Prefrontal cortex and basal ganglia contributions to visual working memory

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Edited by Robert Desimone, Massachusetts Institute of Technology, Cambridge, MA, and approved September 7, 2010 (received for review May 25, 2010)

Visual working memory (VWM) is a remarkable skill dependent on the brain's ability to construct and hold an internal representation of the world for later comparison with an external stimulus. The prefrontal cortex (PFC) and basal ganglia (BG) interact within a cortical and subcortical network supporting VWM. We used scalp electroencephalography in groups of patients with unilateral PFC or BG lesions to provide evidence that these regions play complementary but dissociable roles in VWM. PFC patients show behavioral and electrophysiological deficits manifested by attenuation of extrastriate attention and VWM-related neural activity only for stimuli presented to the contralesional visual field. In contrast, patients with BG lesions show behavioral and electrophysiological VWM deficits independent of the hemifield of stimulus presentation but have intact extrastriate attention activity. The results support a model wherein the PFC is critical for top-down intrahemispheric modulation of attention and VWM with the BG involved in global support of VWM processes.

attention | electroencephalography | lesion | stroke

Even a seemingly simple action such as determining which of two bananas is riper requires us to compare real world visual information, such as the color of the banana you are currently looking at in the store, with your memory of the yellowness of the other banana you just put down. This relies in part on visual working memory (VWM), a remarkable ability wherein we construct and hold an internal model of a real-world visual stimulus that we then later compare against another stimulus. In essence, we construct and hold a model of the visual world and compare that model against subsequent inputs from the external world. VWM relies upon an intact and functioning prefrontal cortex (PFC), and damage to this region, such as from stroke, causes VWM impairments (1–3). However, cognitive processes do not localize to specific brain regions per se and a behavior as complex as VWM recruits a distributed network of cortical and subcortical structures (4–8), including the basal ganglia (BG) (9, 10) and visual extrastriate regions (11–13).

Most computational models of VWM rely upon intercommunication between the PFC and the striatum such that memories are maintained via recurrent activation in fronto-striatal loops (14–16). In vivo, working memory maintenance is associated with sustained delay-period activity in the PFC (5, 17) and BG (18), although the BG are thought to play a role in gating information into the PFC to allow it to update representations where necessary (19). Although neurons in both visual extrastriate and the PFC maintain VWM representations during delay periods, PFC neurons encode more information about the stimuli and are more resistant to distractors than visual extrastriate neurons (20). Animal research shows that the BG rapidly learn task-relevant rules and may send relevant, preprocessed information to the PFC for subsequent selection and further processing (21). Anatomically, the BG are situated in an ideal position to mediate cognitive behavior modulated via reinforcement learning (22, 23). Each striatum receives bilateral inputs from many cortical regions including the PFC and visual extrastriate cortex (24), and these inputs converge with dopaminergic afferents from the substantia nigra (25). The striatum is organized in parallel interconnected loops (24, 26, 27) with frontal cortical regions (including the PFC) via the globus pallidus, thalamus, and subthalamic nucleus. From a neuroanatomical perspective, each striatum receives PFC input bilaterally from both hemispheres (28) and thus both BG have connections to both PFC hemispheres. The BG are anatomically situated such that they receive inputs from many cortical regions, which may allow them to integrate broadly distributed cortical information such as from the PFC and visual extrastriate cortices (29).

Patients with BG pathology, such as from stroke or Parkinson disease, have deficits in a variety of cognitive learning and switching tasks (30–35) similar to the profile observed in patients with lateral PFC lesions (2). The BG deficits are proposed to be due to a general deficit in the manipulation of internally represented stimuli (36). Human neuroimaging shows that activity in the BG and PFC is associated with individual differences in VWM capacity and that BG activity is specifically associated with filtering out irrelevant distracting information (9, 37), consistent with gating models of BG function and stimulus manipulation.

Scalp electroencephalography (EEG) studies show that extrastriate activity increases with the number of items held in VWM up to an individual's VWM capacity limit and that this activity correlates with individual VWM capacity differences (11). Although sustained PFC activity is associated with working memory maintenance, the role of attention in working memory—both to external stimuli and internal representations of the same—cannot be ignored (38–40). This attention/working memory interrelationship has lead to theories of PFC function that highlight the role of the PFC in information integration (41), with interactions between the PFC and BG necessary to build models of complex rules and behavior from discrete components (42).

