Supplementary Information

Structural covariance networks are coupled to expression of genes enriched in supragranular layers of the human cortex

Rafael Romero-Garcia[1,§], Kirstie J Whitaker[1,2], František Váša[1], Jakob Seidlitz[1], Maxwell Shinn[1], Peter Fonagy[3], Raymond J Dolan[4,5,] Peter B Jones[1,6], Ian M Goodyer[1,6], the NSPN Consortium[‡], Edward T Bullmore [1,6,7], Petra E Vértes[1].

[1]Department of Psychiatry, University of Cambridge, Cambridge, CB2 0SZ, UK.

[2]The Alan Turing Institute for Data Science, British Library, 96 Euston Road, London, NW1 2DB, United Kingdom

[3]Research Department of Clinical, Educational and Health Psychology, University College London, London, WC1E 6BT, UK.

[4]Wellcome Trust Centre for Neuroimaging, UCL Institute of Neurology, University College London, London, WC1N 3BG, UK.

[5]Max Planck UCL Centre for Computational Psychiatry and Ageing Research, London, WC1B 5EH, UK.

[6]Cambridgeshire and Peterborough NHS Foundation Trust, Huntingdon, PE29 3RJ, UK.

[7]ImmunoPsychiatry, Immuno-Inflammation Therapeutic Area Unit, GlaxoSmithKline R&D, Stevenage SG1 2NY, UK.

§ **Correspondence to**: Rafael Romero-Garcia PhD, University of Cambridge, Department of Psychiatry, Sir William Hardy Building, Downing Street, Cambridge CB2 3EB, UK Tel: 1223 764673, Email: rr480@cam.ac.uk

Keywords: Allen Brain Atlas, cortical thickness, gene expression, structural brain network, transcriptomic brain network

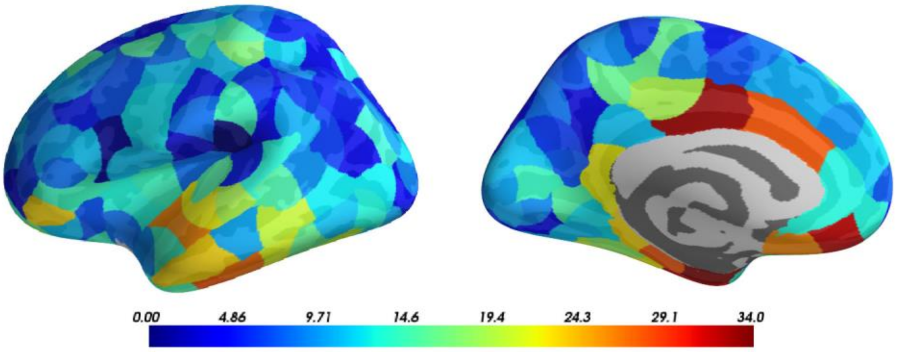

Figure S1: Number of AIBS samples in each cortical region. Inferior supramarginal gyrus was the only parcel that included zero AIBS samples.

