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Separate Modulations of Human V1 Associated with Spatial Attention and Task Structure

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Summary

Functional magnetic resonance imaging (fMRI) was used while normal human volunteers engaged in simple detection and discrimination tasks, revealing separable modulations of early visual cortex associated with spatial attention and task structure. Both modulations occur even when there is no change in sensory stimulation. The modulation due to spatial attention is present throughout the early visual areas V1, V2, V3, and VP, and varies with the attended location. The task structure activations are strongest in V1 and are greater in regions that represent more peripheral parts of the visual field. Control experiments demonstrate that the task structure activations cannot be attributed to visual, auditory, or somatosensory processing, the motor response for the detection/discrimination judgment, or oculomotor responses such as blinks or saccades. These findings demonstrate that early visual areas are modulated by at least two types of endogenous signals, each with distinct cortical distributions.

Introduction

Of the total afferent inputs to primary visual cortex (V1), only a small proportion conveys information from the retina (Ahmed et al., 1994; Peters et al., 1994). In addition to inputs from the lateral geniculate nucleus (LGN), V1 receives feedback projections from visual, auditory, and multimodal cortical areas (Falchier et al., 2002; Rockland and Ojima, 2003) and feedforward projections from subcortical regions such as the pulvinar, claustrum, locus ceruleus, and basal nucleus (Doty, 1983; Graham, 1982). Single-unit and neuroimaging studies have shown that stimulus-induced activity in V1 is modulated by attention to location (Brefczynski and DeYoe, 1999; Gandhi et al., 1999; Martinez et al., 1999; McAdams and Reid, 2005; Motter, 1993; Somers et al., 1999; Tootell et al., 1998). Moreover, Ress et al. (2000) and Kastner et al. (1999) have shown that attentional modulations in V1 from attending to a location occur in the absence of a stimulus; i.e., they are completely endogenous.

To date, however, there has been little to challenge the general assumption that modulations of early visual areas are directly attributable to perceptual processing (but see Shuler and Bear, 2006). The present experiments show that two entirely endogenous modulations coexist within V1: one is related to spatial attention; the other, to task structure. We use a detection task similar to that of Ress et al. (2000) in which participants detect a threshold contrast visual stimulus. We replicate their observation that attending to a location in the absence of a stimulus produces a robust modulation of human visual cortex (V1, V2, V3, and VP). In a series of experiments, by varying the time and frequency of response, and the location and modality of the target, we demonstrate the presence of an endogenous signal time-locked to task events.

The results demonstrate that the modulation due to spatial attention is separable from modulations due to task structure. The attentional modulation is confined to the time period in which the stimulus is presented, its location within V1 changes with the location of the attended stimulus, and it is observed with the same or greater magnitude in retinotopic areas subsequent to V1 (e.g., V2 and V3). The task structure modulation occurs both at the time of stimulus presentation and at the time of response, is biased toward the peripheral representation within V1 irrespective of the stimulus location, is independent of the modality of the target stimulus, and is much stronger in V1 than in subsequent visual areas such as V2 and V3. Control experiments establish that the task structure modulation of V1 is not due to sensory stimulation, spatial attention, motor factors, blinks, or eye movements. In addition, an experiment involving two response intervals, separated in time, demonstrates modulation of V1 associated with an intermediate task event, not just with events marking task onset and offset.

Results

Human Visual Cortex Modulation by Spatial Attention and at Time of Response

Experiment 1 separated activity due to attention and activity associated with response by comparing immediate and delayed response conditions. The task is described in Figure 1A (also see Experimental Procedures). In the delayed response condition, the time between stimulus presentation and response was long enough to resolve the blood oxygenation-level-dependent (BOLD) modulation associated with each event. Behavioral data from this and subsequent experiments can be found in the Supplemental Data.

Figures 2A–2E show a flattened representation of the occipital lobe of a representative participant. Passive retinotopy was used to map the borders of early visual areas and the representation of eccentricity in those areas (Figures 2A and 2B, see Experimental Procedures). Figure 2C shows that immediate response trials produced surprisingly widespread activity throughout V1, with no evidence of stronger activation at the eccentricity corresponding to the stimulus (i.e., the region corresponding to the second largest hot pink semicircle in Figures 2B–2E). Delayed response trials produced two distinct peaks of activity. Figure 2D shows that the first peak in activity, putatively related to attention, was

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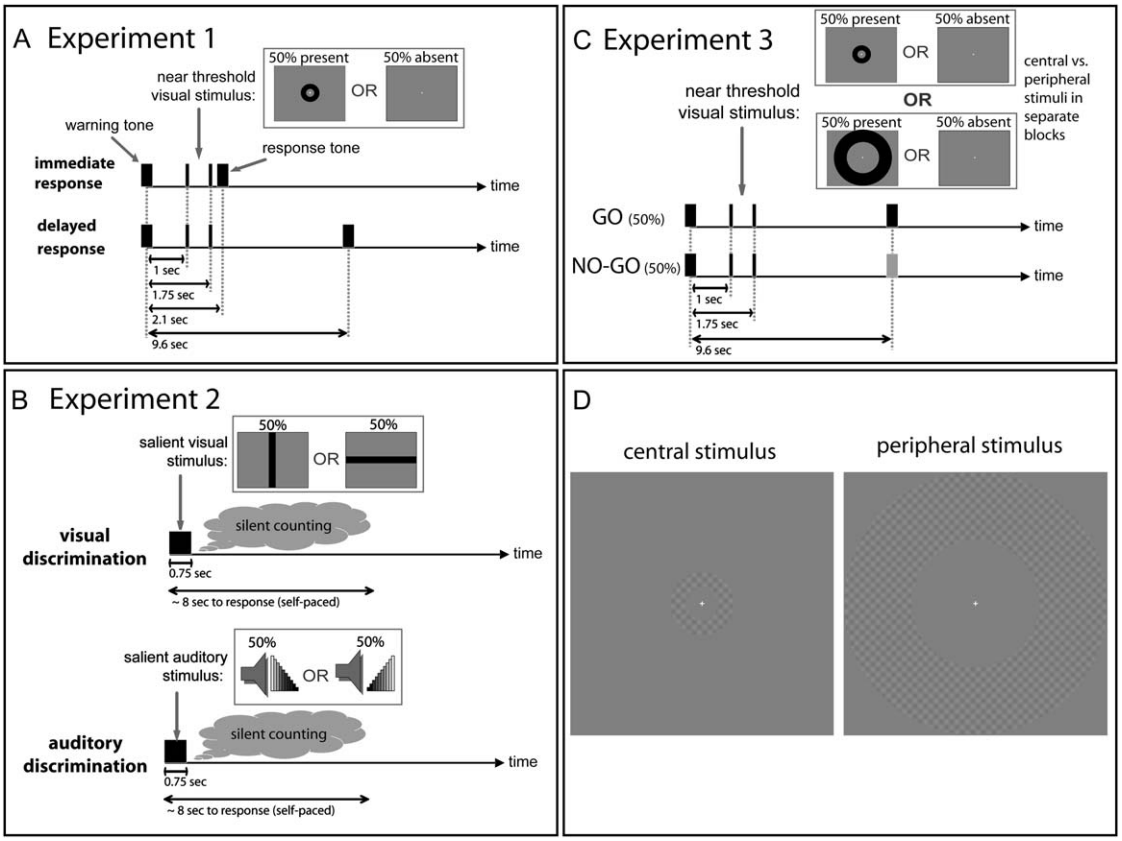

