# Performance Results

## N-back

Mean values for performance on the n-back task are reported in Table 2. As expected, increasing task difficulty was associated with reduced accuracy (model with at-risk and control groups, F(2.16, 90.65) = 38.34, *p* < 0.001; NPE, PE, control model, F(2.16, 88.45) = 39.50, *p* < 0.001). There were no group differences for overall accuracy (at-risk vs control comparison, F(1, 42) = 1.05, *p* = 0.312; NPE, PE, control comparison, F(2, 41) = 0.65, *p* = 0.525) and no interaction effects between groups and difficulty (at-risk vs control comparison, F(2.16, 90.65) = 0.81, *p* = 0.457; NPE, PE, control comparison, F(4.31, 88.45) = 0.59, *p* = 0.686). For reaction times, slower responses were associated with task difficulty (at-risk vs control comparison, F(3, 126) = 60.55, *p* < 0.001; NPE, PE, control comparison, F(3, 123) = 56.76, *p*< 0.001). As with accuracy, reaction times did not differ between groups (at-risk vs control comparison, F(1, 42) = 0.74, *p* = 0.396; NPE, PE, control comparison, F(2, 41) = 2.20, *p* = 0.124) and no interaction effects between group and difficulty were observed (at-risk vs control comparison, F(3, 126) = 0.16, *p* = 0.921; NPE, PE, control comparison, F(6, 123) = 0.28, *p* = 0.945).

Supplementary Table 1 Performance measures for the n-back task for patients and healthy controls.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **N-back** | **Controls** |  | **At-risk** |  | **NPE** |  | **PE** |
| **(N = 20)** |  | **(N = 24)** |  | **(N = 13)** |  | **(N = 11)** |
| **Mean** | **SD** |  | **Mean** | **SD** |  | **Mean** | **SD** |  | **Mean** | **SD** |
| **MRT [ms]** |   |   |   |   |   |   |   |   |   |   |   |
| 0-back | 487 | 88 |  | 507 | 94 |  | 478 | 100 |  | 541 | 77 |
| 1-back | 594 | 134 |  | 621 | 119 |  | 591 | 130 |  | 656 | 100 |
| 2-back | 681 | 200 |  | 719 | 147 |  | 694 | 155 |  | 749 | 138 |
| 3-back  | 724 | 168 |  | 737 | 149 |  | 683 | 162 |  | 800 | 106 |
| **Accuracy [%]** |  |  |  |  |  |  |  |  |  |  |  |
| 0-back | 100 | 0 |  | 100 | 2 |  | 100 | 2 |  | 100 | 0 |
| 1-back | 99 | 3 |  | 99 | 1 |  | 99 | 2 |  | 99 | 1 |
| 2-back | 97 | 5 |  | 96 | 6 |  | 96 | 6 |  | 95 | 5 |
| 3-back  | 94 | 5 |  | 92 | 6 |  | 92 | 5 |  | 91 | 7 |

MRT = Mean Reaction Time (in ms); NPE = No Postpartum Episode; PE = Postpartum Episode; SD = Standard Deviation.

## Fearful Faces

Mean values for performance on the fearful faces task are reported in Table 3. Task condition did not affect accuracy (at-risk vs control comparison, F(1.63, 68.55) = 0.28, *p* = 0.714; NPE, PE, control comparison, F(1.62, 66.39) = 0.31, *p* = 0.686). Accuracy did not differ significantly across groups (at-risk vs control comparison, F(1, 42) = 0.02, *p* = 0.897; NPE, PE, control comparison, F(2, 41) = 0.03, *p* = 0.967) and no interaction effects between group and condition were observed (at-risk vs control comparison, F(1.63, 68.55) = 0.39, *p* = 0.634; NPE, PE, control comparison, F(3.24, 66.39) = 0.43, *p* = 0.748). Task condition significantly affected reaction times (at-risk vs control comparison, F(2, 84) = 6.62, *p* = 0.002; NPE, PE, control comparison, F(2, 82) = 5.85, *p* = 0.004), with all participants, regardless of group, responding significantly slower during standard fear trials compared to lower fear trials (at-risk vs control comparison, *p* = 0.007; NPE, PE, control comparison, *p* = 0.011). Reaction times did not differ significantly across groups (at-risk vs control comparison, F(1, 42) = 0.33, *p* = 0.571; NPE, PE, control comparison, F(2, 41) = 0.40, *p* = 0.671). No interaction effects were observed between group and condition (at-risk vs control comparison, F(2, 84) = 0.15, *p* = 0.860; NPE, PE, control comparison, F(4, 82) = 0.63, *p* = 0.646).

