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Supplemental Information

**Multiplexing of Theta and Alpha Rhythms
in the Amygdala-Hippocampal Circuit Supports
Pattern Separation of Emotional Information**

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1 **Supplementary Information**

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8 **Inventory of Supplemental Information**

9 **Table S1 is related to Figure 1**

10 **Table S2 is related to Figure 1**

11 **Table S3 is related to Figure 2 and Figure 3**

12 **Table S4 is related to Figure 1**

13 **Figure S1 is related to Figure 1**

14 **Figure S2 is related to Figure 2**

15 **Figure S3 is related to Figure 2**

16 **Figure S4 is related to Figure 3**

17 **Figure S5 is related to Figure 3 and Figure 4**

18 **Figure S6 is related to Figure 1**

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20 **Table S1. Subject information and behavioral performance, Related to Figure 1**

Subject number	Gender	Age	Electrode Coverage	Seizure Onset	Hemisphere analyzed	Accurate retrieval accuracy*	RT** (mean \pm s.e.m)
1	Male	21	Bilateral	Left MTL	Right	0.754	2.89 \pm 0.022
2	Female	40	Bilateral	Right SMA	Right	0.786	2.55 \pm 0.011
3	Female	58	Bilateral	Left MTL	Right	0.866	2.46 \pm 0.007
4	Female	32	Bilateral	Right MTL	Left	0.731	2.59 \pm 0.054
5	Male	24	Bilateral	Right MTL	Left	0.841	2.54 \pm 0.014
6	Female	54	Bilateral	Right MTL	Left	0.783	2.51 \pm 0.114
7	Male	23	Bilateral	Right MTL	Left	0.823	2.54 \pm 0.022

21 MTL = Medial Temporal lobe

22 SMA = Supplementary motor area

23 s.e.m = standard error of the mean

24 * Accuracy across all trials including lures, targets and foils. Detailed behavioral information listed in Table
 25 S2

26 ** The response time are corresponding to the stimuli onsets.

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Table S2. Subjects' behavioral performance within each stimulus category, Related to Figure 1

		Target			Lure			Foil			Accuracy Rate
		Negative (n = 16)	Positive (n = 17)	Neutral (n = 16)	Negative (n = 33)	Positive (n = 34)	Neutral (n = 32)	Negative (n = 44)	Positive (n = 49)	Neutral (n = 49)	
S1	Correct/ Incorrect (responded)	16 / 0	17 / 0	16 / 0	17 / 16	22 / 10	25 / 7	32 / 12	33 / 15	37 / 10	75.4%
	Correct/ Incorrect (clean)	15 / 0	15 / 0	15 / 0	15 / 15	21 / 10	25 / 7	32 / 8	31 / 11	36 / 3	
S2	Correct/ Incorrect (responded)	16 / 0	17 / 0	16 / 0	17 / 16	19 / 14	24 / 8	37 / 8	36 / 13	46 / 3	78.6%
	Correct/ Incorrect (clean)	14 / 0	12 / 0	12 / 0	15 / 12	15 / 11	23 / 6	35 / 0	32 / 0	36 / 0	
S3	Correct/ Incorrect (responded)	13 / 2	17 / 0	16 / 0	23 / 10	22 / 12	27 / 6	38 / 6	46 / 3	49 / 0	86.6%
	Correct/ Incorrect (clean)	13 / 1	14 / 0	15 / 0	21 / 10	19 / 10	25 / 5	35 / 3	40 / 0	42 / 0	
S4	Correct/ Incorrect (responded)	16 / 0	14 / 1	16 / 0	18 / 12	24 / 9	25 / 5	32 / 12	23 / 19	29 / 14	73.1%
	Correct/ Incorrect (clean)	15 / 0	13 / 1	16 / 0	18 / 12	22 / 9	24 / 5	30 / 12	22 / 19	28 / 11	
S5	Correct/ Incorrect (responded)	15 / 1	17 / 0	15 / 1	17 / 15	18 / 16	24 / 8	44 / 0	46 / 3	47 / 2	84.1%
	Correct/ Incorrect (clean)	16 / 1	17 / 0	15 / 1	17 / 15	18 / 16	24 / 8	44 / 0	46 / 3	47 / 2	
S6	Correct/ Incorrect (responded)	16 / 0	17 / 0	15 / 1	16 / 17	21 / 13	27 / 5	31 / 13	45 / 4	39 / 10	78.3%
	Correct/ Incorrect (clean)	16 / 0	17 / 0	15 / 1	14 / 17	18 / 12	27 / 5	30 / 13	44 / 3	39 / 8	
S7	Correct/ Incorrect (responded)	16 / 0	17 / 0	16 / 0	14 / 18	18 / 14	25 / 6	36 / 8	41 / 4	49 / 0	82.3%
	Correct/ Incorrect (clean)	14 / 0	15 / 0	15 / 0	12 / 16	16 / 13	24 / 5	34 / 5	38 / 1	41 / 0	
Total Correct / Incorrect Trial (responded)		102 / 3	103 / 1	103 / 2	112 / 104	144 / 88	177 / 45	250 / 59	270 / 61	296 / 39	79.8%
Total Correct / Incorrect Trial (clean)		102 / 2	103 / 1	103 / 2	112 / 97	129 / 81	172 / 41	240 / 41	253 / 37	269 / 24	
Group-level accuracy rate for each stimuli category		97.1%	99.0%	98.1%	51.9%	62.1%	79.7%	80.9%	81.6%	88.4%	

