Transient shifts in frontal and parietal circuits scale with enhanced visual feedback and changes in force variability and error

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J Neurophysiol 109: 2205–2215, 2013. First published January 30, 2013; doi:10.1152/jn.00969.2012.—When subjects perform a learned motor task with increased visual gain, error and variability are reduced. Neuroimaging studies have identified a corresponding increase in activity in parietal cortex, premotor cortex, primary motor cortex, and extrastriate visual cortex. Much less is understood about the neural processes that underlie the immediate transition from low to high visual gain within a trial. This study used 128-channel electroencephalography to measure cortical activity during a visually guided precision grip task, in which the gain of the visual display was changed during the task. Force variability during the transition from low to high visual gain was characterized by an inverted U-shape, whereas force error decreased from low to high gain. Source analysis identified cortical activity in the same structures previously identified using functional magnetic resonance imaging. Source analysis also identified a time-varying shift in the strongest source activity. Superior regions of the motor and parietal cortex had stronger source activity from 300 to 600 ms after the transition, whereas inferior regions of the extrastriate visual cortex had stronger source activity from 500 to 700 ms after the transition. Force variability and electrical activity were closely related, with a positive relation in the parietal cortex and a negative relation in the frontal cortex. Force error was nonlinearly related to electrical activity in the parietal cortex and frontal cortex by a quadratic function. This is the first evidence that force variability and force error are systematically related to a time-varying shift in cortical activity in frontal and parietal cortex in response to enhanced visual gain.

electroencephalography; event-related potentials; low-resolution brain electromagnetic tomography; visual gain; visuomotor

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parietal, and visual cortical circuits. Finally, we will determine if acute changes in specific brain regions, identified using LORETA-based source localization, are consistent with prior functional magnetic resonance imagine (fMRI) studies that have localized the effects of visual gain within superior and inferior parietal cortex, PMv, PMd, M1, and V3/V5 (Coombes et al. 2010).

METHODS

Subjects. A total of 11 participants were recruited for this study (5 women; ages 19–30 yr: mean = 23.45 yr, SD = 3.80 yr). All participants were healthy right-handed subjects with normal or corrected vision. Self-reported measures of handedness were used, and all subjects reported no medical history of neurological and psychiatric conditions. Subjects were asked not to consume any caffeine, to refrain from using any hair products, and to wear prescription glasses instead of contact lenses for corrected vision. All subjects provided informed consent before the experiment. This study was approved by the local Institutional Review Board and performed in accordance with the Declaration of Helsinki.

Experimental design. Subjects sat upright in a chair with their right forearm supported by a rigid arm rest and their thumb and index finger in a pinch grip position against two force transducers (Measurement Specialties, Hampton, VA) (Fig. 1A). The experiment was carried out in a dimly lit room with a computer monitor that was placed ~130 cm (52 in.) in front of the subjects. Before the experimental task, subjects performed three 3-s trials of maximal isometric pinch grip force. The largest force output of the three trials was used as the individual's maximal voluntary contraction (MVC). Next, each subject performed five practice trials that consisted of 11 s of rest followed by 6 s of force production at 15% of their MVC. Subjects were asked to practice a pinch grip force task so that 1) the subjects could become familiar with the equipment and general requirements of the study, and 2) the visual display during force production could be recorded and reproduced onto the screen for the subject during a vision-only condition of the task.

The subjects were required to maintain a steady isometric force output with a change in visual feedback gain level during force production. The visual gain, which is the sensitivity of a system to error, can be varied by manipulating the distance of the eye to the computer monitor and/or changing the spatial amplitude of force output provided to the subject. In this study, the distance between the subject and the computer monitor was kept constant; therefore, visual gain was manipulated by changing the amplitude of the force fluctuations as viewed by the subject. The height of the force fluctuations viewed by the subject was manipulated using the following formula:

\[ \text{White cursor position} = \left[ \left( \frac{F_p - F_t}{G} \right) \times G \right] + F_t, \]  

where \( F_p \) is the force produced by the subject, \( F_t \) is the target force that was always centered on the screen, and \( G \) is the gain level used to change the spatial amplitude of visual feedback (white cursor position). The gain level \( G \) was equal to 0.05 for the low gain and 5.5 for the high gain. The higher value of \( G \) caused more displacement on the video screen (see Fig. 1 from Coombes et al. 2010). Visual gain in degrees of visual angle was calculated by assuming a set force output standard deviation (SD) of 0.3 N (Vaillancourt et al. 2006). The full range (±3SD) of the estimated variance for the height of force fluctuation was approximated by multiplying the SD value by 6 (0.3 N × 6 = 1.8 N). For each gain level G, we determined the height that 1.8 N would lead to in millimeters on the video display. The visual gain for each gain level \( G \) was then calculated using the following formula:

\[ \alpha = 2 \tan^{-1} \left( \frac{H_1}{D} \right), \]

where \( \alpha \) is the visual gain, \( H_1 \) is the height of the total range of motion in the top half of the visual field for each gain level \( G \), and \( D \) is the...
distance to the monitor. The low and high visual gain levels correspond to visual angles of 0.026° and 2.908°. The selected visual angles were well below and above 1°, spanning the range across which a dramatic change in force performance will occur (Coombes et al. 2010; Vaillancourt et al. 2006). The two levels of visual gain will be referred to as low gain (0.026°) and high gain (2.908°).

