SUPPLEMENTAL INFORMATION

Continuous Theta Burst Stimulation to the Right Dorsolateral Prefrontal Cortex May Increase Potentiated Startle in Healthy Individuals

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Supplemental Methods

Participants

Thirty-four right-handed participants between the ages of 18 and 50 were recruited from the Philadelphia, PA, metropolitan area to take part in this study. Exclusion criteria included: current or past Axis I psychiatric disorder(s) as identified with the Structured Clinical Interview (SCID) for DSM-IV, non-patient edition (1), use of psychoactive medications, any significant medical or neurological problems (e.g. cardiovascular illness, respiratory illness, neurological illness, seizure, etc.), and any MRI/TMS contraindications (e.g. implanted metal, history of epilepsy or seizure, etc.). For a complete list, see: www.clinicaltrial.gov (Identifier: NCT03993509).

A total of 28 participants completed the study (21 females, 7 males, mean age = 26.61 years, SD = 7.04). Six consented subjects were excluded from the final sample (2 screen failures; 1 pilot subject; 3 subjects withdrew [2 due to scheduling, 1 withdrew during consent]). All participants signed an informed consent form, and the protocol was approved by the Institutional Review Board for human subject research at the University of Pennsylvania. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

General Procedure

The basic procedure can be seen in Figure 1A. Subjects completed 8 study visits over the course of 4 weeks. During Week 1, subjects completed an intake/pre-test visit that included the consent, screening questionnaires, the No-shock, predictable-shock, unpredictable-shock (NPU) task, and the Sternberg task. They also completed a targeting session in the MRI scanner that

included structural, resting state, and task fMRI runs. During Weeks 2 and 4, subjects completed 2 days (2 sessions per day) of either active or sham cTBS. The order of the visits was counterbalanced across subjects. They also completed a post cTBS testing session 24 hours after the final cTBS session that included the NPU and Sternberg WM tasks.

Consent visit

Consent visit procedure. Subjects began by completing the informed consent form. They then completed the MRI safety form, the TMS adult safety screen (TASS) (2), a medical history questionnaire, a demographics questionnaire, the State/Trait Anxiety Inventory (STAI) (3), the Beck Anxiety Inventory (BAI) (4), Montgomery–Åsberg Depression Rating Scale (MADRS) (5), and an eligibility checklist. Afterward the study coordinator administered the SCID (1). Participants that met screening criteria then completed the pre-stimulation test visit procedure.

Test visits

Test visit procedure. The coordinator began the test visit by cleaning and preparing the skin for electrode placement. Then, electrodes for the blink recording, EDA recording, and shock delivery were attached and tested. Next a startle habituation task was completed, followed by a shock workup procedure. Once this initial setup was complete, the subjects completed 2 runs of the NPU threat task and 2 runs of the Sternberg+threat WM task.

NPU. During each test visit, subjects had 2 runs of the NPU task (Figure 1B). Each run consisted of alternating blocks of neutral (no shock), predictable (at risk for shock only during cue), and unpredictable blocks (at risk for shock throughout) conditions (6–8). Predictable and Unpredictable blocks were always separated by a neutral block to yield the following two block orders: **NPNUNUNP, NUNPNPNU**. Subjects were informed of the contingencies prior to the

task, and the block type was displayed at the top of the screen. Each block contained "cue" and intertrial interval ("ITI") trials where a white noise probe was presented during the presence or absence of a visual cue. Cues were (8 s) simple colored (orange, teal, and purple) shapes (triangle, square, and pentagon), and the color and shape were varied across conditions. Each of the 4 Neutral blocks had 2 trials per conditions, while Predictable (x2) and Unpredictable (x2) blocks had 4 trials per condition for a total of 8 trials per condition per run. Three shocks were presented during each run at random points during either the cue (predictable condition) or the ITI (unpredictable condition). Subjects rated their anxiety from 0 (not anxious) to 10 (extremely anxious) throughout the task using an onscreen numerical scale.

