ABSTRACT: Functional magnetic resonance imaging (fMRI) and neuron electrophysiology (neurophysiology) are two well-established ways to measure brain activity. Even though the spatial and temporal resolution of these techniques is very different, both measurements show a high level of consistency, i.e., for mapping feature preferences of cortical areas. There are, however, other striking differences between fMRI and neurophysiology, for example, fMRI has good accessibility to higher cognitive functions, a bias to measure synaptic activity, and a good sensitivity to detect feedback-related activity, all of which can shed a new light on the function of well-known brain areas like primary visual cortex, V1. Classically, it is believed that V1 cells are exhaustively characterized by their complex receptive field properties. Contrary to this view, however, fMRI shows that response properties in area V1 are spatially unstable, influenced by contextual information, and depend on internal states. This review will highlight some of the most striking new fMRI findings that show V1 is involved in higher cognitive functions.

Received 2 April 2010; accepted 2 April 2010

I. INTRODUCTION

There are several established techniques to measure brain activity. Traditional animal neuron electrophysiology (neurophysiology) was the first to describe the complex receptive field properties of V1 in the seminal, Nobel prize-winning work of Hubel and Wiesel (1959, 2009). Functional brain imaging, especially functional magnetic resonance imaging (fMRI), began its tremendous success in the 1990s (Bandettini et al., 1992; Frahm et al., 1992; Kwong et al., 1992; Ogawa et al., 1992; for recent reviews see: Logothetis, 2008; Friston, 2009; Raichle, 2009) and emerged as the most frequently used method to measure brain activity (Fig. 1).

Functional MRI has revealed new perspectives on how brain functions can be conceptualized (Raichle, 2009) and how brain structures can be separated. For example, a fundamental separation between the extrinsic system, driven by external stimuli, and the intrinsic system, dissociated from external stimulation, has been proposed only recently on the basis of brain imaging data (Golland et al., 2007). Monkey neurophysiology on resting state and spontaneous activity has become more meaningful by the direct comparison to the human default-mode network (Vincent et al., 2007). Brain areas of the default-mode network are deactivated during the experimental conditions and more active for the baseline condition of an experiment, in which the subjects are supposed to do nothing but in fact get involved in the highest cognitive functions, and plan their day, remember important life events, engage in self-cognition and mental time travel (Shulman et al., 1997; Raichle et al., 2001; Buckner et al., 2008). The significance of the discovery of the intrinsic system and the default-mode network is becoming more and more relevant both in the understanding of basic brain processes and the understanding of mental diseases like Alzheimer’s, Dementia, and possibly even schizophrenia and autism (Buckner et al., 2008).

Not only has become possible to investigate brain regions whose cognitive functions were previously unknown (i.e., Hasson et al., 2004; Buckner et al., 2008) and to investigate higher cognitive functions that are difficult to study in primates (i.e., introspection, mental imagery, mental time travel, self-cognition, and language) but also low-level cortical brain areas like V1 can be investigated from a new perspective.

V1 is a well-studied brain area and by the time fMRI contributed to the investigation, neurophysiology had already provided more than 30 years worth of information. It was therefore not expected that fMRI would discover many new properties of V1. However, the great ease with which fMRI can investigate higher cognitive functions has led to the surprising finding that some of the higher cognitive functions are actually contributing to the activation pattern in V1. I will use examples of visual spatial attention, visual illusion processing, visual prediction, and visual memory to discuss this. In doing so, I will argue that (1) the fMRI signal is especially sensitive to cortical feedback, (2) the activity of V1 is modulated to a large extent by cortical feedback from many areas, and (3) the tradition of feed-forward-oriented neuroscience has overlooked some of the most important factors that contribute to V1 activity.

Correspondence to: Lars Muckli; e-mail: lars@psy.gla.ac.uk

Grant sponsors: Biotechnology and Biological Science Research Council Grant on “Visual Prediction” (BB/G005044/1) and the German Federal Ministry of Education and Research (BMBF 01 GO 0508).

© 2010 Wiley Periodicals, Inc.
rewiring (Muckli et al., 2009). Classical receptive fields in V1 are correlated activity and provide robust maps even after substantial effort to define all parameters contributing to V1 activity. Olshausen and Field (2005) estimate the amount of unknown V1 properties as high as 85%.

