Towards layer specific fMRI: investigating feed forward and feedback processing in area V5/MT

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Abstract: High-resolution fMRI has been used to investigate layer specific feedback responses in V1. Currently, no paradigm exists for high-resolution fMRI which enables to investigate both feed forward and feedback processing in an area higher in the visual information processing hierarchy than V1. This study aimed to establish a paradigm with which those processes can be selectively elicited and manipulated in motion sensitive area V5/MT. Two different manipulations of a moving dot stimulus were used to selectively manipulate feed forward and feedback processes. To manipulate feed forward processing, three different motion coherence levels were used. Feedback processing was manipulated using an attentional task where either the motion or the color of the stimulus had to be attended. The results showed that increased motion coherence elicited increased percent signal change in V5/MT while no attention effect was observed in V5/MT. The absence of such an effect might be explained by confounds of task difficulty that could have weakened attentional influences on V5/MT activity. The here proposed paradigm demonstrates an interesting approach to investigate layer specific feed forward and feedback processes in V5/MT. However, additional investigations and improvements of the current paradigm are necessary before using it in a high-resolution fMRI setting.

Keywords: feed forward, feedback, motion, coherence, attention

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Introduction

Recently, high-resolution functional magnetic resonance imaging (fMRI) has been used to measure blood oxygen level dependent (BOLD) signals with high enough spatial resolution, suggesting to measure activity from different layers of the neo cortex (Logothesis, 2008; Kok et al., 2016).

The human neo cortex is organized in six histological layers. Even though the thickness of the layers and the types of neurons vary between regions, a common pattern of interaction between the layers of different regions can be found, which leads to a canonical model of layer specific processing (Douglas & Martin, 2004). Herein, feed forward pathways project from the layers 2 and 3 of one area to layer 4 of the target area. Feedback projections on the other hand project from layer 5 of one area to layers 1, 3 and 6 of the target area (Thomson & Bannister, 2003). Currently, the spatial resolution of laminar fMRI is not sufficient to separate signals from all six cortical layers. Therefore, studies using high-resolution fMRI have typically divided the neo cortex into three evenly spaced chunks to approximate the underlying cortical layers (see Figure 1, adapted from Lawrence et al. 2017). Consistent with the canonical model of layer specific processing, these studies find feedback responses predominantly in deep cortical layers (Lawrence et al. 2017; Kok et al., 2016;).

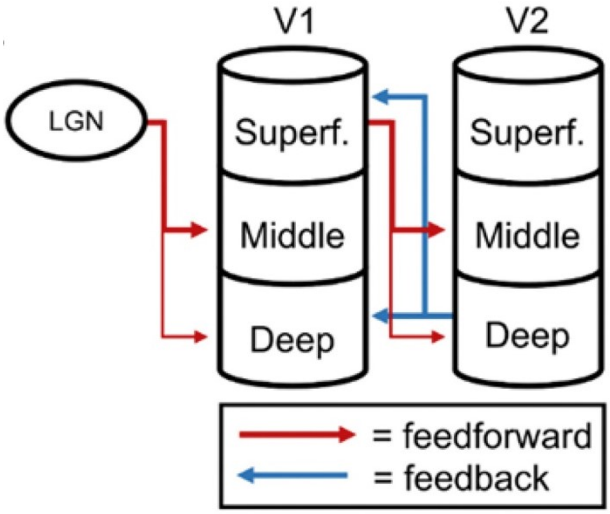

Figure 1. Schematic representation of the feedforward (red arrows) connections between human LGN, V1 and V2 and feedback (blue arrows) connections between V1 and V2. V1 and V2 are split into superficial (≈ layers 1-3), middle (≈ layer 4) and deep (≈ layers 5-6) cortical layers to demonstrate how high-resolution fMRI can be used to estimate feed forward and feedback responses by measuring laminar responses.

For instance, in a recent high-resolution fMRI study, Kok et al. (2016) used illusory figures to examine the laminar activity profile of the human primary visual cortex (V1). When a Kanizsa triangle was presented to subjects, the illusory contour of the triangle elicited stronger activity in deeper layers compared stimuli that did not produce illusory contours. This was interpreted as the result of feedback projections from higher order areas to V1 to generate a percept of the illusory contour. However, this study solely analyzed activity in V1. Whether the canonical model of layer specific processing and the possibility to measure those signals is consistent for brain regions higher in the hierarchy of visual information processing is unknown. Additionally, the source of the feedback signal has not been investigated.

The aim of this pilot study is to establish a paradigm that enables the manipulation of feed forward and feedback processing in a region higher in the information processing hierarchy than V1. The region of interest (ROI) in this project is the visual area 5, also called middle temporal visual area (V5/MT), an area that plays a major role in the perception of motion (Born & Bradley, 2005).

Area V5/MT is interesting because of its functional position in the information processing hierarchy. On the one hand, it receives input from multiple areas lower in the visual processing hierarchy, with the most dominant inputs originating from direction and velocity tuned neurons in layer 4B of V1 (Born & Bradley, 2005; Silvanto et al., 2005). On the other hand, area V5/MT has been shown to receive feedback input from frontal areas. Rahnev et al. (2011) used predictive and non-predictive cues in a dot motion task, asking subjects whether the predominant motion was contracting or expanding. With this fMRI study, they demonstrated that expectations about the direction of motion in the stimulus increased the effective connectivity between V5/MT and the left dorsolateral prefrontal cortex (DLPFC). A subsequent dynamic causal modeling analysis suggested that this connectivity is modulated by feed forward and feedback processes representing a mechanism of how prior information (predictive cues) influences decision making by frontal regions, thereby changing the responsiveness of relevant neurons in sensory cortex.

Investigations about how different aspects of motion influence V5/MT activity have been contradictory. In early fMRI work, McKeefry et al. (1997) investigated V5/MT activity depending on motion coherence of moving dot stimuli. To their surprise, and contrary to what they predicted based on previous electrophysiological studies, incoherently moving stimuli resulted in greater V5/MT activity compared to fully coherent stimuli. This finding was consistent with more recent results from Harrison et al. (2007), which also showed decreased V5/MT activity due to increasing motion coherence. On the other hand, Rees et al. (2000) suggested the opposite, proposing a linear relationship with increasing activity in V5/MT for increasing motion coherence in stimuli.