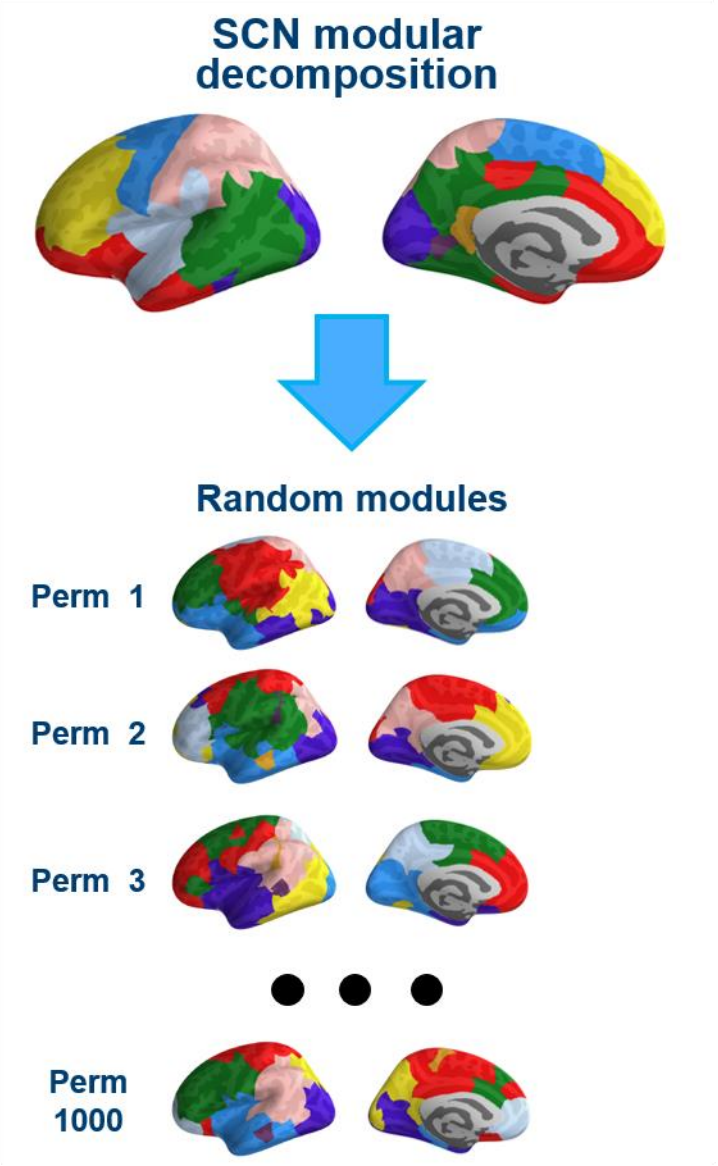

Figure S2: Random modular communities that preserve the number and size of modules, as well as the spatial contiguity of the empirical community partition.

Figure S3: Von Economo atlas. Granular cortex; primary motor/precentral gyrus (light purple), granular association isocortex Type I (yellow), granular association isocortex Type II (grey), secondary sensory cortex (green), primary sensory cortex (pink), limbic regions (red) and insular cortex (dark purple).

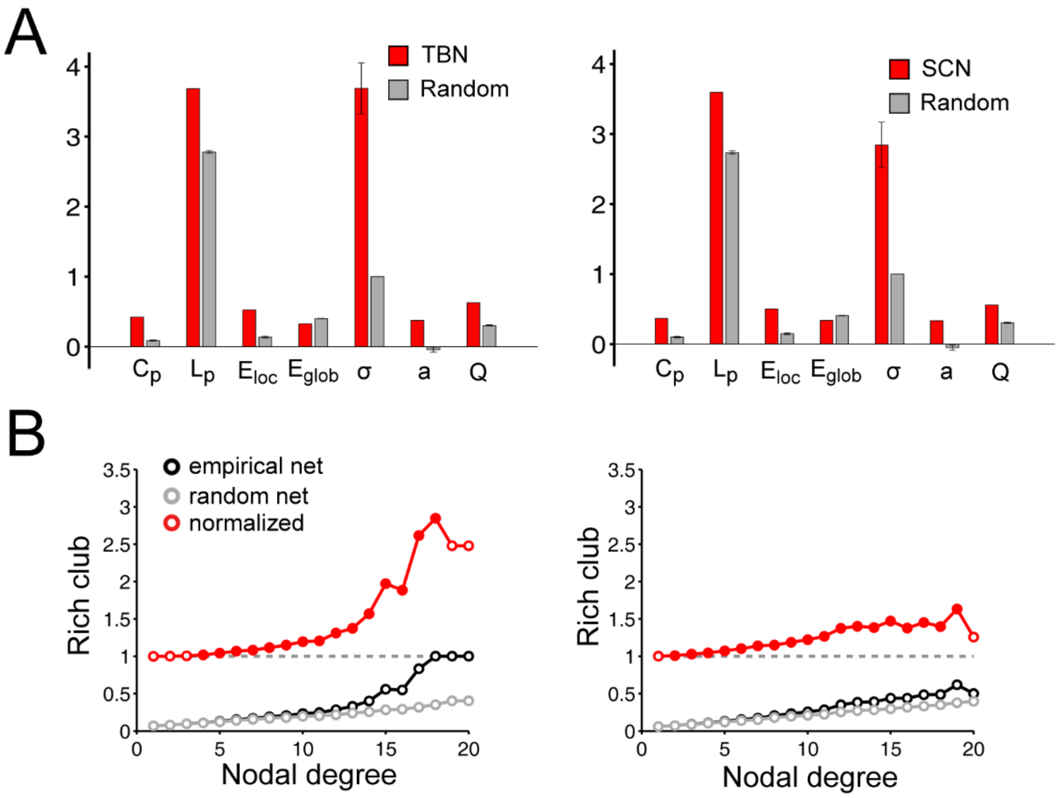

Figure S4: Global topology of gene co-expression (left) and structural covariance networks (right) at 5% connection density. A: Global topological metrics estimated in TBN, SCN and comparable random networks: C_p = clustering coefficient; L_p = path length; E_{loc} = local efficiency; E_{glob} = global efficiency; σ = small-world; a = assortativity; Q = modularity. Error bars represents the standard deviations. **B**: Rich club coefficient curves for TBN, SCN and random networks.

