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# Neural patterns differentiate traumatic from sad autobiographical memories in PTSD

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# Supplementary Information

## Neural patterns differentiate traumatic from sad autobiographical memories in PTSD

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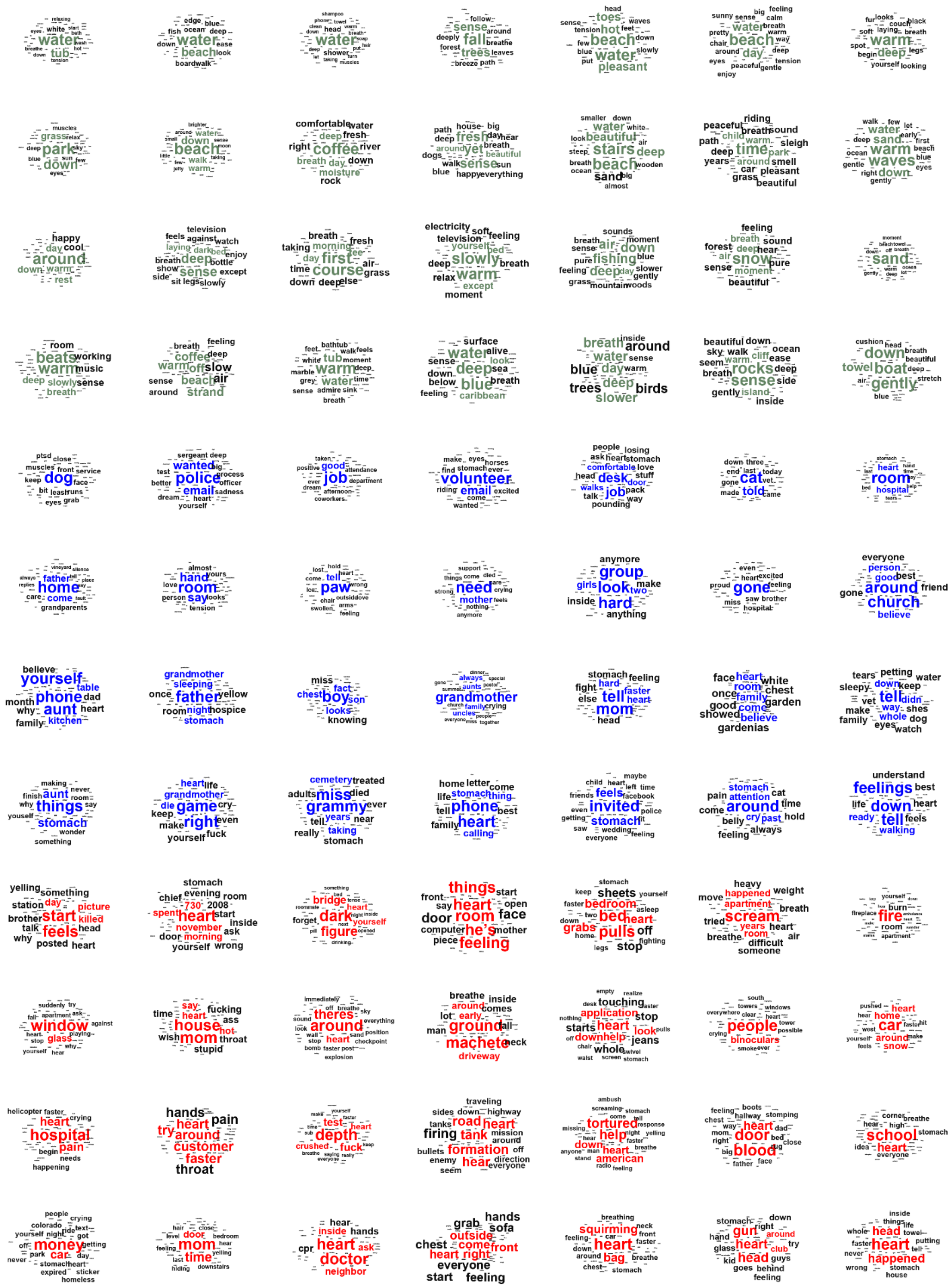
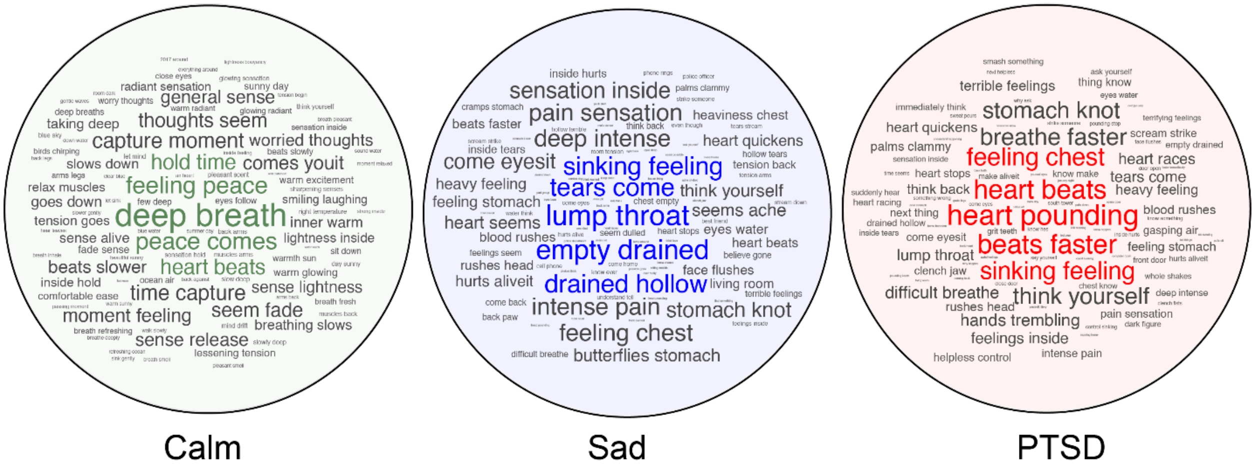


**Supplementary Figure 1 (corresponding to Figure 2):**

***Word-clouds of script content.***

*Word-cloud plots depicting word occurrence per each individual script (N = 84: 28 participants*

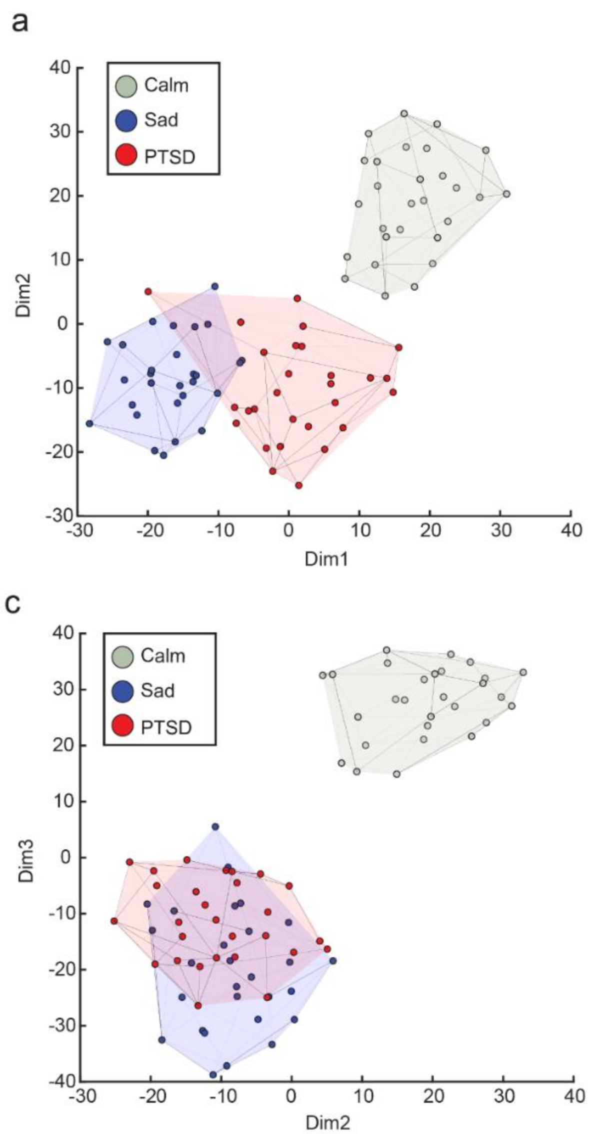
*X 3 script types). The most frequent words are highlighted in color in cloud centers. Text color depicts script type: green – ‘Calm’, blue – ‘Sad’ and red – ‘PTSD’.*