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The correct (green) and incorrect responses (red) within each stimulus category ([stimuli type: target, lure, foil] x [stimuli valence: negative, positive, neutral]) are listed. "N" in the column label indicates the number of stimuli that was presented to the subject. The total numbers of trials that subjects responded (rows with white background) and survived after artifact rejection (rows with gray background) are listed for each stimuli category. Correct response rates (black) for each subject (right column) and group averages (bottom row) are included in the table.

Table S3. ANOVA test across the valence, trial type, and accuracy, Related to Figure 2 and 3

ANOVA test with the amygdala and hippocampal theta and alpha power, Related to Figure 2

Amygdala	Theta power		Alpha power	
	F-number	P-value	F-number	P-value
Emotion	6.22	0.0022**	12.41	0.0000065***
Accuracy	2.23	> 0.05	3.17	> 0.05
Trial type	3.11	> 0.05	5.86	0.016*
Emotion x Accuracy	1.79	> 0.05	1.24	> 0.05
Emotion x Trial type	2.05	> 0.05	14.31	0.0000011***
Accuracy x Trial type	0.86	> 0.05	6.19	> 0.05
Emotion x Accuracy x Trial type	3.77	0.024*	4.97	0.0075**

Hippocampus	Theta power		Alpha power	
	F-number	P-value	F-number	P-value
Emotion	2.33	> 0.05	2.96	> 0.05
Accuracy	3.04	> 0.05	2.22	> 0.05
Trial type	5.43	0.02*	4.14	0.043*
Emotion x Accuracy	2.01	> 0.05	1.15	> 0.05
Emotion x Trial type	11.07	0.000023***	6.66	0.0015**
Accuracy x Trial type	1.96	> 0.05	0.78	> 0.05
Emotion x Accuracy x Trial type	5.51	0.0044**	4.13	0.017*

Emotion x Accuracy	Lure		Foil	
	F-number	P-value	F-number	P-value
Amygdala theta power	2.56	> 0.05	1.07	> 0.05
Amygdala alpha power	4.99	0.0076**	1.23	> 0.05
Hippocampus theta power	6.44	0.0019**	1.62	> 0.05
Hippocampus alpha power	4.96	0.0078**	2.03	> 0.05

ANOVA test with the amygdala-hippocampal phase synchrony, Related to Figure 3

AMY-HPC PLV	Theta PLV		Alpha PLV	
	F-number	P-value	F-number	P-value
Emotion	2.89	> 0.05	0.79	> 0.05
Accuracy	10.38	0.0014**	2.16	> 0.05
Trial type	3.12	> 0.05	1.68	> 0.05
Emotion x Accuracy	3.01	> 0.05	1.74	> 0.05
Emotion x Trial type	3.44	0.033*	5.76	0.0035**
Accuracy x Trial type	2.51	> 0.05	1.19	> 0.05
Emotion x Accuracy x Trial type	4.02	0.019*	4.33	0.014*

Emotion x Accuracy	Lure		Foil	
	F-number	P-value	F-number	P-value
Theta phase synchrony	5.53	0.0045**	2.19	> 0.05
Alpha phase synchrony	4.79	0.0092**	1.23	> 0.05

The bolded values are results with significant main effect or interactions (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$).

Table S4. Visual attributes of stimuli within each valence group, Related to Figure 1

Visual attributes	Negative		Positive		Neutral	
	Target	Lure	Target	Lure	Target	Lure
Width	1512.87 ± 6.35	1515.04 ± 7.70	1503.91 ± 7.01	1492.92 ± 8.33	1519.95 ± 6.88	1525.66 ± 7.32
Height	1277.89 ± 7.02	1284.96 ± 7.69	1311.12 ± 7.89	1307.08 ± 8.03	1289.41 ± 6.99	1274.34 ± 7.31
Luminance	115.05 ± 0.97	113.88 ± 1.34	116.88 ± 1.43	117.54 ± 1.39	116.06 ± 1.29	117.76 ± 1.47
Contrast	65.93 ± 0.91	66.49 ± 0.52	66.13 ± 0.48	67.01 ± 0.52	67.72 ± 0.79	66.69 ± 0.58
JPEG_size80	310917.38 ± 5523.74	301919.23 ± 5387.31	320231.09 ± 5497.13	314258.85 ± 5615.25	318633.29 ± 5572.47	322750.41 ± 5724.86
LABL	48.29 ± 0.60	47.15 ± 0.53	48.88 ± 0.59	48.58 ± 0.55	48.44 ± 0.57	48.61 ± 0.59
LABA	1.94 ± 0.60	1.95 ± 0.31	2.04 ± 0.29	2.10 ± 0.33	2.11 ± 0.37	2.03 ± 0.28
LABB	7.84 ± 0.41	7.81 ± 0.39	7.96 ± 0.44	8.05 ± 0.40	7.88 ± 0.40	7.93 ± 0.38
Entropy	7.83 ± 0.011	7.78 ± 0.014	7.76 ± 0.015	7.54 ± 0.019	7.49 ± 0.011	7.52 ± 0.018

