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Spatiotemporal tuning of brain activity and force performance

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Abstract

The spatial and temporal features of visual stimuli are either processed independently or are conflated in specific cells of visual cortex. Although spatial and temporal features of visual stimuli influence motor performance, it remains unclear how spatiotemporal information is processed beyond visual cortex in brain regions that control movement. We used functional magnetic resonance imaging to examine how brain activity and force control are influenced by visual gain at a high visual feedback frequency of 6.4 Hz and a low visual feedback frequency of 0.4 Hz. At 6.4 Hz, increasing visual gain led to improved force performance and increased activity in classic areas of the visuomotor system – V5, IPL, SPL, PMv, SMA-proper, and M1. At 0.4 Hz, increasing gain also lead to improved force performance. In addition to activation in M1/PMd and IPL in the visuomotor system, increasing visual gain at 0.4 Hz also corresponded with activity in the striatal-frontal circuit including DLPFC, ACC, and widespread activity in putamen, caudate, and SMA-proper. This study demonstrates that the frequency of visual feedback drives where in the brain visual gain mediated reductions in force error are regulated.

Keywords

basal ganglia; memory; prediction; visuomotor; fMRI

Introduction

Spatial and temporal features of visual feedback influence motor output and much is now known about the brain regions that underlie this visuomotor process (Coombes et al., 2010; Ledberg et al., 2007; Vaillancourt et al., 2006b). In the cortex visual motion is initially processed in the striate and extrastriate visual cortices (McKeefry et al., 2008; Mikami et al., 1986; Moutoussis and Zeki, 2008; Paradis et al., 2000; Perrone, 2006; Sack et al., 2006). Populations of neurons in the primary visual cortex (V1) are tuned for spatial, temporal, and spatiotemporal properties of visual stimuli (Priebe et al., 2006). V1 neurons project to area V5/MT, and neuronal activity in V5/MT corresponds with the integrated spatiotemporal

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properties of motion stimuli (Priebe et al., 2003). Priebe and colleagues (2006) have argued that V5/MT may refine the representation of motion for real-world objects to create outputs that are specialized for the needs of downstream motor processes. While it is clear that spatial and temporal properties of visual input are conflated in visual cortex, it is not fully understood how this conflation influences downstream motor processes.

Movements that are guided by visual feedback rely on a distributed visuomotor system comprised of inferior parietal cortex (IPL), superior parietal cortex (SPL), dorsal premotor cortex (PMd), ventral premotor cortex (PMv), supplementary motor area (SMA), primary motor cortex (M1), putamen, V5, and lobule VI/Crus I of the cerebellum (Coombes et al., 2010; Dannenberg et al., 2009; Debaere et al., 2003; Ebner and Fu, 1997; Krakauer et al., 2004; Lee and van Donkelaar, 2006; Roitman et al., 2009; Vaillancourt et al., 2006b; Vaillancourt et al., 2003). Empirical findings show that separately changing either spatial or temporal features of visual feedback leads to changes in brain activity in the visuomotor system and changes in force performance (Coombes et al., 2010; Vaillancourt et al., 2006b). The spatial features of visual feedback can be manipulated by changing the gain at which visual feedback is presented. Increasing visual gain increases the spatial amplitude of the feedback, thereby magnifying error. Increasing visual gain below 1 degree at a high feedback frequency improves force performance and increases brain activity bilaterally in V3, V5, and left M1 (Coombes et al., 2010). In addition, large increases in visual gain above 1 degree leads to the maintenance of accurate force performance and an increase in brain activity bilaterally in PMd, PMv, and right IPL.

Temporal features of visual feedback can be manipulated by altering the frequency at which visual feedback is presented. Increasing the temporal frequency of visual feedback at a relatively high visual gain also leads to improved force performance and increased brain activity in right IPL, right PMd, right PMv and bilaterally in lobule VI/Crus I of the cerebellum (Vaillancourt et al., 2006b). These regions are part of the parietal-premotor visuomotor circuit that underlies the generation of externally guided movements (Debaere et al., 2003; Goldberg, 1985). Despite our understanding for how independently manipulating spatial and temporal visual feedback affects the visuomotor system, less is understood about how altering the spatiotemporal properties of visual feedback affects circuits both within and beyond the visuomotor system. Circuits beyond the visual system may be involved in motor tasks in which the visual stimulus needs to be processed by visuospatial memory, and previous studies suggest the involvement of prefrontal and basal ganglia regions in this process (Debaere et al., 2003; Goldberg, 1985; Goldman-Rakic, 1995; Wasson et al., 2010).

The current study manipulates the spatiotemporal features of visual feedback and measures brain activity using functional magnetic resonance imaging (fMRI). Brain activity and force performance were examined in humans while the spatial amplitude of visual feedback was manipulated at both high and low visual feedback frequencies. One hypothesis was that activity in regions of the visuomotor system including V5, M1, PMd, PMv, and IPL would increase in activity with an increase in visual gain at both high and low visual feedback frequencies. The alternative hypothesis was that increasing visual gain at low but not high visual feedback frequency would lead to increased activity in brain regions both within and beyond the visuomotor system. More detailed spatial information at slow intermittent temporal frequencies may require movements to be generated internally using prediction and working memory related processes which rely on striatal-frontal circuits. These circuits are outside of the traditional visuomotor system used during visually-guided motor control (Debaere et al., 2003; Pochon et al., 2001; Wasson et al., 2010).

Methods

Subjects

Fifteen healthy right-handed subjects with normal or corrected to normal vision participated in the study (8 females and 7 males, ages 19–31 years: $M = 22.3$, $SD = 3.72$). Prior to the experiment, each subject provided informed consent to all procedures, which were approved by the local Institutional Review Board and were in accord with the Declaration of Helsinki.

Force data acquisition

Subjects produced force against a custom fiber optic force transducer (Aither Engineering) using their right thumb and right index finger. The force transducer was constructed from rigid, nonmetallic material to allow for its use inside the magnetic resonance environment. The force signal was transmitted via fiber optic wire to the Si425 Fiber Optic Interrogator (Micron Optics) outside the fMRI environment. The Si425 Fiber Optic Interrogator digitized the force data at 125 Hz and customized software written in LabVIEW collected the force data and converted it to Newtons. The force transducer was factory calibrated by Aither Engineering and had a resolution of 0.025 Newtons. The output from the force transducer was presented to the subject using a visual display inside the MRI scanner. The feedback was projected via the parallax biofeedback system (Thulborn, 1999), similar to previous experiments (Coombes et al., 2010; Spraker et al., 2009). A mirror located inside the MR environment displayed visual feedback onto a video screen located 35 cm from the subject's eyes. The force output was displayed on the screen at a resolution of 640×480 pixels and a refresh rate of 60 Hz. The force data were lowpass filtered using a Butterworth filter at 20 Hz (4th order dual pass).

