Grasby, Katrina L., 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, Ch[illegible]topher D., Witt, Stephanie H., Wittfeld, Katharina, Wolf, Christiane, Wolfers, Thomas, Wu, [illegible] Qin, Yasuda, Clarissa L., Zaremba, Dario, Zhang, Zuo, Zwiers, Marcel P., Artiges, Eric, A[illegible]sare[illegible] 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, Nyberg, Lars, Oosterlaan, Jaap, Ophoff, Roel A., Pantelis, Christos, Paus, Tomas, Pausova, Zdenka, Penninx, Brenda W. J. H., Polderman, Tinca J. C., Posthuma, Danielle, Rietschel, Marcella, Roffman, Joshua L., Rowland, Laura M., Sachdev, Perminder S., Sämann, Philipp G., Schall, Ulrich, Schumann, Gunter, Scott, Rodney J., Sim, Kang, Sisodiya, Sanjay M., Smoller, Jordan W., Sommer, Iris E., St Pourcain, Beate, Stein, Dan J., Toga, Arthur W., Trollor, Julian N., Van der Wee, Nic J. A., van t Ent, Dennis, Völzke, Henry, Walter, Henrik, Weber, Bernd, Weinberger, Daniel R., Wright, Margaret J., Zhou, Juan, Stein, Jason L., Thompson, Paul M. and Medland, Sarah E. 2020. The genetic architecture of the human cerebral cortex. Science 367 (6484) , eaay6690. 10.1126/science.aay6690 file

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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 199 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 306 loci that were genome-wide significant in the principal meta-analysis ($P \leq 5 \times 10^{-8}$; Fig. 1B; table S5). Of these, 118 have not been previously associated with either intracranial