Supplemental Information for ‘Salience and Central Executive Networks Track Overgeneralization of Conditioned Fear in Post-Traumatic Stress Disorder’

**Method**

**Participants**

Demographic, psychological, and psychiatric characteristics of participants are reported in Tables S1 and S2. Psychiatric diagnoses other than PTSD were determined via Structured Clinical Interview for DSM-IV (SCID-I) (First *et al.* 1996). The following exclusion criteria were applied: pre-deployment history of Axis I psychopathology; current or past history of bipolar depression, psychosis, or delusional disorders; history of substance abuse or dependence within 6 months of participation; use of antipsychotics, mood stabilizers, anti-parkinsonian agents, anticonvulsants, anti-hypertensives, or alpha/beta adrenergic agents, or inability to refrain from use of as-needed medications such as benzodiazepines, sleep medications or pain medications within 12 hours prior to testing; current Axis 1 psychiatric disorders in trauma controls; significant suicidal ideation or behavior; any medical condition not safe for MRI; major medical conditions; and current illicit drug use. Seven participants (4 PTSD, 2 SubPTSD, 1 TC) were excluded because they did not have conditioned fear responses available for generalization (i.e., perceived risk to CS+ ≤ CS-). Six additional subjects (2 from each group) were removed because of excessive head motion during scanning (absolute displacement >1.5mm during any fMRI run [Wisner *et al.* 2013b; Siegel *et al.* 2014]), reflecting one additional TC and 2 additional SubPTSD subjects than were excluded previously (Kaczkurkin et al., 2017), since current network-based analyses required a more conservative criterion for excessive motion. Final analyses were thus conducted on 20 PTSDs, 19 SubPTSDs, and 19 TCs. The study was approved by IRBs at both the Minneapolis VA and the University of Minnesota, and informed consent was obtained from all participants prior to testing. All participants received reimbursement for their time.

**Generalization Paradigm**

 A previously validated fMRI task designed to assess generalization of conditioned fear (Lissek *et al.* 2014) was applied. As can be seen in Figure 1, stimuli serving as conditioned stimuli (CS: CS+, oCS-) and generalization stimuli (GS: GS1, 2 GS2, 2 GS3) consisted of 5 checkerboard textured rings of parametrically increasing size, and one “V-shaped” stimulus (vCS-) of the same checkerboard texture, all presented on a rear-projection viewing screen mounted to the scanner. The paradigm includes one CS+ and the following two CS-: 1) either the largest or smallest ring, referred to as oCS-, and 2) a “V” shaped stimulus, referred to as vCS-. Extreme sizes served as oCS- and CS+ with big and small sizes of oCS- and CS+ counterbalanced across subjects. The three intermediately-sized rings served as GSs (GS1, GS2, GS3) and formed a continuum-of-size between oCS and CS+. The vCS- was included to test a broader form of generalization in which fear generalizes to all things circular. The unconditioned stimulus (US) was a 100ms electric shock (3-5mA) delivered to the right ankle.

The checkerboard patterned conditioned and generalization stimuli counterphase-flickered at a rate of 10 Hz. Such stimuli were designed to activate the calcarine sulcus along a continuum of visual eccentricity (Murray *et al.* 2006) as part of a longer-range goal to use this generalization paradigm to retinotopically map representations of CSs and GSs in sensory cortex. Important for the purposes of the current paper is the size and shape of these stimuli rather than their retinotopic-mapping characteristics, as retinotopy was unsuccessful in the current study.

*Design*. CSs and GSs were presented for 4s in quasi-random order (ITI=2.4-4.8s), across three phases: 1) *Pre-acquisition:* 20 of each stimulus (CS+, GS1, GS2, GS3, oCS-, vCS-) without shock; 2) *Acquisition:* 15 CS+, 15 oCS-, and 15 vCS-, with 12 of 15 CS+ co-terminating with shock; and 3) *Generalization-test:* 20 of each stimulus (unreinforced CS+, GS1 ,GS2, GS3, oCS-, vCS-), and an additional 10 CS+ co-terminating with shock to prevent extinction during generalization, while leaving 20 unreinforced CS+ to index responses uninfluenced by US.

