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Neural Correlates of Saccadic Suppression in Humans

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Summary

When you look into a mirror and move your eyes left to right, you will see that you cannot observe your own eye movements. This demonstrates the phenomenon of saccadic suppression: during saccadic eye movements, visual sensitivity is much reduced. Given that humans make more than 100,000 eye movements each day, it is clear why suppression is needed: without it, the motion on the retina would prevent us from seeing anything at all. Psychophysical data show that suppression is stimulus selective: it is strongest for the kind of stimuli that preferentially activate magnocellular thalamic neurons. This has led to the hypothesis that saccadic suppression selectively targets the magnocellular stream. We used fMRI to find brain areas with a stimulus-selective suppression of the BOLD signal that matches the psychophysical data. We found such a neural correlate of saccadic suppression in the dorsal stream (hMT+, V7) and in ventral area V4. These areas receive magnocellular input; hence our findings are consistent with the magnocellular hypothesis. The range of effects in our data and in single cell data, however, argues against a single thalamic mechanism that suppresses all cortical input. Instead, we speculate that saccadic suppression relies on multiple mechanisms operating in different cortical areas.

Results

Many psychophysical studies have investigated saccadic suppression and have generally concluded that suppression of visibility starts approximately 75 ms before a saccade and returns back to normal 100 ms after saccade onset (for review, see [1]). In laboratory setups, visibility is not reduced to zero [2–5], but it has been reported as tenfold poorer during saccades [6, 7]. Suppression is stimulus selective; several groups have shown that those visual stimuli typically processed by the magnocellular, dorsal visual stream are suppressed the most [6–10]. Given the role of the dorsal stream in processing motion information, this fits well with the purported role of saccadic suppression to eliminate retinal image motion due to saccadic eye movements.

Electrophysiological studies have shown that saccades affect single cell visual responses in the lateral geniculate nucleus (LGN) [11, 12], the middle temporal (MT), middle superior temporal (MST) [13], and ventral intraparietal area (VIP) (Bremmer et al., 2002, Soc. Neurosci., abstract). These single-unit responses are at times either enhanced or suppressed when compared to fixation. In humans, positron emission tomography studies have shown that activity in human visual areas decreases when subjects make saccades in total darkness [14–16]. This confirms that there is extraretinal (i.e., nonvisual) suppression of metabolic activity in the visual cortex, but this approach does not allow one to investigate the stimulus-specific, perceptual nature of the suppression.

We used event-related fMRI in combination with high temporal resolution eye-position monitoring in the scanner to determine which brain areas are involved in saccadic suppression. Our experimental design relied on the finding of Burr et al. [6] that saccadic suppression selectively reduces the visibility of stimuli with low spatial frequencies that are defined by luminance contrast, but not those defined by isoluminant color contrast. We translated this finding to a testable hypothesis about BOLD signal changes: in an area that is involved in the psychophysical phenomenon of saccadic suppression, we expect to find a perisaccadic reduction in BOLD signal for luminant gratings, but not for isoluminant gratings. In the main experiment we therefore compared the BOLD signals evoked in four stimulus conditions: a luminant or isoluminant grating presented either long before a saccade or around saccade onset. These four conditions will be referred to as pre-lum, pre-iso, peri-lum and peri-iso, respectively (see Figure 1 and Experimental Procedures for details).

Regions of Interest

To look for suppression we first had to find areas that were activated by our stimuli. We selected as regions of interest (ROI) for subsequent analysis the areas in which both the luminant and isoluminant stimuli in the pre-epochs led to significant activation. Although the isoluminant stimulus generally led to somewhat smaller activation, the difference with the luminant gratings was not statistically significant in any of the areas. The threshold set for inclusion was deliberately low ($p < 0.01$, uncorrected, cluster size >50 voxels) to avoid missing potentially interesting areas. Based on their Talairach coordinates, we tentatively identified these areas with V1/V2, V3, V4, V7 [17], hMT+, and an activation in the intraparietal sulcus (IP). The corresponding Talairach coordinates of the peak activation were V1/V2: ± 11, -67.5; V3, -41,-80.10; V4: ± 23, -62, -12; V7: ± 16, -77.32; hMT+: ± 48, -64.6; and IP: -40, -49.34. The bilateral activations were treated as one ROI. We defined a stimulus-specific BOLD reduction index as one minus

