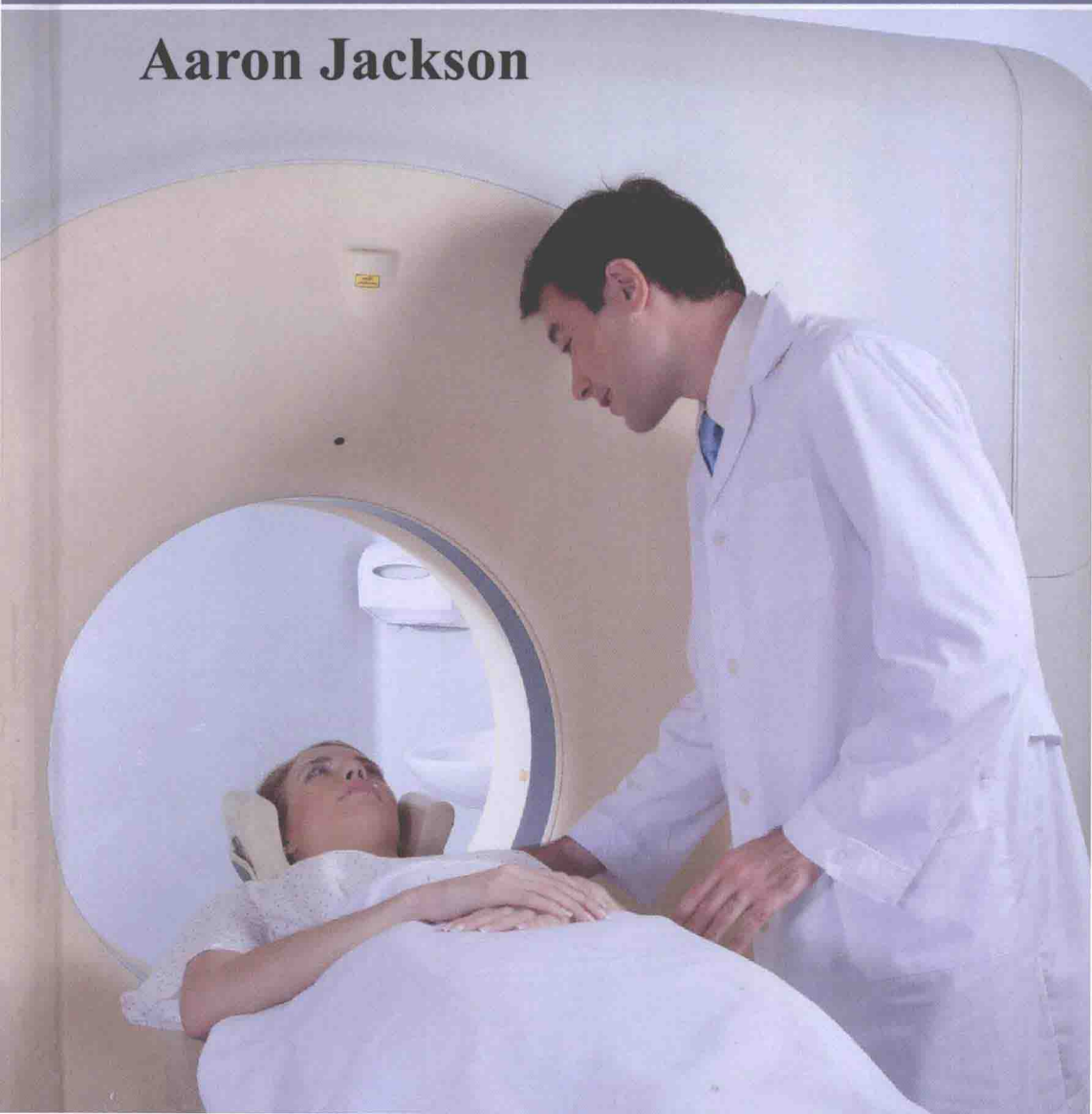
Functional Magnetic Resonance Imaging

Clinical Neuroimaging Applications

Aaron Jackson



Functional Magnetic Resonance Imaging: Current Neuroimaging Applications

Edited by **Aaron Jackson**

New Jersey

Published by Foster Academics,
61 Van Reypen Street,
Jersey City, NJ 07306, USA
www.fosteracademics.com

Functional Magnetic Resonance Imaging: Current Neuroimaging Applications
Edited by Aaron Jackson

International Standard Book Number: 978-1-63242-194-4 (Hardback)

Printed in China.