CS and GS trials for all 3 phases of the study were arranged in quasi-random order such that no more than two stimuli of the same class occurred consecutively. An additional constraint for the generalization sequence was the arrangement of trials into 10 blocks of 13 trials (2 unreinforced CS+, 1 reinforced CS+, 2 oCS-, 2 vCS-, 2 GS1, 2 GS2, 2 GS3) to ensure an even distribution of trial types throughout runs. During all phases, a behavioral task developed to maintain visual gaze at the center of the visual field (Schwartz *et al.* 2005) was applied. This task consists of a stream of colored crosshairs (blue, yellow, red, green, purple) presented serially for a duration of 800 ms each in the center of the screen for the duration of each CS/GS, with 5 crosshairs of different color during each 4 second CS/GS. Participants were instructed to monitor the stream and quickly rate their perceived risk for shock following each red crosshair using a 3-button response pad (Lumina LP-404 by Cedrus), where 0=‘no-risk’, 1=‘moderate-risk’, and 2=‘high-risk’. These online behavioral risk ratings were recorded with Presentation software (Neurobehavioral Systems). For half of CS/GS trials during all 3 phases of the study, 1 of 5 crosshairs was red, and the remaining trials included no red crosshairs (i.e., behavioral ratings were collected on half of trials). Additionally, on reinforced CS+ trials, the red crosshair never appeared in the fourth or fifth position to avoid interference from shock on behavioral responses. Thus, for all stimuli other than shock-reinforced CS+, risk ratings were assessed at either 0 ms, 800 ms, 1600 ms, 2400 ms, or 3200 ms post-stimulus onset, while risk ratings to reinforced stimuli were assessed at 0 ms, 800 ms, or 1600 ms post-stimulus onset.

 *Procedure.* Participants were not instructed of the CS/US contingency but were told they might learn to predict the shock if they attend to the presented stimuli. Shock electrodes were then attached and a shock workup procedure was completed. During this workup, participants received between 1-3 sample shocks, and levels of shock were adjusted to achieve a level rated by participants as ‘highly uncomfortable or mildly painful’. Participants next practiced using the button box to respond to red crosshairs appearing both at the center of CSs and GSs. Participants were then placed in the magnet with foam pads placed to limit head movement. Structural scans were acquired followed by pre-acquisition, acquisition, and generalization.

**Image Acquisition and Pre-Processing**

Functional magnetic resonance imaging (fMRI) acquisition parameters were the same as those reported in Kaczkurkin et al. (Kaczkurkin *et al.* 2017). Briefly, T2\*-weighted echo-planar images (EPIs) of the BOLD signal were collected (TR: 2300 ms; TE: 23 ms; flip: 90°) and consisted of axially-oriented slices of 3.5 mm thickness and 1.745x1.745mm in-plane resolution (matrix: 128Å~128, FOV: 22 cm). T1-weighted anatomical-scans (MP-RAGE) were acquired to serve as anatomical reference. Standard pre-processing was completed using FMRIB Software Library (FSL) and included slice-timing correction for interleaved slice acquisition, motion correction, brain extraction, grand-mean intensity normalization of the 4D data set (all volumes) by the same multiplicative factor, temporal filtering set at 100s, B0 field unwarping, 5-mm FWHM smoothing, and spatial normalization and nonlinear registration to MN152.Motion regression with six parameters, including three rotational and three translational parameters was then conducted**.**

**Selecting and Classifying ICNs of Interest**

Spatial ICA is a well-validated, data-driven approach that decomposes brain activity into a set of spatially independent brain components (i.e., ICNs) and their activity over time. ICNs generated with spatial ICA have been found to have good replicability across samples, reproducibility over time (Wisner *et al.* 2013a), and direct functional interpretations (Smith *et al.* 2009, 2018; Laird *et al.* 2011; Gratton *et al.* 2018). Spatial ICA was applied because (a) the resulting ICNs can overlap spatially, which may more realistically characterize networks than methods generating non-overlapping clusters (Poppe *et al.* 2013; Abram *et al.* 2015), and (b) ICA is able to extract functionally coherent subnetworks instead of simply using one larger network that may have facets that are differentially related to generalization processes.