Visual attributes	Main effect across valence	Main effect across Trial type	Valence x Trial type
Width	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05
Height	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05
Luminance	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05
Contrast	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05
JPEG_size80	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05
LABL	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05
LABA	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05
LABB	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05
Entropy	<i>P</i> > 0.05	<i>P</i> > 0.05	<i>P</i> > 0.05

Seven visual attributes, including image width, image height, luminance, contrast, complexity (JPEG_size80), color composition (LABL, LABA, LABB) and entropy was calculated for each image. The average and standard error mean for each valence group were listed in the table (mean ± s.e.m.). One-way ANOVA test was performed to examine whether any visual attributes differ from three valence groups.

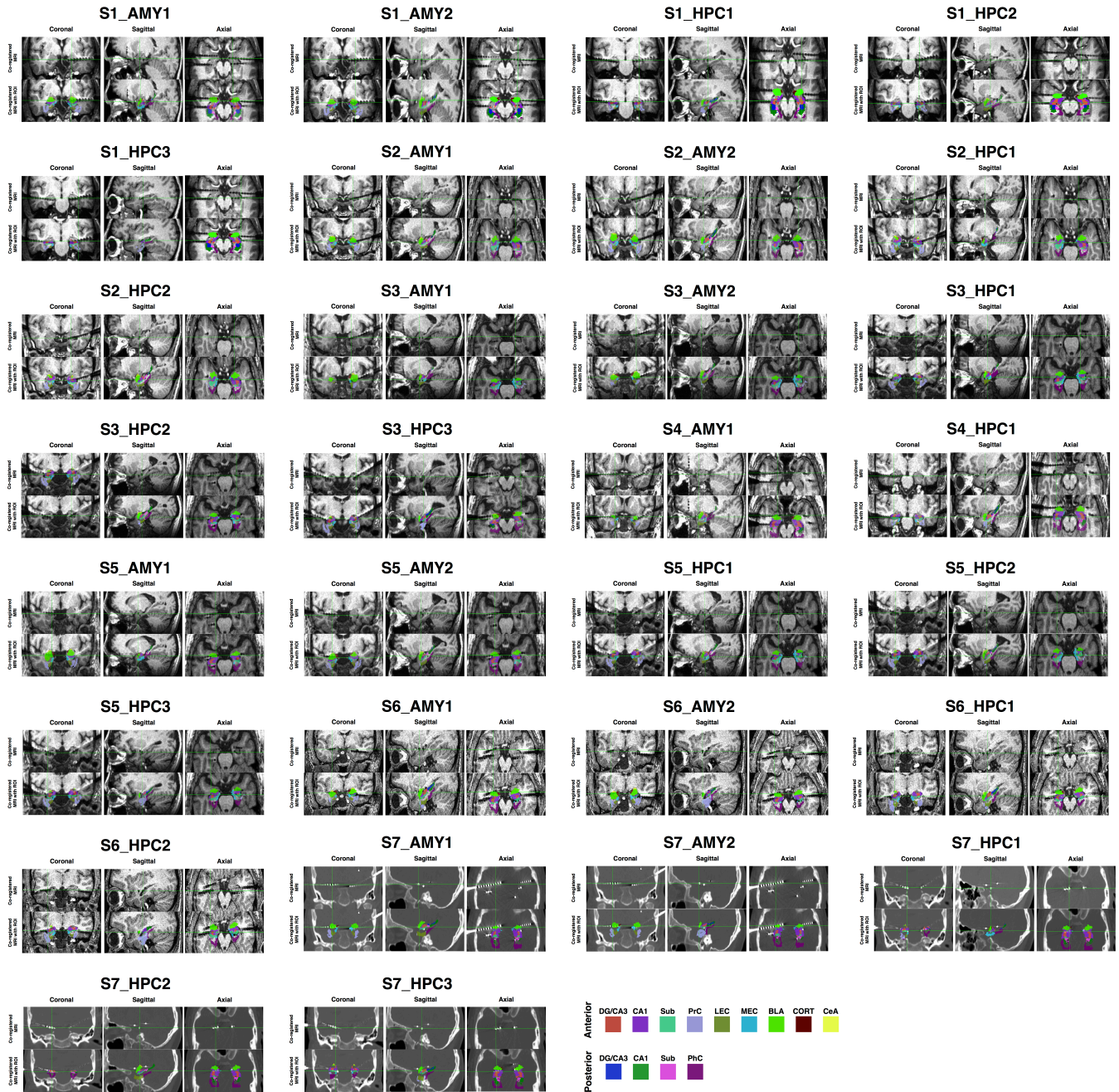


Figure S1. Localizations of electrodes within the amygdala (AMY) and the hippocampus (HPC) for all seven subjects, Related to Figure 1. Post-implantation MRI (Subject 1-6) or CT (Subject 7) aligned using rigid body alignment to the pre-implantation MRI (lower panel for each subject). Translucent registered regions of interests (ROIs) were overlaid on the post-to-pre aligned MRI or CT (upper panel for each subject) for three views (Coronal, Sagittal and Axial), including the dentate gyrus/CA3 (DG/CA3), CA1, subiculum (Sub), parahippocampal cortex (PrC), lateral entorhinal cortex (LEC), medial entorhinal cortex (MEC), basolateral amygdala (BLA), corticomедial amygdala (CORT) and central nucleus of the amygdala (CeA). Cross hairs are centered on the electrode within the amygdala and the hippocampus.