MRI data acquisition

Magnetic resonance images were collected using a volume head coil inside a 3 Tesla MR Scanner (GE Healthcare 3T94 Excite 2.0). The subjects lay supine in the scanner while performing the task. The subject's head was stabilized using adjustable padding and then fitted with the projector-visor system for displaying visual feedback. The functional images were obtained using a T2*-sensitive, single shot, gradient-echo echo-planar pulse sequence (echo-time 25 ms; repeat-time 2500 ms; flip angle 90°; field of view 200 mm²; imaging matrix 64×64; 42 axial slices at 3 mm thickness; 0 mm gap between slices). The high-resolution anatomical scans were obtained using a T1-weighted SPGR (spoiled gradient echo) pulse sequence (echo-time 3 ms; repeat-time 25 ms; flip angle 40°; field of view 240 mm²; imaging matrix 256×256; 120 axial slices at 1.5 mm thickness; 0 mm gap between slices).

Experimental design

Control scans—Figure 1 shows the experimental design. Subjects made two separate visits to the laboratory (0.4 Hz Day, 6.4 Hz day). Mean duration between visits was 12 days. Figure 1A shows the characteristics of the 3 scans completed by each subject during the 0.4 Hz day. A control scan was conducted first. The control scan provided a baseline measure of force performance and brain activity across the two testing days. The control scan cycled between 25 s blocks of Rest and 25 s blocks of force with vision (FV). One cycle of Rest and one cycle of FV is shown in Figure 1A. A total of 5 Rest blocks and 4 FV blocks were completed during the control scan. The scan began and ended with a Rest block. Subjects viewed a red/green target bar which was set at 15% of each subject's maximum voluntary contraction (MVC). A white bar was also visible to the subject. The white force bar was stationary during the Rest condition, and fluctuated in real time according to the subject's force production in the FV condition. During the Rest condition subjects were instructed to

fixate on the red target bar. During the FV condition, which began when the red target bar turned green, subjects were instructed to produce force as accurately as possible to the target level. During the FV condition subjects received online visual feedback.

Experimental scans—Figure 1A also shows the design of the experimental scans. Experimental scans followed the same pattern and timing parameters as the control scan; alternating 25 s blocks of Rest (×5) and 25 s blocks of FV (×4). The scan began and ended with a Rest block. Two experimental scans were completed on the 0.4 Hz day. Figure 1B shows that during the 0.4 Hz day a 20 ms sample of visual feedback was presented every 2.5 s to the subject during the FV portion of each experimental scan. The independent variable that was manipulated between the two scans was the visual gain of the feedback during the FV condition. An increase in visual gain leads to an increase in the spatial displacement of the visual feedback (i.e., white force bar) viewed by the subject. Figure 1C shows the example individual data which demonstrates the impact of visual gain on the spatial amplitude of the visual feedback viewed by the subject. Since the distance from the subject's eye to the projection screen surface remained constant, the height of the force fluctuations was manipulated to alter visual gain. The height of the force fluctuations viewed by the subject was manipulated using the following formula:

$$\text{Cursor Position} = (F_p - F_t) * G + F_t \quad (1)$$

in which F_p is the force produced by the subject, F_t is the target force, and G is the gain level used to manipulate the spatial amplitude of visual feedback. Based on prior work (Vaillancourt et al., 2006a), we calculated the visual angle by assuming a set force output standard deviation of 0.3 N. This estimate was derived from previous studies (Laidlaw et al., 2000; Slifkin and Newell, 1999). The value of the standard deviation was multiplied by 6 to approximate the full range (plus/minus 3 standard deviations) of estimated variance for the height of the force fluctuations. The visual angle for each gain level was then calculated using the following formula:

$$\alpha = 2 \times \tan^{-1} \left(\frac{H1}{D} \right) \quad (2)$$

in which α is the visual angle, D is the distance to the display, and $H1$ is the height of the total range of motion in the top half of the visual field. The two visual gain levels corresponded to visual angles of: 0.018°, 0.623°. These gain levels were chosen because they span the range across which a dramatic change in force performance occurs. Previous evidence has demonstrated that a visual gain of 0.018° leads to high performance error. When visual gain is increased to 0.623° performance error is dramatically reduced. Importantly, improvements in force performance beyond a visual gain of 0.623 are minimal (Coombes et al., 2010). The two levels of visual gain will be referred to as low gain (0.018°), and high gain (0.623°) throughout the remainder of the manuscript. Figure 1C shows that increasing visual gain leads to an increase in the spatial amplitude of the visual feedback. Figures 1D-F detail the characteristics of the control scan and experimental scans during the 6.4 Hz day. The only independent variable that was manipulated across the 0.4 Hz day and the 6.4 Hz day was the frequency at which the visual feedback was presented during the FV block of the experimental scans. The 0.4 Hz frequency was chosen because it has previously been shown to lead to severe decrements in force performance (Slifkin et al., 2000; Vaillancourt et al., 2006b). The 6.4 Hz frequency was chosen because previous behavioral evidence has shown that 6.4 Hz represents a critical threshold such that increases in frequency above this level do not lead to improvements in force performance (Slifkin et al.,

2000). The frequency of visual feedback was manipulated by controlling how often visual feedback (i.e., the white force bar) was displayed. In the 0.4 Hz condition a 20 ms visual sample was displayed every 2500 ms (Figure 1B), whereas in the 6.4 Hz condition a 20 ms visual sample was displayed every 156 ms (Figure 1E). Figure 1C and 1F show that an increase in visual gain leads to an increase in the spatial amplitude of visual feedback at 0.4 Hz and at 6.4 Hz.

To summarize, subjects completed 3 functional scans on each day. The first scan was always the control scan and the control scan was identical each day. Subjects then completed 2 experimental scans at high and low visual gain levels but all at the same feedback frequency. Feedback frequency was the only independent variable manipulated across days. Visual gain within each day and feedback frequency across days was randomized for each subject.

Procedure

Prior to entering the magnet on the first day, each subject completed a 1 hr training session to minimize learning effects when inside the scanner. Once in the fMRI environment, the individual's MVC was calculated. The subjects were asked to sustain a contraction of maximum force for three consecutive 5 s trials. Each trial was separated by a 60s period of rest. The MVC was calculated as the average force during the sustained maximum force contraction. Subjects then completed three functional scans followed by one anatomical scan. Each experimental session lasted approximately 45 minutes.

