An investigation of the neural correlates of selective attention in humans using functional imaging

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Abstract

To what extent does perception depend on attention? The work presented here uses functional imaging to explore this question by examining whether stimuli produce brain activity when they are not directly attended. The effects of unattended stimuli on brain activity are explicitly measured by systematically varying the rate of presentation, identity or presence of ignored stimuli. First, the rate of presentation of visual and auditory information was varied to give an index of stimulus processing. Activity evoked by attended and unattended stimuli differs profoundly in a way that suggests that attention operates through two distinct physiological mechanisms. In sensory cortex, even ignored stimuli evoke rate correlated brain activity, suggesting processing of these unattended stimuli. Second, the consequences of such processing were studied by systematically manipulating the identity of ignored distractors. When distractors produced negative priming, subcortical structures including the striatum were active, suggesting a link between negative priming and implicit learning. Finally the determinants of unattended processing were explored in a series of experiments where perceptual load of the primary task was varied. The degree to which ignored stimuli were processed, even when highly salient, depended strongly on the perceptual load of the task and the availability of attention. In the case of single words, eliminating the availability of attention led to inattentional blindness, and no brain activity was evoked that related to their meaning. These findings suggest that attention has a pervasive influence on sensory processing in multiple cortical areas and that the perceptual load of a task is an important determinant of selectivity. Moreover the results suggest an intimate link between the availability of attention and perceptual awareness.
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CONTENTS

CHAPTER 1 INTRODUCTION .....................................................................................................................1-10

1.1 Framing the question ......................................................................................................................1-10
1.2 Psychological approaches .............................................................................................................1-11
1.3 Physiological approaches .............................................................................................................1-16
  1.3.1. Single cell electrophysiology .................................................................................................1-16
  1.3.2. Event related potentials .........................................................................................................1-20
  1.3.3. Functional imaging ...............................................................................................................1-22
     1.3.3.1. Attention to visual features ..............................................................................................1-22
     1.3.3.2. Attention to spatial location ............................................................................................1-24
1.4 Conclusions .....................................................................................................................................1-30
1.5 Thesis Material .............................................................................................................................1-32
  1.5.1. Experimental approach ........................................................................................................1-32
  1.5.2. Overview of work ................................................................................................................1-32

CHAPTER 2 GENERAL METHODS ...........................................................................................................2-34

2.1 Positron Emission Tomography ....................................................................................................2-34
  2.1.1. General overview .................................................................................................................2-34
  2.1.2. PET experimental design .....................................................................................................2-35
2.2 Functional Magnetic Resonance Imaging .....................................................................................2-36
  2.2.1. General overview ................................................................................................................2-36
  2.2.2. fMRI experimental design ...................................................................................................2-38
2.3 Comparing PET and fMRI .........................................................................................................2-40
2.4 Statistical Methodology .............................................................................................................2-42
  2.4.1. Realignment ........................................................................................................................2-42
  2.4.2. Spatial normalisation & smoothing ......................................................................................2-42
  2.4.3. Statistical Inference ............................................................................................................2-43

CHAPTER 3 NEURAL CORRELATES OF SELECTIVE ATTENTION ..........................................................3-45

3.1 Introduction .....................................................................................................................................3-45
  3.1.1. Single neuron mechanisms of selection ..............................................................................3-45
  3.1.2. Evoked potentials in humans ...............................................................................................3-46
  3.1.3. Functional imaging studies ..................................................................................................3-47
3.2 Two Physiological Correlates of Attention ..................................................................................3-51
  3.2.1. Introduction ........................................................................................................................3-51
  3.2.2. Methods ............................................................................................................................3-52
     3.2.2.1. Subjects and stimuli ......................................................................................................3-52
     3.2.2.2. Data acquisition and analysis .......................................................................................3-53
  3.2.3. Results .................................................................................................................................3-53
     3.2.3.1. Behavioural ..................................................................................................................3-54
     3.2.3.2. Functional Imaging ......................................................................................................3-54
  3.2.4. Discussion ..........................................................................................................................3-62
CHAPTER 4 NEURAL CORRELATES OF NEGATIVE PRIMING ..................................................... 4-86

4.1 INTRODUCTION ................................................................................................................. 4-86

4.2 METHODS ............................................................................................................................... 4-90

4.2.1. Subjects ......................................................................................................................... 4-90

4.2.2. Materials ....................................................................................................................... 4-90

4.2.3. Data acquisition and analysis ...................................................................................... 4-91

4.3 RESULTS .................................................................................................................................. 4-91

4.3.1. Behavioural .................................................................................................................... 4-92

4.3.2. Functional imaging ........................................................................................................ 4-94

4.4 DISCUSSION ............................................................................................................................. 4-101

4.4.1. Distractor processing ..................................................................................................... 4-101

4.4.2. Neural correlates of negative priming ............................................................................ 4-104

4.5 CONCLUSION ......................................................................................................................... 4-106

CHAPTER 5 PERCEPTUAL LOAD AS A DETERMINANT OF SELECTIVE ATTENTION .... 5-108

5.1 INTRODUCTION ..................................................................................................................... 5-108

5.1.1. A direct test of the perceptual load hypothesis ............................................................. 5-109

5.2 METHODS ............................................................................................................................... 5-110

5.2.1. Subjects and stimuli ...................................................................................................... 5-110

5.2.2. Data acquisition and analysis ...................................................................................... 5-113

5.3 RESULTS .................................................................................................................................. 5-114

5.4 DISCUSSION ............................................................................................................................. 5-118

5.5 ARE ATTENTIONAL RESOURCES SHARED BETWEEN VISION AND AUDITION? ..... 5-123

5.6 INTRODUCTION ..................................................................................................................... 5-124

5.7 METHODS ............................................................................................................................... 5-125

5.7.1. Subjects and stimuli ...................................................................................................... 5-125

5.7.2. Data acquisition and analysis ...................................................................................... 5-126

5.8 RESULTS .................................................................................................................................. 5-127
CHAPTER 6 INATTENTIONAL BLINDNESS FOR WORDS .............................................................6-141

6.1 INTRODUCTION ........................................................................................................6-142
6.2 METHODS ................................................................................................................6-144
  6.2.1. Subjects and stimuli .........................................................................................6-145
  6.2.2. Data acquisition and analysis ..........................................................................6-146
6.3 RESULTS .....................................................................................................................6-146
  6.3.1. Recognition memory .........................................................................................6-146
  6.3.2. Imaging ..............................................................................................................6-147
    6.3.2.1. Main effect of attention to pictures ...............................................................6-147
    6.3.2.2. Main effect of attention to letters .................................................................6-147
    6.3.2.3. Simple main effect of word identity under attention to letters ..................6-147
    6.3.2.4. Interaction between word identity and attention ........................................6-148
    6.3.2.5. Simple main effect of word identity under attention to pictures ...............6-148
6.4 DISCUSSION .............................................................................................................6-156
6.5 CONCLUSION ............................................................................................................6-160

CHAPTER 7 GENERAL DISCUSSION ...............................................................................7-161

7.1 RELATING SINGLE CELL STUDIES AND POPULATION MEASURES ....................7-162
7.2 WHAT IS PERCEPTUAL LOAD? ................................................................................7-166
7.3 WHAT IS THE RELATIONSHIP BETWEEN ATTENTION AND VISUAL AWARENESS? 7-171
7.4 CONCLUSION ............................................................................................................7-173

CHAPTER 8 APPENDIX: THE EFFECT OF VARYING STIMULUS PRESENTATION RATE ON RESOURCES IN BOTH PET AND FMRI .................................................................8-175

8.1 DIFFERENCES BETWEEN PET AND FMRI EXPERIMENTS ..................................8-175
8.2 MATERIALS AND METHODS ..................................................................................8-177
  8.2.1. Behavioural session .........................................................................................8-177
  8.2.2. fMRI session ...................................................................................................8-178
  8.2.3. PET session .....................................................................................................8-178
  8.2.4. Data analysis ..................................................................................................8-179
  8.2.5. Results ............................................................................................................8-181
8.3 DISCUSSION .............................................................................................................8-187
  8.3.1. Stimulus dependency of rCBF measurements ...............................................8-187
  8.3.2. Stimulus dependency of BOLD measurements ..............................................8-188
  8.3.3. Why is there a difference between the BOLD and rCBF measurements? ........8-188
  8.3.4. Relationship between BOLD contrast and deoxyhaemoglobin concentration 8-189
  8.3.5. Mechanisms causing changes in deoxyhaemoglobin concentration ..............8-191
Figures

Figure 3-1: Theoretical illustration of modulatory effects of attention..............................3-50
Figure 3-2: Attention to visual conjunctions......................................................................3-56
Figure 3-3: Decreases in cerebral blood flow correlated with rate of stimulus presentation.........................................................3-57
Figure 3-4: Two modulatory effects of attention on rCBF ...................................................3-60
Figure 3-5: Two modulatory effects of attention on rCBF ...................................................3-61
Figure 3-6: Positive and negative correlations with rate of stimulus presentation......3-74
Figure 3-7: Effects of attention on visual and auditory cortex .............................................3-77
Figure 4-1: Counting reaction times ..........................................................................................4-93
Figure 4-2: Distractors compared to baseline...........................................................................4-95
Figure 4-4: Time-dependent distractor activity .......................................................................4-96
Figure 4-4: Activity due to negative priming distractors......................................................4-99
Figure 5-1: Illustration of visual display..................................................................................5-112
Figure 5-2: Interaction of perceptual load and visual motion ............................................5-117
Figure 5-3: Timecourse of attentional modulation...............................................................5-119
Figure 5-4: Motion after-effect duration...........................................................................5-121
Figure 5-5: Effects of visual motion .......................................................................................5-128
Figure 5-7: Main effect of high auditory perceptual load ...................................................5-131
Figure 5-8: Interaction between perceptual load and visual motion.................................5-133
Figure 6-1: Recognition Memory for words ..........................................................................6-150
Figure 6-2: Attention to pictures or words .............................................................................6-152
Figure 6-3: Activation by word identity and modulation by attention ............................6-154
Figure 6-4: Time-course of evoked brain activity ...............................................................6-155
Figure 8-1: Word listening in PET and fMRI........................................................................8-180
Figure 8-2: PET rate dependency .............................................................................................8-182
Figure 8-3: fMRI rate dependency...........................................................................................8-184
Figure 8-4: fMRI rate dependency...........................................................................................8-185
Figure 8-5: Relationship between T2* and blood oxygenation........................................8-190
Tables

Table 3-1: Activity related to stimulus presentation rate ...................................................... 3-58
Table 3-2: Areas that show both stimulus dependent and task dependent activity .... 3-59
Table 3-3: Areas showing correlation with stimulus presentation rate ......................... 3-72
Table 3-5: Attention to visual or auditory streams ............................................................... 3-75
Table 3-7: Attention to identity compared to intensity ....................................................... 3-78
Table 4-1: Distractor-related activations ........................................................................... 4-98
Table 4-2: Negative priming activations ........................................................................... 4-100
Table 5-1: Interaction of perceptual load and visual motion ........................................... 5-116
Table 5-2: Main effect of visual motion ............................................................................ 5-129
Table 5-4: Main effect of perceptual load ........................................................................ 5-132
Table 5-4: Interaction between auditory perceptual load and visual motion .......... 5-134
Table 6-1: Effects of directing attention to picture or letter stream ......................... 6-151
Table 6-2: Effects of word identity .................................................................................. 6-153
Table 8-1: Orthogonal polynomial regression (PET) ....................................................... 8-186
Table 8-2: Orthogonal polynomial regression (fMRI) .................................................... 8-186
Chapter 1 Introduction

To what extent does perception depend on attention? This issue has been a central question in attention theory over the past forty years, yet remains unresolved. Two contrasting positions have emerged. Some studies have suggested the importance of attention for perception, showing that unattended stimuli apparently receive very little processing beyond a rudimentary analysis of sensory attributes (Broadbent, 1958; Treisman and Gelade, 1980). Other studies, however, have implied that unattended stimuli can be processed extensively and have some effect on behaviour as measured by indirect methods (for example, reaction times and evoked potentials) (Neill et al., 1995). Evidence has accumulated over the last forty years from behavioural, electrophysiological and functional imaging experiments for both positions, without consensus or resolution. The issue hinges on the degree to which unattended stimuli are processed, and the determinants of such processing.

1.1 Framing the question

This thesis addresses this question from a neurobiological perspective. Modern brain imaging techniques are used to assess directly the brain areas and mechanisms involved in processing unattended stimuli. The general goal to which this work contributes is the development of a mechanistic account of how visual and auditory stimuli are processed by the brain. A complete description of such processes should account for the observation that humans are able to choose to process stimuli selectively while ignoring others. The behavioural consequences of this ability, selective attention, appear to be the enhanced processing of attended stimuli leading to improved detection and discrimination (e.g. (Yeshurun and Carrasco, 1998)).

One approach to this question is to seek evidence for an ‘attentional system’ in the human brain. This approach is not favoured in the experimental work presented here, which attempts to remain neutral about whether there are specific brain areas that represent such a system. A potential difficulty with such an approach is that it seeks to directly associate (folk) psychological categories with brain mechanisms. In doing so, there is often an implicit assumption that attention represents a unitary mechanism subtended by dedicated cortical circuitry. This may be misleading, as areas of the brain that are active during
Neural correlates of selective attention

attention demanding tasks may be active simply by virtue of their association with some particular process whose resultant effects we see behaviourally as selective attention. The work presented here manipulates ‘attention’ primarily through instruction to the subjects, and seeks to characterise the resultant effects on sensory processing. In this sense, attention is one way of manipulating the internal state of an organism, while holding sensory stimulation constant, and investigating how brain activity changes as a result.

The experiments presented here address the following questions. What is the difference between signals related to attended and unattended stimuli? What determines whether unattended stimuli produce brain activity? Is attention necessary for stimuli to produce certain types of brain activity? Experimental paradigms are therefore explored that attempt to assess the degree to which ignored stimuli are nevertheless processed. This is carried out by developing explicit measures of brain activity evoked by unattended stimuli, together with converging behavioural evidence of their effects.

Before the experimental material is presented, there follows a brief and selective literature review that highlights the main findings relevant to the subject matter of this thesis. It is suggested that the use of brain imaging together with convergent behavioural measures is well suited to elucidate the brain mechanisms involved in selective sensory processing. First, the classic behavioural and physiological results showing how sensory evoked responses are modulated by attention will be reviewed. The functional imaging literature that has investigated these issues is then examined. A dominant concern of the imaging community has been the study of covert spatial attention, and this review will illustrate that little information has yet been gleaned about the nature of processing outside the focus of attention.

1.2 Psychological approaches

Detecting changes in reaction time or error rates and subsequently inferring the existence of different processing stages has a long and distinguished history in the psychology of attention (Brozek, 1970; Donders, 1969; Sternberg, 1969). This approach has been applied to detecting the processing of ignored stimuli in a number of ways. Processing of a distracting stimulus can be inferred by measuring how its presence affects observers’ ability to perform a primary task. The presence of a particular type of distractor may cause a slower reaction time or increased error rate. Alternatively a subsequent
Neural correlates of selective attention

assessment of memory for the distracting stimulus may serve as a measure of processing. Here key experimental findings are briefly reviewed: the intention is to serve as the foundations for discussing the later experimental work rather than as a comprehensive literature review.

The Stroop task (Stroop, 1935) is often cited by authors and reviewers alike as a ‘classic’ attention demanding task. Subjects are asked to name the ink colour of successive words presented visually. When the word name represents a conflicting colour, naming is slower and error rates increased compared to when the word names a neutral thing. This pattern of findings is taken to suggest that the distracting information (the semantic identity of the word), although irrelevant to the task, is nevertheless processed and conflicts with the primary task of colour naming. This general approach can be used to study how the processing of irrelevant distracting information conflicts with a primary task. A distracting stimulus that is processed to the level of meaning will evoke semantic associations that can interfere with responses to the primary stimulus. In this way, the irrelevant distracting stimulus serves as a ‘probe’ that interferes with processing of the primary task. This approach requires that the ‘probe’ shares some processing stage (such as the evocation of semantic associations) with the primary task. For example, in the Stroop task there is a semantic conflict between the word identity and the ink colour. In order to make correct inferences about the way in which processing of attended and unattended stimuli differ, then it is essential that this shared processing stage be identified accurately. A more subtle consequence of using distractors that interfere with the primary task is that the experimenter is forced to create circumstances where such conflicts exist. It is not, however, particularly clear whether this reflects everyday circumstances (Neisser, 1967). Moreover, the processing of an attended stimulus might be impaired even in the absence of a semantic (or other obvious) relationship between distractor and attended stimulus. In such cases it is not necessarily clear what aspect of processing is important. Such nonselective effects are predicted by some attentional theories that postulate a limited pool of resources. Often it is unclear how such theoretical constructs as ‘resources’ are implemented physiologically, and detailed physiological investigation of such effects has only just begun.

A more important difficulty with making inferences about processing stages from the demonstration of interference is that the mapping from postulated cognitive processes onto brain mechanisms is not necessarily clear. Even in the case of systems that appear
Neural correlates of selective attention

It is not at all correct to assume that such systems must therefore occupy a single location in the brain. For example, Fodor (Fodor, 1983) is widely cited as supporting the notion that cortical mechanisms might have an encapsulated, modular architecture. However, it is often overlooked that modularity in this sense is a concept that applies solely to information processing. It is entirely possible, indeed probable, that an encapsulated information processing architecture is subserved by a distributed neural system throughout the brain (Fodor, personal communication). Similarly, a modular neural architecture (such as the putative localisation of face specific activity to an area in the fusiform gyrus) need not reflect a modular information processing architecture. It is therefore an open question whether there is a direct, one-to-one mapping between mechanisms postulated on functional grounds by psychological experiments, and brain processes involved in processing unattended stimuli. This point was made forcefully several years ago by the initial wave of enthusiasm for parallel distributed processing computational models. Such models illustrate that complex computational abilities may be distributed throughout a system and not necessarily functionally localised.

Although demonstrating interference between a distractor and a target implies that they are both processed to a common stage, the converse is not true. A failure to demonstrate interference may not reflect absence of processing of unattended information. One demonstration of this comes from the work of Driver and Tipper (Driver and Tipper, 1989) who investigated an experimental paradigm where the distractors did not interfere with the attended targets (Francolini and Egeth, 1980). However, using an alternative behavioural measure they were able to show that the distractors were nevertheless processed. They suggested that the production of interference and the processing of distractors are not necessarily coextensive.

Driver and Tipper demonstrated that ignored stimuli were nevertheless processed by showing that they produced negative priming. The study of negative priming is a second important way that the processing of ignored stimuli has been investigated (for a review see Fox, 1995). Negative priming refers to a slowing in reaction times (the opposite of ‘positive’ repetition priming) that occurs when subjects respond to a target item (on ‘probe’ trials) that has previously been ignored (on ‘prime’ trials). The standard explanation for this phenomenon has been that the process of ignoring a distractor involves inhibiting information or responses associated with that item (Tipper and
Neural correlates of selective attention

Cranston, 1985; Tipper, 1985). Subsequent responses to a previously ignored distractor will be retarded due to this inhibition persisting over a short time. Negative priming has been demonstrated in many experimental contexts, both for spatial location and for the identity of objects. It appears to have a time course that can be extended over several seconds (Fox, 1995) or perhaps even longer (DeSchepper and Treisman, 1996). Negative priming effects specific to the semantic content of ignored stimuli are seen (Tipper and Driver, 1988) providing prima facie evidence that ignored stimuli are processed to the level of meaning. However, several empirical issues have emerged that suggest that the attribution of negative priming to an inhibitory attentional mechanism is not entirely straightforward (Milliken and Tipper, 1998; Neill et al., 1995). In addition the relationship between the higher-order psychological construct of 'negative priming' with the physiological determinants of such an effect is obscure: it may be the case, for example, that the brain processes underpinning negative priming are not inhibitory but excitatory. However there has been little empirical neurophysiological study in this area.

Processing of ignored stimuli has not only been assessed by studying how their presence affects reaction times or error rates. A third way that the processing of ignored stimuli has been explored psychologically has been to examine whether subjects are able to remember stimuli that they have been previously ignoring. Some of the first experiments using the dichotic listening paradigm measured memory for words presented on the unattended channel. The absence of any significant memory for ignored words (Cherry, 1957) led Broadbent (Broadbent, 1958) to postulate that only certain basic physical properties of stimuli (for example, pitch) were initially analysed and stored in a short term memory buffer. A selective filter then ensured that only the behaviourally relevant contents of short term memory are subject to further attentive analysis, while stimuli not selected were thought to decay passively within the sensory buffer. However this account soon ran into difficulties as investigators reported that subjects sometimes recognise their own name when it is inserted in an ignored message during a shadowing task (Moray, 1959). This implies that processing of unattended material can proceed to the level of semantic analysis, and this prompted modification of the idea of a selective filter (Treisman, 1960). Other investigators abandoned this idea altogether, suggesting that all processing proceeds to the level of semantic analysis and the locus of selection is post-perceptual (Deutsch and Deutsch, 1963; Duncan, 1980; Neisser, 1967).
Neural correlates of selective attention

With the development of interest (e.g. (Eriksen and Eriksen, 1974; Treisman and Gelade, 1980)) in the investigation of visuospatial determinants of selective attention and visual search, interest in mnemonic aspects of the processing of ignored stimuli declined. More recently, Rock and colleagues have spurred a renewal of interest in mnemonic measures with their provocative studies of inattentional blindness (Mack and Rock, 1998; Rock et al., 1992). They studied a series of paradigms in which a naive observer is typically engaged in a demanding primary task. For example, observers viewed a postmasked stimulus made up of a vertical and horizontal line overlapping in the form of a cross, and determined which line was longer. On the critical trial a small diamond shape was presented unexpectedly for 200ms in one of the four quadrants of the cross. Subsequently subjects were asked if they saw anything unusual on that trial, and if they reported seeing the diamond, in which quadrant it was seen. Surprisingly, the large majority of subjects did not report seeing anything unusual, and many of those who did report seeing the diamond mislocated it in one of the other three quadrants. This finding is supported by a number of other studies using different paradigms, all of which share the common feature that if attention is not drawn to an unexpected stimulus, subjects apparently fail to perceive it. Rock and colleagues dubbed this phenomenon 'inattentional blindness'.

However, just as with measuring interference, the use of mnemonic measures of unattended processing is also fraught with potential difficulties. One obvious pitfall is the implicit inference from 'no memory' to 'no processing' that is obscured by the use of the phrase 'inattentional blindness'. Rock and colleagues claim that subjects do not remember stimuli because they do not perceive them at the time of presentation. However the way in that stimuli are presented always involves unexpected presentation of unattended stimuli to naive subjects. It is well established that the depth to which stimuli are processed at the time of perception strongly influences the degree to which they are subsequently recalled. Memory for previously studied word lists is greater if subjects are asked to perform an encoding task that relies on the semantic aspects of the words compared to the physical characteristics of the words (Fletcher et al., 1997). It is therefore possible that subjects do not remember stimuli because although they are perceived at the time of presentation, they are not subsequently encoded in memory to any depth and so fail to elicit recognition memory. This alternate explanation would suggest that 'inattentional blindness' should be more properly titled 'inattentional amnesia'.
Neural correlates of selective attention

In summary, it has been argued that although behavioural measures of unattended processing have provided fundamental insights that have shaped our understanding of selective attention, there are a number of important drawbacks to these techniques. These drawbacks limit their use in understanding the brain mechanisms that underpin performance on selective attention tasks. Many of these difficulties are potentially circumvented by direct recording of brain activity with the use of techniques such as single cell electrophysiology, evoked potentials (ERP), positron emission tomography (PET) and functional MRI (fMRI). These techniques all allow a direct measure of brain activity (at varying temporal and spatial resolutions) during task performance. This in theory allows a direct answer to such questions such as: are ignored stimuli processed in the absence of interference? Is negative priming an inhibitory phenomenon? Do subjects suffer from inattentional blindness or inattentional amnesia?

The major neurophysiological techniques are now reviewed in order to provide an empirical background for the remainder of the thesis. Taken together, these techniques have demonstrated that attending to an object or feature modulates the sensory responses evoked by that feature in a number of ways. While this indicates how the processing of attended stimuli and unattended stimuli differ, without some systematic manipulation of the type or presence of unattended stimuli it is difficult to draw strong conclusions about the nature and extent of processing of ignored stimuli. After reviewing the physiological literature I will discuss how experimental paradigms for functional imaging might seek to systematically manipulate the presence and identity of distractors in order to characterise the nature and determinants of unattended processing, before proceeding to the experimental sections of the thesis.

1.3 Physiological approaches

1.3.1. Single cell electrophysiology

The development of extracellular recording techniques in awake behaving animals in the 1970s and 1980s {e.g. (Mountcastle et al., 1981)} allowed the first direct examination of neural mechanisms that might underlie the attentional modulation of visual processing. Broadly speaking these studies, reviewed below, have established that attention enhances the sensory processing related to visual stimuli in single neurons. The review will
Neural correlates of selective attention

concentrate primarily on processing in the ventral visual stream (Ungerleider and Haxby, 1994).

Moran & Desimone (Moran and Desimone, 1985) presented pairs of stimuli in the receptive fields of neurons in V4 or IT. One of these was chosen to be effective in driving the cell (i.e. it matched the colour or orientation preference of the recorded cell) and the other was ineffective. The stimuli were presented twice and the monkey was trained to report whether the stimuli remained the same or whether a slight change in orientation had taken place. When the monkey attended to the effective stimulus, the neural responses elicited were much the same whether the effective stimulus was presented alone or together with the ineffective stimulus. However when the monkey attended to the ineffective stimulus, the responses to the effective stimulus were suppressed. Moran and Desimone suggested that one interpretation of these results was to suppose that attention ‘shrank’ the neuronal receptive field so as to exclude all but the attended stimulus. Interestingly, when the two stimuli were placed one within and one outside the receptive field, there was no modulation of cell responses by attention in V4, and only a weak modulation of responses in inferotemporal cortex (IT). Unlike receptive fields in V4, those in IT are much larger and often extend across the whole of the visual field. Moran & Desimone suggested that “The results from area V4 and the IT cortex indicate that the filtering of irrelevant information is at least a two-stage process. In V4 only those cells whose receptive fields encompass both attended and unattended stimuli will fail to respond to unattended stimuli. In the IT cortex, where receptive fields may encompass the entire visual field, virtually no cells will respond well to unattended stimuli”.

These findings show that sensory responses in the ventral visual pathway are affected by attention, but do not uniquely specify the mechanism involved. The requirement that both stimuli be within the receptive field of a cell to show attentional modulation of responses suggests a mechanism based on lateral interactions within a cortical area. However, such a response pattern might also be based on response competition at a previous cortical area with convergent inputs to the cell recorded in a subsequent area. Support for attention modulating the competition between cells with similar orientation preferences within a cortical area came from a follow up study investigating another orientation discrimination task (Spitzer et al., 1988). These authors, who used a task with two levels of difficulty, established that as monkeys’ discriminative tasks improved when the task became more difficult, corresponding neuronal responses to stimuli became larger and more selective.
Neural correlates of selective attention

This could not be accounted for by changes in general arousal, and so it was concluded that increasing the amount of attention directed toward a stimulus can enhance both the responsiveness and selectivity of the neurons that process it. This suggests a possible mechanism whereby attention might enhance competition between functionally specified visual attributes within a cortical area, leading not only to an enhancement of responses (like a gain control or multiplicative scaling of responses) but also increased selectivity (a change in the receptive field preferences or shape). However, a more recent experiment may cast doubt on this account (McAdams and Maunsell, 1999). Here the animals were trained on a rather different task in which oriented stimuli were presented to the receptive field of cells being recorded in a delayed match-to-sample task. Orientation tuning curves were constructed for both attended and unattended oriented stimuli. Although attention enhanced the responses of V1 and V4 neurons, selectivity as measured by the width of the orientation tuning curve was not systematically altered by attention. Instead, the results of attention were consistent with a multiplicative scaling of the driven response to neurons. Whether this difference is due to differences in the experimental paradigm used, or reflects more fundamental distinctions in the mechanism of attention, remains to be established.

The previous experiments suggested that competition may be important for attentional effects to emerge. This idea has been given substantial support by the work of Brad Motter (Motter, 1993; Motter, 1994a; Motter, 1994b). In one experiment (Motter, 1993), he presented stimuli that were oriented at several locations in a circle around fixation, with one stimulus positioned to fall into the receptive field of a neuron in either V1, V2 or V4. The monkey was cued to discriminate the orientation of one of the stimuli, that was either inside or outside the receptive field of the neuron being recorded. Neural responses were greater to an attended stimulus than the same stimulus when unattended. When there were no distractors, this attentional modulation disappeared. This study was one of the first to show attentional modulation of neural responses as early as V1. For example, Moran & Desimone (Moran and Desimone, 1985) were unable to show any attentional modulation in striate cortex; the first appearance of such modulation was at the level of V4. It appears that the presence of distracting stimuli in the visual display is particularly important to see these early effects.

Early experiments sought evidence for attentional modulation in ventral visual cortical areas related to object recognition. More recently activity related to visual motion in
Neural correlates of selective attention

cortical areas MT/V5 and MST has been investigated. Treue & Maunsell (Treue and Maunsell, 1996) investigated the attentional modulation of moving stimuli by presenting one or two moving dots in the receptive field of neurons in MT/MST, together with a third moving dot outside the receptive field. The dots moved back and forth; where two dots were present in the receptive field they moved in antiphase. The monkey was trained to monitor one of the dots and report whether it changed its velocity. With only one dot in the receptive field, responses were 20% (MT) or 40% (MST) larger when the dot was attended than when it was unattended. With two dots in the receptive field the responses were 90% (MT) or 110% (MST) larger. These results show that attention could modulate motion specific neural responses, and that the size of the modulation (as with the V4 results) was greater when there was more than one stimulus in the display. In this study the modulatory effects were comparatively strong; however this may not always be the case in area V5. Newsome and colleagues recently reported a study where monkeys were spatially cued to attend to the direction of motion of one of a pair of coherent dot patches (Seidemann and Newsome, 1999). In contrast to the previous study, these authors found a modest 8% increase in response in MT associated with attending to the coherent dots. Moreover was little effect of stimulus competition comparing situations where the ignored and attended dot patches were in the same receptive field and when they were in different receptive fields. However the interpretation of this latter study is complicated by the sheer difficulty of the task. Surprisingly, both monkeys tested found the task extremely challenging and performance was often poor even after extended training. Furthermore the design of the task displays allowed the animals to perform the task without necessarily directing attention to one or the other test stimulus. The modest attentional modulations seen may reflect these factors. Nevertheless, the discrepancy between the two studies indicates that task demands may potentially modify the size of attentional effects.

In summary, neural responses in the ventral visual stream to attended stimuli are enhanced by attention, though usually only when distracting stimuli are also present. Responses to unattended stimuli are sometimes suppressed. These studies provide important information that relates to possible mechanisms of attentional selection and whether unattended information is processed. However there are a number of important limitations of the work to date. All the studies have sought to produce evidence that the response to an attended stimulus is enhanced relative to an unattended stimulus. However it is often not clear whether the response to an unattended stimulus is simply attenuated,
Neural correlates of selective attention

or whether it is abolished altogether. This distinction is important, as an attenuated response could still progress through the visual system, receiving further processing and influencing responses at subsequent stages of processing. The relationship of single cell studies to the psychological study of attention in humans is made harder to interpret by the interspecies differences in cortical anatomy. Animals are also difficult to train and so more complex dual task paradigms {e.g.(Braun and Julesz, 1998)} that might better characterise attentional mechanisms are not feasible in their original forms. Furthermore, the studies to date have typically used non-linguistic meaningless stimuli such as gratings or coloured patches so cannot address the central question: to what extent are unattended stimuli processed, and are stimuli that are ignored processed to the level of identity?

It should also be clear from this review that no consensus exists in the single cell literature regarding the mechanism by which attention changes responses evoked by sensory stimuli. While some studies are consistent with a gain control mechanism, others suggest that the tuning properties of the cell also change. Very recent work combining psychophysical observations with computational modelling may prove useful in bridging the gap between behavioural observations in humans and single cell electrophysiology in primates, and thus assist in resolving questions about neurobiological mechanisms. Itti and colleagues developed a simple computational model of early spatial vision and constrained its parameters with data from a range of dual task experiments (Lee et al., 1999). In these experiments a variety of spatial vision thresholds were measured with full attention and in the absence of attention. Itti et al found that a parsimonious way to constrain the model to simulate the experimental findings was to assume that attention enhanced the competition between similarly tuned spatial filters. This is analogous at a biological level to attention enhancing the competition between hypercolumns of neurons with similar functional properties. The use of such computational models mediating between observations using different physiological and psychophysical techniques is potentially very powerful and will be explored more fully in the general discussion.

1.3.2. Event related potentials

Electrophysiological studies in humans use surface electrodes to measure the scalp distributions and time courses of electrical currents evoked by changes in cortical activity (Hillyard et al., 1995). The chief advantage of such techniques is their exquisite temporal resolution; however their spatial resolution is rather limited due to lateral spread of
Neural correlates of selective attention current in the scalp layers. The most important finding from ERP studies is that components arising very soon after the presentation of a stimulus clearly differ as a function of whether the stimulus is attended or ignored (Hillyard et al., 1995). The visually evoked component P1 is smaller when a stimulus is ignored because of its location. When selection is based on stimulus attributes other than location, such as colour, an additional component is superimposed on the N1 and P1. This colour selection component is substantially reduced when the stimulus is in an ignored spatial location, suggesting that the location and colour selection are organised hierarchically with location-selection dominant (Mangun et al., 1993). The location of the generators of these components in early sensory processing areas (Heinze et al., 1994a) suggests that the mechanism of selection not only operates very soon after stimulus presentation but also very early in the anatomical hierarchy of processing areas (Woldorff et al., 1993). More recently Hillyard has argued that very early components, such as the C1 component that is thought to arise from striate cortex, are not modulated by spatial attention (Hillyard et al., 1998). This suggests a model of spatial selection in which processing is modulated in extrastriate (but not striate) areas early in the course of visual processing. However it is important to recognise that even observing differential enhancement of processing early temporally and spatially in the ventral visual pathway does not establish the level to which unattended stimuli are produced. It has been emphasised already that a signal attenuated in amplitude early in the processing pathway, may nevertheless in principle continue, and be processed to the level of semantic associations or beyond.

It is difficult to relate these ERP findings to the single cell data because it is not always clear what the neural correlates of a modulation of ERP signal represent. The complex summation of electrical activity within and between cortical areas then is filtered through the scalp and recorded at multiple electrodes. It is not clear, for example, whether an increase in ERP amplitude reflects increased spiking or the same degree of spiking but with increased synchrony. Stimuli in ERP studies are also frequently presented alone to aid interpretation of the resultant waveforms, presenting interpretational differences when comparing single cell experiments with cluttered displays and ERP experiments. The experimental paradigms used in ERP also utilise relatively austere visual displays. This may be particularly important given the electrophysiological evidence that competing stimuli are required to produce some attentional effects (Motter, 1998).
Neural correlates of selective attention

ERPs have also been used to study visual search and non-spatial aspects of selective attention, but there is insufficient space to review these experiments here. There are a number of good reviews available (Hillyard et al., 1995; Luck, 1998).

1.3.3. Functional imaging

In the last ten years there has been an explosive growth in the ability to image brain function non-invasively in human subjects. The newer techniques of PET, fMRI and magnetoencephalography (MEG) have augmented and supplanted the established use of evoked potentials to assess cortical function (Frackowiak et al., 1980; Toga and Mazziotta, 1996). Here the functional imaging literature relevant to studies of visual selective attention is reviewed. By far the dominant issue addressed by imaging studies to date has been the investigation of the mechanisms of allocation of covert spatial attention. In particular, functional imaging has not been used to explicitly examine the processing of unattended stimuli. This is puzzling, as one of the most attractive features of brain imaging techniques is the ability to observe directly activity related to ignored stimuli, without having to index that activity through, for example, producing interference with the attended stimuli.

1.3.3.1. Attention to visual features

Maurizio Corbetta conducted one of the first functional imaging studies of selective attention (Corbetta et al., 1990; Corbetta et al., 1991a). In this study he asked subjects to attend to different aspects of a composite visual display such as shape, colour and speed. Using $H_2^15O$ PET imaging, he found increases in cerebral blood flow in areas of extrastriate visual cortex when subjects attended to different attributes of the visual stimuli compared to when they passively viewed the stimuli. Moreover the areas modulated were different when different attributes were attended. This feature specific modulation of specialised cortical areas is in keeping with the idea of a functionally specialised visual system (Zeki et al., 1991). Subsequent observations have broadly supported Corbetta's initial observations. Directing attention to a moving stimulus modulates activity in the human homologue of V5/MT (Buchel et al., 1998a; O'Craven et al., 1997). Similarly, covert spatial attention to faces modulates activity in areas of the fusiform gyrus (Wojciulik et al., 1998) that appear to have differential sensitivity to the visual presentation of a face (Kanwisher et al., 1997) but see (Allison et al., 1994).
In addition to showing modulation of activity in the ventral visual pathway, Corbetta (Corbetta et al., 1990; Corbetta et al., 1991b) also compared selective attention to individual features of the display and divided attention, where subjects were asked to attend to all features simultaneously. These two different conditions, compared to a low level baseline condition, activated non-overlapping sets of brain regions. In particular, divided attention activated the anterior cingulate and dorsolateral prefrontal cortex, areas that have been associated with response selection and the prevention of response conflicts. The different pattern of activity also suggests that different attentional requirements led to the involvement of different neural systems. Vandenberghhe and colleagues (Vandenberghhe et al., 1997) further investigated the difference between different task requirements by comparing attention to one and two features of objects presented in left and right visual fields. Behaviourally, subjects can identify two features of the same object concurrently without loss of accuracy, while performance falls when the features belong to different objects (Duncan, 1984; Duncan, 1993; Egly et al., 1994). The neural correlates of this apparently simple behavioural finding proved more complex. When subjects attended to a single feature, areas of parietal, premotor and anterior cingulate cortex were activated, particularly in the right hemisphere. Activity in these areas was enhanced when subjects identified two features of the same object compared to a single feature. These feature discriminations on a single object were not affected by the direction of attention to either left or right visual fields. However, direction of attention (regardless of task) did affect activity in right and left lateral frontal cortex, with activity ipsilateral to the direction of attention being higher. Activity in these areas during divided attention to both objects (i.e. two features, but of different objects in right and left visual field) was intermediate between that seen during attention to either right or left visual field alone. This complex pattern of findings suggests that enhanced activity in structures associated with peripheral selective attention is associated with the maintenance of accuracy when subjects are asked to identify more than one feature of an attended attribute. Note that this is an example where changes in brain activity are not reflected in a change in performance (which remained equally accurate during single and dual feature discrimination for a single object).

Recent work has focused on demonstrating attentional modulation of motion processing in human homologues (Watson et al., 1993) of area V5/MT. Initial work has shown that attending to visual motion (compared to passive viewing) modulates activity in these
Neural correlates of selective attention

areas (Buchel et al., 1998a; O’Craven et al., 1997). Recently, Watanabe (Watanabe et al., 1998a; Watanabe et al., 1998b) has shown that attention to motion appears to be task dependent. The authors found that activity in V5/MT was enhanced by attention to motion whatever local component was attended, while activity earlier in area V1 was significantly higher only in the translation condition. This combines a demonstration of attentional modulation affecting area V1, and thus early in the cortical hierarchy, with the idea that task demands affect feature selective processing in these motion sensitive areas differently. This is an important extension to the feature specific modulation shown by Corbetta (Corbetta et al., 1991b). Even when attending to a single feature, different tasks may modulate activity in different areas associated with processing that particular feature.

1.3.3.2. Attention to spatial location

Many studies to date have focused exclusively on spatial attention using paradigms originally described by Posner (Posner and Snyder, 1975). These studies have examined how processing of a simple visual stimulus is modified by prior knowledge of the location at which it is likely to appear. As such, this work might more properly be characterised as studying attentional ‘set’ or expectation, rather than selective attention per se. Although this topic, and the mechanisms of spatial attention, are not directly studied in this thesis, such functional imaging studies have been very influential in the field and are therefore reviewed for completeness (see also footnote ii for some mechanistic speculations).

The ‘Posner paradigm’ (Posner and Snyder, 1975) and its variants are perhaps the most frequently studied tasks, in which an austere visual display comprising two boxes and a central fixation mark is shown to subjects. Subjects are asked to fixate on the central marker and to provide a detection or discrimination (depending on paradigm) response to a visual stimulus that appears briefly in either right or left boxes. The experimental manipulation is to provide a cue that may predict the subsequent target location some time before target appearance. This cue can either be peripheral (brightening of the box; ‘exogenous’ attentional cueing thought to reflect stimulus-driven orienting of peripheral attention) or central (symbolic arrow cue at fixation; ‘endogenous’ attentional cueing thought to reflect deliberate covert centrally driven shifts of attention). The crucial manipulation is that while for most of the trials (typically 80%) the cue is valid, on some of the trials the cue is invalid. The validity of the cue has a strong effect on reaction
Neural correlates of selective attention

times. Valid trials are responded to faster than invalid trials, showing that prior knowledge about the likely spatial location of an upcoming target in some way facilitates processing of, and responses to, that target. Posner went on to show that patients with right parietal lesions and visual neglect had particular difficulty on invalid trials. He hypothesised that the right parietal lobe is important for 'disengaging' attention from a covertly attended spatial location prior to a shift of attention (Posner et al., 1984), but a discussion of these results is beyond the scope of this review. The basic invalid/valid trial distinction has been replicated many times, although there are a series of methodological and interpretational issues that complicate a simple assertion that the effect of a cue is to enhance processing of a subsequent target (see (Pashler, 1998) for a discussion). For example, it has not always been possible to show that shorter reaction times to valid cues reflects a benefit (over neural uninformative cues) rather than a cost.

Variants of the Posner task have been studied with functional imaging by both Corbetta and Nobre (Corbetta et al., 1993; Nobre et al., 1997). Both groups concluded that attention to spatial location evoked activity in a distributed cortical network that was predominantly right lateralised and involved prefrontal and parietal areas. Corbetta went on (Corbetta et al., 1995) to show that right parietal cortex is also differentially involved in visual search for conjunctions of features, suggesting a role for this structure in the direction of the 'spotlight' of spatial attention. These findings are consonant with some large scale network theories of attentional function that propose that 'attention' is subserved by distributed activity in a network involving anterior cingulate, right
Neural correlates of selective attention

prefrontal and right posterior parietal cortex (Mesulam, 1990; Posner and Dehaene, 1994; Posner and Petersen, 1990). However, these theories (Mesulam, 1990), while supported by the findings of Corbetta and Nobre, postulate functional specialisation within such a network and this has been more difficult to establish. Indeed, it is possible that the areas involved in the shifting of covert spatial attention might be more restricted. In particular, the study of Nobre and colleagues used a very simple reference state (fixation) with which to compare activations produced by covert allocation of attention. As a consequence the ‘network’ of areas subsequently ascribed to attention may in fact contain components solely associated with the visual and motor aspects of the task. Performance of the Posner task comprises cerebral activity associated with the presence of the visual display, the onset of the targets and the motor responses associated with target presentation in addition to any enhancement of the target processing caused by covert spatial attention. Consequently the comparison of this task with visual fixation (where no

Although not directly relevant to the argument developed here, there are some important problems with these conclusions from Corbetta’s study (Corbetta et al., 1995). Corbetta compared visual search for features with search for conjunctions of features in a simple visual display. The data presented shows that superior parietal cortex is more active during the conjunction task than during the feature task. Corbetta and colleagues argue that this is compatible with Feature Integration Theory (FIT; (Treisman and Gelade, 1980)) suggesting that the spatial direction of attention is controlled by superior parietal cortex. However parietal cortex is also active (compared to baseline) during the feature search, which is not explained or predicted by FIT. Treisman’s theory is not particularly clear as to whether attention is ever required for feature perception. Conjunction and feature tasks also differ in their degree of difficulty, so it is possible that an alternate explanation of parietal activation during the conjunction task is that it reflects task difficulty. Moreover careful examination of the manuscript shows that analysis of the data was restricted to parietal cortex alone. Although the figures presented in the manuscript show strong activation elsewhere (in frontal structures), the relative contribution of these areas to the visual search paradigm, which might alter interpretation of the differential parietal activity, is not described. Finally, another important problem with the interpretation of the functional imaging studies of spatial attention discussed here is that they appear to activate the superior parietal lobule, whereas the focal lesion that produces visuospatial neglect appears to be located in the inferior parietal lobule (Driver and Mattingley, 1995), well away from the locus of activation described. This discrepancy has not been satisfactorily explained.
Neural correlates of selective attention

visual stimuli are presented and no motor responses produced) cannot be said to isolate solely the structures subserving the spatially specific enhancement of visual processing. More recently some authors have begun to examine these issues in more detail. Coull and colleagues (Coull and Nobre, 1998) studied an interesting variant of the Posner task in which cues were also provided in time (onset of the target) as well as space. However for the purposes of this review, the interesting aspect of their study was the inclusion of a neutral condition. In this condition, the visual stimulation and motor responses were identical to the valid or invalid trials, but the cue differed only in not being informative. In keeping with previous findings, the informative cues enhanced visual processing and shortened visual processing compared to the non-informative neutral cues. While comparison of the attentional conditions with rest revealed a frontoparietal network similar to that described previously, the more stringent comparison with the neutral cue condition revealed activation only in a small focus located in right parietal cortex. As the visual stimulus and motor output are identical in neutral cue and attentional conditions, this difference must reflect purely attentional effects. This pattern of results suggests that frontal activity in attentional tasks may be related to the motor component of the attentional task (Mesulam, 1990). However a definitive conclusion is difficult to reach. Other studies argue from different results, that the spatial similarity of these 'attentional networks' and the network of areas activated by explicit saccadic eye movements (Corbetta, 1998) indicates that the deployment of covert attention and the programming of saccadic eye movements must be functionally related² (c.f. (Rizzolatti et al., 1987) for theoretical suggestions).

