Relative Timing of Brain Activations Revealed by Ultra-Fast MR inverse imaging (InI)

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INTRODUCTION

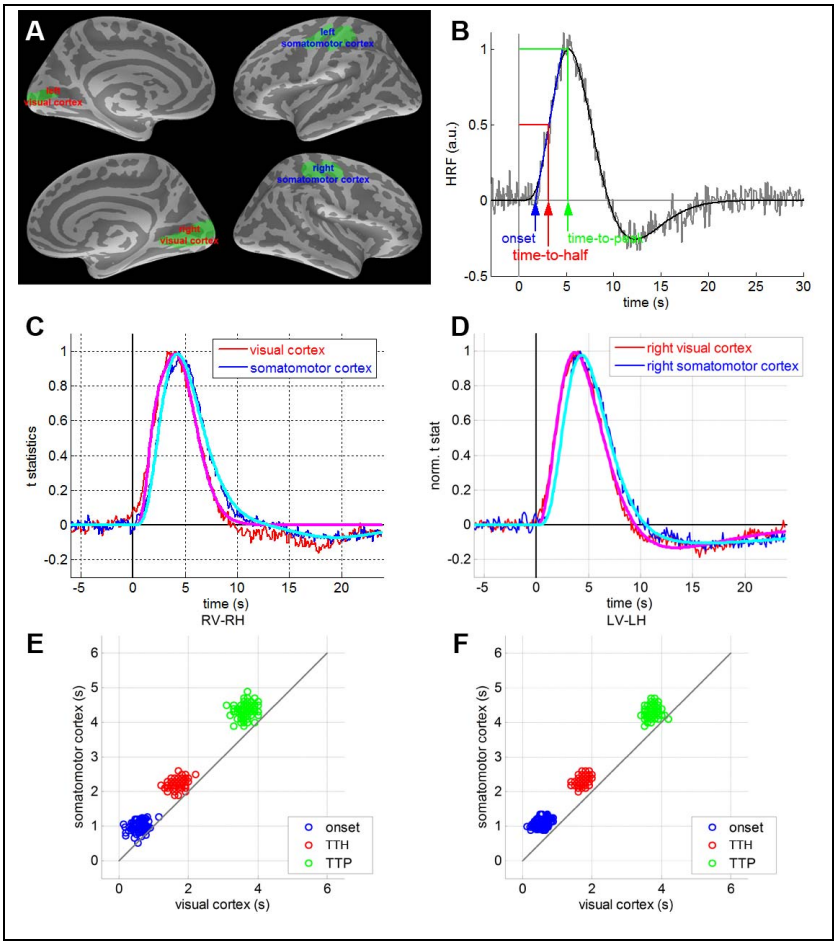
Accurate timing information is crucial for understanding the neuronal basis of human cognition. Unfortunately, despite its high spatial resolution and spatially uniform sensitivity, the prevailing human neuroimaging method BOLD-fMRIhas a poor temporal resolution. Novel techniques to increase the temporal sampling rate of BOLD-fMRI have been recently developed, but their validity has been limited because the regional neurovascular coupling can be so variable across human brain areas that it overwhelms the neuronal timing information. Here, we hypothesize that the regional neurovascular coupling timing variability can be averaged out in a group-level analysis. Using the ultra fast magnetic resonance inverse imaging (InI) [1] capable of 100 ms temporal resolution, 5 mm spatial resolution in cortex, and whole brain coverage, we demonstrate that the hemodynamic responses can elucidate the timing information including neuronal processing and neurovascular coupling in a group. The order of sequential activity in contralateral visual, posterior parietal, premotor, sensory, and motor cortices was found. Considering the two-choice reaction time task experiment as the extreme case of revealing sequential activity in brain, we conclude that the inter-regional neuronal timing can be extracted from fast hemodynamic response timing in a group level to infer sequence of activations across brain areas in tasks and cognition..

METHOD

21 subjects were recruited in this study with informed consent. The task is to use either left or right hand to press the button immediately perceiving a checkerboard flashing (500 ms duration, 100% contrast) at left or right visual hemifield. InI was measured from a 3T MRI scanner (Tim Trio, Siemens Medical Solutions, Erlangen, Germany) and a 32-channle head coil array. The imaging parameters were: TR=100 ms; TE=30 ms, Flip angle=30°. 32 trials of left hemifield stimulus and 32 trials of right hemifield stimulus were randomly presented over in each 4-minute run. Totally 4 runs were collected. The InI analysis was done by first using the general linear model (GLM) to deconvolve the hemodynamic responses using finite impulse basis functions [2]. Subsequent volumetric reconstruction was done by the k-space InI reconstruction [3]. We used a canonical model [4] to quantify the onset, time-to-half, and time-to-peak of the hemodynamic responses. Bootstrap was used to evalulate the groupl-level variability of the hemodynamic timing.

RESULTS

The figure at right summarized our results. The panel A shows the visual and motor cortex ROIs in both hemispheres. The canonical hemodynamc response and three indices: onset, time-to-half (TTH), and time-to-peak (TTP), were indicated in panel B. In the group-level data, we showed that the hemodynamic responses of the visual cortices indeed preceded motor cortical activity (Panels C and D). To evaluate the variance of timing, we used bootstrap with 100 iterations. The results for onset (blue circles), TTH (red circles), and TTP (green circles) timing indices in visual (x-axis) and sensorimotor (y-axis) cortices are shown in Panels E and F for right-visual (RV)-right hand (RH) and left visual (LV)- left hand (LH) conditions, respectively. Values above the 45° gray line indicate a later response in the sensorimotor cortex than in the visual cortex.



DISCUSSION

Here we show using a simple two-choice reaction time task, that the InI BOLD technique can resolve fine temporal delays across cortical areas. The hemodynamic activity in the visual cortex precedes that in the sensorimotor cortex. While this result is logical since it follows the intuitive causal relationship in a visuomotor task, the ability to resolve sequential brain activity using the commonly regarded “sluggish” BOLD-contrast hemodynamic response is still surprising, since the BOLD-contrast fMRI is a secondary measure of the neuronal activity, and it is a mixture of different biophysical mechanisms. The local vasculature varies across brain areas, which is a likely confounding factor when trying to infer inter-regional neuronal latency differences using hemodynamic responses. However, we hypothesize that the hemodynamic response includes a neuronally driven component and a neurovascular coupling component. The former may accurately reflect neuronal timing and is quite constant, while the latter involves uncertainty of CBV, CBF, and $CMRO_2$ transduction and is much more variable. The hemodynamic response looses accurate timing information as both components act together. However, the variability of hemodynamic responses can be suppressed if data from multiple repetitions and multiple subjects are averaged, since the contribution of the more variable neurovascular coupling component cancel out. Validation of the neuronal origin of such hemodynamic timing is under the way.

REFERENCES

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