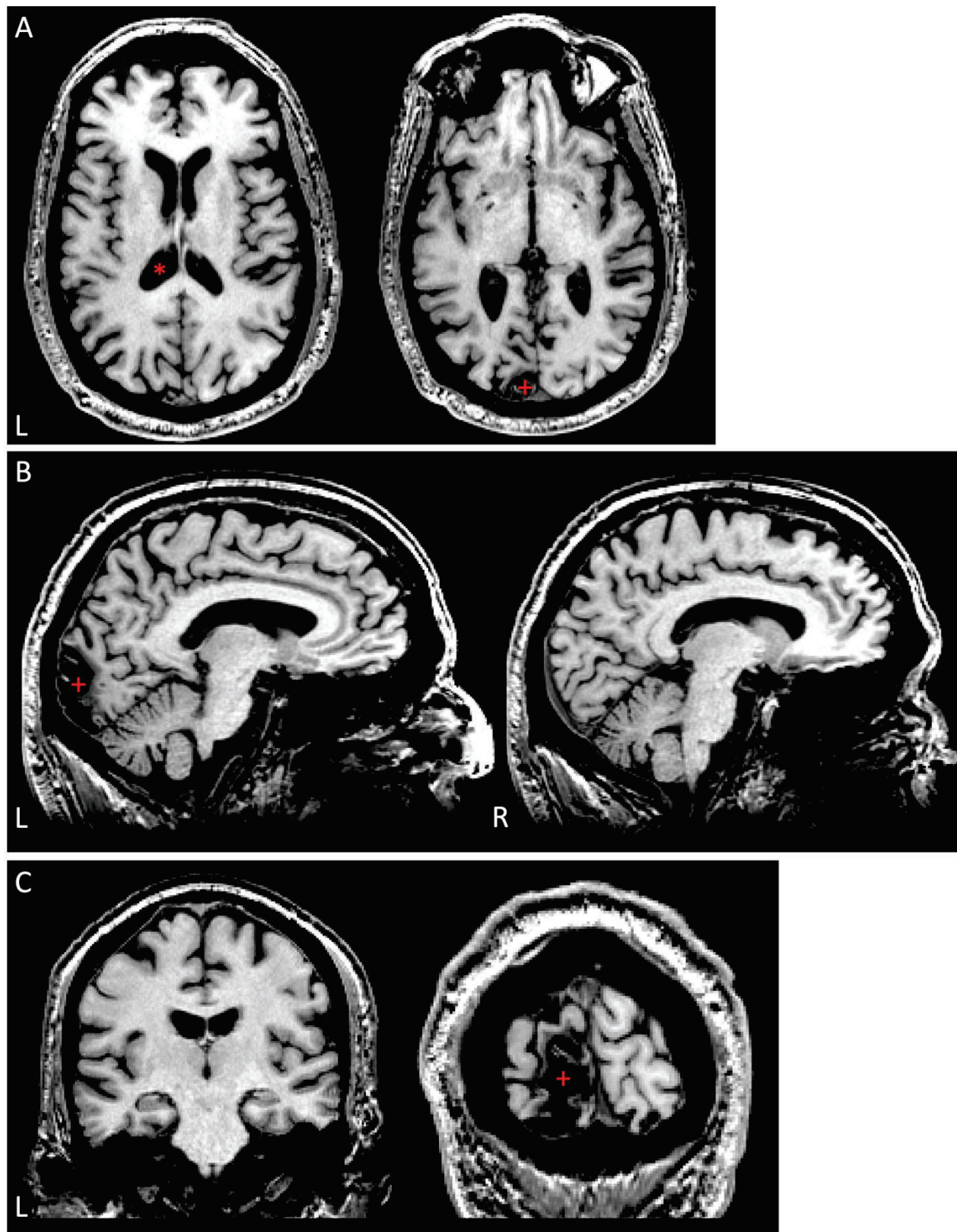
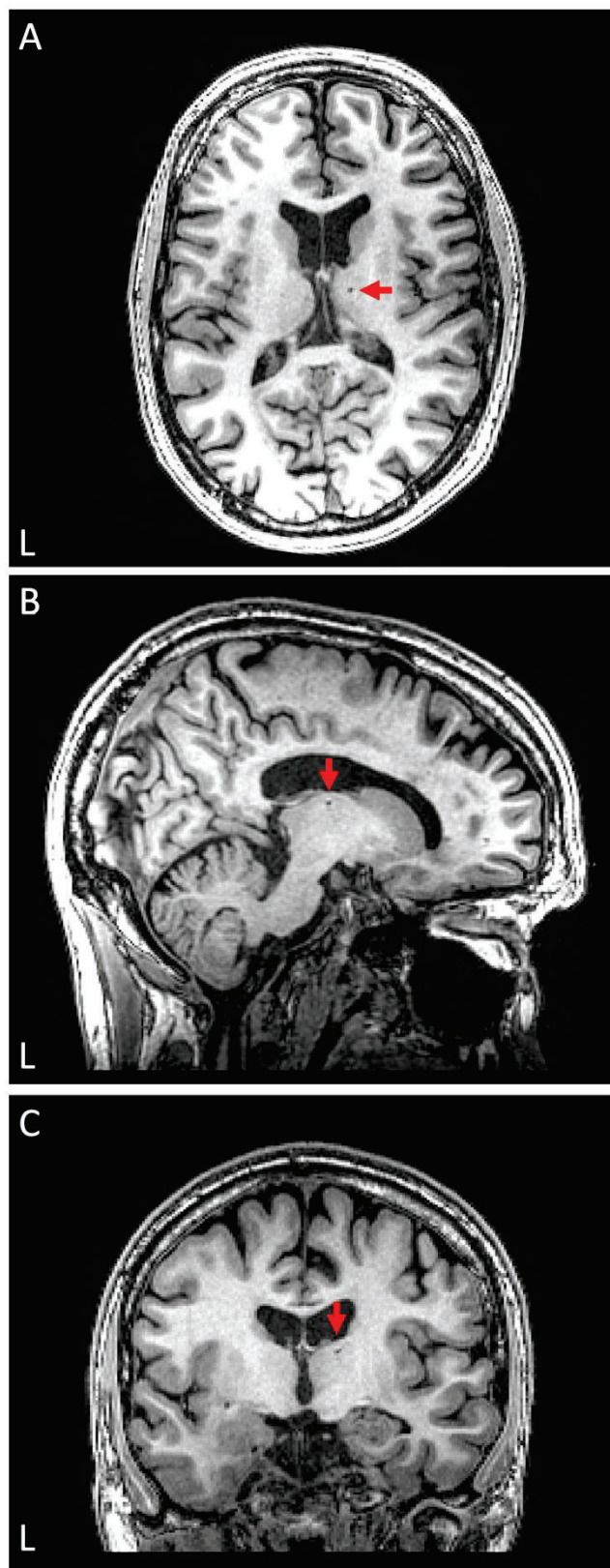


