Supplementary Table S1

Psychological and physiological measures.

	Placebo	Rapid CORT	Slow CORT
Affective State (PANAS)			
Positive affect: baseline	30.78 (1.54)	32.39 (1.28)	32.11 (1.65)
Positive affect: prior to encoding	29.28 (1.40)	30.67 (1.01)	31.50 (1.32)
Positive affect: after encoding	26.00 (1.30)	25.22 (1.24)	28.00 (1.49)
Negative affect: baseline	16.06 (1.97)	13.06 (1.23)	14.50 (1.51)
Negative affect: prior to encoding	16.17 (1.78)	14.78 (1.51)	15.17 (1.53)
Negative affect: after encoding	16.11 (1.83)	15.22 (1.65)	15.22 (1.54)
Heart rate (BPM)	62.00 (1.77)	59.58 (1.41)	61.96 (1.24)
Heart rate variability (ms^2)	134.71 (20.08)	123.39 (16.85)	109.70 (11.58)
Picture rating (# congruent)			
Neutral pictures	77.67 (0.44)	77.17 (0.42)	78.06 (0.41)
Negative pictures	73.39 (0.98)	75.28 (0.64)	74.89 (1.02)
Memory performance			
Free recall: # neutral pictures	15.11 (2.11)	15.06 (2.66)	15.44 (1.88)
Free recall: # negative pictures	29.22 (2.19)	29.17 (2.36)	31.67 (1.75)
Cued recall: # neutral pictures	33.89 (3.27)	34.61 (3.51)	35.67 (2.86)
Cued recall: # negative pictures	42.72 (2.37)	40.39 (3.27)	42.67 (2.30)

Mean values (S.E.M.). PANAS; Positive and Negative Affect Schedule questionnaire (Watson et al. 1988).

Supplementary Table S2

Regions revealing main effects or interactions of picture valence and subsequent memory.

Region	Brodmann area	MNI Coordinates x	y	z	Peak T-score	Cluster-size	*P*-value
Main effect of subsequent memory							
Remembered > Forgotten							
Middle occipital gyrus, L & R	**7,19**	32	-72	38	5.93	746	$P < 0.001$
Inferior temporal gyrus, L	**19,37**	-52	-58	-10	7.78	988	$P < 0.001$
Inferior temporal gyrus, R	**37**	54	-52	-14	5.00	430	$P < 0.001$
Inferior parietal lobule, L	**2,40**	-48	-40	50	6.28	1479	$P < 0.001$
Hippocampus / Amygdala, L	**34,35**	-14	-8	-12	5.95	623	$P < 0.001$
Superior temporal pole / Amygdala, R	**34,36,38**	30	8	-22	4.64	187	$P = 0.041$
Middle cingulate gyrus	**24**	2	-2	36	4.70	240	$P = 0.015$
Inferior & Middle frontal gyrus, L	**6,44,48**	-50	10	26	6.81	1698	$P < 0.001$
Inferior frontal gyrus, R	**44**	50	10	24	5.36	263	$P = 0.010$
Supplemental motor area, L	**6**	-6	10	62	5.34	191	$P = 0.038$
Superior frontal gyrus, L	**9**	-20	32	48	5.20	299	$P = 0.005$
Inferior frontal & Orbitofrontal gyrus, L	**45**	-46	40	14	5.28	789	$P < 0.001$
Forgotten > Remembered							
Precuneus	**7,23,26**	4	-64	36	6.63	2279	$P < 0.001$
Middle temporal gyrus, R	**20-22,37**	56	-48	16	5.63	672	$P < 0.001$
Middle frontal gyrus, R	**10,11,46**	36	48	14	4.28	467	$P < 0.001$
Main effect of picture valence							
Aversive > Neutral							
Cerebellum, L	**/**	-14	-74	-44	9.15	949	$P < 0.001$
Middle temporal gyrus, L	**19-21,37,39**	-50	-64	8	15.97	5821	$P < 0.001$
Middle temporal gyrus, R	**19-22,28,34,**	54	-66	0	16.79	15089	$P < 0.001$
(incl. hippocampus, amygdala, and insula)	**37,41,42,48**						
Precuneus / Posterior cingulate cortex	**23,26**	4	-54	30	9.44	1310	$P < 0.001$
Inferior frontal gyrus, L & R	**45**	-48	32	4	5.16	303	$P = 0.005$
Superior medial frontal gyrus	**8-10,32**	6	52	32	8.97	1821	$P < 0.001$
Rectal gyrus	**11**	4	56	-16	7.54	420	$P < 0.001$
Neutral > Aversive							
Cerebellum, L	**/**	-40	-62	-44	5.37	236	$P = 0.016$
Calcarine, L & R	**17-19,23,27,**	-16	-58	14	9.40	2069	$P < 0.001$

