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THE MODULARITY OF PROCESSING AND PERCEPTION IN THE VISUAL BRAIN

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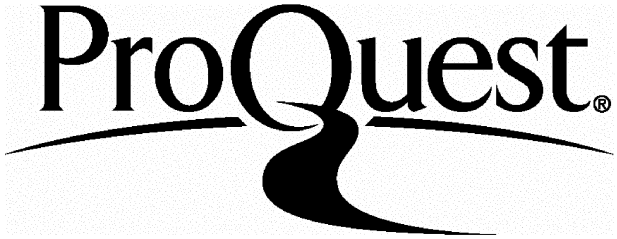

Abstract

Practical and theoretical approaches were applied to try to unravel the relationship of the anatomical processing sites to the relative timing of processing and perception. Psychophysical, imaging and theoretical studies led to the overall conclusion that simultaneously presented attributes that are perceived at the same time are processed at the same site, and ones that are perceived at different times are processed at different sites. This is referred to as to the *theory of perceptual sites.* Functional magnetic resonance imaging (fMRI) experiments charted the organisation of the human colour centre (the V4-complex), and found it to be more complex than previously believed. It has two subdivisions, V4 and V4α, of which V4 is retinotopically organised, while V4α is not. The extent and organisation of the colour centre revealed in this study may account for the variability and severity of the syndrome of achromatopsia (acquired cortical colour blindness). Application of an independent components analysis (ICA) to fMRI data showed that these two subdivisions are coactive and can be isolated together from the remaining brain activity. It was further shown that, because cortical areas enjoy substantial autonomy, they differ in their activation time courses, such that ICA can dissect the brain computationally into its functional units, creating what we call *chronoarchitectonic maps.* The above evidence, when viewed in context of previous experimental and clinical studies, leads us to propose the following: First, that the activity in different visual areas reaches conscious perceptual endpoints at different times; leading to the supposition that consciousness is not unitary but consists of many *microconsciousnesses.* Second, that since activity at each processing site can become perceptually explicit, there is no terminal perceptual stage in the visual brain; leading to the conclusion that activity at each site of the visual brain can be integrated with activity at any other site, and to the *theory of multistage integration.*

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Part 1:

Introduction

Overview

The work submitted herein constitute a body of work that is thematically unified. The starting point is to consider the visual brain conceptually as a system of functionally specialised modules. This raises the following fundamental question: How independent are these modules functionally, and what functions does each have? More specifically, one may ask whether their function goes beyond the processing of a given attribute. Does a functionally specialised area store all the brain's knowledge of the attribute it is specialised for, or does it even include the generation of a conscious percept for that attribute? No matter what the answers may be, the very modular nature of the visual brain raises the following two additional questions, which are interrelated: The first one is that of consciousness: How can we perceive the world in a seemingly unified percept, when in fact every visual attribute is processed at a different anatomical location in the brain? The second relates to knowledge: If the different visual attributes are processed at different sites, is the acquisition of visual knowledge a property of the whole visual brain or are there sub-specialisations in the visual brain for acquiring knowledge?

I address these issues by using two approaches: a practical one (A) and a theoretical one (B), both of which have in common that they try to give some answers to the questions raised above, and both are conceptually outlined in the following two sections. I begin by reviewing the literature on the human colour centre. Arising from this review is a possible explanation for the variation in the duration and severity of lesions in the colour centre. This explanation is fortified by the results of the imaging experiments given here. The latter shows not only that the colour centre has a more complex architecture than previously supposed and that, in addition to computing the ratios that are necessary for generating colour constancy, it is specifically involved during attention to colour. I also describe the use of the recently developed method of independent components analysis (ICA) to show that the colour centre can be isolated from the rest of the brain from fMRI data without any a priori knowledge, since its activity time course differs from that of all other regions in the brain. I then go on to show that this is not only true for the colour centre but for several other specialised visual and non visual areas and probably indeed for all functionally specialised areas. This is so because, as a consequence of their specialisation, each area responds to a stimulus in a different and unique way. Finally, I combine a thought experiment with a review of the literature to propose that each functionally specialised area not only processes the attribute it is specialised for, but that activity in it is also equivalent to a conscious percept of the attribute concerned; this leads me to introduce the concept of *microconsciousness*. I further go on to propose the consequences that this will have for the timing of perception, by introducing the theory of perceptual sites, which states that any two attributes that are processed in different cortical sites will have a perceptual delay, while two attributes processed in the same site will be perceived synchronously when presented at the same time.

(A) Practical

Most of the practical work has been concerned with brain imaging, using the technique of functional Magnetic Resonance Imaging (fMRI), which detects areas of the brain which are especially active when humans perform given tasks. For analysis I used the statistics package developed in this department (SPM) and a more novel technique, the Independent Components Analysis (ICA), which locates independent components of brain activity in space, using maps acquired at different times. Using these techniques, I concentrated on three problems raised above, namely the one of conscious experience, the one of knowledge acquisition, and the one of modularity of the cerebral cortex:

1. The organisation of the colour centre of the visual brain and the extent to which activity in that area results in our capacity to see the world in colour.

The colour system is one of the best examples of the brain's capability of acquiring a constant knowledge from a changing environment, a capability whose significance and consequences mankind has only begun to understand (Zeki, 1999). Schopenhauer was among the first to recognise explicitly that it was the brain that extracted and held this abstract knowledge, and hence recommended the study of colour as a general example of studying the knowledge-acquiring system of the brain, "..because a more precise knowledge and firmer conviction of the wholly subjective nature of colour contributes to a more profound comprehension of the Kantian doctrine of the likewise subjective, intellectual forms of all knowledge, and so it affords a very suitable introductory course of philosophy." (Schopenhauer, 1854).

Our brain needs to compare the ratio of light - for different wavebands separately - reflected from different spatial locations, before it can attach a colour to a surface (Land 1974). This ratio-taking operation must be the same for coloured and black and white surfaces, as it has to occur before any colour can be assigned to them. In our experiments we tried to activate selectively the regions involved in this ratio-taking process, by illuminating various visual scenes with a light-source that changed its wavelength composition continuously; this has the consequence that the wavelength composition of the light coming from every part of the scene changed continuously, without changing the perceived colour of any part (that is to say the perceived colours remained constant). The fMRI studies selectively activated area V4 (the human colour centre) and led to only very restricted activity in the visual areas V1 and V2. Moreover, the same results were obtained whether the scenes viewed were abstract Mondrians or meaningful natural scenes, thus showing that the ratio-taking process is a purely

computational one, not involving memory or stored associations to properties of known objects. Because this is the site which, when damaged, leads to the syndrome of acquired colour blindness (cerebral achromatopsia), the evidence I have obtained suggests that the processing site and the perceptual site for colour are one and the same and that activity generated in V4 by viewing coloured stimuli is not reported to further hypothetical sites which might be involved in the perception of colours. Additionally, we found that the activity in the brain was identical for coloured or black and white stimuli viewed under changing illuminants, confirming that the basic ratio-taking operation involves identical processing areas. The activity was identical both for illuminants changing their wavelength composition or just changing in intensity. ICA isolated the two subdivisions within the V4-complex together from the rest of the brain, showing that their acitivity time courses are highly related.

The activity also revealed that the colour centre has a much more complicated organisation than previously believed. In particular, human V4 appeared to have two subdivisions. We attempted to show that the two parts are indeed two separate areas, both anatomically and functionally, in three steps. First, we re-analysed an earlier study of the retinotopic mapping in V4 (McKeefry & Zeki, 1997) using less spatial smoothing; this revealed not only that both hemifields are completely mapped in both V4 and in the anteriorly lying V4α, but also that only V4 has separate maps for lower and upper hemifield, whereas V4α does not, indicating that the latter has no retinotopic organisation. Second, we show that attention to colour also activates the two subdivisions. Third, by re-analysing data from a study on naturally and un-naturally coloured objects (Zeki & Marini, 1998) we were able to show a functional segregation between V4 and V4α: only the latter was co-active with the even more anteriorly located object recognition area. In the discussion, I compare the organization of the human colour cerntre with that of the macaque (Bartels & Zeki, 2000a).

2. The influence of attention on activity in visual areas.

The general theoretical framework within which I am working supposes that each of the many areas that constitute the visual brain forms a specialised and autonomous unit. One feature of this autonomy would manifest itself in the independent modulation of activity in each area through attentional mechanisms. An initial step in this investigation would then be to show that the areas specialised for one attribute (e.g. colour) will be more activated when we attend to that specific attribute (colour) than when we attend to another (e.g. motion) or when we view passively. We have obtained results that show exactly this. In addition, our results show that attention to colour modulates both V4 and V4α. Attention to different visual hemifields showed the same

retinotopic organisation of V4 as the retinotopic mapping during passive viewing did, revealing a retinotopy of attention in V4 (Bartels & Zeki, 2000a).

3. The chronoarchitecture of the human brain revealed by the computational isolation of functionally specialised cortical areas from fMRI data.

There are several fundamental organisational principles according to which the human brain is organised. One of them is the principle of functional specialisation discussed above. We propose that, since separate cortical areas have different processing properties based on different physiological and anatomical properties, with the consequence that they are involved differently in different tasks, the activity pattern of each should be sufficiently unique to separate one from another. We applied independent components analysis (ICA) to data sets obtained in different fMRI experiments, which had been designed to activate particular sets of areas, which were revealed using an SPM analysis. Surprisingly, without any information about the tasks, ICA isolated regions in the brain that correspond to the different functionally specialised areas that were activated in the tasks, and which had time courses that differed. In a second step, we submitted fMRI data obtained when subjects freely viewed a film sequence to an ICA analysis to see if areas that were not specifically targeted but activated in a situation closer to real live would still show activation patterns so unique that ICA could isolate them. The results showed exactly that. This method thus allows us to create a map of the brain that reveals the location and extent of functionally specialised areas in it, together with the time courses of their activation. We call this map the *chronoarchitecture* of the brain, since it shows a dissection of the brain based entirely on activation time courses. It also shows that, in spite of the wealth of their rich inter-connectivity, the specialised areas have remarkably distinct activity time courses (Bartels & Zeki, 1999; Zeki & Bartels, 1999a; Bartels & Zeki, 2000b).

(B) Theoretical

Based on the published evidence and on our own experimental results, we discuss several conceptual consequences that current evidence has for our understanding of how the brain functions. These can be summarised in the three theories outlined below.

1. The asynchrony of consciousness.

Different visual areas get their input signals at different times (e.g. (Buchner, Weyen, Frackowiak, Romaya & Zeki, 1994; ffytche, Guy & Zeki, 1995) and terminate their tasks at different times (Moutoussis & Zeki, 1997b). The perception of a stimulus is a conscious event. We hypothesise that the asynchrony of percepts corresponding to different attributes of a unitary event in the outside world reflects that the very processing areas themselves generate separate conscious events asynchronously with respect to each other and with respect to the outside world. In other words, we believe that consciousness is not a unitary faculty, but that it is made up of many *microconsciousnesses* (Zeki & Bartels, 1998a).

2. The theory of multistage integration.

The cortical system for colour includes several stages, such as specialised groups of cells in area V1, V2 and V4 and parts of the parietal cortex. Each stage is specialised for processing the attribute at a different level of complexity. We have hypothesised that activity at each stage of a processing system can become perceptually explicit. In other words we can be aware of what happens at each stage, thus perceiving a given scene through several perceptual layers. For example, we perceive not only the correct constant colour of a surface (mediated by activity in area V4) but also whether the surface is illuminated predominantly by 'blue' or 'red' light (areas V1, V2). What happens at each stage can be integrated with activity of any other stage of the same or of another processing system, thus leading to the *theory of multistage integration* in the visual brain. As a corollary, we theorise that there is no strict hierarchy in perception (Bartels & Zeki, 1998b).

3. The theory of perceptual sites.

This is the most critical theory and unifies the above hypotheses. In essence, the theory states that when two attributes which are presented simultaneously are perceived

at the same time, they are processed at the same site, and when two attributes are perceived at different times, they are processed at different sites (Zeki & Bartels, 1999b). For example, colour and motion are perceived at different times, and there is substantial evidence that they are processed at different sites. There is psychophysical evidence in support of our hypothesis (Moutoussis & Zeki, 1997a).

Historical survey

1. The colour centre in the human visual cortex

> *"Tout ceci nous montre combien de questions sont encore à résoudre dans ce domain des localisations cérébrales et combien nous nous mouvons encore sur un terrain peu ferme. Cependant toute nouvelle contribution à cette étude a son importance pour l'édification de ce monument dont Charcot et ses élèves ont été les fondateurs, et c'est là ce qui m'a engagé à publier l'observation précédente"*
>
> Louis Verrey, 1888

With these words, Verrey (1888) ended his description of what he called the centre for the chromatic sense ("le centre du sense chromatique") in the human cerebral cortex. His article should have been a landmark in studies of colour vision, but was not. Instead, it was disputed soon after its publication by Salomon Henschen (1893) and Sir Gordon Holmes (1945) and, according to Damasio (1985), "vanished" from the literature. Verrey almost certainly did not realise the true significance of his findings (Zeki, 1993a). His discovery that the colour centre lies in the lingual and fusiform gyri, and hence outside the calcarine cortex, led him to suppose that the primary visual receptive centre (the "cortical retina" of Henschen, which we now call V1) extended beyond the striate cortex in the calcarine sulcus; the primary visual receptive centre was, therefore, not only much more extensive than supposed by Henschen, Flechsig (1901) and others, but it was also regionally specialised. This supposition brought him into conflict not only with the views of Henschen and Holmes, but also with those of Wilbrand (1884), who, like Poppelreuter (1923) after him, believed that a specialisation for colour in the primary visual receptive centre was organised according to layers. Verrey's evidence of a visual disturbance that was more or less specific to a single visual sub-modality, colour, was also against a climate of opinion which was hostile to the idea of separate localisation for different attributes of vision in the cerebral cortex,

well summarised by Holmes' statement that "...occipital lesions do not produce true dissociations of function with intact retinal sensibility" (Holmes, 1918). The evidence for a colour centre was not to be considered again until after the experimental demonstration of a specialisation for colour in the visual brain of the macaque monkey (Zeki, 1973). It was Meadows (1974) who, reviewing all the published evidence of acquired achromatopsia, found a correlation between the syndrome and the site of the lesion, located ventrally in the occipital lobe, in the territory of the lingual and fusiform gyri. A further insight, though one not remarked upon by him, is present in the title itself of Verrey's paper - "Hémiachromatopsie droite absolue".

The work of Brodmann (1905) and of von Bonin and Bailey (1947) had suggested that the visual "association" cortex is arranged in two concentric rings surrounding the calcarine cortex, area V1, and a quarter of a century of physiological mapping experiments have seemingly supported this notion. Two general features have emerged from this work; one is that the relatively early, physiologically defined visual areas, such as V2 and V3, do in fact form concentric rings around V1, even though they are not coincident with the anatomically defined rings of Brodmann (*i.e.* areas 18 and 19); another is that, broadly speaking, the dorsal part of the occipital lobe registers activity in the contralateral inferior quadrant of the field of view while the ventral half registers activity in the superior contralateral quadrant of the field of view, an arrangement that is radically altered only at the level of the parietal and temporal areas, where the receptive fields of cells are much too large to allow such a simple classification. And yet Verrey's clinical and pathological studies had shown that a lesion located ventrally in the occipital lobe leads to an "absolute" hemi-achromatopsia, i.e. in both upper and lower visual quadrants in one half of field of view. This led Damasio (1980) to write that "...one single area in each hemisphere controls colour processing for the *entire* hemifield. This is so regardless of the fact that such an area is "eccentrically" located, in the lower visual association cortex, classically related to *upper quadrant* processing only...The classic concept of concentrically organised visual association cortex no longer appears tenable" (original emphasis).

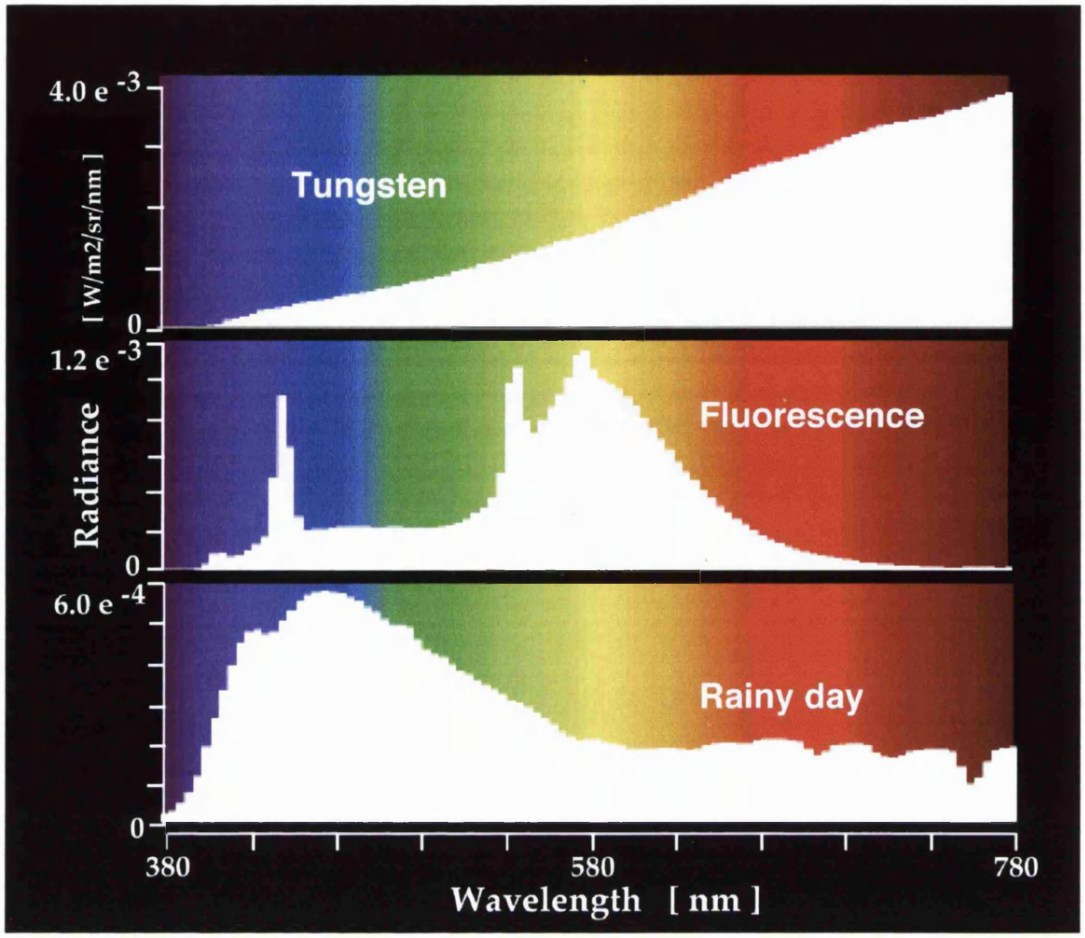

Figure 1. Spectra of light reflected from a piece of white paper which was illuminated by different illuminants. Even though the wavelength composition reaching the observers eye from this surface changes completely in different illuminants, the perceived colour remains constant (white). **Top**: Tungsten light from a standard light bulb. Halogen light and candle light are very similar, the former having a slightly steeper onset in the short-wave region, the latter with a concave, almost exponentially rising curve. **Middle**: Fluorescence light in an office. The 'white' of a computer screen has features comparable to the spectrum shown, in that it also consists of both broad and sharp peaks (e.g. an AppleVision 1710 screen has broad peaks at 440 and 530 nm, and sharp peaks at 620 and 710 nm). **Bottom**: Sunlight after sunset in rainy weather conditions. The light of a blue sky has a more flat spectrum across all wavelengths, whereas the light coming from grey clouds at midday is more intense in the middle and long-wave region than in short-wave. The dips occurring at 690, 730 and 760 nm are typical for all daylight spectra and indicate probably the absorption spectra of compounds such as water.

Mapping experiments, using functional magnetic resonance imaging (fMRI) (McKeefry & Zeki, 1997), have shown that both quadrants of the contralateral hemi-field are indeed contiguously but separately mapped within the colour centre. This, together with antecedent anatomical and physiological work, has established that the colour centre in the fusiform gyrus is one part of a cortical colour processing system that extends from the striate cortex through area V2 to V4, and beyond to the inferior temporal cortex (Zeki & Marini, 1998). Yet the resolution of this problem leaves several questions un-answered, particularly in relation to the role of each stage of this

colour processing system in the generation of colour. One way of trying to answer this question is to study the role of the individual stages of this colour processing system in the generation of the single most important property of the colour system, namely colour constancy. By this we mean an invariance in the colour category of a surface despite a continually varying wavelength composition of the light reflected from it (see **Figure 1**).

Studies of humans with lesions in the colour centre (Kennard, Lawden, Morland & Ruddock, 1995) and experimental evidence from monkeys with V4 lesions (Walsh, Carden, Butler & Kulikowski, 1993) show that both experience difficulty with colour constancy tasks; they are unable to "discount the illuminant" (Helmholtz, 1911). Hence for them the perceived colour of surfaces changes with changes in the wavelength composition of the illuminant and deviates towards the colour of the dominant wavelength reflected from the surface. This suggests that the colour centre is critical for the ratio-taking operations that enable the brain to compare the wavelength composition of the light reflected from one surface and that reflected from surrounding surfaces in order to assign a constant colour to a surface (Land, 1974). However it is not known whether this is a co-operative phenomenon involving all stages of the colour pathways or one that is vested in the colour centre alone. Whether this is the only function of this centre in relation to colour is itself problematic.

The syndrome of colour imperception produced by damage to the colour centre is complex and cannot be characterised by a unique feature (see also Rizzo, Smith, Pokorny & Damasio, 1993). In some cases (the true achromatopsias) the world is reported to be entirely devoid of colour and perceived only in terms of "dirty" shades of grey (e.g. Verrey, 1888; MacKay & Dunlop, 1899; Young, Fishman & Chen, 1980); in others (the dyschromatopsias) the defect is less severe and the perception of some colours may be more affected than others, recovery may be more complete for some patients than for others and more for some colours than for others. In particular, when the damage is unilateral, patients may not even be aware of their hemi-achromatopsia (~~Albert, Reches & Silverberg, 1975~~ Kölmel 1988; Paulson, Galetta, Grossman & Alavi, 1994), suggesting that the colour centre itself may be critically involved both in generating a conscious correlate for the activity in it and in attentional mechanisms related to colour. That these patients are not even aware of the loss of one of their visual modalities suggests that the lesion can erase the very concept of that modality. If so, the erased attribute must have been completely represented in the area specialised for it, without any additional "observing" area, which would be able to notice the nature of the loss. It appears as if the specialised areas must therefore generate a microconsciousness of what is uniquely processed in them (Bartels & Zeki, 1998b; Zeki & Bartels, 1999b).

The variability in severity, degree and characteristics of the recovery suggests at first sight that the colour centre may have been unequally damaged in different cases of achromatopsia (Zeki, 1990a). The issue is difficult to decide on the basis of the published evidence because the colour vision of many of these patients was assessed by asking them to recognise the colours of common objects, rather than to identify the colours of abstract scenes. Unlike the latter, coloured objects activate a large part of the medial temporal lobe, extending from the fusiform gyrus anteriorly and medially (Zeki & Marini, 1998). The colour centre itself, as determined in our previous experiments, is large and extends 2 cm antero-posteriorly (Lueck, Zeki, Friston, Deiber, et al., 1989; McKeefry & Zeki, 1997); this makes it possible to suppose that it is not totally damaged in all cases of achromatopsia or that it may contain further, possibly specialised, subdivisions within it, just as in the macaque monkey (Zeki, 1977).

Another aim of this study was therefore to determine the architecture of the colour centre in the human brain. We therefore designed stimuli which simulated, as far as possible, conditions in which the wavelength composition or the intensity of the light reflected from multi-coloured abstract and natural scenes changed continually (dynamic modes), without entailing a change in the perceived colour. We compared the activity in the brain produced by them with the activity produced by the same coloured scenes when the wavelength composition and intensity coming from every patch of the multi-coloured scene remained the same. Previous work (Corbetta, Miezin, Dobmeyer, Shulman & Petersen, 1991) has shown that attending to colour, which is a means of enhancing one's perception of it, leads to a heightened activity in the colour centre. We therefore wanted to extend these studies to learn whether attention to colour activates the colour centre in a retinotopic fashion. The results showed that the colour centre of the human visual brain, located in the fusiform gyrus, consists of two components, a posterior one (which may contain further subdivisions) and in which the two hemi-quadrants are separately mapped, and an anterior one which is not topographically organised. These two subdivisions are both equally involved in the ratio-taking operations of both abstract and natural scenes; attention to colour reveals an identical architecture, including the retinotopic organisation of the posterior subdivision.

2. Perceptual loss in colour vision following damage to the fusiform gyrus

The discoveries that I have made regarding the architecture of the human colour centre made it interesting to review the clinical literature concerning the visual loss following damage to the region of the fusiform gyrus where the V4 complex (the colour centre) is located).

The literature on cerebral achromatopsia resulting from lesions of the fusiform gyrus is uniform only in the description that achromatopsic patients give of their perception of the visual world in the initial stages after damage to the colour centre; they almost all describe the world as consisting of "dirty" shades of grey. But damage to the colour centre in the fusiform gyrus also causes variant syndromes (dyschromatopsias) in which the defect in colour vision is not total but affects some colours more than the others or leads merely to a defect in colour constancy while sparing a colour vision based on wavelengths (see below). **Table 1** gives examples of different degrees of severity and recovery, from which the variability of the syndrome becomes evident, without recourse to an exhaustive review of the literature. We need only point out here that the patients of Pearlman (1979) and of Victor (1989) for example, had a greater loss for blues and greens, and a relative sparing for reds; that Ogden (1993), Kölmel (1988) and Paulson (1994) report no recovery in six years, two years and ten months, respectively, after onset whereas Bornstein (1959) reports a rapid recovery; that following lesions affecting the colour centres in both hemispheres, colour may return in one rather than both hemifields (Albert, Reches & Silverberg, 1975), implying a recovery in one hemisphere only. Moreover, recovery may not affect all colours equally, patients sometimes recovering their ability to perceive some colours less than others, which may return to normal (e.g. Jaeger, Krastel & Braun, 1989). Unfortunately, the total extent of the lesions are not recorded in many of the published papers, or done so very imperfectly. It is therefore not possible, at present, to draw an exact relationship between extent and type of recovery and the size of the cortical damage. Future studies may be able to relate the variability in the severity and degree of recovery to the extent and architecture of the human colour centre as revealed in this study.

Table 1. Examples reported in the literature of patients with colour deficits and different degrees of recovery.

Sources	Descriptions	Quotations
(Steffan, 1881)	Some improvement over 5 years, but only partial recovery.	
(Critchley, 1965)	Some improvement within about 6 months, but only partial recovery.	"Objects around him seemed to be grey ... a certain amount of improvement set in."
(Wilbrand, 1884)	Recovered upper quadrant after 14 days. Lower quadrant no recovery.	Reported in (MacKay, 1888)
(Meadows, 1974)	No recovery within 6 years.	" ... everything looked black or grey"
(Rondot, Tzavaras & Garcin, 1967)	Recovered from achromatopsia, but not prosopagnosia.	
(von Hagen, 1941)	No recovery noted within a few months of CO poisoning.	"Everything looked grey to her."
(Mohr, Leicester, Stoddard & Sidman, 1971)	Died after 1 year. No recovery.	" A persisting defect occurred ..."
(MacKay & Dunlop, 1899)	Died after 1.5 years. No recovery.	
(Rizzo, et al., 1993)	No recovery mentioned. Time course > 1 year.	" ... red, green and yellow signals appeared only as different shades of grey. Patient 2 noted special difficulty with the identification of hues of less saturated colours ... "
(Albert, Reches & Silverberg, 1975)	No recovery discussed. Condition reported as "stable".	"His visual disorders passed ... to a final point of stability. ... He could not name colours ... "
(Ogden, 1993)	No recovery after 7 years.	" ... he saw everything as shades between black and white."
(Bartolomeo, Bachoud-Lévi & Dene, 1997)	Partial recovery over two months.	"In December 1995 she suffered from a second [lesion]. ... Formal colour testing began on February 1996. By that time Mme D. claimed that her visual world had changed from grey to red-brown."

(Orrell, James-Galton, Stevens & Rossor, 1995)	No recovery. Died within a few months.	"Over a period of two weeks there was some improvement in his vision, but persistence of the loss of colour vision."
(Fine & Parker, 1996)	Recovered after five months.	"This perversion of colour recognition persisted for the best part of five months ... "
(Paulson, et al., 1994)	No recovery in few months.	"color vision ... was profoundly disturbed" [Case 1]
	(Two cases).	"... colour vision was markedly abnormal in this quadrant" [Case 2]
(Mollon, Newcombe, Polden & Ratcliff, 1980)	No recovery after 8 years.	"MS has been repeatedly tested over the period 1972-1978 [original illness in 1970] and his condition is stable in that his colour vision has not improved..."
(Cole & Perez-Cruet, 1964)	No recovery after 1 year.	"Under most conditions, however, he was unable to state the colour of objects shown to him, calling a red pen 'black' and yellow objects 'light'..."
(Bornstein & Kidron, 1959)	Recovery of achromatopsia over the course of a few days leaving profound prosopagnosia and other symptoms.	"While in hospital no disturbance in colour sense was noted, but apparently it did exist before that time ... "
(Ross, 1980)	Case 1: No recovery after 2 years.	"On Feb 6 1974, the patient lost the ability to read, recognize objects, and perceive colours..." "The patient was admitted ... in November 1976."
	Case 2: No achromatopsia.	"(2) a severe inability to recognize and name colours that could not be explained by the patient's congenital colour blindness;"
(Beyn & Knyazeva, 1962)	No recovery after 1 year, but was using compensatory techniques.	"Six months later ... he made greater use of compensatory methods, e.g. comparing the colour of a given object with that of an object such as his own fountain pen ... five months later [12 months since first admission] there was a very slight improvement in recognition of pictures and of facial expression."
(Ogden, 1993)	No recovery after 7 years.	"An extensive optometry examination carried out 7 years post trauma ... MH could not identify any colours whether in isolation or in the context of an object. He commented that he saw everything as shades between black and white."

(Whiteley & Warrington, 1977)	Case 1: No recovery within 9 months. Case 2: No achromatopsia. Case 3: Mild achromatopsia, but no time course information given.	"His symptoms remained unchanged at follow-up nine months later." [Case 1]
(Green & Lessell, 1977)	Case 1: Increasing achromatopsia due to growing carcinoma. Case 2: Carcinoma - no recovery. Case 3: Stroke - no recovery, no time course given. Case 4: Stroke - no recovery, no time course given. Case 5: Stroke - no recovery, no time course given.	"was examined early ... had normal colour vision. Several months later ... he was colour-blind." [Case 1] "Despite good visual acuity she was colour-blind" [Case 2] " ... he retained good visual acuity and colour vision. Subsequently, after a second stroke ... impaired colour vision developed." [Case 3] "... he retained good visual acuity and normal colour vision. After a second stroke ... he had become colour blind." [Case 4] " ... she did show moderate evidence of colour vision impairment ..." [Case 5]
(Ishii, Kita, Nagura, Bandoh & Yamanouchi, 1992)	No recovery after 7 years	Original text in Japanese.
(Damasio, et al., 1980)	Case 1 No recovery within 3 weeks. Case 2 No recovery within 8 weeks	"the defect persisted unchanged for the 3 weeks prior to our initial exam" [Case 1] "Her colour perception defect was unchanged after the onset of the latter problem" [Case 2]
(Brazis, Biller & Fine, 1981)	No recovery in two years	"Two years after the initial result he presented to us because of the persistence of these symptoms."
(Young & Fishman, 1980)	No recovery after 3 years	"Approx. 3 years ago ... was unable to appreciate colours."

This review shows that there are examples of patients with no recovery from the achromatopsia produced by lesions of the fusiform gyrus, and others in whom there is considerable recovery. This diversity raises a question never before addressed, namely what is its cause. Several reasons might explain the differences in symptoms and recovery processes, but an obvious first question is whether the differences reflect differences in the extent of the lesion and whether it involves both subdivisions of the colour centre. It is certainly plausible to assume that if one of two functionally closely related cortical areas is lesioned the second can compensate the loss to some degree, while lesions affecting both would have more severe consequences.

3. Perceptual losses following damage to other parts of the visual brain

The above section revealed the tight relationship of lesions in a particular part of the brain, namely the fusiform gyrus, with a particular perceptual deficit, that of colour perception or at least the ability to construct constant colours. The question arises whether this relationship is unique to the colour system or whether it is also true for other attributes, in other words whether this is an example of the more general phenomenon of the modular organisation of the visual brain. Modular organisation in turn raises the question of the relationship between processing sites, which may be specialised for given attributes, and perceptual sites, which may or may not be the same as the processing sites. If a processing site is also a perceptual site, then we can speak of processing-perceptual sites, a formulation that has far reaching consequences for understanding how the visual brain is organised. A good indication of the independence of these processing-perceptual modules will be given by asking how specific the perceptual consequences of a lesion in a specific cortical site is or can be. An alternative way of asking the question is to enquire into the extent to which the perception of other attributes is affected when that of one is impaired.

The above considerations make it worthwhile to review some of the clinical literature on lesions in the prestriate cortex and their perceptual consequences, which is given below.

3.1. Clinical evidence for a piecemeal understanding of the visual world following damage to the prestriate component of the processing systems

The visual fields are topographically represented in areas V1 (Henschen, 1893; Holmes, 1945) and V2 (Cragg, 1969; Zeki, 1969a), as if both areas are undertaking a "piece-meal" analysis of the visual world (Hubel & Wiesel, 1977). Receptive field sizes of cells also become larger as one proceeds from V1 to V2 to the more specialised areas (Van Essen & Zeki, 1978), an enlargement that is coupled to the emergence of new physiological properties (Hubel & Wiesel, 1962; Zeki, 1974; Desimone, Schein, Moran & Ungerleider, 1985). It could therefore be expected that (*1*) a person with a relatively large lesion in the prestriate cortex but one which spares area V1, either partially or completely, should be capable of a piecemeal analysis of his visual world and (*2*) that a person with a lesion restricted to the prestriate component of a given

processing-perceptual system should be able to experience all attributes of the visual scene, save the one processed by the compromised system; moreover, they should be able to experience something about the attribute processed by the damaged system, and that something must be related to the physiological capacities of the undamaged nodes of that processing-perceptual system, meaning the physiological capacities of area V1 and possibly V2. Below we consider examples from different patients to illustrate these two points, by showing that the well known syndromes of achromatopsia, object agnosia, prosopagnosia and akinetopsia - all caused by specific lesions of the prestriate cortex - share a property in common. That common property is the ability to see and experience details of a given attribute without being able to combine the details into a whole and thus experience the whole. They are, in brief, able to see and understand what the intact nodes of their processing-perceptual systems allow them to see and understand.

3.2. Object agnosia

The ponderous speculations of Lissauer (1890) coupled to the anatomico-pathological discoveries of Henschen (1893, 1910) and the myelogenetic studies of Flechsig (1901) led to a general view that we "see" with V1 and "understand" what we see with the visual "association", or prestriate, cortex, a notion that divided seeing from understanding and assigned a separate cortical seat to each (for a general historical review see Zeki, 1993b). Since that time, belief in the concept of a global agnosia has been apparently supported by the finding that such patients can commonly draw even complex figures, though without being able to make any sense of the figure they have drawn, or to understand it. Yet how is it that these patients draw? There is good agreement that the drawing is piecemeal, small segments of the picture, or of its outline - segments that the patient can see and understand - being drawn, one after another. Once drawn, the patient can still only recognise and understand small segments of his drawing and not its entirety. The patients' report of the process itself is more or less uniform. One patient stated that when he copied a complex figure, "all he saw was a complex pattern of lines, which did not correspond to a particular object". This is well reflected in his description of the difficulty of recognising common objects: "I have come to cope with recognising many common objects, if they are standing alone... When objects are placed together, though, I have more difficulties" (Humphreys & Riddoch, 1987), the latter possibly an example of what has been called simultagnosia, or an inability to perceive more than one object in the field of view at a time. It is the simple components of a figure that the patients are able to see and to understand because the integrative mechanisms necessary to construct simple forms, such as lines, are intact while those needed for more complex forms are compromised. Indeed the

authors of this fascinating report state that the patient "has intact registration of form elements (single lines and edges), but... his ability to integrate these elements into 'perceptual wholes' is in some way impaired. The intact information about the local form elements enables him to make accurate copies of stimuli he cannot identify" (Humphreys & Riddoch, 1987)

The consequences of a large lesion are also illustrated by the famous patient of Adler (1950), who suffered from carbon monoxide poisoning at a Boston night club during the Second World War. She has also described her experiences in piecemeal terms. Shown a green battleship, she mistook it first for a fountain pen, then for a green knife before identifying as "a boat". She explained: "At first I saw the front part. It looked like a fountain pen because it was shaped like a fountain pen. Then it looked like a knife because it was so sharp, but I thought it could not be a knife because it was green. Then I saw the spokes and that it was shaped like a boat, like in a movie where I had seen boats. It had too many spokes to be a knife or a fountain pen". Another patient, "When looking at a picture... could identify individual detail but could not appreciate the significance of the entire scene" (Gomori & Hawryluk, 1984). These descriptions are so representative that they apply to many agnosic patients.

In principle, one should be able to account for some of the characteristics of the syndrome, namely a capacity to see the details but not the whole, by appealing to the physiology of the visual pathways, and in particular the capacities of the nodes that are left undamaged by the lesion. This is not an easy task, because the visual areas which are involved in the recognition of even simple objects, as well as the details of the integrative processes, are not known, especially in man. But there are clues to suggest that the residual capacity of a patient to see the details, the lines in particular, is related to the physiological capacities of areas V1 and V2, partially spared by the lesion. We suppose that the orientation selective cells, a conspicuous feature of the physiology of V1 and V2, are largely intact and that activity of cells at these nodes can become perceptually explicit, that is have a conscious and perceptual correlate. This, to us, is a far more satisfactory explanation than vague references to uncoupling between "seeing" and "understanding".

This incapacity to combine simple elements is also evident in another example, which we interpret to be due to a lesion in V2, although the actual pathology is not available and our interpretation may turn out to be wrong. The case is that of an artist who became agnosic after a cerebral vascular accident and whose agnosia was accompanied by a mental deterioration and, more significantly, a restricted scotoma (Wapner, Judd & Gardner, 1978). Since the patient was able to perceive details, we are

inclined to attribute the scotoma to a lesion of V2, which is also known to cause scotomas (Horton & Hoyt, 1991) although it may have been more extensive. One of the interesting features of this artist was his failure to see illusory contours, for example Kanizsa triangles. When shown such a triangle he described it as "a three cornered thing... I see three edges and three circles". The authors explain that the patient's "descriptions and drawings focused on the individual elements physically present, omitting, despite probing, any reference to the subjective occluding figure" (Wapner, Judd & Gardner, 1978). The patient, in brief, was not able to "fill in" perceptually the gaps in the Kanizsa triangle. This failure is similar to the agnosic patient described above, in whom the failure of integrative mechanisms was such that he commonly failed to "fill in" or complete. Physiological evidence shows that cells which are capable of responding to the illusory borders which are characteristic of the Kanizsa figures are present in V1 and V2 (von der Heydt, 1987; Grosof, Shapley & Hawken, 1993). We thus conjecture that the artist is capable of seeing and understanding what the intact cells of his V1 and V2 are capable of signalling. Such an explanation is as plausible, or even more so, than one which postulates a mysterious breakdown in "understanding" what was seen.