**Supplementary Figure 2 (corresponding to Figure 2):**

***Word-clouds of common bi-grams per script type**.*

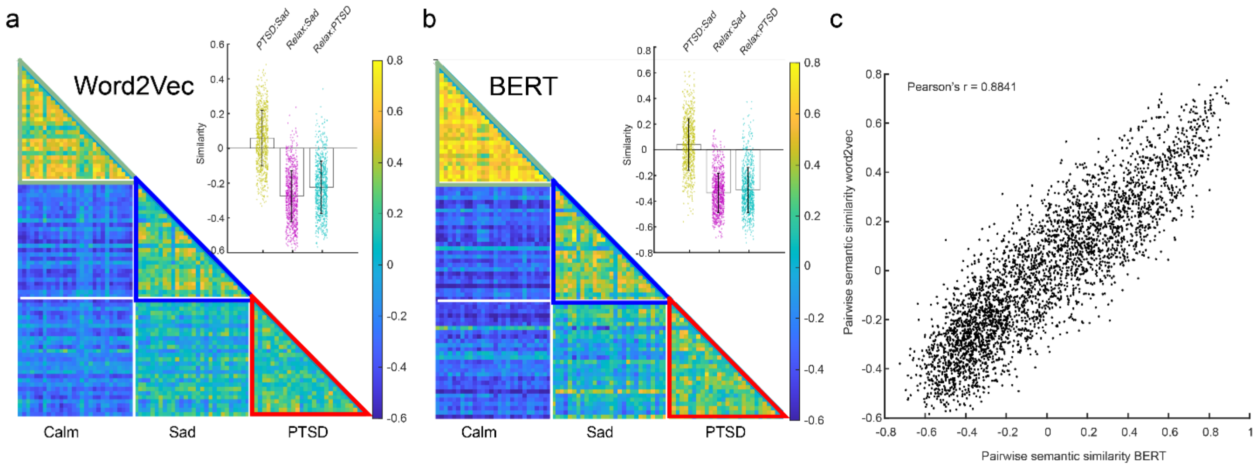
*Bi-gram word-cloud plots clustering two-word phrases common to each script type (‘Calm’, ‘Sad’, ‘PTSD’). The most frequent bi-grams are highlighted in color in plot centers.*




**Supplementary Figure 3 (corresponding to Figure 2):**

***Projections of semantic space based on three principal dimensions***

- ***(a)*** *. t-SNE embedding of scripts projected onto dimensions 1-2. Each dot represents a single script, Colored volumes are continuous spaces occupied by each script type. Color denotes script type ('PTSD': red, 'Sad': blue, 'Calm': green). Note overlap of 'PTSD' and 'Sad' semantic content.*
- ***(b)*** *Same as* ***(a)*** *but projected onto dimensions 1-3.*
- ***(c)*** *Same as* ***(a)*** *but projected onto dimensions 2-3.*



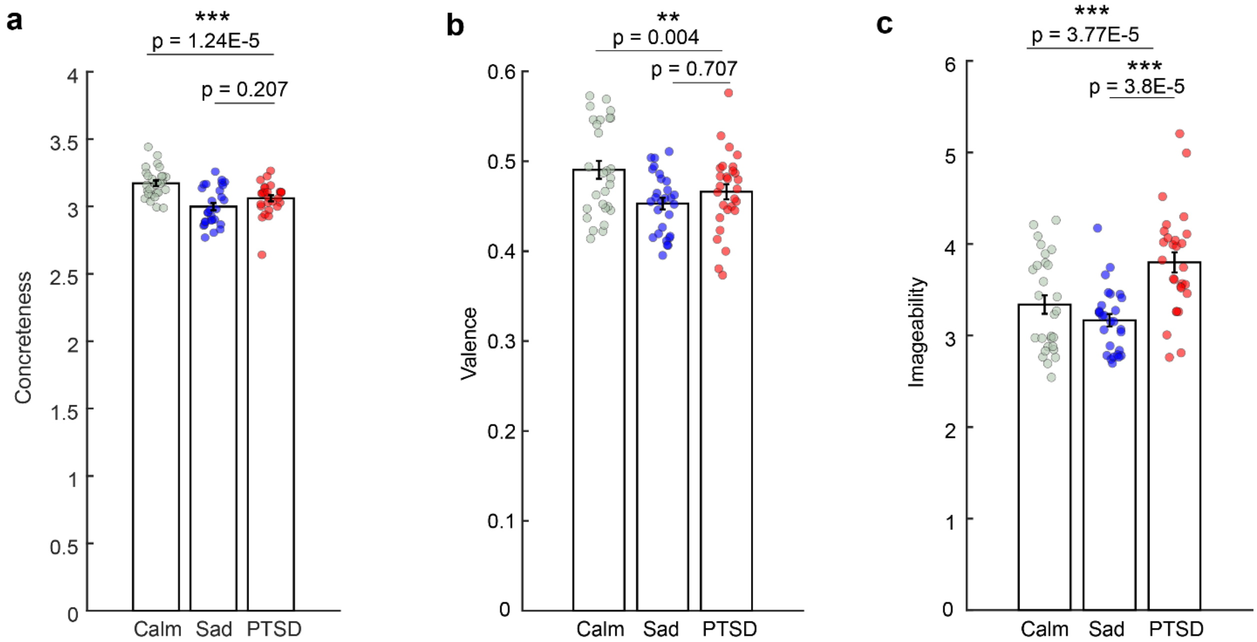

**Supplementary Figure 4 (corresponding to Figure 2):**

**Comparison of word embedding methods – word2vec and BERT**

a. ***Pairwise similarity of semantic content of scripted narratives obtained via word2vec embedding.*** *Semantic pairwise cosine similarity presented for all scripted narratives. Within-category similarity is marked in colored triangles off the matrix diagonal ('PTSD': red, 'Sad': blue, 'Calm': gray). Inlet bar graphs illustrate the distribution of pairwise semantic similarity across script types. Bars depict means (N = 378 per condition), error bars are SEM.*

b. ***Pairwise similarity of semantic content of scripted narratives obtained via BERT contextual embedding.*** *Same as (a) but semantic cosine similarity was obtained using a pre-trained contextual embedding transformer model, BERT, implemented in the MATLAB R2021a NLP toolbox to account for intra-sentence dynamics*

c. ***Scatter plot depicting comparisons of pairwise semantic similarity values obtained using the methods described in (a) and (b).*** *The lower triangles of the two similarity matrices were collapsed and their correlation estimated with Pearson's r. Each datapoint is equivalent to one colored square tile in the matrices.*