² A close functional relationship between the programming of eye movements and covert shifts of spatial attention might be anticipated by careful study of the electrophysiological literature. Duhamel (Duhamel et al., 1992) showed that the visual receptive fields of cells in the lateral intraparietal sulcus (LIP) of macaque monkey moved in retinotopic co-ordinates immediately prior to a saccade. The movement was such that it exactly anticipated the movement of the receptive field (in retinotopic co-ordinates) that would be produced by the subsequent saccade. The authors proposed that this reflected a 'remapping' of the receptive fields in LIP in retinotopic co-ordinates. Cells that show this anticipatory remapping have also been found in other structures implicated in oculomotor control such as the frontal eye fields and superior colliculus (Umeno and Goldberg, 1997; Walker et al., 1995). The existence of this remapping mechanism suggests a possible neurobiological mechanism for the operation of covert spatial attention. If, during covert visual attention, the same structures could be engaged that cause remapping of the visual world prior to saccades, but the final motor output that produces a saccade could be inhibited, then a remapping of the visual world could occur in the absence of eye movements. What functional consequences might this have? In the ventral visual stream, Connor (Connor et al., 1996; Connor et al., 1997) has shown that the deployment of spatial attention near to the receptive field of a V4 cells appears to 'pull' the receptive field of that cell towards the spatial location of attention. Such an effect may be the correlate of remapping in LIP and dorsal stream, and may serve to deploy the superior processing resources available for processing of foveally presented information (Sereno et al., 1995) to peripheral, covertly attended areas of the visual field. This account of mechanism is necessarily speculative, but could be investigated using functional imaging. A prediction of this account of attentional
Functional imaging therefore indicates that right frontoparietal structures are differentially active when subjects engage in covert spatial attention tasks. The inference leading from this that right frontal and parietal cortex forms an 'attentional network' responsible for 'spatial attentional control' has received relatively uncritical acceptance. However even a cursory review of the literature shows a large number of other attentional and nonattentional tasks associated with parietal activity. Right parietal cortex is active in such diverse tasks as (for example) non-spatial working memory (Coull and Frith, 1998), predictive guessing, sound movement perception (Griffiths et al., 1998) and binocular rivalry (Lumer et al., 1998; Lumer and Rees, 1999). It is possible that all these tasks require spatial attention in some way, but arguing in such a way rather begs the question. An alternate possibility is that these structures are not specifically involved in spatial attention, but instead subtend some more general role or cognitive process that is seen in both attentional tasks and others with different demands. We have suggested elsewhere that such a role may be selecting among patterns of neural activity in the ventral stream competing for visual awareness (Lumer and Rees, 1999). Attributing certain structures with the characteristics of 'attentional control' networks seems to reflect an implicit assumption that attention involves an interplay between 'bottom-up', stimulus derived factors and 'top-down' factors. However the origin of such 'top down' factors is rarely made explicit, and seems to imply the existence of homuncular control (Frith et al., 1991).

Allport (Allport, 1993) cautioned that to apply labels such as 'attentional network' to specific brain structures requires care. If attention is a property of whole individuals, then it need not follow that the brain of that individual contains an 'attentional system' in the sense of functionally localised brain areas. To do so may be to make a category mistake (Ryle, 1949). This phrase is associated with the work of Ryle, who used a number of illustrative examples. For example, a visitor to Oxford or Cambridge might, having visited all the colleges and faculties, ask to see where the University is located. This is a category mistake, as the University is not from the same category as the other sights that the visitor has seen, and is subsumed in the distributed interaction of the individual mechanism is that delay period activity in the Posner task should be seen in oculomotor structures. During the delay period spatial attention is covertly maintained at a particular spatial location while awaiting a target. Tonically maintaining attention on a location should result in activity in those structures subtending the remapping process.
Neural correlates of selective attention components. Ryle used these examples to argue (Robinson, 1998) against faculty psychology and the legacy of phrenology (Spurzheim, 1832), with the assignment of different faculties (e.g. intellectual faculties, emotional faculties) to distinct brain regions. From a contemporary perspective, Ryle could be seen not as arguing against the idea that different areas of the brain are functionally specialised, but against the assignment of labels derived from phenomenology directly to regions of the brain. Similar circumspection might therefore be appropriate when invoking the idea of ‘distributed networks’ to ‘explain’ some particular faculty or phenomenological category (attention). This is not an argument to say that different areas do not participate in attentional tasks, but suggests that the (neurobiologically defined) function of these cortical areas that are involved in such tasks is not necessarily attention. In calling these areas ‘attentional’ we may be committing a category mistake.

This worry has not gone unnoticed in the imaging literature. Vandenberghe and colleagues, in a study of feature discrimination (Vandenberghe et al., 1997) cautiously stated that ‘It remains to be seen what cognitive processes are associated with the...parietal activity we observed.’ In previous work, Vandenberghe showed that parietal cortex was differentially active in association with attention to peripheral rather than to central targets (Vandenberghe et al., 1996), suggesting a role in the attentive processing of peripheral events. However, activation of this region during non-spatial tasks (Coull et al., 1996; Pardo et al., 1991) indicates that parietal cortex also fulfils a more general role in maintaining alertness or cognitive readiness. Experimental work presented elsewhere in support of this thesis (see Chapter 9) is consistent with a more general role for parietal cortex than the control of covert spatial attention alone. Our work shows that right frontoparietal structures are differentially involved in generating the spontaneous transitions of perceptual experience seen in binocular rivalry (Lumer et al., 1998), and that covariation between visual and non-visual areas may be important for visual awareness (Lumer and Rees, 1999). These, and other results (Griffiths et al., 1998; Kleinschmidt et al., 1998) suggest that the function of right parietal cortex may be to select between different neuronal events competing for visual awareness. This ‘function’ would be critical in spatial attention tasks, but would not suggest an explanation of parietal function solely on the basis of its involvement in spatial attention tasks as a ‘spatial attention network’.
Neural correlates of selective attention

1.4 Conclusions

The studies reviewed above lead to the broad conclusion that the effect of selective visual attention, in both humans and non-human primates, is to modulate activity in corresponding functionally specialised extrastriate visual areas. However the source of such effects, and the nature of attentional control, have been more difficult to establish consistently. Altering the precise pattern of task requirements can lead to different patterns of modulation across different visual areas associated with processing a given feature. Activation in parietal cortex, especially on the right, is associated particularly with the deployment of covert spatial attention to the periphery. However the involvement of this structure in a wide variety of other tasks suggests a more general role than simply the allocation of peripheral spatial attention.

Although most of the studies involved both attended and unattended stimuli, none have specifically addressed the issue of whether processing of unattended stimuli *per se* occurs. By characterising the difference between brain activity produced by attended and unattended stimuli, information is gained about how behavioural states can modify sensory processing. But as the unattended stimuli are not explicitly manipulated, this falls short of a characterisation of the nature and extent of unattended processing. For example, an attenuated response to an unattended stimulus might receive further processing and propagate fully through the visual system. Only manipulating the type (or presence) of unattended information can provide an explicit measure of unattended stimulus processing. Moreover, physiological studies have most often studied the modulation of sensory responses evoked by meaningless stimuli such as coloured patches or visual motion. Without the use of meaningful stimuli, it is not possible to examine whether meaning is extracted from ignored stimuli. This issue in particular is central to the question of how perception is dependent on attention. Although the presence of attentional modulation of sensory responses appears to be occurring both early in time and in very early cortical areas, these findings do not establish whether unattended processing occurs, and so do not resolve the critical issue.

In humans, this is in part due to the limited spatial resolution of functional imaging techniques when used to study spatial (i.e. retinotopically organised) visual attention. To disambiguate processing of attended and unattended stimuli requires that the activity evoked by each can be separately resolved. Although attended and unattended stimuli are
Neural correlates of selective attention

typically in distant parts of the receptive field, often the separation is not great enough that different activated areas of cortex can be resolved (see (Kastner et al., 1998) for a discussion). Where the separation is great enough - for example across the vertical meridian - the comparison made has been between attending to one hemifield and attending to the other (Heinze et al., 1994b). Because there is no comparison between an unattended hemifield where a stimulus is present and one where a stimulus is absent, there is no effective measure of unattended stimulus processing. Nevertheless, one recent study (Kastner et al., 1998) indirectly addressed this issue in an experiment that compared a single stimulus presented in the upper visual field with the same stimulus presented with three distractors in the lower visual field (experiment 2 of Kastner et al). Because the representations of the upper and lower visual fields are widely separated in extrastriate cortex, these authors were able to selectively visualise the activation caused by the upper visual field target. In the presence of three distractors the activation was reduced compared to the target alone, suggesting that the distractors were indeed processed and influenced the activity produced by the target.

There have been no studies that explicitly address the degree to which processing unattended stimuli occurs by manipulating the type of distractor present. However there are a wealth of suggestions from reported studies that extensive processing of unattended stimuli may occur. A number of investigators have studied attention to visual motion (Buchel and Friston, 1997; Buchel et al., 1998a; O'Craven et al., 1997). Both groups studied the brain activity caused by a visual stimulus in which a number of dots translated radially on the visual display. Subjects were asked either to attend to, or ignore, the moving dots. The primary conclusion of both studies is that attention modulates activity evoked in V5/MT by the moving dots (c.f. (Treue and Maunsell, 1996)). However inspection of the plots of activity in V5 presented by both Büchel (Buchel et al., 1998a) and O'Craven (O'Craven et al., 1997) shows that, even when subjects are asked to ignore the moving stimulus, there is activity in V5. Comparing the activity in V5 with a baseline condition where a fixation cross alone is present, the ignored dots evoke activity in V5 that represents about two-thirds of that when subjects are asked to specifically attend to the dots. This represents an impressive response modulation by attention: however it also shows that subjects have difficulty ignoring the motion. Even when subjects are asked not to specifically attend to motion, activity in motion-sensitive areas of visual cortex occurs. This falls short of a clear demonstration that unattended stimuli are always processed, however, particularly as subjects are asked ‘just to look’ at the moving stimulus and are
Neural correlates of selective attention

not given a distracting task. These issues are explored further in the remainder of the thesis.

1.5 Thesis material

1.5.1. Experimental approach

How might the processing of unattended stimuli be measured? The most basic requirement is for an explicit measure of whether unattended stimuli are processed. By this is meant some comparison between brain activity evoked by unattended distractors of different types, rather than simply between attended and unattended stimuli. The literature reviewed above has emphasised the use of such behavioural measures as interference or negative priming. In functional imaging terms, as the technique is inherently a relative one (comparing different conditions) then the most basic requirement is for two conditions in which unattended stimuli are either present or absent. Alternatively interference or negative priming can be studied by including unattended stimuli that either do, or do not, produce the behavioural measure in question. A more sophisticated approach is to study the interaction of unattended and attended stimuli using a factorial design in which the presence or absence or unattended or attended stimuli is manipulated independently of one another. A final approach is to use a parametric manipulation of unattended stimuli (such as the number of stimuli, or their presentation rate) in order to set up a correlation between evoked activity and the presence of unattended stimuli. The change in the form of such a correlation can be used to measure both how attention changes the processing of ignored stimuli when they become attended, and to index whether unattended stimuli are processed at all (i.e. whether there is any correlation between the parameter being varied and evoked activity). What all these measures have in common is that there is some explicit manipulation of the presence, or the attributes of the unattended stimuli, that can be used to characterise their effect on cerebral activation. A range of such measures are explored in this thesis.

1.5.2. Overview of work

The work presented in this thesis represents a total of seven functional imaging experiments carried out over a three year period investigating the processing of unattended stimuli. After reviewing the general methods in Chapter 2, the first two
Neural correlates of selective attention experiments are presented in Chapter 3. Here the manipulation of stimulus presentation rate is investigated as a way of indexing the processing of attended and unattended stimuli. The modulation of brain activity by attention takes a very different form in separate cortical areas, suggesting that there are at least two physiologically distinct mechanisms by which attention can modulate sensory processing. In the second of the experiments, attention is directed to either visual or auditory streams. When attention is directed away from visual cortex, rate correlated activity is nevertheless seen throughout extrastriate cortex, demonstrating the existence of unattended stimulus processing. In Chapter 4 the consequences of such processing are explored by systematically manipulating the identity of ignored distractors. When the distractors are fully processed they produce negative priming. Subcortical structures including the corpus striatum show time-dependent changes associated with negative priming, suggesting a link between distractor processing, negative priming and implicit learning. Having investigated the neural correlates of distractor processing, the experimental work then turns to investigating the determinants of such processing. Two experiments are described in Chapter 5 that independently manipulate the identity of distractors and the perceptual load of the primary task. The results indicate that perceptual load is a major determinant of selective processing in the visual system, and show how imaging can be used to directly test cognitive psychological theories of attention. Finally, a specific aspect of distractor processing, the extraction of meaning, is explored under conditions of inattention. Under sufficiently demanding conditions, the results presented in Chapter 6 indicate that even highly salient foveally presented stimuli are not perceived. Finally, in an appendix to the main thesis, Chapter 8 describes a further exploration of the rate methodology, suggesting that it may be difficult to use this approach successfully in fMRI due to fundamental differences in the techniques.

To aid comprehensibility, the chapters are self-contained and should be understandable in isolation, though the relevant material in other chapters is cross referenced throughout and the chapters are presented in logical sequence. Taken together, these studies illustrate ways in which functional imaging can be used to give insights into the nature of attentional mechanism, and suggest a neurobiological account of visual attention based strongly on processing constraints within the visual system. Future work is outlined that will test these proposals more fully.
Chapter 2  General Methods

The bulk of the work presented in this thesis combines conventional behavioural measurements of task performance with the biological imaging techniques of Positron Emission Tomography (PET) and functional MRI (fMRI). These techniques allow the direct measurement of components of the cerebral haemodynamic response that can be used as an indirect reference for neural activity. This chapter explains the basic principles behind the two imaging methodologies, and an outline of the approach to data analysis used elsewhere in the thesis. It is not intended to be a comprehensive overview of the techniques, nor an exploration of the relationship between neural activity and cerebral haemodynamics. The interested reader is referred to Chapter 8, where some of the former issues are explored theoretically and experimentally, or to one of the general textbooks of functional imaging now available (Frackowiak et al., 1998; Toga and Mazziotta, 1996).

2.1 Positron Emission Tomography

2.1.1. General overview

Positron Emission Tomography (PET) is a technique that is used to characterise the distribution of radiolabelled probes in biological systems. Positron-emitting isotopes are produced by a cyclotron and used to label molecules of a compound of interest whose distribution can then be examined directly. Atoms of the positron-emitting isotope radioactively decay, emitting a positron and a neutrino. While neutrinos can only be detected by elaborate methods, positrons rapidly lose energy through collision with electrons in tissue and within a very short distance are annihilated through such a collision, giving rise to two high energy gamma rays. The energy of these gamma rays, that are emitted in opposite directions, is such that they escape the body and can be detected by a PET camera. The camera consists of circumferential arrays of scintillation detectors that identify coincidental emission of gamma rays on opposite sides of the head. By combining data from many different detectors simultaneously and using a back projection algorithm the count density within the head can be determined.
The neuroscientific attraction of PET lies in the existence of positron emitting isotopes of carbon, nitrogen and oxygen, that are the major elemental constituents of the human body. This gives PET considerable flexibility in labelling different biological substrates, including neurotransmitters and glucose. However, in the work presented here a single positron-emitting substance, H$_2^{15}$O, was used. This tracer diffuses freely across the blood-brain barrier and so uptake in cerebral tissue is determined by the blood flow to that tissue rather than the diffusion rate of the tracer into tissue. After injection of a bolus of H$_2^{15}$O, the tracer is extracted from plasma into cerebral tissue on the first pass through the brain and the tracer uptake is highly correlated with cerebral blood flow. The PET imaging therefore takes less than two minutes, and the half life of H$_2^{15}$O is relatively short so repeated measurements every 8-12 minutes are possible.

2.1.2. PET experimental design

The studies described in this thesis were performed using the ECAT EXACT HR+ system (CTI Siemens, Knoxville, TN) at the Wellcome Department of Cognitive Neurology (Institute of Neurology, University College London). The scanner was operated in 3D mode with septa retracted (meaning that coincidences are not detected only within a 2D ring of detectors, but across all geometric combinations of detectors) with increased sensitivity to head counts produced by the use of a NeuroInsert (Grootoonk et al., 1996). A venous cannula to administer the tracer was inserted in the left antecubital fossa vein of the subject. Approximately 350 MBq of H$_2^{15}$O in 3ml of normal saline was loaded into intravenous tubing and flushed into subjects over 20s at a rate of 10ml/min by an automatic pump. After a delay of approximately 35s, a rise in counts could be detected in the head that peaked 30-40s later (depending on individual circulation time). The interval between successive H$_2^{15}$O administrations was 8min. The data were acquired in one 90 second frame, beginning 5s before the rising phase of the head curve. Correction for attenuation was made using a transmission scan collected at the beginning of each study. Images were reconstructed by filtered back projection (Hanning filter, cut off frequency 0.5 cycles per pixel) into 63 image planes (separation 2.4mm) and into a 128x128 pixel image matrix (size 2.1mm).

Each study typically involved between five and nine subjects who were studied with twelve separate measurements of cerebral blood flow, every eight minutes, over a two and a half hour period. All subjects gave informed consent for their participation in the
Neural correlates of selective attention

studies, that were approved by the National Hospital for Neurology & Neurosurgery ethics committee. At the end of each study, an anatomical T1 weighted MRI structural image was obtained for subsequent coregistration of the activation data. The radiation dose limitations appropriate for the study of healthy normal individuals with PET mean that each subject is usually scanned only twelve times within a single session. During an individual scan, the experimental paradigm is typically started manually by the experimenter prior to data acquisition. The data are acquired in a single 30s frame, so it is important that task performance is stable during this window. Within these constraints all potential types of experimental design can be accommodated (Frackowiak et al., 1998): in this thesis both simple 2x2 factorial designs and factorial parametric experiments are presented.

2.2 Functional Magnetic Resonance Imaging

2.2.1. General overview

In normal neurological (clinical) use, the magnetic resonance signal produced by brain tissue comes mainly from the protons in tissue water, and this signal varies with the local tissue environment of the protons. Placing a body in the large static magnetic field of an MRI scanner leads to the proton magnetic moments becoming aligned along the axis of that magnetic field. By displacing their alignment through excitation with a radiofrequency pulse, and then measuring the energy produced by the longitudinal relaxation of the magnetic moments back to their original alignment, an image that reflects the tissue environment of the protons can be produced. In addition to this longitudinal (T1) relaxation, differences in the magnetic environment of each spin also lead to differences in the transverse relaxation time (T2) caused by precession of the spins about the longitudinal axis of the static magnetic field. In addition the presence of paramagnetic particles within an object to be imaged (e.g. due to spatial inhomogeneity) cause an additional relaxation, that together with the T2 effect is known as T2* relaxation. In the early 1990s it was realised that variations in T2* could be exploited to measure cerebral blood flow via the injection of a paramagnetic vascular marker such as gadolinium. The combination of this technique with an ultrafast image acquisition technique, echoplanar imaging (EPI) (Mansfield, 1977), allowed dynamic imaging of the passage of such a contrast agent through the brain. This lead to the first measurements of changes in cortical perfusion with MRI (Belliveau et al., 1991), that could be thought of

2-36
Neural correlates of selective attention

as loosely analogous to a PET measurement. In this experiment Belliveau and colleagues compared the signal returned when subjects viewed a flickering visual checkerboard stimulus with a static non-flickering display (Belliveau et al., 1991). Strong activation related to visual stimulation was seen in occipital cortex. The next step was the rediscovery that deoxyhaemoglobin is more paramagnetic than oxyhaemoglobin, meaning that haemodynamic changes that alter the relative proportion of oxy- to deoxyhaemoglobin will change the magnetic environment and therefore the MRI signal around these cortical vessels. The development of EPI sequences specifically sensitive to T2* signal (known as Blood Oxygenation Level Dependent or BOLD contrast) allowed the non-invasive functional imaging of changes in cortical haemodynamics related to cerebral activity (Kwong et al., 1992; Ogawa and al, 1993) This technique is used in the MRI experiments presented in this thesis.

The exact relationship between neural activity and BOLD contrast is still under active investigation (Toga and Mazziotta, 1996), but the basic principles have been established using a combination of optical imaging, single cell electrophysiology and MRI (Malonek and Grinvald, 1996). Neural activity in the brain appears to cause an initial increase in oxygen consumption, leading to a rise in deoxyhaemoglobin concentration and a fall in the MR signal that can be seen at high field strengths (Menon et al., 1995). This brief ‘early dip’ is then superseded by a large rise in the signal that is thought to reflect a transient increase in blood flow to the active area. Because the flow increase temporarily outweighs the consumption, a large transient decrease in deoxyhaemoglobin concentration occurs, giving rise to a large peak in the MRI signal that is easily seen using EPI at field strengths of 1.5T and greater. At the lower field strengths (less than 2 Tesla) used in this thesis, this latter signal is dominant and the ‘early dip’ is usually not seen. Note that the origin of the signal depends on an imbalance of flow and metabolism {see also (Fox et al., 1988)}. If the resupply of oxyhaemoglobin always balanced tissue consumption, no change in the BOLD contrast MRI signal would be seen. Technical issues regarding the origin of the BOLD signal are usually only tangential to the conduct of cognitive experiments. However in this thesis, Chapter 8 contains further discussion and an experiment explicitly addressing the relative stimulus dependencies of PET and fMRI signals, as this is relevant to the rate modulation technique presented in Chapter 3. Similarly the relationship between neurophysiological findings at a single neuron level (from single cell electrophysiology) and those recorded with functional imaging from populations of several hundred thousand or million neurons is not well understood. The
Neural correlates of selective attention

use of fMRI techniques on awake behaving monkeys will begin to address this question (Stefanacci et al., 1998) by allowing the simultaneous recording of single neuron activity and evoked haemodynamic activity from cortical areas.

2.2.2. fMRI experimental design

The studies described in this thesis were performed on the 2T Siemens VISION (Siemens, Erlangen) at the Wellcome Department of Cognitive Neurology using BOLD contrast EPI. Each study typically involved scanning between six and nine subjects. Unlike PET, fMRI acquisition is typically continuous with each volume (comprising multiple contiguous slices) being acquired every 2-6 seconds. The lower signal to noise ratio, continuous acquisition and specific artefacts make a knowledge of potential statistical confounds invaluable in designing effective fMRI experiments. The most important of these are described briefly here: these issues are described in more detail elsewhere (Turner et al., 1998).

Head motion is an important potential confound for both PET and fMRI experiments. The experimenter attempts to minimise head movement through the use of soft padded restraints. The dynamic nature of fMRI data acquisition means that not only the position of the object in the scanner, but also the history of the object within the scanning environment will affect the signal within a slice. This means that even when motion effects are removed through realignment of multislice images (see section 2.4.1.), there may be residual signal changes related to subject motion. Typically the repeat time (TR) in multislice functional imaging studies is of the order of the T1 relaxation time for brain tissue, so out-of-plane motion can create a different spin excitation history for different groups of spins within a slice being imaged. This contaminates the data with motion correlated signal intensity changes, so an additional autoregressive algorithm is used with fMRI realignment to remove this component of the signal (Friston et al., 1996b). This represents a practical problem for paradigms where stimulus-correlated head movement occurs, as any signal evoked by task performance that is also correlated with subject motion will be removed by this algorithm. This particularly affects sensorimotor paradigms in which proximal limb movement occurs. Similarly, paradigms where spoken responses are required also produce task-correlated head movement as well as more subtle changes in the local magnetic field homogeneity. For this reason experiments that require spoken responses are inadvisable.
In addition to motion-related changes in signal, fMRI images contain other sources of noise. Modern scanners remain stable over extended scanning periods, so variability in the signal is mostly physiological in origin (Turner et al., 1998). At a typical repetition time (TR) of a few seconds, the dominant source of this noise is due to the aliasing of cardiac and respiratory cycles. Because cardiac and respiratory cycles are a close, but non-integer multiple of the repetition time, aliasing of these frequency components will create an additional artefactual signal of relatively low frequency. In addition slow changes in blood oxygenation also appear to occur over the course of an experiment (Biswal et al., 1995), giving rise to low frequency drifts and shifts that contaminate the fMRI signal. These low frequency components can be modelled and removed statistically with a Fourier series with a relatively low frequency cut off that effects a high pass filter (Holmes et al., 1997). However the presence of such confounds also informs experimental design. Most experimenters choose to design experiments in such a way that active experimental conditions alternate in ‘epochs’ of between thirty and forty seconds. Experimental conditions alternate with a recurring low level control period, and the objective is to assess the mean level of activity over the course of an epoch in each experimental condition. The variability in the activity of the recurring control condition can be used to characterise low frequency drifts and shifts. More importantly, the alternation of experimental conditions creates a fundamental frequency for the task related activation that is sufficiently high to be clear of the low frequency region of the noise spectrum, without being so high as to be attenuated by the sluggish haemodynamic response.

The slow rise and fall of the haemodynamic response that occurs in response to neural activity means that the haemodynamic activity measured by fMRI is effectively a low pass filtered representation of the neural activity {assuming linearity: see Chapter 8 and (Friston et al., 1998b)}. During an experimental epoch, task performance results in successive haemodynamic responses to repeated neural activity that in effect summate, producing a smooth mean level of activity. Inferences can then be made about the variation in that mean level of activity with some experimental manipulation. As with PET, all conventional psychological designs can be implemented (Frackowiak et al., 1998). In this thesis, both simple 2x2 factorial designs and more complicated parametric factorial designs are used.
Neural correlates of selective attention

More recently, advances in experimental design and analysis have made it feasible to attempt to detect the modulation of haemodynamic activity to individual neural events ('event-related' fMRI). This is equivalent to time locking fMRI acquisition to individual task events, in a manner analogous to ERP, and seeking evidence for modulation of the resultant evoked response. This requires that the individual events be separated in time during performance of a task sufficiently far that the individual haemodynamic responses to task events can be resolved. The timing of individual events can be used to create an event train that is then convolved with a synthetic haemodynamic response to create a regressor that represents the expected haemodynamic response to these task events. The functional imaging data can then be examined for the presence of such event-related modulation. In the supporting material to this thesis, an experiment using this methodology is presented (Lumer et al., 1998). In this experiment, Dr. Erik Lumer and myself investigated the neural correlates of spontaneously occurring transition events in binocular rivalry. By asking subjects to press a button whenever they experienced a transition between different monocular views of a rivalrous stimulus, we were able to look for activity specifically correlated in time with perceptual transitions. Compared to a control condition, differential activity time locked to these transitions in binocular rivalry was seen only in right frontoparietal structures. In recent work we studied how such responses to rivalrous stimuli evoked in visual and extrastriate cortex covaried in space and over time (Lumer and Rees, 1999). Analytic techniques for event related fMRI are still evolving, and the interested reader is directed to the relevant literature (Friston et al., 1998a) for further information.

The other fMRI studies described in the thesis used a conventional alternating epoch design. Each scanning run (comprising 80-300 volumes) is also preceded by six or eight 'dummy' scans to allow for equilibration of T1 relaxation effects. The dummy scans are discarded prior to analysis. All subjects gave informed consent for their participation in the studies, that were approved by the National Hospital for Neurology & Neurosurgery ethics committee. In addition to the T2* weighted BOLD contrast volumes, an anatomical T1 weighted structural image was also acquired for each subject.

2.3 Comparing PET and fMRI

The most important differences between the two techniques is that they differ in spatial and temporal resolution. A typical PET study involves 12 separate measurements, each of
Neural correlates of selective attention

which takes place over some 30 seconds. An equivalent single measurement in fMRI takes place over 3 seconds. The more rapid temporal resolution of the latter technique opens the way to ‘event-related’ designs, where the modulation of the haemodynamic response by brief events is detected. The effective spatial resolution of PET is around 10-15mm; for the fMRI sequences used in our laboratory the effective spatial resolution is 5-10mm. Despite the superior spatial resolution of fMRI, the technique has important spatial limitations that affect the ability to image certain areas of the brain. Near air-filled sinuses (anterior and inferior frontal regions; mid-temporal lobes), artefacts and signal drop out due to dephasing of spins typically mean that these areas are not imaged well with BOLD fMRI. These difficulties vary considerably between subjects, depending on their individual anatomy. Drop out in mid-temporal regions has potentially important implications for imaging this area in language studies. However, this has not been an important issue in the work presented here.

Although fMRI has superior spatial and temporal resolution, this does not mean that innovative use of PET cannot allow inferences about neural activity occurring on a shorter timescale. In Chapter 3 modulation of stimulus presentation rate during PET scanning is used to make inferences about the form of different event-related patterns of neural activity. Furthermore there are important technical difficulties with fMRI that do not always make it the technique of choice. While PET is almost completely silent, fMRI (even with shielded coils) produces noise levels of around 100dB in the bore. Although it is feasible to perform auditory psychophysical experiments [see supporting material & (Griffiths et al., 1998)] in the magnet, the environment is considerably more hostile and stressful for the subjects. This of particular concern where perceptual load is manipulated in the auditory domain. In section 5.5 PET is used rather than fMRI to test whether auditory perceptual load affects visual processing for this reason. Similarly in PET access to the subject is unrestricted if additional apparatus is required; however in fMRI the subject in entirely enclosed in the RF coil and bore of the magnet. This leads to a restricted field of view (compared to PET) for the presentation of visual stimuli, and difficulty introducing any other instrumentation. Both restricted access and the need for materials that are not ferromagnetic provide a challenge to the experimenter who needs to use additional instrumentation. For example, the RF energy produced during imaging produces pronounced electrical artefact on simultaneously recorded EEG or EOG traces making it technically challenging to monitor eye movements and very difficult to simultaneously record EEG potentials.
Neural correlates of selective attention

2.4 Statistical Methodology

Raw images from fMRI and PET scanners require considerable pre-processing before changes in haemodynamic activity produced by experimental conditions can be estimated. In this thesis the package Statistical Parametric Mapping (Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm) was used to perform these steps. The package is implemented in MATLAB (The Mathworks, Inc, Sherborn MA, USA) running on SUN Ultra-2 workstations (SUN Microsystems Inc, Surrey, UK). The essential pre-processing steps prior to statistical inference are realignment, spatial normalisation and spatial smoothing. These steps are outlined here: more detailed expositions are also available (Friston et al., 1995a; Friston et al., 1996a; Friston et al., 1995c; Friston et al., 1996b; Turner et al., 1998).

2.4.1. Realignment

The first six to eight images (fMRI) of a scanning run are typically discarded to allow for T1 equilibration effects. The remaining functional images acquired from a single subject are realigned to the first in order to correct for subject motion. The algorithm used (Friston et al., 1995a; Friston et al., 1996b) is a least squares algorithm for the three affine translations (x, y and z) and rotations (pitch, roll and yaw). Typically, movements of the order of a few millimetres only are seen. Excessive movement can lead to significant artefact in the final statistical analysis, typically affecting the anterior and posterior edges of the images or producing flat 'plate like' activation artefacts. This is a particular problem when scanning patients, who frequently move more than normal subjects. After realignment, the T1 structural image is coregistered to the functional images, thus putting all the images acquired from a single subject in the same anatomical space. The procedure followed with PET images is identical, although only the transmission scan is discarded before realignment.

2.4.2. Spatial normalisation & smoothing

To facilitate comparison between subjects and reporting of the data in a stereotactic reference, the data are then spatially normalised. This is not necessary if only a single subject is analysed, as activations can be related directly to that individual’s surface anatomy; however even then it still facilitates reporting and comparison with other
Neural correlates of selective attention

findings. The normalisation technique used here involves determining a twelve parameter transformation between one of the experimentally acquired images and a template in stereotactic space (Friston et al., 1995a). These parameters are then applied to all the functional and structural images, bringing them into a standard anatomical space. In this thesis the stereotactic space of the Montreal Neurological Institute, that conforms to that of the atlas of Talairach & Tournoux (Talairach and Tournoux, 1988) was used. Typically normalisation parameters are determined from a T1 structural image that has been coregistered with the functional image, or a mean functional image (PET or fMRI) to the appropriate template (rCBF or EPI T2*). After normalisation, a small amount of spatial smoothing is applied using a Gaussian kernel. This both allows for residual intersubject variability when characterising group activations, and permits the use of parametric statistics (see below).

2.4.3. Statistical Inference

The approach used within SPM is a massively univariate approach using the General Linear Model (Friston et al., 1995c). User specified parameters are used to create a design matrix of hypothesised effects either introduced by the experimenter (e.g. experimental conditions), related to the functional images themselves (e.g. global changes in cerebral blood flow) or unknown (e.g. drifts and shifts in the fMRI signal over time). The design matrix contains one column for each hypothesised effect, and one row for each scan. By fitting the design matrix to the time-series data at each voxel independently using multiple linear regression, then at each voxel a set of parameter estimates reflecting the model fit can be derived. The Theory of Random Gaussian Fields allows the use of parametric statistical inference on these parameter estimates provided certain assumptions are met by the data. The most important of these is that the smoothness of the data exceeds a criterion value of approximately 3.5 times the voxel size. This is achieved by applying a small amount of spatial smoothing with a Gaussian kernel to the data (PET 12-20mm; fMRI 5-10mm). Regionally specific differences in cerebral blood flow are assessed using linear contrasts between experimentally interesting parameter estimates. Each contrasts produces a statistical parametric map (SPM) of the t-statistic. Appropriate contrasts between condition-specific effects are generated to test the experimental hypotheses. The SPM\{t\} is typically thresholded at Z=3.09 (p<0.001 uncorrected for multiple comparisons) and the resultant areas characterised in terms of their peak height
Neural correlates of selective attention and/or spatial extent. This procedure yields a $Z$ score for each activated area and a $p$ value that has been corrected for multiple comparisons using a Bonferroni like procedure.

A general property of the statistical inference procedure used in this study is that the whole brain is examined simultaneously, giving rise to a significant problem of multiple comparisons. There are up to 150,000 voxels in a typical fMRI volume, although the smoothness of the data means the effective number of independent measurements within each volume is somewhat smaller. Very recently, small volume corrections for Gaussian Field Theory (Worsley et al., 1996) have become available within Statistical Parametric Mapping software. This allows the analysis (and estimation of $p$ values) to be confined to small regions of interest. However, at the time most of the experimental data presented here was obtained, these were not available. Hence although a $Z$ score is available for each activated region, only two $p$ values are generally available. One is uncorrected for multiple statistical comparisons, which is probably rather too liberal. However the other is corrected for every single voxel in the brain, which is probably rather too conservative (as it is usually possible to make an a priori regional prediction of which lobe the activation is likely to be in, for example). The general convention adopted in the work presented here is therefore to assess significance based on uncorrected $p$ values if the region of interest has been predicted a priori before the data was collected (to within about one full-width half-maximum of the smoothing kernel employed). For all other areas and activations not predicted a priori, corrected $p$ values are used.
Chapter 3  Neural correlates of selective attention

3.1 Introduction

In the first experimental chapter, the rate of presentation of visual and auditory information was varied to give an index of stimulus processing. The primary focus of this work addressed the nature of attentional selection. In particular this work was used to investigate the differences between the brain activity produced by attended and unattended stimuli. Although the material reviewed in Chapter 1 suggested that attention operates by changing the sensory evoked responses to visual stimuli, here the particular mechanism is examined in more detail. Evidence from neurophysiological studies is reviewed that leads to the suggestion that there are two different types of attentional signal that are involved in the selection of visual information. Two functional imaging experiments using PET are presented that suggest that two physiologically distinct types of change in sensory activity are seen in humans. The relationship between these changes and those seen at a single cell level are discussed. Moreover, in visual and auditory cortex the results show that even ignored stimuli evoke rate correlated brain activity, suggesting processing of these unattended stimuli.

3.1.1. Single neuron mechanisms of selection

Moran and Desimone (Moran and Desimone, 1985) investigated whether responses of single cells in visual areas differed depending on whether or not a monkey was attending to a stimulus. In primary visual cortex, there was no difference, but in area V4 the response to an irrelevant stimulus was reduced by about two-thirds. Moreover, this attenuation only occurred when both attended and unattended stimuli were located simultaneously within the receptive field (RF) of the neuron. When the unattended stimulus was outside the receptive field and the attended stimulus inside it, no modulation of neural responses was observed. In inferotemporal cortex (IT), attenuation was always observed, as the receptive fields in this area are large and cover most of the visual field. The effects of attention are invariably seen when both relevant and irrelevant stimuli are presented simultaneously, but effects are also seen when stimuli are presented sequentially, suggesting that competition takes place in both space and time (Luck et al., 1997).
Neural correlates of selective attention

Desimone and Duncan (Desimone and Duncan, 1995) argued that these findings were compatible with a 'biased competition' model of attention, where objects in the visual field compete for processing at the receptive field level. The role of top-down selective influences is to bias the processing at a cellular level towards one stimulus or the other. The results of Moran & Desimone are consistent with this as they show that attention only has an effect when relevant and irrelevant stimuli are competing for the cell’s response. According to the ‘biased competition’ model, perceptual selection is a two-stage process (Desimone and Duncan, 1995). Initially, top-down signals bias activity in neurons representing the relevant object or location. Consistent with this, elevations of baseline firing rates are seen in V4 neurons whenever attention is directed towards their receptive field (Luck et al., 1997); similarly in IT, neurons show elevated activity in the delay period of a delayed match-to-sample task (Chelazzi et al., 1993). These findings are consistent with an extrinsic ‘bias’ signal. In the second stage of perceptual selection, neurons that have received a bias signal gain an advantage in their competitive interactions (mediated through local intrinsic connections) with other neurons. Consistent with this, attention to non-spatial features of objects influences not only baseline (spontaneous) firing rates but also modulates stimulus-evoked responses (Ferrera et al., 1994; Haenny et al., 1988; Luck et al., 1997). Thus it seems that there are at least two different mechanisms at a single cell level that might mediate selective attention. In visual cortex, elevations in baseline firing rate and modulation of stimulus-evoked activity both appear to occur during selective visual discriminations.

3.1.2. Evoked potentials in humans

Electrophysiological studies in humans have been discussed briefly in section 1.3.2. and a more comprehensive review is available (Hillyard et al., 1998). The most important finding from ERP studies is that components arising very soon after the presentation of a stimulus clearly differ as a function of whether the stimulus is attended or ignored (Hillyard et al., 1995). The visually evoked component P1 is smaller when a stimulus is ignored because of its location. When selection is based on stimulus attributes other than location, such as colour, an additional component is superimposed on the N1 and P1. This colour selection component is substantially reduced when the stimulus is in an ignored spatial location, suggesting that the location and colour selection are organised hierarchically with location-selection dominant (Mangun et al., 1993). The location of the
Neural correlates of selective attention
generators of these components in early sensory processing areas suggests that the
mechanism of selection not only operates very soon after stimulus presentation but also
very early in the anatomical hierarchy of processing areas (Woldorff et al., 1993). It is
difficult to relate these ERP findings to the single cell data, because stimuli in ERP
studies are frequently presented alone to aid interpretation of the resultant waveforms.
Furthermore where ERP attention effects have been seen as a function of competition
between relevant and irrelevant stimuli, the stimulus conditions have never led to the
simultaneous presence of attended and ignored stimuli inside a single receptive field in
extrastriate cortex.

3.1.3. Functional imaging studies

In humans, functional imaging studies have shown that attention to different attributes of
visually presented stimuli changes evoked activity in areas of cortex concerned with
processing those attributes. For example, attention to the colour of visual stimuli changes
evoked activity in cortical area V4, compared to attention to the motion of identical visual
stimuli (Corbetta et al., 1990; Corbetta et al., 1991b) Similarly, attention to visual motion
modulates the stimulus-evoked activity in cortical area V5 (Büchel and Friston, 1997;
O’Craven et al., 1997). These functional imaging experiments have demonstrated the
general principle that attention modulates functionally segregated and stimulus-specific
regions of visual cortex, but have not provided any insight into the mechanism of such
processes. The reason for this lies in the experimental design; typically investigators have
compared a state where the subject attends to a certain aspect of a display with a state
where the subject receives identical visual stimulation but does not attend. The difference
in activity between these two states has been attributed to the effects of attention.
However in light of the preceding discussion it can be seen that such a difference between
‘attend’ and ‘no attend’ conditions necessarily conflates both additive and interactive
(stimulus-evoked) components of attention. Intuitively this can be seen by imagining
performing the experiment again but without using a stimulus. Would comparing ‘attend’
and ‘no attend’ reveal a difference in evoked activity (that could be produced by a change
in baseline firing rates or bias signal), or is such a difference contingent on stimulus-
evoked activity (a true modulatory effect of attention)? Such a thought experiment serves
to illustrate the theoretical point that to characterise the effects of attention using
functional imaging requires an experimental manipulation of stimulus-evoked activity
that is independent of the experimental manipulation of attention. The independent
Neural correlates of selective attention

manipulation of attention and stimulus-evoked activity allows the separate
caracterisation of attentional effects due to modulation of the stimulus evoked activity
per se, or due simply to changes in baseline activity independently of that evoked by the
stimulus. Note that the requirement for a measure of stimulus-evoked activity
independent of the attentional manipulation is largely a consequence of the time over
which functional imaging measurements are acquired (of the order of seconds) relative to
the time scale over which the neuronal effects are manifest (of the order of milliseconds).
This means that in any given trial, both stimulus evoked and baseline activity are lumped
together. To separate the effects of attention on each requires some independent
manipulation of stimulus-evoked activity.

Frith & Friston (Frith and Friston, 1996) proposed that such an independent measure of
stimulus-evoked activity might be elicited by varying the rate of presentation of visual
and auditory stimuli. The basis for this proposal is the observation that cerebral blood
flow in primary sensory, primary motor and higher order association cortices increases
with increasing stimulus presentation (Frith and Friston, 1996; Price et al., 1996a; Rees et
al., 1997c; Sadato et al., 1997). The most likely interpretation of these results is that each
stimulus produces a transient increase in blood flow such that the total increase in blood
flow is directly related to the number of stimuli presented during the scan. This means
that the slope of the line relating activity to presentation rate is an index of the amount of
transient activity associated with the presentation of a single stimulus. Attention can now
be investigated by studying how the slope or intercept of this line varies with the direction
of attention (Figure 3-1). A change in slope implies a true modulatory effect of attention;
the amount of activity associated with each stimulus presentation is directly changed. On
the other hand, a change in intercept implies that the activity associated with each
stimulus presentation is unchanged, but instead a 'bias' signal, constant across different
presentation rates, is added. This pattern implies that there may be activity in an area even
in the absence of stimulus presentation.