volume or cortical SA, TH, or volume (*13-18*). Twenty of these were insertions or deletions (INDELs). Eleven INDELs had a proxy single nucleotide polymorphism (SNP) available in the European replication data; no proxies were available for six INDELs and one SNP. Of the 299 loci for which the SNP or a proxy was available, 255 (SA: 241, TH: 14) remained genome-wide significant when the replication data were included in the meta-analysis, with 199 passing multiple testing correction ($P \leq 8.3 \times 10^{-10}$; SA: 187, TH: 12). Of the 255 loci, 244 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 241 of these loci. Of the 244 loci available in the non-European cohorts, 189 had effects in the same direction in both the European and non-European meta-analyses, and 111 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 253 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 $P_{MA} = 2.3 \times 10^{-32}$; replication $P_{rep} = 3.5 \times 10^{-43}$; *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 $P_{MA} = 1.7 \times 10^{-13}$; $P_{rep} = 1.0 \times 10^{-17}$) 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 $FDR_{CommonMind\ Consortium(CMC)} < 1.0 \times 10^{-2}$; 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 $P_{MA} = 2.5 \times 10^{-10}$; $P_{rep} = 2.5 \times 10^{-13}$) 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 $P_{MA} = 8.4 \times 10^{-10}$; $P_{rep} = 8.1 \times 10^{-11}$) 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* $FDR_{FETAL} = 