**Supplementary Data:**

# Central nervous system targeted autoimmunity causes regional atrophy: a 9.4T MRI study of the EAE mouse model of Multiple Sclerosis

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**Supplementary Table S1.** Uncorrected volumes of brain structures at peak clinical EAE disease.

| Anatomical Region | Volume, mean ± SD $mm^3$ | | |
|---|---|---|---|
| | Naïve | CFA | EAE |
| **White Matter** | | | |
| Fimbria | 2.93 ± 0.14 | 2.98 ± 0.14 | 3.26 ± 0.17 |
| Corpus Callosum | 16.4 ± 0.6 | 16.6 ± 0.6 | 17.4 ± 0.5 |
| Posterior Commissure | 0.11 ± 0.01 | 0.11 ± 0.01 | 0.13 ± 0.01 |
| Fornix | 0.60 ± 0.05 | 0.59 ± 0.04 | 0.65 ± 0.05 |
| Stria Medullaris | 0.66 ± 0.05 | 0.65 ± 0.04 | 0.69 ± 0.03 |
| Optic Tract | 1.40 ± 0.07 | 1.38 ± 0.06 | 1.46 ± 0.08 |
| Fasciculus Retroflexus | 0.24 ± 0.01 | 0.23 ± 0.01 | 0.25 ± 0.01 |
| Anterior Commissure: Pars Anterior | 1.22 ± 0.04 | 1.19 ± 0.05 | 1.24 ± 0.06 |
| Internal Capsule | 2.31 ± 0.15 | 2.22 ± 0.15 | 2.37 ± 0.15 |
| Anterior Commissure: Pars Posterior | 0.38 ± 0.04 | 0.36 ± 0.03 | 0.38 ± 0.04 |
| Stria Terminalis | 0.81 ± 0.05 | 0.77 ± 0.04 | 0.79 ± 0.04 |
| Habenular Commissure | 0.03 ± 0.01 | 0.03 ± 0.01 | 0.03 ± 0.01 |
| Mammilothalamic Tract | 0.22 ± 0.01 | 0.22 ± 0.02 | 0.22 ± 0.02 |
| **Grey Matter** | | | |
| Lateral Septum | 2.78 ± 0.11 | 2.77 ± 0.12 | 3.04 ± 0.14 |
| Basal Forebrain | 3.93 ± 0.19 | 3.83 ± 0.21 | 4.21 ± 0.20 |
| Periaqueductal Grey | 3.58 ± 0.16 | 3.57 ± 0.26 | 3.87 ± 0.11 |
| Hippocampus | 18.9 ± 1.1 | 19.1 ± 1.2 | 20.4 ± 0.6 |
| Cerebral Peduncle | 1.88 ± 0.09 | 1.87 ± 0.10 | 2.03 ± 0.15 |
| Amygdala | 11.4 ± 0.6 | 11.4 ± 0.8 | 12.0 ± 0.5 |
| Dentate Gyrus of Hippocampus | 3.32 ± 0.21 | 3.39 ± 0.19 | 3.54 ± 0.13 |
| Medial Septum | 0.92 ± 0.07 | 0.86 ± 0.06 | 0.93 ± 0.07 |
| Stratum Granulosum of Hippocampus | 0.80 ± 0.05 | 0.84 ± 0.05 | 0.86 ± 0.02 |
| Nucleus Accumbens | 3.28 ± 0.19 | 3.21 ± 0.16 | 3.38 ± 0.18 |
| Hypothalamus | 9.19 ± 0.49 | 9.00 ± 0.34 | 9.52 ± 0.79 |
| Fundus of Striatum | 0.11 ± 0.02 | 0.11 ± 0.02 | 0.12 ± 0.02 |
| Thalamus | 15.6 ± 0.7 | 15.4 ± 0.6 | 15.8 ± 0.4 |
| Pre-Para Subiculum | 2.15 ± 0.12 | 2.12 ± 0.13 | 2.18 ± 0.07 |
| Globus Pallidus | 2.40 ± 0.19 | 2.30 ± 0.12 | 2.38 ± 0.14 |
| Bed Nucleus of Stria Terminalis | 1.19 ± 0.07 | 1.16 ± 0.07 | 1.20 ± 0.08 |
| Striatum | 17.7 ± 0.9 | 17.7 ± 0.8 | 18.1 ± 0.8 |
| Mammillary Bodies | 0.46 ± 0.04 | 0.45 ± 0.03 | 0.47 ± 0.04 |

**Supplementary Table S1.** (Continued) Uncorrected volumes of brain structures at peak clinical EAE disease.

| Anatomical Region | Volume, mean ± SD $mm^3$ | | |
|---|---|---|---|
| | Naïve | CFA | EAE |
| **Ventricles** | | | |
| Cerebral Aqueduct | 0.43 ± 0.04 | 0.48 ± 0.04 | 0.52 ± 0.03 |
| Lateral Ventricle | 3.32 ± 0.18 | 3.44 ± 0.17 | 3.85 ± 0.29 |
| Third Ventricle | 0.98 ± 0.06 | 1.02 ± 0.06 | 1.11 ± 0.08 |
| Fourth Ventricle | 0.47 ± 0.04 | 0.40 ± 0.04 | 0.51 ± 0.06 |
| **Cerebral Cortex** | | | |
| Entorhinal Cortex | 10.3 ± 0.5 | 10.6 ± 0.4 | 10.8 ± 0.2 |
| Parieto-Temporal Lobe | 71.1 ± 2.8 | 71.0 ± 3.6 | 72.6 ± 2.0 |
| Occipital Lobe | 5.98 ± 0.33 | 5.85 ± 0.36 | 5.92 ± 0.18 |
| Frontal Lobe | 39.0 ± 1.3 | 39.2 ± 1.6 | 39.2 ± 0.8 |
| **Brainstem** | | | |
| Pons | 14.1 ± 0.9 | 13.8 ± 0.5 | 15.0 ± 0.6 |
| Superior Olivary Complex | 0.55 ± 0.08 | 0.56 ± 0.05 | 0.62 ± 0.03 |
| Corticospinal Tract/Pyramids | 1.11 ± 0.07 | 1.18 ± 0.10 | 1.27 ± 0.10 |
| Colliculus: Superior | 7.72 ± 0.35 | 7.63 ± 0.38 | 8.01 ± 0.19 |
| Pontine Nucleus | 0.59 ± 0.05 | 0.61 ± 0.04 | 0.66 ± 0.05 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | 2.04 ± 0.15 | 2.04 ± 0.12 | 2.19 ± 0.13 |
| Cuneate Nucleus | 0.24 ± 0.03 | 0.25 ± 0.02 | 0.28 ± 0.03 |
| Ventral Tegmental Decussation | 0.11 ± 0.01 | 0.09 ± 0.01 | 0.11 ± 0.01 |
| Medulla | 21.9 ± 1.7 | 21.7 ± 1.1 | 23.7 ± 1.8 |
| Midbrain | 11.4 ± 0.82 | 11.4 ± 0.40 | 12.0 ± 0.23 |
| Inferior Olivary Complex | 0.25 ± 0.03 | 0.27 ± 0.03 | 0.29 ± 0.02 |
| Colliculus: Inferior | 5.21 ± 0.25 | 5.21 ± 0.23 | 5.41 ± 0.16 |
| Interpeduncular Nucleus | 0.23 ± 0.03 | 0.23 ± 0.02 | 0.25 ± 0.03 |
| Facial Nerve (Cranial Nerve 7) | 0.21 ± 0.02 | 0.20 ± 0.01 | 0.21 ± 0.03 |
| **Cerebellum** | | | |
| Arbor Vita of Cerebellum | 8.71 ± 0.62 | 8.50 ± 0.40 | 9.24 ± 0.31 |
| Cerebellar Peduncle: Inferior | 0.66 ± 0.06 | 0.68 ± 0.05 | 0.75 ± 0.06 |
| Cerebellar Peduncle: Middle | 0.98 ± 0.06 | 0.99 ± 0.05 | 1.06 ± 0.06 |
| Cerebellar Cortex | 44.7 ± 2.6 | 45.2 ± 2.1 | 47.0 ± 1.1 |
| Cerebellar Peduncle: Superior | 0.92 ± 0.04 | 0.86 ± 0.04 | 0.92 ± 0.03 |
| **Olfactory** | | | |
| Lateral Olfactory Tract | 1.15 ± 0.05 | 1.14 ± 0.04 | 1.21 ± 0.03 |
| Olfactory Tubercle | 3.19 ± 0.23 | 3.04 ± 0.17 | 3.33 ± 0.12 |
| Olfactory Bulbs | 21.1 ± 1.1 | 21.3 ± 1.0 | 21.5 ± 01.1 |
| Subependymale Zone / Rhinocele | 0.06 ± 0.01 | 0.06 ± 0.01 | 0.06 ± 0.01 |

**Supplementary Table S1.** (Continued) Uncorrected volumes of brain structures at peak clinical EAE disease.

| Cumulative Anatomical Region | Volume, mean ± SD $mm^3$ | | |
|---|---|---|---|
| | Naïve | CFA | EAE |
| Ventricles | 5.19 ± 0.28 | 5.33 ± 0.23 | 6.00 ± 0.37 |
| Cerebral Cortex | 29.2 ± 1.2 | 29.2 ± 1.3 | 30.9 ± 0.9 |
| Cerebral White | 69.2 ± 4.4 | 68.8 ± 2.8 | 73.8 ± 1.4 |
| Cerebellum | 56.0 ± 3.4 | 56.2 ± 2.5 | 58.9 ± 1.4 |
| Total Brain Volume | 405 ± 18 | 405 ± 15 | 422 ± 9 |
| Brain Stem | 220 ± 9 | 220 ± 9 | 227 ± 5 |
| Cerebral Grey | 25.5 ± 1.1 | 25.6 ± 1.1 | 26.1 ± 1.2 |
| Olfactory | 126 ± 5 | 127 ± 5 | 129 ± 2 |

*Volumes mean ± standard deviation.*

**Supplementary Table S2.** Volumes of brain structures corrected for body weight, at peak clinical EAE disease.

| | Volume, mean ± SD $mm^3$ | | |
|---|---|---|---|
| Anatomical Region | Naïve | CFA | EAE |
| **White Matter** | | | |
| Fimbria | 2.96 ± 0.14 | 2.98 ± 0.14 | 3.25 ± 0.17 |
| Corpus Callosum | 16.5 ± 0.6 | 16.5 ± 0.6 | 17.4 ± 0.5 |
| Posterior Commissure | 0.11 ± 0.01 | 0.11 ± 0.01 | 0.13 ± 0.01 |
| Fornix | 0.60 ± 0.05 | 0.59 ± 0.04 | 0.65 ± 0.05 |
| Stria Medullaris | 0.67 ± 0.05 | 0.65 ± 0.04 | 0.69 ± 0.03 |
| Optic Tract | 1.40 ± 0.07 | 1.38 ± 0.06 | 1.46 ± 0.08 |
| Fasciculus Retroflexus | 0.24 ± 0.01 | 0.23 ± 0.01 | 0.25 ± 0.01 |
| Anterior Commissure: Pars Anterior | 1.22 ± 0.04 | 1.19 ± 0.05 | 1.24 ± 0.06 |
| Internal Capsule | 2.31 ± 0.15 | 2.22 ± 0.15 | 2.37 ± 0.15 |
| Anterior Commissure: Pars Posterior | 0.38 ± 0.04 | 0.36 ± 0.03 | 0.38 ± 0.04 |
| Stria Terminalis | 0.81 ± 0.05 | 0.77 ± 0.04 | 0.79 ± 0.04 |
| Habenular Commissure | 0.03 ± 0.01 | 0.03 ± 0.01 | 0.03 ± 0.01 |
| Mammilothalamic Tract | 0.22 ± 0.01 | 0.22 ± 0.02 | 0.23 ± 0.02 |
| **Grey Matter** | | | |
| Lateral Septum | 2.80 ± 0.11 | 2.77 ± 0.12 | 3.04 ± 0.14 |
| Basal Forebrain | 3.92 ± 0.19 | 3.83 ± 0.21 | 4.21 ± 0.20 |
| Periaqueductal Grey | 3.61 ± 0.16 | 3.56 ± 0.26 | 3.86 ± 0.11 |
| Hippocampus | 19.0 ± 1.1 | 19.1 ± 1.2 | 20.3 ± 0.6 |
| Cerebral Peduncle | 1.88 ± 0.09 | 1.87 ± 0.10 | 2.03 ± 0.15 |
| Amygdala | 11.4 ± 0.6 | 11.4 ± 0.8 | 12.0 ± 0.5 |
| Dentate Gyrus of Hippocampus | 3.34 ± 0.21 | 3.38 ± 0.19 | 3.53 ± 0.13 |
| Medial Septum | 0.92 ± 0.07 | 0.86 ± 0.06 | 0.93 ± 0.07 |
| Stratum Granulosum of Hippocampus | 0.81 ± 0.05 | 0.83 ± 0.05 | 0.86 ± 0.02 |
| Nucleus Accumbens | 3.26 ± 0.19 | 3.22 ± 0.16 | 3.38 ± 0.18 |
| Hypothalamus | 9.15 ± 0.49 | 9.01 ± 0.34 | 9.53 ± 0.79 |
| Fundus of Striatum | 0.12 ± 0.02 | 0.11 ± 0.02 | 0.12 ± 0.02 |
| Thalamus | 15.6 ± 0.7 | 15.4 ± 0.6 | 15.8 ± 0.4 |
| Pre-Para Subiculum | 2.16 ± 0.12 | 2.12 ± 0.13 | 2.17 ± 0.07 |
| Globus Pallidus | 2.39 ± 0.19 | 2.31 ± 0.12 | 2.38 ± 0.14 |
| Bed Nucleus of Stria Terminalis | 1.19 ± 0.07 | 1.16 ± 0.07 | 1.21 ± 0.08 |
| Striatum | 17.7 ± 0.9 | 17.7 ± 0.8 | 18.1 ± 0.8 |
| Mammillary Bodies | 0.46 ± 0.04 | 0.45 ± 0.03 | 0.47 ± 0.04 |