In a more recent fMRI study by Kayser et al. (2010a), V5/MT showed a specific parametric modulation to different motion coherence levels in a moving dots task. Subjects had to indicate the predominant motion direction of moving dots with varying coherence levels. They found a parametric decrease in V5/MT activity with increasing motion coherence of the stimulus. In a separate study by Kayser et al. (2010b), subjects had to indicate either the predominant motion direction or color of the stimuli. In this case, a parametric increase in activity in V5/MT for increasing motion coherence was found when motion was unattended, and the contrary (decreasing activity in V5/MT for increasing coherence) when motion was attended. Their behavioral results showed that when subjects had to indicate the direction of motion, low coherence stimuli resulted in lower accuracy compared to high coherence stimuli. This suggests that detecting the predominant direction of motion is more difficult when only a small proportion of dots is moving into the same direction (compared to a large proportion of dots). Under this assumption, low coherence motion would require increased attention to detect the predominant motion direction in a stimulus than high coherence motion, likely resulting in higher V5/MT activity for low compared to high coherence stimuli. This can also be translated to the results from McKeefry et al. (1997) and Harrison et al. (2007), where difficulty increased with decreasing motion coherence in the stimuli and V5/MT activity was higher for low coherence. On the other hand, when motion is unattended, motion coherence should influence V5/MT activity in a pure feed forward way. In this case, Kayser et al. (2010b) found increased activity in V5/MT for increasing motion coherence, suggesting a positive relationship between motion coherence and V5/MT activity.

The question this study aims to answer is whether a paradigm can be established with which feed forward and feedback processes that target motion sensitive area V5/MT can be selectively elicited and manipulated. To do this, two different manipulations of a moving dot stimulus were used to selectively manipulate these processes. To manipulate feed forward processing, different motion coherence levels were used. While in previous studies coherent dots were moving in one direction and incoherent dots were moving in random directions, in this study coherent dots were moving towards the center (contracting motion) and incoherent dots were stationary. This was done to maximize the influence of coherent motion on V5/MT activity, thereby defining coherence as the amount or intensity of motion in the stimulus. Feedback processing was manipulated using an attentional task where either the motion or the color of the stimulus had to be attended, similar to the paradigm used by Kayser et al. (2010b). However, here the focus lay only on area V5/MT, using the attentional difference as a contrast. A staircase procedure was used to make all coherence and attention conditions equally difficult. This was done to ensure that the attention and coherence conditions were not different in terms of exerted attention (as discussed previously for Kayser et al., 2010b).

For the feed forward condition, we hypothesized increased activity in area V5/MT with increasing motion coherence. For the feedback condition, we hypothesized increased activity in V5/MT when attention is directed towards the motion of the stimulus compared to when attention is directed towards the color. If successful, this paradigm could be used in a high-resolution fMRI setting to investigate layer specific feed forward and feedback processes in V5/MT. This could reveal whether layer specific feed forward and feedback processing is consistent for brain areas that are higher in the hierarchy of visual information processing than V1.

Methods

Subjects

Thirteen healthy right-handed subjects participated in this study (7 females; mean age, 25.15 years). All participants had normal or corrected to normal vision and were not colorblind. All participants provided written informed consent in accordance with the guidelines of the local ethics committee.

Task and stimuli

Subjects performed a visual dot motion or color proportion task on a stimulus consisting of multiple colored moving dots in which one of these two features (motion or color) was relevant to the task during a given trial. For all trials, regardless of the attended feature, a subset of dots moved coherently towards the center on a background of randomly distributed stationary dots. All dots were equally distributed into red and green dots (i.e. half of the stationary and half of the coherent dots are in one color, the rest in the other color). For each attend-to-motion trial, subjects were required to identify a probable change in the speed of the coherently moving dots. For each attend-to-color trial, subjects were required to identify a probable change in the distribution of colored dots (are there more red than green dots or vice versa?). However, changes only occurred for the according attention condition, meaning that changes of speed only occurred when motion was attended and color changes only occurred when color was attended. Only 20% of all trials were trials where a change occurred (oddball trials). Subjects were instructed that the actual task contained a lower probability of changes than the practice trials (explained later) and therefore required increased alertness, without stating the actual percentage of oddball trials. For the main experiment, subjects completed a total of 4 blocks with 30 trials each. Each block contained 5 trials of each of the 6 conditions (2 attention [motion, color] x 3 coherence [low, mid, high]) from which one trial per condition was an oddball trial, resulting in 6 (20%) oddball trials per block.

Stimuli were presented using a EIKI LC – CL100 beamer (resolution: 1024 x 768, frame rate: 60 Hz). Projection size was 450 x 341 mm and subjects distance to the projection was 995mm (via a mirror in front of the eyes). Stimuli were presented using the software PsychoPy (Pierce, 2007; Pierce, 2009) in Python. A stimulus contained 300 dots with a diameter of .098° each, presented on a grey background in a circular plane with a radius of 20°. A patch with the same color as the background was used to occlude the center (radius = 2°), overlaid with a black fixation dot (radius = .1°). Half of the dots were green, the other half red, and a proportion of all dots was moving towards the center, depending on the motion coherence level of the current trial. Low, mid and high motion coherence meant that 20, 40 or 80% of all the dots presented were moving towards the center. Motion was induced by multiplying their coordinates by a fixed number (= .975) at every frame, resulting in contracting motion. The incoherent dots were stationary and both coherent and incoherent dots were replotted on a random location after a lifetime of 12 frames (200 ms).

Each trial began with a text cue directing the subject to perform either the motion or the color task for the upcoming trial (see figure 2). The cue was presented for 1 s, followed by a fixation period of the same length. Then, the stimulus was presented for 8 s. Changes in the stimuli occurred at random time points in a range between $\frac{1}{3}$ to $\frac{2}{3}$ of the total stimulus presentation and remained until the offset of the stimulus. An increase in speed meant that the coherently moving dots are multiplied by a number smaller than .975, which results in replotting the dots closer to the center for every frame. A change in color was achieved by a disequilibrium in the distribution of red and green dots (e.g. changing from a 50% / 50% distribution to a 70% / 30% distribution) where the color that became more dominant was always picked at random. Stimuli were followed by a 1 s response interval where subjects had to respond with their index or middle finger whether they perceived a change or not, respectively. Next came feedback interval of the same length. During the response interval, the center of the fixation dot was empty (background color) and was filled with red or green color during the feedback interval, indicating right or wrong (or missed) answers, respectively. A jittered inter trial interval (ITI) of 8 (± 2) s was used between trials, chosen from a uniform distribution without replacement to assure a fixed duration of the whole task. The mean duration of a trial (including ITI) was 20 s resulting in a task duration of 600 s.