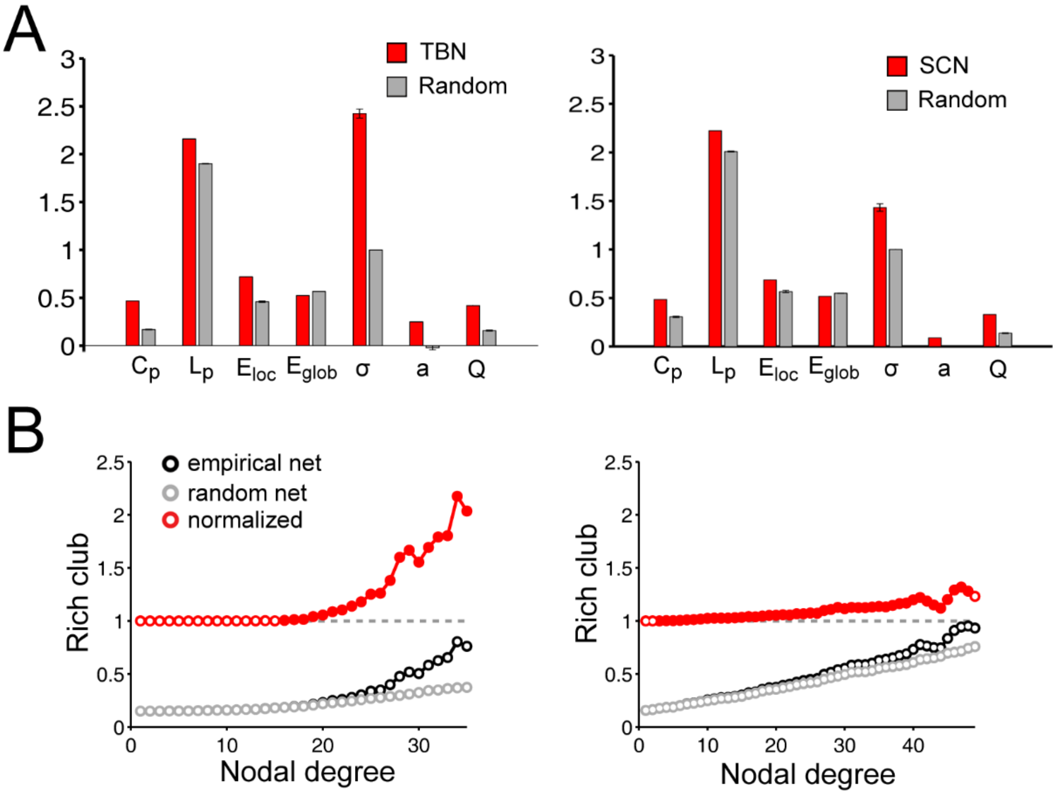

Figure S5: Global topology of gene co-expression (left) and structural covariance networks (right) at 15% connection density. A: Global topological metrics estimated in TBN, SCN and comparable random networks: C_p = clustering coefficient; L_p = path length; E_{loc} = local efficiency; E_{glob} = global efficiency; σ = small-world; a = assortativity; Q = modularity. Error bars represents the standard deviations. **B**: Rich club coefficient curves for TBN, SCN and random networks.