Force data analysis

Force data was analyzed using custom algorithms in LabVIEW. The force-time series data were digitally filtered by using a fourth-order Butterworth filter with a 20 Hz low-pass cut-off. Four dependent measures were calculated (Coombes et al., 2010): 1) duration of force, 2) mean force amplitude, 3) force error measured in Newtons ($RMSE_N$) and 4) visual feedback amplitude measured in centimeters on the visual display ($RMSE_{cm}$). Duration of force represented the entire length of each sustained contraction. The onset of each contraction was identified as the time point where force rose above two times the baseline value. The offset of each contraction was identified as the next time point where force fell below 2 times the baseline value. Baseline values were calculated as the mean force amplitude during the 300 ms prior to each 25 s block. Force error, visual feedback, and mean force were calculated from an 18.5 s portion of each contraction, beginning 4 s after force onset. Force error reflected how accurate force production was relative to the target force level and was calculated in Newtons ($RMSE_N$) using the following equation:

$$RMSE_N = \left(\sum (s - f_i)^2 / n - 1 \right)^{1/2} \quad (3)$$

where s = target force, f_i = i^{th} force sample and n = number of samples. To calculate the spatial amplitude of visual feedback ($RMSE_{cm}$) the force that each subject produced during each time point where feedback was visible for each experimental condition was converted from units of force to units of centimeters. Hence, the force trace was converted to units which reflected the spatial amplitude of the visual feedback as viewed by each subject. We then used the same equation (3) to calculate $RMSE_{cm}$ as was used to calculate $RMSE_N$ but the units were in centimeters.

Potential adaptation effects within each scan were examined with separate one-way repeated measures analysis of variance (ANOVA). However, because no significant effect of Block was found for all four dependent variables (all p 's > 0.05) during control and experimental scans, an average of the four values within each scan served as the summary statistic for

each dependent variable. The effect of day on each measure of force performance (duration of force, mean force amplitude, force error [RMSE_N], visual feedback amplitude [RMSE_{cm}]) during control scans was analyzed with separate paired t-tests (day 1 vs day 2). The effect of visual gain and visual feedback frequency on each dependent measure of force performance during experimental scans was analyzed with separate two-way repeated measures ANOVA's (Visual Gain $\times$ Visual Feedback Frequency). The two levels of visual gain were high and low, and the two levels of visual feedback frequency were 0.4 Hz and 6.4 Hz. Significant interactions were followed up with paired t-tests which were corrected for multiple comparisons using the Bonferroni correction. For each interaction a total of 6 paired t-tests were conducted. Post-hoc t-tests were considered significant if the p-value was less than 0.008.

fMRI data analysis

AFNI, the public domain software was used to process and analyze the fMRI data sets. First, we corrected for head motion using standard procedures. Translational movement parameters never exceeded 1.5 mm in any direction for any subject. All subjects were included in all analyses.

Control scans: ROI analysis

A region of interest (ROI) analysis of the mean BOLD percent signal change during control scans was used to determine the effect of day on brain activity. In this experimental design it was important that there was no effect of day on the control scans. No effect of day on the control scans would allow us to attribute changes in brain activity and behavior in experimental scans to our independent variables: visual gain and visual feedback frequency. First, each individual dataset was motion corrected and then filtered using a Gaussian filter (full-width half-maximum at 4 mm). Next, mean BOLD percent signal change was acquired by calculating the mean signal within each voxel for the FV and Rest blocks across each individual functional time series. The mean BOLD percent signal change within each voxel was calculated using the following equation:

$$\mu_{\text{psc}} = (\mu_{\text{T}} - \mu_{\text{R}}) / \mu_{\text{R}} * 100 \quad (4)$$

where μ_{T} is the mean signal during the FV blocks and μ_{R} is the mean signal during the Rest blocks. Therefore, the output data represented the percent signal change in each voxel for each individual subject dataset. Next, each subject's anatomical and functional datasets were transformed to standardized stereotaxic space using the automated function in AFNI. Mean percent signal change within each ROI was completed for each subject for each day.

Regions of interest were based on functional data from previously published studies which examined the visuomotor and motor memory systems (Coombes et al., 2010; Vaillancourt et al., 2003). Regions of interest were anatomically labeled using the Basal Ganglia Human Area Template (Prodoehl et al., 2008), the Human Motor Area Template (Mayka et al., 2006), and the Schmahmann MRI atlas of the human cerebellum (Schmahmann et al., 2000). Paired t-tests were used to compare activity between day 1 and day 2 to determine whether BOLD activity in specific regions of the visuomotor and motor memory systems varied across the two testing days.

Experimental scans: Voxel-wise analysis

To determine the effect of visual gain on brain activity at each visual feedback frequency separate voxel-wise analyses were conducted. A total of 4 datasets were preprocessed (2 visual gain levels $\times$ 2 visual feedback frequencies). Motion-corrected individual datasets at

each feedback frequency were first normalized by dividing the instantaneous signal in each voxel at each point in the time series by the mean signal in that voxel across each scan. A Gaussian filter was then applied to the datasets (full-width half-maximum at 4 mm). Next, the time-series data were regressed to a simulated hemodynamic response function for the task sequence. The dependent variable at this level of analysis was the estimated β -coefficient of the regressed time series and its associated t-statistic for the FV-R comparison. Before group analyses, each subject's anatomical dataset was transformed into standardized stereotaxic space using the automated function in AFNI. Each subject's individual functional datasets were then transformed to standardized space using the standardized anatomical dataset as a template. Separate paired t-tests were then run for each feedback frequency, and each output data set was corrected for multiple comparisons using a Monte Carlo simulation model (AlphaSim). The datasets were thresholded to remove all voxels with $t < 3.32$ with an activation cluster minimum of $324\mu\text{L}$ ($p < 0.05$, corrected). The independent variable in each t-test was visual gain (high, low).

Experimental scans: Correlation analysis

To examine the relation between force performance and brain activation correlation analyses were conducted between the BOLD signal in selected regions and mean force amplitude, force error, and visual feedback amplitude. Correlations were considered significant if the p-value was less than 0.05.

Results

Control scan: Force data

Figure 2A–C shows the mean duration, amplitude, and error of force production during the FV condition in the control scan for day 1 and for day 2. Together, the data in the figures demonstrate that mean duration, mean force amplitude, and force error was similar during the control scan across days. Paired t-tests revealed non-significant effects of day for each measure (see Table 1).