Sternberg+threat WM task. Following the NPU task, subjects completed 2 runs of the Sternberg+threat WM task (Figure 1C). The task consisted of a series of WM trials presented during safe (no shock) and threat (shock at any time) conditions, designed to also test the effects of arousal on WM performance. Subjects were informed of the contingencies prior to the task, and were shown a blue circle during safe blocks. Each trial started with an instruction keyword to indicate the trial type. Next, subjects viewed a series of 5 letters, presented sequentially. They then retained them in working memory for a brief interval, and then gave a forced choice response during a subsequent response prompt. On "maintain" trials, subjects rehearsed the letters in the order that they were presented. On "sort" trials, subjects rearranged the letters in alphabetical order. When prompted with a letter/number combination, subjects indicated with a button press whether the position of the letter in the series matched the number. Half of the trials were matches, half were mismatches. The duration of the letter series (1.5 – 2.5 s), retention interval (6.5 – 8.5 s), and ITI (5 – 8 s) were jittered across trials. The duration of the instructions (1 s) and response prompt (3 s) were fixed. Two shock trials were presented during each run at

random points during the threat periods. Importantly, these "shock trials" were added to the design, and subsequently discarded from the analysis. Safe and threat blocks alternated and there were 2 of each block type per run. There were 3 trials per condition per block for a total of 6 trials per condition per run. Block order was counterbalanced across run.

White noise. During the NPU task, subjects received periodic 40-ms, 103-dB white noise presentations with an instantaneous rise time. Noises were delivered via standard over-the-ear headphones (Sennheiser HD280PRO, Sennheiser electronic GmbH & Co., Wedemark, Germany) (9).

Startle Habituation. Prior to the NPU task, subjects received 9 unsignaled whitenoise presentations spaced at approximately ~17 s intervals.

Electromyography. Facial electromyography (EMG) was recorded from the left orbicularis oculi muscle at 2000 Hz using a Biopac MP160 unit (Biopac; Goleta, CA) via 15 × 20 mm hydrogel coated vinyl electrodes (Rhythmlink #DECUS10026; Columbia, SC).

EMG processing. EMG data were processed using the `analyze_startle` package developed by Dr. Balderston (https://github.com/balders2/analyze_startle). Data were bandpass filtered from 30 to 300 Hz, rectified, and smoothed using a 20-ms sliding window. Startle responses were extracted from the timeseries and scored as the peak (max during the 20 ms to 120 ms post-noise window) – the baseline (50 ms pre-noise window). Raw startle responses were converted to t-scores (tx = [Zx × 10] + 50). Trials with excess noise (baseline SD > 2x run SD) were excluded. Trials with no detectable blink (peak < baseline range) trials were coded as 0.

Anxiety Ratings. Anxiety ratings were continuously recorded during the NPU task and extracted for analysis at the moment just prior to each white noise presentation.

Shock. Shocks were delivered to the left wrist via disposable 11 mm Ag/AgCl electrodes

(Biopac Item number EL508; Goleta, CA), spaced ~2 cm apart. The shock stimulus was a 100 ms train of 2 ms pulses delivered at 200 Hz using a using a constant current stimulator (Digitimer #DS7A, Ft. Lauderdale, FL). Shock intensity was calibrated prior to each testing session using an individualized thresholding procedure. Subjects rated each shock on a scale from 1 (not uncomfortable) to 10 (uncomfortable but tolerable), and shocks were delivered throughout the experiment at the level that subjects rated as their level 10.

Targeting visit

Targeting visit procedure. Subjects arrived at the scanner and were cleared by the scanning technician or PI to enter the scan room. They were given ear plugs, a button box, an emergency squeeze ball, and padding to minimize head movement. A pulse oximeter and respiration belt were also attached. Once setup was complete, structural scanning was completed from start to finish without intervention. Subjects then completed 1 run of the Sternberg WM task, followed by 2 resting state runs.

Sternberg WM task. During the targeting visit, subjects completed a single run of the Sternberg WM task, while fMRI was recorded. Subjects were explicitly informed that no shock would be administered during this targeting run of the Sternberg WM task. There were 12 trials each for the sort and maintain conditions. All other aspects of the task were similar to the Sternberg+threat task.