A. The Rise of fMRI. Currently “fMRI” research accumulates a publication rate of more than four articles a day, as shown by a simple PubMed database search for “fMRI” (Fig. 1). A comparison to previous years shows that “fMRI” publications increase exponentially with a more or less constant rate of 17% every year. In comparison, publications with “neuron electrophysiology” have a yearly increase rate of less than 3% over the last 20 years (Fig. 1). The success of fMRI might be related to factors including the successful introduction of standardized analysis tools and experimental procedures, and the huge financial investments at many centers likely fostered successful interdisciplinary cooperations. However, to some extent, the lasting success relies on the continuous development of new experimental strategies and analysis tactics allowing the investigation of higher cognitive functions that have been inaccessible or have received less attention in previous animal research. Furthermore, fMRI is not only the preferred method of brain activation measurement of higher cortical areas (i.e., prefrontal cortex, or language areas that might not have homologous regions in nonhuman primate brains) but also the most frequently used method for investigating V1 (more than threefold in 2007 and 2008 when compared with “neurophysiology” or “neuron electrophysiology”). Experimental findings are, however, not always consistent between fMRI and neurophysiology. Indeed, the picture that emerges from fMRI research on V1 is different from the picture that has emerged from 50 years of neurophysiology. However, because of its long-standing use, neurophysiology models and textbooks are dominated by the neurophysiological perspective on V1. In this review, I would like to highlight the challenges to these concepts and models prompted by fMRI.

B. Conceptual Comparison of V1. Comparisons between neurophysiology and fMRI can be drawn from simultaneous measures of the two (see below) or by comparing results of independent studies that investigate homologous brain areas in humans and monkeys. Depending on how activity is measured V1, responds differently across different tasks. V1 is a useful target region as it is probably the best studied region in the primate brain, and for comparison, I will look at the striking differences that occur when V1 responds to visual attention, visual illusions, prediction, and memory tasks. In standard textbooks, none of these cognitive functions are assigned to the properties of V1. Rather, it is well known that V1 cells are driven by contours, edges, and spatial frequencies at localized retinotopic coordinates. Likewise, attention, illusions, prediction, and memory functions are assigned to regions higher up in the proposed cortical hierarchy or in parietal and frontal regions or in areas of the limbic system. However, it is possible that the bias to low-level feature processing in V1 is driven by a methodological bias of neurophysiology. Neurophysiology, with its tradition of response measurement, may be more capable of detecting certain low-level features of neuronal processing, but brain imaging, in spite of less spatial and temporal resolution, may have the advantage in discovering higher cognitive information processing in V1.

Figure 1. Number of publications per year using fMRI and neurophysiology. Results are shown for a simple PubMed search (http://preview.ncbi.nlm.nih.gov/pubmed) using keywords “fMRI” and “neuron electrophysiology.” The absolute numbers vary depending on the precise keywords and databases used, but the general pattern, increase rate, and relative difference between neurophysiology and brain imaging remain more or less the same. For example, Logothetis (2008) used an ISI Web of science keyword search: “fMRI” or “functional MRI” or “functional magnetic resonance imaging,” which finds 70% more publications (i.e., 3,266 for 2008). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

II. V1—THE MODEL REGION

Primary visual cortex, or V1, is one of the first cortical stages in which visual information is processed. In the input layers (IV), area V1 receives thalamic input from lateral geniculate nucleus (LGN), which is transmitted from the retina in a topographic manner, preserving retinotopic neighborhood relationships (Brewer et al., 2005). A topographic neighborhood relationship in the visual system means that adjacent points in the visual field are processed at adjacent positions in the cortex (Wandell et al., 2007; Muckli et al., 2009). Ontogenetic mechanisms are based on molecular cues and correlated activity and provide robust maps even after substantial rewiring (Muckli et al., 2009). Classical receptive fields in V1 are small and below 1° of visual angle. Although V1 receives most of the retinal input (90%), there are other cortical areas that receive smaller proportions of retinal input from the thalamus (LGN, i.e., Bridge et al., 2008), which are able to respond simultaneously or even earlier than V1 (Bullier, 2001; Silvanto et al., 2005). Even though 90% of retinal input projects to V1, this does not mean that V1 cells are only activated by thalamocortical input. Actually, it is estimated that for any given cell, even in layer IV of V1, only 5% of its excitatory synapses receive thalamocortical feed-forward input (Douglas and Martin, 2007). More than 50 years of neuronal electrophysiology has led to an impressive level of understanding of neuronal processing in V1, stirring the hope that it would soon be possible to generate a standard model of V1 (i.e., based on combined set of linear receptive fields). It was assumed that with a precise model, V1 responses could be generalized to any new visual stimulus on the basis of receptive field properties. By now, it is estimated that even the best current models can only explain 40% of variance in V1 (Carandini et al., 2005). 40% is impressive considering that only 5% of excitatory synapses feed forward from retina, however still leaving 60% of variance unexplained and open to modulation influence from elsewhere. Olshausen and Field (2005) estimate the amount of unknown V1 properties as high as 85%.

