Cerebral Metamorphopsia

Perceived spatial distortion from lesions of the adult human central visual pathway

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For every person who cannot achieve their potential due to prejudice and discrimination.

Abstract

Metamorphopsia is the perceived visual illusion of spatial distortion. Cerebral causes of metamorphopsia are much less common that retinal or ocular causes. Cerebral metamorphopsia can be caused by lesions along the central visual pathway or as a manifestation of epileptogenic discharges. Geometric visual distortions may result from structural lesions of the central visual pathway after reorganisation of the retinotopic representation in the cortex. Very few experimental investigations have been performed regarding cerebral metamorphopsia as it is often viewed as a clinical curiousity and analysis of the perceived distortion is difficult due to its subjective nature. Investigations have been undertaken to understand cortical plasticity as an explanation for visual filling-in. There has been much interest in cortical reorganisation after injuries to the peripheral and central visual pathway. Behavioural experiments aimed at quantifying the possible visual spatial distortion surrounding homonymous paracentral scotomas may be able to demonstrate cortical reorganisation afer brain-damage and provide clues regarding the neural processes of visual perception.

The aims of the thesis are:

1. To identify which cases of metamorphopsia, both published and unpublished, might be a consequence of cortical spatial reorganisation of retinotopic projections.

2. To investigate perceptual spatial distortion surrounding homonymous paracentral scotomas in adults with isolated unilateral injuries of the striate cortex.

A review of the literature describing cases of cerebral metamorphopsia was performed. Metamorphopsia caused by retinal or ocular pathology, psychiatric conditions, drugs or medications were excluded. A retrospective case series of eight patients with metamorphopsia from a cerebral cause was performed in two clincal neurology practices specialising in vision disorders. Two cases who suffered from paracentral homonymous scotomas due to isolated unilateral primary visual cortex V1 lesions were identified from a Neuro-ophthalmology practice. Neuropsychophysical experiments to investigate visual spatial perception surrounding their scotomas were developed and tested using MATLAB and Psychtoolbox.

The use of the term 'metamorphopsia' was only in reference to cases in which contours or lines were experienced as distorted. In the published literature, few cases of cerebral metamorphopsia have been identified as being potentially due to cortical reorganisation. The main result is that when compared to a normal control, there is a statistically significant visual spatial distortion surrounding a paracentral homonymous scotoma. There is also a significant distortion of perception in the "unaffected" visual hemifield in the subjects.

After lesions of V1, visual perceptual spatial distortions occur surrounding the homonymous paracentral scotomas. The spatial distortion also occurs in the normal hemifield possibly due to long-range cortical

connections crossing to the other hemisphere through the corpus callosum. A collaborative approach across disciplines within vision science is required to further investigate the mechanisms responsible for perceptual visual illusions. Behavioural testing in brain-damaged cases remains important in developing theories of normal visual processing. New neuroimaging and neuroscience techniques can then test these theories, furthering our understanding of visual percption. An understanding of normal visual perception could allow future modification of neuronal processes to harness cortical reorganisation and restore functional vision in humans with lesions of the visual pathway.

Statement of originality

This is to certify that to the best of my knowledge, the content of this thesis is my own work. This thesis has not been submitted for any degree or other purposes, and does not contain previously published material. I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged.

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List of special names, abbreviations, glossary and acronyms

Throughout the thesis, I have inserted a hyphen in some words to assist the reader who is not familiar with the terminology.

Accommodation	Convergence of the two eyes, pupil constriction and change lens to more convex with shorter focal length
Achromatopsia	Partial or total absence of colour vision
Amodal Completion	Perception of a complete image behind an occluder
Anova	Analysis of variance, a collection of statistical models and their associated estimation procedures, used to analyze the differences among group means in a sample.
anova	An R function for comparing two models
Array	(Array data structure) Data structure consisting of elements (values or variables) each identified by at least one array index or key
Asomatoganosia	Absence of body recognition, most common form of asomatognosia is the lack of recognition and loss of ownership sensation in the left side of the body. This phenomenon is also known as hemiasomatognosia. Most often, this is a transitory symptom.
Bit	A basic unit of information used in computing and digital communications
Bitmap	Mapping from some domain to bits
Code	(Computing) Program instructions
Concatenate	Link together in a chain or series
CRT	Cathode Ray Tube
Dyschromatopsia	Deficiency in colour vision
Dysaethesia	An abnormal unpleasant sensation when touched
Homonymous	Affecting the same part of the visual field in each eye
Ictal	Physiological state or event such as a seizure, stroke, or headache
Interictal	Occurring between ictal episodes
LCD	Liquid Crystal Display
LGN	Lateral geniculate nucleus. A nucleus in the thalamus which acts as a major relay station for visual signals from the retina to the primary visual cortex (V1). The LGN also receives massive feedback signals from V1.
DOVA	Degrees of Visual Angle
EEG	Electroencephalogram
Illusory Contours (IC)	Borders . . .
Kakopsia	Seeing things are ugly, menacing and/or sinister
Kalopsia	Seeing things are beautiful, friendly and/or comforting

Luminance	An objective measurement of the intensity of light emitted from a light sourse or reflected from a surface
Modal Completion	Interpolation of illusory contours between inducing edges and associated brightness enhancement of the perceived figure
MRI	Magnetic Resonance Imaging
fMRI	Functional MRI
Receptive Field (RF)	A delimited medium where some physiological stimuli can evoke a sensory neuronal response
Retinotopic	Organisation of a two-dimensional array of neurons in a given area which correspond topographically (in spatial arrangement) to those on the retina
Pelopsia	Vision perception disorder in which objects appear nearer than they actually are
Primary visual cortex	Also known as V1 or striate cortex. The cortical area which is the main receiver of visual information from the retinae, by way of the lateral geniculate nucleus
Prosopagnosia	Cognitive disorder of facial perception, inability to recognise faces
Scotoma	A circumscribed damaged area to some part of the visual system which eliminates visual input from a certain part of the visual field.
SPECT	Single Photo Emission Computed Tomography
Sprite	(Computer graphics) A two-dimensional bitmap that is integrated into a larger scene
Teleopsia	Vision perception disorder in which objects appear much farther away than they are
VEPs	Visual Evoked Potentials

Contents

Chapter 1

Introduction

"I was taught that the way of progress was neither swift nor easy."

Marie Sklodowska Curie

Vision is one of the most important human senses. A human's perception of the world occurs mostly through their eyes and visual system. The light intensity between the brightest day and a starlit night varies by a factor of ten million. The human visual system is able to adapt to these changes in intensity. It also has the capacity to discriminate between thousands of hues and shades of colour. Vision gives an organism the ability to gain knowledge of its surroundings by sensing light reflected off surfaces [1]. Visual perception allows recognition of objects so the organism can behave appropriately to obtain its objective. Recognising objects requires complex parallel processing of information. However, the perception subjectively appears to be almost instantaneous and effortless. In order to gain new knowledge and progress the understanding of visual perception in humans, a diverse multidisciplinary approach is required. This includes (not exclusively) the discplines of physics, optics, neurobiology, neurophysiology, neuroanatomy, cognitive neuropsychology, mathematics and computer science. The field of clinical medicine is required to develop targeted rehabilitative methods for human visual systems that have lost specific functions. Individual clinical cases with pathologies of specific visual processes are important to investigate what is abnormal. Understanding what is abnormal then allows investigations into what could be done to improve their impairment, decrease their disability, or restore function.

1.1   Visual illusions and hallucinations

Visual illusions and hallucinations are considered positive visual phenomena, in contrast to visual loss which is a negative phenomenon. Hallucinations are defined as perceptions occurring in the absence of a corresponding external sensory stimulus. Visual hallucinations are the result of internal processing. They are characterised by pathological patterns of discharges of impulse generation. There is no evidence of a relationship between visual perception and an external stimulus. Visual hallucinations can be classified as unformed/simple or formed/complex. Illusions are misinterpretations of a true sensory stimulus. One could assume the differences between visual illusions and hallucinations could relate to different pathophysiological pathways. Jean-Etienne-Dominique Esquirol was the first person to differentiate between visual illusions and hallucinations [2, 3].

There is a tendency to believe these visual perceptual disorders are rare and of no consequence. However, unless a patient is specifically asked to describe any past experiences of visual disturbances, they do not often divulge them voluntarily. Patients suffering from visual illusions or hallucinations usually have a concurrent loss of vision or other systemic medical problems. They are so concerned with their other medical issues that they fail to discuss their visual perceptual disturbances with their healthcare providers. Some patients may believe the visual disorder is part of a new onset psychiatric illness or dementia, and so they hide their experiences. With careful history taking, visual phenomena are relatively common, and may be normal or pathological. The diagnosis of visual illusions or hallucinations is commonly based on the clinical setting and the detailed description of the visual symptoms.

The patient's description of the visual phenomenon is often very suggestive of a particular cause. The patient should be asked to describe the hallucinations or illusions in detail with particular attention to content, complexity, static or dynamic features. It is often helpful to have them draw their experiences about what is perceived. Their frequency, duration and repetitiveness should be established. Other accompanying neurologic symptoms can be helpful in the diagnosis. The patient should be asked if they know whether the visual perception is a hallucination or not. Insight is a characteristic of release visual hallucinations, whereas a person suffering from a psychotic hallucination may not be able to differentiate the hallucination from reality.

The causes of visual hallucinations and illusions can be grouped into several major categories [4]:

1. Migraine

2. Release phenomena (in the setting of impaired vision)

3. Entoptic (ocular) phenomena

4. Alcohol and drug-related

5. Seizures

6. Neurodegenerative disease

7. Central nervous system lesions

8. Psychiatric disease

9. Narcolepsy

The focus of this thesis is cerebral metamorphopsia, a visual illusion where distortion of contours or lines is caused by lesions of the central visual pathway.

1.1.1 Visual illusions

Visual illusions result from the transformation of external stimuli. They are often predetermined by the visual processing system and may not necessarily be pathological phenomena. Lesions of the visual pathway can cause a broad spectrum of visual illusions. [5].

Disordered visual function	Visual Illusion
Axis	Tilted or inverted
Distance	Pelopsia/teleopsia
Size	Macropsia/micropsia
Shape	Metamorphopsia
Motion	Slow motion or elapsed time
Number of images	Diplopia/polyopia
Extinction	Perseverations
Memory	Deja vu, jamais vu

1.2 Anatomy and physiology of the visual system

There are four neuronal elements of the visual pathway [6]. The first three are found in the retina:

1. Photoreceptors

2. Bipolar cells

3. Retinal ganglion cells

Axons of the retinal ganglion cells pass through the optic nerve, optic chiasm and optic tract. The fourth neuronal element is found in the lateral geniculate nucleus. These axons then form the optic radiation and terminate in the primary visual cortex in the occipital lobes.

1.2.1   Anatomy of the eye

The eye is the organ of vision and is an extension of the central nervous system. It is the only receptor that is actually part of the central nervous system. The eye is responsible for converting patterns of light energy into neuronal signals. The eye has three layers (or tunics):

1. Cornea and sclera: the outer fibrous tunic

2. Choroid, ciliary body, and iris: the middle vascular and pigmented tunic

3. Retina: the inner neural tunic

The cornea is the clear window allowing rays of light to enter the eye. The majority of light refraction to focus rays on to the retina occurs at the air-cornea interface. The sclera is the tough fibrous coat of the eye that provides its structural rigidity. The lens is suspended by zonules to the ciliary body. The lens separates the anterior chamber from the vitreous. It completes the refraction of light onto the retina.

The middle layer of the eye is highly vascularised providing oxygen and metabolites to the inner photoreceptor layer and the retina. The choroid is the posterior portion of this layer. Its innermost portion is adjacent to the retinal pigment epithelium layer of the retina. The ciliary body comprises of a vascular tunic and the ciliary muscle. It surrounds the lens. The ciliary muscle is the vascular component and the zonules (suspensory ligaments) suspend the lens. The ciliary muscles are used in accommodation. The pupillary muscles of the iris control the aperture size of the pupil. There are two sets of muscles: the sphincter and dilator pupillae.

Embryology: the eye is an outpouching of a neural fold

The retina develops from the optic vesicles of the hindbrain. The optic vesicle forms the optic cup. The optic cup consists of two layers: the outer layer becomes the pigment epithelium of the retina, and the inner layer differentiates into the neural layer of the retina. The optic cup is connected to the brain by the optic stalk which becomes the optic nerve.

1.2.2   Retina

The retina is the innermost structure of the eye. Histologically, the retina contains the following 10 layers (sclera to vitreous):

1. Retinal pigment epithelium (RPE)

2. Photoreceptors: Rods and Cones

3. External limiting membrane (ELM)

4. Outer nuclear layer (ONL): containing the photoreceptor nuclei

5. Outer plexiform layer (OPL): a synaptic layer between photoreceptor cells and bipolar cells

6. Inner nuclear layer (INL): the bipolar cell layer

7. Inner plexiform layer (IPL): a synaptic layer between the cell processes of bipolar cells and ganglion cells

8. Ganglion cell layer (GCL)

9. Retinal nerve fibre layer (RNFL): consisting of the ganglion cell axons

10. Internal limiting membrane(ILM): containing the foot-plates of Muller's cells

The retina is functionally divided into receptive fields (RFs). These receptive fields have a circular RF centre with a surrounding peripheral centre area. There are two types of neurons:

1. ON-neurons: excited by light hitting the centre and inhibited by light hitting the peripheral area

2. OFF-Neurons: excited by light hitting the periphery and inhibited by light hitting the centre

Photoreceptors: rods and cones

The 130 million rods and cones transform electromagnetic waves of light, with wavelengths between 400 and 700 nm, to graded membrane potential changes. Cones are active under bright daylight illumination conditions (photopic). Rods are active under dim illumination conditions such as at night (scotopic). The signal from the photoreceptors continues to the bipolar cells and then to the retinal ganglion cells.

1.2.3 Optic nerve

Approximately one million axons of the retinal nerve fibre layer converge at the optic disc to form the optic nerve head. This is almost 40% of the total number of axons of all the cranial nerves. The optic disc is the part of the optic nerve that can be observed using ophthalmoscopy. The optic nerve then enters the optic foramen in the sphenoid bone. Where the optic nerve exits each eye, there are no photoreceptors. The physiological blind-spot is due to this lack of photoreceptors. This blind-spot correlates to an area plotted on visual fields.

1.2.4   Optic chiasm

Axons coming from the nasal hemiretina are normally crossed in the optic chiasm. The axons from the temporal hemiretina remain uncrossed. See Figure 1.1.
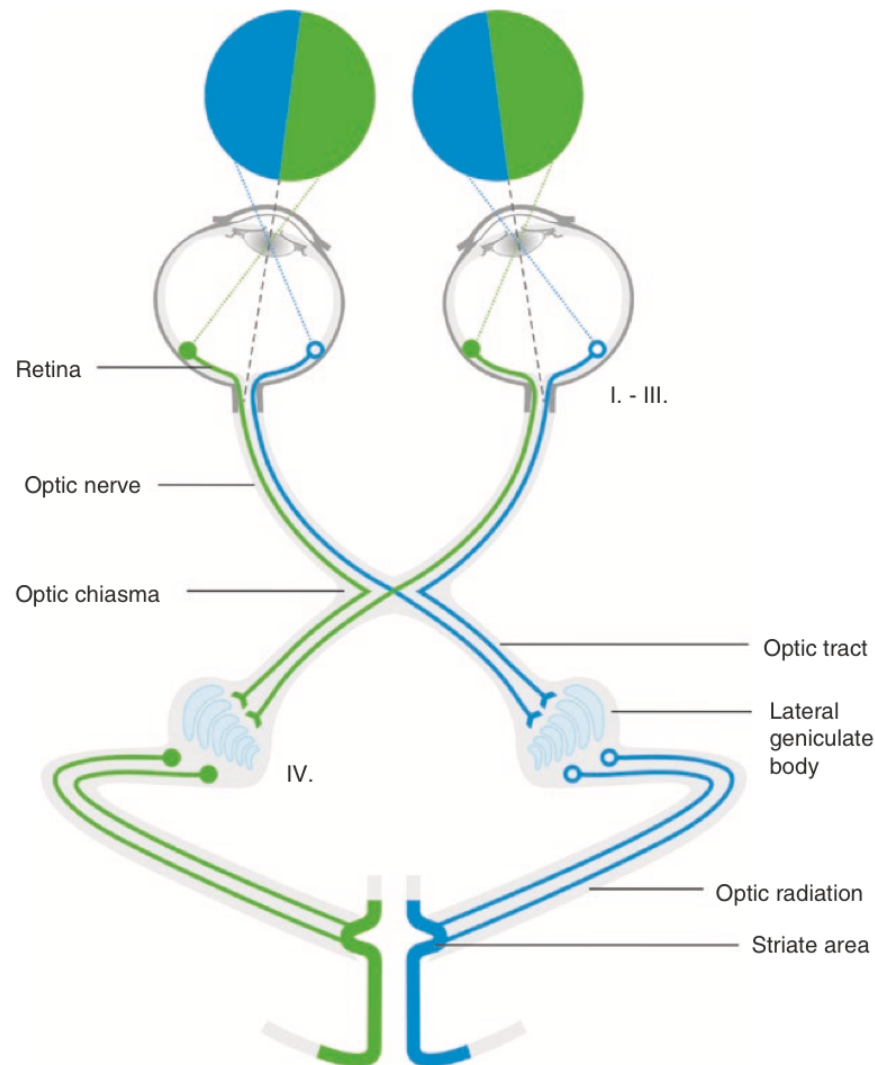
Figure 1.1 – Schematic drawing of the neuronal components of the visual pathway [7]

1.2.5   Optic tract

About half of the axons in the optic tract terminate in the lateral geniculate nucleus (LGN) with the other half bypassing the LGN. This half terminates in the tectum of the superior colliculus, some of these fibres are also involved in light reflexes. An isolated lesion of the optic tract causes a clinical triad of findings:

1. Homonymous hemianopia

2. Relative Afferent Pupillary Defect (RAPD)

3. Atrophy of the optic disc

1.2.6   Lateral Geniculate Nucleus (LGN) of the thalamus

Neurons of the LGN send their axons to the optic radiations. Isolated lesions of the LGN are uncommon and cause an incongruous homonymous hemianopia. Due to the dual blood supply of LGN by the anterior and lateral posterior choroidal artery, there is often a specific wedge-shaped pattern to the visual field defect.

1.2.7   Optic radiations

Lesions of the optic radiations in the temporal lobe cause contralateral upper homonymous quadrantanopia. Lesions in the parietal lobes result in contralateral lower homonymous quadrantanopia. A complete lesion of an optic radiation leads to a contralateral homonymous hemianopia. If there is damage to the internal capsule, there is also a varying degree of hemiparesis or hemianaesthesia.

1.2.8   Occipital lobe

Areas in the occipital lobe: Brodmann areas 17, 18 and 19 (V1-V5). V1, striate cortex, or Brodmann area 17. From V1 to higher visual association areas responsible for visual perception of objects, letters, colours, faces and orientation. Visual association areas are classified into ventral and dorsal pathways [8]. Unilateral lesions of an occipital lobe (Areas V1-V5) typically result in a congruent contralateral homonymous hemianopia with central (macular) sparing.

1.2.9   Temporal lobe lesions

Lead to defects in personality, temporal epilepsy, memory disturbances, Wernicke aphasia, or Kluver-Bucy syndrome (hypersexuality, hyperorality, visual and auditory agnosis and apathy).

1.2.10   Parietal lobe lesions

Patients with parietal lobe legions involving the optic radiations are often unaware of their visual field defects. This is referred to as anosognosia and are most often seen with lesions of the non-dominant parietal lobe. Other dysfunctions of higher sensory integration may exist such as asterognosis, agraphesthesia and impaired two-point discrimination. Deep parietal lesions may lead to homonymous hemianopia and abnormalities in smooth pursuit eye movements to the ipsilateral side. Lesions at the parieto-occipital border or the occipital

lobe can cause cortical blindness, or Balint syndrome, which also includes ocular apraxia and simultanagnosia. These lesions are generally caused by neuro-degenerative disorders.

Dominant parietal lobe lesions

These lesions manifest as conductive aphasia, Wernicke aphasia, alexia with or without agraphia, Gerstmann syndrome (finger agnosis, agraphia, acalculia, failure of left-right orientation), or tactile agnosia.

Non-dominant parietal lesions

These lesions manifest by a left-hand syndrome (also known as alien hand syndrome, where one hand acts on its own free will), neglect, or constructional apraxia and apraxia of dressing in association with left-sided hemianopia.

1.2.11   Corpus callosum

The corpus callosum is a bundle of neural fibres connecting the left and right hemispheres of the brain. It is composed of white matter, millions of axons with their dendrites and terminal buttons/boutons projecting into both right and left hemispheres. The corpus callosum is organised into functional regions. The transfer of visual information takes place in the posterior portion of the corpus callosum known as the splenium [9]. Visual fibres project from the occipital cortex of one hemisphere of the brain and connect through the splenium to the opposite hemisphere [10]. Lesions of the splenium and the immediately-posterior retrosplenium cortex (immediately posterior to the splenium), are known to be associated with metamorphopsia, amnesia and alexia.

1.3   Central visual pathway

The central visual pathway processes and integrates visual information passing through the optic nerves. The brain is responsible for visual perception and cognition. There is a hierarchy in the central visual processing pathway. In an oversimplification, the central visual pathway is comprised of processing stations. Each station tends to preserve the spatial order of outputs from the retina of each eye. The spatial organisation of these output is mostly maintained in the optic nerve fibres as they leave the eye. The order becomes more refined as the outputs terminate in their major brainstem targets. The retinal ganglion cell axons present in the optic nerve project to the lateral geniculate nucleus (LGN), superior colliculus (SC), pretectum, and the pulvinar. There are weaker projections to several small hypothalamic nuclei and the accessory optic system.

There are several largely parallel anatomical pathways processing various different aspects or components of visual input. There are two main classes of retinal ganglion cells: parvocellular and magnocellular. Parvocellular cells have small receptive fields and are specialised in fine spatial analysis of object features. Magnocellular cells have larger receptive fields and specialise in motion detection. A ventral visual processing pathway extending into the temporal lobe is specialised for object processing. The ventral pathways project from striate cortex to the angular gyrus (language processing), inferior temporal lobe (object identification), and limbic structures. The ventral pathway is often referred to the "what" pathway as it serves object recognition. A dorsal stream extends into the parietal lobe and specialises in processing motion and the spatial relationships between objects [11]. Dorsal pathway projects to the posterior parietal cortex and superior temporal cortex (visuospatial analysis) and then continues forward to the premotor frontal cortex. This "where" pathway processes objects in visual space and their movement. Naming these pathways "what" and "where" is an oversimplificaiton of how these cortical areas function as there are interactions among each individual region.

The LGN of the thalamus is the termination site for 90% of the retinal ganglion cells [12]. The LGN is laminated and has retinotopic organisation. Each layer receives input from a specific eye and class of retinal ganglion cell. The LGN appears to be involved in regulating information to V1.

The superior colliculus in the midbrain receives 10% of all retinal ganglion cell projections. It is involved in generating visually guided saccadic eye movements together with the cortical frontal eye fields and the brainstem reticular formation. The superior colliculus is also laminated with retinotopic organisation. The retinal projections remain segregated by eye with alternating columns of left and right eye terminals, forming a banded pattern throughout the superficial layers.

There are several weaker projections of retinal ganglion cells to three of the four subdivisions of the pulvinar nucleus of the thalamus. The pulvinar is the largest nuclear mass in the primate thalamus. It receives a projection from small-calibre fibres from the optic nerve and superior collicular. The pulvinar also projects to several visual cortical areas including V1, extrastriate and parietal areas. Therefore, the pulvinar represents a second pathway that bypasses LGN to get to V1 and may play a role in processing form vision [12].

There is strong evidence in favour of the hierarchical way visual information is processed within different streams. The neurons in V1 have small receptive fields and code simple features of visual input such as the orientation of edges. V1 is retinotopic where neighbouring points in the retinal image are projected onto corresponding neighbouring points of the cortex, retinotopy. This is analogous to somatopic organisation in the somatosensory system and tonotopy in the auditory system. Increasingly complex stimuli are processed at higher levels of visual processing (more anterior in the brain). The sizes of receptive fields become larger

and retinotopy breaks down. Due to the strong retinotopy of V1, there is a possibility that a lesion of the striate cortex may lead to cortical reorganisation changes resulting in a geometric, hard wired, spatial distortion. This could underly some cases of cerebral metamorphopsia.

1.4   Metamorphopsia

The term 'metamorphopsia' comes from the Greek words metamorphoun (to change the form) and opsis (seeing). It translates roughly as 'seeing an altered form' and is a visual illusion. The term 'metamorphopsia' has been used generally in the literature for the visual illusions where various aspects of visual perception are spatially distorted [4]. In this thesis, the term metamorphopsia will only be used to define the visual illusion of cases where contours or lines experienced as distorted. The visual perception of wavy lines or contours has been termed 'dysmorphopsia'. The experience of the metamorphopsia visual phenomenon is subjective and are experienced as either transient, episodic or established long-term. Critchley used the word 'metamorphopsia' to denote an illusory distortion of objects [13]. Metamorphopsia is most often produced by peripheral pathologies within the ocular media and rarely by central, cortical or cerebal causes. In some of the published literature, the term 'metamorphopsia' has been used to describe all visual distortions or dysmetropias, including micropsia and macropsia. Also, 'reversal of vision metamorphopsia' is rare and has been described in the literature where there is a coronal 180 degree alteration of the visual field [14]. Unal et al. described a case who had left parieto-occipital cortical dysplasia on brain Magnetic Resonance Imaging (MRI), where upside-down vision precedes complex partial seizures. This case is an example of the term metamorphopsia being used with a broad definition. The otolith receptors play an important role in the perception of verticality. An illusion where the environment appears tilted or upside-down may follow damage to the peripheral or central vestibular system or its cortical connection. This illusion is not the focus of this treatise as it is not a geometric distortion of visual space.

1.4.1   What is Metamorphopsia?

The term 'metamorphopsia' is used at present in a restricted sense to denote a visual distortion affecting the contours of objects. As a more general term, it is used to denote a variety of qualitative visual distortions which affect the perceived form, size, orientation, colour, and/or speed of perceived objects. As defined in the broader sense, metamorphopsia is an extremely variable visual illusory experience that could be divided into several categories:

Achromatopsia	inability or strongly diminished ability to perceive colour
Akinetopsia	inability to perceive motion
Chromatopsia	seeing things in a single hue, cyanopsia (blue vision), chloropsia (green vision), erythropsia (red vision), ianothinopsia (violet or purple vision), xanthopsia (yellow vision)
Corona phenomenon	an extra contour is visible around objects
Dysmegalopsia	diminished ability to appreciate the size of objects
Dysmetropsia	changes in the apparent size and distance of objects
Dysmetropsia	changes in the apparent size and distance of objects
Dysplatopsia	objects are perceived flattened and elongated
Enhanced stereoscopic vision	exaggeration of depth and detail of visually perceived objects
Entomopia	seeing multiple identical images as if perceived through an insect's eye
Gyropsia	seeing an illusory, circular movement
Hemi-metamorphopsia	only one half of an object or face appears distorted
Illusory splitting	apparent vertical splitting of objects
Inverted vision	objects are perceived as if rotated 180°
Kinetopsia	illusory movement
Loss of stereoscopic vision	things appear two dimensional or 'flat'
Macropsia	seeing things larger than they are
Macroproxiopia	perceived size and distance of objects is altered
Micropsia	seeing things smaller than they are
Microtelepsia	perceived size and distance of objects is altered
Mosaic vision	fragmentation of perceived objects or stimuli into irregular, crystalline, polygonal facets, interlaced as in a mosaic
Pelopsia	objects appear to be closer than they are
Plagiopsia	objects appear to be tilted
Polyopia	seeing multiple identical copies of a single image
Porropsia	stationary objects are seen as moving away from the observer
Prosopometamorphopsia	faces appear to be distorted
Teleopsia	objects appear to be further away than they are
Visual allachaesthesia	objects are perceived as if dislocated into the opposite visual field
Visual perseveration	illusory reoccurrence of visual percepts, as in illusory visual spread, palinopsia, and the trailing phenomenon

Scottish philosopher Thomas Reid (1710-1796) is commonly credited with providing the first case report of metamorphopsia in 1764, after having contracted the condition himself due to a prolonged period of sun

gazing.

Reportedly, the Norwegian expressionist painter Edvard Munch (1863-1944) also suffered from metamorphopsia, caused by an intraocular haemorrhage [15].

Metamorphopsia due to a lesion of a single eye is referred to as 'monocular metamorphopsia'.

When metamorphopsia evokes changes in the affective assessment of the extracorporeal environment, rendering it either beautiful, ugly, or frightening, they are called "complicated metamorphopsia". When such changes are absent the term " simple metamorphopsia" is used [13].

Pathophysiologically, metamorphopsia is divided into two broad categories. Those attributable to an intraocular cause are referred to as peripheral or retinal metamorphopsia. Those attributable to a central cause are termed central, cortical, or cerebral metamorphopsia.

Metamorphopsia tends to be transient or episodic in nature, especially when the underlying neurological condition is transient or episodic in nature. Some examples of these conditions are migraine, epilepsy, and the use of psychoactive substances such as mescaline or LSD. Metamorphopsia occurring in the context of an "aura" or a related seizure disorder are referred to as "ictal illusion" or "ictal metamorphopsia". Long-lasting and permanent metamorphopsia is relatively rare. Pathophysiologically, they are associated primarily with discrete lesions affecting the visual association areas. Aetiologically, they are associated primarily with structural damage, due, for example, to infarction, haemorrhage, or a neoplasm.