Supplementary Table 2 Performance measures for the fearful faces task for patients and healthy controls.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Fearful faces** | **Controls** |  | **At-risk** |  | **NPE** |  | **PE** |
| **(N = 20)** |  | **(N = 24)** |  | **(N = 13)** |  | **(N = 11)** |
| **Mean** | **SD** |  | **Mean** | **SD** |  | **Mean** | **SD** |  | **Mean** | **SD** |
| **MRT [ms]** |   |   |   |   |   |   |   |   |   |   |   |
| Neutral | 949 | 211 |  | 990 | 210 |  | 972 | 232 |  | 1012 | 189 |
| Lower fear | 941 | 218 |  | 966 | 193 |  | 928 | 182 |  | 1012 | 204 |
| Standard fear | 978 | 208 |  | 1008 | 203 |  | 987 | 193 |  | 1032 | 221 |
| **Accuracy [%]** |   |   |   |   |   |   |   |   |   |   |   |
| Neutral | 87 | 7 |  | 86 | 6 |  | 87 | 6 |  | 86 | 7 |
| Lower fear | 87 | 8 |  | 87 | 5 |  | 87 | 5 |  | 87 | 6 |
| Standard fear | 86 | 8 |  | 87 | 5 |  | 88 | 5 |  | 86 | 6 |

MRT = Mean Reaction Time (in ms); NPE = No Postpartum Episode; PE = Postpartum Episode; SD = Standard Deviation.

# fMRI Results

## Brain Activation

### N-back

Supplementary Table 3 Brain activation results during the n-back task for all significant clusters. All *p*≤0.05.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Subject Contrast** | **Cerebral Region**  | **BA** | **Peak MNI Coordinates** | **Cluster Size (voxels)** |
| **x** | **y** | **z** |
| *0-back* |  |  |  |  |  |  |  |
| At-risk > HC | R | Superior Lateral Occipital | 19 | 36 | -74 | 38 | 41 |
| PE > HC | B | Cuneus, Supracalcarine, Intracalcarine, Lingual | 18/17 | 4 | -76 | 20 | 605 |
| *1-back* |  |  |  |  |  |  |  |
| At-risk > HC | R | Superior Lateral Occipital | 39 | 42 | -64 | 34 | 137 |
| PE > HC | B | Cuneus, Supracalcarine, Intracalcarine, Precuneus, Lingual, Occipital Fusiform | 18/30/19 | 4 | -76 | 20 | 1705 |
|  | R | Posterior, Anterior Supramarginal Gyrus | 40 | 46 | -38 | 42 | 73 |
|  | L | Precuneus | 7 | -4 | -80 | 54 | 52 |
|  | R | Occipital Pole | 19 | 4 | -94 | 24 | 20 |
|  | R | Inferior Lateral Occipital | 18 | 46 | -78 | -16 | 18 |
|  | L | Precuneus | 7 | -6 | -74 | 40 | 17 |
|  | R | Superior Lateral Occipital | 7 | 8 | -82 | 50 | 11 |
| *3-back* |  |  |  |  |  |  |  |
| At-risk > HC | L | Posterior Cingulate, Precuneus  | 31 | -6 | -54 | 26 | 279 |
|  | L | Posterior Cingulate, Precuneus  | 31 | -4 | -42 | 42 | 79 |
|  | R | Precuneus | 7 | 8 | -60 | 38 | 44 |
|  | L | Posterior Cingulate | 31 | -2 | -28 | 46 | 10 |
| PE > HC | B | Precuneus, Posterior Cingulate, Cuneus, Supracalcarine, Intracalcarine, Lingual  | 29/23/31/ 30/18/17 | -2 | -58 | 10 | 1453 |

B = Bilateral; BA = Brodmann Area; HC = Healthy Controls; L = Left; NPE = No Postpartum Episode; PE = Postpartum Episode; R = Right.