The above examples share the similarity that the pathological vision described is piecemeal but that subjects can both see and understand the elements in their field of view without being able to combine the details together to form a coherent whole; they thus neither see nor understand the larger picture created by the elements. One of the difficulties of interpreting the syndromes we discuss above in the way that we would like to is that the lesions are not really adequately characterised except for the patient of Humphreys and Riddoch (1987). Carbon monoxide poisoning in particular results in diffuse damage which almost certainly involves many areas but there are reasons to believe that it may spare parts of V1, especially the parts concerned with colour (see below). We are on surer anatomical and pathological grounds when we look at the consequences of more specific damage, to the prestriate component of a given processing-perceptual system.

3.3. Prosopagnosia or the inability to recognise (familiar) faces

The remarkable feature of prosopagnosia is that subjects commonly know that they are looking at a face but cannot recognise it. A somewhat frightening example is the record of the dissolution of facial recognition, while it happened. It is the experience of a man who, while talking to his physiotherapist, suddenly exclaimed, "But Mademoiselle, what is happening is that I can no longer recognise you", although he knew who she was and knew that he was talking to her (Lhermitte, Chain, Escourolle, Ducarne & Pillon, 1972). They do not seem to be able to combine the many individual features, which they are able to perceive, into a whole. One prosopagnosic patient related how "I can see the eyes, nose and mouth quite clearly but they just don't add up" (Pallis, 1955). The point that we emphasise here is the residual ability of such patients, their capacity to see much but not to combine everything into a whole. If we suppose that the area in the fusiform gyrus implicated in the perception of familiar faces, and damage to which leads to prosopagnosia, is a distinct node, then the clear implication of the above is that the patient is able to experience what the antecedent nodes have processed, namely the details of the face (although no one knows where these details are processed). More simply stated, the capacity of the patient is related to the physiological capacities of the intact parts of the processing system.

3.4. Cerebral achromatopsia or the inability to see the world in colour

This somewhat complex syndrome, discussed above, provides even more compelling grounds for supposing that the processing and perceptual systems are one and the same. The syndrome is one in which patients either cannot see colours at all, describing the world in shades of 'dirty' grey or one in which they can see some colours, more often reds, but not others, more commonly greens and blues (Zeki, 1990a), a condition which we refer to as dyschromatopsia. In the latter condition, a patient's ability to "discount the illuminant" (Helmholtz) is much impaired, with the consequence that they are not able to construct constant colours and hence cannot see colours in a stable way, like normals (Kennard, et al., 1995). But V4 is only one node in an extensive colour processing-perceptual system that extends from V1 to the inferior temporal cortex (Zeki & Marini, 1998). Damage to the V4 complex may, and often does, leave the antecedent parts intact. The consequence is interesting and can be related directly to the physiological capacities of the nodes that are left intact by the lesion. It has been found, for example, that achromatopsic patients are able to discriminate remarkably well, and consciously, between lights of different wavelengths, even if they are not able to ascribe colours to them (Victor, et al., 1989; Vaina, 1994). Like humans, monkeys with V4 lesions can also discriminate between light of different wavelengths though with raised thresholds (Heywood, Gadotti & Cowey, 1992). This,

we believe, reflects the physiological capacities of the wavelength selective cells in V1 and probably V2, which respond when light of the appropriate wavelength is flashed into their receptive fields, without being concerned with the colour of the stimulus in their fields (Zeki, 1983b).

An interesting insight is provided by an achromatopsic patient who had retained the ability to detect the border between two equiluminant colours, without being able to distinguish the colours on either side of the border (Heywood, Cowey & Newcombe, 1991). The authors of this study seek a complicated explanation for this residual capacity, by supposing that there are two specialised prestriate areas, one specialised for the conscious perception of colour and the other for extracting contours from colour. But a simpler explanation might lie in the physiology of orientation cells in V1. These cells, though responsive to lines of particular orientation, will respond to a border between two equiluminant stimuli of the same orientation, without caring much about the colour on either side of the border (Gouras & Kruger, 1979; Thorell, De Valois & Albrecht, 1984). This is precisely what the patient could discriminate, without being able at the same time to detect the difference between the two stimuli, just like a V1 interblob cell. V1 constitutes a node of the colour processing system and, in the absence of V4, there is at present no good reason to suppose that the activity of such cells in it does not have a perceptually explicit correlate. And it is interesting to note in this context that cells such as the one described above, located in the interblobs of V1, project to V4, either directly or through the thin stripes of V2 (Livingstone & Hubel, 1984b; Zeki & Shipp, 1989; Nakamura, Gattass, Desimone & Ungerleider, 1993). In brief, the knowledge of these achromatopsic patients reflects such physiological capacities as the wavelength selective cells of V1 and V2 have.

3.5. Akinetopsia or motion imperception

Akinetopsia (Zeki, 1991) is a syndrome of motion imperception following cortical damage, more specifically to area V5, the motion centre in the cerebral cortex (Zeki, Watson, Lueck, Friston, et al., 1991; Watson, Myers, Frackowiak, Hajnal, et al., 1993; Tootell & Taylor, 1995). Perhaps the best example is provided by the patient of Zihl (Zihl, Von Cramon & Mai, 1983; Zihl, Von Cramon, Mai & Schmid, 1991). Because of a bilateral lesion involving area V5, his patient is unable to see objects when in motion but only when they are stationary. This does not mean that she is unable to detect the presence of motion *per se*. Indeed, one study of this patient concludes that "the overall deficit... is characterised by a large discrepancy between detection [of motion], which is relatively unimpaired, and discrimination, which can be severely impaired" (Hess, Baker & Zihl, 1989). This same study, as well as more recent ones

(Shipp, de Jong, Zihl, Frackowiak & Zeki, 1994), have shown that the patient is able to detect certain kinds of simple, slow, motion, leading the authors to say "Thus, the overall results suggest that the local component information necessary for the derivation of motion is intact and thus that the anomaly occurs at a later stage, where a more global analysis takes place" (Hess, Baker & Zihl, 1989). We take this to be a reflection of the capacity of the direction plus orientation selective cells of her intact area V1, and possibly those in areas V2 and V3 as well.

Because V1 is not directly connected to the frontal lobes, it has been suggested that we are not aware of what happens in V1, thus excluding V1 from direct involvement in conscious experience (Crick & Koch, 1995). This may well turn out to be so, and we have no compelling evidence that it is not. On the other hand, the evidence reviewed above could be interpreted to imply that activity in V1 itself has a direct conscious correlate. This is emphasised further by recent experiments in which a patient blinded as a consequence of a severe heart attack nevertheless retained the ability to see colours (Humphrey, Goodale, Corbetta & Aglioti, 1995). But our further examination of him revealed that his colour vision, (which is completely divorced from form vision in that he is not able to perceive the form of the colours which he describes correctly) is wavelength based. In other words, he is not able to construct constant colours. Imaging experiments show that, when he discriminates colours according to wavelength, the activity in his brain is located in area V1 (Zeki, Aglioti, McKeefry & Berlucchi, 1999). Even in spite of this, we are diffident about saying that activity in V1 has a conscious correlate, because we have no means of knowing what residual, and undetected, activity may have occurred elsewhere.

Thus, each of these syndromes provides evidence that activity in the intact part of the processing systems can have a perceptual correlate. There is much in the evidence that is incomplete. We do not have an adequate account of the total extent of the lesions in most cases, and in some none at all. Even if we did have such an account, there is no knowing at present how much of the system is compromised by damage to the output fibres. In spite of these difficulties, collectively the evidence is compelling in showing that there is always a residual visual capacity with lesions of the prestriate cortex, and that this residual capacity is at present best explained by the physiological properties of the cells that are left intact by the lesion.

4. Temporal consequences of the modular organisation of the brain: why the brain can be dissected computationally

If the visual areas of the brain are indeed to some degree autonomous, and the results of my studies on the colour centre, together with a review of the published literature, show them to be so, then one might expect this autonomy to be reflected in activity time courses that differ from area to area, with no area having the same activity time course as any other. I therefore decided to use the technique of independent components analysis to fMRI data, first to show that this is true for the human colour centre and then for other visual and non-visual areas as well, leading me to collect additional fMRI data and to introduce the concept of *chronoarchitecture*.

In fact, the motivation for applying the information theory based ICA to brain activation data stems from a fundamental property of the cerebral cortex: the principle of functional specialisation (Zeki, 1993b). This states that separate cortical areas have different physiological and anatomical and therefore different processing properties, and that they are involved differently in different tasks. Different areas are therefore stimulated independently to varying degrees and are therefore active with varying degrees of independence. A classic example from the visual cortex is that stimulation with colour or motion selectively activates areas V4 or V5, respectively (Zeki, et al., 1991). It is therefore plausible to believe that functionally specialised areas can be identified and segregated using clever computational tools (such as ICA) alone, without a priori knowledge. By analysing whole-brain activity without knowing the type of specialisation, localisation or spatial extent of the areas or anything about the type or time course of the stimulation applied, a computational tool should be able to dissect the brain into its functional components.

In the last century, both, the methods of electrophysiology and functional imaging established that cells in one part of the brain respond very differently to a stimulus than those in another part, and that cells with the same stimulus preference are grouped together in regions to which we refer to as to functionally specialised areas. It has also been shown that some cortical areas differ from each other on anatomical grounds leading to the axiom that areas that differ in structure must also differ in function (Vogt & Vogt, 1919),. There is a close link between anatomical markers and functional specialisation. Since function is derived from anatomical properties, any area

that differs anatomically from others must have a unique function, and, vice versa, any functionally specialised area must differ in at least one anatomical property from all the others. For example, by staining brain slices for myelin, it has been shown that area V5 has higher contents of myelin than others (Clarke & Miklossy, 1990; Tootell & Taylor, 1995). Myelin allows for a higher conductance speed of the axons: a short signal arrival time and fast processing are functional properties of V5, derived from anatomical ones.

In the next section some additional physiological properties are described that have been shown to differ from area to area, and which contribute to differences of the BOLD signals associated with these areas. These properties facilitate their segregation, based purely on the activity time course detected by fMRI.

4.1. Differences in BOLD signal dynamics across cortical areas

Any method trying to segregate different cortical or sub cortical areas from each other using fMRI data has to rely on differences in their BOLD response. Parametric methods such as SPM are designed to exploit such differences when the experimenter can predict these in advance: e.g. by hypothesising that a motion stimulus activates a given area more than a colour stimulus. SPM is therefore limited to identifying brain regions whose response have been predicted in one way or another. In contrast, non-parametric, explorative methods such as ICA can exploit both known and unknown differences in the BOLD response of different regions in the brain. This promises to lead to the discovery of unknown subdivisions of already known areas, of areas that have not been described before, or to the identification of interesting particularities of the BOLD response properties of known areas. In this section, some of the factors that can lead to differences in the BOLD signal in different areas are described. Even though some of these factors are known, they are not known precisely enough to be formulated in terms of clear hypotheses that could be used by SPM. At the same time, these factors almost certainly contributed in this study to the successful segregation of various brain regions by ICA.

The following factors contribute to and cause differences in the activity time courses measured as BOLD signal across different cortical or sub-cortical areas:

First, the recent discovery of previously unknown cortical areas in the early visual cortex such as KO/V3B (Van Oostende, Sunaert, Van Hecke, Marchal & Orban, 1997; Smith, Greenlee, Singh, Kraemer & Hennig, 1998) makes it likely that there are many more functionally specialised areas in the cortex that remain to be described, and

whose BOLD response differs merely because of their particular and unique stimulus preferences.

Second, even though the hemodynamic response function that underlies the BOLD signal appears to be quite similar in different cortical regions, it has been reported that cortical regions differ in the latency of their BOLD response to a given stimulus, but a differential BOLD signal latency across different regions is a disputed and unresolved issue (Guy, ffytche, Brovelli & Chumillas, 1999). This works to the advantage of data-driven brain analyses, but will have to be taken into account for statistical mapping, which commonly assumes a constant and identical response delay for all cortical regions.

Third, stimulated by their preferred stimulus, areas differ in the dynamics of their response. For example, cells in V1 display less spike frequency adaptation than cells in V4, and subdivisions of ORA display differences in their adaptation to repeated stimuli, which led to the discovery of its subdivision (Grill Spector, Kushnir, Edelman, Avidan, et al., 1999). Thus, when a constant stimulus is presented which activates two cortical areas, the two areas can be segregated because they differ in their response to the stimulus over time (e.g. one remains active while the other slowly returns to baseline activity). Similarly, a linear change in stimulation, e.g. word presentation rate, has been shown to elicit different non-linear response changes in BOLD data that differ across cortical areas (Buchel, Holmes, Rees & Friston, 1998), thus allowing a segregation of the areas involved.

Fourth, a segregation of an area from those providing input to it can be facilitated by the fact that many areas can be activated through more than one pathway. An example is the object area ORA: It can be activated via the colour-pathway involving areas V1/V2/V4 by presenting objects derived from isoluminant colours, or it can rely entirely on the motion pathway involving areas V1/V2/V3/V5 when objects are derived from motion as in study 1 (Grill Spector, Kushnir, Edelman, Itzchak & Malach, 1998).

Fifth, attention can modulate areas in ways that differ from that of sensory stimulation. For example, unilateral stimulation with motion always activates bilateral V5 (Tootell, Reppas, Kwong, Malach, et al., 1995b), while attention to motion in one hemifield activates contralateral V5 (Tootell, Hadjikhani, Hall, Marrett, et al., 1998). In the former case, ipsilateral V5 is activated by a direct signal from contralateral V5 through the corpus callosum, with a delay in the range of tens of milliseconds (ffytche,

Howseman, Edwards, Sandeman & Zeki, 2000). Such differences can help to segregate areas that may otherwise be co-active and therefore indistinguishable.

Sixth, interactions between brain areas provide additional means of segregating them: When area A is co-active with areas B and C, but selectively increases its activity when both area B and C are active simultaneously, A can be segregated from the other areas.

Seventh, different areas and even functional subdivisions within areas differ substantially in their vascularisation density (Zheng, LaMantia & Purves, 1991). This constitutes an anatomical difference directly affecting the BOLD signal.

4.2. ICA analysis of fMRI data

The non-parametric, explorative fMRI time series analysis is clearly still in its early days and will probably see an exciting future. In this study we concentrated on the application of a method rather than on evaluating or developing new ones. Other groups have examined in great detail the merits and pitfalls of a variety of explorative analytic techniques, including ICA (Friston, 1998; McKeown, Jung, Makeig, Brown, et al., 1998a; McKeown & Sejnowski, 1998).(McKeown *et al.*, 1998a) and several other techniques, such as PCA (Friston, Frith, Liddle & Frackowiak, 1993; McKeown, Makeig, Brown, Jung, et al., 1998b) and non-linear PCA (Friston, Phillips, Chawla & Buchel, 2000), ICA combined with SPM (McKeown, 2000), clustering techniques (Baumgartner, Ryner, Richter, Summers, et al., 2000a; Baumgartner, Somorjai, Summers, Richter, et al., 2000b) and derivatives of ICA (Nakada, Suzuki, Fujii, Matsuzawa & Kwee, 2000). However, none of these groups have attempted analysis of nearly as substantial data sets as was done here, in which the whole brain is represented, most of the areas in which were highly and differentially activated. It is probable that a very rich and complex data set as the one employed here will not only reveal more details about the strengths and weaknesses of these methods, but it might also lead to a change in their ranking in obtaining useful results.

In a first approach to achieving a purely computational dissection of the human brain into its functional components without using any a priori knowledge, we applied independent component analysis (ICA) (Bell & Sejnowski, 1995) to several fMRI data sets. Previous applications of ICA on much more limited fMRI data sets, which contained only one or few slices, have shown that ICA can isolate voxels whose time course correlates with that of the external stimulation, and that ICA is better in doing so than other techniques, such as principal components analysis (McKeown, Makeig,

Brown, Jung, et al., 1997; Friston, 1998; McKeown, et al., 1998a; McKeown, et al., 1998b). The key weakness of PCA stems from its constraint to isolate components that are orthogonal to each other, such that most variance in the data are accounted for by the first component, while the last component accounts for virtually no variance in the data. This stands in contrast to the brain's organisation, in which each brain area contributes similarly to the overall activity; any algorithm trying to segregate the brain's areas should therefore allow each component to explain a similar amount of the total variance, which ICA does. ICA constrains its components to be as independent as possible (in one of the two dimensions), which does not mean they need to be orthogonal. We applied ICA for the first time to fMRI data with both a high temporal and a high spatial resolution, and discovered that in this case ICA not only isolates voxels that are involved in different tasks, but that it isolates functionally specialised areas (Bartels & Zeki, 1999; Zeki & Bartels, 1999a; Bartels & Zeki, 2000b; Bartels & Zeki, 2000a).

The results obtained herewith show therefore that the brain's modular organisation goes so far that each of its modules can be segregated from the others based entirely on differences in its activity time course, despite the enormous amount of cross-connections between all the cortical areas.

Part 2:

Methods

1. Experiments on colour vision

One major aim of this study, the determination of the cortical site of the ratio-taking, colour-generating operations, through which we also hoped to be able to discern something about the architecture of the colour centre of the human brain, could best be achieved by simulating conditions under which multi-coloured images are viewed in continually changing illumination conditions, such that either luminance or wavelength composition (or both) coming from each patch changes continuously, without affecting the perceived colour (colour constancy).

In total the following five separate experiments were performed, in which twenty seven subjects with normal colour vision took part.

Experiment **(1):** Six subjects viewed statically and dynamically illuminated versions of coloured and achromatic Mondrians.

Experiment **(2):** Three subjects viewed statically and dynamically illuminated versions of a naturally coloured scene consisting of fruits and vegetables.

Experiment **(3):** In the light of the results obtained from (1) and (2), which revealed a subdivision of the human colour centre, we re-analysed the data of four subjects originally collected by McKeefry & Zeki (1997), using less spatial smoothing to obtain a higher spatial resolution. In that experiment, which was essentially a study of the retinotopic organisation of V4, which has been recently confirmed (Hadjikhani, Liu, Dale, Cavanagh & Tootell, 1998; Tootell & Hadjikhani, 1998; Zeki, McKeefry, Bartels & Frackowiak, 1998), the subjects had viewed a coloured Mondrian and its achromatic counterpart presented separately in the upper and lower halves of their visual fields.

Experiment **(4):** The results obtained from (1) - (3) also led us to re-examine data collected by Zeki & Marini, (1998) in which nine subjects had viewed correctly and incorrectly coloured natural scenes and their achromatic counterparts.

Experiment **(5):** We investigated how the human colour centre is affected by attention to colour and to different quadrants of the visual field, in an experiment in which five subjects paid attention to either colour or motion in each one of the four quadrants of the visual field separately.

Stimuli in all studies subtended 24° x 20° degrees and were projected onto a translucent screen viewed via a mirror angled at 45° using an LCD projector. All subjects gave their informed consent and permission to conduct the studies was obtained from the Institute of Neurology Ethics Committee.

1.1. Mondrians

Experiments (1) and (3) relied on multicoloured or achromatic abstract scenes with no recognisable objects, used extensively by Edwin Land in his psychophysical experiments (see Land, 1974; 1986), and by previous imaging studies from this laboratory, as the one shown in **figure 2** (Lueck, et al., 1989; Zeki, et al., 1991; McKeefry & Zeki, 1997). They bear a certain resemblance to the paintings of Piet Mondrian and are hence known as the Land colour Mondrians or Mondrians in brief. By achromatic counterpart we mean the black, white and grey versions of the coloured stimuli. We do not imply that black, white and grey are not colours. They are regarded as colours by scientists such as Hering (1877) and Land (1974), as well as by artists, e.g. Matisse, (1972).

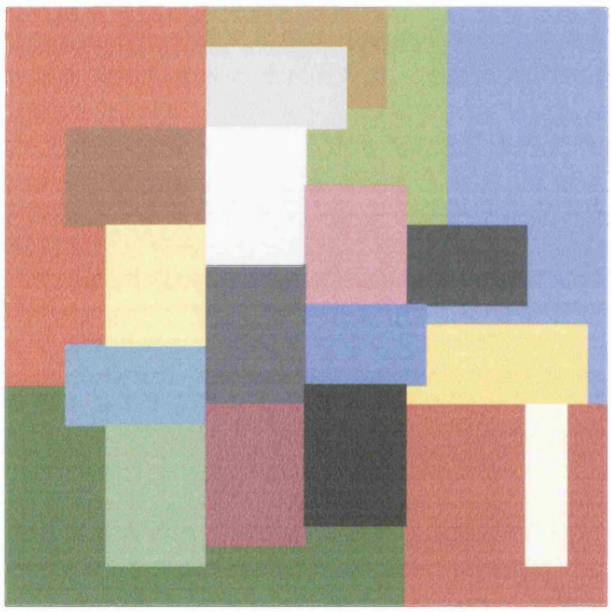

Figure 2. A typical Mondrian.

1.2. Experiment 1

In this study, six subjects viewed statically and dynamically illuminated coloured and achromatic Mondrians, while fixating the centre of the Mondrian. Here we tried to simulate experimentally what would happen when a scene is viewed in lights of continuously changing illuminants, so that the wavelength composition of the light coming from every patch changes (see the Colour Methods Appendix for a detailed description of the illumination simulation methods). Prior to scanning, we

asked subjects to report the colours of nominated patches of a Mondrian while the wavelength composition changed (see below), thus allowing us to ascertain that changes in the wavelength composition did not lead to changes in the perceived colour of any patch in any of our subjects. Colour constancy was thus achieved in the face of a continually changing wavelength composition.

1.2.1. Experimental paradigm

The patches of the achromatic version were made isoluminant to their coloured counterparts as follows: using the radiant spectra of the illuminant and the reflectance spectra of each patch, the reflected light from each was calculated and the intensity re-calculated from this as a CIE 1931 Y value. This was then matched to an equiluminant grey.

Both the coloured stimuli and their achromatic counterparts were presented in three modes, resulting in six different conditions. In the first (*static*) mode, subjects viewed a Mondrian in which the wavelength composition coming from every patch remained constant, with a luminance of 7.7 $cd \cdot m^{-2}$. In the second (*varying intensity*) mode subjects viewed the Mondrians in "white light" whose intensity changed continuously (3.4-12.0 $cd \cdot m^{-2}$ with a period of 9 s), mimicking what would happen if an observer were to view a coloured scene in one illuminant whose intensity alone varies; here the total flux at any given wavelength, reflected from every patch, increases or decreases, without otherwise altering the wavelength composition. In the third (*varying wavelength composition*) mode we simulated a condition in which the Mondrians are viewed in illuminants whose wavelength composition changes continuously; this entailed a change in both flux and wavelength composition of light coming from each square of the Mondrian, the extent of which is shown in **figure 8 c**. For this mode, the Mondrian was illuminated with three simulated light sources (illuminants) that projected predominantly long, middle or short wave light. The illuminants changed their intensity continuously in a sinusoidal fashion, each with a different period. This way, a maximal variety of illuminant-intensity combinations would be achieved. Illuminant I (simulated long wave light) changed from 0.3-2.3 $cd \cdot m^{-2}$ with a period of 18 s; illuminant II (simulated middle wave light) from 2.9-8.7 $cd \cdot m^{-2}$, period=9 s; illuminant III (simulated short wave light) from 0.1-1.0 $cd \cdot m^{-2}$, period=6 s. The mean luminance (of all illuminants) was 7.7 $cd \cdot m^{-2}$. The above values are given for the light coming from the white patch of the Mondrian, with the luminance ratio in our *static* condition between representative patches being [white : yellow : green : red : blue] = [100 : 82 : 57 : 29 : 20]. Since the spectrometer could not be used in the scanner to measure the light transmitted through the translucent screen,

the light reflected from the screen was measured and its transmittance was determined. The actual luminance values were so derived for a few representative conditions and the remaining ones calculated by our simulation software (see Colour Methods Appendix), using the measured values as calibration points. All measurements were performed using a Photoresearch PR650 Spectra Colorimeter.

Conditions were repeated six times within blocks which consisted of different random permutations of the six conditions; each condition lasted 32.8 s, thus allowing 8 whole brain acquisitions to be made.

1.2.2. Ratio-taking operations

The ratios of light, in terms of wavelength composition and flux, are calculated by the brain to generate constant colours and it is indeed for this reason that the perceived colours of the patches remain constant, in spite of the continual changes in the wavelength composition of light reaching the eye from each patch. One of the difficulties is that the changes in wavelength composition and in luminous intensity are perceived, even if they do not alter the stability of the colours. This could lead one to conclude that the greater cerebral activation in response to the dynamic version of the coloured stimuli reflects the changes perceived. But such perceptual changes are impossible to separate from the ratio-taking operation, since a change in overall wavelength composition or in luminosity will at the very least activate different wavelength selective cells in cortical areas involved in colour processing. Even though this will not lead to a change in colours, the shades of the patches will change; for example, when viewing a green surface successively in tungsten light and in daylight it remains green, but we perceive the difference in the shade of green. Hence, these perceived changes are part of the re-calculation process, and cannot be separated from it. We note that the ratios of light of any given waveband across any two patches remained constant in both dynamic modes described above. But the change in absolute values necessitates that these ratios across space and wavebands are retaken. In the *varying intensity mode* the ratio of intensities between wavebands reflected from a given patch remained constant, since the intensity of all wavebands increased or decreased simultaneously.

1.3. Experiment 2

Previous studies have shown that areas in the fusiform gyrus beyond the V4-complex are involved when colours are viewed as parts of recognisable objects (Zeki & Marini, 1998). We therefore designed an experiment to test whether these further areas are involved in the ratio taking operations when natural scenes are involved or whether the ratio-taking is done at a unique site, regardless of the nature of the stimulus. Three subjects viewed a complex natural scene of coloured vegetables, as is shown in **figure 3**. The stimuli were divided into two types. In one, the wavelength composition of the illuminant changed continuously (as described for the Mondrian above) while in the other it remained constant. The stimuli were presented 18 times alternatingly and lasted 32.8 s each. The measurement and analysis techniques were as given for experiment (1).

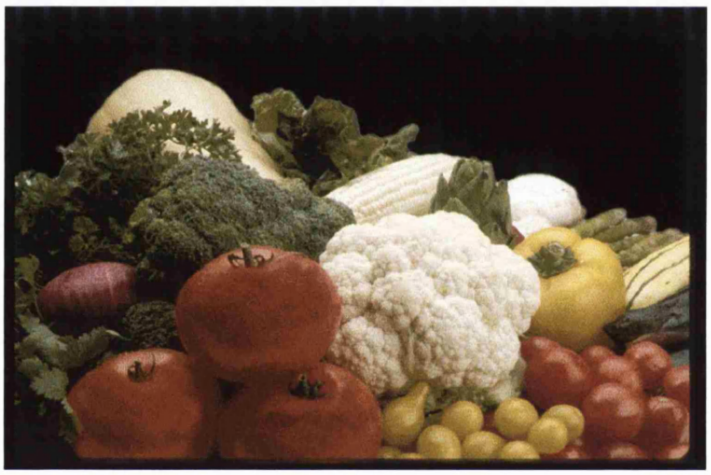

Figure 3. The meaningful visual scene containing coloured vegetables that was displayed in conditions of a dynamically changing illumination and a static illumination.

1.4. Experiment 3

Experiments (1) and (2) revealed two subdivisions of the colour centre in the fusiform gyrus. To learn whether the two subdivisions have different retinotopic organisations - which would be an indicator that they actually are separate cortical maps - we re-analysed the data from four randomly chosen subjects collected by McKeefry and Zeki (1997).

1.4.1. Experimental paradigm

In this study, subjects viewed a grey screen that contained a Mondrian stimulus confined to either the upper or the lower third of the screen, while they fixated a central cross. The Mondrian alternated at 1 Hz with a homogenous surface that had the same mean luminance and mean hue as the Mondrian (see **figure 4**). The Mondrian was either coloured or achromatic, thus leading to four stimulus conditions: (A) Upper field coloured, (B) lower field coloured, (C) upper field achromatic and (D) lower field achromatic. For the colour conditions, the eight patches of the Mondrian were set to isoluminance with the gray background for each subject separately, using the heterochromatic flicker method (Kaiser, 1991). The mean luminance of the coloured Mondrian was equal to the mean luminance of the achromatic version, which contained gray patches that differed in luminance. Each of the four conditions was presented in blocks lasting 30.4 s (5 TRs) and was repeated 16 times in a pseudo-random sequence. The whole scanning session lasted 32 min 27s.

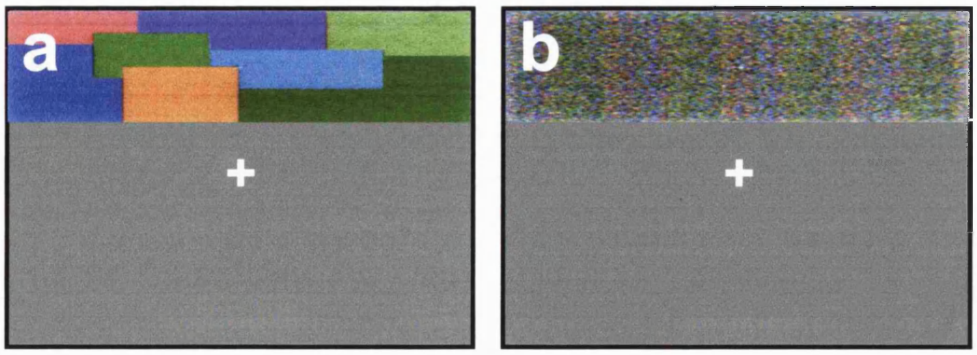

Figure 4. The stimuli used in the retinotopic mapping study of the human colour centre. The two stimuli (a and b) alternated at 1 Hz in the *upper field coloured condition* while the subject fixated the central cross. Lower field stimulation used the same stimulus, but rotated by 180 degrees. For the achromatic conditions, the Mondrian in (a) consisted of gray patches of different luminance and the screen in (b) was homogeneously gray. The stimulation was confined to the upper or the lower third of the screen.

By comparing the colour with achromatic conditions, the human colour centre as a whole would be revealed (see figure 11a). By making the contrast of e.g. (A-C) - (B-D), the colour selective cortical region representing upper field only should become apparent, assuming a topographic map within V4 (see figure 11b).

1.4.2. Re-analysis using less spatial smoothing

The original study by McKeefry and Zeki (1997) had revealed the retinotopic organisation of area V4, but no further subdivisions within the colour centre in the fusiform gyrus. We suspected that both subdivisions had actually been activated, but that the 8 mm FWHM (full width at half maximum) spatial smoothing filter used might have made the two separate areas appear as a single area since they were always co-active, while still allowing the retinotopy of the posterior area to appear due to its differential activation during upper and lower field stimulation and corresponding statistical contrasts. In our re-analysis, we therefore applied a spatial smoothing filter of 6 mm. In general, spatial smoothing of fMRI data is necessary to reduce the noise in the data. The use of large spatial filters can have two potential disadvantages: first, areas of activation that are small with respect to the filter can lose their statistical significance in the subsequent analysis, and, second, spatially neighbouring and co-active areas can appear as a single area. The use of small filters circumvents this whilst having the disadvantage of decreasing statistical significance in the subsequent analysis, since the spatial noise is reduced less effectively. Another risk associated with the use of small spatial filters occurs only in group analyses, in that the activation of a single area with slightly different positions in different subjects can appear in the group analysis as two separate areas of activation. We avoided this by additionally examining whether the two subdivisions were present in the single subjects separately, which turned out to be so (see also **Figures 8 b**, **10 b** and **11 a**).

1.5. Experiment 4

Marini and Zeki (1998) conducted this experiment in order to study the relationship of colours and objects in the cerebral cortex, especially the effect falsely coloured objects would have in terms of cortical activation in the colour centre and beyond it. It seemed interesting to find out whether the newly discovered subdivisions within the human colour centre would be differentially activated by falsely coloured and correctly coloured objects, as compared to gray tone images of the same objects.

1.5.1. Experimental paradigm

Nine subjects had been presented with 16 pictures containing fruits, vegetables, animals and landscapes. The same pictures were presented in the form of three different categories: (A) in normal colours, (B) in abnormal colours and (C) in gray tones. An example of a picture in format (A) and (B) is given in **figure 5**. Each of the three categories was presented to the subjects in blocks lasting 30.12s (5 TRs) each, during which two pictures of the same category were alternated at 1 Hz. The blocks of the different categories were repeated eight times in a random sequence, and each block was followed by a rest condition consisting of a black screen and lasting 30.12s. The scanning session lasted 24min during which 240 whole brain scans were acquired.

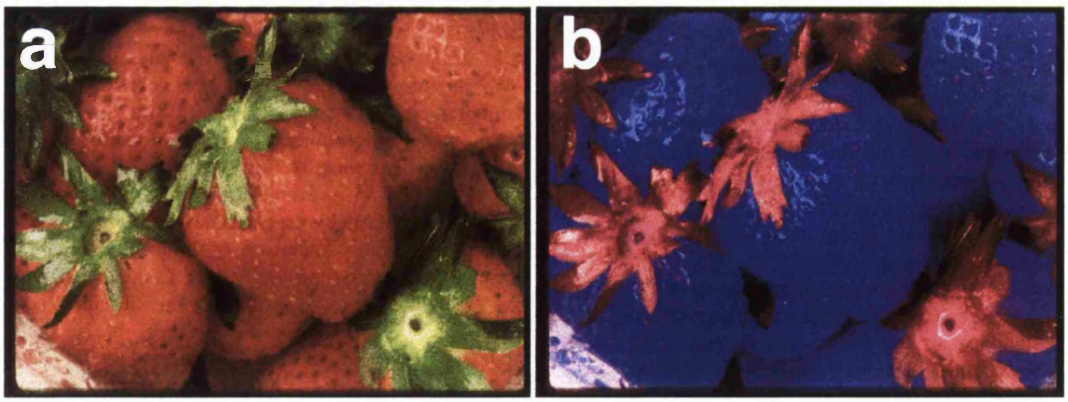

Figure 5. Examples of a meaningful scene shown in natural (a) and abnormal (b) colours.

Contrasts were calculated for (A-C) and (B-C); both were expected to reveal activity in the V4-complex, since both compare coloured with gray tone stimuli. An overlay of these two contrasts at an appropriate threshold should then show whether the intensity of activity differed in the two subdivisions of the human colour centre during processing of naturally or abnormally coloured scenes (see figure 12).

1.6. Experiment 5

This experiment was designed to determine whether the modulatory effects of attention to colour involve both subdivisions of the colour centre in the fusiform gyrus described in this study and to segregate attentional mechanisms involved in attention to colour and to motion. It also served to find out whether the two subdivisions are retinotopically organised. Here we concentrate only on results related to attention to colour.

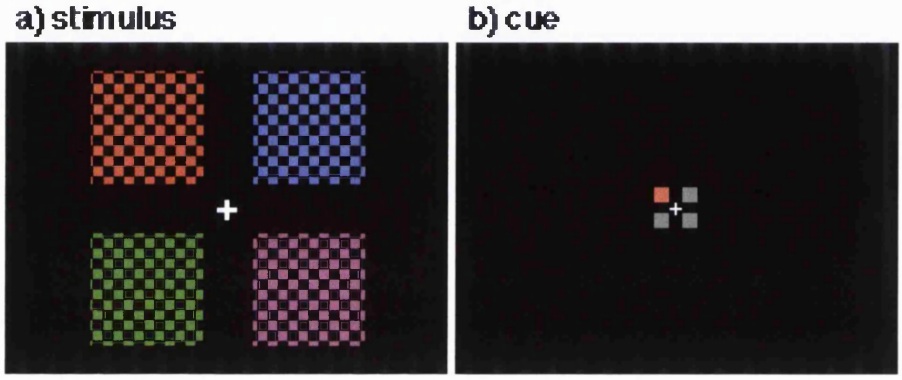

Figure 6. A schematic representation of the stimuli used in the retinotopic attention mapping study of the human colour centre. (a) represents the main stimulus, with each quadrant containing one of four colours and randomly arranged squares moving in one of four directions. Both motion direction and colours changed independently and randomly every 500ms. (b) is an example of a cue shown to the subject during 1.5s at the beginning of each condition. In this example, the subject is cued to count the number of occurrences of the red colour in the top left square (until the main stimulus is interrupted by the next cue).

1.6.1. Experimental paradigm

Five subjects performed 9 tasks each while fixating a central cross throughout the complete scanning procedure. The tasks involved covert attention to four different locations in space and to two visual attributes (colour and motion) within them, plus one control condition. The stimulus used was always the same and consisted of a central fixation cross surrounded by four squares on a black background, one in each visual quadrant (dimensions of each square: 7° x 6.5°, separation between squares: 7° horizontal, 6.5° vertical). Within each square a random array of black pixels (pixel size: 0.8°, with equal numbers of black and coloured pixels) moved in one of four directions (up, down, left or right) at a speed of 5.4 degrees·s^{-1}. The remaining pixels in each square had one of four colours (red, green, blue or violet) set to isoluminance for each subject separately using the heterochromatic flicker method (Kaiser, 1991). Both colour and direction of motion changed independently and randomly every 500 ms in each square. During the scan, subjects were cued to attend covertly (with the eyes

fixating the central cross) to one of the four quadrants, and to either motion or colour within this quadrant (see **figure 6**).

A control condition was included in which the subjects did not attend to anything while viewing the stimulus. To maintain attention, subjects had to count covertly the number of occurrences of a certain colour (e.g. red) in the colour attention task, or the number of occurrences of a certain direction of motion (e.g. up) in the attended square. In the control condition, subjects counted covertly at the same pace that they had counted at in the attention conditions (on average at 0.5 Hz). The cue was presented at the beginning of each condition for 1.5 s and consisted of an iconic representation of the whole stimulus (spanning 2.7°) consisting of four small squares, in which one square was highlighted either with the relevant colour or with an arrow in it that indicated the relevant direction of motion. In separate experiments the covert counting had been replaced with button-presses, and identical results were obtained (not shown). Each condition lasted 32.8 s and was repeated 8 times within blocks that consisted of different random permutations of the nine conditions.