Functional Magnetic Resonance Imaging: Current Neuroimaging Applications

Preface

The current neuroimaging applications of functional magnetic resonance imaging are described in this book. The book deals with practical techniques of Functional Magnetic Resonance Imaging (FMRI) used in evaluation of cognitive applications in brain and neuro-psychological analysis using motor-sensory activities, language, orthographic diseases in children. The book will prove to be useful for readers learning applied neuro-psychological judgment plans in neuro-psychological research experiments, and to the comparatively learned psychologists and neuroscientists. It has been structured in a way to give the readers a fair understanding of the primary ideas of FMRI and also, physiological basis of FMRI. The book covers a variety of subjects starting with event-related stimulus and then moving forward to latest approaches in the practical field of constraint-induced movement therapy, accountability assessment, refractory SMA epilepsy and consciousness states. This book also imparts knowledge on the topics like decree-advised demeanor assessments, orthographic frequency neighbor evaluation for phonological activation and quantitative multi-modal spectroscopic FMRI for assessing varied neuropsychological conditions.

This book unites the global concepts and researches in an organized manner for a comprehensive understanding of the subject. It is a ripe text for all researchers, students, scientists or anyone else who is interested in acquiring a better knowledge of this dynamic field.

I extend my sincere thanks to the contributors for such eloquent research chapters. Finally, I thank my family for being a source of support and help.

Editor

Contents

Section 1

Basic Concepts of fMRI

1

Current Trends of fMRI in Vision Science: A Review

Nasser H. Kashou
Department of Radiology, Children's Radiological Institute, Nationwide Children's Hospital
Department of Radiology, Department of Ophthalmology, The Ohio State University Medical Center
Department of Biomedical, Industrial and Human Factors Engineering, Wright State University
USA

1. Introduction

Studying brain functional activities is an area that is experiencing rapid interest in the field of neuroimaging. Functional magnetic resonance imaging (fMRI) has provided vision science researchers a powerful and noninvasive tool to understand eye function and correlate it with brain activities. In this chapter, we focus on the physiological aspects followed by a literature review. More specifically, to motivate and appreciate the complexity of the visual system, we will begin with a description of specific stages the visual pathway, beginning from the distal stimulus and ending in the visual cortex. More importantly, the development of ascending visual pathway will be discussed in order to help in understanding various disorders associated with it such as monochromacy, albinism, amblyopia (refractive, strabismic). In doing so we will divide the first half into two main sections, the visual pathway and the development of the ascending pathway. The first of these sections will be mostly an anatomy review and the latter will discuss the development of this anatomy with specific examples of disorders as a result of abnormal development. We will then discuss fMRI studies with focus on vision science applications. The remaining sections of this chapter will be highlighting the work done on mainly oculomotor function, some perception and visual dysfunction with fMRI and investigate the differences and similarities in their findings. We will then conclude with a discussion on how this relates to neurologists, neuroscientists, ophthalmologists and other specialists.

2. Background

To motivate the discussion we begin by asking, what is the problem in visual perception? This will be answered briefly. In visual perception, we have both a distal and a proximal stimulus. The distal stimulus is what the subject is looking at, usually at a distance. In the case of vision, it determines the pattern of light arriving at the cornea. The proximal stimulus hits the sense organs directly. In the case of vision, it is the pattern of light arriving at the retina, for instance as a result of looking at the distal stimulus. There are several features that distinguish

