



Interpreting the signal

It is assumed that the changes in blood flow measured during functional brain-imaging studies reflect changes in neural activity. Two recent studies that directly measured blood flow, blood oxygenation and neural activity in animals suggest that this assumption must be reconsidered at least in some circumstances.

Devor *et al.* measured blood oxygenation (using spectral imaging of oxyhaemoglobin, deoxyhaemoglobin and total haemoglobin) and blood flow (using laser speckle imaging) in the somatosensory cortex of anaesthetized rats in response to forepaw stimulation. As expected, both measures increased in the contralateral cortex but decreased on the ipsilateral side. Surprisingly, however, the uptake of labelled 2-deoxyglucose, a measure of metabolic activity, in response to forepaw stimulation increased in both the contra- and the ipsilateral cortex. Moreover, electrophysiological recordings revealed a stimulus-evoked increase in spiking in both sides of the somatosensory cortex. Thus, in the ipsilateral

side, blood flow and oxygenation were decoupled from glucose consumption and neuronal activity, suggesting that energy consumption associated with neuronal activity does not necessarily determine blood flow.

Sirotnin and Das developed an optical imaging technique that allowed them to measure both blood volume and oxygenation in alert monkeys while simultaneously recording neural activity. Their experiments took place in a dark room, with a tiny point of light serving as a visual cue. The colour of this light point alternated at regular intervals; the colours indicated either a 'fixate' phase, in which the monkeys had to stare at the light point for several seconds in order to receive a juice reward, or a 'relax' phase. Importantly, the light point was visible at all times and the cortical area receiving input from the light point fell outside of the area that was being imaged; thus, any observed haemodynamic or neural-activity changes were assumed to be trial-related rather than visually driven.

Blood volume and oxygenation in the primary visual cortex (V1) showed robust periodic changes that followed the rhythm of the trial phases. There was no temporal correlation between these changes and multi-unit spiking and local field-potential measurements in the V1, whereas the haemodynamic signals correlated closely with these measurements in trials in which strong visual stimuli, such as coloured gratings, were used in addition to the light point. Thus, stimulus-induced haemodynamic signals reflected neuronal activity, but the fluctuating, trial-related haemodynamic signals observed in this study did not.

What then underlied the fluctuating haemodynamic signals? The authors found that the signals were directly linked to the timing of the task trials: changing the duration of the trials resulted in an equivalent change in the timing of the haemodynamic signal. Moreover, the signal changes began before the onset of a trial, indicating that they were not triggered by the colour change of the light point; rather, they might have reflected anticipatory responses.

These studies will urge a rethink of the interpretation of functional MRI signals as they show that an increased haemodynamic signal does not always reflect increased neural activity. Sirotnin and Das showed that, depending on the type of stimulus used, the signal might be anticipatory rather than responsive, whereas Devor *et al.* showed that neural activity might in some cases result in vasoconstriction rather than dilation, and thus in reduced blood flow.

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ORIGINAL RESEARCH PAPERS Devor, A. *et al.* Stimulus-induced changes in blood flow and 2-deoxyglucose uptake dissociate in ipsilateral somatosensory cortex. *J. Neurosci.* **28**, 14347–14357 (2008) | Sirotnin, Y. B. & Das, A. Anticipatory haemodynamic signals in sensory cortex not predicted by local neuronal activity. *Nature* **457**, 475–479 (2009)