

## fMRI adaptation revisited

Jonas Larsson<sup>a</sup>  
Samuel G. Solomon<sup>b</sup>  
Adam Kohn<sup>c-e</sup>

- a. Department of Psychology, Royal Holloway, University of London, Egham UK
- b. Department of Experimental Psychology, University College London, London UK
- c. Dominick Purpura Department of Neuroscience, Albert Einstein College of Medicine, Bronx NY USA
- d. Department of Ophthalmology and Visual Sciences, Albert Einstein College of Medicine, Bronx NY USA
- e. Department of Systems and Computational Biology, Albert Einstein College of Medicine, Bronx NY USA

email: Jonas Larsson [jonas.larsson@rhul.ac.uk]  
Samuel Solomon [s.solomon@ucl.ac.uk]  
Adam Kohn [adam.kohn@einstein.yu.edu]

Contact: Adam Kohn  
Dominick Purpura Department of Neuroscience  
1410 Pelham Parkway S, Rm 822  
Bronx NY 10461  
Tel: 718-430-2417  
Fax: 718-430-8821

Jonas Larsson  
Department of Psychology  
Royal Holloway University of London  
Egham Hill  
Egham, Surrey  
TW20 0EX UK  
Tel: +44-7184-414061

## Abstract

1 Adaptation has been widely used in functional magnetic imaging (fMRI) studies to infer  
2 neuronal response properties in human cortex. fMRI adaptation has been criticised  
3 because of the complex relationship between fMRI adaptation effects and the multiple  
4 neuronal effects that could underlie them. Many of the longstanding concerns about fMRI  
5 adaptation have received empirical support from neurophysiological studies over the last  
6 decade. We review these studies here, and also consider neuroimaging studies that have  
7 investigated how fMRI adaptation effects are influenced by high-level perceptual  
8 processes. The results of these studies further emphasize the need to interpret fMRI  
9 adaptation results with caution, but they also provide helpful guidance for more accurate  
10 interpretation and better experimental design. In addition, we argue that rather than being  
11 used as a proxy for measurements of neuronal stimulus selectivity, fMRI adaptation may  
12 be most useful for studying population-level adaptation effects across cortical processing  
13 hierarchies.  
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18 **Key words:** function imaging, adaptation, repetition suppression, surround suppression  
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## Introduction

1 Adaptation has long been used in psychophysics and neuroscience to probe the nervous  
2 system. The usefulness of adaptation in understanding brain function is perhaps best  
3 illustrated by its revealing orientation-tuned mechanisms in the human brain (Blakemore &  
4 Campbell, 1969; Blakemore & Hogue, 1972). In the early 2000s adaptation was embraced  
5 by the neuroimaging community with the use of “fMRI adaptation” to infer neuronal  
6 response properties in human brain areas in a wide variety of sensory stimuli and cognitive  
7 tasks (Grill-Spector & Malach, 2001). The basic logic of the approach is straightforward.  
8 Adaptation causes weakened responses to repeated or prolonged stimuli. If altering the  
9 properties of a stimulus causes fMRI responses to recover, this is evidence that a distinct  
10 population of neurons has been recruited by the stimulus manipulation. Equivalently,  
11 stimulus-specific adaptation effects on fMRI responses indicate the presence of neurons  
12 that are selective along the dimension of stimulus manipulation.  
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17 Despite its widespread use, fMRI adaptation has been criticized for the potentially complex  
18 relationship between neuronal and BOLD (blood oxygenation level dependent) adaptation  
19 effects, which can preclude accurate inferences about neuronal tuning. Perhaps partly as a  
20 result of this critique, fMRI adaptation has fallen out of favour and been largely superseded  
21 by multivariate pattern analysis (MVPA) as the method of choice for inferring neuronal  
22 response properties (Haxby et al., 2001; Kamitani & Tong, 2005). MVPA methods,  
23 however, have their own issues of interpretation (see Op De Beeck, 2010, for a review).  
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27 Here we revisit fMRI adaptation as an experimental approach, motivated by several new  
28 findings. First, there has been progress in understanding the neurophysiological effects of  
29 adaptation, with results that help clarify the interpretation of BOLD measurements.  
30 Second, whereas most of the original critique of fMRI adaptation focused on confounds  
31 arising from the underlying “low-level” neurophysiological mechanisms, recent work has  
32 shown that fMRI adaptation effects can also be influenced by high-level processes such as  
33 attention and expectation. We close by suggesting ways in which fMRI adaptation may still  
34 be useful for understanding perceptual and cognitive function.  
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### What are the concerns with fMRI adaptation?

