Supporting Online Material

Methods

Subjects

Twenty-four right-handed subjects participated (10 females, age range: 19-31). All gave informed consent according to the procedures of Stanford University.

Task and stimuli.

Subjects were trained on 36 critical and 12 filler pairs according to procedures reported previously (*1*). The cue and response of each pair were weakly related. The responses were chosen so that each was a member of a unique category (Fig. 1) to permit later testing of that item with an extralist category. Subjects were trained until they could provide the response to at least 50% of the pairs (average = 73%).

After training, subjects were read the think/no-think instructions, and were then given practice on fillers. Subjects were then given 384 critical trials (192 suppress, 192 respond) in which respond and suppression stimuli were intermixed. On each trial, a cue from one of the pairs appeared for 4000ms in red (Suppress) or green (Respond), followed by a 500ms blank inter-trial interval. For Respond trials, subjects retrieved the response and kept it in mind for 4000ms, while focusing on the cue. For Suppression trials, subjects kept the response out of consciousness for 4000ms while focusing on the cue. No overt responses were required. Suppression and Respond trials were conducted on different pairs, with 12 pairs (repeated 16 times) participating in each. Four blocks of 96 critical trials were presented, separated by 45-second breaks.

After the think/no-think phase, scanning ended and memory for all pairs was tested twice. In both tests, a cue for each pair was presented in black for 5 seconds, or until subjects responded. Twelve pairs from each of the Respond, Suppress, and Baseline conditions were intermixed. In the Same-Probe test (SP test), recall for each response was cued with the stimulus paired with it previously. In the Independent-Probe test (IP test), subjects were cued with the category name for each response along with its first letter. In each case, subjects were asked to recall the studied item that fit the cues. Half the subjects got the Same-Probe test first, and half received the Independent-Probe test first.

MRI acquisition.

Twenty-five axial slices (4mm thick, 1mm gap) were collected at 3T with a T2*-sensitive gradient echo spiral-in/out pulse sequence (*2*) (30 ms TE, 2000 ms TR, 2 interleaves, 60° flip angle, 24 cm field of view, 64x64 data acquisition matrix). T2-weighted flow-compensated spin-echo scans were acquired for anatomical localization (2000ms TR; 85ms TE).

Data Analysis

Functional images were slice time corrected, motion-corrected, and normalized to a standard template brain using SPM99 (Wellcome Department of Cognitive Neurology). Normalized images were interpolated to 2x2x2 mm voxels and spatially smoothed with a Gaussian filter (6 mm full width-half maximum). Low-frequency noise and differences in global signal between participants were removed. Single participants' data were analyzed with a fixed-effects model and group data were analyzed using a random effects

model. Effects were modeled with a canonical hemodynamic response function at the onset of each 4-second trial. For the group analysis, contrast images were created for each participant to summarize differences in brain activation between trial types. One-sample t-tests were performed on these contrast images to create a series of SPM{T} maps depicting these differences across the group. Statistical maps for group analyses were thresholded at $p < .001$ uncorrected for multiple comparisons. Maxima were reported in ICBM152 coordinates, as in SPM99. A 6-voxel extent threshold was applied to all statistical maps.

To identify regions for which level of suppression-related activation was correlated with suppression-related decreases in memory, a regression analysis was performed on the individual images from the Suppress > Respond contrast. Memory inhibition was computed (Baseline percentage recalled – Suppression percentage recalled, averaged over SP and IP tests, z-transformed within each counterbalancing condition to account for item-specific effects across counterbalancing groups) conditioned on correct initial recall during the training phase. Regression analyses were thresholded at $p < .005$. This analysis was supplemented with a quartile split of subjects (matched for item counterbalancing) based on DLPFC activation to illustrate differences in recall for subjects as a function of condition and test type. A mixed Anova was performed on this analysis to determine whether subjects with greater DLPFC activation showed significantly more memory inhibition on both SP and IP tests.

To determine whether memory inhibition modulated hippocampal responses, functionally defined regions of interest (ROIs) were defined for left and right

hippocampus based on the activations from the overall group contrast (Respond > Suppress). ROIs were smoothed with a 6mm spatial filter. Parameter estimates (that model the amplitude of the fMRI response) averaged across all voxels for each ROI were extracted for Sf and Sr items, considering only trials with correct initial recall. These scores were first entered into a 2 x 2 within-subjects Anova with memory status (forgotten versus remembered) and item type (Respond versus Suppress) as factors, excluding subjects with no forgotten items in the Respond condition (7 subjects excluded). This was followed by a correlation analysis, focused on Suppression items only. Difference scores for each ROI for each subject (Sf- Sr) were correlated with inhibition scores. Scores 3 standard deviations from the mean were classified as outliers, which excluded 1 subject (who had only 16 trials contributing to activations) from all ROI analyses; a scanner malfunction corrupted a portion of an additional subject's data (final group, n = 22). This correlation was supplemented with a 2 x 2 x 2 mixed Anova, with the between subjects factor (inhibition group, with low and high levels, defined by median split based on subjects' memory inhibition score) added (Figure 4b) to establish that Sf items showed significantly greater right hippocampal activation than Sr items, for the highest half of inhibitors.