Figure 1. Experimental Tasks in Experiments 1–3

(A) In Experiment 1, three participants performed immediate and delayed response tasks in separate scans. An auditory warning tone marked the start of each trial. The onset and offset of the stimulus window were also marked by brief auditory tones. A further auditory tone indicated the time to respond. On 50% of trials there was no change to the visual scene at any point in the trial (stimulus absent). On the remaining 50% (stimulus present), a contrast-reversing checkerboard pattern was presented in a central annulus throughout the stimulus window (0.75 s). The stimulus was presented at near-threshold contrast (established prior to scanning, see Experimental Procedures), and subtended 0.75°–1.5° visual angle (left side of [D]). (B) Three participants performed visual and auditory discrimination tasks in separate scans. One of two highly salient stimuli, which could be easily distinguished, was presented for 0.75 s at the start of the trial. Participants then counted silently to seven before giving a manual response to indicate which stimulus was presented. In the visual task the stimuli consisted of either a vertical or a horizontal checkerboard pattern, presented at maximum contrast. There were no auditory stimuli in the visual task. In the auditory task, the stimuli consisted of a series of ten tones of either ascending or descending frequency. There were no visual stimuli in the auditory task. (C) Participants were required to detect a near-threshold, contrast-reversing checkerboard pattern, presented either in a central annulus (0.75°–1.5° visual angle, left side of panel [D]) or a peripheral annulus (3°–6° visual angle, right side of [D] in separate scans). The stimulus was present on only 50% of scans. After the stimulus window, participants waited for an auditory cue. On 50% of trials, the auditory cue indicated the time to make a response (GO). On the other 50%, a distinct auditory tone indicated that participants should withhold response (NO-GO). (D) Left side, snapshot of central (0.75°–1.5°) stimulus used in all experiments except Experiment 2. Right side, snapshot of peripheral stimulus (3°–6°) used in Experiment 3.

most evident at the retinotopically appropriate region (near the second largest hot pink semicircle), while the map in Figure 2E shows that the second peak in activity was most pronounced outside the stimulus region in peripheral V1 (i.e., outside the largest hot pink semicircle in Figures 2B–2E). Figure 2F shows time courses averaged across the three participants for regions corresponding to the stimulus eccentricity (blue time courses) and most peripheral mapped eccentricity (red time courses) in V1, V2, and V3/VP. Immediate response trials are shown on the left; delayed response trials, on the right. Statistical analyses of the time courses were conducted separately for each participant using repeated measures analysis of variances (ANOVAs) (see Statistical Methods subsection). The distribution of peak activity can be seen individually for each participant, and for all four eccentricities, in Figure S1 of the Supplemental Data.

The time course for immediate response trials (left panel) showed a single, early peak, while that for delayed response trials (right panel) showed both the early peak and a later peak, consistent with a response-related signal. This difference in the time course for the immediate and delayed conditions was significant for each participant, as indicated by the interaction of Time by Condition (immediate, delayed) (P1, number of trials [n] = 528, $p < 0.001$; P2, n = 548, $p < 0.001$; P3, n = 576, $p = 0.006$).

The attention-related and response-related signals were distinguished not only by their time of occurrence, but also by their retinotopy. Attention-related activity occurred in the retinotopically appropriate location. The right panels of Figure 2F show that during the stimulus window, activity in the stimulus region (shown by the blue lines) was greater than activity in the most peripheral region (shown by the red lines). Repeated

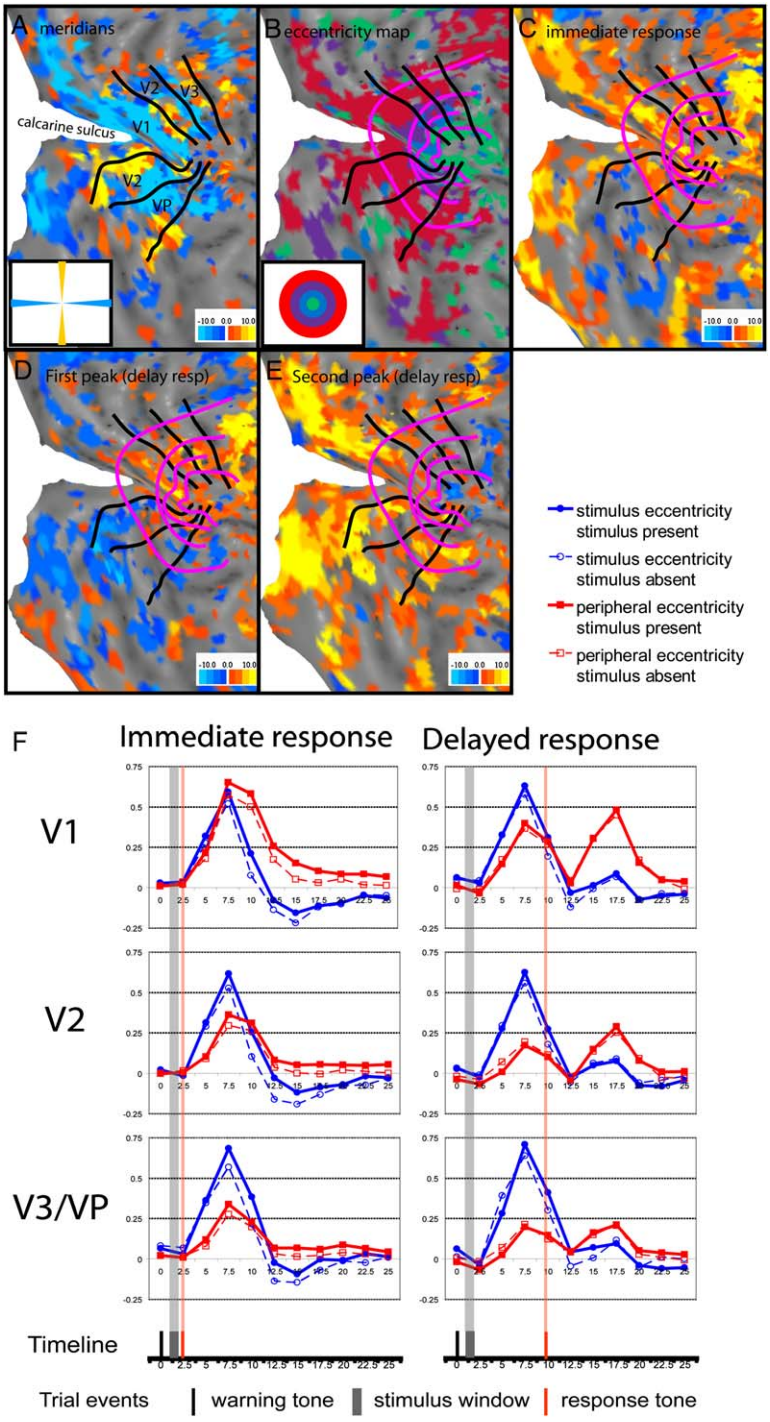

Figure 2. BOLD Modulation of Early Visual Areas for Immediate and Delayed Response Trials for Experiment 1: Immediate/Delayed

(A) to (E) shows a flattened representation of the right occipital cortex of a representative participant (P1). (A) The horizontal and vertical meridians mark the borders between V1, V2, V3, V3A, VP, and V4 . (B) Four annuli were used to map eccentricity (with inner and outer radii of 0.2°–0.75°, 0.75°–1.5°, 1.5°–3°, and 3°–6° visual angle from fixation). The stimulus corresponded to the second largest annulus, colored blue in this panel. (C) shows significant BOLD activity corresponding to the stimulus window in immediate response trials, (D) shows significant BOLD activity corresponding to the stimulus window in delayed response trials, and (E) shows the second peak in BOLD activity in delayed response trials. All maps are thresholded at $p < 0.05$ (two-tailed, uncorrected); scale indicates z score. Black lines marking the borders of visual areas and hot pink lines marking the approximate center of the eccentricity representations are drawn by hand for reference.

(F) Time courses, averaged across participants, for immediate and delayed response trials. In this and all subsequent graphs, the scale is given in percent BOLD modulation unless otherwise indicated. Blue lines show activity in regions corresponding to the eccentricity of the stimulus, determined by passive retinotopy (see Experimental Procedures). Red lines show activity in regions corresponding to the most peripheral passive localizer. Activity is shown separately for V1, V2, and V3 and VP combined. Solid lines with closed symbols show stimulus present trials. Dotted lines with open symbols show stimulus absent trials.

measures ANOVAs on the subset of the data corresponding to the first peak of activation (7.5 s) during delayed trials showed a significant effect of eccentricity in all three participants (P1, n = 264; P2, n = 274; P3, n = 288; $p < 0.001$ for all tests).

In contrast, the response-related signal isolated by the second peak of activity was stronger in the most peripheral region than in the stimulus region (i.e., for the second peak, the red lines are above the blue lines). Inspection of all four mapped eccentricities revealed that the increase in response-related activity for more eccentric regions was highly systematic (see Figure S1). A repeated measures ANOVA on the subset of the data corresponding to the second peak of activation (17.5 s) on delayed trials indicated that all participants showed significantly greater activations in the peripheral than stimulus region (P1, n = 264; P2, n = 274; P3, n = 288; $p < 0.001$ for all tests). The difference in the retinotopic distribution of the two peaks of activity during delayed response trials was statistically significant within V1. A repeated measures ANOVA limited to V1 with the factors Time of Activation (7.5 s versus 17.5 s) and Region

(stimulus region versus peripheral region) yielded a significant interaction of Time of Activation by Region in each of the three participants (P1, n = 264; P2, n = 274; P3, n = 288; $p < 0.001$ for all tests).