Preceding the fMRI session, subjects practiced the task in a 1.5 h behavioral session on a separate day. A staircase procedure was used based on the modeling work from García-Pérez (1998) to make sure that both attentional tasks and the different coherence levels were equal in difficulty to rule out confounding effects of difficulty with attention, resulting in about 80% correct responses. However, difficulty only adapted to responses on oddball trials because those are the only ones where values can be changed to adjust difficulty. Subjects were therefore first trained on a version of the task with a shorter stimulus and ITI duration of 3 s and an oddball occurrence of 50% to speed up the staircase procedure. Subjects practiced 216 trials in this task. Then, the same task was practiced that was used in the fMRI session. Here, subjects practiced another 120 trials with the actual duration of stimuli (8 s) and ITI (8 ± 2 s), and 20% oddball trial occurrence.

The staircase procedure was achieved by applying a three-up-one-down rule in the practice task and a one-up-one-down rule in the fMRI task. All subjects started with a speed change value of .955 in the attend-to-motion trials for all coherence levels and with a color-change distribution of 70/30, both of which were obvious and easy to perceive. During the three-up-one-down rule, the speed change value increased by .001 for every three correct answers in a row, and decreased by that value for every wrong answer (bringing the speed of the dots closer to the default .975 value). The color-change value changed in steps of .01

(e.g. from 70/30 to 69/31) for the same criteria as the speed changes. During the one-up-one-down rule the values changed for every right or wrong answer and the step sizes of the changes were multiplied by 0.2599, which, according to previous modeling work in forced-choice staircases, should result in an 80% performance level (García-Pérez, 1998). Subjects completed 18 oddball trials per condition with the three-up-one-down rule in the practice task and four with the one-up-one-down rule while practicing the fMRI task, resulting in a total amount of 22 oddball trials per condition. García-Pérez (1998) suggested about 20 trials with the changes used here to achieve stable performance levels. Also, the staircaise procedure continued in the experimental fMRI task with the same rules used in the training fMRI task.

Following the main experiment, a localizer was used to map the V5/MT region. The localizer contained two different moving dots stimuli with high (80%) and low (20%) motion coherence levels and a duration of 15 s. Like in the main experiment, 300 dots were presented from which half were red and the other half green. They were presented alternately with ITIs with a duration of 15 s. Subjects had to perform a task where they pressed a button with their right index finger every time the fixation dot flashed white in its center (flash duration: 6 frames, 100 ms).

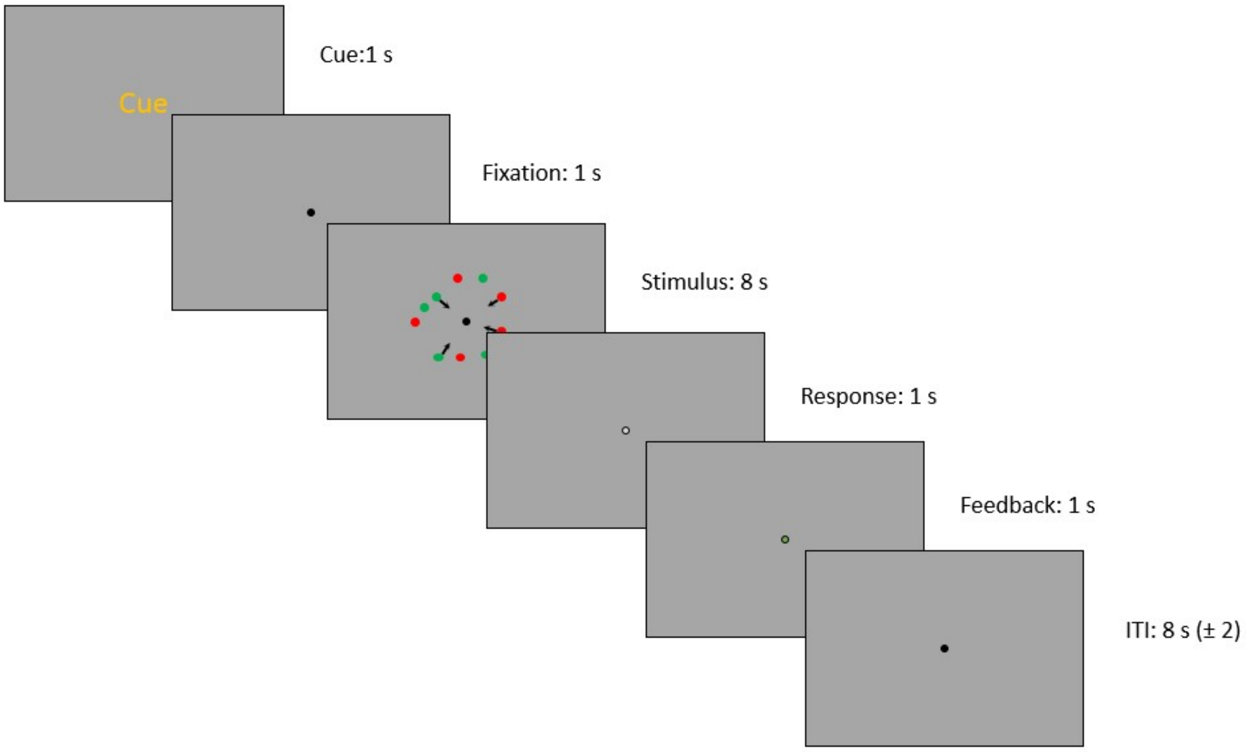

Figure 2. Task design. Each trial began with a text cue indicating whether the motion or color attentional task had to be performed. The cue was presented for 1 s, followed by a fixation period of 1 s. The stimulus was presented for 8 s. 20% of all trials were oddball trials where an aspect of the stimulus would change depending on the cue. If the cue was 'motion', the speed of the moving dots could increase and if the cue was 'color', the distribution of the colored dots could change (resulting in more of one color and less of the other). Stimuli were followed by a 1 s response interval with a proceeding feedback interval of the same length. During the response interval, the center of the fixation dot was empty (background color) and was filled with red or green color during the feedback interval, indicating right or wrong (or missed) answers, respectively. A jittered ITI of 8 (± 2) s was used between trials. The mean duration of a trial (including ITI) was 20 s.