the distal and proximal stimuli. The distal stimulus is 3-dimensional, independent of point of view, upright, and has no lens blur or filter. An example of the latter two is that when we look at a person their head is on top and their feet are on the bottom and the physical person does not get blurred. The proximal on the other hand is 2-dimensional, depends on point of view, inverted, blurred and filtered by the lens. So the main problem in visual perception becomes clearer; that is to retrieve information about the distal stimulus with only the proximal stimulus to work with. This is important because it affects the perceptual representation which is the endpoint of the perceptual process. Perceptual representation is the state of the visually-guided motor behavior (keeps us from bumping into things), visual pattern recognition, visual understanding, and memory. Basically, as the subject sees an object (distal stimulus), the input falls on the retina (proximal stimulus) and an output of the distal stimulus is perceived via perceptual representations. Note, that this is not the same as the distal stimulus, because there are two kinds of perception, veridical and illusory. There are many examples of visual illusions, in which the perceptual representation suggests an incorrect distal stimulus. That is, the apparent distal stimulus differs from the veridical distal stimulus. With this concept, we can now refine the problem in visual perception, as trying to understand how the visual system creates a perceptual representation of the distal stimulus with only the proximal stimulus as an input. Why is this a problem? Because the relationship of distal to proximal is not one to one, that is a distal stimulus can be seen as many proximal stimuli and proximal stimuli can be many distal stimuli. This leads to the inverse problem of trying to recover a visual representation from the input, even when many representations are consistent with the proximal stimulus. Thus, this is a motivation to begin discussing the visual pathway and understand the retinal (proximal) input to the brain.

3. Visual pathway

The visual pathway consists of many stages. We will focus on the ganglion cells, lateral geniculate nucleus (LGN), and the primary visual cortex (V1). The ascending visual pathway begins when light hits the back of the retina and stimulates the photoreceptors (rods and cones). These photoreceptors transform radiant energy into electrical activity, which is transmitted to retinal bipolar cells and then into retinal ganglion cells. The retina has several layers and sub-layers with corresponding cells, such as ganglion, amacrine, bipolar and horizontal. Each of these cells play a role in the visual system and have their own receptive fields. Again, in this chapter we choose to focus and discuss the ganglion cells.

3.1 Ganglion cells

There are two major classes of ganglion cells. The smaller midget, or parvo, cells comprise about 80 percent of these cells and the larger parasol, or magno, cells about 10 percent (Lennie et al., 1990). As with other cells in the retina, these ganglion cells have their own receptive fields known as center surround with either on-center (off-surround) or off-center (on-surround). There are several differences between these two types of cells. Parvo cells are dominant in the fovea as opposed to the magno cells, which are dominant in the periphery. The parvo cells are also characterized as having a sustained response while the magno have a transient response (Purpura et al., 1990; Schiller & Malpeli, 1978). At any given eccentricity, parvo cells have a higher spatial resolution, lower contrast sensitivity, slower conduction velocity, and a more sustained response than do magno cells (Shapley et al., 1981). The parvo cells have low contrast sensitivity and detect color and form, while the magno have high

contrast sensitivity and detect motion. Parvo cells rarely respond well to luminance contrasts below 10%, whereas magno cells often respond to stimuli with contrasts as low as 2% (Purpura et al., 1988; Sclar et al., 1990; Shapley et al., 1981). In addition to these two, there are other types of ganglion axons that exist; the more common of these are the konio cells which are small bistratified cells (Kaas et al., 1978). They are common in the parafovea, have low contrast sensitivity, and detect color. The major difference between the konio cells and the other two is that the konio have a uniform receptive field and thus have no spatial opponency. To many investigators the term konio has become synonymous with the blue-yellow pathway, just as parvo is now equated, too simplistically, with the red-green pathway (Sincich & Horton, 2005). But this is not always the case because, konio cells constitute a heterogeneous population of cells, some lacking blue-yellow color opponency (Hendry & Reid, 2000). The axons of all these ganglion cells exit the eye, forming the optic nerve and synapse in the midbrain. Since the diameter of the optic nerve and the number of the ganglion cell axons it contains are limited by the structure of the skull, not all the information that falls upon the retina is transmitted to the brain proper (Schwartz, 2004). Although there are more than 100 million photoreceptors within the retina, there are only 1 million ganglion cells, revealing an extensive degree of neural convergence (Curcio & Allen, 1990; Osterberg, 1935). At the optic chiasm, ganglion cell fibers from the nasal retina of each eye cross over to join the temporal fibers of the fellow eye to form the optic tract (Schwartz, 2004). The long axons of the retinal ganglion cells leave the eye, form the second cranial nerve (the optic nerve), and synapse in the dorsal lateral geniculate nucleus (dLGN), a midbrain structure (Schwartz, 2004). We will now discuss the LGN.

