Supporting Information

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SI Results

Behavioral Effect of Lesions. We analyzed subject reaction times, response bias (proportion of "match" compared with "non-match" responses), and percent misses. In a three-way ANOVA on reaction time, including all three groups, we found a load by hemifield interaction ($F_{2,42} = 8.61$, $P = 0.001$) and a group by load interaction ($F_{4,42} = 3.38$, $P = 0.017$). There was a main effect of load on reaction time such that all groups were slower to respond with increasing memory load ($F_{2,42} = 69.08$, $P < 0.0005$). There were no group by hemifield interactions ($F_{2,21} = 1.57, P = 0.23$) nor any effect of group ($F_{1,21} = 3.06, P = 0.068$). Although both patient groups showed a main effect of load on reaction time (PFC: $F_{2,10} = 41.77$, $P < 0.0005$; BG: $F_{2,10} = 11.10$, $P = 0.003$) neither group showed an effect of hemifield of stimulus presentation (PFC: $F_{1,5} = 3.20$, $P = 0.13$; BG: $F_{1,5} = 1.31$, $P = 0.30$).

In an analysis of response bias, we found only a main effect of load ($F_{2,42} = 8.62$, $P = 0.001$) where subjects tend to respond "match" more often at higher loads with no effect of group or group interactions ($F < 1.0$ all group effects). No group showed an effect of hemifield of stimulus presentation on response bias (controls: $F_{1,11} = 2.60, P = 0.14$; PFC: $F_{1,5} < 1.0$; BG: $F_{1,5} < 1.0$). In a series of post hoc t tests, no group showed a significant response bias overall ($P > 0.05$, corrected, for all comparisons). Finally, in an analysis of miss rates, we only found a main effect of load ($F_{2,42} = 6.47$, $P = 0.004$) with no effect of group ($F_{1,21} = 1.42$, $P = 0.26$) or group interactions ($P > 0.1$ for all comparisons). To normalize the distribution of miss rates, we performed statistical analyses on transformed miss rates (square root of the proportion of miss responses).

Electrophysiological Effects of Lesions. To examine the behavioral relevance of our electrophysiological findings, we performed a sliding-window correlation analysis at each time point between instantaneous CDA amplitude for each subject at each load with that subject's behavioral performance at the same load. For control subjects, instantaneous CDA amplitude and behavior are significantly correlated from ~250–950 ms poststimulus onset, which corroborates the a priori selection of the 300- to 900-ms time window based upon previous studies (1). This same analysis was performed separately for each group and each hemifield of stimulus presentation. As can be seen in Fig. S3, for ipsilesional stimuli in the PFC group there was no difference in the CDA/behavioral correlation compared with controls ($\chi^2 = 0.78, P = 0.38$); however, for contralesional stimuli, correlations were lower ($\chi^2 = 3.42$, $P = 0.027$). Within the BG group correlations were attenuated for both hemifields (ipsilesional: $\chi^2 = 32.74$, $P < 0.0005$; contralesional: $\chi^2 = 8.68$, $P = 0.003$). These results confirm the CDA and behavioral findings and demonstrate a strong relationship between delay-period electrophysiology and later behavioral outcomes.

It is important to note that although the large hemispheric differences in CDA amplitudes between hemispheres in the patient groups are not significant when assessed using paired-sample t tests and within-subjects ANOVAs, these differences are significant when assessed using independent-samples t tests. For example, if we treat hemifield of stimulus presentation as a between-subjects variable in the PFC analyses, rather than as a within-subjects variable, and run a two-way t test, then we see a significant effect of hemifield of stimulus presentation ($P = 0.022$). We see a similar pattern of results for the BG group. This means that although the distribution of the slopes between the ipsilesional CDA and contralesional sustained negativity do not significantly differ from zero, the distributions for the ipsilesional CDA and contralesional sustained negativity (separately, not the slopes) do significantly differ.

We performed additional analyses to examine the nature of the contralesional sustained negativity in more detail. We began by examining the scalp topographies of our groups during the CDA time window. Scalp topographies for patients differ significantly from that of controls for contralesional stimuli only (contra: $F_{16,168} = 2.88$, $P < 0.0005$; ipsi: $F_{16,168} = 1.20, P = 0.27$; Fig. S2*A*) due to the larger spatial spread and increased amplitude of posterior negativity. We also examined the relationship between CDA/sustained negativity and alpha power. Because posterior sustained negativity in patients is similar between groups, alpha/ERP analyses were performed on controls and a combined patient group (PFC and BG patients). In control subjects, alpha power is greatest over the midline at visual cortical sites. In contrast, posterior alpha power is distributed differently in the combined patient group (group by electrode interaction comparing three posterior electrodes, PO7, POz, and PO8; $F_{2,44} = 7.03$, $P = 0.015$). We examined alpha power in our control and patient groups in relation to posterior ERPs. In the patient group, alpha power is larger over the visual cortex in the damaged hemisphere ($P = 0.045$), whereas power is equally distributed between the left and right visual hemispheres in controls ($P = 0.15$; Fig. S2*B*).