A. Attention. Although neurophysiology studies have made a substantial effort to define all parameters contributing to V1 activity

III. ACTIVITY DISCREPANCIES BETWEEN fMRI AND NEUROPHYSIOLOGY

A. Attention. Although neurophysiology studies have made a substantial effort to define all parameters contributing to V1 activity...
as well as possible, it came as a surprise when in 1998 and 1999 several fMRI studies reported strong V1 responses to visual spatial attention (Kastner et al., 1998; Tootell et al., 1998; Watanabe et al., 1998; Brefczynski and DeYoe, 1999; Gandhi et al., 1999; Martinez et al., 1999; Somers et al., 1999; reviewed by Kanwisher and Wojciulik, 2000). Until then most neurophysiological studies found no (Luck et al., 1997) or only small (Motter, 1993) effects of visual spatial attention in area V1. This discrepancy has been investigated in subsequent studies confirming that using neurophysiology visual spatial attention effects are small (Thiele et al., 2009) but can be huge using fMRI (Silver et al., 2007). Figure 2 illustrates some of the most striking differences: fMRI responses seem to be markedly influenced by visual attention even if no visual stimulus is presented (Fig. 2A), and only minor response differences show if a threshold stimulus is presented (Fig. 2B). An inverted picture emerges for neurophysiology: no difference whether a stimulus is attended or ignored (Fig. 2C), at least for the first part of the response, and attention differences occur only later in time (Fig. 2D). On closer inspection of the literature, we can differentiate two separate visual spatial attention effects, an additive gain control (Boynton, 2009; Deco and Thiele, 2009) and a baseline shift (e.g., Kastner et al., 1998; Silver and Logothetis, 2007). A gain control can be observed in the presence of a visual stimulus for which the response is systematically modulated if attended. The higher fMRI response might be related to the accumulation over time (Fig. 2C). Visual attention effects in V1 appear later in time as a result of cortical feedback (Roelfsema et al., 1998; Roelfsema et al., 2007; Buffalo et al., 2010), and because of the low temporal resolution of fMRI, attention effects are averaged over a long period of time. In contrast, neurophysiology often focuses on the initial processing before feedback modulation (Martinez et al., 1999). Recently, Boynton (2009) compared three fMRI (Buracas and Boynton, 2007; Li et al., 2008; Murray, 2008) and two neurophysiological studies of attentional effects in V1 (Reynolds et al., 2000; Willford et al., 2006). These studies adopted a parametric design in which the attended stimuli were modulated by stimulus contrast. An additive gain control was found in neurons tuned specifically to the visual features (Reynolds et al., 2000), whereas a baseline shift was found in most neurons