Scans. MRI data was acquired on a 3 Tesla Siemens Prisma scanner with a 64 channel head coil (Erlangen, Germany). We acquired a T1-weighted MPRAGE (TR = 2200 ms; TE = 4.67 ms; flip angle = 8°) with 160, 1 mm axial slices (matrix = 256 × 256; field of view (FOV) = 240 mm × 240 mm). We acquired a T2-weighted image (TR = 3200 ms; TE = 563 ms; flip angle = variable) with 160, 1 mm sagittal slices (matrix = 256 mm × 256 mm;

FOV = 240 mm × 240 mm). For each task and rest run, we acquired 615 whole-brain BOLD images (TR = 800 ms; TE = 37 ms; flip angle = 52°; Multi-band acceleration factor = 8) comprised of 72, 2 mm axial slices (matrix = 104 × 104; FOV = 208 mm × 2008 mm) aligned to the AC-PC line.

fMRI Pre-processing. Task data were processed using the afn_proc.py script distributed with the AFNI software package (10), with the following preprocessing blocks: `tshift`, `align`, `volreg`, `blur`, `mask`, `scale`, `regress`. Prior to timeseries regression, 1) the images were slice time corrected, 2) the EPI data were aligned to the T1 data using an Local Pearson Correlation cost function, 3) individual images were registered to the image with the fewest outliers, 4) images were blurred with a 2 mm Gaussian kernel, 5) they were masked using the intersection of the EPI brain mask and the skull-stripped T1, 6) they were scaled so the mean of the run was 100. The subject-level timeseries regression included regressors of no interest corresponding to the 6 primary motion vectors and their derivatives, and a set of polynomial regressors to model the baseline. Additionally, the first 4 TRs and TRs with greater than 0.5 mm displacement or greater than 15% of voxels registered as outliers were scrubbed from the timeseries prior to the regression.

Head modeling. Finite element models representing the head and coil geometries were created with the SimNIBS software package (Version 2.1) using the T1 and T2 scans (11). Images were first segmented into tissue compartments (i.e. scalp, skull, CSF, gray matter, and white matter), then meshed using a Gmsh subroutine (12).

Target localization. The effect of working memory manipulation (i.e. sort > maintain) from the Sternberg WM paradigm was used to identify the target coordinates for each subject (55). Results were first masked with a functional right dlPFC ROI, which was defined using a

group-level functional ROI from a previous study using the same Sternberg WM task to account for variability in the single subject fMRI data (Figure 2A) (25,63). Coordinates for this target site were then projected to the scalp using a nearest neighbor search (Figure 2B).

E-field calculations. E-field models were conducted at 24 evenly spaced orientations centered on the scalp target. The roll and pitch of the coil model were defined tangent to the scalp surface. The yaw of the coil model was varied by 15 degrees from one orientation to the next. The magnitude of the E-field was then averaged within the right dlPFC ROI, and the yaw orientation corresponding to the maximal E-field within this ROI was used for stimulation (Figure 2C) (55,63).

TMS visits

TMS visit procedure. Subjects began the TMS visit by affirming their previous answers to the TASS, and acknowledging any potential changes. The coordinator then secured the neuronavigation sensors using a swimcap and attached the e-stim electrodes. The subject was then registered to their MRI in Brainsight. On the first TMS visit, subjects resting motor threshold (RMT) was obtained (specifications below). Next the subject completed the remaining TMS visit procedures in the following order: Sternberg WM task (pre stim run), cTBS (specifications below), Sternberg WM task (post stim run). They were given a 30 min break and the TMS visit procedures (Sternberg WM task [pre stim run], cTBS, Sternberg WM task [post stim run]) were repeated.

Sternberg WM task. During the TMS visits, subjects completed short runs of the Sternberg WM task before and after cTBS administrations. Like in the targeting session, subjects were explicitly informed that no shock would be administered during the runs, and no shock electrodes were connected to the subject. There were 4 trials each for the sort and maintain

conditions pre run. All other aspects of the task were similar to the targeting session run.

Active stimulation. A Magventure MagPro 100X stimulator with a B65AP (active/placebo) figure-8 coil was used for the cTBS sessions. The active and sham coil sides of the coil were masked and assigned blinded labels (e.g. A = active, B = sham). The label key was maintained by a member of the study staff not directly involved in the collection or analysis of the data. All other study staff were blinded to the label assignments.

Sham stimulation. The placebo side of the B65AP has the same visual characteristics as the active side, but has an internal magnetic shield that limits the output to < 5% of the active side. Active sham electric stimulation was delivered concurrent with each TMS pulse to allow for a similar sensation across active and sham sessions. Importantly, the sham e-stim pulse was titrated to match the TMS sensations for each participant. The pulse was delivered to the scalp adjacent to the stimulation site via 15 × 20 mm hydrogel coated vinyl electrodes (Rhythmlink #DECUS10026; Columbia, SC). These electrodes were connected to the e-stim system via one of two identical cables allowing the operator to deliver either real or sham electrical stimulation. Cables were assigned blinded labels to match the corresponding coil side so that each session always included either active TMS or active e-stim, but never both.