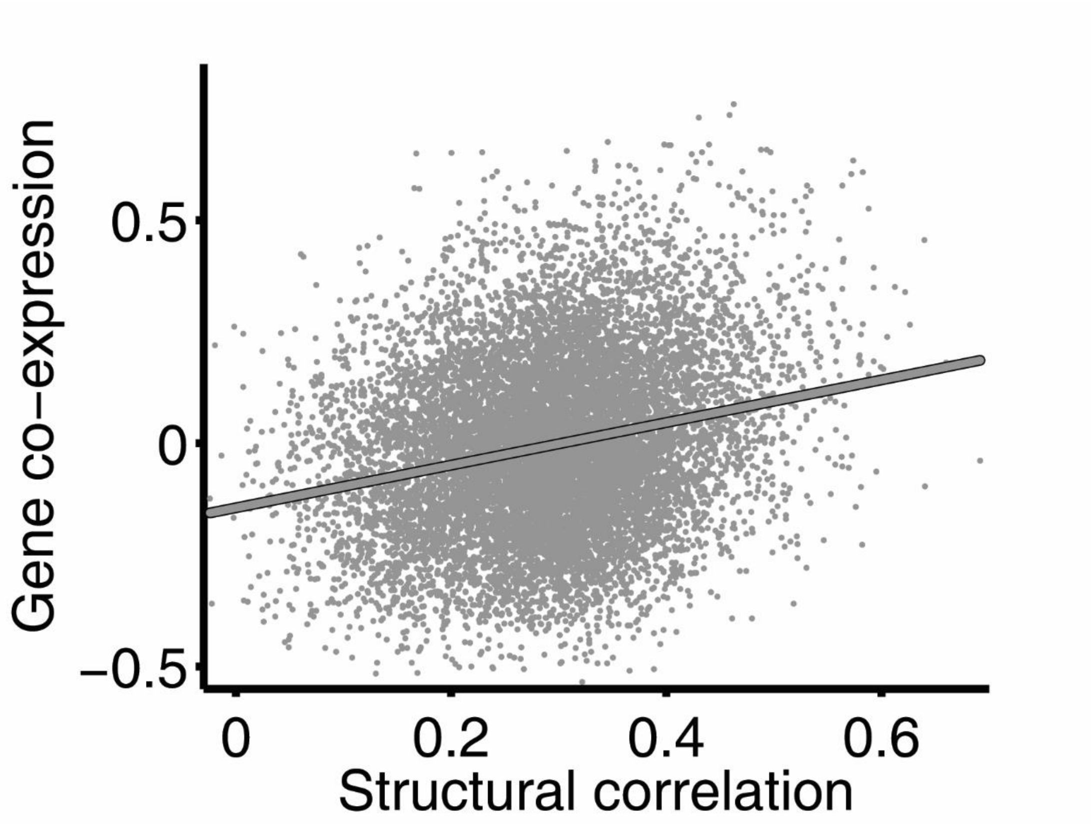

Figure S6: Scatterplot of gene co-expression versus structural covariance after regressing out the effect of the inter-regional distance.

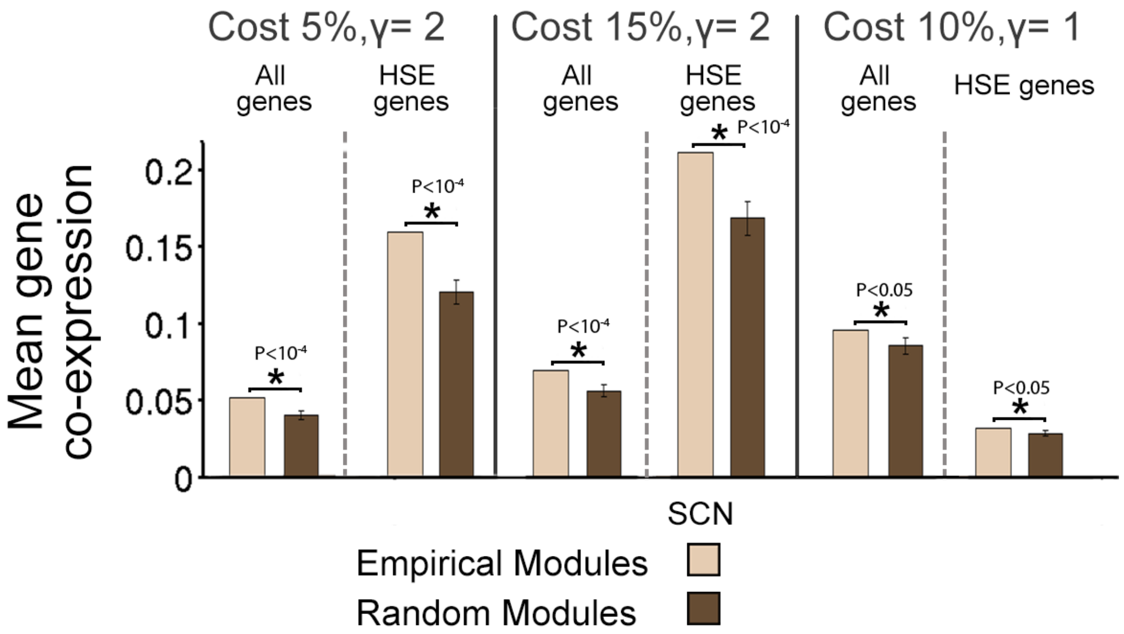

Figure S7: Mean gene co-expression between nodes located in the same SCN module for the empirical modules (light colors) and the random null modules (dark colors). Results replicated for different SCN costs (5%, 10% and 15%) and modularity resolution parameters (γ=1 and γ=2).

