regulations. Some of the data are subject to MTA or DTA and specific details on how to access data for each cohort are available in table S20.

Supplementary Materials:

Materials and Methods

Supplementary Text

Consortium Authors

Additional Cohort Information

Supplementary Acknowledgements

Figs. S1 to S11

Tables S1 to S19

References (70–108)

Fig. 1. Regions of the human cortex and associated genetic loci. (**A**) The 34 cortical regions defined by the Desikan-Killiany atlas. (**B**) Ideogram of loci influencing cortical SA and TH.

Fig. 2. Genetics of Global Measures. (**A**) Genetic correlations between global measures and selected traits (red indicates significant correlation, FDR < 0.05). (**B**) Partioned heritability enrichment in active regulatory elements across tissues and cell types. (**C**) Partioned heritability enrichment in temporally specific active regulatory elements. (**D**) Partioned heritability enrichment in regulatory elements of cell-type specific genes in fetal brain. (**E**) Manhattan plot of loci associated with total SA (*top*) and TH (*bottom*), green diamonds indicate lead SNP in the principal meta-analysis, black diamonds indicate change in *P*-value after replication, dashed

horizontal line is genome-wide significance, solid horizontal line is multiple-testing correction threshold.

Fig 3. Genetic and Phenotypic Correlations Between Cortical Regions. (**A**) Surface Area. (**B**) Thickness. The regions are numbered according to the legend of Fig. 1A. The proportion of variance accounted for by common genetic variants is shown in the first column (h^2_{SNP}). Phenotypic correlations from the UK Biobank are in the upper triangle. Genetic correlations from the principal meta-analysis are in the lower triangle. Only significant correlations are shown.

Fig 4. Genetics of Regional Measures. (**A**) Regional plot for rs1080066, including additional lead SNPs within the LD block and surrounding genes, chromatin interactions in neural progenitor cells, chromatin state in RoadMap brain tissues*, and BRAINSPAN candidate gene expression in brain tissue**. (**B**) Ideogram of 15q14, detailing the significant independent loci and cortical regions. (**C**) rs1080066 (G allele) association with SA of regions. (**D**) rs1080066 association with central sulcus depth and depth of several primate species *TssA:Active Transcription Start Site (TSS); TssAFlnk:Flanking Active TSS; TxFlnk:Transcription at gene 5' and 3'; Tx:Strong transcription; TxWk:Weak transcription; EnhG:Genic enhancers; Enh:Enhancers; Het:Heterochromatin; TssBiv:Bivalent/Poised TSS; BivFlnk:Flanking Bivalent TSS/Enhancer; EnhBiv:Bivalent Enhancer; ReprPC:Repressed; PolyComb; ReprPCWk:Weak Repressed PolyComb; Quies:Quiescent/Low. **DFC:dorsolateral prefrontal cortex; VFC:ventrolateral prefrontal cortex; MFC:anterior cingulate cortex; OFC:orbital frontal cortex; M1C:primary motor cortex; M1C-S1C:primary motor-sensory cortex; PCx:parietal neocortex; S1C:primary somatosensory cortex; IPC:posteroventral parietal cortex; A1C:primary auditory cortex; TCx:temporal neocortex; STC:posterior superior temporal cortex; ITC:inferolateral temporal cortex; Ocx:occipital neocortex; V1C:primary visual cortex.

Fig 5. Genetic correlations with neuropsychiatric and psychological traits. (**A**) Genetic correlations with total SA and average TH positive correlations are shown in red, while negative correlations are shown in blue. (**B**) Regional variation in the strength of genetic correlations between regional surface area (without correction for total surface area) and traits showing significant genetic correlations with total surface area.

Science
AAAS

Supplementary Materials for

The genetic architecture of the human cerebral cortex

Katrina L. Grasby†*, Neda Jahanshad†*, Jodie N. Painter‡, Lucía Colodro-Conde, ‡, Janita Bralten,‡, Derrek P. Hibar,‡, Penelope A. Lind,‡, Fabrizio Pizzagalli‡, Christopher R.K. Ching, Mary Agnes B. McMahon, Natalia Shatokhina, Leo C.P. Zsembik, Sophia I. Thomopoulos, Alyssa H. Zhu, Lachlan T. Strike, Ingrid Agartz, Saud Alhusaini, Marcio A.A. Almeida, Dag Alnæs, Inge K. Amlien, Micael Andersson, Tyler Ard, Nicola J. Armstrong, Allison Ashley-Koch, Joshua R. Atkins, Manon Bernard, Rachel M. Brouwer, Elizabeth E.L. Buimer, Robin Bülow, Christian Bürger, Dara M. Cannon, Mallar Chakravarty, Qiang Chen, Joshua W. Cheung, Baptiste Couvy-Duchesne, Anders M. Dale, Shareefa Dalvie, Tânia K. de Araujo, Greig I. de Zubicaray, Sonja M.C. de Zwarte, Anouk den Braber, Nhat Trung Doan, Katharina Dohm, Stefan Ehrlich, Hannah-Ruth Engelbrecht, Susanne Erk, Chun Chieh Fan, Iryna O. Fedko, Sonya F. Foley, Judith M. Ford, Masaki Fukunaga, Melanie E. Garrett, Tian Ge, Sudheer Giddaluru, Aaron L. Goldman, Melissa J. Green, Nynke A. Groenewold, Dominik Grotegerd, Tiril P. Gurholt, Boris A. Gutman, Narelle K. Hansell, Mathew A. Harris, Marc B. Harrison, Courtney C. Haswell, Michael Hauser, Stefan Herms, Dirk J. Heslenfeld, New Fei Ho, David Hoehn, Per Hoffmann, Laurena Holleran, Martine Hoogman, Jouke-Jan Hottenga, Masashi Ikeda, Deborah Janowitz, Iris E. Jansen, Tianye Jia, Christiane Jockwitz, Ryota Kanai, Sherif Karama, Dalia Kasperaviciute, Tobias Kaufmann, Sinead Kelly, Masataka Kikuchi, Marieke Klein, Michael Knapp, Annchen R. Knodt, Bernd Krämer, Max Lam, Thomas M. Lancaster, Phil H. Lee, Tristram A. Lett, Lindsay B. Lewis, Iscia Lopes-Cendes, Michelle Luciano, Fabio Macciardi, Andre F. Marquand, Samuel R. Mathias, Tracy R. Melzer, Yuri Milaneschi, Nazanin Mirza-Schreiber, Jose C.V. Moreira, Thomas W. Mühleisen,, Bertram Müller-Myhsok, Pablo Najt, Soichiro Nakahara, Kwangsik Nho, Loes M. Olde Loohuis, Dimitri Papadopoulos Orfanos, John F. Pearson, Toni L. Pitcher, Benno Pütz, Yann Quidé, Anjanibhargavi Ragothaman, Faisal M. Rashid, William R. Reay, Ronny Redlich, Céline S. Reinbold, Jonathan Repple, Geneviève Richard, Brandalyn C. Riedel, Shannon L. Risacher, Cristiane S. Rocha, Nina Roth Mota, Lauren Salminen, Arvin Saremi, Andrew J. Saykin, Fenja Schlag, Lianne Schmaal, Peter R. Schofield, Rodrigo Secolin, Chin Yang Shapland, Li Shen, Jean Shin, Elena Shumskaya, Ida E. Sønderby, Emma Sprooten, Katherine E. Tansey, Alexander Teumer, Anbupalam Thalamuthu, Diana Tordesillas-Gutiérrez, Jessica A. Turner, Anne Uhlmann, Costanza Ludovica Vallerga, Dennis van der Meer, Marjolein M.J. van Donkelaar, Liza van Eijk, Theo G.M. van Erp, Neeltje E.M. van Haren, Daan van Rooij, Marie-José van Tol, Jan H. Veldink, Ellen Verhoef, Esther Walton, Mingyuan Wang, Yunpeng Wang, Joanna M. Wardlaw, Wei Wen, Lars T. Westlye, Christopher D. Whelan, Stephanie H. Witt, Katharina Wittfeld, Christiane Wolf, Thomas Wolfers, Jing Qin Wu, Clarissa L. Yasuda, Dario Zaremba, Zuo Zhang, Marcel P. Zwiers, Eric

Artiges, Amelia A. Assareh, Rosa Ayesa-Arriola, Aysenil Belger, Christine L. Brandt, Gregory G. Brown, Sven Cichon, Joanne E. Curran, Gareth E. Davies, Franziska Degenhardt, Michelle F. Dennis, Bruno Dietsche, Srdjan Djurovic, Colin P. Doherty, Ryan Espiritu, Daniel Garijo, Yolanda Gil, Penny A. Gowland, Robert C. Green, Alexander N. Häusler, Walter Heindel, Beng-Choon Ho, Wolfgang U. Hoffmann, Florian Holsboer, Georg Homuth, Norbert Hosten, Clifford R. Jack Jr., MiHyun Jang, Andreas Jansen, Nathan A. Kimbrel, Knut Kolskår, Sanne Koops, Axel Krug, Kelvin O. Lim, Jurjen J. Luykx, Daniel H. Mathalon, Karen A. Mather, Venkata S. Mattay, Sarah Matthews, Jaqueline Mayoral Van Son, Sarah C. McEwen, Ingrid Melle, Derek W. Morris, Bryon A. Mueller, Matthias Nauck, Jan E. Nordvik, Markus M. Nöthen, Daniel S. O'Leary, Nils Opel, Marie-Laure Paillère Martinot, G. Bruce Pike, Adrian Preda, Erin B. Quinlan, Paul E. Rasser,, Varun Ratnakar, Simone Reppermund, Vidar M. Steen, Paul A. Tooney, Fábio R. Torres, Dick J. Veltman, James T. Voyvodic, Robert Whelan, Tonya White, Hidenaga Yamamori, Hieab H.H. Adams, Joshua C. Bis, Stephanie Debette, Charles Decarli, Myriam Fornage, Vilmundur Gudnason, Edith Hofer, M. Arfan Ikram, Lenore Launer, W. T. Longstreth, Oscar L. Lopez, Bernard Mazoyer, Thomas H. Mosley, Gennady V. Roshchupkin, Claudia L. Satizabal, Reinhold Schmidt, Sudha Seshadri, Qiong Yang, Alzheimer's Disease Neuroimaging Initiative#, CHARGE consortium#, EPIGEN consortium#, IMAGEN consortium#, SYS consortium#, Parkinson’s Progression Markers Initiative#, Marina K.M. Alvim, David Ames, Tim J. Anderson, Ole A. Andreassen, Alejandro Arias-Vasquez, Mark E. Bastin, Bernhard T. Baune, Jean C. Beckham, John Blangero, Dorret I. Boomsma, Henry Brodaty, Han G. Brunner, Randy L. Buckner, Jan K. Buitelaar, Juan R. Bustillo, Wiepke Cahn, Murray J. Cairns, Vince Calhoun, Vaughan J. Carr, Xavier Caseras, Svenja Caspers, Gianpiero L. Cavalleri, Fernando Cendes, Aiden Corvin, Benedicto Crespo-Facorro, John C. Dalrymple-Alford, Udo Dannlowski, Eco J.C. de Geus, Ian J. Deary, Norman Delanty, Chantal Depondt, Sylvane Desrivières, Gary Donohoe, Thomas Espeseth, Guillén Fernández, Simon E. Fisher, Herta Flor, Andreas J. Forstner, Clyde Francks, Barbara Franke, David C. Glahn, Randy L. Gollub, Hans J. Grabe, Oliver Gruber, Asta K. Håberg, Ahmad R. Hariri, Catharina A. Hartman, Ryota Hashimoto, Andreas Heinz, Frans A. Henskens, Manon H.J. Hillegers, Pieter J. Hoekstra, Avram J. Holmes, L. Elliot Hong, William D. Hopkins, Hilleke E. Hulshoff Pol, Terry L. Jernigan, Erik G. Jönsson, René S. Kahn, Martin A. Kennedy, Tilo T.J. Kircher, Peter Kochunov, John B.J. Kwok, Stephanie Le Hellard, Carmel M. Loughland, Nicholas G. Martin, Jean-Luc Martinot, Colm McDonald, Katie L. McMahon, Andreas Meyer-Lindenberg, Patricia T. Michie, Rajendra A. Morey, Bryan Mowry, Lars Nyberg, Jaap Oosterlaan, Roel A. Ophoff, Christos Pantelis, Tomas Paus, Zdenka Pausova, Brenda W.J.H. Penninx, Tinca J.C. Polderman, Danielle Posthuma, Marcella Rietschel, Joshua L. Roffman, Laura M. Rowland, Perminder S. Sachdev, Philipp G. Sämann, Ulrich Schall, Gunter Schumann, Rodney J. Scott, Kang Sim, Sanjay M. Sisodiya, Jordan W. Smoller, Iris E. Sommer, Beate St Pourcain, Dan J. Stein, Arthur W. Toga, Julian N. Trollor, Nic J.A. Van der Wee, Dennis van 't Ent, Henry Völzke, Henrik Walter, Bernd Weber, Daniel R. Weinberger, Margaret J. Wright, Juan Zhou, Jason L. Stein§*, Paul M. Thompson§*, Sarah E. Medland,§* on behalf of the Enhancing NeuroImaging Genetics through Meta-Analysis Consortium (ENIGMA)—Genetics working group

Correspondence to: katrina.grasby@qimrberghofer.edu.au; njahansh@usc.edu; jason_stein@med.unc.edu; pthomp@usc.edu; sarah.medland@qimrberghofer.edu.au

This PDF file includes:

Materials and Methods
Supplementary Text
Consortium Authors
Additional Cohort Information
Supplementary Acknowledgements
Figs. S1 to S11
Captions for Tables S1 to S20

Other Supplementary Materials for this manuscript include the following:

Tables S1 to S20 (Grasby_etal_Supplementary_Tables.xlsx)

Contents

Materials and Methods

Imaging

Measures of cortical surface area (SA) and thickness (TH) were derived from *in vivo* whole brain T1-weighted magnetic resonance imaging (MRI) scans using FreeSurfer MRI processing software (*1*) (table S3). SA and TH were quantified for each subject within 34 distinct gyral-defined regions in each brain hemisphere according to the Desikan-Killiany atlas (*10*) (Fig. 1A). SA was measured at the grey-white matter boundary. TH was measured as the average distance between the white matter and pial surfaces. The total SA and average TH of each hemisphere was computed separately. High test-retest correlations have been previously reported for all measures with the exception of the frontal and temporal poles (*7*). Image processing and quality control were implemented at the cohort level following detailed, harmonized protocols.

Site analysts visually inspected the 34 bilateral cortical Desikan-Killiany atlas segmentations for each subject. Visual inspection was conducted to assess extraction of the cortical grey matter ribbon, to identify regional boundary errors on the cortical surface, and ensure the accuracy of anatomical labels. Inspection was slice by slice on an orthogonal view, as well as on the external surface view. Regions marked as "failed segmentations" were excluded from analyses. SA and TH estimates beyond 2.698 SD from the mean were flagged in order to be more carefully inspected by the respective site analysts. A quantitative assessment of quality was not applied; subjects or regions were marked either as acceptable or not by a human rater. As this was a binary "pass" or "fail" flag for each region, no additional metrics were added to the statistical analysis at the site level. For sites that removed subjects for only the region that failed, the number of subjects available varied across regions. For sites that removed subjects entirely for regional fails, the total number of subjects available was the same as for all regions. We also note that some cohorts removed poor quality scans from their database, so for some cohorts the number of quality control issues may be limited. We include the percent of regional data available at the cohort-level in table S3. The protocols that were used for the imaging quality control are available online from the ENIGMA website (http://enigma.ini.usc.edu/protocols/imaging-protocols).

Phenotype distributions for all traits in all cohorts were inspected centrally prior to meta-analysis (fig. S11). Any cohort where the phenotypic distribution for a given trait showed deviation from expectations that could not be resolved through re-analysis or outlier inspection were excluded from analyses of that trait.

Genome-wide association analyses

At each site, genotypes were imputed using either the 1000 Genomes Project (*70*) or Haplotype Reference Consortium (*71*) references (table S4). To ensure consistency in the correction for ancestry and stability of the correction given the relatively small sample sizes, each cohort also ran the same multidimensional scaling (MDS) analysis protocol in which the data from the HapMap 3 populations were merged with the site level data and MDS components were calculated across this combined data set. Within each cohort, genome-wide association (GWAS) was conducted using an additive model including covariates to control for the effects of age, age^2, sex, sex-by-age and age^2 interactions, ancestry (the first four MDS components), diagnostic status (when the cohort followed a case-control design), and dummy variables for scanner (when multiple scanners were used at the same site).