Control scan: Brain activity

Figure 2D–F shows mean BOLD percent signal change values in regions of the visuomotor system during the control scan for day 1 and day 2. In line with the behavioral data, there was no effect of day on BOLD activity in left M1 (Figure 2D) ($t(14) = -0.07$, $p = 0.95$). Figure 2E shows the BOLD response across days in left PMv and Figure 2F shows the BOLD response across days in right lobule VI of the cerebellum. Figure 2G–I shows the BOLD response across days in areas related to motor memory and prediction including left putamen, left caudate and right DLPFC. There was no effect of day on BOLD activity in any visuomotor region or motor memory region, and the corresponding t-value and p-value from each paired t-test for each ROI is shown in Table 1.

Experimental scan: Force analysis

Duration of force production—The duration of each sustained isometric force contraction did not differ as a function of visual feedback frequency ($F(1, 14) = 0.41$, $p = 0.84$), the visual gain of the visual feedback ($F(1, 14) = 0.11$, $p = 0.75$), or an interaction of these two factors ($F(1, 14) = 3.05$, $p = 0.10$). Any changes in the BOLD response can therefore not be attributed to changes in the duration of force production between experimental conditions.

Force amplitude—Figure 3A shows the effect of visual feedback frequency and visual gain on mean force amplitude. The filled circles represent low visual gain and the open

circles represent high visual gain. Visual feedback frequency is on the x-axis. A two-way repeated measures ANOVA revealed a significant main effect of visual feedback frequency ($F(1, 14) = 5.72, p = 0.03$). Mean force amplitude was greater when visual feedback frequency was 6.4 Hz as compared to 0.4 Hz. A main effect of visual gain was also evidenced on mean force amplitude ($F(1, 14) = 19.03, p = 0.001$), with high visual gain as compared to low visual gain leading to a reliable increase in mean force amplitude. This is shown in Figure 3A with the open circles being higher than the closed circles at 0.4 Hz and 6.4 Hz. The mean target force for all subjects was 10.86 N. Together these findings show that mean force amplitude was greatest and the target force was better approximated at a high visual feedback frequency and at a high level of visual gain. The interaction between visual feedback frequency and visual gain was not significant ($F(1, 14) = 0.40, p = 0.54$).

Force error—Figure 3B shows mean force error for all subjects across high (open circles) and low (filled circles) visual gain levels at visual feedback frequencies of 0.4 Hz and at 6.4 Hz (x-axis). The two-way repeated measures ANOVA revealed significant main effects of visual feedback frequency ($F(1, 14) = 5.85, p = 0.03$) and visual gain ($F(1, 14) = 29.03, p < 0.01$), but these main effects were superseded by a significant interaction between visual gain and visual feedback frequency ($F(1, 14) = 7.09, p = 0.02$). Follow-up paired t-tests revealed a significant reduction in error when visual gain increased from low to high levels across both frequencies (p 's < 0.008). Importantly, relative to all other conditions, least error was revealed when high visual gain was paired with high visual feedback frequency (p 's < 0.008). The effect of visual feedback frequency on force error at low visual gain was not significant ($p = .480$).

Visual feedback amplitude—Figure 3C shows the mean amplitude of visual feedback for all subjects across high (open circles) and low (filled circles) visual gain levels at visual feedback frequencies of 0.4 Hz and at 6.4 Hz (x-axis). The two-way repeated measures ANOVA revealed significant main effects of visual feedback frequency ($F(1, 14) = 15.50, p = 0.001$) and visual gain ($F(1, 14) = 35.88, p < 0.001$). A significant increase in the spatial amplitude of visual feedback was evidenced when visual gain increased from low to high and when frequency decreased from 6.4 Hz to 0.4 Hz. A significant visual feedback frequency by visual gain interaction was also evidenced ($F(1, 14) = 16.64, p = 0.001$). Follow-up t-tests revealed a significant increase in the spatial amplitude of visual feedback when visual gain increased from low to high levels across both frequencies (p 's < 0.008). Relative to all other conditions the spatial amplitude of the visual feedback was greatest when high visual gain was paired with the 0.4 Hz visual feedback frequency (p 's < 0.008). The effect of visual feedback frequency at low visual gain was not significant ($p = 0.315$).

Experimental scan: Brain activity

Clusters of voxels where the BOLD response was significantly different between high and low visual gain were identified separately for each visual feedback frequency. At each feedback frequency no brain regions were identified in which the BOLD signal was greater for low visual gain as compared to high visual gain.

When feedback frequency was 0.4 Hz, the group analysis revealed significant gain-related activity in brain regions including bilateral putamen, bilateral caudate, DLPFC, SMA-proper, bilateral IPL, bilateral M1/PMd, right thalamus, anterior cingulate cortex (ACC), and bilateral posterior cingulate. The top panel in Table 2 shows all brain regions which showed gain-related activity at 0.4 Hz with their corresponding cluster size, Talairach coordinates, MNI coordinates, and peak T-value. When the visual feedback frequency was 6.4 Hz the group analysis of brain images revealed significant gain-related activity in bilateral V5, bilateral PMv, left primary somatosensory cortex/IPL, left M1, right middle

occipital gyrus, left superior parietal lobe, and SMA-proper. The bottom panel in Table 2 shows all brain regions which showed gain-related activity at 6.4 Hz with their corresponding cluster size, Talairach coordinates, MNI coordinates, and peak T-value. We next present figures which focus on the specific cortical and subcortical regions in which the pattern of gain-related BOLD signal differed between the 0.4 Hz and 6.4 Hz visual feedback frequencies.

Figure 4 shows maps of cortical and subcortical brain activity overlaid on axial anatomical images when visual feedback frequency was 0.4 Hz (top row) and 6.4 Hz (bottom row). The activation maps correspond with regions where the BOLD signal was greater in the high gain condition as compared to the low gain condition. When comparing gain-related brain activity in the top row (0.4 Hz) to the bottom row (6.4 Hz), it is clear that the patterns in the activation maps are distinct and that the corresponding differences are focused in regions of the basal ganglia and visual cortex. Figure 4 demonstrates that an increase in visual gain at 0.4 Hz as compared to 6.4 Hz corresponded with an increase in BOLD activity in multiple subcortical regions including left putamen (center of mass: $-26.7, 3, -0.2$), right putamen (center of mass: $21.6, 1.6, -1.6$), left caudate (center of mass: $-19.2, -6.8, 23.5$) right caudate (center of mass: $16.9, -6.4, 24.9$), and also in right DLPFC (center of mass: $36.7, 36.7, 9.5$). In contrast, the bottom row in Figure 4 shows that no gain-related activity was found in any regions of the basal ganglia or prefrontal cortex when visual feedback frequency was 6.4 Hz. However, the bottom panel in Figure 4 does show that regions of the dorsal visual pathway, and specifically V5, are sensitive to changes in gain at 6.4 Hz but not at 0.4 Hz. Hence, gain-related changes in brain activity in basal ganglia, prefrontal cortex, and extrastriate visual cortex appear to be mediated by the frequency at which visual feedback is presented.

