Research Paper

Volume : 3 | Issue : 10 | October 2014 • ISSN No 2277 - 8179

Medical Science

KEYWORDS : ocular dominance, fMRI

Fmri and Ocular Dominance

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ABSTRACT

The aim of the study was to determine whether fMRI activation is dependent on ocular dominance. Our sample included 20 eyes of 10 healthy subjects (8 female with mean age 50.25 and two male with mean age 59). None of the subjects in our sample had ocular or neurological disease. All subjects were examined for sighting eye dominance (hole-in-the-hand and pointing-a-finger test) and sensory eye dominance (Worth dot test and fogging test). All the control subjects underwent functional magnetic resonance imaging examinations with stimulation of both eyes and each eye separately using a black-and-white checkerboard of size 25.8x16.2 degrees of the visual field.

We observed different interocular fMRI activity in all subjects. This difference was not statistically significant (P = 0.85). Neither the directional nor sensory ocular dominance correlated with the fMRI activity. We did not even demonstrate hemispheric laterality after separate stimulation of the dominant eye.

Introduction

Over the past three years, we have been intensely evaluating the possible uses of fMRI in clinical ophthalmology[1-7]. We noted that the fMRI activity values are not the same if each eye is examined separately. One possible explanation for this finding is the dominance of one eye. For this reason, the aim of this study to determine whether there is a correlation between eye dominance and fMRI values.

Material and Methods

Our sample included 20 eyes of 10 healthy subjects (8 female with mean age 50.25 and 2 male with mean age 59). Visual acuity(determined on ETDRS optotypes) of all subjects was 1.5, after correction where necessary. (Table 1)None of the subjects in our sample had ocular or neurological disease. All subjects were right-handed and were examined for sighting eye dominance (hole-in-the-hand and pointing-a-finger test) and sensory eye dominance (Worth dot test with red-green glasses and fogging test-blurred test)[8]. (Table 2)

The study protocol was approved by the local Ethics Committee and the study was performed in accordance with Good Clinical practice and the Declaration of Helsinki.

Functional MRI

Functional MRI examinations were carried out on the Philips Achieva 3T TX MR system (Philips Healthcare, Eindhoven, Netherlands) operating with a magnetic field strength of 3 Tesla using the BOLD method. A standard 32-channel SENSE head RF coil was used for scanning. For measuring fMRI with the BOLD technique, the gradient-echo EPI sequence was used with the following parameters: TE = 30 ms, TR = 3 s, flip angle of 90 °. The measured volume contained 39 continuous 2mm-thick slices. The voxel size measured was 2 x 2 x 2 mm (FOV = 208 x 208 mm, matrix 104 x 104, SENSE factor 1.8).

Optical stimulation was provided by a black/white checkerboard alternated with its negative image with a frequency of 2 Hz. The size of black and white checkerboard was 25.8 x 16.2degrees of the visual field and the LCD monitor as a standard graphical interface of the commercial Eloquence (InVivo) stimulation system was used. The measurements consisted of a sequence of five 30-second active phaseperiods and five resting periods of the same length (10 dynamic scans). During the restingphase of each fMRI scan, a static crosshair situated in the centre of the visible field wasprojected. In total, every measurement included 100 dynamics and took 5 minutes.

Functional MRI response and its hemispheric laterality after simultaneous stimulation of both eyes and after unilateral stimulation of each eye separately were observed in all subjects (3 fMRI measurements per subject).

The obtained data were processed using SPM8 software and a general linear model (GLM).

During the pre-process, the data were motion corrected (realignment) and corrected for time shift of individual slices (slice timing) and then smoothed with a Gaussian filter with FWHM 6 x 6 x 6 mm and finally standardised into the MNI_152 space. For statistics on the level of individual subjects, the GLM with canonical HRF (hemodynamic response function) applied to the block scheme of stimulation was used. Statistical maps were thresholded at P = 0.05 with FWE correction.A group statistic using one-sample t-test was also performed and the evaluation was done at P = 0.0001 with minimal cluster size of 50 voxels. Multiple regression analysis was done to find possible dependence of the strength of the fMRI activation on age and refraction correction (P = 0.001, minimal cluster size of 10 voxels).

Lateralisation index (LI) was calculated using LI-toolbox for SPM8 and bootstrap thresholdingmethod[9]. As an inclusive mask, the occipital lobe was selected and all other parameters were used in default settings. For the final statistic, the weighted mean LI as a result of the calculation was utilised. A strong advantage of this approach is the independence on the subjective choice of the statistical threshold and also the ability to equalise differences in the strength of the BOLD effect in individual cases.

