**Supplementary material**

**Table 1: Comparison of sample groups with non-smoking participants only**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Groups** | | | | **Group tests** | |
| **Variables** | **Overweight & depressed**  **N= 58** | **Overweight control**  **N= 32** | **Normal weight & depressed**  **N= 44** | **Normal weight control**  **N= 51** | **Statistic** | ***P*** |
| **Demographics** |  |  |  |  |  |  |
| Median age in years  (range) | 38.5  (25 – 50) | 37  (25 – 48) | 30  (25 – 50) | 30  (24 – 50) | *K* = 15.16 | 0.002 |
| Gender, female  (%) | 36  (62.1%) | 15  (46.9%) | 33  (75%) | 39  (76.5%) | *x*2 = 9.744 | 0.021 |
| BMI  (range) | 29.6  (25.3 – 47.8) | 28.5  (25 – 35.6) | 22  (18.1 – 24.9) | 22.4  (18.8 – 24.9) | *K* = 138.57 | <0.001 |
| Ethnicity, white  (%) | 52  (89.7%) | 26  (81.2%) | 36  (81.8%) | 40  (78.4%) | *x*2 = 2.711 | 0.438 |
| **Clinical** |  |  |  |  |  |  |
| Median HAM-D total score  (range) | 19  (14 – 31) | 0  (0 – 5) | 18  (14 – 26) | 0  (0 – 7) | *K* = 141.16 | <0.001 |
| Currently on antidepressants  (%) | 37  (63.8%) | NA | 31  (70.5%) | NA | *x*2 = 0.245 | 0.621 |
| Mean age of depression onset ± SD | 25 ± 9.8 | NA | 25.4 ± 9.2 | NA | *F* = 1.623 | 0.206 |
| **hsCRP** |  |  |  |  |  |  |
| Median hsCRP (range) | 2.25  (0.2 – 15.3) | 1.4  (0.2 – 11.8) | 0.7  (0.2 – 8.8) | 0.5  (0.2 – 5.2) | *K* = 30.514 | <0.001 |
| Mean log hsCRP mg/L ± SD  Cohen’s *d* effect size *vs* controls | 0.27 ± 0.51  1.11 | 0.09 ± 0.48  0.81 | -0.11 ± 0.43  0.29 | -0.23 ± 0.36 | *F* = 12.07 | <0.001 |
| hsCRP ≥3mg/L  (%) | 23  (39.7%) | 4  (12.5%) | 5  (11.4%) | 3  (5.9%) | *x*2 = 24.405 | <0.001 |
| **Salivary cortisol** |  |  |  |  |  |  |
| Mean CAR AUCi (nmol min/L) ± SD | 99.8 ± 262 | 87.7 ± 238 | 6.79 ± 228 | 89 ± 311 | *F* = 0.889 | 0.448 |
| Mean log AUCg (nmol hour/L) ± SD | 1.66 ± 0.18 | 1.67 ± 0.23 | 1.7 ± 0.18 | 1.72 ± 0.23 | *F* = 0.082 | 0.495 |

BMI= body mass index, HAM-D= Hamilton Depression Rating Scale 17 for depressive symptoms, hsCRP= high sensitivity C-reactive protein, SD = standard deviation, CAR= cortisol awakening response, AUCi= area under the curve with respect to increase, AUCg= area under the curve with respect to ground.

**NIMA (Part 1) Consortium members**

Cambridge

Edward T. Bullmore (MD, PI, EC)1,2,11, Junaid Bhatti1, Samuel J. Chamberlain1,2, Marta M. Correia1,12, Anna L. Crofts1, Amber Dickinson\*, Andrew C. Foster\*, Manfred G. Kitzbichler1, Clare Knight\*, Mary-Ellen Lynall1, Christina Maurice1, Ciara O'Donnell1, Linda J. Pointon1, Peter St George Hyslop1,13,14, Lorinda Turner31, Petra Vertes1, Barry Widmer1, Guy B. Williams1,14

Cardiff

B. Paul Morgan (PI)15, Claire A. Leckey15, Angharad R. Morgan\*, Caroline O'Hagan\*, Samuel Touchard15

Glasgow

Jonathan Cavanagh (PI, EC)3, Catherine Deith\*, Scott Farmer16, John McClean16, Alison McColl3, Andrew McPherson\*, Paul Scouller\*, Murray Sutherland16

Independent advisor

H.W.G.M. (Erik) Boddeke (EC)17

GSK

Jill C. Richardson (EC)18, Shahid Khan11, Phil Murphy19, Christine A. Parker19, Jai Patel11

Janssen

Declan Jones (EC)6, Peter de Boer4, John Kemp4, Wayne C. Drevets6, Jeffrey S. Nye (deceased), Gayle Wittenberg6, John Isaac6, Anindya Bhattacharya6, Nick Carruthers6, Hartmuth Kolb6

Kings College London

Carmine M. Pariante (PI)10, Federico Turkheimer (PI)20, Gareth J. Barker20, Heidi Byrom10, Diana Cash20, Annamaria Cattaneo10, Antony Gee20, Caitlin Hastings10, Nicole Mariani10, Anna McLaughlin10, Valeria Mondelli10, Maria Nettis10, Naghmeh Nikkheslat10, Karen Randall20, Hannah Sheridan\*, Camilla Simmons20, Nisha Singh20, Victoria Van Loo\*, Marta Vicente-Rodriguez20, Tobias C. Wood20, Courtney Worrell\*, Zuzanna Zajkowska\*