1.7. Image acquisition and data analysis

Data for all 27 subjects were acquired as T_2-weighted whole-brain images with a voxel size of 3 x 3 x 3 mm in a 2 Tesla Siemens Vision scanner using an echo-planar imaging (EPI) sequence. The data were analysed using the statistical parametric mapping software (SPM) package developed by Friston et al. (1995b) and were obtained with the following values: Experiments (1), (2) and (5): TR=4.0 s, 48 slices, spatial smoothing: 6 mm FWHM; experiment (3) TR=6.084 s, 64 slices, spatial smoothing: 6 mm FWHM; experiment (4): TR=6.024 s, 64 slices, spatial smoothing: 8 mm FWHM. For all experiments, echo time (TE) was 40 ms. Images were realigned to minimise movement artefacts and then normalised into the anatomical Tailarach space (using the EPI template provided in SPM, which is similar to the average of 305 brains provided by the Montreal Neurological Institute) before they were spatially smoothed with a Gaussian kernel of the size indicated.

1.8. Analysis of fMRI data by the independent components analysis (ICA)

Data from both the dynamic Mondrian experiment (Experiment 2) and the earlier V4 mapping study (10 subjects) of (McKeefry & Zeki, 1997) were submitted to an independent component analysis (ICA) (Bell & Sejnowski, 1995). Even though the application of ICA to fMRI data is treated in much greater depth below, a quick overview is given here. This algorithm is based on information theory and is capable of decomposing or unmixing any signal which is a linear mixture of several independent signals (the sources), which need not be known. It does so by minimising the mutual information between the components that it delivers as output; when the mutual information between the output signals is minimal, they can be assumed to be the original, independent sources that the input signal had been composed of, as long as they were truly independent. During tasks involving conscious perception, as those performed in our fMRI experiments, the brain areas functionally specialised to perform the given task will be active. Different, but maybe overlapping, sets of areas will be active during different tasks, each such set constituting a functional unit across the cortex (Bartels & Zeki, 1998b). Furthermore, some sets of areas will be active throughout a given task whereas others may be activated only at onset or offset. These spatial maps of brain activity will consistently appear whenever a task is repeated during the experiment, with a time-course that is characteristic for each. ICA is the method of choice to isolate such dynamically formed maps of brain activity that might correspond to functional units across the cortex, since ICA does not require any *a priori* knowledge about the time-course of the activity patterns with regard to the stimulation. ICA has been applied to a variety of different data sets, especially successfully in the separation of temporally independent sources in EEG data (Makeig, Jung, Bell, Ghahremani & Sejnowski, 1997). For fMRI data, ICA has been shown to be more powerful than PCA or other non-parametric methods in separating artefacts from task-related brain activity by separating spatially independent maps of brain activation. It has also isolated spatially independent activity maps in fMRI data whose time-courses correlated completely or for parts with the tasks performed during scanning (McKeown, et al., 1998b; Zeki & Bartels, 1999a). However, one would expect that the application of ICA to fMRI data is of limited power, since true independence of activation patterns can hardly be assumed and ICA is limited in picking up non-linear interactions between areas; the poor temporal resolution of several seconds imposes further restrictions (for a discussion, see Friston, 1998). As input signal to ICA, the same 6 mm smoothed data used for statistical parametric mapping (SPM) were submitted to the ICA algorithm (Bell & Sejnowski, 1995). For this, images were re-sliced to obtain voxels of cubes of 4 x 4 x 4 mm to make the task computationally tractable. The data from each brain thus

consisted of up to 320 time-steps with ca. 30,000 voxels each. For ICA, we treated the spatial (voxel) dimension as time and each time-step as a channel, thus obtaining 320 independent spatial maps, each of which had a unique time course associated with it.

1.9. Colour methods appendix:

A computer model of the Land Mondrian Retinex experiment

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In the Land Mondrian Retinex experiment (Land, 1974) a multicoloured abstract scene consisting of rectangular patches is illuminated using three projectors. Each projector is fitted with a coloured filter which passes either predominantly long-wave, medium-wave or short-wave light. The intensity of light from each projector may be independently varied. Constructing a computerised version of this experiment requires two steps; firstly, the colour of each patch must be calculated given the intensities of the three projectors and secondly that colour must be emulated on the graphics output device of the computer (cathode ray tube (CRT) or liquid crystal display (LCD) projector).

1.9.1. Calculation of the colour of each patch for given projector intensities

A cardboard square was made up as shown in **Figure 2** with 20 assorted coloured patches pasted on it. The reflectance spectrum of each of the twenty coloured patches was measured using a Photo Research PR650 Spectra Colorimeter. The reflectance (from 0 to 1) was calculated for 101 wavelengths in 4 nm bins from 380 nm to 780 nm by comparing the intensity of light reflected by the patch with that reflected by a standard reflector for each of the 101 wavelength bins. **Figure A1** shows the reflectance spectrum of a patch which was of an overall reddish colour.

Using the same instrument, the radiant spectra of three illuminators were measured directly; these were predominantly long (reddish), medium (greenish) and short (bluish) wave, respectively. **Figure A2** shows the radiant spectrum of a typical medium-wave illuminator.

Given a reflectance spectrum for a patch and a radiant spectrum for an illuminator, it is a simple matter to calculate the spectrum that would be reflected. Using tables it is possible to convert this spectrum into 1931 CIE XYZ tristimulus values (X, Y and Z). These contain information about both intensity and colour, and can be converted into the CIE xyz chromaticity co-ordinates, which are independent of the intensity, as follows: $x=X\cdot(X+Y+Z)^{-1}$; $y=Y\cdot(X+Y+Z)^{-1}$; $z=Z\cdot(X+Y+Z)^{-1}$. The required colour matching functions are tabulated in Wyszecki & Stiles (1982), Table I (3.3.1).

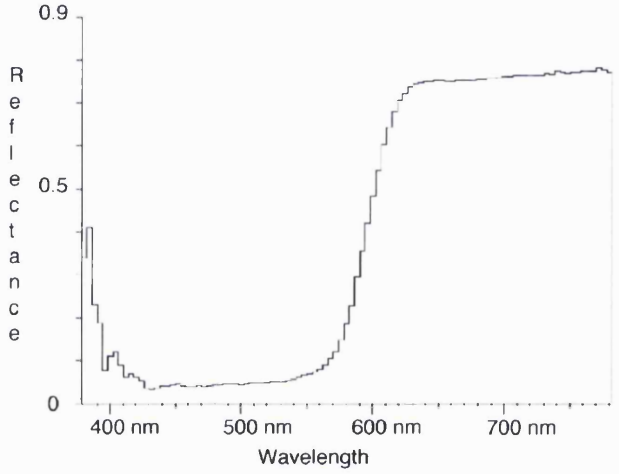

Figure A1. Typical reflectance spectrum of a red patch.

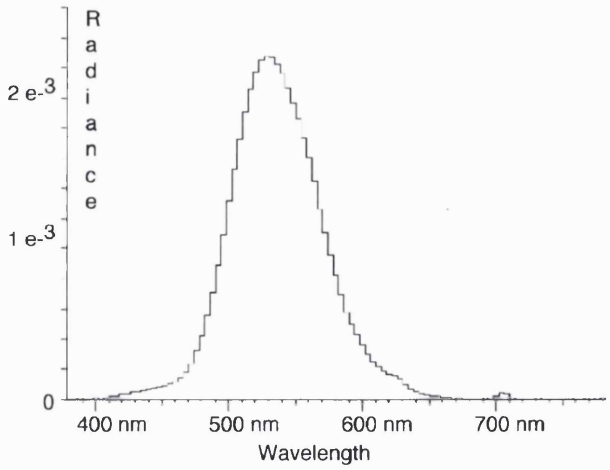

Figure A2. Typical medium-wave illuminator radiant spectrum.

The XYZ values thus obtained are for the respective illuminator at maximum intensity. If the illuminator were at 50% brightness the resulting XYZ values would be at 50% of these values. Thus the XYZ values of the patch can be calculated in simple proportion for any required brightness of that illuminator. Moreover, the XYZ values are additive so that the_XYZ values for each of the three illuminators (long, medium and short-wave) can be calculated separately and then added together to give a combined XYZ for the patch. Using this method the XYZ tristimulus values for any patch can be calculated for any combination of intensities of the three illuminators.

Measuring the full reflectance and radiant spectra as described above has the advantage that XYZ tristimulus values can be generated for any combination of patch and illuminator. However, it is sufficient to measure just the XYZ tristimulus values for each patch in turn when each is lit in turn by each illuminator at maximum intensity.

1.9.2. Emulation of a particular colour on a computer graphics output device

The computer graphics output devices we used employ three variable intensity light sources to generate colours. In the case of a CRT monitor there are three coloured phosphors, red, green and blue (the RGB elements). In the case of LCD projectors there are red, green and blue elements in the LCD panel. In both cases the intensities of the RGB elements may be controlled directly by the computer.

For the purposes of this study two assumptions were made about the RGB elements. Firstly, that the colour of each element does not change for different intensities (i.e. the xyz chromaticity co-ordinates remain constant at different intensities). Secondly, that the elements are independent so that the output of a particular red element for example is constant regardless of the output of surrounding elements.

The XYZ tristimulus values of each of the individual RGB elements at peak intensity were measured. Let these be:-

X_r Y_r Z_r for the red element
X_g Y_g Z_g for the green element
X_b Y_b Z_b for the blue element

The RGB elements can have different intensities denoted by I_r, I_g, I_b, where I varies linearly from 0 to 1. The resulting tristimulus values for the RGB elements combined would be:-

$$X = X_r I_r + X_g I_g + X_b I_b$$
$$Y = Y_r I_r + Y_g I_g + Y_b I_b$$
$$Z = Z_r I_r + Z_g I_g + Z_b I_b$$

Equation E1 - relationship between RGB intensity and output XYZ

The tristimulus values of each of the individual RGB elements are known and so the three simultaneous linear equations above can be solved for any required value of XYZ, giving the required intensities for the three RGB elements I_r, I_g, I_b.

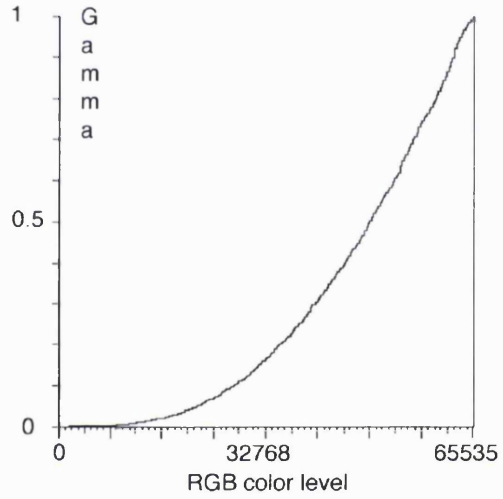

Figure A3. Typical gamma curve.

The next step was to produce these required intensities under program control. Usually there is a graphics command on the computer to set the individual colour levels for the RGB elements. On the Macintosh they can be set on a scale from 0 to 65535. The relationship between colour level (e.g. 0 to 65535 for the Macintosh) and intensity on the graphics output device is usually non-linear and is commonly known as a gamma function (not related to statistical gamma distributions). A typical gamma function for a monitor is shown in **Figure A3**. The gamma functions for the three RGB elements may be obtained using a light meter (although we used the PR650 Spectra Colorimeter). It is not usually necessary to take more than about 64 calibration points along the curve; spline interpolation between these points should be accurate enough for the intervening areas.

1.9.3. Problems arising from the model

Two problems may arise from the solution of equation E1 above:

(1) One or more of the intensities I_r, I_g or I_b is negative.

This means that the graphics output device is unable to generate the required colour. The device can only generate colours that lie within the triangle formed by the CIE 1931 chromaticity co-ordinates of the RGB elements of the device; the XYZ tristimulus values have chromaticity co-ordinates which lie outside that triangle.

(2) One or more of the intensities I_r, I_g or I_b is greater than one.

This means that the graphics output device is unable to generate the required colour at the required intensity; the maximum brightness of the graphics device RGB elements in the required ratio is still not enough to produce the required intensity.

Problem 1 above is difficult to deal with. One approach is to generate a colour close to requirements. This could be done by resetting the negative intensity to zero, by taking the absolute value of the minimum negative intensity and adding it to all the intensities (effectively adding white and desaturating the colour), or by calculating the closest colour on the 1931 CIE colour space which lies within the RGB element triangle. All these methods will produce an approximation to the required colour. Another approach (the one we use) is to modify the experiment so that less saturated colours are required, colours which can be generated by the graphics device. In the case of our Land Mondrian Retinex experiment we do this by limiting the minimum intensity of the three illuminators to say 20% of full intensity rather than allowing them to switch off completely. This effectively reduces the saturation of the colours that are reflected from the Mondrian patches.

Problem 2 above may be dealt with in the following way. First of all we calculate the maximum intensity I_r, I_g or I_b which may be required under any circumstances. This will be for one of the patches when lit by all three illuminators at maximum intensity. Let this value be I_{Max}. The inverse of this can be used as a normalisation factor. If every required intensity is always multiplied by this normalisation factor then all the resulting I_r, I_g or I_b values will be less than or equal to one and therefore they will all be able to be generated on the graphics device. All the required colours will be the same as before and all the relative intensities will also be correct, but the absolute intensities will all be dimmer by the normalisation factor.

1.9.4. Discrepancies between predicted and measured XYZ

The method described above produces a good emulation of the Land Mondrian Retinex experiment but there are still some discrepancies between predicted and measured XYZ values, typically between 5% and 10%. This is due to failure of the two assumptions of the model: inconstancy of the hue of the RGB elements with intensity and non-independence of the RGB elements. Other factors may also have an effect; for example, the colour and intensity of a very small patch may be different from that of a very large patch even though the computer RGB levels may be identical. Also, different areas on the graphics device may have a slight colour cast or different intensity, particularly when comparing the periphery to the centre of the screen. There may also be a temporal effect; transient changes in colour may not be delivered accurately by the graphics device. This has been noted when using LCD projectors.

2. The computational dissection of the brain: ICA analysis of fMRI data

In order to find out whether ICA can isolate activity in several visual and maybe even non-visual areas from brain activity elsewhere, we used two fMRI data sets that were perceptually sufficiently rich and diverse as to ensure activity in several different visual areas.

2.1. Study 1: Objects from motion

The specific question that Bork & Zeki (1998) tried to address in their study was whether the same or different higher cortical areas of the visual brain are activated when the same meaningful and recognisable forms are generated from the two different attributes, namely motion and luminance (Bork & Zeki, 1998). To do so, five different stimulus categories were presented to the subjects in a standard fMRI block-design; they were expected to activate different cortical areas. I have analysed the data gathered by Bork & Zeki (1998) because they activate several, clearly distinct, visual cortical areas. The multiplicity of areas activated thus makes it possible to enquire whether ICA is capable of isolating the areas that are detected with a standard statistical analysis using SPM. Given that ICA would do so without a priori knowledge, any agreement between the results obtained by the SPM method and by ICA would strongly suggest that ICA has the power to detect functionally specialised zones in the cortex. Stimulus generation and data collection were done by Bork & Zeki (1998).

2.1.1. Visual stimuli

Four subjects viewed abstract patterns of black and white squares with no recognisable forms and similar stimuli in which the squares were so arranged as to generate a recognisable form, either from the static arrangement of the squares or from their movement. These stimuli allowed for a comparison of the cortical activity produced by (a) a stationary abstract (meaningless) stimulus made up of black squares, in which there is no recognisable figure (SML=stationary meaningless); (b) the moving version of the same stimulus in which there is no recognisable figure (MML=motion meaningless); (c) a stationary stimulus in which the black squares are grouped together to generate a recognisable (meaningful) form (SMF=stationary meaningful); (d) the moving version of (c) which also results in recognisable (meaningful) shapes but this time from motion alone (MMF=motion meaningful), and (e) a black screen as a control condition (Rest).

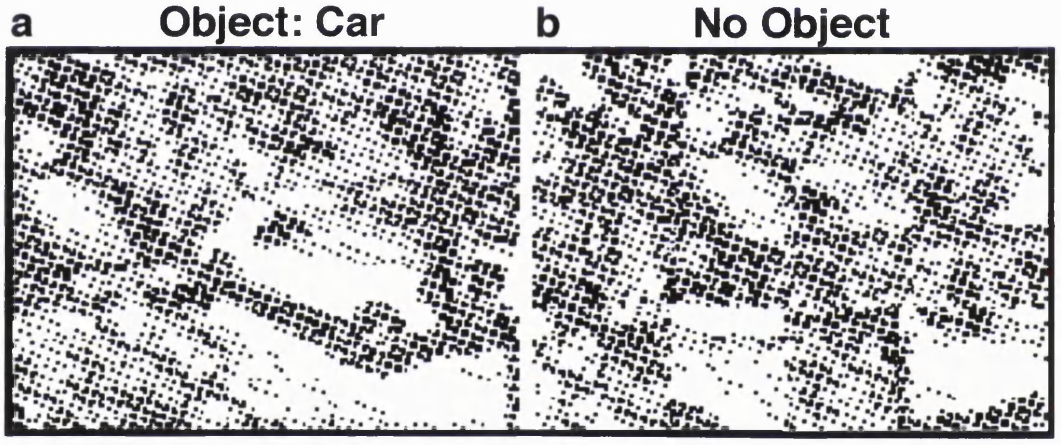

Figure 7. Screen shots of stimuli used for the 'object from motion' recognition study (**a**) An example of a recognisable (meaningful) stimulus, which contains in this case a car. (**b**) An example of a meaningless stimulus, which contains no recognisable object, but shares the general features with that shown in (a).

Meaningful stimuli were generated by choosing film clips of cars, animals and humans moving in their natural environment, changing colours into grey levels, applying an edge detection algorithm and finally translating these black/white rendered edges into small squares, using the packages MATLAB and Adobe Photoshop/Premiere. Image features of foreground and background were modelled equally by this procedure, so that the task of the subjects was not only object recognition but also figure- ground segregation on the basis of the pattern of movement of the squares. Any single frame of this dynamic stimulus consists of apparently randomly assembled squares, not giving rise to any recognisable object. In order to

create meaningless stimuli the same original film clips were locally blurred and then passed through the same sequence of filters, so that global speeds and distribution of squares were left intact. Stationary stimuli contained squares that were either screen shots of the moving stimuli and therefore contained no recognisable objects, or they contained squares that outlined objects such that they were recognisable. Examples of such screen shots are given in **figure 7**.

Each condition lasted 30s (5 TRs) and was repeated eight times in a fixed sequence of the five conditions ([SMF MMF SML MML Rest] for subjects JT, AF, SD, and [MMF SML MML SMF Rest] for subject AB). In total, 160 different stimuli of all types were presented during a total scanning time of 20min during which 200 whole brain scans were acquired.

A comparison of brain activity elicited by stimuli containing motion with that elicited by stimuli containing no motion would therefore reveal areas that are involved in motion processing, while a comparison of activity produced by meaningful versus meaningless stimuli would reveal areas involved in object processing. A comparison of e.g. the activity related to static meaningless stimuli with that related to the rest condition would reveal early visual areas, such as V1 and V2 (see the Results section).

2.2. Study 2: the James Bond 007 movie *Tomorrow Never Dies*

The above studies all used controlled stimuli, arranged in blocks lasting around 30s that were repeated many times. The stimuli were specifically designed to activate one or several specific cortical areas differentially, throughout the duration of the blocks. It seemed important to find out whether different cortical areas have different time courses of activation even without stimuli that are repeated many times and which are specifically designed to activate them, as would happen in natural viewing conditions when a variety of stimuli would activate a number of visual areas. Equally important would be to find out if such differences in activity would be apparent despite the long time intervals of several seconds fMRI data are acquired with. If so, we expected that ICA might be able to isolate different cortical areas, without a priori knowledge.

2.2.1. Visual stimulation

To study this, I asked subjects to view the first 22min of the James Bond movie *Tomorrow Never Dies*, including the sound track. Whole brain images were acquired every 4.1s. The movie was interrupted every 2.5min or 3min with a blank period lasting 30s, in total eight times (leading to a total of 4mins blank period; see figure 24). The blank period consisted of a black screen and no sound track. Colours were alternated with black&white every 30s, which was not analysed in the present study. Excluding dummies, 324 whole brain images were acquired during 22min 25s.

2.3. fMRI parameters, SPM and ICA analyses

Data for both studies were acquired in a Siemens 'Vision' whole body MRI scanner with 2 Tesla, using an echo planar imaging (EPI) sequence for the acquisition of $T2^*$ weighted images to measure the BOLD response.

For the objects from motion study (study 1), whole brain images consisting of 64 slices were acquired with a repetition time (TR) of 6.048s and an echo time (TE) of 40ms using a sinusoidal EPI sequence. Slices had a 0.5mm gap between them, were 2.5mm thick and contained 64x64 3x3mm voxels. 204 images were acquired including four initial dummies.

For the movie study (study 2), whole brain images consisted of 48 slices with the same parameters as above, except for the TR=4.1s. 328 images were acquired including four initial dummies.

Before submitting data to ICA and SPM analyses, they were preprocessed using SPM99b (Friston, Frith, Frackowiak & Turner, 1995a; Friston, et al., 1995b) (http://www.fil.ion.ucl.ac.uk/spm/). The slice-wise acquired whole brain images were time-sliced so that for a given image every voxel corresponded to the same point in time; images were then realigned to minimise movement artefacts, followed by a normalisation to the anatomical Tailarach brain. After this, data were spatially smoothed with a Gaussian kernel spanning 6mm full width at half maximum (FWHM) and temporally smoothed with the hemodynamic response function (hrf) to eliminate non-physiological high-frequency noise. For the normalisation to the Tailarach brain, the EPI image provided with SPM99b was used, which is similar to the average of 305 brains provided by the Montreal Neurological Institute.

The parametric statistical analysis of study 1 was also performed using SPM99b. Data were globally normalised (the mean was subtracted from each image) and the time series were high-pass filtered with a cut-off at 300s to eliminate low-frequency noise, which was not task related. A standard statistical analysis was performed (a multiple regression against the five stimulus conditions), as described elsewhere (Friston, et al., 1995a; Friston, et al., 1995b).

For the ICA analysis, the preprocessed data were fed into the standard Bell-Sejnowski algorithm (Bell & Sejnowski, 1995) as provided in the EEG-package by Makeig et al. (http://www.cnl.salk.edu/~scott/ica-download-form.html) (Makeig, et al.,

1997). The data from each brain thus consisted of up to 328 time-steps with ca. 30,000 voxels each. For ICA, we treated the spatial (voxel) dimension as time and each time-step as a channel, thus obtaining 328 independent spatial maps, each of which had a unique time course associated with it.

2.4. Graphical display methods

The following sections merely fill in some of the technical details that are not given in the results section or the figure captions and should therefore be consulted in conjunction with those.

2.4.1. Glass brain projections

These are maximum intensity projections of the 3D whole brain images. Both, maps of independent components (ICs) and of correlation maps (CMs) have negative and positive values. For each pixel in one of the three 2D projections (sagittal, coronal and transverse) only that voxel is displayed whose absolute value deviates most from zero along the column of the collapsed dimension. Glass brains are displayed using the colour codes shown in the colour bars in e.g. figures 16 and 17.

2.4.2. Chronoarchitectonic maps

To generate chronoarchitectonic maps, each IC was thresholded at 40%, such that only the voxels 'hotter' than 40% from the midpoint are visible. The whole set of these voxels is then given a colour corresponding to the activity that the IC has during a given time. See also the description given in the caption to figure 20.

2.4.3. Correlation maps and Correlograms

For the correlograms only areas that had been clearly isolated by ICA were considered. The BOLD signal time courses that corresponded to the hottest voxel of the areas isolated in the ICA components were used. No global normalisation was applied (subtraction of the mean from each whole-brain image). Global signal changes that affect all voxels contribute therefore to a positive correlation, which explains why most of these maps have a yellowish look. However, a global normalisation can introduce

area-specific distortions, which is why we chose not to apply it. See also the results section and the captions to figure 17 and 18.

2.4.4. Timings for the correlograms of study 2

The movie was interrupted in total eight times every 2.5 or 3 min by 30s blank periods (see figure 24). Purely movie related brain activity, activity related to the blank period and that related to on/offset effects of the blank period were retrieved from the original fMRI time series using the timings shown in figure 22e and 22f. These are the mean times applied to the eight periods; the exact timings jitter ±2s around these since whole brain images were acquired every 4.1s. To extract the activity related to viewing of the movie (figure 22a,b), the data between -2s before onset of the blank period to 22s after offset of the blank period were cut out to ensure no activity related to the blank period remained. This included a generous refractory period of 22s following it: recovery of the BOLD signal was observed for up to about 20s following the blank period (see figure 23). Data related to no visual stimulation were collected between 11s after onset of the blank period to the end of it (figure 22c), while those related purely to on/offset effects corresponded to data during the 11s after onset and 11s after offset of the blank period.

2.4.5. PSTHs (peri-stimulus time histograms) and ICA time courses

PSTHs for study 1 were obtained by averaging the ICA or BOLD time courses for all six repeats of the five conditions. BOLD PSTHs represent the percentage in signal change. ICA time courses and PSTHs have arbitrary units and were normalised for each IC to the same range (0-1).

Part 3:

Results

1. The architecture of the human colour centre

This section describes experiments aiming to identify the cortical regions that are critical for the ratio-taking process that generates colour, and to characterise their extent, retinotopic organisation and involvement in attention.

1.1. Experiment 1 - Dynamically illuminated Mondrians

The primary aim of this experiment was to determine the cortical sites involved in the ratio-taking operations across the field of view that are necessary to generate constant colours. *A priori*, these were not expected to be necessarily identical with the sites determined in previous experiments when humans viewed coloured stimuli, namely the calcarine cortex (V1) and area V4. Here, we focused on comparing cortical activity evoked by stimuli which were either coloured or achromatic, but which we thought differed in the degree to which they would put the ratio-taking system into use.

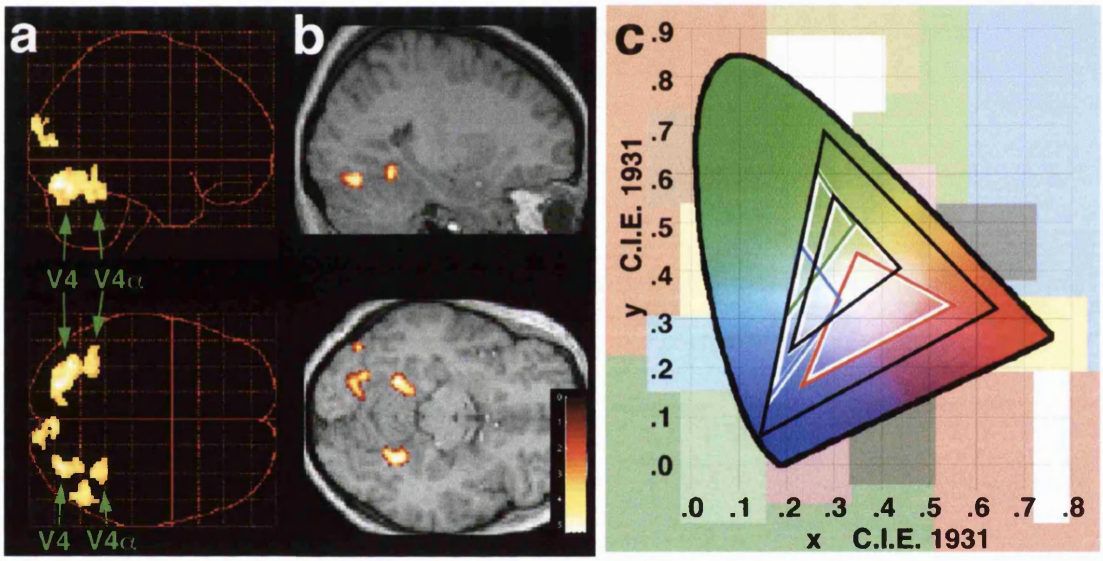

Figure 8. The cortical activity elicited when subjects viewed a dynamically illuminated coloured scene. (**a**) **Left:** Group result of six subjects who viewed a coloured Mondrian, for the comparison of the *varying luminance* and the *varying wavelength composition* mode versus the *static* mode. The perceived colours remained constant at any time. An SPM displayed as a glass-brain reveals that activity was largely constrained to two subdivisions of the V4-complex: V4 and V4α (group of six subjects, random two of whom were scanned twice, thresholded at $p<0.0001$ ($Z=3.72$) for height and at 90 voxels for extent of activation, both uncorrected). There is also activity in the V1/V2 region and lateral to the V4-complex. **Right:** Activity in a single subject for the comparison of *varying wavelength composition* mode vs. the *static* mode in a coloured Mondrian. V4 (posterior) is at this threshold only visible in the right hemisphere, V4α in both ($p<0.001$ uncorrected, slices taken at x: -26, z: -12 mm). (**b**) This graph contains the Mondrian stimulus used (background) and an overview of the range within which the illuminant changed dynamically (foreground). The latter is displayed in a C.I.E. (Comission Internationale de l'Éclairage) colour flowchart (ellipsoid envelope). The three inner coloured triangles show the range of colour space which four Mondrian patches of the corresponding colours would have occupied during the *varying wavelength condition* had they been viewed on their own (the black triangle depicts the same for the white patch). Even though the wavelength composition of each patch of the Mondrian changed continuously, their perceived colours remained constant in the experiment, since they were viewed in context. The range of colours our projection screen is capable of displaying is depicted by the black outer triangle.

Figures 8 a and **b** summarise the main findings, which were the same for comparisons within coloured or achromatic stimuli. Any comparison of a dynamic condition (i.e. *varying wavelength composition mode* or *varying intensity mode*) with a static condition, whether of coloured or achromatic stimuli, led predominantly to activity in the fusiform gyrus, with surprisingly little involvement of areas V1 and V2, compared to studies that used flashed coloured versus achromatic stimuli. But each of these comparisons also revealed that the colour selective region in the fusiform gyrus can be subdivided into at least two parts: a larger posterior zone with co-ordinates very similar to the co-ordinates given in earlier studies for V4 and a smaller anterior one, not previously differentiated as a separate area (see **Table 2**). The calcarine cortex (V1) and V2 showed weak activity, but considerably less than that observed in previous studies which compared activity evoked by flashed coloured versus flashed achromatic stimuli.

Figure 9 shows glass-brain projections for the four separate comparisons of the *varying wavelength* condition with the *static* condition or of the *varying intensity* condition with the *static* condition, for the coloured (**a** and **b**) and the achromatic (**c** and **d**) stimuli separately. These comparisons share a common feature, in that the colour selective region in the fusiform gyrus appears to consist of at least two subdivisions in each hemisphere. We could not find any consistent difference in activity patterns that would allow us to differentiate between coloured or achromatic stimulations nor between the different types of dynamic stimulations. This suggests that similar calculations have to be performed in order to "discount the illuminant" under a dynamic illumination, no matter whether the stimuli are coloured or achromatic, or whether they change in their luminance only or along with changes in their wavelength composition. It is interesting to note that some activity in the V5-complex became apparent. This has not been observed in previous studies or in re-analyses of our earlier studies which used flashed coloured and achromatic stimuli. It might therefore be caused by the dynamic nature of the stimuli used here, which share with moving stimuli the property that they changed predictably over time, even though they were spatially static.

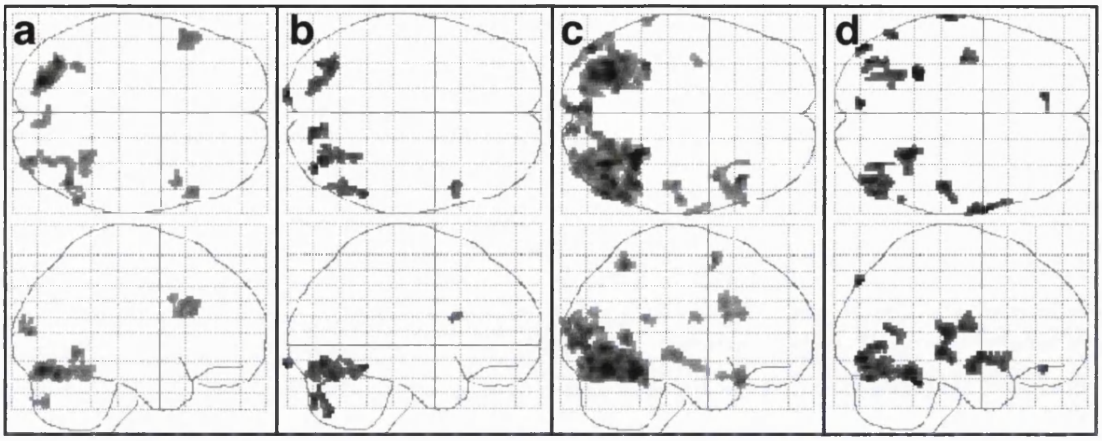

Figure 9. Comparisons of activity obtained by passive viewing of dynamically vs. statically illuminated Mondrians that were coloured (a,b) or achromatic (c,d). **(a)** *Varying wavelength composition* mode vs. *static* mode in a coloured Mondrian. **(b)** *Varying luminance* mode vs. *static* mode in a coloured Mondrian. **(c)** *Varying wavelength composition* mode vs. *static* mode in an achromatic Mondrian. **(d)** *Varying luminance mode* vs. *static* mode in an achromatic Mondrian. All contrasts are shown in glass-brain projections for the group of six subjects, thresholded at $p<0.001$ for height and at $p<0.05$ for extent of activation (both uncorrected).

In all comparisons of equivalent conditions between coloured and achromatic Mondrians (e.g. varying intensity colour vs. varying intensity achromatic) only very weak activity was found in the fusiform gyrus. Specifically, the posterior subdivision within it (V4) was active in the comparison of coloured versus achromatic Mondrians in the *varying intensity* conditions, and the comparison of achromatic versus coloured Mondrians in the *varying wavelength composition* conditions resulted in the same activity pattern. The comparison of colour vs. achromatic for the static conditions led to bilateral activity in both subdivisions of the colour selective region ($p<0.001$, uncorrected). Comparisons of the *varying wavelength composition* condition with the *varying intensity* condition led to activity in both subdivisions of the colour selective region only with the achromatic stimuli but not with their coloured counterparts ($p<0.001$, uncorrected).

Table 2. Colour selective regions identified in the fusiform gyrus. Tailarach coordinates and Z-scores from this and previous studies.

	POSTERIOR (V4)				ANTERIOR (V4α)			
	x	y	z	Z	x	y	z	Z
THIS STUDY (fMRI)								
Dynamic Mondrian (n=6)								
Left	-34	-68	-18	7.25	-28	-54	-18	5.39
Left	-22	-76	-16	6.97	-36	-56	-22	6.03
Right	34	-74	-14	6.9	28	-50	-16	7.18
Dynamic Scene (n=3)								
Right	32	-74	-14	4.34	34	-54	-22	5.14
Left	-28	-76	-16	4.84	-28	-56	-20	4.71
Topography (n=4)								
Chromatic-achromatic								
Right	28	-74	-12	5.63	30	-50	-20	5.36
Minimum extent, right	26	-66	-4	-	24	-44	-10	3.09
Maximum extent, right	38	-80	-24	-	36	-60	-24	3.09
Left	-32	-74	-16	5.39	-34	-54	-14	5.18
Minimum extent, left	-24	-66	-4	-	-26	-48	-10	3.09
Maximum extent, left	-36	-82	-22	-	-38	-62	-22	3.09
Superior field, right	20	-72	-10	8.46	30	-50	-20	3.54
Superior field, left	-22	-72	-12	7.31	-36	-54	-16	3.51
Inferior field, right	32	-76	-10	5.52	30	-50	-20	6.47
Inferior field, left	-30	-76	-8	8.13	-32	-54	-14	5.80
False Colours (n=9)								
Right	32	-74	-12	4.5	34	-56	-12	4.58
Left	-30	-64	-12	5.1	-30	-54	-10	4.24
Left	-28	-76	-16	4.84	-28	-56	-20	4.71
Attention (n=5)								
Right	34	-70	-16	7.63	34	-50	-20	6.85
Left	-30	-78	-12	7.01	-30	-48	-18	5.87
PREVIOUS STUDIES								
Lueck et al. 1989 (PET, n=3)								
Left					-27	-56	-5	-
Right					24	-58	-7	-
Zeki et al. 1991 (PET, n=6)								
Left	-26	-68	-8	-				
Right	20	-66	-4	-				
McKeefry et al. 1997 (fMRI)								
(fullfield: n=12, hemifields: n=6)								
Left full field	-26	-80	-14	7.99				
Left superior	-24	-76	-14	4.61				
Left inferior	-32	-76	-12	4.71				
Right full field	30	-78	-18	8.05				
Right superior	28	-72	-12	4.59				
Right inferior	38	-74	-20	4.71				
Hadjikhani et al. 1998	-	-65	-16	-				
(fMRI, N=13) "area V8"	+33							
Kastner et al. 1998 (fMRI, n=8)								
Left only	-19	-74	-14	-	-27	-59	-14	-
Beauchamp et al. 1999								
(fMRI 100 Hue test, n=12)								
Left	-22	-80	-10	-	-28	-58	-12	-
Right	30	-69	-9	-	-	-	-	

All data from this study were brought into Tailarach space and normalised using the EPI template provided in SPM98, which is similar to the average of 305 brains provided by the Montreal Neurological Institute. Note that although the activation extended posteriorly to include V4 in the study of Lueck et al. (1989), the hottest voxels were in V4α. *n*, number subjects involved.

1.2. Experiment 2 - Dynamic illumination of a meaningful scene

Previous results suggest that area V4 is more concerned with generating colours, regardless of whether they constitute the surface properties of objects or whether they are part of abstract compositions (Bartels & Zeki, 1998a). If this is so, then by using a natural scene viewed in an illuminant whose wavelength composition changes continuously, V4 alone should become active without entailing activity in the more anterior parts of the fusiform gyrus which are activated by naturally coloured scenes but not by coloured Mondrians; such an experiment also promised to tell us whether the anterior or posterior divisions of the colour selective region in the fusiform gyrus are more involved when colour is part of natural objects. In this condition the wavelength composition coming from each point changed, whereas its perceived colour remained constant. **Figure 10** shows a comparison of this dynamic condition with a static one, revealing that activity in the fusiform gyrus was restricted to both subdivisions of the colour selective regions, which were activated bilaterally. The posterior subdivision (V4) was significant at a corrected threshold of $p<0.05$ (group of 3); the activity in the anterior one appeared bilaterally at the uncorrected threshold of $p<0.001$. There was also activity lateral to left V4 and in the parietal cortex.

We thus conclude from the above two experiments that the ratio-taking operation does not involve the entire cortical pathway devoted to colour, but that it primarily involves the colour selective region in the fusiform gyrus, no matter whether the scene viewed is abstract or meaningful. Furthermore, it became apparent that the colour selective region in the fusiform gyrus contains at least two subdivisions, a posterior one (McKeefry & Zeki, 1997; Hadjikhani, et al., 1998) and one anterior to it, which has only recently been described (Zeki & Bartels, 1999a). This finding is confirmed by two reports that describe areas beyond V4 activated with different colour tasks (Kastner, DeWeerd, Desimone & Ungerleider, 1998; Beauchamp, Haxby, Jennings & DeYoe, 1999).