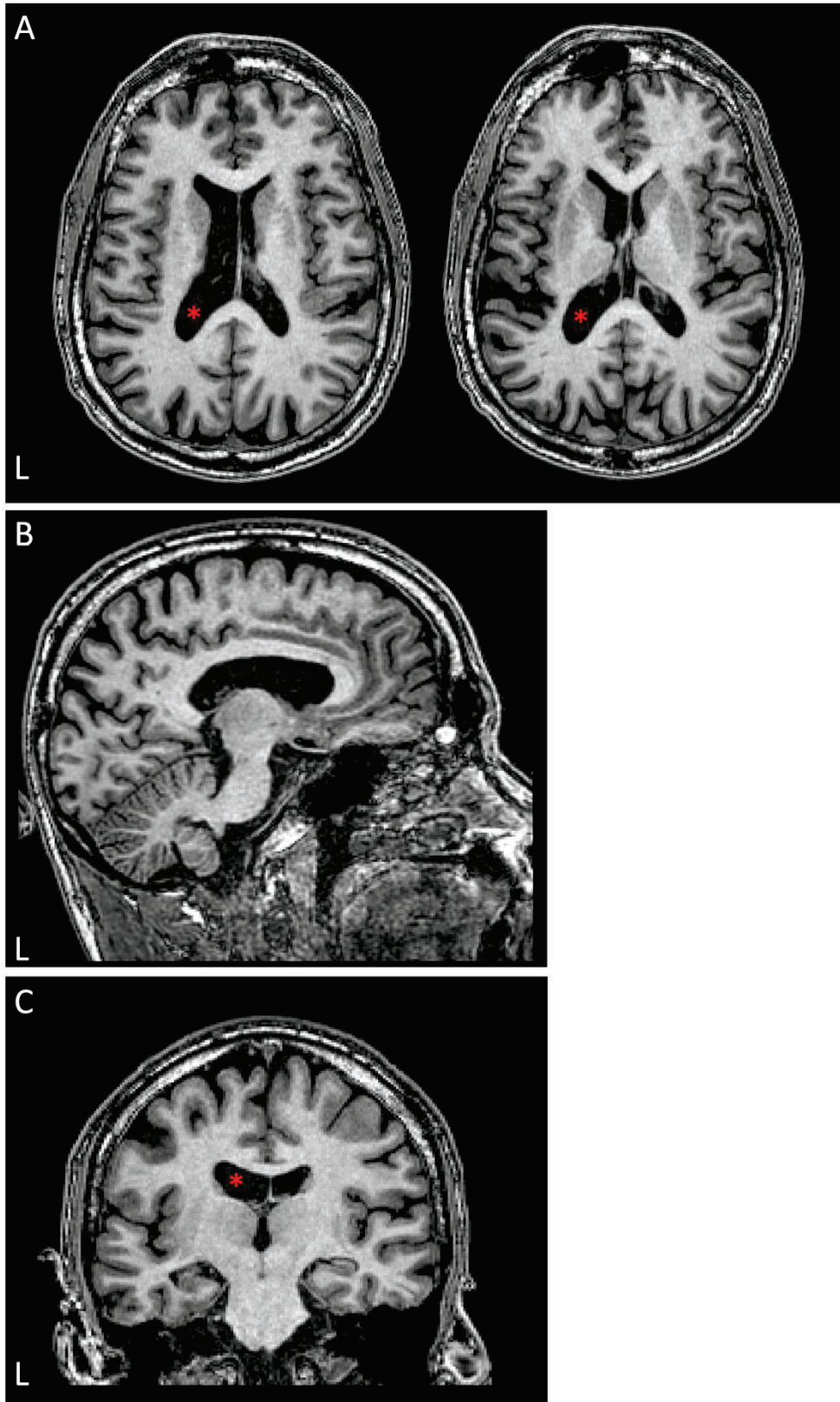
53 **Supplementary Figure 1. P1 structural brain MRI.** Representative (A) axial, (B) sagittal, and (C)
54 coronal images from P1. Images illustrate increased left hemisphere atrophy near the temporal horn