Figure 5 shows gain-related activation maps for the 0.4 Hz (top panel) and the 6.4 Hz (bottom panel) conditions overlaid on axial anatomical images. Each slice is separated by 3 mm and together these images detail activation in progressive inferior to superior (left to right) cortical regions. At 0.4 Hz, prominent gain-related activity was revealed across a large region of SMA-proper which extended in the inferior direction to the cingulate motor area (center of mass: $3.2, -1.4, 45$). Activity in SMA-proper at 0.4 Hz was larger and inferior to the SMA-proper activity that was revealed at 6.4 Hz. At 6.4 Hz, the group analysis also revealed gain-related increases in activity in right PMv, and in left M1 which was contralateral to the hand which produced force.

Our primary analyses showed a frequency specific dissociation between the brain circuits that underlie gain induced changes in force performance. Additional support for these analyses comes from a secondary control analysis in which high and low frequency conditions were directly contrasted with each other after computation of the high versus low gain contrast in each condition. A voxel-wise analysis revealed a gain related increase in activity in the 0.4 Hz condition as compared to the 6.4 Hz condition in areas including left putamen, right putamen, right caudate, right DLPFC, and SMA-proper. In addition, increased activity was found in the 6.4 Hz condition as compared to the 0.4 Hz condition in left V5, right V5, and left SPL.

To examine the relation between force performance and region specific brain activation we conducted correlation analyses. Brain activation data and performance data from the low gain and high gain condition were included in each analysis. All correlations between force amplitude and brain activity were not significant (p 's > 0.05). A significant negative correlation was found between force error and the BOLD signal at the 0.4 Hz condition in right DLPFC ($r = -0.384, p < 0.05$), suggesting that as force error increased the BOLD signal in DLPFC decreased. All other correlations between force error and brain activity

were not significant (p 's > 0.05). Significant positive correlations were found between visual feedback amplitude and the BOLD signal at the 6.4 Hz condition in left M1 ($r = 0.496$, $p < 0.05$), right V5 ($r = 0.359$, $p < 0.05$), left SI/IPL ($r = 0.366$, $p < 0.05$), right PMv ($r = 0.362$, $p < 0.05$), and right middle occipital gyrus ($r = 0.513$, $p < 0.05$). These findings suggest that as the spatial amplitude of the visual feedback increased, the BOLD signal within regions of the occipital-parietal-frontal circuit also increased. All other correlations between the spatial amplitude of visual feedback and brain activity were not significant (p 's > 0.05).

Discussion

This study demonstrates that the frequency of visual feedback drives where in the brain visual gain mediated improvements in force performance are regulated. At 6.4 Hz, increasing visual gain led to a reduction in force error and increased activity in classic areas of the visuomotor system – MT/V5, IPL, SPL, PMv, SMA-proper, and M1. At 0.4 Hz, increasing gain also led to improved force performance. In addition to activation in M1/PMd, and IPL in the visuomotor system, increasing visual gain at 0.4 Hz also corresponded with activity in the striatal-frontal circuit including DLPFC, ACC, and widespread activity in putamen, caudate, and SMA-proper. Correlation analyses between brain activity and force performance demonstrated that these findings were not driven by changes in mean force amplitude or force error between conditions. These findings suggest that increasing visual gain at intermittent feedback frequencies requires activation of additional circuits outside of the classically defined visuomotor system.

Increasing visual gain at 0.4 Hz activates working memory and prediction circuits

Previous evidence shows that increasing visual gain leads to accurate force performance and increased brain activity bilaterally in V3, V5, PMd, PMv, left M1, and right IPL (Coombes et al., 2010). These areas are key regions of the parietal-frontal circuit and the dorsal visual pathway, which together represent the visuomotor system which underlies the generation of externally guided movements (Coombes et al., 2010; Dannenberg et al., 2009; Debaere et al., 2003; Kruse et al., 2002; Lee and van Donkelaar, 2006; Martinez-Trujillo et al., 2007; Oreja-Guevara et al., 2004; Prodoehl et al., 2009; Ungerleider and Mishkin, 1982; Vaillancourt et al., 2006b; Vaillancourt et al., 2003). In the current study we examined whether gain induced changes in brain activity hold true at different visual feedback frequencies. The current findings show that increasing visual gain at 0.4 Hz led to a reduction in error (Figure 3B), and this is consistent with the idea that magnifying visual error improves the accuracy of motor performance (Coombes et al., 2010; Patton et al., 2006; Vaillancourt et al., 2006a). The novel finding was that in addition to activity in the parietal-frontal circuit, increasing gain at 0.4 Hz led to increased BOLD activity in a striatal-frontal circuit which included bilateral putamen, bilateral caudate, right DLPFC, ACC, and SMA-proper. Brain activity in these regions has previously been associated with prediction (Prodoehl et al., 2009; Wasson et al., 2010), working memory (Funahashi et al., 1989; Goldman-Rakic, 1995; Procyk and Goldman-Rakic, 2006), and motor memory (Debaere et al., 2003; Vaillancourt et al., 2003). In the 0.4 Hz condition the time between samples of visual feedback was 2.5 s and this was constant across visual gain levels. Increased activity in the striatal-frontal circuit in the 0.4 Hz condition therefore corresponded with an increase in visual gain. Hence, although we did not explicitly manipulate prediction or working memory processes, one interpretation of our findings is that the visual gain induced improvement in performance at the low visual feedback frequency was related to increased activation of prediction and working memory striatal-frontal brain circuits.

Wasson et al. (2010) required subjects to produce a series of force pulses to visual targets that varied in amplitude. The predictability of the series of force pulses was manipulated such that subjects knew 20%, 40%, or 80% of the required sequence. Coupled with

increased activity in the parietal-frontal circuit, an increase in the predictability of the force pulse series also corresponded with increased BOLD signal in bilateral anterior putamen and left anterior caudate and left DLPFC. These regions have been implicated in the planning and prediction of force generation and with working memory capacity and rule retrieval (Landau et al., 2009; Prodoehl et al., 2009; Wasson et al., 2010).