The approach outlined here relies on measuring the relationship between rCBF and a
stimulus variable (presentation rate), and then examining how a manipulation of attention
changes this relationship. Certain assumptions are implicit in this approach that should be
made clear. Most importantly, the assumption is made that within an area, the gain
control or bias signal factor is constant across different presentation rates. If this
assumption is incorrect then the measured changes in rCBF, although remaining a correct
Neural correlates of selective attention
description of the effects of attention on rCBF, will be falsely attributed to a single underlying mechanism. In other words this approach makes the simplifying assumption of a unitary neurobiological mechanism of attention with a constant gain control or bias signal across the range of presentation rates studied. In these initial experiments a restricted range of presentation rates is used for this reason.
Neural correlates of selective attention

Figure 3-1: Theoretical illustration of modulatory effects of attention.

Activity evoked by a stimulus is modulated by an additive ‘bias’ signal that is constant over time (B) Activity evoked by a stimulus is modulated by a ‘gain control’ or multiplicative scaling (C) Effect of a bias signal on evoked activity integrated over a short time period. The ‘bias’ signal is constant over stimulus presentation rate, so results in a change in the intercept but no change in slope (D) Multiplicative scaling by a ‘gain control’ results in a change in the slope relating stimulus rate to integrated response. In this case there is an interaction between attention and the rate-correlated response.
3.2 Two physiological correlates of attention

3.2.1. Introduction

Selection is the essence of attention, whether of a train of thought, a particular location, or a specific object (Duncan, 1984; James, 1890/1976; Posner and Petersen, 1990; Vecera and Farah, 1994). A general account of selectivity must deal with both spatial and non-spatial selection. The biased competition model (Desimone and Duncan, 1995) suggests that selectivity arises from competition among relevant and non-relevant stimuli according to both bottom-up and top-down factors. Bottom-up factors are those concerning stimulus saliency, whereas top-down factors are a way of biasing bottom-up competition in favour of signals currently relevant to behaviour. The neuroanatomical basis for such a model is not clearly established. Objects in the visual field compete for processing in several cortical areas (Desimone and Duncan, 1995; Duncan, 1993). Signals pass from primary visual cortex into inferotemporal cortex and are important for object recognition, while other signals pass to posterior parietal cortex and are important for spatial perception (Duncan, 1984; Posner and Petersen, 1990; Ungerleider and Mishkin, 1982; Vecera and Farah, 1994). A great deal of work has implicated the parietal lobe in the context of a larger functional network including dorsolateral frontal cortex and prefrontal cortex, in spatial selection through shifts of attention (Corbetta et al., 1995; Eglin et al., 1991; Mesulam, 1990). Object recognition involves selectivity among factors other than spatial location, and one might expect to find a basis for it in inferotemporal structures. Several lines of evidence suggest the involvement of inferotemporal cortex (Haxby et al., 1991; Tanaka, 1993), and it has been suggested that modulatory biases to inferotemporal cortex arise in dorsolateral frontal cortex (Fuster et al., 1985; Wilson et al., 1993). In this experiment, evidence was therefore sought for functional interactions between dorsolateral frontal and inferior temporal cortex during selective attention to objects.

Presentation of a visual stimulus evokes transient neural activity. The neural implementation of selective attention (top-down influences on sensory processing) implies a modulation of that transient activity. The theoretical discussion above suggests that this modulatory influence could take two distinct forms. First, the transient activity...
Neural correlates of selective attention associated with processing of the visual stimulus may be enhanced (or suppressed) directly ("phasic" modulation). It has been suggested that this sort of modulation is active in prestriate cortex during selective attention to visual motion (Corbetta et al., 1991b). However the modulation could act a second way, by increasing the "tonic" neural activity in a cortical area even in the absence of stimulus related neural signals ("tonic" modulation). This type of modulation takes the form of a 'bias' signal that is task dependent, but stimulus independent, and is suggested by the biased competition model. In this experiment PET is used to detect the difference between these two types of modulation by varying the rate of presentation of the stimulus across scans.

On theoretical and empirical grounds it was suggested in section 3.2 that the slope relating brain activity to presentation rate is an index of the amount of transient activity associated with the presentation of a single stimulus. "Phasic" and "tonic" modulation by attention can now be distinguished by their different effects on the relationship between activity and presentation rate (Figure 3-1c & 1d). "Phasic" modulation directly affects the processing of each stimulus, analogous to an amplifier gain control or the contrast control on a television set. However "tonic" modulation represents a change in activity in a rate responsive area that does not alter the correlation between activity and presentation rate. This might be thought of as modifying stimulus processing by adding an offset or bias signal. This is directly analogous to the brightness control on a television set. Note that this analogy is purely illustrative. The neural instantiation of "phasic" modulation might, for example, represent modulation of spiking frequency, number of spiking neurons, or any number of other effects. Functional imaging studies activity in populations of neurons, and so the theoretical analysis developed here should not be thought of as making predictions about the spiking behaviour of individual neurons. This technique was applied by varying the rate of presentation of items in a non-spatial visual attention task, to characterise the anatomy and neural dynamics of selective visual attention.

3.2.2. Methods

3.2.2.1. Subjects and stimuli

Subjects categorised serially presented single visual targets by individual features (colour or orientation), or the conjunction of colour and orientation. All subjects were strongly
Neural correlates of selective attention

right handed males aged 31-76 (mean 40.5 years) who gave their informed consent for participation in this study. Approval for conduct of the study was also obtained from the National Hospital for Neurology & Neurosurgery ethics committee and from ARSAC (UK).

Isoluminant ellipses subtending approximately seven degrees of visual angle were presented at regular intervals (30, 50, 70 and 90 ellipses per minute) for 500ms at fixation on a computer monitor approximately 57cm from the subjects. The ellipses could differ in colour (red, green or blue) and orientation (horizontal or vertical). Subjects indicated their categorisation choice of target or non-target by pressing a button with either right or left index fingers. A response was required for every ellipse presented. The proportion of targets was kept constant across conditions at 50%; in all other respects the stimuli and presentation were identical in all conditions. The assignment of fingers was made before the scanning session, and was the same for all scans for any one subject, but counterbalanced across subjects for the experiment. The order of task presentation was counterbalanced across subjects.

3.2.2. Data acquisition and analysis

Each of these three tasks were performed at four different rates of stimulus presentation during a series of twelve PET regional cerebral blood flow scans with $\mathrm{H}_2\mathrm{O}^{15}$ as the tracer (see section 2.1). Reaction times were recorded during the scanning. Appropriately weighted scans were compared to identify areas with three distinct types of response characteristic. First, those areas were identified that were activated by the conjunction task relative to the feature tasks, but that showed no rate related effects. Second, those areas were identified in which activity covaried with presentation rate to delineate a distributed network responsible for stimulus identification and response production irrespective of task. Finally areas were sought in which there was both stimulus related activity and modulation of activity in the conjunction task. These areas represent the sites of attentional modulation, and the modulatory influence of attention in these areas was characterised as either showing “tonic” or “phasic” effects. “Tonic” effects were indexed as an increase in baseline activity without alteration of the correlation between activity and presentation rate. “Phasic” effects were indexed as a change in the correlation of activity and presentation rate.

3.2.3. Results
3.2.3.1. **Behavioural**

RT for correct responses for the colour, orientation and conjunction tasks respectively was 352ms (standard deviation 86ms), 350ms (standard deviation 95ms) and 368ms (standard deviation 104ms). This significant difference in RT between conjunction and feature tasks is not in accord with Treisman’s Feature Integration Theory (Treisman and Gelade, 1980), if one regards the task as a conjunction search without distractors. However, similar elevated RTs in conjunction search without distractors have been seen in the only functional imaging study previously reported of conjunction search (Corbetta et al 1995; note 21). Reaction time declined with increasing rate of presentation, being 378ms, 358ms, 346ms & 357ms for rates of 30, 50, 70 and 90 ellipses per minute respectively. This may reflect subjects finding it easier to stay “on task” at higher rates, keeping relevant behavioural goals more active. Error rates were highest (15.5%) in the colour condition; for the orientation condition there were 5.05% errors, and for the conjunction condition 6.98% errors averaged over all subjects. There is thus no suggestion from the error data that increased difficulty of the conjunction task might account for the results.

3.2.3.2. **Functional Imaging**

A distributed network of areas was identified in which activity covaried with stimulus presentation rate (Table 3-1) that included striate and extrastriate cortex, motor and premotor cortex and cerebellum. Large relative deactivations with increasing presentation rate were found in medial prefrontal structures and inferotemporal cortex (probably BA 20) bilaterally (Figure 3-3).

The only brain area that showed greater activity in the conjunction task relative to the feature tasks was located in right dorsolateral frontal cortex (Z score 4.22, co-ordinates [42 22 40], p<0.001 uncorrected for multiple comparisons due to our prior hypothesis). The Talairach co-ordinates and surface anatomy derived from an averaged MRI of the six subjects suggested that the activation was located in Brodmann area 8 (BA 8) (Figure 3-2).

Significant modulatory effects due to attention to conjunctions were seen in five areas (Table 3-2). In three areas, left premotor cortex, left cerebellum and left precuneus, the
Neural correlates of selective attention modulation took the form of a change in slope of the relationship between rCBF and stimulus presentation rate; that is, a “phasic” effect of attention (Figure 3-4 & Figure 3-5). In two areas, left inferior temporal cortex and right cerebellum, the modulation took the form of a change in the intercept; that is, a “tonic” effect of attention. In inferior temporal cortex this “tonic” modulation took the form of a decrease in the intercept in the context of a negative relationship between rCBF and rate (Figure 3-4).
Neural correlates of selective attention

Figure 3-2: Attention to visual conjunctions

Activation evoked by attention to visual conjunctions compared to single features is shown rendered on a standard template brain placed in the stereotactic space of Talairach & Tournoux. A threshold of $Z > 3.09$ was used to generate this figure.

right dorso-lateral frontal BA 9
Neural correlates of selective attention

Figure 3-3: Decreases in cerebral blood flow correlated with rate of stimulus presentation.

Decreases in cerebral blood flow correlated with rate of stimulus presentation. Areas that show significant decreases in regional cerebral blood flow with increasing stimulus presentation rate are rendered on a canonical T1-weighted structural MRI placed in the anatomical space of Talairach and Tournoux. The areas deactivated include medial frontal structures and bilateral areas of inferior temporal cortex (arrowed)
Neural correlates of selective attention

Table 3-1: Activity related to stimulus presentation rate

Areas showing activity varying with stimulus presentation rate. All data reaches p < 0.05 level of significance corrected for multiple comparisons, except inferior temporal cortex p < 0.001 uncorrected due to prior hypotheses about these regions

<table>
<thead>
<tr>
<th>Co-ordinates</th>
<th>Area</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-42 -88 -10</td>
<td>Left inferior occipital gyrus</td>
<td>4.60</td>
</tr>
<tr>
<td>48 -60 -18</td>
<td>Right fusiform</td>
<td>4.68</td>
</tr>
<tr>
<td>-32 -66 -22</td>
<td>Left cerebellum</td>
<td>4.87</td>
</tr>
<tr>
<td>2 -54 -8</td>
<td>Right cerebellum</td>
<td>4.75</td>
</tr>
<tr>
<td>-56 -2 50</td>
<td>Left precentral gyrus</td>
<td>4.14</td>
</tr>
<tr>
<td>-12 -10 64</td>
<td>Left premotor cortex</td>
<td>4.36</td>
</tr>
<tr>
<td>Decreases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-2 36 -6</td>
<td>Anterior cingulate</td>
<td>5.13</td>
</tr>
<tr>
<td>22 48 16</td>
<td>Right inferior frontal gyrus</td>
<td>4.46</td>
</tr>
<tr>
<td>62 -20 -24</td>
<td>Right inferior temporal gyrus</td>
<td>4.08</td>
</tr>
<tr>
<td>-62 -16 -18</td>
<td>Left inferior temporal gyrus</td>
<td>4.20</td>
</tr>
</tbody>
</table>
Neural correlates of selective attention

Table 3-2: Areas that show both stimulus dependent and task dependent activity

Data shown reaches p<0.05 level of significance corrected for multiple comparisons

<table>
<thead>
<tr>
<th>Co-ordinates</th>
<th>Area</th>
<th>Z score</th>
<th>Type of modulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>-62 -16 -18</td>
<td>Left inf. temporal gyrus</td>
<td>4.77</td>
<td>“tonic”</td>
</tr>
<tr>
<td>12 -58 44</td>
<td>Right precuneus</td>
<td>4.96</td>
<td>“phasic”</td>
</tr>
<tr>
<td>-16 -12 62</td>
<td>Left premotor cortex</td>
<td>5.69</td>
<td>“phasic”</td>
</tr>
<tr>
<td>-32 -62 -20</td>
<td>Left cerebellum</td>
<td>5.47</td>
<td>“phasic”</td>
</tr>
<tr>
<td>28 -54 -26</td>
<td>Right cerebellum</td>
<td>4.95</td>
<td>“tonic”</td>
</tr>
</tbody>
</table>
Neural correlates of selective attention

Figure 3-4: Two modulatory effects of attention on rCBF

(I) Cerebral blood flow in left inferotemporal cortex (see Table 3-2) plotted as a function of stimulus presentation rate, separately for attention to visual conjunctions (red line) compared to individual features (green line). There is a significant difference in the intercept of these two lines, but no significant difference in slope. This represents an additive effect of attention that is constant across presentation rates (c.f. (B) Cerebral blood flow in left premotor cortex plotted as a function of stimulus presentation rate, separately for attention to visual conjunctions (red line) compared to individual features (green line). There is a significant difference in the slope of these two lines. This effect represents an interaction between stimulus rate-evoked changes in rCBF and attention.
Figure 3-5: Two modulatory effects of attention on rCBF

(II) Plots of regional cerebral blood flow as a function of stimulus presentation rate presented in a similar fashion to the previous figure. The upper panel shows activity taken from the right cerebellar area described in Table 3-2; the lower panel shows activity taken from the left cerebellar area described in that table.
3.2.4. Discussion

Lateralised activity in Brodmann area 8 is uniquely seen with performance of the conjunction task (Figure 3-2). Inspection of the statistical parametric map failed to identify any stimulus rate related activity, even at low statistical thresholds. Because this activity is stimulus and response independent, we suggest that this area is the source of 'top-down' attentional influences on components of the distributed network performing the task. Brodmann area 8 is well placed to be a source of modulatory influence. It receives inputs from dorsal and ventral prestriate cortices (Barbas, 1988; Cavada and Goldman Rakic, 1989; Petrides and Pandya, 1988; Seltzer and Pandya, 1989). Neuronal responses in this area are task-related in go/no go and match-to-sample tasks (for example (Pragay et al., 1987; Sakagami and Niki, 1994)). Moreover, excision of frontal cortex around the posterior arcuate sulcus (BA 8) in the macaque selectively impairs performance on a cross-modal conjunction task compared with the corresponding feature responses. BA 8 in monkey contains the frontal eye fields, and an alternate explanation for these results is that eye movements were responsible for the differences between conjunction and feature tasks. However all stimuli were presented in an identical fashion over all tasks at fixation, and there is no reason to suspect differential eye movements in the conjunction condition. Furthermore in humans the reported co-ordinates for the frontal eye fields are not located within BA 8 (Fox et al., 1985; O'Driscoll et al., 1995; Paus, 1996). The activation observed is lateralised to right BA 8 and there appears to be no clear explanation for this result. Right frontal cortex is selectively implicated in tasks requiring sustained attention (Pardo et al., 1991), but there is no reason to suggest that the conjunction task requires sustained attention whilst the feature tasks do not. One previous functional imaging study has examined the difference between conjunction and feature categorisation (Corbetta et al., 1995), but in the context of a spatial task with analysis restricted to parietal cortex. In the present study, however, the task contained no spatial component and no parietal activation was apparent.

There are five areas that show a modulatory influence of attention in addition to rate effects (Table 3-2). The presence of activity related to both stimulus presentation and to task in these areas suggests that they are the site at which 'top-down' attentional influences act to influence behaviour. The findings in inferior temporal cortex are of
Neural correlates of selective attention

particular interest to the experimental hypothesis of frontotemporal interaction as the basis of object selectivity.

Increases in stimulus presentation rate results in progressive decrements in activity in inferior temporal cortex. Decreases in activity of inferior temporal cortex and cingulate cortex have also been seen in a study where subjects identified familiar stimuli compared with passive observation. Transient suppression of activity in visually responsive single neurons is seen in monkey inferior temporal cortex during match-to-sample tasks (Miller and Desimone, 1994; Miller et al., 1991; Miller et al., 1993). 'Adaptive mnemonic filtering' refers to the reduction in the response from a cell to a stimulus which has been seen recently independently of task. However an extrapolation from single cell data to the evoked haemodynamic response from activity in a population of neurons should be made with caution. Other effects are also seen in inferior temporal cells; for example, an enhancement of response to a stimulus when it matches a searched-for target. The present data are intriguing in that they suggest the aggregate outcome of activity in several subsets of neurons with different response characteristics is an overall decrease in inferior temporal activity. One possibility is therefore that the changes observed here represent neural activity associated with the identification of familiar stimuli.

In one of the areas in inferior temporal cortex, that showed a decrease in activity as presentation rate increased, there was a change in activity due to attending to conjunctions compared to features. The change in activity took the form of a decrease in activity in the conjunction task that was constant across all presentation rates (Figure 3-4). This change in activity must be due to the different attentional demands of the conjunction task, as the visual stimuli were the same across all tasks. In contrast to the attentional modulation seen by Frith & Friston (1996), this modulation takes the form of a baseline shift that is independent of the correlation of cerebral blood flow with stimulus presentation rate. In other words, the slope of the relationship between cerebral blood flow and stimulus presentation rate is unchanged by attention, but the intercept is changed, consistent with a bias signal. The direction of the attentional effect is negative, decreasing evoked activity in inferior temporal cortex. There are at least two possible explanations for this type of effect. An explanation based on Feature Integration Theory (Treisman and Gelade, 1980) would suggest that in the feature task, any relevant feature should trigger a correct response. However, in the conjunction task the separate features of the relevant conjunction will tend to evoke false alarms. They will therefore need to be
Neural correlates of selective attention

inhibited, so that responses are made only to the correct conjunctions. In other words, more inhibition is required in the conjunction task giving rise to a lower overall evoked rCBF in inferior temporal cortex. An alternate explanation may be that conjunctions are coded in inferior temporal cortex as higher order combinations of single features. A hierarchical coding scheme would mean that fewer cells are selective for conjunctions compared to individual features. In such a scheme fewer cells would therefore need to be biased to give rise to selectivity for conjunctions compared to features. Overall neural activity evoked by feature selectivity would therefore be higher than for conjunctions, giving rise to a lower rCBF in the conjunction condition. Convergent functional imaging evidence supports the observation that less activity is evoked in human inferotemporal cortex during the identification of conjunctions compared to individual visual features (Elliott and Dolan, 1997). These authors showed a decrease in rCBF in left inferior temporal cortex when participants perform a visual delayed match to sample task on the basis of conjunctions of colour and form compared to individual features. The location of the area in left inferotemporal cortex identified by Elliott & Dolan is very close to that identified in the present study, suggesting a common effect related to the identification of visual conjunctions of colour and form in both paradigms.

It may therefore be reasonable to speculate that the modulation observed in left inferotemporal cortex is a neural correlate of the 'attentional template' suggested by the biased competition model; it is a bias signal altering the processing of object related signals in inferotemporal cortex. The bias signal may arise in right BA8; a functional interaction between prefrontal and inferior temporal cortex is consistent with both the neuroanatomical connectivity of frontal cortex and the present data (Chavis and Pandya, 1976; Jacobson and Trojanowski, 1977; Jones and Powell, 1970; Pandya and Kuypers, 1969; Webster et al., 1994). Cooling of prefrontal cortex in monkeys results in both increases and decreases of stimulus-evoked and spontaneous neural activity in inferotemporal cortex (Fuster et al., 1985).

Relating the functional imaging findings in inferior temporal cortex to the neurophysiological data in monkeys is more difficult. Cells in inferotemporal cortex in monkeys show a range of different response properties. In delayed match-to-sample tasks, both cue related activity in delay periods and enhanced responses to target stimuli matching a prior cue are seen. The presence of delay-related activity has been suggested as a neural correlate of an attentional bias signal (Desimone and Duncan, 1995). The
Neural correlates of selective attention

Functional imaging data presented here is consistent with an additional signal associated with attention in inferior temporal cortex, independent of and additive to transient stimulus-evoked activity. However whereas the activity of single cells shows an additive increase in activity, the functional imaging data shows an additive decrease in rCBF when conjunctions are compared to features. In other words, the response at the relatively coarse spatial scale detected by functional imaging is not the same as that recorded in a small number of single cells within this area. Intuitively this might seem plausible; for every cell that shows cue specificity and elevated delay related activity within a single trial, most of the population will not show elevated delay related activity. At a population level, the aggregate neuronal dynamics will therefore not necessarily bear a straightforward relationship to the changes in firing rate of a single cell. Indeed, it is possible that although individual neurons show an increase in firing rate due to attention, the overall level of activity in a population of neurons may decrease if (for example) local interactions lead to suppression of activity. However the relationship of single cell activity to that of populations of cells in this area has not been explored experimentally in detail, so such a mechanism remains speculative.

In contrast to the tonic modulatory effect of attention observed in inferior temporal cortex, “phasic” modulation by attention of rate related activity occurs in left premotor cortex (Figure 3-4) and left cerebellum (Figure 3-5). The correlation coefficient between presentation rate and local activity changed significantly in the conjunction task. This demonstrates that attention can act in two physiologically distinct ways to influence neural activity in human cortex. “Phasic” modulation implies that signals specifically associated with stimulus identification and response production are directly enhanced or suppressed. This contrasts with the “tonic” modulation seen in inferior temporal cortex, that represents activity that is additional to, and independent of, stimulus rate related activity. One prediction from this characterisation of “tonic” attentional modulatory influences is that attention-related activity may be present within a cortical area even in the absence of stimulus presentation.

The modulation of multiple areas in temporal cortex, premotor cortex and cerebellum is broadly compatible with theoretical approaches to attention that consider its predominant role as shaping behaviour through influencing motor output (e.g. (Allport, 1987)). Non-spatial selective attention modulates cortical activity in two physiologically distinct ways. These results support a model of visual attention in which prefrontal cortex modulates
Neural correlates of selective attention

activity in a distributed network of cortical and cerebellar structures that are relevant both
to the processing of sensory signals and to relevant motor output.

3.3 Conclusion

This study shows that varying the rate of presentation of a visual stimulus evokes brain
activity correlated both positively and negatively with presentation rate in different
cortical areas. The effect of directing attention to different features or combinations of
features of this stimulus produces two different patterns of effect on this rate correlated
signal. In some areas, a constant additional ‘bias’ signal is added to the rate correlated
signal. In other cortical areas, there is an interaction between attention and rate so that
attention changes the correlation between brain activity and presentation rate. These
findings suggest that changes in the rate of presentation of a visual item can be used to
index stimulus evoked activity, and that selective attention may operate through at least
two distinct physiological mechanisms. In the next experiment this approach is extended
to the study of auditory and visual modalities. Two stimuli are presented together and so
the nature of unattended processing can be investigated for the first time.

3.4 Directing attention to either auditory or visual modalities

3.4.1. Introduction

The previous experiment investigated how brain activity changed when subjects attended
to different aspects of the same stream of information. More generally, humans encounter
information simultaneously in different modality, yet have a remarkable ability to attend
selectively to one out of these many competing streams (Broadbent, 1958).
Electrophysiological studies have shown that attending to a modality alters the evoked
potentials associated with presentation of stimuli in that modality. For example, negative
components of the auditory evoked response become more negative when a signal is
attended to (Woldorff et al., 1987); similar components of the visual evoked response are
enhanced by attention (Luck et al., 1993). The sites of modulation of electrical activity
seem to be located at or near primary cortical areas of the attended modality (Mangun et
al., 1993; Woldorff et al., 1993). Within a single modality, the functional imaging studies
reviewed above (Section 1-22) have shown that increased activity in different
functionally specialised areas of extrastriate cortex is increased with attention to relevant
Neural correlates of selective attention

parts of the same visual display. For example, attention to visual motion increases activity in cortical area V5, whereas attention to the colour in an identical display enhances activity in cortical area V4 (Corbetta et al., 1991b).

The difference in activity in a cortical area when a subject attends to some aspect of the stimulus, compared to when the subject does not attend, has been attributed to the effects of attention. However, discussed in section 3.2, this conclusion is premature. The differential responses of a cortical area actually represent an interaction between the analysis of a particular stimulus attribute and the modulatory effects of attention. The fallacy of attributing a differential response to attention alone would be shown by repeating the experiment in the absence of the stimulus. In this instance, attention should not lead to any activation because there is no stimulus dependent response to modulate. In other words, to understand the effects of attention on analysis of a particular stimulus attribute requires a measure of stimulus-related activity that is independent of the measure of attention. The approach outlined above has been to use a parametric variation of stimulus presentation rate to characterise stimulus related activity. In humans, the experiment presented in section 3.2 showed that both changes in slope and changes in intercept are mechanisms that operate during selective attention to different stimulus attributes (Frith and Friston, 1996). The present study sought to extend this work to two modalities.

Attention is an example of 'top-down' modulation of sensory areas, since the changes in evoked haemodynamics are not caused by a change in the evoking stimulus, but by the decision to attend to the signal. What is the source of such effects? One approach is to compare areas activated by simple manipulations of selective attention in different studies and to look for areas activated in common across studies. In the case of visuospatial attention, a number of studies have shown that different manipulations of visuospatial attentional requirements all lead to enhanced activity in parietal cortex (Corbetta et al., 1993; Corbetta et al., 1995; Heinze et al., 1994b; Nobre et al., 1997; Vandenberghe et al., 1997), consistent with both lesion studies and neurophysiological data from non-human primates. However, this strategy has been less successful in characterising non-spatial aspects of visual attention, perhaps because of the heterogeneity of non-spatial attention tasks. An alternative approach, explored here, is to combine two different manipulations of attention within a single study. If the control of attention relies on a common resource, or cortical area, then such an area should show differential activation according to the
Neural correlates of selective attention

attentional requirements. Moreover, activity in an area truly involved in the control of attention should show an interaction between the effects of the two different manipulations of attention. In other words, the context set by one of the attentional manipulations should modulate the differential response of that cortical area to another attentional manipulation. In the study described above, right dorsolateral prefrontal cortex (BA8) appeared to be such a candidate for the source of top-down modulatory influence. Activity in this area increased when attention was directed to visual conjunctions, but there was no difference in activity when stimulus presentation rate varied. This suggested that this area was not involved in analysing the sensory attributes of the stimulus, but was involved in the control of the direction of attention. The anatomical connectivity of this area to auditory and visual cortex make it well placed to act as such a source of control signals. It was therefore of interest to further study the response characteristics of this area and in particular to investigate whether the effects of two different manipulations of non-spatial visual and auditory attention interact in this cortical area.

This study therefore combined two manipulations of attention with systematic manipulation of stimulus presentation rate to characterise processing of stimulus-related signals independently of attention. The two manipulations of attention explored were asking the subject to attend either to visual or to auditory stimuli (between-stream manipulation), and within that sensory stream to attend to either a physical attribute (intensity) or a semantic attribute (identity). The experiment sought to characterise how brain activity related to stimulus presentation rate was modulated by these two manipulations of attention. It was expected that evoked activity in areas common to the control of between-stream and within-stream direction of attention would show an interaction between these two factors.

3.4.2. Methods

3.4.2.1. Subjects and stimuli

Six male, right handed, healthy volunteers gave written informed consent for the study. The study was approved by the National Hospital for Neurology & Neurosurgery ethics committee and by ARSAC (UK).
Neural correlates of selective attention

On each of twelve scans volunteers were presented with two concurrent streams of signals, auditory and visual. The streams were presented at three different rates, so that stimuli occurred at interstimulus intervals of 0.9s, 1.6s and 6.0s during separate scans. Auditory and visual signals were always presented at the same rate.

The visual stream consisted of large capital letters presented serially for 200 ms at the centre of a visual display. The letters varied in their intensity (grey scale) and their identity. During half of the scans, volunteers were asked to ignore the auditory stream and attend to the visual stream. They were asked to press a button whenever a target appeared. For half of the visual attention scans, the target was a letter of very low intensity grey (clearly different from the other letters); for the other half the target was the letter ‘Z’. In all the scans the target was constrained to occur randomly at a frequency of one target for every five stimuli.

The auditory stream consisted of a series of spoken single letters presented at a volume that was clearly audible in the scanning environment. The letters were presented binaurally through in-ear earphones. The letters varied in intensity (volume), and identity. During half of the scans, volunteers were asked to ignore the visual stream and attend to the auditory stream. They were asked to press a button whenever a target appeared. For half the auditory attention scans, the target was a letter of very low intensity (clearly different from the other letters); for the other half the target was the letter ‘Z’. In all the scans the target was constrained to occur randomly at a frequency of one target every five stimuli.

Subjects were shown the stimuli prior to the scanning period to ensure that they were familiar with the stimuli and targets. All responses were made with their right index finger. Note that although the rate of presentation and of responding is systematically varied, the target probability is kept constant. This paradigm has three independent factors (1) between-modality direction of attention (towards the visual or auditory stream); (2) within-modality direction of attention (towards letter intensity or identity); (3) rate of presentation of stimuli. Subjects underwent one scan for each combination of the three factors.

3.4.2.2. Data acquisition and analysis
Neural correlates of selective attention

Data were obtained from six volunteers scanned twelve times (once every eight minutes) using $\text{H}_2^{15}$O PET. The order of presentation of conditions was fully counterbalanced across subjects. There were not enough subjects to fully counterbalance the order of the three presentation rates, so a partial counterbalancing was used to ensure that high and low rates occurred equally often throughout the twelve scans. Scans were acquired and analysed in the manner described in Chapter 2.

3.4.3. Results

3.4.3.1. Behavioural

Analysis of reaction times and accuracy for all the conditions showed that there were no significant differences between conditions. All the experimental conditions were therefore of equivalent difficulty

3.4.3.2. Functional Imaging

The general convention is adopted here of only reporting areas that reach significance at a level of $p<0.05$ corrected for multiple comparisons, with two important exceptions. First, in areas where there was a prior hypothesis, the lower threshold of $Z=3.09$ is used (equivalent to $p<0.001$ uncorrected for multiple comparisons). These areas are auditory, striate and extrastriate cortex, thalamus and right dorsolateral prefrontal cortex. Secondly, the lower threshold of $Z=3.09$ is also used in those areas reported that show both an effect of presentation rate and an independent effect of attention. A lower threshold is appropriate in such a comparison because the chance of an area showing both effects together is the mathematical product of the chance that each effect alone is seen (as rate and attention are manipulated independently).

Changing stimulus presentation rate (Table 3-3)

A number of areas showed strong modulation of their activity by stimulus presentation rate. Increasing activity with increasing stimulus presentation rate was seen in bilateral areas of fusiform gyrus, bilateral primary auditory cortex (Heschl’s gyrus), and left precentral and postcentral gyrus. Strong decreases in activity with increasing presentation
Neural correlates of selective attention rate were seen in bilateral intraparietal sulcus and surrounding areas of lateral parietal cortex, precuneus bilaterally, right inferior frontal and middle frontal gyrus, and left middle temporal gyrus.
Table 3-3: Areas showing correlation with stimulus presentation rate

Areas where rCBF shows significant changes correlated either positively or negatively with stimulus presentation rate

<table>
<thead>
<tr>
<th>Area</th>
<th>Tailarach co-ordinates</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INCREASES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L Fusiform</td>
<td>-32 -90 -2</td>
<td>7.27</td>
</tr>
<tr>
<td>L fusiform</td>
<td>-32 -82 -6</td>
<td>7.04</td>
</tr>
<tr>
<td>R Fusiform</td>
<td>38 -82 -12</td>
<td>7.02</td>
</tr>
<tr>
<td>L auditory cortex</td>
<td>-64 -18 8</td>
<td>6.69</td>
</tr>
<tr>
<td>R auditory cortex</td>
<td>64 -24 14</td>
<td>5.41</td>
</tr>
<tr>
<td>L Precentral gyrus</td>
<td>-26 -24 72</td>
<td>4.12</td>
</tr>
<tr>
<td>L Precentral gyrus</td>
<td>-54 -4 40</td>
<td>3.82</td>
</tr>
<tr>
<td>L Thalamus</td>
<td>-20 -12 8</td>
<td>3.66</td>
</tr>
<tr>
<td>L postcentral gyrus</td>
<td>-26 -36 80</td>
<td>3.43</td>
</tr>
<tr>
<td><strong>DECREASES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L intraparietal sulcus</td>
<td>40 -60 34</td>
<td>6.31</td>
</tr>
<tr>
<td>Precuneus</td>
<td>-6 -66 42</td>
<td>5.70</td>
</tr>
<tr>
<td>R inf/middle frontal</td>
<td>32 40 -4</td>
<td>4.71</td>
</tr>
<tr>
<td>R middle frontal</td>
<td>46 28 30</td>
<td>4.65</td>
</tr>
<tr>
<td>L inf/middle temporal</td>
<td>-62 -56 -10</td>
<td>4.50</td>
</tr>
</tbody>
</table>
Neural correlates of selective attention

**Effects of attention (Table 3-5 & Table 3-7)**

Here areas are reported that showed both an effect of one of the attentional manipulations and an effect of stimulus presentation rate. The attentional effect could be either an additive effect, independent of presentation rate, or one that interacted with the stimulus presentation rate. To identify the former, we masked the appropriate contrast for the effects of attention with the positive or negative contrast for stimulus presentation rate.

**Changing the modality to which attention is directed**

**Additive effects**

Large bilateral areas of fusiform cortex showed increases in activity with presentation rate that were increased (in a rate-independent manner) by attention to the visual stream. Left auditory cortex and left thalamus showed increased activity with presentation rate that was further enhanced by attention to the auditory stream. Right auditory cortex also showed this pattern of activity, but this did not reach significance at the threshold used (x, y, z = 54, -10, 0; Z=2.70, p=0.003 uncorrected). Two areas of middle occipital gyrus close to the parietal-occipital junction and an area in left lingual gyrus showed activity that decreased with increasing presentation rate, but was enhanced in a rate-independent manner by attention to the visual stream. Left prefrontal cortex showed two areas that decreased their activity with increasing presentation rate, but showed a rate-independent increase in activity with attention to the auditory stream.

**Interaction effects**

Attention to the visual modality increased rate-related activity in right prefrontal cortex. The modulated area was large, encompassing most of area 8 and extending posteriorly into area 6. Attention to the auditory modality, on the other hand, increased the slope of rate-related activity in a large area of right fusiform gyrus.
Figure 3-6: Positive and negative correlations with rate of stimulus presentation

Right and left lateral, superior and inferior views of areas where changes in cerebral blood flow show a significant positive (red areas) or negative (green areas) correlation with stimulus presentation rate. The activations, thresholded at a Z score of Z>3.09, are rendered on a canonical T1-weighted MRI image placed in the standard anatomical space of Talairach and Tournoux.
Neural correlates of selective attention

Table 3-4: Attention to visual or auditory streams

Areas that show a significant change in rCBF in association with attention to visual or auditory streams, and an effect of stimulus presentation rate. The effects of attention reported here are either additive, or interact with the effects of stimulus.

<table>
<thead>
<tr>
<th>Area</th>
<th>Talairach co-ordinates</th>
<th>Z score</th>
<th>Type of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VISUAL STREAM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L fusiform [18]</td>
<td>-32 -84 12</td>
<td>4.57</td>
<td>additive, positive</td>
</tr>
<tr>
<td>R fusiform [18]</td>
<td>30 -90 -6</td>
<td>4.39</td>
<td>additive, positive</td>
</tr>
<tr>
<td>R inf temp [37]</td>
<td>46 -58 -12</td>
<td>3.65</td>
<td>additive, positive</td>
</tr>
<tr>
<td>R hippocampus</td>
<td>34 -36 -20</td>
<td>3.48</td>
<td>additive, positive</td>
</tr>
<tr>
<td>L striate [17]</td>
<td>-20 -80 12</td>
<td>3.40</td>
<td>additive, positive</td>
</tr>
<tr>
<td>R occipital [19]</td>
<td>44 -68 -16</td>
<td>3.38</td>
<td>additive, positive</td>
</tr>
<tr>
<td>L sup occipital [18]</td>
<td>-28 -84 22</td>
<td>4.59</td>
<td>additive, negative</td>
</tr>
<tr>
<td>R sup occipital [18]</td>
<td>28 -82 26</td>
<td>3.56</td>
<td>additive, negative</td>
</tr>
<tr>
<td>R inf frontal [46]</td>
<td>46 642</td>
<td>4.35</td>
<td>interaction</td>
</tr>
<tr>
<td>R sup frontal [8]</td>
<td>16 30 60</td>
<td>4.30</td>
<td>interaction</td>
</tr>
<tr>
<td>R med frontal [10]</td>
<td>36 56 6</td>
<td>4.13</td>
<td>interaction</td>
</tr>
<tr>
<td><strong>AUDITORY STREAM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L auditory cortex</td>
<td>-62 -24 8</td>
<td>3.87</td>
<td>additive, positive</td>
</tr>
<tr>
<td>L Thalamus</td>
<td>-14 -22 10</td>
<td>3.52</td>
<td>additive, positive</td>
</tr>
<tr>
<td>R fusiform</td>
<td>44 -44 20</td>
<td>3.81</td>
<td>interaction</td>
</tr>
</tbody>
</table>
3.4.3.3. Changing the (within-stream) attribute to which attention is directed
(Table 3-7)

Additive effects

Attending to the intensity of the letters compared with their identity evoked increased activity in a small area of right superior parietal cortex that also showed increased evoked activity with increasing rate. Attending to the identity of the letters compared to their intensity resulted in enhanced activity in right and left auditory cortex and left thalamus, areas that also showed enhanced activity with increasing stimulus presentation rate. In areas that showed decreased activity with increasing stimulus presentation rate, an area in left inferior temporal gyrus and in right temporal pole showed enhanced activity with attention to letter identity.

Interaction effects

There were no significant interactions between stimulus presentation rate and attention to within-stream stimulus attributes.

A dorsolateral area of prefrontal cortex x, y, z = [4, 42, 58; Z=3.77], probably BA8, showed an interaction between the activity evoked by changing the attended modality and the activity evoked by changing the attended attribute. This area was situated dorsolateral to, but overlapped with, the area reported above that showed an interaction between attended modality and rate of stimulus presentation.
Neural correlates of selective attention

Figure 3-7: Effects of attention on visual and auditory cortex

Right and left lateral views of areas where changes in cerebral blood flow show a significant positive (red areas) or negative (green areas) correlation with stimulus presentation rate. The activations are rendered on a canonical T1-weighted MRI image placed in the standard anatomical space of Talairach and Tournoux. Below visual (left) and auditory (right) cortex are plotted the relationship between cerebral blood flow and stimulus presentation rate, as a function of attention to the visual signals (yellow line) or the auditory signals (blue line). In both cases there is an additive effect of attention, with no interaction between attention and stimulus presentation rate.
Neural correlates of selective attention

Table 3-5: Attention to identity compared to intensity

Areas that show a significant change in rCBF in association with attention to identity compared to intensity of the within-stream target, and an effect of stimulus presentation rate. The effects of attention reported here are additive.

<table>
<thead>
<tr>
<th>Area</th>
<th>Co-ordinates</th>
<th>Z score</th>
<th>Type of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudate</td>
<td>-16  -2  14</td>
<td>4.00</td>
<td>additive, + rate</td>
</tr>
<tr>
<td>R premotor</td>
<td>12  -6  76</td>
<td>3.48</td>
<td>additive, + rate</td>
</tr>
<tr>
<td>R auditory</td>
<td>62  6  -6</td>
<td>3.39</td>
<td>additive, + rate</td>
</tr>
<tr>
<td>Right inf frontal</td>
<td>58  20 -20</td>
<td>3.30</td>
<td>additive, + rate</td>
</tr>
<tr>
<td>L auditory</td>
<td>-64  -16  5</td>
<td>3.21</td>
<td>additive, + rate</td>
</tr>
<tr>
<td>R temporal pole</td>
<td>46  20 -32</td>
<td>4.12</td>
<td>additive, + rate</td>
</tr>
<tr>
<td>L inf temporal</td>
<td>-66  -14 -24</td>
<td>3.65</td>
<td>additive, - rate</td>
</tr>
<tr>
<td>Caudate</td>
<td>-14  4  14</td>
<td>3.33</td>
<td>additive, - rate</td>
</tr>
<tr>
<td>L intraparietal sulcus</td>
<td>-44 -64 36</td>
<td>3.24</td>
<td>additive, - rate</td>
</tr>
<tr>
<td>R sup frontal</td>
<td>26  58  24</td>
<td>3.19</td>
<td>additive, - rate</td>
</tr>
</tbody>
</table>
Neural correlates of selective attention

3.4.4. Discussion

There are three interesting aspects to these results; the pattern of attentional modulation in auditory and visual cortex, the changes in parietal cortex rCBF produced by varying presentation rate, and the multiple interactions between activity evoked by the experimental manipulations in right prefrontal cortex. Each will be discussed in turn.

Several areas showed a positive relationship between cerebral blood flow and stimulus presentation rate. In accord with expectation, these included bilateral auditory cortex and bilateral areas of striate and extrastriate cortex (Figure 3-6). These effects support the idea that the slope of the line relating cerebral blood flow to stimulus presentation rate indexes the amount of transient activity evoked by each stimulus. It was therefore extremely interesting that bilateral areas of medial and lateral parietal cortex also showed a significant change in cerebral blood flow with stimulus presentation rate. However in this case the form of the effect was opposite to that seen in auditory and visual cortex; cerebral blood flow increased as stimulus presentation rate decreased. Why should this be? One logical possibility is that each stimulus evoked a transient decrease in activity in parietal cortex, giving rise to enhanced deactivation as rate of presentation increased. This explanation seems rather implausible, as neuronal responses in non-human primates show generally enhanced activity to stimuli in attentive states (Mountcastle et al., 1981), and previous functional imaging studies have shown enhanced activity in parietal cortex with manipulations of visuospatial attention (Corbetta et al., 1993; Nobre et al., 1997). This regionally specific effect was not seen in the study presented previously in section 3.2, or in previous studies that varied stimulus presentation rate. Two possible explanations for this discrepancy were considered.

First, it is possible that differences in the stimuli (e.g. simple tones versus spoken letters, abstract shapes vs. visual letters) gave rise to the differences observed. However in studies that did not vary stimulus presentation rate, attentional effects in parietal cortex do not show material or stimulus specificity, so this explanation was considered unlikely. The other way in which the present study differs from previous studies is that the range of stimulus presentation rates used is much greater. In particular, the lowest presentation rate in the present study was sufficiently low (0.17 Hz) that only five stimuli were presented
Neural correlates of selective attention in the scanning window. Both frontal and parietal cortex have been shown to be involved in sustained attention (Coull et al., 1998; Pardo et al., 1990). In the present study, as stimulus presentation rate decreased, the requirement for sustained attention increased considerably. At the lowest presentation rate, a stimulus was presented every 6 seconds, whereas at the highest rate a stimulus was presented every 0.9 seconds. The observation of decreased activity in lateral and medial parietal structures as stimulus presentation rate increased may therefore reflect the involvement of these structures in sustained attention (Coull et al., 1998; Pardo et al., 1990). A practical implication of this finding is that non-spatial attention studies may show different effects in parietal cortex as a function of the rate at which the attentional task is performed.