55 (asterisk) and residua from a small hemorrhage from diffuse axonal injury in the left midbrain (arrows).
56 Coronal image illustrates generalized atrophy. L = Left.
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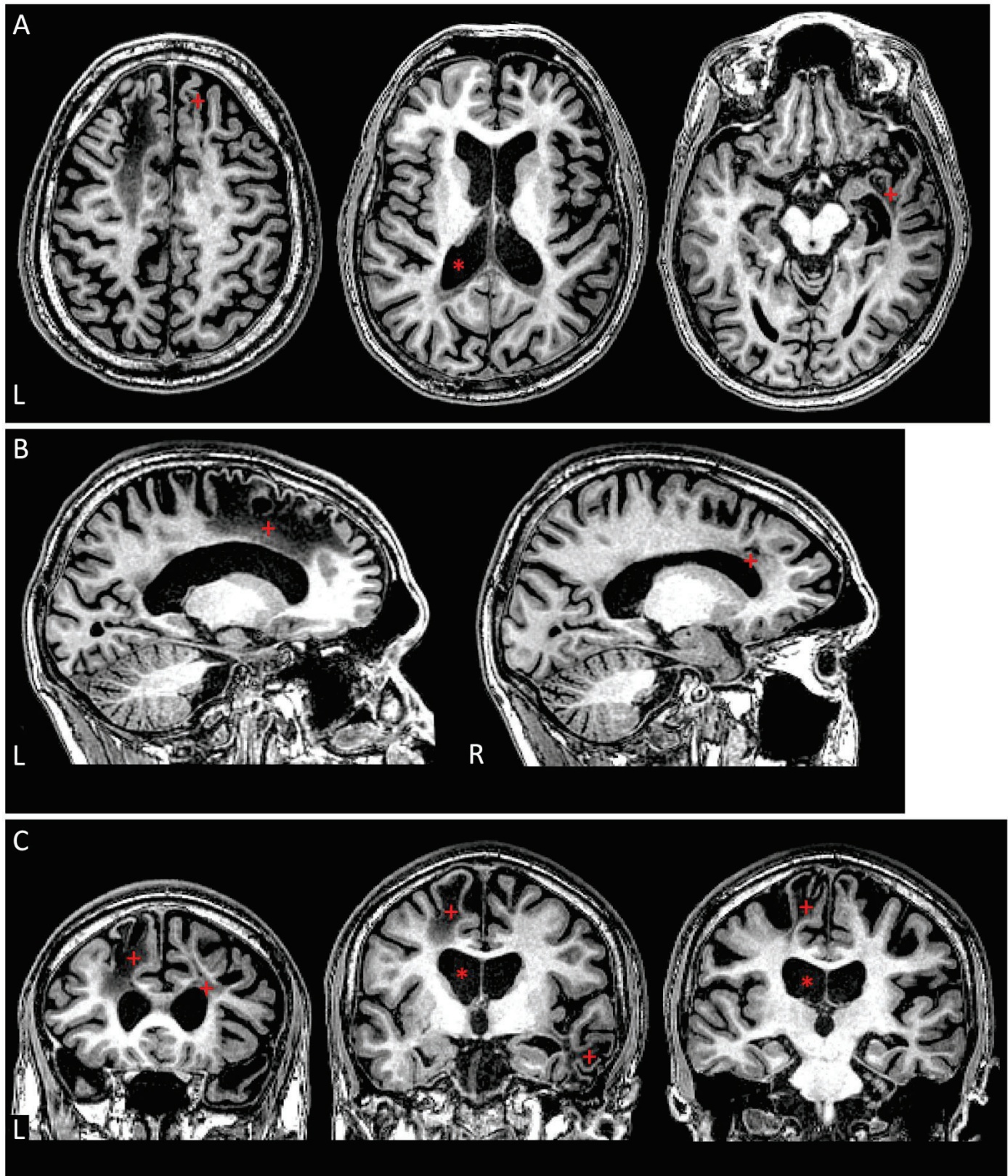