Lesion studies in human and nonhuman primates have provided the strongest evidence for a causal relationship between anatomy and function (1, 43). For example, because PFC lesions lead to working memory deficits, the PFC can be said to play an important, necessary role in working memory networks. Research has shown that unilateral PFC lesions cause lateralized deficits in top-down modulation of visual attention (44, 45). These deficits manifest as errors in target detection specifically to targets that appear in the contralesional hemifield. These target-detection errors are associated with attenuation of visual extrastriate event-related potentials (ERPs), including the early visual N1. This early latency ERP (100–200 ms after stimulus onset) is modulated by attentional state and is enhanced in the stimulated visual hemisphere during lateralized attentional allocation (46) and attenuated in the damaged hemisphere in the presence of a unilateral PFC lesion (44). Because EEG studies provide a direct neural measure of working memory load (11) and attentional allocation (46, 47), we used

Author contributions: B.V. and R.T.K. designed research; B.V. performed research; B.V. analyzed data; and B.V. and R.T.K. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

Freely available online through the PNAS open access option.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1007277107/-/DCSupplemental.

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EEG to assess top-down cognitive deficits associated with unilateral lesions on a within-hemisphere basis.

We hypothesized that the BG plays a visual-field independent role in VWM updating and learning. Conversely, we predicted that the PFC has an executive role in VWM maintenance, attentional control, and top-down facilitation of visual extrastriate cortices on a within-hemisphere basis. Thus, we examined two groups of patients with either unilateral PFC or BG lesions (Fig. 1) performing a lateralized VWM task (Fig. 2*A*) while recording scalp EEG. By making use of a lateralized visual design, we took advantage of the inherent contralateral organization of the mammalian visual system wherein visual input from the right visual field enters the left visual cortex and vice versa. In Fig. 2*B* we illustrate how a patient with a left PFC lesion viewing a stimulus in the left visual hemifield would receive the visual input into the intact cerebral hemisphere; that same patient viewing a right hemifield stimulus would receive the information in the damaged hemisphere, leading to behavioral deficits mainly in the contralesional visual field. By combining a lateralized VWM design with scalp electrophysiology in patients with unilateral brain lesions, we reveal distinct contributions of the PFC and BG to VWM maintenance and examine the role of each region in top-down modulation of extrastriate activity.

Results

Behavioral Effect of Lesions. In a three-way ANOVA including all three groups, we found a main effect of load on accuracy such that all groups were less accurate with increasing memory load ($F_{2,42}$ = 344.45, $P < 0.0005$). There was also a three-way interaction between group, memory load, and hemifield of presentation ($F_{4,42}$ = 12.47, $P < 0.0005$). We performed ANOVAs comparing performance between and within the patient groups to examine the nature of this three-way interaction. Accuracy results are summarized by the group × hemifield effect (collapsed across load) in Fig. 2*C* ($F_{2,21}$ = 10.17, P = 0.001; Table S1 contains all accuracy results).

In a comparison between controls and PFC patients, we found a three-way interaction ($F_{2,32}$ = 14.41, $P < 0.0005$). Consistent with our hypothesis, there was a significant group × hemifield interaction ($F_{1,16}$ = 16.17, P = 0.001). The PFC patients showed a significant hemifield × load interaction ($F_{1,5}$ = 37.46, P = 0.002) and a main effect of hemifield ($F_{1,5}$ = 29.21, P = 0.003) wherein they were less accurate overall for contralesional stimuli. There was no effect of hemifield in the control group ($P > 0.5$). These results suggest that the hemifield × group interactions were driven by deficits in the PFC group in response to contralesional stimuli. This was confirmed in an analysis comparing accuracy by hemifield between groups wherein PFC patients were impaired for contralesional stimuli compared with controls (P = 0.026). In comparing controls and BG patients, we also found a three-way interaction ($F_{2,32}$ = 5.40, P = 0.010). Unlike the PFC group, BG patients showed no main effect of hemifield on performance ($F_{1,5} < 1.0$) and were impaired compared with control subjects in both hemifields (ipsi: P = 0.046; contra: P = 0.025). Analyses of other behavioral measures, including response bias, reaction times, and hit rates (*SI Results*), indicate that the patient behavioral deficits arise from errors in working memory rather than from motoric deficits or systematic response biases.