**Supplementary Table S2.** (Continued) Volumes of brain structures corrected for body weight, at peak clinical EAE disease.

| Anatomical Region | Volume, mean ± SD $mm^3$ | | |
|---|---|---|---|
| | Naïve | CFA | EAE |
| **Ventricles** | | | |
| Lateral Ventricle | 3.35 ± 0.18 | 3.43 ± 0.17 | 3.84 ± 0.29 |
| Cerebral Aqueduct | 0.43 ± 0.04 | 0.47 ± 0.04 | 0.52 ± 0.03 |
| Third Ventricle | 0.98 ± 0.06 | 1.02 ± 0.06 | 1.11 ± 0.08 |
| Fourth Ventricle | 0.47 ± 0.04 | 0.40 ± 0.04 | 0.51 ± 0.06 |
| **Cerebral Cortex** | | | |
| Entorhinal Cortex | 10.4 ± 0.5 | 10.6 ± 0.4 | 10.8 ± 0.2 |
| Parieto-Temporal Lobe | 71.5 ± 2.8 | 71.0 ± 3.6 | 72.4 ± 2.0 |
| Occipital Lobe | 6.02 ± 0.33 | 5.84 ± 0.36 | 5.90 ± 0.18 |
| Frontal Lobe | 39.1 ± 1.3 | 39.1 ± 1.6 | 39.2 ± 0.8 |
| **Brainstem** | | | |
| Pons | 14.1 ± 0.9 | 13.8 ± 0.5 | 15 ± 0.6 |
| Superior Olivary Complex | 0.55 ± 0.08 | 0.56 ± 0.05 | 0.62 ± 0.03 |
| Corticospinal Tract/Pyramids | 1.11 ± 0.07 | 1.18 ± 0.10 | 1.28 ± 0.10 |
| Medulla | 21.8 ± 1.7 | 21.7 ± 1.1 | 23.7 ± 1.8 |
| Pontine Nucleus | 0.59 ± 0.05 | 0.61 ± 0.04 | 0.66 ± 0.05 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | 2.04 ± 0.15 | 2.04 ± 0.12 | 2.19 ± 0.13 |
| Midbrain | 11.5 ± 0.8 | 11.4 ± 0.4 | 12 ± 0.2 |
| Colliculus: Superior | 7.77 ± 0.35 | 7.62 ± 0.38 | 7.99 ± 0.19 |
| Ventral Tegmental Decussation | 0.11 ± 0.01 | 0.09 ± 0.01 | 0.11 ± 0.01 |
| Inferior Olivary Complex | 0.25 ± 0.03 | 0.27 ± 0.03 | 0.29 ± 0.02 |
| Cuneate Nucleus | 0.26 ± 0.03 | 0.25 ± 0.02 | 0.28 ± 0.03 |
| Colliculus: Inferior | 5.23 ± 0.25 | 5.20 ± 0.23 | 5.40 ± 0.16 |
| Interpeduncular Nucleus | 0.23 ± 0.03 | 0.23 ± 0.02 | 0.25 ± 0.03 |
| Facial Nerve (Cranial Nerve 7) | 0.21 ± 0.02 | 0.20 ± 0.01 | 0.21 ± 0.03 |
| **Cerebellum** | | | |
| Arbor Vita of Cerebellum | 8.76 ± 0.62 | 8.49 ± 0.40 | 9.22 ± 0.31 |
| Cerebellar Peduncle: Inferior | 0.66 ± 0.06 | 0.68 ± 0.05 | 0.75 ± 0.06 |
| Cerebellar Peduncle: Middle | 0.98 ± 0.06 | 0.99 ± 0.05 | 1.06 ± 0.06 |
| Cerebellar Cortex | 45.0 ± 2.6 | 45.1 ± 2.1 | 46.9 ± 1.1 |
| Cerebellar Peduncle: Superior | 0.93 ± 0.04 | 0.86 ± 0.04 | 0.92 ± 0.03 |
| **Olfactory** | | | |
| Lateral Olfactory Tract | 1.15 ± 0.05 | 1.14 ± 0.04 | 1.21 ± 0.03 |
| Olfactory Tubercle | 3.20 ± 0.23 | 3.04 ± 0.17 | 3.33 ± 0.12 |
| Olfactory Bulbs | 21.0 ± 1.1 | 21.3 ± 1.0 | 21.5 ± 1.1 |
| Subependymale Zone / Rhinocele | 0.06 ± 0.01 | 0.06 ± 0.01 | 0.06 ± 0.01 |

**Supplementary Table S2.** (Continued) Volumes of brain structures corrected for body weight, at peak clinical EAE disease.

| Cumulative Anatomical Region | Volume, mean ± SD $mm^3$ | | |
|---|---|---|---|
| | Naïve | CFA | EAE |
| Ventricles | 5.22 ± 0.28 | 5.32 ± 0.23 | 5.98 ± 0.37 |
| Cerebral White | 29.3 ± 1.2 | 29.1 ± 1.3 | 30.9± 0.9 |
| Brain Stem | 69.3 ± 4.4 | 68.7 ± 2.8 | 73.7 ± 1.4 |
| Cerebellum Total | 56.3 ± 3.4 | 56.2 ± 2.5 | 58.8 ± 1.4 |
| Total Brain Volume | 407 ± 18 | 405 ± 15 | 422 ± 9 |
| Cerebral Grey | 221 ± 9 | 220 ± 9 | 226 ± 5 |
| Olfactory | 25.4 ± 1.1 | 25.6 ± 1.1 | 26.1 ± 1.2 |
| Cerebral Cortex | 127 ± 5 | 127 ± 5 | 128 ± 3 |

*Volumes mean ± standard deviation corrected for body weight using an ANCOVA analysis.*

**Supplementary Table S3.** Comparing the uncorrected volumes of Naïve, CFA, and EAE mice at peak clinical disease.

| Anatomical Region | % Difference in Between Groups | | | | | |
|---|---|---|---|---|---|---|
| | Naïve vs. CFA | *q-value* | Naïve vs. EAE | *q-value* | CFA vs. EAE | *q-value* |
| **White Matter** | | | | | | |
| Fimbria | -1.6 | 0.680 | 9.3 | 0.008 | 11.1 | 0.009 |
| Corpus Callosum | -1.0 | 0.779 | 5.1 | 0.031 | 6.1 | 0.010 |
| Cerebral Peduncle | 0.6 | 0.884 | 8.6 | 0.027 | 7.9 | 0.078 |
| Posterior Commissure | -2.3 | 0.779 | 14.4 | 0.036 | 17.1 | 0.039 |
| Fornix | 1.7 | 0.761 | 9.2 | 0.029 | 7.4 | 0.128 |
| Stria Medullaris | 2.4 | 0.667 | 7.0 | 0.025 | 4.4 | 0.220 |
| Optic Tract | 1.3 | 0.763 | 5.6 | 0.044 | 4.3 | 0.193 |
| Fasciculus Retroflexus | 5.0 | 0.208 | 6.6 | 0.076 | 1.6 | 0.750 |
| Anterior Commissure: Pars Anterior | 2.7 | 0.259 | 4.1 | 0.088 | 1.3 | 0.721 |
| Internal Capsule | 4.0 | 0.342 | 6.5 | 0.079 | 2.3 | 0.673 |
| Anterior Commissure: Pars Posterior | 7.1 | 0.268 | 6.9 | 0.185 | -0.2 | 0.994 |
| Stria Terminalis | 4.9 | 0.207 | 3.1 | 0.265 | -1.7 | 0.729 |
| Habenular Commissure | -7.8 | 0.440 | 2.6 | 0.861 | 11.3 | 0.375 |
| Mammilothalamic Tract | -1.0 | 0.876 | 1.9 | 0.761 | 2.9 | 0.685 |
| **Grey Matter** | | | | | | |
| Lateral Septum | 0.5 | 0.888 | 9.9 | 0.003 | 9.3 | 0.011 |
| Basal Forebrain | 2.6 | 0.401 | 10.1 | 0.005 | 7.3 | 0.036 |
| Periaqueductal Grey | 0.4 | 0.949 | 8.6 | 0.012 | 8.1 | 0.006 |
| Hippocampus | -1.3 | 0.779 | 6.6 | 0.024 | 8.0 | 0.008 |
| Amygdala | -0.1 | 0.995 | 5.8 | 0.055 | 5.9 | 0.055 |
| Dentate Gyrus of Hippocampus | -1.8 | 0.686 | 4.5 | 0.081 | 6.4 | 0.040 |
| Medial Septum | 7.2 | 0.159 | 8.1 | 0.055 | 0.9 | 0.891 |
| Stratum Granulosum of Hippocampus | -3.7 | 0.310 | 3.1 | 0.292 | 7.1 | 0.054 |
| Nucleus Accumbens | 1.9 | 0.679 | 5.0 | 0.080 | 3.1 | 0.357 |
| Hypothalamus | 2.0 | 0.425 | 5.7 | 0.117 | 3.6 | 0.405 |
| Fundus of Striatum | 8.1 | 0.407 | 13.3 | 0.194 | 4.9 | 0.763 |
| Thalamus | 0.9 | 0.780 | 2.4 | 0.137 | 1.5 | 0.426 |
| Pre-Para Subiculum | 1.3 | 0.783 | 2.8 | 0.267 | 1.5 | 0.473 |
| Globus Pallidus | 4.1 | 0.316 | 3.2 | 0.269 | -0.9 | 0.885 |
| Bed Nucleus of Stria Terminalis | 2.9 | 0.410 | 3.7 | 0.265 | 0.8 | 0.887 |
| Striatum | -0.3 | 0.950 | 2.1 | 0.352 | 2.4 | 0.364 |
| Mammillary Bodies | 1.2 | 0.872 | 3.6 | 0.396 | 2.4 | 0.762 |

**Supplementary Table S3.** (Continued) Comparing the uncorrected volumes of Naïve, CFA, and EAE mice at peak clinical disease.

| Anatomical Region | % Difference in Between Groups | | | | | |
|---|---|---|---|---|---|---|
| | Naïve vs. CFA | *q-value* | Naïve vs. EAE | *q-value* | CFA vs. EAE | *q-value* |
| **Ventricles** | | | | | | |
| Cerebral Aqueduct | -10.5 | 0.053 | 9.0 | 0.043 | 21.9 | 0.006 |
| Lateral Ventricle | -3.4 | 0.270 | 12.0 | 0.008 | 15.9 | 0.008 |
| Third Ventricle | -4.3 | 0.216 | 9.9 | 0.017 | 14.8 | 0.010 |
| Fourth Ventricle | 17.9 | 0.023 | 27.5 | 0.004 | 8.1 | 0.250 |
| **Cerebral Cortex** | | | | | | |
| Entorhinal Cortex | -2.9 | 0.270 | 1.5 | 0.352 | 4.6 | 0.043 |
| Parieto-Temporal Lobe | 0.0 | 0.999 | 2.2 | 0.296 | 2.2 | 0.259 |
| Occipital Lobe | 2.3 | 0.474 | 1.1 | 0.742 | -1.1 | 0.745 |
| Frontal Lobe | -0.4 | 0.891 | 0.1 | 0.954 | 0.6 | 0.781 |
| **Brain Stem** | | | | | | |
| Pons | 1.7 | 0.690 | 8.1 | 0.004 | 6.3 | 0.076 |
| Superior Olivary Complex | -2.2 | 0.779 | 11.0 | 0.011 | 13.5 | 0.030 |
| Corticospinal Tract/Pyramids | -5.6 | 0.227 | 8.1 | 0.078 | 14.5 | 0.013 |
| Colliculus: Superior | 1.1 | 0.781 | 5.0 | 0.026 | 3.9 | 0.067 |
| Pontine Nucleus | -4.2 | 0.341 | 7.3 | 0.078 | 12.0 | 0.037 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | 0.1 | 0.996 | 7.5 | 0.034 | 7.4 | 0.079 |
| Cuneate Nucleus | -3.3 | 0.476 | 10.1 | 0.081 | 13.9 | 0.075 |
| Ventral Tegmental Decussation | 20.0 | 0.044 | 14.1 | 0.044 | -4.9 | 0.353 |
| Medulla | 0.8 | 0.886 | 9.1 | 0.027 | 8.3 | 0.109 |
| Midbrain | 0.3 | 0.946 | 5.2 | 0.010 | 4.9 | 0.101 |
| Inferior Olivary Complex | -7.8 | 0.312 | 7.4 | 0.181 | 16.4 | 0.024 |
| Colliculus: Inferior | 0.0 | 1.000 | 3.8 | 0.069 | 3.8 | 0.110 |
| Interpeduncular Nucleus | -0.7 | 0.949 | 6.1 | 0.213 | 6.8 | 0.320 |
| Facial Nerve (Cranial Nerve 7) | 3.2 | 0.502 | 5.1 | 0.353 | 1.9 | 0.870 |
| **Cerebellum** | | | | | | |
| Arbor Vita of Cerebellum | 2.5 | 0.397 | 8.6 | 0.004 | 6.0 | 0.036 |
| Cerebellar Peduncle: Inferior | -3.2 | 0.423 | 10.7 | 0.024 | 14.4 | 0.013 |
| Cerebellar Peduncle: Middle | -0.5 | 0.914 | 7.6 | 0.025 | 8.1 | 0.054 |
| Cerebellar Cortex | -1.1 | 0.778 | 3.9 | 0.055 | 5.0 | 0.036 |
| Cerebellar Peduncle: Superior | 7.4 | 0.036 | 6.8 | 0.011 | -0.6 | 0.872 |
| **Olfactory** | | | | | | |
| Lateral Olfactory Tract | 0.8 | 0.780 | 6.0 | 0.005 | 5.2 | 0.021 |
| Olfactory Tubercle | 4.8 | 0.236 | 9.7 | 0.004 | 4.7 | 0.159 |
| Olfactory Bulbs | -1.0 | 0.780 | 0.8 | 0.800 | 1.9 | 0.473 |
| Subependymale Zone / Rhinocele | 3.2 | 0.774 | 4.2 | 0.456 | 0.9 | 0.948 |