	29,30,37						
Inferior parietal lobule, L	**7,39,40**	-48	-54	48	6.76	637	$P < 0.001$
Inferior parietal lobule, R	**7,39,40**	50	-48	48	8.36	1017	$P < 0.001$
Inferior temporal gyrus, L & R	**20-22,37,48**	62	-40	-14	8.46	2595	$P < 0.001$
Fusiform, L & R	**17,19,23,27,**	28	-44	-10	9.37	1787	$P < 0.001$
	30,37						
Superior temporal gyrus, L & R	**20-22,43,48**	-58	-4	4	7.25	2798	$P < 0.001$
Middle frontal gyrus, L & R	**8-11,45,46**	42	36	28	8.29	7901	$P < 0.001$
Valence by SME interaction (positive)							
Orbitofrontal cortex, L	**38**	-34	20	-18	4.39	210	$P = 0.026$
Medial superior frontal gyrus	**10,11,32**	0	66	20	5.28	1141	$P < 0.001$

The peak x, y, z coordinates are given in MNI152 standard space coordinates. L and R denote left and right. SME: subsequent memory effect. All effects were analyzed using whole brain family wise error (FWE) correction for multiple comparisons at the cluster-level ($P_{fwe} < 0.05$), after using a height threshold of $P < 0.001$.

Supplementary Table S3

Regions revealing significant slow CORT effects, after correcting for the difference in cortisol level between placebo and slow CORT during scanning.

Region		MNI Coordinates					
	Brodmann area	x	y	z	Peak T-score	Cluster size	*P*-value
Placebo > Slow CORT							
Middle frontal gyrus, R	**9,46,48**	24	36	30	4.48	717***	$P < 0.001$*
Middle frontal gyrus, L	**9,46,48**	-24	34	28	4.42	165^{+}	$P = 0.025^{+}$
Sup orbitofrontal lobule, L	**11**	-24	52	-2	3.82	155^{+}	$P = 0.030^{+}$

The peak x, y, z coordinates are given in MNI152 standard space coordinates. L and R denote left and right. All effects were analyzed using family wise error (FWE) correction for multiple comparisons at the cluster-level ($P_{fwe} < 0.05$), after using a height threshold of $P < 0.001$. *: FWE-corrected for whole brain volume, $^{+}$: FWE-corrected for region of interest

Supplementary Figure S1

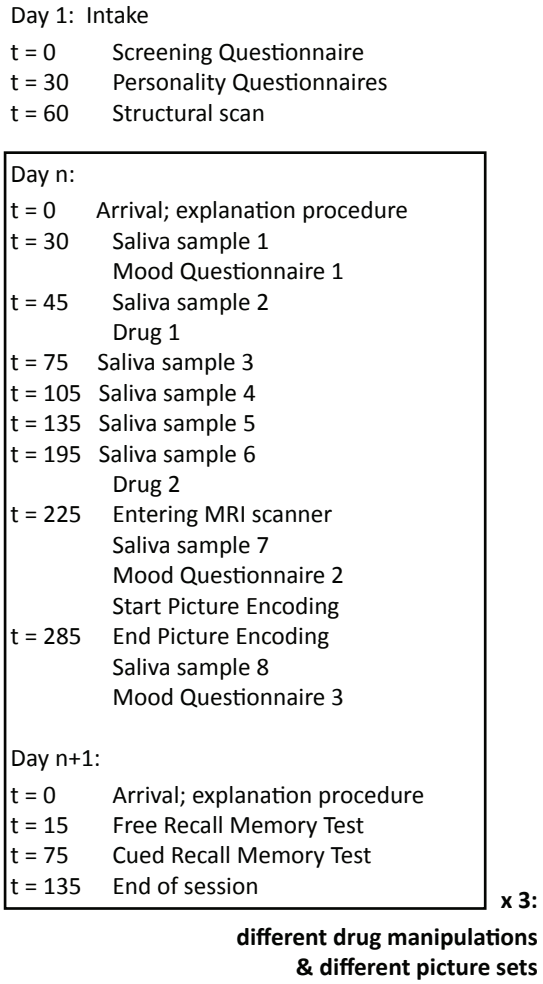

Fig. S1 Time line of the experiment. Participants were first invited for an intake interview, after which they returned for three sessions consisting of two subsequent days and separated by approximately a month. t = time in minutes