A final dissociation between the two types of signals was reflected in their distribution across visual areas V1, V2, and V3/VP. The second peak in activity was strongest in V1, and became progressively weaker moving to V2 and then to V3/VP. In contrast, the first peak, at the eccentricity corresponding to the stimulus, showed, if anything, a small trend to be greater in higher visual areas. A closer examination of the distribution of attentional and nonperceptual modulations across visual areas can be found at the end of the Results section.

Importantly, the time courses from trials in which the stimulus was present (continuous line) or absent (dashed line) were virtually indistinguishable, indicating that the putative attention-related first peak of activity did not reflect sensory activity but was endogenously generated, as previously noted (Ress et al., 2000). Identical stimulus-present and stimulus-absent time courses were also observed for the second peak, indicating that it was also unrelated to sensory activity.

In summary, the results from the time course analysis (Figure 2F) and from the statistical maps (Figures 2A–2E) generated by using an assumed hemodynamic response show that the responses on immediate and delayed response trials consisted of the combination of two distinct endogenous modulations. The first was time-locked to the stimulus window, was stronger at the eccentricity where the stimulus was presented, and was approximately equal across different visual areas. This modulation likely corresponds to that reported by Ress et al. (2000) and is associated with the voluntary orienting of spatial attention to the stimulus location. The other modulation varied with the time of response, was more prominent in V1 than in later visual areas, and was distributed to more peripheral regions.

Although the second modulation was clearly greatest in regions representing more peripheral parts of the visual field, it also appeared in more foveal regions. The time course of activity at the stimulus eccentricity (blue time courses) on delayed response trials showed a small second peak of activity that was not present on immediate response trials. t tests that compared activity on delayed and immediate response trials at the time of the second peak (17.5 s) for each of the four mapped eccentricities and for each of the three participants revealed significantly higher activity for delayed as opposed to immediate response trials for all twelve comparisons (independent samples paired t tests, $p < 0.05$, two-tailed). This effect was significant even at the most central region of the localizer, which abuts the foveal confluence. Therefore, the second modulation occurred throughout V1.

Finally, while Experiment 1 provided strong evidence for modulation of V1 at the end of each trial, the results were also consistent with the presence of a similar modulation at task onset, the time of stimulus presentation. On delayed response trials (right panel, Figure 2F), the magnitude of the first peak of activity in the peripheral region (red time courses) was very similar to that of the second peak. Furthermore, it showed a similar decline across visual areas V1, V2, and V3/VP. This trend was significant for all three participants (repeated measures

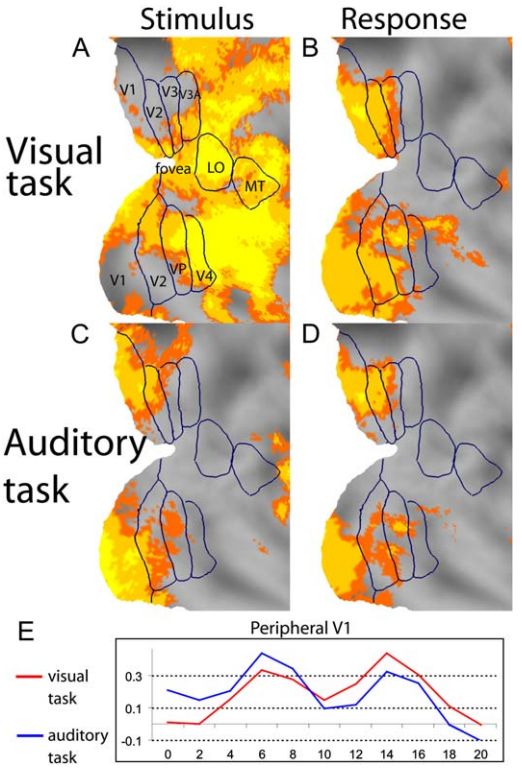

Figure 3. Activation of Early Visual Areas Associated with Stimulus Presentation and with Stimulus Response during Visual and Auditory Discrimination Tasks

(A) to (D) show averaged data from the three participants (P4, P5, P6) that participated in Experiment 2 (visual/auditory), mapped onto the PALS atlas using multi-fiducial surface averaging (Van Essen, 2005). Occipital cortex is shown, with the guideline atlas borders of visual areas outlined in blue. (A) and (C) show BOLD activation when a visual or auditory stimulus was presented. (B) and (D) show BOLD activation when the participant gave a manual response. In each task, participants discriminated between two suprathreshold stimuli. Neither the stimulus nor the response was cued: participants were instructed to count to themselves to delay response. All maps are thresholded with a mean $z > 3$. (E) shows the mean time courses in a region corresponding to the periphery of V1 (3°–6° visual angle, see Experimental Procedures).

ANOVA on the magnitude of the first peak of delayed response trials in the peripheral eccentricity, main effect of visual area: P1, n = 264; P2, n = 274; P3, n = 288; $p < 0.001$ for all tests). The next experiment provides stronger evidence for the presence of a modulation at the time of stimulus presentation, which cannot be easily accounted for by perceptual demands.

Activation of V1 during an Auditory Task

Experiment 2 eliminated the confounding effects of visual stimulation at the start of each trial by including an auditory task condition. The use of an auditory task also allowed a test of whether the second peak in activity occurs in V1 even when the task does not involve any visual perceptual or attentional demands. Three new participants (P4, P5, P6) performed visual and auditory discrimination tasks in alternating blocks (see Figure 1B and Experimental Procedures). Figure 3 shows activity in occipital cortex time-locked to stimulus presentation and response in the two tasks. At the time of response, the pattern of activity is similar for both auditory and visual

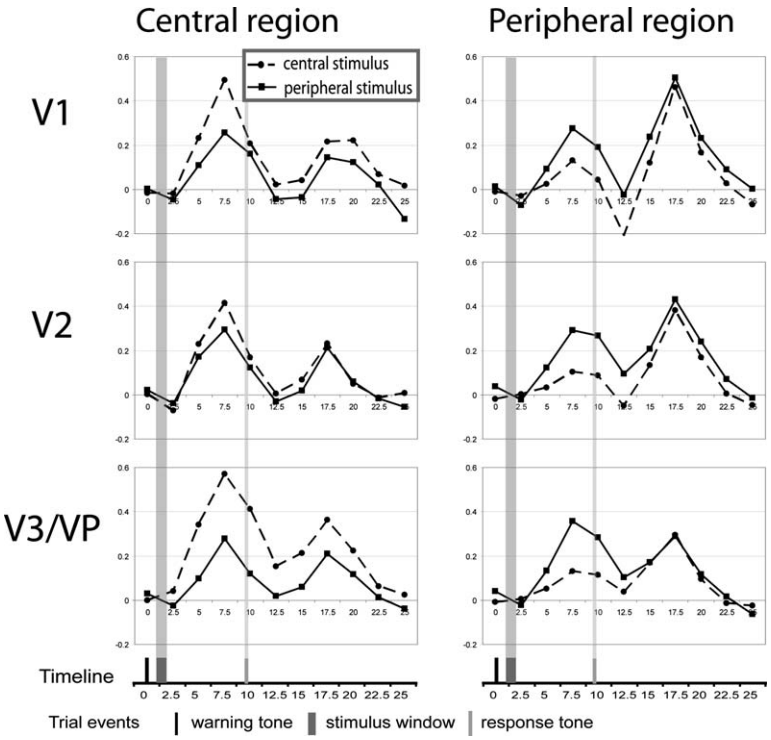

Figure 4. BOLD Activity in Early Visual Areas Is Modulated by Changes in Attended Location

Graphs show mean estimated time courses, averaged across participants, for trials in which no stimulus was present in Experiment 3 (central/peripheral go/no-go). Graphs on the left show activity from regions corresponding to the more central stimulus location. Graphs on the right show activity from regions corresponding to the more peripheral stimulus location. Dotted lines show activity for blocks with central stimuli. Solid lines show activity for blocks with peripheral stimuli.

tasks (Figure 3B and 3D), and is distributed more in the periphery than fovea, consistent with Experiment 1. In addition, however, Figure 3C shows a similar activation at the time of stimulus presentation in V1 during the auditory task, which is remarkable since it cannot be accounted for by visual stimulation or by visual attentional demands. The activation of peripheral V1 during the auditory stimulus presentation was highly significant for two of the three participants, while the third showed a trend in the same direction (P4, $z = 9.08$, $p < 0.001$; P5, $z = 0.36$, $p = 0.36$; P6, $z = 3.07$, $p < 0.001$). When data from the three participants were pooled, it was highly significant, as illustrated by the thresholded maps shown in Figure 3. Finally, the time courses in Figure 3E confirm that peripheral V1 showed very similar stimulus presentation and response-related signals irrespective of task modality. Experiment 2 shows that activations occur both at the time of stimulus presentation and at the time of response, are weighted toward peripheral V1, and occur even during performance of a nonvisual task. These findings suggest a quite general activation of visual cortex. It does not appear to relate to perceptual demands, nor to any specific aspect of the task, but is instead more generally related to task structure—it is time-locked to significant task events. While this characterization will be further tested in subsequent experiments, for convenience we will refer to it from here as the "nonperceptual" modulation of V1.