The experimental trials consisted of the following conditions: 1) rest (R; 5 s), 2) vision only at low gain (LV; 3 s), 3) vision only at high gain (HV; 3 s), 4) force with visual feedback at low gain (LF; 5 s), and 5) force with visual feedback at high gain (HF; 4 s) (Fig. 1B). There was no gap between these five conditions. The vision-only condition provided visual error signals on the screen that were consistent with prior work such that the visual error (root mean square error in cm) on the screen averaged across the subjects was 0.11 cm (+1SE = 0.016 cm) at the low gain and 1.71 cm (+1SE = 0.251 cm) at the high gain (Coombes et al. 2010). The force with visual feedback condition provided visual error signals consistent with the vision-only condition such that the visual error on the screen averaged across subjects was 0.10 cm (+1SE = 0.014 cm) at the low gain and 1.73 cm (+1SE = 0.245 cm) at the high gain. These changes for the low-to-high gain transition are similar to the visual error measurements from the high-to-low gain transition in the study by Poon et al. (2012). In that study, high-gain visual error was 1.69 cm (+1SE = 0.24 cm) and low-gain visual error was 0.10 cm (+1SE = 0.21 cm). Each condition in the current experiment is described in further detail below:

1) R: subjects were asked to rest and look straight ahead at the computer screen. A yellow stationary target bar was displayed and set at 15% of the subject’s MVC. A white stationary force bar was also displayed during the rest condition.

2) LV: subjects were asked not to produce any force but to focus their attention on the screen as the yellow target bar turned green and the white force bar fluctuated in real time according to a reproduction of the subjects’ force output at low visual gain.

3) HV: subjects were asked to continue looking straight ahead at the screen as the white force bar switched to the high-gain condition in real time according to a reproduction of the subjects’ force output. The green target bar remained on the screen.

4) LF: subjects were asked to produce force at 15% of their MVC by matching the white force bar to the green target bar using online visual feedback of the force output set at the low-gain level.

5) HF: subjects were asked to continue matching the white force bar to the green target bar using online visual feedback of the force output set at the high-gain level.

Each trial lasted 20 s, with the trials repeated 25 times in 1 block. Subjects performed a total of 8 blocks equaling 200 trials. To minimize a possible increase in electrocortical activity due to muscle fatigue (Johnston et al. 2001), subjects received a break of at least 3 min after every block in addition to R, LV, and HV conditions that required no force production within each trial. Subjects were instructed to minimize blinking during LV, HV, LF, and HF conditions. The transitions from LF to HF are referred to as the force + vision transitions. The transitions from LV to HV are referred to as the vision-only transitions. The vision-only transitions served as a control where subjects viewed a similar visual stimulus to that observed during the force + vision transitions. This allowed us to parse out the neural activity associated with the visual stimulus and to isolate the neural activity relating to the gain-related acute visuomotor response.

Behavioral data acquisition. The force transducers used were ELFT1600; 16-bit A/D to digital (A/D) amplifiers at an excitation voltage of 5 V. The force signal was transmitted via a 16-bit analog-to-digital converter and digitized at 200 Hz. The summed output from the force transducers was presented to the subject using a visual display on the computer screen (white force bar in Fig. 1B). The force output was displayed on the screen at a resolution of 1,024 × 768 pixels and a refresh rate of 60 Hz. Digital triggers identifying the start of each condition were sent from a program written in LabView to the BioSemi ActiiveTwo acquisition software.

Electrophysiological data acquisition. The electroencephalogram (EEG) was collected using a BioSemi ActiveTwo system with 128 Ag-AgCl ActiveTwo electrodes. The active electrodes were connected to a cap that was in a preconfigured montage covering the entire scalp surface (Fig. 1C). One of three cap sizes was selected for the subjects depending on their head circumference (i.e., 50–54, 54–58, or 58–62 cm). The signals were amplified through the electrodes at the source and had an output impedance of <1 Ω. EEG signals were digitally amplified at DC and sampled at 2,048 Hz. Electrical potentials were recorded between each electrode and the common mode sense (CMS) electrode, which is analogous to a ground. The CMS and a driven right leg (DRL) electrode are located toward the center of the other electrodes as shown in Fig. 1C (black filled circles). The CMS and DRL electrodes were used to drive the average potential of the subject as close as possible to the A/D-box reference potential electrode. The electrode offsets, a running average of the voltage measured between the CMS and each active electrode, were evaluated before the start of each block and during data collection to be within the acceptable range of ±40 mV (BioSemi, Amsterdam, The Netherlands). The electrode offset served as an indirect measure of impedance tolerance to ensure that a stable and high-quality signal was recorded from each active electrode.