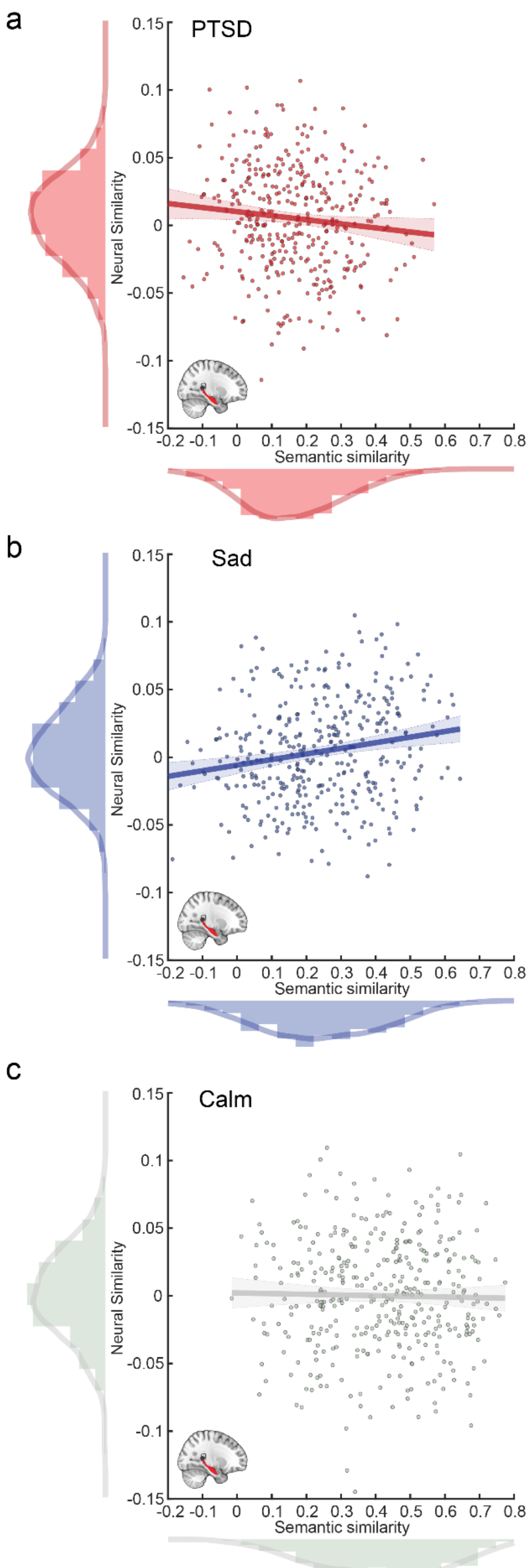

**Supplementary Figure 5 (corresponding to Figure 2):**

**Psycholinguistic ratings of script content**

(a) *Concreteness ratings for individual script content. Bars depict group means, points represent participants, jittered horizontally for visualization. Color denotes script type ('Calm' – gray, 'Sad'- blue, 'PTSD' – red). P values in the top row indicate significance of rmANOVA (across the three conditions); the p values below indicate significance of post-hoc two-sided, paired t-test Bonferroni corrected) comparing the 'Sad' and 'PTSD' conditions. Bars depict means (N = 28 per condition), error bars are SEM.* * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

(b) *Same as* ***(a)*** *but for valence ratings.*

(c) *Same as* ***(a)*** *but for imageability ratings.*


a
PTSD
Neural Similarity
Semantic similarity
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8
b
Sad
Neural Similarity
Semantic similarity
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8
c
Calm
Neural Similarity
Semantic similarity
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8

**Supplementary Figure 6 (corresponding to Figure 3):**

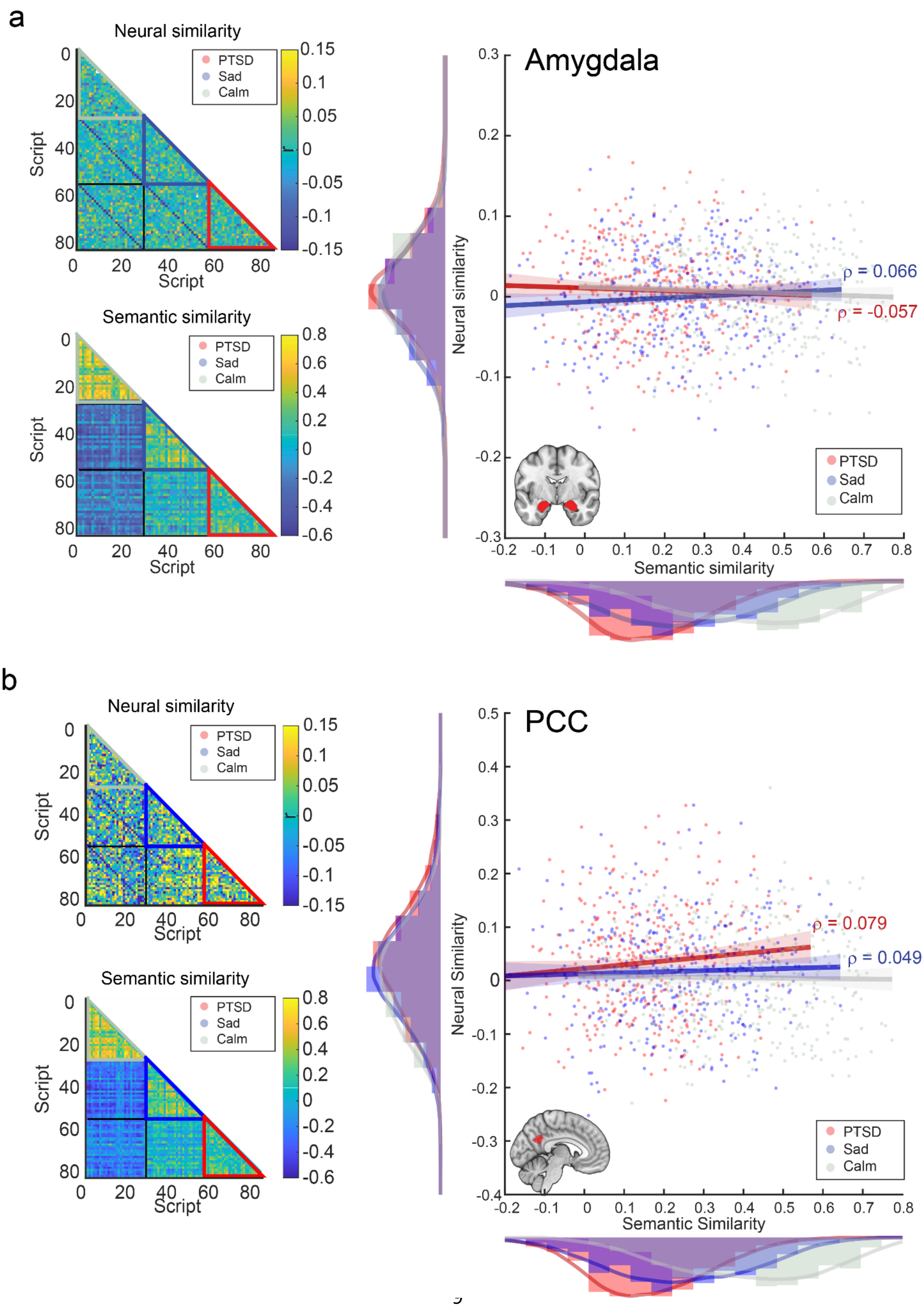
***Hippocampus – semantic-to-neural IS-RSA***

***This figure shows identical data to that presented in Figure 3E in the main text.***

***(a) Hippocampus – semantic-to-neural IS-RSA for 'PTSD' scripts.*** *Intersubject representational similarity analysis conducted on pairwise similarity of semantic content and neural patterns in the hippocampus. Each datapoint is one pairwise comparison. Histograms along axes depict similarity distribution, thick trace depict estimated density, Regression line is an approximate visualization of Spearman correlation ρ coefficient for IS-RSA. Error bands indicate 95% confidence bounds.*

***(b) Hippocampus – semantic-to-neural IS-RSA for 'Sad' scripts.*** *Intersubject representational similarity analysis conducted on pairwise similarity of semantic content and neural patterns in the hippocampus. Each datapoint is one pairwise comparison. Histograms along axes depict similarity distribution, thick trace depict estimated density, Regression line is an approximate visualization of Spearman correlation ρ coefficient for IS-RSA. Error bands indicate 95% confidence bounds.*

***(c) Hippocampus – semantic-to-neural IS-RSA for 'Calm' scripts.*** *Intersubject representational similarity analysis conducted on pairwise similarity of semantic content and neural patterns in the hippocampus. Each datapoint is one pairwise comparison. Histograms along axes depict similarity distribution, thick trace depict estimated density, Regression line is an approximate visualization of Spearman correlation ρ coefficient for IS-RSA. Error bands indicate 95% confidence bounds.*

