Supplemental Materials:

Image Processing

FreeSurfer, which is available for download at http://surfer.nmr.mgh.harvard.edu, was used (standard recon-all pipeline) to process three structural MRI for each subject, reconstructing the cortical surface and segmenting cortical and subcortical volumes. The FreeSurfer automated pipeline is well validated and has been described in the literature. Briefly, recon-all automatically performed normalization of image intensity, motion correction, and averaging of two T1-weighted MPRAGE and skull stripping. Following Talairach transformation, FreeSurfer segments the gray matter (GM), subcortical white matter (WM), and deep gray matter volumetric structures. The GM/WM boundary is then tessellated and overall topology is corrected. To complete individual cortical modeling, the software optimizes the placement of GM/WM and GM/CSF boundaries based on shifts in intensity gradients. FreeSurfer measurements have been validated against histology and manual measurements. These methods use information from the entire brain volume, such as spatial intensity gradients across tissue classes. As mentioned in the manuscript, 10 GM subfields were evaluated based on enhanced subfield segmentation in FreeSurfer 6.0.

Effects of Age and PTSD Symptom Severity on Subfield Volumes

Given that previous studies have reported evidence of age effect on hippocampal volumes, age was included as covariate in all primary analyses. However, to assess whether an interaction between age and PTSD severity existed, we constructed a general linear model (GLM) examining the age x PTSD symptom severity interaction. We found significant CAPS-by-age interaction in the subiculum (F=5.50, p=0.02) and the parasubiculum (F=4.71, p=0.03). No other interactive effects were found. In addition, age did not correlate with any hippocampal subfield, controlling for intracranial volume. The results of these analyses are reported below in columns 1 & 2 of Table S4.

PTSD vs Non-PTSD Group Differences

This study was optimized to conduct an analysis of PTSD symptom severity on a continuum, not to create a contrast between PTSD and non-PTSD groups. However, to inform future studies, we conducted a between group multivariate analysis removing the effect of age and estimated total intracranial volume (eTIV), and using log-transformed volumes as required for normal distribution, consistent with the methods reported in the primary manuscript. No significant differences were found between PTSD and Non-PTSD groups, but the results and estimated marginal means (by group) are reported in columns 3-5 of Table S4 below.

For completeness, we also repeated the post-hoc analyses in the Non-PTSD group, following the exploratory methods described in the manuscript for the PTSD-only group. As described in the manuscript, this post-hoc data was not corrected for multiple comparisons. No significant correlations were identified. The results are reported below in Table S5.
Table S1. Demographic and Population Details (PTSD vs Non-PTSD Subjects)

| Measure                     | Full Group | PTSD | Non-PTSD |
|-----------------------------|------------|------|----------|
|                             | N          | Mean (SD) | n | Mean (SD) | n | Mean (SD) |
| Age                         | 68         | 34.78 (9.55) | 36 | 35.03 (9.26) | 32 | 34.50 (10.00) |
| WTAR IQ                     | 65         | 103.06 (8.14) | 33 | 104.12 (7.45) | 32 | 101.97 (8.77) |
| Gender (Male)               | 61         | —     | 32 | —     | 29 | —     |
| Substance/Alcohol Use Disorder | 13     | —     | 10 | —     | 3  | —     |
| Medication-Free             | 44         | —     | 17 | —     | 27 | —     |
| CES Total Score             | 63         | 18.52 (9.94) | 34 | 21.38 (10.57) | 29 | 15.17 (8.11) |
| BDI Total Score             | 68         | 18.63 (12.50) | 36 | 25.69 (10.24) | 32 | 10.69 (9.81) |
| CAPS Total Score            | 68         | 44.93 (30.75) | 36 | 69.19 (17.23) | 32 | 17.63 (15.96) |
| CAPS Reexperiencing         | 68         | 11.88 (9.33) | 36 | 18.44 (6.73) | 32 | 4.50 (5.55) |
| CAPS Arousal                | 68         | 15.68 (9.91) | 36 | 22.94 (5.48) | 32 | 7.50 (6.92) |
| CAPS Avoidance              | 68         | 5.74 (4.93) | 36 | 8.92 (3.92) | 32 | 2.16 (3.19) |
| CAPS Numbing                | 68         | 11.63 (9.82) | 36 | 18.89 (5.98) | 32 | 3.47 (6.16) |