The primary GWAS of regional measures included the global measure of SA or TH as an additional covariate, to test for genetic influences specific to each region. However, to aid interpretation, the regional GWAS were also run without controlling for global measures. Cohort level GWAS results underwent quality control (excluding variants with an imputation $R^2 \leq 0.5$ and MAF ≤ 0.005). Across all cohorts, for each phenotype, GWAS summary plots (Manhattan and QQ plots) were visually inspected by the central analysis group; if a given trait showed deviation from expectations that could not be resolved through re-analysis, then that cohort was excluded from analyses of that trait.

Meta-analysis

The initial meta-analysis was conducted on all of the ENIGMA European cohorts with genome-wide imputed data, and was then meta-analyzed with the UK Biobank European participants to give the principal results. For replication, we took forward the significant variants from the principal results and meta-analyzed them with an additional ENIGMA cohort and results from the CHARGE consortium. We also extracted these variants from a meta-analysis of non-European cohorts to examine generalization of effects across ancestry. Cohort information is provided in table S2. All meta-analyses were conducted using METAL (*63*). The results of the meta-analyses are summarized in table S5. For the initial and principal meta-analyses we used standard error weighted meta-analyses. In the replication steps we used sample size weighted meta-analyses, in order to include results from the CHARGE consortium for which only sample size weighted results were available. An additional ENIGMA cohort was also included in the sample size weighted meta-analysis because the GWAS was conducted using a program that provided results on an inverse normalized scale. For each meta-analysis, the results were quality controlled, removing strand ambiguous SNPs and INDELs where the effect allele frequency crossed 0.5, and (for the initial meta-analysis) variants where the total sample size was < 10,000. Independent loci were identified by clumping significant loci in PLINK (*72*), with thresholds of 1 Mb and $r^2 < 0.2$. For the chromosome 17 inversion region this was increased to 10 Mb. For clumping, a random sample of 5,000 unrelated individuals (*plink 1.90* genetic relatedness $\leq$ 0.025) of European ancestry from the UK Biobank were used as an LD reference.

Following Rietveld et al. (*73*), we estimated the variance explained R^2 by each variant j as:

$$R_j^2 \approx \frac{2p_j q_j . \hat{\beta}_j^2}{\hat{\sigma}_y^2}$$

where p_j and q_j are the minor and major allele frequencies, $\hat{\beta}_j$ is the estimated effect of the variant within the meta-analysis and $\hat{\sigma}_y^2$ is the estimated variance of the trait (for which we used the pooled variance of the trait across all ENIGMA cohorts and UK Biobank; see table S1). To obtain beta and standard error estimates from the results from the sample size weighted meta-analyses reported in table S5 we used the following equations from Rietveld et al. (*73*):

$$\hat{\beta}_j \approx z_j \cdot \frac{\hat{\sigma}_y}{\sqrt{N_j \cdot 2p_j q_j}} \; and \; SE(\hat{\beta}_j) \equiv \frac{z_j}{\hat{\beta}_j}$$

Where z_j is the Z-score and SE ($\hat{\beta}_j$) is the estimated standard effect of the variant within the meta-analysis and N is the number of contributing alleles.

Multiple testing correction

We analyzed 70 traits (total SA, average TH, and the SA and TH of 34 cortical regions averaged across right and left hemispheres). However, after accounting for the correlation between the traits in the UK Biobank (residuals correcting for sex, age, ancestry and global measures) using matrix spectral decomposition (*12*), the effective number of traits was estimated to be 60. Therefore, we applied the significance threshold of $P \leq 8.3 \times 10^{-10}$ to correct for multiple testing in the GWAS meta-analysis results. Multiple testing corrections applied to each of the follow-up analyses are described below.

Analyses of UK Biobank data

Analyses of the UK Biobank cohort were conducted on the 2018 (version 3) imputed genotypes, imputed to the Haplotype Reference Consortium and merged UK10K and 1000 Genomes (phase 3) panels. UK Biobank bulk imaging data were made available for 12,962 individuals under application #11559 in July 2017, with data from an additional 5,095 individuals made available in August 2019. We processed the raw MRI data using the ENIGMA protocols described above. Following processing, all images were visually inspected. Analyses of UK Biobank participants within 0.02 on the first and second MDS components of the European centroid were included in the meta-analyses of the European ancestry cohorts. Analyses of participants beyond this threshold were included in the meta-analysis of non-European ancestry cohorts.

Gene-based association analyses

We conducted genome-wide gene-based association analysis using the principal meta-analytic results. We used the 19,427 protein-coding genes from the NCBI 37.3 gene definitions as the basis for the gene-based association analysis using MAGMA (*67*). For each gene we selected all SNPs within exonic, intronic and untranslated regions as well as SNPs within 50 kb upstream and downstream of the gene. After SNP annotation, there were 18,048 genes that were covered by at least one SNP. Gene-based association tests were performed taking LD between SNPs into account. We applied a Bonferroni correction to account for multiple testing, adjusting for the number of genes tested as well as the effective number of traits tested (60 independent traits), setting the genome-wide threshold for significance at 4.5×10^{-8}. These results are shown in table S6.

Twin heritability

Twin heritability was estimated in the ENIGMA Queensland Twin Imaging (QTIM) study of healthy adolescent and young adult twins and their siblings (N = 923; 157 MZ pairs, 194 DZ pairs, 221 unpaired twins) using OpenMx (*74*) in R. Structural equation models were fitted to total SA, average TH, and the SA and TH of 34 cortical regions averaged across right and left hemispheres using full information maximum likelihood to decompose the variance into additive genetic and environmental factors. The models included a simultaneous means regression to adjust for effects of sex, linear and nonlinear age effects, interactions between age and sex, MRI acquisition orientation, and for the regional measures we analyzed a version with and one without the corresponding global measures. We performed analyses without controlling for global measures for completeness. The likelihood ratio test was used to select the best fitting most parsimonious model, which was a model explaining the phenotypic differences in variance by additive genetic factors and unique environmental factors (including measurement error). These results are shown in table S7.

Heritability due to common variants

For each of the 70 traits, we used LD score regression (*64, 65*) to estimate the proportion of variance accounted for by common SNPs or SNP heritability (h^2_{SNP}). These results are shown in table S7.

Partitioned heritability

Partitioned heritability analysis was used to estimate the percentage of heritability explained by annotated regions of the genome (*66*). Annotations were derived from either Epigenomics Roadmap (*22*) or a study of chromatin accessibility in mid-fetal brains (*21*). For analyses using Epigenomics Roadmap data, ChromHMM chromatin states (15 state model) were downloaded for available tissue types (http://egg2.wustl.edu/roadmap/web_portal/chr_state_learning.html). For each tissue, genomic regions comprising all active regulatory elements (TssA, TssAflnk, Enh, EnhG) within each tissue type were added as an additional annotation to the baseline model provided with the LDSC package (https://github.com/bulik/ldsc). A separate analysis was conducted by identifying if the same active regulatory elements that were specific to either fetal brain (combining annotations from BRN.FET.F and BRN.FET.M) or adult brain cortex (combining annotations from BRN.CING.GYR, BRN.INF.TMP, BRN.ANG.GYR, BRN.DL.PRFRNTL.CRTX). Those elements present in fetal brain showing no overlap with adult brain cortex were used as "fetal brain specific". Conversely, those elements present in adult brain cortex showing no overlap with fetal brain were used as "adult brain specific". These annotations were added separately to the baseline model. For analyses using chromatin accessibility in mid-fetal brains, the genomic coordinates of peaks more accessible in the germinal zone than the cortical plate (GZ > CP) and peaks more accessible in the cortical plate than the germinal zone (CP > GZ) were added jointly to the baseline annotations. A separate analysis was conducted subsetting to chromatin accessibility peaks defined in fetal brain that showed evidence of regulating cell-type specifically expressed genes in mid-fetal development. Cell-type definitions and genes with cell-type specific expression (log2 fold change > 0.2 between cell-types, BH corrected $P < 0.05$, Expressed in 10% of cells in cluster) were acquired from previously published work (*23*). Peaks near the TSS of cell-type specific genes (promoter peaks) and those with significant chromatin accessibility correlation with promoter peaks were used as cell-type specific annotations. These annotations of all 16 cell-types were added to the baseline model. Partitioned heritability and the enrichment of heritability explained in these annotations was run using LD score regression (*66*). The significance of enrichment was corrected across all annotations displayed in each of the analyses using FDR correction (FDR ≤ 0.05) and the significance and enrichment scores were plotted (Fig. 2B–D, fig S6A–D).

Genetic and phenotypic correlations and clustering of genetic correlations

LD score regression (*64*) was also used to estimate genetic correlations between cortical regions and with global measures. These results are shown in table S14−15. Phenotypic correlations were calculated from the UK Biobank cohort (residuals correcting for sex, age, ancestry, and global brain measures). We used a threshold of $P \leq 8.3 \times 10^{-4}$ (0.05/60) to correct for multiple testing in the genetic and phenotypic correlations shown in Fig. 3.

To identify patterns of genetic correlations of SA and TH (both with and without correction for global measures), we used Mclust (*75*) for hierarchical cluster analysis, which uses expectation-

maximization to fit parameterized Gaussian mixture models to the data. The best-fitting model for number and shape of clusters was selected as the one with the largest Bayesian Information Criterion. These results are shown in fig. S9.

Genetic correlations were calculated to determine if shared genetic influences contributed to both cortical structure and neuropsychiatric disorders or psychological traits. Summary statistics were downloaded from the following published genome-wide association studies: general cognitive function (*54*), insomnia (*55*), antisocial behavior (*76*), educational attainment (*28*), subjective well-being (*57*), depressive symptoms (*57*), neuroticism (*29*), attention deficit hyperactivity disorder (ADHD; *56*), autism (*77*), bipolar disorder (*78*), anorexia nervosa (*79*), major depressive disorder (*58*), obsessive compulsive disorder (*80*), post-traumatic stress disorder (PTSD; *81*), schizophrenia (*82*), anxiety disorders (*83*), aggression (*84*), Alzheimer's disease (*85*), loneliness (*86*), cigarettes smoked per day (*87*), epilepsy (*88*), Parkinson's disease (*27*), and frontotemporal dementia (*69*). LD score regression was used to calculate genetic correlations (*64*). Significance was corrected for multiple comparisons using FDR across all genetic correlations with average TH and total SA, and significant associations were highlighted in Fig. 5A. To explore regional variability in those significant genetic correlations, genetic correlations were conducted between the trait and the cortical regions (without correcting for global measures) are depicted in Fig. 5B.

Polygenic risk score analyses

To examine the extent to which our analyses could predict SA and TH in an independent dataset, we derived polygenic risk scores (PRS) from the primary meta-analysis results. Using data from an additional 5,095 unrelated individuals of European ancestry from the UK Biobank who were unrelated to participants who contributed to the meta-analysis (*plink 1.90* genetic relatedness $\leq$ 0.025). The index variants used to weight the PRS were identified by clumping the meta-analytic results in plink 1.90 using an r^2 threshold of 0.1 with a 1000 kb window using the genotypic data of the prediction cohort as a reference. Following checks for strand alignment, PRS were calculated using the probabilistic imputed genotype dosages to account for imputation uncertainty. PRS were calculated for *P*-value thresholds of $P \leq 5 \times 10^{-8}$, 1×10^{-5}, 0.001, 0.01, 0.05, 0.1, 0.5, 1. The proportion of variance accounted for by a given PRS was estimated by comparing the R^2 of a linear regression analysis that included the PRS and the covariates that were included in the GWAS analyses to a corresponding analysis that only included the covariates (conducted in *R lm*). The results of these analyses are presented in table S7.

Mendelian randomization and latent causal variant analyses

We performed 2-sample Mendelian randomization (2SMR) and latent causal variant (LCV) analyses to investigate whether significant correlations detected by the analyses above could be driven by causal genetic relationships between an exposure (e.g., total surface area) and an outcome (e.g. the correlated traits). The 2SMR analyses were performed using MR-Base (*59*), which performs a series of MR and sensitivity analyses to evaluate evidence for causality and detect the presence of horizontal pleiotropy (where a SNP directly influences an outcome, violating the MR assumption that SNPs only influence the outcome through their effect on the exposure), and MR-PRESSO (*89*), which detects and then corrects for horizontal pleiotropy by removing SNPs with outlying effects on the outcome trait. For each exposure trait, we included only SNPs GWAS *P*-values $< 5.0 \times 10^{-8}$ which were clumped for LD ($r^2 < 0.01$) to ensure only significantly exposure-associated, independent variants were included as the instrumental

variables. SNP effects were standardized prior to analysis. We conservatively set the threshold for significance at $P = 3.13 \times 10^{-3}$ (0.05/16 trait comparisons). Where there was significant evidence of SNP heterogeneity in effect sizes for outcome traits the analyses were re-run in MR-Base with the outlier SNPs removed as further sensitivity analyses to determine the extent to which the relationship between traits was influenced by the outlier SNPs. The results of the MR analyses are presented in table S18. We present the betas and their standard errors for the two associated quantitative traits in the main text following sensitivity analyses suggesting all included instruments (SNPs) were unbiased (*59*). Additionally, we show odds ratios and 95% confidence intervals reflecting risk per standard deviation increase in the relevant exposure calculated from the inverse variance weighted MR model result in table S18.

A key assumption of MR is that the genetic variants included in the analysis are specific instruments for the exposure under investigation: false positive results can occur in the presence of genetic correlation if the correlation is driven by pleiotropy (*19, 90*). Additionally, the exposure trait (and also the outcome trait where a causal relationship exists) is likely to be affected by residual genetic variation that doesn't surpass the genome-wide significance threshold. To overcome these potential limitations we also performed latent causal variable analyses using LCV-Master (*19*). The LCV method mediates genetic correlation through the use of a latent variable that has a causal effect on each trait. The degree of causality of a trait (trait 1) on another (trait 2) is quantified using a *genetic causality proportion* (gcp) that ranges from -1 to 1, with gcp > abs(0.6) implying full or nearly full genetic causality (*19*). All LCV analyses were performed using genome-wide GWAS summary results (Z-scores) using the default settings. As LCV-Master includes tests for causality in both directions the threshold for significance for these analyses was set at $P = 6.25 \times 10^{-3}$ (0.05/8 trait comparisons). The LCV results are presented in table S19.

Multivariate GWAS analysis

We used TATES (*42*) to conduct two multivariate analyses: one for the 34 regional SA measures, and a separate analysis for the 34 regional TH measures. These analyses were run on the meta-analytic results from the second phase of meta-analysis. Briefly, TATES combines the *P*-values from univariate GWAS while correcting for the phenotypic correlations between traits and does not require access to raw genotypic data (*42*). The power of TATES has been shown to be similar or greater than that of multivariate tests using raw data across a range of scenarios for analyses of 20 or more traits (*91*). For these analyses, we used phenotypic correlations calculated from the UK Biobank cohort (residuals correcting for sex, age, ancestry, and global cortical measures).

Gene-set enrichment analyses

Gene-set enrichment analyses were performed on total SA and average TH as well as the multivariate GWAS results for SA and TH using DEPICT (*25*). Within DEPICT, groups of SNPs were assessed for enrichment in 14,462 gene-sets. These analyses were run using variants with $P \leq 1.0 \times 10^{-5}$. Gene-set enrichment analyses were considered significant if they survived FDR correction ($q \leq 0.05$) (*25*). These results are shown in table S10.

Functional annotation

Potential functional impact was investigated for lead variants and their proxies (defined here as $r^2 > 0.6$ to the lead SNP) at each of the 369 loci nominally associated with global and regional SA and TH using a number of publicly available data sources. The majority of the SNP annotations were as provided by FUMA (*30*) which annotates:

- SNP location (e.g., genic/intergenic)
- the potential for functional effects through predicted effects as determined by CADD (*92*) and Regulome (*93*)
- expression quantitative trait (eQTL) effects. We considered eQTLs within cortical structures from GTEx v7 (*94*), the UK Brain Expression Consortium (*95*), the CommonMind Consortium (*96*), and PsychENCODE (*97*).
- the presence of enhancers and promoters in SNP regions (RoadMap tissues E053, E073, E081, E082, E125)
- chromatin state and interactions in numerous brain tissues (GEO GSE87112). We included data for dorsolateral prefrontal cortex and neural progenitor cells, PsychENCODE, and adult and fetal cortex (*98*).