2.0 \times 10^{-24}$, empirical *t*-test of Pearson's *r* $\mathrm{FDR}_{Genotype\text{-}Tissue\ Expression(GTEx)} = 3.3 \times 10^{-40}$; tables S11–S12). On 3p24.1, rs12630663 (*Z*-score $P_{MA} = 1.3 \times 10^{-8}$; $P_{rep} = 1.4 \times 10^{-8}$) 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 $P_{MA} = 8.4 \times 10^{-11}$; $P_{rep} = 3.7 \times 10^{-12}$) is a fetal cortex eQTL (*t*-test $FDR_{FETAL} = 1.8 \times 10^{-4}$) 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 $P_{MA} = 3.2 \times 10^{-10}$;

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 (1–13%) 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 12 with regional TH; of these 175 SA and 10 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 $P_{MA} = 1.8 \times 10^{-137}$; $P_{rep} = 4.6 \times 10^{-189}$; variance explained = 1.03%; Fig. 4A). Across 11 traits we observed 41 independent significant associations from 18 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 $P = 7.9 \times 10^{-21}$), 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 $FDR_{FETAL} = 4.8 \times 10^{-2}$) 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 $FDR_{BIOSgenelevel} = 6.1 \times 10^{-6}$). *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 $P_{MA} = 1.9 \times 10^{-11}$, $P_{rep} = 3.0 \times 10^{-11}$; pericalcarine SA, *Z*-score $P_{MA} = 1.9 \times 10^{-11}$; $P_{rep} = 9.9 \times 10^{-16}$) is an eQTL for *ST7L* and *WNT2B* (*t*-test $\mathrm{FDR}_{CMC} < 1.0 \times 10^{-2}$) in