Research suggests that the BG are critical in learning behavioral requirements (8, 21, 32, 47, 48). Therefore, we examined the temporal evolution of behavioral performance across the first 100 trials (*Materials and Methods*). In comparing controls to PFC patients, there was a main effect of trial on performance ($F_{3,48}$ = 3.14, P = 0.034) and a main effect of group ($F_{1,16}$ = 15.88, P = 0.001) but no group × trial number interaction, which suggests that both groups improved across the first 100 trials and that the PFC group performed worse than controls. In contrast, when we compared the BG group to controls, we found a significant group × trial number interaction ($F_{3,48}$ = 3.64, P = 0.019). Although both the BG and control groups showed a main effect wherein behavior improved across trials (BG: $F_{3,15}$ = 5.13, P = 0.012; controls: $F_{3,33}$ = 2.95, P = 0.047), only the BG group showed a significant deficit during the initial trials (Fig. 2*D*, trials 1–25 compared with 26–51, P = 0.001; $P > 0.05$ for all other pair-wise comparisons between successive trial bins for both BG and control groups). It is important to note that although the behavioral deficits in the BG group were exaggerated during the first 25 trials, they continued to perform worse than controls in all time bins examined ($P < 0.05$ for all other binned analyses). This accuracy deficit was not due to prolonged reaction times extending through the end of the trial, as there was no effect of trial number on number of misses ($F_{3,15} < 1.0$).

Electrophysiological Effects of Lesions. We examined the effects of PFC and BG lesions on delay period EEG activity. We replicated previous findings that in normal subjects (11) the amplitude of contralateral delay activity (CDA) (*Materials and Methods,* Fig. 3, and Fig. S1) increases with memory load in a three-way ANOVA including all three groups ($F_{2,42}$ = 18.84, $P < 0.0005$); visual inspection of the CDA time courses (Fig. 3) showed that patient CDA amplitudes for contralesional stimuli are abnormal for both groups and that this is reflected in a different scalp topogra-

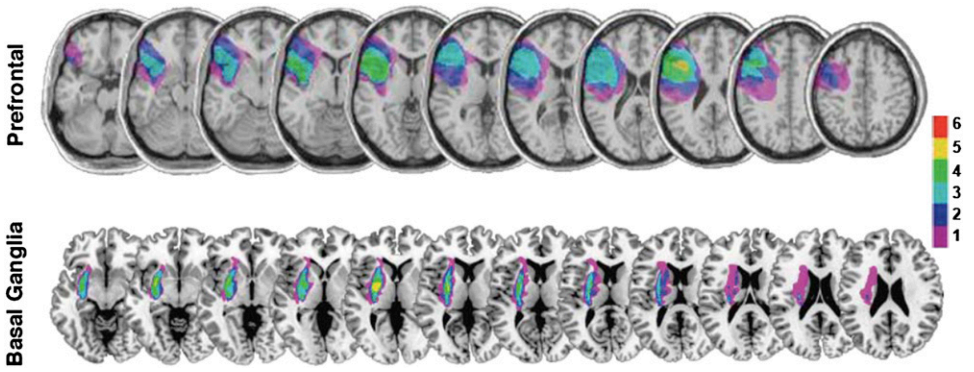

Fig. 1. Patient lesion reconstruction. Structural MRI slices illustrating the lesion overlap across the two patient groups (color represents number of subjects with a lesion at that voxel). For the PFC group (n = 6), mean lesion volume was 58.6 cm^3 and maximal lesion overlap (>50%) was in Brodmann areas 6, 8, 9, and 46 centered in the middle frontal gyrus and including portions of the inferior and middle frontal gyrus in some patients. For the BG group (n = 6), mean lesion volume was 9.7 cm^3 and maximal lesion overlap was in the putamen and encompassed the head and body of the caudate as well as the globus pallidus in some patients. All lesions are normalized to the left hemisphere for comparison; however, two patients in each group had right hemisphere lesions. Software reconstructions were performed using MRIcro (53).

