

The neural network of saccadic foreknowledge

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Received: 8 April 2015 / Accepted: 8 October 2015 / Published online: 26 October 2015
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Abstract Foreknowledge about upcoming events may be exploited to optimize behavioural responses. In a previous work, using an eye movement paradigm, we showed that different types of partial foreknowledge have different effects on saccadic efficiency. In the current study, we investigated the neural circuitry involved in processing of partial foreknowledge using functional magnetic resonance imaging. Fourteen subjects performed a mixed antisaccade, prosaccade paradigm with blocks of no foreknowledge, complete foreknowledge or partial foreknowledge about stimulus location, response direction or task. We found that saccadic foreknowledge is processed primarily within the well-known oculomotor network for saccades and antisaccades. Moreover, we found a consistent decrease in BOLD activity in the primary and secondary visual cortex in all foreknowledge conditions compared to the no-foreknowledge conditions. Furthermore we found that the different types of partial foreknowledge are processed in distinct brain areas: response foreknowledge is processed in the frontal eye field, while stimulus foreknowledge is processed in the frontal and parietal eye field. Task foreknowledge, however, revealed no positive BOLD correlate. Our

results show different patterns of engagement in the saccade-related neural network depending upon precisely what type of information is known ahead.

Keywords Saccade · Antisaccade · Functional magnetic resonance imaging · fMRI · Foreknowledge · Partial foreknowledge

Introduction

Saccades are rapid eye movements that move a target in the visual field on a central retinal location. The speed and accuracy of saccadic eye movements critically determine visual performance (Yarbus 1967). Previous studies on saccadic performance showed that subjects benefit from foreknowledge: making saccadic tasks predictable resulted in reduced reaction time (Abegg et al. 2011; Barton et al. 2006b) and better accuracy of the saccadic landing point (Barton et al. 2006a). This is a consistent finding in studies that provided foreknowledge on all aspects of an upcoming trial (Moschner and Zangemeister 1993; Pare and Munoz 1996; Schiller et al. 2004). Less is known about partial foreknowledge, where only some aspects of an upcoming trial are known leaving other aspects unknown. For saccadic eye movements, it is possible to provide partial foreknowledge on either stimulus location, type of task (prosaccade = looking towards the stimulus, or antisaccade = looking away from the stimulus) or response direction (left or right). In a previous study (Abegg et al. 2011), we examined the impact of different types of partial foreknowledge on saccadic performance by using a pro- and antisaccade task with predictable sequences of either stimulus location, response directions or task. We found that (1) response foreknowledge improves saccadic

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performance, i.e. the combined reaction time and response accuracy, equivalent to that seen with complete foreknowledge, and (2) task foreknowledge has an intermediate benefit, while (3) stimulus foreknowledge has no effect on saccadic performance. Similarly, partial foreknowledge led to distinct changes of switch costs, which were defined as performance loss elicited by the sudden change of a repetitive feature of a trial. We found switch cost benefits from response foreknowledge, but foreknowledge of the task did not reduce task switch costs. These findings suggest that different aspects of foreknowledge are processed differently, possibly involving separate neural networks of the brain with a variable impact on the efficacy of a response. In this report, we used functional MRI to identify the cortical areas involved in the processing of saccadic foreknowledge. We tested whether different types of foreknowledge are processed in distinct cortical areas.

Materials and methods

Subjects

Fourteen healthy subjects, 10 of whom were female, with median age 34 years (range 22–56) participated. All subjects reported normal or corrected-to-normal vision and had no history of neurological disorder. Informed consent was obtained from each participant, and the protocol was approved by the institutional review boards of the University of British Columbia and Vancouver General Hospital, in accordance with the Declaration of Helsinki.

Saccadic paradigm

As in a previous report (Abegg et al. 2011), five conditions of foreknowledge were tested. Foreknowledge was provided by making certain aspects of a trial predictable leaving other aspects unknown. This was achieved by providing information about either task, stimulus location or response direction in a predictable AABBA... sequence. In the *no-foreknowledge condition* (NF), no prior information about the upcoming saccadic task was provided. In the *stimulus-foreknowledge condition* (SF), the side of the stimulus but not the task (antisaccade vs. prosaccade) was known. Thus, two left stimuli were followed by two stimuli on the right, followed by two left stimuli, etc. The *task-foreknowledge condition* (TF) provided information about the task but not about the stimulus side. In the *response-foreknowledge condition* (RF), knowledge about the saccadic goal was provided, but the subjects did not know whether to perform a prosaccade or an antisaccade and thus were uninformed about the stimulus location. Last, the *complete-foreknowledge condition* (CF) was a sequence in which stimulus, task

and response were all predictable. Given that all aspects were predictable in the complete-foreknowledge condition and the AABB sequence was followed, we were forced to select two out of four possible sequences in a given subject. One subject had, for example, two antisaccades to the left followed by two prosaccades to the right, etc., in the first run (see below) and two prosaccades to the left followed by two antisaccades to the right in the second run. This selection was changed between subjects.

