**Failure to deactivate medial prefrontal cortex in people at high risk for psychosis**

Irina Falkenberg a,b\*, Chris Chaddock a , Robin M. Murray a, Colm McDonald d , Gemma Modinos a , Elvira Bramon a,e ,Muriel Walshe a , Matthew Broome a,c , Philip McGuire a , Paul Allen a

a Department of Psychosis Studies, Institute of Psychiatry, King’s College London, London, United Kingdom; b Department of Psychiatry and Psychotherapy, Philipps-University Marburg, Germany; c Division of Mental Health and Wellbeing, Warwick Medical School, University of Warwick, Gibbet Hill, Coventry, CV4 7AL, United Kingdom; d Department of Psychiatry, Clinical Science Institute, National University of Ireland, Galway, Galway, Ireland; e Department of Clinical Neuroscience, Institute of Psychiatry, King’s College London, London, United Kingdom

**\* Corresponding author:** Institute of Psychiatry, King's College London, Department of Psychosis Studies (PO67), 16 De Crespigny Park, London SE5 8AF, UK, Tel: +44 (0)20 7848 0801, Fax: +44 (0)20 7848 0976, E-mail: irina.falkenberg@kcl.ac.uk

**Supplementary Results**

**Table S1:** Linear trend analysis of activation during N-back, covaried for age and IQ. Results are reported at a threshold of p <.001 uncorrected. \* p ≤ 0.05 FWE

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Group Effects  |  | MNI coordinates |  |  |
|  | Side | X | Y | Z | Peak Z-score | Cluster size |
| UHR>FHR>CTRL |  |  |  |  |  |  |
| Precuneus | L | -14 | -50 | 40 | 5.38 | 1279\* |
| Posterior cingulate | R | 22 | -66 | 4 | 4.26 | 290 |
| Insula | L | -30 | -40 | 14 | 4.19 | 364 |
| Hippocampus | R | 32 | -34 | -6 | 3.89 | 124 |
| Parahippocampal gyrus | L | -28 | -58 | -4 | 3.64 | 51 |
| Inferior temporal gyrus | R | 54 | -6 | -24 | 3.50 | 16 |
| Lingual gyrus | L | -16 | -72 | -10 | 3.49 | 47 |
| Superior temporal gyrus | L | -40 | -32 | 0 | 3.47 | 32 |
| Postcentral gyrus | R | 22 | -34 | 48 | 3.40 | 23 |
| Cingulate gyrus | L | -16 | 26 | 28 | 3.39 | 20 |
| Superior frontal gyrus | L | -12 | 58 | 20 | 3.38 | 35 |
| Transverse temporal gyrus | R | 58 | -22 | 10 | 3.30 | 12 |
| Anterior cingulate | L | -16 | 36 | 12 | 3.25 | 18 |
| CTRL>FHR>UHR |  |  |  |  |  |  |
| Precunues | L | -2 | -52 | 32 | 4.75 | 812\* |
| Insula | R | 52 | -22 | 12 | 4.08 | 200 |