The effect of between stream manipulation of attention between visual and auditory streams was to change the evoked activity in large areas of visual and auditory cortex respectively. The form of the change in activity was identical in each case; the slope of the line relating cerebral blood flow to stimulus presentation rate was unaffected, but the intercept changed (Figure 3-7). In other words, attention to a particular modality gave rise to a change in cerebral blood flow in areas concerned with processing signals from that modality that was constant across all presentation rates. This is not in keeping with the common intuition that attention represents a 'cortical gain control', modulating the stimulus-evoked activity in a cortical area. The present findings suggest that the dominant effect of directing attention to visual or auditory modalities is to increase the baseline activity in large areas of extrastriate and auditory cortex respectively. Is there any evidence that baseline shifts occur at a single cell level? In section 3.1.1. experiments in non-human primates were described that showed two different effects of attention on the visual responses of cells in V2, V4 and IT. First, the baseline firing rate was elevated even in the absence of stimuli. Second, the response of a neuron to a visual stimulus was enhanced by attention only when a distractor is also present within the receptive field; if the distractor is outside the receptive field the modulatory effect of attention was substantially attenuated or abolished (Luck et al., 1997; Moran and Desimone, 1985). In other words, multiplicative effects of attentional modulation depend on both stimuli being present in the receptive field of a neuron. Now, as Luck and colleagues noted, previous ERP and PET studies (where it is often assumed that attention acts as a gain control in sensory cortex) use visual displays where attended and ignored stimuli are usually placed far apart, on opposite sides of the vertical stimuli (Heinze et al., 1994b; Mangun et al., 1993). Such stimuli are not likely to be placed within a single receptive field, and so it has
Neural correlates of selective attention
been difficult to account for why ERP and PET studies show an effect of attention on sensory responses. One possibility is that the ERP and PET effects might arise in some other area, such as the human homologue of macaque inferior temporal cortex. Receptive fields in this area are sufficiently large that attention effects could potentially be observed across the vertical meridian. However attention effects across the vertical meridian have now been observed very early in the ventral visual pathway using functional imaging in humans, making this possibility less likely (Kastner et al., 1998). A second possibility is that the ERP and PET effects are related to the baseline shift effect, that was observed in V2 and V4 by Luck (Luck et al., 1997) even when the two locations were in different hemifields. This account would be consistent with the present findings, that show that the effect of directing attention to visual or auditory modalities on the appropriate visual or auditory cortex was equivalent to adding an additional signal, constant across presentation rates (Figure 3-7). This was by far the dominant effect in extrastriate and auditory cortex, with an interaction between presentation rate and attention (representing a modulation of stimulus-evoked activity) much less common. If this account is correct, then there are significant implications for functional imaging studies of attention, as it suggests that PET may be much more sensitive to a modulation of baseline activity by attention, rather than changes in evoked activity.

The dominant response property in areas of extrastriate cortex was of a positive relationship between stimulus presentation rate and rCBF, with an additional increase in the intercept of this line during attention to visual signals. However, in temporoparietal cortex, bilaterally symmetric areas showed a positive relationship between stimulus presentation rate and rCBF, but a negative bias signal (decrease in intercept with attention to visual signals). This finding indicates that the effects of visual attention on extrastriate cortex are heterogeneous; decreases in activity, as well as increases in activity, may be functionally important. This is extremely consistent with the findings discussed in the previous experiment (section 3.2 ), where decreases in activity with attention to conjunctions were functionally relevant in very similar areas of temporal cortex. The attention-related changes in activity in extrastriate cortex seem to be bilaterally symmetrical, whereas there is a marked asymmetry in auditory cortex. Statistically reliable attention effects are seen in left auditory cortex, whereas those in right auditory cortex are less reliable and failed to reach significance at the threshold used. The sounds were presented binaurally so it may be the case that subjects chose to focus their attention
Neural correlates of selective attention

on the left ear alone. However in the absence of a prior hypothesis it is difficult to interpret this intriguing finding.

Although the dominant pattern of attentional modulation in extrastriate and auditory cortex involved a 'tonic' change in activity, the right fusiform gyrus (and left middle temporal gyrus at a lower level of significance) showed a different pattern, with a change in the slope of the line relating evoked activity to presentation rate. As discussed above, this can be interpreted as an effect of the direction of attention (to visual or auditory modalities) on the transient activity associated with presentation of a stimulus in this area. The direction of the effect suggests that there is more transient stimulus-related activity in this area when auditory stimuli are attended, compared to when visual stimuli are attended. This finding is in keeping with those of the previous experiment that suggested two different attentional mechanisms operate in different cortical sensory areas. It also indicates that functional imaging techniques are not in principle insensitive to true modulatory effects of attention. The failure to demonstrate such an effect in extrastriate and auditory cortex discussed above may therefore simply indicate that the dominant effect in these areas caused by attention is a change in baseline firing rates.

Changing the attribute within a stream to which subjects were attended produced a surprising pattern of results (Table 3-7). Attending to letter identity enhanced activity both in areas early in the processing of auditory signals, such as auditory cortex, and in areas such as left inferior temporal cortex that might be expected to participate in later processing stages. This was an unexpected finding. Attention to a physical attribute of the stimulus such as volume might be expected to enhance activity in primary auditory cortex, with attention to a categorical attribute (identity) modulating activity in more distant areas. However, no effect in primary auditory cortex was seen, and the pattern of modulation is not in keeping with such a simple hypothesis. These results are therefore not consistent with models of attention that postulate that areas earlier in a processing pathway are activated during attention to physically more primitive stimulus features. Instead, they suggest that attention to the identity of an item (compared to a physical feature of that item) modulates activity at multiple levels of the processing hierarchy.

Changing the attribute within a stream to which attention was directed did not, however, lead to any significant changes in activity in visual cortex. This may indicate that the modulatory effect of attention on the processing of visual signals differs from its effect on auditory signals. It should also be noted that the tasks performed by the subjects were all...
Neural correlates of selective attention

easy with performance at ceiling throughout. It is possible that more demanding tasks may produce a more consistent and stronger pattern of modulation (see also Chapter 5.5).

Activity in a remarkably restricted area of prefrontal cortex, mainly Brodmann area 8, was modulated by the interaction of stimulus presentation rate and the direction of attention to visual or auditory modalities. A very similar area, overlapping but slightly dorsomedial to this area, also in BA8, showed a pattern of evoked activity corresponding to the interaction of the between-modality and within-modality direction of attention. These areas overlap with the activation in BA8 associated with attention to conjunctions described in section 3.2. The presence of two different modulatory interactions between experimental factors suggests that this area may be involved in the control or direction of the attentional processes we manipulate; it may represent a source of modulatory influence. As has been commented on above, BA 8 is well placed to be a source of modulatory influence for both auditory and visual attention. It receives convergent visual, auditory and somatosensory inputs from a wide area, and lesions to this area in monkey give rise to deficits on cross-modal (auditory-visual) attentional tasks (Petrides and Iversen, 1976). Although in monkey, BA8 is involved in the control of eye movements, the location of the frontal eye fields in humans is well away from BA8 and probably located in BA6 (Paus, 1996). Finally, in the present experiment all the stimuli were presented briefly at fixation so it seems unlikely that eye movements occurred. An interesting feature of the activity evoked in right BA8 in this experiment (especially compared to the previous experiment) is that it is sensitive to rate of presentation (although this is, in turn, modulated by between-modality direction of attention). It has been argued that the range of presentation rates used suggests that the rate-related effects on evoked activity may represent changes in the requirement for sustained attention. If this is the case, then the interaction between stimulus presentation rate and between-modality direction of attention in right BA8 may represent an interaction between sustained and selective attention (Coull et al., 1998). This is plausible, given the involvement of right prefrontal cortex in this area in sustained attention (Pardo et al., 1991). These results may be consistent with an important role for this particular area of prefrontal cortex in both sustaining and directing attention between and within auditory and visual modalities.
Neural correlates of selective attention

3.4.5. Conclusions

This study confirms that varying the rate of visual stimulus presentation evokes rate correlated activity, and extends this finding to auditory stimuli. Like the previous study, attentional modulation changes this rate-correlated activity in two different ways. However the dominant pattern of modulation observed when switching attention between different modalities took the form of a baseline shift. This raises the possibility that PET and electrophysiology may index different neural effects of attention, but the relationship is complex and requires further clarification.

3.5 General conclusions

Taken together, these two experiments present compelling evidence that the difference between the brain activity evoked by attended and unattended stimuli can take two different forms. On the one hand, there is evidence to suggest that some areas show a pattern of modulation consistent with a ‘gain control’ or multiplicative scaling. However many areas show a pattern of modulation that suggests the presence of a ‘bias signal’ that is simply added to stimulus correlated activity. These findings indicate that from a physiological point of view, selective attention has at least two distinct forms of operation in different cortical areas. The relationship of these patterns of modulation observed at the level of cortical areas to those observed in single cells requires cautious interpretation. First, the relationship between single unit activity and population measures of activity such as functional imaging is not necessarily a simple one. For example, attentional effects that are prominent at a single cell level but affect relatively few cells in an area may be drowned out in a population measure of activity where many cells in an area change their activity in a less prominent way. Secondly the relationship between changes in neural activity and changes in cerebral blood flow is not fully understood. This is emphasised in Chapter 8, where it is shown that although variation in stimulus presentation rate evokes a linear relationship with rCBF (PET), fMRI measurements with BOLD contrasts reveal a curvilinear saturating relationship. This difference must relate to the measurement techniques rather than neural activity as the stimuli are the same in each case. This finding emphasises the complex origin of functional imaging measures of activity and that there may be important differences between techniques.
Neural correlates of selective attention

More importantly for the subject matter of this thesis, the second experiment clearly demonstrates that even when attention was directed to the auditory stream, there was a correlation between blood flow and stimulus presentation rate in visual cortex (Figure 3-7). The reciprocal relationship in auditory cortex also holds true. Assuming that visual stimuli do not produce activity in auditory cortex and vice-versa, these observations provide compelling evidence that unattended stimuli are nevertheless processed. The remainder of this thesis described several ways in which this phenomenon is investigated further. In Chapter 4, rather than vary presentation rate, the identity of distracting stimuli is systematically manipulated. This allows characterisation of the neural correlates of the consequences of processing unattended stimuli that produce negative priming. Subsequently the determinants of unattended processing are investigated in Chapter 5 and Chapter 6.
Neural correlates of selective attention

Chapter 4  Neural correlates of negative priming

The work presented in the previous chapter has established that neural correlates of the processing of unattended stimuli can be detected and characterised. The particular measure chosen, parametric variation in stimulus presentation rate, embodies a number of assumptions (see discussion in section 3.2 about the relationship between transient neural activity and the signal returned over the duration of a PET scan). Furthermore, to extend these studies and distinguish more clearly between attended and unattended activity would require separate variation of the presentation rate of attended and unattended stimuli. For these reasons we concluded that this paradigm, while producing extremely interesting results, was not best suited to examine the processing of unattended stimuli and so in this chapter take a different experimental approach. Here a simple subtractive experimental design was used to investigate the neural correlates of the consequences of unattended stimulus processing: negative priming.

4.1 Introduction

Under what circumstances are ignored stimuli processed, and how does such processing come to influence behaviour? This question has become central in the psychology of attention yet remains unresolved (Allport, 1993; Desimone and Duncan, 1995; Johnston and Dark, 1986). Two general classes of behavioural effects, interference and negative priming, have been taken to indicate processing of ignored stimuli (Neill et al., 1995). In both cases responses to attended items take longer in the presence of distractors that interfere or cause negative priming. Because these effects are specific to the identity of the ignored stimuli, they are taken to reflect distractor processing. The neural correlates of interference have been explored largely through functional imaging studies of the Stroop conflict paradigm (Bench et al., 1993; Pantelis et al., 1996; Pardo et al., 1990), in which the anterior cingulate appears to play a crucial role. In this chapter the neural correlates of negative priming, which are largely unknown, were explored.

A commonly used paradigm for investigating selective attention is the Stroop task (Stroop, 1935). Subjects are asked to name the ink colour of successive visually presented words. When the words correspond to colours, subjects are slower at naming the ink colour than when the words are neutral or replaced by coloured items. This finding
Neural correlates of selective attention suggests that the identity of the colour word, though ignored, is processed and interferes with naming of the incompatible ink colour. To this extent the Stroop task is taken to reflect a failure of attention, in that despite subjects' attempts to focus on the ink colour alone, the ignored colour word identity is nevertheless processed. Dalyrymple-Alford and Budayr (Dalyrymple-Alford and Budayr, 1966) extended these findings by using a list in which the ink colour of each item corresponded to the ignored colour word of the immediately previous item. Now in addition to the Stroop-like conflict, there was also a systematic relationship between successive trials in that the ignored colour word became the subsequent naming target. Naming latencies for this 'ignored repetition' list were compared to a list in which no such systematic relationship existed. Subjects were significantly slower at naming the ink colour in the ignored repetition list. This phenomenon was shown to be a more generic one by Tipper and colleagues who conducted a series of experiments where subjects were asked to respond to one of two overlapping stimuli such as letters or line drawings (Driver and Tipper, 1989; Tipper and Cranston, 1985; Tipper, 1985; Tipper and Driver, 1988). The slowing of response latencies on ignored repetition trials was named 'negative priming', in contrast to the more familiar positive priming that is usually seen when an attended item is subsequently repeated. Negative priming is not simply a perceptual effect; it occurs between letters with the same identity but different shapes (Tipper and Cranston, 1985), and between pictures and the names of objects sharing the same semantic category (Tipper and Driver, 1988). This suggests that distractors can be processed at least to the level of semantic and structural descriptions. Theoretically, negative priming is taken to index an inhibitory mechanism of selection. The implication is that ignoring a stimulus is an active process that involves inhibition of its representation. As a result, subsequently generating a response to that stimulus takes longer as the persisting inhibition has to be overcome. However this theoretical interpretation is controversial, and the neural correlates of negative priming are not known (Neill et al., 1995).

These examples illustrate that unattended stimuli that produce negative priming frequently produce interference. Interference differs from negative priming in that it refers to an effect caused by the relationship between a target and distractors presented simultaneously. On the other hand, negative priming is an effect that relates to the contingency between a current target and ignored items from a previous trial. To the extent that both negative priming and interference are a consequence of the processing of distractors, they might be expected to have a reciprocal relationship. Inhibition of
Neural correlates of selective attention
distractor processing should minimise interference on the current trial, but enhance
negative priming on a subsequent trial. Indeed, this is often the case; high levels of
interference are, in general, associated with low levels of negative priming (May et al.,
1995). However the relationship is complex and the reciprocal effects are not always
consistent. It is therefore not entirely clear that interference and negative priming reflect
the same underlying psychological process. This presents a practical problem for
designing a functional imaging experiment to investigate the neural correlates of negative
priming, as interference and negative priming tend to occur together and are therefore
hard to distinguish given the relatively low temporal resolution of functional imaging
techniques. A well characterised behavioural paradigm was therefore modified for the
purpose. The paradigm, in which distractors produce negative priming but not
interference, was originally described by Morton (Morton, 1969). Subjects are asked to
count red items presented briefly on the circumference of an imaginary circle, while
ignoring a variable number of black distractors. Subjects are able to ignore the distractors,
as Stroop-like interference is not produced when the black items are numbers (Driver and
Tipper, 1989; Francolini and Egeth, 1980). However, negative priming can be produced
by the ignored black items on subsequent counting responses (Driver and Tipper, 1989).
This shows that the distractors are processed to the level of identification, although they
produce no interference. This paradigm therefore produces negative priming without
item-specific interference.

The haemodynamic responses associated with negative priming were characterised using
specific modifications of this paradigm for H_2^{15}O Positron Emission Tomography (PET).
In negative priming behavioural experiments, ‘prime’ and ‘probe’ trials are frequently
separated with assessment of the negative priming only on the ‘probe’ trials. To maximise
the sensitivity of the functional imaging measure of cortical activity due to negative
priming, the paradigm was therefore modified so that there was no distinction between
these trial types. On any one trial, the distractors served as a prime for the subsequent trial
and the attended items as a probe for the previous trial. Subjects were always asked to
perform the same task, counting red items, throughout the experiment. The identity and
presence of the black distractors was systematically varied to produce four different
conditions:

- **Baseline.** Each display contained only red letters, and there were no black
distractors.
Neural correlates of selective attention

- **Letters.** Each display contained both red letters and (ignored) black letter distractors. There was no relationship between the number of red items and the number of black items.

- **Numbers.** Each display contained both red letters and ignored black digits that bore no systematic relationship to the number of red items in the current or immediately subsequent display.

- **Ignored repetition numbers.** Each display contained both red letters and ignored black digits whose value corresponded to the number of red items in the immediately subsequent display, and should therefore cause negative priming.

Behaviourally, it was expected on the basis of the previous studies using a similar paradigm (Driver and Tipper, 1989; Francolini and Egeth, 1980) that naming latencies for condition (3) would not differ from condition (2), showing that the ignored numbers do not produce interference. However comparison of naming latencies of condition (4) and condition (3) should reveal a small negative priming effect. Comparisons among the functional images were planned in several different ways. As there are no physical differences in the stimuli presented in conditions (3) and (4), and the task performed by the subjects is identical, any differences in cerebral blood flow should be directly attributable to negative priming. By comparing blood flow in the number distractor conditions (3 & 4) to the letter distractor condition (2), a measure of cerebral activation attributable to the numerosity of the distractors is elicited. Finally comparison of the conditions where distractors were present (2, 3 & 4) with the baseline condition (1) should reveal activation caused by distractors per se, or the increased selection demands associated with performing the primary task in the presence of distractors. Previous experience with paradigms studying distractor processing strongly suggested that time dependent factors may be prominent in the data. In a previous study investigating the Stroop task (Bench *et al.*, 1993); see also (Pantelis *et al.*, 1996), time dependent changes in rCBF were seen that were specific to the type of distractor (in other words, not attributable to some general non-specific effect but associated with distractor activation in a time-by-condition interaction (Friston *et al.*, 1991): see methods). Within the radioactive dose limitations appropriate for H$_2^{15}$O PET, each experimental condition was therefore replicated three times within a twelve measurement scanning session. Here both time-dependent and time-independent effects revealed by the comparisons of rCBF described above are reported.
Neural correlates of selective attention

4.2 Methods

4.2.1. Subjects

The nine subjects (8 men and 1 woman; median age 29 years, range 25-55y) were volunteers who gave their informed consent to the procedure. All were right-handed and had normal colour vision and normal (corrected) visual acuity. The procedures were approved by the local ethical committee and Administration of Radioactive Substances Advisory Committee (UK) (ARSAC).

4.2.2. Materials

Subjects viewed stimuli presented on a computer monitor at a distance of approximately 60cm while lying supine in the scanner. A display containing either red items, or red and black items, was presented for 300ms. The diameter of the display subtended 9 degrees of visual angle, while individual red or black items subtended 0.7 degrees. The subjects were asked to count the number of red items and report verbally. Speed and accuracy were emphasised, and subjects were told that the black items were an irrelevant distraction that they should ignore. Displays were presented sequentially with a constant SOA of 1000ms. During a single scan a total of eighty stimuli were presented. Displays contained a variable number of items that could be either red or black. Each item was located at one of eight equally spaced locations on the circumference of an imaginary circle. The number of items per display varied, depending on the condition. There were always 1, 2, 3 or 4 red items. Red items were always uppercase letters (excluding B, I, O, Q, S and W) and comprised the same letter repeated when more than one was present in an array. Black items were either uppercase letters (excluding B, I, O, Q, S and W) or the digits 1, 2, 3 or 4. The black items in a display were always repetitions of the same item. The number of red items (to which the subject had to respond) could not be predicted by either the number of black items, or the total number of items in those conditions. Before imaging, subjects were shown an example display and given a short period of practice. The functional imaging session lasted about ninety minutes. At the end of the session, the subjects were asked if they had noticed anything about the black items in the displays and then if they noticed that the black items were sometimes digits. If they responded positively to the latter question, subjects were then asked if they had noticed any relationship between the black digits and the red items. If the subjects had not noticed the
Neural correlates of selective attention

contingent relationship between black digits and the subsequent counting response in the numbers-same question, the contingency was explained to them and they were asked if they had noticed it.

4.2.3. Data acquisition and analysis

Each subject underwent twelve H$_2^{15}$O PET scans in a single session using an ECAT EXACT HR+ system (CTI, Knoxville, TN) in a manner similar to that described in section 2.1.2.. There were four conditions using a within-subject subtractive design. There were therefore three replications of each condition per subject, and the order was counterbalanced across subjects.

Subjects' verbal responses were recorded during the scanning session. The recordings from the remaining 106 scan sessions from nine subjects were analysed using voicekey software (Wellcome Department of Cognitive Neurology, UK) implemented in MATLAB (MathWorks Inc, Sherborn, MA) to derive measures of counting RT. The first trial of each session was eliminated from the analysis. All error trials, and the immediately following trial were also eliminated from the analysis.

Functional imaging analysis used Statistical Parametric Mapping, as implemented in SPM96 (Wellcome Department of Cognitive Neurology, UK, http://www.fil.ion.ucl.ac.uk/spm) in a manner similar to that described in Chapter 2. A design matrix was constructed that specified the main effects of each condition, the main effect of time and the interactions between time and condition. In this experiment, the effect of time was modelled by specifying the sequential order of each condition. This models a linear effect of time that is specific to each condition. The counterbalanced design ensures that these effects were not related to condition order. In this chapter two types of effect are therefore reported. First, activity related to distractor processing that does not change over time (a main effect of condition). Second, activity related specifically to distractor processing that shows changes over time (interactions between condition and time). The relevant SPM(t) for each comparison was constructed and then transformed into an SPM(Z). Clusters are reported that are significant at p<0.05 corrected for multiple comparisons (Friston et al., 1996a).

4.3 Results

4-91
4.3.1. Behavioural

Counting reaction times and error rates were available from eight subjects and are shown in Figure 4-1. There was a significant negative priming effect of 20ms (t(7)=2.048, p<0.05 one tailed), but no interference from the number distractors compared to the letter distractors (t(7) = -0.218, p>0.05). These findings replicate those previously observed in behavioural studies using the same paradigm. It is important to establish that these effects are not due to subjects becoming aware of the distractor contingencies, so a structured debriefing took place after the experiment. Four of the nine subjects reported noticing that the black items were on occasion digits. However none noticed the contingency between ignored numbers and subsequent counting response in the ignored-repetition condition, even when it was pointed out. Over the course of the experiment there was a modest decrease in reaction times of 31ms that trended towards, but did not reach, significance (F(2,8)=1.048, p>0.05). There were no significant interactions between condition and replication.
Figure 4-1: Counting reaction times
Condition-specific counting RTs are shown, averaged across eight subjects. Error bars are one standard error. The left panels show condition-specific reaction times, whereas the right panel shows how RT changes across successive replications, collapsed across condition.
4.3.2. Functional imaging

Activity attributable to distractors of any type \((2+3+4)-(1)\)

Comparison of the three distractor conditions with the baseline (no distractor) condition gave a measure of changes attributable to distractors irrespective of their identity (Figure 4-2, Figure 4-4). Activations were seen in bilaterally symmetric areas of right and left fusiform cortex \((x,y,z = 48 -80 -10, Z=5.41; x,y,z = -32, -78, 12, Z=4.22)\) and right parietal cortex \((x,y,z = 30, -60, 64; Z=3.57)\). Other areas showed rCBF changes associated with this condition-specific effect that changed with successive replications (formally, a time-by-condition interaction). These areas were left dorsolateral prefrontal cortex (BA 45; \(x,y,z = -66, 4, 16; Z=4.73\)), right middle frontal gyrus (BA 9 and 10; \(x,y,z = 28, 34, 34, Z=4.08\); \(x,y,z = 42, 48, -10, Z=3.84\)) and left anterior cingulate \((x,y,z = -12, -6, 36; Z=4.71)\). In these regions, differences in rCBF between distractor condition and baseline increased over successive replications (Figure 4-4).

Activity attributable to number distractors \((3+4)-(2)\)

The comparison of the two conditions where number distractors were present (no-repetition and ignored-repetition) with the condition where letter distractors were present (letters) showed activity in the right fusiform gyrus only \((x,y,z = 42 -60 -14; Z=3.83)\). There were no significant changes with replication.
Figure 4-2: Distractors compared to baseline

Activation related to presence of distractors in display compared to baseline. Foci of significant ($p<0.05$ corrected) activation due to distractors that did not show significant interactions with time. The data are displayed superimposed on a T1 weighted anatomical template rendered in Talairach space.
Figure 4-3: Time-dependent distractor activity

The upper panels represent a rendering of foci of activation associated with the presence of distractors that showed a significant \( p<0.05 \) corrected interaction with time. This comparison involved a contrast between the time-dependent effects attributable to the three distractor conditions with the Baseline condition. The data are displayed superimposed on a T1 weighted anatomical template rendered in Talarach space. The lower panels illustrate the regionally-specific differences in rCBF between the average of the rCBF from the three distractor conditions (Letters, Numbers, Ignored repetition numbers) and the rCBF in the no-distractor (Baseline) condition, plotted as a function of time. These graphs represent rCBF differences specifically attributable to distractor processing in these three cortical areas.
Neural correlates of selective attention

Activity attributable to negative priming \{(4)-(3)\}

Comparison of the ignored-repetition and no-repetition conditions provided a measure of changes in activity associated with the negative priming effect. Three areas showed significant effects expressed as interactions with time (Figure 4-4 & Table 4-2): left striatum \((x,y,z = -26,-18,20; Z=4.04)\), left cuneus \((x,y,z = -14, -88, 16; Z=3.82)\) and right anterior cingulate \((x,y,z = 14, 34, 18; Z=3.38 & p=0.06)\). An area in left parietal cortex showed a trend toward significance \((x,y,z = 12, -36, 58; Z=3.29, p=0.146)\). These time-dependent correlates of negative priming are plotted as a function of time for striatum, cuneus and cingulate areas in Figure 4-4. There were no areas that showed an effect of negative priming independent of time.

\[\text{Activity attributable to negative priming \{(4)-(3)\}}\]
Neural correlates of selective attention

Table 4-1: Distractor-related activations

Areas activated in the comparison of conditions where distractors were present (Letters, Numbers & Ignored-repetition numbers) with the baseline condition where no distractors were present.

<table>
<thead>
<tr>
<th>Cortical area</th>
<th>Effect</th>
<th>Co-ordinates</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right fusiform</td>
<td>Main effect</td>
<td>48 -80 -10</td>
<td>5.41</td>
</tr>
<tr>
<td>Left fusiform</td>
<td>Main effect</td>
<td>-32 -78 12</td>
<td>4.22</td>
</tr>
<tr>
<td>Right parietal</td>
<td>Main effect</td>
<td>30 -60 64</td>
<td>3.57</td>
</tr>
<tr>
<td>Left BA [44]</td>
<td>Interaction</td>
<td>4 12 26</td>
<td>4.72</td>
</tr>
<tr>
<td>Left BA [45]</td>
<td>Interaction</td>
<td>16 14 4</td>
<td>4.62</td>
</tr>
<tr>
<td>Cingulate</td>
<td>Interaction</td>
<td>-12 -6 36</td>
<td>4.71</td>
</tr>
<tr>
<td>Right Gfm [9]</td>
<td>Interaction</td>
<td>28 34 34</td>
<td>4.08</td>
</tr>
<tr>
<td>Right Gfm [10]</td>
<td>Interaction</td>
<td>42 48 -10</td>
<td>3.84</td>
</tr>
</tbody>
</table>
Figure 4-4: Activity due to negative priming distractors

The upper panels represent a maximum intensity projection in Tailarach space of an SPM(t) representing the foci of significant ($p<0.05$ corrected) interaction between the negative priming effect and time. This comparison involved the conditions Ignored-repetition numbers and Numbers. The lower panels illustrate the difference between the rCBF in Ignored-repetition numbers and Numbers conditions, plotted as a function of time, showing time-dependent changes in rCBF attributable to negative priming.
Neural correlates of selective attention

Table 4-2: Negative priming activations

Areas activated in the comparison of *Ignored repetition numbers* and *Numbers* conditions. The p values stated are corrected for multiple comparisons across the whole brain volume.

<table>
<thead>
<tr>
<th>Cortical area</th>
<th>Type of effect</th>
<th>Co-ordinates</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left striatum</td>
<td>Interaction</td>
<td>-26 18 16</td>
<td>4.04</td>
</tr>
<tr>
<td>Left cuneus</td>
<td>Interaction</td>
<td>-14 88 16</td>
<td>3.82</td>
</tr>
<tr>
<td>Right anterior cingulate</td>
<td>Interaction</td>
<td>14 4 18</td>
<td>3.38</td>
</tr>
<tr>
<td>Right parietal</td>
<td>Interaction</td>
<td>12 36 58</td>
<td>3.29</td>
</tr>
</tbody>
</table>

(p=0.06)  
(p=0.15)
4.4 Discussion

The experimental manipulation in this study was intended to produce an isolated negative priming effect on naming latencies in the absence of interference from the black distractors. In this respect the behavioural data replicate, both qualitatively and quantitatively, the results of Driver and Tipper (Driver and Tipper, 1989). There was no Stroop like interference from the ignored black digits in the displays. However the same digits that produce no interference do produce a negative priming effect comparable in size to that observed by Driver & Tipper (Driver and Tipper, 1989). Importantly, none of the subjects noticed the systematic manipulation of the relationship between distractor and subsequent response. There is therefore no evidence to suggest that subjects were using an alternative strategy (e.g. remembering the numerical identity of a distractor to produce as the next counting response!) during the negative priming task.

As the subjects always performed the same task (with the same instructions to ignore the black items), differences in activity between experimental conditions must reflect either distractor processing, or the influence of distractors on processing of the attended items. In the comparison designed to identify the correlates of negative priming, the stimuli, task and responses were physically identical so any differences in activity between these conditions must reflect the neural correlates of negative priming. Taking the results as a whole, it is surprising that the differences in brain activity were so widespread and affected not just posterior sensory areas but also prefrontal and subcortical structures. Furthermore the time-dependent nature of many distractor related activations raises questions about how distractor processing may change over time during repeated performance of the same task. The activity evoked by distractors per se will be discussed first, before turning to the neural correlates of negative priming.

4.4.1. Distractor processing

The presence of distractors, irrespective of their identity, activated bilateral areas of fusiform cortex and the right parietal cortex compared to baseline. The fusiform cortex and other areas within ventrolateral areas of extrastriate visual cortex are implicated in the
Neural correlates of selective attention

processing of object related signals in human functional imaging studies (Corbetta et al., 1991b; Ungerleider and Haxby, 1994) so these activations are plausibly related to processing the identity of these unattended stimuli. The activation in parietal cortex was in the superior parietal lobule (BA7) that has been repeatedly implicated in the control of selective attention (Corbetta et al., 1991b; Coull et al., 1996). This finding is of interest because previous functional imaging studies have not been able to distinguish parietal activation due to intention and attention (Corbetta et al., 1995). Selective attention is usually studied by instructing subjects to attend to particular stimulus attributes, and varying that instruction in different scans. This conflates subjects’ (necessarily conscious) intention and the manipulation of attention (selective processing). However in the present study there is no difference in the intention of the subjects during the different conditions, as the instructions are identical in each. The presence of a superior parietal activation might therefore be the result of changing attentional demands, and not intentional. Behaviourally, the presence of distractors in this experiment was associated with a slowing in RT. The slowing of choice responses to a relevant stimulus by the simultaneous occurrence of other visual events is well documented (e.g. (Eriksen and Eriksen, 1974; Eriksen and Schultz, 1978)). Moreover there is evidence that links such ‘filtering costs’ to the spatial allocation of attention (Treisman et al., 1983). These posterior activations may represent the neurobiological correlate of ‘filtering costs’.

In contrast to the posterior activations, that showed constant activity over time, activity related to the comparison of distractor conditions and baseline was also seen in anterior areas of cortex that varied in a time dependent manner with successive replications. Activations were seen in right and left prefrontal cortex and anterior cingulate. The anterior cingulate activation is located caudal, ventral and contralateral to the PET studies showing cingulate activation in response to Stroop stimuli (Bench et al., 1993; Pantelis et al., 1996; Pardo et al., 1990). The interpretation of cingulate activation has often suggested a role in monitoring, response selection or conflict prevention. However the functions of the cingulate cortex appear to differ along its extent, and increased anterior cingulate activity has been observed in PET activation studies involving such diverse phenomena as selective attention, response selection, language and painful stimuli (Craig et al., 1996; Frith et al., 1991; Petersen et al., 1988; Rees et al., 1997a). Recently, Carter and colleagues (Carter et al., 1998) have shown that the anterior cingulate is more active in situations where increased response competition occurs, and suggested that the cingulate monitors competition between processes that conflict during task performance.
Neural correlates of selective attention

Thus in the present study, cingulate activation may be related to distractor processing and the prevention of response conflict between distractor and target representations. In addition to the cingulate, a swathe of predominantly left prefrontal cortex is activated extending forward from precentral gyrus through inferior frontal gyrus (BA44) into BA45. Activations in right and left prefrontal cortex have been seen in tasks involving both implicit and explicit memory (Grafton et al., 1995; Shallice et al., 1994). In particular, implicit memory seems to involve more ventral structures in prefrontal cortex (Hazeltine et al., 1997). Activity in these areas of prefrontal cortex, related to distractors, may therefore represent implicit memory for such unattended stimuli, consistent with some theoretical accounts of distractor processing (Neill et al., 1992).

Over successive replications, the activations due to distractors increased in these anterior areas (Figure 4-3). Given that RT decreased over time, suggesting that task performance was improving, it might seem counterintuitive that distractor-related activity increased over time. Improved task performance in general makes it easier to exclude distracting information, and yet we saw an increase in activation. One possible explanation for this effect is suggested by the perceptual load theory of Lavie (Lavie, 1995). She proposes that perceptual load is a major factor in determining the locus of attentional selection. In this account, perceptual processing is conceived of as a limited resource, but one that proceeds automatically until it runs out of capacity. The role of attention is to direct attention to particular stimuli. If attention to a particular task uses only part of the resources available at any given time (i.e. ‘low perceptual load’), then involuntary processing of unattended stimuli will occur, consistent with late selection theories of selective attention. However, under conditions of high perceptual load, relevant (attended) items exhaust the available processing capacity, and irrelevant (distractor) items are not processed; a claim that is consistent with early selection theories. Lavie’s unifying theoretical approach has received empirical support from both behavioural (Lavie and Tsai, 1994) and functional imaging (Rees et al., 1997b) studies. An important prediction of this theory concerns the interaction between practice and attention. If practice at a task decreases the perceptual load (see Lavie (Lavie, 1995) for a full discussion of the operational definition of this term), then the theory predicts that distractors should actually be processed more, and therefore interfere more, as a function of practice. We suggest that one interpretation of the time by distractor interactions observed in our functional imaging data may be the occurrence of additional distractor processing occurring with practice. An alternative suggestion is that the frontal
Neural correlates of selective attention activations reflect additional inhibitory mechanisms of attention deployed to suppress increased distractor processing over time. It is not possible to decide which of these explanations is correct from the present data. Nevertheless these findings suggest that the degree to which distractors are processed changes as a function of task practice. Although the activations evoked by distractors compared to baseline changes over time, such an interaction is not clear in the reaction time data. However, although this difference is extremely interesting, it is difficult to draw strong conclusions from a failure to reject the null hypothesis.

4.4.2. Neural correlates of negative priming

Stimuli that produced negative priming activated three cortical areas (Figure 4-4); the left striatum, left cuneus and right anterior cingulate (with a trend towards significance in right parietal cortex). In this comparison, the stimuli were perceptually identical in both conditions; the only difference was the delay in RT attributable to the negative priming. The differences in evoked haemodynamic activity are therefore not attributable to the presence of number distractors per se or to any physical difference in the stimuli; they are related to the interaction of previously ignored stimuli with the evoked activity produced by the counting task on probe trials. This shows that at least one component of the negative priming process is due to activity on the probe trial (where counting RT is delayed) rather than on the prime trial. If negative priming was realised neurobiologically solely as an inhibitory process acting on number distractors, then we should see changes in activation occurring whenever number distractors are present, regardless of the behavioural consequences. In other words, if there was an inhibitory process caused by number distractors on the prime trial, we should expect there to be changes in rCBF in both the numbers-same and numbers-different conditions; there should be no difference in activations between these conditions. The observation here of significant differences between the conditions suggests that the underlying process arises as an interaction between the numerosity of previously ignored distractors and the current counting response. This distinction is important in the light of the psychological theories advanced to explain negative priming. There are two main theories, that are not necessarily mutually exclusive (Neill et al., 1995). The first suggests that the representation of an ignored distractor is blocked from access to response mechanisms (Tipper and Cranston, 1985). This is an elaboration of the idea that the representation of an ignored distractor is
Neural correlates of selective attention

simply deactivated or inhibited directly, motivated by empirical evidence that negative priming sometimes depends on whether there is interference on probe trials (Neill et al., 1995). Both the deactivation hypothesis and the blocking hypothesis attribute negative priming to inhibition occurring on the priming trial. This inhibition then carries forward to the probe trial, impeding the response to information related to the ignored distractor. An alternative theory suggests that identification of a target involves obligatory retrieval of past processing episodes in which the current target stimulus has been ignored (Neill and Valdes, 1992; Neill et al., 1992). It is proposed that retrieval of such episodes slows responses to the target stimulus. On this account, the inhibition associated with negative priming is evoked on the probe trial, not the prime trial. The common element unifying the episodic retrieval, blocking and deactivation theories is that negative priming is attributed to the interaction of prior distractor processing with current target identification. The present findings support these theoretical claims, and reveal the functional anatomy associated with this interaction.

Cortical and subcortical activity specific to the negative priming changed over successive replications (Figure 4-4). This interaction between negative priming and time might be explained in terms of Lavie's theory discussed above. If practice results in increased task automatization and decreased perceptual load, her theory predicts that negative priming distractors will be processed more fully. This would result in an enhanced negative priming effect, consistent with our observation of increase in activation over time. Indeed, Lavie and Fox have recently shown that the degree of negative priming produced by distractors is influenced by perceptual load, being greater under low perceptual load (Lavie and Fox, 1999). However although reaction time declined over successive replications, we were unable to demonstrate significant interactions with condition. This is perhaps not surprising given the rather limited power (small number of subjects and replications) of the behavioural component of the experiment. The constraints of PET require combining many probe/prime stimuli sequentially in a single scan. Within a single scan, the unique feature of the numbers-same condition, compared to the other distractor conditions, is that there exists a contingent relationship between the distractor identity on a given trial and the counting response to the next trial. Is it possible that another explanation for the time-dependent effects seen here is that they represent implicit learning of this relationship? There is evidence from the Stroop task that subjects can implicitly learn a systematic contingency between the ink colour and the word name (Musen and Squire, 1993). We speculate that it is possible that such implicit learning may
Neural correlates of selective attention

be occurring in the present study. Our findings demonstrated very prominent activation of the entire left striatum. Theoretical accounts of implicit learning implicate the striatum (Graybiel et al., 1994), and basal ganglia activation has been associated with implicit learning of motor sequences (Grafton et al., 1995; Hazeltine et al., 1997). It is possible that the striatal activation in the present study may therefore reflect implicit learning of the contingency between ignored repetitions of distracting information in the negative priming. The activation was strongly lateralised to the left hemisphere, as are many of the anterior activations seen in the distractor-related comparisons. Predominantly left hemispheric activation is consistent with both the linguistic nature of the stimuli employed (Price, 1998) and the need for processing to proceed to semantic levels of analysis in order to see the behavioural effect of negative priming (because it is the numerical identity of the distractors that is repeated in the counting response).

Anterior cingulate activation was evoked by the negative priming distractors, but in a different location to that seen when comparing all distractor conditions to baseline. The distinction between left anterior cingulate activation produced by distractors of any type, and right anterior cingulate activation by negative priming distractors, emphasises the functional and anatomic heterogeneity of the cingulate. The negative priming activation here is located close to the cingulate focus activated by the Stroop task compared to naming the ink colour of coloured crosses (Bench et al., 1993; expt 2). One interpretation of cingulate activation in the Stroop task is that it is related to the suppression of irrelevant distracting information. In the present study, the similar cingulate activation in the presence of negative prime stimuli therefore might also be related to the suppression of the representations of distractors. Bench (Bench et al., 1993) noted previously that cingulate activation in the Stroop task is exquisitely sensitive to task parameters. Changes in the interstimulus interval by small amounts, and changes in the amount of practice, result in considerable variation in the cortical activations evoked. The time-dependent manner of the activation in the present study further support the idea that time-dependent changes in functional anatomy are important in selective attention experiments that involve presentation of distracting stimuli.

4.5 Conclusion

Negative priming represents an interaction between the processing of ignored stimuli and the task engaging the subject (counting visually presented items in this study). The results
Neural correlates of selective attention presented in this chapter indicate that this interaction evokes neural activity that varies over time, and that the activity is predominantly seen in subcortical structures such as the basal ganglia. Negative priming has commonly been seen as reflecting an inhibitory mechanism; the results presented here might suggest that it is better thought of as related to the learning of associations between ignored and attended stimuli.

In the studies presented here and in section 3.4, simple and austere visual displays and paradigms were used, and this may be one reason why processing of unattended stimuli was seen. While these studies have helped elucidate something about differences between the signals evoked by attended and ignored stimuli, they do not speak to the determinants of such selective processing. In the next two chapters more complex visual displays are now used with direct manipulations of task difficulty in an attempt to effect such a characterisation.
Chapter 5 Perceptual load as a determinant of selective attention

The previous chapters have established that the unattended stimuli can be processed under certain circumstances and evoke specific patterns of cerebral activity related not simply to sensory processing of the stimuli but also related to the behavioural consequences of such processing such as negative priming. In this chapter an attempt is made to characterise in a more explicit fashion the determinants of processing of unattended stimuli. In particular, the role of task demands in modifying the processing of irrelevant and ignored stimuli are examined. Attention is often characterised as some kind of monolithic force or process that acts on sensory processing. Here, an alternative hypothesis is sketched out: that selective processing in the visual system occurs as an automatic result of the availability of processing resources, and is not necessarily under direct control by the subject.

5.1 Introduction

A classic issue in the study of attention is whether identity is extracted from stimuli when they are ignored. The previous chapter showed that, in the context of a relatively easy counting task, the identity of ignored visually presented numbers could interfere with task performance. As this negative priming only occurs when the ignored numbers predict the subsequent counting response, the identity of the ignored numbers must have been extracted by the visual system in order to generate this interference. This type of study shows that ignored stimuli are processed to the level of identity. However other studies show that ignored stimuli receive little processing beyond a rudimentary analysis of sensory attributes (Broadbent, 1958; Treisman and Gelade, 1980). Subjects performing dichotic listening tasks, for example, appear to have little or no access to information about the identity of stimuli presented to the ignored ear. More recently experiments where selection is made between competing stimuli on the basis of spatial location show that modulations of sensory evoked responses occur both early in time and early in the visual processing pathway. Two contrasting positions can be distinguished. According to the first, selective processing begins early in the visual system and unattended stimuli receive little or no processing beyond a rudimentary analysis of their sensory attributes. However the second position suggests on the basis of negative priming and other
Neural correlates of selective attention

phenomena that unattended stimuli are processed beyond a mere analysis of physical attributes to the level of identity. Any selective process such as attention must be operating post-perceptually. How can these two contrasting positions be reconciled, and what are the determinants of selective perception? In this chapter, two experiments are presented that combine functional imaging and behavioural measures to test a new theory that may resolve this longstanding controversy.

5.1.1. A direct test of the perceptual load hypothesis

Lavie’s theory (Lavie, 1995; Lavie and Tsal, 1994) proposes that capacity for perception is limited, but within those limits perception proceeds automatically. Thus, while we may not be able to perceive everything, we are unable to stop perceiving whatever we can. The extent to which a target task exhausts available capacity thus determines the degree to which irrelevant distracting stimuli will be processed. If the processing load of the target task exhausts available capacity, irrelevant stimuli will not be perceived. However, if the target processing load is low attention will inevitably spill over to the processing of irrelevant distractors. The extent to which irrelevant stimuli are excluded from perception does not thus depend simply on subjects’ intentions to ignore them. Irrelevant stimuli are excluded from perception only when the processing load of a task engages full attention under conditions of high load. The concept of perceptual load involves increasing the number of items in a display, or increasing the processing requirement for the same number of items. A review of previous behavioural studies of attention supported the claims of perceptual load theory (Lavie, 1995). Results compatible with selective perception were typically obtained in situations of high attentional load, and results compatible with nonselective perception were typically obtained in situations of low load. For example, the negative priming experiment presented in the previous chapter would be considered a low perceptual load task as there little processing of attended stimuli was required to generate the counting response. Consistent with this, the results indicate nonselective processing with the identity of ignored numbers producing negative priming of the attended items.

This theory was investigated by studying the perception of irrelevant visual motion during performance of a task involving linguistic judgements on single words. Although both these tasks involve visual input, they are thought to rely on completely different psychological processes. Yet if both depend on a common source of attention, as the load
Neural correlates of selective attention

theory suggests, then they should be strongly interdependent. Specifically, the prediction was that subjects will fail to ignore irrelevant visual motion as long as processing load in the linguistic task is low, but that higher load in the linguistic task will prevent perception of the irrelevant motion. Despite subjects' wishes to ignore the motion distractors in all conditions, they will only succeed in doing so under conditions of high load in another task that exhausts their attentional capacity.