 ICNs of interest were defined as ICNs that (a) included brain areas found to underlie generalization of PTSD-related overgeneralization, and (b) instantiated a generalization gradient. 17 candidate ICNs meeting the first criterion were identified via visual comparison of prior findings with the thresholded ICN maps. To determine which of the 17 candidate ICNs met the second criterion, event-relatedness of ICN activity was assessed. Specifically, individual-level BOLD activity within each candidate ICN was derived using the first half of a dual regression procedure, where task fMRI data were regressed onto spatial maps of the ICNs to result in subject-specific time-series corresponding to each ICN (Beckmann *et al.* 2009). Next, we regressed the time-course of each candidate ICN onto an ideal response function for each task stimulus (excluding reinforced CS+), generated by convolving the time-course of each stimulus-type onto a gamma variate hemodynamic response function. This provided subject-specific standardized beta coefficients representing the extent to which the time-course of activity in a given ICN was associated with the time-course of a given stimulus. One-way ANOVAs of Stimulus-type (oCS-, GS1, GS2, GS3, CS+) were conducted for each candidate ICN, and ICN responding across stimuli was visually inspected, to assess the extent to which each candidate ICN coded for generalization elicited by the task. Only ICNs that showed a gradual positive or negative slope as stimuli increased in similarity to the CS+ were considered to code for generalization. Eight ICNs met both criteria and were selected as ICNs of interest.

**Analyses**

Group differences in behavioral and neural responses were analyzed with 3 (Group: TC, SubPTSD, PTSD) x 5 (Stimulus-type: oCS-, GS1, GS2, GS3, CS+) repeated-measures ANOVAs. Because these analyses may not adequately detect important gradient-shape differences across any two subject groups, Group x Stimulus-type ANOVAs were also computed with group defined as PTSD vs. TC, Sub-PTSD vs. TC, and PTSD vs. SubPTSD. Given the disadvantages of dichotomizing continuous variables, we additionally tested the continuous effects of PTSD symptom severity on behavioral and neural responding by analyzing CAPS x Stimulus-type interactions using repeated measures ANOVAs with stimulus-type entered as the independent variable and CAPS scores entered as a covariate. Group x Stimulus-type and CAPS x Stimulus-type interactions were followed by tests of linear and quadratic trends in light of previously found patient-control differences in these components of generalization gradients (Lissek *et al.* 2010; Kaczkurkin *et al.* 2017). Additionally, to identify specific stimuli to which behavioral and neural responses generalized for each group, Hochberg-corrected (Hochberg 1988) paired-sample *t*-tests were computed for each group to compare responses to CS+ and GSs against oCS- for positive generalization gradients, and responses to oCS- and GSs against CS+ for negative gradients.

***Effects of symptom severity on the steepness of generalization gradients.***Significant Group x Stimulus-type and CAPS x Stimulus-type interactions were followed by tests of relations between the steepness of generalization gradients (i.e., generalization magnitudes) and PTSD symptom severity across all participants (*N* = 71). To this end, we correlated CAPS scores with linear deviation scores (LDS (Lissek *et al.* 2014)), reflecting the degree to which subject-level gradients departed from linearity. For positive gradients, LDS = ([GS1, GS2, GS3] ∕3) – ([CS+, CS-] ∕2)); for negative gradients, LDS = ([CS+, CS-] ∕2)) – ([GS1, GS2, GS3] ∕3). Here, [CS+, CS-] ∕2 reflects the theoretical, linear midpoint of the gradient, and [GS1, GS2, GS3] ∕3 reflects the average response to GSs which could fall above the linear midpoint (positive departure), on the linear midpoint (zero departure), or below the linear midpoint (negative departure). This equation thus provides a single number reflecting the steepness of generalization gradients, with more positive versus negative values indicating stronger versus weaker generalization. For all analyses of neural responding, absolute and relative mean framewise displacement (Jenkinson *et al.* 2002) were included in the models as covariates.

 ***Between-network analyses*.**  To test hypotheses that generalization in SN would be correlated with generalization in CEN and DN, magnitudes of generalization (i.e., LDS) for each ICN representing SN were correlated with magnitudes of generalization in ICNs representing CEN and DN. To test predictions of increased SN-CEN and reduced negative SN-DN associations during generalization with increasing PTSD symptom severity, hierarchical regressions were conducted to test the moderating effect of CAPS scores on relations between magnitudes of generalization (i.e., LDS) in SN and CEN as well as SN and DN. For these analyses of between-network group effects, only ICNs showing significant within-network group effects were included to reduce problems associated with multiple comparisons. Of note, these analyses did not directly assess functional connectivity or its relationship to PTSD.

**Results**

**Behavioral Results at Acquisition**

 Online risk ratings were greater to the CS+ versus oCS- and vCS- (*p*s<.001). No main effects of group or Group x Stimulus-type interactions were found (*p*s>.134).

