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Can neuroimaging really tell us what the human brain is doing? The relevance of indirect measures of population activity

Hans op de Beeck^{a,b}, Johan Wagemans^{a,*}, Rufin Vogels^b

^a *Department of Psychology, Laboratory of Experimental Psychology, University of Leuven, Tiensestraat 102, B-3000 KU Leuven, Belgium*

^b *Laboratorium voor Neuro- en Psychofysiologie, KU Leuven, Belgium*

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Abstract

Neuroimaging studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) give an indication towards the localization of mental representations and processes in the human brain. It is not clear to what extent such global measures of neuronal activity, pooling across large populations of neurons, can reveal how certain computations are implemented by the neurons in such population ('computational neuroimaging'). Population activity is related tightly to single-cell activity when all neurons in the population have similar response properties. We describe some evidence from single-cell recordings in monkeys that indicates that neurons with similar response properties are not scattered randomly throughout the visual cortex. Notwithstanding this clustering, populations of nearby neurons are still rather heterogeneous, requiring some prudence in deriving single-cell response properties from population activity. The following review of recent neuroimaging studies of the visual system describes to what degree inferences about computations and representations can be drawn from these studies. © 2001 Elsevier Science B.V. All rights reserved.

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* Corresponding author. Tel.: +32-16-325969; fax: +32-16-326099.

E-mail address: johan.wagemans@psy.kuleuven.ac.be (J. Wagemans).

1. Introduction

Non-invasive neuroimaging techniques like functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) are widely used by cognitive neuroscientists. The subject of cognitive neuroscience (Gazzaniga, 1995, 1999) can be defined broadly as the neuronal implementation of cognitive representations and processes. Some of the more specific topics are related to functional neuroanatomy, that is, trying to disentangle what representations and processes are located where in the brain ('localization'). From their conception, neuroimaging techniques have been viewed as a major tool in this respect. Although localization is important from a neuroscience perspective, it is a pertinent question whether mere localization of function has any relevance for disciplines that are not interested in the exact implementation of representations and processes but in cognitive functions at a more algorithmic level (the subject of cognitive psychology). Indeed, as argued by Marr (1982) (see also Vecera, 1998), the same complex topic can be analyzed at multiple levels. In this paper, we will describe to what degree neuroimaging techniques can go beyond localization of function and can be used as a tool to discover how particular computations are carried out in the human brain. However, in this enterprise, it is necessary to combine the neuroimaging evidence with findings from other techniques like single-cell recordings in macaques.

In the first section, we will focus on the principles and limitations of the current neuroimaging techniques. The main limitation in the context of this paper is their spatial resolution that prevents the investigation of single neurons. The application of these techniques to the study of the functional organization of the brain is limited by the relevance of the population activity of groups of neurons. Results from single-cell recordings in macaque monkeys, as described in this paper, indicate that this population activity can give some limited information about the properties of single-cell responses. We review the application of neuroimaging techniques in the study of the human visual system¹ and show that these techniques can go beyond localization in some cases, especially if converging evidence from single-cell recordings is available.

2. Principles and limitations of non-invasive neuroimaging techniques

Many techniques exist that can be used to investigate the activity of neurons in the brain, but some of these techniques cannot be used in humans because they are invasive. The non-invasive techniques have one general disadvantage: their

¹ In this paper, we provide a selective review of neuroimaging studies on a specific topic, that is, the functioning of the visual system. Given the exponential increase in publication rate of PET and fMRI studies in recent years, an extensive review of the whole field would necessarily focus on general aspects while ignoring the details, which we wanted to avoid (a broad review can be found in Cabeza & Nyberg, 2000).

poor spatial resolution, making it impossible to pinpoint the activity of single neurons. These techniques can be subdivided into two broad groups: those measuring the electrical activity of the brain directly (like the electro-encephalogram (EEG) and magneto-encephalogram (MEG)) and those measuring indirect correlates of it (PET and fMRI). We will concentrate on the more recently developed indirect measures (for a more general and historical introduction to brain mapping techniques, see Savoy, 2001). The direct measures have a better temporal resolution but their spatial resolution is worse, making them more appropriate to investigate processes that are differentiated in time but less appropriate for localization.

Both PET and fMRI measure metabolic changes related to brain activity. Neuronal activity is accompanied by a local increase of oxygen and glucose consumption, which is followed by an increase in blood flow towards the active region. This increased blood flow is delayed relative to the neuronal activity by several seconds, and its rise and fall time together comprises more than 10 s. More extensive methodological reviews of both methods can be found elsewhere (Cohen & Bookheimer, 1994; Posner & Raichle, 1994; Sergent, 1994). In PET, a radioactive molecule is injected into the blood and changes in blood volume become visible by detecting changes in the amount of radioactive emission. This emission is measured cumulatively during a time period depending on the decay period of the radioactive molecule, being at least 40 s. The experimental design is adapted by presenting the experimental conditions in blocks (i.e., the order of trials is not randomized, but trials of each condition are grouped). By comparing ('subtracting') the radioactive signal in different experimental conditions, one infers differences in brain activity from these measured changes in blood supply. The temporal resolution of PET is limited by the cumulative measurement during tens of seconds, while its practical spatial resolution is several millimeters.

In fMRI, concentration changes in deoxyhemoglobine are used as an intrinsic contrast agent. Such concentration fluctuations are reflected in the strength of the fMRI signal that is evoked by disturbing the magnetic equilibrium in a magnetized tissue (in case, the brain). At the moment of increased oxygen consumption, the concentration of deoxyhemoglobine increases, leading to a small decrease in fMRI signal. This increased oxygen consumption is compensated by a subsequent overshoot in blood supply, which causes the concentration of deoxyhemoglobine to decrease rapidly, reflected in a stronger fMRI signal (only this increase is regularly detected with conventional MRI scanners, while the initial signal dip has only been visualized in a few studies, e.g., Hu, Le, & Ugurbil, 1997; Menon et al., 1995). Again, the signal in different conditions can be compared to infer changes in brain activity. The temporal resolution of fMRI depends on the experimental design. Most of the early studies used a design comparable to the traditional PET experiments, and presented trials of one condition in blocks of tens of seconds. However, the temporal resolution in PET was limited by the cumulative way in which the signal was measured, while fMRI can measure changes in blood oxygenation level on-line. The fMRI technique samples this blood flow indirectly as the magnetic perturbation cannot be applied continuously and needs an interval of more than 1 s to allow the

tissue to reach its magnetic equilibrium again (at least in those studies using conventional magnetic field strengths and imaging several brain slices).