3.2 Lateral geniculate nucleus (LGN)

The primary target of the optic tract is the dorsal lateral geniculate nucleus (dLGN), a thalamic nucleus. In higher vertebrates, such as carnivores and primates, axons from the two eyes converge onto their primary target, the dorsal lateral geniculate nucleus (dLGN), but occupy distinct regions (the eye-specific layers) within this target (Guillery, 1970; Kaas et al., 1972; Linden et al., 1981). In primates (Rakic, 1976; 1977), the axonal terminals of ganglion cells of the two eyes initially share common territories within the dLGN, but through a process that eliminates inappropriately placed branches, projections from the two eyes become restricted to their appropriate layer. Most, but not all, retinal ganglion cells synapse in the six-layered structure. Layers 2, 3, and 5 receive input from the ipsilateral eye, whereas layers 1, 4, and 6 receive input from the contralateral eye, Fig. 1. The dorsal four layers, which are constituted of comparatively small neurons called parvo, or P-cells, are the parvocellular layers (layers 3,4,5,6). Larger neurons, commonly called magno or M-cells, comprise the two ventral magnocellular layers (layers 1,2). Axons from midget ganglion cells synapse on P-cells in the dLGN to form the parvo pathway, while axons from the parasol cells synapse on dLGN M-cells to form the magno pathway. The layers between the parvocellular and magnocellular layers contain very small neurons (konio cells). Studies have shown that konio cells provide the only direct geniculate input to layers 1-3 (Hendry & Yoshioka, 1994). The subcortical projection from the retina to cerebral cortex is strongly dominated by the two pathways (M and P pathways) the magnocellular and parvocellular subdivisions of the lateral geniculate nucleus (Shapley & Perry, 1986). The parvo layers receive input from color-opponent midget ganglion cells, whereas the magno layers are supplied by broadband parasol ganglion cells (Perry et al., 1984). Parvo pathway neurons show color opponency of either the red/green or blue/yellow type, which means that they respond to color change regardless of the relative luminance of the colors (Derrington & Lennie, 1984). The blue-yellow ganglion cells project to

the konio layers just ventral to the third and fourth parvocellular layers (Calkins & Hendry, 1996). Layers 5 and 6 have on-center receptive fields, and layers 3 and 4 have off-center receptive fields. Layers 1 and 2 have both on- and off- center receptive fields. These projections from the retina to the LGN then lead to the visual cortex.

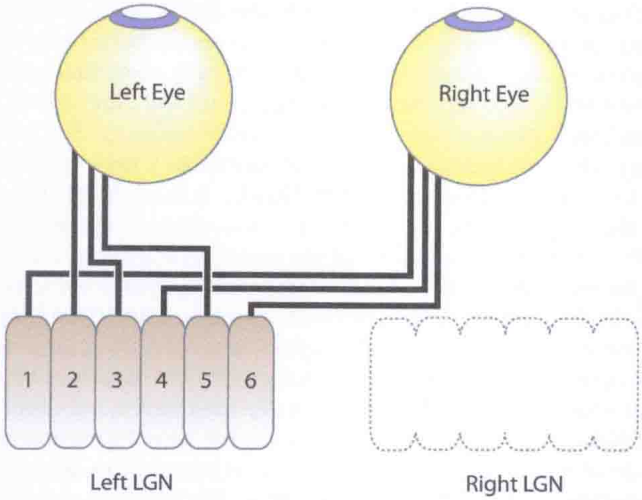


Fig. 1. Retinal ganglion cell projections to the lateral geniculate nucleus (LGN) of the thalamus. Note that layers 1,4, and 6 of the LGN receive visual information from the contralateral retina, whereas layers 2,3, and 5 receive visual information from the ipsilateral retina.