1.4.2   What types of metamorphopsia are there?

There are two types of metamorphopsia: 1. Ocular or retinal (far more common) and 2. Cerebral

Peripheral or retinal metamorphopsia

Structural lesions of the retina may cause perceived distortions in shape or form. These distortions are almost always fleeting in nature, they visual perception is restored to "normal" with time. A review of the retinal causes of metamorphopsia and clinical tests for detection or monitoring has been published by Midena et al [16].

The author Burke suffered from a scotoma produced by a macular hole. He found that a line positioned near the scotoma was perceptually deflected toward the scotoma. The thicker the line, the larger the deflection. However, the structural distortion of the remaining photosensitive foveal structures could account for this result [17].

Central, cortical or cerebral metamorphopsia

True cerebral metamorphopsia may be long-lasting and in some cases permanent. The disorder is not commonly experienced by patients. A practising neurologist or ophthalmologist specialising in Neuro-ophthalmology would only be expected to encounter a few patients who describe perceiving visual distortions after an insult to the occipital lobe.

1.4.3 Why does metamorphopsia occur?

The causes of metamorphopsia are rarely central. Ocular causes of metamorphopsia are far more common. Experimental work has been performed to quantify the visual distortion perceived from structural retinal abnormalities. Retinal pathology causing metamorphopsia can be seen on fundoscopy and captured on imaging. This allows an objective measure of the displacement of the retinal architecture. However, the patient's visual perception is still a subjective description of what they see. Structural changes in the retina may not necessarily cause distortion due to higher visual processing.

Disease of the occipital lobes is usually attributed as the cause of cerebral metamorphopsia. Lesions along the central visual pathway or cerebral seizure activity could however also cause vision distortion. Occipital cortical visual distortion can be commonly seen in neurodegenerative disorders where the subject's cognitive capacity limits the accuracy of their description. There has been little experimental work done regarding cerebral metamorphopsia as it is often viewed as a clinical curiosity. It is difficult to assess metamorphopsia as the examiner relies on the subject for an elaborate description of the visual distortions. The examiner is not able to check the accuracy of the description and relies on the subject's intelligence, articulation, and observation or skill in analysing the phenomena they are experiencing. This could possibly allow two extremes of description to be observed which could potentially limit the analysis of cerebral metamorphopsia. At one end of the spectrum, the subject may take little or no interest in the distortion, does not understand what is happening and therefore, does not fully voice their experiences. On the other extreme, the subject may excessively complicate or elaborate descriptions of their experiences. Occasionally the sufferer is able to express the visual distortion through drawing. Again this relies on the person's ability to accurately draw their visual experiences. It is hoped that the drawings by patients with cerebral metamorphopsia will be as useful as those demonstrating the visual experiences of migraine sufferers [18]. Analysis of visual distortion is difficult due to the difficulties in developing behavioural experiments that consistently demonstrate the distortion across a group of individual subjects.

1.5   Visual perceptual completion

Objects in the visual scene are often covered or partly visible. Therefore, the human visual system needs to fill the gap to perceive the whole object. There are two forms of completion. One is amodal completion, when a target is partly covered by an occluder. Amodal completion forms the perception of the hidden parts that lack visible attributes (colour, texture, etc.). The other is modal completion, in which completion of objects appears to occur in front of the supposedly occluded object. See figure 1.2.

1.6   Visual filling-In

Filling-in is a perceptual phenomenon where visual features of the surrounding area are perceived in a certain area of the visual field even though these features are not physically present. The empty region of visual space appears filled-in with colour, brightness or texture of its surround. The human brain fills-in the naturally occurring optic disc blind-spot, borders, surfaces and objects [20, 21]. Edges and contours are important in filling-in colours, brightness and testures into surfaces. There are two main theory types: 1. Isomorphic; 2. Symbolic. Under scotopic (dim illumination) conditions, objects that are just off to the midline of sight disappear once focus shifts to them. However, there is no trace of their disappearance and the visual field looks homogenous (uniformly the same) or filled-in. This is due to: 1. There are no rod photoreceptors in the fovea, only cones are present. Therefore, the fovea does not contain suitable receptors to capture photons of under these conditions; 2. The lack of rod photoreceptors spans approximately one degree of visual angle. However, although the visual cortex does not receive any input, no gap is vision is seen or perceived.

1.6.1   Isomorphic filling-in theory

In this theory, a visual surface to be filled-in is represented in the brain by a two-dimensional array of neurons [21, 20]. These fire under the influence of excitation spreading inwards from the edges. It is proposed that colour signals spread in all directions until stopped by a luminiance border which acts as a barrier. The analogy used here is physical diffusion.

1.6.2   Symbolic filling-in theory

In this theory, there is no spread of activity within the surface [21, 20]. The visual properties of the surround such as texture, contrast polarity and colour are tagged and applied to the enclosed surface. This process of filling-in is economical and resembles a vector graphics method of representation. The minimalist version of
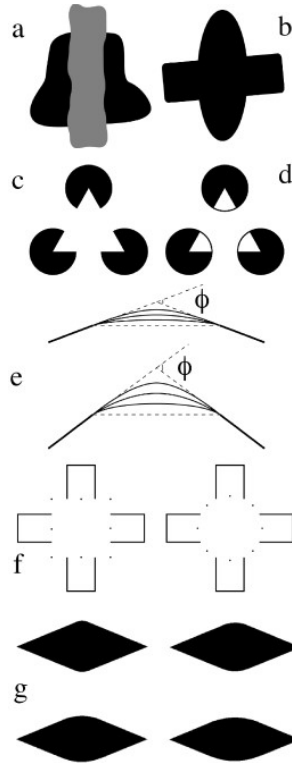
Fig. 1. Illustrations of visual completion. In the example of amodal completion (a), the two black regions are disparate fragments in the image, but are perceived to belong to a single amodally completed surface extending behind the gray occluder. The self-splitting figure (b) is perceived to contain two overlapping objects that undergo spontaneous depth reversals—thereby switching which object is modally completed (in front) and which one is amodally completed (in the back). In the modal version of the Kanizsa triangle (c), a unitary white surface is seen to partly occlude three black disks. In the amodal version of the Kanizsa triangle (d), a unitary white surface is seen to extend behind a surface containing three portholes. The identity hypothesis was motivated by the observation that the modal and amodal variants of both the self-splitting figure and the Kanizsa displays generate identical completed shapes. The illustration in (e) shows that inducer pairs with smaller turning angles (top) allow less room for the shape of the interpolating contour to vary than do those with larger turning angles (bottom). Small turning angles thus make any shape differences between modal and amodal completion less likely to be detected. The *Koffka crosses* in (f) demonstrate that the placement of a small number of dots can alter the perceived shapes of illusory contours. The illustration in (g) shows four levels of smoothing applied to a diamond shape with a turning angle of $45°$. This configuration served as the comparison display in the experiments. Participants adjusted the degree of smoothing applied to its top and bottom vertices, in order to match the shape of the perceived interpolated contour in a standard completion display. The four levels depicted have normalized smoothing measures of .2, .4 (top row), .6, and .8 (bottom row), respectively.

Figure 1.2 – Illustrations of visual completion. Figure 1 from [19].

symbolic filling-in is the retinal blind-spot could be ignored as there are no neurons in the brain dedicated to processing this area.

1.6.3 Evidence for isomorphic filling-in theory

The following papers are of particular interest: Paradiso and Nakayama 1991 [22]; Murakami 1995 [23]; and Motoyoshi 1999 [24]. Motion aftereffects(MAE)around the blind-spot offer strong support for the isomorphic filling-in theory. If one first inspects a striped moving pattern, when the motion stops, the stripes appear to move back in the opposite direction. This MAE can be established in one eye monocularly and then elicited in the other eye. In Murakami's study, an annular (ring-shaped) stimulus was presented on the blind-spot of the right eye with drifting stripes [23]. A small striped disk, smaller than the diametre of the hole or empty space in the annulus, was then viewed in the corresponding intact retina of the left eye. Murakami's study found adaptation to filled-in motion caused MAE well inside the blind spot. This study suggests motion activity filled-in the blind spot of the right eye and filled-in motion is processed by the same mechanisms as MAE. This study also suggested the likely representation of filling-in of motion is in the retinotopic and elementary stages of the visual system. Paradiso and Nakayama used masking experiments to investigate filling-in of brightness in a uniform luminance area [22]. Motoyoshi used masking experiments to investigate filling-in of texture [24].

1.6.4 Phenomenology of filling-in

A review article by Komatsu classifies filling-in events into three main groups [21].

Blind-spot or scotoma

Blind-spot is the region of the visual field corresponding to the optic disc. The optic disc has no photoreceptors, it is where the optic nerve exits the retina. Therefore, there is no visual input from this area as the eye is unable to detect photos of light in this section. One can demonstrate or perceive their own blind-spot by performing the following:

1. Close one of your eyes

2. Extend one arm straight in front of you

3. Spread the fingers of your hand wide with your palm facing away from you

4. Focus your gaze at your thumbnail

5. Wiggle your little finger

Your little finger will fall within your own blind-spot and you will be unable to see it.

The blind-spot approximately measures 5-6 degrees of visual angle in diametre and its centre is 15 degrees of visual angle medial to the fovea, slightly above the horizontal meridian. Humans still visually perceive the same colour and/or pattern as the surround within the region of the visual field corresponding to the blind-spot [25, 26, 27].

When viewing the visual scene in normal binocular vision, the cortical representation of the other eye compensates for the lack of visual input. However, monocular viewing does not cause a perception of a blank patch in the visual field. The visual system perceptually fills-in visual information from surrounding colour and texture information.

Patients with damage to the retina or a slowly progressing optic neuropathy, such as caused by glaucoma, develop a scotoma. Patients often do not realise they have an area missing or damage in their visual field until an objective test is performed. Perceptual filling-in of the scotoma has occurred so no missing or strange region is perceived in their visual field. Unfortunately, often the patient is not aware of their vision loss until substantial irreversible damage has occurred [25, 28, 29, 20].

Steady fixation and stabilised retinal image, fading peripheral objects

Filling-in also occurs when there is no deficit of visual input. For example, stabilisation of the border of a surface on the retina causes filling-in. When steady fixation is maintained, the contrast of an object in the peripheral visual field gradually decreases until the object fades away to being invisible. The visual features of the surround fill-in the part of the visual field which was originally occupied by the object. This phenomenon is called the Troxler effect [30, 31, 32, 33]. In 1804, Troxler reported a small, low contrast target when presented in the peripheral field and viewed with strict fixation, became embedded in the background and disappeared from view [30]. The fading process is acclerated if the edges of the object are blurred. The process occurs even faster and more completely if the edges are stabilised against the micro-saccades caused by small eye movements. See [20] for examples.

Texture filling-in occurs in a small region surrounded by a texture consisting of a large number of elements. When steady fixation is maintained, the originally empty region is perceived as having the same texture as what is surrounding it [25, 34, 35]. This filling-in does not happen instantaneously. It usually requires at least several seconds to occur. When eye movements occur, this breaks the filling-in process as it refreshes the information so the original percept is restored.

Neon colour spreading

Neon-like glow of a colour escapes the boundaries of a real figure. The speading seems to fill the surrounding area until limited by the boundaries of an illusory figure [36]. It was first observed in 1971 by Dario Varin [37] and Harrie van Tuijl in 1975 [26].

Higher visual processing areas may be involved in filling-in, however, no attempt has been made to study the role of these areas. A similar strategy used to investigate early visual areas cannot be used in higher areas as neurons have larger receptive fields and complex stimulus selectivity. Filling-in and spatial distortion have been interpreted as a result of cortical plasticity. Cortical plasticiy in the visual system is related to changes in receptive fields [38].

1.6.5   Filling-in of retinal scotomas

Studies observing or investigating filling-in of retinal scotomas have been performed [39, 40, 41, 42, 28, 43, 44, 17]. There are limitations in blind-spot and artificial scotoma studies. The physiological blind-spot is normal and therefore, the filling-in mechanisms may not exist in other areas. The blind-spot is also small in size and peripherally located. Using artificial scotomas to investigate filling-in dose not take into account pathological retinal atrophy from disease and the consequences of long-term cortical reorganisation. These artificial scotoma studies also exclude the foveal region and the scotomas are small.

Active completion as a mechanism for filling-in is supported by the results of a study investigating retinal scotomas from macular degenerations [39]. The range of perceptual completion was increased compared to artifical scotomas. The retinal scotomas from macular degeneration in this study were larger and more central compared to artificial scotoma studies. Also, long-term cortical reorganisation had already occurred. The study also suggests there are filling-in mechanisms involved beyond V1 units as under some conditions, the filling-in of the scotomas fails [39].

A study suggests higher-level processing of image completion is involved in filling-in of pathologic retinal scotomas [40]. They investigated alignment thresholds over the physiological blind-spot in controls and pathologic retinal scotomas. They also suggests perceptual filling-in across retinal scotomas does not include low-level receptive field organisation. The alignment thresholds over pathologic retinal scotomas were not significantly lower than thresholds measured across equally eccentric retina in the intact retina of the healthier fellow eye [40].

1.7 Cortical plasticity of the visual cortex

In his Ferrier Lecture, Gordon Holmes questioned whether there is any evidence of plasticity in the organisation of the visual cortex [45]. At the time of this lecture in 1945, there were only two definite differentiations of visual function: 1. Central or macular, greater acuity, greater power of discrimination, more accurate projection into space of images perceived and more exact fixation of objects; 2. Peripheral sight. Gordon Holmes' clinical observations suggested that under pathological conditions, the properties of the macular vision might have been taken over by extra-macular or peripheral vision due to modifications of the functional activity of the cortex. He had observed that men with complete destruction of one striate area had hemianopia, complete blindness of the opposite half of the visual field of each eye. This extended up to and often bissected fixation. However, the patient affected by the hemianopia was frequently unaware of this loss of half of his visual space and only learnt it through experience. The visual space that remained appeared unrestricted to him and appeared to perceptually extend, as the normal field of vision does. The objective visual field is halved although the subjective field is perceived as whole.

Brain imaging techniques are still not sensitive enough to detect the cellular mechanisms of cortical reorganisation. Therefore, animal studies have been the main focus of research regarding the neural substrate. The earlier stages of cortical reorganisation, thought to be 'unmasking' of previously silent connections: 1. Horizontally between adjacent cortex; 2. Vertically between cortex and thalamus. The unmasked connections are thought to be strengthened by long-term potentiation (LTP). LTP is the persistent strengthening of synapses based on their recent pattern of activity. Longer-lasting changes could be consolidated by: sprouting of new axon branches, elongation of dendrites,or formation of new synaptic connections. Animal studies suggest axons and dendrites can grow for distances of up to 3mm during reorganisation of the somatosensory cortex. Representations in the motor cortex can rapidly shift by up to 2mm [46].

1.8 Visual psychophysics in humans

The term "psychophysics" is due to Fechner [47, 48]. Psychophysics studies the quantative relationship between environmental stimulation (physical dimension) and sensory experience (psychological dimension). The two basic parameters of human performance measured by psychophysical methods are accuracy and precision. Studying visual psychophysics in human beings requires the subject to be taught how to respond to a stimulus with the primary interest being the decision processes preceeding those responses. The goal of visual psychophysics is to quantify the perceptual experience. This requires an understanding of the relationship between the external stimulus, the internal representation and then the response.

1.9   Investigation of the visual processing pathway using cognitive neuropsychology and neuropsychophysics

Historically, single-case investigations of individuals with brain-damage or brain injuries have substantially contributed to our understanding of human cognitive processes [49]. The primary goal of cognitive neuropsychology is to use information gathered from brain-damaged individuals to draw inferences about the organisation of the normal human cognitive system. Recently, the role of single-case cognitive neuropsychology has faded with the development and increased availability of non-invasive techniques measuring neural activity in humans. A currrent popular approach in cognitive neuroscience is large-scale informatics where data is gathered from hundreds of neuroimaging studies or 'big data'. Using cognitive neuropsychology, the single-case approach focuses on developing models of cognitive processing. This approach is able to address several of the weaknesses inherent in the informatics approach.

A significant benefit of single-case investigations is the serendipitous nature of exploration and investigations. The investigator or observer has no control over how an individual will behaviourally respond to testing. The investigator then has to determine how to characterise the cognitive impairment from the brain-damage. Unexpected behaviours lead to new experiments which could lead to new cognitive models. During experiments performed in this thesis, an unexpected persistent visual hallucination was created in one of the subjects (POV), see results section on Filling-In experiment.

There are barriers to performing single-case studies. The special nature of the population undergoing testing means it is very difficult to find individuals with specific lesions of the brain who are willing to participate in substantial amounts of research. It is extremely difficult to recruit a large enough sample for sufficiently powered studies to potentially determine neural correlation of function. An enormous effort is required to gather the data. Experiments have to be generated, adjusted and run specifically for each individual factoring their cognitive impairment. Unfortunately, single-case subjects have suffered from subsequent medical events before the study is complete which may render the partially collected dataset useless. For the experiments in this thesis, I am indebted to the subjects POV and DSS for their time, effort, and patience. There were substantial delays in the acquistion of data from POV due to a prolonged respiratory illness. Fortunately, he recovered and is presently in good health.

The major technological advances in cognitive neuroscience have occurred in neuroimaging. There has been a shift of interest towards neural activity over developing cognitive models. There appear to be two streams of investigation in cognitive neuroscience: 1. Biomedical: investigating neurophysiology and neural substates; 2. Cognitive: investigating theories of information processing.

Behavioural studies usually contain small sample sizes. Neuroimaging studies have been argued as superior to behavioural studies. There has been an explosion of published functional MRI (fMRI) papers. Meta-analyses of neuroimaging studies has become possible from the ability to share neuroimaging data, automated methods to extract data from the literature and increased computing power. 'Big data' has the potential to transform our understanding of cognition. The informatics approach to neuroimaging addresses the weaknesses of single studies of a lack of statistical power, reverse inference and experimental design. This could lead to structure-function mapping which could create neural data used to develop cognitive theories. There is potential in the informatics approach if investigations are theory driven. If the input into 'big data' is atheoretical and not driven by cognitive processes, then the output will also be atheoretical and lack specificity. If one simply increases the amount of data, nothing substantial will be revealed about the brain-behaviour relationship and/or cognitive processes.

This thesis is aimed at developing a theory of the cognitive processes of the human visual system which could be further investigated using other single-case subjects and neuroimaging.

1.10   Hypothesis

Cortical reorganisation of the visual cortex occurs in adult humans and can be demonstrated through psychophysical testing surrounding homonymous paracentral scotomas caused by lesions to only V1. Cortical reorganisation of the retinotopic map in the adult human visual pathway can be investigated, measured and plotted on a cartesian map.

1.11   Aims

1. To determine to what extent can metamorphopsia in cases of occipital lobe damage be explained by retinotopic remapping

2. To gain a better understanding of the general mechanisms in the human visual system

3. To understand the mechanisms and functions of cortical reorganisation with general implications to study plasticity and learning in the visual system

4. To explore the possibility of using cortical reorganisation to visually enhance impaired individuals

Chapter 2

Cerebral metamorphopsia

2.1 Preface

In this thesis, the term 'metamorphopsia' is used to describe visual distortion of lines and contours. Throughout the published literature, metamorphopsia is used inconsistently [50, 13, 51, 52]. Some articles extend the definition of metamorphopsia to distortion of visual hallucinations as well as true percepts [53]. The term 'dysmorphopsia' has also been used to describe visual distortions of lines and contours, or distortion of fixed objects [13, 54, 5]. However, dysmorphopsia has also used interchangeably with "dysmegalopsia", objects appear to be modified in size [55]. Another article defines dysmetropsia as subjective distortions in size and metamorphopsia as distortion of shape [56]. Dysmorphopsia is not universally used to describe only visual spatial distortions [51]. A general search and broad review of the literature regarding metamorphopsia/dysmorphopsia in adult humans is presented in this chapter. Cases of metamorphopsia from clinical practice have also been included. An attempt has been made to categorise the articles and clinical cases. They have been grouped according to anatomical location of the cerebral pathology and the likelihood of cortical reorganisation of the retinotopic map as the cause of the distortion. The term "reorganisation" will refer to structural reorganisation or long-term plastic changes within the visual cortex in response to neuronal loss such as potential axonal sprouting with cortical remapping [57]. It should be noted that in the literature, some groups use "reorganisation" to include fuctional organisation. This relates to long-term functional changes such as long-term potentiation or depression, uncovering or re-weighting of signals mediated by pre-existing cortical connections between V1 and other visual areas [58]. Also, "reorganisation" should not be confused with adaptation. Adaptation is the short-term functional modifications of neuronal interactions within the visual cortex such as adjustments to neuronal responses.

When attempting to further understand the general mechanisms of the human visual system, one could assume studying the mature adult would decrease potential variables. A 14-year-old published case and a 16-year-old clinical case have been included in this chapter. However, in these teenage cases, there may be additional or alternative visual processing mechanisms at play. Deciphering the complex long-term mechanisms leading to persistent abnormal visual perception, may lead to manipulation of the visual processing 'code'. After injury to the human visual system, reprogramming the 'code' could minimise an individual's visual impairment.

2.2 Review of the literature

A search was performed using PubMed, Web of Science, Medline and Google Scholar. Articles of all languages were included in the initial search and there were no limitations to the date of publication. The search terms used were: human, adult, metamorphopsia, prosopometamorphopsia, dysmorphopsia, visual distortion, visual perception disorder, positive spontaneous visual phenomena, cerebral, cortical, striate cortex, V1, visual pathway, visual processing. Some older articles were not found through searching databases as their date of publication preceded the database limits. These articles were found through references made by other articles. There were difficulties sourcing older articles and those that were inadequately referenced by authors. There were also difficulties obtaining formal translations of articles not published in the English language. However, English language abstracts were published by some authors and these have been included. Articles were excluded if the visual distortions were drug-induced, migrainous or due to sensory deprivation. However, some illustrative cases have been included for comparative purposes. A summary table is in the appendices.

2.2.1 Drug-induced cerebral metamorphopsia

The pathophysiology of cerebral metamorphopsia caused by pharmacological drugs is likely due to diffuse neurotransmitter and neuroreceptor alterations. Drug-induced metamorphopsia is unlikely to result from cortical reorganisation of the retinotopic map and will not be discussed in detail in this thesis. However, an example case is presented here for comparative purposes [59].

A 57-year-old Caucasian man presented to his optometrist with blurred distance vision. He had no previous ocular injury, surgery or disease. He had a 40-year history of perceiving "trailing images". His past medical history included hypertension, depression, suicide attempts, panic disorder and polysubstance drug use. He also had multiple head traumas and experienced painful non-throbbing headaches without visual auras for the previous 15 years. He had a recent history of alcohol, tobacco, and marijuana use. Use of crack

cocaine, amphetamine, heroin, and LSD were reported to all be in sustained remission. Regular medications included allopurinol, loratadine, trazodone 100 mg, hydrocodone/acetaminophen, lisinopril, mirtazapine, and amlodipine. Trazodone helped him sleep at night, although he reported nightmares secondary to its use.

Best-corrected visual acuity was 20/20 in each eye with subjective refraction. He had normal pupillary responses and no visual field defect.

The patient first experienced "tracers" shortly after using LSD in his teenage years. These tracers occurred whilst he was awake and in all fields of gaze. They appeared when an object moved relative to its background. The result was full-color, translucent, comet-like trails, often with a row of multiple distinct images of a brightness and intensity similar with the original object (palinopsia). Occasionally, the tracers resembled a "movie, but slowed down". He also perceived "beams of light" coming down from light bulbs and lamps, appearing like halos. He describes metamorphopsia when viewing parallel lines such as a doorway. The two parallel walls comprising the doorway would change size in a "teeter-totter" fashion. He had experienced these phenomenon constantly for 40 years so he thought they were benign in nature.

Enhanced MRI of the brain performed 3 years previously was normal apart from a "small old lacunar infarct in the belly of the pons". It was concluded that the palinopsia was primarily related to LSD use as the onset of his symptoms preceded the head traumas and trazodone therapy. However, multiple head traumas and trazodone could have exacerbated his visual symptoms.

Summary of visual phenomena:

- Palinopsia

- Metamorphopsia, distortion of parallel lines

Possible aetiology of visual distortion:

- Hallucinogen persisting perception disorder or trazadone (diffuse neuro-transmitter/receptor changes from psychoactive drug use)

2.2.2 Demyelination

Multiple sclerosis (MS) causes central nervous system demyelination. This can affect the anterior and posterior visual pathways. Increased inflammatory cytokines and synaptic hyperexcitability is associated with demyelination [60]. The metamorphopsia experienced from demyelination is unlikely to be due to long-term cortical reorganisation of the retinotopic map. An example of acute demyelination causing prosopometamorphopsia has been included here for comparative purposes [61].

A 32-year-old right-handed woman with a 2-year history of relapsing-remitting MS presented with altered visual perception. She was receiving treatment with interferon beta-1a injections. She experienced distorted faces in her right field of vision. When looking at any face, the left side of that face, which she perceived in her right visual field, appeared distorted or elongated. People's eye appeared stretched-out in an almost ovoid shape on the affected side of their face. She did not experience visual distortion of any other objects. She also saw persistent translucent 'after-images' of previously witnessed visual images (palinopsia).

MRI performed during a symptomatic episode, showed an extensive area of T2-hyperintense and T1-hypointense signal, with enhancement in the left periatrial region, extending into the occipital subcortical white matter with minumal mass effect. There was a second enhancing lesion in the left frontal area. Additional non-enhancing smaller lesions were noted in the bilateral periventricular, pericallosal and corpus callosal regions.

Her visual symptoms lasted several week and spontaneously improved without steroid treatment, but never returned to baseline. She continued to experience these visual phenomena episodically without identifiable triggers.

Summary of visual phenomena:

- Pure hemi-prosopometamorphopsia

- Palinopsia

- No visual field defect

Other neurological symptoms or signs:

- Difficulty performing tandem gait

Possible aetiology of visual disorder:

- Epileptogenic discharge, deafferentation, active demyelination involving either the optic radiations or the visual association area in the temporo-occipital region of the left hemisphere.

2.2.3   Possible cortical reorganisation of the retinotopic map

The following articles published cases suffering from visual spatial distortions possibly due to cortical rewiring or remapping.

Left occipital lobe gunshot wound [62]

In his book written in 1917, Poppelreuther described a case who suffered a gunshot wound of the left occipital lobe. This case described objects would visually appear to dance paroxysmally and were elevated forcing him to look upwards. There was a wave-like distortion of objects. After he experienced this distortion, his gunshot wound would hurt. He also had paroxysmal blurring of his vision, two perimacular scotomas, and confused the colours blue and green. He was observed to have these symptoms for nine months and had no futher follow-up after this period.

Summary of visual phenomena:

- Metamorphopsia, wave-like distortion of objects

- Dyschromatopsia

- Movement disturbance

- Visual symptoms were present for at least 9 months

Possible aetiology of visual distortion:

- Deafferentation

- Cortical irritation or epileptic discharge during wound healing

- Probably temporal and/or parietal lobe damage or oedema as well

Left or midline occipital gunshot wound [63]

Case 1 was a 24-year-old male with a gunshot wound causing a left or midline occipital lesion. He experienced distortions of vertical lines and components. Lines would appear "geknickt" (bent/broken/fragmented) like a branch stuck into the water ("wie ein ins Wasser gesteckter Stab"). He had a right hemianopia, and vertigo associated with double vision.

Summary of visual phenomena:

- Distortions of vertical lines

- Right hemianopia

- Vertigo (vestibular involvement)

- Diplopia

Possible aetiology of visual distortion:

- Possible residual vision in right hemifield or an incomplete hemianopia

- Cortical irritation or epileptic discharge from healing

- Cortical deafferentation

Left occipital lobe lesion from shrapnel [63]

Case 2 was a male of unknown age who had a left occipital lesion from shrapnel. He had a right paracentral scotoma and visual distortion of contours. He also had apparent movement of the right side of objects. He experienced a loss of "Tiehensechen" (spatial vision) with depth appearing shallower.

Summary of visual phenomena:

- Visual distortion of contours

- Depth perception problems (shallow appearance)

- Illusion of movement of the right side of objects

- Right paracentral scotoma

Possible aetiology of visual distortion:

- Possible parietal lobe involvement

- Cortical irritation or epileptic discharge from healing

- Cortical deafferentation

Right occipital lesion [64, 65]

Case 2 was a 58-year-old male casemaker who suffered from decompensated arterial hypertension. When he got up from bed in the mornings, he did not see a portion of the objects in his room. His employer would find his work lying on the left side of the desk. He thought something was restraining his left foot. He did not have a headache. A few days later, he experienced dizziness but no problems with his speech.

His vision progressively worsened and he noticed objects appeared visually distorted after eight months. Lines were wavy both vertically and horizontally, lines that were vertical were more distorted. He had difficulty "finding the centre". When he looked at his desk from above, it appeared arched more so on the left. Sometimes it was convex and other times it was concave. He did not describe macropsia or micropsia.

Whilst reading, he sometimes was not able to read the left side of the print and used his finger to follow the lines. He read better with one eye open rather than bionocularly. There was no difference between using each eye to read. His fundi were normal. Visual field testing of the right eye demonstrated a severe defect in the upper left (nasal), at times he had "concentric constriction (for white and red)". In both eyes, the left upper border seemed narrower and the upper half seemed narrower than the lower half.

The symptoms of visual distortion had appeared three years previously when his tools appeared too short or obscured. He often feared objects would slip off his table due to the convex bending appearance. Straight lines became especially bent after he focused on something: "it suddenly became bent, wavy, with the bend in the wave mostly towards the left". Visual field testing at this time revealed bilateral concentric constriction.

He suffered from cardiac issues with occasional throbbing headaches, especially the left temple. He had optokinetic nystagmus more pronounced to the right than the left, upward weaker than downward. It was concluded that poorly controlled hypertension was the cause of his symptoms with the "formation of red softenings during decompensated hypertension" and perhaps "multiple, bilateral small vascular lesions". The author also suggested another small lesion in the striate area of the right hemisphere as the cause of the "hemianopic visual field defect of the left upper quadrant during repeated examinations of the right eye" which was "more constant, clearer and extensive than in the left eye".