Supplementary Figure S2

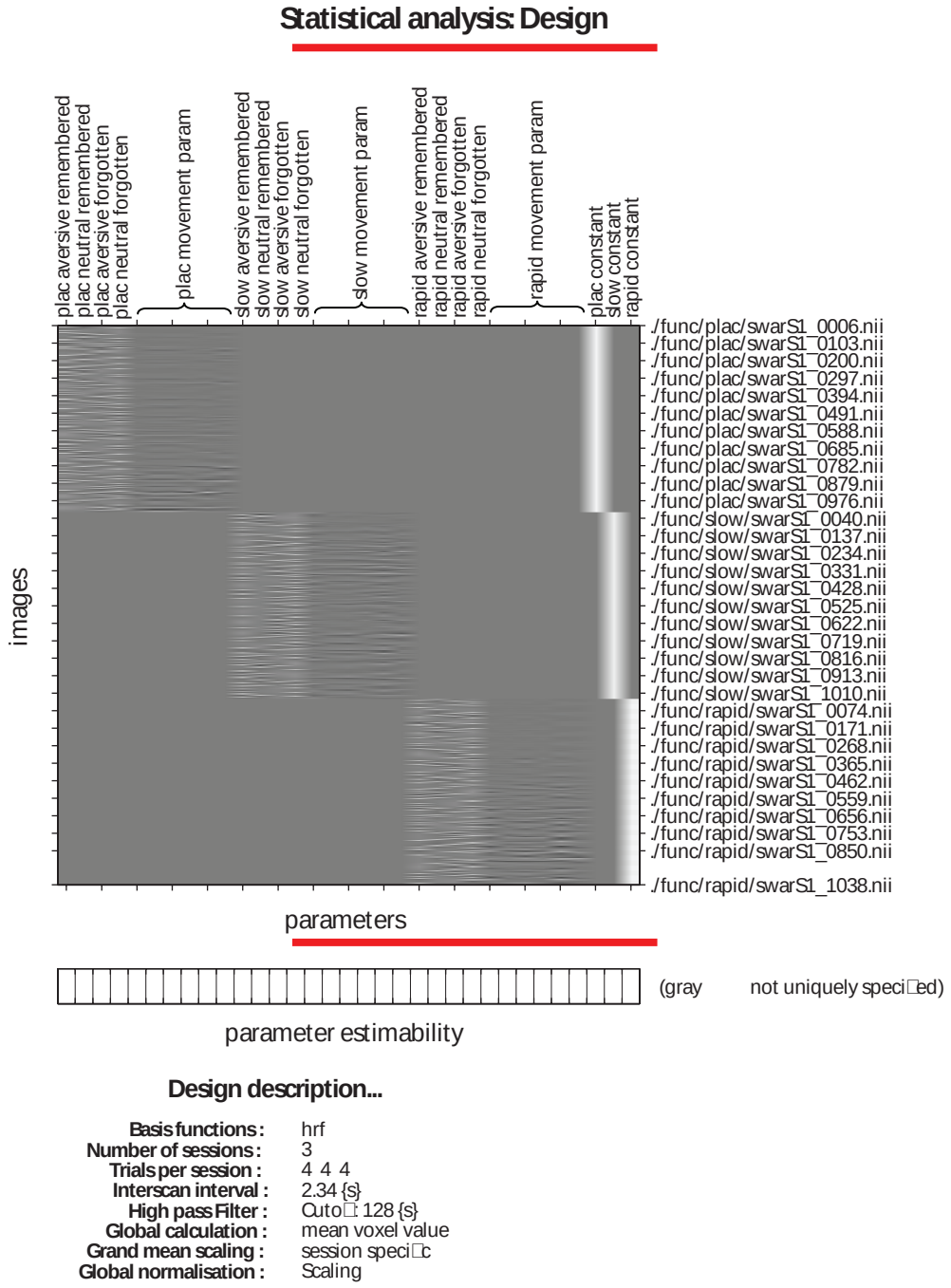

Fig. S2 Exemplary design matrix for the first model used in fMRI data analysis. All individual events were modeled based on drug condition (slow CORT vs. rapid CORT vs. placebo), subsequent memory (remembered vs. forgotten), and item aversiveness (aversive vs. neutral). Besides these regressors the six covariates corresponding to the movement for every session were included in the model, as well as a constant.