Four different runs were constructed, and two of them were randomly assigned to each subject. One run contained six different blocks (five foreknowledge blocks and one fixation block) in a pseudorandom order; each block was repeated twice in one run. Thus one run contained a total of 12 blocks. The order of the foreknowledge blocks from the first half was mirrored in the second half of each run to balance for fatigue and learning effects. While the order of the foreknowledge blocks was pseudorandomized, the fixation block was always presented once after the first five foreknowledge blocks and again at the end of the run. The only difference between the runs was the order of the foreknowledge blocks within the runs. Duration of one run was 740 s. The fixation block consisted of 20 s of fixation on a central fixation cross, and all the other blocks contained 20 events each. Each event had a duration of 2 s, which corresponds to the time of repetition (TR) of the BOLD fMRI. Each block contained ten prosaccades, ten antisaccades and also balanced numbers of left and right stimuli and left and right responses. To introduce a temporal jitter, which allows for rapid functional magnetic resonance imaging (fMRI) analysis, null events, i.e. fixation intervals (2, 4, 6 or 8 s), were interleaved between events of the foreknowledge blocks. A total of 20 s of null events were distributed in each block, so that the total duration of each foreknowledge block was 60 s. Thus for the entire experiment, 80 trials per foreknowledge condition were performed: 40 antisaccades and 40 prosaccades.

Before each block, an instruction screen explaining the type of foreknowledge and the order of sequence was shown for 10 s. The screen contained an explanatory text and examples illustrating the trials. Care was given, only to provide information about the desired aspect. Thus foreknowledge was present in the first trial of the instruction screen. Moreover, subjects were trained for all the conditions during at least 25 min within 24 h before the scan, and they were again briefly trained immediately before going into the scanner.

Stimuli

Each trial started with a fixation on a central fixation cross during 1 s. The fixation cross was then replaced with simultaneous stimulus and cue onset. The cue consisted of a

green circle spanning about 2° of visual angle or a red cross of the same diameter. The green circle indicated prosaccade task and the red cross indicated the antisaccade task. In half of the subjects, this was inverted, so that green circle indicated the antisaccade task and the red cross indicated the prosaccade task. Simultaneous with cue onset, a stimulus consisting of a black disc of 1° of visual angle was presented 10° off centre horizontally. After one second, this screen was replaced by a fixation cross to indicate start of the next trial. Possible stimulus locations (and thus possible response locations) were indicated with a grey circle of 1.5°, which remained on the screen permanently, except during the instruction screen.

MR acquisition

All scans were acquired in a 3.0-Tesla Philips (Andover, MA, USA) scanner. Stimuli were presented using Presentation 9.81 software (Neurobehavioral Systems Inc, Albany, CA, USA) and rear-projected onto a mirror mounted on the head coil. Whole-brain anatomical scans were acquired using a T1-weighted gradient echo sequence, consisting of 170 axial slices of 1 mm thickness (1 mm gap) with an in-plane resolution of 1 mm × 1 mm (FOV = 256 mm). T2*-weighted functional scans (TR = 2 s; TE = 30 ms) were acquired using an interleaved ascending EPI sequence, consisting of 36 axial slices of 3 mm thickness (1 mm gap) with an in-plane resolution of 1.875 mm × 1.875 mm (FOV = 240 mm). The functional scans consisted of 740 functional volumes per subjects in total.

MR data analysis

Data analysis was conducted using Brain Voyager QX 1.10 (Brain Innovation, Maastricht, The Netherlands). The functional scans underwent slice scan time correction, 3D motion correction and temporal filtering with a high-pass filter. Functional and anatomical data set of each subject were coregistered, aligned and spatially smoothed with a 6-mm full-width at half-maximum (FWHM) Gaussian Kernel and then transformed to the Talairach space (Talairach and Tournoux 1988). A total of 27 functional data sets were included (one run was excluded due to erroneous data). Loci of significant increases in the BOLD signal were calculated with a random effect analysis using a general linear model. The time course of the different conditions was convolved with a standard double- γ hemodynamic response function ($\gamma_1/\max[\gamma_1] - \text{dip} \times \gamma_2/\max[\gamma_2]$) scaled so that its total integral is zero (positive peak/FWHM, 5.4/5.2 s; negative peak/FWHM, 10.8/7.35 s; coefficient of the negative dip, 0.35). A t-contrast image was generated per subject from the single-subject level for any condition as described above and the map used to inform a second level analysis