Summary of current visual phenomena:

- Metamorphopsia eight months after first symptoms, lines were wavy vertically and horizontally, vertical lines were more distorted

- Depth perception issues

- Right monocular severe upper left (nasal) visual field defect, at times he had concentric constriction

- Optokinetic nystagmus more pronouced to the right than the left

Three years previously:

- Visual distortion of tools appearing too short or obscured, straight lines became bent after focusing on something

- Visual space curved to the left, sometimes convex and other times concave

- Bilateral concentric constricted visual field testing

Possible aetiology of visual distortion:

- Deafferentation

- Potential parietal and/or temporal lobe involvement from posterior cortical artery hypoperfusion, right worse than left.

Left optic radiation haemorrhage [66]

A 63-year-old right-handed male presented with acute right hemiparesis. He had a past medical history of hypertension. On examination, he had a right homonymous hemianopia, right inferior facial palsy and right hemiparesis without sensory involvement. The right homonymous hemianopia resolved on the third day. However, on the fourth day, the left cheek of his doctor appeared to be 'scraped'. The doctor's left hand was tortuous and some of the fingers of the hand seemed to be missing. He did not have a visual field defect at this time with confrontation examination and Goldmann perimetry. On the fifth day, the patient described visual hallucinations of the "right half of curtain in front of me suddenly transforms into animal's face. It rotates there for a while and finally flows to the right and then disappears. At the next moment, another face springs up at the very portion. . . ". These visual hallucinations lasted for three to four days. One month after presentation, he was able to walk without assistance and was discharged from hospital.

CT brain showed left putaminal haemorrhage without ventricular extension or mass effect. The putamen is the largest and most lateral part of the basal ganglia. A pattern shift VEP showed moderately delayed latency of P100 during right visual hemifield stimulation compared to stimulation of the left hemifield, indicating involvement of the left visual pathway posterior to the optic chiasm. This article claimed to be the first reported case of a left optic radiation lesion causing metamorphopsia.

Summary of visual phenomena:

- Prosopometamorphopsia

- Metamorphopsia of hand and face

- Complex visual hallucinations, lasting 3-4 days

- Right homonymous hemianopia, which resolved on the third day

Other neurological symptoms or signs:

- Right hemiparesis without sensory involvement

- Right inferior face palsy

Possible aetiology of visual distortion:

- Most likely release phenomenon visual hallucinations, resulting from interrupted input to the striate cortex. There could be rewiring of the deprived retinotopic maps posterior to the optic radiation.

Lateral right occipital lobe [67]

A 71-year-old right-handed female noticed everything on the left appeared smaller in size, shrunk and distorted. It was as if she "was looking at reflections from a broken mirror" whilst she was watching the television. Reading was difficult due to letters appearing to overlap one another, and the lines of the text were not properly aligned. Her general and neurological examinations were normal. She was able to recognise objects and name colours. Everything on the left side appeared distorted in size. However, when she was dreaming or imagining objects with her eyes close, there was no distortion. Visual field testing performed three days after the onset of her visual symptoms was normal. She had a past history of hypertension and ischaemic stroke in the left parieto-occipital region three years previously. After this stroke, she had a right homonymous hemianopia for a few days but this spontaneously resolved. A second stroke was diagnosed as the cause of her current symptoms. One month after onset, her perceptual deficits remain unchanged.

Eight neuropsychological and experimental investigations of 'dysmetropia' were performed over a two month period.

MRI demonstrated two lesions:

1. An older lesion on the left side involving inferior parietal lobe (Brodmann areas BA39 and BA40) and part of the superior parietal lobe (BA5 and BA6)

2. More recent lesion involving the lower part of the lateral aspects of the right occipital lobe, included parts of BA18 and BA19

When correlated to recent functional maps based on functional MRI in humans, the presumptive location of the lesion was posterior to area MT (V5) involving ventral V4 (V4V) and part of the lateral occipital area.

Summary of visual phenomena:

- Hemi-metamorphopsia

- Normal visual fields (transient right homonymous hemianopia from previous left parieto-occipital infarction)

Possible aetiology of visual disorder:

- Reorganisation of the visual processing system could be possible. Higher visual processing areas affected on the right, and previously on the left three years ago. V1 presumed to be intact both sides as normal visual field tests. Visual spatial distortion was long-standing so this could be reorganisation of the retinotopic map of higher visual processing areas.

Several questions are raised by this case:

- Did the previous damage to left parieto-occipital region cause the distortion to be experienced after the recent right occipital infarction?

- How much influence does each hemisphere have on the final visual scene that is perceived?

Chapter 6: Cerebral Metamorphopsia, from [68]

The authors reviewed 708 patients admitted to the Psychiatric-Neurological University Hospital in Vienna during the period 1.1.1950 to 31.12.1963. These patients had verified localised lesions of the cerebral hemispheres. The location of each lesion was verified anatomically. The localisation was checked by autopsy in 99 cases (41.1%) and in 142 cases (58.9%) by operation/surgery. There were 110 women (45.6%) and 131 men (54.4%). The average age was 57.2 years (range 6-87 years). The diagnoses were 95 gliomas, 51 encephalomalacias, 34 meningiomas, 21 metastases, 20 traumatic lesions, 8 angiomas, 7 intracerebral haematomas, 3 brain abscesses and 2 sarcomas.

The authors use the term 'metamorphopsia' only for cases who experienced contours and lines as distorted. They excluded dysmetropsia and also the blurring of contours in cerebral asthenopia. They compared the incidence of cerebral metamorphopsia with each anatomical location. There were 10 cases due to brain stem lesions and 53 cases due to lesions of the cerebral hemispheres out of the total of 708 patients.

The distorted vision was reported as occurring transiently in all the cases. However, the term 'transient' was not defined in the article and the distortion was associated with epilepsy in some cases. The distorted vision did not cause mistakes or misinterpretations of visual objects. Also, these cases did not have spatial agnosia due to the cerebral metamorphopsia.

Metamorphopsia occured in 53 cases with cerebral hemisphere lesions and 10 cases who had brainstem lesions.

[68], Cerebral metamorphopsia (distorted vision); Localisation of lesions

Table 2.1 – Table 2 of [68], L = left-handed or ambidextrous patients

Localisation	Left cerebral hemisphere	Right cerebral hemisphere	Bilateral	Total number
Occipital	11	17	10	38
Parieto-occipital	11 (4 L)	23 (1 L)	13	47 (5 L)
Temporo-occipital	15 (1 L)	18 (1 L)	6	39 (2 L)
Parieto-temporo-occipital	70 (7 L)	32 (6 L)	15	117 (13 L)
Total number (occipital and adjacent areas)	107 (12 L)	90 (8 L)	44	241 (20 L)
Parieto-temporal	33 (6 L)	25 (1 L)	3	61 (7 L)
Temporal	33 (1 L)	19	1	53 (1 L)
Parietal	49 (3 L)	49 (7 L)	4 (1 L)	102 (11 L)
Fronto-temporal	16 (1 L)	16 (1 L)	5	37 (2 L)
Fronto-parietal	39 (5 L)	37 (5 L)	5	81 (10 L)
Fronto-temporo-parietal	16 (1 L)	9 (1 L)	2	27 (2 L)
Frontal	36 (3 L)	38 (2 L)	32	106 (5 L)
Total Number: Non-occipital	222 (20 L)	193 (17 L)	52 (1 L)	467 (38 L)
Total Number: Cerebral hemispheric lesions	329 (32 L)	283 (25 L)	96 (1 L)	708 (58 L)
Lesions of the brainstem and cerebellum				120 (- L)

Localisation	Left hemisphere	Right hemisphere	Bilateral	Total Number
Occipital	-	2	-	2
Temporo-occipital	-	3	-	3
Parietooccipital	4 (2L)	2	3	9 (2L)
Parietotemporooccipital	5 (1L)	11 (2L)	2	18 (3L)
Parietotemporal	-	4	- 4	
Temporal	-	7	-	7
Parietal	-	5	-	5
Frontoparietal	1	2	-	3
Frontotemporal	-	1	-	1
Frontal	-	1	-	1
Hemispheric lesion	10 (3L)	38 (2L)	5	53 (5L)
Brainstem lesion	-	-	-	10
Total number	-	-	-	63

The cerebral lesions associated with metamorphopsia were mostly in the right non-frontal regions (i.e. occpital, parietal, temporal) and the brainstem. The authors postulated that a lesion within the brainstem and the non-frontal regions of the non-dominant cerebal hemispheres may produce the phenomenon of cerebral metamorphopsia.

Cerebral metamorphopsia was associated with agnosia in 21 cases, polyopia in 4 cases, oblique vision in 2 cases, dysmetropsia in 3 cases and cerebral blindness in 2 cases. As noted above, the distorted vision itself did not result in spatial agnosia.

The authors performed a systematic investigation where stimulation of the subjects labyrinths was compared with the occurrence of positive visual phenomena. Form their results, the authors surmised that stimulation of the vestibular apparatus may produce cerebral metmorphopsia in a great number of patients who have a lesion of the occipital, temporal or parietal regions of the right hemisphere. These lesion locations were similar to those in which metamorphopsia may occur spontaneously in their cohort of cases.

2.2.4   Probably not cortical reorganisation of the retinotopic map

Critchley 1949 [13]

Critchley concluded cerebral metamorphopsia mostly occurs when lesions are close to the visual cortex (V1) and the geniculo-striate radiations, but without actually involving these anatomical areas.

1. Focal lesions of the brain Four cases with lesions adjacent to the occipital lobes were quoted in this paper:

   (a) Right middle cerebral artery thrombosis, "all the mats were crooked". Most likely right parietal lobe affected.

   (b) Left parieto-occipital glioma, "The furniture seemed to be turned around"

   (c) Right temporo-parietal glioblastoma, "Things for a minute or so seem smaller than they actually are"

   (d) Right parietal area puerperal venous thrombosis, "Objects looked different and blurred. Her husband seemed too big, and yet unduly far away"

2. Metamorphopsia occurring within a portion of the visual field Critchley quoted the following two cases:

   (a) "A woman with a post-encephalitic state was subject to recurring oculogyric crises in which her eyeballs would involuntarily become deviated towards the right. During these attacks, her vision became altered, so that the lower part of the objects looked at were obscured, while the upper portions were seen with greatly exaggerated detail."

   (b) "A woman with signs pointing to a left-sided rapidly growing cerebral tumour, developed a distortion of her sight. Objects to her right side looked more distant and larger than to the left, while objects to the left side appeared diffuse, distorted, and smaller than usual."

Epilepsy or epileptiform discharges

Visual distortion experienced in epilepsy or epileptiform discharges cannot be due to cortical reorganisation unless caused by a structural cortical lesion. Also, the perceptual visual disorder should occur in the inter-ictal periods as well as ictal episodes.

1. Critchley 1949 [13] Metamorphopsia described to arise in two circumstances in the context of epilepsy:

   (a) As an aura to an attack. Dysmetropsia (micropsia and macropsia) preceed attacks of unconsciousness

   (b) As an important part of an episode of psychical epilepsy (visual hallucinations, not an illusion)

   Critchley describes the illusion of movement as a form of epileptic metamorphopsia. He remarks that this form of visual illusion can be difficult to distinguish from characteristic vertigo.

2. Stauder 1934, unknown lesion causing seizures [69] A 32-year-old male with an unknown lesion experienced visual distortion during epileptic aura, absence and generalised seizures. He describes the wallpaper pattern disappearing and doctors' faces were distorted or oblique with an enlarged nose. Objects could also appear distant. He had the illusion or dreamy experience where the scenery and people around him would appear ancient or like in the mountains. He also had possible hemineglect or hemianopia of the hallucinating visual field.

3. Brain 1947, right posterior cerebral artery circulation disturbance due to malignant hypertension [70] A 43-year-old right-handed female had malignant hypertension. Her symptoms were of migrainous visual aura in the left half of her visual field. She had epileptiform attacks. During an attack of left-sided partial continuous epilepsy, she experienced macropsia, micropsia, metamorphopsia and more elaborate visual hallucinations. She also experienced hyperacuisis and sounds synaesthetically aroused visual hallucinations. The author suggested the visual symptoms could have been due to temporary impairment of circulation through the right posterior cerebral artery.

   Summary of visual phenomena:

   - Migrainous visual aura (simple visual hallucinations) in left hemifield

   - Dysmetropsia (macropsia and micropsia)

   - Metamorphopsia (no definition or elaborate description)

   - Complex visual hallucinations

Possible aetiology of visual disorder:

- Right posterior cerebral artery hypoperfusion due to malignant hypertension

- Epileptiform discharges or transient deafferentation

4. Bender 1968, patient 4, bilateral occipito-temporal epileptogenic activity [71] The term 'metamorphopsia' in this case was in reference the patient's description of "All the doctors in the room had green beards".

A 58-year-old female, unknown handedness, presented with acute bilateral blindness of cerebral origin. During her recovery, she had confusion and homonymous field defects worse on the left. Objects appeared "strange". Examiner's skin appeared reddish, his fingers were shorter than normal. Palinopsia, simple visual hallucinations of lights and complex visual hallucinations. Door to her room looked like "butter were smeared on it". The examiner's or her own fingers looked abnormally short. Orange appeared purple on pseudoisochromatic plates and she could not identify numbers. She had cognitive deficits including inability to state her age, do simple calculations or to name the year.

She was certain that all of these visual phenomena were unreal. Visual symptoms persisted for about six weeks and all resolved spontaneously. There was gradual resolution of the field defect and cognitive deficits. However, when reading pseudoisochromatic plates, she consistently made errors on the left side.

EEG during visual hallucinations showed "moderate voltage spikes and polyphasic sharp complexes at the right and left occipital and right posterior temporal electrodes". Left and right brachial angiograms were normal.

Summary of visual phenomena:

- Metamorphopsia

- Palinopsia

- Simple and complex visual hallucinations

- Polyopia

- Dyschromatopsia

- Chloropsia with complex visual hallucination: green beards on men's faces and green flies when there were none

- Teleopsia: some people appeared far away

- Lilliputianism: some people seemed very small

- Transient bilateral homonymous visual field defects, worse on the left

Other neurological symptoms or signs:

- Transient agnosia

- Transient disorientation in time and place

Possible aeitiology of visual distortion:

- Bilateral occipital and right posterior epileptogenic activity of unknown cause

5. Nass 1985, right parieto-temporo-occipital arteriovenous malformation [72] A 14-year-old caucasian right-handed female described visual distortions affecting faces and objects. People looked different than their known appearance, their faces appeared older. She was still able to identify the faces. The known white walls of the kitchen appeared yellow and shapes of objects were distorted. She also continued to fill a glass with milk even though it was full.

EEG demostrated posterior temporal slow and sharp wave activity synchoronously bilaterally, as well as independently from the right hemisphere. VEPs were normal. Brain CT revealed a calcified right parieto-temporo-occipital lesion with slight contrast enhancement. Cerebral angiography was normal. She underwent partial excision of the thrombosed and calcified AVM. After the surgery and commencing carbamazepine, she rarely experienced episodes of visual distortion. Two-and-a-half years later, she developed severe headaches and had a follow-up brain CT. This CT brain demonstrated haemorrhage into the AVM. She again underwent surgery for resection of the AVM and a CT brain six months later demonstrated a small residual calcified lesion. Following the second surgery, she had no further seizures whilst taking carbamazepine.

Summary of visual phenomena:

- Object metamorphopsia

- Dyschromatopsia

- Prosopometamorphopsia

- Depth perception issues

- Episodic, resolved with partial resection of arteriovenous malformation (AVM) and carbamazepine

- Normal visual fields

Possible aetiology of visual disorder:

- Epileptogenic discharges from AVM

6. Young 1989, right parietal astrocytoma with PLEDs [73] This case has a very similar description of visual phenomena compared with two of the clinical cases, see Section 2.3.1.

A 38-year-old right-handed female experienced a tonic-clonic seizure four months before hospital admission. CT brain demonstrated an enhancing right parietal mass. A biopsy III-IV astrocytoma was partially resected. She also received radiotherapy. She suffered from the occasional focal seizure, however, EEG correlation was not obtained. During the focal seizure, she experienced left arm and shoulder numbness and clumsiness.

Months after her neurosurgery and radiotherapy, she experienced palinopsia where the first object she looked at would be superimposed on the next in her left visual field. These symptoms resolved with increased corticosteroid treatment. The day before her admission, she experienced a five hour period of left arm dysaethesia and involuntary movements of her left limbs. For one hour, she also experienced increased intensity in street lights and coloured objects. The following morning, she experienced palinopsia and visual perseveration. She had prosopometamorphopsia where faces appeared distorted. Her "son's head appeared split between the eyes and nose with the two parts separated horizontally". She also felt decreased body awareness, incoordination and spatial disorientation.

The Goldmann visual field test was normal. CT brain scan demonstrated no change from previous scans. EEG demonstrated PLEDs with repetitive rate of 1 to 1.5 Hertz in the right parital region and right-handed slowing. Her dose of lorazepam and phenytoin were increased. However, during her six day hospital admission, she developed bizarre prosopometamorphopsia where "one day visitors had beards sprouting from their faces; on another day they were balding; at one time, eyes left the skull and rotated in front of their heads; chins deviated to the right; and features of people disappeared and reappeared". She decribes her bed appearing shorter and objects in front of her getting smaller. She commenced carbamazepine and her condition improved.

After the visual symptoms resolved, an EEG demonstrated a 9 Hertz posterior rhythm had replaced the PLEDs. However, there were still changes consistent with focal cerebral dysfunction and a skull defect in the right posterior quadrant.

Summary of visual phenomena:

- Bilateral prosopometamorphopsia

- Unilateral palinopsia in the left visual field

- Polyopia

- Micropsia

- Dyschromotopsia

- Spatial disorientation

- Loss of depth perception

- Normal visual field test

Other neurological symptoms and signs:

- Seizures

Possible aetiology of visual disorder:

- Periodic lateralised epileptiform discharges (PLEDs) are semi-regular EEG findings that predominate in a hemisphere or focal region of the brain. This subject only had visual symptoms when there were PLEDs on EEG.

7. Satoh 1997, left occipital epilepsy [74] A 55-year-old right-handed man suddenly noticed unformed visual hallucination of rainbow-coloured balls coming out of the lower quadrant of his right visual hemifield. Visual field examination demonstrated a right lower quadrant homonymous hemianopia. Metamorphopsia of the hand or face appeared six days later whilst observing his hands or face in the mirror. This visual distortion persisted for around ten minutes.

1231-IMP SPECT demonstrated marked increase in cerebral blood flow of the left occipital pole during the visual symptoms, and marked decrease in cerebral blood flow after the symptoms resolved. T1- and T2-weighted brain MRI were normal. Gd-DTPA-enhanced T1-weighted MRI brain showed high signal subcortical white matter of the left occipital pole.

Summary of visual phenomena:

- Ten minute episode of metamorphopsia of hand and face

- Simple visual hallucinations

- Right lower homonymous quadrantanopia

Possible aetiology of visual disorder:

- Metamorphopsia was probably induced by an epileptogenic mechanism in the left occipital lesion. However, the nature of the lesion remained unclarified.

8. Heo 2004, right temporo-occipital epilepsy [75] A 56-year-old right-handed female was admitted to hospital after experiencing recurrent flickerings and continuous metamorphopsia. She had a past medical history of hypertensive cerebral haemorrhage in the right occipital region seven years before the onset of these visual symptoms. She also suffered from severe chronic renal failure, hypertension and diabetes mellitus. She had the sensation of objects being closer to her (pelopsia). These episodes were short-lived and disappeared spontaneously. Four months before her admission to hospital, she experienced repeated flickerings in her left visual hemifield, objects appeared neither nearer (pelopsia) or farther that they were in reality (teleopsia). This was followed by a headache in the right occipital region. MRI brain demonstrated focal cerebromalacia at the right temporo-occpital junction. She was commenced on valproate. Two months later, she ceased the valproate due to epigastric discomfort and nausea. She did not have any seizures whilst she was not taking valproate.

Ten days prior to her admission, whilst looking at human faces she observed a continuous visual illusion of the faces appearing distorted, swollen and grotesque. Four days later, she experienced repetitive flickering in the left or whole visual field. The flickering also appeared to be moving towards her. The episodes of flickering lasted a few minutes each time and recurred 15-30 times per day. On many occasions during these episodes, objects in front of her appeared to be nearer (pelopsia) or farther away (teleopsia), or they seemed to rock from side-to-side. She did not lose consciousness at any stage during these episodes. Her blood pressure at this time was 110/70 and she had a dense left homonymous hemianopia. The metamorphopsia was restricted to only faces. Bodies, animals and other objects appeared normal. She did not have prosopagnosia. Repeat MRI brain did not reveal any interval changes. She recommended sodium valproate.

Two days after admission, she was experiencing a continuous state of metamorphopsia and less frequent episodes of flickering. By day three, the frequency of the flickering episodes decreased further. However, the metamorphopsia persisted and was continuous. EEG for 40 minutes showed poorly developed alpha activity in the right occipital region. This was frequently intruded by rhythmic slow waves lasting 5-20 seconds, with little evidence of evolving change. By day four, the metamorphopsia disappeared and repeat EEG showed well-developed and symmetric posterior alpha activity.

She ceased the anti-epileptic medication valproate due to recurrence of epigastic discomfort and nausea. However, the seizure activity had ceased when she commenced regular peritoneal dialysis for her chronic renal failure. She still had the left homonymous hemianopia, however, she could recognise crude stimuli

in the scotoma.

SPECT imaging demonstrated an increased blood flow region in the ventrolateral aspect of the right temporo-occipital junction (middle and inferior occipital, and inferior temporal gyri). This area was adjacent to the cerebromalacia.

Summary of visual phenomena:

- Prosopometamorphopsia only: distorted, swollen grotesque faces
- No other objects distorted
- Simple visual hallucinations
- Pelopsia
- Teleopsia
- Illusion of movement
- Dense left homonymous hemianopia

Other neurological symptoms or signs:

- Right occipital headache
- No prosopagnosia

Possible aetiology of visual disorder:

- Epileptogenic discharge in cortex surrounding cerebromalacia
- Deafferentation
- Metabolic disorder from chronic renal failure

9. Orjuela-Rojas 2015, right temporo-parieto-occipital epilepsy due to right temporo-occipital neurocystocercosis [76] The detailed description of this case's experiences is an example of how a patient's background, education or interests can influence the communication of their subjective perceptions to others.

A 36-year-old woman, with a bachelor's degree in psychology, worked as a housewife due to the frequency of her seizures. At the age of 5, she presented suddenly with fever, headache, left-ward gaze deviation, vomiting, and generalised tonic–clonic seizures. At age 9, she intermittently saw colourful lights for a few seconds in the inferior and temporal quadrant of her left eye. During her adolescence, she experienced distortion of form and the contour of objects located in her left hemifield for a few

seconds: "I see something like a bubble that appears in the left side of my eye, as if it was a kaleidoscope distorting the people, the lines, everything. . . It's like putting a drop of water in a glass. . . Or like a magnifying glass moving upwards".

The visual illusion continued to appear repeatedly during her life, sometimes once a week. On some occasions, it was followed by generalised tonic–clonic seizures. Between ages 5-17, just after the metamorphopsia: "Sometimes I saw a luminous dot, a white and bright light. Inside it I could see different things. . . Once I saw my deceased grandmother; sitting down, wearing a beige dress. It was a very clear image, as if I was watching the television. I was fond of her. . . She died when I was very young. . . After that I had a strong seizure. On another occasion, I saw the image of an aerialist: it was a young woman with a white suit, juggling on a trapeze, jumping from one place to another. I have also seen the school janitor screaming, wearing a white and blue striped polo shirt." She could not hear this janitor, but she thought he appeared to be screaming. Her visual experiential hallucinations lasted between one and five minutes. They always appeared before a generalized seizure.

At age 16, she experienced a phenomenon related to recognition of her own body (hemi-asomatognosia): "I was going to take a glass, so I extended my left hand to reach it and I asked myself: what is it that is moving? And then I realized it was my hand!". She had a generalized seizure a minute after the asomatognosia. She again experienced this phenomenon at age 28 and repeatedly since then. "I feel strangeness in my left side. It's not asleep, I perceive pain, I can move it, the only strange thing is the feeling that it's not mine. At the beginning it was only the arm, then it spread to the leg and the half of my face. It's as if I was not there, I need to touch my leg in order to know I have one. I know it's mine because I see it, but not because I feel it." This phenomenon occurred twice a month and lasts from seconds to minutes.

She had no other medical problems in addition to her epilepsy. Her physical and neurological examinations were normal. Her mental status examination was also normal regarding cognitive functions and emotional state. She did express concerns relating to her hemi-asomtognosia. "My husband doesn't believe me, but sometimes I feel that my left arm and leg are not mine; I have to lay down on my left side to make some pressure on them because I feel they are so strange." Aside from these subjective abnormalities, she did not have any delusions or somatoparaphrenia (delusion where one denies ownership of a limb or an entire side of one's body). Her family had not observed any psychotic symptoms. Her reality test was normal, and her main explanation for her symptoms agreed with the medical explanations.

Blood tests, inter-ictal EEG and neuro-ophthalmological assessment were normal. MRI brain demon-

strated a rounded, hypointense, well-defined lesion in the right occipito-temporal cortex without peri-lesional oedema. The lesion was classified as a nodular calcification due to neurocysticercosis. CT brain demonstrated the density of the lesion was similar to bone, supporting the calcified nature of the lesion.

PET study showed mild hypometabolism in two regions: right posterior temporal cortex and right parietal cortex. The rest of the PET study was within normal limits. She was given a diagnosis of focal temporo-parieto-occipital symptomatic epilepsy due to brain cysticercosis. Treatment with valproic acid (500 mg twice a day) and levetiracetam (500 mg twice a day) successfully reduced her seizure frequency.

The authors' hypothesis for the cause of her symptoms was an epileptogenic lesion corresponding to calcification located in the right occipito-temporal cortex. They postulated this cortex receives inputs from different unimodal areas located in the occipital, temporal, and parietal areas. Inter-ictal hypometabolism of the right posterior temporal cortex and right parietal cortex, suggest epileptic activity arises from these areas. The epileptogenic zone is associated with the symptomatogenic zones, meaning abnormal epileptic activity propagates through several topographic routes which generates symptoms beyond the epileptic origin. Propagation of activity through the occipital lobe is related to simple visual hallucinations. Propagation through the occipito-temporal pathway could account for the metamorphopsia. The complex experiential visual hallucination probably arises when the epileptiform discharge reaches the anterior and medial temporal regions (amygdala and hippocampus). Her hemi-asomatognosia could be related to extension through the parietal lobe, corresponding to an area of functional deficit which was revealed by the inter-ictal hypometabolism seen on PET.

Summary of visual phenomena:

- Metamorphopsia

- Left hemi-asomatognosia

- Simple, complex and experiential visual hallucinations

Other neurological symptoms or signs:

- Fever, headache, left-ward gaze deviation, vomiting and generalised tonic-clonic seizures

Possible aetiology of visual distortion:

- Epileptogenic discharge due to right temporo-occipital neurocystocercosis

Structural optic radiation pathology

1. Geyer 1963, case 2, left optic pathway lesion posterior to chiasm or optic radiation (possibly aneurysm) and subarachnoid haemorrhage [77] A 24-year-old male experienced a sudden, severe headache the day before he was admitted unconscious with neck stiffness and bilateral pyramidal tract signs. He had bloody CSF on sub-occipital cistern puncture. Four days after his admission, he was able to describe his first headache being associated with the strange sensation of the left side of his face stretching and expanding suddenly "like a balloon". He also experienced vertigo which lasted approximately two minutes. After the episode had resolved, he observed his face in the mirror and discovered the left side of his face appeared deformed. Also, the left side of his head appeared grotesquely elongated. The left side of all the objects in the room appeared to be stretched vertically. He compared his visual distortion to the long shadow cast by objects when the sun is low in the sky. He then suffered the attack which caused him to lose consciousness and be admitted to hospital. By the time the history of the visual distortions was taken four days after his admission, they had resolved.

   Angiography suggested a small clinoidal posterior communicating artery aneurysm. However, this aneurysm could not be identified at craniotomy. The surgical team concluded an intrathalamic location for the lesion seen on angiography. The patient had a right homonymous quadrantanopia which they assumed to be due to a lesion of the left optic pathway immediately posterior to the chiasm or the optic radiation.

   Summary of visual phenomena:

   - Hemi-macropsia

   - Hemi-metamorphopsia

   - Right homonymous quadrantanopia

   Other neurological symptoms and signs:

   - Headache, unconscious with neck stiffness

   - Bilateral pyramidal tract signs

   - Vertigo

   Possible aetiology of visual disorder:

   - Epileptogenic discharge

   - Deafferentation

- Cortical irritation

- Vestibular involvement

Structural occipital lobe pathology

1. Bender 1968, patient 2, right occipital meningioma [71] A 49-year-old female who had a right occipital menigioma experienced visual distortion or enlargement of objects. When she fixatated on the examiner's nose, as the examiner's finger was held at their right ear, the finger appeared "broadened" and "increased" in size. A 6 millimetre white disc held in the same position appeared "larger and larger" in about fifteen seconds. Sometimes not only the real but also the false image increased in size a number of seconds after the real image appeared to do so. The distance of the object from the patient did not change. Macropsia and metamorphopsia occurred only in the left homonymous half fields, particularly the superior quadrants.