Motor threshold determination. Each participant's RMT was determined using EMG recordings from the first dorsal interosseous muscle (FDI) and the adaptive parameter estimation by sequential testing (PEST) algorithm (15). Because the MT procedure required active stimulation, a separate B65 coil was used. Importantly, this coil was calibrated against the B65AP coil to ensure comparable output.

cTBS parameters. During each cTBS session, a single 600 pulse cTBS train was delivered during each stimulation session at 100% of RMT. The train consisted of 50 Hz bursts,

repeated at intervals of 200 ms (5 Hz) for 40 sec.

Neuronavigation. We used the Brainsight (Rogue Research Inc, Montreal, Canada) frameless stereotaxic neuronavigation system for neuronavigation. Prior to the cTBS sessions, target coordinates and orientation vectors were loaded into Brainsight along with the subject's reconstructed T1 image. Scalp and cortical surfaces were generated from the T1. During the visits, the subject's head was co-registered to the T1 using fiducial points at the nasion and tragi, and 50 – 100 refinement points distributed across the scalp. TMS pulses were delivered to the target at the E-field optimal orientation, and the accuracy of this targeted stimulation was monitored and tracked by the Brainsight software.

Analysis

Sample size determination. We expected a moderate effect size of (f=0.5) (8, 16). We set power at 0.8 and used a corrected two-tailed alpha of 0.025 (each tail) which suggested a sample of 26 subjects to detect a main effect.

Targeting session whole-brain BOLD. In addition to the a priori ROI analysis based on the dlPFC mask used for targeting, we also conducted a confirmatory voxelwise analyses at the whole-brain level. We extracted first-level GLM betas corresponding to the retention interval and performed a paired-sample t-test using the AFNI program `3dttest++`. We used the standard cluster-based thresholding procedure implemented in the AFNI program `3dClustSim` (17) with a t-tailed voxelwise p-value of 0.001, a non-Gaussian (i.e. autocorrelation function) (18) estimation of the smoothness of the BOLD data, and clusters defined as thresholded voxels with adjoining faces or edges. Running 10,000 Monte Carlo simulations with these parameters resulted in a minimum cluster size of 33, 2-mm isotropic voxels.

Targeting session performance and dlPFC BOLD. For performance, percent correct

and reaction time were calculated for the sort and maintain trials. For dlPFC BOLD, first-level GLM betas corresponding to the retention interval were extracted from the voxels within the dlPFC targeting mask. Paired sample (Sort > Maintain) t-tests were then conducted on these values.

Testing session NPU anxiety ratings and startle. Anxiety ratings at the time of each WN presentation were extracted and averaged across trials. Likewise, EMG data were processed, and startle magnitude was averaged across trials. For both ratings and startle, difference scores were calculated to correspond to Fear (FPS: Predictable Cue – Predictable ITI), Anxiety during the ITI (APS_iti: Unpredictable ITI – Neutral ITI), and Anxiety during the cue (APS_cue: Unpredictable Cue – Neutral Cue). A 2 (Coil: Active vs. Sham) x 3 (Trial type: FPS vs. APS_iti vs. APS_cue) repeated measures ANOVA was conducted on these values.

Testing session Sternberg threat WM performance. Percent correct and reaction time were calculated for the sort and maintain trials during safe and threat blocks. WM-related effects were calculated by creating WM-related difference scores (Sort – Maintain). A 2 (Coil: Active vs. Sham) x 2 (Condition: Safe vs. Threat) repeated measures ANOVA was conducted on these difference scores.

TMS session Sternberg WM performance. Percent correct and reaction time were calculated for each coil, session, and run. WM-related effects were calculated by creating WM-related difference scores (Sort – Maintain). A 2 (Coil: Active vs. Sham) x 4 (Session: 1-4) x 2 (Run: Pre-cTBS vs. Post-cTBS) repeated measures ANOVA was conducted on these difference scores.

For all measures, outliers (i.e. values greater than 2x SD) were truncated to 2 standard deviations from the mean (i.e. $x(|x > M \pm 2*SD|) = M \pm 2*SD$). Significant 2-way interactions

and multi-level 1-way main effects were probed using *post hoc p*aired-sample t-tests.