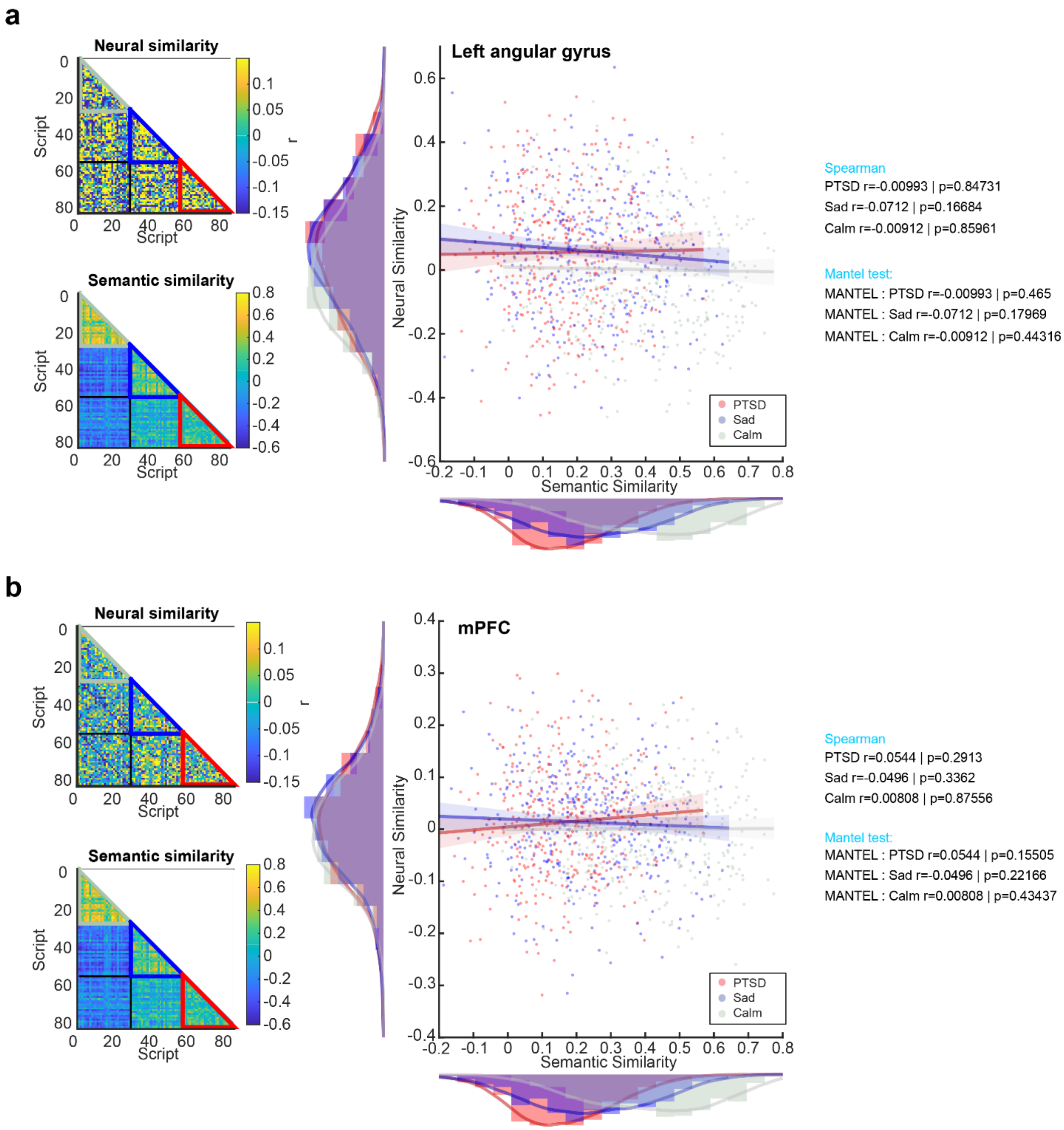

a
Neural similarity
Semantic similarity
Script
PTSD
Sad
Calm
r
Amygdala
ρ = 0.066
ρ = -0.057
Neural similarity
Semantic similarity
b
Neural similarity
Semantic similarity
Script
PTSD
Sad
Calm
r
PCC
ρ = 0.079
ρ = 0.049
Neural Similarity
Semantic Similarity

**Supplementary Figure 7 (corresponding to Figure 3):**

***Semantic-to-neural IS-RSA in amygdala and PCC***

*(a)* ***Top Left: Amygdala – neural similarity matrix.*** *Script-by-script neural similarity matrix for spatial patterns extracted from the amygdala during script reactivation. Within-category similarity is marked in colored triangles off the matrix diagonal (‘PTSD’: red, ‘Sad’: blue, ‘Calm’: green).* ***Bottom Left: semantic similarity matrix.*** *Semantic cosine similarity of scripted narratives. Within-category similarity is marked in colored triangles off the matrix diagonal (‘PTSD’: red, ‘Sad’: blue, ‘Calm’: gray).* ***Right: Amygdala – semantic-to-neural IS-RSA.*** *Intersubject representational similarity analysis conducted on pairwise similarity of semantic content and neural patterns in the amygdala. Each datapoint is one pairwise comparison. Analysis was iterated per script type (‘PTSD’: red, ‘Sad’: blue, ‘Calm’: gray). Histograms along axes depict similarity distribution, thick trace depict estimated density, colors correspond to main legend. Regression lines are approximate visualization of Spearman correlation ρ coefficients for IS-RSA in ‘PTSD’ and ‘Sad’ scripts (red and blue resp.). Error bands indicate 95% confidence bounds.*

**(a)** *Same as in* ***(a)*** *but for signals extracted from the posterior cingulate cortex (PCC).*



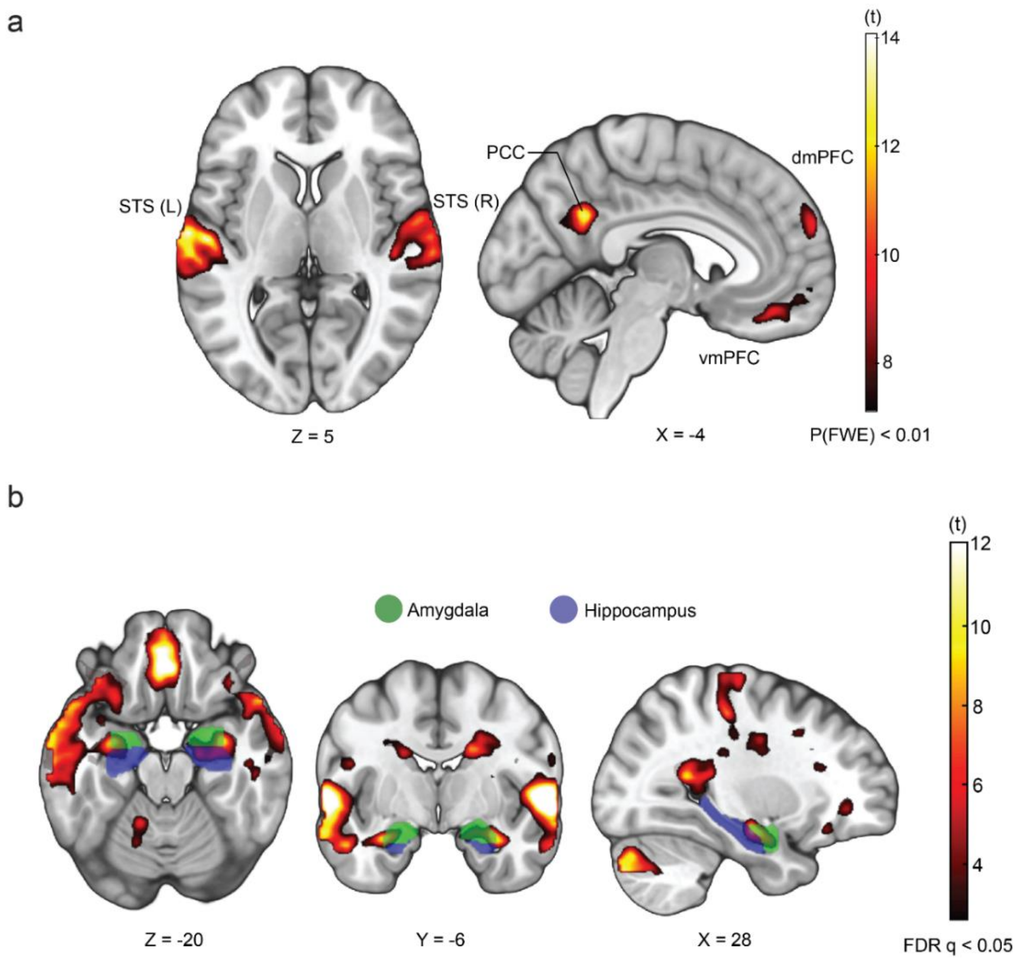
a
Neural similarity
Script
r
Semantic similarity
Left angular gyrus
Neural Similarity
Semantic Similarity
PTSD
Sad
Calm
Spearman
PTSD r=-0.00993 | p=0.84731
Sad r=-0.0712 | p=0.16684
Calm r=-0.00912 | p=0.85961
Mantel test:
MANTEL : PTSD r=-0.00993 | p=0.465
MANTEL : Sad r=-0.0712 | p=0.17969
MANTEL : Calm r=-0.00912 | p=0.44316
b
Neural similarity
Script
r
Semantic similarity
mPFC
Neural Similarity
Semantic Similarity
PTSD
Sad
Calm
Spearman
PTSD r=0.0544 | p=0.2913
Sad r=-0.0496 | p=0.3362
Calm r=0.00808 | p=0.87556
Mantel test:
MANTEL : PTSD r=0.0544 | p=0.15505
MANTEL : Sad r=-0.0496 | p=0.22166
MANTEL : Calm r=0.00808 | p=0.43437