These data were used by FUMA to map coding and non-coding (e.g. lncRNA) genes to each lead SNP and high LD proxies based on an eQTL effect with FDR-corrected *P*-values ≤ 0.05 in cortical tissue and/or chromatin interactions between the region harboring the lead SNP and a gene promoter in a second chromosomal region (including interactions with an FDR correction ≤ 1×10^{-6}) (*30*). Default FUMA settings were used. In the main text we indicate the FDR values for significant eQTL effects (i.e. FDR Q ≤ 0.05: both the nominal *P*-values and the FDR-corrected values are provided in table S12). FDR values for adult eQTL data from GTEx reported in text as FDR_{GTEx} were derived from beta distribution-adjusted empirical *P*-values of nominal *P*-values from *t*-tests of Pearson product-moment correlation coefficients that were FDR corrected using the Storey Tibshirani method (*30, 94*). FDR values for adult eQTL data from the CommonMind Consortium (CMC) reported in text as FDR_{CMC} were derived from linear regression coefficient *t*-tests that were FDR corrected and accessed by FUMA in Q-value bins (e.g. $Q < 1.0 \times 10^{-2}$). These bin values are reported as whole numbers by FUMA (e.g. the $Q < 1.0 \times 10^{-2}$ bin is reported as $Q = 9.0 \times 10^{-3}$). We report the CMC bin value in the main text, although table S12 (FUMA "gene" output) reports the corresponding FUMA-assigned values. For rs1080066, we also investigated if it was reported as an eQTL in adult blood (*99*), the FDR value reported in text as $FDR_{BIOSgenelevel}$ was derived from meta-analytic *Z*-scores and FDR corrected against permuted data. Fetal eQTL data were taken from O'Brien et al (*34*). FDR values for fetal eQTLs reported in text as FDR_{FETAL} were derived from nominal *P*-values from *t*-tests of Pearson product-moment correlation coefficients reported in the original paper that were FDR corrected for our significant loci using the Benjamini-Hochberg method. HaploReg (*100*) was used to annotate transcription factor binding across multiple tissues, and whether SNPs modified transcription factor binding motifs. The potential for a detrimental effect on protein function due to lead or proxy SNPs located within gene exons was investigated using SIFT and PolyPhen as reported by SNPNexus (*40*).

In Fig. 4A we annotate the genomic context of rs1080066 and high LD proxies associated with additional traits, chromatin state in relevant tissues, and gene expression in pre- and post-natal brains. Chromatin state represents the degree to which 200 bp genomic regions are accessible for transcription. Around each of our associated loci chromatin state was annotated by FUMA (*30*) utilizing the core 15-state model (table S11). In Fig. 4A, genomic regions in three tissues/cells

most relevant to our study (RoadMap E073 dorsolateral prefrontal cortex [Adult cortex], E081 female fetal brain [Fetal brain], and E125 NH-A Astrocytes Primary Cells [Astrocytes]) are indicated as one of the 15 possible chromatin states as predicted by Roadmap Epignomics using ChromHMM, based on data for 5 chromatin marks (H3K4me3, H3K4me1, H3K36me3, H3K27me3, H3K9me3) in 127 epigenomes (*22*). Chromatin states are as follows: TssA:Active Transcription Start Site (TSS); TssAFlnk:Flanking Active TSS; TxFlnk:Transcription at gene 5' and 3'; Tx:Strong transcription; TxWk:Weak transcription; EnhG:Genic enhancers; Enh:Enhancers; ZNF/Rpts:ZNF genes & repeats; Het:Heterochromatin; TssBiv:Bivalent/Poised TSS; BivFlnk:Flanking Bivalent TSS/Enhancer; EnhBiv:Bivalent Enhancer; ReprPC:Repressed; PolyComb; ReprPCWk:Weak Repressed PolyComb; Quies:Quiescent/Low. Pre- and post-natal gene expression data across multiple brain regions was obtained from the BrainSpan Atlas of the Developing Human Brain (http://www.brainspan.org/). These data include gene expression information for cortical tissues indicated on a scale from low (dark blue) to high (dark red) expression on a $\log_2$ RPKM scale (RPKM = Reads Per Kilobase [of transcript per] Million [mapped reads], which normalizes expression levels to account for sequencing depth and gene length). The BRAINSPAN cortical tissues, organised in ontological order, are as follows: DFC:dorsolateral prefrontal cortex; VFC:ventrolateral prefrontal cortex; MFC:anterior (rostral) cingulate (medial prefrontal) cortex; OFC:orbital frontal cortex; M1C:primary motor cortex (area M1, area 4); M1C-S1C:primary motor-sensory cortex (samples); PCx:parietal neocortex; S1C:primary somatosensory cortex (area S1, areas 3,1,2); IPC:posteroventral (inferior) parietal cortex; A1C:primary auditory cortex (core); TCx:temporal neocortex; STC:posterior (caudal) superior temporal cortex (area 22c); ITC:inferolateral temporal cortex (area TEv, area 20); Ocx:occipital neocortex; V1C:primary visual cortex (striate cortex, area V1/17).

For each locus, we evaluated functional annotations for the lead SNP and for additional SNPs considered to be credible causal variants (CCVs) if they were either i) in reasonable LD ($r^2 \geq 0.6$ in individuals of European ancestry) with the lead SNP and/or ii) had *P*-values within 2 orders of magnitude of the lead SNP. As lincRNAs show considerable cell/tissue specificity, in the main text we detail SNP location based on neighboring coding genes, but detail lincRNAs when our lead SNPs show eQTL effects and/or chromatin interactions to these non-coding transcripts. Genes at each associated locus were determined to be potential candidates by considering whether the lead SNP (or a proxy) was an eQTL for a particular gene in adult or fetal cortical tissue (listed above) and/or when chromatin interactions were observed to occur between the region harboring the lead/proxy SNPs and a gene promoter in relevant brain tissues (dorsolateral prefrontal cortex and/or neural progenitor cells).

Analysis of the central sulcus

To follow-up the precentral surface area association with rs1080066, 10,557 UK Biobank MRI scans were further analyzed using BrainVISA-4.5 Morphologist pipeline for the extraction and parameterization of the central sulcus. Quality controlled FreeSurfer outputs (orig.mgz, ribbon.mgz and talairach.auto) were directly imported into the pipeline to use the same grey and white matter segmentations. Sulci were automatically labeled according to a predefined anatomical nomenclature of 61 sulcal labels per hemisphere (*101, 102*). Extracted meshes for the left and right central sulcus were visually quality checked; subjects with mislabeled central sulcus were discarded from further analysis; 6,045 individuals had good quality extractions for both the left and right hemispheres. An additional 52 individuals were removed for genotyping

quality or ancestry reasons. The central sulcus depth profile was measured by extending the method introduced in Cykowski et al. (*47*) and Hopkins et al. (*103*). The ridges at the fundus of the sulcus and at the convex hull, along with the two extremities, were automatically extracted. Using these landmarks, two coordinate fields (x and y) were extrapolated over the entire mesh surface (*104*). Sulcal depth was defined as the distance between paired points at the sulcal fundus and brain envelope that shared the same y coordinate (*105*). For each individual, the parametrized surface was divided into 100 equally spaced points along the length of the sulcus, and the depth at each point was recorded for comparison. We averaged the corresponding depth measurements across the left and right sulcus and calculated the effect of the rs1080066 G allele on the bilaterally averaged depth at each point. These results are shown in Fig. 4D.

Fine mapping

In order to identify putatively causal variants at each associated locus for future functional validation experiments, we performed fine-mapping with CAVIAR (*68*). For each associated locus (defined in table S5), all SNPs with $r^2 > 0.6$ (using 1000G EUR reference panel) to the index SNP for that locus and $P < 0.001$ to the brain trait of interest were input into the CAVIAR program (v2.2). CAVIAR was then run for each locus specifying two causal variants per locus and using LD patterns from 1000G EUR reference panel to identify the set of SNPs that have a 95% probability of containing the causal variants. These are output in table S13. For those loci where the index SNP was not found in 1000G data, only the index SNP was identified as putatively causal.

Supplementary Text

The Desikan-Killiany atlas

The Desikan-Killiany atlas (*10*) used here to define the 34 regions of interest is one of many possible atlases. This atlas was chosen as it is a common output of FreeSurfer, and it is one of the coarser atlases, yielding larger, more consistent regions, defined by the common folding patterns visible on standard MRI. More recent efforts partitioning the cortex into 180 regions have used high-resolution multimodal assessments (MMPC; *106*). Other atlases based on functional partitions have also been used, particularly for analyzing function MRI data (*107, 108*). The breakdown of the cortical surface into 34 large parcels yields clear boundaries between the regions, and allows for anatomically driven quality assessments (see Imaging in the Supplementary Materials and Methods).

The choice of atlas will not have an effect on the global measures; however, the choice of atlas would influence our regional findings, and possibly limit findings, as we may not be able to detect genetic influences on functionally coherent cortical regions, or refined cortical regions partitioned by multimodal MRI measures, for example myelin content, which may have more pathway-specific genetic influences. Assessing the genetic influences on the cortex at a finer scale is an important future effort. However, for multi-cohort efforts such as that performed here, the reliability and accuracy of the parcellations should be assessed across multiple age ranges and MRI acquisition parameters, such as field strength. Automated, and reliable, quality assurance and label accuracy assessments would be an important aspect of this next step.

Our choice of atlas is also likely to influence our findings of regional genetic correlations. It is possible that the correlations between adjacent structures, seen in our analysis, may reflect suboptimal partitioning of the cortex by the atlas; for example, we see a positive genetic correlation between the inferior parietal and the superior parietal gyri, whereas in the MMPC atlas, a portion of each of these two regions is included under a new label, the intraparietal label. Portions of these genetically correlated regions may be re-assigned based on other advanced imaging data, such as multimodal myelin mapping, which may better define cortical cellular architecture.

Sulcal development

Positive genetic correlations between the SA of neighboring regions may also be driven by the development of the sulcus, separating the regions. The pre- and post- central regions (also known as the primary motor and sensorimotor cortices, respectively) are consistently labeled across many cortical atlases as the regions directly anterior and posterior to the central sulcus, which appears early in development (*109*). The SA of all four regions surrounding the calcarine sulcus (the pericalcarine, lingual, cuneus, and lateral occipital region) show positive genetic correlations. The same is also true for the SA of the insula and superior temporal gyri surrounding the lateral sulcus (or Sylvian fissure). These major, early-forming sulci show positive genetic correlations between the regions that directly surround them for SA, but not TH. These observations may imply that part of the genetic influences we observe to be underlying regional SA, may actually be driving the formation of the separating folds, or sulci, during fetal development.

Consortium Authors

Alzheimer's Disease Neuroimaging Initiative (ADNI)

Data used in preparing this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, many investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators may be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf. *ADNI Infrastructure Investigators:* Michael Weiner (UC San Francisco), Paul Aisen (University of Southern California), Ronald Petersen (Mayo Clinic, Rochester), Clifford R. Jack, Jr. (Mayo Clinic, Rochester), William Jagust (UC Berkeley), John Q. Trojanowki (U Pennsylvania), Arthur W. Toga (USC), Laurel Beckett (UC), Davis Robert C. Green (Brigham and Women's Hospital/Harvard Medical School), Andrew J. Saykin (Indiana University), John Morris (Washington University St. Louis), Leslie M. Shaw (University of Pennsylvania). *ADNI External Advisory Board (ESAB):* Zaven Khachaturian (Prevent Alzheimer's Disease 2020 (Chair)), Greg Sorensen (Siemens), Maria Carrillo (Alzheimer's Association), Lew Kuller (University of Pittsburgh), Marc Raichle (Washington University St. Louis), Steven Paul (Cornell University), Peter Davies (Albert Einstein College of Medicine of Yeshiva University), Howard Fillit (AD Drug Discovery Foundation), Franz Hefti (Acumen Pharmaceuticals), David Holtzman (Washington University St. Louis), M. Marcel Mesulam (Northwestern University), William Potter (National Institute of Mental Health), Peter Snyder (Brown University). *ADNI 3 Private Partner Scientific Board (PPSB):* Veronika Logovinsky, (Eli Lilly (Chair)). *Data and*

Publications Committee: Robert C. Green (BWH/HMS (Chair)). *Resource Allocation Review Committee:* Tom Montine (University of Washington (Chair)). *Clinical Core Leaders:* Ronald Petersen (Mayo Clinic, Rochester (Core PI)), Paul Aisen (University of Southern California). *Clinical Informatics and Operations:* Gustavo Jimenez (USC), Michael Donohue (USC), Devon Gessert (USC), Kelly Harless (USC), Jennifer Salazar (USC), Yuliana Cabrera (USC), Sarah Walter (USC), Lindsey Hergesheimer (USC). *Biostatistics Core Leaders and Key Personnel:* Laurel Beckett (UC Davis (Core PI)), Danielle Harvey (UC Davis), Michael Donohue (UC San Diego). *MRI Core Leaders and Key Personnel:* Clifford R. Jack, Jr. (Mayo Clinic, Rochester (Core PI)), Matthew Bernstein (Mayo Clinic, Rochester), Nick Fox (University of London), Paul Thompson (UCLA School of Medicine), Norbert Schuff (UCSF MRI), Charles DeCarli (UC Davis), Bret Borowski (RT Mayo Clinic), Jeff Gunter (Mayo Clinic), Matt Senjem (Mayo Clinic), Prashanthi Vemuri (Mayo Clinic), David Jones (Mayo Clinic), Kejal Kantarci (Mayo Clinic), Chad Ward (Mayo Clinic). *PET Core Leaders and Key Personnel:* William Jagust (UC Berkeley (Core PI)), Robert A. Koeppe (University of Michigan), Norm Foster (University of Utah), Eric M. Reiman (Banner Alzheimer's Institute), Kewei Chen (Banner Alzheimer's Institute), Chet Mathis (University of Pittsburgh), Susan Landau (UC Berkeley). *Neuropathology Core Leaders:* John C. Morris (Washington University St. Louis), Nigel J. Cairns (Washington University St. Louis), Erin Franklin (Washington University St. Louis), Lisa Taylor-Reinwald (Washington University St. Louis – Past Investigator). *Biomarkers Core Leaders and Key Personnel:* Leslie M. Shaw (UPenn School of Medicine), John Q. Trojanowki (UPenn School of Medicine), Virginia Lee (UPenn School of Medicine), Magdalena Korecka (UPenn School of Medicine), Michal Figurski (UPenn School of Medicine). *Informatics Core Leaders and Key Personnel:* Arthur W. Toga (USC (Core PI)), Karen Crawford (USC), Scott Neu (USC). *Genetics Core Leaders and Key Personnel:* Andrew J. Saykin (Indiana University), Tatiana M. Foroud (Indiana University), Steven Potkin (UC Irvine), Li Shen (Indiana University), Kelley Faber (Indiana University), Sungeun Kim (Indiana University), Kwangsik Nho (Indiana University). *Initial Concept Planning & Development:* Michael W. Weiner (UC San Francisco), Leon Thal (UC San Diego), Zaven Khachaturian (Prevent Alzheimer's Disease 2020). *Early Project Proposal Development:* Leon Thal (UC San Diego), Neil Buckholtz (National Institute on Aging), Michael W. Weiner (UC San Francisco), Peter J. Snyder (Brown University), William Potter (National Institute of Mental Health), Steven Paul (Cornell University), Marilyn Albert (Johns Hopkins University), Richard Frank (Richard Frank Consulting), Zaven Khachaturian (Prevent Alzheimer's Disease 2020). *NIA:* John Hsiao (National Institute on Aging). *ADNI Investigators by Site: Oregon Health & Science University*: Joseph Quinn, Lisa C. Silbert, Betty Lind, Jeffrey A. Kaye – Past Investigator, Raina Carter – Past Investigator, Sara Dolen – Past Investigator. *University of Southern California:* Lon S. Schneider, Sonia Pawluczyk, Mauricio Becerra, Liberty Teodoro, Bryan M. Spann – Past Investigator. *University of California – San Diego:* James Brewer, Helen Vanderswag, Adam Fleisher – Past Investigator. *University of Michigan:* Jaimie Ziolkowski, Judith L. Heidebrink, Joanne L. Lord – Past Investigator. *Mayo Clinic, Rochester:* Ronald Petersen, Sara S. Mason, Colleen S. Albers, David Knopman, Kris Johnson – Past Investigator. *Baylor College of Medicine:* Javier Villanueva-Meyer, Valory Pavlik, Nathaniel Pacini, Ashley Lamb, Joseph S. Kass, Rachelle S. Doody – Past Investigator, Victoria Shibley – Past Investigator, Munir Chowdhury – Past Investigator, Susan Rountree – Past Investigator, Mimi Dang – Past Investigator. *Columbia University Medical Center:* Yaakov Stern, Lawrence S. Honig, Karen L. Bell, Randy Yeh. *Washington University, St. Louis:* Beau Ances, John C. Morris, David Winkfield, Maria Carroll,

