Utilization of Binocular inhibitory Interaction for Reliable fMRI Mapping of Human Ocular Dominance Columns

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Introduction Ocular dominance column (ODC) mapping in human primary visual cortex (V1) using blood oxygenation level dependent (BOLD) based fMRI, is an ideal model for testing the spatial specificity and spatial resolvability of fMRI at the submillimeter level. The ability to obtain such maps robustly is very important because columnar level functional parcellation appears to be a fundamental property of cerebral function. To date, fMRI imaging of ODCs in the human brain mostly relies on differential mapping using the hyperoxic phase of the BOLD response to monocular photic stimulations. This technique has to assume symmetric BOLD responses from neighboring ODCs so as to subtract out the "flooded" BOLD signal from the neighbor ODCs due to the BOLD point spread function. Any deviation from this assumption can lead to either overestimation or underestimation of the territories of the ODCs in the map. In this study, an alternative ODC mapping method that is insensitive to this assumption based on the characteristics of binocular inhibitory interactions between the left and right eye ODCs is proposed. The proposed method should improve the specificity and reliability of the ODC mapping, which has been examined from multiple aspects in this study.

Rationale We have already demonstrated that the selective stimulation of one eye can considerably suppress the activity induced by subsequent stimulation of the other eye if the delay between the monocular stimulations is as short as 30-90 ms; this suppression gradually disappears when the delay exceeds 300~400 ms[1]. This characteristic can in principle be used to differentiate two ODC groups. Specifically, the fMRI data at long inter-stimulus interval (ISI) of ~300 ms can generate fMRI maps including the activated pixels covering both eyes ODCs in V1, while at short ISI (~40ms), the regions activated by the eye experiencing the second stimulation are significantly suppressed. Consequently, the separation of the left and right eye ODCs depends on the degree of suppression in terms of the BOLD responses between the two stimulation conditions (short ISI vs. long ISI). Since this method uses the reference of intrinsic neuronal activities within the same ODC group at different conditions instead of referring to the activities from the neighboring ODCs, it does not rely on the assumption of symmetric BOLD activities from the neighbor ODCs, and therefore can further improve the spatial specificity of fMRI mapping. Moreover, the reliability of ODC maps generated using this technique can be independently examined from multiple aspects: human ODC morphology, difference between low-resolution and high-resolution maps and mapping reproducibility. In addition, the mapping reliability can be further examined by switching the order of the paired-monocular stimuli between two different sessions (e.g. session one uses the stimuli of 'left-eye first, right-eye trailing', session two uses the stimuli "right-eye first, left-eye trailing'). In reliable ODC maps, one should expect the suppressed ODC population in the first session become unsuppressed ODC population and vice versa.

Method All the fMRI scans were performed on a 7T 90-cm bore magnet (Magnex Scientific, UK) interfaced with a Varian INOVA console (Varian Inc., Palo Alto, CA). One oblique slice adjacent and parallel to the calcarine fissure was chosen for the fMRI study. On this selected slice, gradient echo planar images (GE EPI) with an in-plane resolution of 0.5×0.5 mm^2 were acquired. In each fMRI run, the paired-monocular stimuli to both eyes with two different ISIs, corresponding to the strong inhibition and no inhibition conditions, respectively, were repeatedly presented (every 600 ms) in two stimulation periods using block task design. The ODC map was generated by comparing the BOLD signals for each activated pixels between the two stimulation conditions. The quantitative criterion for ODC designation and the definition of ODC Index (ODCI) were described in details elsewhere[2]. A small region in V1 was chosen as region of interest (ROI) for each subject. Three subjects participated in this study and multiple sessions on different days were conducted for each subject.