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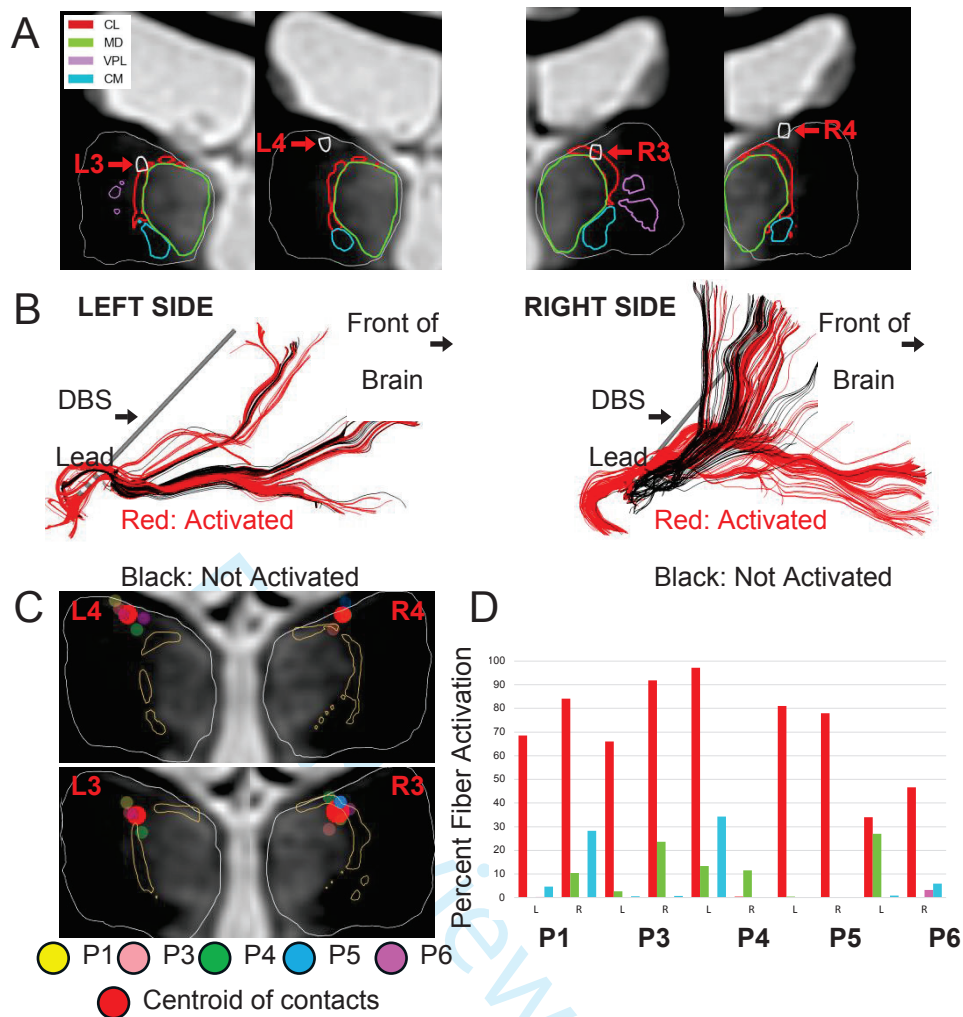
Supplementary Figure 3. P4 structural brain MRI. Representative (A) axial, (B) sagittal, and (C) coronal images from P4. Images illustrate right thalamic residua from a hemorrhage secondary to diffuse axonal injury (arrows). L = Left.