### Fearful Faces

Supplementary Table 4 Brain activation results during the fearful faces task for all significant clusters. All *p*≤0.05.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Subject Contrast** | **Cerebral Region**  | **BA** | **Peak MNI Coordinates** | **Cluster Size (voxels)** |
| **x** | **y** | **z** |
| *Standard Fear > Blank* |  |  |  |  |  |
| At-risk > HC | B | Anterior Cingulate, Paracingulate, Superior Frontal | 32/6 | 2 | 28 | 28 | 1743 |
|  | B | Thalamus, Lateral Ventricle | 50 | -6 | -2 | 4 | 1070 |
|  | L | Middle Frontal, Inferior Frontal, Precentral | 9/6 | -48 | 12 | 30 | 653 |
|  | R | Precentral, Middle Frontal | 6 | 40 | -6 | 32 | 528 |
|  | R | Middle Frontal | 9/8 | 48 | 16 | 40 | 465 |
|  | R | Caudate, Lateral Ventricle, Putamen | 48 | 12 | 22 | 6 | 186 |
|  | B | Superior Frontal, Frontal Pole | 8 | 2 | 48 | 52 | 164 |
|  | B | Anterior, Posterior Cingulate, Supplementary Motor Area | 31/24 | -2 | -14 | 46 | 101 |
|   | R | White Matter | 9 | 18 | 36 | 22 | 33 |

B = Bilateral; BA = Brodmann Area; HC = Healthy Controls; L = Left; R = Right.

## Psychophysiological Interaction

### N-back

Supplementary Table 5 Functional connectivity results during the n-back task for all significant clusters. All *p*≤0.05.