**Supplementary Figure 8 (corresponding to Figure 3):**

***Semantic-to-neural IS-RSA in default mode network ROIs***

(a) ***Top Left: Angular gyrus – neural similarity matrix.*** *Script-by-script neural similarity matrix for spatial patterns extracted from the angular gyrus during script reactivation. Within-category similarity is marked in colored triangles off the matrix diagonal ('PTSD': red, 'Sad': blue, 'Calm': gray).* ***Bottom Left: semantic similarity matrix.*** *Semantic cosine similarity of scripted narratives. Within-category similarity is marked in colored triangles off the matrix diagonal ('PTSD': red, 'Sad': blue, 'Calm': gray).* ***Right: Angular gyrus – semantic-to-neural IS-RSA.*** *Intersubject representational similarity analysis conducted on pairwise similarity of semantic content and neural patterns in the angular gyrus. Each datapoint is one pairwise comparison. Analysis was iterated per script type ('PTSD': red, 'Sad': blue, 'Calm': gray). Histograms along axes depict similarity distribution, thick trace depict estimated density, colors correspond to main legend. Regression lines are approximate visualization of Spearman correlation* ρ *coefficients for IS-RSA in 'PTSD' and 'Sad' scripts (red and blue resp. Statistical information is provided next to the figure in text. All tests are two-sided, Error bands indicate 95% confidence bounds.*

(b) *Same as* ***(a)*** *but for the left medial prefrontal cortex (mPFC),*

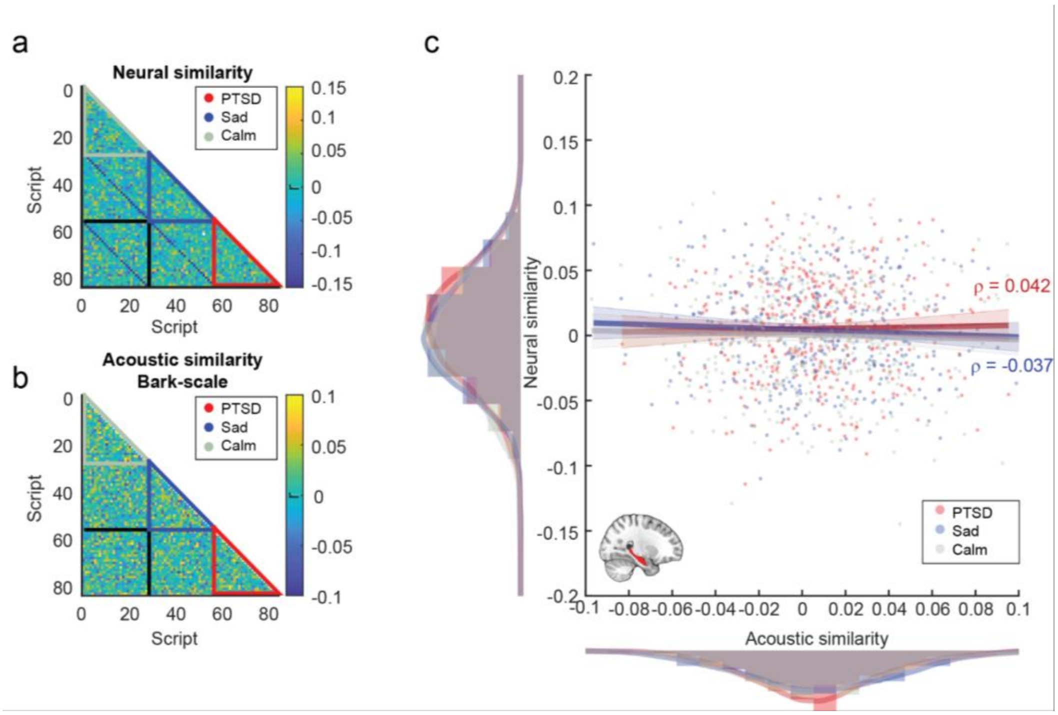



**Supplementary Figure 9 (corresponding to Figure 3):**

***GLM results***

**(a)** *A whole-brain contrast comparing the condition of 'script on' (all script types included) to baseline (group t map, $p_{(FWE)} < 0.01$, k = 50). Clusters of activation as labeled. STS, superior temporal sulcus; PCC, posterior cingulate cortex; dmPFC, dorsomedial prefrontal cortex; vmPFC, ventromedial prefrontal cortex.*

**(b)** *A whole-brain contrast comparing the condition of 'script on' (all script types included) to baseline (group t map $p_{(FDR)}$ q < 0.05) targeting view of the amygdala and hippocampus. Anatomical masks of bilateral amygdala and hippocampus appear in green and purple shades, respectively. Note that the main GLM-derived ROIs (see panel* ***a****) were extracted following a stricter threshold of $p_{(FWE)} < 0.01$*