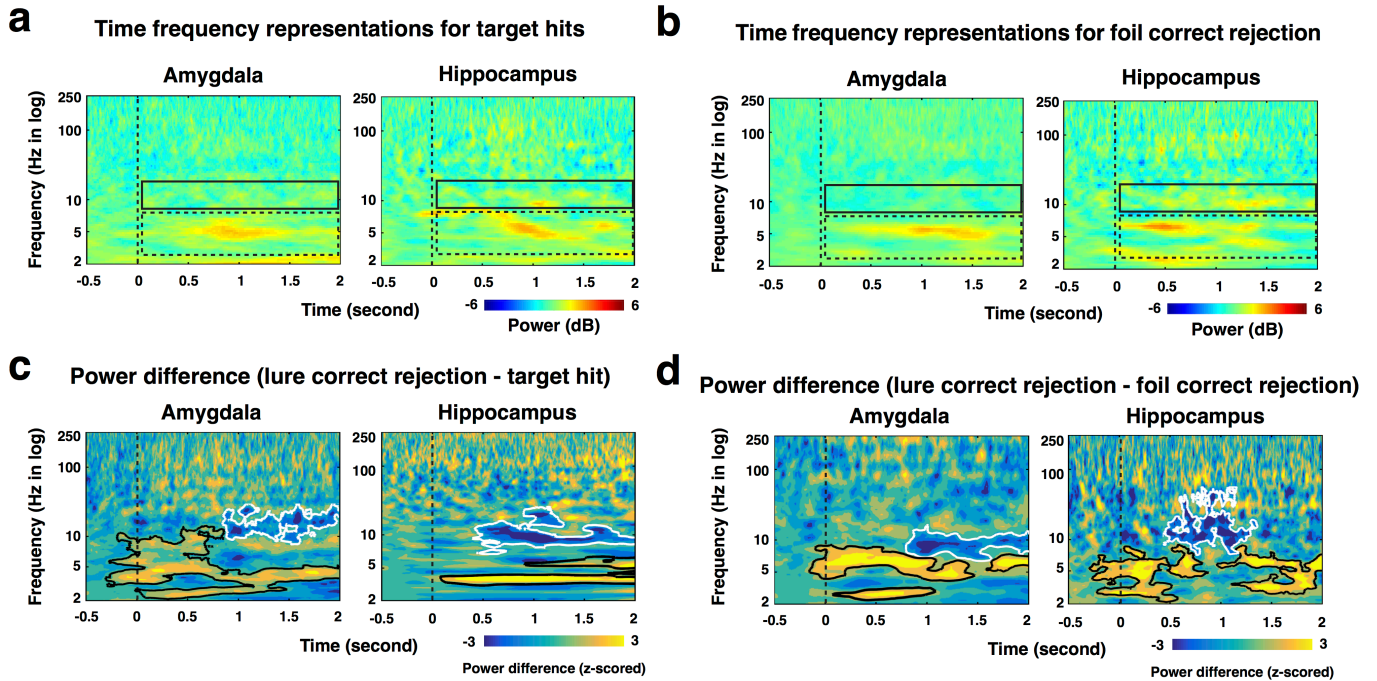


Figure S2. Task-evoked spectrotemporal power in the amygdala and the hippocampus during task performances for target and foil items, Related to Figure 2. Task-induced power in the amygdala and the hippocampus averaged across all the subjects, normalized to pre-trial baseline (500-ms fixation period) and grouped as target hits **(a)** and foil correct rejections **(b)**. Warmer colors denote task-induced power increases from the baseline, while the colder colors refer to power decrease from the baseline. Vertical dashed lines indicate the stimulus onset. The theta (dashed square box) and alpha (solid square box) frequency range were highlighted. Averaged power difference **(c)** (lure correct rejections (Fig. 2) – target hits) and **(d)** (lure correct rejections (Fig. 2) – foil correct rejection) across all seven subjects. Positive values (yellow colors) indicate greater power in the correct discriminated lures compared to the target hits / foil correct rejections, while the negative values (green colors) refer to a greater power in the target hits / foil correct rejections. The significant conditional power differences ($P < 0.05$, corrected based on the clustered based permutation test) were highlighted with black (lure correct rejections $>$ target hits / foil correct rejections) and white contours (lure correct rejections $<$ target hits / foil correct rejections). Dashed vertical lines indicate the stimuli onset.