Behavioral data analysis. Individual force trials were first visually inspected using a custom-written program in LabView to ensure that subjects were completing the requirements of the task (i.e., producing force during force + vision transitions and not producing force during the vision-only transitions). The force data were low-pass filtered using a fourth-order dual-pass Butterworth filter at 10 Hz. Force output was examined in 100-ms time bins from 0 to 800 ms after the force + vision transition. Mean force output, SD of force, coefficient of variation (CV) of force, and root mean square error (RMSE) of force were calculated. SD represented the variability about the mean force. CV represented the relative variability about the mean force (CV = SD/mean). RMSE represented the error about the target. The effect of time on force output was analyzed with one-way repeated-measures ANOVA using Greenhouse-Geisser corrections. Significance was determined with a P value <0.05. Significant effects were followed with individual t-tests to determine the first 100-ms time bin that was significantly different immediately after changes in visual feedback. Since eight t-tests were conducted, we adjusted the t-tests to be significant with a P value <0.00625.

Electrophysiological data analysis. All EEG data were imported into EMSE Suite software (Source Signal Imaging, San Diego, CA) for analysis. The data processing was consistent with prior work (Poon et al. 2012). The data were first re-referenced to a common average reference. The average reference was chosen to provide the best approximation of an absolute reference with a net source of zero (Srinivasan et al. 1998). This also allowed us to avoid the violation of quasi-stationarity for source estimation (Michel et al. 2004). Slow drifts across entire trials were removed by polynomial detrend and baseline corrected to DC offset. Next, channels were band-pass filtered at 0.5–70 Hz. Signals were then downsampled from 2,048 to 512 Hz. Trials were manually inspected for movement and eye artifacts and were discarded from further analyses if they contained visible artifacts. Trials were automatically excluded from averaging with individual t-tests to determine the first 100 ms that was significantly different immediately after changes in visual feedback. Since eight t-tests were conducted, we adjusted the t-tests to be significant with a P value <0.00625.

Electrophysiological data analysis. All EEG data were imported into EMSE Suite software (Source Signal Imaging, San Diego, CA) for analysis. The data processing was consistent with prior work.
to be reconstructed. The average number of valid trials per subject was 139 trials (SD 22.99 trials) for the vision-only transitions and 165 trials (SD 20.54 trials) for the force + vision transitions.

The event-related potentials (ERPs) were extracted by averaging across all valid trials for each subject from 0 to 800 ms after the vision-only and force + vision transition. A total of eight 100-ms time bins were analyzed (Fig. 1D). The effect of time and transition on each region of interest (ROI) was analyzed using separate two-way repeated measures ANOVA with Greenhouse-Geisser corrections (8 time bins × 2 transitions). Thirteen ROIs were selected to cover frontal, central, parietal, temporal, and occipital regions of the visuo-motor system (Fig. 1C). These ROIs were selected a priori and based on prior EEG and fMRI studies that suggested where the gain effects would be observed (Anguera et al. 2009; Coombes et al. 2010; Poon et al. 2012). Each ROI consisted of an average cluster of three electrodes. Each significant time × transition interaction was followed with individual t-tests and corrected for multiple comparisons using Bonferroni corrections. For each interaction, eight t-tests were conducted and considered significant with a P value <.00625. Electrophysiological results are reported in terms of positive or negative polarities, but no inferences are made regarding the nature of the polarities, i.e., the structure and orientation of dipoles(s) or the type of postsynaptic cells (excitatory or inhibitory).

Correlation analysis for low-to-high gain transition. To examine if there was a relationship between behavioral measures of force production and electrophysiological patterns of event-related brain activity, correlation analyses were performed using Pearson’s correlation coefficient, from which we reported the correlation coefficient (r). The dependent measures were the average amplitude across each 100-ms grand-averaged ERP voltage across subjects correlated with each force measure (SD, CV, RMSE) that was the grand average across subjects and trials for each measure. The behavioral and electrophysiological measures across each 100-ms time bin from 0 to 800 ms after changes in visual gain were plotted, and best-fit linear or nonlinear regression lines were determined for each individual ROI.