adult cortex (tables S11–S12). On 14q23.1, we observed 20 significant loci (table S5) from four LD blocks. Our strongest association here was for the precuneus SA (rs73313052: *Z*-score $P_{MA} = 1.1 \times 10^{-24}$; $P_{rep} = 2.2 \times 10^{-35}$). 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 $FDR_{CMC} < 1.0 \times 10^{-2}$) 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 $P_{MA} = 1.6 \times 10^{-10}$; $P_{rep} = 3.1 \times 10^{-14}$) is an eQTL in adult cortex for *LMO4* (*t*-test $FDR_{CMC} < 1.0 \times 10^{-2}$), with chromatin interactions between the region housing both this SNP and rs59373415 (which is associated with the precuneus SA: *Z*-score $P_{MA} = 1.6 \times 10^{-10}$, $P_{rep} = 5.3 \times 10^{-12}$) 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 precentral thickness and general cognitive function (r_G = 0.27, *Z*-score P_{rG} = 2.5 x 10^{-5}) and educational attainment (r_G = 0.25, *Z*-score P_{rG} = 4.0 x 10^{-4}) as well as between the inferior parietal thickness and educational attainment (r_G = -0.19, *Z*-score P_{rG} = 5.0 x 10^{-4}). 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 x 10^{-8}; LCV gcp = 0.40, 95% CIs [0.23–0.57], *t*-test $P_{gcp=0}$ = 1.4 x 10^{-9}) and educational attainment ($b_{MR\text{-}IVW}$ = 0.12, SE = 0.01, *Z*-score *P* = 2.1 x 10^{-21}; gcp = 0.49, 95% CIs [0.26–0.72], *t*-test $P_{gcp=0}$ = 8.0 x 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).