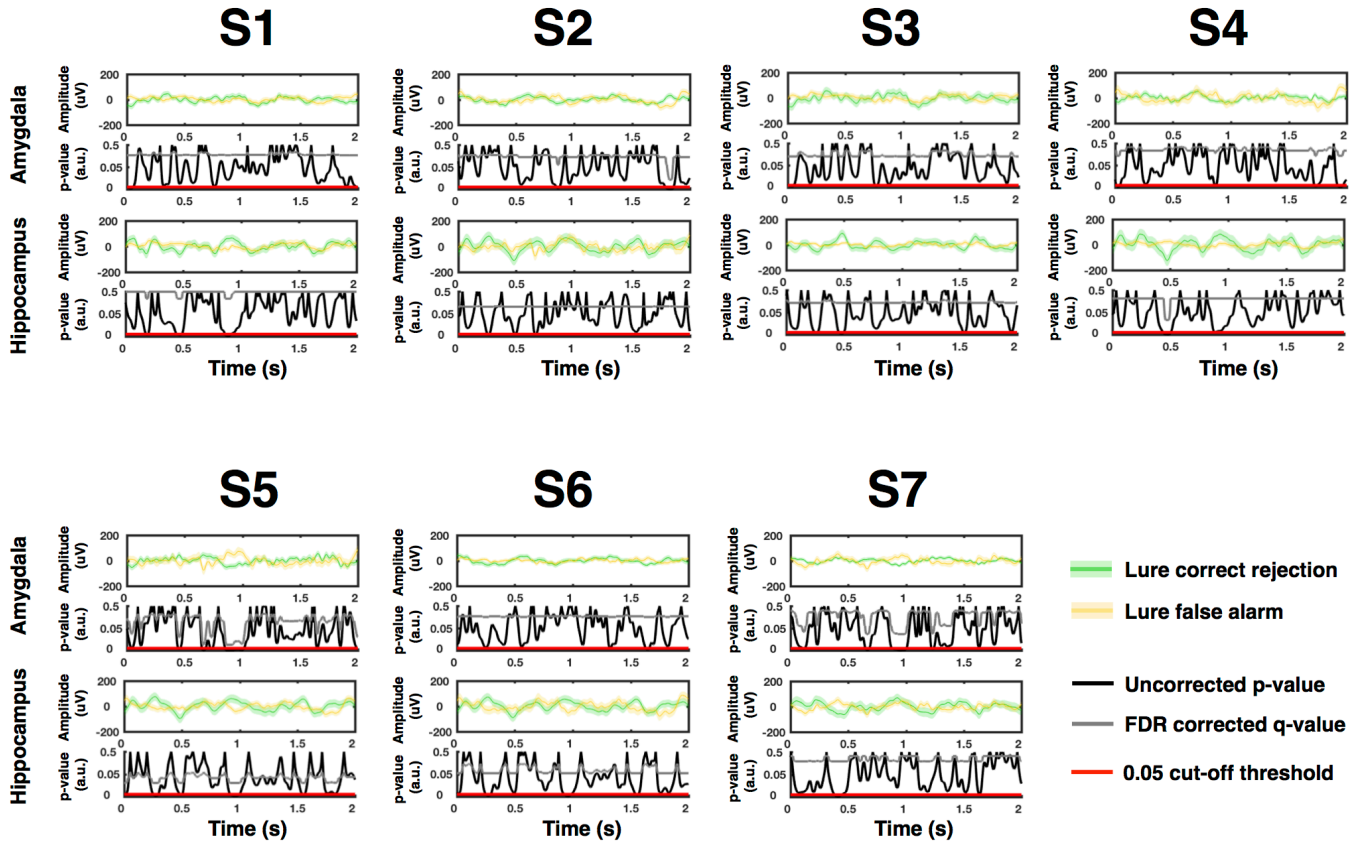


Figure S3. Event-related potentials (ERPs) in each subject for the amygdala and the hippocampus, Related to Figure 2. Comparisons of ERPs (upper plots) between lure correct rejections (green traces) and lure false alarms (yellow traces) lure trials and point-by-point t-test (bottom plots). Significant group differences in ERP amplitudes with uncorrected $P < 0.05$ threshold were found for a small number of time points (amygdala = 5.25%; hippocampus = 7.43%). No data points survived correction for multiple comparisons. Shaded regions = s.e.m. across trials.