Figure 2. Attentional effects in V1 measured with fMRI and neurophysiology. (A) fMRI attention effects are prominent even in the absence of any visual stimulus. fMRI activity at the attended location when no stimulus is presented is shown in blue and at the unattended location in green (adapted with permission from Silver et al., J Neurophysiol, 2007, 97, 229-237, © American Physiological Society). (B) Small signal differences at attended locations can be observed for threshold stimulation (adapted with permission from Ress et al., Nat Neurosci, 2000, 3, 940-945, © Nature Publishing Group). (C) Electrophysiology, in contrast, shows no signal differences for attended versus unattended stimuli in V1 (adapted with permission from Luck et al., J Neurophysiol, 1997, 77, 24-42, © American Physiological Society). (D) Differences between attended and unattended locations can build up over time as seen in a selective attention task (adapted with permission from Roelfsema et al., Neuron, 2007, 56, 785-792, © Cell Press). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
within the attended visual field not specifically tuned to the stimulus orientation. In a brain imaging voxel, there are only few neurons tuned to the presented stimulus and the vast amount of other neurons are more likely to express the baseline shift effect. As fMRI averages over all neurons in a voxel, it is therefore expected to find a stronger baseline shift effect in human fMRI than in animal neurophysiology (Boytton, 2009). However, the study by Boyont (2009) failed to consider neuronal synchronization in his model. Neuronal synchronization appears to be the key factor underlying attention effects in area V4 (Fries et al., 2001; Taylor et al., 2005; Womelsdorf et al., 2006; Deco and Thiele, 2009; Fries, 2009) and might contribute via feedback connections to attention processes in V1 (Deco and Thiele, 2009). Given that fMRI is specifically tuned to incoming projections (including feedback from higher areas) and to γ-hand synchronization (Goense and Logothetis, 2008), it is likely that the increased baseline shift is modulated by synchronized oscillatory feedback projections. However, there is only one study so far that has directly compared attention-related baseline shifts measured with BOLD imaging (optical recordings of the blood oxygenation level–dependent (BOLD) signal comparable to the (fMRI signal) to neuronal recordings (Siroton and Das, 2009). The surprising outcome of this comparison was a negative result with a missing neuronal correlate of the BOLD signal. There are many possible ways to explain this negative finding. One possibility is that the neuronal activity sums to a “closed electrical field” that cancels each other because the active neuronal population is not coaligned (Raichle, 2009). There have been suggestions that the study of Siroton and Das might have been related to methodological limitations (Kleinschmidt and Muller, 2010); however, latest data seem to support the original set of data (personal communication and CCNI-debate, Glasgow, March 4, 2010). The findings of Siroton and Das (2009) will lead to further investigations on how various neuronal activities can average to a measured BOLD signal (see below and Logothetis, 2008).

B. Size Illusion. Quite unexpectedly on the basis of knowledge gained from neurophysiology, fMRI findings suggest that retinotopic space, and therefore receptive fields, can flexibly adapt to contextual information. Murray et al. (2006) demonstrated that the spatial extent of retinotopic activation in V1 follows a size illusion induced by surrounding context information. In the eye, the physical size of visual stimuli determines precisely the stimulated region of photoreceptors (by physical laws of optics). It appears however that in V1 the activated space can flexibly adapt to the presence of a visual spatial size illusion. This flexibility is inconsistent with the rigid projection patterns from retinal ganglion cells to LGN and from thalamus to visual cortex. Moreover, it is inconsistent with the model that the response of a V1 cell can predict new stimuli once its basic feature tuning has been measured (orientation, spatial receptive field, etc.; Carandini et al., 2005).

The visual size illusion used by Murray is shown in Figure 3A and is based on the classical Ponzo illusion. Although the two checkerboards have the same size, the rearmost checkerboard is perceived as much larger. When visual focus is in the centre, both checkerboards will activate the identical retinal space and presumably the same retinal ganglion cells project their information to LGN from where it is relayed to V1. Receptive fields of V1 cells are believed to be rigid and independent from its surrounding context. The results of Murray demonstrate, however, that the receptive fields in V1 are either flexible or exposed to flexible feedback effects that vary as a function of the perceived size illusion. Figure 3C shows a model (MacEvoy and Fitzpatrick, 2006) highlighting this idea of flexible receptive fields. An alternative explanation is that V1 cells are strongly modulated from outside of their classical receptive field (Angelucci and Sainsbury, 2006).