**Abbreviations:** WTAR, Wechsler Test of Adult Reading; CES, Combat Exposure Scale; BDI, Beck Depression Inventory 2nd Edition; CAPS, Clinician Administered PTSD Scale for DSM-IV.
**Table S2. Demographic and Population Details (Medicated vs Non-Medicated Subjects)**

| Measure                          | Full Group          | Medicated         | Non-Medicated       |
|---------------------------------|---------------------|-------------------|---------------------|
|                                 | N       | Mean (SD) | n    | Mean (SD) | n    | Mean (SD) |
| Age                             | 68      | 34.78 (9.55) | 24   | 34.21 (9.79) | 44   | 35.10 (9.51) |
| WTAR IQ                         | 65      | 103.06 (8.14) | 22   | 103.59 (9.67) | 43   | 102.80 (7.34) |
| Gender (Male)                   | 61      | —         | 22   | —         | 39   | —         |
| Substance/Alcohol Use Disorder  | 13      | —         | 4    | —         | 9    | —         |
| CES Total Score                 | 63      | 18.52 (9.94) | 23   | 21.35 (11.62) | 40   | 16.90 (8.58) |
| BDI Total Score                 | 68      | 18.63 (12.50) | 24   | 26.67 (9.18) | 44   | 14.25 (11.94) |
| CAPS Total Score                | 68      | 44.93 (30.75) | 24   | 59.54 (23.82) | 44   | 36.96 (31.39) |
| CAPS Reexperiencing             | 68      | 11.88 (9.33) | 24   | 15.58 (7.88) | 44   | 9.86 (9.53) |
| CAPS Arousal                    | 68      | 15.68 (9.91) | 24   | 20.46 (7.45) | 44   | 13.07 (10.18) |
| CAPS Avoidance                  | 68      | 5.74 (4.93)  | 24   | 7.42 (4.30)  | 32   | 4.82 (5.05)  |
| CAPS Numbing                    | 68      | 11.63 (9.82) | 24   | 16.08 (8.71) | 44   | 9.21 (9.62)  |

**Abbreviations:** WTAR, Wechsler Test of Adult Reading; CES, Combat Exposure Scale; BDI, Beck Depression Inventory 2nd Edition; CAPS, Clinician Administered PTSD Scale for DSM-IV. *Full Group details are repeated from Table S1 for convenience.*
### Table S3. Raw Intracranial and Bilateral Hippocampal Subfield Volumes

| Volume             | Full Group  | PTSD       | Non-PTSD   | Medicated | Non-Medicated |
|--------------------|-------------|------------|------------|-----------|---------------|
|                    | (n=68)      | (n=36)     | (n=32)     | (n=24)    | (n=44)        |
|                    | Mean (SEM)  | Mean (SEM)| Mean (SEM)| Mean (SEM)| Mean (SEM)    |
| eTIV               | 1573970.59  | 1574444.44 | 1573437.50 | 1561250.00 | 1580909.09    |
|                    | (18360.29)  | (25434.15) | (26954.30) | (33607.46) | (21887.22)    |
| Hippocampus        | 8417.84     | 8301.88    | 8548.31    | 8149.11   | 8564.43       |
|                    | (107.01)    | (135.75)   | (167.77)   | (181.09)  | (128.80)      |
| Subiculum          | 869.19      | 865.48     | 873.36     | 846.19    | 881.73        |
|                    | (12.44)     | (16.80)    | (18.74)    | (21.44)   | (15.10)       |
| Presubiculum       | 628.10      | 631.65     | 624.11     | 609.77    | 638.09        |
|                    | (9.63)      | (13.23)    | (14.24)    | (18.53)   | (10.80)       |
| Parasubiculum      | 128.09      | 131.37     | 124.40     | 129.41    | 127.37        |
|                    | (2.41)      | (3.31)     | (3.45)     | (5.09)    | (2.52)        |
| CA1                | 1296.90     | 1286.51    | 1308.59    | 1254.62   | 1319.96       |
|                    | (17.11)     | (21.04)    | (27.81)    | (28.25)   | (20.90)       |
| CA2/3              | 453.92      | 448.60     | 459.90     | 435.67    | 463.88        |
|                    | (7.34)      | (9.93)     | (10.95)    | (11.39)   | (9.24)        |
| CA4                | 530.85      | 526.40     | 535.85     | 509.90    | 542.27        |
|                    | (7.23)      | (8.79)     | (11.85)    | (10.43)   | (9.25)        |
| Dentate Gyrus      | 618.84      | 613.95     | 624.33     | 594.63    | 632.04        |
|                    | (8.54)      | (10.34)    | (14.04)    | (12.33)   | (10.94)       |
| Molecular Layer    | 1169.13     | 1161.09    | 1178.18    | 1131.79   | 1189.50       |
|                    | (15.06)     | (18.62)    | (24.41)    | (24.82)   | (18.41)       |
| HATA               | 132.17      | 129.99     | 134.63     | 128.74    | 134.04        |
|                    | (1.84)      | (2.47)     | (2.73)     | (3.24)    | (2.20)        |
| Hippocampal Tail   | 1095.33     | 1083.32    | 1108.84    | 1053.90   | 1117.93       |
|                    | (16.61)     | (23.18)    | (23.94)    | (29.77)   | (19.29)       |