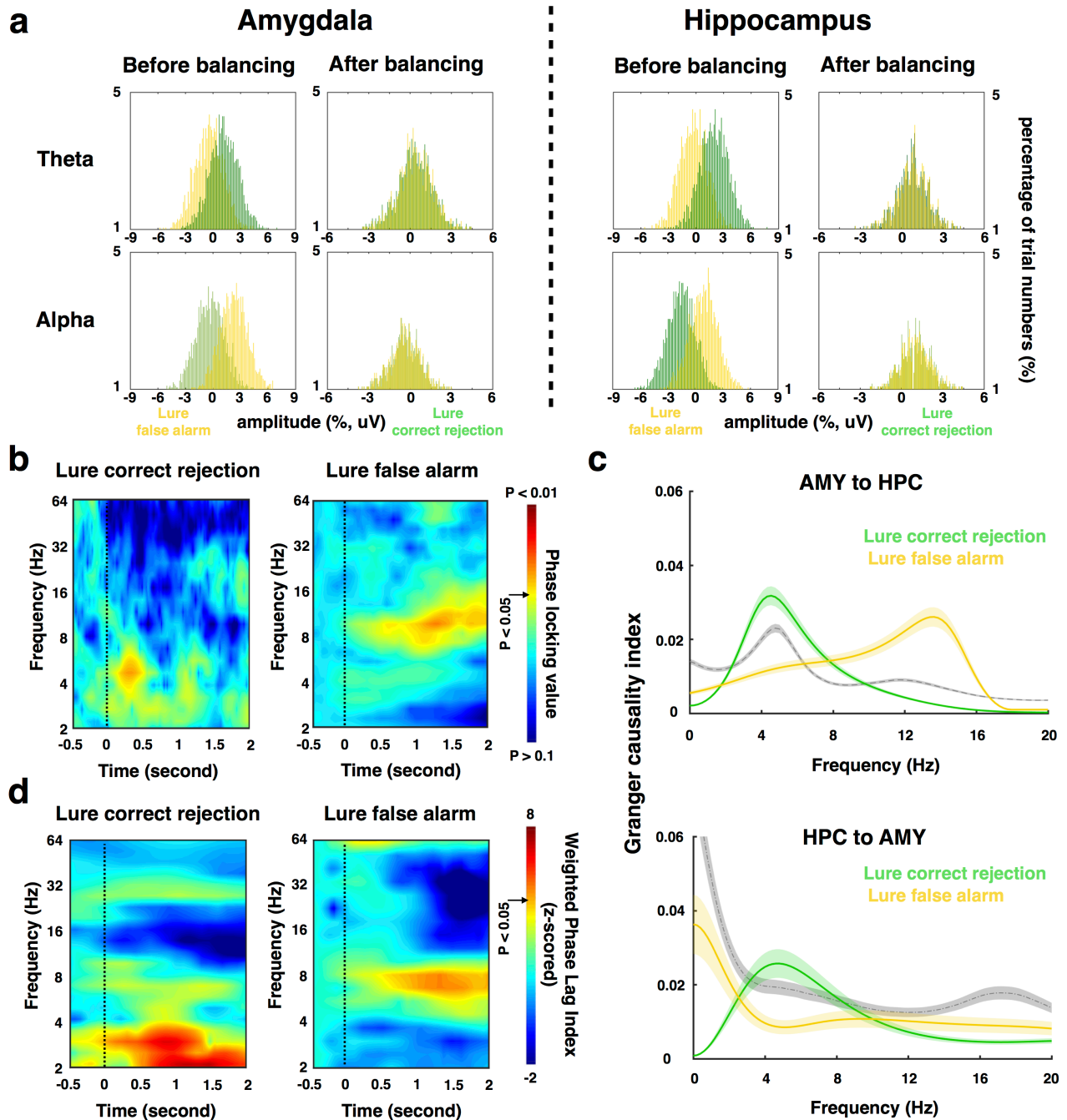


Figure S4. Additional analyses confirmed observed amygdala-hippocampal synchrony and Granger causality effects, Related to Figure 3. (a) Power balancing was performed using a stratification method that trims trials with extreme power values from each condition until the histogram of trial power values is closely matched between compared conditions (lure correct rejection versus lure false alarm). (b) Averaged amygdala-hippocampal phase locking values across all subjects for both conditions (lure correct rejection: left panel; lure false alarm: right panel) using power balanced trials. The frequency specific theta and alpha synchrony remained significant after power balanced analysis ($P <$

0.05, permutation test). **(c)** Frequency-domain Granger causality for data subsets calculated using trials with balanced theta and alpha power between lure correct rejections and lure false alarms. Bidirectional theta mediated interactions for lure correct rejections and alpha mediated amygdala to hippocampus directional influence remained significant after power balanced analyses. **(d)** Average z-score standardized debiased WPLI-square estimator as a function of time and frequency during lure correct rejection (left panel) and lure false alarm (right panel). WPLI quantifies the contribution of the observed phase leads and lags between signals from the amygdala and the hippocampus, and is weighted by the magnitude of the imaginary component of the cross-spectrum. Warm colors denote strong phase-synchronization. Dashed lines indicate the stimuli onsets. This further confirms that the frequency-specific inter-regional phase synchrony is not due to the volume conduction in the amygdala-hippocampal circuit.