**Supplementary Table S3.** (Continued) Comparing the uncorrected volumes of Naïve, CFA, and EAE mice at peak clinical disease.

| Anatomical Region | % Difference in Between Groups | | | | | |
|---|---|---|---|---|---|---|
| | Naïve vs. CFA | *q-value* | Naïve vs. EAE | *q-value* | CFA vs. EAE | *q-value* |
| Ventricles | -2.6 | 0.342 | 12.5 | 0.004 | 15.5 | 0.004 |
| Cerebral White | 0.1 | 0.992 | 5.9 | 0.012 | 5.8 | 0.024 |
| Brain Stem | 0.6 | 0.884 | 7.3 | 0.006 | 6.6 | 0.043 |
| Cerebellum Total | -0.4 | 0.917 | 4.8 | 0.025 | 5.3 | 0.033 |
| Total Brain Volume | 3.7E-03 | 0.998 | 4.2 | 0.024 | 4.2 | 0.044 |
| Cerebral Grey | -7.0E-03 | 0.999 | 2.8 | 0.096 | 2.8 | 0.111 |
| Olfactory | -0.2 | 0.954 | 2.1 | 0.343 | 2.4 | 0.356 |
| Cerebral Cortex | -0.3 | 0.949 | 1.4 | 0.376 | 1.7 | 0.271 |

*% volume difference compares average volume between groups (positive indicates increase in size, negative indicates decrease in size). q-values (significance = <0.1) represent FDR-adjusted p-values*.

**Supplementary Table S4.** Comparing volumes, corrected for body weight, of Naïve, CFA, and EAE mice at peak clinical disease.

| Anatomical Region | % Difference in Between Groups | | | | | |
|---|---|---|---|---|---|---|
| | Naïve vs. CFA | *q-value* | Naïve vs. EAE | *q-value* | CFA vs. EAE | *q-value* |
| **White Matter** | | | | | | |
| Fimbria | 0.5 | 0.882 | 9.7 | 0.002 | 9.2 | 0.003 |
| Corpus Callosum | 0.5 | 0.871 | 5.5 | 0.024 | 5.0 | 0.031 |
| Cerebral Peduncle | -0.4 | 0.936 | 8.2 | 0.024 | 8.6 | 0.048 |
| Posterior Commissure | 1.2 | 0.896 | 15.7 | 0.029 | 14.3 | 0.038 |
| Fornix | -1.5 | 0.798 | 7.6 | 0.030 | 9.3 | 0.093 |
| Stria Medullaris | -2.9 | 0.388 | 3.8 | 0.038 | 6.9 | 0.275 |
| Optic Tract | -1.3 | 0.756 | 4.2 | 0.048 | 5.6 | 0.188 |
| Fasciculus Retroflexus | -5.1 | 0.192 | 1.1 | 0.062 | 6.6 | 0.815 |
| Anterior Commissure: Pars Anterior | -2.6 | 0.319 | 1.4 | 0.081 | 4.1 | 0.696 |
| Internal Capsule | -3.9 | 0.343 | 2.3 | 0.086 | 6.5 | 0.676 |
| Anterior Commissure: Pars Posterior | -7.0 | 0.249 | -0.7 | 0.215 | 6.8 | 0.920 |
| Stria Terminalis | -4.7 | 0.193 | -1.7 | 0.306 | 3.1 | 0.723 |
| Habenular Commissure | 8.0 | 0.488 | 10.7 | 0.854 | 2.6 | 0.389 |
| Mammilothalamic Tract | -3.6 | 0.798 | 0.3 | 0.730 | 4.1 | 0.417 |
| **Grey Matter** | | | | | | |
| Basal Forebrain | -2.4 | 0.418 | 7.4 | 0.003 | 10.1 | 0.035 |
| Lateral Septum | -1.1 | 0.780 | 8.7 | 0.002 | 9.8 | 0.008 |
| Periaqueductal Grey | -1.3 | 0.737 | 7.0 | 0.004 | 8.5 | 0.029 |
| Hippocampus | 0.4 | 0.900 | 6.9 | 0.012 | 6.5 | 0.021 |
| Amygdala | -0.8 | 0.843 | 4.8 | 0.041 | 5.7 | 0.118 |
| Dentate Gyrus of Hippocampus | 1.2 | 0.760 | 5.6 | 0.080 | 4.4 | 0.063 |
| Medial Septum | -6.1 | 0.194 | 1.6 | 0.059 | 8.2 | 0.791 |
| Stratum Granulosum of Hippocampus | 3.1 | 0.356 | 6.3 | 0.283 | 3.0 | 0.080 |
| Nucleus Accumbens | -1.5 | 0.752 | 3.5 | 0.084 | 5.1 | 0.287 |
| Hypothalamus | -1.5 | 0.779 | 4.2 | 0.098 | 5.8 | 0.289 |
| Fundus of Striatum | -8.3 | 0.413 | 3.8 | 0.194 | 13.2 | 0.792 |
| Thalamus | -1.1 | 0.717 | 1.3 | 0.195 | 2.4 | 0.486 |
| Pre-Para Subiculum | -1.9 | 0.460 | 0.8 | 0.262 | 2.7 | 0.820 |
| Globus Pallidus | -3.5 | 0.345 | -0.3 | 0.314 | 3.3 | 0.939 |
| Bed Nucleus of Stria Terminalis | -2.4 | 0.487 | 1.3 | 0.263 | 3.8 | 0.794 |
| Striatum | 0.2 | 0.938 | 2.3 | 0.365 | 2.1 | 0.389 |
| Mammillary Bodies | -0.9 | 0.895 | 2.7 | 0.394 | 3.6 | 0.721 |

**Supplementary Table S4.** (Continued) Comparing volumes, corrected for body weight, of Naïve, CFA, and EAE mice at peak clinical disease.

| Anatomical Region | % Difference in Between Groups | | | | | |
|---|---|---|---|---|---|---|
| | Naïve vs. CFA | *q-value* | Naïve vs. EAE | *q-value* | CFA vs. EAE | *q-value* |
| **Ventricles** | | | | | | |
| Lateral Ventricle | 2.5 | 0.467 | 14.6 | 0.003 | 11.9 | 0.002 |
| Cerebral Aqueduct | 10.5 | 0.048 | 20.4 | 0.033 | 8.9 | 0.003 |
| Third Ventricle | 4.1 | 0.328 | 14.3 | 0.014 | 9.8 | 0.005 |
| Fourth Ventricle | -14.2 | 0.042 | 9.4 | 0.002 | 27.6 | 0.152 |
| **Cerebral Cortex** | | | | | | |
| Entorhinal Cortex | 2.5 | 0.247 | 4.0 | 0.388 | 1.4 | 0.073 |
| Parieto-Temporal Lobe | -0.7 | 0.789 | 1.3 | 0.250 | 2.1 | 0.475 |
| Occipital Lobe | -3.0 | 0.269 | -2.0 | 0.749 | 1.0 | 0.419 |
| Frontal Lobe | 1.7 | 0.924 | 3.7 | 0.950 | 2.0 | 0.897 |
| **Brain Stem** | | | | | | |
| Pons | -1.8 | 0.655 | 6.1 | 0.009 | 8.1 | 0.055 |
| Superior Olivary Complex | 2.6 | 0.730 | 14.0 | 0.029 | 11.0 | 0.025 |
| Corticospinal Tract/Pyramids | 6.0 | 0.250 | 14.6 | 0.060 | 8.1 | 0.014 |
| Medulla | -0.7 | 0.897 | 8.4 | 0.030 | 9.2 | 0.072 |
| Pontine Nucleus | 4.4 | 0.364 | 12.0 | 0.081 | 7.3 | 0.030 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | -0.1 | 0.981 | 7.4 | 0.038 | 7.5 | 0.070 |
| Midbrain | -0.7 | 0.845 | 4.5 | 0.033 | 5.2 | 0.092 |
| Colliculus: Superior | -2.0 | 0.309 | 2.9 | 0.012 | 4.9 | 0.149 |
| Ventral Tegmental Decussation | -16.8 | 0.026 | -5.0 | 0.047 | 14.1 | 0.406 |
| Inferior Olivary Complex | 8.1 | 0.267 | 16.0 | 0.198 | 7.3 | 0.039 |
| Cuneate Nucleus | -2.0 | 0.755 | 8.0 | 0.078 | 10.2 | 0.059 |
| Colliculus: Inferior | -0.5 | 0.873 | 3.2 | 0.073 | 3.7 | 0.188 |
| Interpeduncular Nucleus | 0.6 | 0.940 | 6.7 | 0.275 | 6.1 | 0.306 |
| Facial Nerve (Cranial Nerve 7) | -3.0 | 0.752 | 2.0 | 0.366 | 5.2 | 0.814 |
| **Cerebellum** | | | | | | |
| Arbor Vita of Cerebellum | -3.0 | 0.246 | 5.3 | 0.002 | 8.6 | 0.048 |
| Cerebellar Peduncle: Inferior | 3.2 | 0.468 | 14.2 | 0.021 | 10.7 | 0.013 |
| Cerebellar Peduncle: Middle | 0.6 | 0.896 | 8.2 | 0.030 | 7.6 | 0.041 |
| Cerebellar Cortex | 0.3 | 0.899 | 4.1 | 0.043 | 3.8 | 0.058 |
| Cerebellar Peduncle: Superior | -7.8 | 0.003 | -1.6 | 0.004 | 6.6 | 0.388 |
| **Olfactory** | | | | | | |
| Lateral Olfactory Tract | -0.8 | 0.758 | 5.1 | 0.004 | 6.0 | 0.025 |
| Olfactory Tubercle | -5.0 | 0.136 | 4.2 | 0.005 | 9.6 | 0.198 |
| Olfactory Bulbs | 1.5 | 0.724 | 2.4 | 0.784 | 0.9 | 0.388 |
| Subependymale Zone / Rhinocele | -3.6 | 0.798 | 0.3 | 0.730 | 4.1 | 0.417 |

**Supplementary Table S4.** (Continued) Comparing volumes, corrected for body weight, of Naïve, CFA, and EAE mice at peak clinical disease.

| Anatomical Region | % Difference in Between Groups | | | | | |
|---|---|---|---|---|---|---|
| | Naïve vs. CFA | *q-value* | Naïve vs. EAE | *q-value* | CFA vs. EAE | *q-value* |
| Ventricles | -0.3 | 0.671 | 1.1 | 0.002 | 1.4 | 0.003 |
| Cerebral White | -0.3 | 0.870 | 4.4 | 0.034 | 4.7 | 0.011 |
| Brain Stem | -0.4 | 0.815 | 3.7 | 0.038 | 4.1 | 0.011 |
| Cerebellum Total | -0.4 | 0.901 | 2.3 | 0.046 | 2.8 | 0.019 |
| Total Brain Volume | -0.5 | 0.875 | 5.3 | 0.072 | 5.9 | 0.029 |
| Cerebral Grey | 1.9 | 0.869 | 14.6 | 0.235 | 12.4 | 0.098 |
| Olfactory | 0.5 | 0.875 | 2.7 | 0.302 | 2.2 | 0.322 |
| Cerebral Cortex | -0.9 | 0.898 | 6.3 | 0.662 | 7.3 | 0.363 |

*% volume difference compares average volume between groups (positive indicates increase in size, negative indicates decrease in size). q-values (significance = <0.1) represent FDR-adjusted p-values*.