C. Apparent Motion Illusion. Another unexpected demonstration of activity in nonstimulated parts of primary visual cortex arises from the use of long-range apparent motion, in which two alternating dots induce the visual illusion of back and forth motion. In my laboratory, we used this illusion to investigate the cortical activity related to the illusory motion trace, the nonstimulated path between the blinking dots (Fig. 4A). The concept of rigid retinotopic receptive fields would predict that the nonstimulated path between the blinking dots should not be activated. However, we, and others, were able to demonstrate that the apparent motion path can be stimulated by the visual motion illusion (Mackli et al., 2005; Larsen et al., 2006; Sterzer et al., 2006). Previous neurophysiological investigations had failed to find these effects in V1 using single-cell neurophysiology (Mikami et al., 1986), but more recent findings were able to replicate the illusion-related activity in ferret area 17 (the ferret homologue to primate area V1). It is assumed that the illusory path activity was found because a voltage-sensitive dye imaging technique was used (Ahmed et al., 2008). This technique shares some of the properties of fMRI, especially its sensitivity to synchronized oscillatory subthreshold membrane fluctuations, see discussion below. Moreover, it has been shown in previous studies to be sensitive on feedback signal (Roland et al., 2006) and on other visual illusions (Jancke et al., 2004). The activation in Figure 4A is shown from a region that does not respond to the location of the blinking dots (shown in red and yellow) but only to stimulation along the apparent motion trace (blue and orange). During apparent motion perception, the illusory trace is not stimulated but nevertheless activated (green in Fig. 4A). The apparent motion trace covers a substantial 16.5° visual angle, whereas Murray’s size illusion affects a smaller part of the visual field—so where does this big illusion-related effect originate from? Our original suggestion that V1 apparent motion trace activity is related to feedback from motion-sensitive visual area hMT/V5 was first confirmed by Sterzer et al. (2006) and later by Wibral et al. (2009) and Ahmed et al. (2008). Wibral et al. (2009) used EEG to confirm a temporal sequence of trace activity in retinotopic areas (V1/V2/V3) following motion-sensitive V5 activity, and Ahmed et al. (2008) replicated a temporal sequence of trace-related activity in ferret cortex areas 19, to 18, to 17.

Importantly, apparent motion and attention can be modulated independently to one another (Kohler et al., 2008), and V1 activity to the apparent motion trace is independent to attention (Mackli et al., 2005). We also found traces of retinotopic specific activation in V1 during visual motion imagery (Kaas et al., 2010). For example, if subjects imagined motion in the right upper visual field the corresponding section in the left ventral V1 shows slightly more activity, which in our experiment was seen as less negative fMRI signal. Previous studies investigated motion imagery in V1 with designs that included recovery of sensory stimulation (Goebel et al., 1998; Slotnick et al., 2005). In contrast to previous findings, our study showed negative fMRI signal in V1 for motion imagery. This example demonstrates again how V1 is exposed to feedback activity and its involvement in higher cognitive function in the absence of retinal input.
D. Prediction in V1. What is the functional role of cortical feedback to area V1 during illusory perception? We proposed the hypothesis that higher visual areas automatically generate predictions that are fed back to V1. Predictions in V1 are compared to the incoming sensory stimulation. In the case that a cortical prediction is confirmed, less activity is needed for further processing. Only when a cortical prediction is wrong is additional processing required and an error signal might be passed on to subsequent processing stages. Comparable models of predictive coding have been suggested time and again (Mumford, 1992; Rao and Ballard, 1999; Friston, 2005; George and Hawkins, 2009; Hawkins et al., 2009; Friston, 2010; Spratling, 2010). Prediction-related activation and sensory stimulation will normally overlap at a given cortical processing stage. The cortical processing of apparent motion might be a very special case: For the perception of apparent motion, predictive feedback is generated (comparable to the processing of regular visual motion)—however, for apparent motion there is no sensory stimulation along the apparent motion trace, which allows us to investigate the cortical prediction system in more detail.

We first tested whether predictable stimuli along the apparent motion trace are easier to detect. We tested our hypotheses by presenting a visual blinking stimulus along the apparent motion trace in temporal accordance and in violation with the presumed cortical prediction (Fig. 4B). We found behavioral advantages for predictable stimuli (Schwiedrzik et al., 2007) and investigated in a subsequent study whether this effect relates to processing at the level of V1 (Alink et al., 2010). Our results confirmed that predicted stimuli induced less fMRI activation in V1 (Fig. 4B). Finding reduced activity related to increased performance fits well with the framework of predictive coding (Mumford, 1992) but is difficult to explain otherwise.

The prediction-related (illusion-related) activity might only be detectable with functional brain imaging methods that are able to measure subthreshold membrane fluctuations (fMRI, voltage sensitive dyes, EEG) and not with neurophysiological methods that rely on spiking feed-forward activation (see below).