Spatial Attention Signals Are Modulated by Attended Location

Experiment 3 shows that the cortical distribution of the attention signal changes with the attended location. Experiment 3 also provided an initial test of the hypothesis that activation of V1 occurs independently of motor execution by including both response (go) and no-response (no-go) conditions (the effect of the go/no-go variable will be discussed in the next section, which describes several control experiments).

Three participants performed a variation of the delayed response condition of Experiment 1 (see Figure 1C and Experimental Procedures). Figure 4 shows time courses, averaged across the three participants and over go and no-go trials, for regions corresponding to the central and peripheral stimulus locations in V1, V2, and V3/VP. Only trials on which the stimulus was absent are shown. The magnitude of activity that was time-locked to the stimulus window followed the pattern predicted by passive retinotopy. In cortical regions corresponding to the central stimulus (Figure 4, left column), the first peak of activity was greater when participants attempted to detect the central stimulus (dotted lines) rather than the peripheral stimulus (solid lines). In cortical regions corresponding to the peripheral stimulus (right column, Figure 4), the first peak of activity was greater when participants attended to the peripheral stimulus as opposed to the central stimulus. We tested the reliability of the change in the attention-related signal with stimulus eccentricity using a repeated measures ANOVA on the data corresponding to the first peak of activation (7.5 s) on stimulus-absent trials (see the Statistical Methods subsection). The interaction of stimulus location (central versus peripheral) with retinotopic region (central versus peripheral), tested separately for each participant and for each visual area (V1, V2, and V3/VP), was highly significant ($p < 0.001$) in 8 of the 9 tests (P1, $n = 168$; P2, $n = 159$; P3, $n = 166$). The only exception was for V1 in participant P1 ($n = 168$, $p = 0.47$), where the trend was in the predicted direction. Conversely, there was no consistent effect of attended location on the magnitude of the second peak of activity, confirming that this signal is independent of the

distribution of spatial attention. (In peripheral V1, z stats for the contrast attend central minus attend peripheral for stimulus absent trials were: P1, z = −2.42, p = 0.016; P2, z = 0.82, p = 0.412; P3, z = 0.53, p = 0.596). In conclusion, varying the location of attention produces a reliable and retinotopically appropriate modulation of endogenous activity in early visual areas, but has no effect on the second peak of activity in V1 that occurs in delayed response trials.

Control Experiments for Cross-Modal and Motor Factors

While the endogenous modulation of early visual areas associated with spatial attention has been anticipated in the literature (Kastner et al., 1999; Ress et al., 2000), we do not know of any reports of nonperceptual activation in V1 associated with task structure. We conducted a number of control studies to check that this activation could not be accounted for by other perceptual or motor factors. Our first goal was to rule out an explanation related to sensory processing of auditory stimuli, which were used in Experiments 1 and 3 to mark both the time of visual stimulus presentation and of response. This possibility had been partly ruled out in Experiment 2, which demonstrated a second peak in activity even when the response was self-paced rather than cued by an auditory tone. However, it is important to carefully consider this hypothesis, since it is known that V1 receives back projections from auditory cortex, which are weighted toward the periphery (Falchier et al., 2002; Rockland and Ojima, 2003). To directly test whether auditory input has any influence on the second peak, Experiment 4 compared two conditions, one in which participants waited for an auditory tone before making their response, as in Experiment 1 (immediate/delayed), and a second condition in which participants self-paced their own delayed response by silently counting to a fixed number before responding, as in Experiment 2. The two conditions were made directly comparable by yoking the timing of the auditory tones in one block of trials to the time of the self-paced responses in the previous block (see Experimental Procedures; response times are given in Supplemental Data). A second goal of this experiment was to investigate the relationship between the second peak in activity and motor factors by measuring the effect of responding with the left hand, held on the left side of the body, versus responding with the right hand, held on the right side of the body (see Experimental Procedures).

The most important result was that the second peak in activity was present in both the self-paced and auditory cue conditions (Figure 5A). The self-paced condition (and yoked auditory cue condition) resulted in a less sharp second peak than that observed for auditory cue trials with a fixed timing (compare time courses in Figure 1F to the present time courses), because trials with fixed timing allow a more precise time-locked synchronization with task structure.

In order to compare the auditory cue and self-paced conditions, we took the maximum BOLD response in the interval from 12.5 to 22.5 s as the peak magnitude for each trial. The delayed activation in peripheral V1 actually showed a trend for greater activity when no auditory stimulus was present (i.e., during self-paced responses) (independent samples t tests: P1, t = 6.4, p < 0.001; P2, t = 0.9, p = 0.4; P3, t = 1.3, p = 0.2), showing that the second peak in activity cannot be attributed to auditory stimulation.

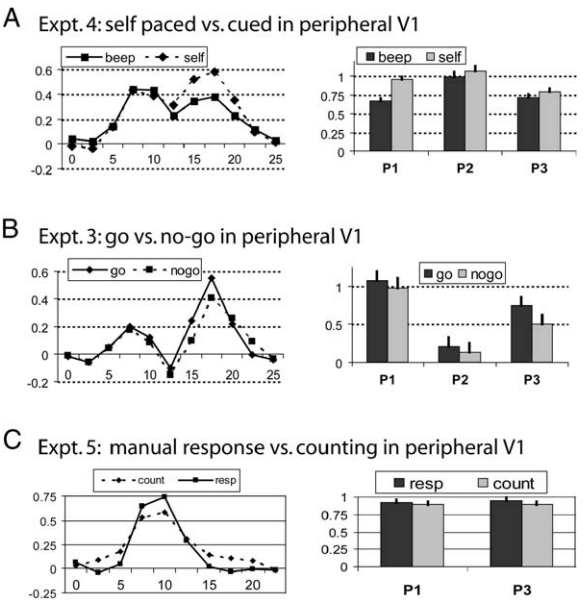

Figure 5. Nonperceptual Activation of Peripheral V1 Is Not Due to Auditory or Tactile Stimulation or to the Act of Making a Manual Response

(A) The left panel shows mean time courses, averaged across participants, for self-paced and auditory cued trials in Experiment 4 (cued/self-paced left-/right-handed). The right panel shows the mean peak magnitudes (taken from 12.5 to 22.5 s inclusive) of the delayed peak for each participant. Error bars = SEM.

(B) Left panel shows mean peripheral V1 time courses for go and no-go trials in Experiment 3 (central/peripheral go/no-go). The right panel shows the magnitude of the delayed peak for each participant. Error bars indicate standard error of the estimate.

(C) Left panel shows mean peripheral V1 time courses for counting and response trials in Experiment 5 (respond/count). The right panel shows the mean peak magnitudes (taken from between 7.5 and 17.5 s inclusive) for each participant. Error bars = SEM.

An alternative hypothesis is that activation of V1 may result from the act of making a manual response, either because of some intrinsic connection between perceptual and motor processes (e.g., see Astafiev et al., 2004) or because V1 is involved in processing somatosensory information (as has been shown in the blind e.g., see Sadato et al., 1998). However, in Experiment 4, we found that the delayed responses in right and left visual cortex did not vary as a function of the responding hand. The go/no-go manipulation of Experiment 3, in which half the trials (randomly interleaved) were signaled as "no-go" trials by a change in the auditory tone, provided a further test of this hypothesis.