53 **Supplementary Figure 4. P5 structural brain MRI.** Representative (A) axial, (B) sagittal, and (C)
54 coronal images from P5. Images illustrate dilated left ventricular system marking asymmetric
55 hemispheric atrophy (asterisks). L = Left.



53 **Supplementary Figure 5. P6 structural brain MRI.** Representative (A) axial, (B) sagittal, and (C)
54 coronal images from P6. Images illustrate severe bilateral fronto-temporal injuries (plus symbols) and
55 left-greater-than-right dilation of the lateral ventricles (asterisks) secondary to the large medial frontal
56 lesion. L = Left. R = Right.
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Supplementary Figure 6. Activation of CL/DTTm fibers in a representative participant and

group summary. Example placements of the therapeutic DBS contacts (left: L3, L4; right: R3, R4) are shown for participant P4 in **(A)** coronal slices in the participant's brain and in **(B)** P4's diffusion tensor imaging model showing that CL's connections to the prefrontal cortex via the DTTm were activated by DBS. **(C)** Therapeutic contacts for all participants are shown in coronal slices in a study-specific group brain. Light brown outline indicates CL. Small circles show the therapeutic contacts, color-coded for each participant, and rendered dim if out-of-plane or bright if in-plane. Bright red larger circles indicate the group centroid of all top or bottom contacts. **(D)** Histogram showing the percentage of activated fibers that were part of the targeted CL/DTTm fiber tract versus those of adjacent nuclei (MD, VPL, and CM) from each participant's diffusion tensor imaging model. Note that CL/DTTm was primarily activated over adjacent fibers in each participant. Modified with permission from Schiff ND, Giacino JT, Butson CR, *et al.* Thalamic deep brain stimulation in traumatic brain injury: a phase 1, randomized feasibility study. *Nat Med.* Dec 2023;29(12):3162-3174.