3.3 Primary visual cortex (V1)

The cells of dLGN send most of their axons to the cerebral cortex, specifically, the primary visual cortex (V1) along with the visual field representation in the retina and primary cortex. Inputs to V1, which are stratified by magno, parvo, and konio, become thoroughly intermingled by passage through the elaborate circuitry of V1 (Sincich & Horton, 2005). There are about 8 or 9 layers in V1. Layer 4 consists of three sublayers, 4A, 4B, and 4C. Layer 4C also is subdivided into 4Cα, and 4Cβ. The projections from the LGN go specifically to layer 4C and the information flows up and down from there (Merigan & Maunsell, 1993). The projections from parvocellular layers terminate primarily in layers 4A and 4Cβ, whereas those from magnocellular geniculate terminate in layer 4Cα (Fitzpatrick et al., 1985). Layer 4B receives direct input from 4Cα (M pathway), but not 4Cβ (P pathway) (Lund & Boothe, 1975; Lund et al., 1979). Layer 4Cβ projects to the blobs and interblobs (Horton & Hubel, 1981; Humphrey & Hendrickson, 1980). The blobs also receive major inputs from the M pathway by way of layers 4B and 4Cα (Blasdel et al., 1985; Fitzpatrick et al., 1985; Lachica et al., 1992; Lund, 1988). Fig. 2 gives the details of these connections.

More recently, Yazar et al. (2004) have found that some geniculate fibers terminate in both layers 4Cβ and 4A, implying either a direct parvo input to 4A or a konio input to 4Cβ. In layer 3B the cells in blobs and interblobs receive input from parvo (4Cβ), magno (4Cα), konio (4A), or mixed (4B) layers, in a range of relative synaptic strengths (Sawatari & Callaway, 2000). Cells in both 4Cα and 4Cβ project to layers 5 and 6 (Callaway & Wiser, 1996; Lund & Boothe, 1975). Feedback from layer 6 to the LGN is segregated only partially with respect to magno

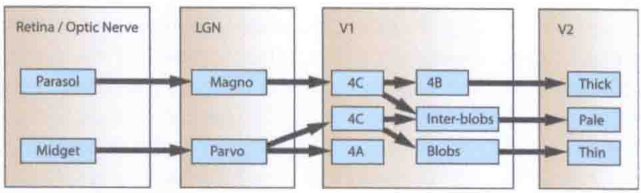


Fig. 2. Block diagram of ganglion cell mapping from retina through LGN, V1, and other cortical areas.

and parvo, thus mixing the geniculate channels (Fitzpatrick et al., 1994). There are two main types of cells in V1, stellate and pyramidal. The stellate cells are small interneurons found in layers 2-6 and the pyramidal cells are large relay neurons found in layers 2, 3, 5, and 6. The stellate cells are simple cells because of their receptive fields. The pyramidal cells are complex cells. The simple cells' receptive fields are of a certain size, are oriented in a certain way, and are sensitive to phase. They increase their rate of firing when stimulated in some places, and reduce it when stimulated in other places. The simple cells respond to a single spot of light and are additive and linear. The complex cells do not respond to a single spot of light, rather they respond to edges and bars, and are not sensitive to spatial phase. Many of the complex cells respond best to stimuli that move in one direction. So, if the stimulus is stationary, in the opposite direction, or a spot of light then the complex cells' receptive field will have no response. The complex cells are non-additive and are non-linear. Both the simple and complex cells respond to most proximal stimuli. All together, these cortical cells are tuned for spatial frequency, position, and orientation. This distinction is important in designing visual stimuli for fMRI studies to understand normal and abnormal visual function.