Figure 5B shows that the time courses on go and no-go trials were very similar, contrary to the hypothesis that the second peak in activity was caused by motor execution. However, there was a trend for a greater response in go than no-go trials, suggesting a possible role for motor or premotor processes in generating the V1 activation. (Contrast of go minus no-go [see Statistical Methods subsection]: P1, z = 1.13, p = 0.26; P2, z = 0.17, p = 0.87; P3, z = 2.83, p = 0.005).

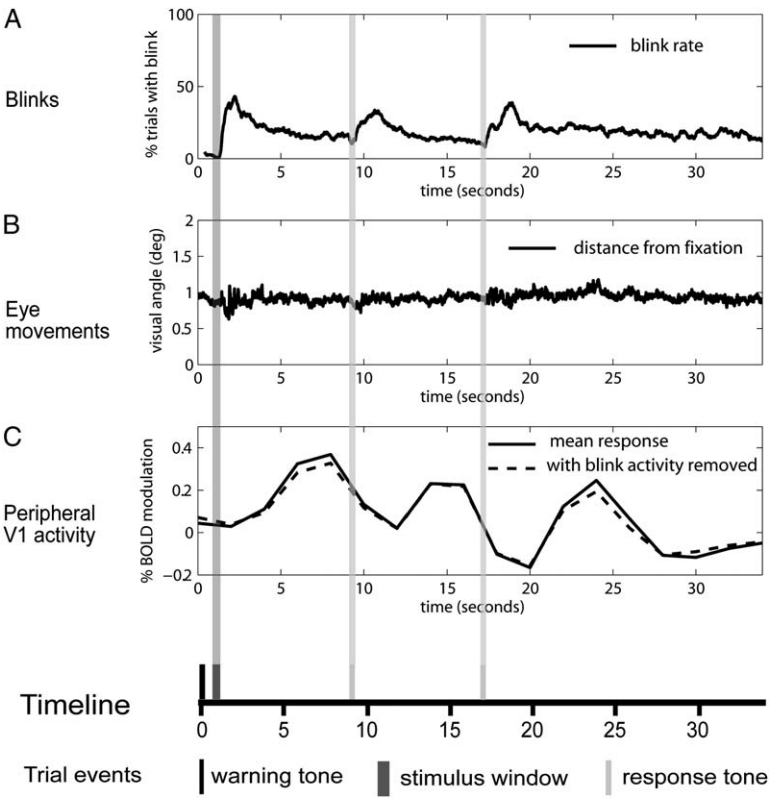

Figure 6. Blinks, Eye Movements, and BOLD Response during a Task Involving Two Separate Delayed Responses to a Single Stimulus in Experiment 6

(A) Mean percentage of trials on which participants blink, demonstrating a tendency to blink after each task event.

(B) Root mean square distance from fixation, indicating that participants did not break fixation in time with the task.

(C) BOLD response in peripheral V1, demonstrating activation associated with the stimulus window and with both the first and second responses. The dotted line shows that the nonperceptual modulation remains the same after BOLD activity attributable to blinking has been covaried out.

A further control experiment, Experiment 5 (respond/count), assessed activity in peripheral V1 in the complete absence of motor preparation and response. This experiment compared activity between a condition in which a manual response was made (identical to immediate response trials in Experiment 1) and a condition in which participants kept a covert count of the total number of stimuli presented, giving a verbal response after the end of each scan (16 trials). An immediate response task was used, instead of a delayed response task, since it was not feasible to ask participants to delay a covert action. Figure 5C shows that the time course of activity in the two conditions in peripheral V1 was similar, with the counting condition perhaps showing a smaller peak magnitude but a broader sustained response. This difference may simply reflect greater variation in task timing during the counting condition. A t test comparing the two conditions, using the maximum BOLD response in the interval from 7.5 to 17.5 s as the peak magnitude for each trial, revealed no difference between the conditions (independent samples t tests: P1, $t = 0.64$, $p = 0.5$; P3, $t = 1.0$, $p = 0.3$). This null result cannot rule out a role for motor factors in modulating activity in peripheral V1. However, it is notable that robust activation of peripheral V1 persists in a task that does not involve any overt action or limb movement. This result, consistent with the motor manipulations in Experiments 3 and 4, and with the finding of activation of V1 at the time of stimulus presentation in Experiments 1 and 2, indicates that any contribution of motor factors to the observed activation of V1 must occur at an abstract premotor level, such as motor planning.

Control for Eye Movements, Blinks, and Intermediate Task Events

The nonperceptual modulation of V1 has been found to occur whenever a significant task event has occurred, regardless of whether that event corresponds to stimulus presentation or response. However, the experiments reported so far have involved a maximum of two task events, capable of being distinguished given the temporal resolution of BOLD, which occurred at the start and end of each trial. One possibility, suggested by studies of BOLD activity at block transitions (Dosenbach et al., 2006; Fox et al., 2005; Konishi et al., 2001; Shulman et al., 2003), is that activation of medial occipital cortex is specifically associated with task onset and offset. Experiment 6 (dual response) served to test this hypothesis by using a design in which three temporally distinct task events occurred on each trial. Four new participants discriminated two features (orientation and frequency) of a sinusoidal grating and made separate responses to report on each feature (see Experimental Procedures). The delays between task events were sufficient to resolve BOLD activation time-locked to the stimulus window and to each response individually. In addition, we used an eye tracker to monitor the participants while in the fMRI scanner, to control for the potential confounding effects of eye movements and blinks (see Experimental Procedures).

Figure 6A shows the mean percentage of trials in which participants blinked (see Experimental Procedures). There was a tendency for blink rate to peak immediately after stimulus presentation and immediately after each response. To assess statistical reliability,

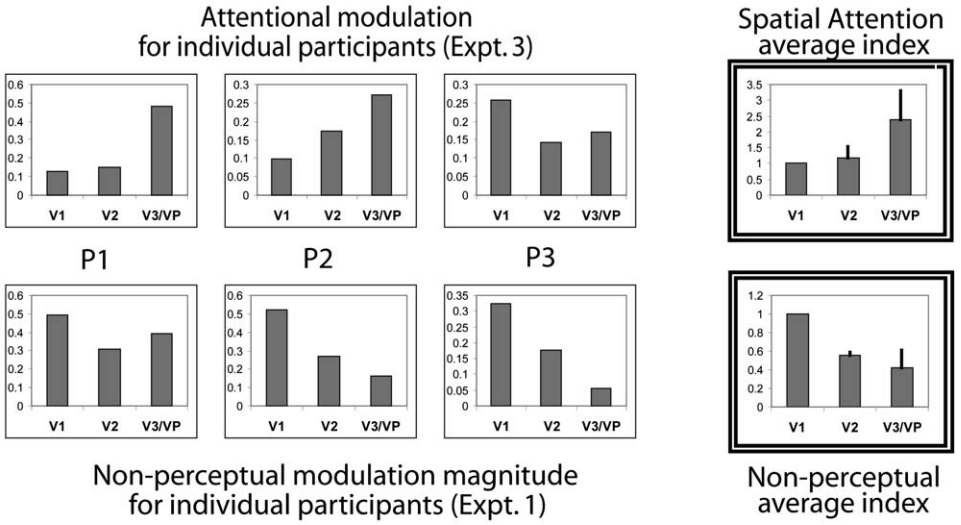

Figure 7. Distribution of Endogenous Modulations across Early Visual Areas

Magnitudes of attentional modulation (top row) and the nonperceptual modulation (bottom row) are shown for three participants. Data are derived from Experiments 1 and 3, as explained in the Results. The graphs on the far right show average magnitude of attentional modulation and nonperceptual activation in V2 and V3/VP, normalized to V1. Error bars = SEM.

the data was averaged in 2 s bins to render it comparable to the BOLD data, then entered into a repeated measures ANOVA with repeated factor of time and no other factors (see Experimental Procedures). There was a highly significant effect of time ($p < 0.001$) for all participants (P7, n = 144; P8, n = 132; P9, n = 120; P10, n = 144). Thus, blink rate did covary in time with task events, and further analyses, described below, were required to rule it out as a potential confounding factor.