See Schiff *et al.* Extended Data Figures 3-7 for detailed localizations and histograms for each participant. CL = central lateral thalamic nucleus. DTTm = medial dorsal tegmental tract. MD = mediodorsal thalamic nucleus. VPL = ventral posterior lateral thalamic nucleus. CM = centromedian thalamic nucleus. DBS = deep brain stimulation. P = Participant. L = Left. R = Right.

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Supplementary Table 1 Therapeutic DBS settings

| Participant | Therapeutic Contacts* | Amplitude | Frequency (Hz) | Pulse Width (μ s) |
|--------------|-----------------------|-------------------|----------------|------------------------|
| Left | | | | |
| P1 | L2-C, L3-C | 3.4 V | 160 | 90 |
| P3 | L2-C, L3-C | 4.0 V | 185 | 60 |
| P4 | L1-A, L2-C, L3-C | 3.5 V | 150 | 60 |
| P5 | L2-C, L3-C | 3.1 – 3.2 V | 150 | 60 |
| P6 | L2-C, L3-C | 3 mA each contact | 150 | 90 |
| Right | | | | |
| P1 | R10-C, R11-C | 3.3 V | 160 | 60 |
| P3 | R10-C, R11-C | 4.0 V | 185 | 80 |
| P4 | R9-A, R10-C | 3.5 V | 150 | 60 |
| P5 | R10-C, R11-C | 3.1 – 3.2 V | 150 | 60 |
| P6 | R9-C, R10-C, R11-C | 3 mA | 150 | 90 |

*A = anode. C = cathode.

Reproduced with permission from Schiff ND, Giacino JT, Butson CR, *et al.* Thalamic deep brain stimulation in traumatic brain injury: a phase 1, randomized feasibility study. *Nat Med.* Dec 2023;29(12):3162-3174.

Supplementary Table 2 Participant-specific distant and recent time periods in the AM Recall task

| Participant | Distant Time Period (Pre-injury) / Years Ago | Recent Time Period (Post-injury) |
|--------------------|---|---|
| P1 | High School / 25 | 6mo – 1yr ago |
| P3 | Age 30's / 30 | 6mo – 1yr ago |
| P4 | High School / 7 | 6mo – 1yr ago |
| P5 | High School / 15 | 6mo – 1yr ago |
| P6 | High School / 15 | 6mo – 1yr ago |

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Supplementary Table 3 Number of trials per response type in the AM Recall task

| Participant | Baseline 1 | Baseline 2 | 3 Months Treatment | 6 Months Treatment | 9 Months Treatment | 13 Months Treatment |
|---------------------------|------------|------------|--------------------|--------------------|--------------------|---------------------|
| P1 | | | | | | |
| Timepoint Exceptions | | | | | | |
| DBS on/off during testing | OFF | | OFF | | | |
| Correct | 21 | | 34 | | | |
| Omit | 14 | | 2 | | | |
| Incorrect | 1 | | 0 | | | |
| P3 | | | | | | |
| Timepoint Exceptions | | | | 5 months* | 8 months* | |
| DBS on/off during testing | OFF | | | ON | ON | ON |
| Correct | 9 | | | 9 | 10 | 13 |
| Omit | 11 | | | 10 | 9 | 9 |
| Incorrect | 16 | | | 17 | 17 | 14 |
| P4 | | | | | | |
| Timepoint Exceptions | | | | | | |
| DBS on/off during testing | OFF | | ON | ON | OFF | |
| Correct | 8 | | 9 | 13 | 11 | |
| Omit | 15 | | 15 | 19 | 16 | |
| Incorrect | 13 | | 12 | 4 | 9 | |
| P5 | | | | | | |
| Timepoint Exceptions | | | | 7 months* | 10 months* | |
| DBS on/off during testing | | OFF | ON | ON | ON | |
| Correct | | 17 | 18 | 20 | 19 | |
| Omit | | 11 | 14 | 14 | 11 | |
| Incorrect | | 8 | 4 | 2 | 6 | |
| P6 | | | | | | |
| Timepoint Exceptions | | | | | | |
| DBS on/off during testing | OFF | OFF | OFF | ON | OFF | |
| Correct | 3 | 4 | 2 | 7 | 12 | |
| Omit | 0 | 17 | 5 | 23 | 20 | |
| Incorrect | 33 | 15 | 29 | 6 | 4 | |

