Connectivity Reveals Sources of Predictive Coding Signals in Early Visual Cortex During Processing of Visual Optic Flow

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Abstract
Superimposed on the visual feed-forward pathway, feedback connections convey higher level information to cortical areas lower in the hierarchy. A prominent framework for these connections is the theory of predictive coding where high-level areas send stimulus interpretations to lower level areas that compare them with sensory input. Along these lines, a growing body of neuroimaging studies shows that predictable stimuli lead to reduced blood oxygen level-dependent (BOLD) responses compared with matched nonpredictable counterparts, especially in early visual cortex (EVC) including areas V1–V3. The sources of these modulatory feedback signals are largely unknown. Here, we re-examined the robust finding of relative BOLD suppression in EVC evident during processing of coherent compared with random motion. Using functional connectivity analysis, we show an optic flow-dependent increase of functional connectivity between BOLD suppressed EVC and a network of visual motion areas including MST, V3A, V6, the cingulate sulcus visual area (CSv), and precuneus (Pc). Connectivity decreased between EVC and 2 areas known to encode heading direction: entorhinal cortex (EC) and retrosplenial cortex (RSC). Our results provide first evidence that BOLD suppression in EVC for predictable stimuli is indeed mediated by specific high-level areas, in accord with the theory of predictive coding.

Key words: connectivity, feedback, fMRI, MST, predictive coding, V1

Introduction
It is now generally accepted that the ascending visual pathway accounts only partially for stimulus processing in early visual cortex. In fact, substantial evidence suggests that processing in V1 is significantly modulated by top-down processes such as attention, expectation, or stimulus context (Roelfsema et al. 1998; Ito and Gilbert 1999; McManus et al. 2011; Coen-Cagli et al. 2015). Accordingly, neurons in early visual cortex receive strong input connections from areas that process higher level stimulus features as motion, shape, color, spatial attention, and stimulus category (Muckli and Petro 2013). Along these lines, a series of fMRI studies has found abstract stimulus representations in early visual cortex that were interpreted as feedback from higher areas. V1 has been shown to represent perceived stimulus size in the Ponzo-illusion (Murray et al. 2006) as well as for after images (Sperandio et al. 2012). In addition, V1 was shown to be suppressed by objects versus object scrambles (Murray et al. 2002), foveal V1 encoded object shapes of peripherally presented objects (Williams et al. 2008), V1-encoded illusionary motion traces (Muckli et al. 2005), and context-dependent feedback in the visual field (Smith and Muckli 2010). Our own prior work showed suppression of V1 during motion processing in natural scenes (Bartels, Zeki, et al. 2008), that it signaled predictable high-level grouping effects of global Gestalt (Zaretskaya et al. 2013), and...
that it encoded the real-world colors of gray-scale object images (Bannert and Bartels 2013).

A prominent framework for all these findings is the theory of predictive coding (Rao and Ballard 1999). According to it, high-level areas send expectations with regard to low-level features to areas earlier in the hierarchy, which in turn compare sensory input with the top-down expectations and forward the mismatch (i.e., prediction errors). Crucially, in this arrangement, highly predictable stimuli are expected to induce less neuronal activity in early areas than unpredictable but otherwise matched counterparts. Exactly, this has been observed in several neuroimaging studies in context of coherent visual motion (McKeefry et al. 1997; Braddick et al. 2001; Harrison et al. 2007; Bartels, Zeki, et al. 2008; Helfrich et al. 2013; Costagli et al. 2014). While this relative suppression effect was initially interpreted as driven by local stimulus differences picked up by the small receptive fields in V1 (McKeefry et al. 1997; Braddick et al. 2001), recent studies suggested it to be mediated by feedback from higher level areas (Harrison et al. 2007; Bartels, Zeki, et al. 2008; Costagli et al. 2014). At present however, the sources of these feedback signals are largely unknown.