Recently, the focus has shifted towards other designs that make optimal use of the temporal resolution of fMRI (event-related fMRI; for review, see D'Esposito, Zarahn, & Aguirre, 1999; Rosen, Buckner, & Dale, 1998). These advances have gone in two directions. First, the alternation of conditions in blocks can be changed into a randomized trial order, avoiding all artefacts that could be related to the blocked design (e.g., the use of particular cognitive strategies). If trials of different conditions are randomized, then one can detect differences in fMRI signal between these conditions, even if they are separated by only 2 s (e.g., Dale & Buckner, 1997). This design is nevertheless far less powerful compared to the blocked design. As the changes in blood oxygenation level appear to be smooth, the block designs are still the most powerful designs as they provide the maximum contrast in signal strength (see Fig. 1). The randomized trial order has some power in detecting signal differences between trial conditions because the stimulus order contains some low-frequency components (a simple alternation of the trials of the conditions would reveal no differences, see Fig. 1(c)). This trade-off between power and order randomization can be solved using an intermediate design that augments the low-frequency components in the trial order relative to a completely randomized order ('stochastic designs', Friston, Zarahn, Josephs, Henson, & Dale, 1999; see Fig. 1(d)).

A second alternative design that improves the temporal resolution of fMRI, allows to discriminate temporal differences in the time course of the fMRI signal in different conditions. By manipulating the time delay between trial onset and the moment at which the magnetic perturbation is applied (e.g., ranging from simultaneous measurement in some trials to a delay of several seconds in other trials with intermediate steps of 100 ms), it is possible to map this time course with a higher resolution than one data point in several seconds (D'Esposito et al., 1999).

The spatial resolution in the initial fMRI studies was comparable to the results with PET. However, recent developments have increased this resolution. Theoretically, the signal point spread of fMRI seems comparable to optical imaging, an invasive high-resolution technique (Engel, Glover, & Wandell, 1997a,b). Such resolution can only be reached with fMRI by using strong and ultra-expensive magnetic fields that are not regularly used with human subjects. However, recent studies (Grinvald, Sloviter, & Vanzetta, 2000; Kim, Duong, & Kim, 2000) indicate that the limiting factor for the spatial resolution becomes unrelated to aspects of the measurement of the metabolic changes, but is related to the non-specificity of the increase in blood supply following neuronal activity. Several studies (Hu et al., 1997; Kim et al., 2000) found that this increase is not specific for the activated neuronal populations and is rather global (i.e., if the activated neurons are grouped in a very specific part of a brain area, then blood volume is increasing in a more extended area). As the small initial dip in the fMRI signal seems to be more local, it can be expected that more studies will try to increase their sensitivity in order to measure it reliably.

Fig. 1. A comparison of the efficiency of different fMRI designs. (a) An idealized hemodynamic response function used to generate the other curves. The function represents the signal change following the presentation of a brief stimulus. The ordinate in all graphs is in arbitrary units. (b,c) The hemodynamic changes related to different trial orders. Each pulse above a graph indicates the occurrence of a brief stimulus. (b) A blocked design: stimuli are presented repeatedly during 20 s followed by a 20 s baseline interval. A comparison of signal strength in both conditions (stimuli presented or not) reveals a strong difference. (c) If stimulus presentations and baseline intervals were simply alternating, then a similar comparison would reveal no substantial difference. (d) In a stochastic design, trial order is randomized with a manipulation of condition probability. In the figure, the probability of trials with stimulus presentation was 0.7 in the first 20 s and 0.3 in the following 20 s interval. This design is more efficient than a simple alternation or a randomization without probability manipulation.

3. The application of non-invasive neuroimaging techniques

Neuroimaging techniques only provide a global measure of population activity. If we want to know how computations are carried out in a particular brain region, then we need more information as we lack detailed knowledge about what individual neurons are doing. A priori, the correspondence between population activity and the

activity of single neurons can vary. If all neurons in the population are doing exactly the same, then the population activity is a perfect reflection of single-cell activity. If the activity of each neuron would be completely unrelated to the activity of other neurons in the population, then population activity is not informative about what is going on (what is computed) in the population. So, before describing the application of neuroimaging techniques to the study of the human visual system, we give some background on the organization of the visual system in macaque monkeys. We focus on the question whether neurons that carry out similar computations are clustered in homogeneous populations.

3.1. Background: single-cell recordings in the macaque visual system

Neurons with similar stimulus preferences are not scattered randomly throughout the visual cortex in non-human primates. We will discuss two levels of clustering. First, neurons with similar response properties are grouped in more than thirty visual areas. Second, within these areas, there is a further grouping of neurons according to the position of their receptive fields and according to other response properties.

In addition, evidence in non-human primates has shown that neuronal activity in the visual system is strongly modulated by attention and memory, suggesting less segregation of these cognitive systems than thought previously.

3.1.1. Modularity and hierarchical processing

The combination of cytoarchitectonical, neuroanatomical and electrophysiological studies has provided evidence for the existence of at least 30 visual areas (Felleman & Van Essen, 1991). These areas are ordered in two ways (Fig. 2). First, they can be divided into two processing streams. Ungerleider and Mishkin (1982) differentiated both visual subsystems in terms of the attributes they encode, with the dorsal stream being involved in the processing of stimulus location and motion while the ventral stream is involved in the computation of object attributes. Electrophysiological studies in the macaque confirmed this hypothesis by showing that neurons in the ventral visual stream are strongly selective for object attributes such as shape elements, texture and color (Desimone, Albright, Gross, & Bruce, 1984; Pasupathy & Connor, 1999; Tanaka, Saito, Fukuola, & Moriya, 1991; Zeki, 1983), while the responses of neurons in the dorsal stream are strongly dependent on stimulus position in the frontoparallel plane (Blatt, Andersen, & Stoner, 1990; Duhamel, Bremmer, BenHamed, & Graf, 1997; Motter, Steinmetz, Duffy, & Mountcastle, 1987), and in depth (De Angelis & Newsome, 1999; Sakata, Taira, Kusunoki, Murata, & Tanaka, 1997), and on motion (Albright, 1984; Colby, Duhamel, & Goldberg, 1993; Sakata et al., 1997).