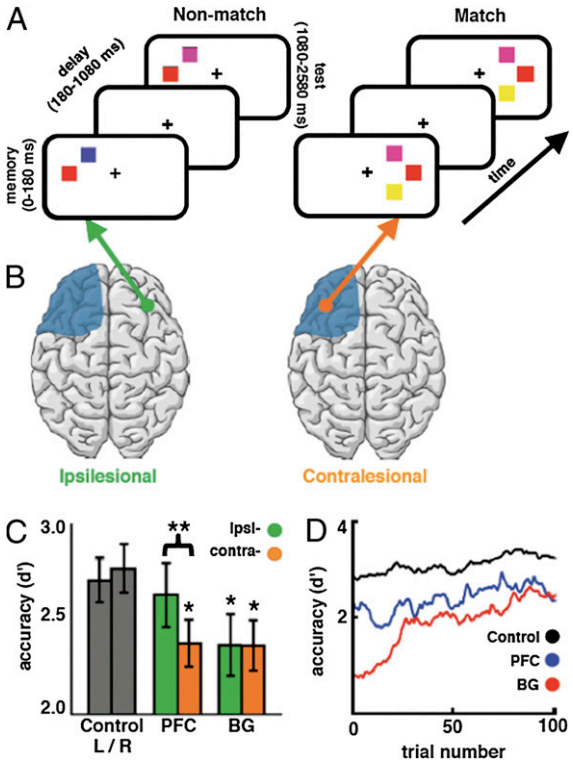

Fig. 2. Behavioral paradigm and performance. (*A*) Diagram of task design. (*B*) For a patient with a left unilateral PFC lesion, as illustrated here, stimuli that appear in the left visual hemifield are ipsilesional, and the visual information selectively enters the intact cerebral hemisphere, whereas stimuli that appear in the right visual hemifield are contralesional and selectively enter the damaged hemisphere. (*C*) Plots of average behavior by group and hemifield. Patients with unilateral PFC lesions performed as well as controls when stimuli were presented ipsilesionally but were impaired for contralesional stimuli. In contrast, patients with unilateral BG lesions performed more poorly overall, regardless of the hemifield of stimulus presentation. (*$P < 0.05$ compared with controls, **$P < 0.0005$, error bars represent SEM). (*D*) Control subjects and PFC patients performed equally well across trials. BG patients were significantly impaired in early trials.

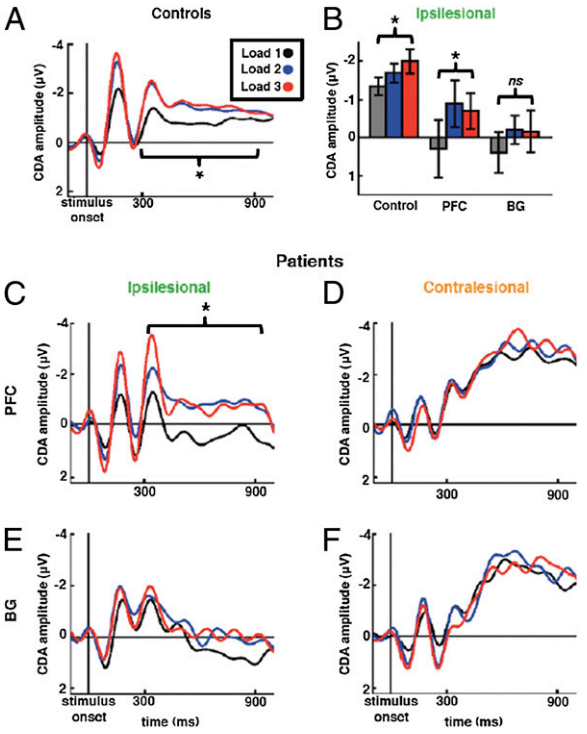

Fig. 3. Electrophysiological analyses (group grand averages). (*A*) Average CDA for control subjects collapsed across hemifield. For controls, CDA amplitude increases with memory load (*main effect of load, $P < 0.0005$). (*B*) Summary of CDA findings for ipsilesional stimuli in the two patient groups (shown in detail in *C*–*F*) and for left hemifield stimuli for controls. For ipsilesional stimuli (*C* and *E*), both controls and the PFC group show a significant effect of memory load on CDA (*$P < 0.05$, error bars represent SEM) that is not seen in the BG group (*ns*, not significant). For contralesional stimuli (*D* and *F*), the relationship between CDA and load is abolished in both patient groups. Both patient groups generated a sustained negative shift for contralesional stimuli that was not sensitive to VWM load (*SI Results*).

