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Discussion forum

Dissociating learning-induced changes in fMRI signal from structural modifications: A comment on Dorjee and Bowers (2011)

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In a recent commentary, [Dorjee and Bowers \(this issue\)](#) raise several issues concerning the interpretation of functional MRI (fMRI) studies that examine learning in general and perceptual learning in particular. The authors rightly criticize an implicit assumption that differences in blood oxygen level dependent (BOLD) levels before and after training can be used to exhaustively determine the brain areas where learning leads to structural changes associated with information retention. However, there are several problematic aspects in Dorjee and Bowers' line of reasoning. Here we would like to underline the importance of the issues raised by Dorjee and Bowers and at the same time prevent misunderstandings about the actual scope of the problem.

One problem with the argument of [Dorjee and Bowers \(this issue\)](#) is their claim that learning studies using fMRI usually assume BOLD-signal changes to reflect learning-related structural modifications. This statement is probably too general. Similarly, the authors' distinction between learning studies and research on what they call "on-line processing" does not constitute a valid simplification, because any form of learning that is behaviorally relevant will affect neural structure as well as future on-line processing. Finally, an isolated discussion of retention aspects of learning may be counter-productive for assessing the relevance of BOLD-fMRI to the study of learning. Both human and animal research suggests that learning involves several steps, each characterized by dynamic interactions between many brain regions, including

areas specialized in sensory processing, executive functions, and memory storage, before the new skill or information stabilizes ([Diekelmann and Born, 2010](#); [Henson and Gagnepain, 2010](#); [Nader and Hardt, 2009](#); [Wang and Morris, 2010](#); [Winocur and Moscovitch, 2011](#)). By ignoring these multiple dimensions of learning, [Dorjee and Bowers \(this issue\)](#) run the risk of fostering misunderstandings concerning the contribution of fMRI to the study of learning processes in general.

All of these issues are linked to our main concern with [Dorjee and Bowers' \(this issue\)](#) commentary, which relates to their use of the term "locus of learning". Our understanding is that this refers to learning-induced structural modifications at the cellular and/or systems levels that are relatively stable over time. When used in this sense, an important unit of analysis for studying the locus of learning must be the synapse, where a wide range of structural and functional modifications support memory formation (e.g., [Redondo and Morris, 2011](#)). While our knowledge concerning the origins of the BOLD signal remains incomplete, current models suggest that its generation is closely linked to synaptic input to and synaptic activity within a given brain region ([Logothetis, 2002, 2008](#)). Assuming that learning-induced structural modifications at the synaptic level entail corresponding functional changes in an important fraction of cases, BOLD-fMRI should in fact be able to provide insights concerning the locus of learning as defined above. Specifically, the most parsimonious

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explanation for long-lasting BOLD-signal changes following learning is that they are caused by persistent changes in local synaptic activity; and that these persistent changes are intimately linked to structural changes at the synaptic level, without which learning effects cannot be stabilized (Redondo and Morris, 2011). Consequently, the hypothetical scenarios invoked by Dorjee and Bowers (this issue) to explain different patterns of BOLD-signal changes in visual cortex appear physiologically implausible, since they (models c–f) assume long-lasting changes in BOLD activity in the absence of any structural modifications at the synaptic level.

As an example, consider the study by Yotsumoto et al. (2008) cited by Dorjee and Bowers (this issue). Training on a standard perceptual learning task led to significant BOLD-signal changes selectively in V1. Importantly, these functional changes remained stable over several days. According to Dorjee and Bowers (this issue), this result could be explained by learning-related structural changes elsewhere in the brain impinging on V1, without any structural modifications in V1 itself. In light of the known characteristics of the BOLD signal on the one hand and synaptic plasticity on the other, this interpretation of Yotsumoto et al.'s (2008) data seems far-fetched and would require an empirical demonstration of a prevailing dissociation between BOLD-signal changes and structural modifications.

The preceding points do not invalidate Dorjee and Bowers' (this issue) claim that, based on our current knowledge, there is no direct way of linking BOLD-signal changes to learning-induced structural modifications. Thus, we agree with the authors' recommendation that BOLD studies should clearly distinguish between findings of functional modifications following learning on the one hand, and hypotheses about underlying structural changes on the other. However, we believe that existing research has demonstrated sufficiently strong links between BOLD-signal changes and the neural mechanisms underlying learning: first, because these mechanisms are not restricted to information retention, but include processes related to encoding and recall to which the BOLD signal is highly sensitive; and second, because findings of locally specific BOLD-signal changes can contribute important – albeit indirect – insights into the likely involvement of brain

regions in information retention. Considering the limitations of alternative methods as reviewed by Dorjee and Bowers (this issue), we believe that such indirect insights should not simply be discarded. More generally, in the context of multiple less-than-perfect techniques, the most promising way forward to us seems to be an attempt at their integration, both in methodological and theoretical terms.

In summary, Dorjee and Bowers (this issue) are correct to draw our attention to some limitations in the interpretation of fMRI studies examining learning processes. However, their critique should not be taken as evidence against the usefulness of BOLD-fMRI in the study of learning in general.

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