   Summary of visual phenomena:

   - Palinopsia

   - Dysmetropia

   - Metamorphopsia

   - Cerebral polyopia

   - Left homonymous superior quadrantanopsia

   Possible aetiology of visual disorder:

   - Epileptic discharge, deafferentation

   - Angiogram: right occipital meningioma = medial, ventral and anterior portion

2. Lance 1976, case 7, right occipital infarction (vertebrobasilar insufficiency) [78] A 53-year-old man had an attack of frontal headache with tinnitus, vertigo and vomiting. He had experienced a similar episode three months previously. On the second occasion, he developed a right intention tremor and dense left homonymous hemianopia splitting the macula. For the next two weeks, her reported distortion of objects (fingers became thicker and thinner, shorter then fatter), and additional fingers and hands appeared to be present on his left side. "A man who had just walked past his bed would be seen to make the journey again a moment afterwards (palinopsia). Two weeks later, he experienced formed complex visual hallucinations on the left side. He saw his beagle sitting on his bed and cats running

along a picture rail to his left. A group of visitors standing in front of him multiplied until the ward to his left was filled with a hundred people or so. There were occasional unformed hallucinations such as pairs of lights on an aircraft descending on a dark landing strip."

All visual phenomena ceased one week later.

Isotope brain scan demonstrated a "wedge of intensely increased uptake in the medial occipital lobe on the right side". Vertebral angiogram showed "some stenosis of the proximal part of the right posterior cerebral artery". The brain scan returned to normal after three months, however, his left homonymous hemianopia persisted.

Summary of visual phenomena:

- Non-geometric metamorphopsia

- Palinopsia

- Cerebral polyopia

- Simple and complex visual hallucinations

- Dense left homonymous hemianopia splitting the macula

Other neurological symptoms and signs:

- Frontal headache

- Tinnitus

- Vertigo

- Vomiting

- Right intention tremor

Possible aetiology of visual disorder:

- Deafferentation

3. Lance 1976, case 9, right occipital infarction (vertebrobasilar insufficiency) [78] A 62-year-old female music teacher experienced the illusion of movement "when the room seemed to rock backwards and forwards and she had to hang on to furniture to retain her balance". She noted a posterior headache. She veered to the left when she attempted to walk. She did not realise she was unable to see to the left until she was admitted to hospital. When she returned home and sat at her piano, she "could not see any not below middle C unless she turned her head to the left". She adjusted to her visual field defect

and began teaching music again. Four months later, she noticed a "rippling, whirling movement in her left half visual fields. This sensation recurred intermittently for two days but on the third day, the hallucinations assumed a definite form. She saw a life-sized stream of people coming towards her on the left side. Their faces were solemn but otherwise featureless and, as they passed by, some of them look at her, some bowed their heads, some shook their heads and others turned their heads away. She said she felt as though she were lying in Lenin's tomb in the Red Square of Moscow. Occasionally, a dog would pass by with its tail wagging 'just like my dog at home'. The next day, the visions partly subsided but any sensory stimulus or excitement started the hallucinations again. The siren of an ambulance or fire engine was enough to start 'a crowd of people scurrying about on my left side'. On another occasion, she smelt actual food cooking and it then appeared as though smoke was pouring from the wall on the left side. This impression continued on and off for two hours as long as the smell of food persisted. After one week, she saw no more people or smoke but the perception of any sudden movement in her field of vision would make it appear as thought the roof were flapping up and down and the walls of the room were undulating on the left side."

She also described palinopsia. When she was looking at a person, a second image of that person would detach itself from the real image and disappear into the background. On other occasions, she would see someone walk across a room and, a fraction of a second later, an identical image would repeat the action. She described a lady in a blue dress walking, seen 'with her right eye' and, a moment later, the same blue lady was seen in an identical performance 'with her left eye'. She had a similar experience with her own actions. She remembers placing some paper in an basket under her wash basin and then, when she turned the water on in the wash basin, she could see an image of herself placing the paper in the basket again. When she walked out of the bathroom she encountered five or six apparitions of herself, all doing things she had done a short-time beforehand.

A brain scan demonstrated increased uptake in the right occipital area which resolved over a period of three months. When she was given carbamazepine 600mg daily, the hallucinations lessened. When the dose was increased to 1200mg daily, the hallucinations disappeared.

Summary of visual phenomena:

- Movement of the visual scene

- Palinopsia

- Cerebral polyopia

- Illusion of movement

- Left homonymous hemianopia

- Transient left hemiparesis during the original episode

- Resolved with carbamazepine

Other neurological symptoms and signs:

- Posterior headache

- Imbalanced gait

Possible aetiology of visual disorder:

- Epileptic discharge, deafferentation

Structural parietal lobe pathology

1. Loss of depth perception or stereoscopic vision

   (a) Riddoch 1917, case 3, shrapnel bullet wound from left frontal vertex to right occipital pole [79], was quoted by Critchley in his 1953 book "The Parietal Lobes" [80] Quoted by Critchley in his 1949 article "Metamorphopsia of central origin" [13]: 'Everything he saw was flat. People had the appearance of cardboard figures; they had outline, but no depth. If two persons were standing in front of him, he could differentiate them only by their outlines, for they were featureless and had no rotundity. Their noses might have been painted on their flat faces. Friends were recognized only by their voices. A landscape was like a piece of stage scenery. Trees, hills, everything he saw, were at the same level; and yet he could recognize light and shade. A ball was simply a circle, an egg an oval, and a box a rectangle. This phenomenon was evident only if the objects were more than a foot away from him.'

   Quoted description of the case from the original article by Riddoch in 1917 [79]: "Case 3 - Captain de W. was wounded at Gallipoli on December 4, 1915, by a shrapnel bullet. He never lost consciousness, and he was aware, almost from the first, that he was blind in the left half fields. Though his right leg and arm were weak, he was able to hop to the dressing station.

   The entry wound, in the left frontal region, was enlarged the same night by Mr. Warren Low. There was no exit wound. By X-ray examination the bullet was found to be lying just inside the skull, near the right occipital pole. On January 7 it was removed, and an abscess evacuated.

   The fields of the patient were examined at Alexandria by Col. Bason a few days after he was wounded. There was a complete left homonymous hemianopia up to the fixation point. He missed food on the left side of his plate.

To Dr. Farquhar Buzzard, who examined him on May 31, 1916, I am indebted for the following note: "Vision in the left upper quadrant lost. Some return of vision in the left lower quadrant." The patient had two fits, the first on March 20 and the second on March 30. He was admitted to the Empire Hospital for treatment in the beginning of September under Dr. Buzzard. He gave a history of having been unable, during the earlier months of his illness, to perform purposive movements with his right hand, and a few symptoms of right motor apraxia remained, though it had apparently cleared up to a great extent. He had much less difficulty in knowing what to do with things, but he still had to think about every action. He could not perform movements spontaneously. There was only slight loss of power of sensation in the right arm. There was no agnosia, and he never failed to recognize the use of an object which he saw or felt.

He noticed first some recovery of vision in May, 1916. The movement of objects only was perceived, and solely in the periphery of the lower quadrant. The patient, describing this vision in a small strip of the half field, said that he saw the movement of objects below and to the left momentarily, but only to lose them again as they approached the centre of his field. When walking in the street he could see what he knew must be people's feet, though they had no shape, moving on the left, but he saw nothing to represent the body above the ankles.

Since May he has become aware that the narrow strip has increased in area from the margin towards central vision, and upwards towards the left upper quadrant. He still cannot see stationary objects on his left, even in the lower peripheral fields. The moving things, he says, have a vague grey shadowy appearance."

Quoted from the original article by Riddoch in 1917 [79]:

> Case 3 of this series presents many symptoms which are parallel to those described by Smith and Holmes. He was, as already mentioned, blind in the left half fields, though now he can appreciate movements in the periphery of their lower quadrants. His ability to orientate in space things that he sees quite well is almost entirely lost, and thickness and depth mean nothing to him visually. He has lost stereoscopic vision.
>
> I will describe his symptoms in detail as they seem to throw light on the nature of stereoscopic vision and on the relation of cerebral defects of vision to those of general sensation.
>
> In the earlier months of his illness, he was quite unable to combine simple movements into complete purposive acts with his right hand and arm. He had, it is true, some weakness and sensory loss of the right side, and for this reason I suppose his symptoms should not be described as apraxic; but the disability was out of all proportion to the amount of paresis and loss of sense of position. From the first there was no agnosia. He still hesitates before he uses things correctly with his right hand. Purposive movements lack spontaneity. The disability has always been, so far as can be ascertained, limited to the right side.
>
> Though he has no difficulty in bringing objects which he sees at once into central vision, this was not always so; for when in hospital at Alexandria he was frequently unable to get his eyes fixed on anything he was asked to look at, even when he knew quite well its position in space,

e.g., his hand.

He quickly looks in any direction to order or when a light is suddenly flashed from either side, or a sudden noise made. Strictly speaking, however, he does not rotate the eyes, but turns his head, keeping his eyes more or less stationary. Similarly when asked to follow a finger with his eyes, though he has no difficulty in keeping them fixed on it, the movement is not of the eyes but of the head. He said in explanation: " I am so accustomed to moving my head about when I read that I do it unconsciously." He has no trouble in keeping his eyes fixed on an object when his head is passively moved; nor in following it with his eyes when his head is kept fixed by the observer.

On being asked to explore the surface of a table with his eyes and to count the coins placed on it, he did it correctly. He believed however, that this would have been impossible for him in the earlier days of his illness.

His visual memory is apparently intact; and, at all events now, his ability to retain visual impressions is not affected, e.g., when a box, a pen, a test-tube and a patellar hammer were shown to him in quick succession and then hidden he described them accurately. There is no visual agnosia.

Visual orientation, however, is grossly upset. He is unable to localize in space the position of an object seen. When told to take hold of a matchbox which was held in front of him, though he saw it at once and kept looking at it, his hand groped about searching for it before it was finally grasped. The task was equally difficult whichever hand he used. He makes poor attempts at touching a spot on a piece of paper with his finger, and the plane in which the paper is held makes no difference.

The length of a room, in reality 18 ft., was thought by him to be 30 ft. Sitting about 3 ft. away from him, he said we were separated by a distance of at least 6 ft.; but he declared he was only guessing as he had no real idea of my relation in space to himself. He can tell only if an object is very near or very far away. He is able, however, to judge with a fair degree of accuracy the height or length of different objects, e.g., a walking-stick, a pencil, a house, but occasionally he makes gross mistakes.

Similarly, he is unable to estimate correctly relative distances and lengths. On a piece of paper held flat on a table before him, two large dots 4 in. apart and one nearer to him than the other, appeared to him to be side by side. When the dots were placed equidistant from the eyes, by shifting the paper round they were recognized to be so. The relative position of the two dots was, nevertheless, easily recognized when he was allowed to move his finger from the one to the other. His answers are equally wrong whether the objects are far away from him or near to him. He never says that the nearer object is the more distant.

Curiously enough, however, he can choose correctly, often several times in succession, the longer of two lines drawn on paper, irrespective of whether they are parallel or not. But if tested with the same lines a short time afterwards he may give a series of answers which are mostly incorrect. It is impossible to predict what his answers will be. With the line tests he appears to have, if anything, more difficulty when the paper is held some distance from him, say 6 ft. away, than when it is nearer.

When I was carrying out some of the tests one day ne suddenly said: "Everything seems to be really the same distance away. For example, you appear to be as near to me as my hand " (he was holding his hand 1 1/2 in. from his face and I was sitting about 5 ft. away from him). This loss of appreciation of the relative positions of things that he sees quite well has been the means of giving him many a fright. Two vehicles approaching one another in the street always seem to be about to collide. A person who is crossing the street is sure, he thinks, to be run over by a taxi that is really yards away. He used to stand and stare aghast till he found he was registering wrong impressions, and that the accidents which he expected to occur every minute did not come off. If two people walking together come towards him on the pavement and separate to let him pass, he loses sight of the one who goes to his left, as he is almost completely blind in the

left half field, and very frequently walks into the one on his right. He can see the man but he cannot judge how far away he is. When waiting with his wife to cross the street, the houses on the other side, the policeman and the refuge all seem to be the same distance away and quite near to him.

His most interesting defect is inability to appreciate depth or thickness in objects seen. The case described by Smith and Holmes had not apparently this difficulty, for they make no mention of it; so that visual localization and orientation may be dissociated from visual appreciation of depth. This symptom, in Captain de W., is very pronounced, and is a source of great trouble to him. The most corpulent individual might be a moving cardboard figure, for his body is represented by an outline only. He has colour and light and shade, but still to the patient he has no protruding features; everything is perfectly flat. One of the unfortunate results of this phenomenon is that friends are recognized only by their voices. A man can be distinguished from a woman because, on account of his dress, his outline is different, and he may possibly wear a beard or a moustache.

To the patient a chair is flat, though he knows from experience that his visual impressions are cheating him. Similarly a sphere is merely a circle, a cylinder a flat rectangle, a cube a square, and a pyramid a triangle. He appreciates shape perfectly.

A stair is a flat inclined plane with no protruding steps, and yet he knows from the light and shade that he ought to see the steps. It was only a few months ago that he began to recognize visually that the top of the flight was farther away from him than the bottom, when he stood a few feet away and looked at it. A landscape is like a painted picture or a piece of stage scenery. I was walking along the street with him on a bright day, when the pavement threw a deep shadow, and he mentioned that strictly speaking the pavement did not seem to him to be elevated above the street. He quite realized that the shadow meant that it was so, but, as he put it, " something else that indicates depth has been taken away, and, despite the difference in light and shade, to me they are both on the same plane."

Hollow vessels appear to have simply shape and no depth. Looking into a kidney-tray he sees only a flat kidney-shaped white metal plate, part of it in the shade and part not. Similarly a bowl viewed from the side is a flat semicircular disc, and if presented to him face on is a circular plate.

His visual pictures are just the same whether he examines objects with one or with both eyes; but immediately he uses his fingers he can tell that the things have depth as well as shape.

The visual defects shown by this case and by several others in the literature seem to me to be analogous to the defects in spatial discrimination found in sensory disturbances of cerebral origin.

Summarizing briefly the defects in visual orientation and in visual appreciation of depth which this patient shows, they are:— (1) Inability to localize an object which he sees; he can only distinguish whether it is very near or very far away. (2) Inability to tell which of two objects is the nearer to him; provided they are not separated by a great distance, they appear to be equidistant from him. He never chooses the one which is the farther away as being the nearer of the two. On the other hand, he frequently chooses correctly the longer of two lines drawn on a piece of paper, or the taller of two persons who are standing near one another; but he shows a certain inconstancy in this, so that one cannot foretell whether an answer will be right or wrong. (3) Inability to appreciate visually depth and thickness in objects, notwithstanding perfect consciousness of light and shade and possession of binocular vision. In his own words, " Something else that indicates depth has been taken away."

He can, however, describe correctly the forms of different objects which are presented in his visual field, e.g., a rectangle, a circle, a square, or a triangle.

Defects in spatial discrimination, similar in type to the visual dissociations enumerated above, are evident in his right hand. (1) Localization of a touch is defective in the first three fingers.

(2) Each finger has to be passively moved on an average through eight or nine degrees before he is conscious that the position has been altered; whereas he recognizes a change of posture when a finger of the left hand has been moved through one degree. (3) Appreciation of relative thickness of things is not nearly so acute with his right as with his left hand, e.g., when he was given, one after the other, two spheres of unequal size to feel with his right hand—though their diameters differed by almost 1/2 cm., he thought they were the same. He chose the larger of the spheres quite readily when he was tested in the same way with his left hand.

Discrimination of weights and estimation of shape are not measurably impaired; neither is the appreciation of two compass points when they are separated by 1 cm. and applied simultaneously.

It would appear from this and similar cases which have been recorded that stereoscopic vision depends on something more than the possession of binocular vision and the ability to appreciate differences in light and shade.

Summary of visual phenomena:

- Not a geometric visual distortion

- Complete left homonymous hemianopia, some recovery in the left lower quadrant

- Visual spatial disorientation

- Permanent loss of stereoscopic vision, no depth perception

Other neurological symptoms and signs:

- Two post-craniotomy seizures

- Transient right hand motor apraxia, almost full recovery

- Loss of sensation in right upper limb

- No agnosia

Reported visual recovery:

- Five months after his injury he was able to perceive movement in the periphery of the lower quadrant, still unable to see stationary objects

Possible aetiology of visual distortion:

- The patient had sustained a shrapnel bullet wound extending from the left frontal vertex to the right occipital pole. The bullet and an abscess were surgically removed.

- Parietal lobe damage is likely

- Deafferentation

- Inflammation from wound healing

(b) Hoff 1935, right parietal displaced skull fracture [64, 65] A 53-year old male acquired a right parietal skull fracture on the edge of the lambdoid suture. There were numerous small skull splinters with attached hair displaced about three centimetres into the brain. During excision or

exploration of the wound, the brain substance oozed continually and the patient noticed paralysis of his left arm. He experienced a visual disorder where he observed a "portion of the opposite wall of the room arched like an alcove; to the right and the left the wall appeared flat". This visual phenomenon was persistent for eight days. No other objects or persons were distorted. He later stated he observed the roof of the opposite house was distorted in a wavy manner, both the edge of the roof as well as its steeply inclined surface. This distortion was apparent in the whole visual field. The wavy contours were in the centre of the visual field, larger towards the outside and overall corresponded to irregular arches. These distortions disappeared at the same time as when the arching of the opposite wall of the room resolved.

The authors of the article surmise the visual distortion was a general disturbance of depth perception due to the parietal lobe injury. The patient had fluctuating ischaemia which probably caused oedema. The authors reasoned that the striate cortex was intact in the right hemisphere so one could attribute the depth perception disorder to an indirect effect of the parietal brain injury. They could not exclude a combination of cerebral and labyrinthe damage as a cause of the metamorphopsia. Since severe cranial trauma had occured, a commotio cerebral injury could not be excluded. The authors concluded the clinical findings suggest the cause of the visual distorion is "indirect effects of the interparietal region on the optic projection apparatus".

Summary of visual phenomena:

- Wave-like distortion of walls and roof of house for eight days, spontaneously resolved
- No other objects affected
- Depth perception disorder

Other neurological symptoms or signs:

- Paralysis of left arm

Possible aetiology of visual disorder:

- Fluctuating ischaemia and oedema of the right parietal lobe after surgical exploration of the wound
- Epileptogenic discharges, focal cortical irritation, deafferentation

2. Lance 1976, case 8, right parietal infarction [78] A 60-year-old female underwent a vagotomy and gastroenterostomy for a prepyloric ulcer. During her postoperative recovery, she developed a left hemiplegia with anosognosia which resolved after hours. She also had a dense left homonymous hemianopia which resolved over one week. Brain scan demonstrated "diffusely increased uptake in the right parietal

area". At the time of her collapse, she perceived herself as a "tiny figure, two feet long, wrapped in a green bundle on the floor. Subsequently her room appeared very small, like a tiny caravan with the walls close to her." She had simple unformed visual hallucinations of black spots on the wall which moved across her gaze and disappeared to the left. She later experienced formed complex visual hallucinations in the left visual field of "two or three people with big heads and discoloured brown skin with black spots. She was not sure who they were; they were possibly relatives but she found them very alarming and had doubts about her sanity. When her hallucinations disappeared after five days she said with relief, 'Thank God they've gone, that lot!'".

Summary of visual phenomena:

- Alice-in-Wonderland Syndrome

- Micropsia

- Simple and complex visual hallucinations

- Dense left homonymous hemianopia, resolved over one week

Other neurological symptoms or signs:

- Transient left hemiplegia

- Transient anosognosia

Possible aetiology of visual disorder:

- Right parietal lobe infarction

- Epileptogenic discharges

- Deafferentation

Structural parieto-occipital pathology

1. Geyer 1963, case 1, right parieto-occipital glioma [77] The visual disturbance described by this case is very similar to Safran's "thin man" phenomenon [81].

   A 44-year-old male railworker for two days experienced all objects and approaching people in his left visual field as distorted. People appeared to have elongated, "egg-shaped" heads; their limbs appeared mis-shapen and enlarged, and all objects appeared tall and thin. Frequently, the outlines of objects shimmered in his left visual field with associated marked vertigo and nausea. He also experienced headaches. The visual distortion was not present in his right visual hemifield. On examination, he

had brisk left ankle jerk but no other long tract signs. EEG demonstrated abnormal signal over the entire right hemisphere with a focus over the right occipito-parietal region. Pneumoencephalogram and angiography were suggestive of a space occupying lesion with midline shift to the left. On craniotomy, the sulci appeared "spread apart", maximally in the right parieto-occipital region. A large subcortical tumour with appearance consistent with a glioma, was identified lying deep to the posterior temporal cortex. The tumour was resected at the cost of almost the entire occipital lobe and most of the parietal lobe. The patient died in hospital shortly afterwards.

Summary of visual phenomena:

- Hemi-metamorphopsia

- Shimmering outlines of objects

Possible aetiology of visual disorder:

- Epileptogenic discharges

- Deafferentation

2. Mooney 1965, left parasagittal parieto-occipital meningioma [82] A 45-year-old commercial male artist was first seen in 1962. He had an eight year history of sudden attacks of visual disturbance, each episode lasting a few seconds. He experienced a moving pattern of coloured (particularly red, but also yellow and blue) lights. He compared these lights to the flickering of a coloured television screen. The pattern of coloured lights rapidly increased in intensity, exploded and disappeared, leaving a blankness in his vision for a moment, before his vision returned to normal. The right visual field was always affected by the moving coloured lights. When the lights were present, he could still see on his left side with difficulty. His judgement of position in the left hemifield during an episode was impaired. He had experienced difficutly seeing the right half of a written word for two years.

Prior to admission to hospital, he experienced his usual attack of moving coloured lights. As his visual symptoms progressed, he felt a peculiar tense feeling described as "an agony that was not pain". He felt ill and was unable to speak nor did he know what he was trying to say. He then collapsed and was unconscious for 30 minutes. On examintion, he did not have any neurological signs. Ophthalmic examination demonstrated normal visual acuity for distance and near. Examination of his fundi examination was normal. Perimetry demonstrated a complete right lower quadrantopia with macular sparing and incomplete involvement of the right upper homonymous quadrants with wide macular sparing. The hemianopia was congruous.

Radiologic studies: Left carotid angiogram revealed slight displacement of the anterior cerebral artery to the right. Venous phase, the internal cerebal vein showed a greater shift to the right of the midline. This indicated the presence of a posteriorly situated space-occupying lesion. Lateral view of the arterial phase, branches of the middle cerebral artery were separated and kinked anteriorly. This suggested the presence of an occipito-parietal space-occupying lesion. Venous phase, some abnormal vessels were seen in the occipital zone. Left external carotid angiogram lateral view demonstrated prominence of the posterior branch of the middle meningeal artery, seen running to the occipital region, where there was a prominent small group of abnormal vessels. A faint "blush" in this region was noted on a late venous film. The angiogram findings indicated the presence of a prominent left meningeal vessel running along the floor of the posterior fossa toward the left superior occipital region in the midline in the anteroposterior projection. Vertebral angiogram arterial phase, there was marked elevation and separation of the branches of the left posterior cerebral artery, one of which had a kinked and stretched circumscribed course. Venous phase, an irregular homogenous "blush" was demonstrated in the occipital region, consistent with a meningioma.

Operation: A left parasagittal parieto-occipital osteoplastic craniotomy was performed. A large parasagittal meningioma was indenting the medial aspect of the parieto-occipital hemisphere in the region of the precuneous lobule. The tumour was embedded in the parietal lobe. The tumour was removed apart from the roots in the wall of the sagittal sinus.

Postoperative progress: Within 24 hours of the craniotomy, the patient experienced visual hallucinations which occurred intermittently during the first week. The hallucinations were synchronised with subjective recovery in the right upper homonymous visual fields. He made colour drawings of his hallucinations and wrote the following description: "The distortions of vision I experienced after my operation were of two kinds: (a) with my eyes open; (b) thoses I saw when my eyes were closed. "The very first were a series of lights, patterns in color, something of this nature and always moving, and always on my right-hand side with other balls of light and colors and quite an amount of type script, that is, words and letters. They always disappeared on my right. "This was replaced by images of a human nature. When I was talking to a nurse standing at the end of my bed, her left eye became extraordinarily staring and fierce, the iris was of an unnatural cobalt blue and the white part very brilliant. She left the ward, but her eye remained vividly where she had been standing; when I closed my eyes the image became even more visid and horrible. This state of affairs rapidly developed for the worse. Everything about every person became grotesque. A man's face, for example: the eye became a ghastly staring hole, cheek bone a cavity; he had teeth on the upper lip, often had two ears. "Every-

thing seemed to be predominated by a sickly flesh colour offset by shining purple and reds. "There was an eye which I saw quite often when my eyes were closed: the lid was shiny red, the iris vivid blue, the pupil jet black. The nose was flesh colored, vividly higlighted and the pores very visible. There was a series of laughing faces of girls like one might see on magazine covers; one, like all the rest, would be laughing horribly; she had bright yellow hair but her lips (screaming, vermillion red color) and very white teeth were the main features of this apparition. Everything was always moving. The girl would start off normal enough but rapidly her lips would get coarser, her mouth more open, and her teeth long and pointed. I have tried to give an impression of this in the colour plate (H and I). I had just as many vision of men's faces going through similar contortions, very red and shiny under a fishlike eye, the lower part of the lid dragged down, showing a very bloodshot white. (Impressions of other eyes I have seen when my eyes were closed.) "Hands were another feature. Their fingers became numerous and often one would start extending to great lengths before dissolving. "If there were two or three people talking together in the ward, another person, either would appear about three feet from them on my right and disappear immediately I tried to see them clearly. "When my eyes were closed I would often see a metal wall painted pink with dark circular hole in it out of which a long metal rod would start moving; this was repeated quite often very vividly. All pipes had a tendency to extend and twist snake-like. "Another oddity I should have mentioned in the earlier context about eyes was that, if any person was wearing spectacles, the left lens (that would be on my right) would visibly rotate to right angles and then float across the room. "I noticed if I looked at a patient's hand and then looked down at the bed, I would carry an image of his hand right down with me. The images usually appeared to be a fraction ahead of my direct vision. This would happen to the side of a man's face, and did happen quite often; his moustache, on his left (my right-hand side), would become a kind of witch's broom and disappeared quickly to my right. This happened with quite a lot of objects. "I noticed that I was inclined to carry shadowy impressions on top of other objects, even when I switched my eyes. In this impression, persons standing at a table might create a kind of negative replica of themselves behind them on my right. "In the ward, the wall opposite to me was usually dim, thus creating very contrasting patches of light in the windows, particularly when the sun shone through a thickly leaved tree and onto walls, buildings, roof tops, etc., creating planes and lines and masses of tone and color which, when the wind blew and the lighting lifted and fell, all too easily created images (as one can see pictures in a fire) and shapes recognizable as men and women. So I often saw people running out of the tree peeping over the wall or through the window. They moved off rapidly to my right. I had similar experiences with lemonade bottles and syphons of various shapes on people's lockers, particularly in the fading light of the evening."

Course: The attacks were controlled by phenobarbitone. The postoperative recovery from craniotomy was otherwise uneventful. The patient returned to work four months after the operation and did not have a recurrence of his visual symptoms at the time the article written. "Perimetry showed rapid functional recovery, with filling out of the affected homonymous fields, there being only a slight residual right inferior quadrantic defect for 2/2,000 white."

Summary of visual phenomena:

- Preoperative:
  - Simple hallucinations
  - Complete right lower quadrantopia with macular sparing and incomplete right upper quandrantopia

- Postoperative:
  - Simple and complex hallucinations
  - Palinopsia
  - Prosopometamorphopsia
  - Illusion of movement

3. Lindgren 1992, right occipito-parietal infarction [83] A 62-year-old right-handed man (a professor of neurosurgery) experienced attacks of 15-20 minutes duration consisting of fortification illusions in his left visual field without headache. Occasionally, he experienced a right-sided headache a few days before the acute attack. Over four days, he had headaches lasting a few hours every morning. He had a sensory deficit of his left arm, his left visual field was blurred, his right pupil was smaller than his left and he vomited. One hour later, he felt blind and everything was gray in hospital. When he awoke the next morning, the left-sided homonymous hemianopia and anisocoria remained.

A few hours after the first acute symptoms, CT brain was normal. Two days later, CT brain showed an area of low attenuation in the medial and posterior part of thr right occipital lobe including most of the calcarine region including the cuneal tip. This region extended close to the ventricle and posteriorly to the occipital lobe. The anisocoria, right cranial nerve neuralgia and hiccups were possibly due to additional lesions in the brainstem not seen on CT.

One year after the acute attack, the patient experienced no feeling of a hemianoptic defect in daylight. This was as long as he was not turning toward an object to the left. However, if he was tired, a gray left hemianoptic field was clearly recognised in daylight but was less noticed in full darkness. A few

occasions after three to four weeks of illness, whilst reading he would experience isolated larger letters floating into the intact visual field from the blind side.

Twenty-one months after the acute attack, the patient had a transient attack of marked numbness of the left hand for one hour followed by clumsiness for some hours. He had simultaneous distortion of spatial vision. He had a feeling of distorted or oblique vision for several hours. A square room looked like a pentagon with a the triangular apex far away in the centre of the visual field. When he moved fixation from a door opening to a flat wall, the apex fold moved along and deformed the appearance of the wall. When reaching for a plate at the kitchen table, the plate seemed to be far away, the peripheral part of his right arm and hand look abnormally long.

Summary of visual phenomena:

- Distortion of spatial vision, feeling of distorted or oblique vision

- Left homonymous heminanopia and transient total cortical blindness

- Simultangnosia

- Depth perception issues

- Complex hallucinations

Other neurological symptoms or signs:

- Acute severe transient sensory deficit of his left arm

- Environmental orientation deficit

- Anisocoria

Possible aetiology of visual disorder:

- Epileptogenic discharges

- Deafferentation

4. Werring 1999, left occipito-parietal tuberculous granulomata [84] Summary of visual phenomena: Unsure whether metamorphopsia was perceived Coloured positive visual symptoms, simple hallucinations Palinopsia No visual field defect

Other neurological symptoms and signs: Posterior headache

Probable aeitiology of visual disorder: Focal cortical irritation from tuberculoma

A 35-year-old man experienced a "starburst" in his right visual field. He also had a posterior headache. He described the persistence of objects images seen in his right hemifield. He did not have a visual field defect. These episodes happened over two months. MRI brain discovered a ring enhancing lesion in the left occipital lobe. This lesion contained tuberculous granulomata on biopsy. He responded to anti-tuberculous medications and remained symptom free after two years. The coloured positive visual symptoms could have been mistaken clinically for a migraine. However, palinopsia is highly suggestive of a structural occipito-parietal lesion. His visual symptoms were thought to be caused by focal cortical irritation from the tuberculoma.