Behavioral data analysis

To investigate if the staircase procedure indeed resulted in all conditions of the experiment to be equally difficult, a 2 x 3 repeated measures ANOVA was done with attention (motion, color) and coherence (high, mid, low) as dependent variables and performance as independent variable. To do this, binary feedback (correct = 1, incorrect =0) was averaged for each condition per subject.

fMRI acquisition

Images were acquired on a 3 tesla Trio MRI system (Siemens) at the Donders Center for Cognitive Neuroimaging, Nijmegen. Functional images were acquired using a 32-channel coil, with a 2D echo planar imaging sequence using multi band 4 (repetition time, 1500 ms;

echo time, 39.6 ms; 68 interleaved slices; voxel size, 2 x 2 x 2 mm; flip angle, 75°; field of view, 210 mm). A high-resolution anatomical image was acquired using a T1-weighted MPRAGE sequence (repetition time, 2300 ms; echo time, 3.03 ms; voxel size, 1 x 1 x 1 mm).

fMRI data analysis

Analysis was performed using SPM12 (Wellcome Department of Imaging Neuroscience, London, UK). The first 3 volumes of each scan were discarded to allow for scanner equilibration. Preprocessing consisted of realignment through rigid-body registration to correct for head motion, co-registration of the functional and anatomical images, segmentation of the anatomical image, normalization to Montreal Neurological Institute (MNI) space using the gray matter image obtained from the segmentation, interpolation of functional images to 2 x 2 x 2 mm, and smoothing with a Gaussian kernel with a full-width at half-maximum of 4 mm. A high-pass filter (cut-off, 128 s) was applied to remove low frequency signals, such as scanner drift.

Regressors for the first-level analysis were obtained by convolving the unit impulse time series for each condition with the canonical hemodynamic response function. The six different cue–stimulus types (attention [motion, color], coherence [low, mid, high]) were modeled separately for all trials. The onsets of the trials were defined at the onset of the stimulus presentation, and the duration was set to 8 s. Button presses were added as a nuisance regressor of non-interest. We included 18 nuisance regressors related to head motion: three regressors related to translation and three regressors related to rotation of the head, as well as their derivatives (Lund et al., 2005) and their squared derivatives (Power et al., 2014). Unless stated otherwise, the reported activations are at $p < 0.05$ corrected at the cluster level for multiple comparisons using an uncorrected voxel threshold of $p < 0.001$.

For the random effects analysis subject specific contrast of the main effects (high > low coherence, motion > color attention) were entered into one-sample t-tests. Additional random effects analyses were done as a sanity check for the main effects of stimulus versus baseline and attention to color versus attention to motion. Brain regions associated with significant clusters were defined using the SPM Anatomy Toolbox (Version 2.1; Eickhoff et al., 2007).

ROI selection and analysis

To avoid ROI selection bias, the intention was to use the high > low coherence contrast of the localizer. Given the absence of significant activity in V5/MT for some subjects in the first level analysis and in the random effects analysis (see results), a different approach was used. An area V5/MT mask was generated based on a reverse inference image (z-score map) from the online data base Neurosynth (http://neurosynth.org/). The image is generated based on a meta-analysis comparing the coordinates reported for studies with and without a term of interest (Yarkoni et al., 2011). For the term “motion”, 383 studies were involved in the analysis that produced the image. The image included clusters in V1 and the parietal cortex, which were excluded for the generation of the mask. The mask was generated for left and right V5/MT based on the z-scores (threshold at 3.09, $p < .001$) of the image. The location of the 100 highest T-values (from the localizer contrast: high > low coherence) that were within the area of the mask were defined as a subject-specific ROI for the subsequent analysis. The six beta values from the GLM of the main task at the location of the ROI were averaged per subject, per hemisphere and computed into percent signal change. To investigate the influence of the different attention or coherence conditions on V5/MT activity, a 2 x 3 x 2 repeated measures ANOVA was done with attention (motion, color), coherence (high, mid, low) and hemisphere (left, right) as dependent variables and percent signal change as independent variable.

Results

Behavioral results

Neither attention ($F_{(1,12)} = .984$, $p = .341$) nor coherence ($F_{(2,11)} = 1.164$, $p = .348$) nor their interaction ($F_{(2,11)} = .724$, $p = .506$) had a significant influence on task performance, suggesting that the staircase procedure resulted in all conditions being equally difficult (Figure 3). However, mean performance ($M = 89\%$) was higher than the aimed 80% performance, suggesting that the task in general might have been easier than intended. Performance reached ceiling for 15 of 78 cases (2 attention x 3 coherence x 13 subjects, see Figure s1). Regarding the feed forward conditions, performance in low, mid and high coherence stimuli reached ceiling in a total of 4, 7 and 4 cases respectively. Concerning the feedback conditions, performance for attention to motion reached ceiling in 10 and attention to color in 5 cases. Eight of the 13 participants reached ceiling in at least one of the six conditions of the task. Contrary to the main task, mean performance on the behavioral training task was close to the aimed level (*M* = 83%) and ceiling was reached by only one subject in one condition.