To fill this gap, in the present study, we examined potential sources of feedback signals to EVC. We replicated the observation of BOLD suppression during coherent optic flow relative to random dot motion matched in low-level features in EVC. In a second step, we ran a whole brain functional connectivity analysis, selecting the most suppressed voxels in early visual cortex as seed region, to look for potential brain areas that showed a change in connectivity between both conditions. We used retinotopic mapping to allow evaluation of suppressive feedback in early visual areas V1, V2, and V3, and examined connectivity with motion responsive regions V5/MT, MST, V3A, V6, CSv, and Pc. We found a specific link between BOLD suppressed EVC and visual motion regions processing optic flow and also with V3A. Additionally, a whole-brain analysis revealed that 2 areas known to encode heading direction showed a change in functional connectivity to EVC during optic flow processing: entorhinal cortex (EC) and an area in prefrontal cortex (RSC). Our results provide first evidence that BOLD suppression for predictable stimuli may indeed be mediated by stimulus-specific high-level areas as predicted by the theory of predictive coding.

Methods

Observers

Twelve normal observers took part in the study (6 females, 6 males, age 22–34 years). All gave written informed consent prior to participation. The study was approved by the ethics committee of the University Clinic Tübingen.

Stimuli and Paradigm

The data used in the present study were acquired within a counterbalanced design involving 7 conditions of different kineticomatograms. For the purpose of the present study, 2 conditions were used for analysis (see Fig. 1): 3D optic flow and random motion, while the others were used to localize V5/MT, MST, and V3A. In the 3D optic flow condition, observers were presented with full-field coherent motion of a random dot pattern with 3D flow (expansion/contraction). In the random motion condition, dot positions were scrambled and motion directions (x and y) randomly mirrored. This approach matched stimuli in trajectory, speed, and acceleration profiles (Fischer et al. 2012a,b) (Fig. 1). All stimuli were generated using MATLAB (http://www.mathworks.de/) and Psychtoolbox (http://psychtoolbox.org/). Both conditions contained random dot patterns of black and white dots on a gray (90 cd/m²) background, presented at 100% contrast. Stimuli were presented on a visual display subtending 24 x 18°, viewed at 80 cm distance. The 3D flow condition simulated a dot-cloud in front of the observer that approached or retracted from the observer. Each stimulus block involved 1 expansion and 1 retraction period following a sinusoidal velocity trajectory that peaked at 120 cm/s, with a period of 12 s. The order of flow expansion and retraction was randomized across blocks. The visibility of the dot-cloud began at 430 cm and ended at 80 cm. In average, 1200 dots were displayed on the screen, with peak motion velocities ranging between 0.2 and 47°/s (mean: 5°/s, median: 5°/s). Dots did change size with distance and subtended a maximal diameter of 2.5°.

The stimuli were back-projected using a projector onto a screen positioned behind the observers’ head and viewed via a front-surfaced mirror mounted on the head coil, with 1280 x 1024 pixels resolution at 60 Hz. All conditions were presented in blocks lasting 12 s and repeated 7 times during 1 imaging run. A total of 5 to 6 imaging runs were acquired for each subject.

Attention Task

To ensure vigilance and balanced attention across all conditions, observers performed a letter back matching task during all conditions presented within the fixation disc (1° diameter). Observers were asked to press a button, whenever an alphabetical letter (a–z, size: 0.6°) with same identity appeared twice in a row. Letters appeared every 800 ms with repetitions occurring on average every 4 s.

Imaging Parameters

Functional gradient-echo echoplanar $T_2^*$-weighted images (EPI) were acquired on a Siemens TIM 3T scanner with a 64-channel phased-array head coil (Siemens, Erlangen, Germany), with the following parameters: TR 2.320, TE 35 ms, flip angle 79°, field of view 192 x 192 mm. Images consisted of 34 slices with 64 x 64 pixels (2.6 mm thick plus 0.4 mm gap), resulting in 3 x 3 x 3 mm voxels. We acquired 5 to 6 runs of the experiment each consisting of 255 images. The initial 4 images of each run were discarded to allow for equilibration of $T_1$ signal. A high-resolution anatomical

Figure 1. Stimuli used in the present study. The 3D optic flow condition involved a full-field coherent motion dot kinematogram with 3D flow (expansion/contraction). For the random motion condition, dot positions were scrambled and motion directions (x and y) randomly mirrored. This approach matched stimuli in trajectory, speed, and acceleration profiles.
ROI Definition