Structural temporo-occipital pathology

The posterior cerebral artery supplies the occipital lobe, inferomedial temporal lobe, a large portion of the thalamus, the upper brainstem and midbrain.

1. Seron 1995, right occipito-temporal haemorrhage [85] (French article, English abstract) A 19-year-old patient (unknown gender) suffered transient metamorphopsia restricted to familiar faces and familiar objects. They had a right occipito-temporal haemorrhage due to a sub-cortical metastasis. Faces appeared distorted and more pleasant. No visual field defect or visual agnosia was reported.

   Summary of visual phenomena:

   - Prosopometamorphopsia
   - Familiar objects distorted
   - No visual field defect

   Possible aetiology of visual disorder:

   - Epileptogenic discharge, focal cortical irritation, deafferentation

2. Sun 2004, right occipital and left temporal hypoperfusion [86] A 59-year-old right-handed illiterate female with untreated hypertension suffered a stroke. Nine months later, she experienced visual distortion. Her stroke episode symptoms were described as dizziness, and unsteady gait without focal weakness. These symptoms spontaneously resolved within one week. The lesion was not localised.

   One morning whilst she was in a chair, she suddenly developed dizziness, and an unsteady gait with no focal weakness or numbness. She also had slurred speech. On examination, she had a left hemiparesis. Her visual fields were not examined at this time. She was admitted with a diagnosis of a right supratentorial infarction.

Ophthalmologic examination on admission revealed normal reactive pupils, normal visual acuity, full range of eye movements, and a dense left homonymous hemianopia on confrontation visual fields. Her speech was slurred but her language functions were grossly normal. She did not have left-sided neglect on the line-bisection test. She had inattention to the left side with double simultaneous stimulation tests using auditory and tactile stimuli. Apart from a wide-based gait and unsteady tandem gait, her neurological examination was normal.

The following day, her visual field defect recovered. Visual perseveration with movement of the object was present in the left visual field. On the third day, the visual perseveration resolved and she saw the left edge of the bed tilting downward and the left railing of the bed became distant to her. She felt she was going to fall down from the left side. Her quilt became triangular and she tried to fold it back as a square. These symptoms persisted for 12 hours. On discharge from hospital, she did not have any neurological symptoms.

MRI brain performed the day after onset of her symptoms did not demonstrate any recent infarction. However, there was an old infarction present in the right occipital region. EEGs performed on the third and sixth day showed a few isolated independent sharp waves over both temporal areas with right posterior extension. SPECT on the eight day demonstrated hypoperfusion of the right occipital and left temporal areas. VEP and brainstem auditory evoked potential studies were noraml. SPECT and EEG were repeated four months later; EEG remained unchanged and hypoperfusion areas were more prominent on SPECT.

Summary of visual phenomena:

- Transient visual distortion: tilted, square became triangle (3rd day for 12 hours)

- Transient visual perseveration, left visual field (2nd to 3rd day)

- Transient dense left homonymous hemianopia (1st day)

Other neurological symptoms and signs:

- First stroke episode (spontaneous resolution): dizziness, unsteady gait without focal weakness

- Second stroke episode: dizziness, unsteady gait with no focal weakness or numbness, slurred speech, left hemiparesis (transient)

- No left sided neglect with line-bisection test

- Left inattention with double simultaneous stimulation using auditory and tactile stimuli

Possible aetiology of visual disorder:

- Deafferentation

3. de Souza 2017, bilateral temporo-occipital hypoperfusion after cardiac arrest [87] A 47-year-old-male with acute precordial chest pain in shock was found on ECG to have an acute anteroseptal myocardial infarction. He developed complete heart block and he was referred to the regional cardiology center. En-route, he had three episodes of cardiac arrest and was revived successfully from each episode within three minutes. A primary coronary angioplasty with stenting to the left main coronary artery was performed. This resulted in good recovery of left ventricular function and resolution of the arrhythmia. No neurologic deficits were noted on the second day of admission. Intravenous inotropic support was withdrawn the next day, and he remained in the cardiology unit for a week on oral medication. One week after presentation, he woke up with acute visual loss in both eyes. He was unable to see hand movements but could perceive light. Ophthalmologic examination was normal with normal pupillary reflex and fundoscopy. He had no other neurologic deficits. Blood chemistry and CT brain were normal. VEPs showed attenuated waveforms from either eye. Gradual recovery was noted from the third day, with slow improvement in visual acuity. He complained of metamorphopsia: straight lines or fluorescent tube lights – appeared curved when viewed directly. By the tenth day, he was able to read and his visual acuity was 6/60 in each eye. MRI brain at this time showed subtle hyperintensity of the cerebral cortex in both temporo-occipital regions on fluid-attenuated inversion recovery and diffusion-weighted imaging (DWI), and visual fields were normal. He continued to improve steadily, and one month later he only had minor visual complaints. He had normal visual acuity, color vision, field of vision, and reading ability.

Summary of visual phenomena:

- Distortion of straight lines (unsure how long it persisted, maybe day 3-10 after acute visual loss)

- Transient bilateral acute visual loss (recovered to normal visual fields in 10 days, and normal acuity in 1 month)

Possible aetiology of visual disorder:

- Epileptogenic discharge, deafferentation from bilateral temporo-occipital hypoperfusion

Structural parieto-temporo-occipital pathology

1. Vogeley 1998, right temporo-parieto-occipital defect [88] A 64-year-old man had a asymptomatic right parieto-occipital glioblastoma resected after routine brain CT demonstrated a lesion. He was diagnosed with neurofibromatosis when 49-years-old. Aged 58, his right arm was amputated because of neurosarcoma. After surgery, he had a dense homonymous left lower quadrantanopia. Four months later, he noticed metamorphopsia. The body of his son appeared bent to the left from the hip upwards. At first, he considered that his son might walk in this distorted way. However, he soon discovered all other people and all vertical lines in his visual environment were bent to the left. Later, he experienced distortion of vertical contours of persons, furniture, windows, doors, etc, which seemed to expand and constrict rhythmically. Each of these metamorphoptic episodes developed suddenly and lasted for several seconds. He also had visual pseudo-hallucinations of context-induced human figures confined to his anopic left lower quadrant. He later recognised these visual hallucinations as being unreal. He had one instance where he perceived a person selling soft drinks on the street he was driving along. However, the torso above the waist appeared amputated and one arm (delivering the soft drinks) appeared out of nowhere in an anatomically plausible position in relation to hip and legs at the height of the cut torso (see patient's drawing in the publication). The visually perceptible figure parts were correctly scaled and appropriately localised in relation to the street environment. The patient could not relate this scene to any past experience.

   An ophthalmological examination between these episodes disclosed the persisting homonymous quadrantanopia for the left lower quadrant. He had normal visual acuity and colour vision. He had no impairment for reading, spoken language, short or long term memory, praxis, or object recognition on bedside examination. He had no disturbances of visual or supramodal attention during simultaneous bilateral stimulation. Muscle tone was slightly increased in the left leg without any other pathological motor signs or somatosensory disturbances. Brain MRI showed a right temporo-parieto-occipital white matter and cortex defect near to the posterior horn of the lateral ventricle. EEG disclosed alpha rhythm with some focal right occipital slowing, but no epileptic elements. No EEG could be obtained during the short episodes of his pseudohallucinations. Brain HMPAO-SPECT demonstrateda relative hyperperfusion in the right (plus 8%) compared with the left temporo-parietal cortex rostral to the lesion.

   Summary of visual phenomena:

   - People and vertical lines were bent to the left

- Complex visual hallucinations

- Dense homonymous left lower quadrantanopia

Possible aetiology of visual disorder:

- Deafferentation, epileptogenic discharge

2. Gonzalez 2011, right occipital intraparenchymal haemorrhage [89] A 64-year-old female presented with sudden onset visual disturbances over the previous 36 hours preceded by intense headache. The patient reported monocular and binocular alterations in her vision. Firstly, she reported constant variations in the shape of objects and people. They appeared to be extremely long and thin (macropsia), short (micropsia), wide, etc. Secondly, dyschromatopsia where objects changed in colour or even in intensity. Thirdly, she described transposition of objects from one side to the other (allesthesia). The rest of the neurological examination was normal. CT brain revealed a right occipital intraparenchymal haemorrhage.

On MRI brain T1 sequence, a hyperintense lesion could be seen located in the right occipital region, maximum diametre of 42 mm and very discreet perilesional oedema, compatible with parenchymal haemorrhage.

Possibility of occipital lobe epileptic seizures was considered despite the waking EEG failed to reveal any alterations. A decision was made to initiate treatment with levetiracetam 1000 mg/day. After 24 hours of treatment, the visual symptoms remitted and the patient was asymptomatic without any residual visual field alterations.

Summary of visual phenomena:

- Variations in the shape of objects and people (dysmetropsia)

- Dyschromatopsia

- Optical allesthesia

Other neurological symptoms and signs:

- Intense headache

Possible aetiology of visual distortion:

- Epileptogenic discharge, deafferentation from left occipital lobe haemorrahge

Basilar artery compromise

1. Brau 1986, bilateral occipital ischaemia from multiple intracranial artery spasm after cerebellar tumour resection [90] A 57-year-old right-handed Caucasian woman developed difficulty walking and standing, severe leg weakness, frequent falls, generalised tremors, severe occipital headaches, tinnitus, dizziness, visual disturbances, nausea and occasional morning vomiting. She also had scotomas which appeared as brilliant lights. She had cerebellar dysfunction signs on neurological examination. She had no corticospinal tract or sensory abnormalities. She had optic disc swelling with flame-shaped haemorrhages. CT brain demonstrated a left cerebellar paracentral low density intraparenchymatous lesion with moderate hydrocephalus. A right temporal ventriculoperitoneal medium pressure shunt was inserted without complications. Her raised intracranial pressure symptoms resolved after the shunt. She had a left vertebral and left internal carotid artery angiogram. This showed the basilar artery pushed forward and stretched, the posterior inferior cerebellar artery complex was distorted, and the left internal carotid artery was normal. She underwent an posterior fossa craniectomy in the sitting position. A large intraparenchymous cerebellar epidermoid tumour was identifed and resected. There were no intraoperative complications.

   One day after craniotomy, she had a left seventh supranuclear cranial nerve palsy. She experienced dizziness and the ceiling light appear to rotate 180 degrees intermittently. People also seemed shorter than they actually were. Day three postoperative, the rotated ceiling lights appeared farther away. Relatives and hospital staff appeared consistently shorter and sometimes upside-down. There were a few episodes where only the upper-half of a person appeared upside-down. Her postoperative visual disturbances were thought to be caused by acute psychosis with associated visual hallucinations. Corticosteroid medication was withheld as it was assumed to be contributing to her psychosis. Fourth day postoperative, she could not see at all. She had normal pupillary light reflexes and full extraocular eye movements. Corneal reflexes were normal and she had no other neurological deficits. She was clinically diagnosed with bilateral occipital ischaemia. CT brain demonstrated no occipital low-density areas, no midline shift and no blood in the subarachnoid spaces.

   On her seventh postoperative day, she clinically deteriorated with left hemiparesis and left hemibody cortical sensory deficit. This was thought to be due to right middle cerebral artery ischaemia. Two weeks postoperative, repeat angiogram demonstrated severe diffuse spasm of the basilar artery, posterior cerebral artery, right supraclinoid internal carotid artery, and anterior cerebral artery. Four weeks postoperative, angiography showed bilateral occipital low-density lesions and a large left cerebellar hemisphere low-density lesion associated with ex-vacuo distortion of the fourth ventricle.

Summary of visual phenomena:

- Pre-craniotomy: Simple visual hallucinations

- Post-craniotomy:

  - People appeared shorter

  - Reversal-of-vision metamorphopsia

  - Depth perception issues

  - Developed permanent cortical blindness

  - Complex visual hallucinations

Other neurological symptoms or signs:

Pre-craniotomy	Post-craniotomy
Lower limb weakness	Left seventh supranuclear cranial nerve palsy
Cerebellar dysfunction	Left hemiparesis
Dizziness	Left hemibody cortical sensory deficit
Generalised tremors	Dizziness
Occipital headaches	People appeared shorter and sometimes upside-down
Tinnitus	Ceiling lights episodically rotated 180 degrees
Nausea and vomiting	Teleopsia
Optic disc swelling	Cortical blindness

Possible aetiology of visual distortion:

- Ocular: optic disc swelling with possible retinal oedema

- Vestibular: epileptogenic discharge, deafferentation, cortical irritation after craniotomy from bilateral occipital ischaemia and; diffuse spasm of basilar artery, posterior cerebral artery, right supraclinoid internal carotid artery and anterior cerebral artery.

Neurodegenerative disease

1. Creutzfeldt-Jakob Disease (CJD). CJD is a rare neurodegenerative disease which commonly presents with rapid onset dementia. It is fatal with death within 12 months of diagnosis occuring in around 90% of patients. CJD is a transmissible spongiform encephalopathy. The term 'prion' was adopted to refer to these 'infectious proteins'. Visual disturbance is reported in more than a third of patients during the course of the disease.

(a) McElvanney 1999 [91]. A 57-year-old man presented with visual distortion. He had noticed a visual field defect whilst working on his computer keyboard. Over the next 2-6 weeks, he complained images became fragmented. Pictures appeared to be moving. Faces were moving, distorting and separating from their bodies. Colours seemed more intense than normal, especially green, orange and red. He also had a mild frontal headache and occasional nausea.

Visual acuity was normal. His ocular examination was normal apart from mild arteriovenous nipping of the vessels consistent with hypertension. Visual field testing revealed a left incongruous homonymous field defect. CT brain was reported as normal. Fundus fluorescein angiography showed areas of hyperfluorescence in the papillomacular area consistent with defects of the retinal pigment epithelium.

His symptoms progressively worsened and his visual acuity decreased. He developed intermittent expressive dysphasia and mild short-term memory loss. He was increasingly sleepy, emotionally labile and his gait became unsteady. MRI brain showed an incidental meningioma of the fourth ventricle and EEG showed bursts of slow activity with posterior spikes and long runs of occipital spikes. With intravenous diazepam, the EEG discharges lessened and his visual symptoms improved. Cerebral angiography did not detect any abnormaility. He was presumed to have occipital lobe epilepsy until he developed more pronounced myoclonic jerking. Repeat EEG showed classic periodic complexes of CJD.

Post-mortem examination confirmed the diagnosis of CJD. Sections of the cerebral cortex demonstrated widespread spongiform encephalopathy, particularly in the occipital cortex. There was widespread neuronal loss and astrocytic gliosis of the occipital cortex (the side that was sectioned was not described, presumed right occipital cortex as the homonymous field defect was on the left). Immunocytochemistry for prion protein was positive. Spongiform change was noted in the basal ganglia, thalamus and hypothalamus.

Summary of visual phenomena:

- Scotomata

- Illusion of movement

- Increased intensity of colours

- Left incogruous homonymous field defect

2.2.5 Unknown aetiology or pathophysiology

A 53-year-old right-handed male was reading a newspaper when the text went from black to white. A few hours later, he noticed distortions of faces and other objects. The objects also appeared rotated. From the article, the site of lesion and the cause of the visual disturbance is unclear. If the objects appeared rotated, it is possible there was a vestibular component and it is not related to cortical reorganisation [92].

2.2.6 Inadequate description of metamorphopsia

Due to the inadequate description of the visual symptoms experienced, it was unclear in the following articles what was meant by the use of the term 'metamorphospia'.

Right posterior cerebral artery hypoperfusion [93]

Case 3 in this article was a 58-year-old right-handed woman who suddenly realised she could not recognise anything around her. Her home of 20 years seemed entirely unfamiliar. On Goldnmann perimetry, she had a left visual field defect involving the entire superior quadrant and a small portion of the adjacent inferior quadrant. Her gait was unsteady. She did not have left-sided neglect. She had prosopagnosia.

CT scan showed a hypodense area in the territory of the right posterior cerebral artery. EEG revealed slow-wave activity in the right posterior temporal area.

One week after discharge from hospital, she awoke with generalised dimness of vision. Four months later she experienced visual hallucinations, including simple light flashes and complex hallucinations of a man repeatedly walking from her left to the right. Palinopsia also occurred. On one occasion, she noted after looking at a dog in the lap of a fellow bus passenger, all the people on the bus seemed to have the dog's face. Ten months later, she suddenly lost consciousness. Her visual orientation worsened and she had a complete left homonymous hemianopia. Visual hallucinations, palinopsia and "metamorphopsia" transiently worsened. A description of the metamorphopsia was not provided in the article. Repeat CT brain demonstrated no significant change. Repeat EEG demonstrated more extensive slowing over the right posterior temporal region.

Summary of visual phenomena:

- "Metamorphopsia" (no description provided)

- Palinopsia

- Visual spatial disorientation

- Prosopagnosia

- Simple and complex hallucinations

- Complete left homonymous hemianopia

Other neurological symptoms or signs:

- Unsteady gait

- Inability to recognise familiar handwriting, including her own

- Inability to recognise familiar pet animals

Possible aetiology of visual disorder:

- Epileptogenic discharge, deafferentation

Bilateral occipital lobe pathology [94]

A 40-year-old Japanese woman with no relevant past medical history developed "metamorphopsia" and right facial palsy in February 2007. A description of the metamorphopsia was not provided in the article. Brain MRI demonstrated T2-weighted high-intensity lesions in both occipital lobes suspicious of malignant lymphoma. Six months later in August 2007, although a brain biopsy was performed, the diagnosis was indefinite, and only inflammatory changes were observed. Her symptoms gradually improved with steroid pulse therapy. In December 2007, at which time the prednisolone dose was tapered, she developed a new lesion in the left thalamus.

In June 2011, four years after presentation, she developed dizziness, hearing loss and a new pontine lesion. In April 2012, she exhibited paraesthesia and weakness in the left upper and lower extremities, with progression of hearing loss and the onset of neurogenic diabetes insipidus. She was again given steroid pulse therapy and commenced on methotrexate and a higher dose of prednisolone. In December 2012, she was admitted to hospital after she developed diplopia, right ophthalmalgia and an ataxic gait. Physical examination revealed mild splenomegaly, however, her superficial lymph nodes were not palpable. Her pupils were round and equal, with a weak light reflex in the right eye. Abduction and adduction of the right eye was limited, she had a peripheral right facial palsy with hearing loss on the left. Finger-to-nose, knee-heel and hand pronation-supination tests revealed mild ataxia in the right upper and lower extremities.

A bone marrow examination revealed no invasion of abnormal cells. However, brain contrast-enhanced MRI disclosed small enhanced T2 high-intensity lesions in the left parietal, left frontal and bilateral occipital lobes as well as the pons and bilateral cerebellar hemispheres. Thickening of the oculomotor nerve and T1

high-intensity lesions in the posterior pituitary were also noted. There were no lesions detected in the right orbit.

The biopsy specimen of the occipital lobe collected in August 2007 was retrospectively assessed and was finally diagnosed as grade 1 lymphomatoid granulomatosis, an angio-centric and angio-destructive lympho-proliferative disease involving extranodal sites composed of Epstein-Barr virus (EBV) - positive B-cells with reactive T-cells.

Summary of visual phenomena:

- "Metamorphopsia" (no description provided)

Other neurological symptoms or signs:

- Right facial palsy

- Dizziness

- Hearing loss

- Paraesthesia and weakness in the left upper and lower extremities

- Diabetes insipidus

- Diplopia

- Ataxic gait

Possible aetiology of visual disorder:

- Inflammatory lesion in both occipital lobes, left parietal and left frontal lobes

2.2.7   Prosopometamorphopsia: visual distortion of faces only

Metamorphopsia restricted to only faces should not be considered to be caused by the same mechanisms as metamorphopsia of other objects. The visual processing mechanisms involved with faces are different than those underlying processing of other objects. Prosopometamorphopsia has been confusingly defined in some of the literature as visual hallucinations of faces rather than visual illusions [95]. Another article includes polyopsia, micropsia and macropsia as metemorphopsia of faces [96]. Visual distortion of faces could be considered an entirely separate category of cerebral metamoprhopsia due to the specific visual areas and complexity of the visual processing involved. The following articles on prosopometamorphopsia have been included for completeness.

Previous reports of prosopmetamorphopsia following splenial or retrosplenial lesion have been summarised in Table 1 from McCarty et al. 2017 [97], they added their case report to the table previously published by Lee [98]. The retrosplenial cortex is highly connected to the anterior thalamic nuclei and to the medial temporal structures important for memory. The splenium of the corpus callosum contains fibres connecting the visual cortices. Other cerebral injuries, apart from those affecting the splenium and retrosplenium, have been reported with descriptions of prosopometamorphopsia.

Age/Sex	Handedness	Side of distortion in opposing face	Side of lesion	Cause	Reference
68/F	Right	Right	Right retrosplenium	Cerebral haemorrhage	Ebata et al. [99]
58/F	Right	Left	Left splenium	Cerebral infarction	Cho et al. [100]
53/M	Right	Left	Right splenium	Cerebral infarction	Cho et al. [100]
68/F	Unknown	Left	Left retrosplenium	Resection of an AVM	Ganssauge et al [54]
61/F	Left	Right	Right splenium	Cerebral infarction	Saito Y et al. [101]
70/F	Right	Left	Right splenium	Cerebral infarction	Hishizawa et al. [102]
52/F	Right	Left	Left splenium	Cerebral infarction	Lee [98]
79/F	Right	Left	Right splenium	Cerebral infarction	Nagaishi et al. [103]
62/M	Right	Not described	Left splenium	Cerebral infarction	McCarty et al. [97]

Right retrosplenial lesion [99]

A 60-year-old right-handed Japanese female experienced unilateral metamorphopsia of the face after a small haemorrhage in the contralateral retrosplenial region. The right side of a face, including her own in the mirror, appeared to be smaller than the left. The side that was affected was the left side when looked at by the patient. Her drawings of faces also showed some distortions. Apart from faces, other objects appeared normal. She had normal visual acuity and visual fields.

CT brain scan demonstrated a small high density in the right posterior part of the cingulate gyrus just behind the splenium with a partial involvement of the adjacent corpus callosum. There were also small low density areas noted in each putamen. The right one most likely represents the putaminal haemorrhage from 11 years previously. She was unable to recall an event to account for the left putaminal lesion. MRI brain demonstrated high signal area in the right retrosplenial region extending into part of the adjacent splenium. Cerebral angiography and EEG were normal.

Visual symptoms resolved at the end of her five week admission to hospital and were attributed to a

small haematoma in the right retrosplenial region.

Summary of visual phenomena:

- Hemi-prosopometamorphopsia

- No prosopoagnosia

- No visual field defect

Left infarct between retrosplenium and cingulate gyrus [104]

This article was published in Japanese with an English abstract. The timing of the visual symptoms is unclear from the English abstract.

A 51-year old female complained she had blurring of the right side of her face. Also, the right margin of all objects in her visual field also appeared blurred. Neurological function and visual field testing was normal. CT brain and MRI revealed a left spotty infarct lesion between the retrosplenium and cingulate gyrus.

Summary of visual phenomena:

- Hemi-prosopometamorphopsia

- Other objects also distorted

- No visual field defect

Left splenial infarction just medial to occipital horn [97]

A 62-year-old right-handed Caucaian male complained of distorted vision. In particular, the mouths of people's faces were distorted and enlarged. Other features of the face, such as the nose and eyes, were not distorted. No other objects were distorted. Not even the patient's own mouth was distorted in the mirror. He did report having trouble recognising faces. He had primarily central visual field distortion, occurring monocularly and binocularly. He had difficulty reading numbers and letters on the computer, however, his ability to write was normal.

He had a an episode of transient global amnesia about three years prior to the onset of the visual distortions. After the short period of anteriograde amnesia, he had investigations including MRI, ECHO, MRA and cardiac assessments, all were negative.

Ocular examination was essentially normal apart from Amsler Grid testing. He had very mild distortion centrally in both eyes with the Amsler grid, the right eye being slightly more distorted than the left. Retinal

examination and imaging (OCT and fluorescein angiography) did not reveal any retinal pathology that would explain the metamorphopsia.

T2-weighted brain MRI revealed late subacute infarct within the left splenium of the corpus callosum, just medial to the occipital horn.

Summary of visual phenomena:

- Distortion of other people's mouths only

- Prosopoagnosia

- Alexia without agraphia

- Distortion on Amsler grid, right greater than left

Left parieto-occipital gunshot wound [105, 80]

Metamorphopsia in this case is not geometric and unlikely to be cause by cortical reorganisation. The symptoms were also episodic and varied.

A 24-year-old male acquired a gunshot wound to his left parieto-occipital region. Contours of objects appeared fuzzy. Human faces all looked alike and appeared expressionless. He had episodes where contours would look alive or moving. Things would look brighter than usual without colour, however, this phenomenon excluded faces. During other episodes, faces would appear different and turn very pale. The eyes would look smaller, the mouth and nose would turn black, and the whole face would look flat without contour for about 20 minutes. Initially after the injury, he had complete blindness for several days, object agnosia, simultanagnosia, alexia, colour agnosia, and bilateral paracentral scotomas.

Summary of visual phenomena:

- Prosopometamorphosia

- Achromatopsia

- Illusion of movement

- Transient complete blindness, bilateral paracentral scotomas

Other neurological symptoms and signs:

- Object agnosia

- Simultanagonisa

- Alexia

- Colour agnosia

Possible aetiology of visual disorder:

- Epileptogenic discharge, focal cortical irritation, deafferentation after gunshot wound to left parieto-occipital region

Left occipital shrapnel wound [105, 80]

A 22-year-old male had a left occipital wound caused by shrapnel from bomb splinters. He had a right hemianopia. Only faces would appear distorted, oblique or strange. An English translation of the distortion was published by Critchley in 1953: "All faces were strangely contorted and the features displaced; e.g. the ward sister's nose was deviated to the side by several degrees; one eyebrow was higher than the other; the mouth lay at a diagonal; the hair was dishevelled like a wig askew. Objects, places, colours, contours, in fact anything other than a face, were seen correctly just as before his wound" [80].

Summary of visual phenomena:

- Prosopometamorphopsia: distorted, oblique or strange

- No other objects distorted

- Right hemianopia (was blind for 2 days)

- Dyslexia

Possible aetiology of visual distortion:

- Other visual areas (including the splenium or retrosplenium) may have been affected by the injury, oedema or scarring.

Right parieto-occipital meningioma excision [106]

Case 3 in this article had removal of a large right parieto-occipital meningioma. This resulted in a bizzare type of prosopometamorhopsia.

The following are descriptions of prosopometamorphopsia in the article. However, it is not clear from the information published which description is specifically from case 3: One case said to her physician "You have stretched lips, a thick nose, and you are grinning. You don't look nice at all. Your eyes are stretched and have big circles under them." Faces which this case revisualised were also distorted. She had no difficulty

recognising faces in photographs due to the "immobility of the features." Another case stated "Faces don't look normal any more: they are quite distorted and contorted like some sketches of Picasso, I should say."

Probable infarction of a posterior cerebral artery territory [95]

Two cases were published describing visual hallucinations after probable infarction of a posterior cerebral artery territory. Case 1 did not describe metamorphopsia during her visual hallucinations that lasted two weeks. She had a "dense right homonymous hemianopia with a crescentic sparing of peripheral vision (i.e. large right homonymous hemianopic paracentral scotomas)". Skull roentgenograms and a technetium 99m brain scan were normal. EEG was normal, including sleep tracing; neither occipital region drove to photic stimulation. VEPs were abnormal, compatible with left suprastriate cortical abnormality. ERG was normal. She was followed-up for 18 months with no further hallucinations or other symptoms. The visual field defect remained unchanged. It could be concluded that case 1 had a left posterior cerebral artery territory infarction.

Case 2 suffered from a right posterior cerebral artery infarction affecting the right posterior temporo-occipital lobes: A 44-year-old right-handed man observed red and green lines at right angles to each other in the left upper visual field "like a checkerboard". This lasted approximately three minutes and occurred a few times each hour. The lines seemed to be moving towards him. After a few days, the lines changed to red and blue spots that seemed to enlarge. The colour of the spots was duller than the lines and occupied the lower as well as the upper visual field. However, the coloured spots did not affect his peripheral visual field. The right half of people's faces seemed to transiently melt "like clocks in a Dali painting" and took on a yellow or violet colours. The distortion only affected faces and was sharply demarcated to only one half of the face. The duration of the facial distortion is not described in the article.

EEG during an episode of typical hallucinations demonstrated frequent sharp forms in the right posterior temporo-occipital area with decreased amplitude of the alpha rhythm on that side.

A month after the start of the visual hallucinations, he became aware of left homonymous hemianopic scotomas which improved over a few weeks. During this recovery period, he would see a black-and-white pulsation in the left lower visual field that lasted for around ten minutes. This pulsation would evolve into a coloured spot which slowly enlarged and persisted for two to three hours. The enlarged coloured spot would then pulsate for half-an-hour and finally flickered out, leaving denser left visual field scotomas for the following few days. Where the scotomas were most severe, he would experience formed hallucinations of past experiences for days following each episode. Sometimes a formed visual hallucination would occur only a few minutes after he saw a real object.

On examination, he had large left homonymous paracentral hemianopic scotomas that split the macula

and spared the peripheral vision. CT brain showed a right posterior temporal lucency that did not enhance with contrast, thought to be a small area of underperfusion.