4. Development of the ascending pathway

We now describe how the visual pathway develops and the effects of abnormal development. During development anatomical projection patterns are restructured and functional reorganization takes place (Campbell & Shatz, 1992; Hubel & Wiesel, 1977; Shatz & Kirkwood, 1984; Wiesel, 1982). There are at least two ways by which neurons can be wired up accurately: connections may be specified from the outset, or synapse formation may initially follow an approximate wiring diagram, with precision achieved by the elimination of inappropriate inputs and the stabilization and growth of appropriate connections (Goodman & Shatz, 1993; Purves & Lichtman, 1985). The ganglion cells, LGN, and V1 are all wired up in a "retinotopic" fashion; meaning that the order of points on the retina (proximal stimulus) are preserved. In this mapping, the points that are further away from each other on the retina will be further away on the brain. It is easy to see that the proximal image is retinotopically related to the distal stimulus, simply because of the optics of the eye. However the retinotopic mapping from the retina to the LGN and from the LGN to V1 is harder to appreciate. Studies of patients with localized cortical damage showed that the receptive fields of neurons within area V1 are retinotopically organized (Holmes, 1918; 1944; Horton & Hoyt, 1991). As a matter of fact, the development of the retinotopic map is a general process for the central nervous system. Cell bodies are born early in embryogenisis; axons and dendrites come later. The nerve growth is then guided mechanically, probably by glial cells, to their overall destination. The patterns of activity of the neurons themselves determine the exact position of the synapses that are formed. Ganglion cells travel up the concentration gradient to the LGN. Target cells send guiding chemical messages, giving crude directions to the cells' overall destination by

their concentration gradient. These chemical signposts act like beacons that attract the cells to project to approximately the correct part of the target tissue. At the same time the chemical signposts repel growth cones from the wrong axons. These guidance molecules also govern the decussation at the optic chiasm by signaling the retinal ganglion cells to either cross or not to to cross. The activity of adjacent retinal ganglion cells is correlated (Galli & Maffei, 1988), and "waves" of activity sweep across the retina during early life (Meister et al., 1991). Although the waves could potentially underlie the refinement of many retinal projection patterns, activity may not be required for establishing the M and P pathways of the primate retina that develop prenatally, and which show no apparent gross structural refinement with ensuing development (Meissirel et al., 1997). The immature and light-insensitive retina spontaneously generates a pattern of rhythmic bursting activity during the period when the connectivity patterns of retinal ganglion cells are shaped (Wong, 1999.). After the cells find a region, the wave then enforces precise ordering at the target. Thus the retinotopic map is finalized via the wave. Prenatal refinement of the retinotopic projections is achieved by these spontaneous waves of activation that propagate across the retina. Here ganglion cells are linked together by means of electrical synapses in a rough network and charge fluctuates randomly. The random response of one cell starts a wave of activity and the cells that fire together will eventually wire together. These spontaneous waves cause neighboring retinal regions to fire at about the same time. In fact, the correlation between the responses of cells is directly related to their separation on the retina (Wong, 1999.). So, the first principle of refinement is that cells that are neighbors tend to respond together. The second principle of refinement is that cells that fire together wire together. If there are two cells, 1 and 2, that are close to each other on the retina then when they fire together they will form neighboring synapses at the LGN. But cell 3, which is far from the first two on the retina will fire separately and thus synapse at the LGN separately. This is how the LGN is retinotopically wired up at birth along with V1 and other retinotopic cortical areas. Hence, the waves in the prenatal retina setup the relation between retina and brain. As for the postnatal retina, responses to stimuli set up the relation between the proximal stimulus and the brain. The postnatal wave may help guide the formation of synapses and determine which erroneous synapses are cut out for the normal mapping. When they arrive at their destinations, each process synapses over a relatively large area. Since target cells have lots of cells synapsing onto them, there are a lot more synapses present in V1 at 6 months and 1 year than in an adult. The process of the synapse starts as each axon from different cell bodies tries to take over a large piece of visual cortex and inevitably overlap occurs. At these regions of overlap a competition occurs, and the cell with the most or strongest synapse claims that region and the other synapses pull back. This synaptic elimination is a key element in the refinement of connectivity in both the central and peripheral nervous systems (Cowan et al., 1984; Goodman & Shatz, 1993; Lichtman et al., 1999; Nguyen & Lichtman, 1996; Purves & Lichtman, 1985). This produces a retinotopic map that has less overlap than before, and has many fewer synapses. If there is a vacant area then other nearby cells synapse onto it without meeting any competition and in turn increase their synaptic field. This process of being able to change as a result of experience is called plasticity, and is required for normal development. It determines how the visual system is wired up during normal development. The synaptic development occurs at different time scales across the brain. For V1 the development ends from about 8 to 16 years and culling happens at about 1-2 years. If there is any difficulty or blur in one eye or an eye turn while these synapses are being formed and refined, the subject will develop a visual disorder. This leads us into the next section.