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40 The pitfalls of using fMRI adaptation effects to infer neuronal response properties were  
41 reviewed by Krekelberg, Boynton, and van Wezel (2006); Bartels, Logothetis, and  
42 Moutoussis (2008); and Grill-Spector, Henson, and Martin (2006). Briefly, these  
43 perspectives identified three key issues. First, adaptation effects may involve a range of  
44 effects at the neuronal level, including fatigue, sharpened tuning, response facilitation, and  
45 altered response dynamics. Depending on the relative importance of these neuronal  
46 effects in a given experimental paradigm, one may see a range of behaviours in the BOLD  
47 response, making it difficult to infer accurately the underlying neuronal selectivity. Second,  
48 it is not clear when adaptation effects reflect changes in the imaged brain area, and when  
49 they reflect effects inherited from upstream areas. That is, adaptation can alter the signals  
50 sent from early sensory areas to subsequent processing stages, thereby altering the  
51 downstream responses. Interpreting adaptation effects as evidence of neuronal response  
52 selectivity in the imaged area may therefore be misleading. Third, adaptation effects in  
53 fMRI BOLD signal may reflect changes in neurovascular coupling rather than in neuronal  
54 responsivity. In the following, we focus on new experimental findings that allow insight into  
55 these issues.  
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## *Tuning changes*

1 Adaptation is usually thought to reduce neural activity, but there is clear evidence that it  
2 can also enhance responses. Numerous studies have shown that adaptation with a  
3 stimulus matched to the classical receptive field of a neuron causes a stimulus-specific  
4 loss of responsivity. As a result, neurons driven with their preferred stimulus become less  
5 responsive, and the tuning of neurons with slightly offset preferences is repelled away from  
6 the adapter (Muller, Metha, Krauskopf, & Lennie, 1999; Dragoi, Sharma, & Sur, 2000). By  
7 contrast, adaptation effects induced by stimuli larger than the receptive field can lead to a  
8 stimulus-specific reduction in surround suppression, and thus to disinhibition and response  
9 enhancement (Webb, Dhruv, Solomon, Tailby, & Lennie, 2005; Camp, Tailby, & Solomon,  
10 2009; Wissig & Kohn, 2012). Because the adaptation-induced weakening of surround  
11 suppression is stimulus specific, it can also alter neuronal tuning—causing tuning to shift  
12 toward the adapter rather than be repelled from it (Kohn & Movshon, 2004; Patterson,  
13 Wissig, & Kohn, 2013). Thus, the distinct effects of adaptation on tuning considered by  
14 Grill-Spector, Henson, and Martin (2006) — suppression, sharpening and facilitation —  
15 can in fact be expressed in the same neurons, and which effects are observed will depend  
16 on the balance of excitatory and suppressive inputs that are recruited by the adapter and  
17 test stimuli (see Solomon & Kohn, 2014 for review).  
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23 fMRI adaptation relies on the logic that stronger adaptation effects—that is, a greater  
24 reduction in response to a stimulus matched to the adapter than to an altered test  
25 stimulus—indicate greater neuronal selectivity for the manipulated stimulus dimension.  
26 Often, fMRI adaptation studies have reported a gradual increase in adaptation magnitude  
