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Functional magnetic resonance imaging (fMRI) is an increasingly popular way to probe the activity of the human brain. The key to its success is the blood-oxygen-level-dependent (BOLD) signal, which, as its name indicates, measures not neural activity but changes in the haemodynamic properties of the cerebral vasculature. As a result, fMRI is an indirect measure of neural activity that relies on neurovascular coupling — the ability of changes in neural activity to alter vascular properties.

As D'Esposito and colleagues point out in this issue (p. 863), this raises potential problems. Neurovascular coupling can be altered in a number of conditions and also in normal ageing. So if we wish to compare, for example, neural activity in aged individuals with that in younger people, how are we to distinguish between differences in neural activity and differences in neurovascular coupling?

One important aspect is recruitment of subjects. It would be counter-productive to exclude the aged or those with medical conditions that might affect neurovascular coupling from all fMRI studies; but careful screening for such conditions could be undertaken. Another consideration is experimental design. Rather than comparing the performances of two groups, such as older versus younger subjects, on one task, it can be more informative to look at such group-by-task interactions.

Perhaps most importantly, we should continue in our efforts to understand more about neurovascular coupling itself, and how the BOLD signal is generated. By elucidating the chain of events that leads from alterations in neural activity to changes measured by fMRI, we should be able to improve our interpretation of fMRI studies in all subjects — not just the aged or those with altered neurovascular coupling.