Correlation analysis for high-to-low gain transition. To better understand the transition from low to high gain during precision grip force, we analyzed previously published data during the same grip force task from high to low gain (Poon et al. 2012). The purpose was to compare the correlation between behavioral and electrophysiological data using the same approach described above. If the same correlation pattern is observed between behavioral and electrophysiological data for the low-to-high gain and high-to-low gain transitions, this finding would be consistent with more general sensorimotor adaptation. Alternatively, if the correlation for the two transitions is different, then this would suggest that the findings observed for low-to-high gain are specific to increased visual feedback. The grand-averaged ERP and SD of force from the high-to-low gain study (Poon et al. 2012) were examined in the same ROIs identified for the current study examining the low-to-high gain transition. The behavioral and electrophysiological measures across each 100-ms time bin from 0 to 800 ms after changes from high to low gain were plotted, and best-fit linear regression lines were determined for each individual ROI.

Source analysis. To further understand the spatial pattern of brain activity during the immediate transition of the visuo-motor system to gain-induced changes in visual feedback, we performed source localization on the time bins that were significantly different in the electrophysiological analysis. Hence, LORETA was applied at each 100-ms time bin for the periods that were identified as significant from the time × transition interactions and post hoc tests. The difference wave obtained by subtracting the grand-averaged event-related response during the vision-only transition from that during the force + vision transition was used to compute three-dimensional linear solutions to the inverse problem within the constraints of a realistic finite element modeling (FEM) of an average brain (EMSE Suite).

FEM is a volume-based modeling technique that considers individual anisotropic conductivities of each tissue type (skin, skull, and brain/ cerebrospinal fluid) to determine the solutions to the forward model. The distribution of neuronal generators as a current density value at each voxel resulted in a spatial resolution of 5 mm. LORETA solutions are characterized with the assumption that there is highly synchronized activity among neighboring neurons and that the smoothest of all possible distributions is the most plausible to explain the data (Pascual-Marqui et al. 2002). Human Motor Area Template and prior fMRI studies from our laboratory were used to identify brain regions from the LORETA solutions (Mayka et al. 2006; Vaillancourt et al. 2003). It is important to note that LORETA solutions are estimates and that many factors and assumptions can affect the outcome of the LORETA solutions (Michel et al. 2004; Pizzagalli 2007). Some of these factors include the number of electrodes, whether the template was from individual subjects or a normalized template, and which anatomic constraints were placed on the solutions. The current study used a MNI152 template, and LORETA solutions were constrained to the cortex.

RESULTS

Behavioral results. The target force level across subjects ranged from 4.2 to 12.0 N with a mean target force of 8.44 N (SD 2.23 N). The analyses examined the dependent measures in consecutive 100-ms time bins from 0 to 800 ms after visual gain changes. One-way repeated-measures ANOVA for mean force output was not significantly different, indicating that mean %MVC force did not change across time [F(7,70) = 2.74, P = 0.12] (Fig. 2A), although there was a clear trend for the mean force level to get closer to the 15% target force level with the increase in visual gain. SD of force was significantly different across time [F(7,70) = 12.40, P = 0.0014] (Fig. 2B). Individual t-tests found significant increases in SD of force between 400 and 800 ms after increased visual gain (all P values <0.00625). CV of force was also significantly different across time [F(7,70) = 14.38, P = 0.0008] (Fig. 2C). Individual t-tests found significant increases in CV of force between 400 and 800 ms after increased visual gain (all P values <0.00625). The RMSE of force production was significantly different across time [F(7,70) = 44.56, P = 0.00002] (Fig. 2D). Significant decreases in RMSE were detected between 400 and 800 ms (all P values <0.00625). Thus the adaptation to increased visual gain led to increased variability and reduced force error.

Electrophysiological results. Figure 3 illustrates the grand-averaged waveforms of all recorded electrodes during force + vision and vision-only transitions. The ROIs that were further analyzed are labeled and highlighted with dashed circles. Figure 4 represents the topography map of the grand-averaged waveforms projected onto a standardized head shape. First, a frontal-central positivity and posterior-occipital negativity was observed between 200 and 300 ms in the force + vision transition (Fig. 4B) and in the vision-only transition (Fig. 4A). This pattern was followed by a frontal negativity and parietal positivity in the force + vision transition between 300 and 800 ms (Fig. 4B). Figure 4C shows the topography map obtained by subtracting the grand-averaged waveforms during the vision-only transition from the those during the force + vision transition. Significant time × transition interactions were found in 8 of the 13 ROIs (i.e., midline prefrontal, midline frontal, left frontal, right frontal, midline parietal, left parietal, right parietal, and midline occipital channel groups) (Table 1), followed by significant t-tests in 6 of the 8 significant interactions after Bonferroni corrections (i.e.,
midline prefrontal, midline frontal, left frontal, right frontal, midline parietal, and right parietal channel groups). Post hoc tests revealed that significant differences occurred as early as 300 ms after the increase in visual gain and as late as 700 ms. The first regions with significant changes in ERPs were detected over the midline prefrontal, left frontal, right frontal, and midline parietal channel groups. At 400 ms, significant differences were found in the midline frontal and right parietal channel groups. The 300- to 700-ms time period is used in Source estimation analysis to examine how source activity changed across this time.