Functional and Anatomical ROI Definitions

V5/MT and MST were identified in 24 hemispheres using a previously established protocol (Huk et al. 2002); MST was defined as the ipsilateral response in lateral occipital cortex near the ascending limb of the inferior temporal sulcus (Dumoulin et al. 2000) for the contrast of an optic flow stimulus confined to the left or right 3/5 of the display, respectively, with static dots. MT/V5 was defined as contiguous sets of voxels in the same region, activated in the contrast of optic flow versus the static condition, excluding voxels belonging to MST. Area V3A was defined in 24 hemispheres using a contrast between pursuit eye movements with planar co-moving background motion versus pursuit eye movements on a static background (Fischer et al. 2012a,b). Areas V6, Pc, and CSv were defined in 22 hemispheres using the contrast between optic flow and random motion.

Additionally, we defined 2 anatomical ROIs of entorhinal cortex and Brodmann area 23 using the SPM anatomy toolbox (Eickhoff et al. 2005) and a brain atlas of the MRicron package (http://www.mccauslandcenter.sc.edu/mricro/mricron/), respectively, in 24 hemispheres. To independently examine BOLD suppression and functional connectivity in the putative LGN, we used the “visual thalamus” ROI that was defined previously based on anatomical connectivity between thalamus and occipital cortex (Behrens et al. 2003) that is now included in the SPM anatomy toolbox 2.0 (Eickhoff et al. 2005).

Retinotopy and Eccentricity of V1–V3

In a subset of 8 observers (16 hemispheres), we also defined areas V1, V2, and V3 using a phase-encoded retinotopy paradigm (Swisher et al. 2007). The mapping stimulus consisted of a gray background, with a superimposed wedge of 70° angle that extended to the edges of the screen. The wedge consisted of a radial achromatic checkerboard (100% contrast) with a check radius that was scaled logarithmically with eccentricity. The checkerboard inverted contrast at 6 Hz. The wedge rotated about fixation with a periodicity of 49.9 s. A red dot appeared at a random location on the wedge for 200 ms in average every 4 s (probability of 5% every 200 ms). Observers were instructed to maintain fixation across the entire session while directing their attention to the stimulus wedge. They pressed a button whenever they saw a red dot. For each observer, 6 runs were acquired. The stimulus rotated clockwise in half of the runs and counterclockwise in the other half. Data were analyzed using the freeSurfer package (Fischl 2012). Polar angle maps of visual areas V1, V2, and V3 were defined on the inflated surfaces of individual observers.

To obtain foveal and peripheral ROI estimates of early visual cortex, we divided each retinotopic surface label of areas V1, V2, and V3 into 2 parts at half of their cortical surface distance along the eccentricity axis. This procedure yielded ROIs that represented about 0°–2° and 2°–12° eccentricity, respectively, given on our horizontal field of view of 24° (Engel et al. 1997; Eijima et al. 2003). We then combined foveal (0°–2°) and peripheral (2°–12°) subparts of V1, V2, and V3 to obtain 1 foveal and 1 peripheral ROI of EVC, respectively.

Data Analysis

Data were processed using SPM5 (http://www.fil.ion.ucl.ac.uk/spm/) including slice-time and head-motion correction and spatial normalization to MNI space. Images were spatially smoothed with a Gaussian Kernel of 12 mm full-width at half maximum (fwhm) for the whole brain random-effects group analyses and with a Gaussian Kernel of 6 mm fwhm for ROI analyses, respectively. Each observer was analyzed separately using a GLM. Each of the conditions was modeled separately (including the 5 conditions not relevant here), with an additional 6 regressors of the realignment parameters obtained from the motion correction, plus 1 regressor containing the mean of each functional volume (Desjardins et al. 2001; Van Dijk et al. 2010). A high-pass filter with 128 s cutoff removed low-frequency signal drifts. For the group analysis we performed a 1-sample t-test using the contrast images from the single subject GLMs. For ROI analyses, condition βs were extracted in each observer individually, and β contrasts were tested for significance across hemispheres using 1-sample t-tests.