| **Subject Contrast** | **Cerebral Region**  | **BA** | **Peak MNI Coordinates** | **Cluster Size (voxels)** |
| --- | --- | --- | --- | --- |
| x | y | z |
| *0-back* |  |  |  |  |  |  |  |
| At-risk > HC | L | Cerebellum | - | -36 | -76 | -26 | 151 |
|  | L | Superior Temporal, Postcentral, Central Opercular | 42 | -68 | -28 | 16 | 52 |
| *1-back* |  |  |  |  |  |  |  |
| At-risk > HC | L | Cerebellum, Parahippocampal, Temporal Occipital Fusiform | - | -36 | -74 | -26 | 2760 |
|  | R | Superior Temporal, Supramarginal, Postcentral, Central Opercular, Parietal Operculum, Planum Temporale | 22/42/40/2/13/43 | 66 | -34 | 20 | 1598 |
|  | L | Superior Temporal, Supramarginal, Postcentral, Central Opercular, Parietal Operculum, Planum Temporale | 22/42/40/2/13/43 | -68 | -30 | 16 | 1504 |
|  | L | Superior Lateral Occipital, Occipital Pole, Cuneus  | 19/18 | -28 | -88 | 26 | 1460 |
|  | R | Occipital Pole, Intracalcarine, Supracalcarine, Precuneus, Lingual, Occipital Fusiform | 17/23/30/31/18 | 14 | -90 | 2 | 577 |
|  | R | Superior Lateral Occipital, Occipital Pole, Cuneus  | 19 | 32 | -88 | 24 | 568 |
|  | R | Cerebellum, Temporal Occipital Fusiform | - | 24 | -74 | -28 | 401 |
|  | R | Cerebellum | - | 24 | -50 | -52 | 186 |
|  | R | Inferior Lateral Occipital, Middle Temporal | 37/19/39 | 52 | -64 | 10 | 155 |
|  | R | Temporal Occipital Fusiform, Lingual | 20/37 | 34 | -42 | -22 | 127 |
|  | R | Occipital Pole  | 19 | 14 | -88 | 32 | 15 |
|  | L | Planum Polare, Central Opercular | 22 | -54 | -8 | 4 | 14 |
|  | R | Angular | 40 | 62 | -54 | 24 | 11 |
| NPE > HC | L | Superior Temporal, Supramarginal, Postcentral, Central Opercular, Parietal Operculum, Planum Temporale, Precentral, Insula, (B) Thalamus | 22/42/40/2/13/43/4 | -66 | -32 | 18 | 6847 |
|  | L | Superior Lateral Occipital, Occipital Pole | 19/18 | -42 | -82 | 28 | 802 |
|  | R | Superior Lateral Occipital, Occipital Pole | 19 | 34 | -86 | 26 | 324 |
|  | L | Precentral | 5 | -16 | -30 | 52 | 137 |
|  | R | Occipital Pole  | 17 | 16 | -90 | 0 | 136 |
|  | L | Cerebellum | - | -36 | -74 | -26 | 98 |
|  | L | Cuneus | 18 | -8 | -82 | 24 | 98 |
|  | R | Lingual, Occipital Fusiform | 18 | 16 | -80 | -8 | 86 |
|  | R | Supracalcarine, Precuneus | 31 | 24 | -60 | 18 | 73 |
|  | R | Precuneus | 30 | 22 | -52 | 12 | 43 |
|  | R | Intracalcarine | 23/18 | 8 | -74 | 14 | 40 |
| PE > HC | L | Cerebellum | - | -38 | -80 | -38 | 1118 |
| *2-back* |  |  |  |  |  |  |  |
| At-risk > HC | B | Superior Temporal, Supramarginal, Postcentral, Central Opercular, Parietal Operculum, Planum Temporale, Precentral, Precuneus, Cuneus, Superior Lateral Occipital, Occipital Pole, Intracalcarine, Supracalcarine, Lingual, Temporal Occipital Fusiform, Occipital Fusiform, Superior Frontal, Middle Frontal, Anterior Cingulate, Posterior Cingulate, Temporal Pole, Supplementary Motor Area, Insula, Caudate, Putamen, Thalamus, Posterior Parahippocampal, Cerebellum | 22/42/40/ 2/13/43/7/6/5/4/24/31/23/19/17/18/29/30/37/48 | -66 | -32 | 18 | 54208 |
|  | R | Precentral | 4/3 | 36 | -18 | 50 | 110 |
| NPE > HC | B | Superior Temporal, Supramarginal, Postcentral, Central Opercular, Parietal Operculum, Planum Temporale, Precentral, Precuneus, Cuneus, Superior Lateral Occipital, Occipital Pole, Intracalcarine, Supracalcarine, Lingual, Temporal Occipital Fusiform, Occipital Fusiform, Anterior Cingulate, Posterior Cingulate, Temporal Pole, Supplementary Motor Area, (R) Caudate, (L) Putamen, Thalamus, Posterior Parahippocampal, Cerebellum | 22/42/40/2/43/7/6/5/4/24/31/23/19/17/18/29/30/37/48 | -66 | -32 | 18 | 21826 |
|  | L | Cerebellum | - | -34 | -74 | -28 | 4055 |
|  | L | Posterior Parahippocampal | 35 | -14 | -30 | -10 | 46 |
| PE > HC | B | Cerebellum, Occipital Fusiform, Inferior Lateral Occipital, Temporal Occipital Fusiform, Lingual, Occipital Pole, Intracalcarine, Supracalcarine, Superior Lateral Occipital, Precuneus, Cuneus, Angular, Anterior Cingulate, Posterior Cingulate, Supplementary Motor Area, Postcentral, Precentral, Superior Temporal, Central Opercular, Planum Temporale, Planum Polare, Temporal Pole, Posterior Parahippocampal, Putamen, Amygdala, Thalamus | 22/42/40/2/43/7/6/5/4/24/31/23/19/17/18/29/30/37/48 | -40 | -82 | -40 | 48355 |
|  | R | Frontal Medial, Frontal Pole, Paracingulate | 11/10 | 4 | 52 | -20 | 499 |
|  | R | Frontal Pole | 10 | 24 | 62 | 20 | 374 |
|  | L | Parietal Operculum | 13 | -34 | -32 | 26 | 56 |
| PE > NPE | R | Middle Temporal | 21 | 58 | -4 | -26 | 164 |
| *2- > 0-back* |
| At-risk > HC | B | Cerebellum, Occipital Fusiform, Inferior Lateral Occipital | 18 | -10 | -92 | -20 | 4416 |
|  | R | Posterior Cingulate, Anterior Cingulate, Precentral, Central Opercular, Superior Temporal | 6/31/24/40/22 | 34 | 0 | 38 | 3648 |
|  | B | Cerebellum, Hippocampus, Parahippocampal | 28/36 | -22 | -46 | -32 | 2483 |
|  | B | Precuneus, Posterior Cingulate | 31/23 | 8 | -54 | 20 | 1709 |
|  | B | Frontal Pole, Superior Frontal, Middle Frontal | 9/10/8/6 | -2 | 60 | 28 | 1410 |
|  | L | Middle Frontal, Superior Frontal  | 6/8 | -32 | 16 | 48 | 291 |
|  | R | Temporal Fusiform  | 20/21 | 38 | -12 | -34 | 184 |
|  | R | Postcentral, Precuneus, Superior Parietal Lobule | 5/7 | 12 | -46 | 66 | 151 |
|  | R | Frontal Pole, Superior Frontal, Middle Frontal | 8 | 20 | 36 | 44 | 141 |
|   | R | Occipital Fusiform, Temporal Occipital Fusiform | 37 | 40 | -64 | -18 | 29 |