to test for group effect. BOLD correlates at the group level were evaluated using a one-sample *t* test. BOLD correlate clusters were considered significant at $p < 0.05$ corrected for multiple testing combining an arbitrary statistical height threshold of $t = 3.1$ as applied in recent group analyses recordings (Fahoum et al. 2012; Kobayashi et al. 2009; Wiest et al. 2013) and applying a spatial extent thresholding according to Forman et al. using the spatial extent thresholding plug-in of BrainVoyager (Forman et al. 1995). The estimated cluster sizes to correct for a p value < 0.05 were 21 functional voxels in all contrasts except RF, which required a cluster size of 20 voxels. In a first step, we reproduced the well-known oculomotor network of prosaccades and antisaccades (Domagalik et al. 2012; McDowell et al. 2008; Pierrot-Deseilligny et al. 2003, 2004) with our dataset. For this purpose, all prosaccades of our data sets (regardless of the foreknowledge condition) were compared with the all the fixation intervals (2, 4, 6 or 8 s). Also all antisaccade events (regardless of the foreknowledge condition) were compared with the fixation events. This resulted in the contrast of prosaccade and fixation and a second contrast of antisaccade and fixation (Figs. 1, 2).

Next we analysed foreknowledge specific signals. For this, we included all events in a given foreknowledge condition, i.e. prosaccades, antisaccades and fixation intervals (2, 4, 6 or 8 s), resulting in a block design. With this approach, we hoped to smooth differences in neuronal activation during movement execution and resting state (=fixation) and get the best approximation to the BOLD signals driven by foreknowledge only.

We explored the different types of foreknowledge separately. For this, we compared each foreknowledge condition (CF, RF, TF, SF) with the no-foreknowledge condition.

Results

Neuronal network of prosaccades and antisaccades

In order to validate our fMRI dataset, we explored the activation and inhibition patterns of prosaccades and antisaccades in our subjects and compared the findings to the well-known saccadic network that was described in the past by other groups (Domagalik et al. 2012; McDowell et al. 2008; Pierrot-Deseilligny et al. 2003, 2004). For this we compared the BOLD response of all events requiring a prosaccade with the BOLD response during fixation events. This contrast showed a significant increase in BOLD activity in bilateral medial frontal eye fields (FEF), the left supplementary eye field (SEF), bilateral parietal eye fields (PEF), the right inferior parietal lobe, the primary and secondary visual cortex (V1/V2), the left middle occipital gyrus, bilateral cerebellar cortex and the right vermis (Fig. 1). Peak-voxel

Fig. 1 Neuronal network of prosaccades. Brain regions activated by prosaccades. The contrast of all trials that required a prosaccade with fixation trials shows that prosaccades provoke a significant increase in the BOLD response in bilateral medial frontal eye fields (MFEF), the supplementary eye fields (SEF), parietal eye fields (PEF), the primary and secondary visual cortex (V1, V2) and the cerebellum (CER). **a** Coronal slice at $y = -4$. **b–d** Axial slices at $z = 39$ (**b**), 16 (**c**) and -28 (**d**) according to Talairach and Tournoux (1988). For abbreviations, see Table 3