Behavioral and electrophysiological correlation. Next, the relation between force variability and event-related activity and force error and event-related activity was examined within the six ROIs that were significant following the post hoc tests described above. Robust and significant linear relationships were demonstrated between force variability (SD) and the event-related brain activity in these six ROIs following the increase in visual gain. The strongest relationship was found between SD and the midline parietal region (Fig. 5A). The linear functions resulted in a significant correlation at midline parietal ($r = 0.96, P = 0.0002$), right parietal ($r = 0.84, P = 0.0095$), midline prefrontal ($r = -0.89, P = 0.0033$), left frontal ($r = -0.87, P = 0.005$), midline frontal ($r = -0.84, P = 0.0088$), and right frontal regions ($r = -0.81, P = 0.015$) (Fig. 5). It is clear that as force variability increases, event-related activity of parietal regions increases (Fig. 5, A and B) and event-related activity of frontal regions decreases (Fig. 5, C–F). As expected from the data in Fig. 2, the CV of force showed the same pattern of findings as the SD of force: midline parietal ($r = 0.95, P = 0.0002$), right parietal ($r = 0.83, P = 0.01$), midline prefrontal ($r = -0.89, P = 0.003$), left frontal ($r = -0.87, P = 0.006$), midline frontal ($r = -0.84, P = 0.009$), and right frontal regions ($r = -0.81, P = 0.02$). However, Fig. 6, A–F, shows that the RMSE and event-related activity revealed a quadratic function that best characterized the relation such that the correlations were as follows: midline parietal ($r = 0.97, P = 0.001$), right parietal ($r = 0.86, P = 0.03$), midline prefrontal ($r = 0.93, P = 0.007$), left frontal ($r = 0.89, P = 0.02$), midline frontal ($r = 0.88, P = 0.03$), and right frontal regions ($r = 0.84, P = 0.05$).

The correlation for SD of force and event-related activity was examined between behavioral and electrophysiology data for the high-to-low gain transition using the data from Poon et al. (2012). The correlation between the behavioral and electrophysiology data for the high-to-low gain transition resulted in nonsignificant correlations for each ROI (all $P$ values $>0.22$).

Source estimation analysis. The results of the source analysis are shown in Fig. 7 and focused on the 300- to 700-ms time period. Observed solutions are overlaid on the SPM 152 template included in EMSE Suite and distributed within SPM (Statistical Parametric Mapping). The intense red color indicated the most prominent sources of activation from the three-dimensionally distributed LORETA solution. Figure 7 shows the unthresholded current density values from the LORETA source analysis. We focused the analysis between 300 and 700 ms, since this is the time period over which the ERP findings were significant in Table 1. The solution illustrated the strongest focus of activity in the left superior parietal cortex from 300 to 400 ms (Fig. 7, axial). Greater source activity was evidenced within left superior parietal lobule (SPL) compared with right SPL. At 300–500 ms, there was also activity in the left and right primary motor cortex (M1), left and right PMv, left and right inferior parietal lobule (IPL), and left and right V3/V5 regions. At 500–600 ms, the left SPL source activity decreased, whereas the left and right IPL source activity increased. Also, left PMv source activity increased compared with that at the early time periods. The most prominent source at 500–600 ms was in the left and right V3/V5 regions. At 600–700 ms, the source activity from most regions decreased compared with that at prior time periods, with the exception of the source activity in right V3/V5. In summary, there was a shift in the strongest source activity with time from superior regions of the motor cortex and parietal cortex to inferior regions of the extrastriate visual cortex.

DISCUSSION

The behavioral finding of this study is that the immediate transition from a low visual gain to a high visual gain caused an inverted U-shaped function for force variability and reduced force error. Corresponding changes in cortical activity varied

Fig. 2. Behavioral results: mean force output (%MVC; A), standard deviation (SD; B), coefficient of variation (CV; C), and root mean square error (RMSE; D) of force. Vertical dashed lines represent time of force vision transition. Arrows represent the earlier time intervals of significant behavioral change. Error bars represent SE. *$P < 0.05$, significant time bins after force vision transition.
across time and correlated with force variability and force error in region-specific ways. There was a strong positive, linear relation between electrical activity in the parietal cortex and force variability and a negative, linear relation between electrical activity in the frontal cortex and force variability. This observation was not evident during a transition from high to low visual gain. Also, the relation between event-related activity and force error was characterized by a quadratic function. There was an immediate change in event-related activity from 200 to 300 ms for both the vision-only condition and the force vision condition (Fig. 4). This response was most likely related to the visual stimulus that was similar in both conditions. From 300 to 700 ms, the changes in cortical activity were specific to the force vision condition and were shown in superior and inferior parietal cortex, M1, PMd, PMv, V3, and V5. There was a shift in the strongest source activity across time with superior regions of the motor cortex and parietal cortex from 300 to 600 ms and with inferior regions of the extrastriate visual cortex showing stronger activity from 500 to 700 ms.