**Abbreviations:** CA, cornu ammonis; eTIV, estimated Total Intracranial Volume; HATA, hippocampus-amygda transition area; Mean is volume in mm$^3$. SEM, Standard Error of the Mean.
Table S4. Effects of Age, CAPS Severity, and PTSD Group Status on Hippocampal Subfields

| Volume                | CAPS x Age A | Age B | Group Difference C | PTSD EMM (SEM) | Non-PTSD EMM (SEM) |
|-----------------------|--------------|-------|--------------------|----------------|-------------------|
|                       | $F (p)$      | $r (p)$ | $F (p)$            |                |                   |
| Subiculum             | 5.50 (0.02)* | -0.18 (0.14) | 0.17 (0.68) | 865.61 (12.65) | 873.21 (13.42)  |
| Presubiculum          | 2.66 (0.11)  | -0.12 (0.35) | 0.28 (0.60) | 631.66 (9.87)  | 624.10 (10.47)  |
| Parasubiculum         | 4.71 (0.03)* | -0.06 (0.62) | 2.71 (0.11) | 131.37 (2.91)  | 124.40 (3.08)   |
| CA1                   | 0.98 (0.33)  | -0.12 (0.35) | 0.90 (0.35) | 1286.46 (16.02) | 1308.64 (16.99) |
| CA2/3                 | 0.04 (0.84)  | -0.04 (0.74) | 0.86 (0.36) | 448.55 (8.46)  | 459.97 (8.98)   |
| CA4                   | 0.83 (0.37)  | -0.12 (0.35) | 0.74 (0.39) | 2.72 (0.01)    | 2.73 (0.01)     |
| Dentate Gyrus         | 1.34 (0.25)  | -0.13 (0.29) | 0.59 (0.45) | 2.79 (0.01)    | 2.79 (0.01)     |
| Molecular Layer       | 1.89 (0.17)  | -0.20 (0.11) | 0.53 (0.47) | 3.06 (0.01)    | 3.07 (0.01)     |
| HATA                  | 0.64 (0.43)  | 0.08 (0.50)  | 2.55 (0.12) | 129.93 (2.04)  | 134.69 (2.17)   |
| Hippocampal Tail      | 0.58 (0.45)  | -0.03 (0.82) | 0.87 (0.35) | 1083.15 (19.01) | 1109.03 (20.16) |

A) Interaction from multivariate general linear model. B) Partial correlation between subfield and age, controlling for eTIV. C) Multivariate general linear model analysis comparing PTSD and Non-PTSD groups. Abbreviations: CA, cornu ammonis; eTIV, estimated Total Intracranial Volume; HATA, hippocampus-amygda transition area; EMM, Estimated Marginal Mean (mm$^3$); SEM, Standard Error of the Mean. *Effects are significant where $p$ is less than or equal to 0.05 ($p \leq 0.05$).
Table S5. Post-hoc Correlations of PTSD Symptom Severity in Subjects Without PTSD

| Volume                  | CAPS Exploratory (Non-PTSD group) |  |
|-------------------------|-----------------------------------|--|
|                         | r       | p   | df |
| Total Hippocampus       | -0.08   | 0.68| 28 |
| Parasubiculum           | 0.02    | 0.94| 28 |
| Presubiculum            | -0.02   | 0.93| 28 |
| Subiculum               | -0.10   | 0.61| 28 |
| CA1                     | -0.04   | 0.83| 28 |
| CA2/3                   | 0.03    | 0.89| 28 |
| CA4                     | 0.10    | 0.60| 28 |
| Dentate Gyrus           | 0.11    | 0.57| 28 |
| HATA                    | -0.17   | 0.36| 28 |
| ML of Hippocampus       | -0.07   | 0.73| 28 |
| Hippocampal Tail        | -0.16   | 0.39| 28 |

**Abbreviations:** r, partial correlation controlling for age and total intracranial volume; CA, cornu ammonis; ML, molecular layer; DG, granule cell and molecular layers of the dentate gyrus; HATA, hippocampal-amygdala transition area; CAPS, Clinician Administered PTSD Scale for DSM-IV. Correlations were conducting controlling for the effects of age and total intracranial volume. * indicates significance if p is less than or equal to 0.05 (p ≤ 0.05). Exploratory analysis—not corrected for multiple comparisons. For Full Group and PTSD-Only Group results, see Table 2 in the primary manuscript.
Video Legends:

**Video S1. 10 Gray Matter Subfields of the Hippocampus – Animated 3D Model.** This video was created in Blender using meshes from one of the combat control (non-PTSD) participants described in the manuscript. It demonstrates the gray matter subfields of the hippocampal formation, and steps through the anatomy to better visualize the more hidden subfields.
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