phy and a general loss of top-down facilitation as indexed by increased alpha power in posterior electrodes in the lesioned hemisphere (detailed analyses are in *SI Results*; see Fig. S2). For this reason, we will refer to the abnormal patient visual cortical ERPs as "sustained negativity" and not CDA. In the three-way ANOVA, there was a significant quadratic three-way interaction between group, memory load, and hemifield of presentation ($F_{2,21} = 3.74$, $P = 0.041$), driven by the effects of the lesion leading to the abnormal patient contralesional sustained negativity. This was reflected in a significant group × hemifield effect ($F_{2,21} = 6.65$, $P = 0.006$; Table S1 contains all CDA results).

In comparing PFC patients to controls, there was a significant group × hemifield interaction ($F_{1,16} = 7.45$, $P = 0.015$), although neither group showed a significant effect of hemifield in separate ANOVAs of each group (controls: $F_{1,11} = 2.95$, $P = 0.11$; PFC: $F_{1,5} = 3.21$, $P = 0.13$). This interaction was driven by a crossover effect wherein CDA amplitude is reduced in the PFC group for ipsilesional stimuli ($P = 0.001$) but is higher for contralesional stimuli ($P < 0.0005$). In separate planned contrasts, we examined the effects of hemifield of presentation on CDA amplitude within the patient groups for ipsilesional and contralesional stimuli. When this analysis was done in the control group, effect of load was significant for both hemifields (left: $F_{2,22} = 7.37$, $P = 0.004$; right: $F_{2,22} = 6.44$, $P = 0.006$). In the PFC group there was a significant effect of load for ipsilesional stimuli ($F_{2,10} = 4.17$, $P = 0.048$), driven by an effect wherein CDA amplitude increased from one to two items ($P = 0.003$) but not from two to three items ($P = 0.69$), similar to the pattern seen in control subjects (one to two: $P < 0.0005$; two to three: $P = 0.13$). As predicted due to the loss of top-down facilitation, for contralesional stimuli there was no effect of load ($F_{2,10} < 1.0$) in the PFC group.

In an analysis comparing CDA between the BG and control groups, there was also a significant group × hemifield interaction ($F_{1,16} = 13.20$, $P = 0.002$), although neither group showed a significant effect of hemifield in separate ANOVAs of each group (controls: $F_{1,11} = 2.95$, $P = 0.11$; BG: $F_{1,5} = 3.39$, $P = 0.13$). Just as with the comparison between controls and PFC patients, this interaction appears to be driven by a crossover effect wherein CDA amplitude is reduced in the BG group for ipsilesional stimuli ($P < 0.0005$) but is higher for contralesional stimuli ($P < 0.0005$). In contrast to PFC patients, in an analysis of hemifield of presentation on CDA amplitude within the BG group there was no effect of load for either ipsilesional or contralesional stimuli (ipsilesional: $F_{1,5} = 1.52$, $P = 0.27$; contralesional: $F_{1,5} < 1.0$).

In a final analysis, we examined the effects of lesions on the attention-related N1. Because of the relatively rapid nature of our task and the brief stimulus presentation time (180 ms), we hypothesized that the observed behavioral deficits in the patient groups could be partly due to the effects of the lesion on attentional control. In a three-way ANOVA including all three groups, we found a main effect of load on N1 amplitude such that increasing perceptual load lead to more negative N1 amplitude ($F_{2,42} = 23.54$, $P < 0.0005$). There was also a three-way interaction between