E. Working Memory in V1. Possibly, the best example that V1 is involved in higher cognitive tasks is given by recent investigations of working memory by Harrison and Tong (2009). In their fMRI study, subjects were instructed to remember one of two presented gratings over a delay period of several seconds. Although activity returned to baseline during the retention period, there was enough information stored in V1 to readout with fMRI which grating was kept in working memory by the subjects. Previous to this finding, prefrontal areas have been shown to be involved in coding
for the content of a working memory task (Miller et al., 1996; Linden et al., 2003; Histed and Miller, 2006). The finding that V1 is involved in the retention period is surprising because fMRI activity returns to baseline. The information was retrieved not from the overall activation but from the voxel-to-voxel activation patterns used in a multivariate pattern classification approach (Mur et al., 2009). To learn more about the nature of this information, the authors tested the classifier performance when trained with an actual low-contrast visual stimulus. A multivariate pattern classifier that was trained on this visual response was able to later classify the working memory content during the retention period (when no stimulus was shown). The cross validation approach showed that the same classifier can be used during working memory tasks and during visual image processing. The neuronal processing is therefore overlapping for vision and memory (Fig. 5).

**F. The Small Difference Between fMRI and Neurophysiology.** BOLD fMRI activity and neurophysiology are treated as comparable for good reasons, as simultaneous and parallel measurements of neurophysiology and fMRI have shown for the most part good consistency. Increased brain activity usually leads to higher fMRI signal and higher single-cell activity as well as summed local field potentials (LFPs). A linear correspondence between single-cell recordings and fMRI response was proposed, for example, by comparison of human and monkey V5 responses (Heeger et al., 2000) and by comparison of human auditory cell responses and fMRI signal (Mukamel et al., 2005). However, this paradigm failed in many other examples and was therefore replaced by a more complex correspondence between the fMRI signal and synchronized high gamma LFP signal (Logothetis et al., 2001; Niessing et al., 2005; Goense and Logothetis, 2008).

Another important difference that became clearer over time is that fMRI has a strong bias toward indicating the activity that is related to incoming projections, compared with the spiking output of a given area (Viswanathan and Freeman, 2007). The spiking output can be seen as the result of the computation occurring at that cortical stage—although the precise code of the outgoing signal is still to be understood (Singer, 2009). In contrast, the pre- and postsynaptic activities that occur before a spiking output can be seen as being related to the actual computation. FMRI seems to be a signal that is highly related to the computation and less so to its output (Logothetis, 2008).

**Figure 4.** Apparent motion-related activity along the illusory motion trace in V1 (green). (A) Left: Long-range apparent motion is induced by blinking dots 16° visual angle apart. The cortical representation of the blinking spots is indicated by the red and yellow rings. Right: Example of fMRI activation along the apparent motion trace. The sample region does not respond to the blinking dots (red or yellow time courses) but to mapping stimuli shown on the apparent motion trace (orange and blue time courses). The apparent motion path in V1 is activated when the blinking stimuli induce an apparent motion illusion (green time course) (adapted with permission from Muckli et al., PLoS Biol, 2005, 3, 1501-1510, © Public Library of Science). (B) Left: Activity to a predictable stimulus is reduced in V1. Right: The blinking test stimulus is easier to detect if the stimulus fits to the spatial-temporal prediction pattern of the apparent motion illusion (adapted with permission from Alink et al., J Neurosci, 2010, 30, 2960-2966, © Society for Neuroscience). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