Our findings support prior EEG literature and the idea that event-related activity is sensitive to changes in a visual display that lead to transient visuomotor error, because behavioral adjustments in force production occurred very closely in time with the detection of event-related activity that resembled both error-related negativity and error-related positivity. Error-related negativity is often linked to evaluation processes, whereas error-related positivity is often linked to error monitoring (Coles et al. 1995; Falkenstein et al. 1991, 2000). The sustained event-related pattern observed during the increase in visual gain covered a wide range of frontal and parietal regions. Error-related activity in these same regions has previously been observed during sensorimotor adaptation tasks (Anguera et al. 2009; Falkenstein et al. 2000; Krigolson and Holroyd 2006). In the current study, changes in force variability, force error, error-related negativity, and error-related positivity were all detected between 300 and 400 ms after increases in visual gain. A study by Anguera et al. (2009) was able to show a scaling of the amplitude of error-related negativity in relation to error magnitude during a sensorimotor adaptation task. Our observations provide novel evidence that associate error-related negativity and error-related positivity with increased force variability when the force error is being reduced.
during force production when transitioning from a low to high visual gain (Figs. 2 and 5).

In addition, results from the behavioral and electrocortical correlation analysis after the increase in visual gain provide support to the idea that changes in the magnitude of isometric force variability is related to the inherent properties of event-related brain activity. As force variability increased, event-related activity of parietal regions increased while event-related activity of frontal regions decreased (Fig. 5). The strongest correlation was found at the midline parietal area, and this region was also identified through source analysis as one of the brain regions primarily responsible for the observed event-related activity between 300 and 400 ms after the increase in visual gain. This same correlation pattern was not observed from high to low gain. Also, since the visual stimulus was similar between vision-only and force+vision conditions, the visual gain. This same correlation pattern was not observed from high to low gain. Also, since the visual stimulus was similar between vision-only and force+vision conditions, the effects of visual input were minimized in the experiment.

The results for force error and event-related activity revealed a nonlinear quadratic relation. When force error was high and low, event-related activity was similar. Upon visual inspection of Figs. 2 and 6, it can be observed that when force error was reduced after the transition to high visual gain, the quadratic function reached either a minimum or maximum depending on the region of interest. This is the same time period when force variability was at its maximum (Fig. 2). These results support the conclusion that force performance is coupled with the event-related activity in the parietal and frontal cortex.

Cortical localization (LORETA) in the 300- to 700-ms transition period following low to high visual gain indicated source activity in SPL, IPL, M1, PMd, PMv, V3, and V5. One might argue that the source activation observed in these regions could be the product of changing a visual stimulus during force production. However, the input to source analysis had already subtracted the voltages during the vision-

Table 1. ANOVA results for time \times transition interaction and follow-up t-tests