Supplementary Figure S3

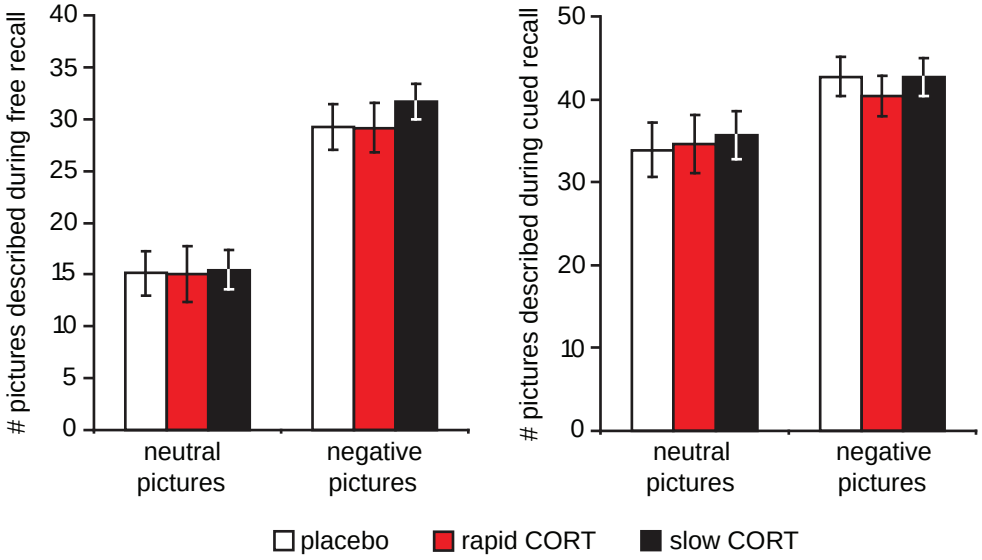

Fig. S3 Number of pictures recalled in the free and cued recall tests. CORT; hydrocortisone

Supplementary Figure S4

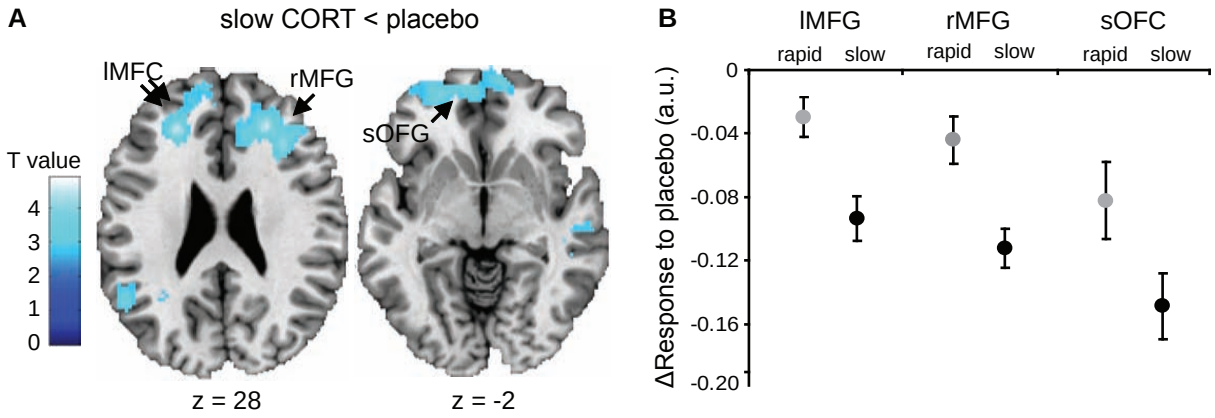

Fig. S4 Brain regions displaying decreased activity compared to placebo due to the slow effects of hydrocortisone (CORT). To correct for the residual elevation in salivary cortisol levels still present during scanning, the absolute difference was entered as a covariate in the general linear model. **A**, This did not change the results: activity in middle prefrontal gyrus (MFG) and orbitofrontal cortex (OFC) was strongly reduced in the slow CORT condition. **B**, parameter estimates of the observed activation clusters in Fig S4A revealed significant downregulation due to the slow effects of corticosteroids.