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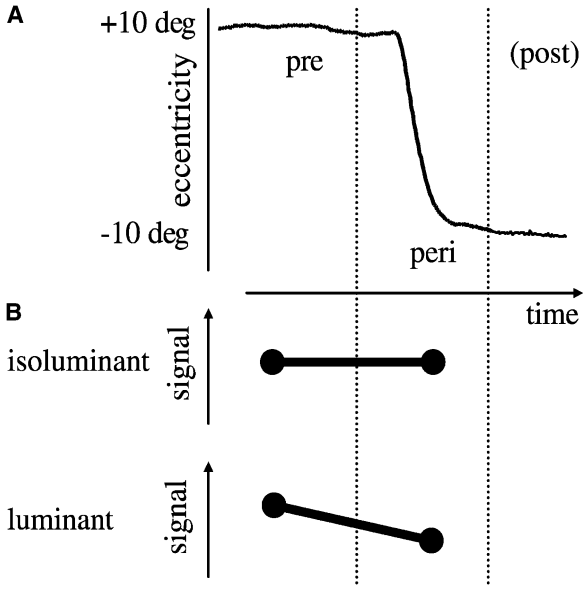

Figure 1. Experimental Paradigm

(A) A leftward saccade. The graph shows the eye position as sampled in the scanner long before (pre), during (peri), and after the saccade.

(B) The hypothesized BOLD signal in areas involved in saccadic suppression. For the red/green isoluminant grating, we expect no suppression and hence the same level of BOLD signal in the pre and peri epochs. For the yellow/black luminant stimulus, we expect that the reduced visibility is reflected in a decrease in BOLD signal during the peri epoch.

the ratio of the perisaccadic BOLD signal and the presaccadic BOLD signal. A value of 0% indicates that the saccade had no effect on the BOLD response, and 100% indicates that the perisaccadic BOLD signal was reduced to zero.

Controlling for Confounds

In our paradigm, the difference between pre- and peri conditions was not just the absence and presence of the hypothesized saccadic suppression. Clearly, the perisaccadic period differed additionally in terms of neural activation related to the eye movement itself, small but nonzero retinal motion, less certainty about the precise retinal location of the stimuli, and possibly even a different mindset of the subject. In principle, such confounds could have led to an artifactual reduction in BOLD signal in the perisaccadic period that one would—erroneously—interpret as saccadic suppression of a visual stimulus. However, there should be no saccadic suppression for the isoluminant stimuli, hence an upper bound to the combined influence of the confounds could be calculated. Specifically, the combined effect of all confounds could at most be the size of the BOLD reduction found for isoluminant stimuli. Hence, to quantify the saccadic suppression that cannot be due to the experimental confounds, we subtracted the BOLD reduction measured for isoluminant stimuli from the reduction measured for luminant stimuli. Statistically, we quantified saccadic suppression in the ROIs by determining the main effects of epoch (pre and peri) for the two stimulus types as well as their interaction.

Saccadic Suppression

In area hMT+ we found a significant perisaccadic BOLD reduction for the luminance stimuli (34%; $p < 0.05$) but no significant reduction for the isoluminant stimuli (5%; $p = 0.4$). The interaction between the two main effects was significant ($p < 0.05$). Estimating the upper bound of the confounds with the isoreduction, we can attribute at least 29% of the perisaccadic change in BOLD signal to a stimulus-selective process of saccadic suppression. In area V4, we found significant ($p < 0.05$) reduction for luminance stimuli (50%) but again no significant reduction for isoluminant stimuli (4%; $p = 0.9$). Hence there was at least 46% stimulus-selective saccadic suppression. The variability in the data, however, was larger in V4; the statistical interaction did not reach significance ($p = 0.1$). A similar pattern of activation was found in V7: significant reduction for luminance (46%; $p < 0.05$), no significant reduction for isoluminant stimuli (28%; $p = 0.2$), and no significant interaction ($p = 0.4$). In V3, the trend was similar, but neither the luminant (29%; $p = 0.3$) nor the isoluminant stimuli (17%; $p = 0.7$) showed a statistically significant perisaccadic reduction in BOLD signal. In areas V1/V2 the reduction for both luminant (24%; $p < 0.05$) and isoluminant stimuli (21%; $p < 0.05$) was statistically significant. Similarly, the IP activation showed 14% ($p < 0.05$) perisaccadic BOLD reduction for luminant and 13% ($p < 0.05$) for isoluminant stimuli. This leaves a lower bound of only 1% for stimulus selective saccadic suppression.