Visual motion was used as a distracting stimulus as it is known to activate a distinct area of the brain, V5, whose location has been reliably identified in previous functional imaging studies (Sereno et al., 1995; Tootell et al., 1995; Tootell and Taylor, 1995; Watson et al., 1993; Zeki et al., 1991). Activation of V5 by a moving stimulus should therefore allow determination of whether processing of irrelevant visual motion has occurred. Previous functional imaging, psychophysical and single cell electrophysiological studies have all suggested that motion perception may depend to some extent on attention (Buchel et al., 1998a; Chaudhuri, 1991; Corbetta et al., 1991b; O'Craven et al., 1997; Treue and Maunsell, 1996). However, none of these studies have provided a critical test for the claim made here, that the crucial factor determining when subjects can ignore motion distractors is the attentional load in an unrelated task. Every previous study has compared explicit attention to motion with explicit ignoring of motion. Any difference in motion related brain activity between these two conditions can be attributed to an enhancement of perception with deliberate attention to the moving stimulus, rather than successful ignoring of motion in the unattended condition. These previous studies therefore cannot provide any clear answer to the principal issue in attention theory: whether irrelevant distractors can be excluded from perception. Here the load theory is tested by characterising changes in selective processing of a motion stimulus that is always irrelevant, while varying the attentional load of an unrelated target task.

5.2 Methods

5.2.1. Subjects and stimuli

For the irrelevant motion stimulus an optic flow field was used with a full field of dots moving radially towards the screen (Figure 5-1). This type of motion may be particularly difficult to ignore due to its biological relevance. Optic flow is continuously used in
Neural correlates of selective attention

judgements about motion direction in the environment (for example, an expanding field indicates approaching to the source of the expansion) (Gibson, 1950; Gibson, 1977). Irrelevant motion processing was characterised by measuring brain activity in motion-related areas during changes in the demands of an imposed (and unrelated) linguistic task.

Subjects viewed a display with two different components (Figure 5-1). In the periphery of the display were placed scattered white dots. Motion perception was assessed by comparing conditions where these dots moved with conditions where the dots were static. This component of the display comprised four hundred single white dots each subtending 0.1 degrees scattered randomly outside a central ellipse in a display 17 degrees across. When the display was moving, each dot moved radially outwards at a constant velocity of approximately 5 degrees per second. As dots left the edge of the display new dots were added at the periphery of the central ellipse surrounding the words to ensure the dot density of the display remained constant. Subjects were asked to ignore the white dots throughout and were told that they were always irrelevant to the experiment, and might produce unpleasant motion after-effects if they were not ignored. In the centre of the display single words were presented successively in a blank ellipse that separated them from the dots. High frequency five letter nouns were presented in the centre of the display, surrounded by a blank ellipse to distinguish the words from the peripheral display. Each word subtended approximately 1.4 degrees and the ellipse 2.7 (vertical) by 4.1 (horizontal) degrees. Each word was presented for 750ms, followed by a blank interval of 250 ms. During each experimental epoch, there were eight targets and twenty-four foils. The words were identical for each subject in high load and low load conditions, though their order within an epoch was randomised. The position of targets within an epoch was constrained to be matching in both high and low load conditions. The condition order and stimulus materials were counterbalanced across subjects.
Neural correlates of selective attention

Figure 5-1: Illustration of visual display

The illustration is schematic and the dotted ellipse and arrows were not part of the stimulus presented to subjects. Words were presented in a stream at fixation in a black ellipse without border. Scattered dots were placed elsewhere on the stream, and in movement conditions moved radially outwards. As dots left the edge of the stream new ones were added at the boundaries of the ellipse in order to keep the dot density constant.
Subjects were asked to focus on these words, and during low load conditions, press a key whenever a word was printed in uppercase letters. Under high load conditions, they saw the same letter strings but were now asked to press the button whenever they saw a bisyllabic word. Each subject performed both high and low load tasks, with and without irrelevant visual motion, while undergoing functional magnetic resonance imaging (fMRI). Informed consent was obtained from six subjects (five female, one male; mean age 24.5yrs; age range 22-29; five right handed, one left handed). All used their dominant hand to respond.

5.2.2. Data acquisition and analysis

A Siemens VISION system (Siemens, Erlangen) operating at 2T was used to acquire both T1 anatomical and gradient-echo echo-planar T2* weighted image volumes with Blood Oxygenation Level Dependent (BOLD) contrast in the manner described in section 2.2. The experiment began with the acquisition of a T1 weighted anatomical image from each subject. Functional imaging was then performed in four separate runs, acquiring a total of two hundred and eighty functional volumes per subject. Each functional image volume comprised forty-eight 3mm axial slices with in-plane resolution 3x3mm positioned to cover the whole brain. During each run, volumes were acquired continuously every 4100ms, while subjects performed either epochs of the experimental task lasting 32.8s (eight volumes), or epochs of rest (visual fixation lasting 32.8s or eight volumes). Each run began with six ‘dummy’ volumes that were subsequently discarded to allow for T1 equilibration effects. Periods of rest then alternated with the experimental conditions as described above for the duration of each run. The total duration of the experiment was thus around 20-25 minutes, during which time two hundred and eighty functional image volumes were acquired of which two hundred and fifty-six were subsequently analysed.

The imaging time series was realigned, spatially normalised to the stereotactic space of Talairach & Tournoux and smoothed with a Gaussian kernel of 8mm full width half maximum (Friston et al., 1995a; Friston et al., 1995b; Friston et al., 1995c; Friston et al., 1996b; Talairach and Tournoux, 1988). Condition-specific effects were estimated using the General Linear Model with a delayed boxcar waveform in the manner previously described. The statistical contrast between the condition-specific effects (low load & motion - low load & no motion) - (high load & motion - high load & no motion)
Neural correlates of selective attention represents the interaction term of interest, and was used to create an $\text{SPM}_t$ that was transformed into an $\text{SPM}_Z$ and thresholded at a Z value of 3.09 (corresponding to $p<0.001$ uncorrected for multiple comparisons). Masking with the contrast between motion conditions and baseline fixation was used to restrict our analysis to areas activated by visual stimulation. The interaction analysis was deliberately confined to the subset of voxels that showed significant activation when comparing the motion conditions (irrespective of load) to fixation. This masking procedure does not alter the Z scores or affect statistical inference for the interaction term, but represents a way of limiting the interpretation of the data to areas plausibly activated by visual stimulation.

Resultant areas of activation were characterised in terms of their peak heights. In cortical area V5, due to the prior hypothesis, activations are reported above a threshold corresponding to $p<0.001$ uncorrected. To account for the variability in position in human V5 (Watson et al., 1993) activations were sought within the stereotactic co-ordinates defined by Watson et al. (Watson et al., 1993), plus or minus half the width of the smoothing kernel. However outside this area a correction (based on the theory of Random Gaussian fields) for multiple comparisons was made across the whole brain volume examined and only areas of activity above a threshold corresponding to $p<0.05$ corrected are reported.

5.3 Results

Data from all six subjects were analysed as a group to identify areas activated in common across all subjects. The critical test of the hypothesis is whether evoked activity related to irrelevant visual motion (compared to no motion) is smaller under conditions of high processing load (compared to low load). This pattern of modulation is represented by the interaction term in the factorial design of the experiment. The statistical parametric map was therefore constructed that reflects this interaction between processing load and visual motion, using SPM (for further details, see chapter 2). This analysis identified several areas (Table 5-1) in which the effect of visual motion (compared to no motion) was greater under conditions of low load (compared to high load). The discussion will be limited to those areas at or before V5 in the pathway for the processing of visual motion.

Confirmation that processing load was manipulated appropriately was obtained by recording subjects' responses in the linguistic task. Behavioural data were unavailable
Neural correlates of selective attention from two subjects for technical reasons. Subjects detected significantly more targets during the low load condition compared to the high load condition (80% versus 63%; t=3.7, p<0.05). Subjects also made more false positive errors in the high load condition compared to the low load condition (2.0 errors per block vs. 0.9 errors per block; t=3.1, p=0.052). Processing load was thus effectively manipulated by the two tasks.

Robust bilateral modulation of V5 complex activity, related to visual motion by load in the target task, was identified (Table 5-1). The right and left hemisphere activations identified were tested to see whether they were significantly different from each other by comparing the subject-specific effect sizes for conditions of high and low perceptual load. This is formally equivalent to testing for a (load x motion x hemisphere) interaction and was not significant (t=0.832, p>0.4).
Neural correlates of selective attention

Table 5-1: Interaction of perceptual load and visual motion

Areas where evoked activity during visual motion (compared with the no motion conditions) was significantly greater under conditions of low load (compared with high load). Only areas that are also active during the comparison of visual motion (irrespective of load) and rest (fixation) are shown, to ensure that only areas concerned with the processing of visual motion are considered. Only areas that reach $p<0.05$ after correction for multiple comparisons are reported, except in V5 where a threshold of $p<0.001$ uncorrected was used (due to the prior anatomically specified hypothesis for this area).

<table>
<thead>
<tr>
<th>Area</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
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<td>-44</td>
<td>-64</td>
<td>4</td>
<td>6.69</td>
</tr>
<tr>
<td>Right V5 complex</td>
<td>42</td>
<td>-66</td>
<td>-8</td>
<td>3.40</td>
</tr>
<tr>
<td>Right V1/V2</td>
<td>26</td>
<td>-96</td>
<td>-8</td>
<td>5.67</td>
</tr>
<tr>
<td>Superior colliculus</td>
<td>-2</td>
<td>-26</td>
<td>-2</td>
<td>5.02</td>
</tr>
<tr>
<td>Left fusiform</td>
<td>-40</td>
<td>-74</td>
<td>-14</td>
<td>5.52</td>
</tr>
<tr>
<td>Left lingual gyrus</td>
<td>-8</td>
<td>-80</td>
<td>-12</td>
<td>5.14</td>
</tr>
<tr>
<td>Right premotor cortex</td>
<td>10</td>
<td>2</td>
<td>68</td>
<td>5.06</td>
</tr>
<tr>
<td>Left superior parietal lobule</td>
<td>-26</td>
<td>-64</td>
<td>32</td>
<td>4.79</td>
</tr>
<tr>
<td>Right superior frontal gyrus</td>
<td>8</td>
<td>58</td>
<td>26</td>
<td>5.62</td>
</tr>
</tbody>
</table>
Neural correlates of selective attention

Figure 5-2: Interaction of perceptual load and visual motion

(Left and central panels) Lateral views of the right and left hemispheres of a T1-weighted volume rendered anatomical image that conforms to the stereotactic space of Talairach and Tournoux. On this image, superimposed in red, are shown those loci from Table 5-1 where brain activity in the group of subjects showed the predicted interaction between the effects of visual motion and linguistic processing load. The locations of the right and left V5 complex activity described in the text and Table 5-1 are indicated by the arrows. (Right panel) A sagittal slice through the same canonical anatomical image, on which is superimposed the locus of activity in superior colliculus (arrow) due to the interaction of visual motion and linguistic processing load.
5.4 Discussion

The experimental findings indicate a robust bilateral modulation of activity in the motion processing area V5 by perceptual load. This interaction of motion and load is in accord with the experimental hypothesis. Under conditions of low load, the moving dots produce strong activation compared to the static dots (and baseline fixation), suggesting motion perception. However, under conditions of high load, there is no increase in activity associated with the moving dots. Thus, under conditions of high load it can be inferred that distracting visual motion was not processed, whereas under low load it was processed. In other words, despite the instructions to subjects to always ignore the dots, their perception of irrelevant visual motion was in fact determined by the experimental manipulation of load in an unrelated task, and not by their intentions alone.

This result was tested further in a second experiment that adapted Chaudhuri’s psychophysical procedure (Chaudhuri, 1991) to make it suitable for testing the load theory. Prolonged exposure to visual motion, followed by viewing of a static stimulus, produces an illusory perception of opposing motion in the static display that fades over time. This motion after-effect is contingent on V5 activity (Tootell et al., 1996) and has been shown to be sensitive to attention (Chaudhuri, 1991; Shulman, 1993). The duration of this after-effect can therefore serve as a behavioural probe for the extent of irrelevant visual motion processing in the present task, allowing a convergent test of the load hypothesis. The pattern of evoked activity observed in V5 complex suggests that the motion after effect should be substantially reduced under high load conditions of the linguistic task. Four subjects viewed displays identical to those used in the functional imaging experiment while performing either the high load or the low load task. The surround was always moving, and was followed by a static full field of dots that produced a vivid motion after-effect, where the static dots appeared to radially contract. This motion after-effect was significantly shorter under conditions of high load than under conditions of low load for all subjects. For each subject, the mean (SD) motion after-effect duration for
Neural correlates of selective attention

Figure 5-3: Timecourse of attentional modulation

Mean activity over all subjects and replications of each experimental condition taken from the left V5 complex area described in Table 5.1. Activity during baseline periods (light grey shading) is shown alternating with that during experimental conditions (dark grey shading). The order in which the conditions are displayed is illustrative and does not correspond to that used in the experiment (because order of conditions was counterbalanced across subjects). Note that the statistical comparisons reported in table 5.1 and the text refer to the comparison of the experimental conditions (dark grey). The scale bar represents a value of 0.1% BOLD signal change.
Neural correlates of selective attention

seven repetitions of low and high load conditions respectively was 9.3s (2.0) & 6.4s (1.0),
t=3.26, p=0.01 (one-tailed throughout); 3.4s(0.9) & 2.5s(0.4), t=2.74, p=0.02;
13.73s(2.2) & 11.7s(1.8), t=1.92, p=0.05; 14.9s(1.6) & 11.4s(0.9), t=5.02, p=0.002. There
was thus a significant decrease in the motion after-effect duration under high load
conditions in every subject. This result is consistent with both our theoretical predictions
and our observation in the fMRI study that motion specific responses were suppressed
with high load in the linguistic task.

One interesting aspect of this motion after-effect data is that under conditions of high
perceptual load there is still a perceptual after-effect. Although under similar viewing
conditions in the fMRI scanner there appears to be no motion related activity in V5 under
conditions of high load, similar displays outside the magnet succeed in evoking a motion
after-effect. This may be simply explained by the different physical configurations of the
display used in the scanner compared to during measurement of the motion after-effect.
Alternatively it may reflect non-specific effects of the auditory perceptual load induced
by the scanner environment (see section 5.5 for further discussion). Although V5 activity
has been shown to relate very closely to the timecourse of the motion after-effect (Tootell
et al., 1996), this correlation may reflect merely the perceptual correlation between
activity in V5 and awareness of an after-effect. The mechanism responsible for generating
the after-effect need not be located in V5: indeed, it seems likely that motion-sensitive
neurons levels at multiple levels of the visual hierarchy are responsible for the genesis of
the motion after-effect (Mather et al., 1998).
Figure 5-4: Motion after-effect duration

Mean motion after-effect duration is displayed for each of the four different subjects. Error bars represent one standard error. The duration of the after-effect elicited after performing the high load task is shown in dark grey; that after performing the low load task is shown in light grey. In each subject there is a significant decrease in after-effect duration under conditions of high load compared to low load.
Neural correlates of selective attention

In the functional imaging data, a number of other areas, predominantly visual, showed a significant modulation of motion-related activity by processing load in addition to V5. These results suggest that the effects of processing load become manifest at multiple levels of the sensorimotor network, including very early visual areas. Differential activation was seen at the V1/V2 border on the right, and at a lower significance on the left. Reciprocal connections between V1/V2 and V5 have been demonstrated by reversible cooling of V5 and neuroanatomical studies in monkey (Girard et al., 1992; Shipp and Zeki, 1985; Shipp and Zeki, 1995). Changes in neural responses in early visual cortex due to attention have previously been shown in monkey (Desimone and Duncan, 1995; Motter and Mountcastle, 1981); the current results show that early visual areas in humans are also sensitive to the effects of attention. Modulation of motion-related activity by attentional load was also seen in superior colliculus (figure 5.1). This pattern of evoked responses is compatible with an ablation study in primates that demonstrated that the impairment in visual discrimination after a lesion in SC is manifest only when the unaffected part of the visual field contained a competing item (Desimone et al., 1990).

The present data suggest that the SC is sensitive to attentional load (rather than just low level visual competition between stimuli), since motion-related activity in SC was modulated in our study by varying the processing requirements in a target task without adding more visual stimuli. Thus there is greater competition for attention with either an increased number of items, or with more processing for the same items (Desimone and Duncan, 1995). Moreover, the superior colliculus has direct reciprocal anatomical connections with V5, and both SC and striate cortex contribute to visual function and motion-specific neural response properties in V5 (Gross, 1991; Rodman et al., 1990; Ungerleider et al., 1984). It is interesting, therefore, that modulation is observed here of motion processing by load in an unrelated cognitive task in both the geniculostriate (V1/V2) and retinotectal (SC) pathways by which motion related signals can reach V5. Although SC has been implicated in oculomotor control, eye movements do not provide a plausible explanation for these findings. A number of factors make this unlikely. Typically, eye movements do not occur with radial optic flow stimuli (see K. O'Craven (O'Craven et al., 1997) for a full discussion and experimental evidence). The optic flow display was widely separated from the single words, that were presented foveally for a brief duration, all factors that would be further expected to minimise eye movements. Nevertheless, to be certain, eye movements were recorded during the experimental paradigm. Technical limitations impede accurate recording of EOG whilst functional images are acquired, so EOG was therefore measured in a single subject performing the
Neural correlates of selective attention

experimental paradigm within the experimental apparatus, but without acquisition of functional images. The measurement was calibrated and sensitive to saccadic movements of approximately one degree. During the experimental conditions, no significant eye movements were detected.

In conclusion, these results demonstrate the use of functional imaging to test a cognitive theory of attention. Specifically, a resolution has been proposed to the long-standing issue of whether perception of irrelevant stimuli depends on attention. These results show that subjects' intentions to avoid irrelevant distractors are not always sufficient for ignoring them. As long as the target task imposes only a low load on attention, irrelevant stimuli such as motion will still be perceived. However, this irrelevant perception is strongly reduced if load of the unrelated task is increased. Selective perception is therefore only possible under conditions of high load. Under such conditions, even the perception of biologically significant stimuli such as optic flow can be reduced by a demanding but entirely unrelated task.

5.5 Are attentional resources shared between vision and audition?

The results presented above suggest that when the difficulty of a visual task is increased, this has a strong effect on the processing of other visual stimuli even when they are irrelevant to the task at hand. In information processing terms, this is accounted for by postulating a pool of limited resources to which visual processing has access. The neurobiological instantiation of such limited resources is not specified (see further discussion in Chapter 7) but in principle there are several possibilities. In the visual system, processing occurs within functionally specialised areas. There are dense interconnections both within visual cortex and between visual cortex and other non-visual areas such as parietal cortex. Thus, in principle a resource limitation could occur because two processes compete to access the same neuronal machinery. This might involve either a single cortical area, or a distributed set of areas within the visual system, or a distributed set of areas both within and outside the visual system. In the first two cases, the resource limitation would occur within the visual system, whereas in the latter case the resource limitation would represent some more general resource that might therefore be shared between visual and nonvisual sensory processing. It is of course possible that multiple levels of resource limitation exist that are tapped by different tasks, but for simplicity I here assume that there is a single neurobiological locus for resource limitation.
Neural correlates of selective attention

In everyday life people encounter both visual and auditory information about the environment simultaneously, and it is frequently useful to attend to both visual and auditory characteristics of an object simultaneously. The different models of perceptual resource limitation make different predictions about how easy this should be. If the major site of resource limitation is limited to the visual modality alone, then focusing attention on the auditory domain should have little effect on the visual system. Any effects of focusing attention should be seen purely in the auditory domain on ignored auditory stimuli; attentional resources are domain specific. Note that this does not preclude that links between visual analysis and auditory analysis exist (as they surely must in order to analyse both visual and auditory characteristics of a single stimulus), but merely indicates that these links do not represent shared attentional resources. If, on the other hand attentional capacity is undifferentiated, then focused attention on the auditory domain should result in decreased processing in the visual domain (and vice versa).

5.6 Introduction

In this section these different accounts of attentional resource limitation are explored by using a crossmodal paradigm and manipulating perceptual load in the auditory domain while ignored visual stimuli are presented. Conceptually the experiment is identical to that presented in the previous section. Subjects are asked to ignore an irrelevant visual motion stimulus while listening to sequentially presented single words. Perceptual load is manipulated by asking subjects to perform either a simple task requiring analysis of the physical attributes of the words, or a hard task requiring phonological analysis of the words. If attentional resources are shared between vision and audition, then Lavie’s theory and the results above lead to the prediction that increased auditory perceptual load should lead to decreased processing of the ignored visual motion stimulus. On the other hand, if attentional resources are largely modality specific, then manipulating auditory perceptual load should have little effect on visual processing.

An important consideration in this experiment was the choice of imaging technique, as the acoustic environment may potentially influence the effectiveness of auditory perceptual load manipulation. As discussed briefly in section 2.3, functional MRI is an extremely noisy environment, with the sound level in the bore of the magnet exceeding 90dB. This added background noise is attenuated somewhat by the acoustic tubephones.
Neural correlates of selective attention
used to present auditory stimuli, and sounds can be clearly and comfortably heard above
the ambient background. However the background noise introduces both an element of
auditory figure-ground segregation and increases the baseline level of perceptual load
from which any manipulation must start. This would have decreased the effective range
of any perceptual load manipulation that was introduced. For these reasons, PET was
chosed as the imaging modality of choice. PET is virtually silent and high fidelity insert
earphones can be used to deliver sounds to the subjects. Although the technique has a
lower overall spatial resolution than fMRI, the absence of ambient noise meant that a far
wider range of auditory perceptual load could be manipulated effectively.

5.7 Methods

5.7.1. Subjects and stimuli

Five subjects (4 men and 1 woman), mean age 33.6 (range 22-43) years were volunteers
who gave their informed consent to the procedure. All were right-handed and had normal
colour vision, normal hearing and normal (corrected) visual acuity. The procedures were
approved by the National Hospital for Neurology & Neurosurgery ethical committee and
by ARSAC (UK).

On each of twelve scans volunteers were presented with both visual and auditory stimuli.
The visual stimuli consisted of an optic flow field identical to that described in the first
experiment, except that it extended over the entire screen from a fixation point in the
centre. Motion perception was assessed by comparing scans where these dots moved with
scans where the dots were static This component of the display comprised four hundred
single white dots each subtending 0.1 degrees scattered randomly outside a central ellipse
in a display 17 degrees across. When the display was moving, each dot moved radially
outwards at a constant velocity of approximately 5 degrees per second. As dots left the
edge of the display new dots were added at the periphery of the central ellipse
surrounding the words to ensure the dot density of the display remained constant.
Subjects were asked to fixate, and to ignore the white dots throughout. Fixation and eye
opening was ensured by monitoring subjects’ gaze using a closed-circuit TV camera
relayed to the PET control room.
Neural correlates of selective attention

The auditory stimuli consisted of a series of spoken words. The volume of the words was chosen to be either just audible in the scanning environment, or loud and clearly audible (without being painful). The words were selected from the lists that had been previously used in the experiment presented in section 3.2 and therefore varied in both identity and the number of syllables. In the experiment, words were presented binaurally through in-ear earphones. The words lists were identical in every scan, presented in a random order. Subjects were asked to focus on these words, and during low load conditions, press a key whenever a loud word was heard. Under high load conditions, they heard the same words but were now asked to press the button whenever they heard a bisyllabic word. All used their dominant hand to respond. The relative intensity of the target words was chosen to be clearly audible so that the intensity discrimination task was of low perceptual load. It was made clear to subjects beforehand that the variation in intensity of the stimuli was sufficient to make the low load task very easy, while emphasising that they should concentrate on every word regardless of intensity during the high load task to ensure accurate performance.

Two factors were manipulated independently to produce four separate conditions in a 2x2 factorial design formally identical to that presented above in section 3.2. One factor was perceptual load (high or low); the other factor was the presence or absence of motion in the visual display.

5.7.2. Data acquisition and analysis

Each subject performed both high and low load tasks, with and without irrelevant visual motion, while undergoing PET imaging with an ECAT EXACT HR+ scanning system using the protocol described in section 2.1. Twelve scans were acquired per subject, representing three replications of the four conditions discussed above.

Data analysis used SPM98 (http://www.fil.ion.ucl.ac.uk) and followed the general plan specified in Chapter 2. The imaging time series was realigned, spatially normalised to the stereotactic space of Talairach & Tournoux and smoothed with a Gaussian kernel of 14mm full width half maximum (Friston et al., 1995a; Friston et al., 1995b; Friston et al., 1995c; Friston et al., 1996b; Talairach and Tournoux, 1988). Global activity was modelled with a subject-specific ANCOVA and local cerebral blood flow change assessed by modelling the appropriate condition-specific effects for each subject.
Neural correlates of selective attention

statistical contrast between the condition-specific effects (low load & motion - low load & no motion) - (high load & motion - high load & no motion) again represents the interaction term of interest, and was used to create an SPM(t) that was transformed into an SPM(Z) and thresholded at a Z value of 3.09 (corresponding to \( p<0.001 \) uncorrected for multiple comparisons). Masking with the contrast between motion conditions and the conditions where no visual motion occurred was used to restrict our analysis to areas activated by visual stimulation. This does not change the Z scores, but as the conjoint probability of appearing in the mask and the interaction SPM is the product of the individual probabilities, activations are reported above a threshold of \( Z>3.09 \), corresponding to \( p<0.001 \) uncorrected for multiple comparisons. Note that the masking procedure is slightly different to the first experiment, where masking with the contrast between all the visual conditions and fixation was used. The radiation dose limitations of PET mean that it was not possible to include such a low level control condition. In the main effects of load and visual motion, only areas that reach \( p<0.05 \) corrected for multiple comparisons are reported as no such masking procedure took place.

5.8 Results

5.8.1. Main effect of visual motion

Comparing the conditions where the visual display contained radially moving dots with those conditions where the dots were static provides a measure of activity evoked by the ignored visual motion irrespective of perceptual load. This comparison showed strong bilateral activation of striate and extrastriate cortex (Figure 5-5 & Table 5-4). The peak foci of activation were located in right occipital gyrus, left lingual gyrus and left inferior occipital gyrus (Table 5-4). However inspection of Figure 5-5 makes clear that the activated area was extremely large. Areas activated by visual motion spread extensively throughout occipital and extrastriate cortex to encompass the Talairach co-ordinates of the human V5 homologue (Watson et al., 1993). Comparing the conditions where the display was static with the moving display conditions revealed two foci of activation in right frontal cortex (Table 5-4). The pattern of activity in these areas may represent either activation by static dots compared to moving dots, or equally a deactivation by moving dots compared to static dots.
Two views of the left and right lateral surfaces of the T1-weighted anatomical template image in Talairach space, on which are superimposed areas where evoked activity was greater during those conditions where the visual display contained radially moving dots, compared to when the dots were static. A statistical threshold of Z=3.09 (corresponding to p<0.001, uncorrected) was used for display purposes; peaks of activation reaching statistical significance after correction for multiple comparisons are shown in Table 5-4.
Table 5-2: Main effect of visual motion

Shown in the table are loci where activity is greater during visual displays containing radial motion compared to static displays. Only the most significant peaks within each area of activation are reported in the table (p<0.05, corrected for multiple comparisons).

<table>
<thead>
<tr>
<th>Area</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R occipital gyrus</td>
<td>32</td>
<td>-92</td>
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<tr>
<td>L lingual gyrus</td>
<td>-6</td>
<td>-82</td>
<td>-12</td>
<td>7.69</td>
</tr>
<tr>
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<td>-40</td>
<td>-82</td>
<td>2</td>
<td>7.39</td>
</tr>
<tr>
<td>Decreases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R inf frontal gyrus (BA47)</td>
<td>40</td>
<td>32</td>
<td>4</td>
<td>5.56</td>
</tr>
<tr>
<td>R middle frontal gyrus (BA 6)</td>
<td>26</td>
<td>2</td>
<td>44</td>
<td>4.40</td>
</tr>
</tbody>
</table>
5.8.2. Main effect of auditory perceptual load

Areas associated with performance of the high perceptual load task were identified by comparing conditions where subjects performed the high load task with those where subjects performed the low load task, irrespective of the state of the visual display. Changes in activity in a distributed network of areas was observed. These included right dorsolateral prefrontal cortex, left inferior frontal gyrus including Broca's area, and left posterior basal temporal gyrus. The reverse contrast, comparing low load with high load, also showed several foci of activation. These were mainly situated in the left hemisphere around the supramarginal gyrus.

5.8.3. Interaction between auditory perceptual load and ignored visual motion

If resources are shared between visual and auditory modalities, then our hypothesis predicted that changing auditory perceptual load would modulate the activity produced by motion. This is represented by the interaction term in the factorial design. Three areas showed a significant interaction between auditory perceptual load and visual motion in accord with the hypothesis (Table 5-4). Only one of the areas, in right occipital gyrus, was located in visual cortex. Statistically, this interaction was extremely weak and only just above the uncorrected threshold used. There was no significant modulation of activity in areas homologous with human MT/V5 (Watson et al., 1993) even at lower statistical thresholds.
Neural correlates of selective attention

Figure 5-6: Main effect of high auditory perceptual load

Two views of the left and right lateral surfaces of the T1-weighted anatomical template image in Talairach space. Superimposed on the rendered image are areas where evoked activity was greater during those conditions where the subjects performed the high load (syllable discrimination) auditory task compared to those where the subjects performed the low load (intensity detection) auditory task. A statistical threshold of Z=3.09 (corresponding to p<0.001, uncorrected) was used for display purposes; peaks of activation reaching statistical significance after correction for multiple comparisons are shown in Table 5-4.
Neural correlates of selective attention

**Table 5-3: Main effect of perceptual load**

Effects of perceptual load. Shown in the table are loci where activity is increased (or decreased) when subjects perform the high auditory perceptual load task compared to the low perceptual load task. Only the most significant peaks within each area of activation are reported in the table (p<0.05, corrected for multiple comparisons).

<table>
<thead>
<tr>
<th>Area</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>Z score</th>
</tr>
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<tbody>
<tr>
<td>Increases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L inf temporal gyrus (BA37)</td>
<td>-56</td>
<td>-56</td>
<td>-20</td>
<td>5.38</td>
</tr>
<tr>
<td>L parahippocampal</td>
<td>10</td>
<td>-24</td>
<td>-4</td>
<td>5.27</td>
</tr>
<tr>
<td>Brainstem</td>
<td>4</td>
<td>-36</td>
<td>-20</td>
<td>5.22</td>
</tr>
<tr>
<td>Right (BA9)</td>
<td>46</td>
<td>32</td>
<td>32</td>
<td>5.25</td>
</tr>
<tr>
<td>Right insula</td>
<td>36</td>
<td>22</td>
<td>4</td>
<td>5.14</td>
</tr>
<tr>
<td>R middle frontal gyrus (BA46)</td>
<td>42</td>
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<td>16</td>
<td>5.02</td>
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<td>L middle/inf frontal gyrus (BA45/46)</td>
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<td>28</td>
<td>22</td>
<td>4.92</td>
</tr>
<tr>
<td>L middle frontal gyrus (BA8)</td>
<td>-42</td>
<td>10</td>
<td>30</td>
<td>4.56</td>
</tr>
<tr>
<td>L insula</td>
<td>-34</td>
<td>22</td>
<td>6</td>
<td>4.46</td>
</tr>
<tr>
<td>Decreases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L precentral gyrus</td>
<td>-32</td>
<td>-24</td>
<td>54</td>
<td>5.12</td>
</tr>
<tr>
<td>L supramarginal gyrus</td>
<td>-46</td>
<td>-58</td>
<td>36</td>
<td>4.73</td>
</tr>
<tr>
<td>L supramarginal gyrus</td>
<td>-48</td>
<td>-60</td>
<td>28</td>
<td>4.63</td>
</tr>
<tr>
<td>L inf temporal gyrus</td>
<td>-56</td>
<td>-22</td>
<td>-30</td>
<td>4.95</td>
</tr>
<tr>
<td>Right inf occipital gyrus</td>
<td>28</td>
<td>-94</td>
<td>2</td>
<td>4.37</td>
</tr>
</tbody>
</table>
Figure 5-7: Interaction between perceptual load and visual motion

Two views of the left and right lateral surfaces of the T1-weighted anatomical template image in Talairach space. Superimposed on this template image are areas where the difference in activity between motion and no-motion visual displays was greater under conditions of low perceptual load, in keeping with the perceptual load hypothesis. A statistical threshold of $Z=3.09$ (corresponding to $p<0.001$, uncorrected) was used for display purposes; peaks of activation reaching statistical significance after correction for multiple comparisons are shown in Table 5-4.
Neural correlates of selective attention

Table 5-4: Interaction between auditory perceptual load and visual motion

Shown in the table are loci where the difference in activity between moving and static visual displays is greater during the low perceptual load task in accordance with the perceptual load hypothesis predictions. Only the most significant peaks within each area of activation are reported in the table.

<table>
<thead>
<tr>
<th>Area</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>L hippocampal gyrus</td>
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<td>3.30</td>
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<td>R inferior frontal gyrus (BA45)</td>
<td>56</td>
<td>30</td>
<td>4</td>
<td>3.21</td>
</tr>
<tr>
<td>R occipital gyrus (BA18)</td>
<td>30</td>
<td>-98</td>
<td>4</td>
<td>3.10</td>
</tr>
</tbody>
</table>
Neural correlates of selective attention

5.9 Discussion

The findings of the present study contrast sharply with the study presented earlier in this chapter. In that study, V5 activity evoked by ignored visual motion changed as the perceptual load of the primary task changed. Here, the failure to demonstrate an interaction between motion and perceptual load suggest that the interaction between auditory perceptual load and visual motion may be negligible. The difficulty of detection of targets in the auditory modality had no discernable effect on the activity in V5 evoked by visual motion. Indeed, throughout visual cortex there was only one area, in right occipital cortex, that showed any modulation of activity, even at marginal levels of significance. However, before concluding that this study provides no evidence for shared attentional resources between vision and audition, a number of alternative explanations for these results must be considered.

First, it is possible that the study had insufficient sensitivity to detect such a modulation. In particular, if the visual motion display produced only a small increment in activity in visual cortex compared to the static display, then even a relative large relative change in this activity produced by auditory perceptual load would be small in absolute terms, and therefore difficult to detect. However inspection of the data does not support this possibility.

There was a strong increase in striate and extrastriate visual cortex activity when viewing visual motion. Comparing the response to viewing the moving visual stimulus with a static version revealed large areas of activation in striate and extrastriate cortex bilaterally. This is consistent with findings in macaque that neurons located within these cortical areas are sensitive to the motion energy contained in a moving stimulus, and with other functional imaging studies that have investigated cortical responses to moving stimuli. Thus, there is no evidence to suggest that the failure to detect modulation of V5 activity by perceptual load reflects a more general failure to evoke activity in this area by the visual stimulus alone.

A second possibility is that the manipulation of perceptual load was insufficient to modulate activity in visual cortex. Informal debriefing of the subjects confirmed that they...
Neural correlates of selective attention

felt the high load task to be considerably more difficult than the low load task. This is reflected in the behavioural results, where accuracy was close to ceiling for the low load task while being considerably worse during the high load task. The functional imaging data show strong differences between high and low load tasks in bilateral areas of frontal cortex and left posterior basal temporal gyrus. The location of these activated areas is consistent with the idea that the high load task required explicit identification of the words and phonological analysis in order to make syllable judgements. Previous neuroimaging studies have shown that left inferior frontal cortex near Broca’s area and left inferior basal temporal gyrus (BA37) are active when subjects are asked to perform semantic or phonological judgements on single words. Such a distributed system appears to be involved in the processing of word identity, as it is activated by written words, visual objects and auditory words irrespective of whether the task concerned involved associative decision, size decisions, animacy judgements, abstract words or concrete nouns. These previous findings are consistent with the present study. Under conditions of high load, subjects made syllable judgements about the auditorily presented words. This is a demanding task that mandates processing of word identity and retrieval of phonological information about each item. However in the low load task, that required judgements about the relative loudness of the words, there was no such requirement. The relative loudness of target (loud) and nontarget (quiet) words was manipulated to produce an extreme difference, so subjects had no incentive to listen to the words or process them to the level of identity. The differential activation that was observed in areas of left frontal cortex and left temporal cortex is consistent with this. Activity in left inferior frontal cortex near Broca’s area may reflect subjects internally rehearsing the sound of the word in order to make syllabic judgements. In passing it is worth noting that the bilaterally symmetric pattern of activation in inferior frontal gyrus is remarkably similar to that elicited by attention to visually presented letters that will be discussed in Chapter 6. It is therefore possible that these areas may represent a source of ‘top down’ control for the analysis of linguistic stimuli in both visual and auditory modalities, though this conclusion is speculative. Outside frontal cortex, strong modulation of sensory areas by perceptual load was seen only in left posterior basal temporal gyrus. It is noteworthy that although the task manipulation increased attentional demands in the auditory modality, no enhancement of activity in or around primary auditory cortex or auditory association areas was seen. However areas of the left inferior basal temporal gyrus (BA37) near the activation seen in the present study have consistently been associated with single word processing. Lesions to this areas in humans produce anomia. Functional imaging studies
Neural correlates of selective attention have shown activation in this area when normal subjects view and make judgements on visually presented words, and also when blind Braille readers perform similar tasks (Buchel, 1998; Buchel et al., 1998b; Fiez and Petersen, 1998; Price, 1998). The activation observed here extends these findings to auditorily presented words and supports the suggestion that this area is a multimodal sensory integration area concerned with word identity (Buchel et al., 1998b).

Apart from left inferior frontal gyrus, other areas of right inferior frontal gyrus and right dorsolateral prefrontal cortex also showed activation due to high perceptual load. Activity in right dorsolateral prefrontal cortex has previously been associated with intention and the generation of deliberate willed actions (Frith et al., 1991). In previous chapters, it has been suggested that this area may also be involved in the 'top down' control of visual and auditory attention. The present findings are also consistent with a role for this area in the control of attention, although the area activated is more lateral and ventral to the activation in Brodmann area 8 discussed in Chapter 3.

A third possibility to consider is that the visual stimulus may have been particularly difficult to ignore, and may have differed in some important respects to the one used in the previous study. In the previous experiment, single words were presented foveally with the motion stimulus being presented in the periphery. In the current study, the moving stimulus extended not just in the periphery but throughout the foveal region. Stimuli presented foveally may be particularly difficult to ignore, but there is little evidence available to objectively assess this possibility. One contrary piece of evidence is that greater inattentional blindness is seen for foveally presented distractors than for those presented parafoveally, that suggests that foveally presented stimuli do not enjoy an attentional advantage in visual processing (Mack and Rock, 1998). However, the possibility cannot be excluded that modulation of a peripherally presented motion stimulus may be seen with manipulation of auditory perceptual load.

Taken together, the strength of the main effects of visual motion (Table 5-2) and perceptual load suggests that the failure to detect a modulation of activity in V5 was not due to insufficient experimental power. Although the size of interactions, by their nature, must be smaller than main effects, the strength of the visual activations here was qualitatively comparable to or greater than that seen in the study presented earlier in the chapter. The present findings therefore suggest that the resources that are consumed by

5-137
Neural correlates of selective attention

Increasing the auditory perceptual load are not required for processing visual motion. This is consistent with the idea that attentional resources are not unitary and shared by both vision and audition, but to some extent are separated between the two modalities. Thus consumption of resources in one modality need not lead to reduced processing in the other modality. Psychophysical evidence to support this notion has come from a recent study by Duncan and colleagues (Duncan et al., 1997). They investigated the ability of subjects to detect targets occurring close together in various combinations of auditory and visual streams of rapid sequentially presented letters. When asked to attend to two streams in the same modality (either both auditory or both visual), identification of a target led to a transient reduction in the ability to identify a second target presented within a few hundred milliseconds of the first. This reduction in the ability to identify a second target is known as the ‘attentional blink’. Critically, when subjects were asked to attend to visual and auditory streams simultaneously, they were easily able to identify two target and no attentional blink occurred. The authors concluded that attentional resources were restricted within a single modality, leading to the attentional blink effect, but not between modalities. Their findings are supported by previous suggestions that searching for a target over two inputs in different modalities is more efficient than searching over two inputs in the same modality (Treisman and Davies, 1973). Similarly, there is little difference between focused and divided attention when inputs are presented from different modalities (Lindsay et al., 1968; Massaro and Warner, 1977). In the present study, the visual stimulus was always irrelevant to the task performed by the subjects, and there was no requirement to detect targets in the visual domain. Despite this, subjects were unable to ignore the visual information and brain activity was evoked relating to the presence of visual motion, regardless of perceptual load. These findings are consistent with the behavioural studies if attentional capacity is restricted within but not between modalities.

In Section 3.4 data from an experiment was presented where visual and auditory streams of information were presented concurrently, and subjects asked to attend to one while ignoring the other. Strong modulatory effects were seen in visual and auditory cortex when subjects attended to the appropriate modality. Such strong attentional effects are not inconsistent with the present findings that indicate little influence of auditory perceptual load on visual processing. The previous study measured primarily the enhancement due to the active direction of attention to a modality; changing the attended modality changed activity in the appropriate primary sensory cortex. However in the present work the effect
Neural correlates of selective attention

of an ignored stimulus on modality-specific cortex is examined. The visual stimulus was always to be ignored and never task relevant. In other words, there is a clear distinction between the potential enhancement of processing produced by attending to a given stimulus or modality, and the degree to which unattended and ignored stimuli are nevertheless processed. Consistent with this, the results presented previously in section 3.4 show that even when stimuli in a particular modality are ignored, there is a correlation between their rate of presentation and evoked changes in cerebral blood flow. This indicates that unattended stimuli were processed to some extent, although this was not the primary focus of the study. In principle, the processing of attended and ignored stimuli are potentially independent though in practice high levels of attentional enhancement are associated with relatively low levels of unattended stimulus processing. The issue of whether attenuated unattended stimuli can nevertheless receive further processing is taken up further in the following chapter.

Although the behavioural studies reviewed above indicate that there is previous evidence to support the idea that perceptual resources are restricted within but not between modalities, there are also a considerable number of studies that show strong crossmodal links between audition and vision. One common example is the ventriloquism effect, where a ventriloquist's voice appears to emanate from their dummy despite the sound actually coming from a different spatial location. Similarly a series of studies by Spence and Driver (Driver and Spence, 1998a; Driver and Spence, 1998b) have shown that visual stimuli can interfere with auditory and tactile judgements if they are presented in the same spatial location. In these studies, spatial location appears to be the key determinant of whether crossmodal interference effects takes place; as the spatial separation between target and distractor increases, so does subjects’ ability to ignore the distractor. In the present study the visual stimulus is presented at a location clearly distinct from the location of the sounds to which the subject is asked to attend. The sounds, presented through insert earphones, appear at a virtual location within the head while the computer monitor on which the visual stimulus is presented is mounted in front of and above the subject. Similarly, in the study conducted by Duncan (Duncan et al., 1997), although explicit information is not given about the spatial location of auditory and visual stimuli it seems reasonable to presume that they are spatially separate. Such a spatial separation is potentially challenging for the Duncan et al study. The observations of Spence and Driver (Spence and Driver, 1996; Spence and Driver, 1997) suggest that subjects’ ability to detect targets in both auditory and visual modalities simultaneously may decline as the
Neural correlates of selective attention

spatial separation of auditory and visual streams decrease. If spatial location is a key
determinant of crossmodal interference, then such interference should increase as the
spatial separation of auditory and visual streams decreases. The conclusion that
attentional capacity is restricted within but not between modalities may therefore depend
heavily on the spatial separation of the two modality specific streams. In the present study
spatial separation was not explicitly manipulated, so no data is available that bears on this
question. However the predictions derived from the studies of crossmodal spatial
attention would be quite different in the case of the present study. Subjects are always
asked to ignore the visual stimulus, and the data of Spence and colleagues indicates that
ignoring a stimulus in another modality becomes more difficult as stimuli are made
spatially coincident. So paradoxically the situation in the present experiment, with spatial
separation between the to-be-attended and to-be-ignored streams, should enhance the
ability of subjects to ignore the visual stimulus. Despite this, subjects were unable to
ignore the stimulus even under conditions of high perceptual load, and brain activity was
evoked that reflects the visual motion of the display.