Second EEG demonstrated decreased amplitude of alpha rhythm on the right, especially in the right posterior temporal region, and decreased driving of the right occiput to photic stimulation. However, there was no epileptiform activity. VEPs were reduced in amplitude at the right occiput and normal at the left, suggesting a right occipital lesion.

Once or twice a month for the following 18 months, he continued to have unformed left visual field hallucinations followed by palinopsia in the scotomatous region. He commenced phenytoin 300mg daily and had three episodes of a small pulsating black spot in the left visual field without progression into the usual symptoms for a further one and a half months. After this period, he had no further attacks whilst taking phenytoin.

Summary of visual phenomena:

- Hemi-prosopometamorphopsia, left hemifield

- No other objects distorted

- Palinopsia

- Dyschromatopsia

- Simple and complex visual hallucinations

- Left homonymous paracentral scotomas splitting the macula

Possible aetiology of visual disorder:

- Epileptogenic discharge, deafferentation from right posterior temporo-occipital hypoperfusion

Right occipital glioblastoma [107]

A 66-year-old man with a past history of 'tension headache' awoke one month before his hospital admission with a dull and steady non-localised headache. This was accompanied by nausea and vomiting, frequent bowel movements, abdominal discomfort, inability to think clearly, subjective vertigo, and unsteady gait. These symptoms recurred episodically.

One day, he experienced a visual disturbance where numbers and letters were reversed, accompanied by visual obscuration. Two days later, he saw a man on the sidewalk. When he arrived at his physician's office, he noticed all of the individuals inside, including his wife, looked alike. Their faces were similar to the man

he had seen earlier on the sidewalk. Their faces appeared wavy, flat and with a tan complexion, and their eyes looked tired. They appeared to be wearing identical clothing. He could not recognise his wife unless she spoke. The whole episode lasted several minutes.

The following day, he experienced lightheadedness and was found by his wife sitting on a chair, confused, pale and diaphoretic. He was admitted to hospital. General and neurological examinations were normal except for subtle left homonymous hemianopia on formal visual field testing and mild difficulty with tandem gait. He continued to complain of a headache localised to the right occipital region and gastrointestinal symptoms. EEG and skull roentgenograms were normal. Chest roentgenograms demonstrated bilateral parenchymal scarring in the lower lung fields. CT brain demonstrated a right occipital mass with ring enhancement. He underwent an uneventful craniotomy and right occipital lobectomy. A histological diagnosis of glioblastoma multiforme was made and he underwent postoperative radiation therapy.

Summary of visual phenomena:

- Prosopometamorphopsia: wavy, flat, dyschromatopsia (tan complexion), tired eyes

- Palinopsia

- Reversal of numbers and letters

- Subtle left homonymous hemianopia

Other neurological symptoms and signs:

- Headache

- Nausea and vomiting

- Frequent bowel movements

- Vertigo

- Unsteady gait

Possible aetiology of visual disorder:

- Epileptogenic discharges, focal cortical irritation, deafferentation

Right occipito-temporal infarction [108]

A 62-year-old right-handed man presented with sudden onset of prosopagnosia. A month before his hospital admission, he was watching television and suddenly the faces on the screen appeared blurred and he could

not recognise them. The faces also appeared reddish and the right eye appeared excessively bright. He could no longer recognise faces of family, friends or famous people in photographs. He had a left upper quadranopia in the right eye. He could recognise people by their voices but not their faces. Faces were partically distorted, the right eye of people were twinkling and the right palpebral aperture appeared "long and narrow as a fox's eye". The visual distortion was restricted to human faces. T2-weighted MRI brain demonstrated an infarction in the posterior cerebral artery territory with an area of hyperintensity in the cortical and sub-cortical areas of the right occipito-temporal areas. Other high intensity areas included the fusiform gyrus, lingual gyrus, tapetum, inferior longitudinal fascicle and part of the optic radiation. PET demonstrated a reduction in regional cerebal blood flow and cerebral metabolic rate of oxygen in the areas of infarction seen on MRI.

Summary of visual phenomena:

- Unilateral prosopometamorphopsia

- Prosopagnosia: He regained the ability to recognise familiar faces, however, he was unable to recognise faces of people he met after disease onset.

- Dyschromatopsia of faces

- No other objects distorted

- Left upper quadranopsia in the right eye

Possible aetiology of visual disorder:

- Epileptogenic discharge, deafferentation

Right occipito-temporal hypoperfusion [109]

A 64-year-old right-handed man experienced two short episodes of light-headedness with paraesthesiae in left hand, chin, lips and tongue. He also had dysarthric speech, and a visual disturbance confined to the left visual hemifield. He experienced oscillating and rotating monochromatic geometrical figures within horizontally moving larger circles, which moved slowly from the left to the right side. For a short duration in one episode, the visual disturbance occurred on a polychromatic yellow and green background. Partial form distortions of faces strictly confined to the person's right facial side with associated loss of colour perception. Visual fields normal and higher cortical function normal. CT brain revealed no abnormality. Brain mapping demonstrated theta-wave slowing of the curve posteriorly over the right hemisphere. Brain SPECT demonstrated definite focal hypoperfusion in right occipito-temporal region. Cerebral angiogram

revealed occlusion of right posterior cerebral artery. Ticlopidine 250mg twice a day was commenced and the visual hallucinations subsided after a few weeks. He had residual blurring of vision restricted to the left visual hemifield. Repeat SPECT demonstrated partial normalisation. However, a discrete hypoperfusion in the right occipito-temporal region persisted. Repeat CT brain remained negative.

Summary of visual phenomena:

- Hemi-prosopometamorphopsia

- Dyschromatopsia and achromatopsia

- Simple visual hallucinations

- Transient visual disturbance confined to left visual hemifield

- Normal visual field tests

Other neurological symptoms or signs:

- Light-headedness

- Paraesthesia left hand, chin, lips and tongue

- Dysarthric speech

Possible aetiology of visual disorder:

- Epileptogenic discharge, deafferentation from right occipito-temporal hypoperfusion

Right temporal lobe brain abscess [96]

A 56-year-old right-handed male presented with generalised convulsions and a high fever. A few days before, he had a headache and generalised fatigue. The convulsions ceased spontaneously.

CT brain scan showed a low-density area occupying the right temporal lobe. The lesion appeared irregular and was surrounded by oedema with contrast enhancement. A diagnosis of a brain abscess was made and it was aspirated. There was no bacterium identified on culture of aspirate. After surgery and antibiotics, he recovered with no neurological or cognitive/psychiatric impairments. Seven months later, he developed generalised convulsions. EEG demonstrated delta wave activity in the right temporal region. This was thought, by the authors, to represent epilepsy caused by scarring of the healing abscess. Antiepileptic medication was able to control the seizures. However, EEG delta activity may not necessarily indicate epilepsy.

Occasionally, the right half of a person in front of him appeared swollen. This particularly affected the lower half of the face. It was consistently the right side of faces in front of him and only when the face was rounded. The distortion did not affect other objects or if the face was thin. There was no epileptic seizure activity during these episodes. He did not experience any visual hallucinations or prosopagnosia. Visual acuity and visual fields were normal. He did not have impairment in visuoperceptual performance or hemineglect.

SPECT did not reveal high tracer uptake suggestive of epilepsy. Increasing doses of antiepileptic medications did not improve the metamorphopsia. The metamorphopsia persisted periodically for 4 years until the paper was published.

Summary of visual phenomena:

- Prosopometamorphopsia

- No other objects distorted

- No prosopangosia

Other neurological symptoms and signs:

- Fever

- Generalised convulsions (resolved spontaneously)

- Headache

- Generalised fatigue

Possible aetiology of visual disorder:

- Cortical irritation or scarring from healing abscess that was aspirated. Possible reorganisation or rewiring.

Right temporo-occipital infarction [110]

A 79-year-old right-handed woman realised on waking, the faces of her family members appeared distorted. She consulted an ophthalmologist and was diagnosed with left homonymous hemianopia. MRI brain revealed a right temporo-occipital cerebral infarction. She had no other significant neurological signs. She described her metamorphopsia: "left half of the faces of people walking on the street in the opposite direction appeared distorted; they looked like monsters." Her condition improved with conservative medical treatment. However,

the right visual field metamorphopsia persisted for over three years. The authors suggest metamorphopsia can occur due to lesions in not only the contralateral parieto-occipital lobe. Metamorphopsia can occur with lesions in other regions including the ipsilateral hemisphere.

Summary of visual phenomena:

- Hemi-prosopometamorphopsia, persitent for over three years

- Left homonymous hemianopia

Possible aetiology of visual disorder:

- Epileptic discharge or deafferentation after right temporo-occipital infarction

Acute demyelination lesion in the left temporo-occipital region [61]

See Section 2.2.2.

Left temporo-occipital cortex infarction [111]

Case MZ was reported as a 60-year-old waoman had a haemorrhagic infarction of the temporo-occipital cortex with face specific distortion lasting 6 weeks. She suffered haemorrhagic venous infarction of the left temporo-occipital cortex with sub-cortical extension after embolization of a dural arteriovenous fistula. She was neuropsychologically examined 9 days poststroke. She complained (parts of) faces in her right visual field appearing to become smaller and to bulge. On confrontation visual field testing, she had no signs of any visual field defects, neglect,or extinction. She described 'When looking at a face, the right side starts to distort within seconds; the right side becomes smaller and the eye starts to disappear outside the face. Nose, mouth, and eye brows are displaced as well and bulge, but are still seen inside the face'. These distortions only affected faces. However, when a cup with two spoons was shown at eye level, she reported that the right spoon became somewhat distorted as well, although not as much as the face. She could still recognise familiar faces.

During neuropsychological experimentation, an observation during shape discrimination with right-sided presentation is incorrect judgments were made especially when the odd-one-out was presented in the upper right position. She described the stimuli as 'most of the time the upper square is much smaller'. When asked to indicate the width and height of the upper right square, it became apparent that a rectangle of 6.4 x 1.6 cm as well as a square of 3.2 x 3.2 cm appeared much shorter in width and only mildly shorter in height (approximately 4.1 x 1.4 cm and 2 x 2.6 cm). With presentations on the left, size estimations were much more adequate: approximately 6 x 1.5 cm and 3 x 3 cm."

Right posterior TIA [111]

CM was reported as having a haemodynamic TIA of the right posterior hemisphere resulting in face-specific distortions lasting 5 weeks. She suffered a haemodynamic TIA in the right posterior hemisphere (arteria cerebri media) and was neuropsychologically examined 4 days post-stroke. After the stroke, her perception of only faces was altered; both real faces and in pictures (e.g. in magazines). The faces become distorted within seconds after perceiving them. She had no signs of neglect, extinction, or hemianopia upon confrontational visual field testing. She described it was hard to look at faces, as the distortions made the faces look ugly on one side only, namely the left. The left side of faces appeared 'as through a glossy mirage'. She could still recognise familiar faces. After 5 weeks, CM reported the facial distortions were not as obvious as before. However, it is no clear whether the facial distortions had actually become less obvious or whether she had become more familiar with them.

2.3   Clinical cases

Eight clinical cases with various visual spatial distortions after cerebral pathology are summarised. Seven cases were from a neurology clinical practice in London, United Kingdom. One case (Case 8) was from a neurology clinical practice in Sydney, Australia. The seven cases from the London practice were described in detail in my master treatise. Further clinical information for the same cases was discovered since completion of the treatise. The case histories have been revised given this new information to improve accuracy in the cortical locations of the lesions or damage. The accurate localisation of the pathology and time course of the visual distortion is important in creating psychophysical behavioural tests to investigate potential cortical reorganisation of the visual pathway and the pathophysiology of cerebral metamorphopsia.

2.3.1   Cortical reorganisation of the retinotopic map possible

Case 1 (DOB 23/01/1945), left extrastriatal occipital lesion

Summary of visual phenomena: Episodic hemi-prosopometamorphopsia, featureless faces Simple hallucinations Right hemifield grey blur Paracentral scotomas

Other neurological symptoms or signs: None

Aetiology of visual disorder: Deafferentation

A 48-year-old female with Monospot positive Epstein-Barr Virus illness described visual disturbances in her right hemifield. Six days after the commencement of symptoms the viral infection, she suddenly noticed

Table 2.2 – Clinical Cases, RH = right-handed

Case	Age	Side of lesion	V1 damaged	Other cortical areas damaged	Type of Metamorphopsia	Geometric Cortical Reorganisation
1	48/F	Left	N	Left extra-striatal	Hemi-faces	Possible, but only faces distorted
2	62/F RH	Left	N	Left optic radiation	Oblique	Unlikely
3	50/F	Bilateral	Y	Y	Bizzare faces/hands, bowed straight lines	Possible
4	61/M	Right	Y	Y	Faces, hands, feet, objects	
5	86/F	Right	Y	Parietal (agnosia, neglect)	Selected objects, faces	
6	55/F RH	Left	Possible	Yes		
7	48/M	Right	Likely	Parieto-occipital likely		
8	16/F	Left (presumed)				

a grey blur located within the right side of her visual field. There were flecks or strands of colour present throughout the grey blur.
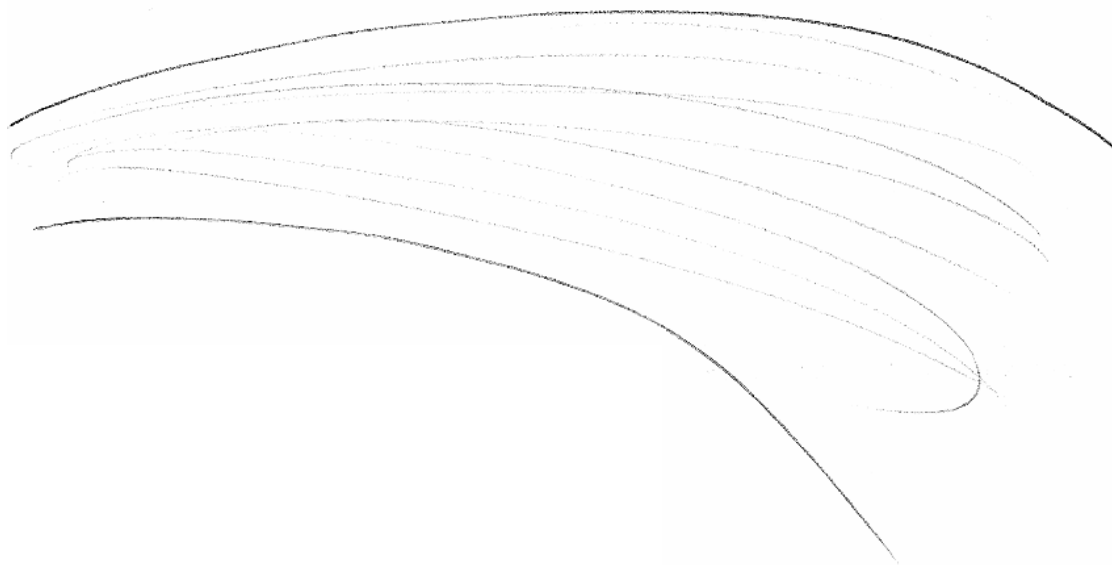
Figure 2.1 – Case 1 drawing of grey blur with flecks of colour in the right half of her visual field

Four days later, she made a full systemic recovery from the viral illness, however, her visual symptoms persisted. Over the following weeks, the coloured areas within the grey blur resolved resulting in a grey featureless blur. Over 18 months, this grey featureless blur dispersed to form smaller scotomatous areas. She was still able to read, however, the small paracentral scotomas created missing areas within the printed text. When she was tested with an Amsler grid, she noticed irregular scotomas in the temporal side of the Amsler grid in each eye.

However, no distortion of the lines of the Amsler grid were observed.

Eighteen months after the onset of her viral illness, she began to experience visual spatial distortions. Faces appeared distorted when they were observed with each eye in turn and also binocularly. Only the right side of each face she was looking at appeared distorted. When she viewed her own face in the mirror, the left side appeared smaller and further away than the right side of her face.

As she varied the viewing distance from the mirror, one of her eyes or other facial features would disappear.If she looked at a face, the eye would appear displaced and the cheeks sunken in. The face appeared to curve backwards. If an eye disappeared altogether, the face no longer appeared to be flesh.

It appears flesh coloured but featureless, the skin has no texture such as lines or wrinkles. Where the eye should be looks like a depression with the walls caved in. When she viewed faces in photographs, the distortion of the face was not observed. However, the face did appear to be missing an eye. Profiles of faces or the back of the head did not cause distortion. If she was looking at a face more than 1.8 meters away, the
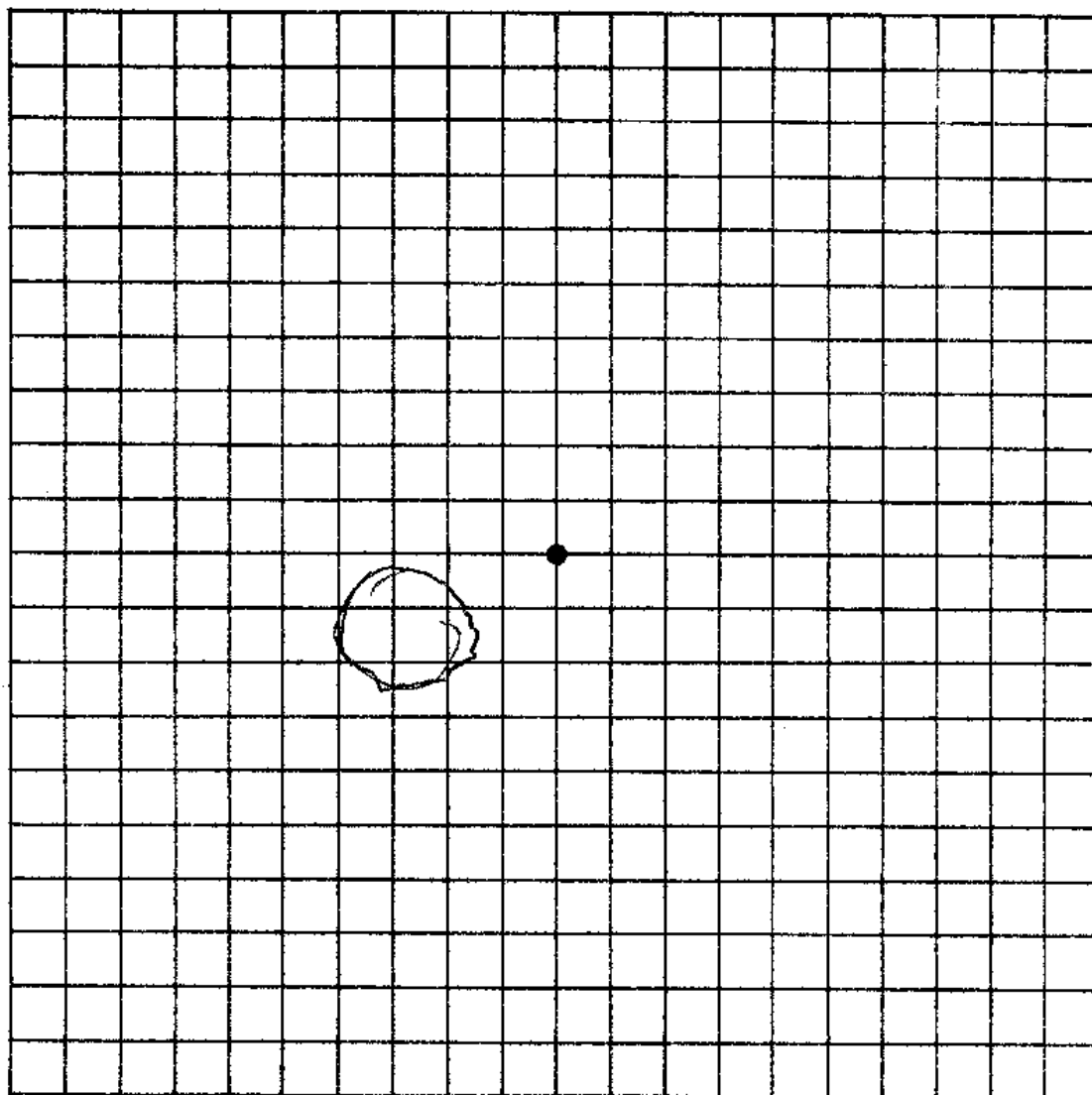
Figure 2.2 – Case 1 Amsler grid left eye demonstrating temporal scotoma
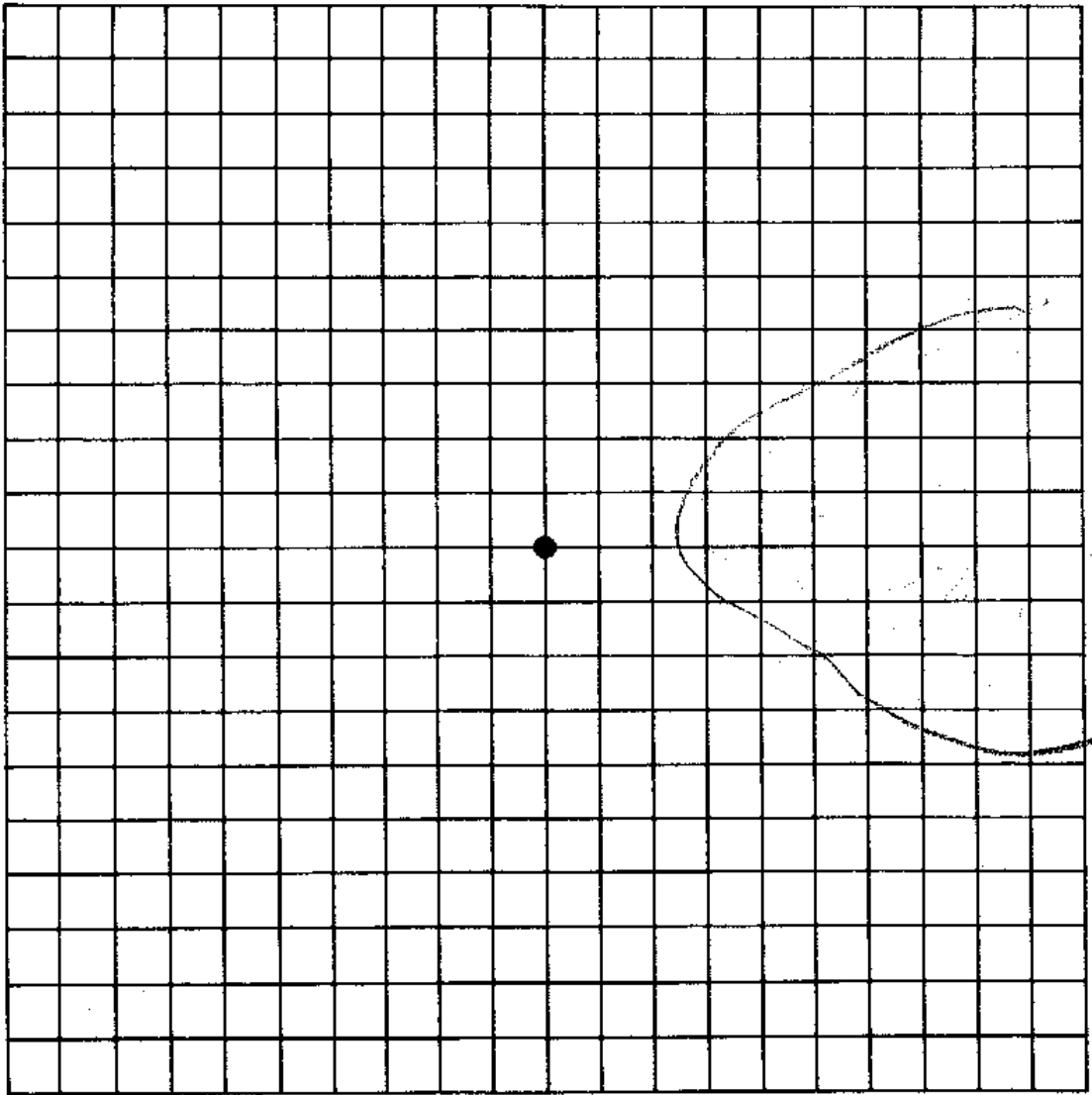
Figure 2.3 – Case 1 Amsler grid binocular viewed at 50cm and 4 months later
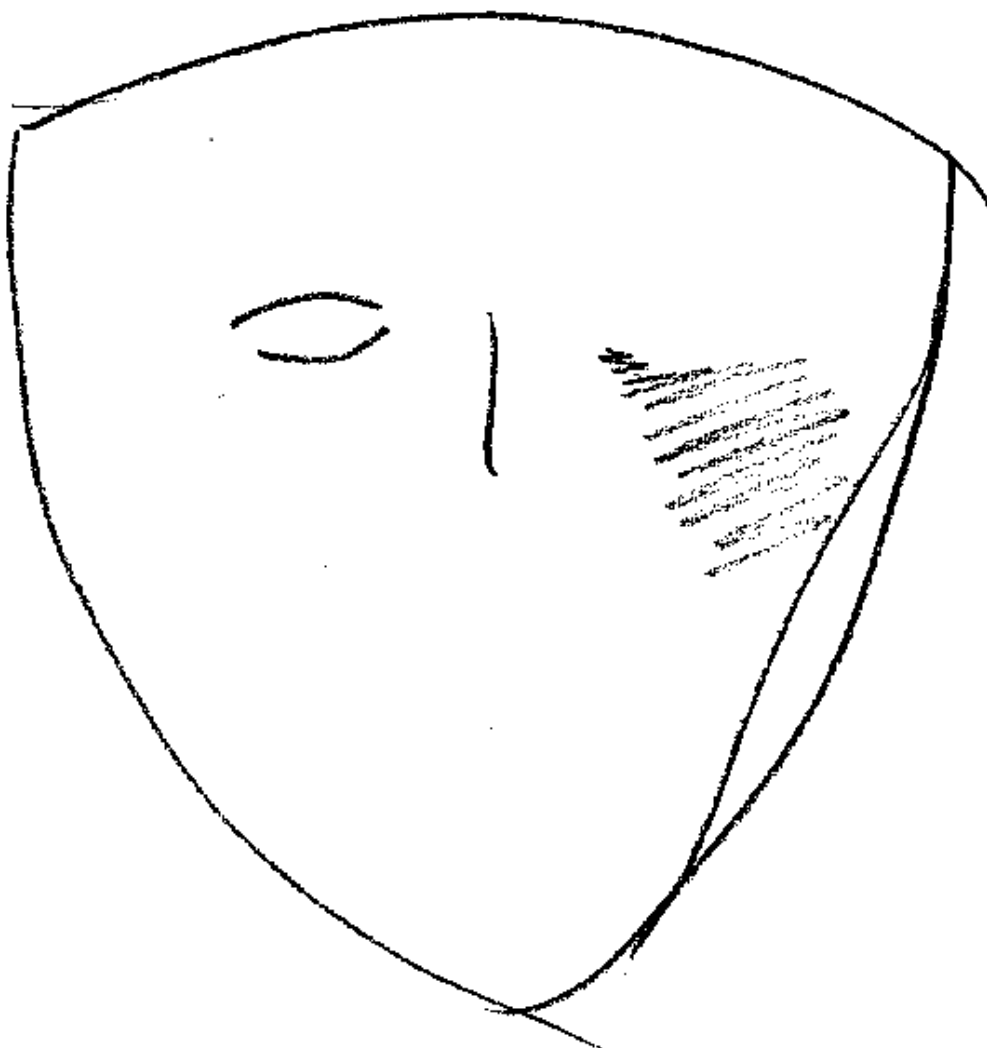
Figure 2.4 – Case 1 drawing of face missing left eye
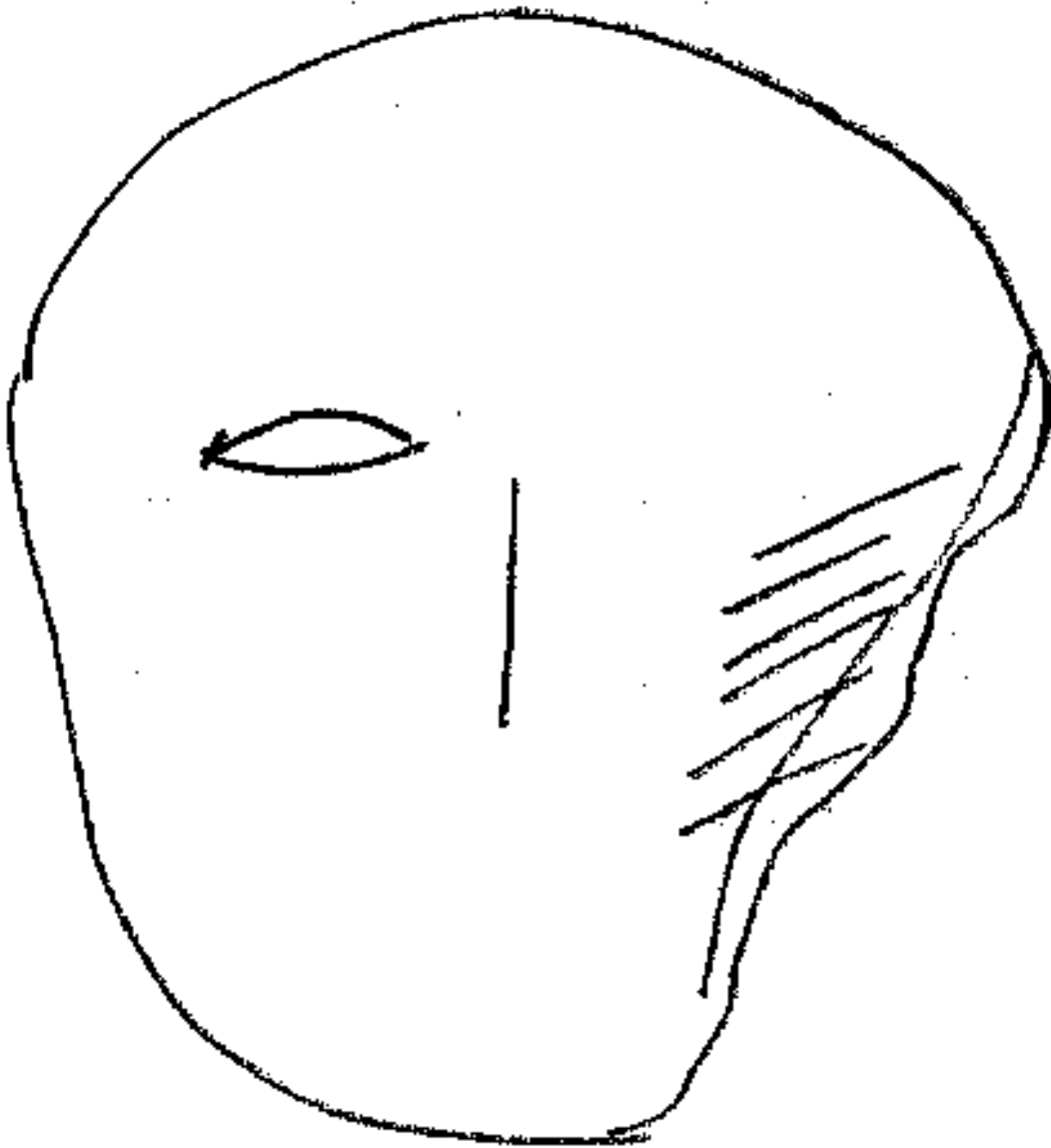
Figure 2.5 – Case 1 drawing of face with sunken flesh

distortion was worse. If she was tired, the distortion was greater and the face appeared closer to her. She observed the distortion occurring with faces on the television if she was also experiencing the facial distortion of real people.

