

1 **Supplementary Material To:**

2 **Title:** Intracranial Fluid Redistribution But No White Matter Microstructural Changes
3 During a Spaceflight Analog

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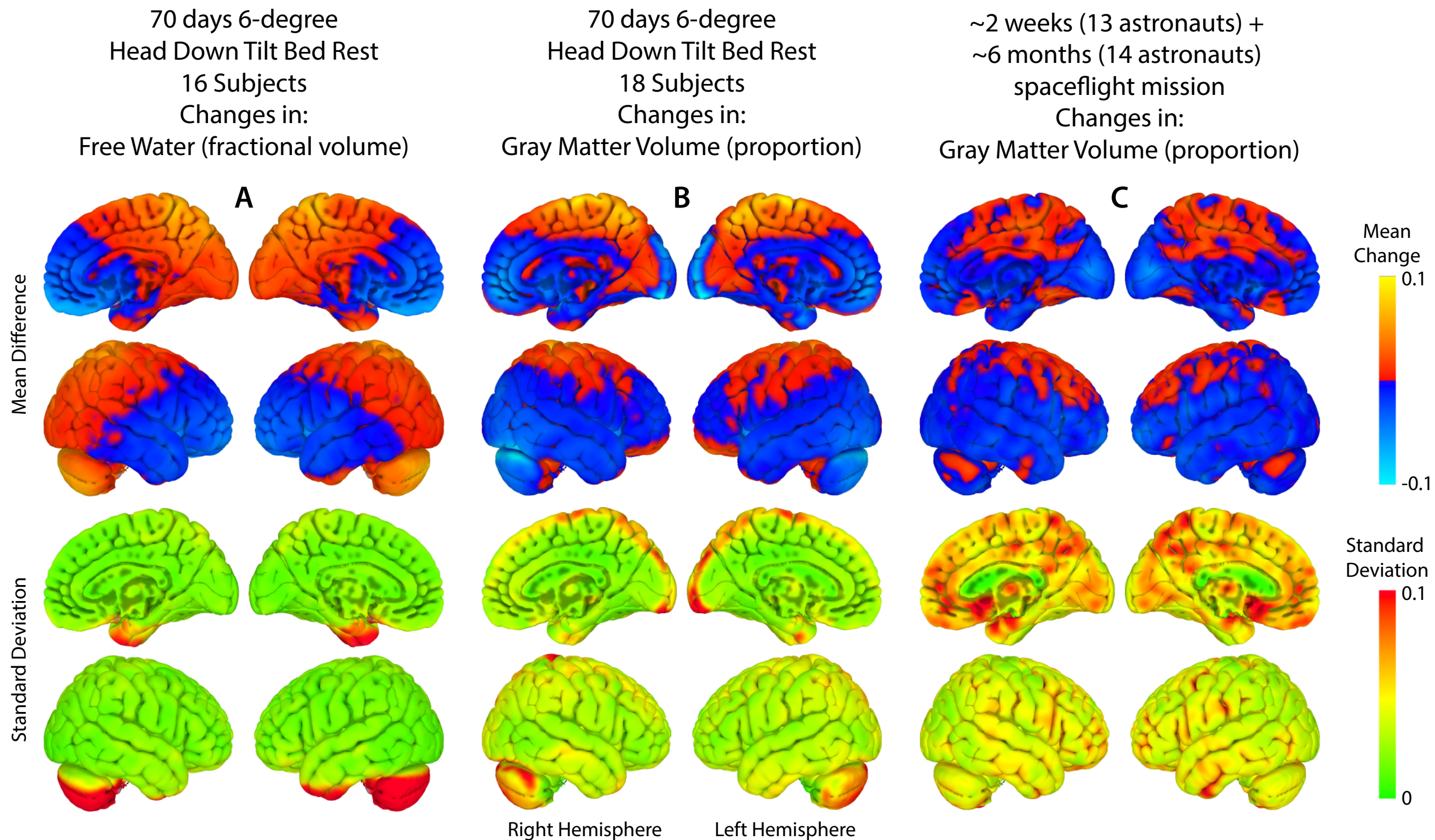
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Similarities between A) Free Water Distribution Changes from pre- to post-Bed Rest, B) Gray Matter Volume Changes from pre- to post-Bed Rest, and C) Gray Matter Volume Changes from pre- to post-Spaceflight