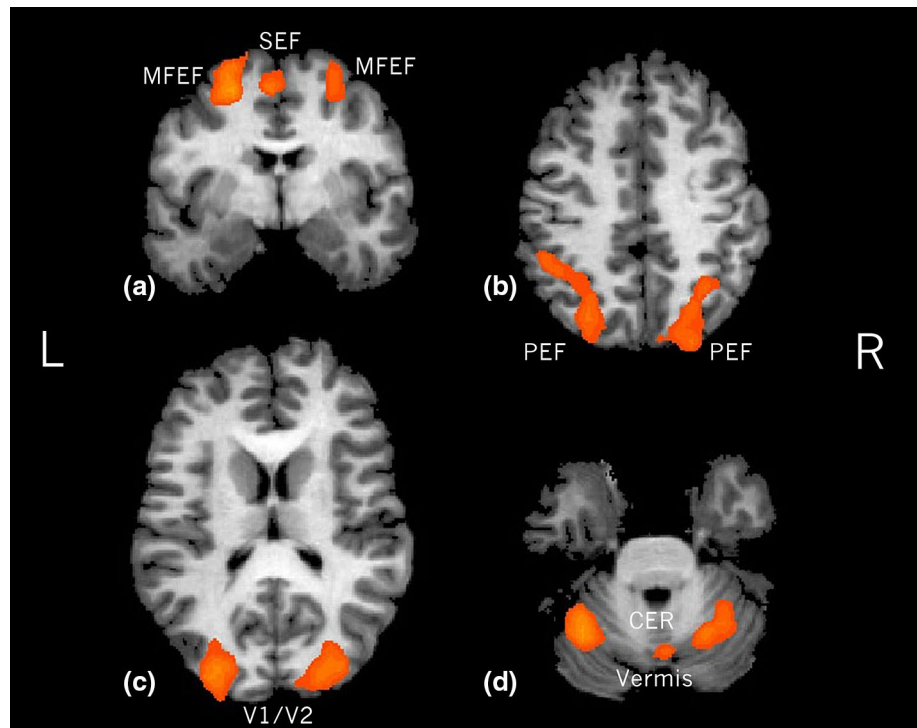
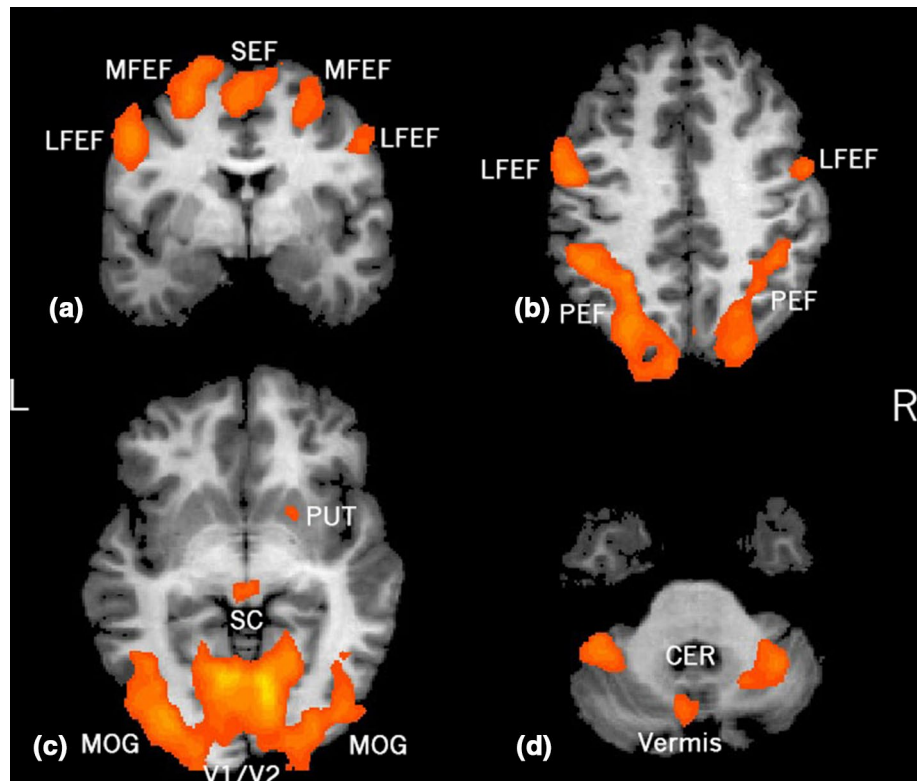


Fig. 2 Neuronal network of antisaccades. Brain regions activated by antisaccades. The contrast of trials containing antisaccades with trials containing fixation only (2, 4, 6 or 8 s) reveals a significant activation of a larger network than for prosaccades only. In addition to regions that were described in the prosaccadic network, we found a significant activation of both lateral frontal eye field (LFEF), middle occipital gyrus (MOG), superior colliculus (SC) and the putamen (PUT). **a** Coronal slice at $y = -3$. **b–d** Axial slices at $z = 37$, -2 , -34 according to Talairach and Tournoux (1988). For abbreviations see Table 3



activations are summarized in Table 1. The contrast of anti-saccade events with fixation events showed a significant increase in BOLD levels in the following regions: bilateral medial and lateral FEF, left SEF, bilateral PEF, right inferior

parietal lobe, bilateral $V1/V2$, bilateral middle occipital gyrus and right inferior occipital gyrus. Furthermore we found positive BOLD correlates in bilateral cerebellar cortex, superior colliculus and right putamen (Fig. 2; Table 1).