Other observations she described include real objects appearing more solid on the right side of vision compared to the left. Objects with straight edges and corners, such as picture frames, appeared normal. She did not describe distortion of any other real objects.

On examination, her visual acuity was 6/6 bilaterally, near vision N5 each eye, Humphrey visual field 24-2 and 10-2 were normal. Confrontation visual field testing with a red pin revealed a small homonymous scotoma one degree of visual angle in diameter. This scotoma was located within one degree of fixation in the right hemifield. MRI brain revealed an extra-striatal left occipital lobe abnormality, thought to be an area of infarction.

The area of infarction was thought to be caused by either arterial or venous ischaemia during her acute viral illness. At the onset of this ischaemia, a substantial right homonymous scotoma would have been present (the grey blur within the right side of her visual field). However, this scotoma decreased in size leaving a very small right sided paracentral scotoma which was quite disabling when reading.

Cortical reorganisation could have possibly caused distortion of visual perception as it was only observed after eighteen months. The distortion also only appeared to consistently affect the right half of faces, there was no visual distortion experienced in the left hemifield. However, she did not perceive visual distortion of any other objects which contridicts a geometric distortion or reorganistion of the cartesian map. The damage was to the extra-striatal occipital cortex, which is a higher visual association area.

Case 3 (DOB 25/03/1945), cerebral hypoperfusion

Summary of visual phenomena: Hand movements left hemifield, light perception right hemifield; improved to count fingers left hemifield and hand movements in right hemifield; dense homonymous right upper quadrantanopia Visual distortion: normal straight lines would be bowed, television appeared rounded, affect vertical and horizontal Grotesque, bizarre prosopometamorphopsia Grotesque, bizarre distortion of hands People observed walking with a strange gait Spontaneous resolution of visual symptoms Achromatopsia, dyschromatopsia

Aetiology of visual disorder: Intraoperative hypoperfusion causing deafferentation in multiple higher visual processing areas. Possible reorganisation of the retinotopic representation of visual space.

A 50-year-old female was admitted from a chest clinic with shortness of breath, cough and chest pain. She was found to have a right malignant pleural effusions. A pleural biopsy diagnosed adenocarcinoma. She underwent a laparotomy which disclosed peritoneal carcinomatosis. Post-laparotomy on the hospital
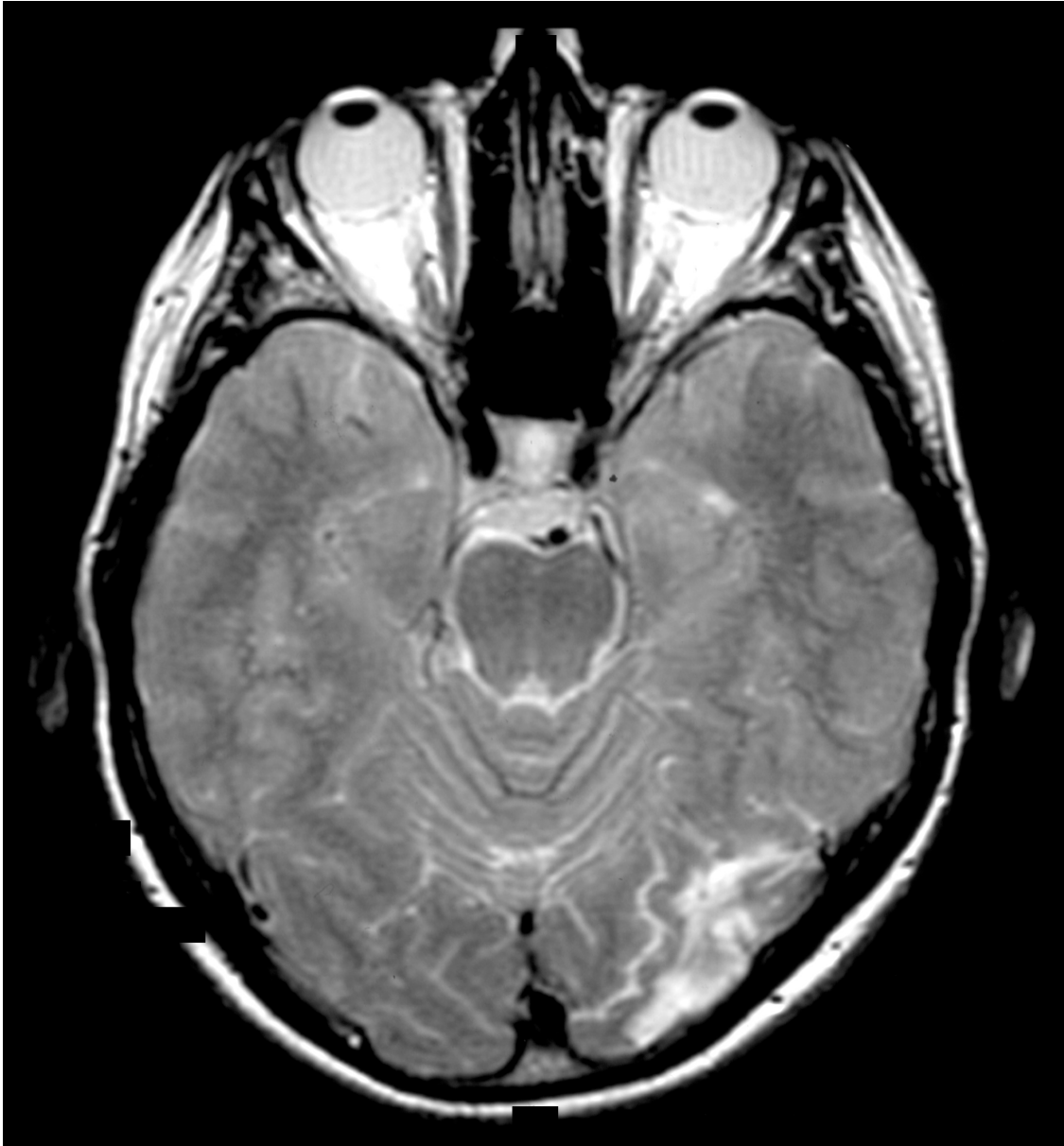
Figure 2.6 – Case 1 T2 weighted MRI axial, extra-striatal left occipital lobe abnormality, thought to be an area of infarction
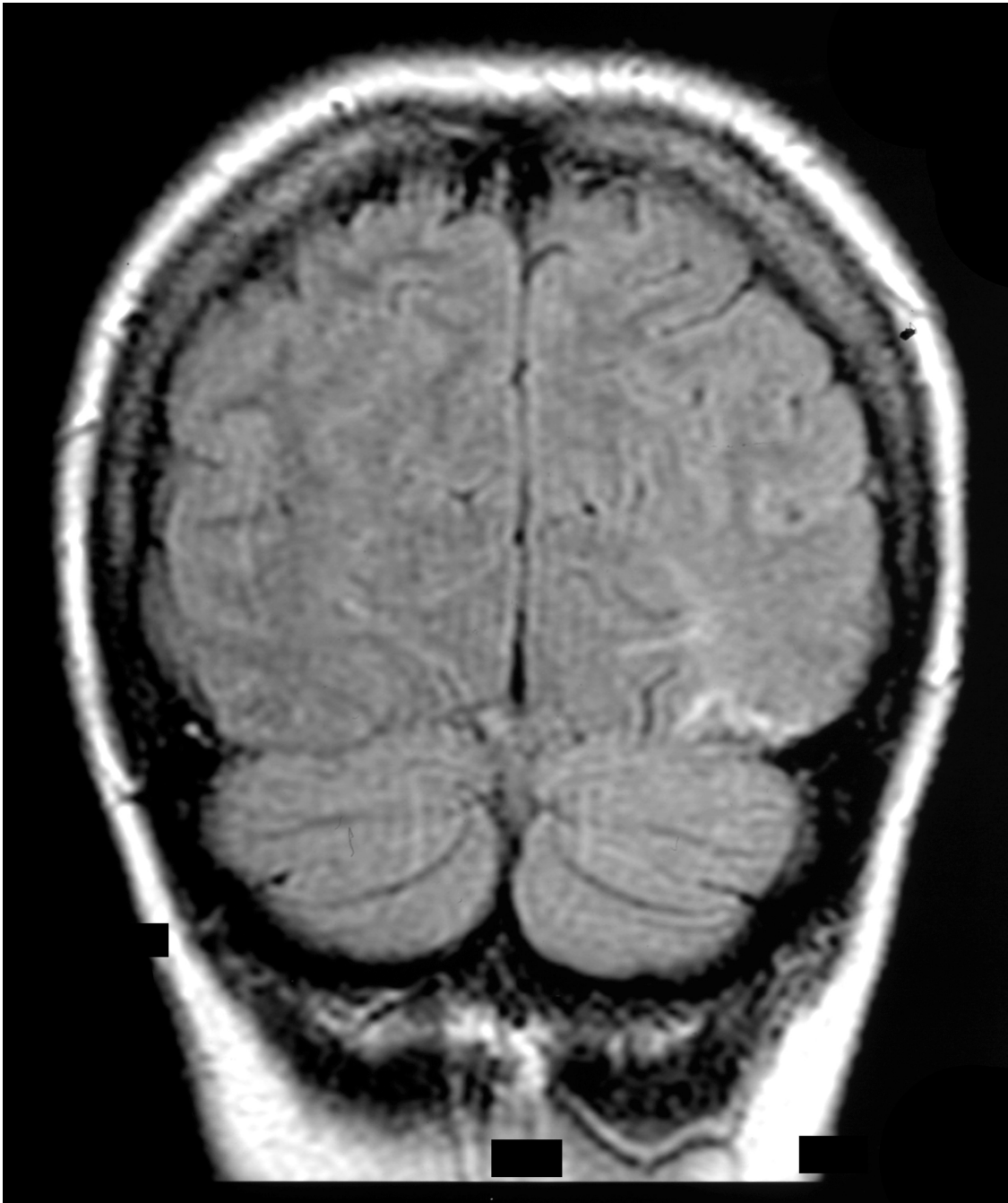
Figure 2.7 – Case 1 T2 weighted MRI coronal, extra-striatal left occipital lobe abnormality, thought to be an area of infarction

ward, she could see very little. She could only make out shapes and people walking around her rooom. On examination, her visual acuity was decreased to hand movements in the left hemifield and light perception in the right hemifield. Over the following few days, her vision gradually improved. She could see objects and people walking around, but only very dimly. Her vision improved to count fingers in the left hemifield and hand movements in the right hemifield. She then became aware of a distinct visual distortion where normal straight lines of a wardrobe would be quite bowed and the television appeared rounded. This affected both vertical and horizontal contours. Also, she described a grotesque and bizarre visual distortion of faces where people appeared "most odd". Faces were perceived as "horrible Picasso portraits", with exaggerated features and "crooked eyes". The facial features of familiar people were so disordered that she was unable to recognise them without auditory cues. Hands also appeared distorted and "horrific with bulbous fingers, as though the had leprosy". The patient's own hands were simiarly affected by this distortion. People appeared to be walking with an strange gait, "as though disabled". The prosopometamorphopsia and visual distortions of hands spontaneously resolved in less than a week. The distortion of objects not being straight or perceived as rounded, lasted longer.

Fourteen days post-operatively, her visual acuity had improved to 6/9 bilaterally. She had a dense homonymous right upper quadrantanopia. Her visual distortion of objects spontaneously improved over weeks, however, a degree of prosopagnosis persisted over several months. She reported difficulty interpreting facial expressions despite having an appreciation of the individual features. Colour vision was profoundly affected initially. She could not perceive any colours and viewed the world in "black and white". She was unable to distinguish between the skin tones of different races. At times people appeared "almost as if in negative". Although her colour perception improved over weeks, she had difficulty choosing appropriately coloured clothes. Some months later, she reported her own eyes to be "creamy colour" (her eyes were brown in reality).

During her laparotomy, potentially many visual cortical areas were affected by hypoperfusion and not just the occipital lobes. She had agnosias such as colour perception, facial recognition, difficulty reading. Therefore, she also had parietal lobe injury. The timing of the prosopometamorphopsia is unlikely to be due to cortical reorganisation. However, the more persisting curved distortion of horizontal and vertical lines could be due to cortical reorganisation of the retinotopic map.

Case 4 (DOB 16/01/1943), right occipital lobe infarction

Summary of visual phenomena: Transient bizarre prosopometamorphopsia and body distortion Distortion of hands and feet Dyschromatopsia Chromatopsia Prosopagnosia Palinopsia Left hemianopia (not aware)

Other neurological symptoms or signs: Transient paraesthesia left arm Unconcious movement of left

upper limb

Aetiology of visual disorder: Deafferentation, possible cortical reorganisation of undamaged cortex of higher visual association areas

A 61-year-old male, with a background of hypertension and atrial fibrillation, suffered a large infarction of his right occipital lobe. He had several transient ischaemic attacks (TIAs) before his stroke. One year prior to his admission to hospital, he experienced an episode of transient physical and visual disturbances. He described sitting in an armchair when his left arm suddenly rose up as if to give a salute. His left arm moved around in a circle and came down again. These left arm movements occurred unconsiously and repeated, so he grabbed his moving arm with his right hand and placed it on the left arm of his armchair. He also had paraesthesia of his left arm. The sensation returned to normal, however, he noticed something wrong with his vision.

He had a bizarre visual distoriton where people appeared to have come from the "Planet of the Apes". For a period of one to two hours, every person he observed appeared a funny shape and had a hunched body. They also had the same colour hair. He was unable to recall looking at his own face in the mirror at this time. The distortion happened most often when the face was in profile. If he then observed the same face front on, they had the same distorted appearance as was observed in profile. This bizarre distortion resolved spontaneously.

The day after his large right occipital lobe stroke, he felt his vision was out of focus but colours appeared normal. He had difficulty recognising people but he could recognise their voices. After his visual acuity improved, the bizarre distortions of faces appeared once again. The facial distortion was intermittent and the patient correlated the visual disturbance with stress. Other objects began to take on the shape of other items he had seen previously. For example, mirrors took on the shape of a vase. His hands and feet looked distorted with each of the digits a different size to what he remembered. Each digit also appeared fatter or thicker. He could not recall any triggers causing an object to take on the shape of something he had seen previously. He remembered an object appeared distorted into a horseshoe shape but he was unable to recall which object it was.

Four weeks after his stroke, his vision gradually improved. He no longer experienced the "Planet of the Apes" distortion. However, the digit distortion of hands and feets remained. This distortion affected other people's hands and not just his own. He had a left sided hemianopia. However, he did not notice the left half of his visual field was missing. He described that he was unable to see anything distinct in the left side of his visual field.

The visual distortions occurred inconsistently, it was observed only some of the time with some objects. It is unknown whether rotating the objects by 90 degrees would have changed the orientation of the dis-

tortion i.e. whether it was purely geometric and unaffected by orientation. It seems unlikely that cortical reorganisation played a role in the bizarre distortion of faces as the symptoms occurred acutely and resolved spontaneously. Also, rewiring would not explain the perception of objects taking on the shape of other objects previously seen, as this was also experienced acutely. The more persisting intermittent distortion of hands and feet could possibly be due to cortical reorganisation. However, the large occpital lobe infarction affected the extra-striatal occipital cortex as well as the striatal cortex. Higher visual proceesing association areas were probably damaged, not only the retinotopic projections.

Case 7 (DOB 15/11/1946), presumed right occipital lobe ischaemia

Summary of visual phenomena: Intermittent loss of left visual hemifield (1st) Continuous horizontal stretching distortion (2nd), vertical lines appeared curved, sometimes complicated Bizarre distortion of hands and faces Partial left non-homonymous inferior quadrant visual field defect

Other neurological symptoms or signs: Right occipito-parietal headache for one to two hours after visual disturbance Prolonged severe throbbing headache lasted 10 days before the second visual phenomenon Bilateral pale optic discs Broken pursuit eye movements Mild ataxia of gait and upper limbs (previous cerebellar astrocytoma age 14 years)

Aetiology of visual disorder: Deafferentation

A 48-year-old male factory worker experienced frequent intermittent episodes where his entire left visual hemifield would "disappear" for seconds to a few minutes. He described seeing half of his wife's face suddenly vanish, and this also occurred with other objects such as clock faces. There were no positive visual phenomena. As the visual disturbance resolved during these episodes, around five minutes after their onset, a moderate to severe right occipito-parietal headache often occurred. Each time the headache persisted for one to two hours. Six months after onset of these visual symptoms, an otherwise typical episode was followed by a prolonged severe throbbing headache which lasted ten days. Shortly after the onset of this headache, after about one day, he experienced second visual phenomenon which was continuous rather than intermittent. He described objects, people, faces etc. to be "stretched" horizontally. Thus, squares appeared as a horizontal rectangles, car wheels appeared to be oval shaped, doorways seemed "small and wide". In addition, vertical lines appeared curved. For example, telegraph poles looked "squashed and bowed". The distortion was worse the closer he was to the object and appeared to be complicated rather than geometric. Distortions of body parts was particularly prominent: fingers appeared to be "fat and short". If he rotated his hand, this made no difference to the distortion. However, he did not observe a compressing or stretching of an object as it was rotated such as the second hand on a clockface. Facial features were accentuated with "big noses and eyes". Familiar faces were recognisable but appeared "in caricature", particularly when viewed close up. This

also affected faces in photographs. Colour vision was unaffected, however, he had a known congenital colour deficit. He did not not experience any true visual hallucinations and had no history suggestive of visual perseveration. Reading was possible but only with a magnifying glass as the lines of printed text appeared to "run together". The distortion was severe for three to four weeks, and then gradually lessened over the following three to four months. As the distortion decreased, he continued to have intermittent headaches and he became aware of reduced peripheral vision which was not distorted.

A cerebellar astrocytoma had been excised and treated with radiotherapy 34 years previously at the age of 14 years. He also underwent multiple operations as a child for bilateral dense congenital cataracts.

He was clinically reassessed nine months after the onset of his prolonged visual distortions. Corrected visual acuity was 6/9 left eye and 6/24 right eye. Near vision was reduced to N12 in the right eye. Colour vision was grossly reduced bilaterally (known to have congenital colour anomaly). Goldmann perimetry revealed a partial left non-homonymous inferior quadrant visual field defect. His optic discs appeared pale bilaterally. Pupillary responses were normal. Extraocular pursuit movements were broken but full. He had mild ataxia of gait and both upper limbs. The remainder of his neurological and general physical examination was normal.

MRI of his brain revealed post-surgical changes in the right cerebellar hemisphere and vermis. There was periventricular signal change consistent with small vessel ischaemia but no focal occipital lesions. MRA of his brain and neck was normal. The IgG antiphospholipid antibody was mildly elevated (9.8 GPLU/ml). An extensive pro-thrombotic screen was otherwise normal. He was treated with low-dose aspirin. Even though the MRI did not demonstrate a focal occipital lesion, it was presumed he had occipital lobe ischaemia.

If he was experiencing cortical ischaemia each time he noticed a paroxysmal scotoma, the continuous visual distortion could be attributed to possible cortical reorganisation. However, if the episode of a prolonged headache for ten days is considered as the only ischaemic event, the visual distortions are unlikely to be due to cortical reorganisation. This is because the visual distortion occurred one day after the headache started which is more likely to be due to release phenomenon or deafferentation. The visual distortions could be due to a combination of cortical reorganisation as well as a release phenomenon as the distortion consistently affected objects in a similar way and he had a bizarre distortion of faces. It is also possible his right parieto-occipital area was affected by ischaemia, the superior and central nerve fibre bundles of the optic radiation as well, considering he had a partial left non-homonymous inferior quadrant visual field defect.

Case 8 (DOB 27/02/1986), presumed small left posterior circulation vascular event

Summary of visual phenomena: Prolonged migrainous visual aura affecting entire right visual hemifield Distortion of hands and faces Bizarre distortion of faces and hands, particularly in the right hemifield

Chromatopsia, green Dyslexia Simple hallucinations Normal formal visual field tests

Other neurological symptoms or signs: History of migraines Persistent retro-ortibal headache for a week with visual distortions

Aetiology of visual disorder: Deafferentation, epileptogenic discharge

A 16-year-old female experienced visual disturbances twelve months after a protracted migraine. Her visual symptoms were thought to be due to a small posterior circulation vascular event. She described metamorphopsia for both hands and faces, as well as chromatopsia (a visual aberration where objects appear abnormally coloured) and visual confusion when reading.

Her first experience of a migraine headache was at the age of ten years. Her migraines were associated with a variety of visual auras from their first onset. Visual blurring and scotomas predominantly developed in the right visual field and occasionally, the scotomas had a "checkered" edge. The visual aura lasted ten to fifteen minutes. Fifteen to thirty minutes after the visual aura commenced, a unilateral mostly right-sided retro-orbital pain would begin. This pain fluctuated but was not throbbing in nature. The pain was usually associated with mild nausea but no vomiting. She also experienced marked photophobia and phonophobia. The headache could last several hours to a day if untreated. The headache frequency was almost monthly but were not necessarily timed with her menstrual cycle. Abortive migraine medication included paracetamol and aspirin, the latter was effective. She had tried sumatriptan once, however, this resulted in nausea. She had also tried a three month course of propranolol which was only partially beneficial. She had not tried any other prophylactic therapies.

Twelve months before presenting to the neurologist, she was in the middle of her high school examinations when she developed a visual aura. This visual aura appeared to affect her entire right visual field. This was followed by retro-orbital pain which became severe over minutes and persisted continuously for an entire week despite simple analgesia. During this week, she had an ongoing disturbance of her vision and her mother noted her to be "a bit out of it". Although the headache had resolved, her vision had not completely returned to normal at the time of consultation. She volunteered her visual perception was distorted or altered. This phenomenon was most pronounced when looking at faces, which occassionaly assumed Picasso-like distortions, particularly involving the eyes, "horrible Picasso faces". On direct questioning, she also noted her hands appeared to be "abstract" in nature some times. The distortion of faces particularly seemed to affect the right visual field i.e. the left side of faces the patient was looking at. She denied any difficulty in recognising faces.

In addition to the metamorphopsia, she had mild difficulty reading. Letters seem to "run into one another" and occassionally apppear to have a pulsating white light around them. She was also aware of a greenish tinge to certain objects as though they are overlaid by a translucent green film.

On examination, she was well and in sinus rhythm. There were no carotid bruits. Her visual fields were full to confrontation on bedside examination. Her visual acuity was 6/6 bilaterally. Fundoscopy was normal with spontaneous venous pulsations present in both eyes. Extraocular version movements were normal and saccades were of normal velocity. Lower cranial nerve examination was intact. Complete neurological examination of limbs and gait were normal. Humphrey visual field testing was normal both eyes. She had almost normal formal neuropsychometric testing.

CT scan of the brain was reported as normal, however, the neurologist thought there was a small abnormal region in the left occipital lobe which was of cerebrospinal fluid density. A MRI scan was requested and did not demonstrate any abnormality.

Case 6 (DOB 28/08/1944), after debulking of left parieto-occipital ependymona

Case 6 experienced a consistent visual spatial distortion where the right half of the visual field appeared to be stretched down and to the right. This was after she suffered from a left occipital lobe lesion. However, the timing of the lesion and her visual symptoms is not known.

Summary of visual phenomena: Distortion in right hemifield, hemi-macropsia, stretching down and to the right Bizarre prosopometamorphopsia Palinopsia Non-homonymous right sided visual field defect, denser inferiorly Depth perception issues Movement perception problems

Other neurological symptoms or signs: Aphasia

Possible aetiology of visual disorder: Post-operative oedema, focal cortical irritation, epileptogenic discharges, deafferentation

A 55-year-old right-handed female telephonist presented with deteriorating non-fluent aphasia over 12 months and subsequently underwent debulking of a left parieto-occipital WHO Grade II ependymona. Post-operatively, she became aware of distortion confined to the right hemifield. The most prominent abnormality was magnification of both objects and people in the right visual field. Objects, faces etc crossing the vertical meridian appeared to be divided by a vertical strip of bright white light. To the right of this strip, was the magnified segment of the object. This distortion was present when the patient viewed her own face in the mirror. All faces appeared "ugly and awful", however, she could only attribute this to the distortion described above. All contours in the right hemifield appeared "fuzzy". She also described an phenomenon when watching television. Speech and lip movements appeared to be desynchronised so words would appear to be articulated a split second after hearing them. This phenomenon was less obvious when interacting with live people. She denied any abnormality of colour perception.

Clinically examination two weeks postoperatively demonstrated a non-homonymous right sided visual field defect, predominantly affecting the inferior quadrant. Fourteen months later, the visual field defect

had diminished in size which is presumably due to the resolution of postoperative oedema. However, the distortion persisted unchanged.

She experienced a variety of visual disturbances. The right hemifield of her vision appeared fuzzy. She was aware of movement in the affected field but everything appeared much larger and closer on the right side compared to the left. Also, everything in the right hemifield was stretched down and to the right like the surface of a balloon. The stretching down and to the right affected all objects she was looking at. Across the horizontal midline, there was a horizontal section where see was unsure of what she was seeing. Moving objects coming from the left were perceived as jumping or suddenly appearing into the right hemifield. If objects were moving in the opposite direction, from the right into the left hemifield, they were perceived normally. She described that her right hemifield appeared like a bright sun shining all of the time.

She drew a few pictures demonstrating her visual distortion, it appears to be a geometric distortion.

2.3.2   Cortical reorganisation unlikely

Case 2 (DOB 15/07/1939), left occipital lobe infarction

Summary of visual phenomena: Persistent visual distortions, 10 days Oblique distortion Normal visual field tests

Aetiology of visual disorder: Deafferentation

A 62-year old right-handed female experienced ten day history of persistent visual distortions. She described an oblique distortion. Objects with sharp angles which she knew to have straight edges and corners, such as picture frames and light switches, appeared slightly crooked. The dimensions of the object were not distorted. Her symptoms spontaneously resolved. Her visual field tests were normal. A MRI scan demonstrated a linear area of signal abnormality in the left occipital lobe close to the left optic radiation (geniculocalcarine tract). This may have represented an ischaemic lesion (MRI scan could not be found in the medical or radiological hospital records). Her final diagnosis was an acute left occipital lobe infarction causing metamorphopsia.

Her visual symptoms were experienced acutely they resolved spontaneously. This makes it unlikely that cortical reorganisation occurred. The occpital lobe lesion was close to the optic radiation. The distorted visual perception could have been due to a geometric change that occurs when input to the retinotopic map of the striate cortex is affected. The distortion could also be due to disinhibition of pre-exisitng long-range horizontal neural connections (a release phenomenon) with the resolution of the symptoms being due to adaptation of these connections.

No drawings are available demonstrating her distortion or MRI documenting the occipital lobe lesion.

2.3.3 Higher visual processing areas damaged

Case 5 (DOB 26/05/1909)

Summary of visual phenomena: Decreased visual acuity Achromatopsia Prosopometamorphopsia: bizarre Metamorhpopsia Palinopsia Visual hallucination Left neglect Aperceptive agnosia

An 86-year-old woman was admitted to hospital with left ventricular heart failure due to ischaemic heart disease. She also had non-insulin dependent type 2 diabetes. Soon after her admission to hospital, she became aware of a visual disturbance. Her vision became "misted over" in both eyes. Both objects and people had a "gingery-brown discolouration". Outlines objects were blurred and she had great difficulty distinguishing between different objects. She also had difficulty distinguishing between objects and people. Faces were particularly affected by her visual disturbance: they appeared "ugly, old and wizened", were "covered in gingery hair" and grossly elongated. Facial features were exaggerated: noses appeared to "spread across the face". In the initial two to three days of these visual experiences, the distortion was such that faces were indistinguishable from one another. The patient relied on on voice recognistion to identify individual people. Interestingly, the faces of family members appeared to be less affected by the distortion.

Bodies and hands also appeared "mis-shapen". During a car trip outside of the hospital, she noticed a "string of horses, hundreds of them, all ginger" on a single occasion. In reality, the car had passed only two horses (she was unsure what colour they werein reality).In addition, floors did not appear to be flat. Instead, the floor appeared to slope or had multiple levels. Items of clothing appeared "lop-sided", with one side higher than the other. After sewing a vest, she held it up her work and was under the impression that one strap was longer than the other. On several occasions, she reported seeing fleeting movements, some of the time it resembled a "small animal scurrying across the floor".