Angela Oliver, Mary L. Creech – Past Investigator, Mark A. Mintun – Past Investigator, Stacy Schneider – Past Investigator. *University of Alabama - Birmingham:* Daniel Marson, David Geldmacher, Marissa Natelson Love, Randall Griffith – Past Investigator, David Clark – Past Investigator, John Brockington – Past Investigator. *Mount Sinai School of Medicine:* Hillel Grossman, Effie Mitsis – Past Investigator. *Rush University Medical Center:* Raj C. Shah, Melissa Lamar, Patricia Samuels. *Wien Center:* Ranjan Duara, Maria T. Greig-Custo, Rosemarie Rodriguez. *Johns Hopkins University:* Marilyn Albert, Chiadi Onyike, Daniel D'Agostino II, Stephanie Kielb – Past Investigator. *New York University:* Martin Sadowski, Mohammed O. Sheikh, Jamika Singleton-Garvin, Anaztasia Ulysse, Mrunalini Gaikwad. *Duke University Medical Center:* P. Murali Doraiswamy, Jeffrey R. Petrella, Olga James, Salvador Borges-Neto, Terence Z. Wong – Past Investigator, Edward Coleman – Past Investigator. *University of Pennsylvania:* Jason H. Karlawish, David A. Wolk, Sanjeev Vaishnavi, Christopher M. Clark – Past Investigator, Steven E. Arnold – Past Investigator. *University of Kentucky:* Charles D. Smith, Greg Jicha, Peter Hardy, Riham El Khouli, Elizabeth Oates, Gary Conrad. *University of Pittsburgh:* Oscar L. Lopez, MaryAnn Oakley, Donna M. Simpson. *University of Rochester Medical Center:* Anton P. Porsteinsson, Kim Martin, Nancy Kowalksi, Melanie Keltz, Bonnie S. Goldstein – Past Investigator, Kelly M. Makino – Past Investigator, M. Saleem Ismail – Past Investigator, Connie Brand – Past Investigator. *University of California Irvine IMIND:* Gaby Thai, Aimee Pierce, Beatriz Yanez, Elizabeth Sosa, Megan Witbracht. *University of Texas Southwestern Medical School:* Kyle Womack, Dana Mathews, Mary Quiceno. *Emory University:* Allan I. Levey, James J. Lah, Janet S. Cellar. *University of Kansas, Medical Center:* Jeffrey M. Burns, Russell H. Swerdlow, William M. Brooks. *University of California, Los Angeles:* Ellen Woo, Daniel H.S. Silverman, Edmond Teng, Sarah Kremen, Liana Apostolova – Past Investigator, Kathleen Tingus – Past Investigator, Po H. Lu – Past Investigator, George Bartzokis – Past Investigator. *Mayo Clinic, Jacksonville:* Neill R Graff-Radford (London), Francine Parfitt, Kim Poki-Walker. *Indiana University:* Martin R. Farlow, Ann Marie Hake, Brandy R. Matthews – Past Investigator, Jared R. Brosch, Scott Herring. *Yale University School of Medicine:* Christopher H. van Dyck, Richard E. Carson, Pradeep Varma. *McGill Univ., Montreal-Jewish General Hospital:* Howard Chertkow, Howard Bergman, Chris Hosein. *Sunnybrook Health Sciences, Ontario:* Sandra Black, Bojana Stefanovic, Chris (Chinthaka) Heyn. *U.B.C. Clinic for AD & Related Disorders:* Ging-Yuek Robin Hsiung, Benita Mudge, Vesna Sossi, Howard Feldman – Past Investigator, Michele Assaly – Past Investigator. *Cognitive Neurology - St. Joseph's, Ontario:* Elizabeth Finger, Stephen Pasternak, William Pavlosky, Irina Rachinsky – Past Investigator, Dick Drost – Past Investigator, Andrew Kertesz – Past Investigator. *Cleveland Clinic Lou Ruvo Center for Brain Health:* Charles Bernick, Donna Muni. *Northwestern University:* Marek-Marsel Mesulam, Emily Rogalski, Kristine Lipowski, Sandra Weintraub, Borna Bonakdarpour, Diana Kerwin – Past Investigator, Chuang-Kuo Wu,– Past Investigator, Nancy Johnson – Past Investigator. *Premiere Research Inst (Palm Beach Neurology):* Carl Sadowsky, Teresa Villena. *Georgetown University Medical Center:* Raymond Scott Turner, Kathleen Johnson, Brigid Reynolds. *Brigham and Women's Hospital*: Reisa A. Sperling, Keith A. Johnson, Gad A. Marshall. *Stanford University:* Jerome Yesavage, Joy L. Taylor, Steven Chao, Barton Lane – Past Investigator, Allyson Rosen – Past Investigator, Jared Tinklenberg – Past Investigator. *Banner Sun Health Research Institute:* Edward Zamrini, Christine M. Belden, Sherye A. Sirrel. *Boston University:* Neil Kowall, Ronald Killiany, Andrew E. Budson, Alexander Norbash – Past Investigator, Patricia Lynn Johnson – Past Investigator. *Howard University:* Thomas O. Obisesan, Ntekim E. Oyonumo, Joanne Allard, Olu Ogunlana.

Case Western Reserve University: Alan Lerner, Paula Ogrocki, Curtis Tatsuoka, Parianne Fatica. *University of California, Davis – Sacramento:* Evan Fletcher, Pauline Maillard, John Olichney, Charles DeCarli, Owen Carmichael – Past Investigator. *Neurological Care of CNY:* Smita Kittur – Past Investigator. *Parkwood Institute:* Michael Borrie, T-Y Lee, Dr Rob Bartha. *University of Wisconsin:* Sterling Johnson, Sanjay Asthana, Cynthia M. Carlsson. *Banner Alzheimer's Institute:* Pierre Tariot, Anna Burke, Joel Hetelle, Kathryn DeMarco, Nadira Trncic – Past Investigator, Adam Fleisher – Past Investigator, Stephanie Reeder – Past Investigator. *Dent Neurologic Institute:* Vernice Bates, Horacio Capote, Michelle Rainka. *Ohio State University:* Douglas W. Scharre, Maria Kataki, Rawan Tarawneh. *Albany Medical College:* Earl A. Zimmerman, Dzintra Celmins, David Hart. *Hartford Hospital, Olin Neuropsychiatry Research Center:* Godfrey D. Pearlson, Karen Blank, Karen Anderson. *Dartmouth-Hitchcock Medical Center:* Laura A. Flashman, Marc Seltzer, Mary L. Hynes, Robert B. Santulli – Past Investigator. *Wake Forest University Health Sciences:* Kaycee M. Sink, Mia Yang, Akiva Mintz. *Rhode Island Hospital:* Brian R. Ott, Geoffrey Tremont, Lori A. Daiello. *Butler Hospital:* Courtney Bodge, Stephen Salloway, Paul Malloy, Stephen Correia, Athena Lee. *UC San Francisco:* Howard J. Rosen, Bruce L. Miller, David Perry. *Medical University South Carolina:* Jacobo Mintzer, Kenneth Spicer, David Bachman. *St. Joseph's Health Care:* Elizabeth Finger, Stephen Pasternak, Irina Rachinsky, John Rogers, Andrew Kertesz – Past Investigator, Dick Drost – Past Investigator. *Nathan Kline Institute:* Nunzio Pomara, Raymundo Hernando, Antero Sarrael. *University of Iowa College of Medicine:* Delwyn D. Miller, Karen Ekstam Smith, Hristina Koleva, Ki Won Nam, Hyungsub Shim, Susan K. Schultz – Past Investigator. *Cornell University:* Norman Relkin, Gloria Chiang, Michael Lin, Lisa Ravdin. *University of South Florida: USF Health Byrd Alzheimer's Institute:* Amanda Smith, Christi Leach, Balebail Ashok Raj – Past Investigator, Kristin Fargher – Past Investigator.

<u>CHARGE</u> <u>Consortium</u>

Edith Hofer (Clinical Division of Neurogeriatrics, Department of Neurology, Medical University of Graz, Graz, Austria), Gennady V. Roshchupkin (Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, The Netherlands), Hieab H. H. Adams (Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, The Netherlands), Maria J. Knol (Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands), Honghuang Lin (Section of Computational Biomedicine, Department of Medicine, Boston University School of Medicine, Boston, MA, USA), Shuo Li (Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA), Habil Zare (Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, UT Health San Antonio, San Antonio, USA), Shahzad Ahmad (Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands), Nicola J. Armstrong (Mathematics and Statistics, Murdoch University, Perth, Australia), Claudia L. Satizabal (Department of Epidemiology and Biostatistics, Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, UT Health San Antonio, San Antonio, USA), Manon Bernard (Hospital for Sick Children, Toronto, Canada), Joshua C. Bis (Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA, USA), Nathan A. Gillespie (Virginia Institute for Psychiatric and Behavior Genetics, Virginia Commonwealth University, VA, USA), Michelle Luciano (Centre for Cognitive Epidemiology and Cognitive Ageing, University of Edinburgh, Edinburgh, UK), Aniket Mishra (University of Bordeaux, Bordeaux Population Health Research Center, INSERM UMR 1219, Bordeaux, France), Markus Scholz (Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig,

Leipzig, Germany), Alexander Teumer (Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany), Rui Xia (Institute of Molecular Medicine and Human Genetics Center, University of Texas Health Science Center at Houston, Houston, TX, USA), Xueqiu Jian (Institute of Molecular Medicine and Human Genetics Center, University of Texas Health Science Center at Houston, Houston, TX, USA), Thomas H. Mosley (Department of Medicine, University of Mississippi Medical Center, Jackson, MS, USA), Yasaman Saba (Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging, Medical University of Graz, Graz, Austria), Lukas Pirpamer (Clinical Division of Neurogeriatrics, Department of Neurology, Medical University of Graz, Graz, Austria), Stephan Seiler (Imaging of Dementia and Aging (IDeA) Laboratory, Department of Neurology, University of California-Davis, Davis, CA, USA), James T. Becker (Departments of Psychiatry, Neurology, and Psychology, University of Pittsburgh, Pittsburgh, PA, USA), Owen Carmichael (Pennington Biomedical Research Center, Baton Rouge, LA, USA), Jerome I. Rotter (Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute and Pediatrics at Harbor-UCLA Medical Center, Torrance, CA, USA), Bruce M. Psaty (Cardiovascular Health Research Unit, Departments of Medicine, Epidemiology and Health Services, University of Washington, Seattle, WA, USA), Oscar L. Lopez (Departments of Psychiatry, Neurology, and Psychology, University of Pittsburgh, Pittsburgh, PA, USA), Najaf Amin (Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands), Mohsen Ghanbari (Department of Epidemiology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands), Sven J. van der Lee (Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands), Qiong Yang (Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA), Jayandra J. Himali (Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA), Pauline Maillard (Imaging of Dementia and Aging (IDeA) Laboratory, Department of Neurology, University of California-Davis, Davis, CA, USA), Alexa S. Beiser (Department of Neurology, Boston University School of Medicine, Boston, MA, USA), Charles DeCarli (Imaging of Dementia and Aging (IDeA) Laboratory, Department of Neurology, University of California-Davis, Davis, CA, USA), Sherif Karama (McGill University, Montreal Neurological Institute, Montreal, Canada), Lindsay Lewis (McGill University, Montreal Neurological Institute, Montreal, Canada), Mat Harris (Centre for Cognitive Epidemiology and Cognitive Ageing, University of Edinburgh, Edinburgh, UK), Mark E. Bastin (Centre for Cognitive Epidemiology and Cognitive Ageing, University of Edinburgh, Edinburgh, UK), Ian J. Deary (Centre for Cognitive Epidemiology and Cognitive Ageing, University of Edinburgh, Edinburgh, UK), A. Veronica Witte (Department of Neurology, Max Planck Institute of Cognitive and Brain Sciences, Leipzig, Germany), Frauke Beyer (Department of Neurology, Max Planck Institute of Cognitive and Brain Sciences, Leipzig, Germany), Markus Loeffler (Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Leipzig, Germany), Karen A. Mather (Centre for Healthy Brain Ageing,School of Psychiatry, University of New South Wales, Sydney, Australia), Peter R. Schofield (Neuroscience Research Australia, Sydney, Australia), Anbupalam Thalamuthu (Centre for Healthy Brain Ageing,School of Psychiatry, University of New South Wales, Sydney, Australia), John B. Kwok (Brain and Mind Centre - The University of Sydney, Camperdown, NSW, Australia), Margaret J. Wright (Queensland Brain Institute, The University of Queensland, St Lucia, QLD, Australia), David Ames (National Ageing Research Institute, Royal Melbourne Hospital, Victoria, Australia), Julian Trollor (Centre for Healthy Brain Ageing,School of Psychiatry, University of New South Wales, Sydney, Australia), Jiyang Jiang (Centre for

Healthy Brain Ageing,School of Psychiatry, University of New South Wales, Sydney, Australia), Henry Brodaty (Dementia Centre for Research Collaboration, University of New South Wales, Sydney, NSW, Australia), Wei Wen (Centre for Healthy Brain Ageing,School of Psychiatry, University of New South Wales, Sydney, Australia), Meike W. Vernooij (Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, The Netherlands), Albert Hofman (Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA), André G. Uitterlinden (Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands), Wiro J. Niessen (Imaging Physics, Faculty of Applied Sciences, Delft University of Technology, The Netherlands), Katharina Wittfeld (German Center for Neurodegenerative Diseases (DZNE), Site Rostock/ Greifswald, Germany), Robin Bülow (Institute for Diagnostic Radiology and Neuroradiology, University Medicine Greifswald, Greifswald, Germany), Uwe Völker (Interfaculty Institute for Genetics and Functional Genomics, University Medicine Greifswald, Greifswald, Germany), Zdenka Pausova (Hospital for Sick Children, Toronto, Canada), G. Bruce Pike (Departments of Radiology and Clinial Neurosciences, University of Calgary, Calgary, Canada), Sophie Maingault (University of Bordeaux, Institut des Maladies NeurodégénrativesUMR5293, CEA, CNRS, Ubordeaux, Bordeaux, France), Fabrice Crivello (University of Bordeaux, Institut des Maladies NeurodégénrativesUMR5293, CEA, CNRS, Ubordeaux, Bordeaux, France), Christophe Tzourio (University of Bordeaux, Bordeaux Population Health Research Center, INSERM UMR 1219, Bordeaux, France), Philippe Amouyel (Centre Hospitalier Universitaire de Bordeaux, France; Inserm U1167, Lille, France), Bernard Mazoyer (University of Bordeaux, Institut des Maladies NeurodégénrativesUMR5293, CEA, CNRS, Ubordeaux, Bordeaux, France), Michael C. Neale (Virginia Institute for Psychiatric and Behavior Genetics, Virginia Commonwealth University, VA, USA), Carol E. Franz (Department of Psychiatry, University of California San Diego, CA, USA), Michael J. Lyons (Department of Psychological and Brain Sciences, Boston University, Boston, MA, USA), Matthew S. Panizzon (Department of Psychiatry, University of California San Diego, CA, USA), Ole A. Andreassen (NORMENT, KG Jebsen Centre for Psychosis Research, Institute of Clinical Medicine, University of Oslo and Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway), Anders M. Dale (Departments of Radiology and Neurosciences, University of California, San Diego, La Jolla, CA, USA), Mark Logue (National Center for PTSD at Boston VA Healthcare System, Boston, MA, USA), Perminder S. Sachdev (Centre for Healthy Brain Ageing,School of Psychiatry, University of New South Wales, Sydney, Australia), William S. Kremen (Department of Psychiatry, University of California San Diego, CA, USA), Joanna M. Wardlaw (Centre for Cognitive Epidemiology and Cognitive Ageing, University of Edinburgh, Edinburgh, UK), Arno Villringer (Department of Neurology, Max Planck Institute of Cognitive and Brain Sciences, Leipzig, Germany), Cornelia M. van Duijn (Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands), Hans Jörgen Grabe (Department of Psychiatry and Psychotherapy, University Medicine Greifswald, Germany), William T. Longstreth Jr (Departments of Neurology and Epidemiology, University of Washington, Seattle, WA, USA), Myriam Fornage (Institute of Molecular Medicine and Human Genetics Center, University of Texas Health Science Center at Houston, Houston, TX, USA), Tomas Paus (Bloorview Research Institute, Holland Bloorview Kids Rehabilitation Hospital, Toronto, Ontario, Canada), Stephanie Debette (University of Bordeaux, Bordeaux Population Health Research Center, INSERM UMR 1219, Bordeaux, France), M. Arfan Ikram (Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, The Netherlands), Helena Schmidt (Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging, Medical

University of Graz, Graz, Austria), Reinhold Schmidt (Clinical Division of Neurogeriatrics, Department of Neurology, Medical University of Graz, Graz, Austria), Sudha Seshadri (Department of Epidemiology and Biostatistics, Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, UT Health San Antonio, San Antonio, USA).