**Supplementary Table S5.** Uncorrected volumes of brain structures at long-term EAE disease duration.

| | Volume, mean ± SD $mm^3$ | | | |
|---|---|---|---|---|
| Anatomical Regions | Naïve | CFA | Low Score EAE | High Score EAE |
| **White Matter** | | | | |
| Corpus Callosum | 17.4 ± 0.5 | 17.5 ± 0.6 | 17.4 ± 0.5 | 16.1 ± 0.9 |
| Stria Terminalis | 0.82 ± 0.05 | 0.85 ± 0.03 | 0.83 ± 0.06 | 0.77 ± 0.05 |
| Optic Tract | 1.48 ± 0.04 | 1.51 ± 0.06 | 1.46 ± 0.06 | 1.40 ± 0.07 |
| Anterior Commissure: Pars Anterior | 1.28 ± 0.06 | 1.28 ± 0.06 | 1.27 ± 0.08 | 1.21 ± 0.05 |
| Internal Capsule | 2.43 ± 0.12 | 2.45 ± 0.11 | 2.38 ± 0.20 | 2.28 ± 0.15 |
| Stria Medullaris | 0.72 ± 0.04 | 0.70 ± 0.04 | 0.71 ± 0.05 | 0.67 ± 0.04 |
| Fasciculus Retroflexus | 0.24 ± 0.02 | 0.25 ± 0.02 | 0.25 ± 0.01 | 0.23 ± 0.02 |
| Fimbria | 3.13 ± 0.18 | 3.18 ± 0.16 | 3.22 ± 0.10 | 3.05 ± 0.21 |
| Anterior Commissure: Pars Posterior | 0.41 ± 0.04 | 0.40 ± 0.03 | 0.39 ± 0.04 | 0.37 ± 0.04 |
| Fornix | 0.63 ± 0.03 | 0.63 ± 0.02 | 0.62 ± 0.04 | 0.61 ± 0.03 |
| Habenular Commissure | 0.03 ± 0.01 | 0.03 ± 0.01 | 0.03 ± 0.01 | 0.03 ± 0.01 |
| Posterior Commissure | 0.12 ± 0.01 | 0.12 ± 0.01 | 0.13 ± 0.01 | 0.12 ± 0.02 |
| Mammilothalamic Tract | 0.23 ± 0.01 | 0.23 ± 0.01 | 0.23 ± 0.01 | 0.23 ± 0.01 |
| Cerebral Peduncle | 2.03 ± 0.09 | 2.02 ± 0.09 | 2.03 ± 0.07 | 2.00 ± 0.14 |
| **Grey Matter** | | | | |
| Striatum | 18.5 ± 0.7 | 18.4 ± 0.6 | 18.4 ± 0.6 | 17.2 ± 0.8 |
| Thalamus | 16.1 ± 0.7 | 16.3 ± 0.3 | 16.3 ± 0.5 | 15.4 ± 0.5 |
| Pre-Para Subiculum | 2.26 ± 0.11 | 2.23 ± 0.10 | 2.20 ± 0.09 | 2.07 ± 0.11 |
| Periaqueductal Grey | 3.68 ± 0.25 | 3.82 ± 0.16 | 3.74 ± 0.09 | 3.48 ± 0.24 |
| Nucleus Accumbens | 3.47 ± 0.17 | 3.44 ± 0.16 | 3.42 ± 0.14 | 3.23 ± 0.14 |
| Bed Nucleus of Stria Terminalis | 1.27 ± 0.05 | 1.25 ± 0.05 | 1.24 ± 0.06 | 1.17 ± 0.06 |
| Hippocampus | 19.9 ± 1.0 | 20.2 ± 1.0 | 20.1 ± 0.5 | 19.0 ± 0.9 |
| Dentate Gyrus of Hippocampus | 3.57 ± 0.18 | 3.60 ± 0.20 | 3.55 ± 0.09 | 3.37 ± 0.17 |
| Basal Forebrain | 4.22 ± 0.21 | 4.14 ± 0.18 | 4.16 ± 0.17 | 3.97 ± 0.16 |
| Medial Septum | 1.00 ± 0.09 | 0.97 ± 0.07 | 0.97 ± 0.06 | 0.92 ± 0.05 |
| Stratum Granulosum of Hippocampus | 0.84 ± 0.04 | 0.88 ± 0.07 | 0.85 ± 0.04 | 0.82 ± 0.06 |
| Hypothalamus | 10.0 ± 0.4 | 9.83 ± 0.40 | 9.71 ± 0.47 | 9.44 ± 0.52 |
| Amygdala | 12.2 ± 0.5 | 12.4 ± 1.0 | 12.2 ± 0.4 | 11.8 ± 0.7 |
| Lateral Septum | 3.13 ± 0.20 | 3.09 ± 0.18 | 3.02 ± 0.14 | 3.02 ± 0.22 |
| Globus Pallidus | 2.52 ± 0.13 | 2.50 ± 0.13 | 2.46 ± 0.18 | 2.39 ± 0.17 |
| Mammillary Bodies | 0.50 ± 0.05 | 0.50 ± 0.03 | 0.50 ± 0.05 | 0.50 ± 0.04 |
| Fundus of Striatum | 0.14 ± 0.03 | 0.14 ± 0.05 | 0.13 ± 0.03 | 0.13 ± 0.02 |

**Supplementary Table S5.** (Continued) Uncorrected volumes of brain structures at long-term EAE disease duration.

| Anatomical Regions | Volume, mean ± SD $mm^3$ | | | |
|---|---|---|---|---|
| | Naïve | CFA | Low Score EAE | High Score EAE |
| **Ventricles** | | | | |
| Cerebral Aqueduct | 0.46 ± 0.06 | 0.50 ± 0.05 | 0.47 ± 0.04 | 0.44 ± 0.05 |
| Third Ventricle | 1.12 ± 0.08 | 1.13 ± 0.10 | 1.07 ± 0.07 | 1.07 ± 0.10 |
| Fourth Ventricle | 0.42 ± 0.07 | 0.40 ± 0.05 | 0.45 ± 0.04 | 0.45 ± 0.09 |
| Lateral Ventricle | 3.77 ± 0.26 | 3.71 ± 0.19 | 3.75 ± 0.20 | 3.69 ± 0.37 |
| **Cerebral Cortex** | | | | |
| Parieto-Temporal Lobe | 72.5 ± 2.3 | 72.4 ± 2.7 | 72.2 ± 2.2 | 66.8 ± 3.9 |
| Frontal Lobe | 40.6 ± 1.6 | 40.4 ± 1.2 | 40.0 ± 1.2 | 37.8 ± 1.8 |
| Entorhinal Cortex | 10.9 ± 0.4 | 11.0 ± 0.5 | 11.00 ± 0.5 | 10.1 ± 0.6 |
| Occipital Lobe | 6.09 ± 0.28 | 6.07 ± 0.24 | 5.93 ± 0.21 | 5.55 ± 0.34 |
| **Brain Stem** | | | | |
| Colliculus: Inferior | 5.33 ± 0.29 | 5.37 ± 0.23 | 5.22 ± 0.12 | 4.84 ± 0.31 |
| Colliculus: Superior | 7.91 ± 0.49 | 7.94 ± 0.30 | 7.83 ± 0.22 | 7.21 ± 0.37 |
| Midbrain | 11.9 ± 0.7 | 12.1 ± 0.4 | 12.2 ± 0.5 | 11.5 ± 0.6 |
| Ventral Tegmental Decussation | 0.11 ± 0.01 | 0.11 ± 0.01 | 0.10 ± 0.01 | 0.10 ± 0.01 |
| Inferior Olivary Complex | 0.30 ± 0.05 | 0.28 ± 0.05 | 0.28 ± 0.03 | 0.29 ± 0.04 |
| Facial Nerve (Cranial Nerve 7) | 0.21 ± 0.3 | 0.21 ± 0.2 | 0.21 ± 0.2 | 0.22 ± 0.2 |
| Corticospinal Tract/Pyramids | 1.21 ± 0.20 | 1.16 ± 0.18 | 1.24 ± 0.14 | 1.25 ± 0.15 |
| Pontine Nucleus | 0.66 ± 0.07 | 0.64 ± 0.04 | 0.65 ± 0.06 | 0.65 ± 0.07 |
| Superior Olivary Complex | 0.62 ± 0.08 | 0.62 ± 0.05 | 0.60 ± 0.05 | 0.61 ± 0.06 |
| Pons | 14.5 ± 1.0 | 14.5 ± 0.5 | 14.7 ± 0.5 | 14.3 ± 0.9 |
| Medulla | 22.6 ± 1.8 | 22.0 ± 2.0 | 22.8 ±1.1 | 22.9 ± 2.1 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | 2.2 ± 0.19 | 2.2 ± 0.17 | 2.2 ± 0.13 | 2.2 ± 0.17 |
| Interpeduncular Nucleus | 0.25 ± 0.03 | 0.26 ± 0.02 | 0.26 ± 0.02 | 0.25 ± 0.02 |
| Cuneate Nucleus | 0.26 ± 0.03 | 0.26 ± 0.03 | 0.26 ± 0.03 | 0.25 ± 0.04 |
| **Cerebellum** | | | | |
| Arbor Vita of Cerebellum | 8.90 ± 0.29 | 9.00 ± 0.41 | 8.81 ± 0.29 | 8.16 ± 0.27 |
| Cerebellar Cortex | 45.0 ± 2.1 | 45.7 ± 2.3 | 45.3 ± 1.6 | 42.4 ± 2.3 |
| Cerebellar Peduncle: Inferior | 0.73 ± 0.04 | 0.71 ± 0.06 | 0.75 ± 0.03 | 0.72 ± 0.05 |
| Cerebellar Peduncle: Middle | 1.08 ± 0.07 | 1.06 ± 0.06 | 1.06 ± 0.05 | 1.03 ± 0.08 |
| Cerebellar Peduncle: Superior | 0.90 ± 0.07 | 0.90 ± 0.04 | 0.91 ± 0.07 | 0.90 ± 0.06 |
| **Olfactory** | | | | |
| Olfactory Tubercle | 3.33 ± 0.20 | 3.38 ± 0.22 | 3.37 ± 0.24 | 3.16 ± 0.17 |
| Lateral Olfactory Tract | 1.24 ± 0.08 | 1.26 ± 0.06 | 1.24 ± 0.06 | 1.18 ± 0.07 |
| Subependymale Zone / Rhinocele | 0.06 ± 0.01 | 0.06 ± 0.01 | 0.06 ± 0.01 | 0.06 ± 0.01 |
| Olfactory Bulbs | 24.4 ± 2.5 | 23.2 ± 2.1 | 22.7 ± 1.3 | 22.7 ± 1.2 |

**Supplementary Table S5.** (Continued) Uncorrected volumes of brain structures at long-term EAE disease duration.

| | Volume, mean ± SD $mm^3$ | | | |
|---|---|---|---|---|
| Summed Regions | Naïve | CFA | Low Score EAE | High Score EAE |
| Cerebral Cortex | 130 ± 4 | 130 ± 4 | 129 ± 4 | 120 ± 6 |
| Cerebral Grey | 229 ± 8 | 230 ± 7 | 228 ± 6 | 215 ± 10 |
| Total Brain Volume | 427 ± 15 | 423 ± 13 | 422 ± 9 | 399 ± 16 |
| Cerebral White | 30.6 ± 0.8 | 31.1 ± 0.8 | 30.9 ± 0.9 | 29.1 ± 1.3 |
| Cerebellum | 57.2 ± 2.4 | 57.0 ± 3.2 | 56.8 ± 1.9 | 53.2 ± 2.7 |
| Olfactory | 29.0 ± 2.6 | 27.9 ± 2.1 | 27.4 ± 1.4 | 27.1 ± 1.3 |
| Brain Stem | 71.5 ± 3.9 | 71.4 ± 3.1 | 72.3 ± 1.8 | 70.1 ± 3.8 |
| Ventricles | 5.80 ± 0.33 | 5.74 ± 0.30 | 5.74 ± 0.20 | 5.65 ± 0.43 |

*Volumes mean ± standard deviation. EAE mice divided into above (High Score) and below (Low Score) average cumulative long-term disease scores.*