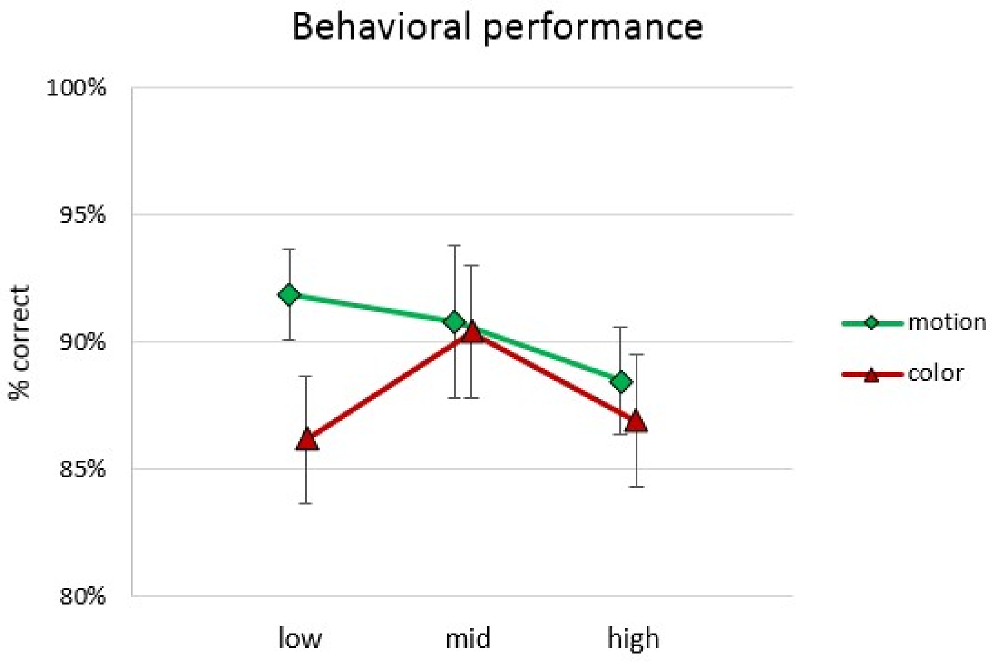

Figure 3. Behavioral performance plotted as a function of motion coherence (low, mid, high) and attention condition (motion, color). No significant main or interaction effects on task performance were found. Error bars show the SEM.

fMRI results

Results from a random effects analysis of the main effect of high coherent relative to low coherent motion for the experimental task resulted in no significant clusters. Results of the main effect of attention to motion relative to attention to color (and vice versa) are summarized in table 1. Figure 4 shows the T-values of the stimulus versus baseline and attention to motion versus attention to color contrasts (threshold: $T > 3.93$, $p < .001$) mapped to a spatially normalized and inflated cortical surface. The yellow area shows the V5/MT mask from which the voxels with the 100 highest T-values (based on the localizer contrast high > low coherence) were chosen as subject-specific ROI for the subsequent ROI analysis. For the attend-motion versus attend-color contrast, no active voxels are found within the mask. Results from a random effects analysis of stimulus versus baseline in the experimental task were performed as a sanity check. The active voxels inside the area of the mask are part of the bilateral occipital cortex clusters (see Table 1).

Due to the absence of significant results in the random effects analysis for the localizer contrast high versus low coherent motion, activity at the individual level inside the mask of V5/MT was investigated. V5/MT activity in the left hemisphere occurred for 4 of the 13 subjects and in the right hemisphere for 7 of the 13 subjects. This was consistent with the activity at the individual level from the main task when the contrast high versus low coherence was used. However, size and locations of activity inside the mask were inconsistent between subjects.

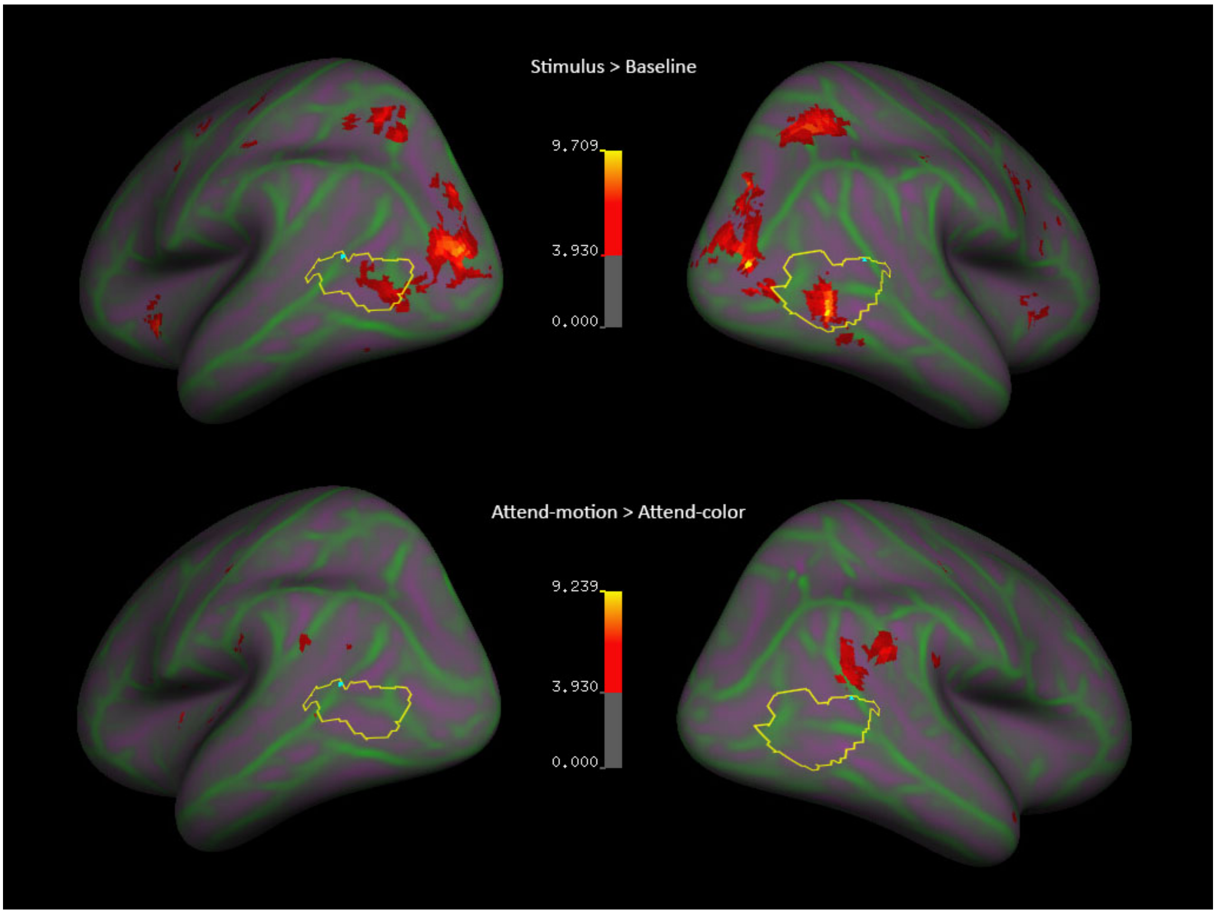

Figure 4. Group level statistical parametric maps of the stimulus versus baseline and attention to motion versus attention to color contrasts with a threshold of $p < .001$ uncorrected for multiple comparisons ($T \geq 3.93$) overlaid onto an inflated average surface using the FreeSurfer software (Dale et al., 1999). The yellow labels show the area V5/MT mask from which the locations of the 100 highest T-values from the localizer were used to extract the percent signal change for the subsequent ROI analysis. The stimulus versus baseline contrast resulted in significant clusters inside the mask of V5/MT. The attention to motion versus attention to color contrast did not result in significant clusters inside this area.

