Impaired Suppression of Delay-Period Alpha and Beta Is Associated With Impaired Working Memory in Schizophrenia

Supplemental Information

Working Memory Capacity Estimation

Parameters for each person were fit using the Bayesian Monte Carlo sampler Stan (Stan Development Team, 2013) in R (R Development Core Team, 2016). The model was fit according to the full model in Rouder et al. (1). For each person, the hit rate (h) and false alarm (f) rate for each set size i:

$$h_i = A(d_i + (1 - d_i)G_j) + (1 - A)G$$

$$f_i = A(i - d_i)G + (1 - A)G$$

where

$$d_i = \min(1, k/M_i)$$

The priors for working memory capacity K_{MAX}, *attention A*, and guessing parameter G were described by uniform distributions:

$$K_{MAX} \sim U(0, 6)$$

$$A \sim U(0,1)$$

$$G \sim U(0,1)$$

with the likelihood function for the data for change (C) and same (S) trials assuming independent binomial distributions:

$$H_i \sim B(h_i, N^C_i)$$

$$F_i \sim B(f_i, N^S_i)$$

Priors for each parameter were uniform priors bounded between 0 and 1 for G and A, and bounded between 0 and 6 (max set size) for K_{MAX}. The use of uniform priors for each parameter coincides with the maximum likelihood estimate. The model was run across four chains with 1000 iterations per chain (500 burn-in and adaption; 500 sampling) for a final posterior sample of 2000 iterations. Convergence was assessed with plots of the posterior and the Gelman-Rubin statistic (2) where numbers close to 1 indicate good mixing of the chains. The mean number of effective samples per person was ~ 1500 for each parameter.

Exploratory Analysis of Suppression Response

As part of a *post hoc* exploratory analysis, we examined two different components of the suppression response (*peak suppression* and *maintenance suppression*) separately for alpha and beta frequency bands at frontal and posterior electrode sites. The measurement window for the peak suppression component was identified by taking the average latency of the peak suppression response ± 2 standard deviations (see Supplementary Figure S5; light gray panel). The maintenance suppression measurement window was defined as the remainder of the delay period (dark gray panel).

The t-tests and pearson correlations were corrected using corrections for false discovery rate (FDR; 3) and correlations are presented in Supplementary Table S6. Similar to findings reported in the main text, we found that PSZ exhibited significantly reduced peak suppression in both frequency bands and in both frontal and posterior sites (all t's > 3.03; all p's < 0.01), as well as significantly reduced maintenance suppression in both frequency bands and in both frontal and posterior sites (all t's > 3.83; all p's < 0.001). We next asked the question of whether the peak suppression component or the maintenance suppression component exhibited a stronger relationship with K_{MAX}. The results of this analysis are presented in Supplementary Table S6. In general, maintenance suppression exhibited a numerically stronger relationship to K_{MAX} than did peak suppression in HCS, whereas peak suppression exhibited a numerically stronger relationship to K_{MAX} than did maintenance suppression in PSZ. Statistically, the relationships between K_{MAX} and the two suppression components were not significantly different from one another (all z's < 1.64; all p's > 0.10); however, these findings suggest that different phases of the alpha/beta suppression response may be contributing differently to working memory capacity between the two groups.

Supplementary Table S1. Demographic information (mean ± SD)