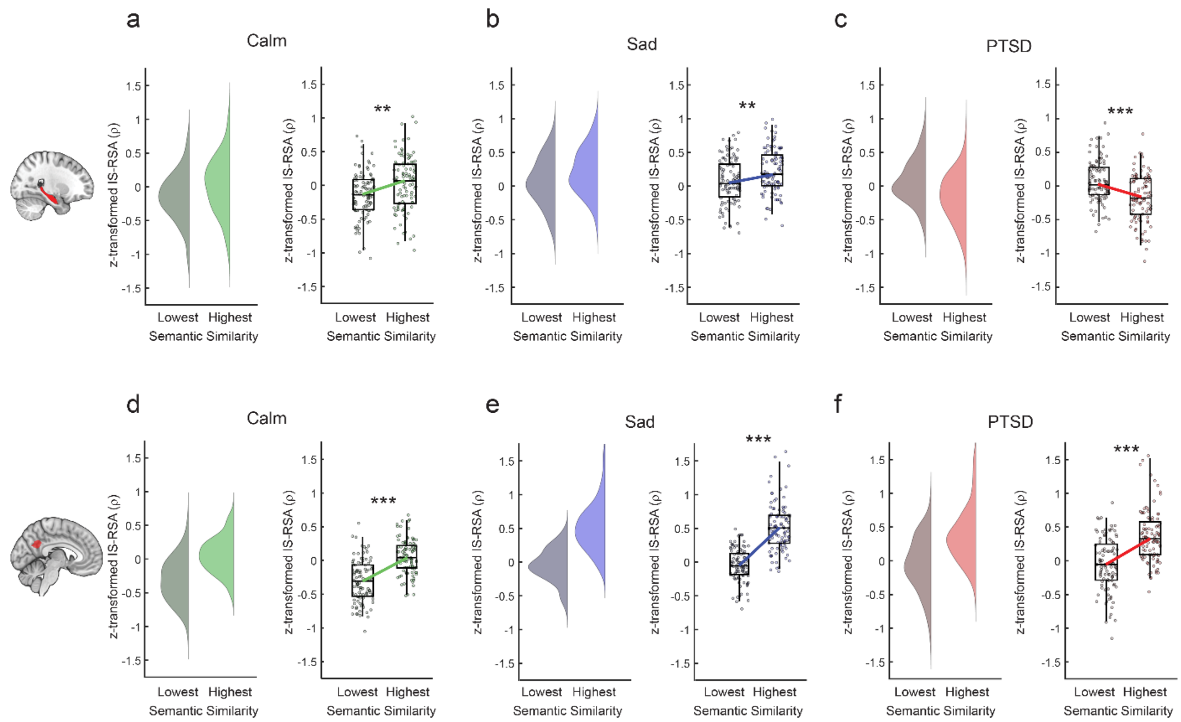

**Supplementary Figure 10 (corresponding to Figure 3):**

***Acoustic-to-neural IS-RSA in the hippocampus***

*(c)* ***Hippocampus – neural similarity matrix.*** *Script-by-script neural similarity matrix for spatial patterns extracted from the hippocampus during script reactivation. Within-category similarity is marked in colored triangles off the matrix diagonal ('PTSD': red, 'Sad': blue, 'Calm': gray).*

*(d)* ***Acoustic similarity matrix.*** *Acoustic similarity of scripted narratives. Within-category similarity is marked in colored triangles off the matrix diagonal ('PTSD': red, 'Sad': blue, 'Calm': gray).*

*(e)* ***Hippocampus – acoustic-to-neural IS-RSA.*** *Intersubject representational similarity analysis conducted on pairwise similarity of acoustic and neural patterns in the hippocampus. Each datapoint is one pairwise comparison. Analysis was iterated per script type ('PTSD': red, 'Sad': blue, 'Calm': gray). Histograms along axes depict similarity distribution, thick trace depict estimated density, colors correspond to main legend. Regression lines are approximate visualization of Spearman correlation ρ coefficients for IS-RSA in 'PTSD' and 'Sad' scripts (red and blue resp.). Error bands indicate 95% confidence bounds*




**Supplementary Figure 11 (corresponding to Figure 3):**

***IS-RSA on script subsets***

(a) *Left: Raincloud plots illustrating the distribution of IS-RSA correlation coefficients computed for subsets of the 'Calm' scripts with lowest- and highest-semantic similarity (N = 100 for each). IS-RSA was computed for the subsets' corresponding hippocampal neural patterns. Right: box plot portraying the same data. Each datapoint is a unique subset. Median-centered boxes show 25th and 75th quantiles, whiskers extend to 2nd and 98th quantiles. two-sample two-sided t-test, FDR corrected at $q < 0.05$ for multiple comparisons, $t(198)= -3.21$ $p = 0.0015$ ** $p < 0.01$, *** $p < 0.001$. Refer to Supplementary Table 3 for central tendency measurements for all panels.*

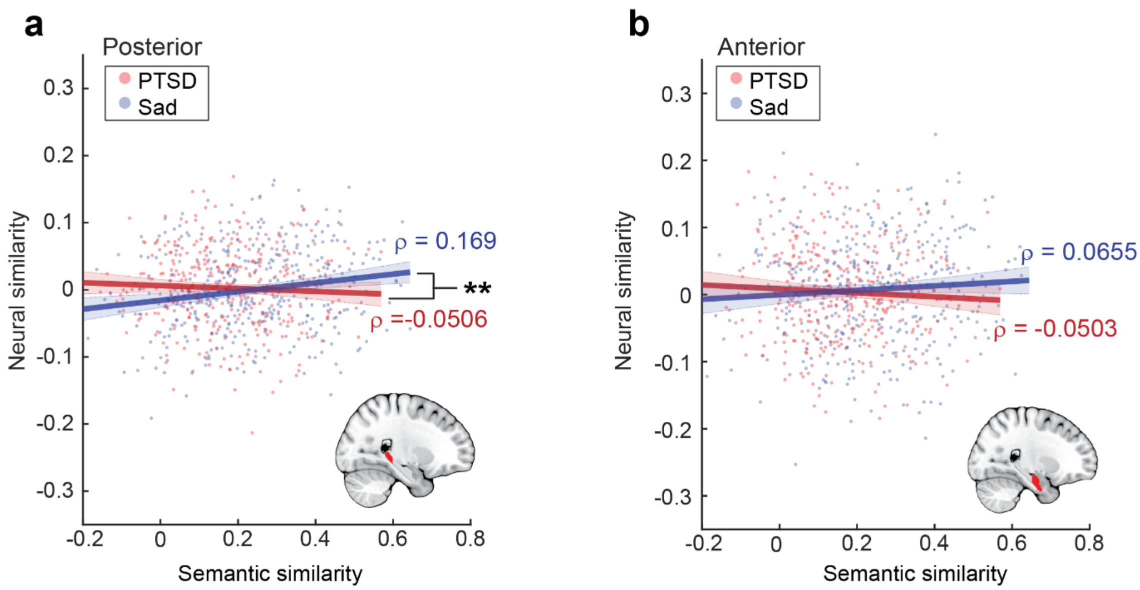
(b) *Same as **a** but for 'Sad' scripts. $t(198)= -3.22$ $p = 0.0015$.*

(c) *Same as **a** but for 'PTSD scripts. $t(198)= 5.09$ $p = 9.21E-07$*

(d) *Same as **a** but showing IS-RSA values computed for posterior cingulate cortex patterns. $t(198)= -8.97$ $p = 6.93E-16$.*