Discussion

Absence of Evidence Is Not Evidence of Absence

In the areas where the perisaccadic BOLD reduction was of comparable magnitude for both stimuli, we effectively lose our ability to control for the confounds in the design. This does not mean that there is no saccadic suppression in these areas, just that our paradigm cannot exclude the possibility that the signal changes are related to the inevitable confounds in the experimental design. Specifically, our data should not be interpreted as to imply that there is no saccadic suppression in V1/V2, V3, or IP. In fact, saccadic suppression in the fundus of the intraparietal sulcus is in agreement with single-cell recordings from the ventral intraparietal area in the macaque (Bremmer et al., Soc. Neurosci. Abstract). However, it seems likely that some of the perisaccadic changes in activation we found in the intraparietal sulcus were related to saccade planning and execution [18] or spatial updating [19] rather than the visual stimulus; this would explain why they were independent of stimulus type. Note also that our stimuli only stimulated a limited set of areas long before a sacccade; clearly we cannot make any claims about the nature of saccadic suppression in areas that were never activated.

Mechanisms

Recordings from the LGN—the thalamic gateway to the visual cortex—have shown that LGN neurons typically

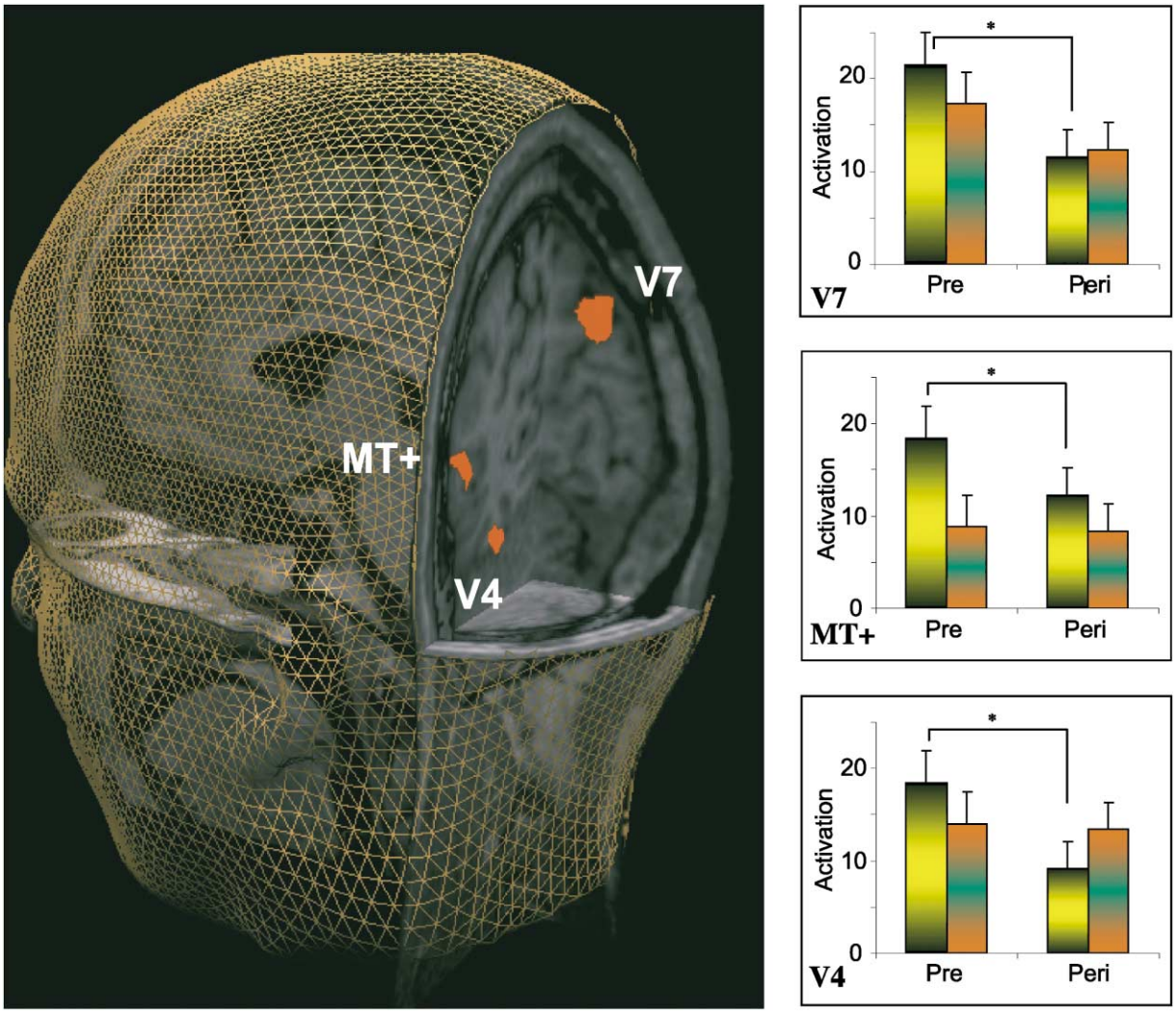

Figure 2. Saccadic Suppression in the Human Brain

The central panel shows a three-dimensional view of the brain with (in red) the areas in which we found clear stimulus selective saccadic suppression (hMT+, V4, and V7). The bar graphs show the activation—as assessed by the regression parameters in the GLM—of these areas long before a saccade (pre) and during a saccade (peri) by luminant (yellow/black) and isoluminant (red/green) stimuli. Although shown in the left hemisphere here, the suppression was bilateral.

have higher firing rates perisaccadically [12]. This would seem to preclude a simple reduction of all cortical input as an explanation of saccadic suppression. On the other hand, phosphenes evoked by transcranial magnetic stimulation of the retina but not the occipital cortex are saccadically suppressed; this would seem to implicate the LGN as a site of saccadic suppression [20]. Our data cannot resolve this controversy, but they show a wide range of changes that saccades cause in the visual activity of several cortical areas. We