Table 1 Neuronal network of prosaccades and antisaccades

Global cluster maxima bilateral	Local maxima	Talairach coordinates			T (voxel level)	p value	Cluster size
		x	y	z			
a. Neuronal network of prosaccades							
Parietal/occipital lobe		9	70	1	7.41	<10 ⁻⁵	1,18,427
	<i>Right</i>						
	Superior parietal lobe (PEF)	27	-52	34			
	Inferior parietal lobe	24	-73	28			
	Lingual gyrus (V1/V2)	9	-70	1			
	Cerebellum	27	-34	-23			
	Vermis	6	-64	-23			
	<i>Left</i>						
	Superior parietal lobe (PEF)	-24	-70	22			
	Lingual gyrus (V1/V2)	-15	-70	-11			
	Middle occipital gyrus	-30	-76	-5			
	Cerebellum	-36	-61	-23			
	<i>Right</i>						
Precentral gyrus		24	-7	58	4.48	<0.0001	1747
	Medio-lateral (MFEF)	24	-7	58			
	<i>Left</i>						
Precentral gyrus		-24	-10	58	5.91	<10 ⁻⁵	5202
	Medio-lateral (MFEF)	-24	-10	58			
	Medial (SEF)	-3	-7	55			
b. Neuronal network of antisaccades							
Parietal/occipital lobe		12	-70	1	7.98	<10 ⁻⁵	1,78,963
	<i>Right</i>						
	Superior parietal lobe (PEF)	27	-64	49			
	Inferior parietal lobe	27	-73	31			
	Lingual gyrus (V1/V2)	12	-70	1			
	Middle occipital gyrus	33	-79	10			
	Inferior occipital gyrus	42	-55	-20			
	Cerebellum	27	-58	-17			
	<i>Left</i>						
	Superior parietal lobe (PEF)	-27	-58	52			
	Middle occipital gyrus	-27	-85	16			
	Lingual gyrus (V1/V2)	-3	-85	4			
	Cerebellum	-27	-64	-17			
Superior colliculus		-9	-22	-8	4.23	<0.0003	745
	Right	6	-22	-8			
	Left	-9	-22	-8			
	<i>Right</i>						
Precentral gyrus	Medio-lateral (MFEF)	27	-10	49	5.40	<0.0001	4274
Precentral gyrus	Lateral (LFEF)	51	2	31	5.00	<0.0001	1140
Putamen		18	11	10	4.92	<0.0001	1147
	<i>Left</i>						
Precentral gyrus		-24	-10	55	7.26	<10 ⁻⁵	17,656
	Medial (SEF)	-3	-10	58			
	Medio-lateral (MFEF)	-24	-10	55			
	Lateral (LFEF)	-48	-4	40			

Coordinates of significant cluster maxima for the contrasts prosaccades versus fixation and antisaccades versus fixation. For abbreviations, see Table 3

The neural network activated by antisaccades was thus larger than the one activated by prosaccades.

Neuronal network of partial foreknowledge

Next, we built contrasts for each partial foreknowledge condition with the no-foreknowledge condition. The comparison of the *response-foreknowledge* block with the no-foreknowledge block showed positive BOLD correlates in right medial and lateral FEF. A negative BOLD correlate was found in left V1 and V2 areas (Fig. 3, Table 2). The comparison of *stimulus foreknowledge* with no foreknowledge revealed a positive BOLD correlate in bilateral medial FEF and left PEF. Negative BOLD correlates were found in right orbitofrontal gyrus, the left precuneus and left V1 and V2 areas (Fig. 4, Table 2). The comparison of *task foreknowledge* with no foreknowledge showed negative BOLD correlates in the right orbitofrontal gyrus, left superior frontal gyrus (dorsal), bilateral inferior temporal gyrus and the left V1 and V2 areas (Fig. 5, Table 2). No positive BOLD signals were found in this condition. In contrast to *complete foreknowledge* with no

foreknowledge, we found negative BOLD signals in bilateral V1 and V2 areas and left cuneus (Fig. 6). Also for this condition, no positive BOLD signals were found.

Discussion

Our analysis of BOLD activity in conditions requiring complete and partial foreknowledge provides several insights: First we found that our paradigm and analysis protocol are well suited to confirm the localization of the saccadic network as was described by other groups before (Domagalik et al. 2012; McDowell et al. 2008; Pierrot-Deseilligny et al. 2003, 2004). This indicates the validity of our data set. Second, we found that foreknowledge-associated BOLD responses are confined to the saccadic network, thus indicating that saccadic foreknowledge is processed within the saccadic network. Third, we found that partial foreknowledge leads to distinct patterns of activation, thus indicating that different aspects of foreknowledge are indeed processed in distinct cortical networks. Fourth, for each foreknowledge