Another view differentiates the dorsal and the ventral system by their functionality (Goodale & Milner, 1992; see Creem & Proffitt, 2001, for further discussion). According to this model, both systems would analyze overlapping aspects of visual scenes, but with a different goal: The dorsal system provides the information needed for visuomotor integration, while the ventral system analyzes the visual input in

Fig. 2. The organization of the visual areas into two processing streams with a hierarchical organization; V1, primary visual cortex; TEO and TE located in the inferior temporal lobe; TG – temporal pole; TF – parahippocampal area; PO – parieto-occipital area; MT – middle temporal area; DP – dorsal prelunate area; PG – the inferior parietal cortex; VIP and LIP – the ventral and lateral intraparietal area; PP – the posterior parietal area; MST – the medial superior temporal area; FST – the fundus of the superior temporal sulcus; STS – the superior temporal sulcus; the numbers in the frontal lobe represent the Brodmann nomenclature (based on Ungerleider, 1995).

order to perceive and recognize objects. While this view would still predict some segregation of the coding of some visual attributes (e.g., color is not that important for visuomotor integration), it would predict a much larger overlap compared to the earlier version. Recent neurophysiological results have indeed focused on shape selectivity in the parietal cortex (Serenó & Maunsell, 1998) and on position selectivity in the inferotemporal cortex (Op de Beeck & Vogels, 2000).

Despite the relative differences between the ventral and the dorsal visual stream, these systems are not isolated from each other. Strong anatomical connections exist between them (e.g., Andersen, Asanuma, Essick, & Siegel, 1990; Neal, Pearson, & Powell, 1990). Furthermore, single-cell recordings have suggested that the ventral visual stream has access to information that is primarily encoded in the dorsal stream (e.g., Sárosy, Vogels, & Orban, 1993).

Apart from the organization of the visual areas in several pathways, a second ordering of the visual areas is a hierarchical one. Visual information enters the cortex at the occipital pole in area V1 and is propagated forward into the dorsal visual areas (from V2, V3, V3A, MT, to parietal cortex) and the ventral areas (from V2, V4, TEO, to TE). Neuronal selectivities differ between hierarchical levels in a systematic way.

Neurons in V1 have small receptive fields; they only respond to stimulus presentations in a restricted part of the visual field (e.g., Van Essen, Newsome, &

Maunsell, 1984). They respond selectively to simple stimulus features like orientation, spatial frequency, wavelength, direction of motion, and binocular disparity (e.g., Gizzi, Katz, Schumer, & Movshon, 1990; Hubel & Wiesel, 1968; Poggio, 1995; Schiller, Finlay, & Volman, 1976). V2 neurons have somewhat larger receptive fields and in addition to selectivities for simple stimulus features such as orientation, wavelength and disparity, some V2 neurons respond to more complex stimuli such as illusory contours (Peterhans & von der Heydt, 1989) and relative disparity (Thomas, Cumming, & Parker, 1999). The responses of many V1 and V2 neurons are modulated in a feature-specific way by stimuli outside their “classical” receptive field (e.g., Lee, Mumford, Romero, & Lamme, 1998; Sillito & Jones, 1996; see also Lamme, 2001). Neurons in the ventral area V4 respond selectively to color and relatively simple shape features (e.g., Kobatake & Tanaka, 1994; Pasupathy & Connor, 1999; Zeki, 1983). Furthermore, strong interactions between stimuli within and outside their classical receptive field have been observed (Moran & Desimone, 1985; Reynolds, Chelazzi, & Desimone, 1999). At the end-point of the ventral stream, area TE, neurons have large receptive fields of on average about 10 visual degrees, and they prefer more complex shape features and shape and color combinations (e.g., Tanaka et al., 1991). In addition, some TE neurons respond selectively to highly complex stimuli such as faces and hands (e.g., Baylis, Rolls, & Leonard, 1985; Gross, Rocha-Miranda, & Bender, 1972).

In the dorsal visual stream, some areas (MT/V5, MST, FST) display strong selectivity for several motion parameters, whereas neurons in parietal areas are selective for stimulus position in relation to motor components (e.g., Albright, 1984; Sakata et al., 1997).

However, one should bear in mind that all these differences are relative, both at lower levels (e.g., Burkhalter & Van Essen, 1986; Felleman & Van Essen, 1987) and higher levels (Sereno & Maunsell, 1998; Op de Beeck & Vogels, 2000). For example, although it has been suggested that V4 contains the highest proportion of neurons with wavelength-selective responses that display color constancy (Zeki, 1983), direct comparisons with several other areas (e.g., V2) are lacking. Furthermore, many cells in V4 lack color selectivity, suggesting that the term ‘color area’ neglects the functional diversity of response properties in this area. It would be too simplistic to assume that there exists a one to one mapping of the coding of particular stimulus attributes and single brain areas. Each stimulus attribute is coded by a system encompassing several cortical areas and each area seems implicated in the coding of several stimulus attributes.

3.1.2. Retinotopic and columnar organization

In V1, only the contralateral visual field is represented completely. Neurons are ordered according to their receptive field (RF) position (‘retinotopy’; e.g., Van Essen et al., 1984). Neurons with foveal RFs are situated laterally, whereas neurons with more eccentric RFs along the horizontal meridian are situated medially along the calcarine sulcus. The upper visual field is represented in the lower part of V1 and the lower visual field in the upper part of V1. A similar clustering according to RF position is present in visual areas at higher levels in the hierarchy, but the strict

retinotopical organization weakens at progressively higher levels. A retinotopic organization can still be found in areas V2, V3 and V3A. Also V4 has a retinotopic organization (e.g., Gattass, Sousa, & Gross, 1988), but it should be noted that once beyond V2, the retinotopy appears less clear and the areal boundaries (and number of areas) are still a matter of debate (e.g., Stepniewska & Kaas, 1996; Kaas, 1997). Even in area TEO, but not TE, there is evidence for a weak systematic organization of RF position (Boussaoud, Desimone, & Ungerleider, 1991; Hikosaka, 1998). In addition, the amount of the ipsilateral visual field representation increases in this hierarchy, with neurons in area TE commonly receiving strong callosal-dependent input from the ipsilateral retina (Rocha-Miranda, Bender, Gross, & Mishkin, 1975).

In addition to a retinotopic organization, neurons also tend to cluster according to other response properties. For example, in area V1, small-scale columns have been found for ocular dominance and orientation preference (Hubel & Wiesel, 1968). Some studies have indicated that the existence of columns is not restricted to low-level visual areas, but can even be found at higher levels in both visual streams (for review, see Mountcastle, 1997). The clustering in these areas does not involve the same stimulus attributes as found in V1, but is related to the typical selectivities in these areas, like direction selectivity and disparity tuning in MT/V5 (Albright, Desimone, & Gross, 1984; De Angelis & Newsome, 1999) and moderately complex object features in area TE (Fujita, Tanaka, Ito, & Cheng, 1992).

Despite the impressive evidence that a clustering of neurons with similar response properties is a fundamental organizational principle in the visual cortex, this clustering is incomplete in two ways. First, even if some clustering is found for a particular stimulus parameter, then it is only relative and nearby neurons will rarely display exactly the same response properties for this parameter. Large variations are still likely. Second, only some stimulus parameters are clustered (and not necessarily the most important ones from a computational point of view), leaving much variation in other response characteristics between nearby neurons.