For reasons outlined in the discussion we group both subdivisions in the V4-complex and refer to the posterior subdivision as area V4 and to the anterior one as area V4α.

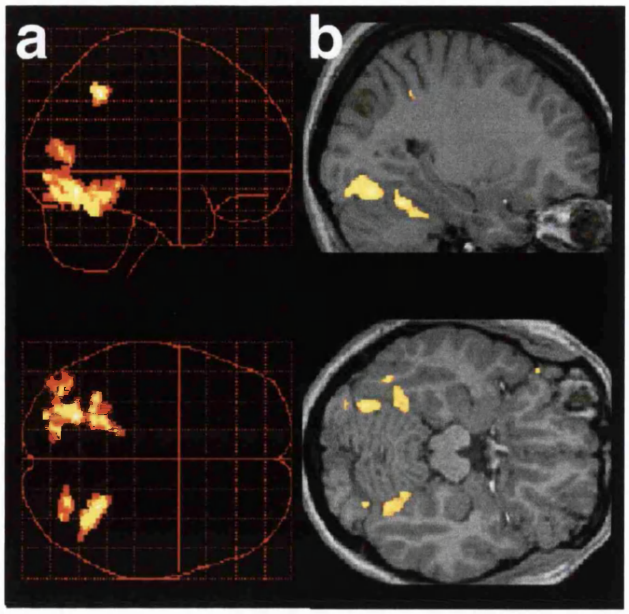

Figure 10. The V4-complex was activated when subjects maintained colour constancy while viewing a dynamically illuminated meaningful scene of vegetables. (**a**): The SPM of brain activity for the comparison of the *varying wavelength composition* mode vs. the *static* mode, viewed as a glass-brain, shows the two subdivisions of the V4-complex in much the same way as in the study using the (abstract) Mondrians (group of three subjects, $p<0.001$ uncorrected for height and $p<0.05$ corrected for the extent). (**b**): Sections through the SPM and the structural image of one of the subjects (same thresholding, slices taken at x: -28 and z: -17 mm).

1.3. Experiment 3 - The retinotopic organisation of V4 but not V4α

The novel finding in the present study (experiment 1) of an anterior and posterior subdivision within what we call the V4-complex and the clear separation between them encouraged us to re-analyse the results of McKeefry and Zeki (1997), using less spatial smoothing to enhance spatial resolution (see methods). The study of McKeefry and Zeki (1997), recently confirmed by Hadjikhani et al. (1998), has shown that, consistent with earlier clinical observations, there is a complete representation of the contralateral field in V4, with a retinotopic map in V4. First, a re-analysis allowed us to confirm the presence of two colour-selective subdivisions within the V4-complex (**Figures 11 a** and **b**) in this independent and rather different study ($p<0.05$; Z-score>5, corrected for multiple comparisons); second, it seemed interesting to learn whether the more anterior subdivision (V4α) also contained a representation of the complete contralateral hemifield and whether it was also mapped retinotopically. Comparisons of either superior or inferior field colour stimulation to their achromatic counterparts

revealed that both subdivisions had a representation of the contralateral hemifield ($p<0.001$; $Z>3.5$, uncorrected) that was colour selective, but only the posterior subdivision (V4) was retinotopically organised (**Figure 11 b**). V4α is therefore activated by stimulation of both upper and lower hemifields but does not show the topography that is characteristic of V4 (McKeefry & Zeki, 1997). However, stimulation of the inferior fields led to more activity in V4α than stimulation of the upper fields; a comparison of the superior colour vs. superior achromatic condition with its inferior counterpart did not result in an activation of V4α, while the reverse comparison did ($p<0.05$, corrected). Tailarach co-ordinates for the subdivisions and the retinotopy are given in **Table 2.** We conclude that the two subdivisions of the V4-complex can also be distinguished from one another by the presence of a distinct retinotopic representation in V4. If present, the retinotopic representation is less clear in V4α.

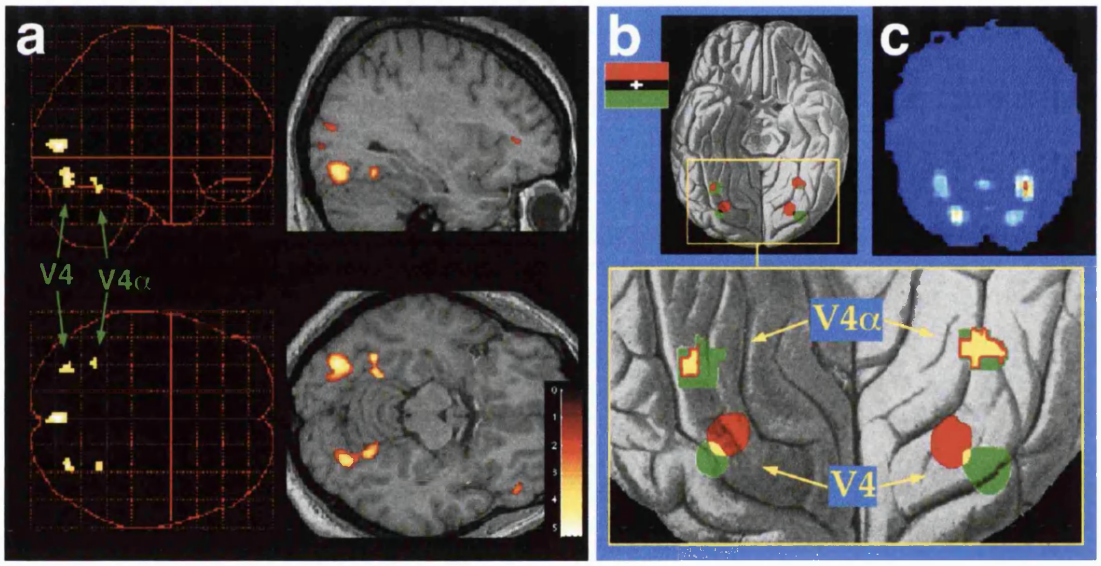

Figure 11. The segregation of the colour selective region in the fusiform gyrus (the V4-complex) into two areas, the posterior retinotopically organised area V4 and the anterior area V4α, as revealed by the re-analysis of the V4 mapping study (McKeefry & Zeki, 1997). (**a**) **Left:** Statistical parametric map (SPM) viewed in glass-brain projections of the comparison of all chromatic stimuli vs. their achromatic counterparts for both upper and lower visual field stimulation (group of four subjects; threshold: $Z>4.81$, $p<0.05$, corrected for multiple comparisons, equivalent to $p<0.000001$ uncorrected). **Right:** Slices taken through an SPM of a single subject, superimposed on its structural image (slices at x: -33 and z: -14 mm). (**b**) Projection of the comparison of either upper field (in red) or lower field (in green) stimulation with colour vs. their achromatic counterparts onto a ventral view of a human brain (overlapping regions are shown in yellow). For V4 (bottom), the SPM of the following comparison is projected onto the drawing: (superior coloured vs. [superior achromatic + inferior coloured + inferior achromatic]); (group of four subjects; threshold: $Z=4.81$, $p<0.05$ corrected). For V4α (top), SPMs of a comparison of colour vs. achromatic stimuli within the corresponding hemifield is projected onto the drawing (threshold: $Z=3.09$, $p<0.001$ uncorrected). (**c**) An independent component analysis (ICA) separates spatially independent maps of brain activity without *a priori* knowledge about the stimulus conditions. ICA isolated the complete V4-complex, including the posterior (V4, bottom) and the anterior (V4α) subdivisions in both hemispheres, shown here in the glass-brain view of a single subjects' brain.

We add that both subdivisions were subsumed into one area in earlier publications from this laboratory and probably in the publications of others.

This study could be turned into a study on the retinotopy of visual areas not specifically related to colours by simply comparing upper vs. lower field stimulation and vice versa. By doing so we found significant activity in areas V1, V2, V3 and V4 and V4α but were unable to find any independent activity in the region of 'V4v', reported by Sereno *et al.* (1995) and Hadjikhani *et al.* (1998) to lie posterior to V4 on the fusiform gyrus and to represent upper fields only ($p<0.001$, uncorrected). In this, our finding is consistent with the similar recent results of Kastner *et al.* (1998).

1.4. The co-operative activity of the two subdivisions within the fusiform gyrus: ICA analysis

The two subdivisions of the V4-complex were evident in all single comparisons of dynamic conditions with their static counterparts, whether achromatic or coloured, but often in conjunction with other areas lateral to the fusiform gyrus, in the temporal and in the prefrontal cortices. If it is true that the V4-complex constitutes a functional unit of closely interacting areas, it would be interesting to learn whether the V4-complex can be isolated from all other brain activity on the basis of its activity patterns throughout the experiments. An independent component analysis (ICA) seems the method of choice to isolate spatially independent areas of functional activity, since it can isolate independent maps of brain activation without *a priori* knowledge about the stimulation. We submitted data from both the dynamic Mondrian and the V4 mapping study (in total 10 subjects) to an ICA (Bell & Sejnowski, 1995). Since the application of ICA to fMRI data has some limitations (Friston, 1998) (see Methods) it was gratifying that it isolated, in 6 out of 10 subjects, areas amongst which V4 and V4α were the only ones in ventral occipital cortex that occurred bilaterally as pairs, suggesting that they can function as a closely interacting unit in colour processing (**Figure 11 c**).

1.5. Experiment 4 - Segregation of V4 and V4α with falsely and correctly coloured objects

In all the other experiments described here (1,2,3 and 5) we observed the presence of at least two separate and colour selective areas in the fusiform gyrus. We did not find any stimulation paradigm that would activate preferentially one subdivision, even though the posterior part (V4) seemed always more active than the anterior one (V4α). The existence of the two subdivisions and the difference in retinotopic organisation between the two subdivisions encouraged us to re-analyse other earlier results with a view to learning whether the two subdivisions also differ in their functional specialisation. One earlier study (Zeki & Marini, 1998) had compared, in nine subjects, the brain activity produced by naturally and un-naturally coloured scenes of fruits and vegetables with that produced by their equiluminant achromatic counterparts. Our re-analysis showed that the naturally coloured scenes activated the anterior part of the V4-complex (V4α) much more powerfully than the posterior one (V4), plus other areas situated even more anteriorly in the fusiform gyrus (**Figure 12 b**), while the un-naturally coloured scenes activated both V4 and V4α equally, as did all the other experiments described here (**Figure 12 a**). The region of overlap between the two experiments is therefore restricted to V4α alone (**Figure 12 c**).

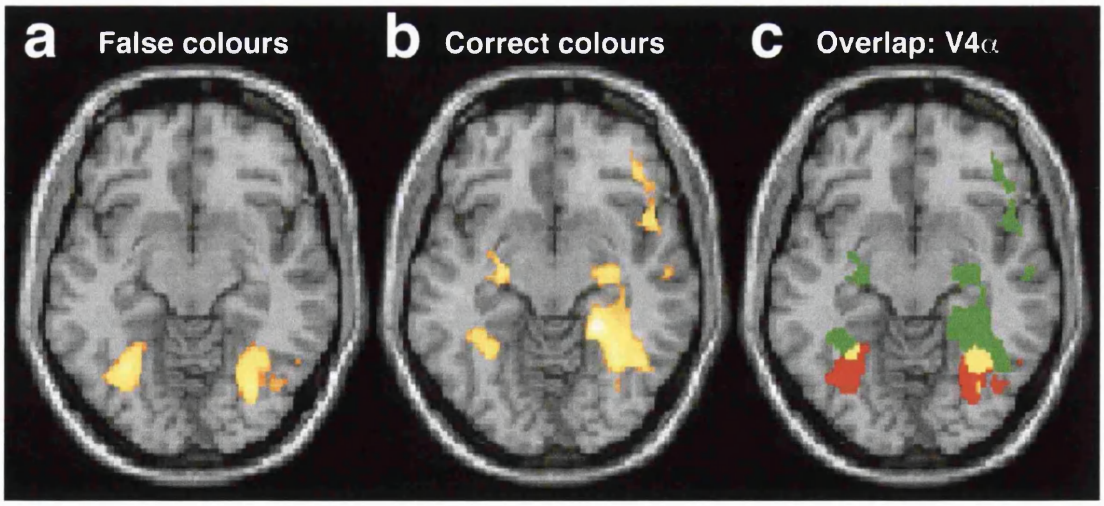

Figure 12. Functional segregation of the posterior (V4) and anterior (V4α) areas within the V4-complex. (**a**): Activity revealed by the comparison of false-coloured scenes vs. their black and white counterparts activated the complete V4-complex (both V4 and V4α) in the fusiform region, but did not involve more anterior areas. (**b**): Correctly-coloured scenes vs. their black and white counterparts led to activity of V4α and more anterior areas, whereas the weak activity in V4 is shown by a streak in (b) and (c). (**c**): Superposition of the contrasts described in (a) (red) and b (green) reveals a functional segregation between V4 and V4α (overlapping regions are shown in yellow and coincide with V4α). All slices were taken at z: -10 mm, and SPMs were thresholded at $p<0.001$, uncorrected.

These results, using the comparisons [naturally coloured scenes vs. achromatic versions] and [un-naturally coloured scenes vs. achromatic versions], not only highlighted the entire V4-complex, but also showed that V4 and V4α are functionally segregated; V4α can be co-active with the posteriorly lying V4 alone or with areas lying directly anterior or lateral to it that are known to be implicated in object and face perception (Haxby, Horwitz, Ungerleider, Maisog, et al., 1994; Kanwisher, McDermott & Chun, 1997; Orban, Dupont, Vogels, Bormans & Mortelmans, 1997; Rosier, Cornette, Dupont, Bormans, et al., 1997).

1.6. Experiment 5 - Attention to colour co-activated V4 and V4α and modulated V4 retinotopically

We were curious to learn whether the two colour selective subdivisions in the fusiform gyrus would also be activated by attentional modulation alone and whether that would be retinotopically organised. Previous studies (Corbetta, et al., 1991) had shown an activation of the fusiform gyrus with selective attention to colour. By asking five subjects not only to pay attention to different locations in their visual field while fixating a central cross, but also to attend to either colour or to motion within these locations, we were able to confirm that there are areas that are specifically modulated by attention to colour, and to discern whether attention modulated them in a retinotopic fashion.

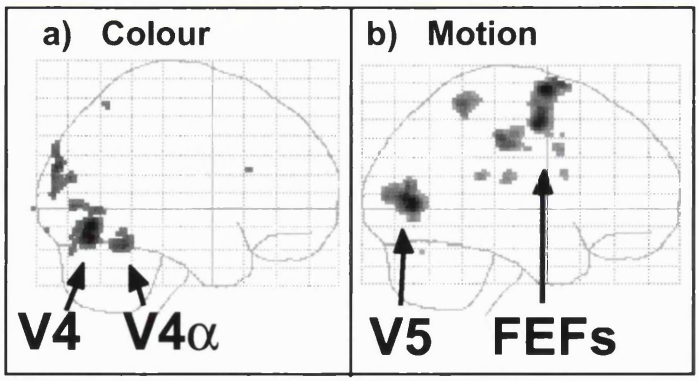

Figure 13. Selective attention to colour or to motion activated the areas specialised for processing these attributes: the V4-complex and area V5 While all four quadrants of the visual field were stimulated with both motion and colour simultaneously, subjects fixated the centre and paid attention either to colour or to motion within one quadrant at a time. Displayed are the comparisons of **(a)** attention to colour in quadrants of the left hemifield vs. attention to motion in all four quadrants and **(b)** attention to motion in quadrants of the left hemifield vs. attention to colour in all four quadrants. Glass-brain projections are SPMs thresholded at $p<0.05$, corrected for multiple comparisons, group of five subjects.

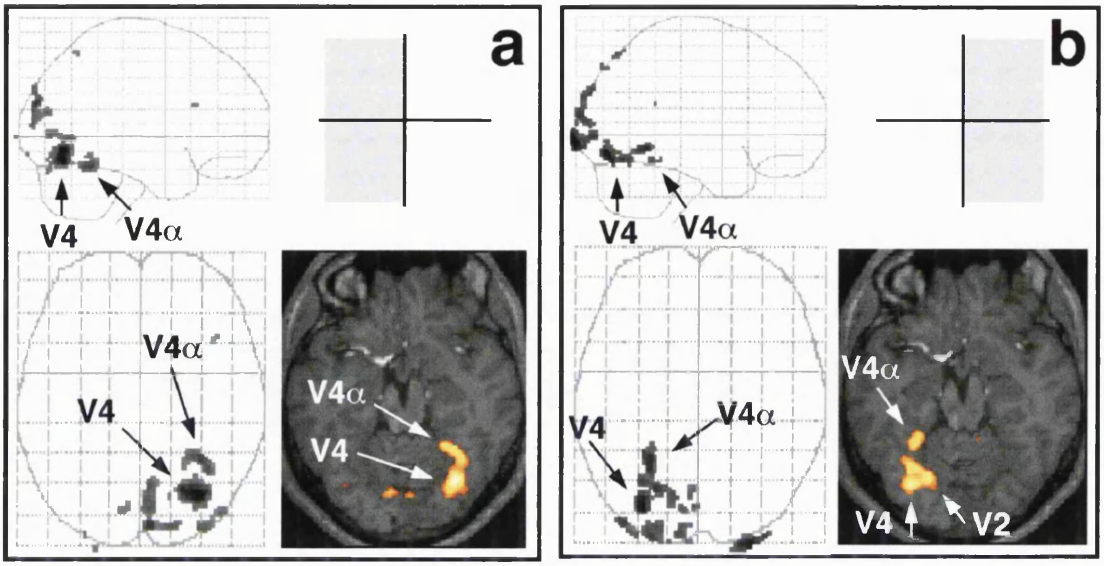

Figure 14. Selective attention to colour activated both subdivisions of the V4-complex, V4 and V4α. While all four quadrants of the visual field were stimulated identically, subjects paid attention to colour within one quadrant at a time while fixating the centre. Displayed are the comparisons of **(a)** attention to colour in quadrants of the left hemifield vs. attention to motion in all four quadrants and **(b)** attention to colour in quadrants of the right hemifield vs. attention to motion in all four quadrants. Glass-brain projections are SPMs thresholded at $p<0.05$, corrected for multiple comparisons, group of five subjects; Slices were taken at z: -18 mm from the same SPMs at $p<0.001$, uncorrected, superimposed on a representative structural scan.

Here we will concentrate mainly on results related to colour. But just to demonstrate how modality specific the effects of attention to a certain attribute are, we contrast in **figure 13** the effects of attention to colour with those to motion. We found that selective attention to colour led in all respects to the same activity patterns in the visual cortex as observed in the experiments described above, while attention to motion does not affect the V4-complex but area V5, along with the parietal cortex and the frontal eye fields.

Figures 14 a and **b** show glass-brain projections and slices for the comparison that displays the two subdivisions, V4 and V4α, best (attention to colour in one hemifield vs. attention to motion in both hemifields) for $p<0.05$, corrected for multiple comparisons. The hottest voxels in both hemispheres were in contralateral V4 and V4α, whose co-ordinates are given in **Table 2**. Activation was also present in contralateral V2, V3 and the calcarine cortex. The ipsilateral activation mainly visible in the occipital pole of the right hemisphere (**Figure 14 b**) is unrelated to attention to colour but is due to inhibition of both occipital poles in tasks involving attention to motion. This became evident in comparisons of the control condition vs. attention to motion, carried out separately for each quadrant.

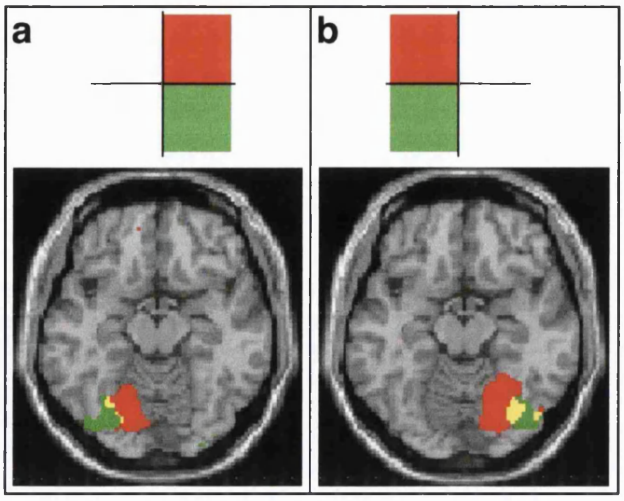

Figure 15. Attentional modulation of V4 was retinotopic when subjects paid attention to quadrants in the upper and lower hemifields. Horizontal slices were taken through SPMs at z = -14 mm for the contrasts [attention to both colour and motion in one quadrant vs. attention to both attributes in the remaining three quadrants] (5 subjects, $p<0.001$, uncorrected; red: top quadrant, green: bottom quadrant) for quadrants within the right (a) or left (b) hemifields. Note the distinctly topographic organisation of the activity produced, which respects the topography of V4 as determined in previous studies (McKeefry & Zeki, 1997) and as shown in **Figure 11b**. The medial part of the black patches include area V2 which, at this ventral level, represents the upper quadrant.

The retinotopic modulation within V4 became apparent by comparisons involving attention to quadrants in upper or lower parts of the visual field; activity evoked by attention to quadrants in the upper visual field was restricted to the more medial part of V4, whereas attention to quadrants in the lower visual field activated the more lateral part of V4, as is shown in **Figure 15** for both hemispheres separately. We used the comparison involving attention to both attributes in this figure since it makes the retinotopic organisation of V4 more clear, but this was also apparent for the corresponding comparison, involving attention to colour alone.

In sum, these results suggest that attention to colours (which are not attached to meaningful scenes) modulates activity of both subdivisions of the V4-complex, V4 and V4α, in the same way as the viewing of colour does, and they also reveal that attention modulates V4 in a retinotopic fashion. This should not come as a great surprise, since so far most imaging studies essentially show a close correlation between subjective experience and specific cortical activity; in this case attention enhances the percept of colours, just as external stimulation with colour would do.

2. The computational dissection of the human brain

The previous section demonstrated that the human V4-complex can be selectively activated by appropriate stimulation, making it possible to isolate it with a parametric statistical analysis. It also showed that an independent components analysis was able to isolate the V4-complex from the rest of the brain. Both methods showed that the V4-complex can be activated selectively, and that both its components, V4 and V4α, are highly related in their activity, which is why they were isolated together in both approaches. This section serves to illustrate in more detail the method, power and implications of applying ICA to fMRI data. By generalising the results obtained for the V4-complex, it tries to show that any specialised area in the cortex can be isolated based on its unique activity time course, highlighting the dramatic modularity of the human brain.

2.1. Why it should not work

In the colour experiments reported above, which used a very customised stimulation paradigm, it was possible to differentially activate the V4-complex in such a way that it had a time course of activation that differed from that of all remaining regions in the brain. It seems rather daring to propose that the V4-complex might have a unique activity time course in uncontrolled, natural viewing conditions, i.e. that the customised stimulus was not really necessary to activate it differentially, and that this can be exploited to segregate the V4-complex from the rest of the brain.

It is daring for several reasons: first, without a tailor-made stimulus other areas might be equally activated as the V4-complex, making it impossible to distinguish them. Second, the temporal resolution of fMRI is in the range of seconds, while neural

processing happens several orders of magnitudes faster. This is for example reflected in the latency difference of 80ms between the perception of colour and the direction of motion, implying that the processes in the colour and the motion systems reach perceptual end-points at different times. So, even if the V4-complex was activated in a unique way, fMRI might just not have the temporal resolution to distinguish it from other regions when the stimuli change rapidly. Third, even if the V4-complex is activated in a unique way with another, maybe much more complex, stimulus we do not have a method to segregate it from the rest of the brain, unless we can precisely predict its expected activity time course in order to use statistical methods to then isolate it.

However, if this proposition should be true, and the time course of activity in the colour centre is different from that of all other regions in the brain, there is no reason to believe that this should not be true for any other specialised area in the brain. And if this is true, this property of functionally specialised areas could then be exploited to identify yet uncharted functional subdivision of the brain. Given this theoretical possibility, it was worth taking the risk. It therefore seemed worthwhile trying to find out whether the method of ICA is able to isolate not only the colour centre from ongoing brain activity as measured using fMRI, but any other functionally specialised area. Further, it seemed interesting to try this out not only for data obtained using stimuli optimised for fMRI analysis, but also using stimuli that are more natural. If successful, then this would give further evidence for the supposition made here, namely that these different areas are autonomous, not only spatially but also temporally.

To illustrate this attempt, data from two studies are presented: the first (study 1) is a classical fMRI study in which subjects were stimulated by alternating blocks of five types of visual stimuli (see methods). Because this data set is well controlled, i.e. both the exact timing of brain data and of the visual stimulation are known, it lends itself to both ICA and statistical parametric mapping (SPM). This data set is used here to demonstrate that ICA does analyse fMRI data in a meaningful and reliable way, using absolutely no a priori knowledge, which is verified in this case using standard statistical tools, that use a priori knowledge. It is shown that the functionally specialised regions identified using SPM are the same that ICA segregates, proving that ICA can isolate functionally specialised areas. The second data set (study 2) is the more interesting one, because it shows that ICA can even isolate these same brain regions and many more when the brain is stimulated more naturally with a movie and in free viewing conditions. This cannot be analysed using SPM, and makes the strengths of ICA apparent. But much more important is that it shows that the unique activity time course different cortical areas have can still be observed at the slow time resolution fMRI data offer.

2.2. Study 1 - Recognition of objects derived from motion

2.2.1. Task dependence: ICA and SPM

ICA was performed on the complete fMRI time series for each of the four subjects separately, and for each very similar components were isolated.

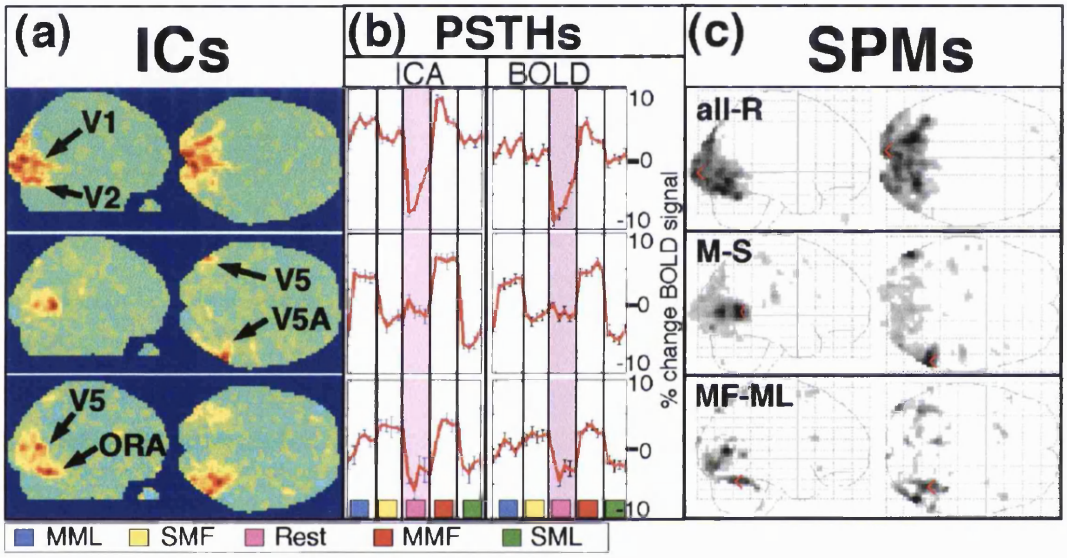

Figure 16. Independent components (ICs) and statistical parametric maps (SPMs) reveal the same functionally specialised areas, which are differentially involved in different tasks. All data are from subject AB. **(a)** The three ICs whose time courses were most correlated to the different task conditions. Each IC contains separate functionally specialised areas or groups of areas that were highly coactive (V1 with V2, V5 with V5A, V5 with ORA). **(b)** Peristimulus time histograms (PSTHs) of the time course associated to the ICs (left, arbitrary y-scale) and those of BOLD signals of the hottest voxel of the IC, which is also indicated on the right (c) with a red arrow (right, y-scale: percentage of change in the BOLD signal). The five stimulus conditions are indicated at the bottom using a colour code (see below). Each condition lasted 30s and was repeated six times in a fixed sequence, with scans acquired every 6s. Error bars: ± standard error. **(c)** SPMs of following contrasts between different types of visual stimuli (thresholded at $p<0.001$, uncorrected): top: all vs. Rest [MMF+MML+SMF+SML vs. Rest]; middle: motion vs. stationary [MMF+MML vs. SMF+SML]; bottom: meaningful vs. meaningless [MMF+SMF vs. MML+SML]. MMF=motion meaningful; MML=motion meaningless; SMF=stationary meaningful, SML=stationary meaningless, Rest=black screen.

Figure 16a shows the three components containing visual areas of subject AB: The first contains areas V1+V2, the second V5+V5A, and the third V5+ORA (the object recognition area, which is part of the larger area LO (Malach, Reppas, Benson, Kwong, et al., 1995), to which we refer here to with the term indicating its function:

ORA). If these three components contain brain regions that are differentially involved in processing the different visual stimuli, the same brain regions should become apparent in a classical statistical analysis using parametric mapping (SPM). This is exactly what we found (**figure 16c**): the three contrasts [all vs. Rest], [Motion vs. Static] (=[MMF+MML vs. SMF+SML]) and [Meaningful vs. Meaningless] = ([MMF+SMF vs. MML+SML]) obtained with SPM reveal three brain maps that precisely coincide with those isolated by ICA without a priori knowledge. V1 and V2 are active in all conditions except for the Rest condition, V5 (l) and V5A (r) are active in all motion conditions, no matter whether they contain recognisable objects or not, while V5 (r) and ORA are active in all conditions containing recognisable objects, no matter whether associated with motion or not. ICA recognised these relationships without any knowledge of brain organisation, the type of the data or the different visual stimuli and their time courses, while the analysis with SPM required knowledge of the inter-scan-interval and the duration and the type (1 to 5) of the visual stimuli applied. Even more informative than the statistical maps is a look at the time courses associated with the three ICA components (**figure 16b**). These indicate how active the components were at any given time throughout the scan, and are shown in figure 16b in the form of peri stimulus time histograms (PSTHs), which are the time courses averaged over the six repetitions of each stimulus condition. For example, V1+V2 were basically always equally active (with a little peak in the MMF condition), and completely inactive during the Rest condition. These ICA time courses correspond precisely to the time courses of the actual BOLD signal taken from the hottest voxel of the corresponding ICA component (see also the correlation coefficients shown in figure 17).

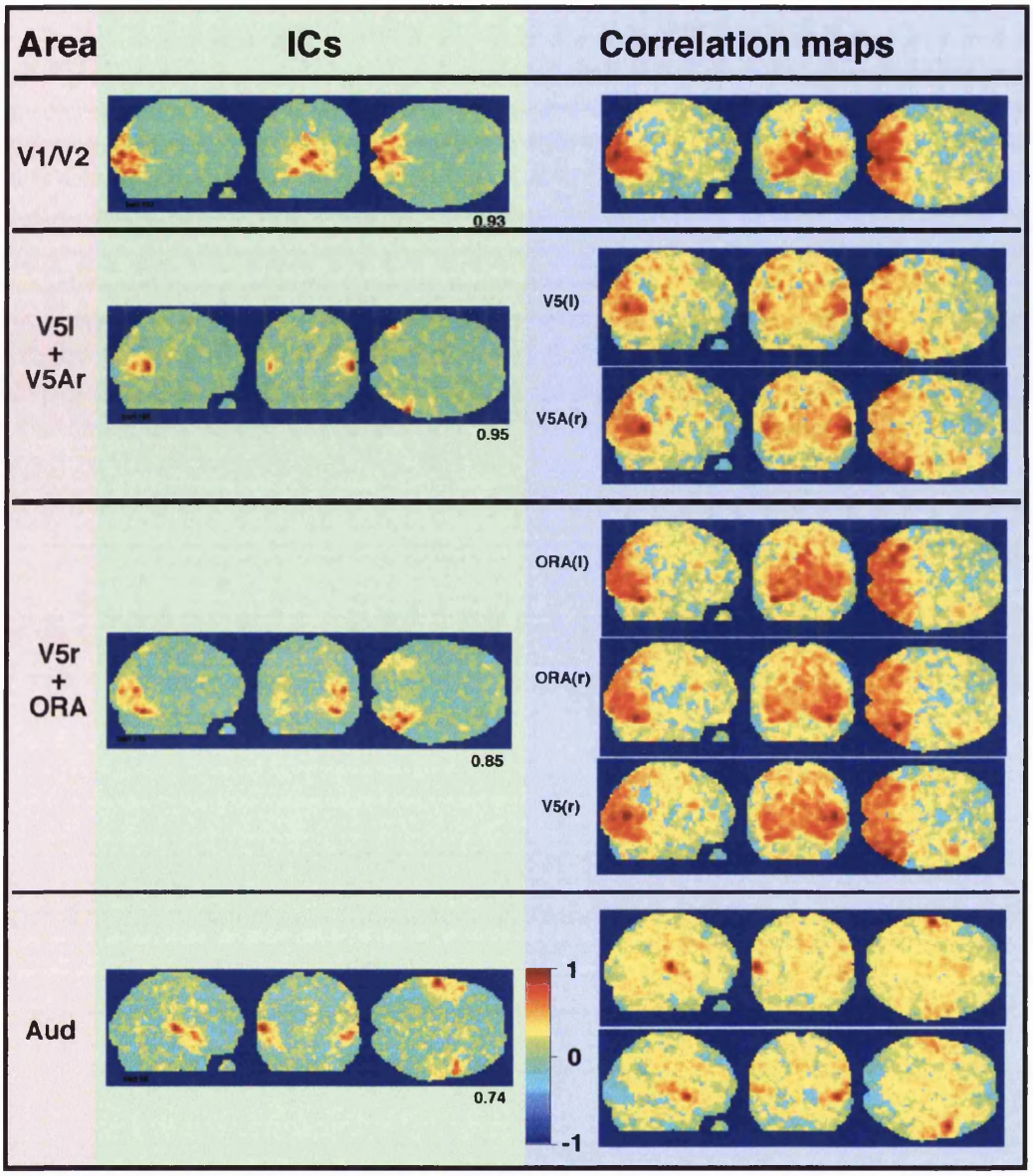

Figure 17. Independent components (ICs) and correlation maps (CMs). CMs show how well the time courses of BOLD signals of all voxels in the brain correlate with that of the hottest voxel of a hot-spot in an IC (shown as glass brain views). **Left:** ICs. ICA isolated functionally specialised areas or groups of areas in separate ICs, no matter whether these areas were involved in the task (in this case object recognition from motion: visual areas, first three ICs) or not (e.g. auditory and language areas(Binder, Frost, Hammeke, Bellgowan, et al., 2000), fourth IC). **Right:** CMs. The similarity of the ICs with the CMs reveals that the hot-spots within a single IC consist of voxels whose BOLD signal time courses are highly correlated, and that only rarely are voxels excluded from that IC whose time courses are highly correlated to those of the IC's hot-spot. The time course associated to an IC correlates highly with that of the BOLD signal of its hottest voxel: correlation coefficients between IC-time course and BOLD signal of its hottest voxel is given below to each IC. For each IC, separate CMs were calculated for each hot-spot this IC contains, using the corresponding hot-spots' hottest voxel as a seed. We refer to the 'seed' voxel as to the voxel whose BOLD signal time course is used for the correlation with those of all the remaining voxels to create a CM. The seed voxel for the first CM was the hottest voxel of the first IC, located in left V1. The seed voxels for the CMs for the remaining ICs were taken from the hottest voxels in the IC of the area indicated on the left of the CM; in the case of bilateral areas in a single IC, the top CM has the seed from the hottest voxel in the left hemisphere and the bottom CM that from the right hemisphere. ICs and CMs are shown using the same colour map, shown in the middle at the bottom of the figure. Data are from same subject (AB) as those in figure 16.

2.2.2. Correlation maps

ICA is used here as spatial ICA, which optimises independence of the isolated components in space, while it does not apply the constraint of independence to the time courses associated with each isolated component. The constraint of spatial independence (e.g. that areas do no overlap in space) is physiologically plausible - separate cortical areas will occupy different spatial locations. It is less straightforward to explain how ICA exploits the relationships of the time courses of the different voxels for the separation process, which clearly plays a crucial role for it: Out of the thousands of possibilities of dissecting the cortex into spatially independent components (e.g. into areas that do not overlap), ICA dissects out functionally specialised areas, which consist of voxels whose time courses have a high temporal correlation and whose time course differ substantially from each other.

The question that arises is the following: what do voxels that ICA grouped together as being independent of the others *in space*, have common *in time*?

The most simple relationship in time is that of linear dependence or correlation: In other words, the degree to which voxel A's time course can be explained by the one of voxel B, in the form of

$$\text{timecourse (A)} = \text{timecourse (B)} * N + K. \qquad \{1\}$$

(with N and K being any real number).

A more complex relationship between A and B's time courses could be e.g.

$$\text{timecourse (A)} = \text{timecourse (B)}^{N}. \qquad \{2\}$$

or the like, in which case they would still depend on each other, but a linear correlation would no longer detect this.

A simple way of finding out whether the voxels of hot-spots of a single spatial IC have in common that their time courses are linearly correlated is by calculating whole brain correlation maps (CMs) of BOLD signals to hot spots within a single IC (**figures 17 and 21**): a map of correlation-coefficients of the BOLD signal time course of every voxel in the whole brain to the BOLD signal time course of a voxel in a 'hot-spot' of an IC (we refer to the latter voxel as to the 'seed' voxel). CMs can be calculated for seed voxels in each hot-spot of a given IC, so that it becomes apparent if there are any two hot-spots in the same IC whose voxels are not correlated, or if there are voxels

that are highly correlated with those in an IC's hot-spot, but that do not form a hot-spot in that IC. For example, if the voxels from left V5 and right V5A, which are combined in a single IC (second IC in figure 16), have highly correlated time courses, then a CM to a seed voxel in left V5 should show a peak region in right V5A, and vice versa. This would indicate that the brain regions concerned have correlated activity time courses, and that ICA exploits this to group voxels together (scenario 1).

Correlation maps also answer two additional questions: are there peaks in CMs that are excluded in the corresponding IC? This would mean that ICA does not necessarily group all highly correlated voxels into a single IC (scenario 2). And: are there hot-spots in the ICs that do not show up in the correlation maps? This would mean that the brain regions concerned have a more complex, non-linear relationship in time (e.g. the one shown in equation {2}), and that ICA exploits this to group voxels into a single IC (scenario 3).