**Supplementary Table S6.** Volumes of brain structures corrected for body weight at long-term EAE disease duration.

| | Volume, mean ± SD $mm^3$ | | | |
|---|---|---|---|---|
| Anatomical Regions | Naïve | CFA | Low Score EAE | High Score EAE |
| **White Matter** | | | | |
| Corpus Callosum | 17.3 ± 0.61 | 17.5 ± 0.50 | 17.3 ± 0.48 | 16.2 ± 0.88 |
| Stria Terminalis | 0.81 ± 0.03 | 0.85 ± 0.05 | 0.82 ± 0.06 | 0.77 ± 0.05 |
| Optic Tract | 1.47 ± 0.06 | 1.51 ± 0.04 | 1.46 ± 0.06 | 1.40 ± 0.07 |
| Anterior Commissure: Pars Anterior | 1.28 ± 0.06 | 1.28 ± 0.06 | 1.27 ± 0.08 | 1.21 ± 0.05 |
| Internal Capsule | 2.43 ± 0.11 | 2.45 ± 0.12 | 2.38 ± 0.20 | 2.30 ± 0.15 |
| Stria Medullaris | 0.72 ± 0.04 | 0.70 ± 0.04 | 0.71 ± 0.05 | 0.67 ± 0.04 |
| Fasciculus Retroflexus | 0.24 ± 0.02 | 0.25 ± 0.02 | 0.25 ± 0.01 | 0.23 ± 0.02 |
| Fimbria | 3.12 ± 0.16 | 3.18 ± 0.18 | 3.20 ± 0.10 | 3.07 ± 0.21 |
| Anterior Commissure: Pars Posterior | 0.41 ± 0.03 | 0.39 ± 0.04 | 0.39 ± 0.04 | 0.37 ± 0.04 |
| Fornix | 0.63 ± 0.02 | 0.63 ± 0.03 | 0.62 ± 0.04 | 0.61 ± 0.03 |
| Habenular Commissure | 0.03 ± 0.01 | 0.03 ± 0.01 | 0.03 ± 0.01 | 0.03 ± 0.01 |
| Posterior Commissure | 0.12 ± 0.01 | 0.12 ± 0.01 | 0.13 ± 0.01 | 0.12 ± 0.02 |
| Mammilothalamic Tract | 0.23 ± 0.01 | 0.23 ± 0.01 | 0.23 ± 0.01 | 0.23 ± 0.01 |
| Cerebral Peduncle | 2.03 ± 0.09 | 2.02 ± 0.09 | 2.02 ± 0.07 | 2.00 ± 0.14 |
| **Grey Matter** | | | | |
| Striatum | 18.5 ± 0.55 | 18.4 ± 0.74 | 18.5 ± 0.62 | 17.2 ± 0.76 |
| Thalamus | 16.1 ± 0.27 | 16.3 ± 0.71 | 16.2 ± 0.47 | 15.4 ± 0.51 |
| Pre-Para Subiculum | 2.26 ± 0.10 | 2.23 ± 0.11 | 2.21 ± 0.09 | 2.06 ± 0.11 |
| Periaqueductal Grey | 3.66 ± 0.16 | 3.82 ± 0.25 | 3.73 ± 0.09 | 3.49 ± 0.24 |
| Nucleus Accumbens | 3.47 ± 0.16 | 3.44 ± 0.17 | 3.42 ± 0.14 | 3.22 ± 0.14 |
| Hippocampus | 20.1 ± 1.02 | 20.2 ± 1.02 | 20.0 ± 0.54 | 19.0 ± 0.86 |
| Bed Nucleus of Stria Terminalis | 1.26 ± 0.05 | 1.25 ± 0.05 | 1.23 ± 0.06 | 1.17 ± 0.06 |
| Dentate Gyrus of Hippocampus | 3.56 ± 0.20 | 3.60 ± 0.18 | 3.55 ± 0.09 | 3.37 ± 0.17 |
| Basal Forebrain | 4.21 ± 0.18 | 4.14 ± 0.21 | 4.16 ± 0.17 | 3.96 ± 0.16 |
| Medial Septum | 1.00 ± 0.07 | 0.97 ± 0.09 | 0.97 ± 0.06 | 0.91 ± 0.05 |
| Stratum Granulosum of Hippocampus | 0.85 ± 0.07 | 0.88 ± 0.04 | 0.85 ± 0.04 | 0.82 ± 0.06 |
| Hypothalamus | 10.0 ± 0.40 | 9.83 ± 0.44 | 9.69 ± 0.47 | 9.45 ± 0.52 |
| Amygdala | 12.4 ± 1.04 | 12.4 ± 0.50 | 12.3 ± 0.42 | 11.9 ± 0.72 |
| Lateral Septum | 3.12 ± 0.18 | 3.09 ± 0.20 | 3.02 ± 0.14 | 3.03 ± 0.22 |
| Globus Pallidus | 2.51 ± 0.13 | 2.50 ± 0.13 | 2.46 ± 0.18 | 2.38 ± 0.17 |
| Mammillary Bodies | 0.51 ± 0.03 | 0.50 ± 0.05 | 0.50 ± 0.05 | 0.49 ± 0.04 |
| Fundus of Striatum | 0.13 ± 0.03 | 0.13 ± 0.05 | 0.13 ± 0.03 | 0.13 ± 0.02 |

**Supplementary Table S6.** (Continued) Volumes of brain structures corrected for body weight at long-term EAE disease duration.

| | Volume, mean ± SD $mm^3$ | | | |
|---|---|---|---|---|
| Anatomical Regions | Naïve | CFA | Low Score EAE | High Score EAE |
| **Ventricles** | | | | |
| Cerebral Aqueduct | 0.47 ± 0.05 | 0.50 ± 0.06 | 0.47 ± 0.04 | 0.44 ± 0.05 |
| Third Ventricle | 1.12 ± 0.10 | 1.13 ± 0.08 | 1.08 ± 0.07 | 1.06 ± 0.10 |
| Fourth Ventricle | 0.43 ± 0.05 | 0.40 ± 0.07 | 0.44 ± 0.04 | 0.46 ± 0.09 |
| Lateral Ventricle | 3.74 ± 0.19 | 3.70 ± 0.26 | 3.74 ± 0.20 | 3.72 ± 0.37 |
| **Cerebral Cortex** | | | | |
| Parieto-Temporal Lobe | 72.9 ± 2.7 | 72.3 ± 2.3 | 72.3 ± 2.2 | 66.6 ± 3.9 |
| Frontal Lobe | 40.9 ± 1.2 | 40.4 ± 1.6 | 40.1 ± 1.2 | 37.7 ± 1.8 |
| Entorhinal Cortex | 11.1 ± 0.5 | 11.0 ± 0.4 | 11.0 ± 0.5 | 10.1 ± 0.6 |
| Occipital Lobe | 6.07 ± 0.24 | 6.07 ± 0.28 | 5.94 ± 0.21 | 5.53 ± 0.34 |
| **Brain Stem** | | | | |
| Colliculus: Inferior | 5.32 ± 0.23 | 5.37 ± 0.29 | 5.24 ± 0.12 | 4.80 ± 0.31 |
| Colliculus: Superior | 7.88 ± 0.30 | 7.93 ± 0.49 | 7.82 ± 0.22 | 7.21 ± 0.37 |
| Midbrain | 12.1 ± 0.4 | 12.1 ± 0.7 | 12.1 ± 0.5 | 11.5 ± 0.6 |
| Ventral Tegmental Decussation | 0.11 ± 0.01 | 0.11 ± 0.01 | 0.10 ± 0.01 | 0.11 ± 0.01 |
| Inferior Olivary Complex | 0.29 ± 0.05 | 0.28 ± 0.05 | 0.28 ± 0.03 | 0.29 ± 0.04 |
| Facial Nerve (Cranial Nerve 7) | 0.21 ± 0.2 | 0.21 ± 0.3 | 0.21 ± 0.2 | 0.22 ± 0.2 |
| Corticospinal Tract/Pyramids | 1.20 ± 0.18 | 1.15 ± 0.20 | 1.23 ± 0.14 | 1.27 ± 0.15 |
| Pontine Nucleus | 0.67 ± 0.04 | 0.64 ± 0.07 | 0.64 ± 0.06 | 0.66 ± 0.07 |
| Superior Olivary Complex | 0.63 ± 0.05 | 0.62 ± 0.08 | 0.60 ± 0.05 | 0.62 ± 0.06 |
| Pons | 14.6 ± 0.5 | 14.5 ± 1.0 | 14.7 ± 0.5 | 14.4 ± 0.9 |
| Medulla | 22.6 ± 2.0 | 22.0 ± 1.8 | 22.8 ±1.1 | 23.0 ± 2.1 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | 2.15 ± 0.17 | 2.23 ± 0.19 | 2.19 ± 0.13 | 2.19 ± 0.17 |
| Interpeduncular Nucleus | 0.25 ± 0.02 | 0.26 ± 0.03 | 0.26 ± 0.02 | 0.25 ± 0.02 |
| Cuneate Nucleus | 0.26 ± 0.03 | 0.26 ± 0.03 | 0.26 ± 0.03 | 0.25 ± 0.04 |
| **Cerebellum** | | | | |
| Arbor Vita of Cerebellum | 8.89 ± 0.41 | 9.00 ± 0.29 | 8.79 ± 0.29 | 8.14 ± 0.27 |
| Cerebellar Cortex | 45.4 ± 2.3 | 45.7 ± 2.1 | 45.4 ± 1.6 | 42.2 ± 2.3 |
| Cerebellar Peduncle: Inferior | 0.73 ± 0.06 | 0.71 ± 0.04 | 0.75 ± 0.03 | 0.71 ± 0.05 |
| Cerebellar Peduncle: Middle | 1.07 ± 0.06 | 1.06 ± 0.07 | 1.06 ± 0.05 | 1.03 ± 0.08 |
| Cerebellar Peduncle: Superior | 0.90 ± 0.04 | 0.90 ± 0.07 | 0.91 ± 0.07 | 0.90 ± 0.06 |
| **Olfactory** | | | | |
| Olfactory Tubercle | 3.33 ± 0.22 | 3.38 ± 0.20 | 3.37 ± 0.24 | 3.15 ± 0.17 |
| Lateral Olfactory Tract | 1.26 ± 0.06 | 1.26 ± 0.08 | 1.24 ± 0.06 | 1.18 ± 0.07 |
| Subependymale Zone / Rhinocele | 0.06 ± 0.01 | 0.07 ± 0.01 | 0.06 ± 0.01 | 0.06 ± 0.01 |
| Olfactory Bulbs | 24.5 ± 2.09 | 23.2 ± 2.49 | 22.8 ± 1.27 | 22.8 ± 1.17 |

**Supplementary Table S6.** (Continued) Volumes of brain structures corrected for body weight at long-term EAE disease duration.

| | Volume, mean ± SD $mm^3$ | | | |
|---|---|---|---|---|
| Summed Regions | CFA | Naïve | Low Score EAE | High Score EAE |
| Cerebral Cortex | 130 ± 4 | 131 ± 4 | 129 ± 4 | 119 ± 6 |
| Cerebral Grey | 230 ± 7 | 231 ± 8 | 228 ± 6 | 214 ± 10 |
| Total Brain Volume | 423 ± 13 | 426 ± 15 | 421 ± 9 | 399 ± 16 |
| Cerebral White | 31.1 ± 0.8 | 30.8 ± 0.8 | 30.8 ± 0.9 | 29.1 ± 1.3 |
| Cerebellum | 56.9 ± 3.2 | 57.1 ± 2.4 | 56.9 ± 1.9 | 53.0 ± 2.7 |
| Olfactory | 27.9 ± 2.1 | 29.1 ± 2.6 | 27.4 ± 1.4 | 27.1 ± 1.3 |
| Brain Stem | 71.4 ± 3.1 | 72.0 ± 3.9 | 72.1 ± 1.8 | 70.2 ± 3.8 |
| Ventricles | 5.74 ± 0.30 | 5.76 ± 0.33 | 5.73 ± 0.20 | 5.68 ± 0.43 |

*Volumes mean ± standard deviation corrected for body weight using an ANCOVA analysis. EAE mice divided into above (High Score) and below (Low Score) average cumulative long-term disease scores.*

**Supplementary Table S7.** Comparing the uncorrected volumes of Naïve, CFA, and Low Score EAE mice to High Score EAE mice.

| Anatomical Region | % Difference in Volume Versus High Score EAE | | | | | |
|---|---|---|---|---|---|---|
| | Naïve | *q* | CFA | *q* | Low Score EAE | *q* |
| **White Matter** | | | | | | |
| Corpus Callosum | -7.8 | 0.001 | -8.4 | 1.2E-04 | -7.0 | 0.001 |
| Stria Terminalis | -6.0 | 0.095 | -9.7 | 0.001 | -6.1 | 0.039 |
| Optic Tract | -5.5 | 0.051 | -6.4 | 0.009 | -5.7 | 0.015 |
| Anterior Commissure: Pars Anterior | -7.9 | 0.014 | -7.7 | 0.006 | -4.0 | 0.181 |
| Internal Capsule | -7.5 | 0.058 | -8.1 | 0.014 | -4.0 | 0.288 |
| Stria Medullaris | -8.2 | 0.031 | -5.8 | 0.106 | -5.0 | 0.153 |
| Fasciculus Retroflexus | -5.9 | 0.195 | -7.1 | 0.053 | -6.0 | 0.093 |
| Fimbria | -3.6 | 0.402 | -5.0 | 0.113 | -4.5 | 0.134 |
| Anterior Commissure: Pars Posterior | -10.4 | 0.086 | -6.7 | 0.261 | -5.6 | 0.342 |
| Fornix | -3.4 | 0.336 | -4.1 | 0.134 | -1.0 | 0.829 |
| Habenular Commissure | 6.7 | 0.811 | -10.6 | 0.442 | -2.5 | 0.906 |
| Posterior Commissure | -3.1 | 0.835 | -3.9 | 0.733 | -7.7 | 0.262 |
| Mammilothalamic Tract | -3.2 | 0.338 | -2.3 | 0.454 | -0.5 | 0.906 |
| Cerebral Peduncle | -2.3 | 0.988 | -1.9 | 0.918 | -0.5 | 0.994 |
| **Grey Matter** | | | | | | |
| Striatum | -7.9 | 4.2E-04 | -7.4 | 2.0E-04 | -6.5 | 4.4E-04 |
| Thalamus | -5.0 | 0.009 | -6.0 | 3.5E-04 | -5.1 | 0.001 |
| Pre-Para Subiculum | -8.7 | 0.002 | -7.5 | 0.002 | -6.9 | 0.003 |
| Periaqueductal Grey | -5.5 | 0.118 | -8.9 | 0.001 | -7.2 | 0.006 |
| Nucleus Accumbens | -8.5 | 0.001 | -7.4 | 0.001 | -5.4 | 0.015 |
| Bed Nucleus of Stria Terminalis | -8.8 | 0.001 | -7.4 | 0.002 | -4.5 | 0.061 |
| Hippocampus | -6.5 | 0.014 | -6.2 | 0.007 | -5.8 | 0.008 |
| Dentate Gyrus of Hippocampus | -6.1 | 0.035 | -6.8 | 0.006 | -5.8 | 0.014 |
| Basal Forebrain | -6.6 | 0.012 | -4.9 | 0.038 | -4.8 | 0.032 |
| Medial Septum | -10.5 | 0.009 | -6.8 | 0.071 | -5.1 | 0.182 |
| Stratum Granulosum of Hippocampus | -5.2 | 0.297 | -8.1 | 0.025 | -4.1 | 0.330 |
| Hypothalamus | -6.3 | 0.035 | -4.6 | 0.093 | -2.3 | 0.474 |
| Amygdala | -6.3 | 0.101 | -5.8 | 0.081 | -4.4 | 0.197 |
| Lateral Septum | -5.6 | 0.149 | -4.2 | 0.248 | 1.2 | 0.839 |
| Globus Pallidus | -5.5 | 0.196 | -4.8 | 0.201 | -3.7 | 0.329 |
| Mammillary Bodies | -4.5 | 0.549 | -3.1 | 0.717 | -3.3 | 0.603 |
| Fundus of Striatum | 0.5 | 0.990 | 0.7 | 0.988 | -7.9 | 0.599 |