Psycho-Physiological Interaction Connectivity Analyses

To identify potential sources of BOLD suppression in early visual cortex during the processing of coherent optic flow compared with the matched random motion stimulus, we performed a psycho-physiological interaction (PPI) analysis (Friston et al. 1997) using the “Generalized form of context-dependent psycho-physiological interactions” SPM toolbox (McLaren et al. 2012). At the observer level, each gPPI analysis included the regressors corresponding to the psychological variables of interest (e.g., the optic flow and random dot conditions but also the other remaining 5 conditions), the time course of the seed area (the physiological variable), and the critical cross-products (i.e., the psycho-physiological interaction terms) between the psychological variables and the time course of the seed area. As in the GLM analysis, the head-motion realignment parameters and the mean of each functional volume were included as covariates of no interest.

Dependent on the analysis, we selected either the peak 500 voxels in the contrast random dot motion > 3D optic flow (which were all located near the occipital poles, that is, covering V1–V3) or the retinotopically mapped regions of V1, V2, or V3, as separate seeds, respectively. To test for changes in connectivity of the seed region with the rest of the brain at the group level, the resulting individual gPPI contrast images were entered into a 2nd level group analysis. Changes in connectivity were assessed using a 1-sample t-test.

Results

BOLD Signal Suppression in Areas V1, V2, V3

First, we performed a whole brain analysis contrasting the less predictable random motion condition to the predictable flow stimulus. In line with previous evidence, we observed strong BOLD responses to random motion in early visual cortex despite the close match in motion features between both stimuli (Fig. 2A). Given that several prior studies reported predictive signals only in V1, but not in V2 or V3 (Murray et al. 2006; Sperandio et al. 2012; Bannert and Bartels 2013), we tested whether the BOLD signal suppression during optic flow affected all early visual regions or only specific ones. We thus performed a region of interest analysis comparing responses with random motion and optic flow in retinotopic V1, V2, and V3, in a subset of 8 observers for whom retinotopic data were available. Figure 2B shows that all 3 areas showed higher BOLD responses to random motion than to optic flow, and Figure 2C shows that most activated voxels...
of the whole-brain contrast shown in Figure 2A fell in V1–V3. Beyond suppression in EVC, we also found reduced BOLD responses to coherent flow in a region close to putative LGN (see Fig. 2A).

Changes in Functional Connectivity with EVC

To identify sources of this optic flow-dependent suppression in EVC, we looked for differences in functional connectivity of the suppressed regions during predictable and unpredictable motion. This approach would identify brain regions whose residual (i.e., nonstimulus driven) responses had higher correlations (i.e., increased functional connectivity) with the suppressed areas during the optic flow condition compared with the matched unpredictable random motion stimulus. We thus carried out a generalized psycho-physiological interaction analysis (gPPI; McLaren et al. 2012) using the 500 voxels with the highest suppression as a seed region for the gPPI in each observer.

The whole-brain result of this analysis is shown in Figure 3A. The condition of optic flow compared with random motion led to a very specific increase in connectivity between suppressed early visual cortex and a network of areas known to process visual motion (Fig. 3A). This network involved the V5/hMT+ complex, V3A, V6, Pc, and CSv. All these regions have previously been shown to respond to ego-motion compatible flow as opposed to control motion stimuli (Wall and Smith 2008; Cardin and Smith 2010; Fischer et al. 2012a,b). Notably, while V3A is more associated with processing of object-motion (Caplovitz and Tse 2007; Bartels, Zeki, et al. 2008) recent evidence also points to a role for it in optic flow processing (Helfrich et al. 2013).

To confirm these whole brain results in a ROI analysis, we functionally defined V5/MT, MST, and V3A using previously established protocols (see methods), and V6, Pc, and, CSv using the net BOLD contrast “Optic Flow” versus “Random Motion.” The results of this ROI analysis are shown in Figure 3B and confirmed the functional links from EVC to MST, V3A, V6, CSv, and Pc, but not for V5/MT.

Figure 4A shows that there was also a specific decrease in connectivity between suppressed early visual cortex and 2 areas known to be involved in visually guided navigation: entorhinal cortex (EC) and an area that has been referred to as functional retrosplenial cortex (RSC) but that is actually adjacent to anatomical RSC (BA 29/30) and overlapping with BA23 (Vann et al. 2009; Baumann and Mattingley 2010). In the present study, we thus refer to the latter region as BA23. In line with these whole-brain
results, we observed the same effects when performing region of interest analyses using anatomical definitions of EC and BA23 (see Fig. 4B and methods).

