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FUNCTIONAL IMAGING

Peeling back the layers of BOLD

Functional MRI (fMRI) is one of the most important techniques in neuroscience today. It uses the BOLD (blood-oxygenation-level-dependent) signal to make inferences about neural activity in the brain, but the detailed relationships between BOLD signal, neural activity and blood flow in the brain are still unclear. Now, Goense *et al.* show that positive and negative BOLD responses in the cortex arise from different, layer-specific haemodynamic processes.

The authors used ultra-high-resolution fMRI to detect BOLD contrast, cerebral blood volume and cerebral blood flow in specific cortical layers. The brains of monkeys were imaged while they viewed a rotating visual stimulus consisting of a central circle surrounded by a gap and then a checked ring. In the visual cortex, this pattern creates a positive BOLD response in areas that represent the central circle and checked ring, with a negative BOLD response in areas representing the space between the two.

Their findings were intriguing. First, as expected, they found that both blood volume and blood flow increased in areas of cortex that showed a positive BOLD response. However, in adjacent areas that showed a negative BOLD response, blood flow decreased but blood volume increased — a result that is somewhat hard to explain.

When the authors looked at layer-specific responses, the results raised even more questions. When there was a positive BOLD response, both blood flow and blood volume increased most strongly in the central layers of cortex, possibly because these layers are the most metabolically active and have the densest microvasculature.

However, the areas of cortex that showed a negative BOLD response revealed a different pattern. Here, blood volume also increased selectively in the central layers of cortex, but the decrease in blood flow occurred only in the more superficial layers. As Bandettini discusses in an accompanying

article, it is not clear why this should be so. One potential explanation for the increase in blood volume in the central layers relates to a possible increase in inhibitory neuronal activity in this region. It is also possible that these changes arise from autoregulatory or redistribution effects in the vasculature, which Bandettini calls ‘plumbing’ effects.

Much more work is needed to make sense of these intriguing findings and to clarify the nature of the neurovascular coupling that gives rise to the negative BOLD signal. For now, these results and the techniques behind them raise the tantalizing possibility of using fMRI to investigate layer-specific neural processing in the human cortex.

Rachel Jones

“ Now, Goense *et al.* show that positive and negative BOLD responses arise from different, layer-specific haemodynamic processes. ”

ORIGINAL RESEARCH PAPER Goense, J., Merkle, H. & Logothetis, N. K. High-resolution fMRI reveals laminar differences in neurovascular coupling between positive and negative BOLD responses. *Neuron* **76**, 629–639 (2012)
FURTHER READING Bandettini, P. A. The BOLD plot thickens: sign- and layer-dependent hemodynamic changes with activation. *Neuron* **76**, 468–469 (2012)