# Corticothalamic Neuronal Interaction Revealed by Dynamic fMRI

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## Introduction

For a long time, the major function of lateral geniculate nucleus (LGN) has been seen as a relay for transferring visual information from the retina to visual cortex However, the number of backward projection fibers from the primary visual cortex (V1) to LGN is ten times larger than the forward projection ones[1]. This large-scale corticothalamic feedback connection makes it intriguing to assume that there must be a strong feedback control from V1 to LGN. It has been suggested that the key function of these modulatory inputs to LGN is to control the response mode, burst or tonic, of relay cells. When geniculate cells are in the tonic mode, retinogeniculate transmission is linear (i.e. LGN can faithfully transmit the visual information from the retina to the visual cortex), whereas when geniculate cells are in the burst mode, the transmission of visual information is not as effective. In this study, we investigated the transfer function at LGN and V1 using fMRI and a paired-stimulus paradigm[1]. The results indicate that there is additional suppression occurs in LGN compared to V1.

## Method

Cats were anesthetized with 0.9-1.2 isoflurane in a 70%$N_2O$/30%$O_2$ gas mixture. The fovea area of the cat retina was located with the aid of a fundus camera (Zeiss, Germany) ensuring that the cat eyes were focused on the visual stimulus. The head position of cat was fixed by a homebuilt head-holder with mouth-bar and ear-bars. Visual stimulation presented as short flashing light (10 ms duration per flash) was generated by a red LED checkerboard. All the fMRI studies were performed on a 9.4T horizontal magnet (Magnex Scientific, UK) interfaced with a Varian INOVA console (Varian Inc., Palo Alto, CA). The multi-slice $T_1$-weighted anatomical images were acquired first to ensure appropriate choice of slices located at the cat LGN and V1. Then, multi-slice gradient echo planar images (TR/TE = 252/14 ms, FOV = 5×5 $cm^2$, 780μm×780μm in-plane resolution, 1 mm slice thickness, 1 mm gap, 5 adjacent axial slices covering both LGN and V1) were applied for fMRI studies using an event-related paradigm design. Visual stimuli were displayed in the full visual field either singly or in pair separated by an inter-stimulus interval (ISI) ranging from 0ms to 4000ms. Successive trials of single or paired stimuli were separated by an inter-trial interval (ITI) of 20 seconds to allow the hemodynamic response to return to the baseline. During the baseline condition, cats were in uniform darkness. All stimuli were time locked to TR. For each single or paired task, 15 trials were repeated in one run. A total of 15 fMRI runs corresponding to 15 tasks (1 single and 14 paired tasks) were acquired in a pseudo-randomized order for each experiment. All BOLD time courses were normalized to the single-flash task.

## Results

Figure 1 shows the normalized BOLD amplitudes in the ROIs of LGN and V1 at all ISIs. At both ROIs, BOLD responses are significantly suppressed (i.e., below the dotted line) at short ISIs of < 1sec when the visual system is in the refractory period; when ISI gets longer, this suppression gradually becomes smaller. A very different behavior in BOLD response between V1 and LGN is that suppression in V1 activity disappears when ISI ≥ 1sec, whereas BOLD suppression in LGN sustains for even longer ISIs (e.g. 4sec). Furthermore, for short ISIs (< 1sec) when both V1 and LGN are in suppressed states, relative BOLD amplitudes in V1 are always larger than those in LGN. Taken together, the data suggest that there is additional suppression occurs in LGN compared to V1. Given the observation that the BOLD response to the second stimulus recovers to the same level of the response to the single stimulus in V1 at ISI > 1sec, this additional suppression in LGN must come from the inhibitory effect of corticothalamic feedback. To further validate this view, we measured the visual evoked potential in V1 to the same paradigm (shown in Figure 2). The normalized VEP amplitudes in response to paired stimuli at different ISIs have a very similar pattern with BOLD activity. This can be further confirmed from a high correlation between the normalized VEP and normalized BOLD amplitudes (Figure 3). Figure 4 and Figure 5 show the averaged time courses of BOLD signals at single- and paired-stimulus conditions in LGN and V1, respectively. In these figures, the BOLD time course at the single-stimulus condition was subtracted from those at paired-stimulus conditions.