Given that the suppression effects spanned from V1 to V3, we repeated our connectivity analyses using each area separately as a seed region to test whether each of these regions or only a subset drove the connectivity results with high-level motion regions. As presented in Figure 5, V1, V2, and V3 all showed robust increases in optic flow-driven functional connectivity to high-level motion processing regions with only marginal differences between areas.

Optic Flow-Specific Responses in High-Level Motion Regions

We next examined whether the regions that engaged in increased functional connectivity with EVC during optic flow also showed a specific net BOLD signal increase to our 3D flow compared with the random motion stimuli. We thus quantified the $\beta$ difference “Optic Flow”–“Random Motion” for MT, MST, and V3A as well as BA23 and EC in Figure 6A. Given that V6, CSv, and Pc were defined by this contrast, we illustrate their responses to optic flow by a whole-brain group analysis “Optic Flow” versus “Random Motion” in Figure 6B. Except for area V3A, all regions that showed changes in functional connectivity to EVC also showed net BOLD responses to optic flow.

Examining the Robustness of EVC Connectivity

We performed several additional analyses to probe the robustness of the EVC connectivity results.

First, the joint findings of change in net BOLD and functional connectivity in most areas raise the question whether our PPI results might be driven by remaining condition effects due to an insufficient GLM fit of the hemodynamic model in the PPI analysis (O’Reilly et al. 2012). To rule this out, we repeated the analysis shown in Figures 3 and 4 but used the assumption-free finite impulse response (FIR) function model to regress out all condition effects in the PPI. This analysis allowed us to replicate all results in all areas except for the entorhinal cortex (see Supplementary Fig. 2).

Second, we examined to which extent the results might depend on the number of seed voxels selected. We hence performed an additional connectivity analysis using half the number of seed voxels, that is, the 250 voxels with the highest suppression in each observer rather than the top 500 voxels in EVC. Again, this analysis replicated our results shown in Figures 3–5 (see Supplementary Fig. 3). Supplementary Figure 4 shows the spatial distribution of the top 250 and top 500 suppressed voxels, respectively, across observers.

Third, we examined whether foveal and peripheral visual field representations of EVC, respectively, would differ in their connectivity with higher level regions. We performed 2 connectivity analyses using foveal (0–2°) and peripheral (2–12°) visual field representations of EVC as seeds (see Methods). Both analyses turned out very similar and replicated the results shown in Figures 3 and 4, with 1 notable difference: peripheral EVC had a significant flow-specific functional link to V5/MT (see Supplementary Fig. 5).

Finally, we provide single observer results for net BOLD modulation in motion responsive regions for the contrast optic flow > random motion in Supplementary Figure 6A and for EVC-seeded functional connectivity increases in the same regions for the same contrast in Supplementary Figure 6B.

BOLD Suppression and Functional Connectivity in pLGN

To quantify the flow-dependent net BOLD signal suppression in putative LGN (see Fig. 2A), we examined the contrast between
optic flow and random motion in the “visual thalamus” ROI, defined by anatomical connectivity between thalamus and occipital cortex (Behrens et al. 2003). While we found flow-dependent suppression (see Supplementary Fig. 7A), evidence for connectivity changes in reaction times was not reliable (see Supplementary Fig. 7B). While a classic gPPI analysis revealed an apparent functional link to V6, CSv, and Pc, none of these findings could be replicated in a more conservative FIR-based connectivity analysis. We also tested whether suppression effects in pLGN might be mediated by an increase in connectivity to EVC. However, we found no functional link between pLGN and V1, V2, or V3 (see Supplementary Fig. 8).

**Behavior**

To assure that none of our findings presented here could be explained by attentional confounds, we tested for systematic differences in reaction times ($F_{6,66} = 1.23; P = 0.28$) and task performance ($F_{6,66} = 1.04; P = 0.41$; average performance: 89%) between conditions using repeated-measures ANOVA but found none.