1 **Supplementary Figure Captions**

2 **Supplementary Figure 1. Qualitative comparison of Free Water and Gray Matter** 3 **changes over the course of HDBR and Gray Matter changes from pre- to post-** 4 **spaceflight**

5 Mean difference images (top 2 rows) show the average of the difference images (8 days pre-
6 HDBR to ~70 days in HDBR, or pre-spaceflight to post-spaceflight). Standard deviation
7 images (bottom 2 rows) show the standard deviation over the difference images of all
8 subjects. Over groups, mean difference images and standard deviation images have been
9 scaled identically for comparison. A (left two columns)= Free Water changes from 8 days
10 pre-HDBR to ~70 days in HDBR (data from the current report); B (middle two columns)=
11 Gray Matter changes from 8 days pre-HDBR to ~70 days in HDBR (Koppelmans et al., npj
12 Microgravity 2016; doi:10.1038/s41526-016-0001-9; same participants as A); C (right two
13 columns)= Gray Matter changes from pre- to post-Spaceflight (Koppelmans et al., npj
14 Microgravity 2016; doi:10.1038/s41526-016-0001-9)

Supplementary tables to:

Intracranial Fluid Redistribution and White Matter Microstructural Changes During a Spaceflight Analog

Vincent Koppelmans, Ofer Pasternak, Jacob J. Bloomberg, Yiri E. De Dios, Scott J. Wood, Patricia A. Reuter-Lorenz, Igor S. Kofman, Ajitkumar P. Mulavara, Rachael D. Seidler

This sheet contains an overview of locations in which we observed free water changes:

- 1) HBDR vs. Normative: Free Water Increase (non-parametric)
- 2) HDBR vs. Normative Free Water Decrease (non-parametric)
- 3) Δ Contrast: Free Water Increase with HDBR *
- 4) Δ Contrast: Free Water Decrease with HDBR *

Anatomical labels of all peak voxels with a minimum distance of 1cm within clusters showing significant (family wise error corrected) free water changes are reported. Coordinates refer to the MNI coordinate system in mm. Changes reflect changes in free water from pre-HDBR to the end of HDBR relative to changes in normative control subjects over a similar time interval.

* The Δ contrast is described in the manuscript (see Figure 1B). In terms of focal free water it assumes a stable baseline (no changes before bed rest) with increases/decreases during bed rest and recovery post bed rest.

Regions highlighted in green are obtained from the **Harvard-Oxford Cortical Structural Atlas**

Regions highlighted in green are obtained from the **Harvard-Oxford Subcortical Structural Atlas**

Regions highlighted in orange are obtained from the **Cerebellar Atlas in MNI152 (normalization with FNIRT)**

These atlases are bundled with Oxford Centre for Functional MRI of the Brain Software Library

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL>

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases>

4) Δ Contrast: Free Water Decrease with HDBR *

Regions in which Free Water was stable at baseline, **DECREASED** from pre-HDBR to ~70 Days in HDBR and recovered post-HDBR (also see Figure 2B)