5.10 General conclusions

The two studies presented in this chapter indicate that the effect of different tasks on the
processing of ignored stimuli differs, depending on the modality of task and distractor.
The first experiment illustrates that concurrent processing within the visual modality has
strong effects on other processing in the same modality. Subjects’ ability to ignore a
visual stimulus was strongly dependent on task difficulty of an unrelated task, indicating
an important role for the mediating construct of perceptual load in determining selective
perception. The theme of how perceptual load effects might be mediated in the visual
system is taken up further in Chapter 7. The second experiment presented in this chapter
explored the crossmodal effects of varying auditory perceptual load on visual processing,
and reached a quite different conclusion. Although strong effects of perceptual load and
visual processing were seen, there was little interaction between the two. Although there
are many interesting aspects of these findings that warrant further investigation, they
suggest that attentional capacity may be restricted within but not between modalities.
Chapter 6  Inattentional blindness for words

The evidence presented in the previous chapter suggests that the processing of unattended visual stimuli is neither mandatory nor under voluntary control. On the one hand, when subjects perform a difficult concurrent visual task, ignored visual stimuli evoke little activity suggesting that processing of such stimuli is not obligatory. On the other hand, when subjects are engaged in an easy concurrent task, extensive processing of ignored visual stimuli takes place despite instructing the subjects to ignore such information. In the context of Lavie's theoretical position (Lavie, 1995) these data suggest that the degree to which ignored visual stimuli evoke activity in extrastriate cortex depends on the perceptual load of the primary task that subjects are engaged in. This is an important finding in the light of the longstanding debate in the psychology of attention between proponents of 'early' and 'late' selection. According to the former view, unattended stimuli undergo little processing other than a rudimentary analysis of physical attributes. However proponents of 'late' selection argue that not only are the physical attributes of an unattended stimulus processed, but also its identity or semantic associations. Selection by attention takes place only after perception has occurred.

Lavie's theory and the data presented previously suggest a resolution to this debate, with perceptual load as a mediating construct. Under conditions of low perceptual load, unattended stimuli undergo more or less extensive processing and selection is 'late'. However under conditions of high perceptual load, unattended stimuli are little processed other than an analysis of physical attributes. Although the data presented in the previous chapter are consistent with such an account, they are not conclusive for a number of reasons. The most important of these reasons is that the psychological accounts of early and late selection are couched in terms of information processing models, where stimuli are analysed initially in terms of their physical attributes before they evoke semantic associations related to their identity. Early and late selection models make different predictions about the stage of processing that unattended stimuli should reach. However the physiological experiments presented in the previous chapter did not use a visual stimulus that was 'meaningful' in the sense it evoked semantic associations. Radially moving dots carry no identity distinct from their physical attributes. It is therefore difficult to conclude from the data presented which stage of information processing is affected by attention without using stimuli that evoke semantic associations. Furthermore
Neural correlates of selective attention

suppression of unattended stimulus processing was seen at multiple locations, making it an open question as to whether other areas concerned with stimulus identity show such suppression.

These difficulties are shared with many other experiments that have studied the physiological effects of attention e.g. (Corbetta et al., 1991a; Corbetta et al., 1991b; Moran and Desimone, 1985; O'Craven et al., 1997; Treue and Maunsell, 1996). Such studies have typically examined responses to meaningless abstract stimuli such as patches of colour, gratings or moving dots. As these stimuli have no identity or semantic associations that is distinct from their physical attributes, it is therefore difficult from the physiological findings to establish the stage to which unattended stimuli are processed (in information processing terms). These studies have typically shown modulation of responses evoked by visual stimuli occurring at multiple levels of striate and extrastriate cortex, often beginning very early in time after the stimulus is presented (Hillyard et al., 1995). However, demonstrating early modulation of sensory responses is not sufficient to resolve the issue. First, the mapping between information processing stages and anatomical location within the visual system is unclear. More importantly, if responses to unattended stimuli are simply attenuated rather than extinguished, such an attenuated response may still propagate through the visual system and receive further processing. The question of whether unattended stimuli evoke activity related to their identity, though a central issue in the psychology of attention, is therefore not settled.

6.1 Introduction

In this chapter cortical responses to unattended stimuli that have both physical attributes and a distinct identity or meaning are investigated. Lavie’s theory makes the strong prediction that under conditions of high perceptual load, processing of stimulus identity will be suppressed although a rudimentary analysis of the physical attributes may take place. This prediction is tested using words as visual stimuli.

Words are a clear example of visual stimuli in which the identity of the stimulus can be dissociated from the physical attributes of their component letters. Although individual letters can be combined in many different ways, only certain combinations produce words that have semantic associations and represent some object or concept in the world. Moreover the relationship between signifier and signified is arbitrary and not determined
Neural correlates of selective attention

by the physical attributes of the word but fixed by custom and convention. On theoretical and empirical grounds the processing of single letters has been thought to be logically prior to, but distinct from, the analysis of meaning or semantic associations. This dissociation has been extensively investigated recently with functional imaging studies (for reviews see (Fiez and Petersen, 1998; Price, 1998)). Word perception has been compared with control situations where subjects view consonant letter strings or ‘false font’ words where the stimuli share many of the physical attributes of words, but do not evoke semantic or phonological associations. Typically such comparisons reveal differential activity in frontal, parietal and temporal areas of the left hemisphere that is thought to reflect semantic and phonological processing of these words. Strong claims have been made that such activity is evoked by the mere presentation of a single word, irrespective of the context. For example, Price and colleagues (Price et al., 1996b) studied the implicit processing of written words by asking subjects to perform an unrelated task (identify the presence of an ascender in the letter string) on visually presented letter strings and words. Despite the task being unrelated to the semantic content of the letter strings or words, the comparison of words and letter strings revealed activation in areas previously associated with semantic processing of words. Their conclusion was that extensive implicit processing of words occurs even when this is irrelevant to the task at hand, and this involves classical language areas.

The activation of classical language areas outside visual cortex by single words despite performance of a concurrent task for which the semantic associations of the words are irrelevant is in keeping with the widespread assumption that word perception is effortless and automatic. The Stroop effect (Stroop, 1935), discussed briefly in chapter 4, has persistently been cited as a good example of such an effect (MacLeod, 1991). Subjects attempt to name the ink colour of each word in a list of words. When the words are colour names that conflict with the ink colour, then subjects name or respond to the ink colour slower than if the word was a neutral (non colour-name) word. This is thought to reflect automatic processing of the word identity, irrespective of subjects’ wishes, producing semantic interference with colour naming. On this account, the Stroop task represents a failure of attention, because word perception is automatic.

Words are therefore a good example of stimuli whose physical attributes can be dissociated from their identity, and whose perception appears to be automatic. However Lavie’s theory, and the evidence presented in the previous chapter, predicts that word
Neural correlates of selective attention

perception should not be automatic and that processing of word identity should be subject to attention. A crucial question for theories of early and late selection is not only the degree to which processing of word identity may be suppressed when attention is not available, but whether it occurs at all. One source of evidence about the processing of the identity of pictorial and word stimuli comes from the work of Rock and colleagues (Mack and Rock, 1998). They presented unattended meaningful outline drawings in situations where naive subjects were engaged in a demanding task and did not expect any other stimuli to be presented. Surprisingly, the unexpected presentation of an extraneous visual stimulus frequently went undetected by the subject (Rock and Gutman, 1981; Rock et al., 1992). When attention was directed away from the fovea, even a foveally presented suprathreshold visual stimulus went undetected as much as 70% of the time (Mack and Rock, 1998). Rock suggested that these results showed that the availability of attention is required for the processing of stimulus identity (and subsequent awareness). However this account can be challenged on a number of grounds. Most importantly, these experiments relied on a retrospective assessment of awareness of stimulus identity, through testing memory for the unexpected event. It may be wrong to assume that amnesia some time after a stimulus is presented reflects an absence of brain activity or processing at the time of presentation. As depth of processing strongly affects subsequent memory recall, it is possible that subjects perceive the unattended stimuli but fail to remember them. Thus, 'inattentional blindness' may be in fact a post-perceptual 'inattentional amnesia'. To decide between these two possibilities requires a direct measure of brain activity due to an unattended stimulus. In this chapter measurements of brain activity are combined with subsequent evaluation of memory for ignored stimuli in investigating the processing of word identity under conditions of inattention. The results suggest not only that areas outside extrastriate cortex involved in processing word identity are strongly modulated by the availability of attention, but also that activity related to word identity in these areas is absent under conditions of inattention.

6.2 Methods

Visual stimuli were used that consisted of overlapping line drawings and short non-word consonant letter strings, presented rapidly and sequentially at fixation. Attention was directed to either picture or letter streams while the experimenter surreptitiously introduced words into the letter stream. Thus perception of words compared to perception of non-word consonant letters strings could be compared while attention was directed to
Neural correlates of selective attention

either the letter stream or the picture stream. Memory for the unattended words was assessed by a surprise recognition test after scanning, while brain activity evoked by unattended words was measured with fMRI.

6.2.1. Subjects and stimuli

Six subjects (2 men and 4 women; mean age 25.3 years, range 23-29y) were volunteers who gave their informed consent to the procedure. All were right-handed and had normal colour vision and normal (corrected) visual acuity. The procedure was approved by the local ethical committee.

Subjects viewed stimuli while lying supine in the scanner using an LCD projector and projection box mounted above the head coil. A display containing an overlapping picture (coloured red) and letter string (coloured green) was presented every 500ms for 250ms. Pictures were presented as an outline drawing from the Snodgrass picture set (Snodgrass and Vanderwart, 1980) and were rotated either 15 degrees clockwise or counterclockwise from the veridical position to increase task difficulty. Overlapping letter strings were comprised either of five consonant letters, or a five letter concrete noun. Both letter strings and pictures were centred on the natural fixation point at the centre of the display. The diameter of the whole composite stimulus subtended approximately 5 degrees of visual angle.

Subjects were asked to perform a repetition detection task on either the picture stream or the letter stream. They were asked to indicate with a single button press when items were repeated immediately in that stream. During scanning this task was performed for periods of 28 seconds, alternating with rest periods of equal duration in which the subject fixated centrally and no stimuli were presented. During scanning, a speeded button press response was required and auditory feedback was given (correct/incorrect/time-out).

Subjects were not informed beforehand that during half the conditions presented, words would be introduced into the letter stream. Words were introduced at a proportion of 50%, with the first 8 trials of any single condition always containing 100% consonant letter strings, in order to disguise the experimental manipulation during an extended scanning period. Words were drawn from three lists (attended/unattended/foils) that were balanced for word frequency, imageability and concreteness and counterbalanced across
Neural correlates of selective attention

subjects. During scanning words were presented only from the attended & unattended lists. The subjects saw each attended word as a repetition target once during the duration of the experiment. At the conclusion of scanning, subjects remained in the scanner and were informed that a surprise recognition memory test followed. Single words from all three lists (attended, unattended and never seen foils) were presented sequentially at fixation. Subjects were asked to indicate with a button press whether they thought that each word had been presented during the preceding scanning session.

Two factors are manipulated independently in this experiment: the direction of attention (either to the letter stream, or the picture stream), and the presence or absence of words in the letter stream. In all conditions the displays are physically identical and viewed in the same way.

6.2.2. Data acquisition and analysis

A Siemens 2T Vision system was used (Chapter 2) to acquire 32 slice T2* BOLD weighted volumes (TR 2.8s; slice thickness 3mm; in-plane resolution 3x3mm). Acquisition took place in four runs of 80 image volumes; the first 8 volumes of each run were discarded to allow for T1 equilibration effects, yielding a total of 288 volumes per subject. During each run, active conditions alternated with rest every 28 seconds (10 TR). Data analysis used SPM99 and followed the general plan outlined in Section 2.4. Separate box-car waveforms were generated for each subject and condition, convolved with a canonical haemodynamic response and used as regressors in a multiple linear regression on the imaging data. A high pass filter of 512 seconds cut-off was used for each subject.

6.3 Results

6.3.1. Recognition memory

Subjects reported remembering on average \( 70.5\% \) of the attended words (SD 11.6%), \( 24.7\% \) of the unattended words (SD 18.3%) and \( 25.0\% \) of the (never seen) foils (SD 15.1%). A repeated measures ANOVA showed a highly significant effect of category (\( F(2,10) = 23.496, p=0.0002 \)) that posthoc tests showed was entirely due to the difference between attended and unattended words (\( p<0.0001 \)). The difference between responses to unattended words and never-seen foils was not significantly different (\( p=0.97 \)).
Neural correlates of selective attention

These results (Figure 6-1) indicate that subjects remembered almost all the attended words. However when they were attending to the pictures, even though the words were presented foveally, their memory did not differ significantly from chance.

6.3.2. Imaging

6.3.2.1. Main effect of attention to pictures

Attending to the picture (red) stream modulated activity in widespread areas of extrastriate cortex extending down the fusiform gyrus into the temporal lobe (Table 6-1 & Figure 6-2). There was a slight asymmetry, with greater activation seen in the right hemisphere compared to the left hemisphere. Notably, all the significant activations were located posterior to the anterior commissure and no frontal activation was seen.

6.3.2.2. Main effect of attention to letters

Attending to the letter (green) stream modulated activity in a more restricted set of visual and non-visual areas. Only one area in visual cortex proper showed a change in activity, in the left inferior occipital gyrus. Outside visual cortex, the most striking activation was seen in bilaterally symmetric areas of right and left inferior frontal gyrus, together with an area of right middle frontal gyrus. The left cerebellum was also activated and an area of the right anterior cingulate trended towards significance.

6.3.2.3. Simple main effect of word identity under attention to letters

When attention was directed to the letter stream, the comparison of activity when words were presented compared to when only letter strings were presented provides a measure of activation specific to word identity when attention is available. The areas significantly activated in this comparison were almost exclusively located in the left hemisphere and include left inferior frontal, left posterior basal temporal (BA37) and left parietal cortex. Significant activation was seen in only one area in the right hemisphere in a location in posterior parietal cortex homologous to a similar activation on the left.
6.3.2.4. Interaction between word identity and attention

The modulation of processing specific to word identity by attention is represented by the interaction term in this design. A number of areas showed a greater difference between the conditions where words were presented, compared to letters alone, when attention was directed to the letter stream (compared to the picture stream). These areas, shown in Figure 6-3, extensively overlapped those areas that showed a simple main effect of word identity under attention to letters. In other words, those areas that showed activity related to word identity when attention was directed to the letter stream, also showed a reduction in that identity-specific activity when attention was directed away from the letter stream toward the pictures.

6.3.2.5. Simple main effect of word identity under attention to pictures

Given that all the areas that show a simple main effect of word identity under attention to letters also show an interaction, it is of interest to determine whether these areas show any differential activity comparing words and letter strings when attention is directed towards the picture stream. The SPM[Z] was constructed that reflected this simple main effect, masked by the simple main effect of word identity under attention to letters (at a lower statistical threshold). This masking procedure does not alter the Z scores or p values for the comparison, but ensures that the analysis is restricted to that subset of voxels activated in the mask. This ensures that a difference in activity between words and letters when attention is directed to the picture stream is only sought in those voxels that show an effect when attention is directed toward the letter stream. Spurious activations that only occur in one of the two comparisons are not recorded.

Remarkably, no cortical areas showed a significant difference between words and letters when attention was directed toward the pictures. This analysis was repeated at a lower statistical threshold of $Z > 3.09$ that corresponds to an uncorrected $p < 0.001$, yet still no areas showed a significant difference between words and letters under attention to pictures. Lowering the statistical threshold still further in a group analysis runs an unacceptable risk of false positives, so the analysis was repeated in individual subjects. This allows evaluation of inter-subject differences that the group analysis may have obscured inadvertently. However at the higher ($p < 0.05$ corrected) threshold, none of the
Neural correlates of selective attention

subjects showed activation related to word identity under attention to pictures. At the lower threshold of $Z > 3.09$ ($p < 0.001$ uncorrected), one of the six subjects showed an activation in an isolated voxel in right temporal cortex that was marginally significant. The important of this finding is unclear as it lies outside classical visual and language areas.
Figure 6-1: Recognition Memory for words

Percent correct recognition judgements for attended words (1), unattended words (2) and never seen foils (3). Values are averaged over the six subjects; error bars represent one standard deviation.
Neural correlates of selective attention

Table 6-1 Effects of directing attention to picture or letter stream.

Shown in the table are loci where activity is greater during attention to pictures (compared with letters) or during attention to letters (compared to pictures). Only the most significant peaks within each area of activation are reported in the table (p<0.05, corrected for multiple comparisons).

<table>
<thead>
<tr>
<th>Area</th>
<th>Talairach coordinates</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention to pictures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R fusiform</td>
<td>24</td>
<td>-66</td>
</tr>
<tr>
<td>R fusiform.inf temp</td>
<td>45</td>
<td>-60</td>
</tr>
<tr>
<td>R lingual</td>
<td>12</td>
<td>-75</td>
</tr>
<tr>
<td>L fusiform/inf temp</td>
<td>-33</td>
<td>-30</td>
</tr>
<tr>
<td>L fusiform</td>
<td>-30</td>
<td>-45</td>
</tr>
<tr>
<td>L middle temporal</td>
<td>-48</td>
<td>-69</td>
</tr>
<tr>
<td>L superior parietal</td>
<td>-21</td>
<td>-54</td>
</tr>
<tr>
<td>L inf parietal</td>
<td>-45</td>
<td>-24</td>
</tr>
<tr>
<td>Attention to letters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L inferior frontal</td>
<td>-36</td>
<td>21</td>
</tr>
<tr>
<td>R inferior frontal</td>
<td>48</td>
<td>24</td>
</tr>
<tr>
<td>L inferior occipital</td>
<td>-33</td>
<td>-93</td>
</tr>
<tr>
<td>L cerebellum</td>
<td>-12</td>
<td>-81</td>
</tr>
<tr>
<td>R middle frontal</td>
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<td>54</td>
</tr>
<tr>
<td>Anterior cingulate</td>
<td>3</td>
<td>36</td>
</tr>
</tbody>
</table>

6-151
Figure 6-2: Attention to pictures or words
Three views of the ventral and lateral surfaces of the T1-weighted anatomical template image in Talairach space, on which are superimposed areas where evoked activity was greater during attention to the picture stream (red) or the letter stream (green). A statistical threshold of $Z=3.09$ (corresponding to $p<0.001$, uncorrected) was used for display purposes; peaks of activation reaching statistical significance after correction for multiple comparisons are listed in Table 6-1.
Neural correlates of selective attention

Table 6-2. Effects of word identity

(Left columns) Tabulated are those loci where activity when attention was restricted to the letter stream was greater during word presentation (compared to non-word letter strings). Only the most significant peaks within each area of activation are reported in the table (p<0.05, corrected unless otherwise specified). (Right columns) Shown are those loci (p<0.05, corrected) where activity due to words (compared to non-word letter strings) was greater when attention was directed to the letter stream compared with attention to the picture stream.

<table>
<thead>
<tr>
<th>Area</th>
<th>Simple main effect</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Talairach</td>
<td>Z score</td>
</tr>
<tr>
<td>L inferior frontal</td>
<td>-39 6 27 4.61</td>
<td>-39 6 27 4.32 (p=0.141)</td>
</tr>
<tr>
<td>L post parietal</td>
<td>-33 -33 57 4.56</td>
<td></td>
</tr>
<tr>
<td>L med parietal</td>
<td>-27 -72 33 4.44 (p=0.089)</td>
<td></td>
</tr>
<tr>
<td>R parietal</td>
<td>24 -48 57 4.34 (p=0.131)</td>
<td>36 -57 36 5.20</td>
</tr>
</tbody>
</table>
Figure 6-3: Activation by word identity and modulation by attention

Effects of word identity. (A) Four views of a T1-weighted anatomical template in Talairach space, on which are superimposed areas where words produced significant activation when attention was directed to the letter stream (simple main effect) (B) Four similar views of the T1 template on which are superimposed areas where there was a significant interaction between word identity and the direction of attention (effect of words greater when attention directed towards the letter stream).
Figure 6-4: Time-course of evoked brain activity

(A) Timecourse plots of the area in left inferior frontal gyrus shown in Figure 6-3. In the left panel are plotted evoked BOLD contrast as a function of time when attention is directed to the picture stream for both words (green) and non-words (red). The right panel illustrates the same conditions during attention to letters (B) Identical plots with the same colour key are displayed for the left posterior basal temporal gyrus (BA37) area illustrated in Figure 6-3.
Neural correlates of selective attention

6.4 Discussion

Attention to pictures changed activity in widespread areas of posterior occipital cortex, extending through striate and extrastriate areas down into the fusiform gyrus (Figure 6-2). The pattern of modulation was roughly bilaterally symmetric, with a slight right-sided predominance. The areas that changed their activity have been previously associated with the processing of different aspects of visual stimuli. In contrast to the widespread modulation when attention was directed toward pictures, attention to the letter stream modulated more circumscribed areas of cortex. The predominant posterior area of modulation was located in the left lingual/fusiform gyrus close to but not contiguous with areas that showed a modulatory effect of attention to pictures. The location of this area is identical to an area described in a previous study that investigated the neural correlates of attention to global and local aspects of a figure. When subjects reported the local aspect of a hierarchical Navon figure made from small letters, activity in this area was enhanced compared to when attention was directed to the global aspect of the Navon figure. The authors of that study suggested that activation in this area was associated with attention to local aspects of a figure. However this interpretation became less tenable when the same authors investigated hierarchical Navon figures made from small objects, and found that a similar area in the opposite hemisphere was modulated by attention to local aspects of the Navon figure. The present findings suggest a natural interpretation of these apparently discrepant findings is that this area is concerned not with attention to local aspects of a figure, but simply associated with attention to printed letters rather than figures. This hypothesis accounts for why, when Navon figures are made from local components other than letters, this area does not show differential activity when comparing locally and globally directed attention. However this does not clearly account for why this area is not active when attention is directed to the global aspect of Navon figures that (globally) represent letters. It may be that global Navon figures made out of letters are a highly unusual stimulus that involves processing in extrastriate areas away from this cortical area. Such an account is highly speculative, as this study was not designed to investigate such a hypothesis.

In addition to enhancing activity in extrastriate cortex, it is also notable that attention to the letter stream enhanced activity in bilaterally symmetric areas of prefrontal cortex, in left and right inferior frontal gyrus. These areas might potentially be the source of ‘top-
Neural correlates of selective attention

down’ signals to more posterior areas, directing attention to the letter stream. It is interesting to compare these areas with the very similar pattern of bilateral frontal activation evoked by the manipulation of auditory perceptual load in the previous chapter (Figure 5-6). In that study the stimuli were also single words, but presented auditorily rather than visually. These areas in frontal cortex may therefore be involved in the direction of attention to words irrespective of modality. However, it is also possible that these areas represent a site rather than source of attentional modulation. The area of inferior frontal cortex activated on the left is close to Broca’s area. Although classically involved in speech production, this area has been considered by some authors as involved in word perception. If this is the case, then modulation of this area by attention to the letter stream reflects a modulation of sensory processing rather than a source of attentional modulation. However this account may be less likely as the involvement of Broca’s area in word perception is often thought to involve explicit internal rehearsal of the individual words. The speed of presentation of items in the current study, together with the mixture of words and consonant letter strings, makes this an extremely unlikely and difficult strategy for the subjects to engage in.

Changing the direction of attention primarily modulated activity in extrastriate cortex. The effects of this modulation on sensory processing can be investigated by comparing the activity evoked by the other experimental manipulation, the introduction of words into the letter stream. Comparing words and consonant letter strings isolates differential activity that is related not to the physical attributes of the stimuli (that are matched) but to the specific identity or meaning and phonological associations of the words. When attention was directed to the letter stream, greater activity was seen when words were presented compared to non-word consonant letter strings in a network of predominantly left hemisphere areas (Figure 6-3). Robust activation due to words was seen in left prefrontal, left parietal and left posterior basal temporal cortex (BA37). The location of these areas is highly consistent with previous lesion and functional imaging studies of higher order linguistic processing. The activation in left posterior basal temporal cortex (BA37) was located in the ventral processing pathway and strategically situated between the visual cortex and more anterior temporal cortex. While more posterior occipital regions are activated equally by visual words and non-words, the more anterior (temporal) regions responded differentially to words. A number of studies have shown activation in this area during both implicit and explicit reading tasks. A recent neuroimaging study (Buchel et al., 1998b) showed that words (compared to letter strings)
Neural correlates of selective attention

specifically activated BA37 in both normally sighted and blind Braille readers, suggesting that this area is an important association area that integrates converging inputs from many brain regions. The data presented here extend these earlier findings by showing that the activity in BA37 related to word identity is critically dependent on attention. An interaction between attention and word-specific activity is also seen in multiple areas of left prefrontal cortex. Neuroimaging studies have found that left prefrontal cortex including Brodmann's areas 44, 45, 46 and 47, responds most strongly during semantic tasks (Fiez and Petersen, 1998). The area around the left frontal operculum, in concert with BA37 appears to be involved in phonological retrieval (Price, 1998).

Taken together, these findings suggest that when words are presented in the attended stream, activation of a circumscribed left hemisphere language network takes place. Activation of left hemisphere areas by word identity has been well described previously, and it was assumed on the basis of some studies that their activity was obligatory whenever a word was presented. However in the present study, when attention is directed away from the letter stream toward the picture stream, a strong modulatory interaction is seen between attention and activity evoked by words (compared to non-word consonant letter streams). The cortical areas that show this modulatory interaction are coextensive with the same classical language areas. These findings show that word specific processing in these areas is not independent of attention. Directing attention away from the words in a demanding task resulted in a diminution of the activity evoked by words. The failure of previous studies to demonstrate such a strong modulation may be due to the care taken in the present study to establish a particularly demanding attentional task. If any spare attentional capacity can be used to process unattended stimuli, then a failure to demonstrate attentional modulation of sensory processing may simply be due to the availability of such resources.

Not only did the activity evoked by word presentation change when attention was directed from the letter to the picture stream, but also subjects’ ability to remember the words changed dramatically (Figure 6-1). All subjects showed a striking difference in their ability to remember attended and unattended words, despite the stimuli being physically identical and presented in a clearly visible way on the most sensitive part of the retina, the fovea. There was no evidence that subjects were able to remember any of the unattended words, as the performance for these words was no different to subjects’ tendency to (falsely) identify foil stimuli as having been previously presented. To ensure
Neural correlates of selective attention

these results were not produced by some unique aspect of the scanning environment (such as the additional difficulty created by a noisy and claustrophobic environment), the experiment was repeated on a new group of subjects outside the scanner. An identical mnemonic dissociation was obtained (data not shown). These results show that when attention is engaged by a sufficiently demanding task, there is inattentional amnesia for other stimuli. Such an effect cannot be mediated by the differential allocation of spatial attention, as the pictures and letters to which the subjects attend are presented in the same spatial location. These findings therefore reflect a non-spatial effect of attention, and extend earlier work showing inattentional amnesia for meaningful figure drawings to another much more salient class of stimulus.

Directing attention to words produced both better explicit memory and greater word-specific activation in cortical language areas. This strongly suggests that the failure to remember unattended words is due to a perceptual deficit at the time of word presentation, rather than a post-perceptual loss of information about word identity. The crucial test of such a perceptual hypothesis is whether words produce any differential activation when attention is directed toward the letter stream. If the response to words is simply attenuated under conditions of inattention, then it is possible that subjects difficulty in remembering such words arises from a difficult in memory encoding or recall rather than from a perceptual difficulty. However, the results were clear. Under conditions of inattention, there was no detectable difference in activation by words compared to letter strings when attention was directed to the picture stream (Figure 6-4). Although left hemisphere language areas were strongly activated by words when attention was directed to the letter stream, this activation was abolished when attention was no longer available. Even in individual subjects, and at an uncorrected statistical threshold (see Results) no consistent activation was observed within left hemisphere language areas. While the failure to observe a differential activation cannot be taken as evidence that a differential activation does not exist (as this would require affirmation of the null hypothesis), the present results suggest that any difference that may exist must be extremely small. The presence of word specific activation under conditions of attention shows that fMRI is sufficiently powerful to detect such activation. Under conditions of inattention, the present findings therefore do not provide evidence to suggest that words produce cortical activation related to their identity. It is important to emphasise that this result is not due to some subterfuge in the presentation of the words. Each word was presented clearly for 150ms to the fovea of the subjects. Despite this, the words failed to
Neural correlates of selective attention evoke activity related to their identity (although of course they may still evoke activity related to their physical attributes; the activity specifically evoked by the component letters was not assessed in this study). These findings strongly suggest that the absence of word-specific activation under conditions of inattention is sufficient to account for subjects' amnesia. The subjects therefore suffered inattentional blindness due to a failure of perception of the unattended stimulus at the time it was presented.

6.5 Conclusion

These results show that subjects are blind to the identity of words that are presented under conditions of inattention. This work does not address the question of whether subjects are also blind to the mere presence of visual stimuli. Here the comparison was between words and letter strings that differ only in meaning, not in physical characteristics. Informal debriefing of the subjects suggested that they were blind, not to the presence of two streams of visual stimuli, but to the identity of individual items within the unattended stream. It is also important to realise that these findings do not preclude the possibility that under other experimental conditions, unattended stimuli might be perceived. The observations presented here show that word perception is strongly modulated by attention, which suggests in turn that if attention is not fully engaged elsewhere then greater incidental processing of unattended words will take place compared to when attention is fully engaged. The success of the method used here most probably relates to the taxing demands of the task that exhaust available attentional resources and establish conditions of full inattention. The importance of these findings therefore lies in establishing that under such conditions there as specific aspects of stimulus processing that are abolished, and therefore wholly dependent on attention. Even looking directly at a highly salient, familiar stimulus such as a single word does not evoke activity related to its identity when attention is not available. Diverting attention therefore fully eliminates the cognitive operation of establishing word identity.
Chapter 7  General discussion

The studies presented in this thesis all address, directly or indirectly, the issue of whether stimuli away from the focus of attention nevertheless produce activity in the brain. The underlying supposition is that functional imaging, is well placed as a technique with which to explore such issues. Other techniques, whether behavioural or electrophysiological, can provide useful information about these issues. However, the ability to acquire whole-brain images at reasonable spatial and temporal resolution in human subjects provides an unprecedented ability to visualise brain structures involved in processed unattended stimuli. Three different ways of quantifying unattended processing have been presented in this thesis. In the first experimental chapter, identifying stimulus-related processing by varying stimulus presentation rate allowed the disambiguation of attended and unattended stimulus processing. In the second experimental chapter, by producing situations where unattended stimulus processing interfered (by negative priming) with attended stimulus processing, the neural correlates of a particular psychological phenomenon, negative priming, were elucidated. This technique involves taking a psychological paradigm and scanning subjects while performing that paradigm. However the resulting imaging data shows that reaction time data alone do not necessarily capture the changes in brain activity that reflect performance of such a task: the predominance of time-related changes in activation. Finally, in the last two experimental chapters, ignored stimuli are used that activate clearly circumscribed cortical areas that are anatomically well described (V5/MT and the classical language areas, respectively). The presence of activity in such areas can then be used to infer processing of ignored stimuli.

The purpose of undertaking such studies of ignored stimulus processing has been in order to make inferences about attentional mechanisms in the human brain. In this the approach differs from some previous work in that the intention is not simply to identify the anatomical correlates of some hypothesised attentional mechanism. Rather, the claims made here are most often functional ones: for example, about constraints on visual processing leading to selective processing such as perceptual load, and about the way in which attention modulates processing in extrastriate cortex. The intention is to emphasise how functional imaging techniques can be used to address questions about attentional processes as well as identifying anatomical structures associated with attentional function.
Neural correlates of selective attention

The general discussion is divided into three parts. In the first section the possible neuronal correlates of attentional modulation in extrastriate cortex are discussed, with reference to the difficulties in relating data from single cells in monkeys to population activity in humans. In the second section the question of what represents the neural correlates of perceptual load is addressed. Finally the question of the relationship between attention and visual awareness is revisited and some speculative comments offered. The discussion will refer primarily to the studies presented previously in the experimental chapters of the thesis, but will also make reference where appropriate to some of the supporting material presented as part of this thesis and bound in following the principal chapters.

7.1 Relating single cell studies and population measures

Whereas single cell neurophysiology records extracellularly from one of a small number of cells within a hypercolumn, contemporary functional imaging has a typical spatial resolution of about 5mm (although claims have been made at high field that individual ocular dominance columns can be resolved (Menon et al., 1997)). Given a typical packing density in cortex of $1 \times 10^5$ neurons per cubic millimetre, the $3 \times 3 \times 3$mm cubic voxels recorded in the fMRI experiments contain around $27 \times 10^5$ neurons (Wandell, 1995). In other words, in a single voxel are sampled the population responses of more neurons than have ever been published in all the electrophysiology experiments ever conducted in non-human primates. A single imaging experiment typically samples 150,000 such voxels around 500 times per subject! Given these discrepancies, is it completely unrealistic to expect that there will be any systematic relationship between what is observed at a single cell level and that obtained by sampling population responses?

Surprisingly perhaps, basic homologies have been clearly established. It is striking that in the visual system, topographic aspects of cortical organisation described at a single cell level can be visualised easily with functional MRI (Sereno et al., 1995). However it is important to distinguish between topographic properties of the cortical surface, that may change relatively slowly with distance over the cortical sheet, and functional properties of neurons within a cortical area. The selectivity of cells within a cortical area for certain classes of stimuli such as moving objects (Tootell et al., 1995; Watson et al., 1993; Zeki
Neural correlates of selective attention

et al., 1991), coloured patches (Lueck et al., 1989) and faces (Kanwisher et al., 1997) appears to be reflected in a population response that shows specificity for such features. However it is not clear whether such homologies can be extended to include more subtle observations about the functional properties of neurons and cortical areas. For example, although it is tempting to interpret the inferotemporal rate-related activation described in chapter 3.2 in terms of the established properties of mnemonic neurons in monkey IT, a number of other possible explanations are equally plausible. Such questions will ultimately be resolved by being able to record extracellularly from single cortical areas while also measuring fMRI signals. However even with a combination of techniques like this, the sampling density of extracellular recording will still be low by comparison to the number of cells within a single fMRI voxel. This discrepancy suggests that a computational model may be required to mediate between what is measured at a number of extracellular recording sites and the population response. A synthetic computational model allows the construction of synthetic networks from a large number of simulated neuronal elements, allowing the behaviour of large populations of simulated neurons in aggregate to be examined and compared with the behaviour of individual elements of that population. By constraining the model with either single cell or fMRI data, it may be possible to understand the relationship between the two. It is also possible to contrast computational models that are not synthetic, made up of individual (simulated) neurons, but analytic. This type of model in effect describes the transfer function that relates the spiking activity of a population of neurons with the measured population (haemodynamic) response. Whatever the type of model, if is probably that the relationship between population response and single cell activity is described by some nonlinear function. In other words, as intuition suggests the population response is not likely to reflect the simple addition of all the individual responses. The anatomical location or physiological process reflecting such nonlinearities may in principle occur at a number of points. One particularly important location or process highlighted by work presented in chapter 3 is the point at which the spiking activity of a single neuron is transduced into the haemodynamic activity that is measured by functional imaging techniques (see also (Friston et al., 1998b)). However other relationships, such as that between the purely electrical activity of a single neuron and that of the whole population are equally likely to be nonlinear. In this context it is worth noting that the difficulty of inferring the nature of single cell responses from population measures of activity is not restricted to functional imaging with PET and fMRI alone. Both MEG and ERP techniques measure the aggregate electrical activity of the cortex either through the
induced magnetic fields that result, or directly. In the case of ERP the potentials recorded are filtered and conducted through the scalp, and frequently changes in DC potentials are removed by signal averaging and normalisation to the baseline. This DC normalisation adds a further interpretational difficulty. In addition to difficulties in inferring how changes in the ERP relate to changes in single unit firing (for example, does an increase in the P300 reflect increased firing, decreased firing, more synchronised firing, or a combination of all three?) the normalisation renders such measures blind to any changes in DC activity that would be produced by differences in baseline firing, unless this is specifically measured (Hillyard and Anllo Vento, 1998). In principle, conventional ERP is therefore blind to changes in baseline firing caused by attention as opposed to modulation of stimulus-evoked responses. The experimental work presented in Chapter 3 took advantage of the manipulate stimulus presentation rate in order to distinguish effects of attention presumed to reflect changes in baseline firing rate from changes in stimulus-evoked activity. Such a distinction is not in principle impossible to obtain with ERP measurements, but conventional practice would discard the former of these effects.

Some of the work presented in this thesis anticipates a nonlinear response between population measures of activity and single cell findings. A nonlinearity was observed in the BOLD response to increasing word presentation rate in auditory cortex, with the response beginning to saturate at a presentation rate of around 60 words per minute. Our subsequent modelling of this result with Volterra kernels (Friston et al., 1998b) formalises these findings in terms of a nonlinearity in the haemodynamic response. As interstimulus intervals start to fall below 2 or 3 seconds, the haemodynamic response to an immediately repeated stimulus begins to fall off. In this study there is no direct measure of electrical activity in cortex, so it is difficult to draw a strong conclusion about the location of such a nonlinearity in the BOLD response. However recent work using optical imaging and simultaneous electrical recording in rat whisker barrel, auditory cortex and human somatosensory cortex has striking similarities (Cannestra et al., 1998). These authors found that although the electrical response to an immediately repeated stimulus was maintained, the haemodynamic response measured with optical imaging of intrinsic signals fell off as the interstimulus interval decreased below about 3 or 4 seconds. This is consistent with my imaging work, suggesting there may be a response nonlinearity between the electrical and evoked haemodynamic activity in auditory cortex. Further work is needed to clarify the issue.
Neural correlates of selective attention

In the study presented in the second half of Chapter 3, when switching attention from auditory to visual modalities, the dominant form of modulation of evoked visual responses in large areas of extrastriate cortex took the form of a superadded 'bias' signal. There appeared to be only one small area in the fusiform gyrus that showed a pattern of activation more typical of the 'gain control' mechanism of attention. In awake behaving monkeys performing purely visual attention tasks, some groups have found changes in the baseline firing rate that might be a correlate of this 'bias' signal (Ferrera et al., 1994; Luck et al., 1997). However recent work has suggested that the dominant form of response modulation may be simply a multiplicative 'gain control' with no changes in bias (McAdams and Maunsell, 1999). Leaving aside possible implications this sort of finding might have for the biased competition model of visual attention, the discrepancy between my results and those seen at a single cell level is of considerable interest. One possibility is that the differences may simply reflect task differences. Differing task demands cause different patterns of attentional modulation, and so when attention is switched between visual and auditory modalities this may evoke a different pattern of modulation to when attention is switched to different features within the visual modality. A more intriguing possibility is that the two techniques, electrophysiology and functional imaging, may be differentially sensitive to modulations of baseline and evoked activity. Recent simulation work suggests that this may be a possibility worth investigating (Scannell and Young, 1999). Using a simple linear spike-counting approach, these authors calculated the possible evoked response from a population of realistic V5/MT neurons (Britten et al., 1992). This is an example of the use of an analytic computational model referred to earlier. The surprising finding from this work was that the population response was much more sensitive to changes in the baseline firing rate of the neurons than to changes in tuning parameters such as the width of the speed tuning curve or by multiplicative scaling of the tuning curve. Small changes in baseline firing rate produced large changes in population responses, while more dramatic changes in tuning parameters of the neurons produced relatively little change in the population response. The comes about because only a relatively small number of the population of V5 neurons respond to any given stimulus (because they are tuned for that particular speed). Changes in the tuning width therefore affect relatively few neurons – only the ones that are responding to that stimulus at that time. However, changes in baseline firing rate, even if small, affect the whole population. Thus small changes in the firing of the entire population have a substantial impact on the population firing rate. This reciprocal relationship is based on a very simple computational model (aggregating the neural firing rate over all neurons) and
Neural correlates of selective attention

does not take account of local interactions within an area. However the congruence with my functional imaging findings is interesting and may bear further investigation. Note that the results of Scannell & Young do not indicate the relative importance of changes in baseline firing rate or of stimulus-evoked responses for processes such as selective attention. Indeed, work discussed elsewhere in the thesis (Lee et al., 1999) suggests that one unifying model for selective visual attention that accounts for a wide range of psychophysical data is the assumption that attention operates by strengthening competition among functionally defined cortical columns. Such a model predicts that selective visual attention acts primarily through changing the width of the tuning of individual cortical neurons.

In summary, the relationship between single cell and functional imaging measures of cortical activity related to a particular task is rich and complex. Although strong homologies exist, at a functional level it will be necessary to characterise more fully the transfer function relating electrical and haemodynamic activity, and between single cells and populations. Such an undertaking is necessarily interdisciplinary in nature and is not simply a methodological enquiry, but ultimately essential for a complete understanding of how psychological processes map onto brain mechanisms.

7.2 What is perceptual load?

The experiments in Chapter 5 investigated the psychological theory of Lavie (Lavie, 1995) and provide compelling evidence for the existence of limited resources in the visual system. Somewhat surprisingly, the processing of motion in the periphery of the display was nevertheless strongly influenced by the difficulty of an otherwise unrelated visual task that subjects were engaged in. This is an example of how it is possible to use imaging to test the relatively abstract predictions of a psychological theory. In this case the most important claim of the psychological theory is that the perceptual system possesses limited processing resources, and that their allocation to stimulus processing over and above the current task is automatic. The idea that attention is necessary because there are limited resources at some point in our cognitive system has a distinguished history. Broadbent (Broadbent, 1958) formulated the first information processing theory of selective attention, based on Cherry's observations of dichotic listening paradigms (Cherry, 1957). Cherry found that subjects were able to describe the message they had
Neural correlates of selective attention

shadowed but could report very little about the unattended message. On the basis of this and other similar observation, Broadbent formulated an information processing theory of attention. According to this theory, all incoming signals are analysed for their physical (nonsemantic) characteristics, whether attended or not. However only attended messages are processed further to the point of identification. Broadbent suggested that the reason why such selection occurred was due to the limited capacity of central executive processes following semantic analysis. This account of selection has been called ‘early selection’. However experimental results became available after Broadbent formulated his theory that suggest that unattended stimuli may be processed more extensively than this theory would suggest. For example, semantically salient stimuli (such as the subject’s own name) in the unattended channel may be remembered (Treisman, 1960). Subjects also tend to switch the ear shadowed when the message is switched between ears, that suggests that the unattended material must be analysed semantically. Finally the existence of negative priming also shows that unattended material can be processed to the identity. As negative priming occurs not only when an unattended item is subsequently repeated, but also when a semantic associate is subsequently presented (see Chapter 4 and (Tipper, 1985)) this indicates that the semantic associations of the unattended item are extracted and may influence behaviour. To account for this and other evidence showing that unattended stimuli received a variable degree of processing, a number of solutions were proposed. One possibility was that the early ‘filter’ in Broadbent’s theory did not completely exclude further signals from processing but merely attenuated them (Treisman, 1960). On this account, particularly strong unattended signals (such as highly salient words) might be processed to the level of identity. Other theorists proposed a radically different theory, suggesting that all message, whether attended or not, undergo semantic analysis (Deutsch and Deutsch, 1963; Duncan, 1980). On this account analysis proceeds in parallel and without capacity limits: selection by attention takes place after perception, when identity has already been extracted from the stimuli.

Lavie’s theory and the present results are interesting because they suggest the outlines of a theoretical resolution to the potential impasse between early and late selection theory. Our results suggest that if resources are exhausted by the task the subject is engaged in, then selectivity of processing will occur. V5 activity associated with the processing of irrelevant motion was lower under conditions of high load. On the other hand, if resources are available under low load conditions then even an irrelevant stimulus that subjects have been asked to ignore will be processed. Here an ignored stimulus (visual
Neural correlates of selective attention

Motion) is used that has biological ‘meaning’ (in terms of providing information about observer movement through the environment) but not ‘meaning’ in a semantic sense. So it would be wrong to say from these results that selection is ‘early’ under high load or ‘late’ under low load. However the experimental findings strongly suggest that the degree to which unattended visual stimuli are processed depends critically on the availability of visual attention. This suggestion is given additional weight by the experiment presented in Chapter 6 where inattentional blindness for words is demonstrated in subjects monitoring overlapping word and picture streams. When attention is directed to the picture stream, subjects neither remember the words presented in the ignored stream nor is brain activity evoked that relates to their meaning. The availability in this experiment of a measure of meaning (by comparing the activity evoked by words to that evoked by consonant letter strings) provides information about the locus (in information processing terms) of selection. Under these exceptionally high load conditions, the locus of selection unequivocally occurs before semantic analysis. These findings are compatible with the general outline of Lavie’s theory, and suggest that the locus of selectivity does indeed vary with perceptual load.