**Quadratic Effects of CAPS on the Steepness of ICN Gradients of Generalization**

Bilateral-SN and Bilateral-CEN showed significant or trend-level Group by Stimulus-type interactions with group defined as PTSD versus TC (*p*’s<.075), but not with group defined by SubPTSD versus PTSD (*p*s>.213; Table 3). This pattern of results raises the possibility that increases in neural gradients of generalization from TC to SubPTSD to PTSD form quadratic rather than linear increases. To test this, the six significant correlations between magnitudes of generalization in ICNs and CAPS scores (see Figure 4) were followed by tests of the quadratic fit of CAPS, via regressions in which CAPS and mean-centered squared CAPS were entered as predictors of generalization magnitudes for each of these 6 ICNs. The quadratic fit of CAPS was non-significant for both linear deviation scores in bilateral-SN, bilateral-CEN, or right-CEN, and broad generalization scores in left-CEN, dorsal-striatum and striatum/thalamus (all *p*s>.14). The significant linear but not quadratic effects of CAPS on levels of generalization in these 6 ICNs indicate that levels of generalization in ICNs representing SN and CEN linearly strengthen with increasing levels of PTSD symptom severity.

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Table S1. Sample characteristics.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | PTSD (*n*=20) | SubPTSD (*n*=19) | TC(*n*=19) |  |
| *Mean* | *SD* | *Mean* | *SD* | *Mean* | *SD* | *p* |
| Age | 33.50 | 9.63 | 36.05 | 9.26 | 33.32 | 10.01 | .620 |
| Education | 5.10 | 1.07 | 5.11 | 1.56 | 5.21 | 1.62 | .964 |
| STAI-State | 17.75 | 8.10 | 12.95 | 7.75 | 9.58 | 7.52 |  <.001\*\*\* |
| STAI-Trait | 47.60 | 11.81 | 43.00 | 11.05 | 33.21 | 9.44 |  .005\*\* |
| BDI | 50.45 | 10.45 | 44.89 | 12.31 | 37.89 | 11.54 |  .007\*\* |
| CAPS-Total | 59.60 | 15.17 | 32.00 | 7.57 | 14.05 | 6.56 |  <.001\*\*\* |
| CAPS-B | 16.55 | 7.02 | 8.63 | 2.75 | 2.89 | 2.28 |  <.001\*\*\* |
| CAPS-C | 21.25 | 6.48 | 10.26 | 3.09 | 3.95 | 3.19 |  <.001\*\*\* |
| CAPS-D | 21.80 | 5.15 | 13.63 | 4.86 | 7.21 | 4.94 |  <.001\*\*\* |
|  |  |  |  |  |  |  |  |
| Ethnicity | *N* | % | *N* | % | *N* | % |  |
|  African American | 2 | 10.0 | 1 | 5.3 | 1 | 5.3 | -- |
|  Caucasian | 18 | 90.0 | 18 | 94.7 | 16 | 84.2 | -- |
|  Hispanic | 0 | 0 | 0 | 0 | 0 | 0.0 | -- |
|  Asian Pacific | 0 | 0 | 0 | 0 | 1 | 5.3 | -- |
|  Other | 0 | 0 | 0 | 0 | 0 | 0 | -- |

SubPTSD = subthreshold PTSD; TC = trauma controls; CAPS=Clinician Administered PTSD Scale for the DSM-IV; CAPS-B=Re-experiencing subscale; CAPS-C = Avoidance/Numbing subscale; CAPS-D = Hyper-arousal subscale; STAI=State-Trait Anxiety Inventory. *p*-values reflect results of one-way ANOVAs on Group (PTSD, SubPTSD, TC). \**p*<.05; \*\**p*<.01; \*\*\**p*<.001.

Table S2. Psychiatric diagnosis and current use of psychotropics.

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | PTSD(*n*=20) | SubPTSD (*n*=19) | Trauma Control(*n*=19) |
| *N* | % | *N* | % | *N* | % |
| PTSD diagnosis |  |  |  |  |  |  |
|  Delayed onset |  1 |  5.00  |  3 |  14.00 |  0 | 0.00 |
|  Chronic | 19 |  95.00 | 19 | 100.00 |  0 | 0.00 |
| Fear/horror/helplessnessa | 20 | 100.00 | 18 |  94.70 | 13 |  68.40 |
| Current diagnoses |  |  |  |  |  |  |
|  Depressive disorder |  5 |  25.00 |  2 |  10.53 |  0 | 0.00 |
|  GAD |  2 |  10.00 |  0 |  0.00 |  0 | 0.00 |
|  Anxiety disorder NOS |  1 |  5.00 |  2 |  10.53 |  0 | 0.00 |
|  Sub abuse/depend |  0 |  0.00 |  0 |  0.00 |  0 | 0.00 |
| Past diagnoses |  |  |  |  |  |  |
|  Depressive disorder | 10 |  50.00 |  7 |  36.84 |  4 |  21.05 |
|  GAD |  0 |  0.00 |  0 |  0.00 |  0 |  0.00 |
|  Anxiety disorder NOS |  1 |  5.00 |  0 |  0.00 |  1 |  5.26 |
|  Sub abuse/depend | 14 |  70.00 |  9 |  47.37 |  9 |  47.37 |
| Current psychotropics |  |  |  |  |  |  |
|  Antidepressant |  4 |  20.00 |  3 |  15.79 |  1 |  5.26 |