We interpret this larger alpha power in the lesioned hemisphere as representative of the loss of top-down facilitation due to PFC or BG damage. We hypothesized that subjects who show larger relative visual cortical alpha power in the damaged hemisphere will have the least amount of task-related modulation of the sustained negativity because those subjects have the least amount of top-down facilitation. In Fig. S2*C Left*, we show that, for ipsilesional stimuli, there is no relationship between damaged visual cortical alpha power and CDA load effect. In contrast, in Fig. S2*C Right*, we see that patients with larger alpha power in the damaged visual cortex show the least amount of load modulation in the ERP. That is, patients with the most top-down dysregulation (most posterior alpha in the damaged hemisphere) show the least normal sustained negativity.

Recent evidence suggests that alterations in alpha power may account for the load-dependent modulation of posterior scalp negativities in memory tasks (2). Visual cortical alpha activity is related to cortical "idling" and reductions in alpha power are associated with visual attention and processing (3) that may influence local neuronal activity (4). Research using combined EEG and PET shows that EEG alpha power correlates with activity in the thalamus and parieto-occipital cortices (5). Parieto-occipital regions are strongly related to alpha power but the thalamus appears to regulate cortical alpha. The fact that both the PFC and BG groups show visual cortical alpha dysregulation is in accord with the known fronto-basal ganglia-thalamo-cortical anatomy. We demonstrate that PFC or BG damage leads to increased visual cortical alpha activity and that the patients with the greatest alpha power show the least load modulation of the contralesional sustained negativity. This suggests that PFC or BG lesions lead to failures of top-down mediated visual extrastriate excitation. Because striatal activation ultimately leads to disinhibition of the thalamus, which in turn provides excitatory input to the cortex (6), our subjects' BG lesions may impair thalamocortical excitation resulting in abnormal visual cortical alpha and sustained negative polarity ERPs as also seen in the PFC group.

SI Materials and Methods

We examined the correlation between CDA and behavior across time by correlating each subject's accuracy for each memory load with their respective CDA amplitude at that load. This was done on the average CDA amplitude across a 100-ms sliding window from 300 to 900 ms. To compare differences in correlation between EEG and behavior between groups and hemifields, we performed χ^2 tests for equality of correlation coefficients using the correlation coefficients from the 300- to 900-ms range.

1. Vogel EK, Machizawa MG (2004) Neural activity predicts individual differences in visual working memory capacity. *Nature* 428:748–751.
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3. Pfurtscheller G, Stancák A, Jr. Neuper C (1996) Event-related synchronization (ERS) in the alpha band—an electrophysiological correlate of cortical idling: A review. *Int J Psychophysiol* 24:39–46.
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5. Schreckenberger M, et al. (2004) The thalamus as the generator and modulator of EEG alpha rhythm: A combined PET/EEG study with lorazepam challenge in humans. *Neuroimage* 22:637–644.
6. Voytek B (2006) Emergent basal ganglia pathology within computational models. *J Neurosci* 26:7317–7318.

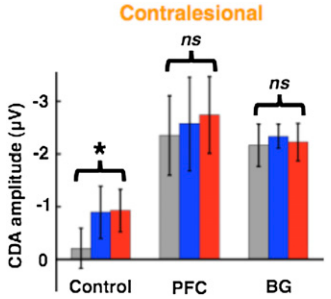

Fig. S1. CDA to contralesional stimuli. Summary of CDA findings for contralesional stimuli in the two patient groups (shown in detail in Fig. 3 *C–F*) and for right hemifield stimuli for controls (*P = 0.006; *ns*, not significant; error bars represent SEM).