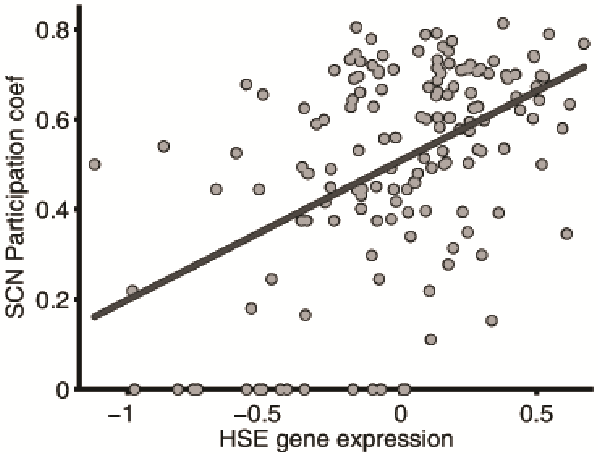

Figure S8: Association between expression of HSE genes and participation coefficient of the SCN.

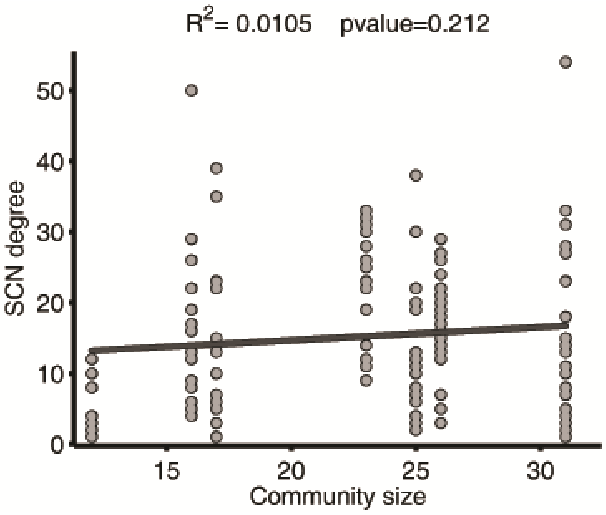

Figure S9: Nodal degree of the SCN was not associated with community size (number of regions belonging to each module).

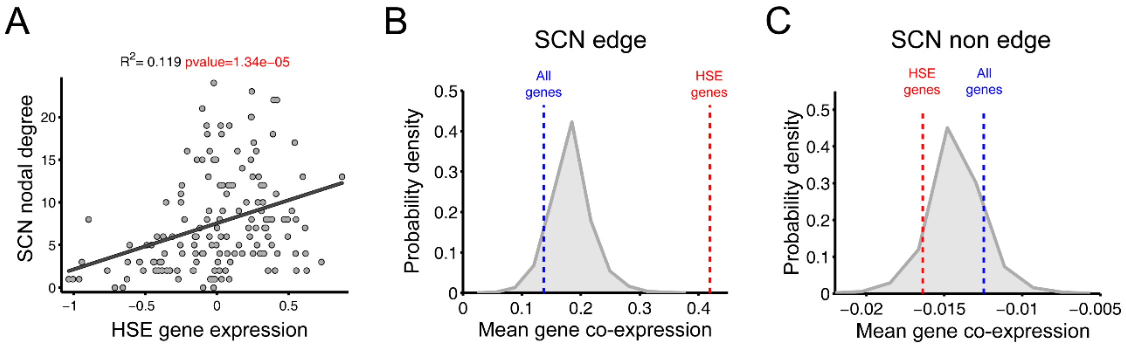

Figure S10: Gene co-expression and SCN at 5% connection density. **A:** Nodal degree in structural covariance network versus HSE gene expression**. B:** Co-expression (whole genome, blue; HSE genes only, red and each of the 5917 gene ontologies, grey distribution) for SCN edges. **C:** Co-expression (whole genome, blue; HSE genes only, red and each of the 5917 gene ontologies, grey distribution) for SCN non edges (unconnected regions).