3.1.3. Overlapping neuronal substrates of different cognitive functions

One fundamental issue in cognitive psychology has been the division of the human mind into separate cognitive functions (Donders, 1969; Sternberg, 1969). These cognitive functions are organized in larger cognitive systems. For example, numerous functions (e.g., contour integration, figure/ground segmentation, ...) have been distinguished within the visual system (Palmer, 1999). Other cognitive systems are attention (Parasuraman, 1998), mental imagery (Farah, 1995; Kosslyn, Behrmann, & Jeannerod, 1995a,b), short-term memory (Baddeley, 1986) and long-term memory (Schacter & Tulving, 1994).

Studies of the neuronal implementation of these systems have revealed that they are partly located within the same neuronal substrates (e.g., the visual areas). For example, single-cell recordings in non-human primates have shown modulations by attention throughout the visual cortex (e.g., McAdams & Maunsell, 1999; Miller & Desimone, 1994; Reynolds, et al., 1998; Roelfsema, Lamme, & Spekreijse, 1998; Treue & Maunsell, 1999; see also Lamme, 2001). Likewise, neuropsychological studies showed that lesions to particular regions can have detrimental effects on

functions from different systems (e.g., Farah, 1990; Ungerleider, 1995; Zeki, 1993; but see Bartolomeo et al., 1998). Several models have suggested that parts of different cognitive systems can share the same organizational structure and neuronal substrate, while the actual computations underlying the different functions can be qualitatively different (Farah, 1995; Sakai & Miyashita, 1993). Some, but not all, processes related to attention, memory, and mental imagery seem to implicate visual areas. For example, several non-visual cortical and subcortical structures seem to be involved in the consolidation and retrieval of long-term memory, but there are indications that memory storage itself is related to visual regions (Ungerleider, 1995). While a single-unit study can often differentiate these different processes according to some distinct characteristics (e.g., their temporal properties), these findings are more problematic for the interpretation of population activity. Given an overall activation in a particular region, it could still reflect computations that are fundamentally different.

3.2. Computational neuroimaging in the human visual cortex

PET and fMRI provide a global indirect measure of neuronal activity. Despite likely further improvements in their spatial resolution, the indirect measurement will impose an upper limit because the metabolic changes are related to the activity of groups of neurons. On the other hand, the clustering of neurons with similar response properties, as described in the previous section, makes such population activity more relevant. Further results indicate that one has to sample the right area size in order to make strong inferences. Scannell and Young (1999) argued persuasively that the relation between neuronal population activity and the activity of single neurons is highly dependent on the homogeneity of the responses of the single neurons in the population. As a result, the effect of stimulus presentations and task manipulations on population activity can be very different. On the single-cell level, the presentation of a stimulus strongly modulates the activity of neurons that are selective for this stimulus during stimulus presentation, while other manipulations like attention can affect the baseline firing rate and responsiveness of a larger subsample of neurons at longer time scales, possibly – as indicated in the previous section – in one and the same brain region (Maunsell, 1995).

If neurons in a particular population are tuned to several stimulus dimensions (as found for all visual areas), then only a relatively small proportion of them will be driven strongly by any given stimulus. Manipulations that change the baseline firing rate of more neurons on a longer time scale will have a much larger impact on population activity. Scannell and Young (1999) concluded that it is likely that neuroimaging signals that sample across broad regions in which neuronal tuning is diverse are dominated by changes in attention (see Fig. 3). Because attentional modulations are quite different from more specific stimulus effects, it is necessary that both can be distinguished. The better the spatial resolution approximates the area size in which neurons with similar response properties are clustered, the stronger the inferences one can draw from neuroimaging results about the actual computations that are performed in particular brain regions. As this clustering seems to be in-

complete, resulting in populations with heterogeneous response properties, inferring single-cell response properties from neuroimaging results is not straightforward.

In the following sections, we will bear these considerations in mind while reviewing the contribution of PET and fMRI to our understanding of the functional organization of the human visual system. In the first section, we will describe the

Fig. 3. A hypothetical comparison of the modulation of population activity by stimulus presentations and attentional processes. The two rectangles on top of the figure represent two parts of the visual field. The symbols LH (left-horizontal) and LV (left-vertical) refer to a cortical population of neurons responding to horizontal and vertical bars, respectively, presented at the position of the left rectangle. Likewise, RH and RV stand for right-horizontal and right-vertical, respectively. LHV and RHV refer to the population of neurons responding at bars of both orientations at the left and the right rectangle, respectively. The plots represent the mean response in each of these neuronal population when a stimulus is presented or attention is directed as indicated in the two corresponding rectangles. Focus of attention is represented by a bold rectangle. The ordinate is in arbitrary units. A neuroimaging signal representing the activity of a population of all neurons responding at a particular position would not be able to distinguish between effects that are specific for particular features (e.g., horizontal versus vertical orientation; see plots in top and middle rows) and more general modulations (see plots in bottom row). In contrast, if the signal could differentiate between neurons with horizontal and vertical bar preferences, it would be able to distinguish specific and more general modulations.

conclusions that have been drawn about the functional organization of the human visual cortex into multiple visual areas. We will focus on the potential of these techniques for revealing how computations are implemented in neuronal populations. Next, we describe some studies showing that other cognitive systems affect the activity of these visual areas, as found convergently in electrophysiological studies.

3.2.1. Visual areas and their organization

Early studies confirmed already the general division of the visual cortex into two processing pathways (Haxby et al., 1991; Köhler, Kapur, Moscovitch, Winocur, & Houle, 1995). In a direct comparison of relative position discrimination with shape discrimination, these studies found that a stimulus position task increases the activity in parietal cortex, while object discrimination activates the occipitotemporal cortex. Later studies have found that the human visual cortex is also composed of multiple areas with a retinotopic organization (DeYoe et al., 1996; Sereno et al., 1995; Tootell et al., 1998a,b). Because a systematic study of retinotopy requires a parametric variation of stimulus position, these studies have been done mainly with fMRI. To map all retinotopical features, stimuli were varied in their angular position (assessed by rotating stimuli) and in their eccentricity (assessed by contracting and expanding stimuli). Within a retinotopically organized area, a rotating or contracting stimulus will produce a continuously changing signal with a frequency that is related to the stimulus speed. Different positions in a particular area consisting of neurons with different RF positions, will have a different temporal phase. Using these stimuli, several retinotopic areas have been mapped in human visual cortex. The relative location of these areas is generally consistent with the organization in macaque monkeys, and the human areas are given the same names as the monkey counterparts: V1, V2, VP, V3, and V4v. Later studies revealed additional areas with a less strict retinotopic organization (V3A, V7, V8; see Tootell et al., 1998a,b). Macaque homologues of these areas have also been proposed, but this point is still highly controversial.