X	Y	Z	Brain Region	Counts
28	-72	44	Lateral Occipital Cortex; superior division	1 Angular Gyrus
1	-51	55	Precuneous Cortex	1 Cingulate Gyrus; anterior division
0	-60	45	Precuneous Cortex	2 Cuneal Cortex
1	-41	59	Precuneous Cortex	1 Intracalcarine Cortex
37	-53	51	Angular Gyrus	2 Juxtapositional Lobule Cortex
12	-77	36	Cuneal Cortex	2 Lateral Occipital Cortex; inferior division
-32	-53	48	Superior Parietal Lobule	7 Lateral Occipital Cortex; superior division
-26	-73	42	Lateral Occipital Cortex; superior division	1 Left Crus I
40	-38	52	Superior Parietal Lobule	1 Lingual Gyrus
-11	-80	37	Cuneal Cortex	2 Middle Frontal Gyrus
-23	-29	65	Postcentral Gyrus	5 Occipital Pole
-32	-27	60	Postcentral Gyrus	6 Postcentral Gyrus
-43	-35	50	Postcentral Gyrus	4 Precentral Gyrus
29	-28	64	Postcentral Gyrus	4 Precuneous Cortex
14	-31	72	Postcentral Gyrus	2 Right Crus I
-2	-76	32	Precuneous Cortex	4 Superior Parietal Lobule
-22	-42	64	Postcentral Gyrus	1 Vermis VI
-30	-40	57	Superior Parietal Lobule	
25	-40	63	Superior Parietal Lobule	
0	-29	55	Precentral Gyrus	
-25	-85	25	Lateral Occipital Cortex; superior division	
24	-90	23	Occipital Pole	
2	-19	67	Precentral Gyrus	
1	0	65	Juxtapositional Lobule Cortex (formerly Supplementary Motor Cortex)	
-12	-73	48	Lateral Occipital Cortex; superior division	
-6	-95	17	Occipital Pole	
-41	-14	49	Precentral Gyrus	
2	-89	20	Occipital Pole	
0	-12	47	Cingulate Gyrus; anterior division	
29	-3	58	Middle Frontal Gyrus	
0	3	49	Juxtapositional Lobule Cortex (formerly Supplementary Motor Cortex)	
-8	-94	-2	Occipital Pole	
46	-66	35	Lateral Occipital Cortex; superior division	
10	-85	6	Intracalcarine Cortex	
37	-87	2	Lateral Occipital Cortex; inferior division	
-19	-95	11	Occipital Pole	
-1	-70	-22	Vermis VI	
21	-81	-25	Right Crus I	
-10	-63	-8	Lingual Gyrus	
37	-74	-27	Right Crus I	
-31	-73	-24	Left Crus I	
43	-13	44	Precentral Gyrus	
-45	-63	27	Lateral Occipital Cortex; superior division	
-26	-2	54	Middle Frontal Gyrus	
-29	-89	5	Lateral Occipital Cortex; inferior division	
-44	-70	18	Lateral Occipital Cortex; superior division	

3) Δ Contrast: Free Water Increase with HDBR *

Regions in which Free Water was stable at baseline, **INCREASED** from pre-HDBR to ~70 Days in HDBR and recovered post-HDBR (also see Figure 2B)

X	Y	Z	Brain Region	Counts
0	42	-11	Paracingulate Gyrus	3
-33	20	-8	Insular Cortex	1
-38	24	0	Frontal Operculum Cortex	2
43	20	1	Frontal Operculum Cortex	9
29	55	2	Frontal Pole	1
38	45	-11	Frontal Pole	1
34	35	-12	Frontal Pole	1
-25	55	1	Frontal Pole	4
-28	38	-11	Frontal Pole	2
1	38	6	Cingulate Gyrus; anterior division	1
44	41	0	Frontal Pole	1
-50	6	-2	Central Opercular Cortex	1
-39	45	-5	Frontal Pole	1
-40	10	1	Insular Cortex	3
-39	43	8	Frontal Pole	2
33	10	-22	Temporal Pole	3
49	3	-2	Planum Polare	
23	38	-17	Frontal Pole	
12	23	3	Right Caudate	
56	-1	6	Central Opercular Cortex	
1	22	-20	Subcallosal Cortex	
54	13	9	Inferior Frontal Gyrus; pars opercularis	
40	15	-13	Insular Cortex	
1	16	-8	Subcallosal Cortex	
-55	-7	9	Central Opercular Cortex	
-46	31	5	Inferior Frontal Gyrus; pars triangularis	
-36	16	-26	Temporal Pole	
-30	7	-22	Temporal Pole	
17	4	-21	Parahippocampal Gyrus; anterior division	
-12	21	-18	Subcallosal Cortex	
-43	-3	9	Insular Cortex	
53	4	-24	Middle Temporal Gyrus; anterior division	
55	-5	-16	Middle Temporal Gyrus; anterior division	
48	-2	-36	Inferior Temporal Gyrus; anterior division	
62	-18	-4	Superior Temporal Gyrus; posterior division	
-55	-12	-10	Superior Temporal Gyrus; posterior division	