This correlation analysis procedure was applied to determine whether the DLPFC regions from our regression analysis predicted differential hippocampal activation for Sf and Sr items. ROIs for left and right DLPFC were defined functionally as above. Difference scores for DLPFC (Sf – Sr) were correlated with difference scores (Sf-Sr) for the hippocampus.

1.) Overall Contrast: BRAIN AREAS THAT ARE MORE ACTIVE DURING SUPPRESSION THAN DURING RESPOND TRIALS IN THE GROUP ANALYSIS (p < .001 uncorrected, n = 24)

							MNI Coordinates			Talairach Coordinates		
	Hemisphere	Structure	Area	Cluster voxel #	t-statistic	voxel p (uncorrected)	X	Y	Z	X	Y	Z
Frontal	Left	Middle Frontal Gyrus	BA6/9/8	92	5.82	0.001	-42	4	50	-42	6	46
		Middle Frontal Gyrus	BA46/45	138	4.64	0.001	-42	28	24	-42	28	21
		Inferior Frontal Gyrus	BA47/45/ Insula 13	103	4.53	0.001	-38	22	2	-38	21	1
	Right	Middle Frontal Gyrus	BA6/9	456	6.8	0.001	48	2	48	48	4	44
		Middle Frontal Gyrus	BA6	14	3.95	0.001	30	4	50	30	6	46
		Inferior Frontal Gyrus	BA45/46	11	3.73	0.001	58	28	20	57	28	17
		Inferior Frontal Gyrus	BA47/13	183	6.02	0.001	38	24	0	38	23	-1
	Medial	Medial Frontal Gyrus	BA6/32	1173	6.01	0.001	10	2	66	10	5	61
		Cingulate Gyrus	BA32	11	3.76	0.001	14	18	32	14	19	29
Parietal	Left	IntraParietal Sulcus	BA7	29	4.31	0.001	-20	-62	46	-20	-58	45
	Right	IntraParietal Sulcus	BA7	234	4.43	0.001	24	-64	38	24	-60	38
		IntraParietal Sulcus	BA7	22	4.05	0.001	14	-58	48	14	-54	47
Temporal	Left	Inferior Temporal Gyrus	BA20	12	4.15	0.001	-54	-30	-24	-53	-30	-19
	Right	Inferior Temporal Gyrus	BA20	21	4.97	0.001	50	-16	-36	50	-17	-29
Occipital	Left	Middle Occipital Gyrus	BA19	19	3.74	0.001	-46	-70	-8	-46	-68	-3
Subcortical	Right	Basal Ganglia	Putamen	220	4.7	0.001	22	8	4	22	8	3
		Corpus Callosum		11	3.86	0.001	16	-44	8	16	-42	9

NOTE: CLUSTERS WITH 10 OR FEWER VOXELS ARE NOT REPORTED.
VOXELS ARE 2 X 2 X 2 MM.

2.) OVERALL CONTRAST: BRAIN AREAS THAT ARE MORE ACTIVE DURING RESPOND THAN DURING SUPPRESSION TRIALS IN THE GROUP ANALYSIS (p < .001 uncorrected, n = 24)

							MNI Coordinates			Talairach Coordinates		
	Hemisphere	Structure	Area	Cluster voxel #	t-statistic	voxel p (uncorrected)	X	Y	Z	X	Y	Z
Frontal	Left	Superior Frontal Gyrus	BA9	46	4.21	0.001	-24	58	34	-24	58	28
	Right	Superior Frontal Gyrus	BA9	72	4.83	0.001	18	50	38	18	50	32
		Superior Frontal Gyrus	BA10	26	4.38	0.001	14	60	24	14	59	19
		Middle Frontal Gyrus	BA6	28	4.7	0.001	14	38	58	14	39	51
Temporal	Left	Hippocampus		63	4.83	0.001	-32	-8	-18	-32	-9	-15
	Right	Hippocampus		36	5.4	0.001	34	-8	-18	34	-9	-15
Insula	Left	Posterior Insula	BA13	104	5.36	0.001	-38	-14	4	-38	-13	4
	Right	Posterior Insula	BA13/ 43	18	4.02	0.001	48	-16	14	48	-15	14
		Posterior Insula	BA13	23	3.87	0.001	42	-14	-4	42	-14	-3
Parietal	Left	Post-Central Gyrus	BA40	48	4.67	0.001	-62	-24	16	-61	-23	16
Occipital	Left	Cuneus / Middle Occipital Gyrus	BA18/ 17/19	580	4.81	0.001	-10	-96	6	-10	-93	10
		Lingual Gyrus	BA18	23	3.89	0.001	-8	-78	-12	-8	-76	-6
	Right	Cuneus / Middle Occipital Gyrus	BA18	167	5.25	0.001	12	-104	10	12	-100	14