Total number of trials per testing session = 36.

Correct refers to an AM recalled from the indicated memory time period within the 15-second time window. Incorrect refers to any other recollection that does not meet the criteria for a successful AM recall, such as a vague memory, semantic information, AM from a wrong memory time period, or a correct AM that appeared in a previous trial. Omit refers to nothing recalled during the 15-second time window.

*Small deviations in the 6-month and 9-month time points for P3 and P5.

Supplementary Table 4 Percent of distant/pre-injury recalled AMs in the AM Recall task

| Participant | Baseline | Treatment |
|----------------------------|-----------------|------------------|
| P1 | 23.8% | 47.1% |
| P3 | 33.3% | 46.9% |
| P4 | 63.6% | 58.8% |
| P5 | 52.9% | 63.8% |
| P6 | 100%* | 38.1% |
| Average | 54.7% | 50.9% |
| Paired t-test (<i>P</i>) | | 0.82 |

No significant difference in the frequency of memory time periods (distant/pre-injury or recent/post-injury) of successfully recalled AMs with CL/DTTm DBS treatment in the AM Recall task. Significance was assessed with a two-tailed paired t-test.

*Calculated from recalled AMs from two baseline timepoints.

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Supplementary Table 5 Alertness and valence of recalled AMs in the AM Recall task

| Participant | Alertness | | | Valence | | |
|----------------------------|-----------|-------------------|----------------|----------|-------------------|----------------|
| | Baseline | Average Treatment | Percent Change | Baseline | Average Treatment | Percent Change |
| P1 | - | - | - | - | - | - |
| P3 | 4.6 | 3.9 | -15.2 | 0.9 | 0.4 | -55.6 |
| P4 | 3.3 | 3.2 | -3.0 | 0.3 | 0.1 | -66.7 |
| P5 | 3 | 3.3 | 10.0 | 0.0 | 0.3 | - |
| P6 | 2.3* | 3.1 | 34.8 | 1.7* | 1.3 | -23.5 |
| Paired t-test (<i>P</i>) | | | 0.83 | | | 0.34 |

No significant change in the alertness during testing or valence of successfully recalled AMs with CL/DTTm DBS treatment in the AM Recall task. Alertness was measured on a 5-point scale from 1 to 5. Valence was measured on a 6-point scale from -2 to 2. Significance was assessed with a two-tailed paired t-test.

*Average rating of recalled AMs from two baseline timepoints.

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Supplementary Table 6 Vividness of AMs in the Autobiographical Interview task

| Participant | Baseline | Average Treatment | Percent Change |
|----------------------------|-----------------|--------------------------|-----------------------|
| P3 | 4.3 | 5 | 16.3 |
| P4 | 3.5 | 3.5 | 0.0 |
| P5 | 3.8 | 3.7 | -2.6 |
| P6 | 4.3* | 2.8 | -34.9 |
| Average | 4.0 | 3.8 | -5.3 |
| Paired t-test (<i>P</i>) | | | 0.33 |

No significant change in the average vividness ratings ("how clearly can you visualize this event on a 1-6 scale?") of AMs in the Autobiographical Interview with CL/DTTm DBS treatment. Significance was assessed with a one-tailed paired t-test.

*Average score from AMs from two baseline timepoints.

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