2) HDBR vs. Normative Free Water Decrease (non-parametric)

Regions with Focal Free Water **DECREASES** from pre-HDBR to ~70 Days in HDBR relative to Free Water Changes in Normative Subjects over a similar time course (also see Figure 2A)

X	Y	Z	Brain Region	Counts
30	-75	44	Lateral Occipital Cortex; superior division	4
36	-51	53	Superior Parietal Lobule	1
-44	-50	48	Supramarginal Gyrus; posterior division	1
18	-60	59	Lateral Occipital Cortex; superior division	3
-44	-35	51	Postcentral Gyrus	2
42	-43	54	Superior Parietal Lobule	1
-6	-73	29	Precuneous Cortex	3
2	-46	46	Precuneous Cortex	11
9	-77	34	Cuneal Cortex	2
-10	-82	36	Cuneal Cortex	2
-25	-71	44	Lateral Occipital Cortex; superior division	2
-2	-37	44	Cingulate Gyrus; posterior division	2
-32	-26	60	Postcentral Gyrus	8
-33	-43	57	Superior Parietal Lobule	1
-19	-52	62	Superior Parietal Lobule	8
-19	-27	61	Precentral Gyrus	5
-23	-38	62	Postcentral Gyrus	5
31	-38	57	Postcentral Gyrus	2
49	-50	44	Angular Gyrus	1
-15	-31	71	Postcentral Gyrus	4
0	-62	43	Precuneous Cortex	5
14	-50	66	Superior Parietal Lobule	2
-17	-72	50	Lateral Occipital Cortex; superior division	1
-19	-61	57	Lateral Occipital Cortex; superior division	1
0	-86	31	Cuneal Cortex	2
-27	-84	24	Lateral Occipital Cortex; superior division	
32	-28	62	Postcentral Gyrus	
-43	-67	32	Lateral Occipital Cortex; superior division	
4	-40	64	Postcentral Gyrus	
-3	-94	11	Occipital Pole	
32	-83	23	Lateral Occipital Cortex; superior division	
-2	-60	61	Precuneous Cortex	
1	-4	55	Juxtapositional Lobule Cortex (formerly Supplementary Motor Cortex)	
-17	-88	26	Lateral Occipital Cortex; superior division	
-10	-94	-1	Occipital Pole	
21	-91	24	Occipital Pole	
11	-85	4	Intracalcarine Cortex	
2	-10	46	Cingulate Gyrus; anterior division	
10	-96	13	Occipital Pole	
-13	-84	2	Intracalcarine Cortex	
-15	-67	23	Precuneous Cortex	
-41	-14	47	Precentral Gyrus	
20	-98	-1	Occipital Pole	
-2	-20	71	Precentral Gyrus	
2	-31	68	Precentral Gyrus	
-21	-95	-3	Occipital Pole	
23	-97	9	Occipital Pole	
18	-31	60	Precentral Gyrus	
55	-40	41	Supramarginal Gyrus; posterior division	
-11	14	65	Superior Frontal Gyrus	
16	-31	73	Postcentral Gyrus	
-27	-90	5	Lateral Occipital Cortex; inferior division	
55	-60	29	Lateral Occipital Cortex; superior division	
-5	23	62	Superior Frontal Gyrus	
-17	-96	8	Occipital Pole	
54	-47	28	Angular Gyrus	
-15	-10	70	Superior Frontal Gyrus	
-52	-51	33	Angular Gyrus	
43	-65	41	Lateral Occipital Cortex; superior division	
8	8	68	Superior Frontal Gyrus	
-46	-59	21	Angular Gyrus	
-14	8	39	Paracingulate Gyrus	
-36	-82	7	Lateral Occipital Cortex; inferior division	
40	-81	8	Lateral Occipital Cortex; inferior division	
-17	-77	-23	Left Crus I	
-3	-65	-18	Vermis VI	
5	-62	-10	Right V	
28	-79	-31	Right Crus I	
14	-83	-25	Right Crus I	
-13	-62	-9	Lingual Gyrus	
-12	-72	-15	Left VI	
1	-73	-34	Vermis Crus II	
-23	-69	-22	Left VI	
-32	-75	-24	Left Crus I	
18	-67	-13	Lingual Gyrus	
-2	-78	-16	Vermis VI	
38	-72	-16	Occipital Fusiform Gyrus	
-24	-87	-17	Occipital Fusiform Gyrus	
-47	-60	-22	Temporal Occipital Fusiform Cortex	