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<tr>
<th>Location of Channel Groups</th>
<th>F Value</th>
<th>P Value</th>
<th>0 to 100 ms</th>
<th>100 to 200 ms</th>
<th>200 to 300 ms</th>
<th>300 to 400 ms</th>
<th>400 to 500 ms</th>
<th>500 to 600 ms</th>
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<tr>
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<td>3.40 0.01</td>
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<td>-4.14 0.002</td>
<td>-2.44 0.03</td>
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<td>0.0004</td>
<td>2.92 0.02</td>
<td>1.34 0.21</td>
<td>1.30 0.22</td>
<td>-3.99 0.003</td>
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<td>-2.76 0.02</td>
<td>-1.18 0.27</td>
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<tr>
<td>Midline frontal</td>
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<td>0.009</td>
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<td>Midline central</td>
<td>0.93</td>
<td>0.440</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Right central</td>
<td>0.57</td>
<td>0.660</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>Left parietal</td>
<td>5.54</td>
<td>0.018</td>
<td>-1.89 0.09</td>
<td>-1.31 0.22</td>
<td>-1.44 0.18</td>
<td>3.19 0.01</td>
<td>4.26 0.002</td>
<td>4.23 0.002</td>
<td>4.18 0.002</td>
<td>2.37 0.04</td>
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<tr>
<td>Midline parietal</td>
<td>11.81</td>
<td>0.0004</td>
<td>3.78 0.006</td>
<td>-1.60 0.14</td>
<td>-1.65 0.13</td>
<td>4.73 0.001</td>
<td>4.26 0.002</td>
<td>4.23 0.002</td>
<td>4.18 0.002</td>
<td>2.37 0.04</td>
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<tr>
<td>Right parietal</td>
<td>7.75</td>
<td>0.001</td>
<td>-3.11 0.01</td>
<td>-0.58 0.58</td>
<td>-1.68 0.12</td>
<td>2.97 0.01</td>
<td>3.90 0.003</td>
<td>3.16 0.01</td>
<td>3.76 0.004</td>
<td>2.27 0.05</td>
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<tr>
<td>Left temporal</td>
<td>0.47</td>
<td>0.750</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>Right temporal</td>
<td>0.69</td>
<td>0.620</td>
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<tr>
<td>Midline occipital</td>
<td>3.68</td>
<td>0.030</td>
<td>-1.55 0.15</td>
<td>-0.54 0.60</td>
<td>-1.15 0.28</td>
<td>2.34 0.04</td>
<td>3.29 0.01</td>
<td>2.61 0.03</td>
<td>1.98 0.08</td>
<td>0.85 0.42</td>
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Two-way repeated-measures ANOVA (8 time bins \times 2 transitions) was performed; corresponding F values and Greenhouse-Geisser-corrected P values are shown. Each significant interaction was followed up with individual t-tests and considered significant with a Bonferroni-corrected P value <0.00625; corresponding t values and P values are shown. Regions of interest with significant interactions followed by significant t-tests are shown in bold type. Significant P values are shown in bold type.
only condition. Also, prior work did not observe the same pattern following a transition from high to low visual gain (Poon et al. 2012), suggesting that these effects were specific to the increase in visual gain during the production of force. In addition, the current findings in SPL, IPL, M1, PMd, PMv, V3, and V5 from the LORETA source analysis are consistent with a prior study that used fMRI to examine brain activity during a similar precision grip force control task in which visual gain was manipulated (Coombes et al. 2010). The localization of premotor and parietal regions during increases in visual gain is also consistent with previous evidence identifying connections between SPL and PMd during visuomotor tasks in nonhuman primates (Binkofski et al. 1999; Caminiti et al. 1996; Wise et al. 1997). An fMRI study in humans identified regions along the dorsal premotor cortex and posterior parietal cortex with increased activity during responses to randomly triggered reach errors (Diedrichsen et al. 2005). It is important to note that we are not claiming the results from LORETA are the same as those from studies using fMRI, because the spatial resolution of LORETA-based source reconstruction (~5 mm) is not at the same level as that of fMRI (~1–3 mm). It is worth noting though that the regions identified with each technique are largely consistent during a similar type of force production task.

The findings for left SPL shown in Fig. 7 are also consistent with prior studies that have studied visually guided grasping. The human anterior intraparietal sulcus (hAIP), which is generally believed to be part of the SPL, is a region that has been linked with visually guided grasping (Binkofski et al. 1998; Castiello 2005; Culham et al. 2006). Several studies have demonstrated the importance of AIP in grip force scaling through transcranial magnetic stimulation (TMS)-induced inactivations of the AIP (Dafotakis et al. 2008; Davare et al. 2007; Tunik et al. 2005). In the context of these previous studies, the changes in activity in the superior parietal region in the current study may be interpreted as reflecting the detection and correction of errors in grip force scaling. Our behavioral finding of significant differences in force variability by 400 ms, along with prominent source activity in the left SPL between 300 and 500 ms, complements earlier evidence that this region plays an important role during grip force error correction. In addition, our findings are in agreement with previous studies that specifically showed left parietal activation during visuomotor adaptation tasks (Clower et al. 1996; Danckert et al. 2008). A more recent study by Mutha et al. (2011) identified deficits in patients with left, but not right, parietal lesions during adjustments to visuomotor rotations. Although we cannot rule out the possibility that the greater activity observed in the left hemisphere is due to hand laterality, our results do
suggest that the superior parietal region is involved in the ability to correct an ongoing visually guided movement when the visual gain of the feedback is increased. Further neurophysiological studies that focus on acute responses to visual gain during a visuomotor task performed by the nondominant hand will be necessary to clarify this issue.

There are other potential explanations for the current findings. The stimulus change from low to high gain was predictable, and it is possible that some of the findings reflect a prediction error from low to high gain. However, when Table 1 and Fig. 4 representing the low-to-high gain transition in the present article are compared with Table 2 and Fig. 6 representing the high-to-low gain transition in the article by Poon et al. (2012), it is evident that different patterns of event-related activity occurred. Both the low-to-high gain and high-to-low gain transitions had predictable timing for each transition, and the unique patterns for each transition would suggest that the predictable timing is an unlikely factor. In addition, since the patterns of event-related activity are different between low-to-high and high-to-low gain transitions, it is possible that the predictability of the error response was a factor and should be explored in future studies.