For most of the ICs, scenario 1 is true: ICA groups voxels together whose BOLD signal have a high correlation. There are some ICs displaying scenario 2, but only in a weak form: Some voxels that are highly correlated with other voxels displayed as hot spots in an IC are not included in that IC (see e.g. the lack of left ORA in the IC containing V5 in figure 21 and the correlogram in figure 22: right ORA is included in this IC, and correlates highly with the omitted left ORA. This is only a weak form of scenario 2, since the omitted voxels do only correlate well with one of the at least three hot spots present in this IC). A simple explanation is that of spatial independence, which is an important limitation of ICA: Once ICA has assigned a group of voxels (e.g. left ORA) to one IC, it cannot assign it to another IC anymore, because of its constraint to produce spatially independent ICs. Both ICs might have other voxels highly correlated with left ORA, but only one can take it up, e.g. the one with the highest mutual correlation coefficients with it and another hot-spot. If the same set of voxels were included in both ICs, the criterion of spatial independence would be violated, which has a high cost in ICA's optimisation procedure. Two variations can be observed in this context: First, sometimes several ICs get the same voxels, just with very decreased intensity (yellow voxels) (see figure 21: ICs containing KO and ORA: both have a weak left ORA; figure 17: ICs containing V1/V2 and right V5: both contain traces of left ORA). Secondly it can be observed that ICA splits up a single area (e.g. ORA) into several sub-components, because some voxels correlate more with area V5, others more with KO, and a third group forms its own IC (see ICs containing ORA in figure 21).

This is a finding of enormous importance on its own: If it can be shown that a single functionally specialised area, such as ORA, has distinct paths of communication with separate specialised areas, several important questions and consequences would follow: First, it might provide an answer to the question whether an area such as ORA can selectively send its output or receive input to/from just one other area, as opposed to send/receive signals indiscriminately from other areas. Secondly, one might consider the notion that ORA might actually be a composite of several areas that have all the same function, namely object recognition, but that each performs this task only for input of a single visual modality, such as motion (provided by V5) or edges from motion (provided by KO). We intend to investigate ORA's subdivisions and their distinct relationships with surrounding visual areas in the future. Here, we put the emphasis on giving an overview of the application of ICA on fMRI data, and merely mention this important finding briefly to highlight the wealth of neurophysiological facts brought to light by this new approach to imaging data.

Scenario 3 was not observed: voxels were never part of an IC hot-spot without being highly correlated with at least some of the other voxels in the same IC.

2.2.3. Correlograms

Once different cortical areas have been identified, it is possible to ask questions about their mutual relationship in time: Which areas have the most correlated activity time courses? Are there non-linear relationships between different areas? To which degree is one area influencing another? Can the direction of information transfer across the areas be identified? Can excitatory, inhibitory or modulatory connections be differentiated? In addition it will be important to relate all this information, which is entirely derived from the time course of activity, to the wealth of anatomical information we have about these areas and their mutual connections: Are strong anatomical connections necessarily associated with a strong dependence of activity in time? To which degree can the strength of such a mutual dependence in time be modulated in time? And, last but not least, can these relationships in time help us to detect unknown anatomical connections?

The investigation of these questions alone will provide plenty of material for future work. We put therefore the emphasis on answering just the first question, by displaying the linear dependence of all the visual areas that were identified by ICA in a correlogram (**figure 18 and table 3**); this shows graphically the correlation coefficients of BOLD signals between the hottest voxel of each pair of all areas. This very simple approach already reveals a wealth of information: e.g. it shows that left V5 has an

extremely high correlation with right V5A, while its correlation with right V5 is comparably small. V1 has its strongest correlation with the ipsilateral ORA (the BOLD signal from V1 was taken from its hottest voxel, located in the left hemisphere). It is also interesting to note that only right V5 entertains a high correlation with both left and right ORA, while neither left V5 nor right V5A have much in common with the ORAs.

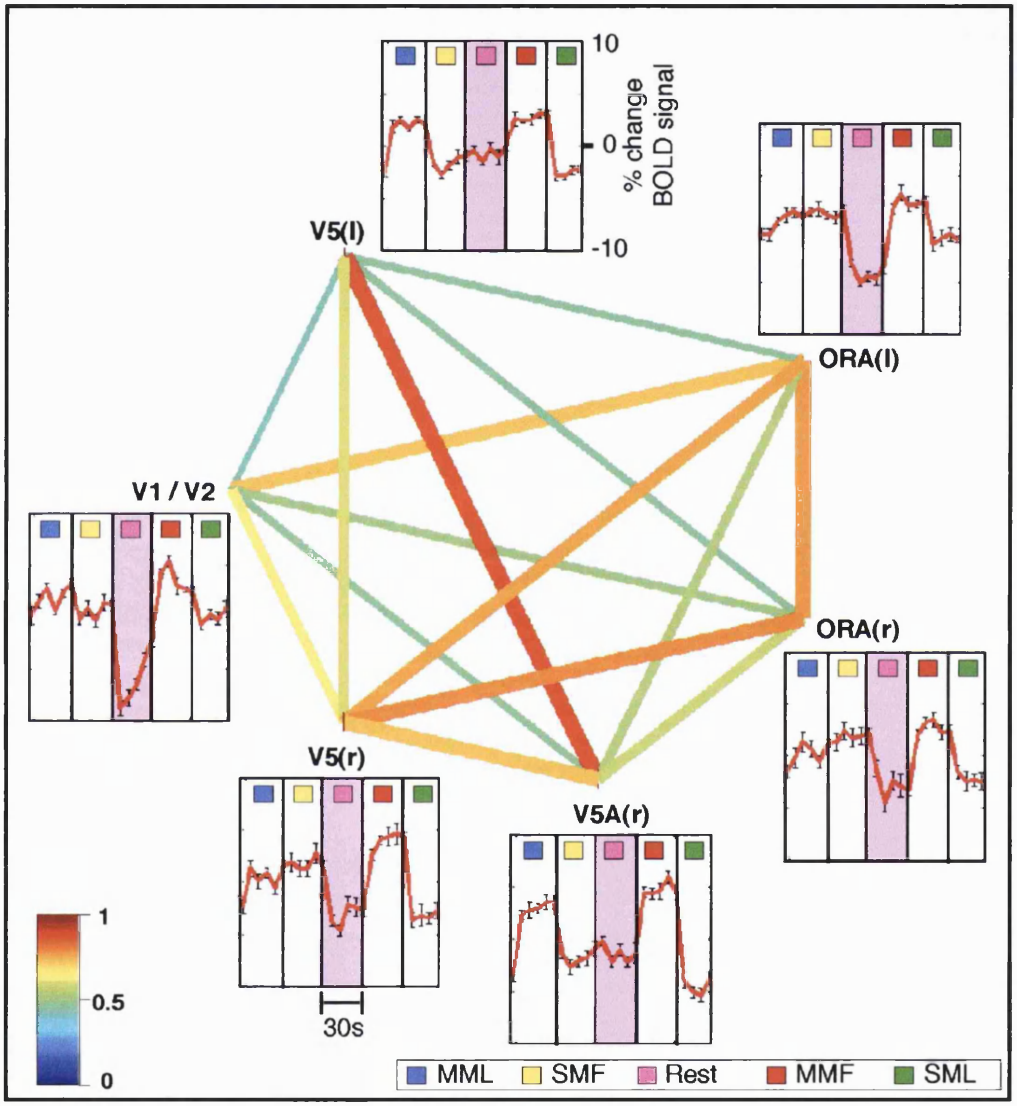

Figure 18. Correlogram of the time courses of the visual areas isolated by ICA. Plotted are the correlation coefficients (r) between BOLD signal time courses taken from the hottest voxel of each area isolated by ICA (r is visualised by a proportional line width and by colour). Insets are PSTHs of the BOLD signal, indicating the percentage in BOLD signal change, with error bars indicating the standard error (for a key of the stimulus conditions, see figure 16). Note that those areas with the highest correlation coefficients were grouped by ICA into single components (see figure 17; V5(l) with V5A(r), and bilateral ORA with V5(r)). Data are from subject AB.

Table 3. Correlation coefficients (r) of six visual areas in the object-from-motion experiment (subject AB).

Area	V1 / V2	V5 l	V5 r	V5A r	ORA l	ORA r
V1/V2	1.00	0.42	0.62	0.47	0.72	0.51
V5 l	0.42	1.00	0.60	0.85	0.46	0.46
V5 r	0.62	0.60	1.00	0.72	0.76	0.78
V5A r	0.47	0.85	0.72	1.00	0.54	0.58
ORA l	0.72	0.46	0.76	0.54	1.00	0.77
ORA r	0.51	0.46	0.78	0.58	0.77	1.00

2.2.4. Consistency and reproducibility across subjects

Four subjects were analysed for study 1. To illustrate how reproducible and consistent the results are, the two ICs containing V1 and V5 are shown for all four subjects in **figure 19** along with the peri-stimulus time histograms (PSTHs) of the associated time courses. There are some minor individual differences, e.g. in the extent to which V2 or V3 were included in the component containing V1, or whether V5A was included in the component containing V5. Much more striking however is the degree to which the time courses are consistent, for both V1 and V5: they are almost indistinguishable across subjects. This is important for two reasons: first, because it shows how similarly different brains react to the same visual stimuli, and second because it demonstrates that ICA performs its tasks in a very reliable and consistent way on different data sets. A third point is important to note with regards to the analysis of imaging data using parametric statistics, such as SPM: While the time courses of both V1 and V5 are highly similar across different subjects, the time courses differ substantially across the different areas (here V1 and V5), not only in their amplitude in different conditions, but also in their wave form within a given condition. The latter fact forms a major limitation for any parametric model that assumes that every voxel in the brain has an identical stimulus response wave form, which differs only in amplitude. Parametric mapping methods have been developed to accommodate these different dynamics(Friston, et al., 1995a), and should be used whenever possible. Most studies still analyse fMRI time series using the standard box-car response function, which allows an easier comparison between different conditions (because only one a priori defined regressor per condition is used for the comparisons, rather than a whole set of regressors per condition), but does so at the cost of reduced Z-scores.

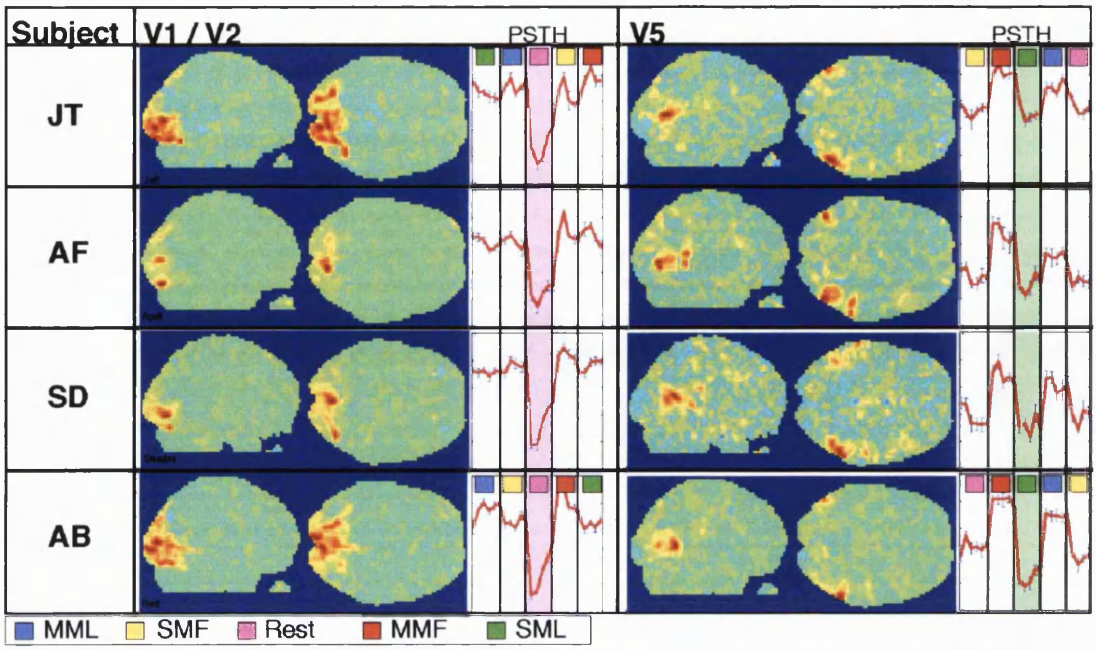

Figure 19. Consistency of activity and ICA performance across subjects. For each of the four subjects (JT, AF, SD, AB) the two ICs containing V1 and V5 are displayed, along with their PSTHs. Both the spatial extent and the time courses associated with each are extremely reliable across subjects, showing that the activity in these areas was very similar across subjects, and that ICA performed its segregation of functionally specialised areas in a highly reproducible and reliable way. Note that not only does the task related activity differ between V1 and V5, but their dynamics within a given condition as well: e.g. in the rest condition, the BOLD signal in V1 shows a steep rebound after about 15s, whereas that of V5 remains low throughout the period. The experiments were identical for all four subjects, except for a different sequence of the five stimulus conditions for subject AB. See figure 16 for a key of the stimulus abbreviations.

2.2.5. The chronoarchitecture of the cerebral cortex

To visualise the degree of activity that several areas have at a given time, the areas isolated in various ICs are superimposed into a single image and colour coded according to their activity. We term this type of mapping, in which the brain is dissected and mapped entirely on the basis of activity time courses "chronoarchitectonic mapping" (see introduction and discussion). **Figure 20** shows four ICs along with their time courses, the three visual ones of which are task related (V1/2, V5 and ORA), while the fourth is not (auditory and language areas). Five chronoarchitectures are shown, each of which taken when the subject was viewing one of the five types of stimuli displayed.

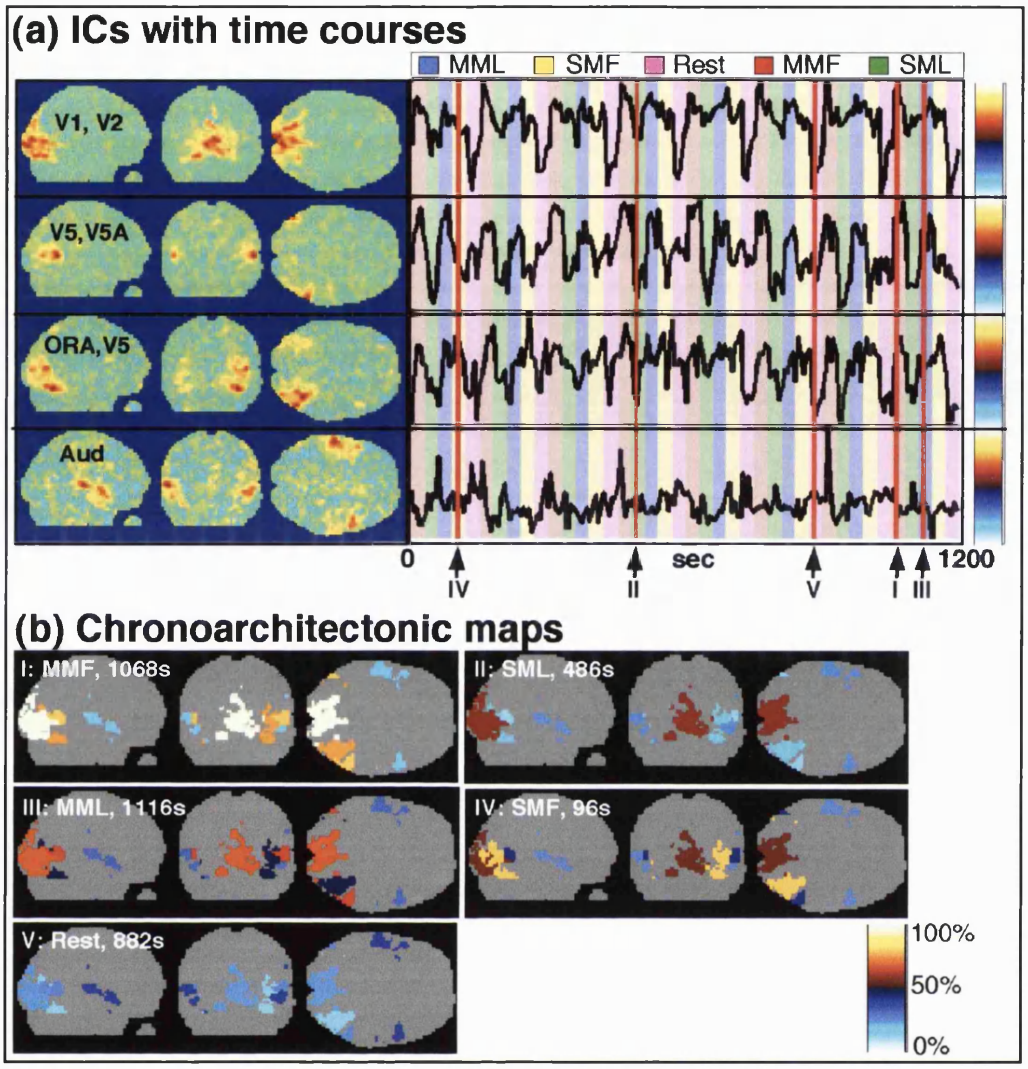

Figure 20. ICs, their time courses and *chronoarchitectonic maps*. (**a**) ICs (left) of the visual areas and one non-visual area are displayed, along with the time courses associated to each IC (right), which have arbitrary units. The colour of the background of the time courses corresponds to the five different stimulation conditions, each lasting 30s (see figure 16 for a key of the stimulus abbreviations). The colour bar to the right of each time course was used to colour code the corresponding thresholded IC according to its activity at a given time for the chronoarchitectonic maps shown in (b). (**b**) ICs were thresholded (voxels exceeding 40% of baseline value of the map were preserved), superimposed, and colour coded according to their percentage of activity at a given time (using the colour bar to the right of the time courses shown in (a) and at the bottom right in (b)), forming a chronoarchitectonic map. Five such maps are displayed, taken at times that correspond to the five stimulation conditions. The times at which each map was taken are given for each map and indicated by the red lines crossing the time courses in (a) with the labels I-V. Data are from subject AB.

2.3. Study 2 - The human brain in natural viewing conditions: Watching the James Bond 007 movie *Tomorrow Never Dies*

The initial twenty minutes of this film were shown to three subjects (CG, JW and LP). All the data obtained for this study are presented in much the same way as those shown for the object from motion study (study 1), such that figures [17,18,19,20] from study 1 correspond to figures [21,22,23,25] of this study. By analogy to the object from motion study, the single-subject data presented for this study in the correlation maps (figure 21), the correlograms (figure 22) and the chronoarchitectonic maps (figure 25) are shown for the same subject (CG) to maintain consistency across figures. We limit therefore the description of the results of the movie study to novel findings that add to those described in the object from motion study, and do not repeat previous descriptions, either in the text or in figure captions.

The correlation maps shown in **figure 21** demonstrate that the ICs contain voxels whose BOLD signals are highly correlated, and that the time course of a given IC is practically identical to the BOLD time course of its hottest voxel. Interesting to note here is that again, as in the object from motion study in a different subject, right ORA is isolated along with bilateral V5. This was true for all three subjects (see figure 23).

The two most important findings in this movie study are the following:

2.3.1. The richer the stimulus the more individualistic are the areas.

First, ICA isolated many more visual areas in this data set than it did in object from motion study (see figures 21 and 25). This is exactly what we had hoped for, because the stimulation by a movie provided a much richer and more diverse stimulus than an epoch design in which five classes of stimuli were repeated over and over again. A correspondingly richer and more diverse activity pattern in the brain was the consequence, in which each area was activated and inactivated over time in a way that differed from that of all remaining areas, even at the relatively slow time scale at which these BOLD data were sampled. This enabled ICA to dissect out more areas.

2.3.2. Brains are all alike.

Second, despite the fact that the stimulus in the movie study was completely uncontrolled, enormously rich and therefore containing many different details that each subject could have focused on, highly similar results were obtained for each of the three subjects: **figure 23** shows ICs and a period of their associated time courses superimposed for all three subjects, to illustrate the consistency of spatial and temporal activation of visual and non-visual areas, and the reliability of ICA to isolate those consistently. In addition to being an interesting finding in its own right, since it shows that the same areas in different individuals have highly correlated time courses when these individuals freely watch a movie, it also provided a convenient control for the performance of ICA: it allows us to prove that the regions isolated by ICA have the same spatial and temporal activity pattern across different subjects, therefore verifying that these ICs are physiologically meaningful.

2.3.3. Left and right brains are alike.

The correlation coefficients of the activity in the many visual areas ICA isolated in the movie study are shown in the correlograms in **figure 22**, which have many more nodes than the one in the object from motion study. It was revealed that the pairs formed by the left and right part of the same area (e.g. left V5 and right V5) have the highest correlation coefficients. This can be explained by two reasons: First, each of these areas has the same stimulus specificity (such as left and right V5 respond to motion), and is therefore activated in a highly correlated way, even if they did not communicate with each other. Second, bilateral areas have strong interconnections across the corpus callosum, and their activity is therefore correlated.

2.3.4. The correlation between cortical areas is stimulus dependent.

In addition, we were in a position to segregate three different states of brain activity in terms of correlograms: every three minutes the movie was interrupted by a 30s blank period (black screen, no sound). This allowed us to examine the dynamic relationship of the BOLD signal between cortical visual areas during free viewing of a movie (**figure 22a,b**), during the absence of visual stimulation (**figure 22c**), and during on/offset of visual stimulation (**figure 22d**).

At first sight it becomes apparent that the correlation coefficients are overall much higher between all areas only during the the periods of stimulation offsets and onsets than during the rest period or the movie period. In the latter two periods, each

area has low correlation coefficients with most other areas and high correlation coefficients only with very few other select areas, indicating that the specificity of the activation or of the cross-communication between areas is much more selective during the stimulation or the blank periods than during the periods of stimulus on- and offsets. During the latter, all areas are driven by the sharp transient of these on- and offsets.

It is surprising to find that the specificity of activity is not only higher during the movie stimulation, but also during the blank periods: both correlograms have a high similarity. This might be explained by visual imagery our subjects might have had during the blank period, making the areas as differentially active as if they were during external stimulation.

2.3.5. The brain's BOLD signal needs more than 30 seconds to recover.

This similarity between stimulation and absence of stimulation as opposed to on/offset effects is even more striking considering the fact that the 30s blank period might not have been enough to capture brain activity related to the absence of visual stimulation, as it is suggested by the data presented in figure 23: the activity throughout the whole blank period seems to have been affected by the stimulus offset: BOLD signal decreased rapidly for 15s, followed by a rebound lasting at least another 15s. These issues are discussed in more detail in the Discussion. The methods section and **figure 22e,f** give more details on the time windows used for the analysis.

2.3.6. Eye movements and their relation to BOLD signals.

In addition to BOLD signals related to brain activity ICA also isolated the signal induced by eye movements in each subject. It seemed interesting to find out whether eye movements as measured by fMRI had any correlation with the activity in visual areas. **Figure 24** shows for each subject the three ICs containing eyes, V1 and V5, along with the associated time courses. A high anti-correlation of the time course related to eye movements with those of the visual areas is apparent (correlation coefficients range from -0.21 to -0.56), but is mainly due to a common change of the signal induced by the blank periods: there is no apparent correlation when the blank periods are cut out of the time courses (correlation coefficients range from -0.05 to -0.13).

2.3.7. Brains watching brains watching movies.

Thirteen different ICs containing cortical and subcortical areas were combined to create chronoarchitectonic maps, four of which are shown in **Figure 25**. Only ICs containing bilateral activity were selected to create these chronoarchitectonic maps in order to avoid the inclusion of artefacts, which are very unlikely to be bilateral. These ICs include visual areas, but also frontal eye fields, parietal and prefrontal areas, and even the putamen. It is possible to interpolate the time courses of the ICs and to display their activity in form of a dynamic chronoarchitecture in a movie, which can be displayed next to the movie the brain was viewing while being scanned. Such a movie of subject CG viewing 3min of the Bond movie starting from t=580s (see figure 23) is available from the author.

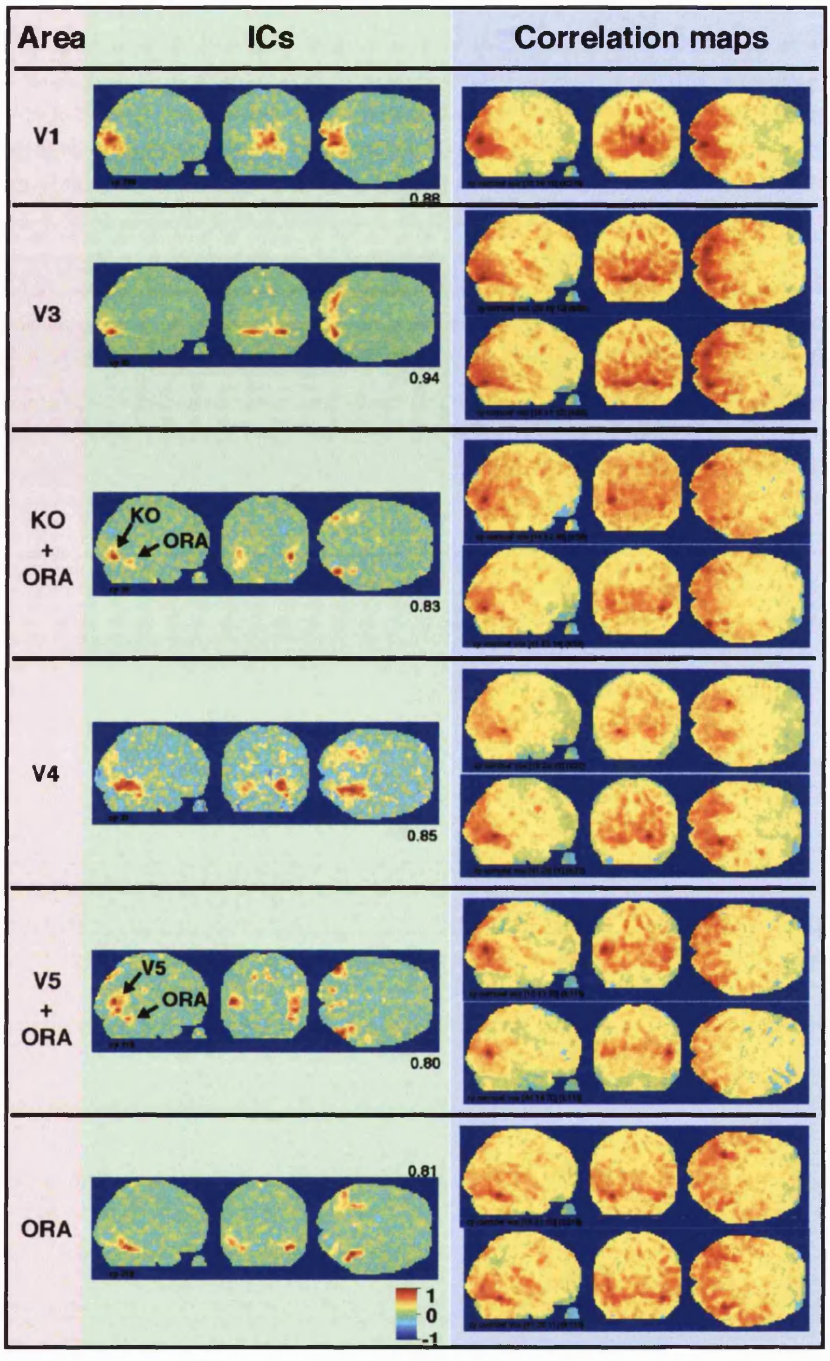

Figure 21. ICs isolated from a single subject (CG) watching the 007 movie (left), and CMs calculated for the hottest voxels of each IC (right). For each IC, two CMs were calculated, each showing the correlation coefficients (r) of the BOLD signal time course of the IC's hottest voxel in left (top CM) and right (bottom CM) hemisphere with those of the remaining voxels in the whole brain. The number underneath each IC is the r of the time course associated to that IC with the BOLD signal time course of that IC's hottest voxel. Interesting to note is that different parts of ORA were separated in different ICs, each associated to another visual area (KO and V5). (See also figure 17 for a description).

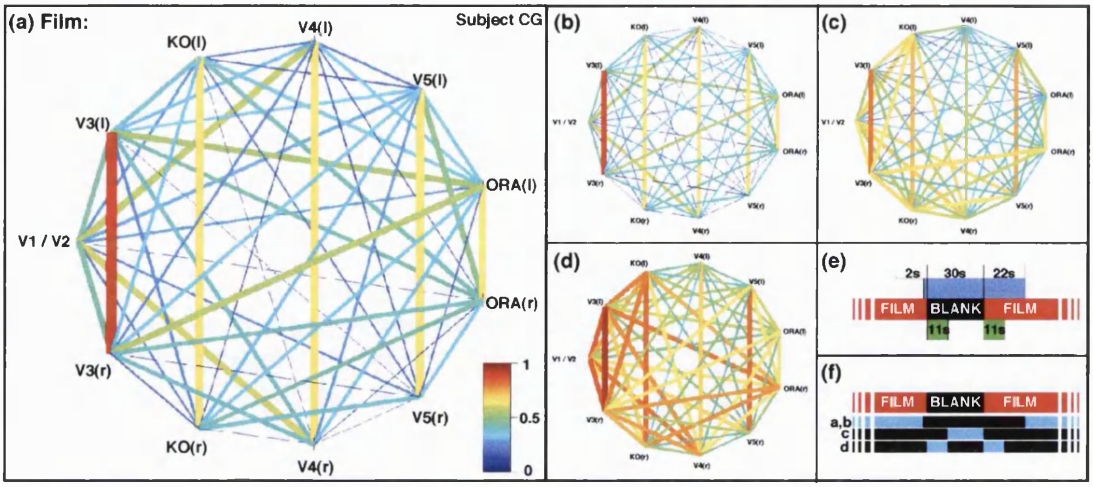

Figure 22. Correlograms of activity in the visual areas while the subject (CG) is watching the 007 movie. The movie was interrupted eight times by 30s blank periods, and separate correlograms were calculated for different sections of the BOLD signal with respect to the blank periods: (**a, b**): Correlograms derived from activity related to watching the 007 movie alone, with no effects from the blank periods (a and b are identical, b is shown at the same scale as (c) and (d) to provide a better comparison). (**c**): Correlogram calculated for the periods while the subject viewed the blank screen during the blank period. (**d**): Correlogram for the periods affected most strongly by the onset and the offset of the blank period. (**e, f**): The exact timings of the periods considered for the different correlograms (see methods section for a detailed description). Three facts are worth pointing out: First, left and right parts of the same areas have the highest correlation coefficients, especially during natural viewing conditions (a). Second, the on/offset periods make the correlations between different areas much less specific, in that all areas become highly correlated that were not so during viewing the film or the blank period alone. Third, viewing the film or the blank period alone leads to very similar correlograms.

Table 4. Correlation coefficients of eleven visual areas watching a James Bond movie (subject CG), corresponding to the correlogram shown in figure 22a,b.

Area	V1/2	V3l	V3r	V4l	V4r	KOl	KOr	V5l	V5r	ORAl	ORAr
V1/2	1.00	0.45	0.27	0.58	0.29	0.27	0.04	0.22	0.60	0.22	0.44
V3l	0.45	1.00	0.39	0.30	0.32	0.54	0.42	0.02	0.40	0.24	0.87
V3r	0.27	0.39	1.00	0.20	0.16	0.38	0.41	0.19	0.08	0.66	0.31
V4l	0.58	0.30	0.20	1.00	0.20	0.32	0.14	0.15	0.66	0.13	0.24
V4r	0.29	0.32	0.16	0.20	1.00	0.35	0.48	0.65	0.27	0.30	0.34
KOl	0.27	0.54	0.38	0.32	0.35	1.00	0.62	0.17	0.31	0.34	0.55
KOr	0.04	0.42	0.41	0.14	0.48	0.62	1.00	0.32	0.13	0.43	0.41
V5l	0.22	0.02	0.19	0.15	0.65	0.17	0.32	1.00	0.09	0.39	-0.01
V5r	0.60	0.40	0.08	0.66	0.27	0.31	0.13	0.09	1.00	0.07	0.40
ORAl	0.22	0.24	0.66	0.13	0.30	0.34	0.43	0.39	0.07	1.00	0.18
ORAr	0.44	0.87	0.31	0.24	0.34	0.55	0.41	-0.01	0.40	0.18	1.00

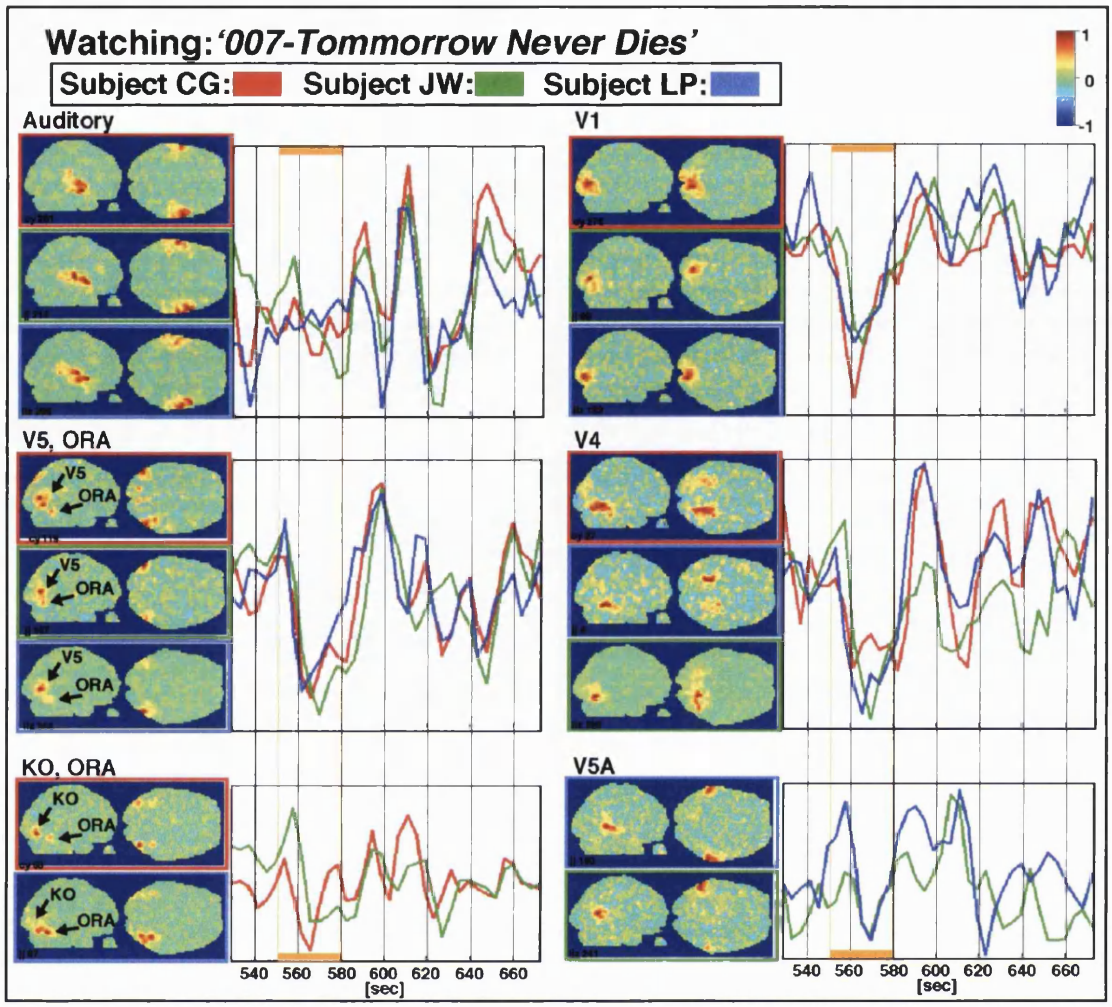

Figure 23. Consistency of activation of the same areas across different brains. Different cortical areas isolated by ICA are shown for all three subjects, next to the time courses associated to the ICs. The time courses of ICs from different subjects that contain the same area are superimposed across the different subjects (arbitrary units). It is evident that the same area (e.g. ORA) had highly similar activity in each subject when they were watching the same section of the movie. In addition, it also becomes apparent that different areas have different time courses. The orange bar at the bottom indicates the duration of a blank period, during which the movie was interrupted by a black screen.

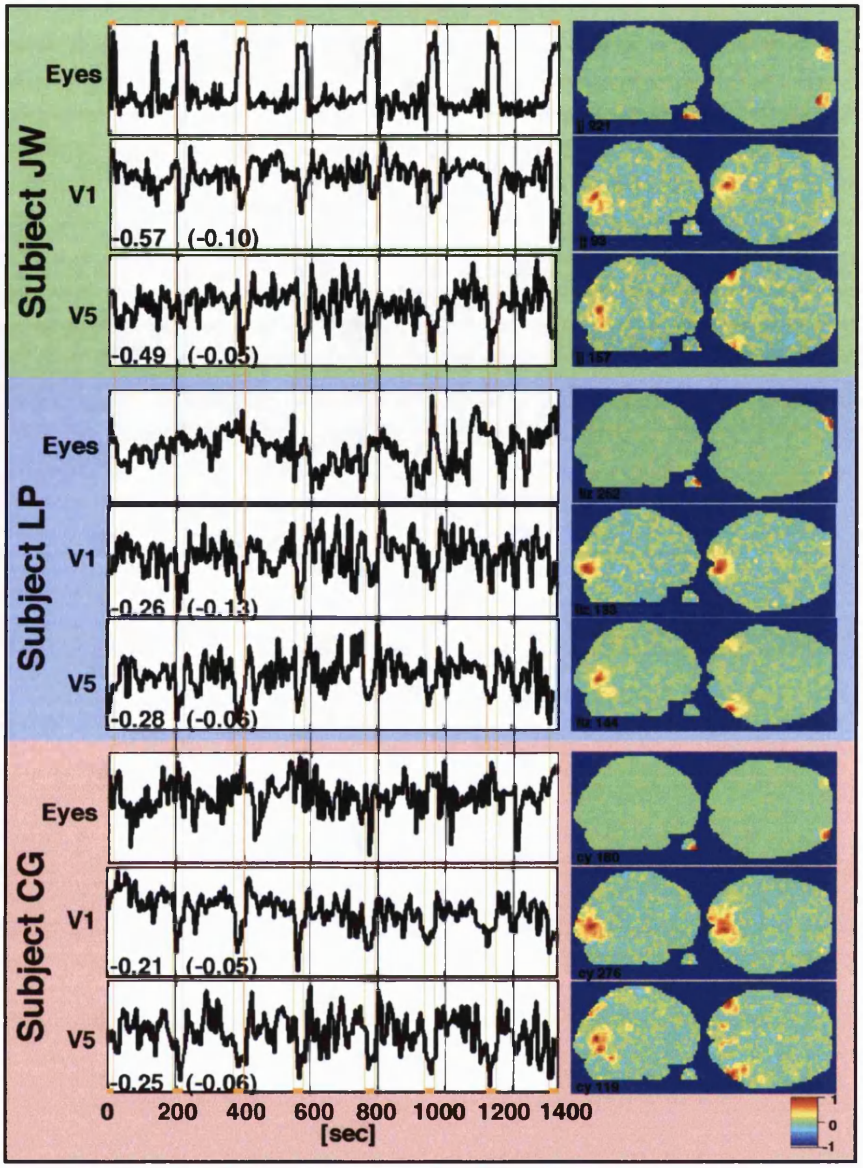

Figure 24. Relation of eye movements and activity in visual areas V1 and V5, for all three subjects. Blank periods are indicated in orange. For each subject, the three ICs containing eyes, area V1 and area V5, respectively, are shown, along with the associated time course (arbitrary units). ICA isolated several ICs containing eye movement related signals in each subject. Here, the one whose time course correlated most with that of V1 was selected. The numbers underneath the time courses of V1 and V5 indicate the correlation coefficients (r) to those of the eyes. In brackets is r obtained when the activity related to the blank periods (indicated by yellow bars) was cut out of the time courses. The anti-correlation between eye movement related signals and BOLD signals can be entirely explained by changes induced by the blank periods. Eye movements as measured by fMRI are therefore not correlated to BOLD signals of visual areas during natural viewing conditions.