Supplemental Results

TMS session Sternberg WM performance. There were no significant main effects of coil, visit, or run for either accuracy (session: ($f(3,81) = 1.72$; $p = 0.17$; eta-squared = 0.06); run: ($f(1,27) < 0.001$; $p < 0.999$; eta-squared < 0.001); coil: ($f(1,27) = 0.15$; $p = 0.7$; eta-squared = 0.01); session*run: ($f(3,81) = 0.31$; $p = 0.82$; eta-squared = 0.01); session*coil: ($f(3,81) = 0.79$; $p = 0.5$; eta-squared = 0.03); run*coil: ($f(1,27) = 0.33$; $p = 0.57$; eta-squared = 0.01); session*run*coil: ($f(3,81) = 0.12$; $p = 0.95$; eta-squared < 0.001)) or reaction time (session: ($f(3,81) = 0.88$; $p = 0.46$; eta-squared = 0.03); run: ($f(1,27) = 0.3$; $p = 0.59$; eta-squared = 0.01); coil: ($f(1,27) = 0.07$; $p = 0.79$; eta-squared < 0.001); session*run: ($f(3,81) = 0.47$; $p = 0.7$; eta-squared = 0.02); session*coil: ($f(3,81) = 0.37$; $p = 0.78$; eta-squared = 0.01); run*coil: ($f(1,27) = 0.03$; $p = 0.87$; eta-squared < 0.001); session*run*coil: ($f(3,81) = 0.77$; $p = 0.52$; eta-squared = 0.03); See Tables 5 and 6).

Supplemental Discussion

In addition to the primary findings of the study, there are several other findings from the NPU and Sternberg tasks that should be discussed. For the NPU task, we observed main effects for trial type for both the anxiety ratings and the startle measures. For startle, we observed larger potentiated startle responses for the predictable compared to the unpredictable condition. This is indeed the typical pattern of findings for this task, and a replication of our previous work (20,56). In contrast, we observed smaller differences in ratings for the predictable condition compared to the unpredictable condition. We believe that this is an artifact of the analysis method. For the

unpredictable condition (APS_cue/APS_iti), the comparison is typically made with the neutral condition (i.e. APS_iti = Unpredictable ITI – Neutral ITI). In contrast, for the predictable condition, the comparison is between the cue and the ITI (i.e. FPS = Predictable cue – Predictable ITI). In the current version of the task, individuals showed qualitatively elevated anxiety ratings during the predictable ITI compared to the neutral ITI, leading to artificially reduced FPS scores for the ratings measure.

For the Sternberg task, we observed a main effect of threat on accuracy. These results suggest that threat selectively interfered with WM manipulation compared to working memory maintenance, which is a replication of previous work (22–24). Similarly, the effect of cTBS on accuracy during the Sternberg task seems to be selective for the sort trials, consistent with the fact that we explicitly targeted the right dlPFC region involved in WM manipulation (i.e. peak voxel in the sort > maintain contrast) (55). In contrast, RT seemed to be marginally slower during maintain trials following active stimulation, suggesting that although accuracy was not impaired, active stimulation may have led to increased effort in the maintain condition, resulting in a reduction in efficiency (3).

Strengths and Limitations

Among the strengths of the study are the relatively large sample-size (N = 28) for a double-blind placebo-controlled fMRI-guided TMS study. Additionally, our power was improved by the use of a within-subject design, and the fact that we used fMRI to individualize the TMS targets (55), E-field modelling to optimize target stimulation (63), and online neuronavigation to ensure accurate and consistent targeting of the stimulation site. We also chose a task that clearly and robustly engages the right dlPFC to identify single-subject targets and to demonstrate engagement of those targets (25). We used a double-blind design, custom-designed

active sham placebo to ensure effective blinding, and we measured concurrent anxiety ratings to assess placebo effects online during the unpredictable threat task (55). Despite no effects of stimulation on these ratings, we show clear effects of active stimulation on both fear and anxiety (during both the unpredictable cue and ITI periods).

Despite these strengths, the following limitations should be noted. First, the results were counter to our hypotheses. Although not technically a limitation, these data need to be replicated in an independent sample. Another limitation is that we included a single baseline visit, rather than a within-week baseline visit for the NPU paradigm, which would have provided a more flexible baseline that could have potentially accounted for any plasticity effects related to order of administration. Although counterbalancing should control for this, it could be argued that a baseline closer in temporal proximity to the cTBS/sham would have been preferable.