**Supplementary Table S7.** (Continued) Comparing the uncorrected volumes of Naïve, CFA, and Low Score EAE mice to High Score EAE mice.

| Anatomical Region | % Difference in Volume Versus High Score EAE | | | | | |
|---|---|---|---|---|---|---|
| | Naïve | *q* | CFA | *q* | Low Score EAE | *q* |
| **Ventricles** | | | | | | |
| Cerebral Aqueduct | -5.9 | 0.468 | -11.2 | 0.033 | -6.9 | 0.232 |
| Third Ventricle | -6.2 | 0.286 | -6.7 | 0.161 | -1.7 | 0.836 |
| Fourth Ventricle | 5.3 | 0.751 | 11.9 | 0.234 | 4.6 | 0.739 |
| Lateral Ventricle | -3.1 | 0.644 | -1.3 | 0.870 | -1.4 | 0.833 |
| **Cerebral Cortex** | | | | | | |
| Parieto-Temporal Lobe | -9.4 | 1.13E-04 | -8.3 | 1.17E-04 | -8.6 | 5.36E-05 |
| Frontal Lobe | -8.3 | 1.77E-04 | -6.9 | 3.49E-04 | -6.4 | 4.50E-04 |
| Entorhinal Cortex | -9.7 | 4.07E-04 | -8.2 | 0.001 | -8.5 | 2.12E-04 |
| Occipital Lobe | -9.4 | 0.001 | -9.1 | 1.83E-04 | -7.6 | 0.001 |
| **Brain Stem** | | | | | | |
| Colliculus: Inferior | -8.2 | 1.16E-03 | -9.2 | 9.64E-05 | -9.6 | 2.66E-05 |
| Colliculus: Superior | -8.2 | 1.29E-03 | -8.6 | 1.89E-04 | -9.0 | 7.50E-05 |
| Midbrain | -4.7 | 0.095 | -5.3 | 0.022 | -4.7 | 0.035 |
| Ventral Tegmental Decussation | -7.8 | 0.195 | -3.9 | 0.572 | 2.9 | 0.741 |
| Inferior Olivary Complex | -4.7 | 0.777 | -0.1 | 1.000 | 1.5 | 0.918 |
| Facial Nerve (Cranial Nerve 7) | 3.7 | 0.721 | 6.6 | 0.296 | 3.7 | 0.598 |
| Corticospinal Tract/Pyramids | 3.6 | 0.823 | 8.2 | 0.401 | 2.4 | 0.854 |
| Pontine Nucleus | -2.4 | 0.823 | 2.9 | 0.751 | 0.7 | 0.934 |
| Superior Olivary Complex | -3.3 | 0.751 | -1.3 | 0.897 | 2.9 | 0.734 |
| Pons | -2.5 | 0.591 | -1.6 | 0.750 | -1.9 | 0.612 |
| Medulla | 0.2 | 0.988 | 3.4 | 0.602 | 0.2 | 0.992 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | -1.5 | 0.868 | 1.8 | 0.816 | 0.02 | 1.000 |
| Interpeduncular Nucleus | -3.2 | 0.762 | -3.8 | 0.602 | -0.6 | 0.944 |
| Cuneate Nucleus | 0.3 | 0.995 | -1.4 | 0.918 | -2.0 | 0.876 |
| **Cerebellum** | | | | | | |
| Arbor Vita of Cerebellum | -8.6 | 2.19E-04 | -9.6 | 2.02E-05 | -7.6 | 1.08E-04 |
| Cerebellar Cortex | -7.5 | 0.006 | -7.9 | 0.001 | -7.5 | 0.001 |
| CBL Peduncle: Inferior | -2.0 | 0.789 | 1.5 | 0.829 | -6.0 | 0.072 |
| CBL Peduncle: Middle | -5.4 | 0.221 | -4.1 | 0.317 | -2.6 | 0.585 |
| CBL Peduncle: Superior | -1.7 | 0.836 | -1.4 | 0.840 | -0.8 | 0.899 |
| **Olfactory** | | | | | | |
| Olfactory Tubercle | -7.0 | 0.075 | -8.3 | 0.011 | -5.9 | 0.069 |
| Lateral Olfactory Tract | -7.3 | 0.021 | -8.2 | 0.002 | -4.1 | 0.155 |
| Subependymale Zone / Rhinocele | -11.7 | 0.080 | -12.6 | 0.024 | 2.8 | 0.804 |
| Olfactory Bulbs | -6.7 | 0.287 | -1.45 | 0.700 | 0.9 | 0.953 |

**Supplementary Table S7.** (Continued) Comparing the uncorrected volumes of Naïve, CFA, and Low Score EAE mice to High Score EAE mice.

| Summed Regions | % Difference in Volume Versus High Score EAE | | | | | |
|---|---|---|---|---|---|---|
| | Naïve | *q* | CFA | *q* | Low Score EAE | *q* |
| Cerebral Cortex | -9.1 | 8.2E-05 | -7.9 | 9.0E-05 | -7.9 | 4.9E-05 |
| Cerebral Grey | -8.0 | 1.1E-04 | -7.2 | 1.1E-04 | -6.6 | 1.1E-04 |
| Total Brain Volume | -7.1 | 2.4E-04 | -6.1 | 2.8E-04 | -5.8 | 2.7E-04 |
| Cerebral White | -6.6 | 0.001 | -7.3 | 1.00E-04 | -5.6 | 0.001 |
| Cerebellum | -7.5 | 0.006 | -7.2 | 0.002 | -7.3 | 0.001 |
| Olfactory | -6.5 | 0.237 | -2.3 | 0.342 | -0.1 | 0.842 |
| Brain Stem | -3.1 | 0.369 | -2.1 | 0.548 | -3.1 | 0.238 |
| Ventricles | -3.3 | 0.496 | -2.3 | 0.623 | -1.5 | 0.795 |

*% volume difference compares average volume between High Score EAE and other groups (positive indicates increase in size, negative indicates decrease in size). No significant differences in volume were detected between Naïve, CFA, and low score EAE groups. q-values (significance = <0.1) represent FDR-adjusted p-values.*

**Supplementary Table S8.** Comparing the volumes, corrected for body weight, of Naïve, CFA, and Low Score EAE mice to High Score EAE mice.

| Anatomical Region | % Difference in Volume Versus High Score EAE | | | | | |
|---|---|---|---|---|---|---|
| | Naïve | *q* | CFA | *q* | Low Score EAE | *q* |
| **White Matter** | | | | | | |
| Corpus Callosum | -7.5 | 0.003 | -6.5 | 9.5E-05 | -6.7 | 3.5E-04 |
| Stria Terminalis | -9.2 | 0.074 | -5.2 | 0.001 | -6.2 | 0.029 |
| Optic Tract | -7.0 | 0.062 | -5.0 | 0.001 | -4.3 | 0.059 |
| Internal Capsule | -7.1 | 0.107 | -6.3 | 0.023 | -4.4 | 0.230 |
| Anterior Commissure: Pars Anterior | -6.0 | 0.099 | -5.8 | 0.033 | -4.7 | 0.128 |
| Fasciculus Retroflexus | -5.8 | 0.369 | -4.1 | 0.089 | -5.6 | 0.104 |
| Stria Medullaris | -4.2 | 0.092 | -6.1 | 0.222 | -4.6 | 0.164 |
| Fimbria | -3.6 | 0.539 | -1.7 | 0.223 | -4.2 | 0.140 |
| Anterior Commissure: Pars Posterior | -5.6 | 0.123 | -8.7 | 0.310 | -4.7 | 0.436 |
| Habenular Commissure | -11.1 | 0.755 | 5.6 | 0.359 | -3.1 | 0.777 |
| Fornix | -3.4 | 0.481 | -2.6 | 0.213 | -1.7 | 0.630 |
| Posterior Commissure | -3.2 | 0.794 | -1.7 | 0.709 | -6.5 | 0.359 |
| Mammilothalamic Tract | -0.8 | 0.694 | -1.5 | 0.763 | -1.7 | 0.619 |
| Cerebral Peduncle | -1.1 | 0.731 | -1.5 | 0.758 | -1.1 | 0.752 |
| **Grey Matter** | | | | | | |
| Striatum | -6.6 | 0.001 | -6.7 | 1.3E-04 | -6.2 | 2.7E-04 |
| Thalamus | -5.3 | 0.020 | -4.1 | 2.6E-04 | -4.8 | 0.001 |
| Pre-Para Subiculum | -7.6 | 0.001 | -8.7 | 0.001 | -6.5 | 0.004 |
| Periaqueductal Grey | -8.6 | 0.132 | -4.8 | 4.0E-04 | -6.4 | 0.010 |
| Nucleus Accumbens | -6.2 | 0.004 | -7.2 | 0.004 | -5.9 | 0.007 |
| Hippocampus | -5.6 | 0.016 | -5.4 | 0.003 | -4.9 | 0.011 |
| Bed Nucleus of Stria Terminalis | -6.0 | 0.006 | -7.1 | 0.008 | -4.9 | 0.038 |
| Dentate Gyrus of Hippocampus | -6.3 | 0.043 | -5.2 | 0.003 | -5.0 | 0.023 |
| Basal Forebrain | -4.4 | 0.016 | -5.9 | 0.047 | -4.8 | 0.028 |
| Medial Septum | -5.4 | 0.025 | -9.0 | 0.180 | -6.1 | 0.112 |
| Hypothalamus | -4.0 | 0.050 | -5.6 | 0.122 | -2.6 | 0.394 |
| Stratum Granulosum of Hippocampus | -6.4 | 0.630 | -2.7 | 0.051 | -3.6 | 0.369 |
| Amygdala | -4.9 | 0.179 | -5.1 | 0.115 | -4.1 | 0.220 |
| Globus Pallidus | -4.6 | 0.210 | -5.1 | 0.180 | -3.2 | 0.411 |
| Lateral Septum | -1.8 | 0.570 | -2.8 | 0.686 | 0.5 | 0.947 |
| Mammillary Bodies | -3.1 | 0.529 | -4.3 | 0.630 | -2.5 | 0.695 |
| Lateral Ventricle | 0.4 | 0.966 | -0.5 | 0.966 | -0.6 | 0.949 |

**Supplementary Table S8.** (Continued) Comparing the volumes, corrected for body weight, of Naïve, CFA, and Low Score EAE mice to High Score EAE mice.

| Anatomical Region | % Difference in Volume Versus High Score EAE | | | | | |
|---|---|---|---|---|---|---|
| | Naïve | *q* | CFA | *q* | Low Score EAE | *q* |
| **Ventricles** | | | | | | |
| Cerebral Aqueduct | -11.7 | 0.386 | -6.2 | 0.012 | -5.6 | 0.366 |
| Third Ventricle | -5.8 | 0.387 | -5.0 | 0.197 | -1.3 | 0.773 |
| Fourth Ventricle | 13.2 | 0.618 | 6.5 | 0.139 | 3.8 | 0.737 |
| Lateral Ventricle | 0.4 | 0.966 | -0.5 | 0.966 | -0.6 | 0.949 |
| **Cerebral Cortex** | | | | | | |
| Parieto-Temporal Lobe | -8.0 | 4.9E-05 | -8.7 | 3.0E-05 | -7.9 | 3.3E-05 |
| Frontal Lobe | -6.8 | 9.7E-05 | -8.0 | 1.3E-04 | -6.0 | 0.001 |
| Entorhinal Cortex | -7.5 | 2.5E-04 | -8.5 | 2.2E-04 | -7.7 | 1.5E-04 |
| Occipital Lobe | -8.8 | 2.5E-04 | -8.8 | 5.3E-05 | -6.8 | 0.001 |
| **Brain Stem** | | | | | | |
| Colliculus: Inferior | -10.5 | 1.2E-04 | -9.7 | 1.7E-05 | -8.3 | 1.4E-04 |
| Colliculus: Superior | -9.1 | 2.5E-04 | -8.5 | 2.5E-05 | -7.8 | 1.4E-04 |
| Midbrain | -4.4 | 0.037 | -4.9 | 0.028 | -4.8 | 0.015 |
| Ventral Tegmental Decussation | -2.0 | 0.360 | -5.9 | 0.756 | 1.2 | 0.792 |
| Corticospinal Tract/Pyramids | 9.7 | 0.629 | 5.7 | 0.241 | 2.8 | 0.752 |
| Facial Nerve (Cranial Nerve 7) | 6.5 | 0.653 | 3.7 | 0.250 | 3.8 | 0.573 |
| Medulla | 4.2 | 0.777 | 1.4 | 0.419 | 0.8 | 0.943 |
| Pontine Nucleus | 3.0 | 0.760 | -1.8 | 0.660 | 2.0 | 0.747 |
| Superior Olivary Complex | -0.2 | 0.763 | -1.9 | 0.996 | 2.6 | 0.710 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | 2.3 | 0.946 | -0.7 | 0.685 | 0.7 | 0.808 |
| Pons | -0.9 | 0.712 | -1.6 | 0.762 | -1.8 | 0.626 |
| Inferior Olivary Complex | 2.8 | 0.978 | -0.8 | 0.762 | 2.6 | 0.763 |
| Interpeduncular Nucleus | -2.3 | 0.771 | -1.8 | 0.734 | -2.4 | 0.734 |
| Cuneate Nucleus | -3.6 | 0.773 | -2.5 | 0.707 | -1.2 | 0.946 |
| **Cerebellum** | | | | | | |
| Arbor Vita of Cerebellum | -9.6 | 1.0E-04 | -8.5 | 8.9E-06 | -7.4 | 9.3E-05 |
| Cerebellar Cortex | -7.7 | 0.005 | -7.0 | 4.7E-04 | -7.0 | 0.001 |
| CBL Peduncle: Inferior | 0.8 | 0.645 | -2.5 | 0.796 | -5.0 | 0.146 |
| CBL Peduncle: Middle | -2.8 | 0.406 | -3.8 | 0.509 | -2.8 | 0.516 |
| CBL Peduncle: Superior | -0.5 | 0.958 | -0.6 | 0.953 | -1.0 | 0.775 |
| **Olfactory** | | | | | | |
| Olfactory Tubercle | -6.9 | 0.186 | -5.4 | 0.028 | -6.6 | 0.038 |
| Lateral Olfactory Tract | -6.0 | 0.205 | -4.7 | 0.029 | -4.9 | 0.107 |
| Subependymale Zone / Rhinocele | -9.0 | 0.321 | -7.8 | 0.138 | -0.7 | 0.974 |
| Olfactory Bulbs | -2.2 | 0.102 | -7.3 | 0.693 | -0.3 | 0.975 |