group, load, and hemifield of presentation ($F_{4,42} = 5.63, P = 0.001$; Table S1 contains all N1 results). The N1 results are summarized by the group × hemifield effect in Fig. 4. In separate analyses comparing controls with PFC patients and controls with BG patients, we also observed significant three-way interactions in both comparisons (PFC: $F_{2,32} = 8.89, P = 0.001$; BG: $F_{2,32} = 5.78$, $P = 0.007$). The control versus BG interaction arose from a group × load interaction ($F_{2,32} = 8.01, P = 0.002$) that was mediated by group differences for one-item arrays wherein BG patients had lower N1 amplitudes ($P = 0.024$). These differences disappeared for higher loads (two items: $P = 0.41$; three items: $P = 0.23$). In a post hoc analysis of the control versus PFC interaction, we examined the a priori hypothesis that PFC patients would have attention deficits in response to contralesional stimuli. Looking across all memory loads, there was no significant difference in N1 amplitude between groups for ipsilesional stimuli ($P = 0.43$). However, N1 amplitude was attenuated in the PFC group for contralesional stimuli ($P = 0.003$). As a comparison, there were no differences between controls and BG patients for either hemifield (ipsilesional: $P = 0.42$; contralesional: $P = 0.24$).

Discussion

These results highlight the distinct roles of the PFC and BG in VWM maintenance. We tested two separate groups of patients with either unilateral PFC or unilateral BG lesions, and age-matched controls while they performed a lateralized VWM task. By making use of a lateralized VWM design with a scalp EEG, we were able to take advantage of the anatomical separation of visual inputs into the neocortex by visual hemifield of presentation and examine the effects of lesions on top-down VWM maintenance. This lesion by hemifield design allowed us to assess behavioral and electrophysiological responses on a within- and between-subjects basis. That is, because patients' lesions were unilateral, we could assess differences in response to contralesional stimuli versus ipsilesional stimuli. Previous studies have shown this to be an effective means in highlighting top-down attention deficits associated with PFC lesions (44).

We found that patients with unilateral PFC lesions performed just as well as controls for ipsilesional stimuli and that accuracy dropped only when stimuli were lateralized to the contralesional hemifield. When we examined the evolution of performance over time, we found that PFC patients performed as well in the first few trials as they did in later trials, similar to the results of normal control subjects. In contrast to PFC patients, the BG group performed worse than controls regardless of the hemifield of stimulus presentation. Furthermore, BG patients performed worse during the initial 25 trials than they did in later trials. This was despite the fact that subjects were able to explicitly restate the rules and requirements of the task when questioned before the experiment began. The fact that the number of misses did not change across early trials argues against the possibility that this learning effect is an artifact due to BG patients making more responses outside of the response window. Interestingly, although patients in the BG group understood the task, they had difficulties initially engaging the neural mechanisms necessary to correctly perform it. The stabilization of behavioral performance at ~30 trials suggests that the BG group adopted a new strategy for performing the task.

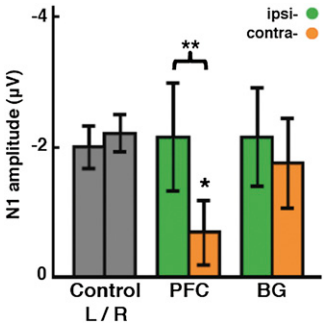

Fig. 4. Attention-modulated ERPs. N1 amplitudes from the contralateral visual cortex in response to the memory array. In the PFC group there is a significant effect of hemisphere (**$P = 0.023$) where N1 amplitudes are attenuated for contralesional stimuli and are lower than control amplitudes (*$P = 0.003$). The BG group shows no such deficit (error bars represent SEM).

Previous EEG research using a paradigm similar to ours in normal subjects has shown that delay-period CDA activity increases in magnitude with increasing memory load up to a subject's VWM capacity (11). We replicated this scaling effect for VWM load in our control group and extended this work to show that individuals' CDA amplitudes at each load correlate with their later behavioral performance (*SI Results* and Fig. S3). These results suggest that CDA accurately indexes behavioral performance. Within our PFC group, we found similar CDA effects for ipsilesional stimuli only. That is, the PFC group, as with controls, showed an increase in CDA from one- to two-item loads. CDA amplitude in response to ipsilesional stimuli also correlated with later behavioral performance. Similar to their behavioral performance, patients with unilateral PFC lesions showed no scaling of CDA amplitude in response to contralesional stimuli nor did CDA amplitude correlate with later behavioral outcomes.