**Discussion**

We examined whether suppression of activity in early visual cortex during processing of a predictable motion stimulus is accompanied by increased functional connectivity with higher level motion processing regions, a hypothesis derived from predictive coding theory (Rao and Ballard 1999; Bastos et al. 2012). Our results show that this is indeed the case. We found increased functional connectivity of EVC during optic flow in areas MST, V3A, V6, CSv, and Pc, all of which are high-level motion processing regions that are involved in optic flow processing (see Fig. 6A,B; Wall and Smith 2008; Cardin and Smith 2010; Fischer et al. 2012a,b).

**V1–V3, LGN**

Suppression in EVC as well as the accompanying functional connectivity changes with high-level regions were not limited to V1 but were also found in V2 and in V3 (see Figs 2 and 5). This extends previous studies that provided evidence for modulatory feedback signals from high-level regions mainly for V1 (Murray et al. 2006; Sperandio et al. 2012; Bannert and Bartels 2013). Beyond EVC, we also found coherent flow-induced BOLD suppression in putative LGN. While we are not aware of previous studies pointing to a role of LGN in coherent motion processing, future studies may examine this finding in more detail. We did not find evidence for a flow-dependent functional link between LGN and higher level motion areas or between LGN and EVC. However, this absence of connectivity changes with LGN cannot be taken for proof of absence of feedback-related effects, as evidence for the presence has in principle also been demonstrated in prior studies for LGN in context of attention or perceptual modulations related to binocular rivalry, respectively (Haynes et al. 2005; Wunderlich et al. 2005; Schneider and Kastner 2009). However, as with the suppression effects in EVC, suppression may also have been induced by local processing such as differential lateral inhibition between the 2 conditions.

**High-Level Motion Network**

Given the assumption that EVC is modulated by feedback, the most likely source candidates given our coherent flow stimulus are the high-level motion regions identified to have increased connectivity with EVC during flow. All motion regions that showed a flow-dependent functional link to EVC had also been reported to be involved in optic flow processing previously (Moreno et al. 2000; Fattori et al. 2009; Cardin and Smith 2010; Fischer et al. 2012a,b; Helfrich et al. 2013). We also observed that while the magnitude of flow response and functional connectivity was correlated across regions, there were also exceptions such as V3A that had pronounced connectivity changes but lacked a flow preference (see also Supplementary Results and Fig. 9). The only region that did not have a preference to coherent versus random flow in our stimulus set was V3A. There is however evidence from other studies for a preference to coherent compared with random motion in V3A (Helfrich et al. 2013) and also for a functional link between V3A and RSC suggesting the involvement of V3A in optic flow-driven goal-directed navigation (Sherill et al. 2015). Finally, V3A has a very specific function in egomotion, as it integrates efference copies of eye movements with planar visual motion to extract motion in real-world coordinates (Fischer et al. 2012a,b). The lack of net BOLD modulation to optic flow in V3A in the present study (see Fig. 6A) may therefore be explained by the presence of several neural populations in it with distinct preferences whose net responses balanced out in our stimulus set (Logothetis and Wandell 2004; Bartels, Logothetis, et al. 2008; Logothetis 2008; Arnoldussen et al. 2011). A change of interaction with V1 of one of those subpopulations during expansion flow processing may thus account for the observed change in connectivity in the absence of net modulation. Beyond that, the finding of an area with no net BOLD increase, but a net functional connectivity increase, adds additional support that our results are not spuriously accounted for by an increase in signal-to-noise ratio of the top-down sending areas (see also Supplementary Results and Fig. 9 for analysis of net BOLD signal vs. connectivity change).
Compared with other visual motion areas, flow-dependent functional connectivity between V5/MT and EVC was less pronounced. In fact, the only functional link to V5/MT we found was specifically restricted to the visual periphery representation of EVC. Prior evidence points to V5/MT as a source for predictive signals in the context of apparent motion (Vetter et al. 2015), and predictability of apparent motion has also been shown to modulate V1 responses (Alink et al. 2010). In the same vein, callosal interhemispheric connections between left and right V5/MT+ have been shown to predict the strength of the horizontal component of apparent motion in the motion quartet stimulus (Genc et al. 2011). The discrepancy between those and our findings might be explained by the 2 types of visual motion compared in the present study. Coherent optic flow compared with random motion have in the past been shown to evoke either no or comparably smaller responses in V5/MT when compared with MST and other high-level motion regions (Smith et al. 2006; Becker et al. 2008; Fischer et al. 2012a,b). In fact, the well-controlled stimuli used here did not evoke significantly differential activity in V5/MT at all (see Fig. 6). Predictions of coherent optic flow may thus predominantly be mediated by motion areas sensitive to this stimulus, that is, MST and further regions downstream rather than V5/MT. Our finding of functional connectivity between peripheral visual field representations of EVC with V5/MT will require future studies to fully understand, as velocities in the periphery were higher than in the fovea. The general finding of differential top-down signals to foveal and peripheral EVC is however in line with previous observations in the context of visual object perception (Williams et al. 2008) or auditory processing and imagery (Vetter et al. 2014).