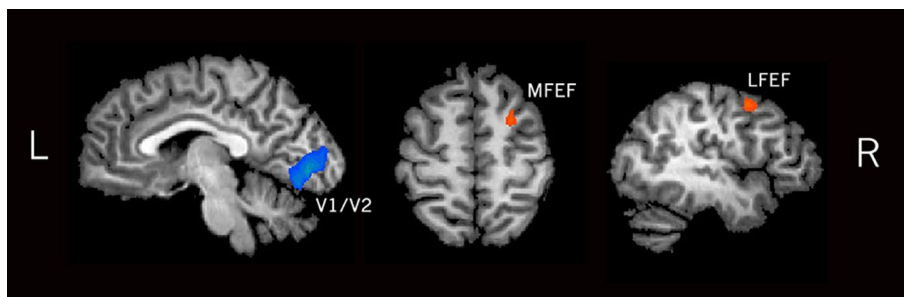


Fig. 3 Response foreknowledge versus no foreknowledge. Areas with significant BOLD responses during the response-foreknowledge (RF) condition contrasted with no-foreknowledge block. Response foreknowledge leads to significant increased BOLD responses (*red*) in the frontal eye field and to a decrease in the BOLD response (*blue*)

in visual associated areas. *Left panel* shows sagittal slice at $x = -5$. *Middle* shows axial slice at $z = 50$ and *right panel* shows a sagittal slice at $x = 45$ according to Talairach and Tournoux (1988). For abbreviations see Table 3 (colour figure online)

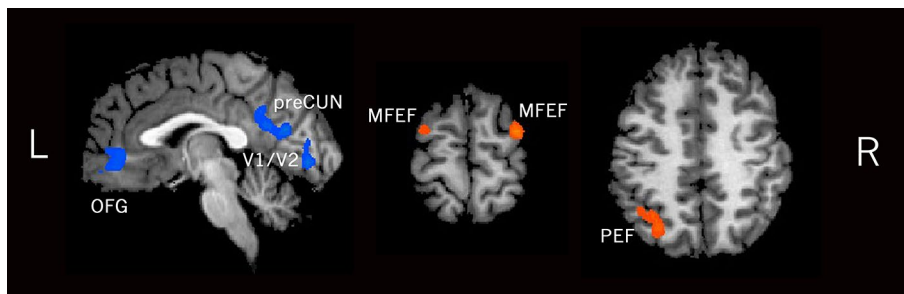


Fig. 4 Stimulus foreknowledge versus no foreknowledge. Areas with significant BOLD responses during stimulus-foreknowledge (SF) block contrasted with no-foreknowledge block. Stimulus foreknowledge leads to a significant activation (*red*) in the frontal eye fields and to a significant decrease (*blue*) in activity in visual associated areas

and the frontal cortex. *Left panel* shows sagittal slice at $x = -2$. *Middle* and *right panels* show axial slices at $z = 61$ and $z = 40$, respectively (according to Talairach and Tournoux 1988). For abbreviations, see Table 3 (colour figure online)

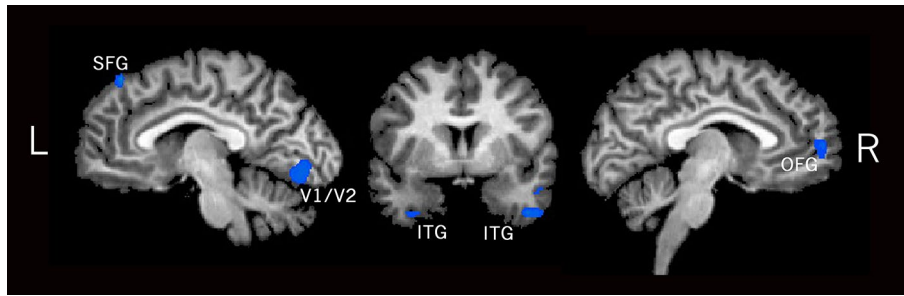


Fig. 5 Task foreknowledge versus no foreknowledge. Areas with significant BOLD level decreases during task-foreknowledge (TF) block contrasted with no-foreknowledge block. No increased BOLD response was observed during events with task foreknowledge. A significant decrease in the response (*blue*) was found in visual asso-

ciated areas, frontal cortex and temporal cortex. *Left panel* shows a sagittal slice at $x = -6$. *Middle panel* shows a coronar slice at $y = 1$. *Right panel* shows a sagittal slice at $x = 7$ according to Talairach and Tournoux (1988). For abbreviations, see Table 3 (colour figure online)