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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.,

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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. 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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.

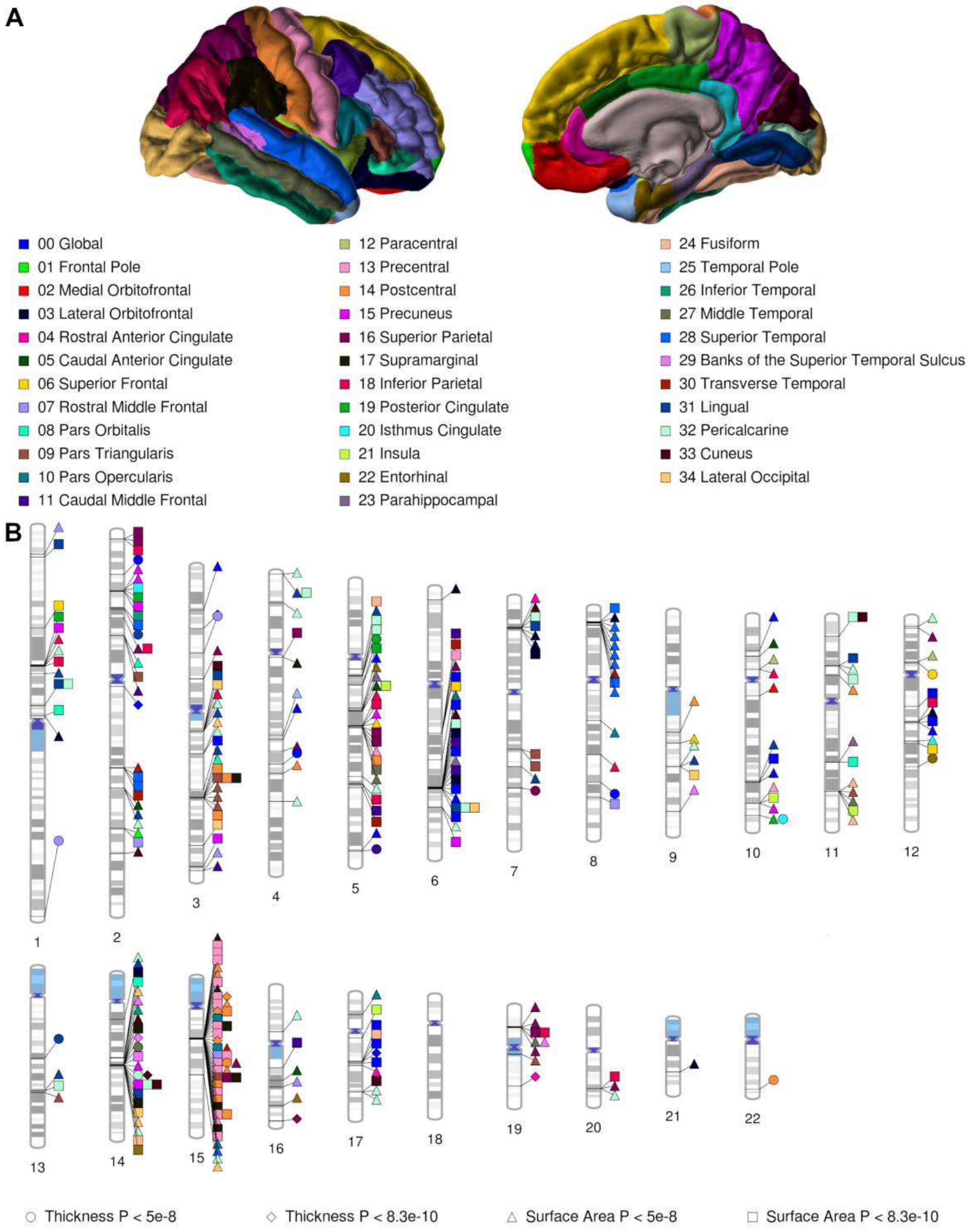
Fig. 2. Genetics of Global Measures. (**A**) Genetic correlations between global measures and selected traits (red indicates significant correlation, FDR < 0.05). (**B**) Partioned heritability enrichment in active regulatory elements across tissues and cell types. (**C**) Partioned heritability enrichment 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

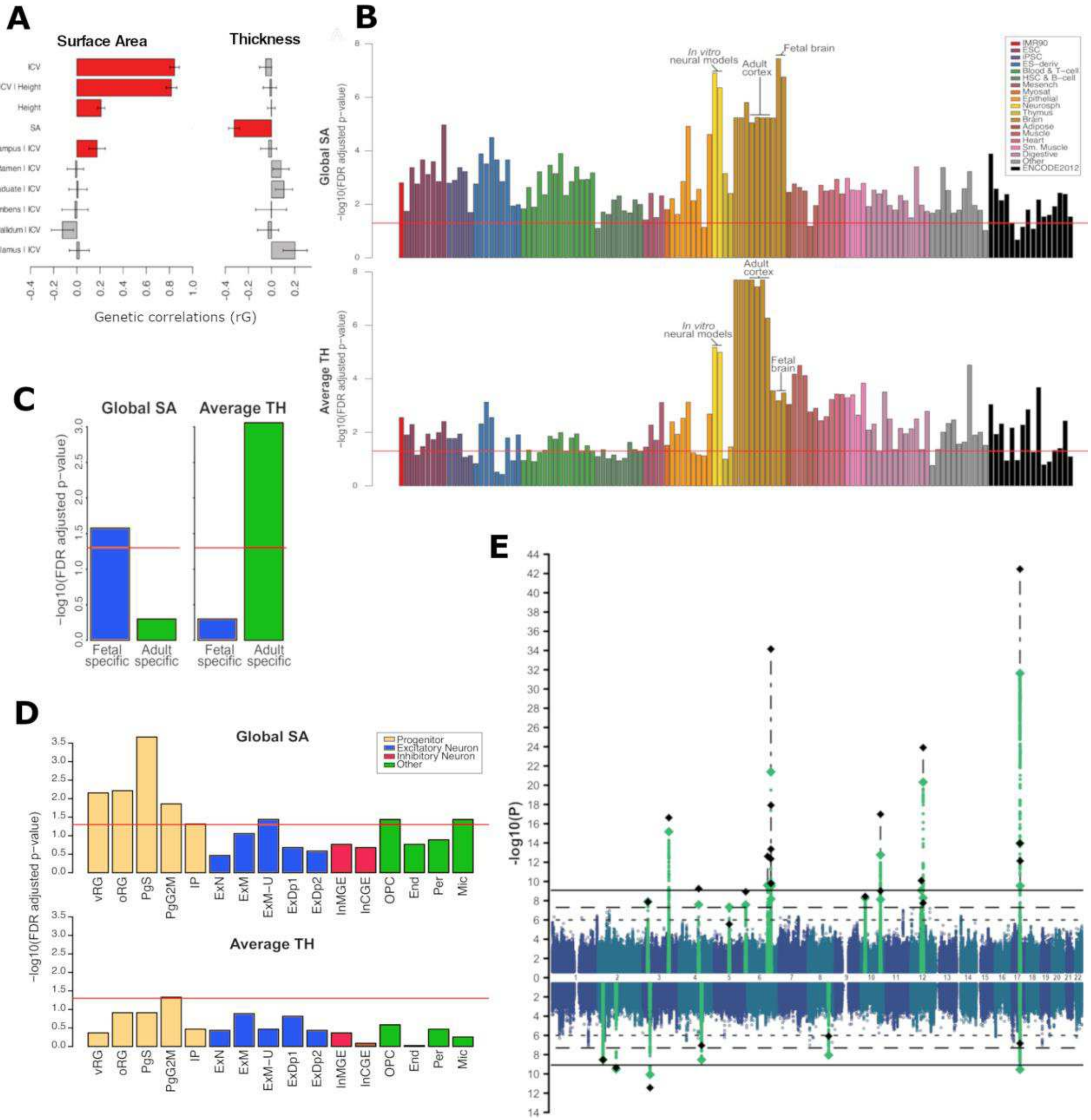
horizontal line is genome-wide significance, solid horizontal line is multiple-testing correction threshold.

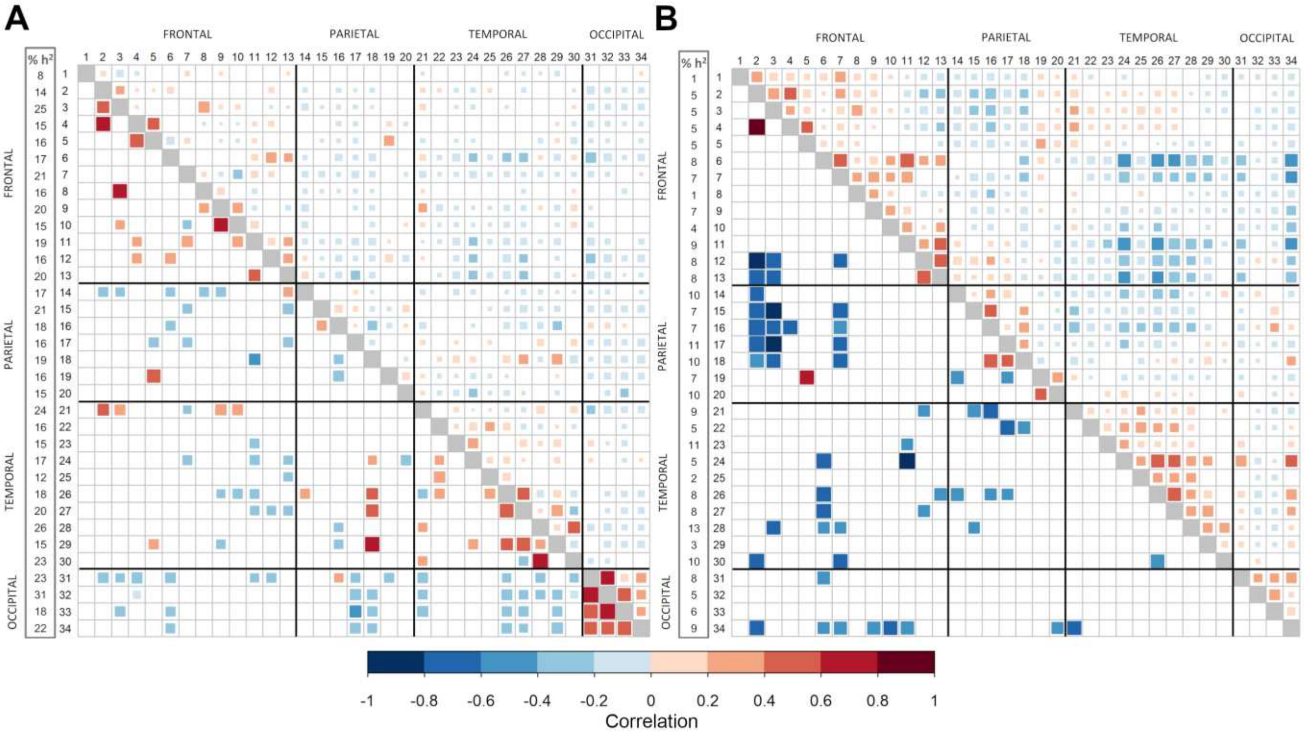
Fig 3. Genetic and Phenotypic Correlations Between Cortical Regions. (**A**) Surface Area. (**B**) Thickness. The regions are numbered according to the legend of Fig. 1A. The proportion of variance accounted for by common genetic variants is shown in the first column (h^2_{SNP}). Phenotypic correlations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

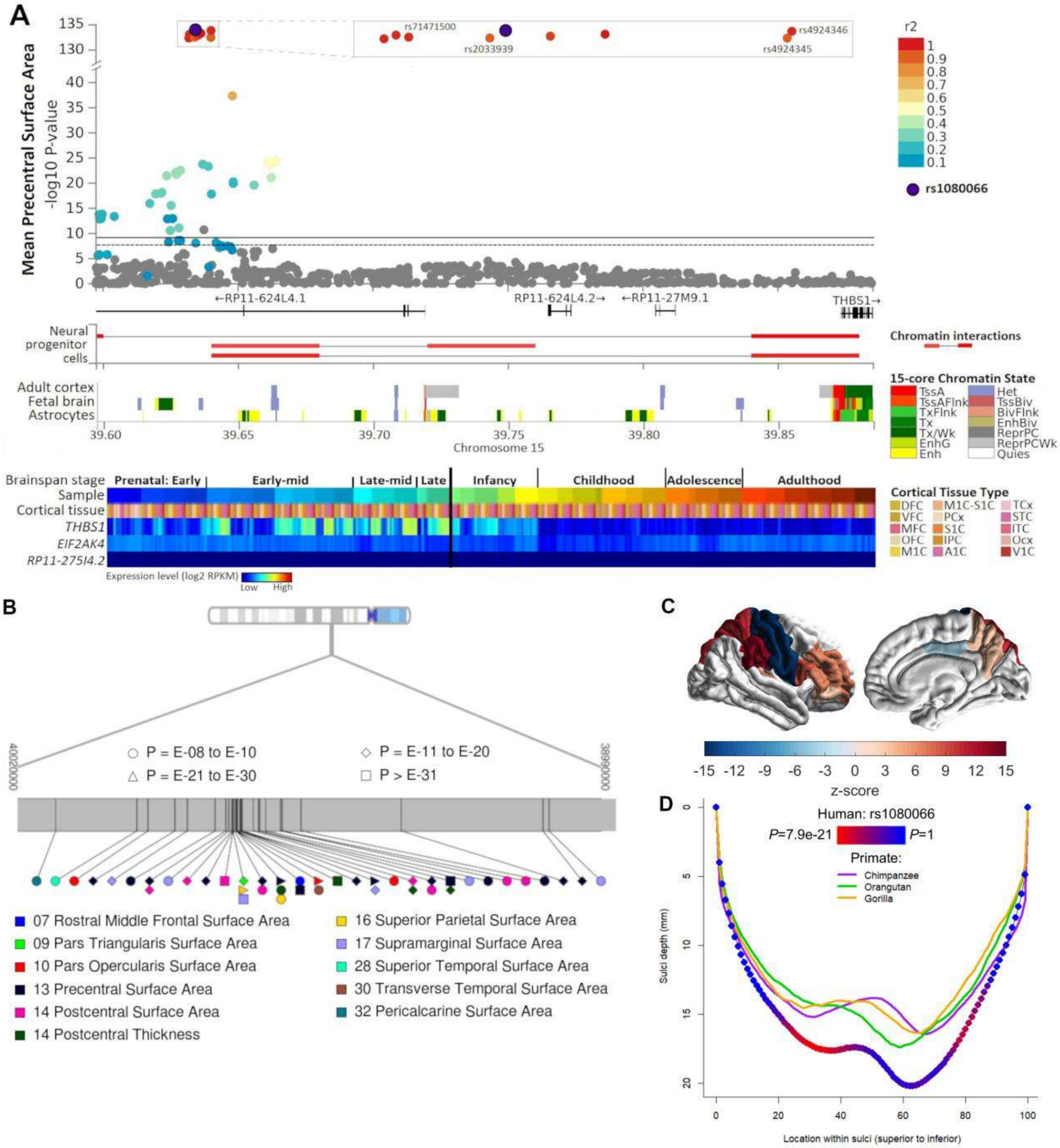
Fig 4. Genetics of Regional Measures. (**A**) Regional plot for rs1080066, including additional lead SNPs within the LD block and surrounding genes, chromatin interactions in neural progenitor cells, chromatin state in RoadMap brain tissues*, and BRAINSPAN candidate gene expression in brain tissue**. (**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.