Entorhinal Cortex and BA23

While our stimulus did not involve an active navigation task, we also found functional connectivity changes between EVC and 2 regions involved in navigation: BA23 in close adjacency to RSC and EC. In the rat, RSC and EC are both substrates of head-direction cells that encode the animals’ heading direction during navigation (Taube 2007) and also in humans EC is known to contain heading direction selective cells (Jacobs et al. 2010). The region in BA23 described here has previously been shown to encode allocentric heading (Baumann and Mattingley 2010). In contrast to the connectivity pattern between EVC and the high-level motion network, functional connectivity between EC, BA23, and EVC was decreased during optic flow compared with random motion. While we interpreted the increase in connectivity with the motion regions as reflecting increased top-down predictions in context of the more predictable flow stimulus, it is at first sight difficult to see why or how this relation would be significantly inversed for a subset of regions. However, the framework of predictive coding would in principle also allow for this inverse change in connectivity: for less predictable stimuli, early sensory regions are expected to send more error signals to higher level regions. Hence, a priori, either direction of connectivity change is plausible in this framework. However, given the limited data on this topic, this idea remains speculation, and further studies are needed to examine the specific role of the functional link between navigation-related regions and EVC during motion perception. Nevertheless, the change in connectivity between these areas suggests that EVC may also provide information relevant for navigation such as heading direction. This idea is in line with the previous evidence showing that feedback to EVC can even convey information about stimulus semantics as category or memory color (Williams et al. 2008; Bannert and Bartels 2013).

Predictive Coding Account

Given that our connectivity results were most likely not driven by spurious correlations, the highly specific connectivity pattern could be interpreted in the following way: during optic flow the network of optic flow processing areas extract a robust heading signal that provides feedback to early visual cortex. This robust feedback signal matches relatively well with the sensory stimulation and correspondingly leads to negligible prediction errors in early visual cortex and thus to minimal BOLD activation. In contrast, during the random motion stimulus with no sensible prediction signal available, the unreliability or absence of feedback to early visual cortex leads to an increase in prediction error that is accompanied by a relative increase in BOLD activation.

Of course, the present findings do not exclude the possibility that additional modulation in EVC is due to stimulus-driven effects of local processing. However, the increase of functional connectivity between V1 and higher level motion processing regions in the face of a decreased net BOLD response do indeed speak for specifically altered communication mediating at least part of the observed suppression.

Our results provide first evidence that BOLD suppression in early sensory areas associated with the predictability of a given stimulus may indeed be mediated by high-level areas that send their stimulus interpretations to regions lower in the processing hierarchy. The present findings therefore complement the evidence provided by numerous prior studies that showed BOLD suppression in early visual regions during coherent flow compared with less predictable control stimuli. In fact, a prior study found evidence consistent with ours, accounting for the positive activation of unstimulated patches of V1 during apparent motion perception, showing that connectivity to V5/MT mediated this increase (Sterzer et al. 2006). Our evidence pinpoints a likely high-level cortical source that may mediate the observed suppression in early visual cortex. While further studies are needed to
examine the interplay between BOLD suppression and underlying neural activity, our results suggest that the BOLD suppression in EVC associated with stimulus predictability could indeed be mediated by high-level regions.

Supplementary Material
Supplementary material can be found at http://www.cercor.oxfordjournals.org/.

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Notes
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References