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Supplemental Tables

Table S1: Whole Brain Results for Sort > Maintain Contrast.

Glasser Label	MNI Coordinates			t-score	Volume
	X	Y	Z		
L_Medial_IntraParietal_Area	-22.8	-62.6	48.9	4.4083	16328
L_Area_posterior_24	-3.2	41.8	-0.7	-4.1748	14071
L_Area_8Av	-42.6	13.4	37	4.2867	11764
R_Area_PFm_Complex	38	-54.2	46.1	4.2826	10530
R_Area_8C	46	19.2	30.3	4.1408	6238
Left Cerebellum (Crus 2)	-41.3	-63.9	-35.9	4.1914	4706
R_RetroInsular_Cortex	53.5	-29.9	24.7	-4.5763	3601
Right Cerebellum (VIII)	38	-62.6	-40.1	4.2077	3357
L_Hippocampus	-25.9	-8.4	-17.5	-4.4087	3061
R_Middle_Insular_Area	34.2	23.2	-0.1	4.6652	2831
R_Hippocampus	25.7	-9.4	-15.9	-4.1872	2137
R_Area_6m_anterior	27.2	14	60.6	4.0821	2061
R_Superior_Frontal_Language_Area	1.5	22.4	56.4	4.1176	1973
L_Area_TE1_anterior	-56.7	3.3	-20.8	-4.0683	1603
L_Anterior_Ventral_Insular_Area	-32.2	22.2	1.3	4.3592	1375
L_Area_PF_Complex	-52.2	-32.8	24.7	-4.0849	934
R_ParaHippocampal_Area_2	31.5	-32.9	-12.7	-4.2828	917
GP_left	-17.4	4.5	8.7	4.4164	809
Left Cerebellum (Crus 2)	-8.7	-85.9	-28.7	4.1446	769
Right Cerebellum (Crus 2)	8.2	-82.2	-30	4.0425	710
L_Area_47s	-38.4	22.5	-19.6	-3.8818	509
L_Area_anterior_9-46v	-42.6	48.5	12.3	3.9642	498
R_Area_47s	28.7	18.6	-22.7	-4.1264	404
R_Area_43	52	-1.1	5.8	-4.055	374
PPtha_right	16	-8	13.4	4.1626	359
L_Area_ventral_23_a+b	-8.4	-51.9	18.9	-4.2872	317
L_Frontal_Opercular_Area_3	-38.1	1.7	13.9	-3.9512	306
R_Area_Posterior_Insular_1	37.3	-14.2	6.1	-3.8651	282
L_Area_OP1/SII	-45.6	-18.2	24.7	-4.0564	280
R_Area_46	43.4	49.5	17.1	3.8424	271
R_Area_11l	22.8	44.9	-14.4	4.0836	268
L_Area_TG_dorsal	-38.5	13.2	-39.8	-4.0735	256
Right Cerebellum (VIII)	31.7	-45.5	-45.7	3.967	227
R_Area_OP1/SII	40.7	-15.7	20.9	-3.8344	225
Cerebellar Vermis (4/5)	1.5	-54.3	-8.5	3.9134	223
L_Dorsal_Area_24d	-6.2	-12.3	44.8	-3.8315	217
L_Primary_Sensory_Cortex	-47.7	-21.5	52.9	-3.9813	210
R_Dorsal_area_6	42.4	-10.2	57.1	-3.884	184
L_Area_13l	-29	28.5	-13.3	-3.9488	175
Left Cerebellum (IX)	-3.3	-57.7	-31.1	3.876	172
R_Area_9_anterior	8.5	67.3	20.9	-3.8962	168
R_Auditory_4_Complex	62.2	-31.4	9.5	-3.8428	157
R_Area_TE1_anterior	54.1	-4.9	-26.6	-3.8352	144
L_Primary_Motor_Cortex	-12.5	-22.3	56.1	-3.9068	144
R_Area_47s	38.3	31.9	-19.5	-3.9027	134
R_Area_45	55	33.3	3.7	-4.0267	129
L_Primary_Motor_Cortex	-6.4	-21.7	78.2	-4.031	128
R_Area_FST	42	-61.4	6.8	-3.8046	122
R_Area_9_Middle	6.4	54.3	15.1	-3.8553	122
L_ParaHippocampal_Area_2	-29.9	-38.9	-5.6	-4.0145	112
mPMtha_left	-16.5	-9.3	3.4	3.9622	84
cTtha_right	10.2	-23	16	4.0214	74
L_Primary_Visual_Cortex	-14.6	-76.1	4.4	3.7989	69
L_Area_8C	-35.1	7.3	38.5	3.8511	68
L_Area_TA2	-53.1	-2.8	0.1	-3.8214	58
L_Primary_Visual_Cortex	-13.6	-99.7	-5.2	3.8281	53
L_Area_9_Middle	-7.5	65.3	25.2	-3.7977	49
R_posterior_OFC_Complex	21	9.1	-18.3	-3.9257	44
L_Insular_Granular_Complex	-36.6	-20.9	14.7	-3.7467	44
R_Area_TG_dorsal	41.2	20.3	-41.2	-3.9618	43
L_Area_STGa	-46.6	16.3	-17.5	-3.7782	37
R_Area_6mp	12.3	-6	70.3	-3.8656	35