	Healthy Controls	Schizophrenia Patients
Gender (M : F)	20 : 11	21 : 9
Age	36.48 ± 10.39	36.47 ± 11.06
Race (AA : C : Other)	13 : 16 : 2	11 : 18 : 1
Education (years)	15.45 ± 2.10	13.50 ± 2.39**
Parental Education	14.60 ± 2.62	14.40 ± 2.60
Chlorpromazine dose equivalent (mg/day)		461.01 ± 316.22
BPRS		31.57 ± 8.69
SANS		22.50 ± 12.22
LOF (social + occupational subscales)		8.45 ± 4.18
WASI	112.83 ± 10.83	103.00 ± 15.08**
WRAT-4	112.63 ± 12.22	102.45 ± 17.81**
WTAR	113.50 ± 9.28	103.55 ± 18.03**
MATRICS Total	51.87 ± 9.03	38.17 ± 12.34***
Processing Speed	54.17 ± 9.18	43.72 ± 9.75***
Attention/Vigilance	50.07 ± 7.46	45.97 ± 11.20
Working Memory	52.67 ± 7.56	44.41 ± 10.28***
Verbal Learning	50.83 ± 8.54	38.83 ± 8.50***
Visual Learning	48.53 ± 10.17	40.48 ± 14.08*
Perceptual Reasoning	50.53 ± 9.58	46.83 ± 10.10
Social Cognition	53.20 ± 9.42	39.90 ± 11.15***

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$
BPRS = Brief Psychiatric Rating Scale; SANS = Scale for the Assessment of Negative Symptoms; LOF = Level of Functioning; WASI = Wechsler Abbreviated Scale of Intelligence; WRAT = Wide Range Achievement Test; WTAR = Wechsler Test of Adult Reading; MCCB = MATRICS Consensus Cognitive Battery

Supplementary Table S2. Percentage trials retained by set size (± SD)

	Set Size 1	Set Size 2	Set Size 4	Set Size 6
HCS	70.5% (±17.4%)	72.7% (±15.5%)	72.9% (±14.2%)	73.7% (±13.9%)
PSZ	69.2% (±15.9%)	71.5% (±11.7%)	72.8% (±11.1%)	71.6% (±13.4%)

Supplementary Table S3. Pearson correlations between K, AL, clinical, and cognitive variables.

	Healthy Controls		Schizophrenia Patients	
	K	AL	K	AL
Age	-0.20	-0.09	-0.51**	0.04
Education	0.19	0.10	0.38*	0.11
Parental Education	0.32$^+$	0.17	0.20	-0.05
WASI IQ	0.54**	0.29	0.42*	0.20
WRAT	0.23	0.16	0.37*	-0.10
WTAR	0.30	0.28	0.26	-0.12
MATRICS Total	0.44*	-0.05	0.23	0.27
Processing Speed	0.37*	-0.09	0.17	0.26
Attention/Vigilance	0.08	0.12	0.20	0.30
Working Memory	0.31	-0.01	0.24	0.13
Verbal Learning	0.32$^+$	0.03	0.07	0.05
Visual Learning	0.29	-0.01	0.13	0.00
Problem Solving	0.34$^+$	-0.11	0.12	0.36$^+$
Social Cognition	0.24	-0.12	0.15	0.30
LOF Total	--	--	-0.01	0.41*
BPRS Total	--	--	-0.02	-0.34$^+$
SANS Total	--	--	0.27	-0.57**
Chlorpromazine Dose Equivalent	--	--	-0.11	-0.10

$^+$p < 0.10; *p < 0.05; **p < 0.01; ***p < 0.001

MCCB = MATRICS Consensus Cognitive Battery; WASI = Wechsler Abbreviated Scale of Intelligence; WTAR = Wechsler Test of Adult Reading; WRAT = Wide Range Achievement Test; BPRS = Brief Psychiatric Rating Scale; LOF = Level of Functioning

Supplementary Table S4. Correlation between average alpha/beta suppression and demographic & cognitive variables (posterior sites only).