B = Bilateral; BA = Brodmann Area; HC = Healthy Controls; L = Left; NPE = No Postpartum Episode; PE = Postpartum Episode; R = Right.

### Fearful Faces

Supplementary Table 6 Functional connectivity results during the fearful faces task for all significant clusters. All *p*≤0.05.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Subject Contrast** | **Cerebral Region**  | **BA** | **Peak MNI Coordinates** | **Cluster Size (voxels)** |
| x | y | z |
| *Lower Fear > Blank* |  |  |  |  |  |
| HC > At-risk | L | Superior Lateral Occipital, Superior Parieral Lobule, Angular, Supramarginal | 7/19 | -28 | -66 | 56 | 900 |
|  | L | Postcentral, Precentral | 6/3 | -58 | -10 | 40 | 345 |
|  | L | Superior Parietal Lobule, Postcentral | 40/7 | -24 | -42 | 56 | 126 |
|  | L | Postcentral, Supramarginal, Central Opercular | 3 | -58 | -16 | 26 | 115 |
|  | L | Precentral | 6/4 | -28 | -16 | 58 | 78 |
|   | L | Supramarginal | 40 | -32 | -36 | 36 | 22 |

BA = Brodmann Area; HC = Healthy Controls; L = Left.

# Comparison between controls and women at risk of PP with a diagnosis of bipolar disorder

## Methods

To explore the impact of bipolar disorder diagnosis on the observed results in the current sample, we performed a secondary comparison between healthy controls and women at risk of PP with an existing diagnosis of bipolar disorder (BD). Ten women from the at-risk group (PE = 2, NPE = 8) were identified as having received a diagnosis of BD. They were compared to the same groups of 20 healthy controls, as used in the analysis of PP. fMRI analysis was conducted for brain activation (general linear model (GLM)) and functional connectivity (psychophysiological interaction (PPI)) during n-back and fearful faces tasks following an identical pipeline as in the main analysis of PP effects.

## Results

### Brain Activation

No significant differences were observed when comparing healthy controls with BD women during both n-back and fearful faces tasks.

### Psychophysiological Interaction

#### N-back

Increased right DLPFC connectivity with a number of regions was observed in the BD group relative to controls during 0- and 2-back (see Supplementary Figure 1 and Supplementary Table 7).

#### Fearful Faces

Reduced functional connectivity between the left amygdala and numerous ipsilateral regions was observed in the BD group compared to controls during lower fear contrasted with the null condition (see Supplementary Figure 1 and Supplementary Table 8).