Table 2 Neuronal network of partial foreknowledge

Cluster maxima	Talairach coordinates			T (voxel level)	p value	Cluster size
	x	y	z			
a. Response foreknowledge versus no foreknowledge						
<i>Right</i>						
Superior frontal gyrus (MFEF)	21	8	55	4.42	$<2 \times 10^{-4}$	671
Medial frontal gyrus (LFEF)	51	11	40	4.10	$<4 \times 10^{-4}$	719
<i>Left</i>						
Lingual gyrus (V1/V2)	-3	-79	-2	-5.79	$<4 \times 10^{-6}$	5592
b. Stimulus foreknowledge versus no foreknowledge						
<i>Right</i>						
Middle frontal gyrus (MFEF)	30	-1	61	4.99	<0.0001	948
Orbitofrontal gyrus	6	38	4	-5.16	<0.0001	2320
<i>Left</i>						
Middle frontal gyrus (MFEF)	-24	-1	64	4.65	<0.0001	788
Superior parietal lobe (PEF)	-27	-61	40	4.16	<0.0001	1161
Precuneus	-9	-55	19	-5.13	<0.0001	2553
Lingual gyrus (V1/V2)	-3	-79	-2	-4.67	<0.0001	825
c. Task foreknowledge versus no foreknowledge						
<i>Right</i>						
Orbitofrontal gyrus	6	59	10	-4.05	$<5 \times 10^{-4}$	669
Inferior temporal gyrus	57	-13	-14	-4.58	$<2 \times 10^{-4}$	589
Inferior temporal gyrus	48	-1	-32	-4.84	<0.0001	735
<i>Left</i>						
Superior frontal gyrus (dorsal)	-9	38	52	-5.00	<0.0001	953
Inferior temporal gyrus	-39	8	-32	-4.95	<0.0001	979
Lingual gyrus (V1/V2)	-3	-79	-5	-6.50	<0.0001	2209
d. Complete foreknowledge versus no foreknowledge						
<i>Right</i>						
Lingual gyrus (V1/V2)	0	-70	-8	-5.63	$<6 \times 10^{-6}$	1918
Cuneus	-3	-94	1	-5.72	$<5 \times 10^{-6}$	1127

Coordinates of significant cluster maxima for the indicated contrasts. For abbreviations, see Table 3

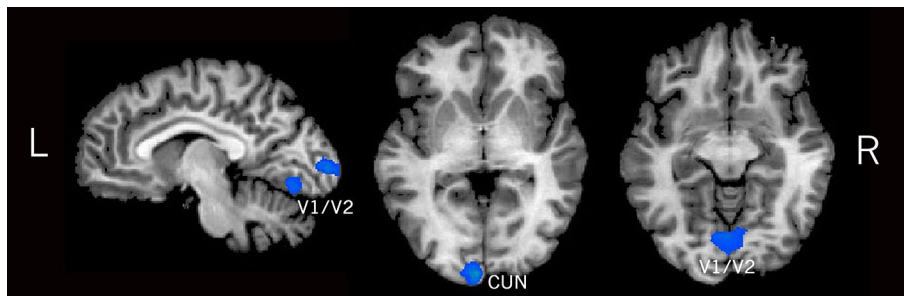


Fig. 6 Complete foreknowledge versus no foreknowledge. Areas with significant BOLD responses during the complete-foreknowledge (CF) block contrasted with no-foreknowledge block. No increased BOLD responses were found during complete-foreknowledge events. A significant decrease in activity (*blue*) was observed in visual asso-

ciated areas. *Left panel* shows sagittal slice at $x = -7$. *Middle and right panels* show axial slices at $z = 1$ and $z = -7$ according to Talairach and Tournoux (1988). For abbreviations, see Table 3 (colour figure online)

condition we found a consistent decrease in the BOLD response in visual and visual associated areas. This indicates that visual associated areas require a significantly smaller BOLD activation if foreknowledge is provided, independent of the type of foreknowledge. How foreknowledge is actually used is unknown, and we cannot rule out that foreknowledge exerts its effect via modulation of attention, motor activity or possibly even by modulating perception.

The decreased BOLD response in left V1/V2 that we found in every foreknowledge condition is intriguing. As suggested in the literature, BOLD activity in visual cortices may not only be the result of direct sensory input via the visual pathway but is also strongly associated with visual attention (Buchel et al. 1998; Luck et al. 1997; Motter 1993). On this background, the decreased BOLD levels in all conditions of foreknowledge may indicate a decrease in visual attention for the upcoming task: if the future is known ahead, less attention is required to successfully fulfil a task.

Table 3 Abbreviations

BA	Brodmann area
CER	Cerebellum
IOG	Inferior occipital gyrus
IPL	Inferior parietal lobe
IPS	Inferior parietal sulcus
ITG	Inferior temporal gyrus
LFEF	Lateral frontal eye field
MFEF	Medial frontal eye field
MOG	Middle occipital gyrus
OFG	Orbitofrontal gyrus
PEF	Parietal eye field
PUT	Putamen
SC	Superior colliculus