**Supplementary Table S8.** (Continued) Comparing the volumes, corrected for body weight, of Naïve, CFA, and Low Score EAE mice to High Score EAE mice.

| Summed Regions | % Difference in Volume Versus High Score EAE | | | | | |
|---|---|---|---|---|---|---|
| | Naïve | *q* | CFA | *q* | Low Score EAE | *q* |
| Cerebral Cortex | -7.6 | 2.2E-05 | -8.5 | 3.0E-05 | -7.3 | 3.2E-05 |
| Cerebral Grey | -6.6 | 2.8E-05 | -7.2 | 8.8E-05 | -6.1 | 9.1E-05 |
| Total Brain Volume | -5.7 | 1.2E-04 | -6.3 | 1.7E-04 | -5.4 | 2.2E-04 |
| Cerebral White | -6.3 | 1.1E-04 | -5.3 | 0.004 | -5.4 | 0.001 |
| Cerebellum Total | -6.9 | 0.001 | -7.1 | 0.004 | -6.9 | 0.001 |
| Olfactory | -2.9 | 0.499 | -6.9 | 0.070 | -1.3 | 0.756 |
| Brain Stem | -1.6 | 0.616 | -2.3 | 0.485 | -2.6 | 0.325 |
| Ventricles | -0.9 | 0.763 | -1.3 | 0.754 | -0.8 | 0.773 |

*% volume difference compares average volume between High Score EAE and other groups (positive indicates increase in size, negative indicates decrease in size). No significant differences in volume were detected between Naïve, CFA, and low score EAE groups. q-values (significance = <0.1) represent FDR-adjusted p-values.*

**Supplementary Table S9.** Comparing the relative changes in volume from peak clinical (days 14-16) to long-term (66+) disease duration of Naïve, CFA, to EAE mice.

| Anatomical Region | Percent change in volume; peak to long-term mean ± SD % | | | Post-hoc *q* values | | |
|---|---|---|---|---|---|---|
| | Naïve | CFA | EAE | Naïve vs. CFA | Naïve vs. EAE | CFA vs. EAE |
| **White Matter** | | | | | | |
| Fimbria | 4.7 ± 5.51 | 3.29 ± 3.78 | -4.22 ± 5.80 | 0.721 | 0.007 | 0.029 |
| Corpus Callosum | 4.0 ± 4.07 | 4.25 ± 4.09 | -2.88 ± 5.66 | 0.987 | 0.016 | 0.025 |
| Optic Tract | 5.8 ± 2.67 | 7.36 ± 4.41 | -0.61 ± 7.19 | 0.687 | 0.038 | 0.024 |
| Cerebral Peduncle | -8.5 ± 5.22 | 6.48 ± 6.28 | 0.09 ± 6.50 | 0.631 | 0.016 | 0.096 |
| Stria Medullaris | 10.5 ± 9.61 | -1.66 ± 5.96 | -1.89 ± 7.96 | 0.026 | 0.010 | 1.000 |
| Fornix | 7.48 ± 8.09 | 0.59 ± 6.47 | -4.16 ± 8.62 | 0.174 | 0.010 | 0.328 |
| Anterior Commissure: Pars Anterior | 7.45 ± 6.00 | 2.27 ± 3.67 | -1.41 ± 6.45 | 0.202 | 0.015 | 0.268 |
| Fasciculus Retroflexus | 6.91 ± 7.81 | 0.89 ± 5.64 | -2.54 ± 6.72 | 0.096 | 0.037 | 0.064 |
| Internal Capsule | -9.47 ± 8.89 | -4.55 ± 8.92 | -1.97 ± 9.93 | 1 | 0.032 | 0.424 |
| Anterior Commissure: Pars Posterior | 14.63 ± 13.31 | -2.09 ± 11.17 | 0.65 ± 15.96 | 0.471 | 0.177 | 0.499 |
| Stria Terminalis | 6.29 ± 6.62 | 5.99 ± 6.55 | 0.49 ± 6.35 | 0.268 | 0.205 | 0.834 |
| Habenular Commissure | -2.60 ± 31.27 | 26.74 ± 40.56 | -3.66 ± 24.81 | 0.735 | 0.230 | 0.169 |
| Posterior Commissure | 7.28 ± 12.85 | 2.56 ± 9.87 | -2.55 ± 20.66 | 0.706 | 0.013 | 0.343 |
| Mammilothalamic Tract | 5.63 ± 7.11 | 2.22 ± 5.61 | 3.07 ± 7.45 | 0.484 | 0.532 | 0.878 |
| **Grey Matter** | | | | | | |
| Hippocampus | 5.11 ± 2.36 | 3.11 ± 3.10 | -3.35 ± 3.14 | 0.282 | 3.76E-05 | 0.001 |
| Basal Forebrain | 10.00 ± 4.26 | 1.86 ± 4.32 | -3.93 ± 5.00 | 0.013 | 4.08E-05 | 0.049 |
| Lateral Septum | 12.95 ± 5.41 | 5.74 ± 1.13 | -2.08 ± 7.70 | 0.085 | 3.63E-04 | 0.047 |
| Periaqueductal Grey | 3.35 ± 7.95 | 3.73 ± 3.79 | -7.32 ± 5.86 | 0.976 | 0.006 | 0.010 |
| Dentate Gyrus of Hippocampus | 5.43 ± 1.62 | 3.17 ± 4.58 | -0.25 ± 4.39 | 0.328 | 0.006 | 0.114 |
| Nucleus Accumbens | 7.52 ± 4.51 | 2.77 ± 2.75 | -1.23 ± 5.94 | 0.156 | 0.004 | 0.205 |
| Amygdala | 8.95 ± 5.64 | 3.31 ± 3.07 | 0.69 ± 5.72 | 0.114 | 0.010 | 0.454 |
| Pre-Para Subiculum | 5.58 ± 3.58 | 1.49 ± 2.64 | -0.71 ± 5.28 | 0.127 | 0.010 | 0.427 |
| Medial Septum | 16.55 ± 13.22 | 4.43 ± 4.93 | 2.36 ± 9.70 | 0.304 | 0.016 | 0.471 |
| Bed Nucleus of Stria Terminalis | 8.76 ± 6.36 | -2.48 ± 5.80 | -0.72 ± 7.34 | 0.084 | 0.019 | 0.13 |
| Thalamus | 4.14 ± 3.29 | 2.96 ± 3.30 | -0.02 ± 3.50 | 0.169 | 0.022 | 0.784 |
| Hypothalamus | 10.79 ± 5.76 | 3.16 ± 4.02 | 1.85 ± 8.14 | 0.593 | 0.019 | 0.454 |
| Striatum | 4.00 ± 3.05 | 2.03 ± 3.25 | -0.49 ± 4.72 | 0.151 | 0.084 | 0.783 |
| Fundus of Striatum | 36.81 ± 55.29 | 15.48 ± 10.17 | 9.74 ± 28.78 | 0.992 | 0.115 | 0.319 |
| Globus Pallidus | 8.86 ± 8.64 | 4.90 ± 5.96 | 1.96 ± 8.89 | 0.785 | 0.157 | 0.513 |
| Stratum Granulosum of Hippocampus | 1.92 ± 6.39 | 2.92 ± 3.42 | -0.94 ± 6.19 | 0.706 | 0.691 | 0.454 |
| Mammillary Bodies | 10.56 ± 13.67 | 3.71 ± 2.98 | 5.93 ± 9.86 | 0.340 | 0.452 | 0.765 |

**Supplementary Table S9.** (Continued) Comparing the relative changes in volume from peak clinical (days 14-16) to long-term (66+) disease duration of Naïve, CFA, to EAE mice.

| Anatomical Region | Percent change in volume; peak to long-term mean ± SD % | | | Post-hoc *q* values | | |
|---|---|---|---|---|---|---|
| | Naïve | CFA | EAE | Naïve vs. CFA | Naïve vs. EAE | CFA vs. EAE |
| **Ventricles** | | | | | | |
| Cerebral Aqueduct | -1.39 ± 8.12 | 13.17 ± 8.00 | -11.08 ± 6.84 | 0.008 | 0.025 | 7.25E-05 |
| Lateral Ventricle | 8.48 ± 4.32 | 5.41 ± 5.50 | -3.95 ± 6.53 | 0.442 | 0.001 | 0.014 |
| Fourth Ventricle | 8.68 ± 22.04 | -17.92 ± 15.46 | -16.38 ± 9.78 | 0.018 | 0.010 | 0.918 |
| Third Ventricle | 10.40 ± 9.18 | 10.40 ± 6.12 | -0.22 ± 10.20 | 0.201 | 0.034 | 0.291 |
| **Cerebral Cortex** | | | | | | |
| Entorhinal Cortex | 3.51 ± 3.39 | 3.39 ± 2.50 | -1.19 ± 3.44 | 0.994 | 0.010 | 0.021 |
| Parieto-Temporal Lobe | 2.48 ± 1.90 | 0.83 ± 1.79 | -1.65 ± 3.75 | 0.392 | 0.013 | 0.343 |
| Occipital Lobe | 3.58 ± 4.44 | -1.02 ± 1.94 | 0.68 ± 4.08 | 0.084 | 0.068 | 0.694 |
| Frontal Lobe | 3.16 ± 3.55 | 2.48 ± 1.82 | 1.47 ± 3.14 | 0.600 | 0.23 | 0.543 |
| **Brain Stem** | | | | | | |
| Cuneate Nucleus | 2.58 ± 12.03 | 10.21 ± 14.32 | -13.6 ± 9.93 | 0.339 | 0.017 | 0.004 |
| Midbrain | 4.98 ± 4.27 | 2.00 ± 4.53 | -2.57 ± 4.05 | 0.290 | 0.004 | 0.047 |
| Colliculus: Superior | 3.23 ± 6.57 | 3.26 ± 5.18 | -4.89 ± 4.78 | 1.000 | 0.011 | 0.021 |
| Colliculus: Inferior | 1.65 ± 6.58 | 3.90 ± 3.42 | -5.04 ± 5.74 | 0.576 | 0.037 | 0.017 |
| Ventral Tegmental Decussation | 22.57 ± 21.14 | -11.89 ± 10.69 | -6.71 ± 13.53 | 0.004 | 0.004 | 0.632 |
| Pons | 5.60 ± 5.50 | 0.83 ± 3.72 | -3.64 ± 5.27 | 0.165 | 0.004 | 0.170 |
| Medulla | 4.72 ± 8.02 | -0.53 ± 6.28 | -4.54 ± 7.71 | 0.455 | 0.038 | 0.784 |
| Superior Olivary Complex | 12.44 ± 13.36 | 1.37 ± 11.07 | -0.78 ± 9.83 | 0.314 | 0.042 | 0.319 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | 8.53 ± 9.07 | 2.63 ± 5.28 | 0.51 ± 7.57 | 0.076 | 0.115 | 0.187 |
| Interpeduncular Nucleus | 7.79 ± 13.63 | 11.03 ± 22.47 | -2.83 ± 12.81 | 0.165 | 0.138 | 0.595 |
| Inferior Olivary Complex | 12.85 ± 19.34 | 7.33 ± 9.67 | 0.96 ± 12.34 | 0.488 | 0.206 | 0.606 |
| Facial Nerve (Cranial Nerve 7) | -5.52 ± 14.11 | -3.76 ± 11.18 | 2.44 ± 12.44 | 0.828 | 0.294 | 0.63 |
| Pontine Nucleus | 8.33 ± 14.87 | 4.87 ± 11.31 | 0.70 ± 11.31 | 0.286 | 0.294 | 0.646 |
| Corticospinal Tract/Pyramids | 2.62 ± 14.00 | 1.54 ± 10.63 | -1.38 ± 12.12 | 0.938 | 0.594 | 0.735 |
| **Cerebellum** | | | | | | |
| Arbor Vita of Cerebellum | 3.58 ± 4.36 | -0.21 ± 2.30 | -8.19 ± 3.20 | 0.111 | 3.59E-05 | 0.002 |
| Cerebellar Cortex | -0.17 ± 2.70 | -0.14 ± 2.60 | -6.13 ± 4.58 | 1.000 | 0.004 | 0.009 |
| CBL Peduncle: Inferior | 9.33 ± 8.19 | 8.21 ± 5.67 | -1.46 ± 6.93 | 0.826 | 0.008 | 0.025 |
| CBL Peduncle: Superior | 4.90 ± 7.31 | -5.40 ± 2.22 | -5.33 ± 6.69 | 0.015 | 0.006 | 1.000 |
| CBL Peduncle: Middle | 8.93 ± 5.72 | 4.58 ± 6.23 | 0.14 ± 7.23 | 0.631 | 0.018 | 0.779 |