 

Supplementary Figure 1 A. Functional connectivity with the right DLPFC during the n-back working memory task. Regions showing significantly higher functional connectivity in the bipolar disorder group compared to healthy controls during 0-back (purple), 1-back (cyan), 2-back (blue). B. Functional connectivity with the left amygdala during the fearful faces task. Hypoconnectivity in the bipolar disorder group compared to controls during the lower fear contrasted with neutral condition.

Supplementary Table 7 Functional connectivity differences between controls and bipolar disorder patients during the n-back task for all significant clusters. All *p*≤0.05.

|  |  |  |  |
| --- | --- | --- | --- |
| **Cerebral Region**  | **BA** | **Peak MNI Coordinates** | **Cluster Size (voxels)** |
| **x** | **y** | **z** |
| *0-back* |  |  |  |  |  |
| L | Postcentral Gyrus | 43 | -64 | -16 | 14 | 52 |
| L | Superior Temporal Gyrus | 42 | -70 | -30 | 16 | 45 |
| L | Insula | 13 | -38 | 4 | 16 | 43 |
| L | Insula | 13 | -42 | -6 | 22 | 26 |
| L | Parietal Operculum  | - | -34 | -32 | 24 | 26 |
| *2-back* |  |  |  |  |  |
| B | Superior Temporal, Supramarginal, Postcentral, Central Opercular, Parietal Operculum, Planum Temporale, Precentral, Precuneus, Cuneus, Superior Lateral Occipital, Occipital Pole, Intracalcarine, Supracalcarine, Lingual, Temporal Occipital Fusiform, Occipital Fusiform, Superior Frontal, Middle Frontal, Anterior Cingulate, Posterior Cingulate, Temporal Pole, Supplementary Motor Area, Caudate, Putamen, Thalamus, Posterior Parahippocampal, Cerebellum | 22/42/40/ 2/43/7/6/5/4/24/31/23/19/17/18/29/30/37/48 | -66 | -32 | 16 | 29778 |
| R | Cerebellum | - | 24 | -42 | -26 | 105 |
| R | Cerebellum | - | 18 | -26 | -20 | 28 |

B = Bilateral; BA = Brodmann Area; L = Left; R = Right.

Supplementary Table 8 Functional connectivity differences between controls and bipolar disorder patients during the fearful faces task for all significant clusters. All *p*≤0.05.

|  |  |  |  |
| --- | --- | --- | --- |
| **Cerebral Region**  | **BA** | **Peak MNI Coordinates** | **Cluster Size (voxels)** |
| **x** | **y** | **z** |
| *Lower Fear > Blank* |   |   |   |   |   |
| R | Cerebellum, Temporal Fusiform, Temporal Occipital Fusiform, Lingual, Lateral Occipital  | 19/18 | 14 | -62 | -16 | 13532 |
| R | Inferior Parietal Lobule, Lateral Occipital Cortex, Angular Gyrus | 39/19/7 | 38 | -62 | 44 | 635 |
| L | Cerebellum | - | -14 | -54 | -60 | 470 |
| R | Lateral Occipital, Occipital Pole | 18 | 26 | -88 | 30 | 336 |
| R | Insula | 13 | 40 | -2 | 20 | 162 |
| R | Postcentral Gyrus | 6 | 64 | -12 | 44 | 95 |
| R | Cerebellum | - | 22 | -52 | -52 | 85 |
| R | Frontal Pole | 9 | 52 | 38 | 32 | 11 |

BA = Brodmann Area; L = Left; R = Right.

# Region of interest (ROI) analysis of the n-back working memory task

We conducted a region of interest (ROI) analysis limited to the dorsolateral prefrontal cortex. Two ROI analyses of the dorsolateral prefrontal cortex were conducted with 1) group (at-risk versus healthy controls) as between-subject factor and load (1-, 2-, and 3-back) as within-subject factor for the combined group analysis (2x3) and 2) group (NPE, PE and healthy controls) as between-subject factor and load (1-, 2-, and 3-back) as within-subject factor for the sub group analysis (3x3).

No significant group differences were observed in the ROI analyses.