We mentioned the existence of small-scale columns and clusters throughout the visual cortex. Several studies have been successful in revealing ocular dominance columns in human V1 (Cheng, Waggoner, & Tanaka, 1999; Menon, Ogawa, Strupp, & Ugurbil, 1997). A recent study in anaesthetized cats (Kim et al., 2000, but see Logothetis, 2000, for a critical view) was able to resolve orientation columns and suggested that such high-resolution mapping would require a shift in the techniques in order to use the initial small decrease in fMRI signal that is more location-specific than the subsequent larger signal increase. As the organization of low-level vision in humans as revealed by fMRI generally agrees with monkey visual cortex, these findings strongly suggest that a thorough study of monkey visual cortex is highly relevant for understanding human vision (for a striking discrepancy, see Tootell et al., 1997). Furthermore, by pinpointing particular processes to individual brain areas, it becomes possible to study them in a more integrated way across different species and different methods. Recent developments in the application of fMRI techniques to imaging in macaque monkeys will be highly relevant for a further investigation of similarities and differences between monkey and human visual cortex

using the same paradigms (Logothetis, Guggenberger, Peled, & Pauls, 1999; Van Duffel et al., 1998).

3.2.2. *Functional differences between visual areas*

3.2.2.1. Color. Several groups (e.g., Bartels & Zeki, 2000; Hadjikhani, Liu, Dale, Cavanagh, & Tootell, 1998; Zeki et al., 1991) compared the presentation of colored and grey-scale images and found that colored images activated a region at the ventral surface of the occipital cortex. Zeki and his colleagues argued that the activated region is the human homologue of macaque area V4, which some researchers believe is the area devoted to color processing, whereas another report, providing not only a functional localization of the color area but also additional retinotopic mapping, suggested that this 'color area' is located anteriorly of the human homologue of macaque area V4 (Hadjikhani et al., 1998). Recent studies indicated that other areas (V1 and V2) are also activated more by colored compared to grey-scale stimuli (e.g., Engel et al., 1997a,b), which agrees with the presence of wavelength selective cells in macaque V1 and V2. These additional activations were found to be weaker compared to the robust results in the ventral occipital cortex. This localization of the regions that are primarily involved in the processing of color is a first and important step towards an understanding of the computations underlying color perception. At least, the processing of color seems to involve several cortical stages that are located in a system comprising several cortical areas.

After this first step, researchers have already started with a more detailed investigation of the characteristics of population activation in these areas. Wandell, Baseler, Poirson, Boynton, and Engel (2000) found that V1 and the ventral occipital cortex share a common color tuning. The iso-response curves in both areas to differently colored stimuli were comparable, suggesting that the color tuning in the ventral occipital cortex is not unique. Further studies will be needed to investigate the relation of the responses of both areas in more complex issues related to color perception (e.g., color constancy). Single-cell recordings (Zeki, 1983) suggested that the responses of V1 neurons are primarily affected by wavelength whereas V4 neurons display more color constancy. Bartels and Zeki (2000) investigated the effect of changing illuminant conditions temporally when subjects were viewing colored and achromatic Mondrians. Compared to a condition with a static illuminant, changing the illuminant increased the activation in the ventral occipital cortex. The difference between this region and V1 and V2 became more prevalent compared to the previous studies. These results were found for both colored and achromatic stimuli, suggesting that they reflect a 'ratio-taken' process that is non-specific for color per se (but such process has been suggested to be necessary for color constancy). However, several other processes could differ between these conditions (e.g., attention to the stimuli), and no behavioral control was present (subjects were performing no task). These results can even be interpreted as being contradictory to the predictions made under the assumption that neurons in human ventral occipital cortex simply display color constancy (as suggested for the macaque by Zeki, 1983). In this interpretation, one assumes that the stimulus representation in this area displays a particular

feature, color constancy, whereas the previous interpretation was posed in process terms, that is, the operation of a ratio-taken process (as an activation difference between two conditions can reflect differences in representations as well as processes, analogous interpretational problems can be detected in many studies). If neurons in this area display color constancy, one would predict less differential activation in the ‘color area’ compared to areas without this response property. For neurons with color-constancy, both conditions would consist of the same stimuli, whereas neurons without color-constancy would get adapted in the condition with a static illuminant but not if the luminant varies (similar to the results found with ‘fMR adaptation’ described below). So, the computational difference as suggested in monkeys has not yet been verified in a conclusive way in the human visual cortex.

3.2.2.2. Motion. Strong motion-related responses have been found in primary visual cortex and a region that seems to include the human homologue of monkey MT/V5 (Tootell et al., 1995a,b; Watson et al., 1993; Zeki et al., 1991). More recently, several studies have investigated the relation between the response properties in human MT/V5 (probably also including human MST) and motion perception. A series of studies by Wandell and colleagues (Dougherty, Press, & Wandell, 1999; Seidemann, Poirson, Wandell, & Newsome, 1999; Wandell, Poirson, Newsome, Baseler, & Boynton, 1999) have investigated the effect of stimulus contrast on speed perception, signal strength in human MT/V5 and single-cell responses in macaque MT/V5. At the behavioral level, perceived speed depends on stimulus contrast and color. If stimulus contrast is limited to middle and long wavelengths, then perceived speed is generally independent of contrast, except at very low contrast levels where speed is underestimated. However, if stimulus contrast is limited to short wavelengths, then perceived speed reaches the same asymptotic level at much higher contrast levels. In human MT/V5, Wandell et al. (1999) found that the fMRI signal saturated at lower contrast levels compared to fMRI signal from primary visual cortex. If MT/V5 would contain a representation of motion parameters, independently of other stimulus parameters like contrast, then one would indeed expect more invariance for contrast. Furthermore, as found at the behavioral level, the activity evoked by stimuli at short wavelengths required much higher contrast levels to reach the same asymptotic level as found with middle and long wavelengths.