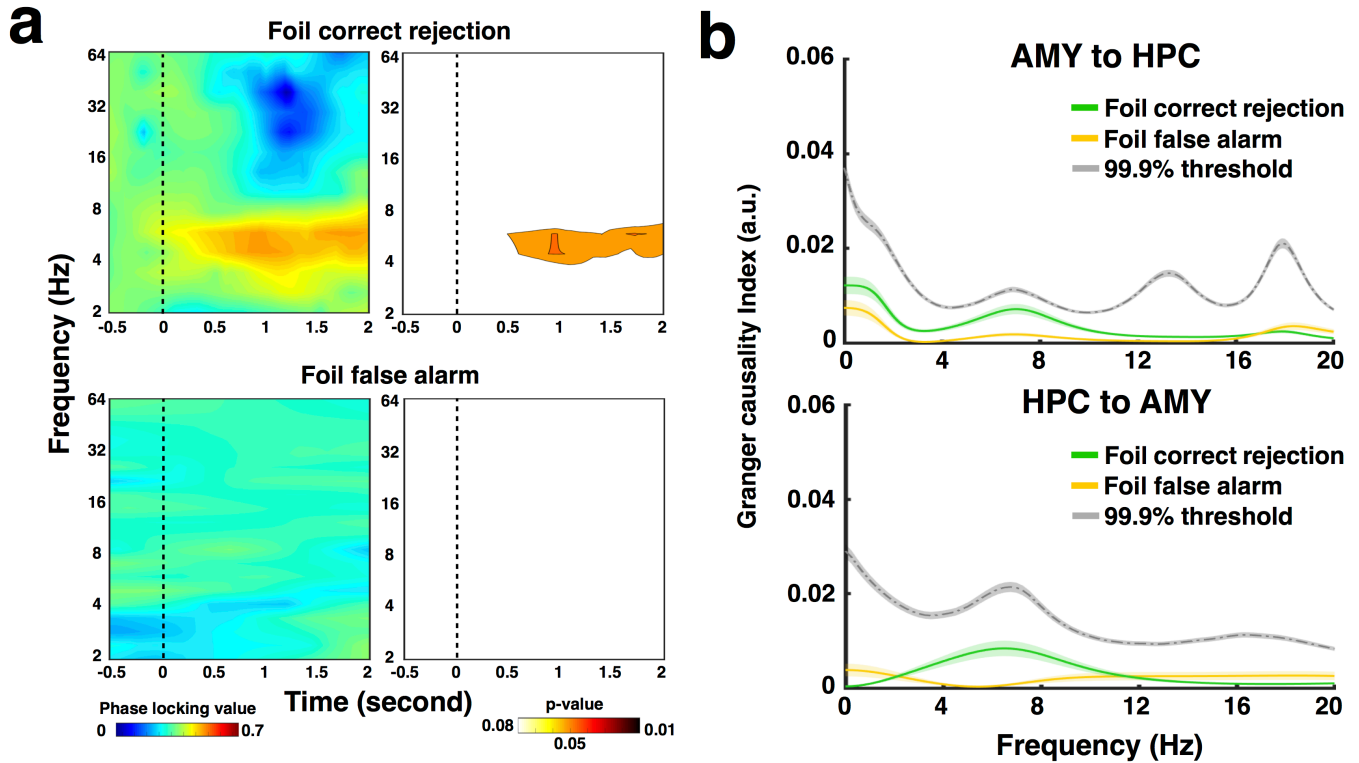


Figure S5. Amygdala-hippocampal phase synchrony and directionality for foils, Related to Figure 3 and Figure 4. (a) Amygdala-hippocampal synchrony (i.e. phase locking value, PLV) averaged across all subjects for foil correct rejections (i.e. reject foil as “new”; left upper panel,) and foil false alarm (i.e. mark foil as “old”; left lower panel). Phase locking value ranges from 0 to 1, with warmer colors indicating greater PLV values and stronger amygdala-hippocampal phase synchrony compared to the baseline. The significant PLV values ($p < 0.05$, permutation test) were plotted for both conditions (right panels) with warm colors denoting lower p-value. The vertical dashed lines indicate stimulus onsets. (b) Averaged Granger causality index across all subjects for foil correct rejections (i.e. reject foil as “new”; green lines) and foil false alarms (i.e. mark foil as “old”; yellow lines). The dashed gray lines represent the 99.9% threshold. Color shaded areas = s.e.m.