EPIGEN Consortium
David B. Goldstein (The Centre for Genomics and Population Genetics, Duke University Institute for Genome Sciences and Policy, Durham, North Carolina, USA), Erin L. Heinzen (The Centre for Genomics and Population Genetics, Duke University Institute for Genome Sciences and Policy, Durham, North Carolina, USA), Kevin Shianna (The Centre for Genomics and Population Genetics, Duke University Institute for Genome Sciences and Policy, Durham, North Carolina, USA), Rodney Radtke (Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA) and Ruth Ottmann (Departments of Epidemiology, Neurology, and the G.H. Sergievsky Center, Columbia University, New York, NY).

IMAGEN Consortium
Dr. Eric Artiges (INSERM), Semiha Aydin (Physikalisch-Technische Bundesanstalt), Prof. Dr. Dr. Tobias Banaschewski (Central Institute of Mental Health), Alexis Barbot (Commissariat à l'Energie Atomique), Prof. Dr. Gareth Barker (King's College London), Andreas Becker (Georg-August-Universität Göttingen), Pauline Bezivin-Frere (INSERM), Dr. Francesca Biondo (King's College London), Dr. Arun Bokde (Trinity College Dublin), Uli Bromberg (University of Hamburg), Dr. Ruediger Bruehl, Prof. Dr. Christian Büchel (University of Hamburg), Dr. Congying Chu (King's College London), Dr. Patricia Conrod (King's College London), Laura Daedelow (Charité Universitätsmedizin Berlin), Dr. Jeffrey Dalley (Cambridge University), Dr. Sylvane Desrivieres (King's College London), Eoin Dooley (Trinity College Dublin), Irina Filippi (INSERM), Dr Ariane Fillmer (Physikalisch-Technische Bundesanstalt), Prof. Dr. Herta Flor (Central Institute of Mental Health), Juliane Fröhner (Technische Universität Dresden), Vincent Frouin (Commissariat à l'Energie Atomique), Dr. Hugh Garavan (University of Vermont), Prof. Penny Gowland (University of Nottingham), Yvonne Grimmer (Central Institute of Mental Health), Prof. Dr. Andreas Heinz (Charité Universitätsmedizin Berlin), Dr. Sarah Hohmann (Central Institute of Mental Health), Albrecht Ihlenfeld (Physikalisch-Technische Bundesanstalt), Alex Ing (King's College London), Corinna Isensee (University Medical Center Göttingen), Dr. Bernd Ittermann (Physikalisch-Technische Bundesanstalt), Dr. Tianye Jia (King's College London), Dr. Hervé Lemaitre (INSERM), Emma Lethbridge (University of Nottingham), Prof. Dr. Jean-Luc Martinot (INSERM), Sabina Millenet (Central Institute of Mental Health), Sarah Miller (Charité Universitätsmedizin Berlin), Ruben Miranda (INSERM), PD Dr. Frauke Nees (Central Institute of Mental Health), Dr. Marie-Laure Paillere (INSERM), Dimitri Papadopoulos (INSERM), Prof. Dr. Tomáš Paus (Bloorview Research Institute, Holland Bloorview Kids Rehabilitation Hospital and Departments of Psychology and Psychatry, University of Toronto), Dr. Zdenka Pausova (University of Toronto), Dr. Dr. Jani Pentilla (INSERM), Dr. Jean-Baptiste Poline (Commissariat à l'Energie Atomique), Prof. Dr. Luise Poustka (University Medical Center Göttingen), Dr. Erin Burke Quinlan (King's College London), Dr. Michael Rapp (Charité Universitätsmedizin Berlin), Prof. Dr. Trevor Robbins (Cambridge University), Dr. Gabriel Robert (King's College London), John Rogers (Delosis), Dr. Barbara Ruggeri (King's College London), Prof. Dr. Gunter Schumann (King's College London), Prof. Dr. Michael Smolka (Technische Universität Dresden), Argyris Stringaris

(National Institute of Mental Health), Betteke van Noort (Charité Universitätsmedizin Berlin), Dr. Henrik Walter (Charité Universitätsmedizin Berlin), Dr. Robert Whelan (Trinity College Dublin), Prof. Dr. Steve Williams (King's College London).

Parkinson's Progression Markers Initiative (PPMI)

Data used in preparing this article were obtained from the PPMI database (http://www.ppmi-info.org/). As such, many investigators within the PPMI contributed to the design and implementation of PPMI and/or provided data but did not participate in analysis or writing of this report. A complete listing of PPMI investigators may be found at: http://www.ppmi-info.org/authorslist/. Kenneth Marek (Institute for Neurodegenerative Disorders, New Haven), Danna Jennings (Institute for Neurodegenerative Disorders, New Haven), Shirley Lasch (Institute for Neurodegenerative Disorders, New Haven), Caroline Tanner (University of California, San Francisco), Tanya Simuni (Northwestern University, Chicago), Christopher Coffey (University of Iowa, Iowa City), Karl Kieburtz (Clinical Trials Coordination Center, University of Rochester), Renee Wilson (Clinical Trials Coordination Center, University of Rochester), Werner Poewe (Innsbruck Medical University, Innsbruck), Brit Mollenhauer (Paracelsus-Elena Klinik, Kassel), Douglas Galasko (University of California, San Diego), Tatiana Foroud (Indiana University, Indianapolis), Todd Sherer (The Michael J. Fox Foundation for Parkinson's Research, New York), Sohini Chowdhury (The Michael J. Fox Foundation for Parkinson's Research, New York), Mark Frasier (The Michael J. Fox Foundation for Parkinson's Research, New York), Catherine Kopil (The Michael J. Fox Foundation for Parkinson's Research, New York), Vanessa Arnedo (The Michael J. Fox Foundation for Parkinson's Research, New York), Alice Rudolph (Clinical Trials Coordination Center, University of Rochester), Cynthia Casaceli (Clinical Trials Coordination Center, University of Rochester), John Seibyl (Institute for Neurodegenerative Disorders, New Haven), Susan Mendick (Institute for Neurodegenerative Disorders, New Haven), Norbert Schuff (University of California, San Francisco), Chelsea Caspell (University of Iowa, Iowa City), Liz Uribe (University of Iowa, Iowa City), Eric Foster (University of Iowa, Iowa City), Katherine Gloer (University of Iowa, Iowa City), Jon Yankey (University of Iowa, Iowa City), Arthur Toga (Laboratory of Neuroimaging (LONI), University of Southern California), Karen Crawford (Laboratory of Neuroimaging (LONI), University of Southern California), Paola Casalin (BioRep, Milan), Giulia Malferrari (BioRep, Milan), Andrew Singleton (National Institute on Aging, NIH, Bethesda), Keith A. Hawkins (Yale University, New Haven), David Russell (Institute for Neurodegenerative Disorders, New Haven), Stewart Factor (Emory University of Medicine, Atlanta), Penelope Hogarth (Oregon Health and Science University, Portland), David Standaert (University of Alabama at Birmingham, Birmingham), Robert Hauser (University of South Florida, Tampa), Joseph Jankovic (Baylor College of Medicine, Houston), Matthew Stern (University of Pennsylvania, Philadelphia), Lama Chahine (University of Pennsylvania, Philadelphia), James Leverenz (University of Washington, Seattle), Samuel Frank (Boston University, Boston), Irene Richard (University of Rochester, Rochester), Klaus Seppi (Innsbruck Medical University, Innsbruck), Holly Shill (Banner Research Institute, Sun City), Hubert Fernandez (Cleveland Clinic, Cleveland), Daniela Berg (University of Tuebingen, Tuebingen), Isabel Wurster (University of Tuebingen, Tuebingen), Zoltan Mari (Johns Hopkins University, Baltimore), David Brooks (Imperial College of London, London), Nicola Pavese (Imperial College of London, London), Paolo Barone (University of Salerno, Salerno), Stuart Isaacson (Parkinson's Disease and Movement Disorders Center, Boca Raton), Alberto Espay

(University of Cincinnati, Cincinnati), Dominic Rowe (Macquarie University, Sydney), Melanie Brandabur (The Parkinson's Institute, Sunnyvale), James Tetrud (The Parkinson's Institute, Sunnyvale), Grace Liang (The Parkinson's Institute, Sunnyvale), Alex Iranzo (Hospital Clinic of Barcelona, Barcelona), Eduardo Tolosa (Hospital Clinic of Barcelona, Barcelona), Shu-Ching Hu (University of Washington, Seattle), Gretchen Todd (University of Washington, Seattle), Laura Leary (Institute for Neurodegenerative Disorders, New Haven), Cheryl Riordan (Institute for Neurodegenerative Disorders, New Haven), Linda Rees (The Parkinson's Institute, Sunnyvale), Alicia Portillo (Oregon Health and Science University, Portland), Art Lenahan (Oregon Health and Science University, Portland), Karen Williams (Northwestern University, Chicago), Stephanie Guthrie (University of Alabama at Birmingham, Birmingham), Ashlee Rawlins (University of Alabama at Birmingham, Birmingham), Sherry Harlan (University of South Florida, Tampa), Christine Hunter (Baylor College of Medicine, Houston), Baochan Tran (University of Pennsylvania, Philadelphia), Abigail Darin (University of Pennsylvania, Philadelphia), Carly Linder (University of Pennsylvania, Philadelphia), Marne Baca (University of Washington, Seattle), Heli Venkov (University of Washington, Seattle), Cathi-Ann Thomas (Boston University, Boston), Raymond James (Boston University, Boston), Cheryl Deeley (University of Rochester, Rochester), Courtney Bishop (University of Rochester, Rochester), Fabienne Sprenger (Innsbruck Medical University, Innsbruck), Diana Willeke (Paracelsus-Elena Klinik, Kassel), Sanja Obradov (Banner Research Institute, Sun City), Jennifer Mule (Cleveland Clinic, Cleveland), Nancy Monahan (Cleveland Clinic, Cleveland), Katharina Gauss (University of Tuebingen, Tuebingen), Deborah Fontaine (University of California, San Diego), Christina Gigliotti (University of California, San Diego), Arita McCoy (Johns Hopkins University, Baltimore), Becky Dunlop (Johns Hopkins University, Baltimore), Bina Shah (Imperial College of London, London), Susan Ainscough (University of Salerno, Salerno), Angela James (Parkinson’s Disease and Movement Disorders Center, Boca Raton), Rebecca Silverstein (Parkinson’s Disease and Movement Disorders Center, Boca Raton), Kristy Espay (University of Cincinnati, Cincinnati), Madelaine Ranola (Macquarie University, Sydney), Thomas Comery (Pfizer, Inc., Groton), Jesse Cedarbaum (Biogen Idec, Cambridge), Bernard Ravina (Biogen Idec, Cambridge), Igor D. Grachev (GE Healthcare, Princeton), Jordan S. Dubow (AbbVie, Abbot Park), Michael Ahlijanian (Bristol-Myers Squibb Company), Holly Soares (Bristol-Myers Squibb Company), Suzanne Ostrowizki (F.Hoffmann La-Roche, Basel), Paulo Fontoura (F.Hoffmann La-Roche, Basel), Alison Chalker (Merck & Co., North Wales), David L. Hewitt (Merck & Co., North Wales), Marcel van der Brug (Genentech, Inc., South San Francisco), Alastair D. Reith (GlaxoSmithKline, Stevenage), Peggy Taylor (Covance, Dedham), Jan Egebjerg (H. Lundbeck), Mark Minton (Avid Radiopharmaceuticals, Philadelphia), Andrew Siderowf (Avid Radiopharmaceuticals, Philadelphia), Pierandrea Muglia (UCB Pharma S.A., Brussels), Robert Umek (Meso Scale Discovery), Ana Catafau (Meso Scale Discovery), Vera Kiyasova (Servier), Barbara Saba (Servier). **SYS Consortium:** Tomáš Paus MD PhD (Bloorview Research Institute, University of Toronto, Canada), Zdenka Pausova, MD (The Hospital for Sick Children, University of Toronto, Canada), G. Bruce Pike PhD (Department of Radiology, University of Calgary, Canada), Louis Richer PhD (Department of Health Sciences, University of Quebec in Chicoutimi, Canada), Gabriel Leonard PhD (Montreal Neurological Institute, McGill University, Canada), Michel Perron PhD (CEGEP Jonquiere, Canada), Suzanne Veillette PhD (CEGEP Jonquiere, Canada) and Manon Bernard BComp (The Hospital for Sick Children, University of Toronto, Canada).

Enhancing NeuroImaging Genetics through Meta-Analysis Consortium (ENIGMA)-— Genetics working group

Katrina L. Grasby, Neda Jahanshad, Jodie N. Painter, Lucía Colodro-Conde, Janita Bralten, Derrek P. Hibar, Penelope A. Lind, Fabrizio Pizzagalli, Christopher R.K. Ching, Mary Agnes B. McMahon, Natalia Shatokhina, Leo C.P. Zsembik, Ingrid Agartz, Saud Alhusaini, Marcio A.A. Almeida, Dag Alnæs, Inge K. Amlien, Micael Andersson, Tyler Ard, Nicola J. Armstrong, Allison Ashley-Koch, Joshua R. Atkins, Manon Bernard, Rachel M. Brouwer, Elizabeth E.L. Buimer, Robin Bülow, Christian Bürger, Dara M. Cannon, Mallar Chakravarty, Qiang Chen, Joshua W. Cheung, Baptiste Couvy-Duchesne, Anders M. Dale, Shareefa Dalvie, Tânia K. de Araujo, Greig I. de Zubicaray, Sonja M.C. de Zwarte, Anouk den Braber, Nhat Trung Doan, Katharina Dohm, Stefan Ehrlich, Hannah-Ruth Engelbrecht, Susanne Erk, Chun Chieh Fan, Iryna O. Fedko, Sonya F. Foley, Judith M. Ford, Masaki Fukunaga, Melanie E. Garrett, Tian Ge, Sudheer Giddaluru, Aaron L. Goldman, Melissa J. Green, Nynke A. Groenewold, Dominik Grotegerd, Tiril P. Gurholt, Boris A. Gutman, Narelle K. Hansell, Mathew A. Harris, Marc B. Harrison, Courtney C. Haswell, Michael Hauser, Stefan Herms, Dirk J. Heslenfeld, New Fei Ho, David Hoehn, Per Hoffmann, Laurena Holleran, Martine Hoogman, Jouke-Jan Hottenga, Masashi Ikeda, Deborah Janowitz, Iris E. Jansen, Tianye Jia, Christiane Jockwitz, Ryota Kanai, Sherif Karama, Dalia Kasperaviciute, Tobias Kaufmann, Sinead Kelly, Masataka Kikuchi, Marieke Klein, Michael Knapp, Annchen R. Knodt, Bernd Krämer, Max Lam, Thomas M. Lancaster, Phil H. Lee, Tristram A. Lett, Lindsay B. Lewis, Iscia Lopes-Cendes, Michelle Luciano, Fabio Macciardi, Andre F. Marquand, Samuel R. Mathias, Tracy R. Melzer, Yuri Milaneschi, Nazanin Mirza-Schreiber, Jose C.V. Moreira, Thomas W. Mühleisen, Bertram Müller-Myhsok, Pablo Najt, Soichiro Nakahara, Kwangsik Nho, Loes M. Olde Loohuis, Dimitri Papadopoulos Orfanos, John F. Pearson, Toni L. Pitcher, Benno Pütz, Yann Quidé, Anjanibhargavi Ragothaman, Faisal M. Rashid, William R. Reay, Ronny Redlich, Céline S. Reinbold, Jonathan Repple, Geneviève Richard, Brandalyn C. Riedel, Shannon L. Risacher, Cristiane S. Rocha, Nina Roth Mota, Lauren Salminen, Arvin Saremi, Andrew J. Saykin, Fenja Schlag, Lianne Schmaal, Peter R. Schofield, Rodrigo Secolin, Chin Yang Shapland, Li Shen, Jean Shin, Elena Shumskaya, Ida E. Sønderby, Emma Sprooten, Lachlan T. Strike, Katherine E. Tansey, Alexander Teumer, Anbupalam Thalamuthu, Sophia I. Thomopoulos, Diana Tordesillas-Gutiérrez, Jessica A. Turner, Anne Uhlmann, Costanza Ludovica Vallerga, Dennis van der Meer, Marjolein M.J. van Donkelaar, Liza van Eijk, Theo G.M. van Erp, Neeltje E.M. van Haren, Daan van Rooij, Marie-José van Tol, Jan H. Veldink, Ellen Verhoef, Esther Walton, Mingyuan Wang, Yunpeng Wang, Joanna M. Wardlaw, Wei Wen, Lars T. Westlye, Christopher D. Whelan, Stephanie H. Witt, Katharina Wittfeld, Christiane Wolf, Thomas Wolfers, Jing Qin Wu, Clarissa L. Yasuda, Dario Zaremba, Zuo Zhang, Alyssa H. Zhu, Marcel P. Zwiers, Eric Artiges, Amelia A. Assareh, Rosa Ayesa-Arriola, Aysenil Belger, Christine L. Brandt, Gregory G. Brown, Sven Cichon, Joanne E. Curran, Gareth E. Davies, Franziska Degenhardt, Michelle F. Dennis, Bruno Dietsche, Srdjan Djurovic, Colin P. Doherty, Ryan Espiritu, Daniel Garijo, Yolanda Gil, Penny A. Gowland, Robert C. Green, Alexander N. Häusler, Walter Heindel, Beng-Choon Ho, Wolfgang U. Hoffmann, Florian Holsboer, Georg Homuth, Norbert Hosten, Clifford R. Jack Jr., MiHyun Jang, Andreas Jansen, Nathan A. Kimbrel, Knut Kolskår, Sanne Koops, Axel Krug, Kelvin O. Lim, Jurjen J. Luykx, Daniel H. Mathalon, Karen A. Mather, Venkata S. Mattay, Sarah Matthews, Jaqueline Mayoral Van Son, Sarah C. McEwen, Ingrid Melle, Derek W. Morris, Bryon A. Mueller, Matthias Nauck, Jan E. Nordvik, Markus M. Nöthen, Daniel S. O'Leary, Nils Opel, Marie-Laure Paillère Martinot, G. Bruce Pike, Adrian Preda, Erin B.