	Healthy Controls		Schizophrenia Patients	
	Average Alpha Suppression	Average Beta Suppression	Average Alpha Suppression	Average Beta Suppression
Age	0.18	0.19	0.23	0.11
Education	-0.22	-0.19	0.21	0.37
Parental Education	-0.24	-0.16	0.19	0.06
WASI IQ	-0.49[+]	-0.57*	0.01	0.02
WRAT	-0.25	-0.30	0.07	0.15
WTAR	-0.40[+]	-0.39[+]	0.10	0.26
MATRICS Total	-0.47[+]	-0.46[+]	-0.18	-0.03
Processing Speed	-0.35	-0.24	-0.05	0.05
Attention/Vigilance	-0.25	-0.40[+]	0.00	0.06
Working Memory	-0.25	-0.31	-0.23	0.02
Verbal Learning	-0.47[+]	-0.45[+]	-0.34	-0.03
Visual Learning	-0.28	-0.26	-0.08	0.03
Problem Solving	-0.13	-0.15	-0.15	-0.11
Social Cognition	-0.34	-0.32	-0.16	-0.23
LOF Social/Occupational	--	--	0.04	0.03
BPRS Total	--	--	-0.07	0.17
SANS Total	--	--	0.07	-0.08
Chlorpromazine Dose Equivalent	--	--	0.13	0.03

[+]$p < 0.10$; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$
MCCB = MATRICS Consensus Cognitive Battery; WASI = Wechsler Abbreviated Scale of Intelligence; WTAR = Wechsler Test of Adult Reading; WRAT = Wide Range Achievement Test; BPRS = Brief Psychiatric Rating Scale; LOF = Level of Functioning

Supplementary Table S5.   Correlation between average alpha/beta suppression and demographic & cognitive variables (frontal sites only).

|	Healthy Controls		Schizophrenia Patients	
	Average Alpha Suppression	Average Beta Suppression	Average Alpha Suppression	Average Beta Suppression
Age	0.30	0.05	0.24	0.16
Education	-0.16	-0.30	0.02	0.25
Parental Education	-0.10	-0.14	-0.02	0.25
WASI IQ	-0.47[+]	-0.46[+]	-0.02	-0.07
WRAT	-0.26	-0.34	-0.15	-0.01
WTAR	-0.32	-0.41[+]	-0.15	0.06
MATRICS Total	-0.60*	-0.28	-0.04	-0.23
Processing Speed	-0.41[+]	-0.31	0.05	-0.21
Attention/Vigilance	-0.34	-0.34	0.13	0.05
Working Memory	-0.43[+]	-0.37	-0.26	-0.20
Verbal Learning	-0.41[+]	-0.13	-0.21	-0.06
Visual Learning	-0.46[+]	-0.10	-0.03	-0.31
Problem Solving	-0.36	0.01	0.18	-0.09
Social Cognition	-0.33	-0.18	-0.05	-0.32
LOF Social/Occupational	--	--	0.13	0.02
BPRS Total	--	--	-0.16	0.24
SANS Total	--	--	-0.07	-0.06
Chlorpromazine Dose Equivalent	--	--	-0.03	0.22

Supplementary Table S6. Correlations between K_{MAX} and suppression components.