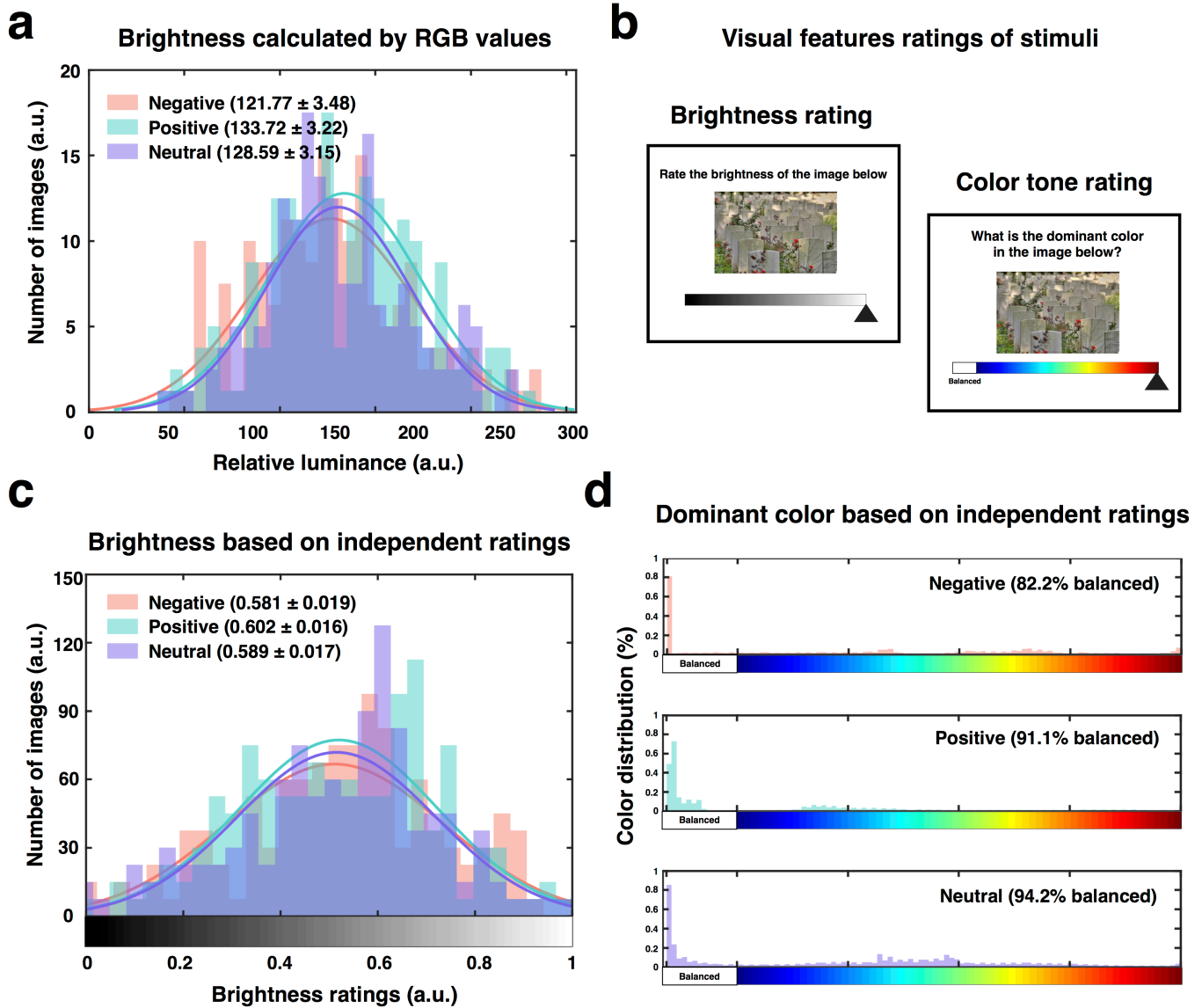


Figure S6. Visual dimensional features of stimuli, Related to Figure 1. (a) Brightness calculated based on the RGB values using the formula: $\text{Brightness} = 0.2126 * R + 0.7152 * G + 0.0722 * B$. Brightness distribution for each valence group was plotted (negative: red; positive: green; neutral: purple) with normal distribution fitted (fitted curve). (b) Examples showing that the visual features (brightness, color tone) of the stimuli were rated by an independent group (4 females, 7 males, age = 26 ± 1.42) via Amazon Mechanical Turk (Mturk). Participants rate each stimulus by moving the triangle to the appropriate position. Notably, for the color tone rating, the white area means the stimuli is color-balanced and no obvious dominant color. (c) Brightness distribution based on 11 subjects' ratings were grouped for three valence groups (negative: red; positive: green; neutral: purple) and fitted by the normal distribution (fitted curves). (d) Dominant color distribution based on 11 subjects' ratings were grouped for three

valence groups (negative: upper panel; positive: middle panel; neutral: lower panel). The percentage of images that were rated as color-balanced was listed on the right corner of each subplot.