1) HBDR vs. Normative: Free Water Increase (non-parametric)

Regions with Focal Free Water **INCREASES** from pre-HBDR to ~70 Days in HBDR relative to Free Water Changes in Normative Subjects over a similar time course (also see Figure 2A)

X	Y	Z	Brain Region	Counts
-43	32	-2	Frontal Orbital Cortex	2
-1	52	-13	Frontal Medial Cortex	1
42	43	-2	Frontal Pole	2
-47	21	4	Frontal Operculum Cortex	1
0	52	4	Paracingulate Gyrus	3
50	20	8	Inferior Frontal Gyrus; pars opercularis	17
39	21	-8	Frontal Orbital Cortex	2
0	40	-19	Frontal Medial Cortex	2
-27	40	-9	Frontal Pole	3
35	55	4	Frontal Pole	2
-37	46	7	Frontal Pole	1
-46	30	13	Inferior Frontal Gyrus; pars triangularis	4
8	49	14	Paracingulate Gyrus	1
-25	56	3	Frontal Pole	2
-35	19	-7	Insular Cortex	1
32	33	-11	Frontal Orbital Cortex	1
-35	49	-8	Frontal Pole	3
23	57	-5	Frontal Pole	
42	42	9	Frontal Pole	
53	7	-20	Temporal Pole	
53	9	8	Precentral Gyrus	
1	37	4	Cingulate Gyrus; anterior division	
-29	54	12	Frontal Pole	
66	-23	-13	Middle Temporal Gyrus; posterior division	
49	31	15	Inferior Frontal Gyrus; pars triangularis	
59	-5	-12	Middle Temporal Gyrus; anterior division	
-40	10	1	Insular Cortex	
50	6	-4	Planum Polare	
53	-1	7	Central Opercular Cortex	
14	58	-10	Frontal Pole	
24	40	-14	Frontal Pole	
55	-6	-31	Middle Temporal Gyrus; anterior division	
-52	10	8	Inferior Frontal Gyrus; pars opercularis	
-2	44	26	Paracingulate Gyrus	
15	63	11	Frontal Pole	
-54	-6	7	Central Opercular Cortex	
63	-10	-4	Superior Temporal Gyrus; posterior division	
-9	61	14	Frontal Pole	
-52	8	-2	Temporal Pole	
10	45	26	Paracingulate Gyrus	
-30	46	27	Frontal Pole	
19	60	22	Frontal Pole	
14	64	1	Frontal Pole	
24	2	-16	Right Amygdala	
41	14	-27	Temporal Pole	
30	42	30	Frontal Pole	
-38	8	-16	Insular Cortex	
59	2	15	Precentral Gyrus	