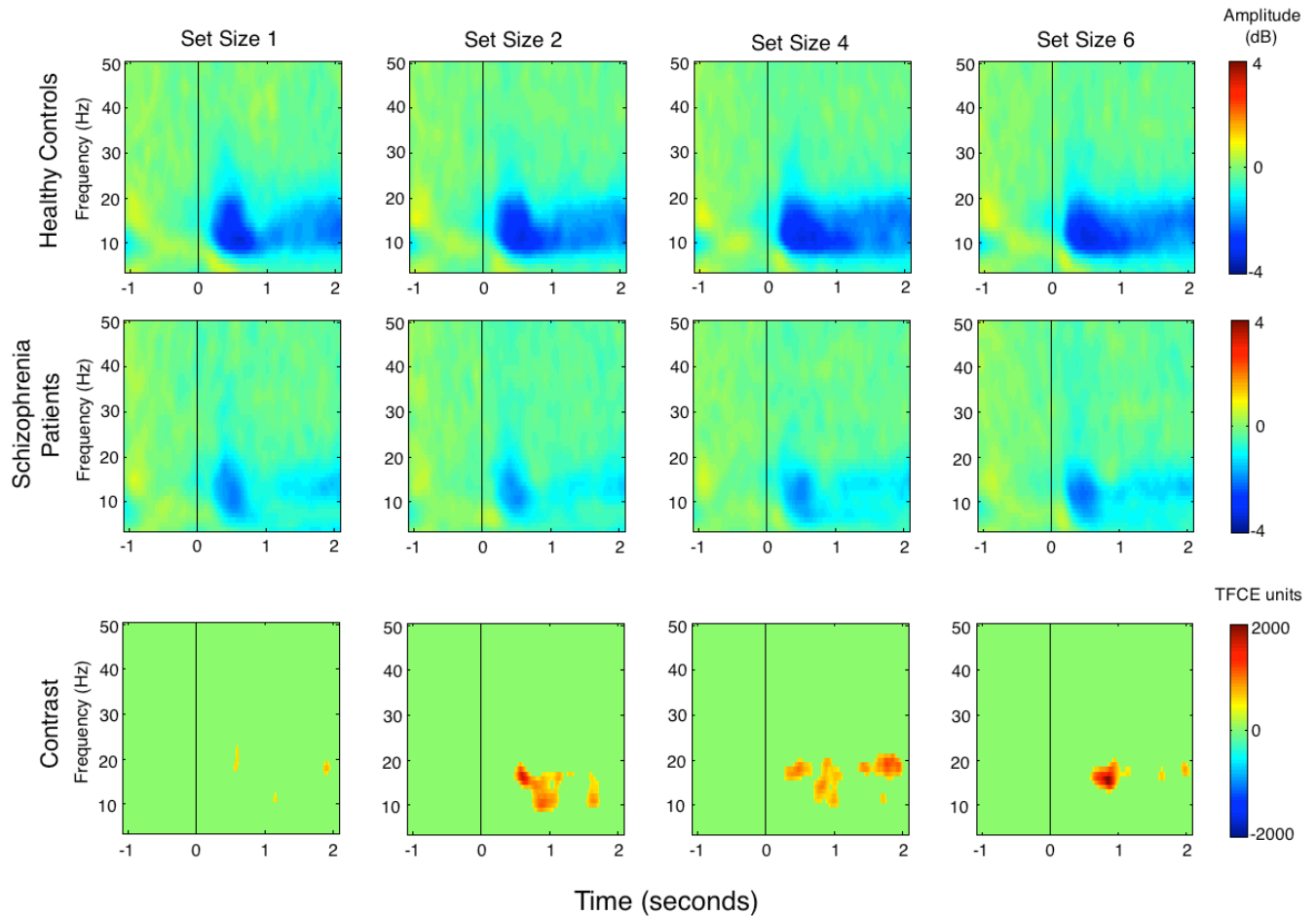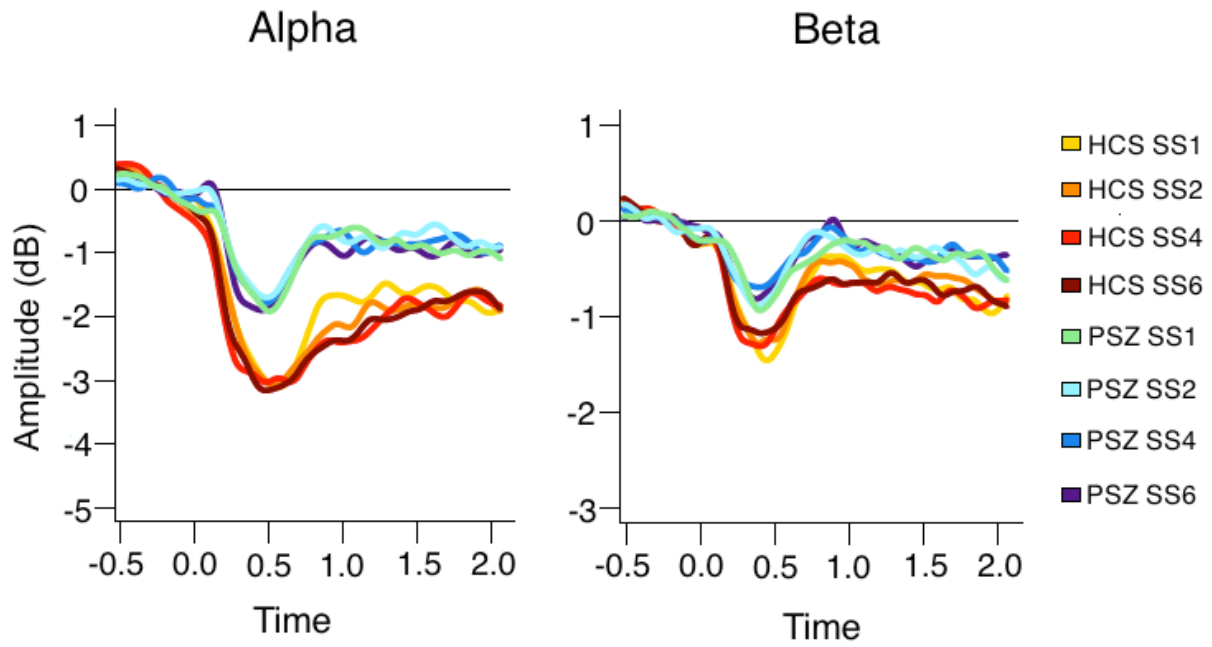|	Healthy Controls K_{MAX}	Schizophrenia Patients K_{MAX}	Group Differences p-value
Posterior Alpha (peak suppression)	-0.23	-0.08	0.569
Posterior Beta (peak suppression)	-0.41*	-0.20	0.390
Frontal Alpha (peak suppression)	-0.44*	-0.25	0.424
Frontal Beta (peak suppression)	-0.44*	-0.33	0.631
Posterior Alpha (maintenance suppression)	-042*	-0.11	0.211
Posterior Beta (maintenance suppression)	-0.50*	-0.09	0.089[+]
Frontal Alpha (maintenance suppression)	-0.57**	-0.24	0.136
Frontal Beta (maintenance suppression)	-0.53**	-0.05	0.046*

