Increased metabolic activity, not preemptive blood flow increase, underlies attentional modulation in primary visual cortex

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Purpose: Determine whether attention affects the coupling of blood flow and oxygen metabolism changes with activation in human visual cortex.

Background: Attentional modulation of sensory information is important in normal perception and in cognitive impairment such as Alzheimer's disease. The physiological mechanisms of attentional enhancement in sensory cortices remain elusive. In particular, the robust attentional modulation of blood oxygenation-level dependent (BOLD) signal in primary visual cortex (V1) appears to be out of proportion to the modest increase in underlying neuronal firing. The essential problem with the interpretation of this phenomenon is the intrinsic complexity of the BOLD signal, with increased cerebral blood flow (CBF) and increased cerebral metabolic rate of oxygen ($CMRO_2$) driving the BOLD signal in opposite directions. Two possible explanations for the discrepancy between attentional modulations of BOLD vs. neural firing are: 1) A pure CBF increase driven in a preemptive fashion by top-down attentional mechanisms, with no increase in $CMRO_2$ and no relation to local neuronal firing [1]; or, 2) an increase of local synaptic activity, not reflected in the local firing rate, with a coupled change in CBF and $CMRO_2$. We tested these ideas by using combined CBF and BOLD measurements to estimate relative $CMRO_2$ changes to the same visual stimulus when the subject was attending and not attending to the stimulus.

Methods: A PICORE arterial spin labeling sequence (QUIPPS II[2], TR=2.5 s, TI_1 = 700 ms, TI_2 = 1500 ms, 20-cm oblique tag, 1-cm tag-slice gap) with a dual-echo gradient echo (GRE) spiral readout (TE_1=9.4 ms, TE_2=30ms, flip angle 90°, FOV 24 cm, matrix 64 × 64) was used to simultaneously acquire cerebral blood flow (CBF) and BOLD responses. Seven volunteers (age 24-35, 3 females) were instructed to fixate at the center of the screen and either perform a one-back memory task on digits appearing at fixation (control condition), or to monitor and report subtle contrast changes of a peripheral grating (attention condition). Stimuli (Fig 1) and task timing were identical in both attention and control runs. Separate localizer runs were used to identify voxels corresponding to the position of the peripheral stimuli. V1 borders were identified in a separate retinotopy session.

Results: The blood flow response in V1 to the peripheral stimulus showed significant attentional enhancement (Fig. 2, p<0.001). BOLD and R2* signals showed a similar pattern (p<0.01). The observed attentional BOLD increase was smaller than predicted for a pure flow increase (Fig 2., dashed curve), or even a proportional increase in $CMRO_2$ and blood flow (i.e., same ratio n=%ΔCBF/%Δ$CMRO_2$, Fig 2., thick curve). Instead, our results suggest that attention increased $CMRO_2$ by 5-10% (p<0.01) while slightly decreasing the blood-flow-metabolism coupling ratio n (Fig. 2, dotted curve). Similar results were obtained using two different models [3-4], and for a wide range of model parameters (Fig. 3).

Conclusions: Attentional enhancement of V1 activity involves an increase of both metabolic activity and blood flow, rather than a preemptive increase in blood flow alone. In addition, our results are consistent with the somewhat surprising picture that the ratio of CBF to $CMRO_2$ change is higher when the stimulus is unattended than when attended. For this reason, the relative magnitude of the BOLD responses (unattended/attended) might actually *underestimate* the underlying changes in CBF and $CMRO_2$ associated with attention.

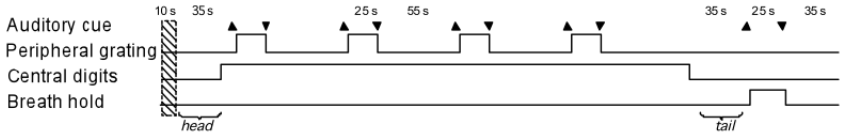

Figure 1. *Stimulation paradigm. Data collected during head and tail sections were used for normalization.*

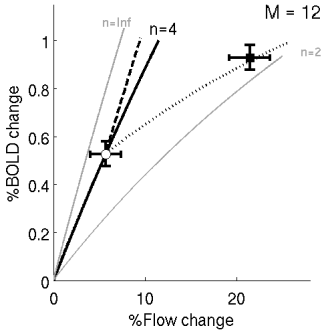

Figure 2*. V1 BOLD vs. blood flow for control (stimulus-driven activity, open circle) vs. attention (stimulus and top-down driven activity, filled square). The black solid curve depicts the BOLD signal when blood flow and metabolic activity increase proportionally with a fixed ratio (n=4). Thin gray curves denote different values of n for comparison. Additional increase in blood flow due to attention (beyond the unattended stimulus-driven activity in the control condition) without an increase in oxygen metabolism is represented by the dashed curve ($n_{attention}$ = infinity[†]). The dotted curve represents additional increase in oxygen metabolism accompanied by a smaller increase in blood flow ($n_{attention}$ = 1.75). M denotes the %BOLD scaling parameter in the Davis model[3].*

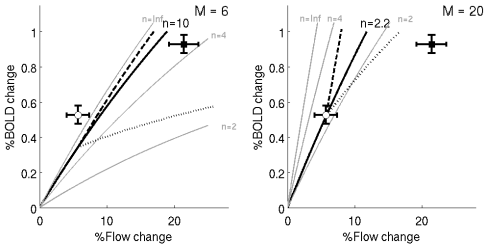

Figure 3. *Same as Fig. 2 but with different values for M. Note that the activity in the attention condition is on the right side of the dashed and black solid curves. Dotted curves represent $n_{attention}$ = 1.75.*

[†] $n_{attention}$=[%CBF(attention)-%CBF(control)] / [%$CMRO_2$(attention)-%$CMRO_2$(control)]

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