27 in extrastriate visual areas compared to primary visual cortex (V1; e.g., Boynton & Finney,  
28 2003; Fang, Murray, Kersten, & He, 2005; Larsson, Landy, & Heeger, 2006; Montaser-  
29 Kouhsari, Landy, Heeger, & Larsson, 2007; Larsson, Heeger, & Landy, 2010), suggesting  
30 greater selectivity in extrastriate cortex. However, these new neurophysiological findings  
31 offer an alternative explanation. Standard fMRI paradigms normally use relatively large  
32 stimuli, and neurons in higher-stages of cortical processing have larger spatial receptive  
33 fields. A large stimulus recruits progressively more excitation, and progressively less  
34 surround suppression, in higher stages of visual processing. Thus, one would expect a  
35 stronger loss of responsivity in higher cortex, where adaptation effects on surround  
36 suppression is reduced, even without a difference in underlying neuronal selectivity.  
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41 However, in many cases stronger adaptation effects in higher extrastriate areas have been  
42 shown to be consistent with known differences in response properties between areas. For  
43 example, stronger and more size-invariant adaptation to objects in ventral stream areas  
44 than in V1 corresponds to differences in neuronal stimulus selectivity measured by direct  
45 recording techniques (e.g. Sawamura, Orban, & Vogels, 2006; Kovács, Zimmer, Harza, &  
46 Vidnyánszky, 2007; Kovács, Cziraki, Vidnyánszky, Schweinberger, & Greenlee, 2008).  
47 Inter-areal differences in susceptibility to adaptation to motion-defined boundaries  
48 measured with fMRI match differences in neuronal selectivity for such boundaries between  
49 macaque visual areas (Larsson, Heeger, & Landy, 2010). Differences in susceptibility to  
50 adaptation across areas may therefore reflect a combination of differential disinhibition  
51 across areas, the inheritance in higher areas of effects induced in lower areas (discussed  
52 below), as well as genuine differences in neuronal stimulus selectivity. Disambiguating  
53 these different contributions is non-trivial.  
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58 A diagnostic way to control for the confounding influence of surround suppression on fMRI  
59 adaptation effects would be to measure how the magnitude of adaptation effects depends  
60 on stimulus size; larger stimuli would be predicted to induce stronger weakening of  
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1 suppressive surrounds, leading to a reduction in adaptation with increasing stimulus size.  
2 To our knowledge, no study has yet systematically addressed the effect of stimulus size on  
3 fMRI BOLD adaptation effects. Recent fMRI work does, however, provide evidence for  
4 both suppressive and facilitatory adaptation effects in the BOLD signal, consistent with  
5 neurophysiological data. Larsson and Harrison (2015) found that adaptation effects for  
6 small patches of gratings depend on the spatial relationship between the adapter and  
7 subsequent test stimuli. When the adapter was in the same location as the test, BOLD  
8 responses in V1 decreased following adaptation (response suppression). When the  
9 adapter was displaced relative to the test, responses in V1 instead increased (facilitation),  
10 consistent with adaptation of suppressive surrounds in human visual cortex.