Many of the theoretical approaches to attention, and Lavie’s theory in particular, make use of the theoretical concept of ‘limited resources’. An important aspect of developing a neurobiological account of how visual attention operates will be to understand how such limited resources might be implemented in the brain. If we consider the processing of a simple feature such as visual motion, there are a limited number of possibilities. First, limited processing capacity could occur because there are a limited number of neurons within a motion-sensitive cortical area capable of processing a motion stimulus. Once all these neurons are allocated to the primary task, then no further processing of visual motion can take place and selectivity (for this feature) occurs. However this is an account of limited motion resources: selectivity for other features would not occur just because all motion processing neurons are engaged. This would not provide a good account of limited resources between different features or aspects of visual processing that are assumed by the theoretical positions outlined above and shown by the results in Chapter 5. Lavie’s theory postulates limited attentional resources that are general to all visual stimuli at least. An explanation of the results in Chapter 5 in terms of limited processing capacity within V5 alone is possible but unlikely. Under high load conditions subjects had to read the words in order to perform the bisyllabic monitoring task. Reading under normal conditions, with eye movements allowed, involves the magnocellular pathway.
Neural correlates of selective attention

that provides a substantial cortical input to V5. If reading specifically involves V5 activity of this kind is conceivable that, although eye movements were disallowed in our experiment, differential involvement of the magnocellular pathway lead to a local exhaustion of motion resources. We believe this explanation to be unlikely, but it remains possible that the effects we observe reflect limited resources within a functionally specialised area of the visual system, rather than throughout the visual system or reflecting more general attentional resources.

In the second experiment addressing the effects of perceptual load (Section 5.5), varying auditory perceptual load failed to produce similar influences on visual processing as changing visual perceptual load. I have argued that this failure to demonstrate a strong effect of auditory perceptual load suggests that attentional capacity is restricted within, but not between, the two sensory modalities. Such an account is at variance with theories that suggest a single undifferentiated attentional system (e.g. (Mesulam, 1990)). The experimental findings do not preclude the existence of such a system, but suggest that under the conditions of our experiment the primary constraint on processing resides within auditory or visual cortex proper. However it is equally clear that while processing of the unattended visual stimulus occurred under both high and low auditory perceptual load, the visual stimulus did not affect behaviour. Some post-perceptual selective mechanism must resolve the potential response conflict between auditory and visual stimuli and ensure the coherence of behaviour. This in turn suggests a multiplicity of processes that may reflect 'attention' and the control of behaviour (Allport, 1993).

To provide a biological account of generalised attentional resources, connections between areas involved in processing a particular attribute and other non-sensory cortical areas must be considered. The V5/MT complex has very rich monosynaptic anatomical connections with posterior parietal and prefrontal cortex near the frontal eye fields (Mesulam, 1990). The effects of perceptual load on motion processing may be due to a limitation in availability of such a 'nonperceptual' resource as these connections with other cortical areas. This suggestion would require that connections from higher cortical areas are in some sense facilitatory. Such 'top-down' connections would have a non-specific facilitatory role: in the absence of top-down activity in a cortical area, processing would be attenuated. The data presented in this thesis do not allow an investigation of this hypothesis, but it would be possible to test this with new analytic techniques. One possibility is that the source of such facilitatory afferents would be more active under
Neural correlates of selective attention

conditions of low load compared to high load. In support of this, in the first perceptual load experiment the reverse interaction (i.e. effects of visual motion greater under low load compared to high load) demonstrated strong biparietal activation (data not shown). However it is also possible that the source of such modulatory top-down effects is equally active under both low load and high load conditions, but with the site of such effects being different. In this case it will be possible to detect a change in the site of such effects using structural equation modelling. A detailed description of this technique is beyond the scope of this thesis but statistical accounts are available elsewhere (Tacq, 1997). The application of this technique to functional imaging involves constructing a simplified anatomical model of the visual system and the connections within this system. By using the physiological functional imaging data collected in an appropriate imaging experiment, the path coefficients between different anatomical areas can be estimated. These coefficients reflect the strength of connections between areas. Christian Büchel has used this technique successfully during a visual attention task (Buchel and Friston, 1997; Buchel et al., 1998a) to investigate the way in which posterior parietal cortex modulates visual areas. He found (Buchel and Friston, 1997) that the physiological data are consistent with parietal cortex modulating the strength of connections between striate cortex and V5 when attention is directed explicitly to a visual motion display. Although in this experiment the visual motion display was always relevant, whereas in our experiments in Chapter 5 the displays were always irrelevant, the finding is supportive of the general approach outlined here. The approach outlined here predicts that under conditions of high load, the connection strength between posterior parietal cortex and V5 would be decreased relative to low load.

Lavie's theory suggests that perceptual selectivity is largely a passive by-product of intention. Subjects choose to perform a particular task and resources are allocated appropriately. Unattended information is then processed automatically and regardless of the subject's wishes until capacity limits are reached. This approach discounts the idea that there is some brain 'mechanism' for selection. However some sort of selective process must still occur, for (as discussed above) under low load conditions multiple attended and nonattended stimuli are processed and can compete to control responses. Under such conditions there must be a selective mechanism to eliminate response competition. Lavie's theory has recently been extended (Lavie, 1999) to incorporate the idea of response competition: interestingly, loading such a post-perceptual selective mechanism would seem to predict results opposite to those obtained here through

7-170
Neural correlates of selective attention manipulations of perceptual load. While the exhaustion of perceptual resources leads to selectivity in processing, exhausting such post-perceptual resources would be expected to lead to less selectivity in responses. These predictions await further testing with brain imaging.

7.3 What is the relationship between attention and visual awareness?

The relationship between attention and awareness has been of enduring interest, although the exact nature of the connection remains elusive. Our observation that the degree to which unattended stimuli are processed depends on the level of perceptual load raises the possibility that allocation of attention is necessary (though not sufficient) for visual awareness. In section 5.1.1., an ignored visual motion stimulus does not produce activity in cortical area V5/MT under conditions of high perceptual load. This study did not directly address whether subjects were aware of the stimulus (by, for example, debriefing them) but nevertheless, given the absence of activity in V5 under high load it is difficult to see how perception would not be altered. Evidence from other studies demonstrates the importance of activity in V5 complex for awareness of visual motion. Activity in V5 is associated with awareness of a moving grating during binocular rivalry and is abolished when the grating is not seen (Lumer et al., 1998; Lumer and Rees, 1999). Similarly, lesions to V5 give rise to an inability to be aware of visual motion. On the basis of these and other findings, it has been proposed that conscious awareness of visual motion is caused by activity in V5 (though we have argued elsewhere that an interaction between different cortical areas is necessary). So were our subjects aware of the visual motion stimulus under conditions of high perceptual load?

A clearer answer to the issue is provided by the experiment presented in Chapter 6. Here we provide an explicit measure of awareness by asking subjects whether they are able to remember attended and unattended stimuli. Even when foveally presented, subjects are unable to recall the identity of single words when unattended. The brain activity evoked by the unattended words is no different to that evoked by meaningless stimuli. This therefore provides information about how a particular aspect of word processing, the extraction of meaning, is affected by the absence of attention. While it is difficult to draw strong conclusions from a null result, our findings strongly suggest that under conditions of full inattention, the brain does not extract semantic information from unattended
Neural correlates of selective attention

stimuli. Moreover, subjects appeared unaware of the presence of such stimuli, showing inattentional blindness. This suggests not only that attention is important for the extraction of meaning from stimuli, but also that this extraction of identity is in some sense important for stimuli to reach awareness.

Taken together, the experiments in Chapter 5 & Chapter 6 suggest that whether unattended visual stimuli are processed depends on the perceptual load of the primary task that subjects are engaged in. The effective locus of selection (in information processing terms) varies accordingly. With a very simple task (Chapter 4) and correspondingly low perceptual load, stimulus processing proceeds to extraction of categorical identity of ignored stimuli. As a result, negative priming occurs and activity is seen in subcortical structures such as the corpus striatum. As perceptual load is systematically increased, activity in a distributed network of cortical areas associated with processing an ignored stimulus is reduced. When load is sufficiently high under very demanding task conditions, unattended stimuli are no longer remembered. Under these conditions the locus of selection appears to be at, or prior to, the extraction of meaning. Unattended stimuli are simply not perceived. These findings do not establish whether unattended stimuli fail to be perceived under all circumstances (e.g. (Treisman, 1960)), but do demonstrate clearly that circumstances exist under which no perception occurs.

Is this true for all classes of stimuli? Earlier work has emphasised that under certain conditions, unattended stimulus processing may occur. However in such experiments it has not been feasible to exclude the possibility that some attention was available, leading to processing of unattended stimuli. In other words, the issue is how to ensure in a rigorous and quantitative manner that attention is truly unavailable when measuring the processing of unattended stimuli. The present findings imply that unattended stimulus processing will occur automatically if attention is available. However, it remains unclear whether the processing of certain stimuli requires so little attention that a stimulus can be detected even when attention is allocated elsewhere in the visual field. These issues have been addressed in a series of experiments by Braun & colleagues (Braun, 1993; Braun and Julesz, 1998; Braun and Sagi, 1991). Braun has used an asymmetrical dual task experiment where attention is focused on a primary letter task that involves discriminating five randomly rotated letters (Ts or Ls) near the centre of the display. This task is particularly demanding, leaving little or no attention available for central tasks. This can be established by producing an attention operating characteristic (directly
Neural correlates of selective attention analogous to a receiver operating characteristic) when performing this central letter task with a particular secondary probe task (identification of a single letter). The authors then combined the central letter task with a number of peripheral tasks, including detection of a texture pop-out stimuli. The results show that a number of peripheral pop out tasks can be performed concurrently with the central letter task with little or no dual task interference. This strongly suggests that certain types of visual processing leading to awareness are possible without attention. The detection of pop out targets preattentively has also been investigated by presented subjects with a task requiring detection of a pop out during the ‘attentional blink’. Joseph and colleagues (Joseph et al., 1997) found that subjects were unable to detect such popouts during concurrent detection of a single target letter in a rapid serial stream. However it appears that this pattern of results is only seen with naive subjects, as repeated training leads to subjects being able to perform both tasks with ease (Braun, 1998). This sensitivity to training is not seen in the work of Braun and colleagues, who invariably use highly overtrained observers.

In summary, while higher level properties of visual stimuli appear to receive very little processing without attention, there is some evidence to suggest preattentive processing of pop-out visual stimuli. These results with asymmetric dual task paradigms are compatible with the present findings if attention is only required for processing certain classes of stimuli (such as the words investigated in Chapter 6) or for certain processing stages (such as the extraction of meaning). The results of Braun and colleagues suggest that certain classes of visual stimuli are privileged in the sense that the detection of such stimuli does not require attention. It will be of considerable interest to see how these psychophysical findings are reflected in future brain imaging studies.

7.4 Conclusion

This thesis has described a number of experiments that share a common theme of investigating the nature and extent of unattended stimulus presentation. The psychological concept of resource limitation has emerged as an important determinant of unattended processing, although its anatomical embodiment is unclear. The work presented here has attempted to start building some links between relatively abstract cognitive theories of attention, functional imaging work in humans and single cell electrophysiology in awake behaving primates. Future work should seek to clarify the nature of resource constraints in anatomical and physiological terms. A mechanistic
Neural correlates of selective attention

account of attention in terms of interacting structures and processes in the brain is highly desirable. To approach such an undertaking requires a synthesis of phenomenology, psychophysics and physiology in order to provide a description of the nature and extent of visual attention and its relationship to visual awareness.
Chapter 8 Appendix: The effect of varying stimulus presentation rate on responses in both PET and fMRI

This appendix is presented after the general discussion as it is more technical in nature, though carried out as part of the logical sequence of experiments in the thesis. The work presented here addresses the nature of evoked haemodynamic responses and how measurements of blood oxygenation level dependent (BOLD) effects are related to changes in regional cerebral blood flow (rCBF). This study particularly investigates the relationship between changes in regional cerebral blood flow measured by positron emission tomography (PET), changes in BOLD contrast measured with functional MRI (fMRI), and the stimulus presentation rate, in human auditory cortex. This work was motivated by the experiments described in Chapter 3, in which the relationship between processing of unattended and attended visual and auditory stimuli was investigated by varying stimulus presentation rate using PET. However as PET and fMRI measure different components of the haemodynamic response, it is not clear that they share the same stimulus dependencies. Motivated by a desire to extend the rate modulation work to fMRI, an empirical investigation of the similarities and differences between the techniques was therefore undertaken.

8.1 Differences between PET and fMRI experiments

The neural activity underlying performance of a cognitive or sensorimotor task is accompanied by focal changes in cerebral blood flow (CBF) (Fox et al., 1986), cerebral blood volume (CBV) (Belliveau et al., 1991; Fox et al., 1988), blood oxygenation (Fox et al., 1986; Fox et al., 1988) and cerebral metabolism (Phelps et al., 1981; Prichard et al., 1991). Measurement of these physiological changes can be used to characterise functional anatomy. Different functional imaging techniques measure different physiological parameters. PET, using an intravascular radiolabelled positron emitting tracer such as H$_2$O, measures regional cerebral blood flow (Frackowiak et al., 1980; Raichle, 1983). By contrast, BOLD fMRI returns a more complex signal reflecting deoxyhaemoglobin concentration (Bandettini et al., 1992; Kwong et al., 1992). The BOLD signal is considered to be predicated on a local mismatch between blood flow and cerebral metabolism in response to neural activity. Oxygen delivery, cerebral blood flow and cerebral blood volume all increase with neural activity. But cerebral blood flow (and so
Neural correlates of selective attention

Oxygen delivery changes usually exceed cerebral blood volume changes, while oxygen utilisation increases only slightly (Fox et al., 1986; Fox et al., 1988). This results in a decrease in the local blood deoxyhemoglobin, that provides the basis of the BOLD contrast. Direct optical imaging of exposed cortex has provided evidence to support this (Frostig et al., 1990; Malonek and Grinvald, 1996). The reflectance signal suggests that there is a biphasic change in deoxyhaemoglobin concentration in neurally active tissue, reflecting an imbalance between oxygen consumption and flow. Initially oxygen consumption rises, producing a fall in oxyhaemoglobin concentration; later there is a rise in flow to that area that exceeds consumption, producing a delayed peak in oxyhaemoglobin concentration. This biphasic response has been shown in primary visual cortex using high field functional MRI (Hu et al., 1997; Menon et al., 1995). In conventional fMRI experiments, the signal primarily reflects the larger, delayed decrease in deoxyhemoglobin. The size of this response therefore depends on the extent and magnitude of both regional cerebral blood flow and local oxygen consumption. This raises the possibility that PET and fMRI signals may not show the same stimulus dependency during functional imaging experiments if the physiological parameters they measure do not share a common stimulus dependency.

A complete interpretation of functional activation studies therefore requires an understanding of the relationship between stimulus characteristics (e.g. presentation rate), the underlying excitatory or inhibitory neural activity and the concomitant regional haemodynamic response. There has been no previous study directly comparing the relationship between stimulus presentation rate and signal in both BOLD fMRI and PET. Separate studies suggest that there may be important differences between these measurement techniques. In primary auditory cortex a strong linear dependence of rCBF changes measured with PET with presentation rate of heard words has been shown (Frith and Friston, 1996; Price et al., 1992). However fMRI studies suggest that the response dependence of primary auditory cortex on rate of presentation of phonemes is highly nonlinear (Binder et al., 1994). This striking difference has not been satisfactorily explained, but there are several possible reasons why there might be a discrepancy between the two experiments. The tasks used were quite different; passive listening to words in one experiment, and active discrimination of phonemes in the other. It is possible that the disparate results are contingent upon differences in paradigm and presentation rather than the measurement technique used. Furthermore, the stimulus presentation environments of PET and fMRI are quite different. PET is virtually silent,
Neural correlates of selective attention

while the echoplanar imaging used to acquire BOLD sensitive images in fMRI studies is relatively noisy. The current generation of MRI scanners produce auditory noise levels within the bore of a magnet approaching 90dB, and it is possible that this affects the responsiveness of primary auditory cortex to acoustic stimuli. A final possibility, that this paper addresses, is that the disparate results obtained with PET and fMRI are due not to differences in paradigm or stimulus environment but to fundamental differences in the temporal dynamics of rCBF and BOLD measurements with respect to stimulus presentation rate.

8.2 Materials and Methods

8.2.1. Behavioural session

Cerebral haemodynamic responses were studied in the subject while listening to words. The PET and fMRI environments are acoustically very different and so considerable effort was made to make the stimulus presentation as closely matched as possible in each environment. To this end, the ambient EPI noise was digitally recorded using a microphone placed close to the bore of the magnet and mixed this with the stimuli for the PET session alone. To ensure that this recording created a similar perception to that actually experienced during EPI, two extended behavioural sessions took place with the subject. In the first session, the subject lay in the magnet while alternately being subjected to real EPI and hearing the pre-recorded EPI sound through the stimulus delivery system (described below). The volume and frequency characteristics of the pre-recorded sound were then adjusted to make the two sounds (recorded and real) perceptually well matched. A second behavioural session was conducted outside the magnet to control for the different characteristics of the stimulus delivery systems (air conduction in fMRI, in ear electromagnetic earphones in PET). The relative volume of the recorded EPI noise played through headphones was adjusted to match that obtained through air conduction.

The stimuli were digital recordings of a female voice speaking a sequence of monosyllabic or bisyllabic nouns. Stimuli were not repeated at any point during the experiment, and the words presented in each experimental condition for both PET and fMRI were matched for frequency, number of syllables, imageability and concreteness. Five different presentation rates were used; 10, 15, 30, 60 and 90 words per minute. The PET stimuli were mixed with the pre-recorded EPI sound obtained by the procedure
Neural correlates of selective attention described above. The order of the conditions was not known to the subject and was determined by a Latin Square within subject design (fMRI) or in a counterbalanced pseudo-random order (PET). A single healthy right-handed male, aged 28 years, was studied with both H$_2^{15}$O PET and BOLD fMRI in two different sessions.

8.2.2. fMRI session

The subject lay in the scanner with eyes closed and room lights extinguished. Digitally recorded stimuli were played at precise intervals with a personal computer, amplified and delivered binaurally to the subject through a pair of plastic tubes approximately five feet long. The plastic tubes ended in occlusive ear inserts allowing free conduction of sound with suppression of the ambient scanner noise. The ambient noise inside the scanner during echoplanar imaging with shielded coils was approximately 90 dB, with an attenuation by the ear inserts of about 20 dB.

Imaging followed the general protocol described in chapter 2, performed using a Siemens Magnetom VISION scanner (Siemens, Erlangen) operating at 2 Tesla and equipped for echoplanar imaging. A gradient-echo echo-planar sequence was used to acquire sixteen slices of thickness 3mm and inplane resolution of 3x3mm (TR/TE 1700ms/40ms). Each scanning run comprised 128 image volumes starting with eight dummy scans to allow for equilibration of T1 saturation effects, followed by 120 images where baseline (no stimuli presented) alternated with activation (auditory stimuli presented) every 20 acquisitions (34 seconds). Ten such series (a total of sixty activation/baseline cycles representing 1200 image volumes) were acquired during a single session. At the beginning of the session a single T1 weighted anatomical image was acquired.

8.2.3. PET session

The subject lay in the scanner with their eyes closed and room lights extinguished. Digitally recorded stimuli were played at precise intervals with a personal computer, amplified and delivered binaurally to the subject through a pair of in ear earphones. PET scans were performed in the manner described in chapter 2. Twelve activation scans were obtained during the PET session, two at each word rate. During two of the scans no words were presented and the subject heard only the pre-recorded fMRI scanner noise.
Neural correlates of selective attention

The subject was unaware of the order of presentation of different rates, that was determined in a random fashion.

8.2.4. Data analysis

Data analysis used the techniques described in Chapter 2, with some important modifications to facilitate inter-modality comparison of imaging data. The first image of each functional series was coregistered with the subject's T1 weighted structural MRI, and the other images aligned to the first (Friston et al., 1995a). Thus all the functional images (both PET and fMRI) were aligned and coregistered with the same T1 weighted MRI image. Spatial normalisation was then performed on both PET and fMRI images using a common parameter set derived from the T1 weighted structural image and a T1 template using an affine and nonlinear transformation (Friston et al., 1995a). The parameter set produced by the normalisation procedure was applied to the coregistered PET and fMRI images. This procedure ensures that exactly the same transformations are applied to both PET and fMRI images; they remain in exact register anatomically and no relative distortions are introduced by the spatial normalisation. The images were smoothed with a Gaussian kernel of FWHM 12mm (PET) or 5mm (fMRI). Each functional image was proportionally scaled to remove the effect of global changes in rCBF or BOLD contrast. This does not change the relative values of the data, but means that the relative changes (figures 2, 3 and 4) are reported relative to a set grand mean rather than with respect to baseline. Statistical parametric maps were generated for both images using a monotonic weighting of condition means to identify areas of interest that covaried positively and negatively with stimulus presentation rate in both data sets. The SPM[Z] was thresholded at $p=0.001$ uncorrected for multiple comparisons and the clusters of voxels above this level characterised in terms of their peak height and spatial extent.
Figure 8-1: Word listening in PET and fMRI

Areas of significant activation in auditory cortex and periauditory areas that correlated positively with stimulus presentation rate. The data from PET and BOLD fMRI datasets are thresholded at p<0.001 uncorrected and displayed on a rendered T1 template image.
Homologous regions of activation to the auditory stimuli that covaried with word presentation rate were identified in primary auditory cortex for both PET and fMRI data sets. Figure 8-1 illustrates the location of these regions in both PET and fMRI datasets. These regions were spatially overlapping in PET and fMRI data, and the peaks of activation in each dataset were within one full width half maximum of each other. Within each region there were several peaks of activation that reached statistical significance, and each was examined separately.

Adjusted rCBF values for each scan were obtained at the voxels of peak activation in auditory cortex from the PET data. The corresponding fMRI data were extracted as a continuous time series. The spatial smoothing of both datasets means that the signal change within a given voxel represents the average signal change in a small region around that voxel, weighted by the smoothing kernel employed. Adjusted rCBF values for the voxels of peak activation in right and left auditory cortex from the PET data are plotted as a function of word presentation rate in Figure 8-2. Inspection of other voxels from the same cluster (data not shown) showed the same relationship between rCBF and word presentation rate. BOLD contrast values from the voxels of peak activation in auditory cortex in the fMRI dataset are plotted as a function of word presentation rate in Figure 8-3. These two voxels represented the most significant voxels within a relatively large area of auditory cortex. Figure 8-4 shows the relationship between BOLD contrast and word presentation rate for four further voxels within the same cluster, each of which represented a subsidiary peak of activation. It is apparent that the stimulus dependency of the voxels in Figure 8-3 & Figure 8-4 is remarkably similar, despite their spatial separation within auditory cortex. The response profiles from the voxels of peak activation (Figure 8-2 & Figure 8-3) were selected for further quantitative analysis.
Neural correlates of selective attention

Figure 8-2: PET rate dependency

Adjusted rCBF values plotted as a function of word presentation rate for voxels of peak activation in right and left auditory cortex. Each open circle represents the adjusted rCBF value during one scan, and the line is drawn through the mean activation at each rate.
Neural correlates of selective attention

Inspection of Figure 8-2 suggests that the dependency of rCBF on word presentation rate is best described between word presentation rates of 10 and 90 words per minute by a linear function. A set of orthogonal polynomial expansions of the word presentation rates was constructed to test this hypothesis. The use of a set of orthogonal polynomial expansions to perform multiple regression on the adjusted rCBF values allows us to test the significance of the regression coefficient for each term of the expansion independently of the others. As expected, only the regression coefficient for the linear term reaches significance (Table 8-1).

Inspection of Figure 8-3 suggests that the dependency of BOLD fMRI contrast on word presentation rate is more complex and best described by a higher order polynomial function. This supposition was tested by constructing a set of orthogonal polynomial expansions of the word presentation rates. The results (Table 8-2) confirm that the regression coefficients of higher order polynomials reach statistical significance.
Figure 8-3: fMRI rate dependency

Adjusted BOLD contrast values plotted as a function of word presentation rate for voxels of peak activation in right and left auditory cortex. Each open circle represents the mean BOLD contrast during one activation epoch (representing 34s of auditory stimulus presentation) and the line is drawn through the mean activation at each rate over all activation epochs.
Neural correlates of selective attention

Figure 8-4: fMRI rate dependency

Adjusted BOLD contrast values plotted as a function of word presentation rate for four subsidiary peaks of activation within the areas displayed in Figure 8-1. Each open circle represents the mean BOLD contrast during one activation epoch (representing 34s of auditory stimulus presentation) and the line is drawn through the mean activation at each rate over all activation epochs.
Neural correlates of selective attention

Table 8-1: Orthogonal polynomial regression (PET)

Multiple regression of orthogonal polynomials created from the word presentation rates (excluding the rest condition) on adjusted rCBF data from right and left auditory cortex voxels of peak activation.

<table>
<thead>
<tr>
<th>ORDER</th>
<th>F-VALUE</th>
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<td>First</td>
<td>133.568</td>
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<tr>
<td>Second</td>
<td>0.013</td>
<td>0.093</td>
</tr>
<tr>
<td>Third</td>
<td>0.127</td>
<td>0.0002</td>
</tr>
<tr>
<td>Fourth</td>
<td>0.061</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 8-2: Orthogonal polynomial regression (fMRI)

Multiple regression of orthogonal polynomials created from the word presentation rates (excluding rest condition) on adjusted BOLD contrast values from right and left auditory cortex voxels of peak activation.

<table>
<thead>
<tr>
<th>ORDER</th>
<th>F-VALUE</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>First</td>
<td>537.851</td>
<td>612.424</td>
</tr>
<tr>
<td>Second</td>
<td>38.707</td>
<td>117.260</td>
</tr>
<tr>
<td>Third</td>
<td>18.201</td>
<td>5.625</td>
</tr>
<tr>
<td>Fourth</td>
<td>5.421</td>
<td>0.175</td>
</tr>
</tbody>
</table>
**8.3 Discussion**

**8.3.1. Stimulus dependency of rCBF measurements**

These findings confirm that stimulus presentation rate determines regional cerebral blood flow in primary auditory cortex. Dependency of rCBF on stimulus presentation rate has been shown previously for primary visual cortex (Fox and Raichle, 1984; Fox and Raichle, 1985) and primary auditory cortex (Frith and Friston, 1996; Price et al., 1992). The nature of the response is of some interest. Measurement of rCBF by the $H_2^{15}$O radiotracer technique requires accumulation of counts over a scanning window of 90 seconds. The rCBF measurements therefore represent an integration over time of the haemodynamic response to neural activity within the scanning window. If the haemodynamic response accompanying each stimulus repetition is uniform, increases in stimulus presentation rate will result in a linear increase in the mean integrated haemodynamic activity. These data show that blood flow in auditory cortex shows an almost exact linear dependency on rate, in accord with previous work (Price et al., 1992). However, when simulated EPI sounds were presented alone, the rCBF was substantially lower than one would expect given the linear relationship between word presentation rate and rCBF. This nonlinearity may have its origins in the effects of selective attention or arousal on auditory cortex. Technical limitations with PET scanning require that the auditory stimulus commence some seconds before the scanning window. The subject therefore became aware before the start of data acquisition whether words were to be presented, and may have turned their attention elsewhere for the duration of the scan. In a similar fashion, for those conditions where words were presented the presence of loud distracting background noise may have forced the subject to attend more intently than in the study of Price and colleagues (1992) where no background noise was present. In addition to the linear responses in auditory cortex, Price et al showed a nonlinear, stepwise responses in left posterior superior temporal gyrus (Wernicke's area). However the data shown in Figure 8-2 comes from an area located well away from posterior superior temporal gyrus, so this is not a plausible explanation for the present results. The difference between the rest condition and those conditions where words were presented was an unexpected finding of this study and requires further investigation. A practical
Neural correlates of selective attention

Implication of this observation is that rCBF measurements made when no stimuli are presented should be interpreted with caution.

8.3.2. Stimulus dependency of BOLD measurements

These results show that there is a nonlinear, saturable relationship between stimulus presentation rate and BOLD contrast measurement. This finding is consistent with the nonlinear dependency of BOLD contrast on rate of presentation of phonemes seen by Binder and colleagues (1994). They studied a phoneme discrimination task with echo-planar imaging of two slices through temporal cortex (TR 3 secs) and showed a monotonic nonlinear dependency of signal on stimulus presentation rate between rest and 2.5Hz. The present findings extend these results to passive word listening. The range of word presentation frequencies used in this study is comparable to that found in everyday conversation. There is therefore no reason to suggest that the saturable relationship between word presentation rate and BOLD contrast is consequent on word presentation frequencies outside the normal physiological range.

8.3.3. Why is there a difference between the BOLD and rCBF measurements?

The difference between the PET and fMRI data, collected in the same subject under the same conditions, is striking. The rigorous and unique approach taken to reproducing the acoustic characteristics of the two imaging environments, with acquisition of an extremely large dataset in a single subject, allows inferences to be made about the specific nature of the relationship between rCBF and BOLD measurements. The differences observed by previous investigators between PET and fMRI auditory studies are not due to differences in paradigm, subject or stimulus environment but reflect fundamentally different stimulus dependencies of PET rCBF and BOLD contrast measurements. The PET data illustrate that, for the conditions where words were presented, rCBF increases linearly with stimulus rate. Therefore, the nonlinearity of the fMRI data over the same range can be unambiguously attributed to factors other than cerebral blood flow. In this section factors other than cerebral blood flow will be discussed, that may be relevant to the observed relationship between stimulus presentation rate and BOLD contrast.

BOLD measurements are contingent on changes in the concentration of paramagnetic deoxyhaemoglobin, an endogenous contrast agent. As a consequence there are two logical
Neural correlates of selective attention

BOLD measurements are contingent on changes in the concentration of paramagnetic deoxyhaemoglobin, an endogenous contrast agent. As a consequence there are two logical possibilities for the observed relationship between stimulus presentation rate and BOLD contrast. Either the relationship between BOLD contrast and deoxyhaemoglobin concentration, or that between word presentation rate and deoxyhaemoglobin concentration, is nonlinear. Each possibility will be examined in turn.

8.3.4. Relationship between BOLD contrast and deoxyhaemoglobin concentration

Under the condition of constant blood volume, changes in tissue transverse relaxation rate ($R_2^*$) are linear with respect to blood oxygenation. However it is not immediately apparent that the relationship between $R_2^*$ and BOLD signal is linear. We can write:

$$R_2^* \propto k \langle [Hb] \rangle$$  \hspace{1cm} (1)

where $k$ describes the proportion of deoxygenated haemoglobin and changes between rest ($k_r \approx 0.3$) and activated ($k_a > 0.3$) states. Now the fractional NMR signal change in going from a rest ($r$) to an activated ($a$) state can be written:

$$\frac{\Delta S}{S_r} = \frac{e^{-m_r R_2^* \tau} - e^{-m_a R_2^* \tau}}{e^{-m_r R_2^* \tau}}$$  \hspace{1cm} (2)

where $S_r$ is the resting signal level at an echo time $TE$. Substituting (1) in (2) at an echo time $TE = T_2^*$ gives:

$$\frac{\Delta S}{S_r} = \frac{e^{-m_a k a} - 1}{e^{-m_r k a}}$$  \hspace{1cm} (3)

Equation (3) is plotted in Figure 8-5. The fractional change in transverse tissue...
Neural correlates of selective attention

Figure 8-5: Relationship between T2* and blood oxygenation

An illustration of the theoretical relationship between fractional change in T2* signal as a function of changes in blood oxygenation
Neural correlates of selective attention

relaxation rate during stimulation is relatively small; experiments on motor cortex suggest that $R_{2*}$ is approximately 97% of $R_{2*}$ (Bandettini et al., 1994). This implies that under normal physiological conditions of brain activation, the changes in NMR signal are located in the region of Figure 8-5 where $k_r/k_l$ is between 0.9 and 1.0. It is immediately apparent that Figure 8-5 is very nearly linear over this range. This suggests that over the physiological range of likely changes in blood oxygenation in response to activation, changes in BOLD signal are likely to be approximately linear with respect to deoxyhaemoglobin concentration. Saturable BOLD effects due to increased blood oxygenation have been shown where resting flow is manipulated pharmacologically (Bruhn et al., 1994). However the flow changes shown in the PET data presented here are substantially smaller and these effects are unlikely to affect this data. The nonlinearity in the BOLD data may thus represent a nonlinear change in deoxyhaemoglobin concentration.

8.3.5. Mechanisms causing changes in deoxyhaemoglobin concentration

The linear relationship between changes in BOLD signal and deoxyhaemoglobin concentration shown above implies that the nonlinear stimulus dependency observed in this experiment is due to a nonlinearity in the relationship between deoxyhaemoglobin concentration and word presentation rate. The presentation of words evokes activity in auditory cortical neurons, that in turn causes changes in oxygen extraction and local changes in blood flow and blood volume. In principle, any one of these components could show a nonlinear dependency on word presentation rate. In other words, either the neural activity or the mapping between neural activity and haemodynamic response may show a nonlinear word presentation rate dependency. It is not possible to distinguish between these explanations using the present data. However it should be noted that blood flow is usually regarded as an index of presynaptic activity (Jueptner et al., 1997), and the present data shows a linear relationship between blood flow and word presentation rate. This observation suggests that the underlying neuronal activity is proportional to word presentation rate. Hence the nonlinear relationship between blood flow and BOLD contrast depends on the mapping between neuronal activity and haemodynamic response. This mapping is realised as changes in blood volume, blood flow and oxygen extraction secondary to changes in neural metabolism. There is increasing evidence to suggest that there is no capillary recruitment during cerebral activation (Gobel et al., 1989),
Neural correlates of selective attention

suggesting that the principal determinants of deoxyhaemoglobin concentration are blood flow and oxygen extraction rather than blood volume per se. These data indicate that changes in blood flow are linear with respect to stimulus presentation rate, so it can therefore be speculated that oxygen extraction is the component of the mapping between neural activity and haemodynamic response that shows a nonlinear rate (and flow) dependency. This is anticipated by contemporary modelling studies of the cerebral circulation (Buxton and Frank, 1997) and qualitatively compatible with the electrical dynamics of single neurons. The explicit modelling of the relationship between neural activity and evoked haemodynamic response suggested by this experiment is addressed in detail elsewhere (Friston et al., 1998b).

Optical imaging data suggest that changes in blood flow and oxygen metabolism occur at different spatial scales (Malonek and Grinvald, 1996). Changes in deoxyhaemoglobin concentration can be seen at a scale of 100 μm, whereas blood flow changes occur in cortex over a scale of 1-2mm. Could this difference account for the differences observed here between rCBF and BOLD contrast measurements? Given that both the scale on which metabolism and flow change locally are smaller than the voxel size used in this experiment, then the difference in spatial scale alone is not enough to account for the present data. This difference may be a contributory factor to these data, but would require that the spatial scale at which flow and metabolism changes occur to vary as different functions of stimulus presentation rate. In other words, assuming constant areas of cortical activity, the spatial scale on which flow is regulated would be a nonlinear function of stimulus presentation rate. At higher rates of cortical activity, the spatial scale at which flow is regulated would have to be larger than the spatial scale at which flow is regulated at low rates of cortical activity.

Is it conceivable that these fMRI results might be contaminated by some unsuspected flow sensitivity? Studies of the dependence of signal change on TE have shown that long-TR gradient echo EPI is very insensitive to flow changes, and that signal change for this sequence is overwhelmingly dominated by BOLD effects (Bandettini et al., 1992). In this study a TR of 1.7 second was used with 16 slice imaging without saturation bands. Nevertheless, the PET data allows us to confidently assert that any unsuspected flow effects would be linear in nature. If any such effects are indeed present in the BOLD fMRI data, the clear implication is that there remains an underlying nonlinearity that is not explained by unsuspected flow sensitivity of the sequence used.
An important question is whether the nonlinearity of BOLD contrast in auditory cortex and periauditory areas demonstrated here will be found in other areas. The BOLD response to a reversing checkerboard in primary visual cortex has a nonlinear dependency on reversal rate (Kwong et al., 1992). This is closely paralleled by a nonlinear dependency of rCBF on reversal rate. This would suggest, that in contrast to the auditory cortex results shown here, that the relationship between rCBF and BOLD is linear in visual cortex. However it may be premature to conclude that the relationship between BOLD and rCBF is different in separate areas of primary sensory cortex. More recent results show that the cerebral metabolic rate of oxygen in visual cortex shows a nonlinear dependency on checkerboard reversal rate, but that this relationship is rather different to that between rCBF and reversal rate (Vafaee et al., 1998). This implies that the coupling between rCBF and oxygen consumption is not the same over all reversal rates, and calls into question the apparent identity of the BOLD and rCBF frequency dependence in visual cortex.

8.3.6. Implications for functional imaging experiments

These results have practical implications for the design of functional activation studies. Stimulus rate is clearly a significant determinant of BOLD contrast in auditory cortex. Moreover the relationship is strongly nonlinear, in contrast to PET measurements. The interpretation of cerebral responses to activation can therefore only be meaningfully interpreted with reference to the stimulus presentation rate. Moreover, the form of the relationships between BOLD contrast, rCBF and word presentation rate suggests that at low stimulus presentation rates, BOLD fMRI is especially sensitive at detecting changes in activation. However at higher stimulus presentation rates fMRI is less sensitive to relative changes in stimulus presentation rate. It is clear that the stimulus-dependency of flow-sensitive fMRI sequences warrants investigation; the present data predicts that such sequences will show linear rate dependency similar to the PET data here.

The importance of these results is twofold. First, they re-emphasise the dependence of regional cerebral blood flow and deoxyhaemoglobin levels on stimulus presentation rate. This dependence can be exploited in the design of experiments that use variation of stimulus presentation rate to study the influence of task requirements on this relationship (Frith and Friston, 1996). Second, they suggest that the relationship between BOLD fMRI
Neural correlates of selective attention

contrast and cerebral blood flow as measured by PET is nonlinear. This has implications for theoretical models of the coupling between cerebral blood flow and oxygen metabolism during neural stimulation. While the present data are not sufficient to identify the proximate cause of the nonlinearity of BOLD image contrast with respect to auditory stimuli, this unique dataset allows confident attribution of the nonlinearity to factors other than rCBF. The temporal dynamics of the mismatch between local blood flow and oxygen metabolism that form the basis of the BOLD contrast are therefore complex. Varying the rate of stimulus presentation will prove to be a useful tool in further study of the interrelationship of neural activity, cerebral blood flow and oxygen extraction.

The nonlinearity in the relationship between BOLD contrast and stimulus presentation rate substantially complicates the interpretation of experiments that characterise attentional effects on stimulus presentation rate, such as those presented in (Chapter 3). The presence of a curvilinear relationship in fMRI between presentation rate and evoked BOLD contrast means that a simple characterisation of attentional effects in terms of altered intercept or altered slope is not possible. For this reason the work presented in Chapter 3 was not subsequently extended into fMRI. Alternative methods of studying the processing of unattended stimuli were used instead. This work is presented in Chapter 5 & Chapter 6.

In a further experiment, event-related fMRI responses to single words presented auditorily every 16 seconds were collected using an identical protocol to that described above. This new dataset was used together with that described above to further investigate the nature of the nonlinear BOLD response and show that this could be accounted for successfully in terms of a significant second-order Volterra kernel. This work is not submitted as part of this thesis: the interested reader is directed to the published peer-reviewed paper (Friston et al., 1998b).
Neural correlates of selective attention

Chapter 9 Supporting material

During the course of my thesis I have engaged in a number of different collaborative projects complementary to the main thrust of the work. Whereas the work presented previously was conducted with myself as primary investigator and author, the work presented here was conducted as a collaborator. This material is presented here for completeness and as it is referred to elsewhere in the thesis where relevant. Original publications are bound in for convenience following this chapter.

9.1 The role of right parietal cortex in perception of sound movement

The function of right parietal cortex has traditionally been associated with the allocation of visuospatial attention. The experimental work presented in the thesis has not emphasised the function of this cortical area. Here I present collaborative work (Griffiths et al., 1998) with Dr. Tim Griffiths (Newcastle University). We use an auditory psychophysical paradigm in which auditory stimuli with physically identical components produce either a vivid perception of lateralised sound movement, or a stationary percept in the midline. Comparing these two conditions reveals differential activity associated with sound movement in a distributed network of areas including right parietal cortex. These findings suggest a more general role for parietal cortex in the processing of both auditory and visual information.

9.2 Right parietal cortex and binocular rivalry

When different images are presented to the two eyes, perception alternates spontaneously between each monocular view, a phenomenon known as binocular rivalry. This spontaneous perceptual phenomenon provides a useful tool to investigate the neural basis of visual awareness, as changes in visual perception occur spontaneously in the absence of any changes in the stimulus. Differences in neural activity associated with such changes can therefore be directly related to changes in visual awareness rather than changes in the stimulus. Dr. Erik Lumer (University College London) and myself investigated binocular rivalry using event related fMRI to identify brain activity time locked to the occurrence of the spontaneous perceptual alternations (Lumer et al., 1998). Cortical regions whose activity reflected perceptual transition included extrastriate areas of the ventral visual pathway, and right parietal and prefrontal cortex. Whereas
Neural correlates of selective attention

modulation of activity in the extrastriate areas was also seen during nonrivalrous perceptual changes, activity in the right prefrontal and parietal cortex was specifically associated with binocular rivalry. In subsequent work we showed that subjects' experience during rivalry was associated with a covariation in activity between a very similar distributed network of visual and nonvisual areas (Lumer and Rees, 1999). More recently, a similar study investigating the perception of bistable figures (such as the Rubins face-vase illusion or the Necker cube) has also shown that right frontoparietal activity is specifically associated with transitions between different perceptual states (Kleinschmidt et al., 1998). Taken together, these findings indicate that areas traditionally associated with the deployment of visuospatial attention are also involved in phenomena such as rivalry where there is no differential allocation of attention. We speculate that this may reflect some underlying operation carried out by prefrontal and parietal cortex that is common to both spatial attention and binocular rivalry. It is striking that both attention and perceptual rivalry entail the suppression of visual information from conscious perception. Monocular stimuli become intermittently invisible during rivalry; similarly unattended stimuli, as shown in this thesis (see, for example, Chapter 6), have a diminished impact on awareness. Both phenomena may therefore call upon a common neural machinery in frontoparietal cortex, involved in the selection of neuronal events leading to visual awareness.
Changes in the delay (phase) and amplitude of sound at the ears are cues for the analysis of sound movement. The detection of these cues depends on the convergence of the inputs to each ear, a process that first occurs in the brainstem. The conscious perception of these cues is likely to involve higher centers. Using novel stimuli that produce different perceptions of movement in the presence of identical phase and amplitude modulation components, we have demonstrated human brain areas that are active specifically during the perception of sound movement. Both functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) demonstrated the involvement of the right parietal cortex in sound movement perception with these stimuli.

The perception of movement in auditory space by humans depends on a number of cues. The movement of sounds in space produces changes in the sound considered at each ear alone and changes in the relative phase and amplitude of the sound's spectral components between the two ears. For broad spectrum sounds, the spatial filtering properties of the pinnae provide another cue for the perception of spatial sound properties and are responsible for the external quality of the perception.

The neural basis for the perception of sound movement is not firmly established by animal work. The detection of differences in sound phase and amplitude at the two ears depends on the convergence of the inputs to each ear. This convergence first occurs in nuclei of the superior olive in the brainstem. Neurons sensitive to changing sound phase or amplitude cues at the two ears have been described in the inferior colliculus and primary auditory cortex. The detection of cues based on the spectral shape of sound may depend on a different brainstem pathway. Neurons in the auditory cortex have also been shown to be selectively activated by the actual movement of sounds in space. Animal lesions that involve the primary auditory cortex produce a deficit in the performance of tasks based on the detection of dynamic phase differences between the ears.