Breaks from fixation were very rare. Figure 6B shows the mean distance from fixation, averaged across participants. As can be seen, there was little tendency for fixation behavior to covary in time with task events. A repeated measures ANOVA similar to that performed on blink data was used to asses the statistical significance of variation in fixation behavior with time (see Experimental Procedures). There was no effect for participants P7, P9, and P10. Participant P8 did deviate from fixation significantly more during the intertrial interval; however, this deviation did not correspond in time with any observed BOLD modulation (see the Supplemental Data: P7, n = 144, $p = 0.7$; P8, n = 132, $p < 0.001$; P9, n = 120, $p = 0.3$; P10, n = 144, $p = 0.5$). Thus, fixation breaks could be ruled out as a potential confounding factor.

In Figure 6C, the solid black line shows the mean BOLD response in peripheral V1, averaged across participants. Three peaks in activity can be clearly seen, corresponding to stimulus presentation, to the first (orientation) response, and to the second (frequency) response. These results indicate that peripheral V1 responses occur to intermediate trial events and are not confined to events that occur at trial onset and offset. Given the observed tendency for the blink rate to increase immediately after these events (Figure 6A), we conducted a second analysis which allowed us to assess the separate contributions of blinks and trial events to BOLD activity (see Experimental Procedures). Blinks did reliably modulate peripheral V1 (P7, $z = 9.0$, $p < 0.001$; P8, $z = 2.0$, $p < 0.05$; P9, $z = 3.3$, $p < 0.001$; P10, $z = 8.2$, $p < 0.001$), although the average magnitude of modulation due to blinks (0.12) was less than half that associated with the two responses (0.29). The dashed line in Figure 6C shows the estimated trial time course when BOLD activity associated with blinks was removed. Notably, this time course is very similar to the mean time course. The two delayed peaks of activity in peripheral V1, time-locked to the two responses, were highly significant even when BOLD activity due to blinks was modeled out ($p < 0.001$ for all participants: First response P7, $z = 12.2$; P8, $z = 8.5$; P9, $z = 5$; P10, $z = 3.3$; Second response P7, $z = 10.1$; P8, $z = 5.0$; P9, $z = 5.1$; P10, $z = 5.2$). This indicates that blinks do not account for the nonperceptual modulation of peripheral V1 observed in these experiments. We report further analyses that support this conclusion in the Supplemental Data. Experiment 6 (dual response) establishes that V1 is modulated by an intermediate trial event, and this modulation is thus not specifically tied to trial onset and offset. It also served to rule out eye movements and blinks as causes of the nonperceptual modulation of V1.

Cortical Distributions of Spatial Attention and Nonperceptual Modulations

While the modulation due to spatial attention was observed with equal or greater strength in later visual areas than in V1 (Figure 3), the nonperceptual modulation was clearly greater in V1 (Figure 1 and Figure 2). The apparent difference in cortical distribution of the two endogenous modulations suggests that they reflect different types of connections. Figure 7 quantifies the distribution of these modulations over visual areas, based on a measure of each modulation from each of the three participants whose cortex was retinotopically mapped. The graphs on the top row show an index of the spatial attention modulation across early visual areas, derived from Experiment 3 (central/peripheral go/no-go) by summing the difference in activity in the central region (central stimulus minus peripheral stimulus) with the difference

in activity in the peripheral region (peripheral stimulus minus central stimulus). This index reflected entirely endogenous signals since only trials on which no stimulus was presented were included. The graphs on the bottom row show the magnitude of the second peak of activity (17.5 s) on delayed response trials in Experiment 1. The far right column of Figure 7 shows two group-averaged summary graphs in which measures in V2 and V3/VP have been normalized relative to V1. The top graph shows a trend for larger spatial attention signals in higher visual areas, while the bottom graph shows the opposite trend of smaller nonperceptual modulations in higher visual areas. The reliability of this difference in the distribution of each modulation across cortical areas was confirmed by entering the raw (unnormalized) magnitudes of each measure for each participant into an analysis of variance. A significant interaction of Area and Measure was observed [number of subjects (n) = 3, $p = 0.022$], confirming the different cortical distribution of the two signals. Post hoc repeated measures ANOVAs on subsets of the data revealed that the trend for greater attentional modulation in higher visual areas was not significant ($n = 3$, $p = 0.305$), whereas the trend for the nonperceptual modulation to be greater in V1 than V2 and V3/VP was significant ($n = 3$, $p = 0.034$).

Discussion

The current experiments have shown that two distinct endogenous activations coexist within V1. While prior studies have reported attentional modulations of V1, we know of only one prior report of nonperceptual modulation of V1 (Shuler and Bear, 2006). This activity cannot be explained by spatial attention, sensory processing in any modality, response-related processes, eye movements, or blinks. It reflects signals in primary visual cortex that appear to play no direct role in visual perception.

Spatial Attention and Nonperceptual Modulations Have Distinct Cortical Distributions

Two results established the presence of an endogenous attention signal in early visual areas V1, V2, and V3/VP that was distinct from the nonperceptual modulation: (1) a peak in BOLD activity occurred in a retinotopically appropriate cortical region at a time corresponding to the peak visual perceptual demands of the task, and (2) the cortical distribution of BOLD activity varied with the attended location. While prior studies using a single, fixed stimulus location have shown that a purely endogenous modulation occurred at the appropriate retinotopic location (Kastner et al., 1999; Ress et al., 2000), the present study shows that the retinotopic distribution of this endogenous modulation changes appropriately with the location of attention.

The two endogenous modulations of early visual areas revealed in these experiments had distinct anatomical profiles. The attentional modulation was seen throughout the early visual areas V1, V2, and V3/VP (Figure 7) and was of approximately equal magnitude in regions corresponding to the central and peripheral visual fields (Figure 4). In contrast, the nonperceptual activations were greater in V1 than in later areas V2 and V3/VP (Figure 7) and were greater in regions that corresponded to more peripheral parts of the visual field (Figure 1).

These differences may be related to two different patterns of connectivity that have been observed for V1. The majority of cortical projections to V1 comes from higher visual areas and is approximately evenly distributed across regions representing different eccentricities. This pattern would fit the modulation due to spatial attention observed here. V1 also receives cortical projections from nonvisual areas, including auditory cortex. These connections have not been seen for higher visual areas and are more numerous in regions corresponding to more peripheral parts of the visual field (Clavagnier et al., 2004; Falchier et al., 2002; Rockland and Ojima, 2003). This pattern would fit the nonperceptual modulation observed here.

Possible Functional Role

It is notable that the experiments reported here all involved brief periods of activity, associated with perception and response, separated by longer periods of rest, during which participants were only required to maintain fixation. A natural interpretation of the nonperceptual modulation of V1 may therefore be that it reflects general arousal and/or may be specifically associated with the psychological process of attentional alerting (Posner and Petersen, 1990). However, a number of factors diminish the likelihood of this hypothesis. First, the modulation we observe is relatively specific in one sense: it is greater in V1 than in other visual regions, and inspection of the whole cortical surface reveals no extensive areas of activity in parietal, temporal, or frontal cortices that cannot be explained by other factors (e.g., motor response). Alerting and generalized arousal would be expected to produce far more widespread cortical activation. Second, there was no clear relationship between the size of the modulation seen in peripheral V1 and task demands (e.g., easy versus difficult task, overt versus covert response, go versus no-go, auditory cued versus self-paced) or even task modality (e.g., visual versus auditory detection). Third, prior work, discussed below, suggests that the same activation occurs when an active and demanding task state comes to end—a transition which should be associated with a decrease in alertness and/or arousal.

An alternative hypothesis is that the nonperceptual activation marks transition points in sequences of behavior. Prefrontal neurons (Fujii and Graybiel, 2003) and field potentials (Fujii and Graybiel, 2005) show activity at the start and end of sequences of saccades. Fujii and Graybiel interpret these signals as marking task boundaries. Some previous neuroimaging studies have reported analogous activity in medial occipital cortex. A study by Shulman et al. (2003) reported evidence of medial occipital activation when the task was completed for a given trial. Studies of BOLD response at block transitions (Dosenbach et al., 2006; Fox et al., 2005; Konishi et al., 2001), which occur between an active block of trials and rest (passive fixation), also demonstrate medial occipital activity. Although none of these studies controlled for perceptual confounds or measured retinotopic maps in individual participants, it is plausible that these findings reflect the same nonperceptual activation of peripheral V1 seen here. Experiment 6 (dual response) demonstrated that the nonperceptual V1 activation occurred at the time of an intermediate task event in

addition to task onset and offset. A reasonable conclusion to draw from the studies presented here and in the literature would be that nonperceptual activation of V1 occurs at task boundaries as well as at other task events.