11 Recent neurophysiological studies thus highlight the interplay of excitation and  
12 suppression in shaping the effects of adaptation on visual neurons. Adaptation effects in  
13 fMRI BOLD measurements are likely to reflect changes in the sensitivity of classical  
14 receptive field, suppressive mechanisms, or both, depending on the configuration of the  
15 adapting and test stimuli. This interplay is likely to be a significant source of variance in  
16 previous fMRI adaptation measurements. These observations also help provide guidance  
17 for interpretation of fMRI adaptation effects, particularly if the experimental design includes  
18 parametric variations of stimulus size. Finally, the neurophysiological work provides  
19 testable predictions about population adaptation effects measured by fMRI (see Box).  
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### 23 *Inherited adaptation*

24 Recordings from neurons in the visual pathway indicate that adaptation effects that  
25 emerge at early stages of visual processing propagate to downstream areas. For example,  
26 spatial adaptation in V1 may reflect convergence of adaptation effects at the level of LGN  
27 (Dhruv & Carandini, 2014). Similarly, adaptation effects in extrastriate area MT seem to be  
28 inherited from early visual cortex, at least when the stimuli are composed of oriented  
29 contours (Kohn & Movshon, 2003, Patterson, Duijnhouwer, Wissig, Krekelberg, & Kohn,  
30 2014). Under other stimulus conditions, however, adaptation effects may arise in area MT  
31 itself (Priebe, Churchland, & Lisberger, 2002). Thus, neural recordings have shown that  
32 adaptation effects can propagate through inter-areal circuits, causing robust effects in  
33 downstream areas.  
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40 Converging evidence also suggests that inherited adaptation effects can influence  
41 downstream processing in unexpected ways. In behavioural studies, adaptation to low-  
42 level cues (e.g. orientation) can distort high-level face and shape perception (Xu, Dayan,  
43 Lipkin, & Qian, 2008; Xu, Liu, Dayan, & Qian, 2012; Dickinson & Badcock, 2012;  
44 Dickinson, Mighall, Almeida, Bell, & Badcock, 2013). In single neurons, adaptation can  
45 alter selectivity for stimulus features other than those present in the adapter, for the simple  
46 reason that complex selectivity is built from the representation of simpler properties  
47 (Patterson, Wissig, & Kohn, 2014). Adaptation effects in low-level representations can thus  
48 derail downstream selectivity for distinct features. Consistent with this, adaptation effects  
49 may even induce response selectivity where there was none previously: for example,  
50 direction-selective responses in V4 may emerge following motion adaptation (Tolias,  
51 Keliris, Smirkanis, & Logothetis, 2005; but see also Ferrera & Maunsell, 2005). Moreover,  
52 the effects of adaptation to low-level stimulus features (e.g., local contrast boundaries) in  
53 early visual areas may propagate to high-level areas, resulting in a much higher degree of  
54 stimulus specificity than expected from the unadapted tuning in these areas (Sawamura,  
55 Orban, & Vogels, 2006).  
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61 Many fMRI studies have also found evidence of widespread adaptation to low-level  
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1 features across extrastriate cortical areas, consistent with inheritance of adaptation effects  
2 from V1 (e.g. Murray, Olman, Kersten, 2006; Larsson, Landy, & Heeger, 2006). Three lines  
3 of evidence suggest that the bulk of extrastriate adaptation to such simple features  
4 originates in V1: first, the tuning of motion adaptation in area MT is very similar to that in  
5 V1 (Lee & Lee, 2012), and contrast adaptation in V2 and V3 (but not V4) is nearly identical  
6 to that in V1 (Gardner et al., 2005); second, the spatial specificity (i.e. tuning) of direction-  
7 selective and orientation-selective adaptation in extrastriate areas is identical to that in V1  
8 (Larsson & Harrison 2015); third, adaptation to motion induces strong motion-selective  
9 responses in areas that normally lack such selectivity, including area V4 (Larsson &  
10 Harrison 2015).

11 This evidence for propagation of adaptation effects from lower (upstream) to higher  
12 (downstream) areas implies that unless the relative contributions of inherited and intrinsic  
13 adaptation can be dissociated, fMRI adaptation effects cannot be interpreted as evidence  
14 of neuronal tuning in the imaged areas. Fortunately, single-unit (Priebe, Churchland, &  
15 Lisberger, 2002, Kohn & Movshon, 2003) and fMRI studies (Larsson & Harrison 2015)  
16 offer a way to dissect the influence of inherited and intrinsic components: by measuring the  
17 spatial specificity of adaptation effects and comparing these to the receptive field sizes of  
18 the imaged areas. If displacing the test stimulus from the adapter results in a recovery of  
19 the fMRI response, then it suggests that the adaptation effect was induced in an area  
20 where the receptive field size is smaller than the distance of the displacement. Using new  
21 tools to estimate population receptive field sizes from fMRI measurements (Larsson,  
22 Landy, & Heeger, 2006; Dumoulin & Wandell 2008) and an understanding that shifting the  
23 location of a test stimulus may enhance responses (Larsson & Harrison, 2015), one can  
24 compare the spatial extent of adaptation effects to estimates of receptive field size in  
25 multiple visual areas, potentially allowing localization of fMRI adaptation effects to specific  
26 areas.  
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### 32 *Missing links between the BOLD signal and single-neuron adaptation effects*