3.) REGRESSION: BRAIN AREAS FROM THE GROUP ANALYSIS (SUPPRESS>RESPOND) THAT PREDICT MEMORY INHIBITION ($p < .005$, $n = 24$)

							MNI Coordinates			Talairach Coordinates		
	Hemisphere	Structure	Area	Cluster voxel #	t-statistic	voxel p (uncorrected)	X	Y	Z	X	Y	Z
Frontal	Left	Middle Frontal Gyrus	BA46/9	164	4.02	0.001	-36	38	34	-36	38	29
		Middle Frontal Gyrus/Precentral Gyrus	BA6	129	3.64	0.001	-32	-12	50	-32	-9	47
			BA6	20	3.22	0.002	-26	-12	68	-26	-8	63
		Middle/Superior Frontal Gyrus	BA11	62	4.55	0.001	-36	60	-16	-36	57	-16
		Middle Frontal Gyrus	BA10	56	4.00	0.001	-42	62	0	-42	60	-3
		Inferior Frontal Gyrus	BA44	55	3.34	0.001	-62	6	22	-61	7	20
		Inferior Frontal Gyrus	BA 13	29	3.51	0.001	-40	22	10	-40	22	8
	Right	Middle Frontal Gyrus	46/9	121	4.36	0.001	32	38	26	32	38	22
		Middle Frontal Gyrus/Precentral Gyrus	BA6	134	4.22	0.001	28	-14	68	28	-10	63
		Precentral Gyrus	BA6	16	3.49	0.001	48	0	46	48	2	42
		Inferior Frontal Gyrus	BA9/6	38	3.44	0.001	44	-2	26	44	-1	24
	Medial	Anterior Cingulate	BA24	11	3.38	0.001	-10	10	30	-10	11	27
		Pre-SMA	BA6	36	3.73	0.001	-12	-16	72	-12	-12	67
			BA6	59	3.85	0.001	2	2	54	2	4	50
Insula	Left	Insula	BA13 / BA38	192	3.87	0.001	-46	4	0	-46	4	2
	Right	Insula	BA13	43	3.68	0.001	48	10	4	48	10	3
Parietal	Left	Superior Parietal Lobule	BA7 IPS	140	4.35	0.001	-16	-72	52	-16	-67	51
			BA7	16	3.13	0.002	-30	-58	66	-30	-53	63
		Inferior Parietal Lobule	BA40	135	3.78	0.001	-50	-36	32	-50	-33	31
			BA 40	82	6.21	0.001	-68	-32	28	-67	-30	27
			BA40	20	3.15	0.002	-42	-58	48	-42	-54	47
		Postcentral Gyrus	BA43	13	3.36	0.001	-52	-76	14	-51	-73	17

Continued . . . .

							MNI Coordinates			Talairach Coordinates		
	Hemisphere	Structure	Area	Cluster voxel #	t-statistic	voxel p (uncorrected)	X	Y	Z	X	Y	Z
Parietal	Right	Superior Parietal Lobule/Middle Temporal Gyrus, Middle Occipital Gyrus	IPS (BA7)/ BA19	712	4.58	0.001	26	-68	50	26	-64	49
			BA7	23	3.24	0.002	8	-68	58	8	-63	57
	Medial	Precuneus	BA7	26	3.52	0.001	2	-52	56	2	-48	54
Temporal	Left	Middle Temporal Gyrus	BA19	180	3.75	0.001	-38	-82	16	-38	-79	19
		Superior Temporal Gyrus	BA22	119	3.9	0.001	-48	4	2	-48	4	2
	Right	Superior Temporal Gyrus	BA38	16	3.58	0.001	50	14	-14	50	13	-12
		Inferior / Middle Temporal Gyrus	BA21	26	3.37	0.001	52	-6	-24	51	-7	-20
		Middle Temporal Gyrus (see Parietal activations)										
Occipital	Left	Middle Occipital Gyrus	BA19	180	3.7	0.001	-38	-84	16	-38	-79	19
			BA19	31	3.52	0.001	-40	-66	-10	-40	-64	-5
		Cuneus	BA19	13	3.38	0.001	-14	-86	34	-14	-82	35
	Right	Middle Occipital Gyrus (see Parietal activations)										
Subcortical	Left	Basal Ganglia	Putamen	88	3.5	0.001	-30	8	-8	-30	7	-7
	Right	Thalamus	Pulvinar	14	3.35	0.001	26	-32	8	26	-31	9
		Brainstem	Pons	31	4.64	0.001	14	-30	-40	14	-31	-32
Cerebellum	Left	Posterior Lobe	Declive	24	3.21	0.002	-26	-60	-24	-26	-59	-17
	Right	Posterior Lobe	Declive	45	3.57	0.001	36	-60	-28	36	-59	-21
		Cerebellar Tonsil		34	4.26	0.001	28	-62	-44	28	-62	-34

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References and Notes

1. M. C. Anderson, C. Green, *Nature* **410,** 131 (2001).

2. G. H. Glover, C. S. Law, *Magn. Reson. Med.* **46**, 515 (2001).