There are three key differences between the experimental design of the current study and the experimental design used by Wasson et al. (2010). In the current study: 1) prediction was not explicitly manipulated, 2) subjects produced force with intermittent visual feedback, and 3) sustained rather than discrete force contractions were executed. Wasson and colleagues (2010) related predictive processes to focally-specific anterior regions of putamen and caudate and memory related processes to left DLPFC. In the current study we found large clusters of activity in anterior and posterior caudate and putamen. The more widespread distribution of activity in the current study may reflect both the planning (anterior) and parameterization (posterior) of force production in the basal ganglia (Prodoehl et al., 2009) because force had to be controlled continually for 25 s. In addition, we found activity in right as compared to left DLPFC, and right DLPFC activation was negatively correlated with force error, suggesting that a reduction in force error was associated with an increase in right DLPFC activity. Increased right DLPFC activity may reflect differences in the working memory process. Wasson and colleagues related left DLPFC activity with rule retrieval which corresponded with the presentation of visual cues, and previous evidence links left DLPFC activity with perceptual decision making that transcends task and response specificity (Heekeren et al., 2006). In the 0.4 Hz condition in the current study there was no rule to learn and the majority of force production occurred without visual feedback. We therefore interpret the gain induced increase in activity in right DLPFC in the current study as reflective of an increased reliance on spatial working memory processes (Goldman-Rakic, 1995).

Converging evidence from inactivation studies and single-unit recordings in monkeys (Funahashi et al., 1989; Johnston and Everling, 2006, 2009; Miller et al., 1996; Sawaguchi and Iba, 2001) and ocular motor lesion studies in humans (Pierrot-Deseilligny et al., 2005; Pierrot-Deseilligny et al., 2003) have localized visuospatial working memory processes to DLPFC (Funahashi, 2006; Funahashi and Kubota, 1994; Goldman-Rakic, 1995). Evidence from single unit recordings in the prefrontal cortex of monkeys has shown that DLPFC activity relates to the prospective coding of visuospatial information rather than the retrospective coding of information (Procyk and Goldman-Rakic, 2006). On a battery of eye movement tasks patients with lesions in DLPFC reported deficits in maintaining memorized information for ongoing intentional saccades (spatial working memory) or facilitating anticipatory saccades (prediction) (Pierrot-Deseilligny et al., 2003). Other evidence suggests that DLPFC is also involved in action selection tasks without a strict working memory component, which suggests a role for DLPFC in action-selection and the control of neural activity in areas that process task-relevant representations (Mars and Grol, 2007). Our findings are also consistent with motor-related brain imaging studies in neurologically intact adults. Evidence shows that whereas the parietal-frontal network has the capacity to store visuospatial information in visuospatial working memory, DLPFC activity is associated with the planning of hand movements which are based on the information that is stored in working memory (Pochon et al., 2001). Other visuomotor studies have demonstrated that DLPFC is associated with early learning prior to 40 minutes of practice across 2 days (Debaere et al., 2004), or early adaptation phases (1st 72 trials of 312 total trials) of visuomotor task performance (Anguera et al., 2010). The current findings are important since they demonstrate that feedback delivered intermittently over a period as short as 2.5 s during precision grip force control, allows a gain induced improvement in force performance which corresponds with increased DLPFC activity in the human brain.

Visual gain related activity in the 0.4 Hz condition was also associated with activity in PMd and evidence has demonstrated that DLPFC and PMd show a functional coupling during cognitive and motor tasks (Abe and Hanakawa, 2009). Our findings provide further evidence for models of prefrontal cortex function which associate prefrontal cortex activity with a top-down control mechanism which coordinates or modulates activity of target structures to which it is connected (Abe and Hanakawa, 2009; Johnston and Everling, 2009; Miller and Cohen, 2001; Sandrini et al., 2008).

In addition to DLPFC, motor memory processes have been associated with BOLD activity in ACC, left insular cortex, left medial gyrus, and left middle frontal gyrus (Vaillancourt et al., 2003). Vaillancourt et al. (2003) required subjects to produce force to a target level for 30 s without any visual feedback. The authors concluded that activity related to motor memory was concentrated in prefrontal regions because no evidence was found for motor memory processes in the parietal cortex, SMA, basal ganglia, thalamus, or cerebellum. There were two key differences between the Vaillancourt et al. study and the current study. First, in the current study visual gain was manipulated, and second, a 20 ms sample of visual feedback was presented every 2.5 s during a 25 s block of force production. The contrast between these studies is important because whereas activity in DLPFC and ACC was present in both studies, activity in parietal cortex, SMA, basal ganglia, thalamus, and cerebellum was only present when visual gain was increased at an intermittent feedback frequency of 2.5 s. These contrasting findings suggest that whereas activity in DLPFC and ACC may be related to motor memory that varies in duration from 2.5 s to 30 s, activity in parietal cortex, SMA, basal ganglia, thalamus, and cerebellum is associated with the frequent updating of motor memory when that memory is driven by an amplified but intermittent error signal.

In contrast to the findings of Vaillancourt and colleagues (2003), Debaere and colleagues demonstrated increased activity in basal ganglia, SMA, cingulate motor cortex, IPL, frontal operculum, and lobule IV–V of the cerebellum during internally as compared to externally generated bimanual hand movements (Debaere et al., 2003). The MNI coordinates reported by Debaere and colleagues for right putamen/globus pallidus (26, -4, -4) are very close to the MNI coordinates for right putamen (24, 0, -6) in the current study. Our findings also show that increases in gain of discrete samples of feedback presented every 2.5 s at 0.4 Hz led to more widespread activity in SMA-proper than increases in gain of discrete samples of feedback presented every 156 ms at 6.4 Hz. As such, the current findings in SMA extend previous evidence which has associated SMA activity with both internally (Debaere et al., 2003; Deiber et al., 1999; Goldberg, 1985) and externally generated movements (Deiber et al., 1999). For instance, Deiber and colleagues showed similar BOLD activity in SMA during visually triggered and internally triggered finger movements and Mushiake and colleagues (Mushiake et al., 1991) showed consistent neuronal activation in SMA during a visually guided task. Further, whereas, repetitive transcranial magnetic stimulation (rTMS) evidence has associated SMA activity with the stabilization of motor memory immediately following and 6 hours after a blocked practice session (Tanaka et al., 2010), the current findings extend the role of SMA to working memory related processes that emerge at a much shorter timescale and involve top-down and bottom-up control mechanisms (Corbetta and Shulman, 2002).