Quinlan, Paul E. Rasser, Varun Ratnakar, Simone Reppermund, Vidar M. Steen, Paul A. Tooney, Fábio R. Torres, Dick J. Veltman, James T. Voyvodic, Robert Whelan, Tonya White, Hidenaga Yamamori, Marina K.M. Alvim, David Ames, Tim J. Anderson, Ole A. Andreassen, Alejandro Arias-Vasquez, Mark E. Bastin, Bernhard T. Baune, Jean C. Beckham, John Blangero, Dorret I. Boomsma, Henry Brodaty, Han G. Brunner, Randy L. Buckner, Jan K. Buitelaar, Juan R. Bustillo, Wiepke Cahn, Murray J. Cairns, Vince Calhoun, Vaughan J. Carr, Xavier Caseras, Svenja Caspers, Gianpiero L. Cavalleri, Fernando Cendes, Aiden Corvin, Benedicto Crespo-Facorro, John C. Dalrymple-Alford, Udo Dannlowski, Eco J.C. de Geus, Ian J. Deary, Norman Delanty, Chantal Depondt, Sylvane Desrivières, Gary Donohoe, Thomas Espeseth, Guillén Fernández, Simon E. Fisher, Herta Flor, Andreas J. Forstner, Clyde Francks, Barbara Franke, David C. Glahn, Randy L. Gollub, Hans J. Grabe, Oliver Gruber, Asta K. Håberg, Ahmad R. Hariri, Catharina A. Hartman, Ryota Hashimoto, Andreas Heinz, Frans A. Henskens, Manon H.J. Hillegers, Pieter J. Hoekstra, Avram J. Holmes, L. Elliot Hong, Hilleke E. Hulshoff Pol, Terry L. Jernigan, Erik G. Jönsson, René S. Kahn, Martin A. Kennedy, Tilo T.J. Kircher, Peter Kochunov, John B.J. Kwok, Stephanie Le Hellard, Carmel M. Loughland, Nicholas G. Martin, Jean-Luc Martinot, Colm McDonald, Katie L. McMahon, Andreas Meyer-Lindenberg, Patricia T. Michie, Rajendra A. Morey, Bryan Mowry, Lars Nyberg, Jaap Oosterlaan, Roel A. Ophoff, Christos Pantelis, Tomas Paus, Zdenka Pausova, Brenda W.J.H. Penninx, Tinca J.C. Polderman, Danielle Posthuma, Marcella Rietschel, Joshua L. Roffman, Laura M. Rowland, Perminder S. Sachdev, Philipp G. Sämann, Ulrich Schall, Gunter Schumann, Rodney J. Scott, Kang Sim, Sanjay M. Sisodiya, Jordan W. Smoller, Iris E. Sommer, Beate St Pourcain, Dan J. Stein, Arthur W. Toga, Julian N. Trollor, Nic J.A. Van der Wee, Dennis van 't Ent, Henry Völzke, Henrik Walter, Bernd Weber, Daniel R. Weinberger, Margaret J. Wright, Juan Zhou, Jason L. Stein, Paul M. Thompson, Sarah E. Medland.

Additional Cohort Information

1000BRAINS

Is a population-based cohort based on the Heinz-Nixdorf Recall Study (HNR) and is supported in part by the German National Cohort. We thank the Heinz Nixdorf Foundation (Germany) for their generous support in terms of the Heinz Nixdorf Study.

ADNI1 and ADNI2GO

Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative database (adni.loni.usc.edu). The ADNI was launched in 2003 as a 5-year public–private partnership, led by Principal Investigator Michael W. Weiner, MD. The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD) and to assess and optimize biomarkers for clinical trials in AD. The initial sample included older adults who were cognitive normal (CN) as well as meeting criteria for MCI and clinical AD. In 2011, ADNI-2 began to recruit an additional CN group as well as individuals with significant memory concerns (SMC), early MCI and late MCI, and AD. These subjects, and others carried forward from ADNI-1, were scanned with an updated neuroimaging protocol. Participants were recruited from over 60 sites across the

U.S. and Canada. For up-to-date information, please see www.adni-info.org. ADNI data are disseminated by the Laboratory for Neuro Imaging at the University of Southern California.

ALSPAC

Pregnant women resident in Avon, UK with expected dates of delivery 1st April 1991 to 31st December 1992 were invited to take part in the study. The initial number of pregnancies enrolled is 14,541 (for these at least one questionnaire has been returned or a "Children in Focus" clinic had been attended by 19/07/99). Of these initial pregnancies, there was a total of 14,676 fetuses, resulting in 14,062 live births and 13,988 children who were alive at 1 year of age. When the oldest children were approximately 7 years of age, an attempt was made to bolster the initial sample with eligible cases who had failed to join the study originally. As a result, when considering variables collected from the age of seven onwards (and potentially abstracted from obstetric notes) there are data available for more than the 14,541 pregnancies mentioned above. The number of new pregnancies not in the initial sample (known as Phase I enrolment) that are currently represented on the built files and reflecting enrolment status at the age of 18 is 706 (452 and 254 recruited during Phases II and III respectively), resulting in an additional 713 children being enrolled. The phases of enrolment are described in more detail in the cohort profile paper (see footnote 4 below). The total sample size for analyses using any data collected after the age of seven is therefore 15,247 pregnancies, resulting in 15,458 fetuses. Of this total sample of 15,458 fetuses, 14,775 were live births and 14,701 were alive at 1 year of age. A 10% sample of the ALSPAC cohort, known as the Children in Focus (CiF) group, attended clinics at the University of Bristol at various time intervals between 4 to 61 months of age. The CiF group were chosen at random from the last 6 months of ALSPAC births (1432 families attended at least one clinic). Excluded were those mothers who had moved out of the area or were lost to follow-up, and those partaking in another study of infant development in Avon. The data used in the present study were collected from 391 males and further description of this subset and the variables used in this study are provided in Tables S2–S4. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. This publication is the work of the authors and they will serve as guarantors for the contents of this paper. The study website contains details of all the data that is available through a fully searchable data dictionary (http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/). Further information can be found in the following papers: Boyd A, Golding J, Macleod J, Lawlor DA, Fraser A, Henderson J, Molloy L, Ness A, Ring S, Davey Smith G. Cohort Profile: The 'Children of the 90s'; the index offspring of The Avon Longitudinal Study of Parents and Children (ALSPAC). International Journal of Epidemiology 2013; 42: 111-127; Fraser A, Macdonald-Wallis C, Tilling K, Boyd A, Golding J, Davey Smith G, Henderson J, Macleod J, Molloy L, Ness A, Ring S, Nelson SM, Lawlor DA. Cohort Profile: The Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. International Journal of Epidemiology 2013; 42:97-110.

BIG

The Brain Imaging Genetics (BIG) database was established in Nijmegen, the Netherlands in 2007. This resource is now part of Cognomics, a joint initiative by researchers of the Donders Centre for Cognitive Neuroimaging, the Human Genetics and Cognitive Neuroscience departments of the Radboud University Medical Center, and the Max Planck Institute for Psycholinguistics (funded by the Max Planck Society). The present study includes two

subsamples of BIG, from successive waves of genotyping on Affymetrix (BIG-Affy) and PsychChip (BIG-PsychChip) arrays. Analyses for this project were carried out on the Dutch national e-infrastructure with the support of SURF Cooperative.

GIG
The GIG (Genomic Imaging Göttingen) sample was established at the Center for Translational Research in Systems Neuroscience and Psychiatry (Head: Prof. Dr. O. Gruber) at Göttingen University.

GSP: Brain Genomics Superstruct Project (GSP): Data were provided [in part] by the Brain GSP of Harvard University and the Massachusetts General Hospital, with support from the Center for BrainScience Neuroinformatics Research Group, the Athinoula A. Martinos Center for Biomedical Imaging and the Center for Human Genetic Research. Twenty individual investigators at Harvard and Massachusetts General Hospital generously contributed data to GSP.

HUNT
The HUNT Study is a collaboration between HUNT Research Centre (Faculty of Medicine and Movement Sciences, NTNU – Norwegian University of Science and Technology), Nord-Trøndelag County Council, Central Norway Health Authority, and the Norwegian Institute of Public Health.

IMpACT
The International Multi-centre persistent ADHD CollaboraTion (IMpACT), is a consortium of clinical and basic researchers from several European countries (The Netherlands, Germany, Spain, Norway, The United Kingdom, Sweden), from the United States of America, and from Brazil.

LBC1936
The work was undertaken as part of the Cross Council and University of Edinburgh Centre for Cognitive Ageing and Cognitive Epidemiology (CCACE; http://www.ccace.ed.ac.uk). The image acquisition and analysis was performed at the Brain Research Imaging Centre, University of Edinburgh (http://www.bric.ed.ac.uk).

MPIP
The MPIP Munich Morphometry Sample comprises images acquired as part of the Munich Antidepressant Response Signature (MARS) Study and the Recurrent Unipolar Depression (RUD) Case-Control study performed at the MPIP, and control subjects acquired at the Ludwig-Maximilians-University, Munich, Department of Psychiatry. **PPMI**: Data used in the preparation of this article were obtained from the Parkinson's Progression Markers Initiative (PPMI) database (www.ppmi-info.org/data). For up-to-date information on the study, visit www.ppmi-info.org.

UK Biobank
This research has been conducted using the UK Biobank Resource under Application Number '11559'.

Supplementary Acknowledgements

International Frontotemporal Dementia GWAS Consortium

Authors: Raffaele Ferrari, Dena G Hernandez, Michael A Nalls, Jonathan D Rohrer, Adaikalavan Ramasamy, John BJ Kwok, Carol Dobson-Stone, William S Brooks, Peter R Schofield, Glenda M Halliday, John R Hodges, Olivier Piguet, Lauren Bartley, Elizabeth Thompson, Eric Haan, Isabel Hernández, Agustín Ruiz, Mercè Boada, Barbara Borroni, Alessandro Padovani, Carlos Cruchaga, Nigel J Cairns, Luisa Benussi, Giuliano Binetti, Roberta Ghidoni, Gianluigi Forloni, Diego Albani, Daniela Galimberti, Chiara Fenoglio, Maria Serpente, Elio Scarpini, Jordi Clarimón, Alberto Lleó, Rafael Blesa, Maria Landqvist Waldö, Karin Nilsson, Christer Nilsson, Ian RA Mackenzie, Ging-Yuek R Hsiung, David MA Mann, Jordan Grafman, Christopher M Morris, Johannes Attems, Ian G McKeith, Alan J Thomas, Pietro Pietrini, Edward D Huey, Eric M Wassermann, Atik Baborie, Evelyn Jaros, Michael C Tierney, Pau Pastor, Cristina Razquin, Sara Ortega-Cubero, Elena Alonso, Robert Perneczky, Janine Diehl- Schmid, Panagiotis Alexopoulos, Alexander Kurz, Innocenzo Rainero, Elisa Rubino, Lorenzo Pinessi, Ekaterina Rogaeva, Peter St George-Hyslop, Giacomina Rossi, Fabrizio Tagliavini, Giorgio Giaccone, James B Rowe, Johannes CM Schlachetzki, James Uphill, John Collinge, Simon Mead, Adrian Danek, Vivianna M Van Deerlin, Murray Grossman, John Q Trojanowski, Julie van der Zee, Marc Cruts, Christine Van Broeckhoven, Stefano F Cappa, Isabelle Leber, Didier Hannequin, Véronique Golfier, Martine Vercelletto, Alexis Brice, Benedetta Nacmias, Sandro Sorbi, Silvia Bagnoli, Irene Piaceri, Jørgen E Nielsen, Lena E Hjermind, Matthias Riemenschneider, Manuel Mayhaus, Bernd Ibach, Gilles Gasparoni, Sabrina Pichler, Wei Gu, Martin N Rossor, Nick C Fox, Jason D Warren, Maria Grazia Spillantini, Huw R Morris, Patrizia Rizzu, Peter Heutink, Julie S Snowden, Sara Rollinson, Anna Richardson, Alexander Gerhard, Amalia C Bruni, Raffaele Maletta, Francesca Frangipane, Chiara Cupidi, Livia Bernardi, Maria Anfossi, Maura Gallo, Maria Elena Conidi, Nicoletta Smirne, Rosa Rademakers, Matt Baker, Dennis W Dickson, Neill R Graff-Radford, Ronald C Petersen, David Knopman, Keith A Josephs, Bradley F Boeve, Joseph E Parisi, William W Seeley, Bruce L Miller, Anna M Karydas, Howard Rosen, John C van Swieten, Elise GP Dopper, Harro Seelaar, Yolande AL Pijnenburg, Philip Scheltens, Giancarlo Logroscino, Rosa Capozzo, Valeria Novelli, Annibale A Puca, Massimo Franceschi, Alfredo Postiglione, Graziella Milan, Paolo Sorrentino, Mark Kristiansen, Huei-Hsin Chiang, Caroline Graff, Florence Pasquier, Adeline Rollin, Vincent Deramecourt, Thibaud Lebouvier, Dimitrios Kapogiannis, Luigi Ferrucci, Stuart Pickering-Brown, Andrew B Singleton, John Hardy, Parastoo Momeni.

Acknowledgements: Intramural funding from the National Institute of Neurological Disorders and Stroke (NINDS) and National Institute on Aging (NIA), the Wellcome/MRC Centre on Parkinson's disease, Alzheimer's Research UK (ARUK, Grant ARUK-PG2012-18) and by the office of the Dean of the School of Medicine, Department of Internal Medicine, at Texas Tech University Health Sciences Center. We thank Mike Hubank and Kerra Pearce at the Genomic core facility at the Institute of Child Health (ICH), University College of London (UCL), for assisting RF in performing Illumina genotyping experiments (FTD-GWAS genotyping). This study utilized the high-performance computational capabilities of the Biowulf Linux cluster at the National Institutes of Health, Bethesda, Md. (http://biowulf.nih.gov). North American Brain Expression Consortium (NABEC) - The work performed by the North American Brain