In contrast to BG patients and controls, we found that PFC patients also had attenuated attention-dependent N1 amplitudes within the lesioned hemisphere only for contralesional stimuli. Previous studies have shown that posterior visual association cortex N1 amplitude is modulated by voluntary attention under top-down PFC control (46). Combined with the impaired CDA to contralesional stimuli, these electrophysiological results suggest that PFC lesions lead to an overall executive functioning deficit affecting multiple cognitive domains within the damaged hemisphere. That is, PFC damage results in a loss of top-down facilitation of visual extrastriate cortex during the working memory delay period, resulting in attention and VWM maintenance deficits contributing to poorer behavioral performance. Although we observed a strong brain/behavior correlation (*SI Results* and Fig. S3), previous research has found that the best predictor of behavioral performance is the load difference in CDA amplitudes rather than the actual amplitudes themselves (49).

Notably, both patient groups showed a pronounced sustained negativity for all contralesional stimuli that was independent of VWM load. Contrary to our findings in the PFC group, patients with unilateral BG lesions showed no load-dependant scaling of CDA amplitudes for either ipsilesional or contralesional stimuli. This was despite the fact that N1 amplitudes within the BG group were intact, even in the lesioned hemisphere. Although patients with unilateral BG neuropathology show deficits in attentional set shifting and general cognitive flexibility (19, 30, 50), the BG do not appear to play a critical role in the rapid allocation of visual attention. Rather, our BG patients show intact electrophysiology related to attentional allocation, whereas our PFC group has attentional impairments for contralesional stimuli. This suggests that the BG play a critical visual-field independent role in VWM maintenance but are not critical for top-down facilitation of early visual extrastriate cortex attentional processes. This adds further support to the specificity of the PFC in intrahemispheric control of top-down visual attention in the visual extrastriate cortex. The behavioral and VWM maintenance impairments in the BG group cannot be explained by a general effect of larger lesion volumes, as overall lesion volumes were significantly smaller in the BG group compared with PFC patients ($P = 0.024$). The fact that BG patients are especially impaired during the first 25 trials provides support for the hypothesis that the BG are critical for rule-based learning and implementation (31).

We hypothesize that unilateral BG lesions lead to a deficit in updating VWM representations, which in turn leads to a degradation in the fidelity of the VWM representation in fronto-extrastriate networks. The deficits may also be due in part to a failure to filter out irrelevant information (9, 37). Even though our protocol had no explicit distractors, the BG have been reported to play an important role in filtering out irrelevant information, and, thus, the stimulus information that is to be reinforced may be degrading over time due to increased ambient noise from the visual world. These results suggest that the PFC plays a broader role in executive functioning including both top-down attentional control and VWM maintenance, whereas the BG are more directly related to global VWM maintenance processes, extending the role of the BG outside the motor domain. Several studies have reported VWM deficits after lateral PFC damage (1–3). In contrast, BG lesions lead to a VWM behavioral impairment associated with maintenance deficits despite intact attention mechanisms. It is important to note that, although patients performed worse than controls in our study, the N1 and CDA deficits we report were from our examination of correct trials only. Thus, despite their pathological electrophysiological responses, patients performed the task well, albeit with impairments. This suggests that there are other mechanisms related to correct behavioral outcomes, possibly including functional reorganization, whereby the unilaterality of the lesions allows other intact cortical structures to compensate for the damaged regions (52).

Materials and Methods

Participants. All subjects gave informed consent approved by the University of California, Berkeley, CA, Committee for Protection of Human Subjects and the Department of Veterans Affairs Northern California Health Care System Human Research Protection Program. Control subjects were matched to patients by age and education. Because there were neither age nor education differences between PFC and BG groups ($P > 0.50$ both comparisons), we compared the results of each group separately to the combined group of 12 controls. For both patient groups, testing took place at least 6 mo after the date of the stroke; lesion etiology was either cerebrovascular accident or hypertensive bleed. A neurologist (R.T.K.) inspected patient MRIs to ensure that no white matter hyperintensities were observed in either patient group.