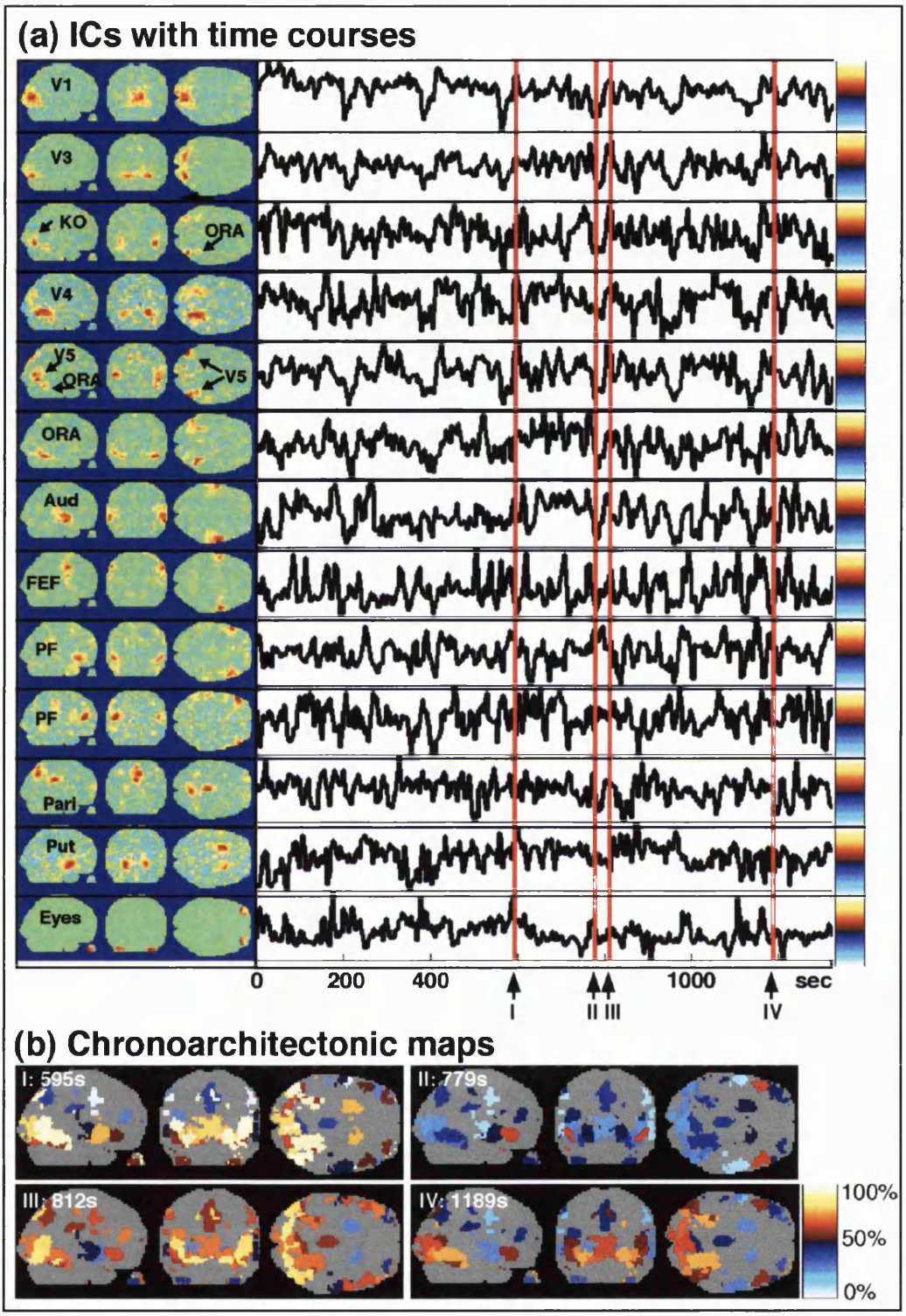

Figure 25. Chronoarchitecture of the human brain during natural viewing conditions (subject CG). (**a**) ICs along with their time courses. (**b**) Chronoarchitectonic maps derived from four arbitrary times. Aud: Auditory or speech areas(Binder, et al., 2000); FEF: frontal eye fields; PF: prefrontal cortex; Pari: parietal cortex; Put: putamen. (See figure 25 for a more detailed description on the making of these maps).

Part 4:

Discussion

In this discussion, I proceed from the particular to the general. The starting point for this work revolved around the question: is there a cortical area that is specific for generating colours and, if so, what is its architecture. The evidence given here and in the published literature, both experimental and clinical, leads me to suppose that there is a colour centre; this forms part of the colour pathway and seems to have, among its functions, the task of generating constant colours by taking ratios of light of different wavebands reflected from different surfaces. This, in turn, raises the question of whether the colour centre is an exception or whether it is a specific example of a more general rule, governing the functioning of the visual brain, namely that different attributes require different processing areas. If so, different attributes should lead to differential activity in each of these areas, making it possible to segregate one from another, even without prior knowledge of their function. From this modular organisation of the cerebral cortex, certain logical consequences follow, and these are traced towards the end of this discussion, which leads to the more general view that activity at individual stations of the visual brain has perceptual and conscious correlates, and that the brain uses a multi-stage strategy to "bind" the activity at different stations of the visual brain.

1. The generation of constant colours

Colour is a remarkable phenomenon which allows the brain to acquire knowledge instantaneously about a constant physical property of objects and surfaces, namely their reflectance for light of different wavebands. It is the end-result of a complex series of operations which depend partly upon the physical properties of light and the surfaces reflecting it and partly upon the operations evolved by the brain to compare the relative efficiency of different surfaces for reflecting lights of different wavebands. When a surface or object is viewed in different illuminants, the wavelength composition of the light reflected from it and from its surrounds changes (see **Figure 1**), but the ratio of light of any given waveband reflected from the two - and determined by the brain - remains the same. It is through such an operation that the brain is able to "discount the illuminant" (Helmholtz, 1911) and thus make itself independent of the continual changes in the wavelength composition of the light reflected from surfaces. The latter, in turn, allows it to assign a constant colour to surfaces in spite of these changes. The nature of the operations that the brain undertakes to construct constant colours is unknown. Computational theories have proposed two general steps, which they suppose are done separately for long, middle, and short wave light (Land, 1974). One is a ratio-taking operation to determine the relative intensities of light reflected from different surfaces and the other a thresholding operation which allows the brain to discard small changes and record large ones. Both steps could be local or global in the sense of involving small or large parts of the visual field but both processes should be indifferent to whether the stimulus is coloured or achromatic, since it is the end-result of this process that allows the brain to assign a colour to a surface.

The relative ratios of the intensities of light of different wavelengths coming from different surfaces determine unambiguously the colour of those surfaces - they are independent of the absolute values and therefore of the illuminant. Changes in wavelength composition are not, of course, the only ones in ambient illumination. A surface can be viewed in the same illuminant but at different intensities, in which case

the ratios of light of different wavebands reflected from the same surface will remain the same. The relative intensities across the different surfaces will have to be continually reassessed by the ratio-taking machinery of the brain. Comparison or ratio-taking thus lies at the heart of the colour generating operations of the brain, which have to be undertaken at any change of the illumination condition.

Little was known about the cortical site of the ratio-taking operation and, until now, not much more about the sites within the pathways of the brain devoted to colour vision where they occur. But the colour pathways themselves are relatively well charted anatomically. They involve areas V1, V2, V4 and the infero-temporal cortex in the monkey (Zeki, 1973; Zeki, 1983c; Livingstone & Hubel, 1984a; Shipp & Zeki, 1985; Hubel & Livingstone, 1987; DeYoe & Van Essen, 1988; Zeki & Shipp, 1989; Komatsu, Ideura, Kaji & Yamane, 1992; Ts'o & Ghose, 1997; Vanduffel, Tootell & Orban, 1997). A similar pathway is involved in the human brain; imaging studies show that V1, V4 and areas located within the fusiform gyrus in the medial temporal lobe are activated by coloured stimuli (Lueck, et al., 1989; Corbetta, et al., 1991; Zeki, et al., 1991; Zeki & Marini, 1998; Beauchamp, et al., 1999). One would intuitively want to involve all areas up to V4, and possibly beyond, in the computational process, partly because they are connected reciprocally (Zeki & Shipp, 1989) and partly because the cells of V1 are the most sensitive to changes in wavelength composition (Zeki, 1983b). Whatever operation areas V1 and V2 undertake is likely, however, to be a local one, given the relatively small size of their cells' receptive fields and their general indifference to what happens outside their receptive fields (Hubel & Wiesel, 1977), although the presence of horizontal connections could, with appropriate stimuli, enlarge the size of the receptive fields beyond the classical one, as recent physiological studies show (Rossi, Rittenhouse & Paradiso, 1996). V2 could also become involved through the double-opponent cells which, it has been argued, are important for colour constancy mechanisms (Livingstone & Hubel, 1984a) and for mediating the initial wavelength differencing stage, which is itself a ratio-taking operation across a border, for different wavelengths (Zeki, 1984). The much larger field size of V4 cells and the apparent indifference of some of them to wavelength composition (Zeki, 1983a) makes of this area a better candidate for long range ratio-taking implementations, though not necessarily to the exclusion of V1 and V2. Finally, the areas in the fusiform gyrus beyond V4 appear to be critical in relating colour to object (Zeki & Marini, 1998) but, until now, it has been unclear whether ratios are taken separately when colours are properties of objects and when they are part of abstract compositions. At any rate, the answer as to the site of these operations seemed to be conjectural enough to be worth investigating.

Our results show that it is the V4-complex that is principally involved in the ratio-taking operation. It was rather surprising that both V1 and V2 were activated only weakly in the comparison of dynamic and static versions of both coloured and black and white stimuli. Our interpretation of these results is therefore that the dynamic and static versions of our stimuli were surprisingly similarly effective in activating V1 and V2, which consequently almost disappeared in the comparisons. However that may be, the fact that the activity was within the territory of V4 in these comparisons reinforces the view that it is V4 that is especially concerned with the computations, not V1 and V2, even in spite of the wealth of anatomical connections that link these three areas reciprocally (Zeki & Shipp, 1989; Felleman & Van Essen, 1991; Nakamura, et al., 1993). It should hardly come as a surprise that the site of the colour generating ratio-taking mechanisms is a relatively advanced stage of the colour pathways. In contrast to the responses of V1 cells, the responses of at least some cells in V4 correlate with perceived colours (Zeki, 1983b) and only V4 has callosal connections that are widespread enough to integrate signals from spatially separated points across the two hemi-fields (Van Essen & Zeki, 1978; Zeki, 1993b), a necessary pre-requisite for colour-generating interactions across the two hemispheres (Land, Hubel, Livingstone, Perry & Burns, 1983).

1.1. The architecture of the human colour centre: the V4-complex

We have shown in this study that area V4 (Lueck, et al., 1989; McKeefry & Zeki, 1997) and a smaller zone just in front of it are the ones principally activated when subjects view multicoloured abstract or natural scenes whose wavelength composition or illumination intensity changes continually, without altering the perceived colour of the individual patches, and hence that these are the areas that must be critically involved in the ratio-taking operations. Additionally we have shown that selective attention to colour as opposed to motion led to a strong and equally selective co-activation of both zones, along with some activation in areas V1 and V2. Given their strong and consistent co-activation by colour, and especially by coloured stimuli that induce additional ratio-taking, we group the two active zones in the fusiform gyrus found in this study into a larger complex, the V4-complex; we designate the posterior part as V4 and the anterior one as V4α. We refer to this entire zone of the fusiform gyrus as the *human V4-complex*, which constitutes the colour centre of the human brain. Of these, V4 proper has a retinotopic map of the contralateral hemifield as revealed by standard techniques (McKeefry & Zeki, 1997). This retinotopic map proved to be too crude to

be detected by the initial polar co-ordinate mapping and cortical flattening techniques (Sereno *et al.*, 1995) but has been recently confirmed by others (Hadjikhani, et al., 1998; Zeki, et al., 1998). V4α resembles V4 proper in that both upper and lower contralateral quadrants are represented in it but differs from it in that the retinotopy that is a feature of V4 is not evident in V4α, at least as revealed by our current methods, which is not to say that it does not exist in a more crude form. We emphasise that a retinotopic organisation within the V4-complex could have been predicted from the published clinical evidence, as indeed it was by (Damasio, et al., 1980), since this shows that the achromatopsia resulting from damage to the colour centre can include both quadrants of the contralateral hemifield, the "hemiachromatopsia" of Verrey (1888) and others. This of course implies that an area located in ventral occipital cortex processes colour for the whole contralateral hemi-field. The evidence of Kölmel (1988), that the achromatopsia can be restricted to a single quadrant, implies a topographic organisation of the colour centre, as does the evidence of Wilbrand (1884) which shows that recovery from achromatopsia can be restricted to a single quadrant.

Even though we are not certain of what functional significance to ascribe to the two subdivisions of the V4-complex, besides the general one of undertaking the ratio-taking operations that are mandatory for generating constant colours, three facts speak in favour of our supposition that V4 and V4α are subdivisions of an area that is broadly involved with an attribute of vision, namely colour: first, both subdivisions were activated in this study and, as a re-analysis shows, in the previous study (McKeefry & Zeki, 1997); second, both were activated with selective attention to colour; third, ICA isolated them without *a priori* knowledge as a spatially independent map, suggesting that they act as a functional unit. We infer from this that the two subdivisions are heavily interconnected, as indeed are the two subdivisions of the V4-complex in the macaque (Zeki, 1977). Our re-examination of an earlier study (Zeki & Marini, 1998) showed that V4 was differentially activated when humans view normally coloured objects compared to abnormally coloured ones, whereas V4α was equally involved in both, once co-active with V4 and once with the areas anterior to it that are associated with face and object recognition. The published literature shows that both V4 and V4α were activated in studies involving object or face perception, but the principal areas specialised in face or object recognition appear to lie directly anterior to V4α and lateral to V4 (Haxby, et al., 1994; Dolan, Fink, Rolls, Booth, et al., 1997; Kanwisher, McDermott & Chun, 1997; Orban, et al., 1997; Rosier, et al., 1997).

1.2. Possible homologies with macaque monkey V4

In macaque, the V4-complex can be distinguished from the surrounding cortex by its low cytochrome oxidase content (**Figure 26**), and studies of the macaque brain have shown convincingly that the V4-complex consists of at least two subdivisions, with further subdivisions within each likely. The subdivision easiest to demarcate in the V4-complex is the one that separates the posterior part, V4, from its anterior part, V4A (Zeki, 1977) (see **Figure 27**). Colour cells are found in both sub-divisions; particularly important in view of the co-activation of V4 and V4α in man is the fact that V4 and V4A in the macaque are strongly interconnected (Zeki, 1971; Xiao & Felleman, 1998) and share some anatomical connections with antecedent visual areas, notably V2 (Zeki, 1977; Zeki & Shipp, 1989; Nakamura, et al., 1993). But each has its own independent system of callosal connections with the opposite hemisphere, a sure sign that each is a separate area (Zeki, 1970). The vertical meridian is represented at the posterior border of V4, the horizontal meridian forms the border between it and V4A and the vertical meridian is re-represented at the anterior border of V4A (Zeki, 1977; Van Essen & Zeki, 1978; Gattass, Sousa & Gross, 1988) but the retinotopic organisation of V4A is coarser than that of V4 (Van Essen & Zeki, 1978; Boussaoud, Desimone & Ungerleider, 1991; Pinon, Gattass & Sousa, 1998). The dorsal part of each subdivision represents the lower contralateral quadrant of the visual field; V4 and V4A extend ventrally and then medially, the ventral extension representing the upper quadrant. It is important to note that area V4A, which has also been called TEO (Boussaoud, Desimone & Ungerleider, 1991) and CIT (Felleman & Van Essen, 1991), has its dorsal border in the dorso-lateral part of the prelunate gyrus (Zeki, 1977) and extends ventrally and then medially into the posterior temporo-occipital region (Boussaoud, Desimone & Ungerleider, 1991), paralleling closely the distribution of V4 (Pinon, Gattass & Sousa, 1998). It is very likely that the posterior part at least of the area that has been called area TEO is in fact the ventral extension of V4A, and therefore part of the V4-complex in the macaque (Zeki, 1996) (**Figure 27**). Physiological evidence shows a further compartmentalisation within the two subdivisions of monkey V4-complex, with cells showing a strong selectivity to colour and wavelength or to orientation or to luminance being grouped together in patches (Zeki, 1983c; Desimone & Schein, 1987; Xiao & Felleman, 1998) even though many of the orientation selective cells in V4 also have colour preferences (Schein & Desimone, 1990), unlike the orientation selective cells of, say, V2, V3 and V3A (see Zeki, 1997). It is likely that the same or further subdivisions may be characterised on the basis of cortical connections (DeYoe, Felleman, Van Essen & McClendon, 1994; Xiao & Felleman, 1998).

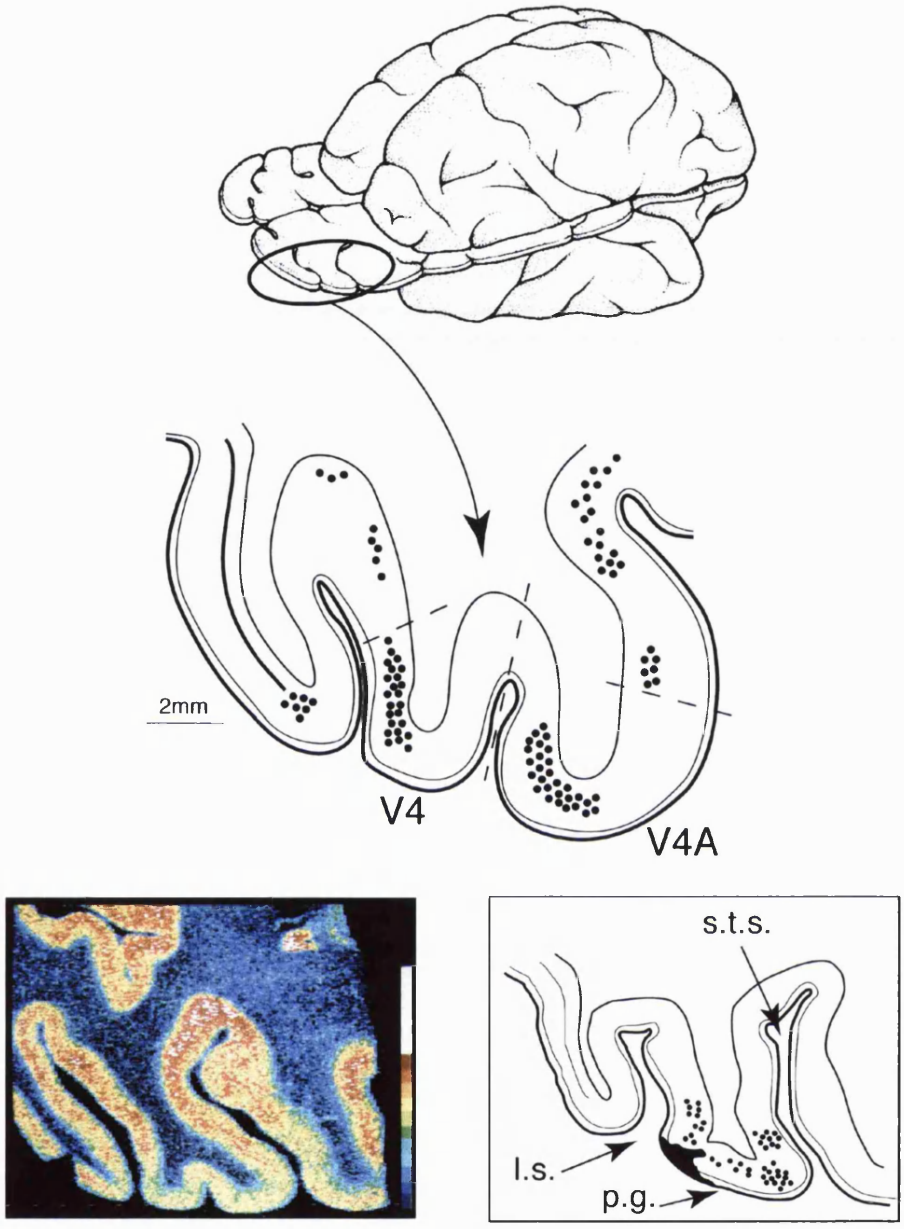

Figure 26. The centre is a drawing of a section taken through the lateral part of the occipital lobe of the macaque brain, at the level shown in the top drawing. The dots represent the distribution of callosal fibres in the cortex, the posterior cluster of callosal fibres belonging to the territory of V4 and the anterior one to that of V4A (re-drawn from Zeki, 1970). The borders of the two subdivisions of the V4-complex are indicated by dashed lines. Below left is a computer enhanced section of the monkey brain, taken at about the same level, to show that the V4-complex can be sharply differentiated from the surrounding areas by its relatively low cytochrome oxidase concentration. Below right is a drawing of a section, taken at roughly the same level as the others, from a macaque brain in which a lesion (shown in black) had been made in V4. The dots in the section show the degeneration produced by the lesion, and indicate the connections between the two subdivisions of the V4-complex (from Zeki, 1977).

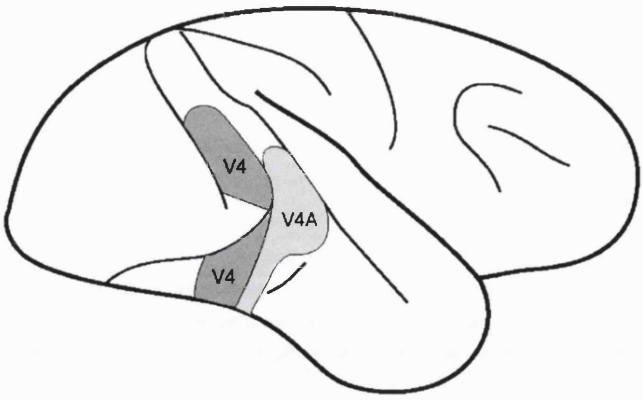

Figure 27. The approximate positions of the two subdivisions of the V4-complex of the macaque brain are shown on this surface drawing.

We possess nothing like this amount of information about the single cell properties or the anatomical wiring of human V4-complex. It would therefore be premature to equate the anterior and the posterior subdivisions found in this study with the ones described in the macaque; not enough is known of the function of these subdivisions in either species and there is a substantial inequality in size between the two subdivisions in the human. But the facts given above suggest analogies compelling enough to raise the question of homology between macaque and man.

Ever since the colour centre in the human brain was determined with imaging methods (Lueck, et al., 1989; Corbetta, et al., 1991; Zeki, et al., 1991; Sakai, Watanabe, Onodera, Uchida, et al., 1995; McKeefry & Zeki, 1997), we have used the term V4 to describe it, implying an homology between it and the area called V4 in the monkey (Zeki, 1971). The reasons for this can be summarised as follows: (a) in both human and monkey, V4 has a complete representation of the visual field, with the upper visual field being mapped more medially in the human and more ventrally in the monkey; the lower visual field is mapped more laterally in the human and more dorsally in the monkey, indicating a ventro-medial displacement in the human (McKeefry & Zeki, 1997; Hadjikhani, et al., 1998); (b) the presence of colour selectivity in both. In monkey the evidence for colour selectivity is derived from single cell physiology (Zeki, 1973; Zeki, 1983c; Schein & Desimone, 1990; Roe & Ts'o, 1995) and from optical imaging experiments (Roe & Ts'o, 1995; Vanduffel, Tootell & Orban, 1997). Especially interesting in this regard is the evidence from positron emission tomography (Mikami, Ando, Kubota, Sawaguchi, et al., 1996) which shows that both V4 and V4A are activated by colour tasks (also Mikami, personal communication). Anatomical tracing studies (Zeki & Shipp, 1989; Nakamura, et al., 1993) have shown a strong input to V4 from the thin stripes of V2, in which wavelength selective cells predominate

(Shipp & Zeki, 1985; Hubel & Livingstone, 1987; DeYoe & Van Essen, 1988), though there is no such direct anatomical evidence in the human. The evidence for the colour selectivity of the V4-complex in the human brain is derived mainly from imaging studies (Lueck *et al.*, 1989; Corbetta *et al.*, 1991; Zeki *et al.*, 1991; Allison *et al.*, 1993; Sakai *et al.*, 1995; Sereno *et al.*, 1995; Hadjikhani *et al.*, 1998; Beauchamp *et al.*, 1999), from electrical stimulation studies in awake patients (Allison, et al., 1993), as well as from clinical studies (see above); (c) behavioural studies (Walsh, et al., 1993) have shown that monkeys with lesions in the V4-complex have problems with colour constancy tasks, just like humans rendered dyschromatopsic by lesions to V4 (Kennard, et al., 1995) (d) the relative position of the V4-complex in both species, being situated anterior to V3 and posterior to motion related cortex (V5). This list of similarities is compelling in drawing attention to a possible homology between monkey and human V4.

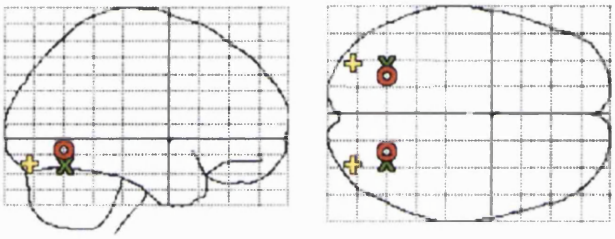

Figure 28. The figure shows the locations of the three areas that are discussed in the text, in a glass-brain projection. The areas were located by using the Talairach co-ordinates of the three areas given in the paper by Hadjikhani et al. (1998): **O** corresponds to area V4 defined in (Lueck, et al., 1989; Zeki, et al., 1991; McKeefry & Zeki, 1997); **X** corresponds to the "new" area "V8" of Hadjikhani *et al.* (1998) and the + to the area V4v defined by Sereno *et al.* (1995).

The latter raises the vexed question of area "V4v", described by Sereno et al. (1995) and by DeYoe et al. (1996) and detected by a novel stimulation technique, that of phase-encoded retinal stimulation, developed by Engel et al. (1994), coupled with fMRI. Here the response phases of individual voxels in the visual cortex are related to the position of a rotating wedge or expanding ring stimulus. Put simply, that part of the visual field which is mapped in a given brain region is given by the retinal location of the stimulating wedge at the time of the region's maximal response, taking into account the time-delay of the response. A reversal in response phase is of particular interest as it marks the transition from one retinotopic map to another. This method is designed to detect retinotopically organised visual areas. The use of the term "V4v" implied a similarity between it and the classical V4, not only because it was the fourth map but also because it was located in territory which was activated by colour. This latter point was emphasised by one of the above reports which, referring to our earlier study

(Lueck, et al., 1989) , reported that "The location of V4v corresponds to some of the locations identified in positron emission tomography studies as having color selective responses" (DeYoe, et al., 1996). The addition of "v" was intended to indicate that it was nevertheless only the isolated ventral part of a much larger V4, in which the upper visual quadrant alone is mapped, which had been charted; the dorsal part, representing the lower quadrant, and thought to be located dorso-laterally in the occipital cortex, had still to be charted (Tootell, Dale, Sereno & Malach, 1996). This itself is cause for concern because it is difficult to imagine why the same stimulation method can chart one half of an area but not the other. More recently, Hadjikhani et al. (1998) have confirmed the existence of a colour centre in ventral prestriate cortex but have misleadingly described it as "a previously undifferentiated cortical area that we call 'V8' ", indicating that colour stimuli "caused preferential activation of V8 but not V4". In fact, the Talairach co-ordinates of their "new" area are identical to the ones published earlier by us for V4 (McKeefry & Zeki, 1997) (see **Figure 28** and **Table 2**) and the two areas are identical, leading Tootell and Hadjikhani to "assume that the cortical area described by McKeefry and Zeki is equivalent to our area V8, ..." (Tootell & Hadjikhani, 1998; Zeki, et al., 1998; Tootell & Hadjikhani, Personal communication). This has misled some authorities (Heywood & Cowey, 1998) into supposing that "the human color center is distinct from area V4", making it a region "responsible for our conscious perception of a colored world". It is likely that area "V4v", described by Tootell et al. (1996) earlier, is to be blamed for this attempted re-naming. We have not been able to confirm the existence of a separate area "V4v", in which the upper visual field alone is mapped, in which there is no colour selectivity and which is therefore distinct from our V4. Others (Kastner, et al., 1998) have also found it difficult to confirm the existence of a separate "V4v". The reason for this difficulty in confirming the results of Tootell et al. (1996) are not entirely clear. They may be related to the phase encoding method itself or the way it is used. While it works in theory, recent evidence suggests that it may not be quite so reliable in practice. Studies of simple, periodic visual stimuli show that similar variations in response phase are present even if the stimulus is not changing in retinotopic position (i.e. not expanding or rotating), since different regions in the human cortex do not have the same latency in the measured BOLD response (Guy, et al., 1999). These inherent physiological phase variations may contaminate phase-encoding methods. It would therefore be appropriate to treat the results obtained by this method with some caution, despite the appealing look of the well-displayed maps on flattened cortices. The fact that successive maps from the same group have significant, but uncommented on, differences (consider, for example, the maps in Sereno *et al.*, 1995; Tootell *et al.*, 1997a; Tootell *et al.*, 1997b; Hadjikhani *et al.*, 1998) emphasises the necessity of attaching statistical significance values to these maps at least in future studies. This is a basic and stringent requirement

for the standard approach and would be useful in order to judge the reliability of the results obtained by this novel method especially when they deviate from those obtained by standard techniques. In summary, there is no present compelling evidence for a separate area "V4v", distinct from V4 and representing upper visual fields only.

1.3. The V4 complex as the ratio-taking site of the colour system

We began this study by supposing that a continual change in the wavelength composition of light coming from every part of the field of view would ensure a high load on the cortical colour generating system, imposing upon it the necessity of re-taking the ratios between all parts with every change in wavelength composition; this, we thought, would allow us to determine the cortical site of these ratio-taking operations. In truth, no one knows whether the ratio-taking operation is continually updated even if there is no change in wavelength composition. What is clear is that, when such changes do occur, the ratio will have to be re-taken. Our finding is, that confronting the brain with either continually changing illuminants or luminance intensities involves extra activity within the V4-complex, which we interpret as being the neurological reflection of the extra computational effort involved in both. But the result also leaves us with a puzzle. Throughout the experiments, our subjects always perceived constant colours, regardless of whether they viewed the dynamic or static versions of the coloured stimuli. Our results thus raise the more general question of how the brain achieves a stable percept - in this case colour constancy - since whether the activity in V4 increases (when viewing the dynamic Mondrian) or decreases (when viewing its static counterpart), the perceived colours remain the same. It is somewhat surprising that V4 decreases its computation so significantly in the static colour condition while permanently providing an equally intense colour percept. Apparently, the percept of colours does not fade over time even when the machinery creating it decreases its activity. This poses a more general neurobiological problem, namely the relationship between the intensity of neural activity and the resulting percept. It is a problem that is difficult to address at the present time but warns us against too facile an equation between intensity of neural activity and conscious perception. One can argue that the increased activity in the V4-complex in the dynamic conditions is reflected perceptually in the perceived changes of the shades of the Mondrian. Finally, it is worth emphasising that comparisons of the dynamic conditions (varying luminance and varying wavelength compositions) with the static versions of the grey stimuli led to an activation that was almost indistinguishable from the corresponding comparisons for

coloured stimuli (**Figure 9**); this is what one might expect on theoretical grounds because the ratio-taking operation that the brain performs should, in theory, be indifferent to whether the stimulus is coloured or achromatic, since the determination that a surface is coloured depends upon the end result of this process. We thus demonstrate that, on neurological grounds, the processing of grey tones involves the same mechanisms that are used for the processing of colours, inclining us to redefine grey as a colour on a neurological basis, just as artists and scientists did on a perceptual one.

1.4. A processing-perceptual system for colour

All the clinical evidence that has accumulated since Verrey published his work has shown that a centre located posteriorly in the fusiform gyrus is necessary for the normal perception of colours and that when this centre is damaged the consequence is a specific inability to see the world in colour, the syndrome of cerebral achromatopsia (for a review, see Zeki, 1990a). It is difficult to be sure, but it is more than likely that most of the lesions in the fusiform gyrus that have resulted in the syndrome of achromatopsia have included the V4-complex as defined here, that is to say both its subdivisions, and that the differences in severity and recovery rates depend on the differential involvement of the two subdivisions. There is no clinically compelling evidence that lesions outside the human V4-complex lead to achromatopsia and it is therefore unlikely that there is an area beyond the V4-complex mediating the perception of the colours computed within it. This evidence, together with the results presented here, which show that the V4-complex is also the site of the ratio-taking operations that are at the heart of the colour generating system, leads us to the concept that the processing system is the same as the perceptual system (Zeki & Bartels, 1998b). This notion is supported by our finding that selective attention to colour as opposed to motion activated most strongly both subdivisions of the V4-complex but no areas beyond it. Furthermore, the perception of afterimages as well as hallucinations involving colours correlate with activity in corresponding regions of the fusiform gyrus (Sakai, et al., 1995; ffytche, Howard, Brammer, David, et al., 1998), which is emphasised by the fact that the syndrome of cerebral achromatopsia can be accompanied by the failure of patients even to imagine or to dream in colours. This notion of processing-perceptual systems can also be derived separately from clinical evidence relating to other specialised systems and from psychophysical evidence which shows that different processing systems reach their perceptual endpoints at different times (see Zeki & Bartels, 1998a), with colour taking precedence over both orientation

and motion (Moutoussis & Zeki, 1997b; Moutoussis & Zeki, 1997a; Zeki & Moutoussis, 1997).

There is other evidence that leads us to this conclusion. Among the interesting features of the syndrome resulting from damage to the V4-complex are (a) its specificity for colour (see, for example, Verrey, 1888; MacKay & Dunlop, 1899; Kölmel, 1988) (b) a failure of colour constancy mechanisms following lesions to the colour centre in the fusiform gyrus (Kennard, et al., 1995) and (c) the ability of achromatopsic patients to discriminate different wavelengths without however being able to ascribe colours to them.

Naturally occurring lesions are of course indiscriminate and, given the many visual areas in the fusiform gyrus, it is obvious that many affect more than one area and thus lead to other syndromes besides achromatopsia, and chiefly to prosopagnosia, the inability to recognise faces. But there are cases of prosopagnosia that are not accompanied by achromatopsia and the reverse is also true (Clarke, Walsh, Schoppig, Assal & Cowey, 1998). Even in spite of the fact that achromatopsia is often accompanied by other syndromes, there remains a small number of cases of isolated achromatopsia that are convincing enough to lead to the conclusion that it can be a specific syndrome.

That patients with incomplete achromatopsia (dyschromatopsia) are, just like monkeys with V4 lesions (Walsh, et al., 1993), unable to assign constant colours to surfaces when the illuminant in which such surfaces are viewed is changed (Kennard, et al., 1995), is consistent with the imaging results given here, that the ratio-taking operations critical for the colour generating system occur within the V4-complex. This adds further support to the view that the processing system and the perceptual system are the same.

The equation of the processing system with the perceptual one raises the interesting question of whether the results of processing at each stage of a multi-stage system - such as the one dealing with colour - can become perceptually explicit at each stage, that is to say without further processing. Our conscious percept would then be a mosaic composed of many microconsciousnesses, each created at an area specialised for the corresponding attribute at a given stage of processing (Bartels & Zeki, 1998b; Zeki & Bartels, 1999b). There is some clinical and experimental evidence to support such a notion, namely the ability of patients and monkeys with V4 lesions to discriminate between different wavelengths, though with an elevated threshold and without being able to assign colours to them (in the case of human patients) (Fries and Zeki, 1983;

Vaina, 1994; Fries and Zeki, unpublished results). This probably reflects the fact that their perceptual capacity in the domain of colour is dictated by the physiology of cells in V1 and V2. Single cell recordings show that the wavelength selective cells in these areas, and especially in V1, respond to the presence and intensity of light of their preferred wavelength in their receptive field, without being concerned with the colour of the surface there (Zeki, 1983a; Zeki, 1983b), presumably because they are not able to effect the long-range comparative mechanisms required of colour vision. If our interpretation is correct, it follows that it is the activity of cells at the level of V1 and V2 that endows the subjects (or the monkeys) with their conscious perceptual capacities. A striking example is to be found in a patient who, after severe cardiac arrest and unconsciousness followed by recovery, became blind but was able to discriminate colours, though his colour vision was very much wavelength based (see also Wechsler, 1933). Imaging studies have shown that the activity in his brain, when he viewed colours, was confined largely to the calcarine region (Zeki, et al., 1999). This in turn implies that his limited, though conscious, vision of colours is largely the result of activity in his V1, and possibly V2. Parallel examples are to be found in the motion system, where subjects deprived of vision in V1 are able to consciously discriminate high contrast fast motion through activity in prestriate cortex, and notably in V5 (Zeki & ffytche, 1998).

Results such as these lead us to the more general view that the conscious perceptual stage is not the result of activity of processing at an hypothetical, final level of a given system. Instead, there are multiple conscious perceptual stages, each dependent upon the processing that occurs at a particular level (Bartels & Zeki, 1998b). Seemingly in support of this view is clinical evidence which shows that patients with unilateral lesions in the V4-complex are sometimes not even aware of their hemi-achromatopsia (~~Albert, Reches & Silverberg, 1975~~ Kölmel 1988; Paulson, et al., 1994 and our own unpublished results). Our hypothesis therefore becomes an interesting one to test, not only to ascertain the relationship of processing to perception at the level of individual areas, but also the relationship of both to conscious experience.

2. The computational dissection of the brain

The past quarter of century of research in neuroscience has shown beyond any reasonable doubt that the brain has a modular organisation, with each module performing a specialised task (Zeki, 1993b). (We use in the following the terms module and area interchangeably.) Here we have shown that, as a consequence of their functional specialisation, the activity time courses of these modules differ sufficiently from each other even at the time scale of several seconds to allow their identification and segregation without any a priori knowledge, using the powerful computational tool of independent components analysis.