believe this variety points to the existence of multiple cortical mechanisms that contribute to the psychophysical phenomenon of saccadic suppression. One such mechanism may involve an active control of visual areas by saccade planning centers [21]. A second mechanism may rely on backward masking [21–23] by the postsaccadic visual scene and could take place entirely within visual areas. Both hypothesized mechanisms have psychophysical evidence to support them [1, 24]. In future work, these mechanisms may be disentangled by investigating the temporal relationship of activation and suppression in saccade-planning areas [25] and the sensory areas we have shown to be suppressed.

Conclusion

Our experiments provide new information on the neural basis of saccadic suppression. We found that the stimulus selective saccadic suppression that Burr et al. reported has a clear correlate in the BOLD signal of areas hMT+, V7, and V4. Even V4 receives considerable magnocellular input [26]; hence, this is consistent with the hypothesis that suppression mainly operates in the magnocellular pathway. Note, however, that these same areas are also strongly modulated by spatial attention [17], indicative of a close link between eye movements and spatial attention [27]. Our data specifically point to

hMT+ as an area that plays a major role in saccadic suppression. Given that hMT+ is considered crucial for the analysis of visual motion, this fits well with the idea that saccadic suppression reflects the visual system's attempt to ignore the retinal image motion induced by saccades.

Experimental Procedures

Stimuli and Procedures

We investigated eight healthy, right-handed subjects (four female, mean age 30 years). The Ethics committee of the Heinrich-Heine University approved the experiments, and they were in agreement with international standards on the use of human subjects in research (Declaration of Helsinki). Subjects lay supine in the scanner and viewed visual stimuli, which were projected onto a screen attached to the front of the head coil through a mirror. Eye movements were monitored during scanning with 500 Hz temporal and better than 0.2° spatial resolution by using a limbus eye-tracking system (CRS, Rochester). Stimuli were generated with the VSG2/5 graphics board (CRS) and projected with an LCD data projector (Sony VPL-S500E) whose output onto the projection screen was linearized by using the VSG calibration procedure and the OptiCal photometer.