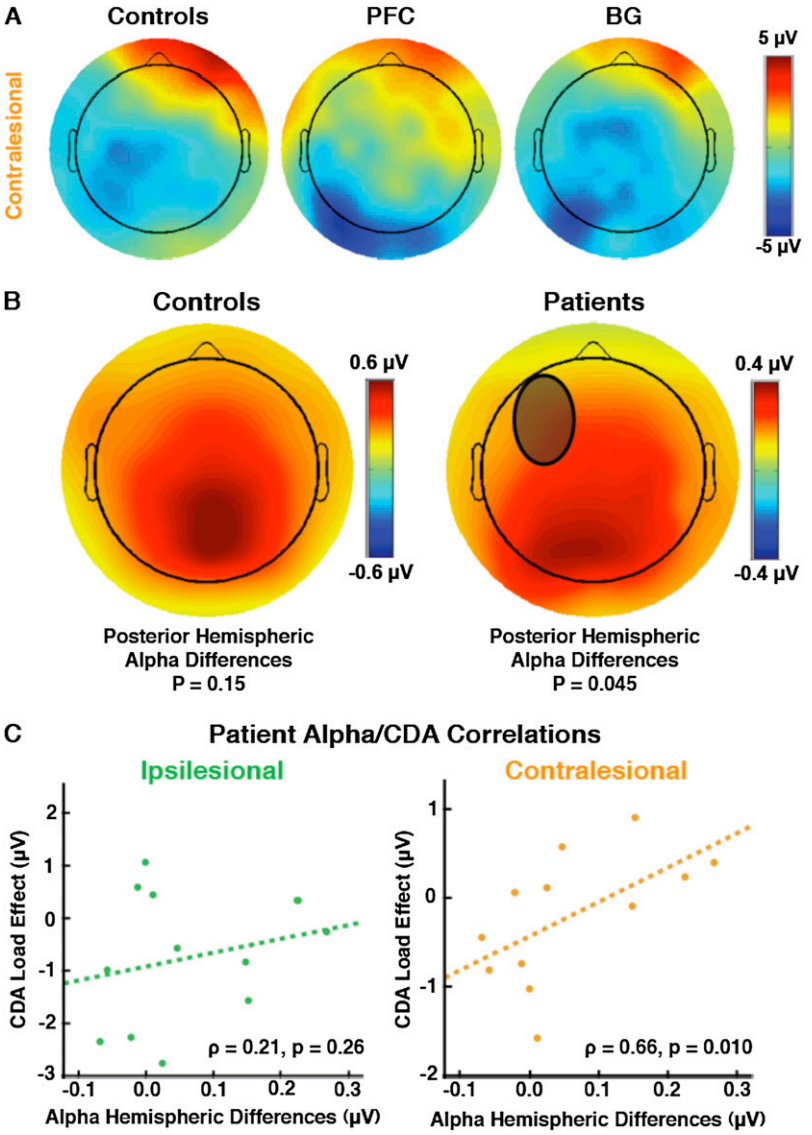

Fig. S2. Posterior alpha asymmetry underlies abnormal patient ERPs. (*A*) Scalp topographies of the ERP for three-item memory loads during the time window of the CDA in response to contralesional stimuli. Patient topographies differ significantly from controls for contralesional stimuli only. (*B*) Scalp topographies of alpha power (8–12 Hz) for controls (*Left*) and patients (*Right*). Because both patient groups showed similar delay period ERP abnormalities for contralesional stimuli, we performed all analyses on combined PFC and BG groups. Over the posterior electrodes used in CDA analyses, controls showed no differences in alpha power between left and right electrodes ($P = 0.15$, paired samples t test). In contrast, the patients showed greater alpha power over posterior electrodes in the lesioned hemisphere compared with the intact hemisphere ($P = 0.045$). (*C*) Within the patient group, there was no relationship between alpha hemispheric power differences and CDA load effect in response to ipsilesional stimuli (*Left*); however, patients with greater posterior alpha power in the damaged hemisphere showed a smaller CDA load effect (*Right*; $P = 0.01$).

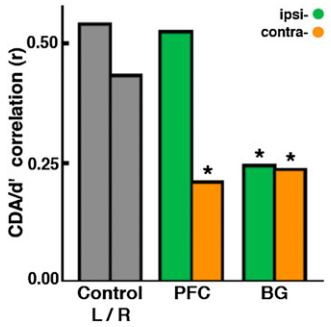

Fig. S3. Correlations between electrophysiology and behavior. CDA activity during the delay period correlates with behavioral accuracy. Here we plot the median correlation coefficients from 300 to 900 ms. The electrophysiology/behavior correlation analyses reflect our previous results wherein the PFC group shows a deficit only for contralesional stimuli, whereas the BG group shows an overall deficit (*$P < 0.05$ χ^2s tests for equality of correlation coefficients, significant deficit compared with controls).

Table S1. Summary of results, mean (SEM)

	Control		PFC		BG	
Memory load	Left	Right	Ipsilesional	Contralesional	Ipsilesional	Contralesional
1-item						
d′	3.23 (0.18)	3.32 (0.22)	3.46 (0.04)	2.91 (0.08)	2.76 (0.20)	2.85 (0.15)
CDA	−1.34 (0.23)	−0.31 (0.35)	0.29 (0.76)	−2.42 (0.72)	0.39 (0.53)	−2.18 (0.42)
N1	−2.16 (0.47)	−1.29 (0.29)	−0.60 (1.21)	−0.08 (0.76)	−0.55 (1.18)	−0.24 (0.93)
2-items						
d′	2.89 (0.13)	2.81 (0.16)	2.64 (0.08)	2.47 (0.08)	2.74 (0.20)	2.41 (0.16)
CDA	−1.69 (0.25)	−1.03 (0.42)	−0.89 (0.62)	−2.57 (0.84)	−0.20 (0.38)	−2.29 (0.23)
N1	−1.70 (0.53)	−2.11 (0.44)	−2.60 (1.30)	−1.29 (0.84)	−2.03 (1.30)	−2.13 (1.12)
3-items						
d′	2.00 (0.09)	2.17 (0.11)	1.79 (0.04)	1.74 (0.06)	1.58 (0.11)	1.82 (0.14)
CDA	−2.00 (0.32)	−0.97 (0.48)	−0.70 (0.47)	−2.74 (0.67)	−0.16 (0.54)	−2.26 (0.33)
N1	−2.13 (0.70)	−3.23 (0.57)	−3.24 (1.76)	−0.68 (1.04)	−3.86 (1.28)	−2.88 (1.42)