aNumber of participants endorsing fear/horror/helplessness during combat-related trauma via the

Clinician-Administered-PTSD-Scale for the DSM-IV. PTSD = posttraumatic stress disorder; GAD =

generalized anxiety disorder; NOS = not otherwise specified; Sub abuse/depend = substance abuse or dependence.

Table S3. ICNs generating responses that fell along generalization gradients.

|  |  |  |
| --- | --- | --- |
| Label | Brain Areas |  Wilks’ λ |
| 1. Bil-SN
 | * L and R AI (BA13), temporal pole (BA38)
* ACC (BA32, BA24), frontal pole, middle frontal gyrus (BA9), superior frontal gyrus
 |  17.658\*\*\* |
| 1. DS
 | * caudate body
* medial thalamus
* putamen
 |  4.086\* |
| 1. S/T
 | * caudate body
* medial thalamus
* nucleus accumbens
* L AI (BA13)
 |  5.532\*\* |
| 1. Bil-CEN
 | * OFC (BA46, BA47), frontal pole (BA9), inferior frontal gyrus (BA44, BA45), AI (BA13)
* superior frontal gyrus (BA8)
* middle temporal gyrus (BA37)
 |  13.563\*\*\* |
| 1. R-CEN
 | * AI, R dmPFC, R dlPFC (BA9), R frontal pole (BA10)
* R IPL, middle temporal gyrus
 |  9.171\*\*\* |
| 1. L-CEN
 | * TPJ, supramarginal gyrus (BA40)
* ACC (BA24)
* L middle frontal gyrus (BA9)
* precentral gyrus (BA6), L central opercular cortex
* lateral occipital cortex (BA19)
 |  4.841\* |
| 1. P-DN
 | * Pc, PCC, angular gyrus (BA39)
* superior frontal gyrus (BA8)
* middle temporal gyrus (BA36, BA37)
 |  10.265\*\*\* |
| 1. A-DN
 | * vmPFC (BA10, BA32), ACC (BA24)
* PCC (BA23, BA30)
 |  5.631\*\* |

Wilks’ lambda (λ) derived from one-way ANOVAs on stimulus type (oCS-, GS1, GS2, GS3, CS+). Brain areas that exceeded the threshold *z/zmax>*.30 for a given ICN are listed; brain areas are bilateral unless otherwise specified. L = left; R = right; Bil = bilateral; BA=Brodmann’s area; SN = salience network; DS = dorsal striatum, S/T = striatum and thalamus; CEN = central executive network; P-DN = posterior default network, A-DN = anterior default network; AI=anterior insula; ACC=anterior cingulate cortex; TPJ=temporoparietal junction; dmPFC=dorsomedial prefrontal cortex; OFC=orbitofrontal cortex; dlPFC=dorsolateral prefrontal cortex; IPL=intraparietal lobule; Pc=precuneus; PCC=posterior cingulate cortex; vmPFC=ventromedial prefrontal cortex. \**p*<.05; \*\**p*<.01; \*\*\**p*<.001.