Our finding of activation in right medial and lateral FEF in the response-foreknowledge condition is consistent with a study by Milea et al. (2007). They found greater BOLD activity in the bilateral medial and lateral FEF when subjects knew the direction of an upcoming saccade compared to when the response direction was unpredictable or compared to fixation (Milea et al. 2007). In contrast to our study they found in addition an activation in left SEF and right pre-SEF. Frontal eye field is essential in planning and execution of saccadic eye movements and plays a role in visual attention (for review see Vernet et al. 2014). Electrical stimulation in the FEF elicits saccadic eye movements. In contrast to FEF, the supplementary eye field SEF does not immediately or directly contribute to saccade initiation. But SEF assists in initiating and controlling saccades made during motor movement of the head and body (Martinez-Trujillo et al. 2004). Gagnon et al. (2002) investigated a condition identical to our response-foreknowledge condition. They too found increased BOLD signals in bilateral medial FEF and left SEF (Gagnon et al. 2002). Curtis et al. (2008) designed a paradigm which combined response foreknowledge and task foreknowledge and compared response foreknowledge with task foreknowledge ($RF + TF > TF$). They found positive BOLD responses in regions corresponding to our bilateral medial and lateral FEF and bilateral PEF (Curtis and Connolly 2008). PEF receives input from visual areas and projects to the frontal eye field and the superior colliculus. It is important for integrating location information for movement planning and is involved in encoding target locations (Li et al. 1999). Taken together, evidence is overwhelming that the FEF is important in foreknowledge processing concerning the direction of a saccade.

For stimulus foreknowledge, we found increased BOLD activity in bilateral FEF and left PEF and decreased BOLD levels in V1/V2, right medial orbitofrontal cortex and left precuneus. We are not aware of any other fMRI studies

that investigated stimulus foreknowledge in a saccade task. There is, however, a good body of literature about the effects of spatial anticipation of an upcoming visual target in paradigms comparing shift of visual attention to a specific location with saccades to that location or fixation (Corbetta et al. 1998; Grosbras et al. 2005; Perry and Zeki 2000). These paradigms are not unlike our stimulus-foreknowledge condition, both provide foreknowledge of spatial properties of visual stimuli. The indicated studies show that a shift of visual attention to a certain localization leads to activations in the same areas as the execution of saccades or, in other words, activates also the oculomotor network (Corbetta et al. 1998; Grosbras et al. 2005; Perry and Zeki 2000). It is though very difficult to distinguish between activation of oculomotor areas due to attentional processes or due to saccade planning and execution. Despite these limitations, the IPS/PEF was reported to play a specific role in spatial anticipation (Pierrot-Deseilligny et al. 2004; Ptak and Muri 2013). Early on this was already described by Bushnell and Goldberg in the monkey (Bushnell et al. 1981). Our involvement of the PEF in the processing of stimulus foreknowledge is thus consistent with these reports.

For task foreknowledge, we were not able to find a positive BOLD signal, instead we found significantly decreased BOLD levels in left V1/V2, right orbitofrontal cortex, left antero-dorsal frontal cortex and bilateral inferior temporal cortex. This is surprising and contradictory to the existing literature. An event-related study showed increase in the bold response of bilateral medial FEF after providing subjects with task foreknowledge. No negative bold answers were reported, but the study only scanned for bold changes in FEF and IPS specifically (Connolly et al. 2002). In the study by Curtis et al. (already referred to above), positive bold correlates were found in bilateral medial and lateral FEF and bilateral PEF in their task-foreknowledge condition. In contrast to our study, they showed the bare effects of task foreknowledge and did not build the contrast with no foreknowledge (Curtis and Connolly 2008). An explanation for our distinct findings could thus lie in the different ways of displaying task-foreknowledge effects. We are not aware of a study directly comparing task foreknowledge to no foreknowledge like in this study, which makes exact comparison to previous results impossible.

Similar as for task foreknowledge, we only found decreased BOLD activity in left V1/V2 and no increased BOLD signals in complete foreknowledge. One possible explanation for this finding is that that complete foreknowledge enables subjects to prepare and perform tasks on a subcortical level, for example, in the reticular formation of the brainstem, leading to a BOLD activity in a region which is poorly accessible with our methods.

In conclusion, we found a distinct cortical network for different types of saccadic foreknowledge. Foreknowledge on the motor response is being processed within the frontal eye field, and stimulus-related foreknowledge additionally involves the parietal eye field. The location of saccadic task foreknowledge is yet unclear. All types of foreknowledge are associated with a decreased activation in primary and secondary visual cortex. All types of saccadic foreknowledge seem to be processed within the network required for saccadic programming.

Acknowledgments MA was supported by the Swiss National Science Foundation. JB was supported by a Canada Research Chair and the Marianne Koerner Chair in Brain Diseases. This work was supported by CIHR grant MOP-81270.

Compliance with ethical standards

Conflict of interest No conflicting relationship exists for any author.

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