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35 Interpreting adaptation effects in fMRI BOLD response requires understanding if  
36 adaptation changes the relationship between neural and vascular activity (neurovascular  
37 coupling). There is a lack of direct evidence for adaptation-induced changes in  
38 neurovascular coupling, but a recent study by Moradi and Buxton (2013) reported that  
39 adaptation changes the coupling between local oxygen metabolism (CMRO<sub>2</sub>, a measure of  
40 energy consumption thought to closely parallel local neural activity) and blood flow, such  
41 that BOLD measurements underestimate the magnitude of adaptation effects. Specifically,  
42 CMRO<sub>2</sub> showed sub-linear summation when doubling the duration of a stimulus block  
43 (consistent with adaptation), whereas BOLD responses increased linearly with stimulus  
44 duration (consistent with no adaptation). Little is known about the effects of adaptation on  
45 neurovascular coupling at finer spatial or temporal scales and no study to date has directly  
46 compared neural activity and blood flow during adaptation. More research is needed, both  
47 to understand the mechanisms linking neural activity, metabolic demand, and BOLD  
48 signals, and in particular how these mechanisms are affected by adaptation.  
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53 A closely related issue is that fMRI measurements are inherently population-based,  
54 whereas most neurophysiological work has concentrated on individual neurons. As a  
55 result, we have a limited understanding of how adaptation affects population neural  
56 responses. Several recent studies have compared adaptation effects in single units and  
57 local field potentials (LFP), an indirect measure of neuronal population activity. Some of  
58 these studies have found population-level effects consistent with those observed in single  
59 neurons (De Baene & Vogels 2010; Kaliukhovich & Vogels 2012; von der Behrens,  
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1 Bauerle, Kossel, & Gaese, 2009), but others report conditions where this is not the case  
2 (Jia, Smith, & Kohn, 2011). Notably, for long interstimulus-intervals (ISIs) adaptation  
3 appears to reduce both the temporal coordination and amplitude of neural population  
4 responses (Kaliukhovich & Vogels 2012), whereas for short ISIs coordination can increase  
5 even though spiking activity decreases following adaptation (Hansen & Dragoi 2011; see  
6 Gotts, Chow, & Martin, 2012 for review). Since hemodynamic responses appear to be  
7 related to the coordination of neuronal activity as well as its amplitude (Niessing et al.,  
8 2005), adaptation-induced changes in BOLD may reflect changes in either network  
9 coordination or firing rates, or both.

10 In summary, it is clear that linking BOLD measurements to neuronal spiking activity is not  
11 trivial. This is not specific to fMRI adaptation, and reflects the greater issues of inferring  
12 single-unit properties from population measurements and of understanding to what extent  
13 BOLD signals are driven primarily by synaptic activity (see Logothetis & Wandell, 2004 for  
14 a review) or spiking output (Lima, Cardoso, Sirotnin, & Das, 2014). This difficulty need not  
15 preclude the use of fMRI to measure adaptation effects, but does point to a need for better  
16 understanding of the relationship between neuronal adaptation effects and adaptation  
17 effects as measured by BOLD, ideally by simultaneous measurements of neuronal and  
18 hemodynamic responses.

### 22 **Low-level vs high-level effects of adaptation: attention and expectation**

23 The neurophysiological evidence reviewed above suggests that fMRI adaptation effects  
24 will be influenced by multiple low-level (“bottom-up”) processing mechanisms. Recent  
25 neuroimaging work suggests that additional, high-level (“top-down”) effects, can also  
26 modulate fMRI adaptation effects. For instance, it is well established that the deployment  
27 of attention can confound the interpretation of fMRI adaptation effects, as highlighted in the  
28 controversy over one of the first applications of adaptation to fMRI: the demonstration of  
29 motion aftereffects (MAE) in human MT+ complex by Tootell et al (1998). The adaptation-  
30 induced change in BOLD, interpreted by Tootell et al. as a neural correlate of the MAE,  
31 was subsequently shown to depend on attention, in that the effect disappeared when  
32 attention was diverted from the adapting and test stimuli (Huk, Ress, & Heeger, 2001). To  
33 minimize such attentional confounds, most subsequent fMRI adaptation studies have used  
34 attention-demanding tasks to maintain a constant level of attention across conditions.

35 The use of an attention-demanding task can be problematic, however, if the task involves  
36 attending to the adapter or test stimuli. Recent studies suggest that under such  
37 circumstances, novelty or “expectation” effects can significantly influence fMRI BOLD  
38 adaptation effects. For example, in work aimed at understanding the source of “repetition  
39 suppression” (a reduction in responses to repeated presentations of stimuli), Summerfield,  
40 Trittschuh, Monti, Mesulam, and Egner (2008) studied the effects of repetitive presentation  
41 of face stimuli on BOLD signals in the fusiform face area (FFA). BOLD signals were larger  
42 when the stimulus was less frequent (i.e. unexpected), than when they were more  
43 frequent. Summerfield et al. concluded that repetition effects were more likely to reflect  
44 stimulus expectation, rather than adaptation. Crucially, however, the study required  
45 subjects to attend to the adapting stimuli. Larsson and Smith (2012) replicated the results  
46 of Summerfield et al., but showed that the effect of expectation disappeared when subjects  
47 performed a demanding task at fixation, diverting attention from the adapting stimuli.  
48 Nonetheless, repetition suppression was still observed when attention was diverted,  
49 consistent with neuronal adaptation effects.