The auditory pathway described in animals from the cochlea to the auditory cortex is therefore necessary for the perception of sound movement. Human lesion work also suggests that the convergence of the inputs to the two ears in the brainstem is important for the detection of interaural cues that produce a perception of sound movement. However, another human lesion study suggests that sound movement perception depends on processing beyond the auditory cortex in the right hemisphere, and that the pathway up to the auditory cortex is therefore not sufficient to underlie the perceptual process.

This study specifically addresses the question of which brain areas are responsible for the conscious perception of sound movement in humans, as opposed to the simple detection of the underlying cues. The study's hypothesis was that sound movement perception depends on processing in cortical areas beyond the primary auditory cortex. We have used novel stimuli that contain identical changes in the phase and amplitude at the two ears but produce different perceptions of sound movement. These stimuli allow us to identify brain areas where activity increases with the perception of sound movement. That activity has been measured in two separate experiments by BOLD (blood oxygen level-dependent) fMRI response and by regional cerebral blood flow as measured by PET.

Results
PSYCHOPHYSICAL DATA
All subjects underwent psychophysical testing using a novel 500-Hz stimulus, presented over one second, containing a linear change in both the phase and the amplitude difference between the ears. Considered alone, both the phase and amplitude changes may be perceived as sound movement toward one side. When the directions of the perceived movements generated by these two cues are opposite to one another, cancellation or trading can occur; the stimulus is a dynamic extension for those used in static time-intensity trading experiments. For all subjects, a point could be defined at which there was exact cancellation of the movement percept due to the two cues and a single static sound image was perceived in the midline (Fig. 1). The point of cancellation for the phase and amplitude ramps varied between subjects (Table 1). The mean amplitude/phase ratio at the point of trading was 0.86 (standard deviation 0.34).

During the PET and fMRI experiments, subjects were presented with two sound conditions (Fig. 2). The cancel condition represents the dynamic time-intensity-traded stimulus discussed above.
During the 'cancel' epochs, subjects listened to repeated stimuli containing phase and amplitude modulations, set at the point of cancellation so that there was no perceived movement. During the 'add' epochs, subjects listened to stimuli containing phase and amplitude changes of the same magnitude as in the cancel condition, but the direction of perceived phase or amplitude change was in the same direction, so that there was a strong resultant perception of movement. For the add condition, all subjects clearly perceived movement of the sound over either the phase or amplitude modulations, set at the point of cancellation. During the 'cancel' epochs, subjects listened to either condition. For the add condition, all subjects performed at a location at least halfway between the midline and the maximum possible lateral displacement. In the add condition, the direction of perceived movement was randomized.

Thus, the add and cancel conditions represent stimuli that produce different percepts despite containing the same component phase and amplitude cues. This allows the stimuli to reveal areas involved in the perception of sound movement, as opposed to the detection of the component cues.

At the start of each scanning session, subjects were played pre-recorded runs of either the add or cancel condition. All subjects reported single fused percepts corresponding to the individual sounds in either condition. For the add condition, all subjects performed at 100% level for the identification of the direction of movement under scanning conditions. For the cancel condition, all subjects scored at 50% (chance) level.

**IMRI STUDY**

During the IMRI study, subjects listened to 40 second epochs of either the add or cancel condition, alternating with rest. Over the 40 seconds, subjects were presented with 33 stimuli. Figure 3a shows the comparison between the IMRI BOLD responses for the add (288 scans) and cancel (288 scans) conditions, based on a group analysis using statistical parametric mapping. Significant activation of posterior parietal cortex occurred in two areas in the right inferior parietal lobule (Brodmann area, BA40), in the right superior parietal lobule (BA7), and in the left inferior and left superior parietal lobules. Analysis of the BOLD signal change between conditions for individual subjects showed a consistent increase in the three subjects in the more superior area in the right inferior parietal lobule (Fig. 3b). An increase in activation was also shown in the left and right prefrontal cortex, the cerebellum, and the right insula. Table 2 lists the areas of activation with their coordinates.

The comparison of the two sound conditions with rest showed significant bilateral activation of the primary auditory cortex (A1) in Heschl's Gyrus\(^1\) (right coordinates -46 -24 10, Z = 6.9; left coordinates -50 -26 8, Z = 6.0); again, there was differential activation in A1. Areas of significant bilateral activation of A1 were also shown in Heschl's Gyrus*\(^*\) (right coordinates 46 -24 10, Z = 6.9; left coordinates -46 -26 8, Z = 6.0). No significant difference at A1 even without correction for multiple comparisons.

**PET STUDY**

During the PET study, subjects were scanned over an 80-second acquisition period while they listened to the add or the cancel condition. Over a typical acquisition period of 80 seconds, subjects were presented with 66 stimuli. Figure 4 shows the comparison between the add (30 scans) and the cancel condition (30 scans) in the PET experiment. A single area of right parietal lobe activation was demonstrated, situated 18 mm from the superior area in the inferior parietal lobule demonstrated in the IMRI experiment (coordinates 24 -40 66, Z = 3.49). The comparison between the two sound conditions showed no significant difference at A1 even without correction for multiple comparisons.

**Discussion**

In this study we have used a novel psychophysical stimulus to demonstrate cortical areas where activity increases when sound movement is perceived. The use of stimuli with the same acoustic structure allows these areas to be interpreted in terms of perceptual and cognitive processing, rather than in terms of the earlier acoustic processing. Thus, this study addresses the question of how sound movement is perceived in general. The IMRI and PET studies converged to show right parietal lobe activation, and additionally are consistent with previous human lesion studies showing posterior right hemisphere involvement in auditory spatial perception.\(^1\)\(^3\)\(^5\)

A striking feature of this work is the demonstration of activity in areas in the IMRI experiment that are not shown by the PET study. Few previous studies have used the same stimulus in the same experiment with both techniques; the demonstration of additional

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**Table 1. Cancellation point for each subject.**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Rate of interaural amplitude change at trade point, k(_a) (s(^{-1}))</th>
<th>Rate of interaural phase change at trade point, k(_b) (s(^{-1}))</th>
<th>Trading ratio amplitude/phase</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>0.10</td>
<td>0.22</td>
<td>0.43</td>
</tr>
<tr>
<td>2</td>
<td>0.10</td>
<td>0.17</td>
<td>1.43</td>
</tr>
<tr>
<td>3</td>
<td>0.15</td>
<td>0.12</td>
<td>1.26</td>
</tr>
<tr>
<td>4</td>
<td>0.10</td>
<td>0.16</td>
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</tr>
<tr>
<td>5</td>
<td>0.15</td>
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</tr>
<tr>
<td>6</td>
<td>0.10</td>
<td>0.14</td>
<td>0.71</td>
</tr>
<tr>
<td>7</td>
<td>0.15</td>
<td>0.16</td>
<td>0.94</td>
</tr>
<tr>
<td>8</td>
<td>0.10</td>
<td>0.14</td>
<td>0.71</td>
</tr>
</tbody>
</table>

One subject (subject 2) took part in both experiments. The rates of amplitude and phase changes have the dimensions of s\(^{-1}\) as the amplitude changes over the one second presentation (proportional change in sound pressure) and phase changes (radians) are both dimensionless.

---

*Fig. 1. Function used to calculate the point of trading between the linear amplitude and phase excursions for subject 1. The rate of amplitude change, k\(_a\), is 0.1 s\(^{-1}\) (see Methods).*
within the stimulus add to produce a strong resultant percept of movement. Stimuli for the cancel condition contain the same areas in the fMRI experiment may be based on methodological differences in the techniques, or due to biological differences in the nature of the task carried out.

**Dynamic Time-intensity Trading**

The two conditions used in the imaging experiments produced different perceptions of movement in the presence of identical interaural phase and amplitude modulation. We have been able to quantify this different perception in terms of psychophysical performance. The variation between subjects in the trade point demonstrated for the dynamic time-intensity trade is notable and a phenomenon that is well established in static time-intensity trading. No subject reported "double images" in the cancel condition used, as have been reported in some studies of static time-intensity trading. This may be because sustained perceptual adjustment of the auditory image is only possible in the static case, in which the stimulus is constant for a prolonged period.

**Common Activation in the fMRI and PET Studies**

The fMRI and PET experiments both showed increased activation in the right parietal cortex during the perception of sound movement. The locations of the single area of significant activation in the PET experiment and the superior area in the inferior parietal lobule in the fMRI experiment are within the combined resolution of the two experiments, being situated 18 mm apart, with the use of a 5 mm filter in the fMRI experiment and 16 mm filter in the PET experiment. PET and fMRI are both indirect measures of regional brain activity; however, the fMRI response and the regional cerebral blood flow obtained with PET are not identical. The fMRI response depends on blood oxygen level, whereas PET indicates local blood flow. It is possible that the maximum changes in blood oxygen level are not at the same position as the maximum changes in local blood flow.

The activation in the right parietal cortex is consistent with the idea that analysis of spatial sound properties, including movement, occurs beyond the primary auditory cortex in the right hemisphere, as suggested by human lesion experiments. One study used a lesion-mapping technique to identify the locus corresponding to a static lateralization deficit demonstrated by interaural amplitude testing. Subjects with deficits were found to have lesions in the posterior right hemisphere. Another study demonstrated a dissociated deficit in sound movement detection due to a posterior right hemisphere lesion that was distinct from the auditory cortex. That lesion involved the right parietal cortex, in addition to the right insula, which was activated in a previous PET auditory movement study using an interaural phase paradigm.

We considered whether the areas differentially activated by the movement task might correspond to areas for the perception of sound movement, or whether they might have a less specific role in the perception of static auditory space. There is a longstanding psychophysical debate about whether sound movement perception depends on detection of velocity per se or sequential static perception. The current experiment was not designed to distinguish between the two, but to demonstrate areas involved in sound movement perception, whatever the underlying mechanism. We have purposely used a low sound velocity (approximately half of the maximum possible lateral sound source displacement in one second); this velocity is clearly perceived as moving by all subjects and can be tracked. This is in contrast to the sudden changes in position that occur with the very rapid sound-movement velocities that have been used in some experiments, in which perceptual explanations based on sequential static perception become much more compelling. The low sound-movement velocity in the current experiment makes either velocity detection or sequential static detection mechanisms possible.

We also considered a possible attentional basis for the activation demonstrated in the movement condition, that is, an activation due to lateralized spatial shifts of auditory attention. In visuomotor attention tasks, parietal cortex is active when subjects have to make a response to a target presented at a location they do not expect. However, this effect depends on the subject being required to make a speeded motor response to an unexpected target, and there is no evidence for such spatial cueing effects in auditory attention. In the present study, the subjects did not make responses, and the loci of significant differences between the add and cancel condition (see Methods) in the fMRI experiment:

<table>
<thead>
<tr>
<th>Region</th>
<th>Area</th>
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<th>Z Score</th>
</tr>
</thead>
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</tr>
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<td></td>
<td>Left postcentral</td>
<td>-44 -32 62</td>
<td></td>
</tr>
<tr>
<td>Frontal</td>
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<td>58 8 46</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Right Gli/insula</td>
<td>34 24 -8</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>Left [6]</td>
<td>-36 0 58</td>
<td>6.5</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
<td>Left Gli</td>
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<td>6.1</td>
</tr>
<tr>
<td></td>
<td>Left [6]</td>
<td>-22 2 60</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>Anterior Cingulate</td>
<td>-10 50</td>
<td>5.6</td>
</tr>
<tr>
<td>Cerebellar</td>
<td>Right hemisphere</td>
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<td>6.1</td>
</tr>
<tr>
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<td>Right hemisphere</td>
<td>-26 -64 -18</td>
<td>4.9</td>
</tr>
<tr>
<td></td>
<td>Medial/vermis</td>
<td>4 -78 -18</td>
<td>5.6</td>
</tr>
</tbody>
</table>

The abbreviations for the individual areas are as in Talairach and are given with the Brodmann area based on that atlas in brackets. LP, parietal lobe; LPi, superior parietal lobe; LPs, inferior parietal lobe; LFS, superior frontal lobe; Gli, inferior frontal gyrus.
Fig. 3. Areas of increased activation using the add condition compared to the cancel condition in the fMRI experiment (see Methods). (a) Group comparison for three subjects superimposed on a T1-weighted template. The posterior parietal areas of maximal signal change are highlighted by arrows. (b) Percentage change in BOLD signal measurements for individual subjects from the superior right posterior parietal areas in (a). (c) Percentage change in BOLD signal measurements for individual subjects from the inferior right posterior parietal areas in (a). (d) Percentage change in BOLD signal measurements for individual subjects from the left posterior parietal area in (a). The BOLD signal bars are relative to an arbitrary origin, and the figure can only be used to compare the blood flow between the conditions. Error bars correspond to one standard error.

The auditory cortex in sound-movement perception

Neither the fMRI nor the PET experiments showed any increase in activation in auditory cortex during sound-movement perception. This is contrary to what might have been predicted from single-unit recordings in animals, showing neurons in the auditory cortex with selective responses to spatial sound cues. However, the actual differences in firing rate of neurons in the auditory cortices that show spatial selectivity are subtle. If neurons in human auditory cortex behaved similarly, such subtle responses might not be apparent using a technique based on the detection of local summed activity, especially under fMRI scanning conditions where saturation effects in the BOLD response are possible. Thus, the absence of a differential response in auditory cortex to the two sound stimuli does not exclude its involvement in the task.

Additional activation in the fMRI study

The fMRI experiment showed areas of activation in the left parietal cortex and in bilateral frontal areas that were not seen with PET. This may be because the contrast between the two sound conditions in the fMRI experiment was based on 288 scans per condition, compared to 30 scans per condition in the PET experiment. The stimuli used for the two functional imaging experiments were identical and presented at the same sensation level relative to background noise, and the psychophysical performance of the subjects under scanning conditions was the same. However, despite the acoustic isolation in the fMRI experiment, the subjects did hear considerable background noise generated by the scanner. The task might then have additionally included an element of auditory streaming in order for the subject to separate the stimulus from the noise. This is the process of separating auditory perceptual objects, analogous to Gestalt processing in the visual system, when the objects would be called figure and ground. This process, and the shorter fMRI epochs, may have increased the attentional load in the fMRI experiment, and thus have engaged attentional mechanisms that may not have been activated to the same degree in the PET experiment.

Frontal and parietal activation have been described in studies of auditory selective attention. A PET study of auditory selective attention, using a paradigm based on pitch change, suggests the existence of an anterior cingulate and predominantly right frontal net-
work, which is supramodal. That study incorporated lateralization to disengage stimulus-dependent and independent effects. However, it cannot be compared directly with the present study, which explored the detection of spatial cues without a specific lateralized attention task. Another study of selective attention by fMRI in consonant-vowel discrimination used binaural and dichotic listening conditions to vary the attentional load (again requiring lateralized attention in the dichotic condition), and showed bilateral increased parietal activation in the task demanding greater selective attention.

The prefrontal activation demonstrated in the present experiment might also be related to spatial monitoring, which has been shown to involve the prefrontal areas in a visual spatial monitoring task. Spatial monitoring refers to the active checking of the incoming spatial auditory information. There was no spatial search strategy or output task required in this experiment, but activation of spatial working memory by a random sequence of moving tones with different directions is also possible. The areas of frontal activation we describe are not within the accepted limits for the frontal eye fields, but a role for these areas in spatial attention linked to eye movements cannot be excluded.

A PERCEPTUAL AND ATTENTIONAL NETWORK

Whatever the mechanism, the additional activation seen in the frontal cortices cannot be explained in terms of abstract spatial representation in the same way as the parietal activation. The frontal activation is hypothesized to be a post-perceptual phenomenon. The activation of both frontal and parietal areas in the movement task represents a form of functional connectivity for which there is an established anatomical basis. The prefrontal areas receive projections from both ventral parietal cortex (area 7) and from area PA/LIP in the monkey. We suggest that the parietal areas, in conjunction with the prefrontal areas that we have demonstrated in the fMRI experiment, form a network involved in sound spatial perception and selective attention.

Methods

Subjects: Three subjects participated in the fMRI experiment and six subjects in the PET experiment. All subjects were right-handed, without hearing or neurological disorder and normal structural MRI scans. All subjects gave informed written consent, and the study was approved by the local hospital ethics committee and conducted under certification from the Administration of Radioactive Substances Advisory Committee (Department of Health, London, UK).

Stimuli: Stimuli for all experiments were 500-Hz tones containing changes in both phase and amplitude between the ears. The mean sensation level was 50 dB in all experiments. The sounds were all one second long. This duration was chosen to ensure that subjects could perceive the movement of the sound, as opposed to a sudden change in position. In all sounds, the phase was linearly advanced at one ear as it was simultaneously retarded at the other, as occurs when a sound moves in the horizontal plane around the head. This change in the instantaneous phase at either ear is identical to a frequency modulation, but subjects are much more sensitive to the phase cue when there is a reference tone in the other ear. Subjects perceived the lateral movement but not the monaural frequency change with the modulation depths used here. The amplitude in all sounds was also linearly increased in one ear and decreased in the other. Considered alone, both the phase and amplitude changes produce a perception of sound movement from the midline to one side. When the perceptions due to the phase and amplitude changes are in the same direction, they add to each other (add condition). When the perceptions due to the phase and amplitude changes move in opposite directions, they can cancel (cancel condition), so that subjects perceived a single stationary sound image in the midline. The add and cancel pressure waveforms, x(t), at either ear for a given subject are represented below for the case of (1) an add stimulus producing perceptual movement to the right and (2) a cancel stimulus:

1. left x(t) = A0 + (1 - k) sin(2πft - kgt),
   right x(t) = A0 + (1 + k) sin(2πft - kgt)
2. left x(t) = A0 + (1 - k) sin(2πft + kgt),
   right x(t) = A0 + (1 + k) sin(2πft - kgt)

f = carrier frequency (500 Hz for all stimuli), A0 = starting amplitude, k = constant determining the rate of amplitude change, k = constant determining the rate of phase change, k generated the rate of phase change necessary to cancel the movement due to the amplitude cue in the cancel condition. The values of k and k were fixed for all stimuli presented to any given subject. The waveforms were smoothed on and off over 20 ms using a cosine squared function. The add and cancel conditions represent stimuli that contain identical magnitudes of component amplitude and phase modulations, but which produce different perceptions of movement. This allows their use in categorical functional imaging paradigms to investigate sound movement perception.

Psychophysical testing: All subjects underwent psychophysical testing in a quiet environment, using headphones. In addition, the subjects for the fMRI experiment were tested using the (fMRI) sound delivery equipment immediately before the scanning session. For all subjects, a point was defined for the cancel condition where the perceived movement was cancelled by varying the interaural phase modulation for a fixed change in interaural amplitude. The rate of interaural amplitude change, k, was fixed at either 0.10 s⁻¹ or 0.15 s⁻¹ for each subject; some subjects required the greater amplitude change because the amplitude change of 0.1, when presented alone, was subthreshold and did not produce a perception of movement. A two-alternative, forced-choice procedure was used with two intervals that both contained the fixed amplitude change. The direction of amplitude change was opposite in the two trials, and the order of trials randomized. The sound also contained ramp phase changes, which produced a perception of movement in the opposite direction to the movement due to the amplitude ramp alone. The stimulus length was one second, and the interstimulus interval was one second. The rate of interaural phase change, k, was randomly varied between zero and a value that always produced a perception of movement in the direction of the phase change. Five levels of phase change were used with at least 20 trials per level. Subjects were required to identify the trial in which the sound appeared to move to the right. A response was counted as correct if the subject chose the interval containing the phase change producing a perception of movement to the right. The percentage of correct trials was determined as a function of phase change to allow a 50% trade point to be defined for each subject. This function is shown in Fig. 1 for subject 1. When the phase cue was insufficient to cancel the amplitude change, the subject chose the interval in which the amplitude signal moved to the right, and therefore scored less than 50%. When the phase cue was more than sufficient to cancel the amplitude change, the subject scored above 50%. The trade point, marked with an arrow on Fig. 1, represents the point where phase and amplitude cancelled each other, and subjects did not perceive movement in either interval and therefore performed at chance. This value of k was used in the imaging experiments.

MRI experiment: Stimuli based on the add or cancel condition were delivered over an acoustically isolated system of speakers and graduated tubes at a sensation level of 50 dB, set when the scanning sequence was running. A combination of external ear defenders and ear plugs around the final tubes within the ear canal was used for passive attenuation of the scanner noise.
All stimuli contained identical phase and amplitude modulations, determined psychophysically prior to the scan. During the movement epochs, subjects were presented with stimuli in which the movement perception added, to give a perception of movement to the left or the right in random order. All subjects were able to correctly identify the correct direction of movement with 100% accuracy, and perceived movements from the midline to a point more than halfway between the midline and the maximum possible excursion toward one ear. In the control epochs, the stimulus with cancellation was used. Epochs of either sound condition were presented alternating with silence. The epochs were approximately 40 s long, and subjects were presented with 33 stimuli during the sound epochs. There was no output task, and subjects were instructed to listen for any changes in the position of the sound and required to base a visual cross-piece placed at the mid-point of the visual axis. Electro-oculogram recording, carried out during a separate session with stimulus presentation but no scanning, demonstrated no eye movements.

fMRI scanning and analysis. BOLD contrast image volumes were acquired at 2.0 T (Siemens Vision, Erlangen) with gradient-echo echo-planar imaging (TR/TE = 6000 ms/40 ms). Each volume comprised sixty-four contiguous 3-mm slices, with an in-plane resolution of 3 × 3 mm. Each subject underwent three consecutive imaging sessions comprising 384 such volumes. The first six volumes of each session were discarded to discount T1 saturation effects. The movement and control conditions were presented in a fixed order alternating with rest (baseline). Each epoch lasted for seven volumes (approx. 42 s). For each subject separately, the TR-echo time-series was realigned to the first image, stereotactically normalized and smoothed with an anisotropic Gaussian kernel of 5 mm FWHM. The entire imaging time-series for each subject was used for a group analysis, representing 1134 image volumes in total. Condition-specific effects were estimated using the general linear model and theory of Gaussian fields as implemented in SPM96. A high-pass filter with a cut-off frequency of 0.19 cycles per min modelled and excluded low-frequency confounding effects in the time-series. A fixed-response, box-car model was used to characterize condition effects, using linear contrasts to test hypotheses about regionally specific condition effects. The SPM(2) analysis for the add minus cancel comparison was thresholded at a Z value of 3.09 (+ = 0.001 uncorrected for multiple comparisons), and the resulting foci were characterized in terms of both spatial extent and peak height corrected for multiple comparisons at the 5% level of significance.

PET scanning. Identical stimulus to those used in the fMRI experiment were delivered over insert earphones at a sensation level of 50 dB. Thus, subjects would attend to approximately 66 stimulus sounds during a typical acquisition period of 80 s. Subjects fixated a cross-piece and carried out no output task, as in the fMRI experiment. Twelve scans were carried out on a Siemens scanner in 3D mode, five with the add condition, five with the cancel condition, and two with silence. The order of scans was randomized across subjects. Statistical parametric mapping[34,35] implemented in SPM96 software (http://www.filion.ucl.ac.uk/spm) was used to compare regional cerebral blood flow between conditions. The data were smoothed with an isotropic Gaussian kernel of 16 mm FWHM.

Acknowledgements

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Neural Correlates of Perceptual Rivalry in the Human Brain

Erik D. Lumer,* Karl J. Friston, Geraint Rees

When dissimilar images are presented to the two eyes, perception alternates spontaneously between two monocular views, a phenomenon called binocular rivalry. Functional brain imaging in humans was used to study the neural basis of these subjective perceptual changes. Cortical regions whose activity reflected perceptual transitions included extrastriate areas of the ventral visual pathway, and parietal and frontal regions that have been implicated in spatial attention; whereas the extrastriate areas were also engaged by nonrivalrous perceptual changes, activity in the frontoparietal cortex was specifically associated with perceptual alternation only during rivalry. These results suggest that frontoparietal areas play a central role in conscious perception, biasing the content of visual awareness toward abstract internal representations of visual scenes, rather than simply toward space.

Bipolar rivalry provides a useful experimental paradigm with which to study the neural correlates of conscious perception (1–3). When dissimilar images are presented to the two eyes, they compete for perceptual dominance so that each image is visible in turn for a few seconds while the other is suppressed. Because perceptual transitions between the two alternative views occur spontaneously without any change in the physical stimulus, neural responses associated with perceptual processes can be distinguished from those due to stimulus characteristics. Psychophysical observations that perceptual fluctuations can also be experienced in normal vision and may therefore reflect a basic perceptual strategy to resolve visual ambiguity (4). Yet despite significant interest in the neural correlates of binocular rivalry (1–3), the mechanisms underlying these perceptual alternations remain unknown.

Here we investigate these mechanisms by characterizing neural activity associated with perceptual transitions per se, rather than activity associated with perceptual state during rivalry. Our results provide evidence for an involvement not only of occipitotemporal visual areas in binocular rivalry, but also indicate a specific and previously unknown role for frontoparietal areas in mediating the perceptual transitions experienced during rivalry. These results were obtained by measuring brain activity with functional magnetic resonance imaging (fMRI) in humans who reported their percepts under different viewing conditions (7). In the first condition, subjects viewed dichoptically stimuli consisting of a red-colored drifting grating shown to one eye and a green-colored drifting grating shown to the other eye. These images were chosen because they are highly dissimilar and readily produce full-field rivalry (7).
viewed through stereoscopic glasses. By manipulating the contrast setting in each image, we were able to bias perceptual dominance in favor of the grating, with long periods during which the grating was seen alone interrupted by shorter incursions of the face in conscious perception (Fig. 1) (8). Subjects used key presses to signal perceptual alternations from the grating to the face or vice versa. To control for motor effects, we compared the activity evoked during rivalry to that elicited in a second, nonrivalrous viewing condition that required the same type of motor responses. In this second condition, subjects were exposed to a "replay" of the rivalry paradigm without the rivalry component. This was achieved by presenting, in a chronology specified by the key reports during rivalry, either the face alone or the grating alone to one eye, and a gray patch of comparable luminance to the other eye. At transition times, physical blends of the face and grating were shown. This stimulation was designed to produce a perception that closely mimics rivalry in both quality and timing, thus resulting in a matched sequence of motor reports in the two conditions (9). Because prolonged periods of stereoscopic fusion can cause ocular fatigue, a third, passive condition was also introduced during scanning to allow visual rest.

Functional MRI scans from six participants were analyzed as a group to identify brain areas where activity was consistently correlated with the perceptual changes reported during either viewing condition (10, 11). To distinguish transient activity associated specifically with perceptual alternation from other, nonselective effects of viewing condition, we modeled the predicted hemodynamic response to each transition event and tested for the presence of such responses in the data while treating the mean condition-specific effects as confounds. Such an event-related modulation of the fMRI signals reflects neural activity that is locked to the time of occurrence of perceptual transitions between face and grating. During rivalry, transient responses associated with shifts of perception were found bilaterally in extrastriate areas of the fusiform gyrus, in right inferior and superior parietal lobules, and in bilateral inferior frontal, middle frontal, and insular cortex (Fig. 2 and Table 1). Event-related activity was also observed in regions of the anterior cingulate cortex, supplementary motor area (SMA), and left primary motor and somatosensory cortex, consistent with the preparation and execution of appropriate motor reports. The estimated hemodynamic response to single transition events is shown for a representative region of activation in Fig. 2 as a function of postevent time (12).

Although neural correlates of rivalrous transitions were expressed at multiple levels of the visual occipitotemporal pathway, such correlates were not observed in primary visual cortex. Perceptual transitions experienced during dichoptic stimulation were highly correlated with activity in extrastriate areas concerned with the representation of higher order properties of the visual scene (13). In particular, we detected transient responses that reflected these perceptual changes in regions of the fusiform gyr that included areas previously implicated in the perception of faces (14). By contrast to higher visual areas, early visual cortical areas showed no significant modulation of activity during rivalrous transitions. The differential involvement of early and higher visual cortical areas in rivalry was further confirmed by an analysis of activity correlated with the perceptual state rather than with the perceptual transitions reported by the subjects (15). These results in humans are consistent with recent findings in monkeys, suggesting that rivalry reflects central processes that take effect subsequent to the analysis of both monocular stimuli (3, 4).

By comparing rivalry to a nonrivalrous viewing condition, the present study also allowed us to provide an answer to the central issue in multistable perception—whether a specific machinery mediates the ongoing selection among sets of neuronal events competing for visual awareness. Because the rivalry and replay conditions yield similar perception and behavior, we expected them to engage common neural pathways associated with the internal representation of visual
scenes and the generation of appropriate motor responses. This was confirmed by the fMRI data: Event-related activity during replay was similar to that evoked during rivalry in visual areas of the fusiform gyri and in areas associated with movement (Fig. 2 and Table 1) (16). However, the rivalry and replay conditions differ fundamentally in the way that they achieve alternation perceiving. Whereas perceptual shifts during rivalry derive from an endogenous neural instability in the absence of changes in the stimulus, during replay they rely on exogenous manipulation of the visual input. Hence, we reasoned that any differential event-related activity between the two conditions would reflect these differences. Such a contrast would expose the mechanisms underlying the ongoing selection between conflicting perceptual interpretations during rivalry, a conflict that is not evoked by the replay condition. In addition, we predicted that the early visual cortex may show less transient activity during rivalry than during replay, because dichoptic stimulation causes little modulation of neuronal activity and possible inhibition at this stage of processing (3, 17), whereas saccadic neuron activity at stimulus onset and offset as generated during replay typically evoke strong cortical responses.

In contrast to the bilateral pattern of event-related activity in common across condition, activity specific to the rivalry condition was strongly lateralized to the right hemisphere. Selective activation during rivalrous perceptual transitions was seen in a region of right extrastriate visual cortex, Brodmann area (BA) 19, and in the right inferior parietal, superior parietal, and inferior frontal cortex (Fig. 3 and Table 1). This pattern of activation was both highly significant and consistent across subjects. We also characterized areas where transient activity associated with perceptual alternations was greater during replay compared with rivalry. Areas that showed such differential activation were located in early visual cortex (medial portion of BA 18), in accord with our prior hypothesis (Fig. 3 and Table 1). The comparison between the rivalry and replay conditions demonstrates a double dissociation: right frontoparietal regions show greater transition-related activity during rivalry, whereas early visual cortex shows greater transient responses during nonrivalrous viewing. These differences cannot be attributed to the generation of motor reports because the two conditions entailed the same sequence of motor responses and produced similar activity in cortical areas associated with movement (9). It is also unlikely that this differential pattern of activity results from nonspecific differences in attentional demands between the two conditions, such as arousal or difficulty. Frontoparietal activity has not been observed during the performance of other visual tasks in which attentional demands were varied systematically (18). Moreover, changes in attentional demands typically result in different levels of activation in ventral areas involved in representation of visual scenes (19), such differences were not observed in the present study when the two viewing conditions were compared. Instead,

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**Fig. 3.** Differential activation during rivalrous and nonrivalrous viewing. (A) Areas where transient activity related to perceptual shifts is greater under conditions of binocular rivalry compared with the replay condition, overlaid onto the average Talairach normalized anatomical MR image of the six subjects. Significant differential activation during rivalry (P < 0.05, corrected) is confined to the right hemisphere and involves frontoparietal structures previously implicated in the shifting of spatial attention. Distance from the anterior commissure is indicated for each coronal section. L, left; R, right. (B) A transverse section through the average normalized anatomical MR image, taken 9 mm below the bicommissural plane, on which are superimposed two foci of activation that represent early visual areas where activity related specifically in time to perceptual transitions is greater under conditions of replay compared with rivalry.

**Table 1.** Coordinates and Z scores for event-related activation. Shown in the table are loci where transient activity during rivalry is greater compared with replay (rivalry > replay); modulation of activity above baseline is measured when viewing dichoptic stimuli (rivalry) or replayed scenes (replay); and event-related activity is greater during rivalry compared with replay (rivalry > replay). Only the most significant peaks within each area of activation are reported in the table (P < 0.05, corrected).

<table>
<thead>
<tr>
<th>Cortical region</th>
<th>Talairach coordinates (mm)</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td><strong>Rivalry</strong></td>
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<td></td>
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<tr>
<td>Right fusiform</td>
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<td>-45</td>
</tr>
<tr>
<td>Left fusiform</td>
<td>-27</td>
<td>-69</td>
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<tr>
<td>Medial anterior cingulate/SMA</td>
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<td>0</td>
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<td>Right inferior frontal</td>
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<td>Right superior parietal lobule</td>
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<tr>
<td>Left motor/somatosensory</td>
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<tr>
<td>Left middle frontal</td>
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<td>39</td>
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<tr>
<td><strong>Replay</strong></td>
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<tr>
<td>Right fusiform</td>
<td>33</td>
<td>-45</td>
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</tr>
<tr>
<td><strong>Rivalry &gt; replay</strong></td>
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<td></td>
</tr>
<tr>
<td>Right inferior parietal</td>
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<td>-30</td>
</tr>
<tr>
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</tr>
<tr>
<td>Right lateral extrastriate (BA 19)</td>
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<td><strong>Replay &gt; rivalry</strong></td>
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<td>Left BA 18</td>
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<td>-78</td>
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</table>
The present results are more consistent with the notion that a distributed frontoparietal system specifically mediates the perceptual switches experienced during rivalry. Right frontoparietal areas have been traditionally implicated in visual tasks requiring spatial shifts of attention and working memory (20–24). Visuospatial neglect syndromes occur most frequently and are more severe after lesions in the right inferior parietal and inferior frontal cortex (21). Moreover, functional imaging experiments have shown that the region of superior parietal cortex identified in the present study is also engaged by successive shifts of spatial attention (22). Finally, differential activation of right extrastriate cortex has been reported in tasks directing attention to global aspects rather than local details of figures (23). But our results show that these cortical areas are also involved in a phenomenon that exhibits a number of differences compared to visuospatial attention. In contrast to shifts of attention, there is no spatial component to the perceptual transitions elicited during rivalry; moreover, where as attentional shifts are subject to top-down influences, rivalrous transitions recur in the absence of voluntary control; finally, spatial attention also engages visual and motor areas that were not activated during rivalry (24). Why then should both phenomena involve overlapping regions of frontoparietal cortex? One possibility is that these areas subtend a common neural machinery for spatial attention and perceptual rivalry. However, it is striking that both phenomena entail the suppression of visual information from conscious perception. Monocular stimuli become perceptually invisible during rivalry; similarly, sensory events associated with unattended stimuli have a diminished impact on awareness during covert attention. These effects occur in both cases in spite of a rather constant retinal input. Both phenomena may therefore call upon a common neural machinery in frontoparietal cortex, involved in the selection of neuronal events leading to visual awareness.

Thus, our results suggest that the role of frontoparietal areas in conscious perception extends well beyond that of spatial processing. Consistent with this notion, lesions of parietal and inferior frontal cortex cause disorders of nonspatial forms of perceptual selection, in addition to spatial disorders (25). Further investigation of frontoparietal function in both human and nonhuman primates may lead to a better understanding of the neural processes underlying the formation of perceptual states and the awareness of sensory stimuli.

REFERENCES AND NOTES

4. The notion that rivalry involves central rather than peripheral processes goes back, at least, to Helmholz [Treatise on Physiological Optics (Optical Society of America, New York, 1911)]. This view contrasts with a later proposal that rivalry results from competition between monocular channels at an early stage of visual processing. For a general review of the psychophysical evidence motivating these alternative accounts, see P. Walker [Psychol. Bull. 85, 370 (1979)] and R. Blake [Psychol. Rev. 93, 145 (1986)]. Recent studies have shown that rivalry occurs normally when conflicting images are rapidly exchanged between the eyes, thus arguing against monocular theories [N. K. Logothetis, D. A. Leopold, D. L. Sheinberg, Nature 382, 621 (1996)].
7. Participants were nonmetamic stereoscopic glasses and viewed a small projection screen through a mirror mounted on top of the IFI coil above the participant's head. Head movements were restrained by foam pads. Stimuli were projected onto the screen by a machine of the Optovue 1 series. They consisted of pairs of square images, each subtending approximately 3.7° of visual angle. Before scanning began, participants used a joystick to modify the lateral separation of the two images used during dichoptic stimulation so that each image could be seen only by one eye and that stereoscopic fusion and binocular rivalry could be comfortably attained. All subsequent stimuli presented during the scanning run were then presented at those locations. Subjects indicated with their index finger when they perceived the transition from face to grating or vice versa, using their dominant hand. A Siemens Vision (Erlangen) operating at 2 T was used to acquire BOLD contrast functional images. Image volumes were acquired continuously every 400 ms, each comprising 49 contiguous 3-mm-thick slices to give whole-brain coverage with an in-plane resolution of 3 mm by 3 mm. Functional imaging was conducted in two scanning runs comprising 1056 volumes in total. In each scanning run, after eight image volumes were discarded to allow for 1.07 s equilibration, each participant performed the rivalry task. Of the 415 (10 s) scans followed by the rivalry condition, 0.017 s remained for each 41 s of rest. Each condition was then repeated for a total of eight repetitions per run. At the beginning of each experimental session a T1-weighted anatomical image was acquired for coregistration with the functional images. 8. Because of the slow time constants of BOLD responses (2–3 s), the contrast of the face and grating stimuli were manipulated to prolong long intervals between consecutive perceptual alternations, and therefore optimize the conditions for detecting neurophysiological correlates of transition events by fMRI. Frequency history limits of dominance time for the face and grating were constructed for each participant from the rivalry reports collected during the scanning session. Of the 10 volunteers that were scanned, 6 had long mean dominance times and were retained for analysis of brain activity (4 males and 2 females; mean age, 31 years; age range, 27 to 34 years; 5 right-handed and 1 left-handed; mean face dominance, 2.9 s; mean grating dominance, 5.7 s).
9. Linear regression analysis demonstrated that the temporal sequence of key-press reports during re-play closely matched that of rivalry (regression slope = 1.02; R² = 1).
10. Analysis was carried out using Statistical Parametric Mapping software (SPM96, http://www.fil.ion.ucl.ac.uk/spm). The imaging time series was realigned, spatially normalized to the stereotactic space of Talairach and Tournois, and smoothed with a Gaussian kernel of 8 mm full width at half maximum. J. Talairach and P. Tournois, Co-Planar Stereotactic Atlas of the Human Brain (Thieme, New York, 1988); K. J. Friston et al., Hum. Brain Mapp. 5, 155 (1996); K. J. Friston et al., ibid., 2, 189 (1995); K. J. Friston et al., NeuroImage 2, 157 (1995); K. J. Friston et al., Magn. Reson. Med. 33, 346 (1995). Voxel-based activations usually and rivalry condition were identified by means of a statistical model containing two components that represent the transition responses produced by the transition events in each condition, together with two boxcar waveforms that modeled active and control events. These models were convolved with the 3-mm fMRI signal in the comparison between conditions. The resulting signal was then multiplied by a binary mask of the head (SPM96) and a correction factor for the effect of multiple comparisons was applied. The factor was a product of the number of significant voxels in the group analysis divided by the number of possible contrasts. The analysis of the contrast between face dominance and grating dominance was carried out by using the contrast between the two conditions as a regressor in a multiple regression analysis. The event-related contrasts, which constitute the effects of interest, were tested to see whether they could account for a significant portion of the variance. Independent of the functional response to the other regressors. All statistical results are based on a single voxel 2 threshold of 3.08 (corresponding to P < 0.0001) within a multiple comparison-corrected volume defined as the extent of the significant regressor. All significant activations were characterized in terms of their peak heights. In assessing statistical significance, we made a correction (based on the theory of random Gaussian fields) for multiple comparisons across the whole-brain volume examined and report only regions of activation above a threshold corresponding to P < 0.005, corrected (K. J. Friston et al., Hum. Brain Mapping 1, 210 (1994).
11. High Z scores in the group analysis reflect a significant activation above the severity level. The consistency of this activation was confirmed by examining positive correlations for contrast against 379, 485 (1996).
12. The reconstructed posterior Roland's four estimates to this estimate as there were events in the 10 seconds preceding the acquisition of the scan. Each sample point was displaced along the time axis by the latency between the acquisition of the scan and the occurrence of the preceding event; its orientation was calculated by adding to the value of the fitted hemodynamic response function at this latency the residual variance after complete model fitting. The sample points were used to construct a posterior histogram, with bins of 1.25 s.
15. To analyze further the hemodynamic activity associated with perceptual changes in the absence of stimulus change, we tested for the presence of activity that correlated with the perceptual dominance or suppression of the face stimulus during rivalry. Compared to our main analysis of multiple transitions per se, we expected that such a test would emphasize areas involved in the visual representation of faces, while de-emphasizing additional areas associated with transition events (22). Areas that were significantly more active when the face was perceived than when it was not seen (P < 0.05 corrected) were largely confined to the fusiform gyrus. Maximally activated loci were located at x = 36, y = -38, z = -25 (Z = 6.37); x = -33, y = -56, z = -15 (Z = 5.77); z = -39 (Z = 5.27).
16. Although both rivalry and transition events yielded similar hemodynamic responses in the anterior cingulate cortex, the location and extent of these activations were significantly different from those observed in the fusiform gyrus.
Proton Transfer Pathways in Bacteriorhodopsin at 2.3 Ångstrom Resolution

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Photosomization of the retinal of bacteriorhodopsin initiates a cyclic reaction in which a proton is translocated across the membrane. The immediate environment of the retinal Schiff base is shown in Fig. 2A. OD1 of bacteriorhodopsin is connected to the proton donor, the Schiff base, through a hydrogen-bonded water and forms a second hydrogen bond with another water. The other carboxyl oxygen atom of Asp86 accepts a hydrogen bond from Thr68. This structure forms the active site. The nearby Arg36 is the center of a network of numerous hydrogen-bonded residues and an ordered water molecule. This network defines the pathway of the proton from the buried Schiff base to the extracellular surface.

Bacteriorhodopsin is a small integral membrane protein that functions as a light-driven proton pump (1). Its seven-helical structure has been described (2–5) at increasing resolutions, most recently at 2.5 Å. The protein crystallizes from cubic lipid phase as a mixture of two or more single crystals. If the twinning in these crystals were ignored, nearly 50% of the scattering matter would be accounted for. Taking twinning properly into account yields a refined structure different in some respects from the one that first used crystals from cubic lipid phase (5). Also, the statistics of the refinement as well as the electron density maps are improved. The previously reported R factor and Rfree were 22.1% and 32.7%, respectively, for data with F > 3σ(F) between 2.5 and 5.0 Å, with an unusually high average B factor of 54 Å^2 (5). Calculating these parameters in the same way (omitting data higher than 5 Å), but not using a σa-based cutoff, we found the following values: R factor, 18.0%; Rfree, 23.6%; and average B, 26.7 Å^2. More detailed statistical information is given in Table 1.

The overall seven-helical structure is similar to those previously determined (3–5). The loop between helices B and C forms a short antiparallel β-sheet in the same orientation as in the electron diffraction structures (3, 4). We observed no density for residues 1 to 5, 154 to 166 (the loop between helices E and F), and 229 to 248 (COOH-terminus). In several positions equivalent to the diacyl lipid positions observed in one of the earlier structures from electron diffraction (3), we also observed long sections of density with various branch points that we interpret as native dihydro­phyll lipids, carried along through solubi­lization and cubic lipid phase crystalli­zation. Model building and refinement for these areas are in progress.

The densities and the refined model at locations of interest are shown in Fig. 2. The immediate environment of the retinal Schiff base is shown in Fig. 2A. OD1 of bacteriorhodopsin is connected to the Schiff base through a hydrogen-bonded water, labeled W401 (8). OD1 of bacteriorhodopsin accepts a hydrogen bond from another water molecule (W402) that in turn accepts a hydrogen bond from the Schiff base, a feature predicted and much discussed (9) but not detected before. This water molecule and Thr68, which is hydrogen-bonded to OD2 of bacteriorhodopsin (see below), should together lower the pK_a (K_a is the acid dissociation constant) of Asp86 and thereby stabilize the otherwise energetically unfavorable Schiff base–Asp86 ion pair in the unphotolyzed protein. If the two hydrogen bond donors were displaced or entered into hydrogen-bonding with other partners after photosomization of the retinal, the pK_a of Asp86 would be raised, and this would be a reason for its protonation by the Schiff base.

The extracellular region where proton release to the surface is induced by protonation of Asp85 (10) is shown in Fig. 2B. Because titration of Asp85 in the dark detects the dependence of its pK_a on the

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Neural correlates of selective attention


10-199
Neural correlates of selective attention


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