(e) *Same as **d** but for 'Sad' scripts. $t(198)= -13.08$ $p = 8.46E-28$.*

(f) *Same as **d** but for 'PTSD scripts. $t(198)= -7.49$ $p = 4.48E-12$.*

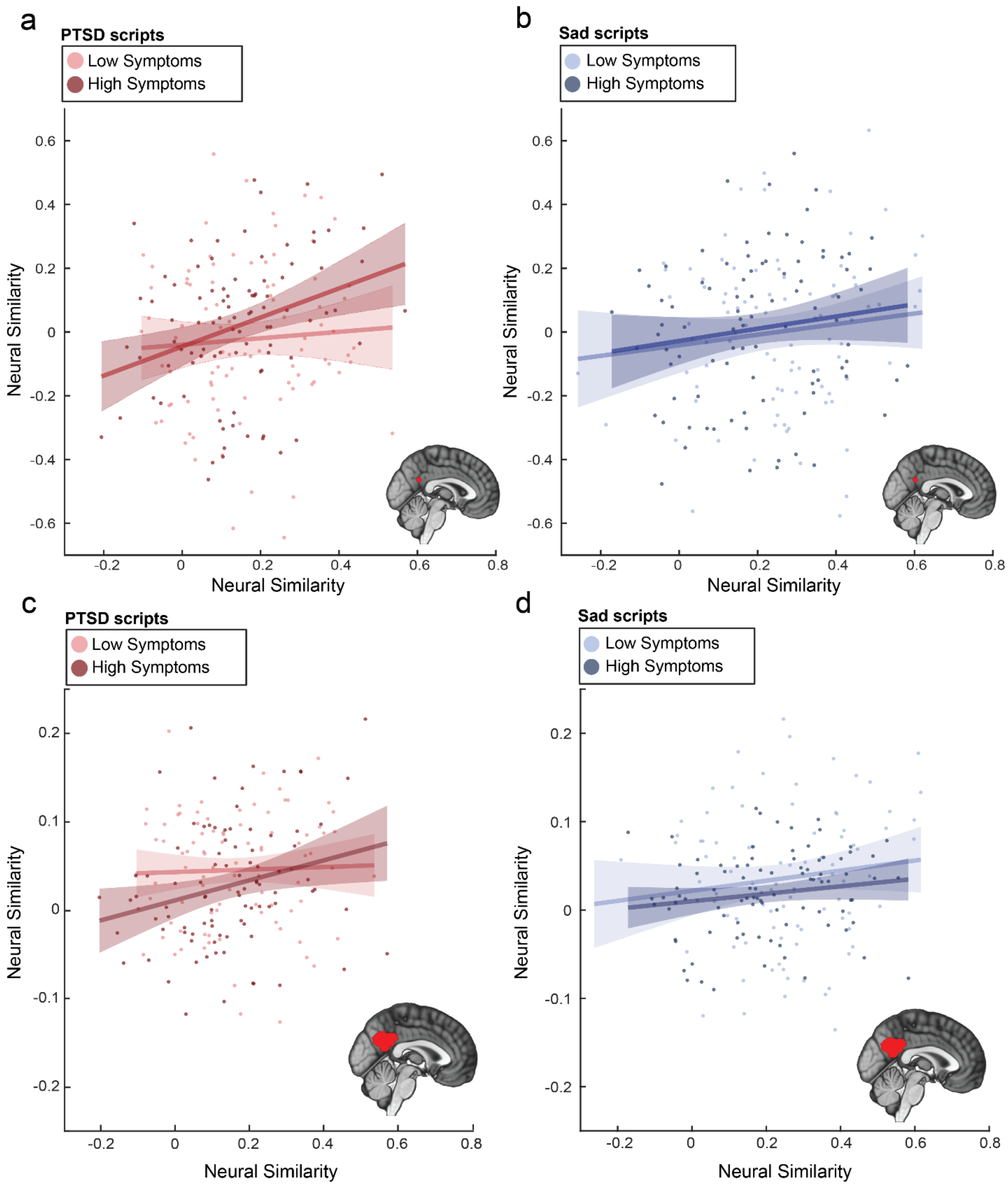



**Supplementary Figure 12 (corresponding to Figure 3):**

***Semantic-to-neural IS-RSA in hippocampal longitudinal parcellation***

*(a)* ***semantic-to-neural IS-RSA in the posterior hippocampus.*** *Intersubject representational similarity analysis conducted on pairwise similarity of semantic content and neural patterns in the posterior hippocampus. Each datapoint is one pairwise comparison. Analysis was iterated per script type ('PTSD': red, 'Sad': blue). Regression lines are approximate visualization of Spearman correlation ρ coefficients for IS-RSA in 'PTSD' and 'Sad' scripts (red and blue resp.). $p = 0.0048$, FDR corrected at $q < 0.05$ for multiple comparisons. Two-sided tests, error bands indicate 95% confidence bounds. ** $p < 0.01$.*

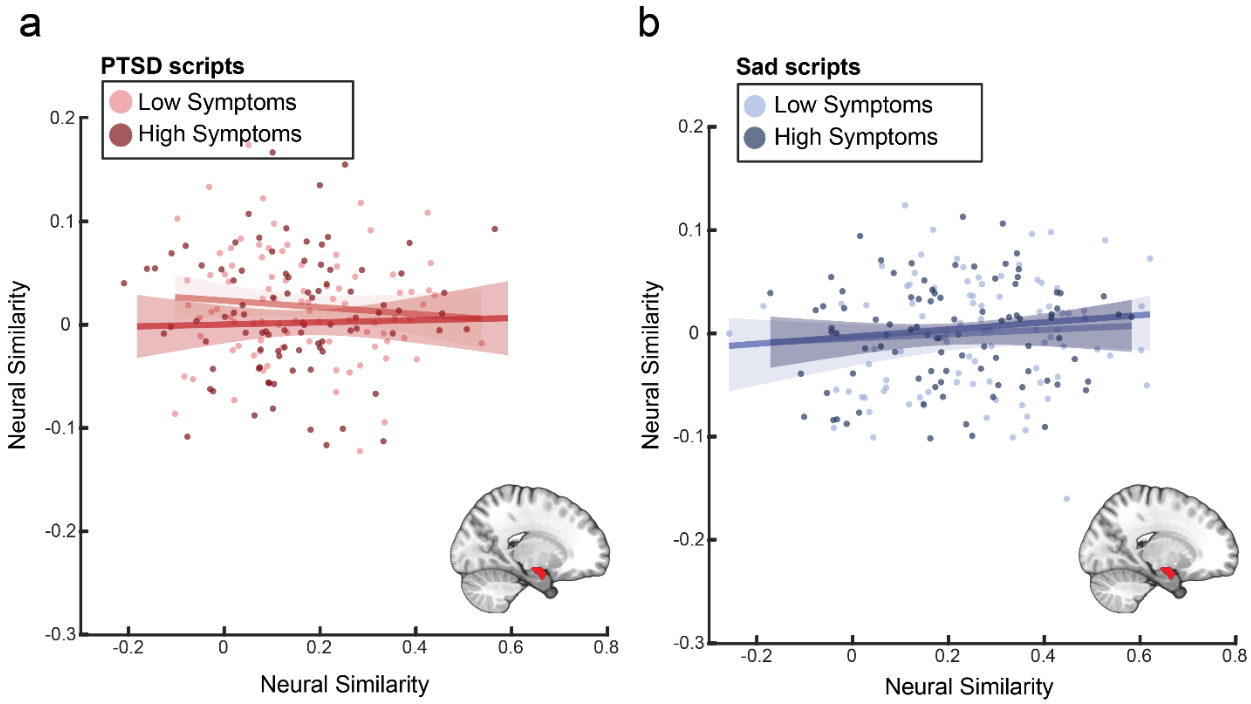
*(b) Same as* ***(a)*** *but for the anterior hippocampus.*


a
PTSD scripts
Low Symptoms
High Symptoms
Neural Similarity
Neural Similarity
b
Sad scripts
Low Symptoms
High Symptoms
Neural Similarity
Neural Similarity
c
PTSD scripts
Low Symptoms
High Symptoms
Neural Similarity
Neural Similarity
d
Sad scripts
Low Symptoms
High Symptoms
Neural Similarity
Neural Similarity

**Supplementary Figure 13 (Corresponding to Figure 5):**

***Semantic-to-neural IS-RSA in additional PCC regions of interest***

- *(a) Intersubject representational similarity analysis in the PCC differed by symptom severity. IS-RSA conducted on pairwise similarity of semantic content of 'PTSD' narratives and neural patterns in the PCC on subgroups differing in symptom severity ('Low' and 'High')***.*** *The PCC ROI was defined using a 4mm sphere located at the center of the anatomical delineation of the PCC. Each datapoint is derived from a pairwise comparison. Analysis was iterated per subgroup. Regression lines are approximate visualization of Spearman correlation ρ coefficients for IS-RSA in 'Low' and 'High' symptoms (light and dark red, respectively). Error bands indicate 95% confidence bounds.*
- ***(b)*** *Same as* ***(a)*** *but conducted on semantic content of 'Sad' narratives and neural patterns in the PCC on subgroups differing in symptom severity ('Low' and 'High' are light and dark blue, respectively).*
- ***(c)*** *Same as* ***(a)*** *but conducted on a PCC ROI defined by the Willlard atlas parcellation.*
- *(d) Same as* ***(b)*** *but conducted on a PCC ROI defined by the Willlard atlas parcellation.*




**Supplementary Figure 14 (Corresponding to Figure 5):**

***Effect of symptom severity on Semantic-to-Neural IS-RSA in amygdala neural patterns***

*(a)* *Intersubject representational similarity analysis on amygdala neural patterns. IS-RSA conducted on pairwise similarity of semantic content of 'PTSD' narratives and neural patterns in bilateral amygdala on subgroups differing in symptom severity ('Low' and 'High'). Each datapoint is derived from a pairwise comparison. Analysis was iterated per subgroup. Regression lines are approximate visualization of Spearman correlation ρ coefficients for IS-RSA in 'Low' and 'High' symptoms (light and dark red, respectively). Error bands indicate 95% confidence bounds.*