What is the origin of this nonperceptual modulation in V1? It is surprising to observe modulation of primary visual cortex that is so nonspecific in nature. Even though V1 contains the most tightly defined topography of any cortical region, the modulation we observe is diffusely distributed across the cortical surface, and it is unaffected by the location of the stimulus or attention. And even though most of what is known about the functional role of V1 links it tightly (under normal conditions) to the processing of visual information, the modulation we observe is apparently completely unaffected by perceptual demands. The nonspecific nature of this modulation suggests that it reflects a general gating signal of some sort. For instance, a hypothesis suggested by V1 activation at task boundaries derives from neural models that feature a nonspecific updating signal that temporarily increases the plasticity of the system, facilitating the transition from one stable state to another (Frank et al., 2001; Grossberg, 1999; Miller and Cohen, 2001).

A related hypothesis is that the nonperceptual signal in V1 is a neural correlate of a transition state between different perceptual-motor schematas (Neisser, 1967). For instance, in Experiment 6 different transient signals in V1 marked the following: a change from rest to task state, which may involve the setting up of two distinct perceptual motor sequences; the execution of a first response, marking the completion of the first perceptual-motor sequence; and, finally, the execution of a second response, marking the completion of the second sequence and transition to rest state. These transitions may involve top-down neuromodulation via subcortical structures. Area V1 has afferents from both cholinergic neurons in the basal nucleus and from noradrenergic neurons in the locus ceruleus (Doty, 1983). Cholinergic modulation has been previously associated with the gating of thalamic inputs to early sensory cortices (for a review see Sarter et al., 2005). Noradrenergic modulation has been previously associated with changes in cortical plasticity (Aston-Jones et al., 2000).

Conclusion

Here we demonstrate modulation of V1 in the absence of any actual, anticipated, or imagined change in the visual scene. These findings show that V1 is endogenously modulated both by signals that are sensitive to perceptual demands and by signals that are sensitive to the temporal structure of a task.

Experimental Procedures

Participants

Ten healthy participants (four female, one left-handed, ages 19–29) with normal or corrected to normal vision participated. Informed consent was obtained according to procedures approved by the local human studies committee.

Apparatus

Stimuli were generated using an Apple G4 Macintosh computer running Matlab (Mathworks) and associated routines from the psychophysics toolbox (Brainard, 1997; Pelli, 1997). The visual image was projected onto a screen at the head of the bore by a Sharp LCD projector. Participants viewed the screen through a mirror attached to the head coil. Manual responses were obtained using an MRI-compatible fiber-optic keypad. Sound was delivered using MR-compatible headphones (Resonance Technology). An eye tracker (ISCAN, Burlington, MA) was used to monitor eye movements in Experiment 6.

Experimental Design

See Table 1 for brief descriptions of each experiment. A more detailed description follows.

Experiment 1: Immediate/Delayed

This replicated the study of Ress et al. (2000), except that the time of response was varied. In addition, the stimulus was presented near the fovea (0.75°–1.5°) rather than in the periphery (3°–6° in Ress et al., 2000). Participants detected the presence/absence of a near-threshold, contrast-reversing (2 Hz) annular Gaussian checkerboard (2 cycles per degree, radius of annulus 0.75°–1.5° visual angle from fixation, duration 750 ms), present on 50% of trials, random but counterbalanced within each scan. Distinct auditory tones occurred 1 s prior to stimulus onset, at stimulus onset, at stimulus offset, and to signal the time of response. In separate blocks, participants were cued to respond either 2.1 or 9.6 s after the initial warning tone. Participants held the keypad with both hands (right index finger for present, left index finger for absent). The trial onset interval (the time between the beginning of one trial and beginning of the next) varied from 27.5 to 32.5 s (mean = 29.4 s). Thus, each trial had a separate BOLD response and could be treated as an independent observation (see Statistical Analysis subsection below).

Table 1. Summary of Experiments

Experiment (Nickname)	Participants	Sessions	Total Scans	Vol./Scan	Trials/Scan	Brief Description
1 (immediate/delayed)	P1, P2, P3	3	44, 46, 48	145	12	threshold detection with immediate and delayed response
2 (visual/auditory)	P4, P5, P6	1	14, 16, 16	185[a]	12	suprathreshold visual and auditory discrimination with delayed response
3 (central/peripheral go/no-go)	P1, P2, P3	1	17, 16, 16	145	20	as Experiment 1 but stimulus central or peripheral and 50/50 go versus no-go delayed response
4 (cued/self-paced left-/right-handed)	P1, P2, P3	1	14, 14, 12	145	12	as Experiment 1 but with self-paced versus auditory cued delayed response using left versus right hand
5 (respond/count)	P1, P3	1	20, 18	143	16	as Experiment 1 but immediate manual response versus covert counting
6 (dual response)	P7, P8, P9, P10	1	12, 11, 10, 12	229[a]	12	discrimination of two features with separate delayed responses

Sessions refers to separate visits to the scanning facility, each lasting 1.5–3 hr. Scans refer to individual runs of data acquisition, lasting 6–8 min. Detailed descriptions can be found in the Experimental Procedures section.

[a] A different acquisition sequence with a shorter TR was used for Experiments 2 and 6; see the Experimental Design subsection.

Participants fixated on a central cross throughout. Threshold was determined in the scanner at the start of each scanning session using a forced choice two-interval detection task and the Quest algorithm (Watson and Pelli, 1983). Prior to scanning, participants practiced the experimental task in at least one behavioral session until performance was stable.

Experiment 2: Visual/Auditory

In separate blocks, participants performed either an auditory or a visual discrimination task. In the auditory task the stimulus was a sequence of 10 contiguous tones that either ascended or descended in frequency. In the visual task participants discriminated between either a horizontal or a vertical line running through the central fixation point (4 Hz contrast-reversing black and white checkerboards). All stimuli lasted 0.75 s. Participants self-paced a delayed response by silently counting from one to seven and responded with their right or left index finger as in Experiment 1. No prestimulus warning cue was presented. In both tasks participants fixated on a central cross throughout. The trial onset interval varied from 28 to 32 s (mean = 29.5 s).

Experiment 3: Central/Peripheral Go/No-Go

This was identical to delayed response blocks in Experiment 1 except for the following two crossed factors: (1) in different blocks the eccentricity of the stimulus annulus alternated between 0.75°–1.5° and between 3°– 6° (2 cycles per degree, duration 750 ms). At the start of the scanning session, threshold was determined as in Experiment 1, separately for each stimulus. (2) On 50% of trials (pseudo-random) participants heard a two-tone beep instead of the usual monotone beep. On these no-go trials, participants withheld a response. The trial onset interval varied from 15 to 20 s (mean = 16.9 s).

Experiment 4: Cued/Self-Paced Left-/Right-Handed

This was identical to delayed response blocks in Experiment 1 except for the following two crossed factors: (1) On odd blocks responses were self-paced rather than cued by a beep and participants counted covertly in order to delay their response. On even blocks the timings of response beeps were yoked to the response times in the previous self-paced block so that the mean and variance of response times were matched across conditions. (2) Participants held the keypad in either the right or left hand, resting on the side of the body, using the index and middle fingers to indicate stimulus present and absent. Participants swapped hands every two blocks. The trial onset interval (the time between the beginning of one trial and the beginning of the next) varied from 27.5 to 32.5 s (mean = 29.4 s).

Experiment 5: Respond/Count

This was identical to immediate response trials in Experiment 1, with the following modifications. The stimulus contrast was raised from threshold until the point where participants reported being able to confidently identify the stimulus (i.e., near 100% correct, see Supplemental Data). The number of present stimuli was varied (random but counterbalanced within participant) from scan to scan between 6 and 10 (/16 trials). On alternating blocks participants either responded immediately after each stimulus window, as before, or kept a covert count of the number of present stimuli, which was reported at the end of the scan. The trial onset interval varied from 20 to 25 s (mean = 21.9 s).