Lundbeck

Niels Plath (EC)21, Jan Egebjerg21, Hans Eriksson21, Francois Gastambide21, Karen Husted Adams21, Ross Jeggo\*, Christian Thomsen21, Jan Torleif Pederson21, Brian Campbell\*, Thomas Möller\*, Bob Nelson\*, Stevin Zorn\*

University of Texas (sub-contracted to Lundbeck)

Jason O'Connor22

Oxford

Mary Jane Attenburrow (PI)7,23, Alison Baird, Jithen Benjamin23, Stuart Clare25, Philip Cowen7, I-Shu (Dante) Huang24, Samuel Hurley\*, Helen Jones23, Simon Lovestone7,(AD, PI, EC) Francisca Mada\*, Alejo Nevado-Holgado7, Akintayo Oladejo\*, Elena Ribe7, Katy Smith23, Anviti Vyas\*

Pfizer

Zoe Hughes\*, Rita Balice-Gordon\*, James Duerr\*, Justin R. Piro\*, Jonathan Sporn\*

Southampton

V. Hugh Perry (PI)27, Madeleine Cleal\*, Gemma Fryatt27, Diego Gomez-Nicola27, Renzo Mancuso32, Richard Reynolds27

Sussex

Neil A. Harrison (PI, EC)28, Mara Cercignani28, Charlotte L. Clarke28, Elizabeth Hoskins\*, Charmaine Kohn\*, Rosemary Murray\*, Lauren Wilcock29, Dominika Wlazly30

University of Toronto (sub-contracted to Cambridge)

Howard Mount13

MD = Mood disorder workpackages lead

AD = Alzheimer’s disease workpackages lead

PI = Principal Investigator

EC = Executive committee member

1 Department of Psychiatry, School of Clinical Medicine, University of Cambridge, CB2 0SZ, UK

2 Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, CB21 5EF, UK

3 Sackler Centre, Institute of Health & Wellbeing, University of Glasgow, Sir Graeme Davies Building , Glasgow, G12 8TA, UK

4 Neuroscience, Janssen Research & Development, Janssen Pharmaceutica NV, Turnhoutseweg 30, B-2340, Beerse, Belgium

5 The Maurice Wohl Clinical Neuroscience Institute, Cutcombe Road, London, SE5 9RT, UK

6 Neuroscience, Janssen Research & Development, LLC, Titusville, NJ, 08560, USA

7 Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford, OX3 7JX, UK

8 Brighton & Sussex Medical School, University of Sussex, Brighton, BN1 9RR, UK

9 Sussex Partnership NHS Foundation Trust, Swandean, BN13 3EP, UK

10 Kings College London, Institute of Psychiatry, Psychology and Neuroscience, Department of Psychological Medicine, London, SE5 9RT, UK

11 Immuno-Psychiatry, Immuno-Inflammation Therapeutic Area Unit, GlaxoSmithKline R&D, Stevenage SG1 2NY, UK

12 MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge CB2 7EF, UK

13 Tanz Centre for Research in Neurodegenerative Diseases, 60 Leonard Avenue, Toronto, ON M5T 2S8 Canada

14 Department of Clinical Neurosciences, University of Cambridge, CB2 0SZ, UK

15 Cardiff University, Cardiff CF10 3AT, UK

16 NHS Greater Glasgow and Clyde, 1055 Great Western Rd, Glasgow G12 0XH, UK

17 University of Groningen, 9712 CP Groningen, Netherlands

18 Neurosciences Virtual PoC DPU, GlaxoSmithKline R&D, Stevenage SG1 2NY, UK

19 Experimental Medicine Imaging, GlaxoSmithKline R&D, Stevenage SG1 2NY, UK

20 King's College London, Department of Neuroimaging Sciences, Institute of Psychiatry, Psychology & Neuroscience, De Crespigny Park, London SE5 8AF, UK

21 H. Lundbeck A/S Ottiliavej 9, 2500, Valby, Denmark

22 University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Dr, San Antonio, TX 78229, USA

23 NIHR Oxford cognitive health Clinical Research Facility, Warneford Hospital, Oxford, OX3 7JX, UK

24 The Kennedy Institute of Rheumatology, Roosevelt Dr, Oxford OX3 7FY, UK

25 Oxford Centre for Functional MRI of the Brain, John Radcliffe Hospital, Oxford OX3 9DU, UK

26 Pfizer, Inc, 1 Portland Street, Cambridge MA, USA

27 Centre for Biological Sciences, University of Southampton, Southampton, UK

28 Clinical Imaging Sciences Centre (CISC), University of Sussex, Brighton, BN1 9RR, UK

29 Sussex Partnership NHS Foundation Trust, Nevill Avenue, Hove BN3 7HZ, UK

30 Brighton & Sussex University Hospitals NHS Trust, Brighton BN2 5BE, UK

31 Department of Medicine, School of Clinical Medicine, University of Cambridge, CB2 0SZ, UK

32 VIB-KU Leuven Center for Brain & Disease Research, Campus Gasthuisberg, Herestraat 49, bus 602, 3000 Leuven, Belgium

\*Former consortium members