Electrophysiological Recording. Subjects were tested in a sound-attenuated EEG recording room at the University of California, Berkeley, CA. EEG data were collected using a 64 + 8 channel BioSemi ActiveTwo (51) amplifier sampled at 1,024 Hz. Horizontal eye movements (HEOG) were recorded at both external canthi, and vertical eye movements (VEOG) were monitored with a left inferior eye electrode and a fronto-polar electrode. Subjects were instructed to maintain central fixation and to respond using the thumb of their unaffected, ipsilesional hand. All data were referenced offline to the average potential of two earlobe electrodes and analyzed in MATLAB (R2009b) using custom scripts and the EEGLAB toolbox (52) and SPSS (Rel. 18; SPSS Inc.). Only correct trials were included in EEG analyses.

Behavioral Task. Subjects were presented with a memory array consisting of a set of one, two, or three colored squares (180-ms presentation; equiprobable presentation of each set size to either the left or right visual hemifield). After a 900-ms delay, a test array of the same number of colored squares appeared in the same spatial location. Subjects were instructed to manually respond to indicate whether the test array was the same color as the initial (memory) array. Behavioral accuracy was assessed using a d′ measure of sensitivity, which takes into account false alarm rate to correct for response bias. To avoid mathematical constraints in the calculation of d′, we applied a standard correction procedure wherein, for any subjects with a 100% hit rate or 0% false alarm rate, performance was adjusted such that $1/(2N)$ false alarms were added or $1/(2N)$ hits subtracted where necessary.

Data Analysis. All statistical analyses on behavior and ERP were first assessed using repeated-measures ANOVAs with group membership (control, PFC, or BG) as the between-subjects factor and memory load and hemifield of stimulus presentation (left/ipsilesional vs. right/contralesional) as the within-subjects factors. Comparisons between control and patient results were such that responses to left hemifield stimuli in controls were compared against ipsilesional responses in patients and right hemifield stimuli were compared with contralesional responses. To test the effects of learning on behavioral performance, we calculated a sliding window d′ measure across blocks of 25 trials moving in one-trial steps looking at overall behavioral performance regardless of memory load or hemifield of stimulus presentation. For analyses on learning, we ran a repeated measures ANOVA with trial number as the within-subjects factor using the mean d′ in the first 100 trials in four bins of 25 trials each. For post hoc analyses, significant effects were reported using one-way independent (between groups) or paired-samples (within group) *t* tests with the predictions that controls would perform better than patients, that patients would be impaired for contralesional stimuli, and that greater memory load would lead to decreased behavioral accuracy and larger amplitude electrophysiological responses.

ERP analyses were performed on bandpass filtered (0.1–20 Hz) data resampled to 256 Hz using a 100-ms prestimulus baseline. Blinks and saccades were identified on raw VEOG and HEOG channels, respectively, and verified with scalp topographies. Events with incorrect or no response, blinks, or saccades were removed from all analyses. CDA values were calculated as the mean amplitude difference from 300 to 900 ms between a group of extrastriate electrodes contralateral to the stimulus and a group ipsilateral to the stimulus. Thus, for controls, CDA for a right hemifield stimulus was calculated as the average of left minus right extrastriate activity from 300 to 900 ms. For patients, CDA was calculated in the same manner but was analyzed relative to the lesion such that, for patients with left hemisphere lesions, CDA for right hemifield stimuli was classified as contralesional and CDA for left hemifield stimuli was classified as ipsilesional (and vice versa). We classified patient behavioral data in the same manner. N1 amplitude was calculated as the maximum negative amplitude over the extrastriate cortex contralateral to the hemifield of stimulus presentation from 100- to 200-ms poststimulus onset.

ACKNOWLEDGMENTS. We thank Matar Davis and Lisa Tseng for assistance with data collection and study design, Richard B. Ivry and Michael Silver for scientific comments on previous versions of this manuscript, Clay Clayworth for lesion reconstruction, and Donatella Scabini for patient recruitment and delineation. This work was supported by American Psychological Association Diversity Program in Neuroscience Grant 5-T32-MH18882 (to B.V.) and National Institute of Neurological Disorders and Stroke Grants NS21135, NS21135-22S1, and PO40813 (to B.V. and R.T.K.).

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