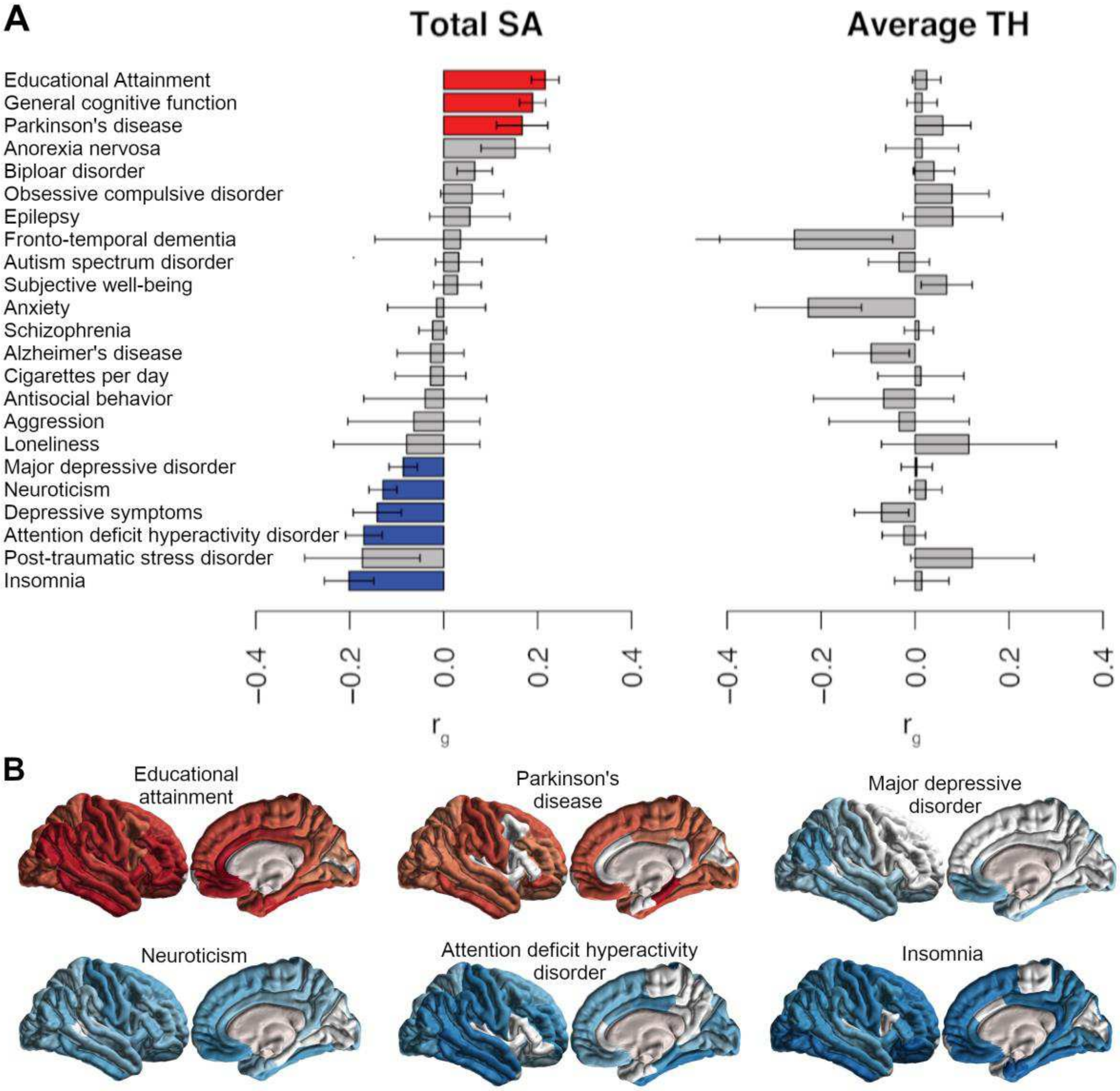
Fig 5. Genetic correlations with neuropsychiatric and psychological traits. (**A**) Genetic correlations with total SA and average TH positive correlations are shown in red, while negative correlations are shown in blue. (**B**) Regional variation in the strength of genetic correlations between regional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


A
00 Global
01 Frontal Pole
02 Medial Orbitofrontal
03 Lateral Orbitofrontal
04 Rostral Anterior Cingulate
05 Caudal Anterior Cingulate
06 Superior Frontal
07 Rostral Middle Frontal
08 Pars Orbitalis
09 Pars Triangularis
10 Pars Opercularis
11 Caudal Middle Frontal
12 Paracentral
13 Precentral
14 Postcentral
15 Precuneus
16 Superior Parietal
17 Supramarginal
18 Inferior Parietal
19 Posterior Cingulate
20 Isthmus Cingulate
21 Insula
22 Entorhinal
23 Parahippocampal
24 Fusiform
25 Temporal Pole
26 Inferior Temporal
27 Middle Temporal
28 Superior Temporal
29 Banks of the Superior Temporal Sulcus
30 Transverse Temporal
31 Lingual
32 Pericalcarine
33 Cuneus
34 Lateral Occipital
B
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
○ Thickness P < 5e-8
◇ Thickness P < 8.3e-10
△ Surface Area P < 5e-8
☐ Surface Area P < 8.3e-10


A
Surface Area
Thickness
ICV
ICV | Height
Height
SA
Hippocampus | ICV
Putamen | ICV
Caduate | ICV
Accumbens | ICV
Pallidum | ICV
Thalamus | ICV