Importantly, whereas Vaillancourt and colleagues (2003) did not find SMA and putamen activity during internally generated sustained grip force production, the present study and the studies reported by Debaere and colleagues (2003) and Wasson and colleagues (2010) did. These contrasting findings may be explained by the intermittent feedback which was common to these later studies. Feedback during the high gain condition at 0.4 Hz in the current study may have mimicked the intermittent sensory feedback generated when the

hands completed a cycle in the bimanual task used by Dabeare and colleagues, and when visual cues initiated force pulses in the task used by Wasson and colleagues. Thus, intermittent sensory feedback to update prediction and working memory processes may be the common thread for studies which show increased activity in the frontal-striatal circuit during internally generated movements.

Increasing visual gain at 6.4 Hz activates the parietal-frontal visuomotor system

Increasing visual gain at 6.4 Hz led to a progressive decrease in force error and an increase in the spatial amplitude of visual feedback. Voxel-wise analyses revealed that these behavioral findings corresponded with increased BOLD signal in core regions of the visuomotor system (Table 2). These findings are consistent with previous studies that have associated visuomotor processes with activity in extrastriate visual cortex and the parietal-frontal network (Coombes et al., 2010; Debaere et al., 2003; Grol et al., 2007; Vaillancourt et al., 2003; Wasson et al., 2010). We extend these findings by showing that the gain related BOLD signal in bilateral V5 was present at 6.4 Hz but not at 0.4 Hz. This suggests that a critical threshold for visuomotor processing may exist at 6.4 Hz. The suggestion that a visual feedback frequency of 6.4 Hz may be a critical threshold in visuomotor processing was first suggested by Slifkin and colleagues (2000). The current study provides a neurophysiological basis to this notion by demonstrating that gain-related activity corresponds with an increase in activity in V5 at 6.4 Hz but not 0.4 Hz. Importantly, V5 is a region of the dorsal visual pathway which is crucial to the processing of the spatial properties of visual feedback (Ungerleider and Mishkin, 1982).

Although activity in area MT in monkeys and V5 in humans has previously been associated with visuomotor processing (Coombes et al., 2010; Dannenberg et al., 2009; Debaere et al., 2003), the current findings show that these areas are only sensitive to changes in visual gain at frequencies greater than or equal to 6.4 Hz. Visual feedback at 6.4 Hz corresponds with a sample of visual information being presented every 156 ms, whereas visual feedback at 0.4 Hz corresponds with a sample of visual information being presented every 2.5 s. TMS studies examining the timecourse of motion perception in visual cortex suggest that V1/V2 and V5 are activated repeatedly through forward and feedback connections, and importantly that these connections can be disrupted via the presentation of TMS approximately 125–200 ms post visual motion onset (Laycock et al., 2007; Prieto et al., 2007). Hence, the timecourse of motion processing in the visual cortex fits well with our findings because presenting visual samples every 156 ms in the 6.4 Hz condition was sufficient to elicit gain-related activity in area V5, whereas visual samples every 2.5 s were not.

Summary

Increases in visual gain at 6.4 Hz corresponded with improved performance and an increase in BOLD signal in the occipital-parietal-frontal circuit. This pattern of brain activity reflected externally guided visuomotor control. In contrast, although increasing visual gain at 0.4 Hz also corresponded with improved performance, these behavioral effects were mediated by a different circuit. We observed changes in the BOLD signal in a striatal-frontal circuit which included bilateral putamen, caudate, right DLPFC, ACC, and SMA-proper, in addition to the parietal-frontal circuit. These regions beyond the visuomotor system have previously been associated with prediction, memory, and internally guided movements, and the current findings extend this notion to sustained visuomotor force control. The current findings show that the spatiotemporal features of visual information profoundly influence force performance. Importantly, these changes in the spatiotemporal features of visual information correspond with top-down internally driven control which relies on a striatal-frontal circuit in addition to the parietal-frontal visuomotor circuit and with bottom-up externally driven control which relies on the occipital-parietal-frontal visuomotor circuit.

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Figure 1.

Experimental design. **1A** shows the experimental design for the 0.4 Hz day. Subjects completed three scans during the 0.4 Hz day. The first scan was a control scan and consisted of 25 s of rest followed by 25 s of force + vision (FV). The next 2 scans were experimental scans. The visual feedback frequency remained constant at 0.4 Hz for the FV portion of each experimental scan. **1B** shows that a 20 ms sample of visual feedback was displayed to the subject every 2.5 s. Visual gain was manipulated between these two scans. **1C** shows an example time-series of the spatial amplitude of visual feedback from 1 subject. The black line represents the spatial amplitude of the feedback and the grey dashed line represents the target. Note that the unit of measurement for the spatial amplitude of visual feedback is cm. **1D** shows the experimental design for the 6.4 Hz day. **1E** shows that a 20 ms sample of visual feedback was displayed to the subject every 156 ms. **1F** shows an example time-series of the spatial amplitude of visual feedback from 1 subject. The black line represents the spatial amplitude of the feedback and the grey dashed line represents the target. Visual gain within each day, and visual feedback frequency across days was counterbalanced for all subjects.

Figure 2.

Control Scans. **2A** shows the duration of force (+ 1SE) for the control scan for day 1 and day 2. **2B** shows mean force amplitude (+ 1SE) and **2C** shows mean force error (+ 1SE). **2D–F** show the mean BOLD response in a subset of visuomotor regions of interest for the control scans for day 1 and day 2. **2G–I** show the mean BOLD response in a subset of motor memory and prediction regions of interest for the control scans for day 1 and day 2. All p-values for the effect of day were non-significant.

Figure 3.

Mean force amplitude, force error, and the spatial amplitude of visual feedback for experimental scans. **3A** shows mean force on the y-axis for low gain (filled circles) and high gain (open circles) for the 0.4 Hz and 6.4 Hz conditions. **3B** shows force error for each visual gain at each visual feedback frequency. **3C** shows the spatial amplitude of the visual feedback for each visual gain at each visual feedback frequency. Error bars represent + 1SE.

Figure 4.