50 Nevertheless, it remains possible that expectation influences fMRI adaptation effects even

1 without a confounding influence of attention. For example, Gardner et al. (2005) found that  
2 the effects of contrast adaptation on BOLD responses in V4 more closely reflected  
3 stimulus novelty (or expectation) rather than contrast changes, even though a demanding  
4 task at fixation was used to divert attention from the adapting stimuli (notably, in V1-V3  
5 there was no effect of novelty). Moreover, expectation effects in EEG measurements  
6 (known as mismatch negativity) have been found even when attention is diverted or  
7 subjects unconscious (see Stefanics, Kremlacek, & Czigler, 2014 for a review).

8 Further studies will be necessary to determine how task manipulations (e.g. varying the  
9 relative probability of stimulus repetitions vs. non-repetitions) can influence and control for  
10 top-down effects, and how to dissociate between bottom-up and top-down contributions to  
11 fMRI adaptation effects. It is also not clear to what extent top-down effects due to attention  
12 and/or expectation might directly interact with adaptation, for example by sharpening the  
13 tuning of neuronal responses (Kok, Jehee, & de Lange, 2012). Further complicating  
14 matters is the fact that single-unit recordings from non-human primates have found no  
15 evidence for expectation effects in neuronal spiking responses (Kaliukhovich & Vogels  
16 2011; Fishman & Steinschneider, 2012; Kaliukhovich & Vogels, 2014), raising the question  
17 of whether fMRI is particularly susceptible to such effects or, alternatively, whether  
18 expectation effects are unique to the human cortex. fMRI studies in non-human primates  
19 and other model species may provide a way to resolve this issue.

## 24 **What can be done?**

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26 The original critiques fMRI adaptation focused on the difficulty of reliably relating BOLD  
27 effects to underlying neuronal response properties. Work over the last decade has  
28 reinforced these concerns. Many of the initial confounds have been confirmed by  
29 experimental studies, and new observations further complicate interpretation of fMRI  
30 adaptation effects.  
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34 Nevertheless, we believe it is a mistake to conclude that measuring adaptation effects with  
35 fMRI has no purpose. fMRI adaptation as a measure of neuronal selectivity suffers from  
36 the limitations outlined above, but (at least compared to MVPA techniques) the approach  
37 does have the virtue of directly tapping into comparatively well defined underlying  
38 neurophysiological mechanisms, allowing testable assumptions to be made about  
39 mechanistic links between neurophysiology and BOLD measurements. Provided the  
40 results are interpreted with caution, and the experiments are carefully designed to  
41 minimize the confounds reviewed above, fMRI adaptation studies can help guide and  
42 provide impetus for more direct measurements. The use of parametric experimental  
43 designs is critical, since these allow the various low-level and high-level influences on  
44 adaptation effects to be systematically disentangled. Used in this manner, fMRI adaptation  
45 can be a useful complement to other measurements, even though it may not always  
46 provide conclusive evidence on its own.  
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51 In addition, we believe that fMRI adaptation has particular promise and merit in light of its  
52 capacity to study population-level consequences of adaptation in its own right. Specifically,  
53 the ability of fMRI to simultaneously measure correlates of neural activity across multiple  
54 brain regions means that fMRI adaptation is particularly suitable to addressing questions  
55 about how adaptation cascades across sensory hierarchies, particularly in brain areas that  
56 are not easily accessible with direct neuronal recordings or invasive neuronal population  
57 measurements, such as LFP or optical imaging. In this context, methods to trace the  
58 inheritance of adaptation effects using spatially selective adaptation (Larsson & Harrison,  
59 2015) hold promise, as well as techniques that measure the tuning of adaptation across  
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cortical areas (Lee & Lee, 2012). A full understanding of the relationship between single-neuron and population measurements of adaptation effects will also require concerted effort to conduct parallel and directly comparable experiments with fMRI and direct neuronal recordings. Key to progress in this area is a better understanding of the mechanisms of neurovascular coupling and how these may be affected by adaptation.

BOX: Open questions

Does adaptation to specific stimulus features occur at multiple stages in the visual hierarchy, or are effects induced at a particular stage?

Do mechanisms and properties of adaptation differ between early and high levels of visual processing?

How does adaptation affect neurovascular coupling at different spatial scales?

How do high-level adaptation effects affect responses at earlier levels?

What is the relationship between adaptation of single neurons and populations?

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