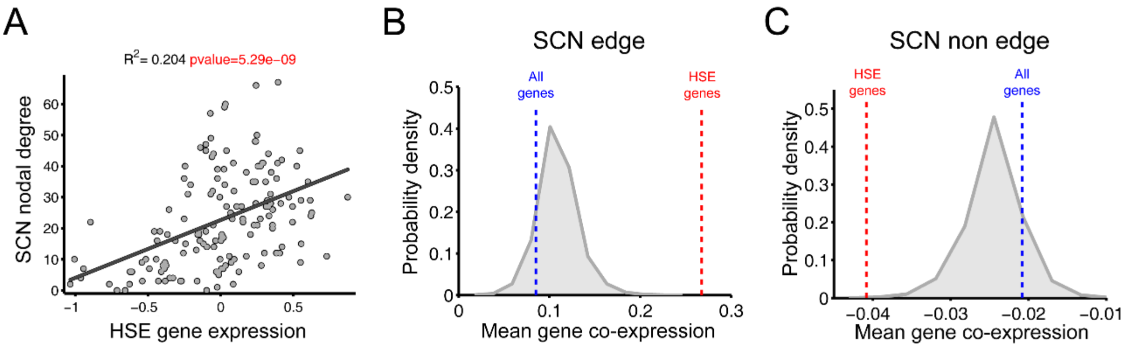

Figure S11: Gene co-expression and SCN at 15% connection density. **A:** Nodal degree in structural covariance network versus HSE gene expression**. B:** Co-expression (whole genome, blue; HSE genes only, red and each of the 5917 gene ontologies, grey distribution) for SCN edges. **C:** Co-expression (whole genome, blue; HSE genes only, red and each of the 5917 gene ontologies, grey distribution) for SCN non edges (unconnected regions).

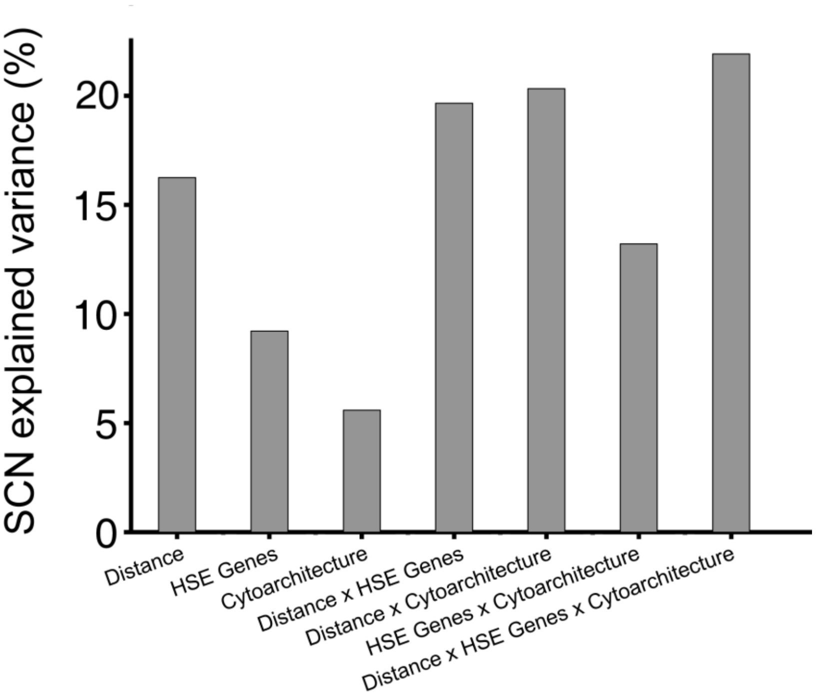

Figure S12: HSE gene expression has effects on structural covariation that are additive to the effects of connection distance. First column represents the SCN variance explained (R^2) by inter-regional distance using the log value of the inter-regional distance. Second and third column show the SCN variance explained by HSE gene expression and the 7 laminar classes defined in the Von Economo atlas. The rest of the columns display the SCN variance explained by a linear multiple regression using combinations of variables.