Region	*Hemi*	*Cluster*	*Cluster*	*Z-score*	*coordinates*

			$p_{(FWE\text{-}corrected)}$	*size*		X	Y	Z
Stimulus > Baseline								
	occipital cortex	L	0	1582	5.19	-24	-76	-8
	occipital cortex	R	0	1493	5.12	28	-72	28
	Thalamus	L	0.031	54	4.99	-20	-30	0
	Thalamus	R	0.01	67	4.67	22	-28	2
	IPS	R	0	345	4.6	28	-56	48
	posterior medial frontal cortex	R	0	334	4.59	4	20	48
	BA2	L	0.001	101	4.4	-38	-42	44
	Insula	L	0	138	4.36	-32	20	-4
	IFG	R	0	403	4.29	48	12	28
	Insula	R	0.001	99	4.19	34	24	2
	IPS	L	0	106	4.04	-28	-58	54
	BA2	R	0.008	69	3.91	50	-38	52
Motion > Color								
	IPL	R	0	158	4.53	60	-54	24
	IPL	L	0.002	89	4.04	-58	-62	8
Color > Motion								
	V4	L	0	679	5.05	-26	-84	-10
	lateral occipital cortex	R	0	132	4.4	38	-84	2
	IPS	R	0	243	3.99	26	-64	36
	V4	R	0	124	3.87	28	-66	-4

Table 1. Region, hemisphere, FEW-corrected cluster-level p-values, cluster size, *Z*-scores and coordinates (MNI-space) of random effects analysis: stimulus > baseline, attend-motion > attend-color & attend-color > attend-motion contrasts. Associated regions were defined using the SPM Anatomy toolbox.

ROI results

We found a significant influence of motion coherence on percent signal change in V5/MT with the 3 x 2 x 2 (coherence x attention x hemisphere) repeated measures ANOVA ($F_{(2,24)} = 10.198$, $p < .001$). Main effects of attention ($F_{(1,12)} = 0.823$, $p = .382$), hemisphere ($F_{(1,12)} = 0.276$, $p = .608$) and all interaction terms (coherence x attention: $F_{(2,24)} = 0.012592$, $p = 0.98749$; coherence x hemisphere: $F_{(2,24)} = 1.3979$, $p = 0.26653$; attention x hemisphere: $F_{(1,12)} = 0.47838$, $p = 0.50232$; coherence x attention x hemisphere: $F_{(2,24)} = 1.2676$, $p = 0.29968$) were not significant. Subsequent T-tests revealed significantly higher percent signal change for high compared to low and mid coherence levels ($T_{(1,12)} = 4.2882$, $p < .001$ & $T_{(1,12)} = 3.3694$, $p < .0028$, respectively). Figure 5 shows percent signal change for low, mid and high coherence trials, error bars represent within-subject error.

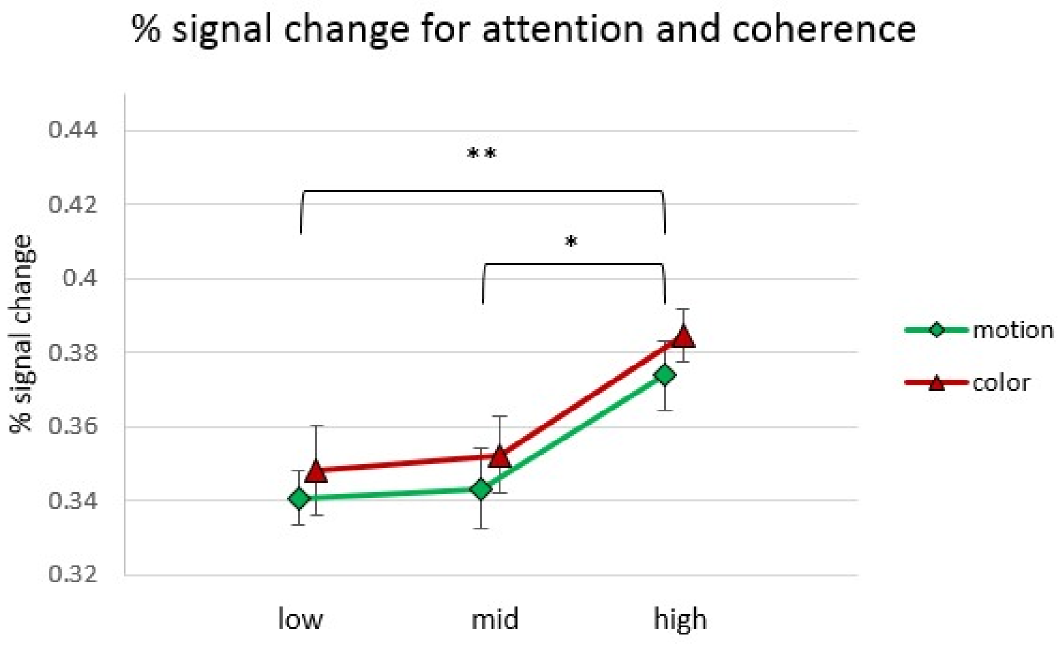

Figure 5. BOLD response to the two attention (motion, color) and the three motion coherence (low, mid, high) conditions. Error bars represent within-subject SEM. *$p < .05$, **$p < .001$.

Discussion

The aim of this pilot study was to establish a paradigm with which feed forward and feedback processes targeting V5/MT can be selectively caused and manipulated. Three motion coherence levels were used to vary feed forward processing and two attentional manipulations were used to manipulate the feedback process.

Feed forward manipulation

The feed forward condition (varying coherence levels) resulted in significant differences in percent signal change in the ROI, but did not result in significant cluster activation in V5/MT at the group level analysis. The ROI analysis revealed significantly increased percent signal change for high (80%) coherence when compared to the two lower coherence levels, with no significant difference between the mid (40%) and low (20%) coherence conditions. It is possible, that the two lower coherence conditions were not different enough to enable detection of a probable change between the two. Rees et al. (2000) reported a linear relationship between stimulus coherence and fMRI response amplitude. It could therefore be that bigger and equal step sizes (e.g. 10%, 50%, 90%) would result in more detectable differences in activation in V5/MT. Whether this is the case cannot be concluded with certainty from the results at hand.