Table S2: Stimulation Site Coordinates.

Subject	MNI Coordinates		
	X	Y	Z
3	51	23	23
4	47	33	23
5	51	35	7
7	57	29	25
8	53	25	29
9	41	3	29
10	49	31	27
11	59	19	29
12	53	31	29
13	53	27	23
15	45	51	9
16	57	19	27
17	45	5	19
18	45	15	33
19	45	39	13
20	57	21	23
21	45	25	17
22	55	13	31
23	49	23	23
24	57	21	25
25	57	15	33
26	49	31	25
28	59	21	25
29	59	17	19
30	55	33	25
32	43	17	29
33	49	27	21
34	53	11	31

Table S3: Rating and Startle Data from the NPU Threat Task.

Stimulation Type	Neutral		Predictable		Unpredictable	
	Cue	ITI	Cue	ITI	Cue	ITI
			Ratings			
Sham	1.17 (1.17)	1.2 (1.18)	2.98 (2.02)	2.67 (2.14)	4.09 (2.21)	4.12 (2.12)
Active	1.1 (0.99)	1.14 (1.01)	2.85 (1.41)	2.53 (1.47)	4.26 (1.94)	4.29 (1.93)
			Startle			
Sham	50.53 (4.57)	48.87 (4.02)	55.12 (3.34)	49.26 (4.08)	53.59 (3.35)	51.24 (2.72)
Active	50.07 (5.74)	47.35 (3.58)	55.23 (3.4)	48.33 (3.85)	54.09 (3.15)	51.3 (3.15)

Table S4: Accuracy and Reaction Time from Sternberg Threat WM Paradigm

Stimulation Type	Safe		Threat	
	Maintain	Sort	Maintain	Sort
		Accuracy		
Sham	88.1 (18.15)	80.36 (19.32)	83.93 (16.82)	83.16 (16.22)
Active	87.2 (14.34)	77.33 (19.64)	85.97 (14.85)	80.1 (16.9)
		Reaction Time		
Sham	1703.88 (457.58)	1835.31 (599.92)	1695.63 (506.39)	1806.01 (516.06)
Active	1753.18 (356.42)	1784.66 (400.43)	1786.08 (497.14)	1771.28 (465.78)

Table S5. Sternberg accuracy during TMS sessions

	Active		Sham	
Session	Pre	Post	Pre	Post
Sesssion 1	-0.12 (0.28)	-0.11 (0.29)	-0.06 (0.26)	-0.11 (0.23)
Sesssion 2	-0.03 (0.26)	-0.01 (0.21)	-0.05 (0.19)	-0.04 (0.25)
Sesssion 3	-0.08 (0.24)	-0.03 (0.18)	-0.06 (0.18)	-0.06 (0.26)
Sesssion 4	-0.06 (0.24)	-0.08 (0.26)	-0.01 (0.25)	-0.04 (0.26)

Table S6. Sternberg reaction time during TMS sessions

	Active		Sham	
Session	Pre	Post	Pre	Post
Sesssion 1	153.21 (540.15)	94.04 (524.92)	-24.04 (430.78)	127.5 (372.34)
Sesssion 2	32.92 (593.8)	42.96 (655.27)	77.05 (438.18)	-19.14 (470.7)
Sesssion 3	40.59 (489.13)	93.4 (462.05)	144.69 (394.68)	165.2 (393.82)
Sesssion 4	51.32 (448.55)	180.65 (759.43)	158.56 (358.7)	161 (432.02)