Results Fig. 1a shows one ODC map created using the proposed method in a representative subject. Alternating ODC-like patches or stripes are clearly observed in the mapped ODCs; most mapped ODCs are largely orthogonal to the interhemispheric fissure; the inter-column distance is ~ 1mm. In contrast, all these features are absent in the map generated identically except with lower spatial resolution (2×2 mm^2, Fig. 1b), in which each pixel contains both left and right eye ODCs. Furthermore, the activated pixels in Fig. 1a are aggregated into two groups, the suppressed ODC group (red color) and the unsuppressed ODC group (yellow color) with the stimuli applied, but this aggregation is not observed in Fig. 1b, in which the majority of the activated pixels are partially suppressed (orange color) due to the partial volume effect. This difference can be further verified from the ODC Index histograms shown in Fig. 1c. Mapping reproducibility was examined by showing the overlap between two ODC maps obtained on different days using the same paradigm in the same subject (Fig. 2). Besides preserving all the ODC features observed in Fig. 1, the major structures of the mapped ODCs are reproducible across the two sessions. Figs. 3a and 3b show the overlaps between different sessions with the same paradigm and the reversed paired-stimuli paradigm, respectively. The color coding for one of the sessions was reversed before the overlaps in Fig. 3b were generated. The maps in Fig. 3b generally resemble those in Fig. 3a, which indicates that the major ODC populations reverse when the order of the paired-stimuli is changed.

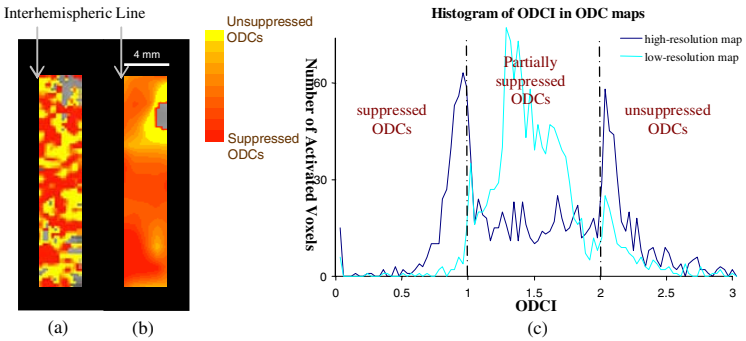

Fig.1 Contrast between high-resolution and low-resolution ODC maps

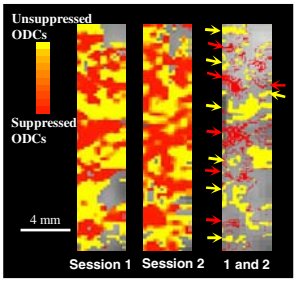

Fig. 2 Reproducibility of ODC maps

Discussion and Conclusion

The features of mapped ODCs in terms of the pattern, orientation and size are consistent with the literature findings in post mortem human brains considering the slice prescription. The remarkable contrast between the high-resolution and low-resolution ODC maps essentially suggests: the mapped ODCs located in V1 are characterized with strong binocular inhibition; they can be spatially aggregated into two distinct groups when the paired-stimuli are applied; they are in the size of about 1mm as the low-resolution map does not show any features or aggregation pattern. The mapped ODCs are reproducible. When changing the order of the paired-monocular stimuli, the suppressed and unsuppressed ODC populations reverse accordingly. These results verify the reliability of the ODC maps obtained using the proposed method. This study also implies that appropriately using the characteristics of neural interaction opens a new door to fMRI mapping down to the column level. It also gives us sufficient confidence in reliable mapping column structures using submillimeter fMRI.

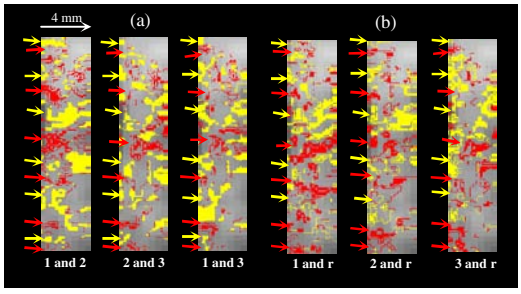

Fig. 3 (a) Overlaps between three sessions (1, 2 and 3) of the same paradigm. (b) Overlaps between one session with the reversed paradigm (r) and the sessions 1, 2 and 3 displayed in (a).

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References

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