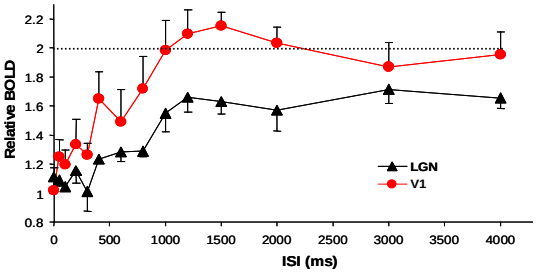


**Figure 1**. Normalized BOLD amplitude at LGN and V1 in response to a pair of visual stimuli at different ISIs.

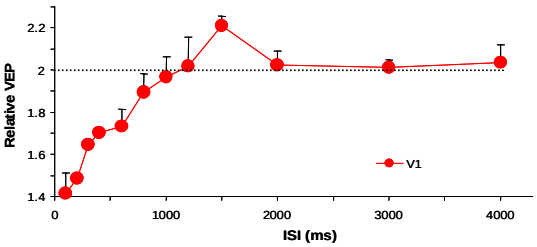


**Figure 2**. Normalized VEP amplitude at LGN and V1 in response to a pair of visual stimuli at different ISIs.

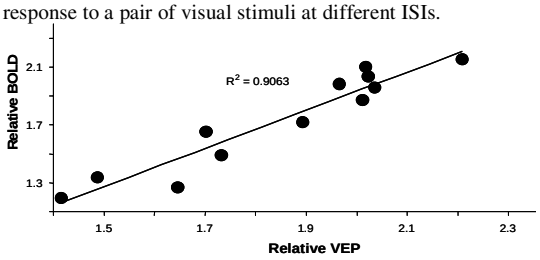


**Figure 3**. Correlation between amplitudes of normalized BOLD and normalized VEP signals at all ISIs.

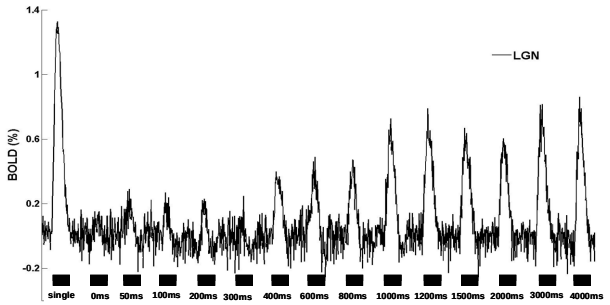


**Figure 4**.Averaged BOLD time courses at single- and paired-stimulus conditions in LGN

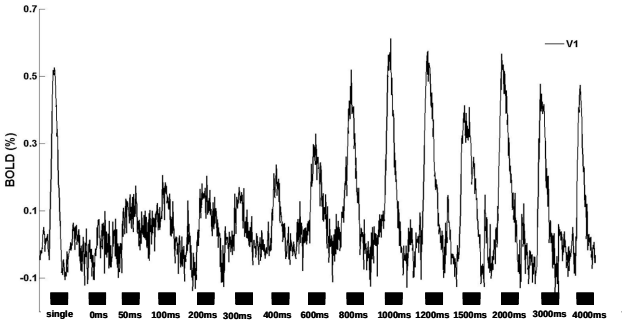


**Figure 5**.Averaged BOLD time courses at single- and paired-stimulus conditions in V1

## Conclusion

BOLD and VEP amplitudes at both V1 and LGN are significantly suppressed when the visual system is within the refractory period. However, there is additional reduction in LGN BOLD activity compared to V1 regardless of ISI. This reduction presumably is induced by the inhibitory effect of corticothalamic feedback. These results suggest that it is feasible of using fMRI to investigate neuronal interaction and neural networks.

## Acknowledgements

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## References:

1. *Murphy PC and Sillito AM, J Neurosci, 1996.*
2. *Ogawa, S. et al, PNAS, 2000.*