Results

Visual acuity (VA) of all subjects was 1.5, after correction where necessary. (Table 1)

No.	RE	LE
1.	0	0
2.	0	0

3.	-0.75	-1.25
4.	-1.5	-1.5
5.	-0.5	-0.5
6.	-3.75	-3.75
7.	+2	+2
8.	+3.5	+3
9.	-0.5	-0.5
10.	-3.25	-2.75

Table 1: Refraction of eyes necessary to achieve VA 1.5

All subjects in our sample showed directional dominance of the right eye. Three subjects had sensory dominance of the right eye; sensory dominance could not be demonstrated in seven subjects. Functional MRI activity expressed in number of statistically significant voxels (or spatial extent) in entire visual cortex after stimulation of the right eye correlated with sensory dominance of the right eye in two of the three subjects (4,5). Where it was not possible to demonstrate sensory dominance, fMRI activity was more extensive after stimulation of the right eye in five subjects (6-10) and after stimulation of the right eye in two subjects (1,3). (Table 2)

No.	Sex/ Age	VA	dominance		fMRI activation [# voxels]			weighted Mean LI	
		RE/LE	sighting	sensory	RE+LE	RE	LE	RE	LE
1.	F/34	1.5/1.5	RE	RE/LE	7 100	8 880	10 710	-0,048	0,012
2.	F/48	1.5/1.5	RE	RE	9 544	7 212	10 013	-0,320	-0,090
3.	F/50	1.5/1.5	RE	RE/LE	11 650	6 627	11 730	-0,420	0,070
4.	F/46	1.5/1.5	RE	RE	6 815	5 882	5 847	0,280	0,085
5.	F/49	1.5/1.5	RE	RE	8 358	9 783	6 754	0,400	0,240
6.	F/50	1.5/1.5	RE	RE/LE	6 799	3 537	2 256	0,064	-0,180
7.	F/60	1.5/1.5	RE	RE/LE	5 973	7 628	6 011	-0,059	-0,100
8.	F/65	1.5/1.5	RE	RE/LE	8 060	6 780	6 415	0,310	0,500
9.	M/58	1.5/1.5	RE	RE/LE	6 809	8 255	6 881	0,200	0,100
10.	M/60	1.5/1.5	RE	RE/LE	7 878	10 580	6 792	-0,510	-0,270

Table 2: Summary table of performed tests. RE/LE sensory dominance means that dominance has not been demonstrated. The extent of the BOLD activation is expressed in number of active voxels (P=0.05 with FWE correction) in the occipital lobe of both hemispheres.

Paired t-test was used for the comparison of right and left eyes. The comparison shows that the values showed no statistically significant difference between right and left eyes in controls. (Figure 1) The average values of fMRI activity and their standard deviations are shown in Table 3.

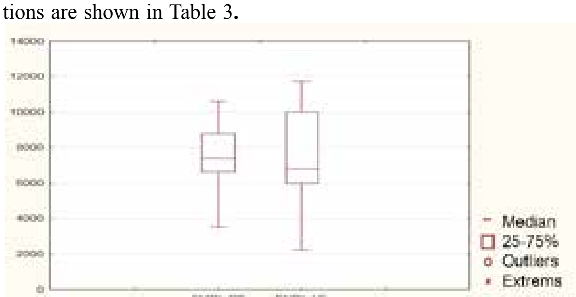

Figure 1: Box plots shows fMRI values after stimulation of the right and left eye.

Eye	FMRI	Standard deviation
RE	7 508.4	2 018
LE	7 340.9	2 775

Table 3: Mean fMRI and their standard deviations after stimulation of the right and left eyes. A statistically significant difference between both eyes was not demonstrated (P = 0.85).

Laterality dominance of the fMRI response after stimulation of each eye is shown in Table 4 Individual values for each hemisphere during the stimulation of RE and LE are shown in Table 2. Negative values indicate directional laterality in the right hemisphere, positive values indicate directional laterality in the left hemisphere.

No.	RE	LE
1	re/le	re/le
2	re	re
3	re	le
4	le	le
5	le	le
6	re/le	re
7	re/le	re
8	le	le
9	le	le
10	re	re

Table 4: Laterality dominance in this table was evaluated by means of thresholding of the LI at the level of 0.07. LI lower than -0.07 is signed as re, LI higher than 0.07 means le and LI between -0.07 and 0.07 is related to the absence of dominance (re/le).

Evaluating the sight dominance (in all subjects right eye) from fMRI experiment, the difference between right and left eye was found only using group statistics (random effects). Using one-sample t-test and significance level of P=0.0001 with minimal cluster size of 50 voxels the resulting number of statistical significant active voxels was 5400 in case of right eye and 3500 for left eye which represent the difference of 35% (fig. 2 and fig. 3). However, paired t-test over the same group of subjects (right versus left eye) did not find any statistical difference between right and left eye. These results corresponds to our results with individual statistics (each subject is evaluated separately and the final number of activated voxels for both eyes is compared) and also support the literature evidence that there is a tendency to activate larger area of the primary visual cortex in stimulation of the dominant eye.

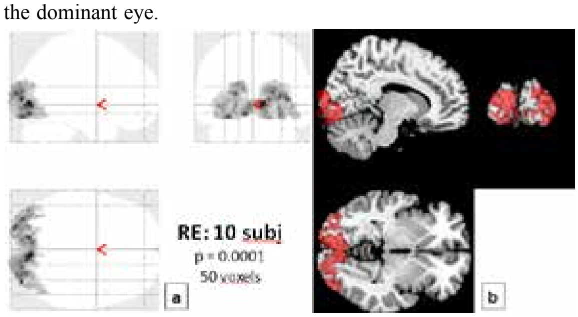

Figure 2 shows results of group analysis (10 subjects) in case of right eye stimulation (P = 0.0001). Three orthogonal maximum intensity projections (MIP) are shown in a) and

b) shows orthogonal representative slices demonstrating the extent of activation in red colour.