*p<0.05
**p<0.01
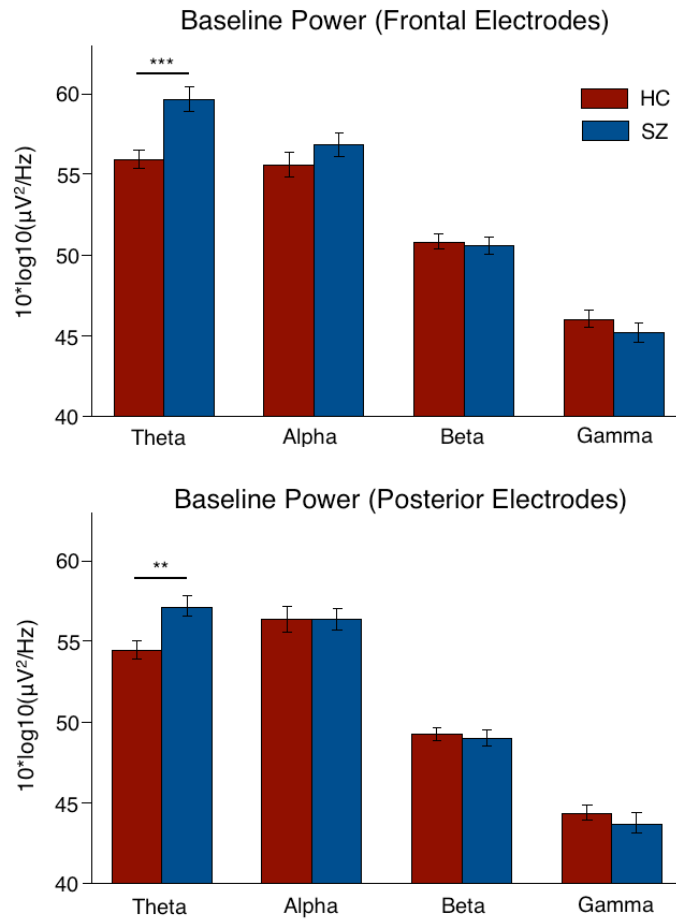
**Supplementary Figure S1.** Pre-stimulus baseline power (± standard error) for each frequency band.
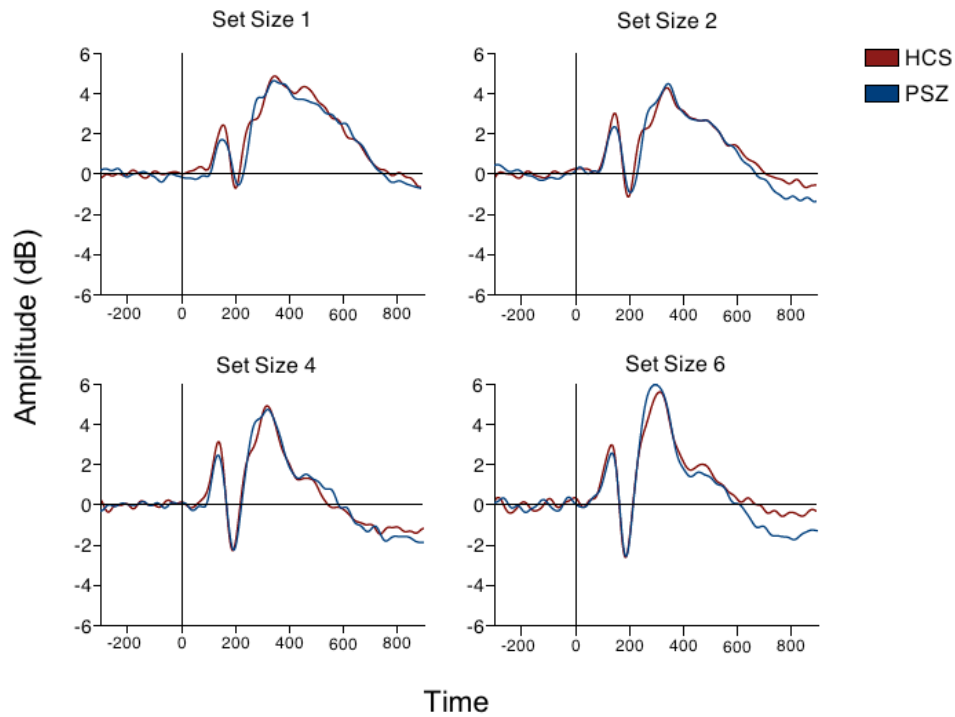
Supplementary Figure S2. Visual evoked potentials for all 4 set sizes. P1, N1, and P2 mean amplitude were measured at the average of PO7/PO8 electrodes, where the grand average signal was maximal. Mean amplitude was not significantly different between the two groups at any set size, and for any of the three components measured (P1, N1, P2; all p's > 0.18).