In a first preexperiment we determined saccadic reaction times in the scanner. These reaction times were used in the main experiment to present stimuli in the temporal vicinity of the onset of saccades. Here, as in the main experiment, subjects fixated a small red dot 10° from the vertical meridian and were instructed to make horizontal saccades to the target dot that appeared on the other side, also at 10° from the vertical meridian. The time of appearance of the target was randomized from 1 to 2 s after a color change in the fixation dot that warned the subjects a target was about to appear. Analog data from the eye tracker were analyzed in Matlab 6.5 (The Mathworks, Inc.). Saccade-onset was defined as the first of three consecutive 2 ms time slices in which the velocity exceeded 10% of the maximum velocity. All saccade trajectories were visually inspected to exclude eye blink and other artifacts. The average saccade latency and standard deviation in our subjects was 200 ± 32 ms.

In a second preexperiment in the scanner, we determined individual isoluminance offsets with the method of Anstis et al. [28]. This offset was used in the main experiment to generate stimuli that were isoluminant for that particular subject. The average isoluminance offset for our subjects, defined as the Michelson contrast between the luminance of the green and the red gun, was 8% ± 4%. Note that any luminance signal remaining in the stimulus after the per-subject calibration will contribute to the experimental confounds; such a signal will always reduce and never increase our estimate of stimulus selective saccadic suppression.

In each trial of the main experiment, we flashed one horizontal grating, covering the central 18° × 10° of visual angle for 32 ms. The background and mean luminance on the screen was always 10 cd/m^2. To generate the stimuli, we first calculated a sinusoidal modulation (spatial frequency: 0.1 cpd) of the red and green guns around a mean value of 5 cd/m^2 with amplitude 3 cd/m^2. The luminance values of these modulations were corrected to take the subject's isoluminance offsets into account and then combined spatially in phase (resulting in a yellow-black grating with 60% luminance contrast) or out of phase (resulting in an isoluminant red-green grating). Both stimuli were well above detection threshold.

The stimulus could appear in one of two epochs. At least 2 s before the saccade (pre) or in the period during which saccadic suppression is known to operate (peri). This factorial experimental design resulted in the four conditions referred to as pre-lum, pre-iso, peri-lum, and peri-iso. The perisaccadic presentation time of the stimuli depended on the consistency with which subjects executed their saccades over time. In the offline analysis, we excluded those stimuli whose onset was after saccade offset or more than 100 ms before saccade onset. This implies that all stimuli in the peri condition fell at least partly inside the saccadic suppression time window; hence, we expected them to be suppressed when compared to the presaccadic stimuli whose presentation was entirely outside the suppression window. Note that even though the stimuli appeared during the saccade, the retinal motion signal was minimal because the saccade was parallel to the bars of the grating.

Imaging and Analysis

We used standard echoplanar imaging (EPI) in a Siemens Magnetom Vision 1.5T MRI scanner (Erlangen, Germany) with a radio frequency head coil for signal transmission and reception. (Parameters: TR 4s, TE 66 ms, flip angle 90°, voxel size 3 × 3 × 4.4 mm^3). Thirty consecutive slices oriented parallel to the AC-PC plane and covering the whole brain were acquired. Total scan duration was 30 min and was repeated once in all but two subjects. The EPI images were coregistered with same-session anatomical T1-weighted 3D MP RAGE scans (180 sagittal partitions, 1 × 1 × 1 mm^3 voxels). Imaging data were analyzed with the BrainVoyager 4.9 software package (BrainInnovation, Maastricht). We realigned functional images to correct for head movements between scans and transformed the structural and functional 3D data into Talairach space by using a piecewise affine and continuous transformation. Preprocessing of the volume time courses involved Gaussian spatial smoothing (FWHM = 10 mm), removal of linear trends, and temporal high-pass filtering with a 10 min cutoff to remove slow periodic drifts. Timing pulses from the scanner and VSG graphics board were combined with the saccade onset times to create event-related protocols for use with BrainVoyager. We used the General Linear Model (GLM) to analyze the fMRI data. One predictor was defined for each of the four conditions (pre-lum, peri-lum, pre-iso, and peri-iso) plus one predictor for periods of no stimulation (baseline/rest). The predictors were given by a convolution of a sum of delta functions (representing the occurrence of a particular stimulus) with a model of the hemodynamic response function [29]. Analysis of single subject data showed that the signals evoked by our brief stimuli were usually too weak to reach significance in all but one or two subjects per ROI. We therefore pooled the data across the eight subjects. To avoid generating spurious results by signal outliers in single subjects, all data were first z scaled. The GLM was then fit to the pooled signal and regression parameters (β) were determined for each predictor. The β parameters represent the contribution of a given predictor/condition to the total signal and are shown as the dependent variable in Figure 2. Because z scaling normalizes the average BOLD signal to zero, this procedure does not allow one to determine a percentage BOLD signal. The nearly identical results by using absolute levels of activation are in the Supplemental Data.