Genetic correlations (rG)
B
Global SA
-log10(FDR adjusted p-value)
In vitro neural models
Adult cortex
Fetal brain
IMR90
ESC
iPSC
ES-deriv
Blood & T-cell
HSC & B-cell
Mesench
Myosat
Epithelial
Neurosph
Thymus
Brain
Adipose
Muscle
Heart
Sm. Muscle
Digestive
Other
ENCODE2012
Average TH
C
Global SA
Average TH
-log10(FDR adjusted p-value)
Fetal specific
Adult specific
D
Global SA
Average TH
-log10(FDR adjusted p-value)
Progenitor
Excitatory Neuron
Inhibitory Neuron
Other
vRG
oRG
PgS
PgG2M
IP
ExN
ExM
ExM-U
ExDp1
ExDp2
InMGE
InCGE
OPC
End
Per
Mic
E
-log10(P)


A
FRONTAL
PARIETAL
TEMPORAL
OCCIPITAL
% h²
8 14 25 15 16 17 21 16 20 15 19 16 20 17 21 18 16 19 16 15 24 16 15 17 12 18 20 26 15 23 23 31 18 22
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34
B
FRONTAL
PARIETAL
TEMPORAL
OCCIPITAL
% h²
1 5 5 5 5 8 7 1 7 4 9 8 8 10 7 7 11 10 7 10 9 5 11 5 2 8 8 13 3 10 8 5 6 9
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34
-1
-0.8
-0.6
-0.4
-0.2
0
0.2
0.4
0.6
0.8
1
Correlation


A
Mean Precentral Surface Area
-log10 P-value
135
130
40
35
30
25
20
15
10
5
0
rs71471500
rs2033939
rs4924346
rs4924345
r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
rs1080066
←RP11-624L4.1
RP11-624L4.2→
←RP11-27M9.1
THBS1→
Neural progenitor cells
Chromatin interactions
Adult cortex
Fetal brain
Astrocytes
15-core Chromatin State
TssA
TssAFlnk
TxFlnk
Tx
Tx/Wk
EnhG
Enh
Het
TssBiv
BivFlnk
EnhBiv
ReprPC
ReprPCWk
Quies
39.60
39.65
39.70
39.75
39.80
39.85
Chromosome 15
Brainspan stage
Prenatal: Early
Early-mid