At the single-cell level, responses of neurons throughout the dorsal stream are direction-selective, i.e., they depend on the direction of motion. Whereas the responses of neurons in primary visual cortex are primarily affected by local motion signals, the response properties of neurons in higher-level areas are more similar to global motion perception (Gizzi et al., 1990). Several groups have tried to investigate the directional interactions in human MT/V5 indirectly (Culham et al., 1999; He, Cohen, & Hu, 1998; Heeger, Boynton, Demb, Seidemann, & Newsome, 1999; Tootell et al., 1995a,b; see also Culham, He, Dukelow, & Verstraten, 2001). This property cannot be studied directly, for example, by comparing activity evoked by two stimuli, each perceived as moving in a different direction. As neurons in MT/V5 with different direction preferences are not clustered over a broad area, it would be difficult to find any difference in the fMRI or PET signal. Direction selectivity in

human MT/V5 has been studied by verifying a close correspondence between MT/V5 activation and the occurrence of a direction-specific visual illusion (MAE or the motion aftereffect). If subjects are adapted to continuous motion, they report that a subsequent stationary test stimulus appears to move in the opposite direction. Through a manipulation of several design parameters, one has confirmed that MT/V5 is activated in those conditions where the MAE is present psychophysically, whereas such correspondence was not found consistently for other areas. For example, the introduction of a blank period between adaptation and test phases extends the total decay time of the MAE. Like the perceptual effect, activity in MT/V5 dropped during the blank period and raised again during the test phase to reach a much higher level compared to the level without introduction of the blank period (Culham et al., 1999). The correspondence between MAE, a direction-specific effect, and MT/V5 activation suggests a direction-selective coding of stimulus motion in this area.

Other approaches have also revealed direction-selective coding of stimulus motion in human MT/V5. Heeger et al. (1999) found a metabolic correlate of psychophysical effects suggesting that motion is mediated by opponent mechanisms for opposite motion directions. If two identical sinusoidal gratings that move in opposite directions are superimposed, then human observers do not perceive a moving stimulus, but rather a flickering, stationary stimulus. Metabolism in human MT/V5 was reduced by taking a single moving grating and superimposing a second grating moving in the opposite direction. No evidence for motion opponency was found in V1. As opponent mechanisms for motion are necessarily based upon direction-selective mechanisms, these results indicate strong directional interactions in human MT/V5.

3.2.3. *Proliferation of modules*

The application of neuroimaging techniques has led to a proliferation of ‘visual areas’ that are defined in a functional way by their unique selectivity for particular stimuli. Some famous examples are the lateral occipital complex (LOC) or ‘shape area’ (Malach et al., 1995), the kinetic occipital cortex (KO) selective for boundaries defined by motion (Van Oostende, Sunaert, Van Hecke, Marchal, & Orban, 1997), the fusiform ‘face area’ (FFA; see Kanwisher, McDermott, & Chun, 1997a,b; Puce, Allison, Gore, & McCarthy, 1995), and the parahippocampal place area (PPA, see Epstein & Kanwisher, 1998). Whereas three distinct criteria had to be reached before one accepted a distinct area in the macaque (cytoarchitectonic differences, differences in the pattern of connectivity with other areas, and functional differences), there is only evidence for the last criterion for these new areas. Furthermore, there is no clear relationship with electrophysiological evidence. So, we can no longer make firm *a priori* predictions about response properties of single neurons. Although some analogies have been suggested with electrophysiological results in monkeys (e.g., Desimone, 1991), no selective clustering of any of these stimuli has been found persuasively in the macaque brain.

The localization of different stimuli to distinct areas is one important piece of information, but it needs to be augmented before we can take these results as a

support for modularity. A simple interpretation would be that these different areas contain neurons with generally the same stimulus selectivities but with altered relative proportions of these selectivities. From this viewpoint, there is no need to interpret the neuroimaging evidence as an indication towards a fundamental difference between human and macaque visual cortex. Moreover, neuroimaging results give only weak indications towards those relative proportions. For example, if human V4 displays the largest difference in activation between colored and grey-scale images, is this because it has the largest proportion of color-selective neurons, or alternatively, because its color-selective neurons fire more vigorously while their proportion is the same? Most defenders of modularity in the human brain will try to make stronger inferences as they argue that there are qualitative differences between the different areas in some computational mechanisms. Taking the example of color selectivity, this interpretation in its most extreme form could state that the strong activation of V4 and not V3 by colored stimuli indicates that only V4 has color-selective neurons. In a more realistic account, it could be argued that this strong activation does not only indicate a higher number of color-selective neurons, but also that these neurons are computing something different compared to the less frequent color-selective neurons in other areas (see the discussion on color constancy). We will review some partial evidence towards such qualitative differences, indicating computational differences between some of these areas.

3.2.3.1. The shape areas. Malach et al. (1995) compared the fMRI signal during the presentation of visual forms with a condition consisting of the presentation of random textures. Several regions in the lateral occipital gyrus (LOC) were activated. Activation in these regions was independent of familiarity, as it was also found with abstract geometric patterns. Interpreted as a group of regions instead of one 'shape area', these data are in line with the electrophysiological results in monkeys that suggested a rather distributed processing of visual form. Other studies have found more medial activation in the fusiform gyrus in a comparison of similar conditions (Kanwisher et al., 1997a,b; Martin, Wiggs, Ungerleider, & Haxby, 1996; Op de Beeck, Batse, Wagemans, Sunaert, & Van Hecke, 2000; Rosier et al., 1997). To date, it is not clear why different studies, all using a diversity of visual forms, result in different localizations.

Subsequent studies, mainly by Grill-Spector and her colleagues, have been able to relate some properties of the fMRI signal in these regions to single-cell response properties in the higher levels of the macaque ventral visual stream (the inferotemporal cortex). First, Grill-Spector, Kushnir, Edelman, Itzhak, and Malach (1998a,b) provided fMRI evidence suggesting that the shape areas contain an abstract representation of shape that is not dependent on the specific cue, as was found previously in the macaque inferotemporal cortex by Sary et al. (1993). Similar activation patterns in LOC were related to the presentation of shape revealed by relative luminance, motion, or texture differences. Although the similarity with the results from single-cell recordings is striking, the population activity found with fMRI cannot prove that individual neurons in the population code shape in a cue-invariant way. It is possible that some neurons code shape from relative luminance

and other neurons code shape from relative motion, and that both types of neurons are intermingled yielding a similar effect on the population response.

In a second study, Grill-Spector et al. (1998a,b) found that scrambled visual forms evoked less response in LOC compared to normal visual forms. The scrambling algorithm divided the original forms into several fragments and randomly intermingled them. Likewise, Vogels (1999) found that scrambled forms evoked less responses in single neurons in area TE of macaque monkeys. Op de Beeck et al. (2000) found a similar effect of scrambling on the fMRI signal using a fundamentally different scrambling algorithm that preserved the overall configuration of the forms while degrading the detailed parts. Apparently, both local and global aspects of visual form are encoded in the shape areas. fMRI signal in these regions is decreasing if one of the two aspects is degraded.