2.1. The independent components of the human brain are functionally specialised areas.

I have shown that ICA can exploit the uniqueness of the spatial extent and the activity pattern in time of each cortical area and separate one area from another, both in conditions of controlled stimulation and in natural viewing conditions. Two data sets were presented to illustrate this: one obtained from a controlled visual stimulation paradigm, the other from presenting subjects with twenty minutes of a movie.

The first data set stems from a standard fMRI study that used an epoch design to study areas involved in processing objects, motion, and objects that are created by motion. It is shown that ICA identifies and isolates visual areas V1/V2/V3, V5, V5A, and the object recognition area ORA in separate components along with their time courses of activation. Furthermore, we demonstrate that areas grouped together by ICA, such as V5 and ORA, are the ones that have the highest mutual correlation coefficients, showing that ICA can and does detect coactive groups of areas. From this one can infer that they are preferentially connected anatomically, or that they have a similar stimulus

preference. A standard statistical analysis (a multiple regression of the BOLD data to the five stimulation conditions) using SPM (statistical parametric mapping) (Friston, et al., 1995a; Friston, et al., 1995b) (http://www.fil.ion.ucl.ac.uk/spm/) was used to show that statistical comparisons of e.g. the object-from-motion-condition with the random-motion-condition reveal the same activity pattern (namely V5 together with ORA) as detected by ICA without any a-priori knowledge. This demonstrates that ICA segregates areas that are differently involved in different tasks, or, in other words, that it segregates functionally specialised areas.

The second data set is used to test whether the activity time courses of different areas differ from each other at the slow time scale as measured by fMRI even when the brain processes more natural stimuli: it stems from three subjects watching the initial twenty minutes of the James-Bond movie *Tomorrow Never Dies* - a type of data set impossible to analyse by classical statistical tools such as parametric mapping. We show that ICA identifies and segregates the visual areas V1, V3, KO, V4, V5 and ORA, and various non-visual areas. This is because each of these areas is activated with different intensities at different times during the movie, which in turn stems from the fact that each of them responds preferentially to different stimuli, such as motion or objects, because each has a different functional specialisation. Since stimuli such as objects, motion, faces, colour, sound and voices occur - in movies as well as in real life situations - if not completely independently of one another, at least in varying combinations, the brain areas specialised to process these different stimuli are also activated in a similarly independent fashion as the stimuli occur, and can be isolated by ICA. Even more surprising however is that these differences are still detectable at a time scale which is by far slower than that of the fast-paced changes occuring in the stimulus.

2.2. Identification of cortical areas: bilaterality as a reliable hallmark

Since ICA is a completely data-driven algorithm, it needs first to be shown that its output is not entirely artefactual and meaningless.

Four reasons make it highly plausible that the areas isolated by ICA are functionally specialised areas: First, the ICs coincide exactly with the anatomical location, the spatial extent and the spatial shape of the human visual areas V1, V2, V3, V4, V5 and ORA, whose anatomical locations in the human brain are well established

and quite consistent across subjects. Second, the correlation maps show that the hot voxels in each IC have high mutual correlation coefficients, making it likely that they belong to one and the same area. Third, the correlograms demonstrate that the symmetrical pairs of left and right-hemispheric cortical areas isolated by ICA had higher correlation coefficients than any two cortical areas. This is exactly what one would expect, since both parts have the same functional specialisation and will therefore respond in a highly similar fashion, and because of the strong inter hemispheric connections between every bilateral cortical area (Zeki, 1970). Fourth, and this applies only to study 1, because the parametric statistical analysis revealed exactly the same areas as ICA, but on the basis of their task preference.

Cortical areas were named here by their most likely identity. The identity of the retinotopically organised areas could have been additionally verified using retinotopic mapping and brain-flattening techniques (Sereno, et al., 1995a; Tootell, et al., 1998). These techniques are very suitable for the identification of the exact borderlines and specific eccentricities of the visual field representation in single subjects. At the same time they have shown that the areas it can reveal reliably (V1, V2, V3 and V3A) have highly consistent anatomical locations across subjects. Areas KO/V3B, V4, V5 and ORA have less or no retinotopic maps, but have also proven to have consistent anatomical locations across subjects and to be linked surprisingly reliably to specific anatomical landmarks (Shipp, Watson, Frackowiak & Zeki, 1995; Tootell & Taylor, 1995; Tootell, et al., 1997b; Van Oostende, et al., 1997; Smith, et al., 1998; Bartels & Zeki, 2000a; Dumoulin, Bittar, Kabani, Baker, et al., 2000). All these factors make us therefore confident that ICA distinguishes functionally specialised areas, and that we could identify these reliably.

2.3. The more complex the better: brain stimuli that lead to its optimal computational dissection

We propose the following, at first sight counter intuitive, hypothesis: the more complex and the more natural the brain stimulation is, the more powerful explorative techniques such as ICA will be in dissecting out the functional units of brain activity. This stands in complete contrast to parametric experimental designs, which should be kept as simple and as well controlled as possible, such that there is only a single and clearly defined difference between two tasks. Our observation that the correlation between different visual areas is lowest while the subjects watch the movie, but highest when the stimulus is simply turned off and on, demonstrates that the more natural and

rich a visual stimulus is, the more specifically each area gets activated (see figure 22), which makes it easier for any algorithm to distinguish them. This is so because each area finds its preferred stimulus within the complex stimulus, which makes its activity more distinct from all the other areas. A dull and simple stimulus in contrast may not contain the ideal stimulus for any of the specialised areas, making several respond to the onset and offset of the stimulus in a more similar fashion, with the consequence that some algorithms might have difficulties in distinguishing between them.

This opens the extremely promising prospect of studying human brain function in less artificial conditions than the ones usually used in fMRI, namely the ones in which the brain is in its natural working environment, processing highly complex and dynamic stimuli. This approach is also likely to reveal more functional subdivisions of the cortex than are known at present.

We further propose that, after a successful identification of an area, a hint to its function could potentially be derived by retrospectively trying to identify a correlation between the time course of its activation and a feature in the stimulus. This stands in contrast to the classical approach used in functional imaging, where stimuli are kept very well controlled and as simple as possible, such that differences of brain activity can be attributed to those in the stimulation.

2.4. The chronoarchitecture of the human brain

The data presented above make it clear that each cortical area has, on the one hand, its own individual activity time course, which is due to its functional specialisation and on the other that areas depend on each other in one way or another, since the output of one is used as the input to the next, even if these relationships are reciprocal. It will be one of the most interesting research fields in the future to uncover how much and what information is passed between different areas, and how much new information is added from the internal 'memory' of a given area. These two factors will define to a large extent the activity pattern of different cortical areas across time.

Equally, a map showing the degree of activity in different regions at a given time, or one illustrating the correlation of brain activity with a given stimulation in time - e.g. maps showing the statistical Z-scores of correlation with the stimulus, commonly known as statistical parametric maps (SPMs), fall within the general class of chrono-architectonic maps. The results allow me to present three types of chrono-architectonic

maps: the first shows how much activity in a given region in the brain correlates with that of all other regions in the brain (correlation maps), the second shows groups of areas that have high mutual correlations (ICs), and the third shows the relative activity of groups of such areas at a given time.

Given two factors, first, the wealth of functional data modern methods provide about the activity in time of the human brain, and second, the fact that the each functionally specialised area differs in its activity time course from all the other areas, we introduce here the concept of *chronoarchitecture*. Quite evidently, chronoarchitectonic maps differ from all those maps that rely on anatomical properties of the tissue, such as myelin maps, cytoarchitectonic or cytochrome oxidase maps, since these rely on static properties of the tissue, and not on their dynamic physiological activity. Since it is the structure that defines the function, some of the anatomical maps might share surprisingly much with chronoarchitectonic maps. For example myelin has a direct relation to the signal conduction speed, rendering myelo-architectonic maps the anatomical face of the chrono-architectonic map in the range of milliseconds. Here we produce chrono-architectonic maps in the most strict sense one can think of, by dissecting the brain into its functional modules entirely based on their activity time course, without any a priori knowledge of the data or the stimuli. However, chronoarchitecture is a conceptual term, and can be used for any type of brain map that relies entirely on activity in time. Several types of chrono-architectonic maps can be created, which might differ in the time scale one takes into account for doing so, or in the method one uses to create them. A map of the brain showing the signal arrival times in different areas after a single external stimulation is based on an entirely different time scale than the type of map introduced here, which segregates independently activated regions in the range of seconds. Our hypothesis, however, is that each of these chronoarchitectonic maps is finally derived from the difference in functional specialisation across cortical areas, thus leading to similar chronoarchitectonic maps, no matter what precise time scale or method is used to derive it.

Here, the term chronoarchitecture is introduced to give these mutual relationships of cortical areas in time - their 'time-architecture' - a conceptual term. The activity pattern of several areas at a single point in time is visualised here by colour-coding each area according to the relative activity it has at that time, which is just one way of creating a 'chrono-architectonic map' - there is no doubt that the future will see much more sophisticated chrono-architectonic maps (figures 20 and 25). Chronoarchitectonic maps stand in contrast to statistical parametric maps (SPMs), because they do not show voxels related to a certain task, but the activity state of the brain at a given time.

2.5. The human brain in natural viewing conditions: Watching the James Bond 007-movie *Tomorrow Never Dies*

In this section the relationship between different areas in terms of their activity time course is discussed. Despite the fact that we restricted ourselves here to the relatively simple measure of the correlation coefficient between pairs of areas, some interesting observations arise (see figure 22). It is striking how little correlation there is across different visual areas, the highest correlation always being between left and right part of the same area, which is true for every area. Apart from these obvious inter hemispheric connections, several interesting groups of highly correlated areas became apparent:

First, the two V4s in each hemisphere are highly correlated with activity in V1/V2. This is exactly what one would suspect, not only because these areas are reciprocally connected (Zeki & Shipp, 1989), but also given that these connections coincide with the colour pathway leading from V1's blobs to V2's thin stripes to V4 as it is charted in the monkey (Zeki, 1973; Zeki, 1983c; Livingstone & Hubel, 1984a; Shipp & Zeki, 1985; Hubel & Livingstone, 1987; DeYoe & Van Essen, 1988; Zeki & Shipp, 1989; Komatsu, et al., 1992; Ts'o & Ghose, 1997; Vanduffel, Tootell & Orban, 1997). In addition, the same areas have cells responding to static orientations, even though with an increasing receptive field size as one progresses from interblob cells in V1 to the interstripes in V2 to V4 (Zeki, 1975; Zeki, 1983c; Desimone & Schein, 1987). In humans, coloured stimuli have activated a similar pathway, including V1, V2 and V4 (Lueck, et al., 1989; Corbetta, et al., 1991; Zeki, et al., 1991; McKeefry & Zeki, 1997; Zeki & Marini, 1998; Beauchamp, et al., 1999; Bartels & Zeki, 2000a).

Second, ORA (also called LO (Malach, et al., 1995), corresponding to IT in the macaque (Tanaka, 1997)) and V5, have very common activity time courses, especially left V5 and right ORA. This relationship is highlighted even more by the fact that these areas were the most correlated ones in study 1. V5, the human motion area (Zeki, et al., 1991), has been shown to be activated together with ORA, even when static images that imply motion are viewed (Kourtzi & Kanwisher, 2000; Senior, Barnes, Giampietro, Simmons, et al., 2000). In fact, even when static images are viewed without implied motion, V5 appears to be activated much beyond its resting activity (Kourtzi & Kanwisher, 2000), which indicates a strong involvement of V5 in mere object recognition that certainly needs to be investigated in more detail. It is worth pointing

out that the strong co-operation of V5 with ORA does not only happen in studies exactly targeting such interactions, as did study 1(Bork & Zeki, 1998; Grill Spector, et al., 1998). The strong correlation of the 'dorsal' V5 with the 'ventral' ORA is one more factor casting doubt on the still widespread view of a strong segregation between a dorsal 'where' and a ventral 'what' pathway (Ungerleider & Mishkin, 1982; Ungerleider & Haxby, 1994).

Third, bilateral area V3 correlates highly with ORA, especially on the left, and with V1/V2. This highlights the probable pathway responsible for contour and object segregation, leading to object recognition. Depth, motion and edge selective cells in V1/V2 provide input into V3, which, with larger receptive field sizes and specialisation for local motion and depth processing, might play an important role in object segregation in complex dynamic visual scenes (Zeki, 1993b). The result of this is then used by ORA for object processing. In monkey, V3 is known to contain both depth and direction sensitive cells (Zeki, 1978b; Zeki, 1979; Poggio, Gonzalez & Krause, 1988; Poggio, 1995), fMRI studies in humans assign it a role in the determination of 3D-structure from motion (Paradis, Cornilleau-Peres, Droulez, Van De Moortele, et al., 2000)

Fourth, but less prominent than the previous two, presumptive area KO (Van Oostende, et al., 1997), which has also been termed V3B (Smith, et al., 1998) has relatively strong correlations with ORA. Its role is presumably similar to the one of V3, in that it might be involved in segregating contours and objects, especially since area KO/V3B has been found to be most activated by kinetic boundaries (Van Oostende, et al., 1997).

Together, the results obtained from this approach show several achievements for the first time: (A): that each functionally specialised area has properties so unique, and that the voxels constituting it have properties that are so common, that functionally specialised areas can be recognised and segregated without a priori knowledge from whole-brain activity measured as BOLD signal; (B): that the subdivision of the cortex into functionally specialised areas is more apparent in natural viewing conditions when many visual attributes are presented simultaneously than in simple on/off paradigms; (C): that in natural viewing conditions, the left- and right-hemispheric parts of a bilateral visual area have a higher correlation of their activity time courses than any other two areas of the cerebral cortex; (D): that a single area, in this case ORA, has distinct parts, each of which preferentially communicates with one of the surrounding areas (KO, V3, V5); (E): that this method can be used to reveal what we call the chronoarchitecture of the brain: the dissection of the brain into its functional modules

entirely based on their activity pattern in time, and their visualisation in terms of their degrees of activity at any given time. In sum, our approach allows the detection of functionally specialised areas and their characteristic activity time course and it allows the identification of groups of co-operating areas. It might be useful to help charting unknown cortical areas, and it might even help in the identification of the function of unknown areas, namely by reversely correlating their activity time courses with properties of the stimulus applied.

3. Toward a theory of visual consciousness

The results obtained from the above two major studies, of the architecture of the colour centre, which shows it to be composed of two subdivisions, and of the chronoarchitecture of the cerebral cortex, which shows it to consist of several, temporally independent areas, have led me to consider theoretically the kind of overall general organisation that the visual brain could have. Given the high degree of specialisation that some of the visual areas have, such as V4 for colour and V5 for motion, the selective perceptual deficits associated with damage to each, and the unique and different time course of activity in each, it seemed important and indeed mandatory to enquire whether all these areas are engaged together in the generation of conscious experience. Undertaking this task, which amounts to another experiment if only a thought experiment, was one of the most exciting outcomes of this work. This is because there is, on reflection, a logic that ineluctably leads to a set of conclusions different from those reached in the past. These conclusions are introduced below under the overall headings of the theory of perceptual sites and that of microconsciousness.

3.1. The modularity of processing and perception

The visual brain consists of several parallel, functionally specialised processing systems, each having several stages (nodes), which terminate their tasks at different times; consequently, simultaneously presented attributes are perceived at the same time if processed at the same node, and at different times if processed by different nodes. Clinical evidence shows that these processing systems can act fairly autonomously. Damage restricted to one system compromises specifically the perception of the attribute that system is specialised for; damage to a given node of a processing system that leaves earlier nodes intact results in a degraded perceptual capacity for the relevant attribute, which is directly related to the physiological capacities of the cells left intact

by the damage. By contrast, a system that is spared when all others are damaged can function more or less normally. Moreover, internally created visual percepts - illusions, afterimages, imagery and hallucinations - activate specifically the nodes specialised for the attribute perceived. Finally, anatomical evidence shows that there is no final integrator station in the brain, one which receives input from all visual areas; instead, each node has multiple outputs and no node is recipient only. Taken together, the above evidence leads us to propose that each node of a processing-perceptual system creates its own microconsciousness. We propose that, if any binding occurs to give us our integrated image of the visual world, it must be a binding between microconsciousnesses generated at different nodes. Since any two microconsciousnesses generated at any two nodes can be bound together, perceptual integration is not hierarchical, but parallel and postconscious. By contrast, the neural machinery conferring properties on those cells whose activity has a conscious correlate is hierarchical, and we refer to it as generative binding, to distinguish it from the binding that might occur between the microconsciousnesses.

Different workers have approached consciousness for different reasons, with different tools and in different experiments. Our approach is dictated in part by a philosophical view of the functions of the brain and in part by the unexpected results of two sets of experiments; these, interpreted against the background of what we have learned about the visual brain in the past twenty five years, have led us ineluctably in the direction which we expose here. Our philosophical view can be summarised by saying that the function of the visual brain - and indeed of much of the brain - is to acquire knowledge about the world. But since humans acquire knowledge mainly in the conscious state and since consciousness is an omnipresent product of human brain function - whether as main product or as unavoidable by-product, as precondition or as consequence - any physiological study of the visual brain, and indeed of the whole brain, becomes unavoidably a study of consciousness. The unexpected results of two sets of experiments previously undertaken in this laboratory gave urgency to this view and enabled us to bring under one heading - that of consciousness - diverse results from different fields of neuroscience. The evidence derived from each one of these sources or from individual experiments, on their own, may seem unsatisfactory and leave many questions unanswered. But when all the results are viewed together, the evidence for the view that we propose here becomes compelling.

The first unexpected result was derived from an experiment which undertaken to study the visual capacities of a subject deprived of vision by a lesion in V1 sustained during childhood. It had been supposed from the published literature on "blindsight" (Weiskrantz, 1990) that the patient would be able to discriminate the direction of

motion of stimuli in his visual field without having a conscious awareness of having seen anything. Imaging results (Barbur, Watson, Frackowiak & Zeki, 1993; Zeki & ffytche, 1998), showed that the subject was not only able to discriminate correctly the direction of motion of fast moving stimuli presented to his blind field but was also conscious of having seen them. This immediately showed that preprocessing or postprocessing of visual stimuli by V1, or reciprocal integration of activity between higher areas and V1, as envisaged by theories of "re-entry" (Edelman, 1989; Engel, Fries, König, Brecht & Singer, 1999), are not necessary conditions for conscious awareness. Indeed it showed that activity in areas disconnected from V1 can have a conscious correlate, a finding instrumental if not unique in leading us to the supposition that activity at any given stage of a processing system can have a conscious correlate. We note that if the result had been what we had predicted from the published literature, namely that such a patient would be able to "see" without having any conscious awareness of having seen, then the theory proposed below would not necessarily be wrong. But then, we may not have formulated it either.

The second set of unexpected results came from psychophysical experiments. Given the unity and wholeness of our vision, most had supposed that different attributes of the visual scene are processed at the same time or at least that an integrator area or process would bring the results of the processings undertaken by the different systems together to provide an integrated image, one in which all the attributes of vision are seen in perfect temporal and spatial registration. But the assumption had not been tested. When this was done, it turned out that when two attributes of vision, for example colour and motion, occur at the same time, they are not necessarily perceived at the same time (Moutoussis & Zeki, 1997b; Moutoussis & Zeki, 1997a; Zeki & Moutoussis, 1997) and that colour is in fact perceived before motion. This argued for an autonomy of the two processing systems and, by extension, for an autonomy of other processing systems as well. Again, if our result had been of the expected variety and had shown that colour and motion are perceived at the same time, one would not conclude that our theory is wrong. But, once again, we would have been less motivated to formulate it in the first place.

As it happens, these two cardinal results are mutually supportive and in turn receive support from other lines of evidence. The whole, taken together, have led us in the direction that we outline below. The two cardinal experiments alluded to above were thus mere catalysts in bringing together conceptually, and under the banner of consciousness, many different studies, including especially new psychophysical ones on relative perceptual times (Zeki & Bartels, 1998c). Each group of results, some old and some new, leads us to a proposition. Some of these are so well known that to repeat

them is to appear trite and invite ridicule; others are more novel and radical. If we thus condense the results of experiments into propositions here, it is because these propositions form a mutually supportive and linked chain which leads us ineluctably to our current view. Our view differs, perhaps significantly, from other views about integration, binding and consciousness. We take little pride in this but only plead that we were driven in our direction by the logic that links the findings that are at the basis of our formulation. We were of course impressed most by the experiments of which we have first hand knowledge, namely our own, and by such reading as curiosity drove us to in the light of our results. In the process, we may have missed other important findings and perhaps even done an injustice to others. For this we apologise.

3.2. The parallel processing systems of the visual brain

We take it as accepted by most, if not all, workers that the visual brain consists of many different visual areas, each having a distinctive pattern of connections and each undertaking its task simultaneously and in parallel with the others (Zeki, 1975). The principle of the multiplicity of visual areas (Zeki, 1969a; Allman & Kaas, 1971; Zeki, 1971; Allman & Kaas, 1974) has now been established beyond doubt through the work of many, even though the actual number of distinct areas has increased and remains uncertain (Felleman & Van Essen, 1991). Each area has highly specific connections, with V1 and V2 on the one hand, and with further areas in the temporal, parietal and frontal lobes on the other. The connections between the blobs of V1, the thin stripes of V2 and V4, all of them involved with colour, and the connections between layer 4B of V1, the thick stripes of V2 and V5, all involved with motion, are good representative examples and too well known to chart in detail here (Livingstone & Hubel, 1984a; Hubel & Livingstone, 1987; DeYoe & Van Essen, 1988; Zeki & Shipp, 1988). We therefore define a processing system as one which includes the specialised cells of V1 and V2 (housed in specialised compartments within these two areas) and the specialised areas to which they project; beyond that, we also include in the processing system the further projections of a specialised area. Examples of the latter may be found in the motion related cortex that surrounds area V5 and is reciprocally interconnected with it (Zeki, 1980; Wurtz, Yamasaki, Duffy & Roy, 1990; Howard, Brammer, Wright, Woodruff, et al., 1996) or the areas to which V4 connects in the medial temporal lobe (Desimone, Fleming & Gross, 1980; Zeki & Marini, 1998). We do not equate these parallel systems with the M and P pathways (e.g. Livingstone & Hubel, 1988). Too many studies have shown that systems previously thought to have been derived exclusively from the M pathway have a significant P input and vice versa (e.g. Saito,

Tanaka, Isono, Yasuda & Mikami, 1989; Maunsell, Nealey & DePriest, 1990). Rather, we believe that a processing system will draw upon any input to undertake its function (Zeki & Shipp, 1988).

We further accept that different processing systems are specialised to undertake different tasks (Zeki, 1978a; DeYoe & Van Essen, 1988; Livingstone & Hubel, 1988; Zeki & Shipp, 1988). The evidence for this is derived from studies of anatomical connections, physiological properties and clinical cases and is alluded to throughout this review. The contrary view, with which we do not agree, states that there is no specialisation within V1 or V2 (Lennie, Krauskopf & Sclar, 1990; Leventhal, Thompson, Liu, Zhou & Ault, 1995; Gegenfurtner, Kiper & Fenstemaker, 1996) or indeed in the visual cortex at large (Schiller, 1997)..

This leads to *Proposition 1*: *The visual brain consists of parallel, distributed, and functionally specialised processing systems.*

3.3. The basic anatomy of the parallel processing systems

There is of course a wealth of detail concerning the connections of the processing systems and the stages that constitute them. We do not review these here but concentrate only on those aspects that are of special interest to us in the context of elaborating views on microconsciousnesses.

(a) Each processing system consists of several stages which we refer to as *nodes* (Bartels & Zeki, 1998b). As an example, we give the motion system consisting of layer 4B of V1, the thick stripes of V2, area V5 and other motion-related areas surrounding it. Each one of these constitutes a node of the motion processing system and the forward connections within this processing system are of the 'like-with-like' variety. By this we mean that the directionally selective cells of layer 4B connect with area V5 which is also rich in directionally selective cells, either directly or through the thick stripes of V2, which also contain directionally selective cells (Zeki, 1969b; Lund, Lund, Hendrickson, Bunt & Fuchs, 1975; DeYoe & Van Essen, 1988; Zeki & Shipp, 1988; Shipp & Zeki, 1989a; Shipp & Zeki, 1989b). Equally, the colour system extends from the blobs of V1, to the thin stripes of V2 and from there to V4, all containing wavelength selective cells; beyond V4, it extends to areas in the inferior temporal cortex. Each one of these stages in this processing system constitutes a node, the

forward connections within the entire processing system being again of the 'like-with-like' variety (Zeki & Shipp, 1989; Nakamura, et al., 1993). By 'node' or 'stage' we therefore refer either to a whole area, such as V4 or V5, or to the functional subdivision of an area, such as the blobs and interblobs of V1, or the thin, thick and interstripes of V2 (Bartels & Zeki, 1998b). The consequence of a 'like-with-like' forward connectivity is to enlarge receptive fields and to confer different, and often more complex, properties on cells in a given node, compared to the antecedent one, in hierarchical fashion (e.g. Hubel & Wiesel, 1962). We emphasise here what we shall detail more generally below, namely that not all of these nodes need be simultaneously or sequentially active for visual perception to occur.

Proposition 2: *Forward connections within a processing system are of the 'like-with-like' variety and lead to cells of increasing receptive field size and complexity in hierarchical fashion.*

(b) There are many anatomical opportunities for the nodes comprising the different processing systems to communicate with each other. These connections, which we refer to collectively as lateral connections because they constitute links between different processing systems, can be conceptually subdivided into three varieties, and share the common property that they differ from the 'like-with-like' variety in that they also include 'like-with-unlike' connections: (i) lateral connections between nodes, which can be of the 'like-with-like' variety as in the 'blob-to-blob' connections within V1 (Livingstone & Hubel, 1984b) or of the 'like-with-unlike' variety, for example the lateral connections that link the thick and thin stripes of V2 (Rockland & Lund, 1983; Rockland, 1985; Lund, Yoshioka & Levitt, 1993; Levitt, Yoshioka & Lund, 1994); (ii) direct connections between the specialised areas, e.g. the direct link between V4 and V5 (see Felleman & Van Essen, 1991 for a review), which in our evidence are not especially strong; (iii) the return connections from the specialised areas, back to the areas feeding them (Shipp & Zeki, 1989b; Shipp & Zeki, 1989a; Rockland, Saleem & Tanaka, 1994; Rockland & Van Hoesen, 1994). All three could be categorised as being of the 'like-with-like' and 'like-with-unlike' varieties: the connections within V1 can be of the blob-to-blob or the blob-to-interblob variety, and much the same is true of the connections between the stripes of V2 (Rockland, 1985). Moreover, in contrast to the forward connections from V1 and V2 to V4 and V5, the return connections from these specialised areas to V1 and V2 are diffuse. For example, while the output from V1 to V2 and from V2 to V5 obeys the 'like-with-like' principle (see above), the return input from V5 to layer 4B of V1 is not restricted to the territory of directionally selective cells in that layer, but is much more diffusely spread and includes the territory of cells that project elsewhere (Shipp & Zeki, 1989a). Similarly,

the return input from V5 to V2 is more diffuse and not restricted to the territory of the thick stripes but includes that of the thin stripes and interstripes as well (Shipp & Zeki, 1989b); a similar diffuse projection has been found from V4 to V2 (Zeki & Shipp, 1989). The motion and colour systems thus have the anatomical opportunity of communicating with each other through these return projections as well as through direct lateral connections. What is surprising, given the wealth of these 'like-with-unlike' anatomical opportunities, is how stable the properties of cells in the visual nodes are. Most orientation and direction selective cells are indifferent to the colour of the stimulus and most wavelength selective cells are indifferent to the form or direction of motion, even after prolonged stimulation with an attribute to which they are not selective. Moreover, many motion selective neurons are indifferent to texture or form of the moving object (Albright, 1992). On the contrary, in spite of these lateral connections, the majority of cells within a given processing system continue to be concerned with a given attribute of the visual scene rather than with all attributes. If these lateral connections mediate any integrative role, then that role and its consequence have yet to be discovered, although it remains possible that they help to derive one attribute (*e.g.* motion) from another (*e.g.* form) (Zeki, 1993b) or be important in conflict conditions, as when, because of their small receptive fields, the directionally cells in V1 signal component motion which does not represent the true direction of motion signalled by cells in V5 (Zeki, 1993b). A central claim of the temporal binding hypothesis (Malsburg & Schneider, 1986; see also Engel, et al., 1999) and of other integrative proposals (Gegenfurtner, 1997) is that the binding of different attributes is mediated by a special temporal relationship (e.g. synchronous firing) between two or more specialised areas. While this imaginative proposal may well turn out to be true, it is worth noting that, in spite of the many anatomical opportunities mentioned above, there is no present compelling evidence for it in terms of activity between visual areas that process different visual attributes of the visual scene. Thus, whereas the properties of the forward projecting anatomical system can be used to account for the properties of cells at successive stages within a processing system, there is no known common characteristic feature that emerges from the lateral connections. Moreover, though the forward 'like-with-like' connections within a processing system are hierarchical, the lateral ones are not, by definition.

This leads to Proposition 3: *The lateral interconnections that link anatomically the different processing systems can be of the 'like-with-like', the 'like-with-unlike' or the diffuse variety and are not exclusively hierarchical; they do not appear to bring about cells that integrate different sub-modalities.*

(c) *Overall anatomical characteristics of nodes*: There are other features of the anatomy of the multi-node processing systems that are worth emphasising. First, there is no node that constitutes a terminal stage in a processing system, since there is no known node that is recipient only. Each node receives inputs and sends outputs (Zeki, 1993b); indeed, each has multiple outputs, as if the result of the operations that each performs is of interest to several other areas. Anatomical evidence shows that there is no single area to which all the specialised visual areas connect, which would enable it to act as an integrator capable of binding signals coming from all the different visual sources. There are in fact common areas to which two different processing systems project. But when this happens each input appears to maintain largely its own territory within the common recipient area, with minimal convergence or overlap with other inputs, thus leading us to speak of a *juxtaconvergence*e (Shipp & Zeki, 1995). Each node is therefore only part of a more extensive processing system, which includes, besides subcortical stations, areas in the temporal, parietal and frontal cortex. The latter areas, too, constitute only parts of the processing system, since they all project to further areas and are reciprocally linked with the earlier visual areas from which they receive input.

This leads to Proposition 4: *There is no 'terminal' station in the cortex for a given processing system and no common 'terminal' area to which the different processing systems connect.*

3.4. Integration and binding within and between processing systems

Most discussions of integration and binding do not give adequate definitions of the terms, assuming them to give one at all. But the intended meaning is quite clear: it refers either to the "integration" or the "binding" of what is processed by the different processing systems (that is, the binding of different attributes) or, more commonly, to the "binding" of the responses of cells within a single processing system. In the latter instance, it is supposed that this binding distinguishes the firing of the "bound" cells from that of all others and constitutes the neural basis for the kind of perceptual salience that is evident in figure-ground segregation (Engel, et al., 1999). A much studied example is whether two cells that are specific for the same orientation but with receptive fields located in different parts of the field of view will synchronise their responses (or have responses that will oscillate together) when a single long line of the appropriate orientation falls on the receptive fields of both, as opposed to a condition in

which the line is discontinuous and more or less restricted to the individual receptive fields of the orientation selective cells (Engel, et al., 1999). Crick & Koch (1990a) have distinguished three kinds of binding. The first two are based on the developmental processes and on expertise; the third one is what they call ad hoc binding. For our purposes, we need a more extensive and inclusive definition of binding or integration. This is not a mere periphrastic exercise but is important for our theory of multiconsciousnesses. This supposes that activity at each node can become perceptually explicit (that is, require no further processing to create a conscious percept) and therefore have a conscious correlate and that visual consciousness therefore consists of many microconsciousnesses (Bartels & Zeki, 1998b; Zeki & Bartels, 1998a). The information that is explicitly present at a node (in the form of neuronal activity) is rendered explicit not only by virtue of the input to it, but also because of its anatomical machinery and specialised physiological capacities, which can partially be thought of as memory and thereby as implicitly stored information. Because nodes within a single processing system are hierarchically connected *(Proposition 2)*, the input to one node may implicitly contain part of the information rendered explicit in it. By implicit information we mean information that requires further processing at the same or at further sites to become perceptually explicit. We consider that the enlargement of receptive fields as one progresses from the lateral geniculate nucleus to V1, or from V1 to V2, or from V1 to V5, are examples of physiological integration which have perceptual and therefore conscious consequences, especially since this kind of binding is accompanied by a modification of receptive field properties. This enlargement therefore confers on cells at a node unique information which is not explicitly present at nodes above or below it; it generates new 'experiential' cells (Zeki, 1993b) whose responses are perceptually explicit, and what becomes perceptually explicit reflects the physiological capacities of the cells at that node. For example, direction selective cells in V1 and V5 signal the motion direction of the components of a moving complex pattern, whereas other V5 cells respond to the motion direction of the whole pattern (Movshon, Adelson, Gizzi & Newsome, 1985; Rodman & Albright, 1989). The combination of physiological and psychophysical experiments in monkey revealed that the reliability and sensitivity of neurons in V5 equals that of the behavioural response (Newsome, Britten & Movshon, 1989; Britten, Shadlen, Newsome & Movshon, 1992), suggesting that a conscious percept might be based on activity of only few cells in a node.

A more compelling example is to be found in the colour system. The enlargement of the receptive field properties of the wavelength selective cells as one progresses from V1 to V4 is accompanied by a qualitative jump - the responses of the cells in V1 correlate with wavelength composition alone whereas the responses of some

cells in V4 correlate with perceived colour, irrespective of precise wavelength composition (Zeki, 1983a). This qualitative jump, we presume, is brought about because the enlargement of the receptive fields in V4, which often have large suppressive or excitatory surrounds (Zeki, 1983b; Desimone, Moran, Schein & Mishkin, 1993) enables them to undertake the comparisons that are critical for generating constant colours (Land, 1986). But we are conscious both of the constancy of colours and of changes in wavelength composition coming from a given part or from the whole of the field of view. Each stage can therefore make a direct contribution to conscious perception, but of a different variety, as is also suggested by the clinical evidence (see below).

We therefore distinguish between two types of binding or integration (two terms which we use interchangeably); these differ from each other in physiological implementation and type of neuronal code used:

(a) *generative binding*, which is always hierarchical and preconscious. It generates cells with new receptive field properties, is accompanied by receptive field enlargement and is mediated by a "like-with-like", "bottom-up" input. It combines the activity of two or more cells onto a third cell in a reliable and reproducible fashion, and the response of the third (receiving) cell depends entirely on the firing of the cells feeding it. The example of V4 cells given above is one among many. Other examples may be found in the generation of simple cells of V1 from centre-surround cells (Hubel & Wiesel, 1962), disparity cells in V3 from the orientation selective cells of V1 (Zeki, 1978b; Poggio, Gonzalez & Krause, 1988), and face selective cells (Perrett, Rolls & Caan, 1982) which combine input from lower level cells. Generative binding thus results in new classes of experiential cells, whose activity has a conscious correlate. Since this conscious correlate is restricted to the visual domain for which that class of cell is specialised, we refer to it as a microconsciousness. We refer to this kind of binding as preconscious because it is the process of binding itself that generates a new class of cell, whose activity can have a conscious correlate. Since, within each system, enlargement of field size and consequent modification of response is strictly hierarchical *(Proposition 2)*, it follows that generative integration is also strictly hierarchical.

(b) *parallel binding*: here we refer to the coupling of the activity of cells - e.g. through synchronous or oscillatory firing or any other form of communication - within a single area or across different areas. In view of our theory, which supposes that activity at each node has a conscious correlate, we consider this binding to be postconscious, since it is the microconsciousness generated at a given node of one processing system

that is bound to the microconsciousness generated at a given node of another (or the same) processing system. We hypothesise that mere communication between areas will not result in a microconscious correlate. It is only the cellular activity at the nodes which does so. Therefore, "binding" must result in a change of the activity at the nodes involved so that altered microconsciousnesses are generated at each. The binding can also be between two groups of cells at a given node, whose activities have a conscious correlates. Unlike its generative counterpart, post conscious integration does not entail receptive field enlargement or modification, since it does not necessarily entail the bringing together of the responses of two cells onto a third cell. It may instead require a form of communication (e.g. synchronous or oscillatory firing) between two sets of cells which are grouped together by a neural code that is different and independent of the one that codes for the feature specificity of cells. Preconscious binding need not affect the cells whose response is integrated because their output is integrated in a third, recipient cell. An example for parallel binding is to be found in the cells of the visual brain that have receptive fields at the midline and that are commonly thought to mediate the interhemispheric integration that links the separate representation of the two hemifields, giving us an unbroken view across the midline. Yet physiological studies show that many, if not most, of these cells, especially in areas V1 and V2, do not have larger receptive fields than cells which represent central, but not midline, parts of the field of view and most commonly have fields that do not cross the midline, or do so only marginally (Van Essen & Zeki, 1978).

As well, unlike generative binding, parallel (postconscious) binding is not hierarchical *(Proposition 3)*; the microconsciousness generated by the activity of cells at any given node of a processing system can be bound to the microconsciousness generated by the activity of cells at any given node of another processing system (see below under the theory of multistage integration). Nor is this restricted to integrating the activity of different nodes between different systems; it could equally apply to integrating the activity of cells within a specialised system. This can be exemplified by the type of binding reported to exist between cells within a given node, namely the synchronisation between the responses of two groups of orientation selective cells with receptive fields at different locations, when they are both responding to a continuous line of the same orientation (see Engel, et al., 1999). Activity at each has a microconscious correlate (our hypothesis) and it is these microconsciousnesses, we believe, that would be brought together in such an example. Here we depart from the more common belief that it is the binding itself that brings about the conscious experience (e.g. Crick & Koch, 1990b; Engel, et al., 1999).

This distinction between generative and parallel binding has not been made before, but it has been proposed that what is called parallel binding facilitates figure-ground separation (binding within a node) or brings different visual attributes such as colour and motion together through the synchronous or oscillatory firing of cells in different nodes (Malsburg & Schneider, 1986; Engel, et al., 1999) and that this is necessary for generating conscious perception (Crick & Koch, 1990b; Singer, 1998; Tononi & Edelman, 1998). Despite its theoretical attraction, there is no unanimity of view that synchronous or oscillatory firing in this context is of functional or perceptual relevance (Lamme & Spekreijse, 1998) nor is it known how the synchrony is generated, that is, whether it is of a top down, bottom up or thalamo-cortical nature (Llinás, Ribary, Contreras & Pedroarena, 1998). The evidence we present below leads us to the view that parallel (or postconscious) binding, supposing it to occur, may not be necessary for the normal functioning of nodes, including the generation of a microconsciousness.