**Supplementary Table S9.** (Continued) Comparing the relative changes in volume from peak clinical (days 14-16) to long-term (66+) disease duration of Naïve, CFA, to EAE mice.

| Anatomical Region | Percent change in volume; peak to long-term mean ± SD % | | | Post-hoc *q* values | | |
|---|---|---|---|---|---|---|
| | Naïve | CFA | EAE | Naïve vs. CFA | Naïve vs. EAE | CFA vs. EAE |
| **Olfactory** | | | | | | |
| Olfactory Tubercle | 9.48 ± 4.86 | 3.20 ± 9.74 | -4.96 ± 6.31 | 0.169 | 0.001 | 0.059 |
| Lateral Olfactory Tract | 7.39 ± 4.77 | 5.88 ± 5.01 | -1.08 ± 4.09 | 0.632 | 0.003 | 0.018 |
| Subependymale Zone / Rhinocele | 9.06 ± 12.28 | 5.47 ± 12.73 | -3.91 ± 17.57 | 0.419 | 0.991 | 0.126 |
| Olfactory Bulbs | 14.28 ± 12.08 | 11.61 ± 5.97 | 7.66 ± 9.13 | 0.607 | 0.396 | 0.306 |

**Supplementary Table S9.** (Continued) Comparing the relative changes in volume from peak clinical (days 14-16) to long-term (66+) disease duration of Naïve, CFA, to EAE mice.

| Anatomical Region | Percent change in volume; peak to long-term mean ± SD % | | | Post-hoc *q* values | | |
|---|---|---|---|---|---|---|
| | Naïve | CFA | EAE | Naïve vs. CFA | Naïve vs. EAE | CFA vs. EAE |
| Total Brain Volume | 4.60 ± 1.01 | 2.32 ± 1.22 | -1.90 ± 2.69 | 0.098 | 3.88E-05 | 0.004 |
| Ventricles | 7.91 ± 4.90 | 4.71 ± 4.54 | -5.04 ± 5.29 | 0.354 | 2.03E-04 | 0.006 |
| Cerebellum | 0.72 ± 2.17 | -0.06 ± 2.43 | -6.29 ± 4.06 | 0.712 | 3.87E-04 | 0.003 |
| Cerebral Grey | 4.43 ± 1.36 | 2.09 ± 1.72 | -0.69 ± 2.80 | 0.099 | 3.35E-04 | 0.038 |
| Brain Stem | 4.62 ± 3.80 | 1.39 ± 4.10 | -4.09 ± 3.74 | 0.208 | 0.001 | 0.026 |
| Cerebral White | 5.33 ± 2.11 | 4.08 ± 4.31 | -2.52 ± 4.52 | 0.650 | 0.002 | 0.011 |
| Cerebral Cortex | 2.94 ± 2.09 | 1.45 ± 1.19 | -0.56 ± 3.14 | 0.369 | 0.014 | 0.191 |
| Olfactory | 13.34 ± 9.83 | 10.12 ± 4.92 | 5.58 ± 8.08 | 0.586 | 0.095 | 0.401 |

*% change in volume compares average volumes at peak and long-term for each group (positive indicates increase in size, negative indicates decrease in size). q-values (significance = <0.1) represent FDR-adjusted p-values*.

**Supplementary Table S10.** Correlations of long-term brain regional volumes and cumulative behavior scores in EAE mice.

| Anatomical Regions | *q* | $R^2$ |
|---|---|---|
| CTX: Entorhinal Cortex | 3.5E-04 | 0.59 |
| CTX: Parieto-Temporal Lobe | 1.6E-04 | 0.57 |
| Colliculus: Superior | 0.001 | 0.50 |
| Cerebral Cortex: Frontal Lobe | 0.001 | 0.49 |
| Striatum | 0.001 | 0.48 |
| Hippocampus | 0.001 | 0.46 |
| Thalamus | 0.001 | 0.46 |
| Corpus Callosum | 0.001 | 0.45 |
| Arbor Vita of Cerebellum | 0.002 | 0.41 |
| Periaqueductal Grey | 0.003 | 0.39 |
| Dentate Gyrus of Hippocampus | 0.004 | 0.38 |
| Cerebellar Cortex | 0.004 | 0.38 |
| Cerebral Cortex: Occipital Lobe | 0.007 | 0.34 |
| Colliculus: Inferior | 0.008 | 0.33 |
| Bed Nucleus of Stria Terminalis | 0.008 | 0.33 |
| Pre-Para Subiculum | 0.009 | 0.32 |
| Olfactory Tubercle | 0.010 | 0.31 |
| Midbrain | 0.013 | 0.29 |
| Amygdala | 0.015 | 0.29 |
| Lateral Olfactory Tract | 0.016 | 0.28 |
| Basal Forebrain | 0.018 | 0.27 |
| Stria Medullaris | 0.018 | 0.27 |
| Nucleus Accumbens | 0.018 | 0.26 |
| Anterior Commissure: Pars Anterior | 0.020 | 0.26 |
| Fasciculus Retroflexus | 0.024 | 0.25 |
| Fimbria | 0.038 | 0.22 |
| Medial Septum | 0.113 | 0.18 |
| Cerebellar Peduncle: Inferior | 0.124 | 0.17 |
| Optic Tract | 0.130 | 0.16 |
| Stria Terminalis | 0.137 | 0.15 |
| Cerebral Aqueduct | 0.202 | 0.11 |
| Cerebellar Peduncle: Superior | 0.267 | 0.09 |
| Anterior Commissure: Pars Posterior | 0.293 | 0.08 |
| Internal Capsule | 0.338 | 0.07 |
| Stratum Granulosum of Hippocampus | 0.362 | 0.07 |
| Interpeduncular Nucleus | 0.356 | 0.07 |
| Cerebellar Peduncle: Middle | 0.366 | 0.06 |

**Supplementary Table S10.** Correlations of long-term brain regional volumes and cumulative behavior scores in EAE mice.

| Anatomical Regions | *q* | $R^2$ |
|---|---|---|
| Facial Nerve (Cranial Nerve 7) | 0.380 | 0.06 |
| Posterior Commissure | 0.408 | 0.05 |
| Corticospinal Tract/Pyramids | 0.519 | 0.04 |
| Pontine Nucleus | 0.520 | 0.04 |
| Pons | 0.525 | 0.04 |
| Hypothalamus | 0.536 | 0.03 |
| Lateral Ventricle | 0.541 | 0.03 |
| Subependymale Zone /Rhinocele | 0.566 | 0.03 |
| Medulla | 0.560 | 0.03 |
| Mammilothalamic Tract | 0.657 | 0.02 |
| Ventral Tegmental Decussation | 0.695 | 0.02 |
| Lateral Septum | 0.713 | 0.01 |
| Habenular Commissure | 0.744 | 0.01 |
| Fornix | 0.766 | 0.01 |
| Inferior Olivary Complex | 0.770 | 0.01 |
| Fundus of Striatum | 0.786 | 0.009 |
| Globus Pallidus | 0.805 | 0.008 |
| Superior Olivary Complex | 0.800 | 0.007 |
| Medial Lemniscus/Longitudinal Fasciculus | 0.827 | 0.006 |
| Mammillary Bodies | 0.860 | 0.005 |
| Olfactory Bulbs | 0.935 | 0.003 |
| Fourth Ventricle | 0.933 | 0.003 |
| Cerebral Peduncle | 0.959 | 0.002 |
| Third Ventricle | 0.962 | 0.002 |
| Cuneate Nucleus | 0.976 | 0.002 |

| Summed Regions | *q* | $R^2$ |
|---|---|---|
| Cerebral Cortex | 1.75E-04 | 0.59 |
| Cerebral Grey | 1.40E-04 | 0.57 |
| Total Brain Volume | 0.001 | 0.52 |
| Cerebral White | 0.002 | 0.41 |
| Cerebellum | 0.003 | 0.40 |
| Ventricles | 0.500 | 0.04 |
| Olfactory | 0.592 | 0.03 |
| Brain Stem | 0.637 | 0.06 |

*q values were corrected for multiple comparisons using the false discovery rate (FDR) method. A 10% threshold was used for significance. Regressions were controlled for bodyweight.

**Supplementary Table S11.** Correlations of relative change in brain volume from peak to long-term and cumulative behavior scores in EAE mice.

| Anatomical Regions | *q* | $R^2$ |
|---|---|---|
| Colliculus: Superior | 0.003 | 0.61 |
| Cerebral Cortex: Entorhinal Cortex | 0.006 | 0.55 |
| Cerebral Cortex: Parieto-Temporal Lobe | 0.007 | 0.54 |
| Cerebral Cortex: Occipital Lobe | 0.012 | 0.48 |
| Mammilothalamic Tract | 0.026 | 0.40 |
| Corpus Callosum | 0.028 | 0.40 |
| Cerebral Peduncle | 0.030 | 0.39 |
| Periaqueductal Grey | 0.031 | 0.39 |
| Dentate Gyrus of Hippocampus | 0.031 | 0.39 |
| Hippocampus | 0.036 | 0.37 |
| Globus Pallidus | 0.048 | 0.34 |
| Facial Nerve (Cranial Nerve 7) | 0.049 | 0.33 |
| Medial Lemniscus/Medial Longitudinal Fasciculus | 0.051 | 0.33 |
| Medulla | 0.068 | 0.30 |
| Fourth Ventricle | 0.106 | 0.24 |
| Cerebellar Cortex | 0.109 | 0.24 |
| Fimbria | 0.112 | 0.23 |
| Hypothalamus | 0.132 | 0.22 |
| Pontine Nucleus | 0.132 | 0.21 |
| Mammillary Bodies | 0.138 | 0.21 |
| Colliculus: Inferior | 0.139 | 0.21 |
| Fornix | 0.215 | 0.15 |
| Arbor Vita of Cerebellum | 0.217 | 0.15 |
| Thalamus | 0.235 | 0.14 |
| Cerebral Cortex: Frontal Lobe | 0.243 | 0.13 |
| Cerebellar Peduncle: Superior | 0.248 | 0.13 |
| Optic Tract | 0.260 | 0.12 |
| Cerebral Aqueduct | 0.267 | 0.12 |
| Cerebellar Peduncle: Middle | 0.319 | 0.10 |
| Third Ventricle | 0.339 | 0.09 |
| Stratum Granulosum of Hippocampus | 0.350 | 0.09 |
| Fundus of Striatum | 0.351 | 0.09 |
| Superior Olivary Complex | 0.384 | 0.08 |
| Inferior Olivary Complex | 0.408 | 0.07 |
| Subependymale Zone / Rhinocele | 0.416 | 0.07 |
| Basal Forebrain | 0.423 | 0.07 |
| Pons | 0.426 | 0.06 |

**Supplementary Table S11.** Correlations of relative change in brain volume from peak to long-term and cumulative behavior scores in EAE mice.

| Anatomical Regions | *q* | $R^2$ |
|---|---|---|
| Nucleus Accumbens | 0.434 | 0.06 |
| Medial Septum | 0.438 | 0.06 |
| Striatum | 0.444 | 0.06 |
| Olfactory Bulbs | 0.445 | 0.06 |
| Ventral Tegmental Decussation | 0.461 | 0.06 |
| Midbrain | 0.489 | 0.05 |
| Stria Medullaris | 0.492 | 0.05 |
| Habenular Commissure | 0.495 | 0.05 |
| Corticospinal Tract/Pyramids | 0.500 | 0.05 |
| Anterior Commissure: Pars Posterior | 0.502 | 0.05 |
| Stria Terminalis | 0.519 | 0.04 |
| Lateral Septum | 0.525 | 0.04 |
| Pre-Para Subiculum | 0.556 | 0.04 |
| Amygdala | 0.558 | 0.04 |
| Lateral Olfactory Tract | 0.573 | 0.03 |
| Internal Capsule | 0.589 | 0.03 |
| Lateral Ventricle | 0.647 | 0.02 |
| Olfactory Tubercle | 0.695 | 0.02 |
| Interpeduncular Nucleus | 0.735 | 0.01 |
| Cerebellar Peduncle: Inferior | 0.803 | 0.007 |
| Anterior Commissure: Pars Anterior | 0.832 | 0.005 |
| Fasciculus Retroflexus | 0.851 | 0.004 |
| Bed Nucleus of Stria Terminalis | 0.870 | 0.003 |
| Posterior Commissure | 0.914 | 0.001 |
| Cuneate Nucleus | 0.993 | 8.0E-06 |

| Summed Regions | *q* | $R^2$ |
|---|---|---|
| Cerebral Cortex | 0.009 | 0.51 |
| Cerebellum | 0.109 | 0.24 |
| Cerebral Grey | 0.131 | 0.21 |
| Cerebral White | 0.238 | 0.14 |
| Total Brain Volume | 0.341 | 0.09 |
| Brain Stem | 0.407 | 0.07 |
| Olfactory | 0.512 | 0.04 |
| Ventricles | 0.901 | 0.002 |

*q values were corrected for multiple comparisons using the false discovery rate (FDR) method. A 10% threshold was used for significance.