Supplemental Data

Supplemental Data showing percentage BOLD signal changes in all ROIs are available at http://www.current-biology.com/cgi/content/full/14/5/386/DC1/.

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Supplemental Data

Neural Correlates of Saccadic Suppression in Humans

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Supplemental Results

To compare absolute levels of BOLD signal in the different conditions, we analyzed the group data without z scaling the individual time courses. This allowed us to determine a percentage BOLD signal change as the ratio of the regression parameters for each condition to the regression parameter for the baseline/rest condition.

The results are very similar to those obtained with z scaling, showing that the group analysis was not driven by outlier data points in single subjects. The figure shows the percentage of BOLD signal for all four conditions (pre-lum, pre-iso, peri-lum, and peri-iso) in all regions of interest. The insets document the statistical analysis. The "lum" p value is the statistical significance level for the main effect of epoch for luminant stimuli, "iso" shows the main effect of epoch for isoluminant stimuli, and "int" shows the p value associated with the statistical interaction between the two main effects.

Here as in the analysis in the main text, stimulus selective saccadic suppression is found in MT+, V7, and V4. V1/V2 and IP show suppression of both luminant and isoluminant stimuli; hence, we lose our ability to control for the confounds, and the suppression in V3 does not reach statistical significance for either stimulus type.

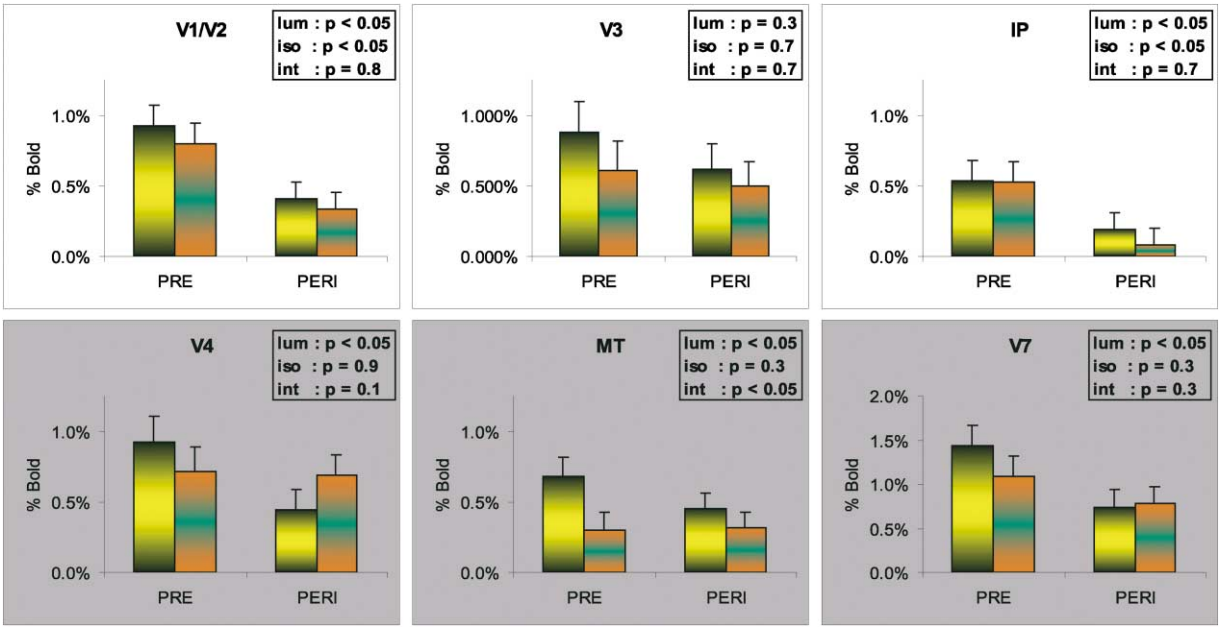

Figure 1. Percentage BOLD Signal Changes in the Regions of Interest

See text for details.