*(b)* *Same as* ***(a)*** *but conducted on semantic content of 'Sad' narratives and neural patterns in bilateral amygdala on subgroups differing in symptom severity ('Low' and 'High' are light and dark blue, respectively).*

## Supplementary Tables

| Cluster size (K) | $P_{(FWE\ corrected)}$ <0.05 | X | Y | Z | Name |
|---|---|---|---|---|---|
| 41 | 0.00330 | -42.5 | 25.5 | -8.5 | Left Inferior Frontal Gyrus |
| 19 | 0.00723 | 51.5 | -16.5 | -8.5 | Right Superior Temporal Gyrus |
| 16 | 0.00633 | -58.5 | -30.5 | -0.5 | Left Middle Temporal Gyrus |
| 8 | 0.00293 | -50.5 | -18.5 | -10.5 | Left Middle Temporal Gyrus |
| 6 | 0.00168 | 47.5 | 21.5 | -14.5 | Right temporal pole |

***Supplementary Table 1**: Values from a group t map conducted on a whole-brain GLM contrasting positive- and negative-valence scripts ([‘PTSD’+’Sad’] > ‘Calm’). Listed are all clusters that survived correction at P(FWE corrected) < 0.05. Coordinates are in Talairach space.*

| Index | Race | Ethnicity | Gender | Age | CAPS-5 | Symptom Severity Group | Length of Diagnosis (Years) | Time from Event (Years) | Major Depressive Disorder - Lifetime Prevalence | Major Depressive Disorder - Recurrent | Major Depressive Disorder - Seasonal Pattern | Major Depressive Disorder - Severity at session | Medication |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | White | Hispanic or Latino | M | 51 | 47 | High | 12 | 12 | Yes | Recurrent | No | Moderate | Divalproex, Prazosin, Sertraline |
| 2 | Native Hawaiian or other Pacific Islander | Hispanic or Latino | M | 31 | 26 | Low | 9 | 9 | Yes | N/A | N/A | Moderate | Cymbalta |
| 3 | Black or African American | Non-Hispanic | M | 27 | 42 | High | 2 | 2 | Yes | Single Episode | No | mood-congruent psychotic features | None |
| 4 | White | Non-Hispanic | F | 30 | 37 | Low | 7 | 7 | Yes | Recurrent | No | N/A | Gabapentin, Strattera, Lexapro |
| 5 | White | Non-Hispanic | F | 41 | 34 | Low | 25 | 25 | Yes | Recurrent | No | Severe | Pristiq, Medical marijuana |
| 6 | White | Non-Hispanic | F | 45 | 56 | High | 33 | 33 | Yes | Recurrent | No | Severe | Prozac, Trazodone |
| 7 | White | Non-Hispanic | M | 52 | 42 | High | 6 | 6 | Yes | Recurrent | No | Moderate | None |
| 8 | White | Non-Hispanic | M | 63 | 37 | Low | 1 | 1 | Yes | Recurrent | No | Moderate | Remeron, Seroquel, Abilify |
| 9 | Unknown | Non-Hispanic | F | 34 | 60 | High | 4 | 4 | Yes | Recurrent | No | Severe, | None |
| 10 | White | Non-Hispanic | M | 30 | 38 | Low | 10.5 | 10.5 | Yes | Recurrent | Yes | N/A | Medical marijuana |
| 11 | White | Non-Hispanic | F | 55 | 29 | Low | >1 | 39 | Yes | Recurrent | No | N/A | Bupropion, Hydroxyzine, Pregabalin |
| 12 | Unknown | Unknown | F | 27 | 54 | High | 5 | 5 | Yes | Recurrent | No | Moderate | Lexapro, Gabapentin |
| 13 | White | Non-Hispanic | M | 49 | 46 | High | **9** | 15.5 | Yes | Single Episode | No | Severe | None |
| 14 | White | Non-Hispanic | M | 29 | 40 | High | 4 | 4 | No | N/A | N/A | N/A | None |
| 15 | White | Non-Hispanic | M | 39 | 38 | Low | 15 | 15 | Yes | Recurrent | No | Moderate | Tramadol, Adderall, Nortriptyline |
| 16 | White | Non-Hispanic | F | 27 | 49 | High | 9 | 9 | Yes | N/A | No | Moderate | None |
| 17 | White | Non-Hispanic | M | 37 | 36 | Low | 15 | 15 | Yes | Recurrent | No | Moderate | None |
| 18 | White | Non-Hispanic | M | 38 | 36 | Low | 15 | 15 | Yes | Recurrent | No | Moderate | None |
| 19 | White | Non-Hispanic | M | 30 | 32 | Low | 10 | 10 | Yes | Recurrent | No | N/A | Duloxetine |
| 20 | Asian | Non-Hispanic | F | 27 | 38 | Low | 11 | 14 | Yes | Recurrent | No | N/A | Venlafaxine |
| 21 | White | Non-Hispanic | M | 24 | 34 | Low | 7 | 7 | Yes | Single Episode | No | N/A | None |
| 22 | Black or African American | Non-Hispanic | M | 27 | 59 | High | 8 | 8 | Yes | Recurrent | No | Severe | None |
| 23 | White | Non-Hispanic | M | 42 | 35 | Low | 34 | 34 | Yes | Recurrent | No | N/A | None |
| 24 | White | Unknown | F | 49 | 45 | High | 11 | 11 | Yes | Recurrent | No | Severe | Lorazepam |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 25 | American Indian or Alaska Native | Non-Hispanic | M | 37 | 36 | Low | 11 | 11 | Yes | Recurrent | No | Moderate | None |
| 26 | White | Non-Hispanic | M | 31 | 43 | High | 8 | 8 | Yes | Recurrent | No | Moderate | Fluoxetine |
| 27 | White | Non-Hispanic | F | 48 | 45 | High | 18 | 18 | Yes | Recurrent | No | N/A | Cannabis, Lamictal |
| 28 | White | Non-Hispanic | F | 51 | N/A | High | 3 | 3 | No | N/A | N/A | N/A | Concerta, Lexapro |

***Supplementary Table 2****: Cohort demographics and comorbidities and psychiatric medication.*

| | **Calm** | **Calm** | **Sad** | **Sad** | **PTSD** | **PTSD** |
|---|---|---|---|---|---|---|
| | Lowest Similarity | Highest Similarity | Lowest Similarity | Highest Similarity | Lowest Similarity | Highest Similarity |
| **Hippocampus** | | | | | | |
| Mean | -0.142 | 0.026 | 0.067 | 0.219 | 0.069 | -0.171 |
| STD | 0.338 | 0.401 | 0.337 | 0.330 | 0.309 | 0.349 |
| Min | -1.082 | -0.962 | -0.693 | -0.586 | -0.674 | -1.116 |
| Max | 0.732 | 1.017 | 0.794 | 0.990 | 0.936 | 0.773 |
| | | | | | | |
| **PCC** | | | | | | |
| Mean | -0.305 | 0.055 | -0.044 | 0.513 | -0.051 | 0.382 |
| STD | 0.311 | 0.255 | 0.242 | 0.351 | 0.392 | 0.425 |
| Min | -1.050 | -0.521 | -0.693 | -0.140 | -1.151 | -0.460 |
| Max | 0.553 | 0.674 | 0.490 | 1.639 | 0.861 | 2.200 |

***Supplementary Table 3:*** Central tendency measurements (mean, standard deviation, minimum and maximum values) for IS-RSA correlation coefficients computed for subsets of the ‘Calm’ scripts with lowest- and highest-semantic similarity (N = 100 for each). Measurements are detailed per script type (‘Calm’, ‘Sad’, ‘PTSD’) and region of interest (Hippocampus and posterior cingulate cortex). STD, standard deviation; Min, minimum; Max, maximum; PCC, posterior cingulate cortex.

## References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