Expression Consortium (NABEC) was supported in part by the Intramural Research Program of the National Institute on Aging, National Institutes of Health, part of the US Department of Health and Human Services; project number ZIA AG000932-04. In addition this work was supported by a Research Grant from the Department of Defense, W81XWH-09-2-0128. UK Brain Expression Consortium (UKBEC) - This work performed by the UK Brain Expression Consortium (UKBEC) was supported by the MRC through the MRC Sudden Death Brain Bank (C.S.), by a Project Grant (G0901254 to J.H. and M.W.) and by a Fellowship award (G0802462 to M.R.). D.T. was supported by the King Faisal Specialist Hospital and Research Centre, Saudi Arabia. Computing facilities used at King's College London were supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London. We would like to thank AROS Applied Biotechnology AS company laboratories and Affymetrix for their valuable input. RF's work is supported by Alzheimer's Society (grant number 284), UK; JBJK was supported by the National Health and Medical Resarch Council (NHMRC) Australia, Project Grants 510217 and 1005769; CDS was supported by NHMRC Project Grants 630428 and 1005769; PRS was supported by NHMRC Project Grants 510217 and 1005769 and acknowledges that DNA samples were prepared by Genetic Repositories Australia, supported by NHMRC Enabling Grant 401184; GMH was supported by NHMRC Research Fellowship 630434, Project Grant 1029538, Program Grant 1037746; JRH was supported by the Australian Research Council Federation Fellowship, NHMRC Project Grant 1029538, NHMRC Program Grant 1037746; OP was supported by NHMRC Career Development Fellowship 1022684, Project Grant 1003139. IH, AR and MB acknowledge the patients and controls who participated in this project and the Trinitat Port-Carbó and her family who are supporting Fundació ACE research programs. CC was supported by Grant P30- NS069329-01 and acknowledges that the recruitment and clinical characterization of research participants at Washington University were supported by NIH P50 AG05681, P01 AG03991, and P01 AG026276. LB and GB were supported by the Ricerca Corrente, Italian Ministry of Health; RG was supported by Fondazione CARIPLO 2009-2633, Ricerca Corrente, Italian Ministry of Health; GF was supported by Fondazione CARIPLO 2009-2633. ES was supported by the Italian Ministry of Health; CF was supported by Fondazione Cariplo; MS was supported from the Italian Ministry of Health (Ricerca Corrente); MLW was supported by Government funding of clinical research within NHS Sweden (ALF); KN was supported by Thure Carlsson Foundation; CN was supported by Swedish Alzheimer Fund. IRAM and GYRH were supported by CIHR (grant 74580) PARF (grant C06-01). JG was supported by the NINDS intramural research funds for FTD research. CMM was supported by Medical Research Council UK, Brains for Dementia Research, Alzheimer's Society, Alzheimer's Research UK, National Institutes for Health Research, Department of Health, Yvonne Mairy Bequest and acknowledges that tissue made available for this study was provided by the Newcastle Brain Tissue Resource, which was funded in part by grants G0400074 and G1100540 from the UK MRC, the Alzheimer's Research Trust and Alzheimer's Society through the Brains for Dementia Research Initiative and an NIHR Biomedical Research Centre Grant in Ageing and Health, and NIHR Biomedical Research Unit in Lewy Body Disorders. CMM was supported by the UK Department of Health and Medical Research Council and the Research was supported by the National Institute for Health Research Newcastle Biomedical Research Centre based at Newcastle Hospitals Foundation Trust and Newcastle University and acknowledges that the views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health; JA was supported by MRC, Dunhill Medical Trust, Alzheimer's Research

UK; TDG was supported by Wellcome Trust Senior Clinical Fellow; IGM was supported by NIHR Biomedical Research Centre and Unit on Ageing Grants and acknowledges the National Institute for Health Research Newcastle Biomedical Research Centre based at Newcastle Hospitals Foundation Trust and Newcastle University. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health; AJT was supported by Medical Research Council, Alzheimer's Society, Alzheimer's Research UK, National Institutes for Health Research. EJ was supported by NIHR, Newcastle Biomedical Research Centre. PP, CR, SOC and EA were supported partially by FIMA (Foundation for Applied Medical Research); PP acknowledges Manuel Seijo-Martínez (Department of Neurology, Hospital do Salnés, Pontevedra, Spain), Ramon Rene, Jordi Gascon and Jaume Campdelacreu (Department of Neurology, Hospital de Bellvitge, Barcelona, Spain) for providing FTD DNA samples. RP, JDS, PA and AK were supported by German Federal Ministry of Education and Research (BMBF; grant number FKZ 01GI1007A – German FTLD consortium). IR was supported by Ministero dell'Istruzione, dell'Università e della Ricerca (MIUR) of Italy. PStGH was supported by the Canadian Institutes of Health Research, Wellcome Trust, Ontario Research Fund. FT was supported by the Italian Ministry of Health (ricerca corrente) and MIUR grant RBAP11FRE9; GR and GG were supported by the Italian Ministry of Health (ricerca corrente). JBR was supported by Camrbidge NIHR Biomedical Research Centre and Wellcome Trust (088324). JU, JC, SM were supported by the MRC Prion Unit core funding and acknowledge MRC UK, UCLH Biomedical Research Centre, Queen Square Dementia BRU; SM acknowledges the work of John Beck, Tracy Campbell, Gary Adamson, Ron Druyeh, Jessica Lowe, Mark Poulter. AD acknowledges the work of Benedikt Bader and of Manuela Neumann, Sigrun Roeber, Thomas Arzberger and Hans Kretzschmar†; VMVD and JQT were supported by Grants AG032953, AG017586 and AG010124; MG was supported by Grants AG032953, AG017586, AG010124 and NS044266; VMVD acknowledges EunRan Suh, PhD for assistance with sample handling and Elisabeth McCarty-Wood for help in selection of cases; JQT acknowledges Terry Schuck, John Robinson and Kevin Raible for assistance with neuropathological evaluation of cases. CVB and the Antwerp site were in part funded by the MetLife Foundation for Medical Research Award (to CVB), the Belgian Science Policy Office (BELSPO) Interuniversity Attraction Poles program; the Alzheimer Research Foundation (SAO-FRA); the Medical Foundation Queen Elisabeth (GSKE); the Flemish Government initiated Methusalem Excellence Program (to CVB); the Research Foundation Flanders (FWO) and the University of Antwerp Research Fund. CVB, MC and JvdZ acknowledge the neurologists S Engelborghs, PP De Deyn, A Sieben, R Vandenberghe and the neuropathologist JJ Martin for the clinical and pathological diagnoses. CVB, MC and JvdZ further thank the personnel of the Genetic Service Facility of the VIB Department of Molecular Genetics (http://www.vibgeneticservicefacility.be) and the Antwerp Biobank of the Institute Born-Bunge for their expert support. IL and AB were supported by the program “Investissements d’avenir” ANR-10-IAIHU-06 and acknowledges the contribution of The French research network on FTLD/FTLD-ALS for the contribution in samples collection. BN is founded by Fondazione Cassa di Risparmio di Pistoia e Pescia (grant 2014.0365), SS is founded by the Cassa di Risparmio di Firenze (grant 2014.0310) and a grant from Ministry of Health n° RF-2010-2319722. JEN was supported by the Novo Nordisk Foundation, Denmark. MR was supported by the German National Genome Network (NGFN); German Ministry for Education and Research Grant Number 01GS0465. JDR, MNR, NCF and JDW were supported by an MRC programme grant and the Dementia Platform UK, the NIHR Queen Square Dementia Biomedical Research

Unit (BRU) and the Leonard Wolfson Experimental Neurology Centre. MGS was supported by MRC grant n G0301152, Cambridge Biomedical Research Centre and acknowledges Mrs K Westmore for extracting DNA. HM was supported by the Motor Neuron Disease Association (Grant 6057). RR was supported by P50 AG016574, R01 NS080882, R01 NS065782, P50 NS72187 and the Consortium for Frontotemporal Dementia; DWD was supported by P50NS072187, P50AG016574, State of Florida Alzheimer Disease Initiative, & CurePSP, Inc.; NRGR, JEP, RCP, DK, BFB were supported by P50 AG016574; KAJ was supported by R01 AG037491; WWS was supported by NIH AG023501, AG019724, Consortium for Frontotemporal Dementia Research; BLM was supported by P50AG023501, P01AG019724, Consortium for FTD Research; HR was supported by AG032306. JCvS was supported by Stichting Dioraphte Foundation (11 02 03 00), Nuts Ohra Foundation (0801-69), Hersenstichting Nederland (BG 2010-02) and Alzheimer Nederland. CG and HHC acknowledge families, patients, clinicians including Dr Inger Nennesmo and Dr Vesna Jelic, Professor Laura Fratiglioni for control samples and Jenny Björkström, Håkan Thonberg, Charlotte Forsell, Anna-Karin Lindström and Lena Lilius for sample handling. CG was supported by Swedish Brain Power (SBP), the Strategic Research Programme in Neuroscience at Karolinska Institutet (StratNeuro), the regional agreement on medical training and clinical research (ALF) between Stockholm County Council and Karolinska Institutet, Swedish Alzheimer Foundation, Swedish Research Council, Karolinska Institutet PhD-student funding, King Gustaf V and Queen Victoria's Free Mason Foundation. FP, AR, VD and FL acknowledge Labex DISTALZ. RF acknowledges the help and support of Mrs. June Howard at the Texas Tech University Health Sciences Center Office of Sponsored Programs for tremendous help in managing Material Transfer Agreement at TTUHSC.

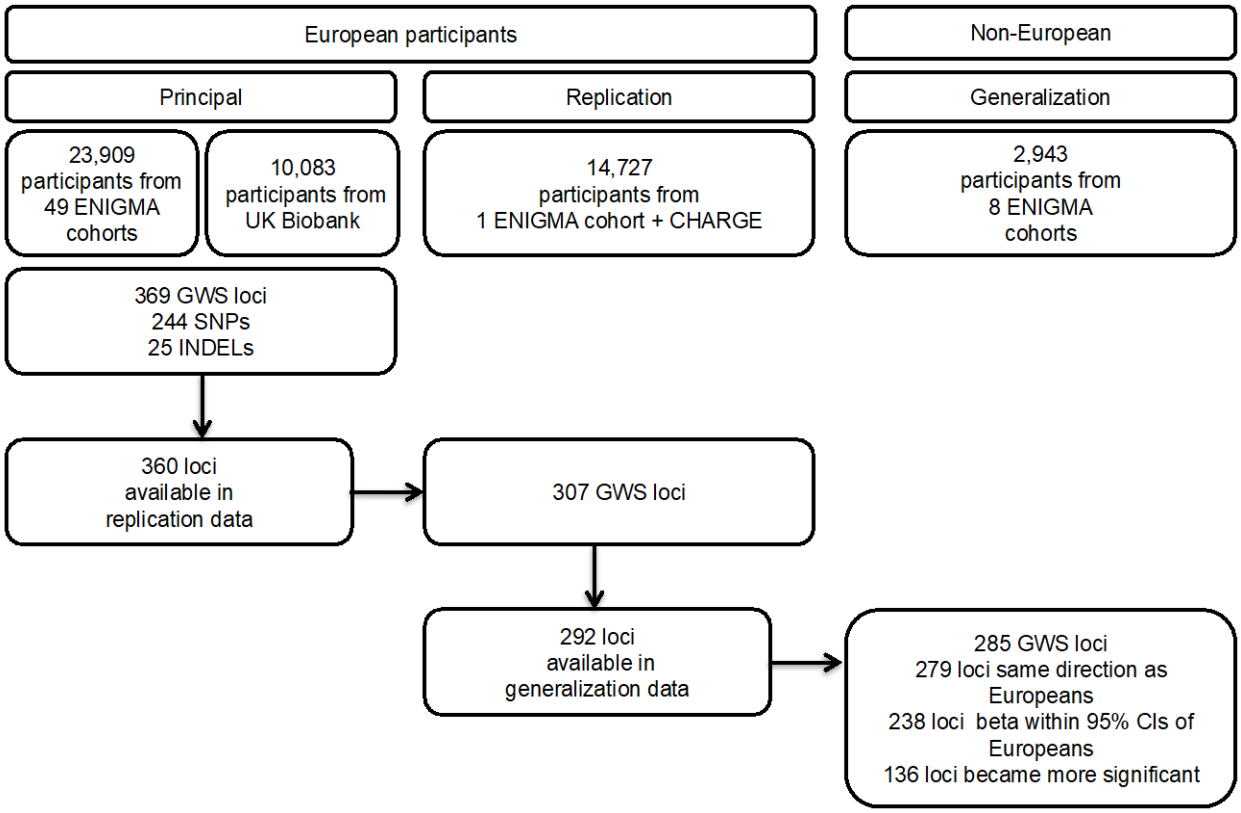

Fig. S1.
Flow chart summarizing the phases of meta-analysis. GWS: genome-wide significant.

Fig. S2. (see external file ManhattanPlots.pdf)
Manhattan plots of each trait from the principal meta-analysis.

Fig. S3. (see external fileQQPlots.pdf)
QQ plots of each region from the principal meta-analysis.

Fig. S4. (see external file Forest Plots.pdf).
Forest plots of the 369 genome-wide significant loci

Fig. S5. (see external file LocusZoom.pdf).
LocusZoom plots of the 369 genome-wide significant loci

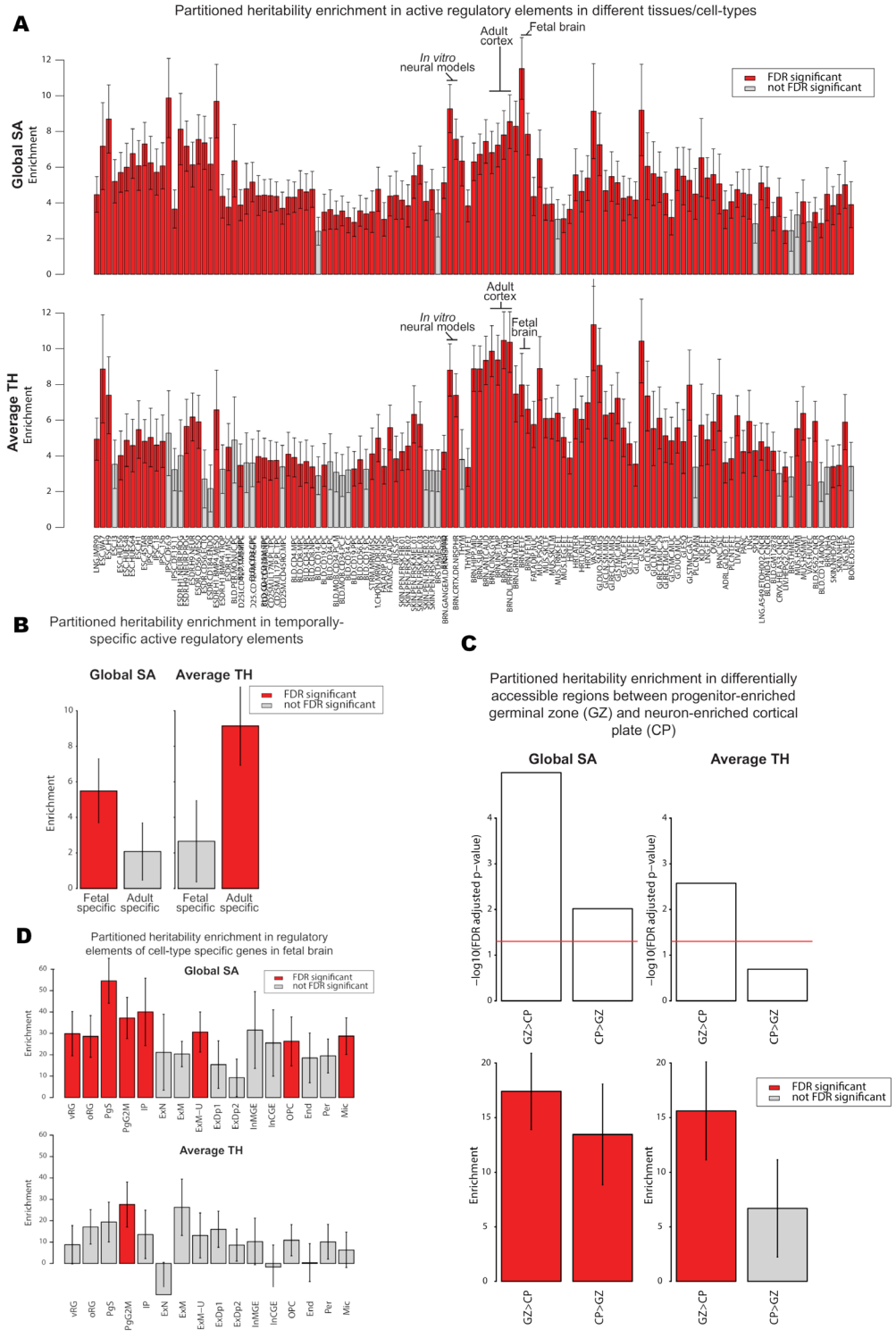

Fig. S6.

Partitioned heritability enrichment analyses (A) active regulatory elements across tissues and cell types, (B) temporally specific active regulatory elements, (C) regulatory elements of cell-type specific genes in fetal brain, and (D) differentially accessible regions between progenitor-enriched germinal zone (GZ) and neuron-enriched cortical plate (CP).