Third, Grill-Spector et al. (1999) (see also Grill-Spector & Malach, 2001) have used a more indirect approach to investigate other response properties of the shape areas. If shape processing in the human shape areas would be similar to shape processing in area TE of the monkey, then one would expect relative size- and position-invariance of the responses of single neurons (i.e., neurons would prefer the same shapes regardless of size and position). However, as with the study of direction-selectivity in human MT/V5, one has to take an indirect approach as activity is averaged across a neuronal population with heterogeneous stimulus selectivities. Grill-Spector et al. (1999) circumvented this problem by using fMR adaptation, i.e., the reduction of the fMRI signal due to repeated presentation of identical images. Possibly, this reduction is related to neuronal adaptation: As identical images evoke responses in the same neurons, these responses will get progressively weaker. If the responses of neurons in a particular area would be invariant for a particular stimulus attribute, then one would expect similar levels of neuronal adaptation whether or not the stimulus attribute remains constant. fMR adaptation was largely invariant for changes in size and position, but less for changes in illumination and viewpoint. These findings suggest that the representation of shape in these areas is more size- and position-invariant than illumination- and viewpoint-invariant. Single-cell recordings in monkeys have revealed the same general trend (e.g., Ito, Tamura, Fujita, & Tanaka, 1995; Logothetis, Pauls, & Poggio, 1995), but provided additional data that these differences are only relative. For example, some size information is still preserved in the responses of single neurons in the macaque inferotemporal cortex (Op de Beeck & Vogels, 2000).

Although the inferences that can be drawn from the neuroimaging results about shape processing in the human shape areas are weaker compared to the single-cell data in macaque monkeys, there is a striking convergence between both lines of evidence. These fMRI studies have given some important cues about how shape is processed in the shape areas. Other fMRI studies have focused on determining what aspect of shape perception is related to activity in these regions. As indicated by several lines of psychophysical and neuropsychological research, shape perception is the outcome of multiple processing stages (e.g., Humphreys & Riddoch, 1987; Marr, 1982). Viewing coherent shapes could evoke more activity compared to viewing incoherent line patterns because of several reasons that are fundamentally different

from a computational perspective (see Fig. 4). At the most general level, viewing incoherent line patterns could evoke less activity because subjects tend to pay less attention to these patterns. This differential amount of processing devoted to the stimuli could be a general difference or it could be restricted to a particular processing stage. Based on the evidence reviewed above, we can only conclude that this activation in the shape area has to reflect differences in visual stages, as it is also found for meaningless shapes (assuming that these shapes do not activate memory representations). Other results suggest that this shape area is not only implicated in visual processing, but can be seen as an interface between shape perception and memory (e.g., Op de Beeck et al., 2000; Rosier et al., 1997; Schacter et al., 1995).

To clarify the role of the fusiform gyrus in shape perception, we (Op de Beeck et al., 2000) manipulated task requirements in addition to the manipulation of shape coherence. Even when task requirements forced subjects to devote more processing to incoherent shapes compared to coherent shapes, we still found less fMRI signal for incoherent shapes in the fusiform gyrus. Apparently, these differences in fMRI signal are related to an unavoidable consequence of the qualitative stimulus difference. Necessarily, degraded object images will provide less information regarding the

Fig. 4. A neuropsychological investigation of visual agnosia has resulted in a model of object recognition with several processing stages (based on Humphreys & Riddoch, 1987). A neuropsychological deficit in shape perception at the behavioral level can reflect a problem at several stages. Likewise, the link between an activated region in a neuroimaging study and a particular stage is indeterminate when the activation is found with subtractions that isolate more than one processing stage.

presented objects, despite all the effort invested by the subjects. It suggests that the fMRI signal reduction in the fusiform shape area is related to the less precise object representation that subjects can build from the available information. This interpretation is in line with previously found modulations in brain regions that appear to be similar to the fusiform part of the shape areas. A study by Schacter et al. (1995) revealed less activation in this brain region when subjects saw impossible (structurally incoherent) objects compared to possible objects. The structural incoherence will necessarily harm the construction of a full object representation. Dolan et al. (1997) investigated the effect of priming on the activation pattern related to two-tone pictures. These pictures are unrecognizable without priming. Primed pictures, from which subjects are able to extract the information necessary to construct an object representation, were related to increased activation in the fusiform gyrus compared to unprimed pictures, again confirming the role of the fusiform shape area in object representation (although alternative hypotheses, e.g. attentional modulations, could explain this individual result). These results illustrate that fMRI studies can allow the isolation of specific processing stages, while inferences about how these representations and processes are carried out can be strengthened by looking at converging evidence from single-cell recordings.

3.2.3.2. Modular processing of different object classes. Several studies have suggested that different activation patterns are related to different object classes like letters versus faces versus everyday objects. Earlier reports suggested that letter recognition is related to specific activation in the left posterior fusiform gyrus (e.g., Petersen, Fox, Snyder, & Raichle, 1990), face recognition to the right fusiform gyrus (e.g., Sergent, Ohta, & MacDonald, 1992), whereas the recognition of everyday objects has not been pinpointed to a particular brain area. However, the earlier reports suggesting these dissociations were not conclusive. Aguirre and Farah (1998) compared the results of many neuroimaging studies and found no systematic differences between different stimuli. However, in the cases where different stimulus classes are compared within the same study and subjects, differences have been found that are consistent across different subjects (e.g., Ishai, Ungerleider, Martin, Schouten, & Haxby, 1999; Kanwisher et al., 1997a,b). The localization of different stimulus classes to different brain areas suggests that these stimuli involve different representations and processes, but it is difficult to clarify the nature of these differences (that is, determining the processing stage they are related to). The available evidence is still rather coarse.