Late-mid
Late
Infancy
Childhood
Adolescence
Adulthood
Sample
Cortical tissue
THBS1
EIF2AK4
RP11-275I4.2
Expression level (log2 RPKM)
Low
High
Cortical Tissue Type
DFC
VFC
MFC
OFC
M1C
M1C-S1C
PCx
S1C
IPC
A1C
TCx
STC
ITC
Ocx
V1C
B
40020000
38990000
○ P = E-08 to E-10
◇ P = E-11 to E-20
△ P = E-21 to E-30
☐ P > E-31
07 Rostral Middle Frontal Surface Area
09 Pars Triangularis Surface Area
10 Pars Opercularis Surface Area
13 Precentral Surface Area
14 Postcentral Surface Area
14 Postcentral Thickness
16 Superior Parietal Surface Area
17 Supramarginal Surface Area
28 Superior Temporal Surface Area
30 Transverse Temporal Surface Area
32 Pericalcarine Surface Area
C
-15
-12
-9
-6
-3
0
3
6
9
12
15
z-score
D
Human: rs1080066
P=7.9e-21
P=1
Primate:
Chimpanzee
Orangutan
Gorilla
Sulci depth (mm)
0
5
10
15
20
0
20
40
60
80
100
Location within sulci (superior to inferior)


A
Total SA
Average TH
Educational Attainment
General cognitive function
Parkinson's disease
Anorexia nervosa
Biploar disorder
Obsessive compulsive disorder
Epilepsy
Fronto-temporal dementia
Autism spectrum disorder
Subjective well-being
Anxiety
Schizophrenia
Alzheimer's disease
Cigarettes per day
Antisocial behavior
Aggression
Loneliness
Major depressive disorder
Neuroticism
Depressive symptoms
Attention deficit hyperactivity disorder
Post-traumatic stress disorder
Insomnia
−0.4
−0.2
0.0
0.2
0.4
r_g
B
Educational attainment
Parkinson's disease
Major depressive disorder
Neuroticism
Attention deficit hyperactivity disorder
Insomnia