Experiment 6: Dual Response

This was similar to delayed response blocks in Experiment 1 except for these changes: (1) the stimulus displayed inside the annulus was a sinusoidal grating, oriented 30° from the vertical either clockwise or counterclockwise, with a frequency of either 1 or 3 cycles per degree of visual angle. The stimulus appeared for just 250 ms, and there was no contrast reversal. (2) The first response tone occurred at 9 s after the initial warning tone and indicated the time to make an orientation response (right index finger for clockwise, left index finger for counterclockwise). The second response tone occurred at 17 s and indicated the time to make a frequency response (right index finger for low frequency, left index finger for high frequency). The trial onset interval (the time between the beginning of one trial and the beginning of the next) varied from 36 to 40 s (mean = 37.5 s), sufficient for the BOLD response to return to baseline.

Image Acquisition and Processing

An asymmetric spin-echo echoplanar imaging sequence was used to measure BOLD contrast on a Siemens Allegra 3T scanner. In Experiments 2 and 6, 31 contiguous 4 mm slices were acquired (4 × 4 mm in-plane resolution, TE = 25, flip angle = 90°, slice TR of 0.0645 s, volume TR = 2 s). In all other experiments, 39 contiguous 3.25 mm slices were acquired (3.25 × 3.25 mm in-plane resolution, TE = 25, flip angle = 90°, slice TR of 0.0641 s, volume TR = 2.5 s). Other details are provided in Table 1. For participants P1, P2, and P3, four sagittal magnetization-prepared rapid acquisition gradient echo (MPRAGE) images (TR = 97 ms; TE, 4 ms; flip angle, 12°; inversion time, 300 ms; voxel size, 1 × 1 × 1 mm) were averaged to produce a high-resolution anatomical image. Surefit and Caret (Van Essen et al., 2001) (http://brainmap.wustl.edu/caret) were used for surface generation and flattening, visual inspection, and drawing and re-embedding of retinotopic regions in these participants. One anatomical MPRAGE was collected for the remaining participants. Functional data were realigned to correct for head movement, coregistered with anatomical data, and transformed to atlas space with a uniform voxel size of 3 mm.

Retinotopy and Definition of Regions

We collected passive retinotopy data for participants P1, P2, and P3 by alternating full field vertical and horizontal meridians (4 Hz contrast-reversing black and white checkerboards, 12.5 s alternating blocks, extending ~13° visual angle from fixation horizontally and ~11.5° vertically, as limited by the scanner bore) and also presenting contiguous annuli at four different eccentricities (4 Hz contrast-reversing black and white checkerboards, 12.5 s stimulus blocks alternating with 12.5 s fixation, random stimulus order, radii of annuli in degrees visual angle: 0.2°–0.75°, 0.75°–1.5°, 1.5°–3°, 3°–6°). Regions V1, V2, V3, and VP were drawn by reference to the established correspondences between their borders and the horizontal and vertical meridians. Regions corresponding to the early visual areas drawn on the cortical surface were then reimbedded into the cortical volume assuming a cortical width of 3 mm. Regions corresponding to separate eccentricities were established objectively within volume space by selecting voxels which showed a significantly greater response to one eccentricity as compared with the other three eccentricities ($z > 3$). In Experiments 2 and 6 (involving participants P4–P10, for whom we had no retinotopy), a region corresponding to peripheral V1 was created from a volume average of participants P1, P2, P3, and three other participants who had undergone identical retinotopic mapping procedures. All regions were bilateral unless otherwise indicated.

Statistical Analysis of BOLD Data

Experiment 1: Immediate/Delayed

For each participant, an 11 frame time course was estimated for each condition using a voxelwise general linear model (GLM) that included terms on each scanning run for an intercept, linear trend, and temporal high-pass filter with a cutoff frequency of 0.009 Hz. The statistical maps shown in Figure 2 were generated by cross-correlating the estimated time course with assumed impulse response functions with appropriate onset times. The voxelwise z statistic for participant P1 was then projected onto the subject's own cortical surface. The time courses shown in Figure 2 were estimated separately for each participant and then averaged across participants. Statistical comparisons of responses in early visual areas were obtained as follows: the general linear model was used to compute 11 frame residual time courses for each region and for each trial, with the baseline, linear trend, and low-frequency components modeled out. Each trial was then entered as an independent observation into a repeated measures ANOVA. The repeated measures were time (frame number), area (V1, V2, V3/VP) and region (central, peripheral). The nonrepeated factors were present/absent and immediate/delayed response. The approach of treating each trial as an independent observation was warranted because the intertrial interval was long enough to allow BOLD response to fall to baseline before the beginning of the next trial. The n reported in the results corresponds to the number of trials.

Experiment 2: Visual/Auditory

The time courses shown in Figure 3 were estimated separately for each participant using a voxelwise GLM as above, except with 14 frames per trial, and averaged across participants. The statistical maps shown in Figure 3 were generated using a voxelwise GLM and cross-correlating assumed impulse response functions, as above, except that 7 frame time courses were estimated separately

for stimulus and response. A mean z stat for the three participants was created by summing the volume z stats for each individual and dividing by root n. This was projected onto the PALS atlas using multi-fiducial mapping in caret (Van Essen, 2005). The z statistics for individual participants in peripheral V1 were computed by cross-correlating assumed response functions with estimates from a regional GLM, which was otherwise identical to that used to produce the voxelwise maps.

Experiment 3: Central/Peripheral Go/No-Go

The 11 frame time courses shown in Figure 4 were estimated using a voxelwise general linear model and averaged across participants, as for Experiment 1. Statistical comparisons of the first peak in response in early visual areas were obtained as follows: the general linear model was used to compute 6 frame (0–12.5 s) residual time courses for each region and for each trial, with the baseline, linear trend, low-frequency components, and mean response due to task offset in the previous trial (frames 7–11, 15–25 s) modeled out. The peak (7.5 s) response for each trial on which the stimulus was absent was then entered as an independent observation into a repeated measures ANOVA, with area (V1, V2, V3/VP) and region (central, peripheral) as repeated factors and stimulus location (central, peripheral) as a nonrepeated factor. The z statistics and magnitudes associated with task offset were computed by cross-correlating assumed response functions with estimates from a regional GLM otherwise identical to that used to produce the mean time courses.

Experiments 4 and 5: Cued/Self-Paced Left-/Right-Handed and Respond/Count

The time courses shown in Figure 5 were estimated separately for each participant using a voxelwise GLM, then averaged across participants. The same GLM was used to derive residual time courses for every trial in peripheral V1, with the baseline, linear trend, and low-frequency components modeled out. This data was analyzed as described in the Results, with every trial treated as an independent observation.

Experiment 6: Dual Response

The time courses shown in Figure 6C were estimated separately for each participant using voxelwise GLMs and averaged across participants. The first model (solid line) estimated an 18 frame time course associated with each trial. The second model (dashed line) simultaneously estimated both an 18 frame time course associated with each trial and a 7 frame time course associated with each blink. Both models included terms for the baseline, linear trend, and low-frequency components. The z statistics for individual participants in peripheral V1 were computed by cross-correlating assumed response functions with estimates from a regional GLM, which was otherwise identical to the second model.

Eye Tracker Methods and Statistical Analysis

A continuous trace of horizontal eye position, vertical eye position, and pupil areas was recorded at 120 Hz and analyzed using Matlab. Blinks were automatically detected by determining when pupil area fell below a threshold (determined by inspection for each participant). The time of onset of every blink that occurred in the scanner run was recorded for use in analyzing BOLD data as described above. The blink rate shown in Figure 6A was created as follows: for the first 34 s of each trial, we created a continuous trace that was set to 1 during blinks (specifically for a period starting 100 ms prior to and ending 200 ms after the pupil diameter fell below a set threshold) and 0 otherwise. These traces were then averaged across trials to determine the proportion of trials on which each participant was engaged in a blink for each time point. This was then averaged across participants to yield Figure 6A. The mean distance from fixation shown in Figure 6B was created as follows: we took the first 34 s of the horizontal and vertical eye position traces for each trial, after removing parts of the trace influenced by blinks or by loss in the corneal reflection. The remaining data was smoothed and any linear trend was removed. Distance from fixation was determined by taking the root mean square difference of the processed horizontal and vertical traces from their median value for the trial. This was averaged across trials to produce an average for each participant, and these were then averaged to yield Figure 6B. Blink and distance data were analyzed independently for each participant as follows: for each trial and for each of 18 2 s bins, the mean value of the blink (or distance) trace was computed. The 18 time points for each trial were then entered into a repeated measures ANOVA, with time as a repeated factor and with each trial treated as an independent observation.

Supplemental Data

The Supplemental Data for this article can be found online at http://www.neuron.org/cgi/content/full/51/1/135/DC1/.

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