First, the differential patterns of activation are delineated with non-familiar members of the stimulus classes (e.g., non-familiar faces). Although it is difficult to reject this explanation completely, this result makes it improbable that the differences would reflect semantic processing. Second, each stimulus category also evokes responses in the regions that responded maximally to other stimuli. For example, the face area is also responsive, albeit weaker, to other objects (Kanwisher et al., 1997a,b; Ishai et al., 1999). Based on their findings, Ishai et al. (1999) suggested that the representation of each stimulus category is not restricted to one region, but is more distributed across a broader cortical range with a partial segregation of

different kinds of information about object form. However, some findings of Gauthier and her colleagues (Gauthier, Tarr, Anderson, Skudlarski, & Gore, 1999) point to another possible explanation (Gauthier, 2000). The pattern of activation in the ventral occipitotemporal cortex does not only depend on the stimuli that are shown, but also on how these stimuli are processed by subjects. The activation pattern related to stimuli from a particular stimulus class (in case, animate-like artificial objects called ‘greebles’) was similar to the activation pattern related to faces, but only in subjects with substantial expertise in differentiating individual objects from this stimulus class. These findings were replicated with car and bird experts (Gauthier, Skudlarski, Gore, & Anderson, 2000). Apparently, the similarity found psychophysically between the processing of faces and the processing of other objects after extensive expertise (e.g., Diamond & Carey, 1986; Gauthier & Tarr, 1997), is also reflected in the human functional neuroanatomy. However, expertise in other domains (e.g., chicken sexing, see Biederman & Shiffrar, 1987) has been suggested to result in contrasting effects on the processing of these stimulus classes. It would be interesting to see whether the effects of Gauthier et al. (2000, 1999) reflect a general effect of expertise, not being related to specific visual processes, or, alternatively, is dependent on the exact computational processes altered by expertise. Furthermore, although activations in the face area evoked by other stimulus classes get larger after expertise, they do not reach the same level as the activations related to face stimuli. The available evidence is not decisive to determine whether these differences are related to the higher amounts of expertise with the face stimuli, or to other properties of these stimuli.

In sum, the distinct localization of different stimulus categories indicates differences in the representation or processing of these stimuli. To date, neuroimaging results have only provided some limited cues towards the nature of these differences, but it is likely that knowledge will accumulate in future years. However, even if we find out which computational differences exist between the processing of different stimulus categories, then the absence of converging evidence from single-cell recordings will make it hard to derive how these computations are carried out within particular brain regions.

3.2.4. Distinct cognitive systems in overlapping visual areas

Fundamental conceptual and computational differences underlie the distinction between cognitive systems as perception, attention, imagery, and memory. Several lines of evidence from neuroimaging studies indicate that some processes from these distinct cognitive systems can be localized partly within the same brain areas. As such, neuroimaging itself augments the body of evidence that suggests that one should be very careful with linking computational conclusions to neuroimaging results. We will only discuss the relation between perception and attention, but similar problems can be highlighted in the interaction between perception and mental imagery, short-term and long-term memory, as several studies have suggested imagery- and memory-related modulations in visual areas (e.g., Bartels & Zeki, 2000; Kosslyn, Pascual-Leone, Felician, Camposano, & Keenan, 1999; Kosslyn et al., 1995a,b;

Martin et al., 1996; Schacter & Buckner, 1998; Schacter et al., 1995; Ungerleider, 1995; Orban & Vogels, 1998).

Behaviorally, attention biases the processing of some stimulus aspects. As a result, these stimulus aspects are processed better while others are neglected. The neural correlate of this bias is a relative enhancement of neural activity in those brain regions that process the favoured stimulus aspects, together with a suppression of activity related to other stimulus aspects. This effect has been shown for most of the stimuli or stimulus attributes described so far as revealing activations in specific regions: color (Bartels & Zeki, 2000; Chao & Martin, 1999; Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991; Price, Moore, Humphreys, Frackowiak, & Friston, 1996), motion (Culham et al., 2001), faces (Wojciulik, Kanwisher, & Driver, 1998) and houses (O'Craven, Downing, & Kanwisher, 1999). The metabolic effect of selective attention can be very specific and early in the processing stream. Tootell et al. (1998a,b) investigated the retinotopy of visual spatial attention in the retinotopic visual areas (see also Brefczynski & DeYoe, 1999). Covert spatial attention to a particular location in the visual field was related to fMRI signal increase at the retinotopically corresponding locations in these areas. Inversely, fMRI signal decreased in the same cortical locations when attention was directed to other locations in the visual field. The strength of the attention-related effects was related inversely to the reliability of the retinotopic mapping (stronger in areas where retinotopy was broader), but it was still found in primary visual cortex.

These results show that a retinotopic and functional mapping of visual cortex not only can be performed by manipulating stimulus characteristics, but also by manipulating attention. If systematic attentional differences are correlated with the manipulation of stimulus parameters, then these two factors become indistinguishable from each other in the neuroimaging signal. As all classical studies showing functional modularity and retinotopy involved a systematic and predictable variation of the stimulus parameters (subjects can predict reliably from the previous trial whether the next stimulus will contain motion, color, or, in the case of retinotopic mapping, where it will be shown), part of these signals could be related to attention instead of purely sensorial processes.

Chawla, Rees, and Friston (1999) used an event-related fMRI paradigm to dissociate both processes. Subjects had to make fine discriminations of either the color or the motion of compound color-motion stimulus events that were presented in an interleaved fashion with a grey, stationary background stimulus. The stimulus events evoked activity in both the ventral occipital cortex and human MT/V5. However, the strength of this activation was modulated by attention. The same compound color-motion stimuli produced more activity in human MT/V5 if attention was directed to motion compared to color. The inverse pattern was found in the ventral occipital cortex. The event-related nature of the design allowed the authors to differentiate this effect of attention (modulation of stimulus-related responses) from changes in baseline activity that are not related to stimulus events. They found indeed that, in addition of modulating stimulus-related responses, attention to color and motion also enhanced activity in ventral occipital cortex and human MT/V5, respectively, even when subjects were viewing a grey, stationary stimulus.

4. Conclusion

By using neuroimaging techniques one has related several stimulus and task manipulations to corresponding metabolic effects in distinct regions of the human brain. A taxonomy of all these manipulations with their localization gives a first indication towards the kind of processes that are located in a particular brain area. We reviewed the potential of neuroimaging techniques to go beyond mere localization and to indicate which computational principles underlie a particular activation. We indicated that there is no simple relationship between the population activity as measured indirectly with neuroimaging techniques and the activity of single neurons in the population because neuronal populations are generally heterogeneous in their response properties. If we want to conclude how particular computations are carried out in a neuronal population, then we need converging evidence from other paradigms like single-cell recordings. Furthermore, meaningful inferences can only be drawn from studies that are able to dissociate the effects of manipulations that bear on different computational principles in the same brain areas.

This paper bears on the important question: What is the most appropriate level of resolution to investigate cognitive processes and their neural implementation? Indeed, neuronal activity at the population level is more relevant to behavior than single-cell activity (like the activity of the whole brain is more relevant to behavior than the activity of one region). However, if one wants to construct a cognitive model of behavior, then a mere localization of these processes is not that important (contrary to its importance for neuropsychology). For a cognitive scientist, it is important which cognitive processes are involved in a task and how these are computed, but it does not matter where they are computed (e.g., it does not matter whether visual cortex is located posteriorly or anteriorly). Paradoxically, the more one is interested in cognitive processes at an algorithmic level (independent of their specific neuronal implementation), the more one needs additional information beyond population activity.

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