**Figure 5.** Involvement of V1 in a working memory task. (A) Time course from V1 during working memory experiment. Stimuli are two differently oriented gratings and a cue stimulus determines whether the first or the second stimulus needs to be remembered for the trial. During the retention period (shaded in blue), fMRI activity returns back to baseline in area V1–V4. (B) A multivariate pattern classifier can be trained on the voxel signal distribution during the retention period to discriminate which stimulus needs to be remembered (adapted with permission from Harrison and Tong, Nature 458 (2009), 632-635, © Nature Publishing Group). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
The precise signaling cascade that allows the link of neuronal activity to the hemodynamic response of BOLD-fMRI remains elusive. Recent findings of fMRI activity without neurophysiologic correlates have reignited the debate (but see Lauritzen, 2005; Devor et al., 2008; Sirotin and Das, 2009; Kleinschmidt and Muller, 2010). However, most views converge on the idea that fMRI is correlated with the many pre- and postsynaptic activities a neuron is involved in prior to the triggering of an outgoing action potential (Logothetis et al., 2001; Viswanathan and Freeman, 2007; Goense and Logothetis, 2008). This synaptic cell activity leads to small membrane potential fluctuations that add up (if in an open field configuration i.e., co-aligned) to observable LFPs in the high gamma range. However, desynchronized membrane potentials and those that are processed by neurons that are not co-aligned (for example, interneurons can give rise to a closed field configuration) and might be impossible to detect with neuron electrophysiology. Therefore, there is always a chance that neurophysiology might miss activity that contributes to the fMRI signal. It is assumed that the sum of pre- and postsynaptic activities is linked to energy consumption, and energy consumption, in turn, is tightly linked to the hemodynamic response (Raichle et al., 2001). Devor et al. (2008) and Lauritzen (2005) show, however, that it is not energy consumption alone that drives the hemodynamic response. Calcium metabolism has been proposed as a central mechanism that can explain the results of Devor et al. (2008) and Lauritzen (2005). However, there are more complex mechanisms that may not be captured in only one model of neurovascular coupling. Future models might incorporate different neurovascular correlates depending on a better understanding of the diverse neuronal mechanisms underlying the BOLD response averaged in each voxel.

IV. CONCLUSIONS

It was assumed that models of information processing in V1 would soon be sufficiently precise so that a V1 neuron could be classified by its response properties to standardized stimuli (i.e., gratings with different size, orientation, contrast, spatial frequency, and position), and that a cell response to any new visual stimulus could be well approximated by this model (Carandini et al., 2005). There is a great beauty in this idea: if it is possible to model one brain area with very good precision then it could be possible to re-engineer more and more cortical areas and extract the computational principles of brain processes. The so-called standard model of V1 has achieved quite some success, and indeed it is estimated that the best models can explain about 40% of the cell response variance, although according to Olshausen and Field (2005), only ~15% of V1 is currently understood. However, this review showed that there are also certain limitations that have not yet been incorporated in the standard model of V1: a strong baseline shift in its activity depending purely on internal processing totally unrelated to external stimuli; external stimuli far away from the receptive field influence the context and trigger visual illusions and predictions that pass through unstimulated regions in V1; mental tasks recruit V1 as a reference for working memory. With these examples in mind, there might actually be different ways to model V1 activity. Only 5–10% of the excitatory input of a V1 cell is from feed-forward thalamocortical connections; the rest comes from neighboring cells and from feedback of other cortical areas. The precise description of V1 activity should therefore not only consist of its receptive field properties to visual stimulation but also to its internal responsive field—receiving input from other areas and including relevant information for conducting cognitive tasks might put ‘‘early visual area V1’’ at a totally different level of the proposed hierarchy. It is conceivable that V1 is, first of all, the target region for cortical feedback and then, in a second instance, a region that compares cortical feedback to incoming information. Sensory stimulation might be the minor task of the cortex, whereas its major task is to reduce surprise (Friston, 2010) and predict upcoming stimulation as precisely as possible (Mumford, 1992; Rao and Ballard, 1999; Hawkins and Blakeslee, 2004).

ACKNOWLEDGMENTS

The author thanks Lucy S. Petro and Petra Vetter for comments on the manuscript and Arjen Alink and Axel Kohler for help on Figure 4.

REFERENCES

A. Angelucci and K. Sainsbury, Contribution of feed forward thalamic afferents and corticogeniculate feedback to the spatial summation area of macaque V1 and LGN, J Comp Neurol 498 (2006), 330–351.
H. Bridge, O. Thomas, S. Jbabdi, and A. Cowey, Changes in connectivity after visual cortical brain damage underlie altered visual function, Brain 131 (2008), 1433–1444.


K.J. Friston, Modalities, modes, and models in functional neuroimaging, Science 326 (2009), 399–403.


A. Kleinschmidt and N.G. Muller, The blind, the lame, and the poor signals of brain function—A comment on Sirotn and Das (2009), Neuroimage 50 (2010), 622–625.


N.K. Logothetis, What can we do and what we cannot do with fMRI, Nature 453 (2008), 869–878.


B.C. Motter, Focal attention produces spatially selective processing in visual cortical areas V1, V2, and V4 in the presence of competing stimuli, J Neurophysiol 70 (1993), 909–919.