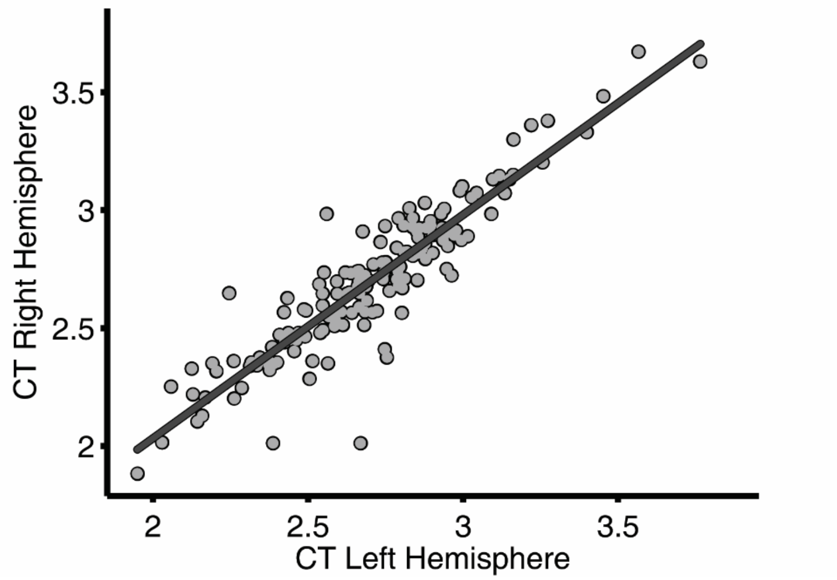

Figure S13: Association between CT values of homologous regions.

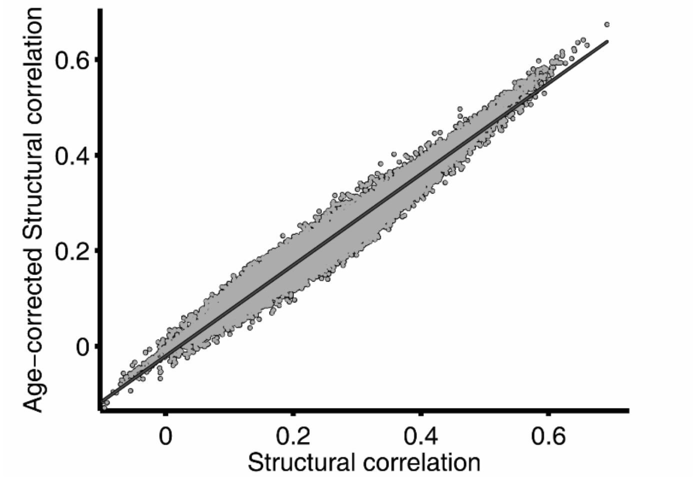

Figure S14. Similarity of structural correlation before and after age correction.

NSPN Consortium member list

Chief investigator:

Edward Bullmore

Principal investigators:

Ian Goodyer
Raymond Dolan
Peter Fonagy
Peter Jones

Associated faculty:

Peter Dayan
Paul Fletcher
John Suckling
Nikolaus Weiskopf
Pasco Fearon

Project managers:

Becky Inkster
Gita Prabhu

Postdoctoral research associates and associated research fellows:

Eran Eldar
Tobias Hauser
Konstantinos Ioannidis
Gemma Lewis
Alda Mita
Michael Moutoussis
Sharon Neufeld
Ela Polek-MacDaeid
Rafael Romero-Garcia
Michelle St Clair
Jan Stochl
Roger Tait
Beata Tick
Umar Toseeb
Anne-Laura van Harmelen
Petra Vértes
Kirstie Whitaker
Geert-Jan Will
Gabriel Ziegler

Jorge Zimbron

PhD & MSc students:

Joost Haarsma
Sian Davies
Juliet Griffin
Michael Hart
Jakob Seidlitz
Maxwell Shinn
František Váša
Konrad Wagstyl

Data managers:
Cinly Ooi
Barry Widmer

Research assistants:

Ayesha Alrumaithi
Sarah Birt
Kalia Cleridou
Hina Dadabhoy
Ashlyn Firkins
Sian Granville
Elizabeth Harding
Alexandra Hopkins
Daniel Isaacs
Janchai King
Clare Knight
Danae Kokorikou
Christina Maurice
Cleo McIntosh
Jessica Memarzia
Harriet Mills
Ciara O'Donnell
Sara Pantaleone
Jennifer Scott
Alison Stribling

Administration team:

Junaid Bhatti
Neil Hubbard
Natalia Ilicheva

Michael Kentell
Ben Wallis
Laura Villis