Table S4. Relations between strength of generalization in the salience (X) and central executive networks (Y), and moderating effects of PTSD symptom severity (CAPS-Total) on such relations.

|  |  |  |
| --- | --- | --- |
|    X |    |  Moderation of X-Y Relations  by CAPS  |
| *R* | *R2* | *ΔR2* | *F* for *ΔR2* |
| Bil-SNa  | Bil-CENa**Y** |  .516\*\*\* | .341 | .051 |  4.209\* |
| DSb | Bil-CENa | .136 | .114 | .010 | 0.600 |
| S/Tb | Bil-CENa | .230 | .152 | .026 | 1.624 |
| Bil-SNa | R-CENa | .229 | .210 | .082 |  5.618\* |
| DSb | R-CENa | -.046 | .192 | .043 | 2.843 |
| S/Tb | R-CENa |  .347\*\* | .187 | .002 | 0.134 |
| Bil-SNa | L-CENb |  .291\* | .394 | .015 | 0.963 |
| DSb | L-CENb |  .404\*\* | .199 | .002 | 0.158 |
| S/Tb | L-CENb |  .359\*\* | .186 | .001 | 0.056 |

Pearson’s correlation (*R*) reflects relations between X (salience network: SN) and Y (central executive network). Moderation results were produced by hierarchical regression models testing moderating effects of PTSD symptom-severity on relations between X and Y. CAPS = Clinician Administered PTSD Scale; *ΔR2* = change in *R2*; Bil-SN = bilateral salience network; DS = dorsal striatum, S/T = striatum and thalamus; Bil-CEN = bilateral central executive network; R-CEN = right-sided central executive network; L-CEN = left-sided central executive network. aLevels of generalization indexed by linear deviation score: ([GS1, GS2, GS3] ∕3) – ([CS+, oCS-] ∕2) . bLevels of generalization indexed by broad generalization: ([oCS-, GS1, GS2, GS3]/4) – (CS+). \**p*<.05; \*\**p*<.01; \*\*\**p*<.001.

Table S5. Relations between strength of generalization in SN (X) and DN (Y)

and moderating effects of PTSD symptom severity (CAPS-Total) on such relations.

|  |  |  |
| --- | --- | --- |
|   X |   Y |  Moderation of X-Y Relations  by CAPS |
| *R* | *R2* | *ΔR2* | *F* for *ΔR2* |
|  Bil-SNa | P-DNa | .088 | .025 | .013 | 0.706 |
|  DSb | P-DNa | -.114 | .065 | .052 | 3.020 |
|  S/Tb | P-DNa | -.007 | .047 | .018 | 1.034 |
|  Bil-SNa | A-DNa |  -.425\*\* | .193 | .006 | 0.425 |
|  DSb | A-DNa | -.177 | .098 | .043 | 2.600 |
|  S/Tb | A-DNa | -.094 | .193 | .016 | 1.087 |

Pearson’s correlation (*R*) reflects relations between X (salience network: SN) and Y (default network). Moderation results produced by hierarchical regression models testing moderating effects of PTSD symptom severity on relations between X and Y. CAPS = Clinician Administered PTSD Scale; *ΔR2* = change in *R2*; Bil-SN = bilateral salience network; DS = dorsal striatum, S/T = striatum and thalamus; P-DN = posterior default network; A-DN = anterior default network. aLevels of generalization measured by linear deviation score: ([GS1, GS2, GS3] ∕3) – ([CS+, CS-] ∕2). bLevels of generalization measured by broad generalization: ([oCS-, GS1, GS2, GS3]/4) – (CS+). \*\**p*<.01.



*Figure S1*. Bivariate relations between magnitudes of generalization and PTSD symptom severity (CAPS-Total) across all subjects (*N*=58). (A) Scatterplots for three ICNs (bilateral-SN, bilateral-CEN, right-CEN) showing increased generalization with increasing PTSD severity. Here the strength of generalization was indexed via linear deviation scores (LDS: ([GS1, GS2, GS3] ∕3) – ([CS+, CS-] ∕2) with larger LDS scores indicative of greater generalization. (B) Scatterplots for ICNs evidencing increased broad generalization in PTSD (left-CEN, dorsal-striatum, striatum/thalamus) for which strength of generalization was indexed via broad generalization scores ([oCS-, GS1, GS2, GS3]/4) – (CS+). CAPS=Clinician Administered PTSD Scale. bilateral-SN = bilateral salience network; bilateral-CEN = bilateral central executive network; R-CEN = right-sided central executive network; L-CEN = left-sided central executive network; \**p*<.05; \*\**p*<.01.



*Figure S2*. Correlations depicting the strength of relations between levels of generalization in SN and CEN for trauma control (TC), subthreshold PTSD (SubPTSD), and PTSD groups separately. Magnitudes of generalization are indexed via linear deviation scores (LDS: ([GS1, GS2, GS3] ∕3) – ([CS+, CS-] ∕2). Bil-SN = bilateral salience network; Bil-CEN = bilateral central executive network; R-CEN = right-sided central executive network. \*\**p*<.01.