This leads to *Proposition 5: Generative or preconscious integration is hierarchical and limited to a given processing system; it leads to a new class of receptive field properties* and to

Proposition 6: parallel or postconscious integration is not hierarchical and can occur between different nodes of different processing systems as well as within a single node.

The distinction between preconscious and postconscious binding is important for the theory of multistage integration proposed later in the thesis.

3.5. The asynchrony of consciousness

We are conscious of what we perceive, and are not conscious of what we do not perceive and do not perceive what we are not conscious of. This makes it interesting to consider whether two visual events which occur together in real time are also perceived simultaneously; this amounts to asking whether we become conscious of the two events simultaneously. Intuitively one would suspect this to be so, since in our daily experience we perceive different modalities coherently (i.e. with precise spatiotemporal registration). But there is a large body of evidence which shows that different modalities (e.g. audition and vision) are perceived with different delays from the time of stimulus onset, in the subsecond range (Woodworth & Schlosberg, 1965). This is also

true of attributes within a modality. An example in vision is when subjects are asked to pair two rapidly alternating states of two attributes, for example a bar having one of two colours and one of two orientations. They are then found to consistently misbind attributes which occur at the same time, because the two attributes are perceived at different times. For example colour is perceived before orientation, which is perceived before motion, with about 30 ms and 40 ms lag times, respectively (Moutoussis & Zeki, 1997b) (**Figure 29**). This perceptual asynchrony within the visual system might presumably form the basis for the much studied illusory conjunctions (Treisman & Schmidt, 1982). It is a perceptual result that confirms psychophysically that neural processing of different visual attributes is segregated in the cortex; it is also one which those who have reported that all cells in visual cortex respond equally to all modalities (e.g. Gegenfurtner, Kiper & Fenstemaker, 1996) should ponder and address in time. The result implies that the colour processing system reaches its perceptual endpoint before the motion processing system. The consequence of this perceptual asynchrony is that, over brief periods of time, subjects misbind what happens in real time, attributing a colour at time *t* to a direction of motion that occurs at time *t - 1*. The brain thus does not necessarily bind together what happens in real time but appears instead to bind the results of the operations undertaken by its different processing systems, which require different amounts of time to complete their tasks. In the subsecond window, the brain therefore misbinds in terms of real time (Moutoussis & Zeki, 1997a; Moutoussis & Zeki, 1997b; Zeki & Moutoussis, 1997). What this result also implies is that there is no central perceptual integrator area that takes into account the different time lags of different systems with regard to real time, before binding their results together. It is important to emphasise that what subjects perceive consciously in these psychophysical experiments is the change in the two states, while they are pairing one with the other; they are not aware of what we measure, namely the difference in relative perceptual times. Given that subjects have to pay equal attention to both attributes in order to pair them, the controversial phenomenon of 'prior entry' (Cairney, 1975) is not relevant here. Collectively, this evidence supports the notion of a general asynchrony in perception, including visual perception.

This leads to the following propositions:

Proposition 7, *Another characteristic of the visual brain is a temporal asynchrony in vision and, reflecting the consequence of functional specialisation in the time domain, visual perception is therefore also modular*, and to

Proposition 8, *When two visual events occur together, they do not have to be integrated for each to be perceived*, and thus *a mutual integration of activity between different processing nodes is not necessary for the creation of a conscious percept.*

Moreover, since perception is accompanied by conscious awareness, we are further led to

Proposition 9, *Activity in each separate processing node generates a microconsciousness for the attribute for which that node is specialised. Consequently, there are several microconsciousnesses, corresponding to the activity of cells at different nodes within different processing systems.*

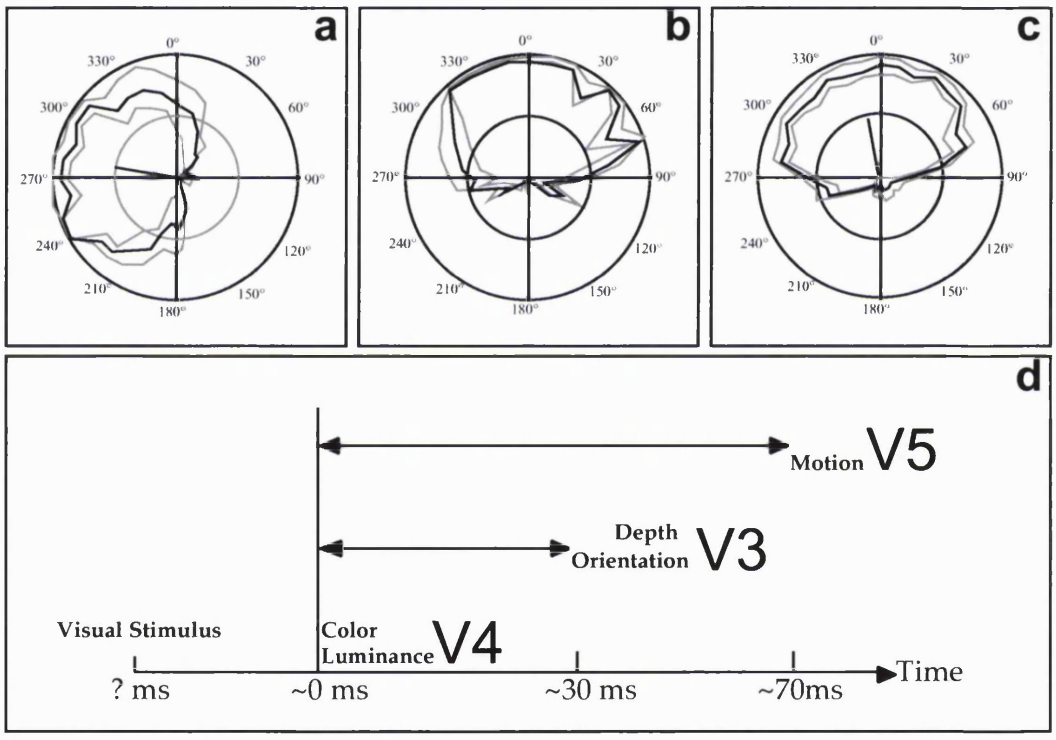

Figure 29. The theory of perceptual sites is based on evidence summarised in this figure. This theory supposes that attributes processed in the same node are perceived simultaneously, whereas attributes processed in different nodes are perceived asynchronously. The diagrams indicate the latencies with which one attribute is perceived with respect to another, averaged over 7 subjects. The full 360°circle corresponds to 573 ms in time. If two attributes (e.g. left-right motion and up-down motion) are perceived at the same time, the vector will show no displacement from 0°. Any displacement of the vector will indicate that one of two attributes is perceived before the other. In the examples given above, colour is perceived before motion (**a**) while left-right motion and up-down motion are perceived simultaneously (**b**). Depth and orientation are perceived at the same time (**c**). The relative perceptual times for different attributes are summarised in (**d**).

But not all visual events that occur together in real time are perceived asynchronously. We can ask subjects to pair two events belonging to the same attribute and known to be processed by the same system. For example, we can ask subjects to pair left-right motion in one half of a TV screen with up-down motion in the other. We then find that they perceive the two events that occur together at the same time (Moutoussis & Zeki, 1997b) (**Figure 29b**). We have used this evidence to enquire into the relative perceptual times of other attributes which the physiological evidence suggests are processed by the same system and even at the same node. A good example is to be found in area V3, in which cells are commonly selective for both orientation and depth (Zeki, 1978a; Zeki, 1979; Poggio, Gonzalez & Krause, 1988). Our experiments show that, when humans are asked to pair two different depths with two different orientations, they perceive the two at the same time (**Figure 29c**). This finding, along with other ones, has led us to our theory of perceptual sites (Zeki & Bartels, 1998c), which states that attributes processed at the same site are perceived at the same time and those processed at different sites are perceived at different times. There are other interesting examples of this perceptual synchrony, which we have used to formulate our theory and which may in fact shed an interesting light on functional specialisation in the visual brain in a roundabout way. It has been argued, for example, that the V4 complex is concerned with orientation, because of the presence of orientation selective cells in it (Zeki, 1975; Zeki, 1983c; Desimone & Schein, 1987), although the orientation selective cells of V4 are more broadly tuned than their counterparts in V1, V2 and V3 (Zeki, 1997). Another view is that V4 is less concerned with orientation as such, but with form in relation to colour (Zeki, 1997). If our theory of perceptual sites is correct, then we should be able to determine whether orientation and colour are actually processed at the same or different sites by simply noting whether they are perceived at the same time; in fact they are not (Moutoussis & Zeki, 1997b). Extending this yet further, we can ask whether orientations generated from random dot motion are perceived at the same time as orientations generated from equiluminant colours. Now we find that when subjects are asked to pair one of two orientations generated from equiluminant colour stimuli and presented in one half of a TV monitor with one of two orientations generated from random dot motion and presented in the other half, the two are perceived at the same time, as if the perception of orientation is mediated by a single area, regardless of how it is generated (Zeki & Bartels, 1998c and our unpublished results). We of course know that there are cells that are able to respond to their preferred orientation if the oriented line is generated from equiluminant stimuli (Gouras & Kruger, 1979; Thorell, De Valois & Albrecht, 1984). So far such cells have been studied in V1 only, but there is little reason to suppose that they may not be found elsewhere, nor any compelling reason to suppose that the V1 cells may not actually be at the basis of the perception. This leads us, as an aside, to suppose that V4 is not

concerned with orientation as such. We have used many such pairings and our studies have led us to a general conclusion, which constitutes

Proposition 10: *When two visual events that occur at the same time are perceived at the same time, it is because they are processed at the same site (node) and when they are perceived at different times, it is because they are processed at different sites (nodes).*

3.6. Microconsciousnesses are functionally specialised

If activity at each node of a given, functionally specialised, processing system can have a conscious correlate, it is obvious that the microconsciousness generated at that node is functionally specialised because it relates to the specialisation of the cells at that node. It would be difficult to conceive of the microconsciousness generated by the activity of cells in V5 to be related to colour or that generated by the activity of cells in V4 to be related to motion. This leads us to

Proposition 11: *The microconsciousnesses are functionally specialised, each microconsciousness being the reflection of activity in a particular, functionally specialised, processing node.*

The concept of microconsciousness perhaps requires some explanation. It has come as a surprise to many with whom we have discussed the issue because of the belief in the unity of consciousness, perhaps best enshrined in the famous dictum of Descartes "Je pense, donc je suis", although he did not intend to imply a unity of experience by that phrase; rather he introduced it to mean that the only sure knowledge that he had isd that of his own conscious existence. But this unity is not at all apparent to us, nor it seems is it apparent to philosophers (e.g. Dennett, 1991). In general, we are not aware of being aware. Instead, we are aware of events, or more generally of that which we are attending to at a given time. It is generally thought that a good guide to being aware is communication through language. But during that communication, we are still not aware of being aware but only aware of our interlocutor or the subject matter. We only become aware that our interlocutor is conscious in an inferential sense, in that he or she is conscious because they are able to conduct this conversation with us and could not do so unless they were conscious. But that awareness of consciousness is elicited only when the question is framed. Even in common conversation, we are conscious of a few things only, and commonly of one thing at a time only. Thus the

term microconsciousness may itself be a misnomer, because it implicitly supposes that there is a higher unified and singular conscious entity, beyond all the microconsciousnesses.

3.7. The processing systems are also perceptual systems

We now address the supposition that we have made in the above discussion, that the processing systems are also perceptual systems and that activity at each node of a processing system can have a perceptual and therefore conscious correlate. The evidence for this comes from electrophysiological and anatomical studies discussed above, greatly fortified by clinical studies, which were reviewed in the introduction.

Implicit in the term 'processing' is the supposition that it is preperceptual, a means of getting to the final percept, whatever that may be. This supposition itself makes implicit assumptions which are worth discussing. The most obvious of these is that there are separate processing and perceptual systems, or at any rate that the processing stages antedate the perceptual ones. In anatomical and physiological terms, this implies that the processing system feeds the results of its operation into the perceptual system. This may be true within an individual node. The results of Logothetis and his colleagues (Logothetis, 1998) have shown, for example, that at each node there are cells whose responses correlate with perception and others whose responses do not, and it is plausible to suppose that, physiologically, the latter are the precursors of the former. Imaging evidence suggests that activity in an area (node) must reach a certain height for a conscious correlate to be generated (Zeki & ffytche, 1998) but does not tell us whether that height is due to the intensity of response of cells, the number recruited or their synaptic activity. The evidence for the supposition that some nodes are purely processing ones and that they feed the results of their operations into other, purely perceptual, nodes does not exist. It would indeed be a somewhat inefficient way of encoding everything twice, once at the processing site and then again at the perceptual site. There is better evidence for our rival suggestion that the processing systems are also perceptual systems (Zeki, 1998), which leads us to speak of *processing-perceptual systems*. We now extend this concept, and *Proposition 9*, by proposing that activity at each node of a processing-perceptual system has a perceptual and therefore conscious correlate (Bartels & Zeki, 1998b). Evidence in favour of this is to be found in electrophysiological experiments which have shown that within each area, including area V1, there are cells whose responses correlate with percepts (Zeki, 1983a; Logothetis, 1998). Our supposition would gain weight if it can be shown that,

with a lesion at a given node of a processing-perceptual system, a patient is not totally deprived of the capacity to experience the attribute for which that system is specialised, but instead has a residual perceptual capacity for that attribute which is a direct reflection of the physiological capacities of the nodes of the affected processing-perceptual system that are left intact by the lesion. It is now generally accepted that, because much of the visual input to the cerebral cortex passes through V1, lesions here usually, but not always (see below), result in total blindness. This is probably also true for V2 (Horton & Hoyt, 1991) which is interposed between V1 and the more specialised areas of the brain and which, like V1, has all the attributes of vision represented in it (Hubel & Livingstone, 1987; DeYoe & Van Essen, 1988; Zeki & Shipp, 1988). What is perhaps more interesting is to look at the perceptual capacities of patients in whom V1 and V2 are not destroyed but who have lesions in the areas of the prestriate cortex to which they project. If there is any substance to our supposition that activity at each node of a processing-perceptual system has a perceptual, and therefore conscious, correlate then we should find that such patients are capable of experiencing every attribute save the one whose processing-perceptual prestriate component is lesioned. The literature on perceptual losses following damage to prestriate cortical areas that is reviewed in the introduction to this thesis confirms this hypothesis. It shows that lesions at specific cortical sites lead to specific perceptual defects, such as prosopagnosia, object agnosia, achromatopsia or akinetopsia, while sparing the remaining attributes. In addition, it shows that a lesion to a 'higher' cortical region does not affect the perceptual capacity of a 'lower' cortical region, highlighting that there is no final perceptual endpoint within a cortical pathway but that each component of a pathway has perceptual capacities, such that e.g. a patient suffering from object agnosia can still see the components objects are made up of while not being able to see the object as a whole.

This leads us to Proposition 12: *Damage to the prestriate component of a specific processing system does not lead to the total loss of the capacity to see and understand the relevant attribute. Instead, the patient is left with a residual capacity to see and experience the elements of that attribute.*

3.7.1. Clinical evidence for conscious experience of an attribute not processed by V1

If processing is separate from conscious perception and antedates it, as is implicit in the term "processing", and if processing and perceptual sites were spatially separated in the brain, then one would expect that removal of a cardinal processing stage would lead to a condition in which neither the percept nor its conscious experience would be possible.

But what if the contrary is true, and activity at each node of a processing system does have a conscious perceptual correlate, even if it is disconnected from an antecedent cortical node which would be expected to process the signals in readiness for its perceptual experience? Such evidence does exist and comes from a study of the Riddoch Syndrome (Zeki & ffytche, 1998). This results from lesions of area V1 and was first described by George Riddoch during the Great War (Riddoch, 1917). So improbable were his conclusions that they were immediately dismissed by Holmes (1918) and relegated to oblivion for about 70 years (Zeki, 1991).

Riddoch had been studying British soldiers hit by enemy fire and blinded by lesions to their occipital cortex, and more particularly area V1. His perimetric studies had shown that, though blind when tested with static perimetry they were not so when tested with dynamic perimetry. Crucially, he repeatedly describes his patients as being "conscious" of the motion, but not of much else besides (Riddoch, 1917). He explains, for example, that "patients with restricted visual fields from occipital wounds...were immediately conscious of 'something' moving" but he also writes that conscious awareness was restricted to the perception of visual motion, the subjects being "...quite sure that neither shape nor colour could be attributed to [the movement]', the nature of the movement being "vague and shadowy" (Riddoch 1917). His explanation for this phenomenon was improbable: he supposed that the mechanisms of visual motion within V1 were spared, which is why his work was so easy to dismiss. But more recent studies confirm his observations. For example, our study of patient GY (Barbur, et al., 1993; Zeki, 1997), blinded by a lesion to his occipital lobe during childhood, showed that the patient could not only discriminate accurately the direction of fast moving, high contrast, objects but that he was conscious of the direction of motion, in that he could describe it verbally. Interestingly, he first told us that the movement he saw was that of shadows, similar to the perception of motion when a normal individual, with eyes closed, can perceive the shadow when a hand moves against daylight. Later, he described this percept as that of a dark shadow against a dark background and a "feeling" that something was moving. An examination of the "blindsight" literature for other patients blinded by lesions in V1 shows similarly that they are commonly conscious of the visual stimuli presented to their blind fields (Zeki & ffytche, 1998). Sometimes subjects have a "feeling" but are "absolutely sure of it" (Weiskrantz, 1986) sometimes they see "shadows" or "pinpoints" of light (Weiskrantz, 1986; Zeki & ffytche, 1998 for a review). Imaging studies show that area V5 is active when GY is shown fast moving stimuli which he can experience consciously (Zeki & ffytche, 1998). It would thus seem that preprocessing by area V1 is not a necessary precondition for the conscious experience of motion and that the notion that "conscious vision is not

possible without V1" (Stoerig & Cowey, 1995; Stoerig, 1996) receives little support from these studies.

The ability of GY to experience consciously fast moving visual stimuli presented to his blind field is almost certainly the consequence of a direct input from the pulvinar to V5, an input that bypasses V1 (Cragg, 1969; Benevento & Rezak, 1976). It is because of this alternative input to V5, curiously described as one "which may not reach consciousness" (Bullier, Girard & Salin, 1994), that one can still obtain specific directionally selective responses from the cells of V5 in monkeys with lesions of V1 (Rodman, Gross & Albright, 1989; Girard, Salin & Bullier, 1992). In fact, the imaging and psychophysical experiments on GY show that the transfer of signals along an equivalent alternative pathway in the human not only activates V5 but that activity has a conscious correlate (Zeki & ffytche, 1998). Electroencephalographic experiments coupled with imaging ones have shown that this alternative pathway delivers signals from fast moving ($> 5^{\circ}$ sec^{-1}) objects to V5, in GY just as in normals, whereas signals from slowly moving ($< 5^{\circ}$ sec^{-1}) objects are delivered to V5 through V1 (Beckers & Zeki, 1995; ffytche, Guy & Zeki, 1995; ffytche, Guy & Zeki, 1996). It is not surprising to find therefore that GY is able to experience consciously fast, but not slow, moving stimuli. We do not suppose that only activity in V5 generates this conscious correlate. Imaging studies show that there are critical sites in the brain stem which are more active during conscious experience (Zeki & ffytche, 1998) and these may act as enabling systems - for example through neuromodulation. The point we are making here is that to perceive fast motion and have a conscious experience of it does not require the mobilisation of nodes antecedent to V5 in the V1-V2-V5 pathway.

The above results lead us to the conclusion that activity at a single node of a processing system, in this case the motion processing system, can have a conscious correlate, without necessarily involving antecedent stages of the visual pathways. This conclusion is supported by further experiments; for example, the fast circular motion that is perceived by humans when viewing the static work of Leviant entitled *Enigma* correlates with the selective activation of one node of the motion processing system, area V5 (Zeki, Watson & Frackowiak, 1993) while the motion after effect as well as mental imagery of motion correlate mainly with activation of V5 (Tootell, Reppas, Dale, Look, et al., 1995a; Goebel, Khorram Sefat, Muckli, Hacker & Singer, 1998). Similarly, the perception of afterimages induced by colour correlates with the selective activation of one node of the colour processing system, the V4 complex (Sakai, et al., 1995). Hallucinations constitute another condition that lends itself to isolating neural processing directly responsible for specific visual experiences. Patients suffering from the Charles Bonnet syndrome have visual hallucinations that can be rather restricted -

e.g. to the perception of objects, faces, colours or textures. The brain activities during such hallucinations have been located to the regions in the ventral occipital cortex that are specialised for the corresponding attributes (ffytche, et al., 1998) without involving V1.

This leads to Proposition 13, which is an extension of Proposition 9: *Activity at a node of a processing system which is deafferented from antecedent nodes can have a conscious correlate, provided there is an input to it.*

Evidence from functional imaging shows that it is the same cortical regions that are activated by a particular attribute which render patients unable to perceive the same attribute when lesioned. Our colour study adds to this by showing that the cortical region which is performing the ratio-taking operation to generate constant colours renders patients achromatopsic when lesioned.

This then adds to the clinical evidence reviewed above to suggest strongly that the processing site that is necessary for the generation of colours is the very site which, when damaged, leads to the syndrome of achromatopsia. It suggests, in summary, that the processing and perceptual site are one and the same.

The evidence presented in the above section leads us to Proposition 14, which is an extension of Propositions 9 and 13: *The processing sites and the perceptual sites are one and the same.*

3.8. The autonomy of the processing systems

Implicit in the above discussion, and especially those of sections III and IV, is the supposition that the different processing-perceptual systems are fairly autonomous of one another, that one can execute its functions more or less satisfactorily without the participation of the others. The admittedly incomplete clinical evidence does in fact suggest that the different processing systems operate with a fair degree of autonomy (Zeki, 1998). It has unfailingly and routinely shown that a lesion affecting the prestriate component of one processing system can lead to a specific perceptual incapacity, without affecting perception globally. This is implicit in all clinical evidence, reviewed above, which shows a specificity of defect. Good examples are those of achromatopsia, akinetopsia, prosopagnosia, and what we shall term kinetic and akinetic object agnosia, conditions in which patients may only be able to perceive forms when they are in

motion (Botez & Sebranescu, 1967; Bender & Feldman, 1972; Kertesz, 1979; Humphreys & Riddoch, 1987) or ones in which they are only able to see objects generated from luminance, not from motion (Regan, Giaschi, Sharpe & Hong, 1992). The pedants would argue that in many examples of lesions in the prestriate cortex, the incapacity is not limited to one attribute, and the pedants are actually quite right, as their habit usually is. Achromatopsia, as mentioned above, is commonly accompanied by prosopagnosia. This is a consequence of the opportunistic nature of lesions which are commonly not restricted to the territory of a given area. There is nevertheless a sufficient number of cases of achromatopsia unaccompanied by prosopagnosia (Michel, Perenin & Sieroff, 1986) , and vice versa (Duvelleroy Hommet, Gillet, Cottier, de Toffol, et al., 1997), to render the pedantic argument nothing more than a tiresome distraction requiring a patient explanation. It is noteworthy that, in the pure state, achromatopsic patients can recognise and name objects, directions of motion and depths; they can read and write and, to all intents and purposes, their general vision is good, apart from the achromatopsia.

The same specificity can accompany lesions that include the territory of human V5 but exclude other areas such as the fusiform gyrus. Here one finds that the resultant akinetopsia is not accompanied by an achromatopsia, prosopagnosia or object agnosia (Zihl, Von Cramon & Mai, 1983; Zihl, et al., 1991). Again, such patients can read, write, and detect depths and colours correctly, thus adding to the evidence of the autonomy of these areas. It needs to be added that the full gamut of defects that patients with specific lesions in the cortex suffer from is not necessarily known; patients are obviously more intensively studied for those defects which they spontaneously complain of. It is therefore possible that when such patients are studied in greater detail, and when more of them become available, the full extent of the disabilities will be better charted. But to a good first approximation, the syndromes described above are remarkably specific.

This leads us to Proposition 15: *The processing systems are fairly autonomous of one another.*

3.9. Integration is a multistage process

There are several lines of evidence which suggest that integration must be a multistage process. Perhaps the most suggestive is to be found in the facts of anatomy. Given that each processing-perceptual system is multinodal (*Proposition 14*), it is worth asking why the connections between the nodes constituting the different processing-perceptual systems occurs right from the start, at the level of V1 and V2 (*Proposition 3*), and why they are not deferred until after some terminal stage. The answer is simple: there is no terminal stage in the cortex (*Proposition 4*). Instead, activity at each node can have a perceptually explicit correlate (*Proposition 9*) and generate its own microconsciousness which is functionally specialised (*Proposition 11*) - if this were not so, the unique information present at each node would be lost for conscious perception. Given that in our ordinary daily life we see all attributes in perfect registration, it seems natural to suppose that the activity in the different processing systems is integrated. One would suppose that the perceptually explicit correlate generated by the functionally specialised cells at a given node must be capable of being integrated with perceptually explicit correlates generated by the activity of cells at other nodes. And hence the nodes are connected with each other, according to both the 'like-with-like' and the 'like-with-unlike' principles (*Proposition 3*). Because the 'like-with-like' pathway is strictly hierarchical and the 'like-with-unlike' pathway is not (*Propositions 2 and 3*), integration itself can be hierarchical or not, depending on whether it is of the preconscious or postconscious variety (*Propositions 5 and 6*). It seems important to emphasise that the connections between different nodes of different processing systems simply allow for communication and integration between them, but that each node can function rather autonomously, and this includes the generation of a microconsciousness. It remains to be investigated when and to which degree such parallel binding between nodes actually occurs in normal subjects in the daily life.

For activity at each node of a processing-perceptual system to have a perceptual (and therefore conscious) correlate (*Proposition 11*) confers advantages in that it increases the number of perceptual repertoires. This would be reduced if the processing systems had to report to a 'terminal' station - either a common one or individual ones - for integration to occur. Such an hypothetical integration area would have to code in a perceptually explicit way the results of the processing at each node separately as well as in the required combinations. A more economical way would be to render the activity at each processing site perceptually explicit, which can then be bound. The number of pairwise connections between N nodes equals N*(N-1)/2. Even given the constraints of cortical connectivity, this would still create a vast repertoire which would not be

possible if integration could only occur between 'terminal' points or 'final' stages. Our conjecture that each node corresponds to a perceptual site (*Proposition 13*) means effectively that there are far more such sites in the cortex than would be possible if there were only a "terminal" perceptual site for each processing system. Moreover, if the result of processing at a given node is not made perceptually explicit, it would be lost in later processing stages and no longer be perceptually accessible. The function of many nodes in a processing system is to discard some information in order to extract more global information. For example a picture of a face composed of small dots will activate areas whose cells respond to dots and other areas whose cells respond to faces. Neither of the two stages codes explicitly information that the other stage explicitly codes for. The only way to preserve both types of information - both the dots and the face - is to make activity in both areas perceptually explicit. It would be wasteful for the brain to make only the information of the anthropomorphically defined 'final stage' - the face area - perceptually explicit. Another example is colour vision. The cells in V1 and V2 which are sensitive to wavelength composition (Zeki, 1983a; Zeki, 1983b) cannot code for colour, which, by definition, remains stable despite changes in wavelength composition (Hering, 1877; Helmholtz, 1911; Land, 1974). It is the activity of cells in V4 that correlates with colour (Zeki, 1983a). The information that the cells in V1 and V2 code for excludes them from coding simultaneously for the information coded for by cells in V4 (and *vice versa*). Nevertheless we are aware of what each set of cells codes for - the colour of a surface and changes in the illumination condition.

If different and often mutually exclusive types of information are made explicit at different processing stages, it becomes tempting to suppose that percepts created at each stage of a processing-perceptual system can be bound to other percepts created by the activity at other stages within a given processing-perceptual system. This is especially so when activity in a single area is important for registering an attribute, no matter how that attribute is derived. For example, recent experiments show that the same area in the fusiform gyrus is activated when humans view objects generated from luminance and from motion (Bork & Zeki, 1998; Grill Spector, et al., 1998). But once generated from motion, for example, one would suppose that the form has to be reintegrated with an earlier stage of the motion pathway to bind the form to the direction of motion. However, the degree to which such binding of percepts is really necessary remains an open question especially since our perception may not be as unified as it is commonly believed to be.

Each processing-perceptual system has a certain hierarchical structure, by which we mean that the visual attribute is processed at a more complex level at a given stage than at the antecedent one (*Proposition 2*). The theory of multistage integration (Zeki,

1990b; Zeki, 1993b; Bartels & Zeki, 1998b) nevertheless supposes that there is no perceptual hierarchy in binding since the perceptually explicit activity of cells at a relatively "low" level in one processing-perceptual system can be bound with the perceptually explicit activity of cells at a relatively "high" level of another, or the same, processing-perceptual system. A good example is provided by a green bus as it emerges from the shade into sunlight. The bus remains a bus and its colour remains green, but the intensity of the light and even its shade change. The recognition of the bus as a bus requires the activity of cells in an area at a high level in the visual pathways (the fusiform gyrus) but the recognition of a change in the shade of green, and in both the intensity and wavelength composition of the illuminating light, depends upon the activity of cells in V1, and possibly V2. A functional corollary of this is that at any given time, many functional units - consisting of stages at different levels of different processing systems - are formed dynamically, with the same stages constituting different units with other stages at another time. The functional units that are formed therefore criss-cross between different stages of different processing-perceptual systems (Zeki & ffytche, 1998). It remains open whether these functional units are defined by binding, or whether the mere activity in an area is sufficient to make the generated percept part of our seemingly unified perception. They are in a dynamic state and the pattern of functional units formed between different stages of different processing-perceptual systems at any given time should be amenable to capture by imaging methods. The functional units formed will be further dynamically shaped by attentional and mnemonic factors.

3.10. Towards a theory of visual consciousness

The propositions that we have given above form a chain which leads us towards our theory of visual consciousness. We have more confidence in some than in others. We are, for example, very confident of Propositions 1 - 4, 7, 12 - 13 and 15. Although the remaining ones do not carry the same levels of confidence on their own, they are so consistent with each other and with the known facts that, when considered as a whole, they are able to lead us towards a theory of visual consciousness, which we outline below, and which might be applicable to other parts of the brain:

We suppose that visual consciousness consists of many, functionally specialised, microconsciousnesses which are spatially and temporally distributed if they are the result of activity at spatially distributed sites (as in the case of colour and motion). This we believe to be the direct consequence of the fact that the several, parallel, multinodal, functionally specialised and autonomous processing systems are also perceptual ones and that activity at each node of each processing-perceptual system can become perceptually explicit. Activity at each node therefore has a microconscious correlate which is functionally specialised and asynchronous with the microconscious correlate generated by that at other nodes. If integration occurs between different nodes, the communication between them must influence the microconsciousness that each creates in a consistent way, leading to consistent, integrated percepts. The communication itself does not create the bound percept. Since activity at each node can become perceptually explicit, it is imperative that the integration that may occur must be multistage and not hierarchical, leading us to the view that perceptual integration itself is multistage (indeed, our theory of multistage integration can be equally well called a theory of perceptual integration). It is therefore not surprising that there is no terminal station in the cortex, since activity at each node represents, in a sense, a terminal stage of its own specialised process, when it becomes perceptually explicit and acquires a conscious correlate. It is, we be believe, the communication between nodes that changes the nature of the microconsciousnesses such that they generate a mutually consistent and integrated image in the brain. This leaves us with the grand problem of how, in physiological terms, the microconsciousnesses are bound together. Indeed, it raises the question of whether they are bound at all, given what appears to be the non-unitary nature of conscious experience.

Conclusions

The studies presented here constitute collectively an investigation into the degree of the modularity of the visual brain and the extent of their autonomy. The literature reviewed makes it clear that the neuroscience community at large accepts the concept of a functional specialisation (Zeki, 1978a) in the cerebral cortex, but at the same time it becomes apparent that the extent of autonomy and specialisation assigned to a single area is still a matter of dispute. Some hold the view that visual areas are only marginally specialised, with each contributing to the processing of many different visual attributes (Schiller, 1997); others not only assign a specific processing function to a given area but go beyond that by suggesting that activity in a specialised area, e.g. V5, is responsible for the creation of a conscious percept (Zeki, 1993b), or plays a direct role in the decision process to initiate a motor action (Britten, Newsome, Shadlen, Celebrini & Movshon, 1996). In the work presented, this problem is attacked at three different levels: first, the localisation of a highly specialised function, namely the ratio-taking process of the colour constancy system, to a single cortical processing site, namely the V4-complex; second, the demonstration that it is possible to computationally dissect the human brain into functionally specialised areas, based entirely on the unique activity time course that distinguishes each area from one another; and third, the development of the theory of perceptual sites, which states that so specialised and autonomous are cortical areas, that their differential, inherent delays in processing lead to measurable delays in perception which are specific to the attributes processed by the respective areas, such that any two attributes that are perceived with a relative delay one to another must be processed in separate sites, while attributes perceived without a relative delay must be processed in the same site.

Our results, together with the literature reviewed, lead us to a viewpoint that might be considered as being rather extreme, in that we assign the highest possible degree of autonomy to individual cortical areas. Our hypothesis, that each cortical area is capable of generating a conscious percept for the attribute it is specialised for, which we refer to as a microconsciousness, is perhaps a rather daring one. But no matter

whether this will turn out to be false or true, we hope that it forms a conceptual basis on which future experiments can build.

Our investigation into the ratio-taking operation of the colour system led to results which confirm a high degree of autonomy of the visual areas. In contrast to previous imaging studies of the human colour system, which activated the whole cortical pathway involved in colour vision, namely V1, V2 and V4, the activation obtained in our study was mostly limited to the V4-complex, with very little or no activity in preceding areas. Instead of comparing brain activity related to coloured and grey stimuli, as was done in previous studies, we compared two types of equally coloured stimuli, one of which put a greater computational load on the ratio-taking system. Firstly, this confirmed the results obtained by electrophysiological recordings in macaque, showing that the cortical site of colour constancy calculations lies in the V4-complex. Secondly, our demonstration that this ratio-taking site consists of two separate cortical areas, V4 and V4α, lends itself to an explanation of the different degrees of colour constancy defects and time courses of recovery patients show after suffering lesions in the fusiform gyrus, since lesions may not always have affected the two subdivisions. We have demonstrated a different retinotopic organisation in the two areas and found an indication of a functional segregation of these two areas with regards to colours as properties of objects. It will be interesting to determine the stimuli that activate V4 and V4α most differentially, which will not be an easy undertaking.

The results obtained by applying ICA to fMRI data may constitute the strongest evidence presented in this thesis for the modularity and autonomy of different cortical areas. Using controlled fMRI paradigms and classical statistics (SPM) to determine functionally specialised areas, we were able to demonstrate that ICA isolated exactly the same functionally specialised areas, but this time entirely based on their differential spatio-temporal activity pattern and without any knowledge of data type or stimulation. The fact that ICA achieved this regardless of the stimulation, even when subjects watched a movie, shows that each of these areas had an associated activity time course which was as unique as a fingerprint - only in this way can an algorithm using no a priori knowledge, like ICA, isolate them. The unique activity time course of each cortical area is astonishing, given the rapidly changing stimulus provided by the movie, the sluggish nature of the BOLD signal that blurs the underlying neural activity, and the wealth of connections between all these areas that allow for their intense feedforward and feedback communication. This can only be explained by a highly distinct function each area undertakes, making it respond differentially to any given stimulus. ICA or similar methods can be used to create a map of the whole brain that reveals its putative subdivisions into distinct, functionally specialised areas, based entirely on their activity

time course: a *chronoarchitectonic* map. Compared to Brodmann's cyto-architectonic maps (Brodmann, 1909) these maps have a higher spatial resolution, because of the subdivision of many Brodmann's areas into several functional areas, and they have an immediate relation to cortical function. In addition to the spatial information they also provide information about the relationship that different areas have in time, e.g. when they - or better, the subject - are freely viewing a movie. The latter gives us for the first time the opportunity to study the temporal relationships of a vast number of cortical areas at once. Apart from making it possible to study the flow of information across the cortex in various conditions, it will also enable us to hierarchically group cortical areas according to the degree of similarity their activities have in time, thus possibly leading to a hierarchical cortical map of anatomical connectivity, which might share similarities with a hierarchical map of relative perceptual times.

As a thought experiment, it is interesting to note how constant chronoarchitectonic maps probably are across vastly different time scales: according to our *theory of perceptual sites*, percepts that have a relative delay to each other must be created by separate cortical areas. If one created a chronoarchitectonic map of the brain with regard to relative perceptual times, this map would turn out to be identical to the chronoarchitectonic map revealed by applying ICA to fMRI data, because both would isolate functionally specialised areas. The former map would be based on a time scale in the range of milliseconds, the latter on one in the range of seconds. But both will ultimately depend upon a pivotal physiological fact, namely that the areas of the visual brain are not only functionally specialised but also largely autonomous.

While the concept of the microconsciousness might be helpful to inspire future studies, it will require much more dramatic concepts to bring neuroscience closer to a solution of one of its grandest problems, namely a scientific explanation of the macro-consciousness, the personal experience of our sensations, and our feeling to be.

A crucial problem arising from the great autonomy assigned to visual areas here is the one of perceptual control: We have proposed that substantial activity in any visual area leads to a conscious percept of the attribute that area is specialised for, while in the absence of activity in the area specialised for an attribute no conscious percept of that attribute can occur: this is a consequence of our proposition that a specialised area creates a microconsciousness for the attribute it is specialised for. This view is confirmed by the literature: specialised areas are active in the absence of a physical stimulus when the subject perceives the attribute concerned (Le Bihan, Turner, Zeffiro, Cuenod, et al., 1993; Zeki, Watson & Frackowiak, 1993; Tootell, et al., 1995a; ffytche, et al., 1998; Goebel, et al., 1998) even if only a subset of the areas involved in imagery

and external stimulation overlap (Howard, Ffytche, Barnes, McKeefry, et al., 1998). The opposite has also been shown, in that the presence of a physical stimulus does not lead to activity in the area concerned, when the subject pays no attention to the attribute concerned, and probably also does not perceive it (Rees, Russell, Frith & Driver, 1999). The problem is that we do not yet understand how the brain can turn on and off the activity in particular areas, e.g. by ignoring a given stimulus, imagining visual scenes, paying attention to another stimulus, etc. There must therefore be ways in which higher cognitive areas can stir up or suppress activity in visual areas in order to arouse or suppress a particular percept, e.g. of a face, at free will. We have only little understanding of how this perceptual control might occur, and which areas are mandatory for this process, apart from the imperative involvement of the visual areas as mediators of the percept, as proposed in this thesis. Our understanding of the subjective sensation associated with activity of the visual areas is extensive and very precise, and stands in sharp contrast to our comparably vague and ambiguous knowledge of the candidate regions exerting control over the activity of these visual areas, probably parietal and prefrontal cortical areas. This sharp boundary of our knowledge between perceptual and decision-making processes might well reflect the qualitative jump in the required understanding which divides the two: while the former deals with the explicit neural representation of a visual feature, the latter touches the much more abstract process of decision making, planning and free will.

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