The absence of significant clusters on the group level for high compared to low motion coherence is interesting. Compared to previous studies that investigated motion coherence, this study tested more subjects with shorter task duration. For instance, the present study approached 13 subjects with 20 trials per condition while Kayser et al. (2010a) recruited a total of 6 subjects with 200 trials per condition (five 1 h fMRI sessions). Still, they reported univariate activity in left and right V5/MT for 3 and 5 subjects, respectively. It seems that even with high number of trials, V5/MT activity has high between-subject variability. The study at hand found univariate V5/MT activity contrasting high and low coherence conditions from the localizer and the main task in 7 of the 13 subjects. However, size and locations of activity inside the mask were inconsistent between subjects, which could explain why the ROI analysis was able to reveal increased activity for increasing coherence while the group level analysis failed to show a similar result.

The localizer also failed to reveal activity in V5/MT for high compared to low coherent motion at the group level. As discussed previously for the main task, this might be the result of the between-subject variability in V5/MT involvement. However, compared to previous studies (e.g. Rahnev et al. 2011), the localizer was not used to contrast moving with stationary dots. Instead, as in the main task, two motion coherence conditions were contrasted (80% vs. 20%). Given that the main task did not result in V5/MT activity for high compared to low coherent motion at the group level, it is not surprising that the localizer, containing fewer trials, did not result in significant clusters at the group level either.

Feedback manipulation

The attentional manipulation did not result in increased activity in V5/MT, neither at the group level, nor in the ROI analysis. Instead, increased activity in the inferior parietal lobe (IPL) for the attention to motion versus attention to color contrast was found. The IPL (especially the right) has been suggested to play a role in "maintaining attentive control on current task goals as well as responding to salient new information or alerting stimuli in the environment" (Singh-Curry 2009). While both attentional conditions in the task at hand required sustained attentive control on the current task goal, the attend-to-motion condition required attention towards a more specific part of the stimulus. In the attend-motion condition, subjects could only infer a probable change in motion from the moving dots, which in 2/3 of all cases made up only 20 – 40% of the stimulus. In the attend-color condition, subjects could use the whole stimulus to detect the probable change in color. The salience in changes in speed might therefore have been higher than changes in color, thereby resulting in higher activity in the IPL.

All conditions versus baseline were investigated to make sure that the task itself did not fail to generate involvement of area V5/MT. Additionally, the random effects analysis of the attention to color relative to the attention to motion contrast resulted in significant clusters in V4 (see figure s2 of the supplementary material). The location of activity is comparable to previous studies reporting color related activity (Beauchamp, 1999; Kayser et al., 2010b).

Given that the stimuli themselves were successful in involving area V5/MT, the question remains, whether task difficulty could have weakened the attentional effects. The results from behavioral performance suggest that the staircase procedure used for the task achieved that all conditions are equally difficult. However, average task performance was 89% instead of the aimed 80%, suggesting that the task in general might have been easier than intended. The fact that eight subjects reached ceiling performance in at least one condition might have substantially weakened the attentional effects in general. This would be comparable to the findings from Kayser et al. (2010a & 2010b), where easier conditions of the task resulted in less V5/MT activity than more difficult conditions. However, given that attention to color resulted in significant activation in V4, it is also possible that only the attention to motion condition was weakened. For instance, performance ceiling was reached more often in the motion attention condition. The attentional effects that were supposed to elicit feedback processes that target V5/MT might therefore have been too weak to elicit increased activity.

One reason why the aimed task difficulty was not reached could be that the training task was more difficult than the main task. If this was the case, the difficulty level of the training task was not transferable to the main task. This would explain why performance during training was close to the aimed level (83%) while performance on the main task was higher (89%). The shorter duration of the stimuli in the training task (3 s) compared to the main task (8 s) could have made it more difficult to detect changes in the stimuli.

Additionally, subjects' knowledge about the reduced amount of oddball trials in the main task compared to the training task (without knowing the true percentages) could have made them rely on that fact when they were guessing. While being unsure whether there was a change in the stimulus or not, subjects might have known that they have a higher chance of being correct when they choose 'no-change' as an answer. Indeed, subsequently reviewing the behavioral data revealed that performance on the main task was better for the trials where no change occurred ($M_{(oddball)}$ = 75% vs. $M_{(no\text{-}oddball)}$ = 93%). This difference was absent for the training task with 50% oddball trial occurrence ($M_{(oddball)}$ = 83% vs. $M_{(no\text{-}oddball)}$ = 84%).

Effective connectivity between V5/MT and the left DLPFC had been reported by Rahnev et al. (2011). However, involvement of frontal areas using the present task paradigm (stimulus versus baseline contrast) could only be reported for the right inferior frontal gyrus (IFG) and the posterior medial frontal cortex (pMFC). The right IFG has been suggested to play a critical role in go/no-go tasks (Aron et al., 2003). More specifically, the right IFG is supposed to be responsible for response inhibition, with damage to the area resulting in disruption of that function (Aron et al., 2003). The fact that subjects had to suppress their response until the offset of the stimulus might explain the involvement of the area. The pMFC has been shown to play a role in performance monitoring in cognitive tasks. Activity in that area has been linked to response conflict and errors with the area supposedly signaling the likelihood of obtaining an anticipated reward (Ridderinkhof et al., 2004). Given that subjects obtained feedback about their performance after each trial, involvement of this area is likely due to reward anticipation.

This pilot study was done with the intention to establish and validate a paradigm that could be used in a high-resolution fMRI setting. Layer specific investigations could determine if the canonical model for layer specific processing is consistent for brain areas higher in the visual information processing hierarchy than V1. However, additional investigations are necessary to establish such a paradigm or to improve the current one. Foremost, improved control over individual difficulties of the different conditions might be necessary to answer the question whether attention to motion elicits increased activity in V5/MT. How feed forward and feedback processing conditions are operationalized could be optimized as well. Further investigation about the relationship between V5/MT activity and motion coherence could reveal the optimal conditions to manipulate feed forward processes that target area

V5/MT. Also, the way incoherent motion influences V5/MT activity could be subject of further investigation. The study at hand defined motion coherence as the intensity of motion in the stimulus in general. How V5/MT responds to incoherent random motion, like it is used in other studies (e.g. Rahnev et al., 2011; Kayser et al., 2010a; Kayser et al., 2010b), when all conditions are equal in difficulty has not been investigated. Given the lack of dlPFC involvement during task performance, the paradigm could include predictive and non-predictive cues as in the paradigm of Rahnev et al. (2011). This could be done to validate the connectivity between the dlPFC and V5/MT and further investigate the layer specific profiles of both areas.