In behavioral and electromyographic (EMG) studies, visual gain has typically been manipulated between trials. When the visual gain increased, young subjects exhibited greater force errors and lower force variability with abduction of the index finger (Baweja et al. 2010), precision pinch grip (Coombes et al. 2010), ankle dorsiflexion (Prodoehl and Vaillancourt 2010), and elbow flexion (Prodoehl and Vaillancourt 2010) tasks. In contrast, the current study manipulated visual gain within a trial. The findings show that when the visual gain increased, subjects transiently decreased force error and increased force variability. Several studies have examined the neural activation of muscle with changes in visual gain across trials. The consensus among three single motor unit studies is that despite the strong effects of visual gain on the force output of young adults, the discharge characteristics of single motor units do not change (Jordan et al. 2013; Schmied et al. 2000; Vaillancourt et al. 2002). This suggests that the effects of visual gain may be realized through the activity of a population of motor units rather than individual motor units. Recent findings support this hypothesis. For example, Kennedy and Christou (2011) demonstrated that young adults increased the normalized power of the EMG signal between 13 and 60...
Hz, whereas older adults did not significantly change this bandwidth when visual gain increased. Thus it is important to note that the current findings for manipulating visual gain within a trial may be different in older adults, and more work is needed to understand the age-associated differences when the visual gain is manipulated within a trial. Furthermore, more work is needed to better understand the neural activation of muscle with manipulation of visual gain within a trial.

An interesting application of visual gain is in the area of error augmentation in rehabilitation of patients following a stroke. It has been suggested that different forms of error magnification can facilitate motor rehabilitation in patients with stroke. For instance, Patton et al. (2006) studied stroke survivors when performing movements in a robot-generated force field. Although subjects adapted to the force fields, greatest adaptation and learning was evident when the training forces magnified the original errors (i.e., high gain) compared with when training forces reduced the errors (i.e., low gain). In a different study of stroke survivors, the authors used a 6-wk randomized crossover design to compare error augmentation using haptic and visual distortions with massed practice alone (Abdollahi et al. 2011). The final evaluations for comparing the two training protocols showed a benefit for error augmentation for patients after stroke. In a study examining the excitability of the motor cortex using TMS during flexion and extension movements, chronic stroke patients had greater ipsilesional cortical excitability at the lowest gain level compared with a gain level of 1 (Bagce et al. 2012), providing additional evidence that the neural mechanism underlying visuomotor transformations remains intact following a stroke. This result may seem contrary to the studies by Patton et al. (2006) on error augmentation in patients following stroke, because the significant effects were at the lowest, compared with the highest, gain levels. However, it is important to note that the study by Bagce et al. (2012) did not augment error. Instead, the ratio between actual movement and the perceived movement was manipulated, which caused movement characteristics to be clamped. This resulted in similar cortical excitability between high-gain and control conditions. Since it is not clear that the current findings would be extended to older adults with or without a history of stroke, future studies should be extended to neurological populations in which the effects of visual gain may have potential therapeutic implications.

Although the current study does not focus on patients following a stroke, the findings provide novel evidence that cortical activity in the frontal cortex and parietal cortex relates to changes in force variability following an immediate transition to an increased gain level. Evidence was presented that after the transition from low visual gain to high visual gain, source activity is strongest in the motor cortex and parietal cortex from 300 to 600 ms and strongest in the extrastriate visual cortex (V3/V5) from 500 to 700 ms. The brain regions identified included superior and inferior parietal cortex, M1, PMd, PMv, V3, and V5, and these regions identified from high-density EEG were consistent with prior studies using fMRI. Finally, a positive, linear relation existed between electrical activity in the parietal cortex and force variability, and a negative, linear relation between electrical activity in the frontal cortex and force variability. Future studies may focus on how damage to the cortex impairs information flow and the relation between cortical physiology and motor performance.

GRANTS
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DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the authors.
AUTHOR CONTRIBUTIONS

C.P., S.A.C., D.M.C., E.A.C., and D.E.V. conception and design of research; C.P. performed experiments; C.P., S.A.C., and D.E.V. analyzed data; C.P., D.M.C., E.A.C., and D.E.V. interpreted results of experiments; C.P., S.A.C., D.M.C., E.A.C., and D.E.V. drafted manuscript; C.P., S.A.C., D.M.C., E.A.C., and D.E.V. edited and revised manuscript; C.P., S.A.C., D.M.C., E.A.C., and D.E.V. approved final version of manuscript.

REFERENCES