**Table S2** Demographic characteristics and means and standard deviations for errors in N-Back task, including an additional sample of patients with first episode psychosis (FEP).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **FEP (n=10)** | **UHR (n=17)** | **GHR (n=10)** | **Controls (n=15)** | **Statistic** |
| **Age** |  |  |  |  |  |
| **Mean (SD)** | 25.5 (5.9) | 24.3 (4.2) | 40.3 (10.7) | 25.6 (4.8) | F (3, 48) = 15.5a |
| **Range**  | 18 - 35 | 20 - 34 | 26 - 59 | 19 - 35 |  |
| **IQ** |  |  |  |  |  |
| **Mean (SD)** | 105.4 (10.5) | 101.7 (11.7) | 111.9 (7.5) | 123.2 (16.2) | F (3, 36) = 6.5a |
| **Range** | 96.6 - 114.1 | 95.5 – 108.0 | 105.0 - 118.8 | 110.7 - 135.7 |  |
| **Gender (n female)** | 3 | 5 | 5 | 5 | Χ2  (3) = 4.5 |
| **Ethnicity (%)** |  |  |  |  | Χ2  (12) = 29.3b |
| **White** | 20 | 76.5 | 100 | 66.7 |  |
| **Black** | 40 | 11.8 | 0 | 26.7 |  |
| **Oriental** | 0 | 11.8 | 0 | 0 |  |
| **Mixed** | 30 | 0 | 0 | 0 |  |
| **Other** | 10 | 0 | 0 | 6.7 |  |
| **Errors in N-back task (Mean ± SD)** |  |  |  |  |  |
| **Total**  | 8.7 ± 10.4 | 4.2 ± 3.8 | 1.9 ± 2.0 | 2.9 ± 3.2 | F (3, 115) = 8.1a |
| **Errors in Instructions** | 1.0 ± 1.8 | 0.1 ± 0.2 | 0  | 0.5 ± 1.3 | F (3, 115) = 6.5a |
| **Errors in 0-back** | 1.7 ± 2.7 | 1.0 ± 1.6 | 0.4 ± 0.9 | 0.7 ± 1.2 | F (3, 115) = 3.3b |
| **Errors in 1-back** | 1.7 ± 2.0 | 0.6 ± 0.9 | 0 | 0.3 ± 0.7 | F (3, 115) = 12.4a |
| **Errors in 2-back** | 3.9 ± 4.5 | 2.5 ± 2.3 | 1.4 ± 1.4 | 1.5 ± 1.7 | F (3, 115) = 5.1b |
| **Medication at baseline (no. of cases)** |  |  |  |  |  |
| **Atypical antipsychotics** | 7 |  |  |  |  |
| **Missing** | 3 |  |  |  |  |

a p ≤ .001

b p < .05

**Table S3:** Linear trend analysis across 4 groups in ascending/descending order of risk of transition to psychosis. Results are reported at a threshold of p <.001 uncorrected.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Group Effects  |  | MNI coordinates |  |  |
|  | Side | X | Y | Z | Peak Z-score | Cluster size |
| CTRL>FHR>UHR>FEP |  |  |  |  |  |  |
| Middle frontal gyrus | R | 30 | -4 | 56 | 3.8 | 23 |
| Inferior parietal lobule | L | -38 | -52 | 40 | 3.69 | 94 |
| Thalamus | R | 8 | -4 | 2 | 3.47 | 28 |
| FEP>UHR>FHR>CTRL |  |  |  |  |  |  |
| Lingual gyrus | R | 26 | -62 | -4 | 4.64 | 734 |
| Precuneus | L | -14 | -48 | 38 | 4.49 | 149 |
| Medial frontal gyrus | R | 2 | 54 | 20 | 4.04 | 158 |
| Lentiform nucleus | L | -18 | -72 | -10 | 3.99 | 133 |
| Paracentral lobule | R | 4 | -30 | 48 | 3.93 | 172 |
| Parahippocampal gyrus | L | -26 | -42 | -14 | 3.72 | 36 |
| Thalamus | L | -42 | -20 | 8 | 3.65 | 86 |
| Cuneus | L | -14 | -70 | 20 | 3.5 | 70 |
| Insula | R | 54 | -30 | 20 | 3.44 | 45 |
| Parahippocampal gyrus | R | 26 | -42 | -12 | 3.41 | 22 |
| Lingual gyrus | L | -12 | -60 | 2 | 3.38 | 31 |
| Cingulate gyrus | R | 2 | -62 | 30 | 3.29 | 47 |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |

**Figure S1:**

Statistical parametric maps (SPMs) showing activation (yellow) and deactivation depending on risk of transition (FEP> UHR > FHR > CTRL). Plots showing contrasts estimates by group

**a)** in the left precuneus and

**b)** the right medial frontal gyrus.

Areas of significance are reported at p <.001 (uncorrected). The left side of the picture corresponds to the left side of the brain.

**a)**



**b)**