Supplementary Figure S3. Time x frequency plots for average frontal electrodes, corrected to pre-stimulus baseline period. Top panel = healthy control subjects; middle panel = schizophrenia patients; bottom panel = contrast in arbitrary units using threshold-free cluster enhancement. Using a repeated measures ANOVA, average frontal alpha suppression (200-2000 ms post-stimulus) showed the expected effect of increased suppression as a function of set size (main effect of set size: $F_{3,177} = 4.28$; $p < 0.01$). Alpha suppression was also significantly greater among HCS compared to PSZ (main effect of diagnosis: $F_{1,59} = 16.09$; $p < 0.001$). The group-by-set size interaction observed in posterior alpha suppression only reached the level of a trend in frontal electrode sites ($F_{3,177} = 2.45$; $p = 0.07$). Within the beta frequency band, average suppression was significantly greater among HCS ($F_{1,59} = 26.52$; $p < 0.001$); however, there was no significant main effect of set size ($F_{3,177} = 0.47$; $p = 0.70$). A group-by-set size interaction in frontal beta suppression was observed at the level of a trend ($F_{3,177} = 2.66$; $p = 0.05$).

Supplementary Figure S4. Time course of alpha and beta suppression in healthy controls and schizophrenia patients in posterior electrode channels.
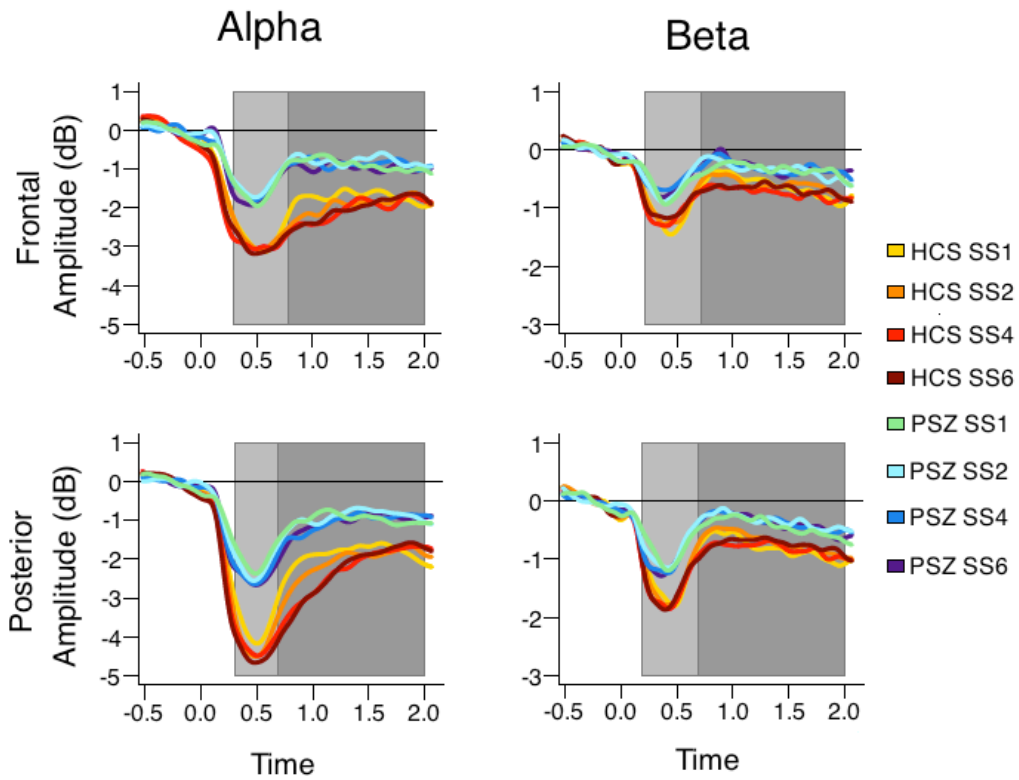
Supplementary Figure S5. Measurement windows for peak suppression (light gray) and maintenance suppression (dark gray) for *post hoc* suppression phase analysis.

Supplemental References

1. Rouder JN, Morey RD, Cowan N, Zwilling CE, Morey CC, Pratte MS (2008): An assessment of fixed-capacity models of visual working memory. *Proc Natl Acad Sci USA*. 105: 5975–5979.
2. Gelman A, Rubin DB (1992): Inference from iterative simulation using multiple sequences. *Statistical Science.* 7: 457-511.
3. Benjamini Y, Hochberg Y (1995): Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society Series B (Methodological).* 289–300.