Brain activity during experimental scans in basal ganglia, visual cortex, and prefrontal cortex. Axial slices showing mean BOLD activation detected by voxel-wise analyses for high visual gain > low visual gain overlaid on a single subjects transformed brain in Talairach space. The color bar ranges from $t=-9$ to $t=+9$ with a group activation threshold of $p<0.05$, corrected. The corrected t -statistics associated with each voxel are displayed. The high visual gain > low visual gain activation map when the visual feedback frequency was set at 0.4 Hz is shown in the top row. Prominent activation is shown in regions of the basal ganglia which include putamen and caudate and in regions of the prefrontal cortex including right DLPFC. No activation was revealed in visual cortex. The bottom row shows the same axial slices, with the same high visual gain > low visual gain activation map but when the visual feedback frequency was set at 6.4 Hz. Prominent activation is shown in V5 which is a region in the dorsal visual pathway. No gain induced change in BOLD signal was revealed in the basal ganglia in the 6.4 Hz condition.

Figure 5.

Brain activity during experimental scans in primary and secondary motor cortices. Axial slices showing mean BOLD activation detected by voxel-wise analyses for high visual gain > low visual gain overlaid on a single subjects transformed brain in Talairach space. The color bar ranges from $t=-9$ to $t=+9$ with a group activation threshold of $p<0.05$, corrected. The corrected t -statistics associated with each voxel are displayed. The top row shows contrast maps when the visual feedback was 0.4 Hz, and shows significant clusters of activation in SMA-proper. The SMA-proper cluster extends into posterior regions of pre-SMA and dorsal regions of the cingulate motor area. Activation in SMA-proper demonstrates that the BOLD signal increased in intensity as visual gain increased in the 0.4 Hz condition. The bottom row shows contrast maps when the visual feedback was 6.4 Hz and shows significant clusters of activation in right PMv, left M1, and SMA-proper. Note that the cluster of SMA-proper activity is smaller and superior in the 6.4 Hz condition as compared to SMA-proper activity in the 0.4 Hz condition.

Table 1**Control scan**

A comparison of Behavioral data and BOLD activity within visuomotor and memory related ROIs for day 1 versus day 2.

		T-value	p-value
Behavior			
Duration		−0.10	0.92
Amplitude		−0.77	0.46
Error		−1.92	0.08
Brain Activity			
M1	L	−0.07	0.95
PMv	L	−1.50	0.16
	R	−0.17	0.86
PMd	L	0.55	0.59
	R	−0.65	0.53
SMA		0.49	0.63
IPL	L	−1.88	0.08
	R	−0.68	0.51
Caudate	L	0.19	0.85
	R	0.89	0.39
Putamen	L	−0.52	0.61
	R	0.33	0.75
V5	L	−0.44	0.67
	R	−1.23	0.24
DLPFC	L	−0.39	0.70
	R	0.10	0.92
Lob VI	L	0.98	0.34
	R	−0.01	1.00

A paired t-test was conducted for each behavioral measure and each ROI and the resulting t-values and p-values are shown.

IPL, inferior parietal lobe; M1, primary motor cortex; PMd, dorsal premotor cortex; PMv, ventral premotor cortex.

Experimental scans

Table 2

Significant activation clusters from the voxel-wise analysis for the high gain > low gain contrast with visual feedback frequency set at 0.4 Hz and 6.4 Hz.

	Talairach coordinates				MNI coordinates				
	Voxels	X	Y	Z	X	Y	Z	max-T	
0.4Hz - High visual gain > Low visual gain									
Putamen	L	9626	-26.7	3.0	-0.2	-27.4	2.2	-3.8	6.7
	R	6452	21.6	1.6	-1.6	24.2	0.5	-6.1	6.4
Caudate	L	1150	-19.2	-6.8	23.5	-19.3	-10.2	21.5	5.2
	R	649	16.9	-6.4	24.9	19.3	-10.2	22.6	5.4
SMA-proper		4542	3.2	-1.4	45.0	4.9	-6.5	45.5	7.4
Cingulate gyrus	L	345	-11.4	22.9	38.3	-10.7	19.8	40.4	4.4
IPL	L	4042	-43.7	-29.2	25.5	-45.5	-33.9	22.0	5.9
	R	897	55.4	-29.8	23.8	60.4	-35.1	18.8	4.6
Thalamus	R	3945	17.8	-35.5	10.3	20.0	-39.7	3.9	5.4
M1/PMd	R	361	12.2	-15.0	1.3	14.1	-17.2	-4.2	5.2
	L	813	-33.5	-15.6	59.3	-34.3	-22.5	60.6	6.0
Posterior cingulate	R	1478	23.8	-14.7	47.7	26.8	-21.0	47.1	5.3
	L	773	-10.9	-61.9	12.0	-10.7	-67.6	3.8	5.1
ACC	L	570	-10.5	-40.1	17.6	-10.2	-45.0	11.9	4.2
	L	717	-18.2	36.6	17.4	-18.1	36.2	18.6	4.9
Lingual gyrus		527	-1.2	-74.7	-7.2	-0.6	-79.5	-18.8	4.4
Supramarginal gyrus	R	699	37.0	-48.7	24.4	40.6	-55.0	18.1	5.9
DLPFC	R	332	36.7	36.7	9.5	40.5	36.6	9.1	4.7
Insula	R	1542	30.2	12.5	9.5	33.5	11.0	7.1	5.1
Lobule IX		947	5.7	-58.4	-31.8	6.7	-60.2	-44.7	6.5
6.4Hz - High visual gain > Low visual gain									
M1	L	1492	-33.3	-13.1	49.4	-34.2	-19.0	49.8	8.8
V5	L	398	-48.5	-70.1	-4.0	-51.1	-74.6	-14.2	4.5
	R	1407	45.1	-69.9	-2.6	49.0	-75.1	-13.8	5.3
S1/IPL	L	653	-40.4	-40.9	60.7	-41.8	-49.4	60.0	7.5
PMv	L	603	-56.8	2.3	36.6	-59.3	-1.5	37.3	5.7

	Voxels	Talairach coordinates			MNI coordinates			max-T
		X	Y	Z	X	Y	Z	
MOG	R	586	-4.4	39.7	57.2	-9.6	38.7	5.5
	R	446	-80.4	18.7	28.9	-88.0	9.1	5.3
		387	-1.5	-1.5	55.7	-0.1	-7.5	4.3
SPL	L	327	-29.2	-58.0	47.3	-30.0	-66.4	5.2

Cluster label, cluster size, Talairach coordinates, MNI coordinates, and maximum T-value are shown.

IPL, inferior parietal lobe; SPL, superior parietal lobe; M1, primary motor cortex; PMd, dorsal premotor cortex; PMv, ventral premotor cortex; ACC, anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; S1, somatosensory cortex; MOG, middle occipital gyrus.