All in all, this pilot study investigated a paradigm to selectively cause and manipulate feedforward and feedback processing in an area that is higher in the processing hierarchy than V1. The selected motion sensitive area V5/MT has been chosen for its functional properties and its location. Manipulation of feed forward processing suggested that increasing motion coherence resulted in increased activity in V5/MT. However, there seems to be large between-subject variability in terms of activation and location concerning area V5/MT. While manipulation of attentional effects resulted in increased activity in the color sensitive area V4 when attention was directed to color, it was not in the anticipated motion sensitive area V5/MT when attention was directed to motion. This was probably due to insufficient control over the difficulty adaptation of the task conditions, which might have substantially wakened the hypothesized attentional effect. Using this paradigm for layer specific fMRI research would require additional investigations with the here proposed improvements.

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Supplementary material

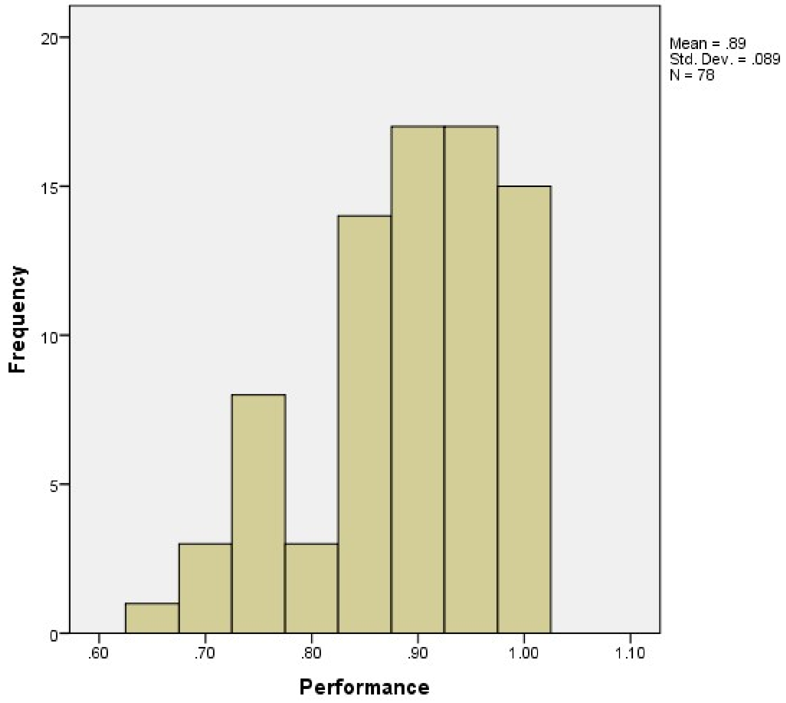

Figure s1. Histogram of the frequency of mean performance on the main task of all cases (conditions x subjects). In total, there were 78 cases (2 attention x 3 coherence x 13 subjects), each with a total of 20 trials. Performance reached ceiling in 15 cases. Of the 13 subjects, eight subjects reached ceiling in at least one condition.

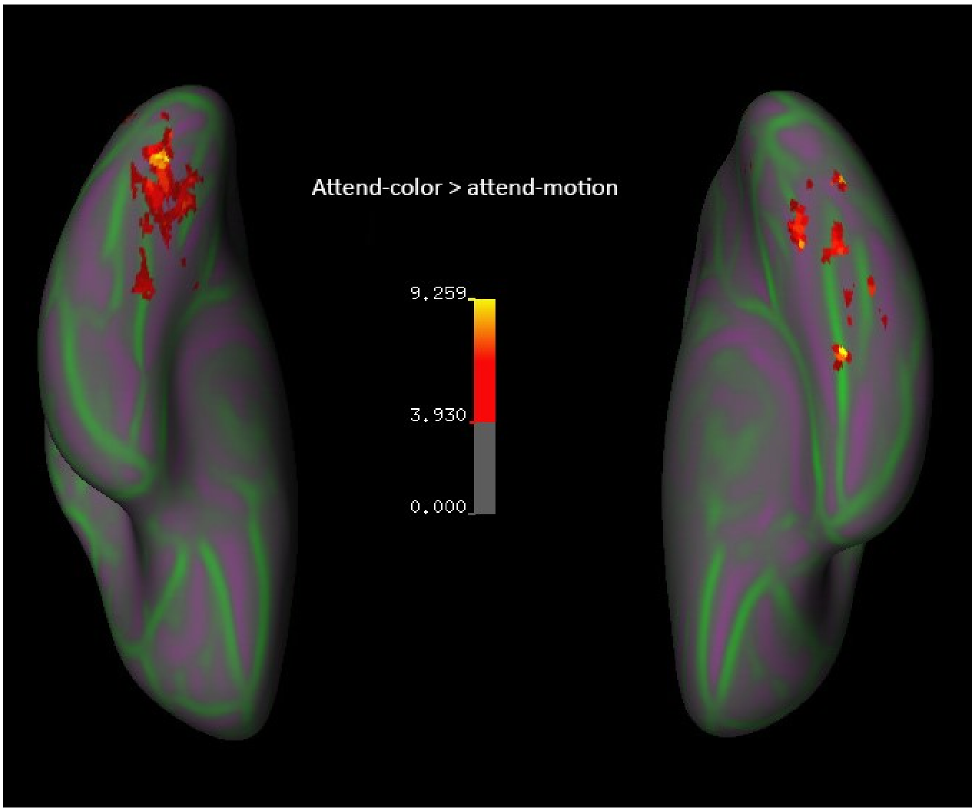

Figure s2. Group level statistical parametric maps of the attention to color versus attention to motion contrast with a threshold of p < .001 uncorrected for multiple comparisons (T ≥ 3.93) overlaid onto an inflated average surface using the FreeSurfer software (Dale et al., 1999).