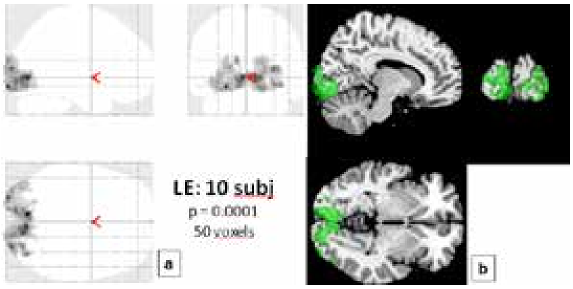

Figure 3: Results of group analysis (10 subjects) in case of left eye stimulation (P = 0.0001). Three orthogonal MIPs are shown in a) and orthogonal representative slices demonstrating the extent of activation in green colour in b).

We found several small areas in primary visual cortexwith the negative age dependency on the fMRI activation using multiple regression analysis (higher age decrease activation in this areas, P = 0.001, figure4). However, there was no correlation with refraction correction found.

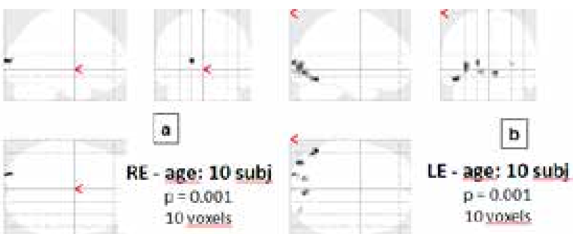

Figure 4 shows areas with the negative dependency of the fMRI activation and age for a) right eye and b) left eye (P = 0.001).

Discussion

The first records of fMRI and ocular dominance were provided by Romboutset al[10]. They used the near-far alignment test for the examination of eye dominance in 26 healthy individuals. Visual stimulation was done with goggles with two LED matrices (red light, 8 Hz), each in front of one eye. In each subject, the left and right eyes were stimulated separately and together, in a randomly alternating order. The authors found differences between activated areas when the left or the right eye was stimulated separately. Twenty-two subjects showed activation, of which eight subjects had a dominant left eye and 14 a dominant right eye. In general the size of the activated area was bigger upon stimulation of the dominant eye. The difference with the area upon stimulation of the non-dominant eye was statistically significant in the right eye dominant group. These results indicate that the dominant eye actually activated a larger area of the primary visual cortex than the non-dominant eye.

Our fMRI results are in agreement with this conclusion but only in case of sighting dominance and only comparing right and left eye in group statistics (10 subjects). However, evaluating all single subjects there was not possible to find the ocular dominance from the extent of the activation stimulating separately right and left eye which would be very attractive from practical point of view. Moreover, the sensory dominance which is not equal every time with sighting dominance is more important for ophthalmologists.

There were differences in methodology of ocular dominance assessment and in the stimulation used to examine the fMRI. Rombouts et al. compared sighting dominance (which differs from sensory dominance) and used diffusion light stimuli for the stimulation[10].

Mendola et al. found that percent change in fMRI BOLD signal was stronger for the dominant eye as defined by the acuity method and this effect was significant for areas located in the ventral occipital territory. In contrast, assigning dominance based on sighting produced no significant interocular BOLD differences. They concluded that interocular BOLD differences in normal subjects exist and may be predicted by acuity measures[11].

Moreover, our results showed the differences in fMRI activity after separate stimulation of right and left eyes. This difference was however not statistically significant and did not correlate with either directional or sensory ocular dominance.

Other studiesreported the difference in fMRI activity after separate stimulation of each eye[12-14].Algaze et al. found interoculardifference of 4.82% + / -0.74% in 6 controls[14]. Our ten controlshad interocular difference of 2.2%, and this difference was not statistically significant (P = 0.85).

Miki et al. found that eye dominance was observed in the contralateral anterior visual cortex. However, the eye dominance in the visual cortex was found not only in the most anterior area corresponding to the monocular temporal crescent but also in the more posterior area, presumably showing the greater sensitivity of the temporal visual field (nasal retina) as compared with the nasal visual field (temporal retina) in the peripheral visual field (peripheral retina)[15].

Our results, comparing laterality of the activity of individual hemispheres after separate stimulation of each eye, did not confirm this finding.

The results of fMRI activity after separate stimulation of each eye and both eyes at the same time were not found in the literature. Our results show that fMRI activity after stimulation of both eyes correlates more with the activity after the stimulation of the left eye (r = 0.6743, P = 0.0325) than after the stimulation with the right eye (r = 0.0372, P = 0.9188). We can only speculate that this finding may be associated with directional dominance of the eye.

Conclusion

We did not demonstrate a dependence of fMRI activity on either directional or the sensory ocular dominance after separate examination of each eye. Other mechanisms are most likely involved in the fMRI activity after visual stimulation.

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