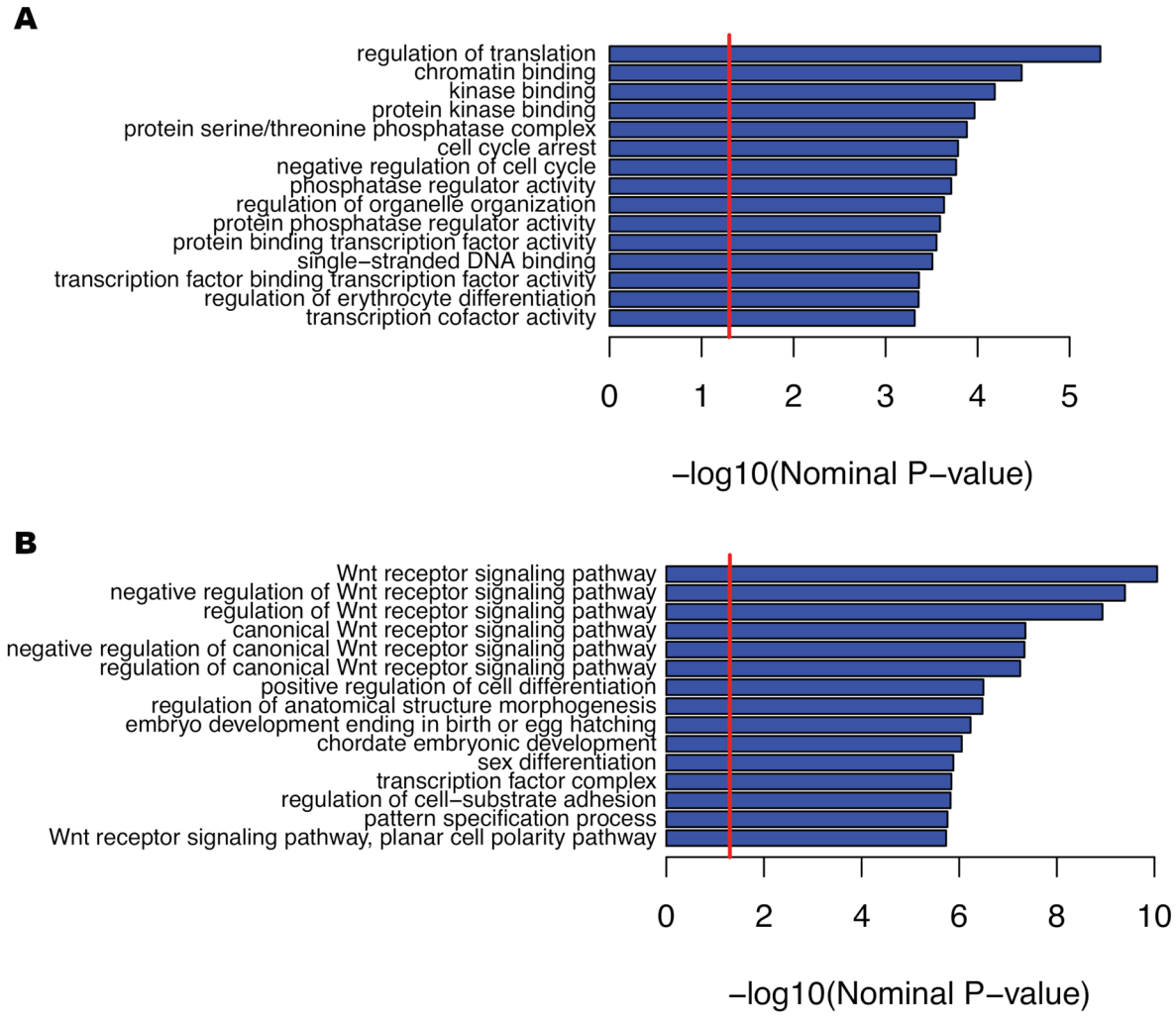

Fig. S7.

Significance of the enrichment of gene ontology annotations for (A) total surface area, and (B) multivariate regional surface area from TATES output.

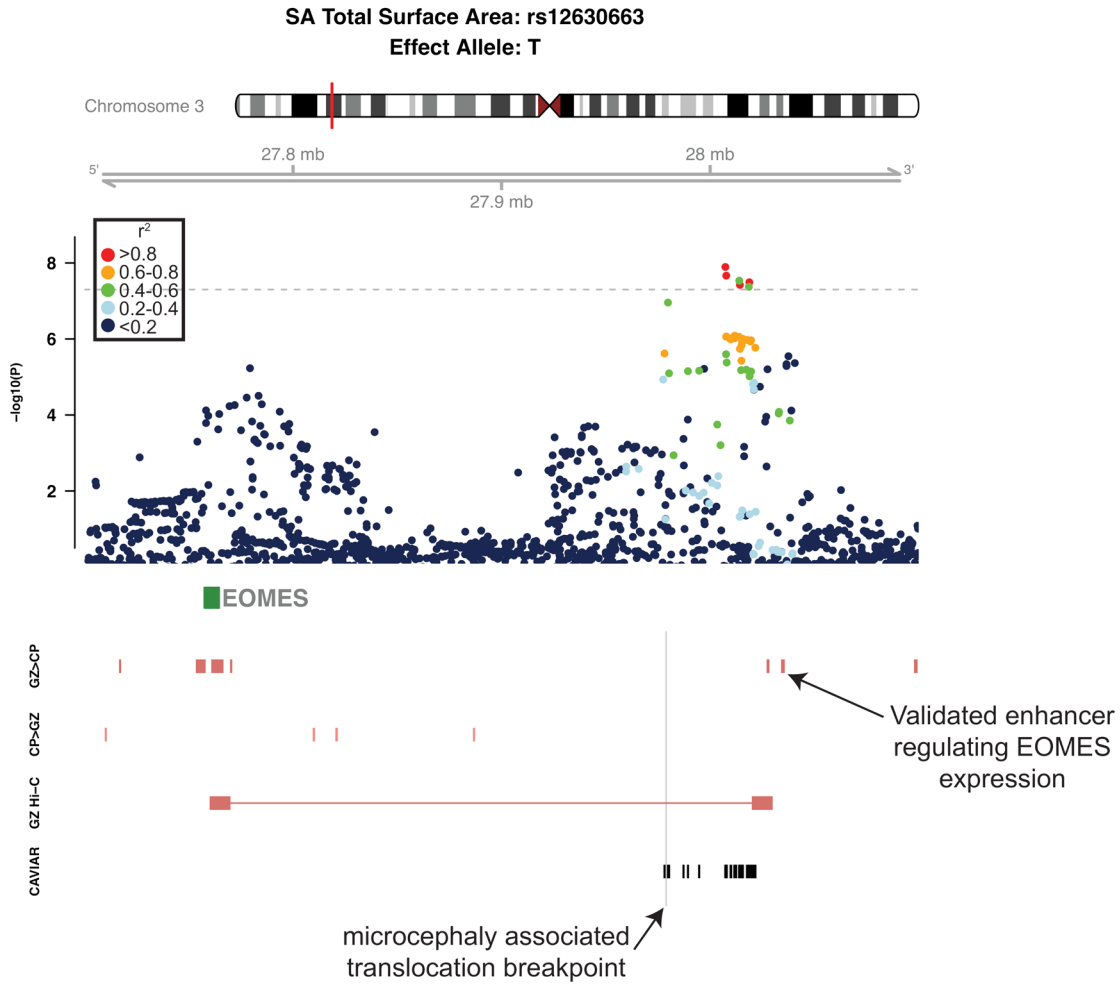

Fig. S8.

Regional association plot for the 3p24.1 locus (rs12630663). Localizing EOMES, validated enhancer regulating EOMES expression, chromatin interaction, and microcephaly associated translocation breakpoint.

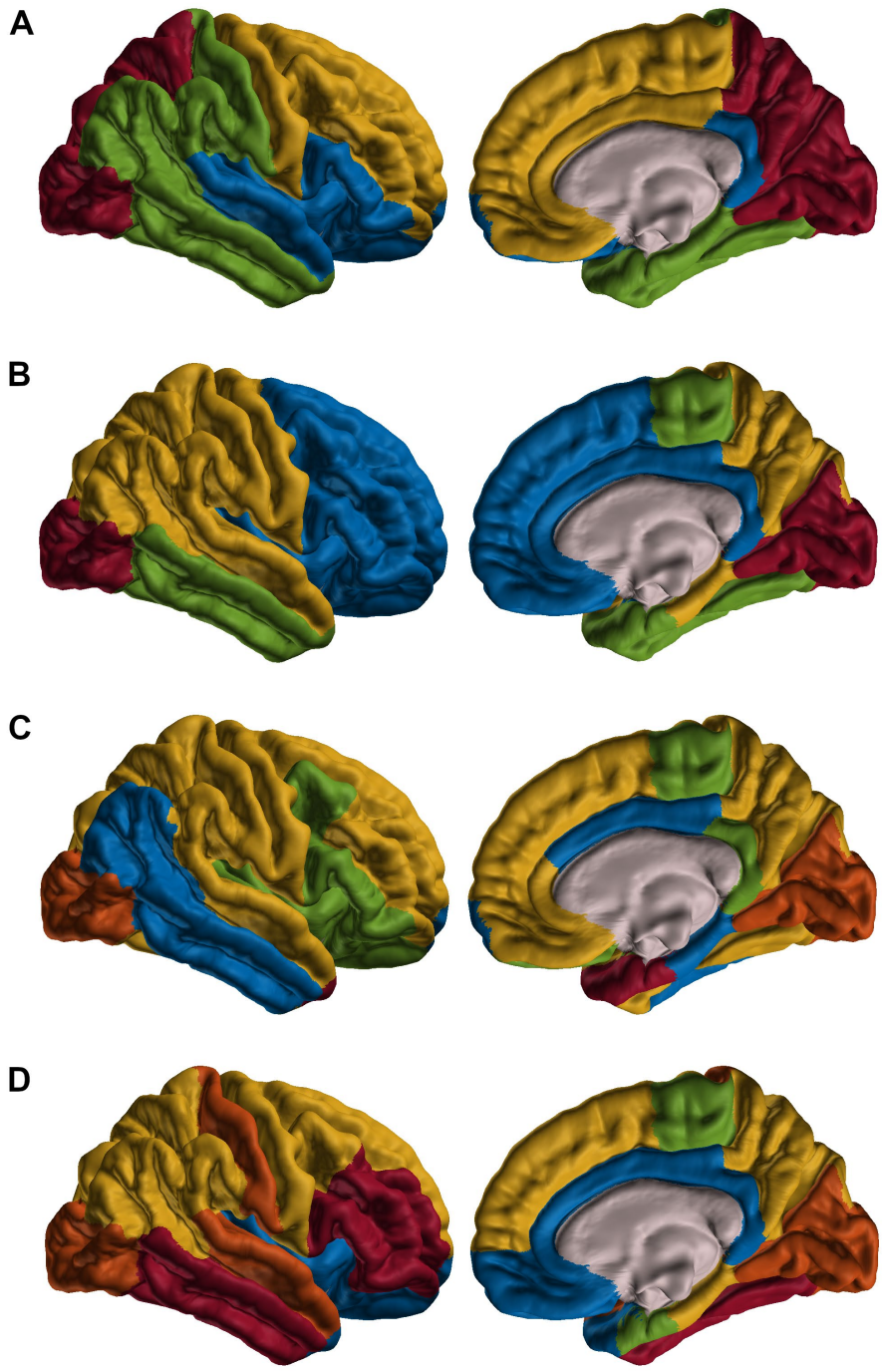

Fig. S9.

Clustering of genetic correlations among (A) surface area and (B) thickness regions after correcting for global measures. Clustering of genetic correlations among (C) surface area and (D) thickness regions without correcting for global measures. The best-fitting model for surface area and thickness with global correction was 4 diagonal components with varying volume and shape. The best-fitting model for surface area and thickness without global correction was 5 spherical components with varying volume.

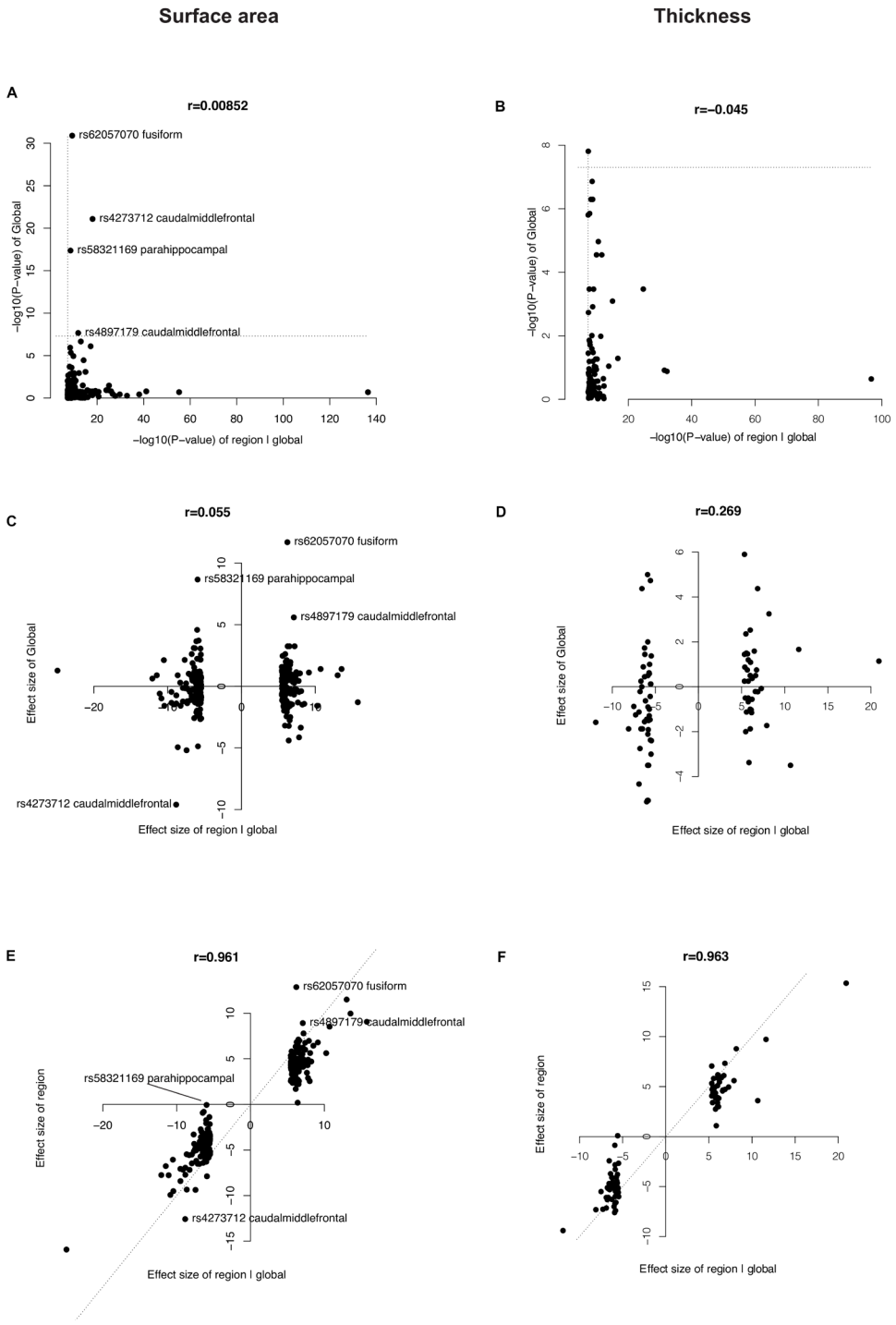

Fig. S10.

P-value of genome-wide significant regional SNPs with global control compared to their *P*-value in the global measure for (A) surface area and (B) thickness. Effect size of genome-wide significant regional SNPs with global control compared to their effect size in global measures for (C) surface area and (D) thickness. Effect size of genome-wide significant regional SNPs with global control compared to regional SNPs without global control in (E) surface area and (F) thickness.

Fig. S11. (see external file PhenotypicPlots.pdf)
Phenotypic distribution plots from each cohort and trait included in the meta-analyses.

Tables S1 to S20 (separate file Grasby_etal_Supplementary_Tables.xlsx).

Table S1.
Phenotype descriptions

Table S2.
Cohort descriptions

Table S3.
Description of the imaging data for each cohort and percentage of individuals retained in each cohort after quality control who were taken forward to the GWAS analyses for each cohort and each trait

Table S4.
Description of the genotype data for each cohort

Table S5.
Meta-analytic GWAS results for the 369 loci taken forward for replication

Table S6.
Results from MAGMA gene based tests

Table S7.
Univariate heritability (twin and SNP) for global and regional surface area and thickness

Table S8.
Polygenic risk score results for global and regional surface area and thickness

Table S9.
Genetic correlations (LD score r_G) calculated between global cortical measures and selected morphological traits

Table S10.
Results from DEPICT pathway based tests

Table S11.
Summary of bioinformatic functional follow-ups

Table S12.
eQTL and chromatin interaction information for lead SNPs and proxies

Table S13.
Results from CAVIAR fine-mapping

Table S14.
Genetic correlations (LD score r_G) calculated from the GWAS of regional measures corrected for global measures

Table S15.
Genetic correlations (LD score r_G) calculated from the GWAS of regional measures not corrected for global measures

Table S16.
Genetic correlations (LD score r_G) calculated between the imaging phenotypes and selected neuropsychiatric disorders and psychological traits

Table S17.
Genetic correlations (LD score r_G) calculated between the imaging phenotypes and selected neuropsychiatric disorders and psychological traits on healthy-only participants

Table S18.
Mendelian randomization analysis results for total SA and 8 correlated neuropsychological traits

Table S19.
Latent causal variable analysis results for total SA against 8 genetically correlated traits

Table S20.
Data access statements