Three weeks after the onset of her visual distortions, her reading vision was N18 bilaterally. Colour vision was impaired. A dense left homonymous hemianopia to hand movements was present. Pupillary responses were normal. Fundoscopy revealed mild diabetic retinopathy changes bilaterally. A mild distal sensory impairment was the only other neurological abnormality.

The video interview performed with GTP of this case was one of the main sources of information as the hospital medical records were unable to be located. The transcript of the interview was included in the appendices of my master treatise. Copies of two neuropsychological reports were found in research records. One of the neuropsychological assessments was performed on the 14/12/1995 whilst she was admitted to The National Hospital for Neurology and Neurosurgery, Queen Square, London, United Kingdom. At the time of this assessment, I was unable to determine how many days she had been experiencing vision loss.

She had very poor vision during this assessment and was unable to read.

Another neuropsychological assessment was performed on the 19/01/1996. Her visual difficulties were assessed using a battery of tests designed to detect early visual processing. Visual acuity was 6/24 using Ffooks symbols test [112] For shape perception, she had a severe deficit on the Efron Test [113]. In the Efron test, patients have to assess whether two orthogonal rectangles (matched for flux: luminance and area) have the same or different dimensions. Failure of this test is an inability to compute shape information. Aperceptive agnosia is attributed to diffuse damage to the right parieto-occipital cortex. She could not attempt the VOSP shape detection test [114]. She had severe left neglect. She had no evideence of any visual disorientation.

CT images of the brain showed a low density region in the right occipital lobe suggestive of early infarction. Follow-up MRI scan images of her brain were not available. However, the MRI brain report confirmed the presence of a mature infarct containing haemosiderin in the right occipital pole.

Case 5 had occipital lobe ischaemia on brain imaging, however, it is unclear whether other visual processing areas were also affected on these images. During her video interview, she described many different visual phenomenon. She experienced a geometric distortion where she could not judge the size of objects. She also experienced a bizarre change in people's appearances. The duration of her symptoms was short once her vision loss partially recovered and she only observed the distortion occurring with selected objects. It is difficult in this case to conclude whether her symptoms could be due to cortical reorganisation as on clinical testing her right parieto-occipital cortex was damaged.

2.3.4   Summary of clinical cases

None of the clinical cases had cortical damage localised to the striate cortex alone. All of the cases potentially had pathology involving higher visual processing areas. Due to the complicated nature of their cortical damage, many of the cases would be unsuitable for developing a psychophysical test to investigate geometric or retinotopic cortical reorganisation. These cases have such varied and complicated pathologies that it would be unclear from subject behavioural testing whether an observation could be attributed to a specific area of cortical injury or remapping.

2.4   Categories of Cerebral Metamorphopsia

Cerebral metamorphopsia could be divided into two categories. Firstly, one which includes geometric distortion of object and could be due to changes in lower-order visual processing. Secondly, an abstract or bizarre distortion of objects involving higher-visual processing areas. These two categories could then be further

sub-divided into when the distortions first appear and their longevity.

2.4.1 Geometric Distortion

A geometric visual distortion of objects could manifest from cortical changes of the lower-order visual processing areas. The perceived distortion may be caused by normal neural cellular processes that have become unmasked or long-term structual reorganisation of the visual cortex.

Instantaneous or acute

In this group, the visual distortions appear instantaneously or acutely after the patient has regained consciouness from their cortical insult. The distortion consistently affects all objects in their visual field. After a duration of time, such as days, the visual distortions resolve. It is likely patients suffering from these acute visual distortions go undiagnosed as they are unlikely to spontaneously volunteer these symptoms during their recovery. Also, their medical team is unlikely to ask them specifically about visual distortions unless they hava a special interest in the area. The cause of these acute geometric visual distortions could be due to a release phenomenon or deafferention of the normal cortex surrounding the area of injury. They could also be due to a normal localised healing process or spontaneous neural activity in the surrounding healthy cortex. These patients are not likely to be reliable subjects for neuropsychological experiments due to the volatile and fleeting nature of their visual distortions.

Manifesting in seconds or minutes after viewing the stimulus

This group only experiences the visual distortion after viewing the scene or object for a short period of time. The visual scene or object changes or transforms from being perceived as entirely normal to geometrically distorted. There is a possibility the normal neuronal adaptatiion processes of healthy neurons surrounding the damaged cortex is responsible. Due to altered or disrupted homeostatic neuronal processes, functional reorganisation transforms the initial normal perception into a distortion. Disruption of normal modulatory neuronal processes in lower-order visual processing could cause the altered perception. The feed-forward and feed-back interactions of early visual processing cortical neurons potentially manifests the distortion. The perceived distortion may be highly stimulus specific in these patients.

Days, weeks, months or indefinitely after initial cortical insult

Patients in this group experience a geometric distortion which is consistent, persistent and develop days after the initial cortical injury. Visual distortions are reported during certain viewing conditions and apparently

appear instantaneously. The visual illusion in these patients could possibly be due to structural reorganisation of the lower-order visual cortical areas. The potential structural changes involved are neuronal sprouting or the establishment of long-range horizontal connections. The participation of this group of patients in research studies is the most promising as there is less variability in their experienced visual distortion.

2.4.2   Bizarre Distortion

Bizarre or abstract visual distortions have been reported after cortical injuries. The cases describe their visual distortion as being jumbled, broken, ugly or grotesque. Disruption to higher-order visual procesing as the cause of their distortion is more likely in these cases.

Instantaneous or acute

The visual distortions in this group are present when the patient regains consciouness after the injury. After a short duration of time, such as hours or days, the distortions resolve. As with the case of acute geometric visual distortions, the umderlying pathology is more likely to be due to a release phenomenon or deafferenation of surrounding neurons. Cortical irritation leading to epileptiform activity could also be a cause of these bizarre distortions. It seems more likely one or many higher-order visual processing areas are involved in causing these disordered visual perceptions. It could be less likely they are caused by structural organisation of residual healthy cortex as they quickly resolve.

Transformation of normal to distorted in seconds or minutes

Normal neuronal adaptation processes or functional reorganisation could account for bizarre distortions that occur with prolonged viewing of a particular stimulus. The feed-forward and feed-back visual processes as well as an overarching mechanism could be disrupted in higher-order visual areas. It is probably less likely structural reorganisation of neurons could be a unique cause of these bizarre distortions as they are not immediately perceived when viewing the object.

Days, weeks, months or indefinitely after initial cortical insult

In this group, there may be structural organisation of healthy cortex including potential neuronal sprouting or the formation of long-range horizontal connection. However, it would be difficult to create robust neuropsychological experiments as the distortions are disordered. This increases the potential variability in the experimental design for each individual subject as well as between different test subjects. Inferences or conclusions made from the results of such experiments would be more open to criticism due to the many

possible visual cortical areas or processes that could be involved or responsible.

2.5 Conclusion

It is difficult from the literature and clinical cases to correlate the timing of the onset of symptoms with when the lesion of the central visual pathway occurred. In some cases, it is likely that areas of the brain apart from the striate cortex were also injured. When other cortical visual areas apart from the V1 are involved, higher-visual processing is more likely influencing the final visual scene perceived by each case.

From reviewing the literature, it is unclear what potential role or roles cortical structural reorganisation plays in the perception of visual distortion. Many of the published cases have unclear pathophysiology and not only V1 is affected by damage. There are many studies using fMRI to investigate cortical reorganisation after brain-damage. fMRI studies, however, do not or are not able to explore the conditions or rates of celluar structural reorganisation, the properties of the reactivated neurons or the mechanisms for such changes in the brain.

The literature review and clinical cases demonstrate the limitations of determining or proving a cognitive theory from subjective experiences. This is especially true when there is no consensus regarding the definition and use of certain terms such a metamorphopsia or cortical reorganisation. An explanation for human visual consciousness remains elusive. The behavioural experiments created and tested in this thesis attempt to examine the loss of function in patients who have brain-damage in an isolated and specfic region early in the cortical visual processing pathway. To investigate the cortical reorganisation of the neurons surrounding damaged cortex, individuals with lesions of only V1 were tested. Limiting the study to subjects injuries to V1 potentially minimises variabilities from higher-order visual processing. If no structural cortical reorganisation were to occur after the brain injury of V1, one could assume the representation of the retinotopic map would remain unchanged. However, if the surrounding undamaged neurons reorganised and made wider permanent connections, it may be possible to demonstrate a geometric change in the retinotopic map on psychophysical testing.

Chapter 3

Methodology

3.1 Preface

The literature review and clinical cases in chapter 2 do not demonstrate strong evidence of cerebral metamorphopsia being caused by structural reorganisation of the visual cortex and retinotopic remapping. In most reported cases of visual distortions, multiple cortical areas are affected. Multiple lesions of visual cortical areas impede the discovery of general mechanisms of human visual perception. We still haven't understood a single discrete visual cortical area, and the dynamics of the visual system are far from being determined. Without knowledge of what is normal, effective treatment of abnormalities is elusive. Our strategy to distinguish normal and abnormal processes, is to carry out thorough experimentation of single subjects suffering discrete well-documented lesions of their early visual processing areas. These lesions result in deficits that can be investigated through neuropsychological testing. By discovering the true nature of these functional deficits and their causes, deductions can be made towards an explanation for normality.

Whilst reading this thesis, it must be kept in mind that the author's background is in clinical medicine and in particular, ophthalmology. When first embarking into the field of vision science, the author had no prevous exposure or experience. During my master degree, I learnt some basic skills as a vision scientist under the supervision of Gordon T. Plant (GTP). However, a critical and systematic approach to the construction of human visual psychophysical experiments was not yet developed. Reflection on the experiments in the author's master degree strongly influenced the methodology of further investigative experiments that were developed and tested in this thesis.

3.2   Previous neuropsychological experimentation

The choice of equipment used for previous experiments during my master degree was made based on what was available in the visual laboratory. One of my supervisors (GTP), had previously created experiments on this system and tested subjects using the same equipment. Due to time constraints of the project and the lack of availability of equipment, assumptions were made during various stages in the creation of the experiments.

An Apple Power Macintosh 7100/80, operating system B1-7.5 was used for all experiments as well as Macromedia Director version 4.0. The monitor was an Apple 12-inch monitor with Macintosh Colour Display.

Table 3.1 – Specifications of Apple 12-inch monitor with Macintosh Colour Display

Federal Communications Commision (FCC) ID	BCGM1212
Family number	M1212
Resolution	640 x 480 pixels
Horizontal display width	10 inches = 254mm
Vertical display height	7.5 inches = 190mm
Trinitron CRT Display type, aperture grille	
Dots Per Inch (DPI)	69
Pixel pitch	0.26mm
Horizontal scan	35kHz
Vertical scan	66.7kHz

The luminance of this monitor was not measured as there was no photometer available. The luminance for all experiments were suprathreshold so it was considered unnecessary to accurately measure the luminance of the sprites for this pilot experiment.

The timing of the presentation of stimuli was not measured so the accuracy of the display timing or response timing was not measured.

The display coordinates of the monitor pixels are from the top-left corner of the screen. The top-left pixel on the monitor is (1,1). All further pixel coordinates are positive integers from this location. The bottom-right pixel on the monitor is (640, 480).

The test subject did not have a button to press to record their responses. Instead, they would verbally state "up", "down" or "straight". This would then be noted by the observer running the experimental array, pressing a button on the mouse/keyboard to record the response.

The size of visual stimuli and their position in the retinotopic map are expressed in degrees of visual angle (DOVA). DOVA reflects the perceived size of a stimulus. The distance between the stimulus and the observer is important in determining the size of the stimulus that falls on the retina. For example, if a 100 x 100 pixel square is displayed on a monitor, the perceived size of the stimulus when an observer is closer to the monitor will be larger than if the observer is further away. In otherwords, if the number of pixels

used to create the square is not increased, the further away the observer is from the monitor, the smaller the perceived size of the square stimulus.

In visual field testing, the centre of the visual field is generally taken to be the where the subject takes up fixation. This is usually where the fovea in the retina is aligned with the fixation target in normal subjects. Afoveal fixation can exist for some individuals with abnormal pathology of their visual system.

In the following experiments, the point of fixation is defined as coordinates in DOVA x=0, y=0 or (0,0); where" x" are the horizontal and "y" are the vertical coordinates. All further coordinates are relative to this fixation location. If the visual field is divided into quadrants, the axes of each quadrant are as follows:

- Right Upper Quadrant $(+, +)$

- Right Lower Quadrant $(+, -)$

- Left Upper Quadrant $(-, +)$

- Left Lower Quadrant $(-, -)$

Conversion of pixels to DOVA when subject is at a distance of 280mm from the monitor:

- Horizontal 30 pixels = 2.435982546

- Vertical 30 pixels = 2.429590809

- Horizontal 2 DOVA = 24.62950894 pixels, therefore rounded to the nearest integer = 25 pixels

- Vertical 2 DOVA = 24.69432344, therefore rounded to the nearest integer = 25 pixels

Therefore, in my earlier experiments the sprites were closer to 2.5 DOVA. Whenever 2 DOVA is seen in the below description of the pilot test, it should be converted to 2.5 DOVA.

The dimensions of the Apple 12 inch monitor in pixels (640 x 480 pixels), and 255mm width and 190mm height. When using a 30 x 30 pixel square sprite on this monitor:

- Centre of screen = 306, 226

- Left bottom of screen = 0, 450

- Right bottom of screen = 610, 450

- Right top of screen = 610, 0

This is calculated because the location or coordinates of where the sprites are presented is determined by the top-left corner of the sprite.

The following experiment was created as a pilot test to investigate whether visual perception was altered surrounding a scotoma caused by cerebral pathology of V1. The method of adjustment was used to find the most appropriate regions for testing in each subject.

3.2.1   Pilot test: Horizontal alignment of two square sprites across a scotoma

In this experiment, the distance between the edges of the sprite closest to the scotoma were the same, and were replicated in the mirror-image across the vertical meridian.

Each subject was seated directly in front of the monitor with their head fixed in position on a chin and forehead rest. The subject's eyes were placed at the same viewing distance to maintain consistent conversion of pixels to DOVA. The chinrest or the monitor height was adjusted vertically so the subject's eyes were level with the fixation target. Testing was performed binocularly, which does not account for pottential problems with convergence and accommodation. No fixation monitoring or eye tracking was used. The author of this thesis was the only investigator who carried out the testing.

The sprites were all 30 x 30 pixels in size which corresponds to 10mm x 10mm squares on the monitor. The fixation target was a circle, 15 pixels in diametre. The reduced size of the fixation target was chosen as a 30 x 30 pixel fixation target size caused an overlap with the test sprites.

Subjects

Three subjects were tested: POV, a Posterior Cortical Atrophy (PCA) case and a control.

The initials POV were kept according to previous publications and are not transparently related to the subject's name. POV presented in 1991 with a 3-year history of paroxysmal visual field disturbances and a 6-month history of headaches. On neurological examination at presentation, the only significant finding was a right-sided homonymous paracentral scotoma. He had a left sided tentorial meningioma and this was excised via craniotomy. On the fifth post-operative day, visual field testing demonstrated a large right-sided homonymous scotoma. This scotoma has remained substantially unchanged since then. There is sparing along the vertical meridian superiorly and inferiorly within the right visual hemifield, and also a spared crescent in the outer periphery (see Figure 3.1). Post-operative brain MRI revealed a left occipital lobe cavity (see Figures 3.2 and 3.3). There was damage to the left striate cortex above and below the calcarine fissure. An extreme anterior portion of the left striate cortex was spared which corresponds to the preserved crescenteric area in his peripheral right visual hemifield. His left posterior fusiform gyrus (putative V4) was damaged). The left dorsal extrastriate areas (dorsal V2 and V3) were considered to be relatively preserved and the left lateral occipital gyri (including V5) were spared.
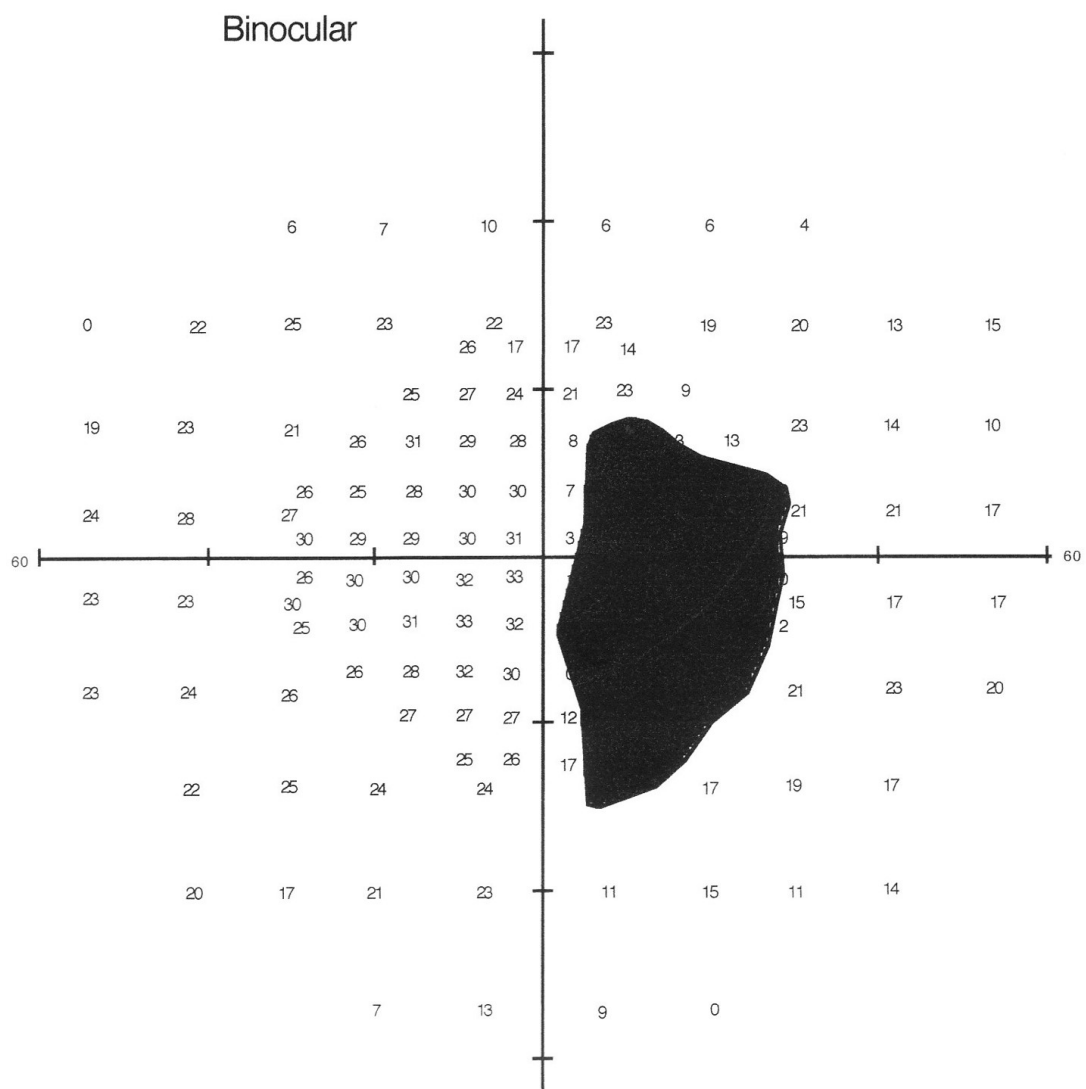
Figure 3.1 – POV Humphrey Visual Field Combined 30-2 and 60-4

Figure 3.2 – POV Coronal T2 Weighted MRI
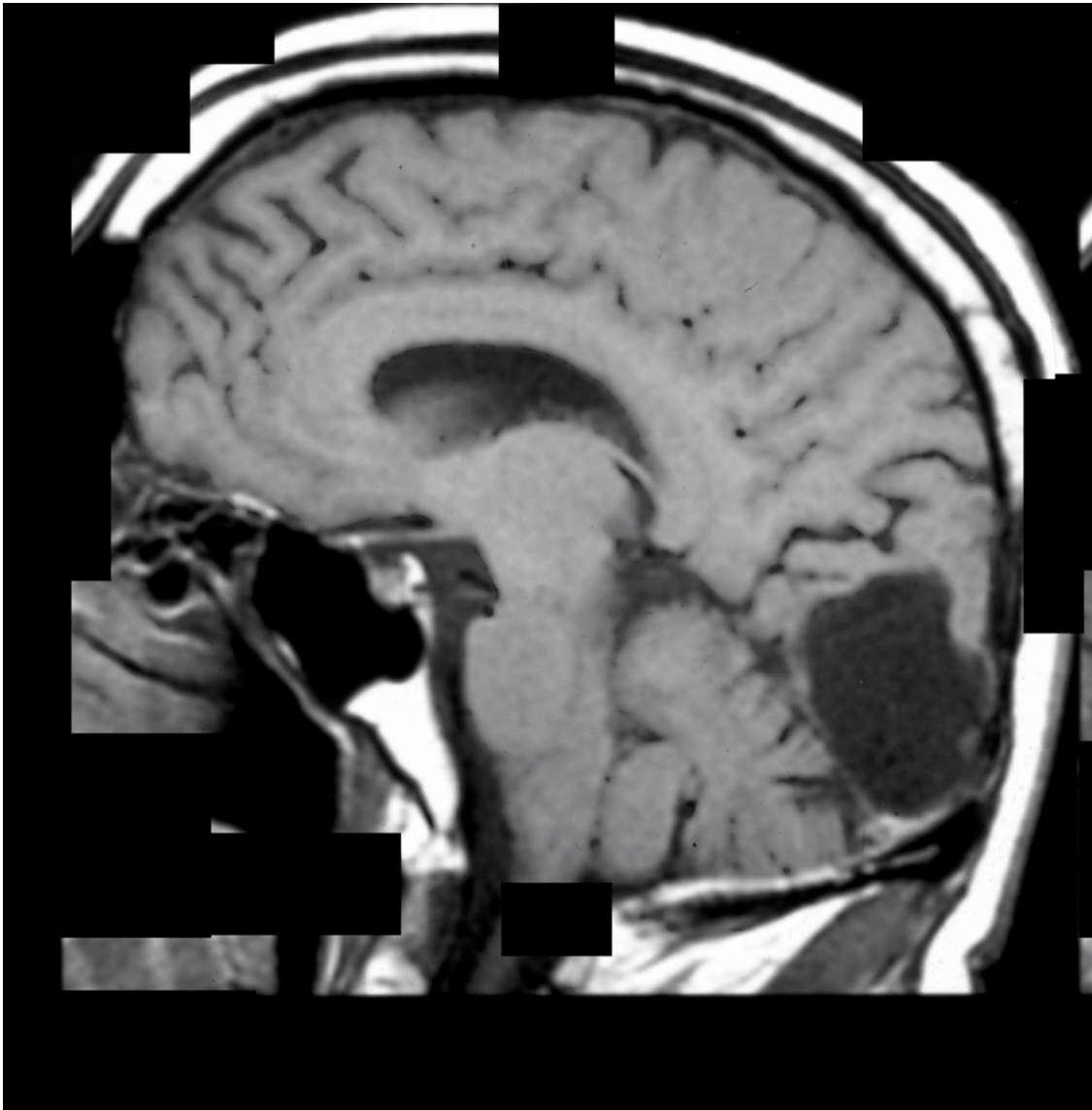
Figure 3.3 – POV Parasagittal T1 weighted MRI

In the immediate post-operative period, POV reported people and objects would "materialize" in their entirety from the right side whilst background scenes were seen as complete. For example, he reported seeing a woman talking to herself and it was only when she had walked further away that a second person came into view on his right side. POV reported that objects were rarely experienced as being occluded by his area of blindness but were either not seen at all (if entirely falling within the scotoma) or were seen as complete. He would misjudge the size of objects and the length of surfaces extending into his blind visual field. The personal reports given by POV and experimental evidence suggest he experiences completes of forms and surfaces.

The PCA subject was 10 years younger than POV and the control subject. She had posterior cortical atrophy which caused visual spatial disorientation. She had no other medical problems and no other visual perception disorders apart from the spatial disorientation.

An age-matched control was the third subject to perform the experiment. She had no ophthalmological or neurological disorders. She had normal visual perception including visual acuity and visual fields. She had no other medical problems.

Details of experiment

POV's scotoma was mapped at 280mm viewing distance to fit the width of the scotoma on the monitor and allow the sprites to be placed (displayed) horizontally on each side of the scotoma. Due to the large vertical dimensions of his scotoma, it was not possible to fit the entire scotoma within the confines of the monitor at the same time. Therefore, the testing area was divided into four quadrants. These four quadrants corresponded to the quadrants of the visual field and were tested separately. The four quadrants are: left-upper, right-upper, left-lower, and right-lower.

During the initial setup of this experiment in the right-upper visual field, POV noted the sprites were not consistently seen as complete squares. Through method of adjustment, the sprites needed to be placed at least 2 DOVA horizontally either side of the scotoma for them to be perceived as complete squares. The sprites also disappeared with prolonged exposure and fixation(Troxler phenomenon [30]). This was presumed to be due to adaptation or due to his filling-in of the scotoma. After the fixation target was presented, the sprites were programmed to display on the monitor and remained on-screen until the subject responded.

The following description relates to testing in the right-upper quadrant of the visual field.

The fixed sprite (Sprite 1) was placed 2 DOVA to the periphery (to the right) of the scotoma edge. The moving sprite (Sprite 2) was placed 2 DOVA to the centre of the visual field (to the left edge of the scotoma). The horizontal distance between the moving and fixed sprites was 28 DOVA. The vertical distance of the fixed sprite from the fixation target was 8 DOVA.

The moving sprite (Sprite 2) was programmed to maintain a fixed horizontal position or "X" coordinate. The vertical position or "Y" coordinate was randomly assigned by the program. The subject was asked to state whether they thought the moving sprite (Sprite 2) was "up, down, or straight" when they compared it horizontally to the fixed sprite (Sprite 1). After each response, a button on the screen was clicked with the mouse to record the response. Also recorded were the vertical and horizontal coordinates of the moving sprite (Sprite 2). A total of 10 responses were recorded for each different vertical position.

The mirror-images of the experiment were then setup for the other three quadrants of the visual field: left-upper, right-lower, and left-lower. The subjects performed the experiments in each quadrant of the visual field as follows: firstly right-upper, then left-upper, right-lower, and finally left-lower.

The moving sprite (Sprite 2) was considered "straight" if it was placed at 8 or 7.2 DOVA. For each of the ten responses, they were assigned a "A" to indicate the subject thought the random moving sprite was up, "B" if down, and "C" if thought to be straight.

The number of vertical positions that were tested was adjusted for each of the three subject tested (POV, PCA and control). If the subject demonstrated consistency in their responses, the starting position of the random moving sprite was adjusted to be closer to the straight position. If there was inconsistency, a wider range of positions was tested.

The total number of vertical positions that could be tested for each subject was limited by the size of the monitor and also by the proximity of the monitor to the subject (viewing distance). The subjects reported difficulty seeing the random moving sprite in the periphery of the monitor. The testing array would be abandoned if the subject voiced difficulty seeing the moving sprite.

The location that the sprite was presented on the screen was defined by the top-left pixel of that sprite. Therefore, the DOVA that are calculated must take this into account. All sprites were presented on a dark background. The background luminance and the luminance of the sprites was not measured as a photometer was unavailable.

Table 3.2 – Pixel coordinates for Horizontal Alignment Experiment

Visual field Quadrant	Left–Upper	Right–Upper	Left–Lower	Right–Lower
Fixation point	(508, 308)	(88, 308)	(530, 100)	(88, 100)
Fixed target	(80, 170)	(500, 170)	(110, 230)	(500, 230)
Moving target x-coord	500	110	530	100

The main data frame `HAlignMaster` for this experiment has a total of 3415 observations, for 3 subjects, and contains the following columns.

The way that this data frame was obtained from the raw data, is explained in the appendix.

Table 3.3 – Main data frame columns for Horizontal Alignment Experiment

Column name	Description
Response	chr "Down" "Up" "Down" "Up" ...
Quadrant	Factor w/ 4 levels "BL","BR","TL",..
Subject	Factor w/ 3 levels "Control","PCA Case",..
Y_{DOVA}	num -12 -5.67 -13.55 -4.05 -15.07 ...

Response histograms for the three subjects.

The response histograms derived from this data are contained in Figures 3.4-3.6.

Statistical tests.

The statistical program used was R [115]. For a given subject, hemifield, and vertical position (value of Y_{DOVA}), one can consider the number of "Up", "Down" and "Straight" responses. For a given vertical position, the response counts form a contingency table when one takes either:

1. A pair of subjects for a given side, or

2. A pair of sides for a given subject.

There are standard statistical tests, such as the chi-square or Fisher's exact test, that can be applied to contingency tables. In the case (1), a rejection of the null hypothesis gives evidence that the two subjects' responses are different for the given hemifield and vertical position. In the case (2), a rejection of the null hypothesis gives evidence that the given individual subject's responses are different for the two hemifields at the given vertical position.

We now provide tables with Fisher p-values comparing left visual hemifield (LVF) and right visual hemifield (RVF) for individual subjects at various vertical positions (Y values), using the R function `LeftRightFisher` described in the Appendix. First for the "Control" subject:

Table 3.4 – Fisher p-values comparing LVF and RVF for Control

Y_{DOVA}	Fisher Test
10.28	p = 0.4921
9.5	p = 0.6247
8.7	p = 0.1885
-8.86	p = 0.2222
-9.65	p = 0.4674
-10.44	p = 1.0000
-11.22	p = 0.5358
-12.0	p = 0.6539

There are no significant differences between the LVF and RVF for Control. However, testing the subject POV:
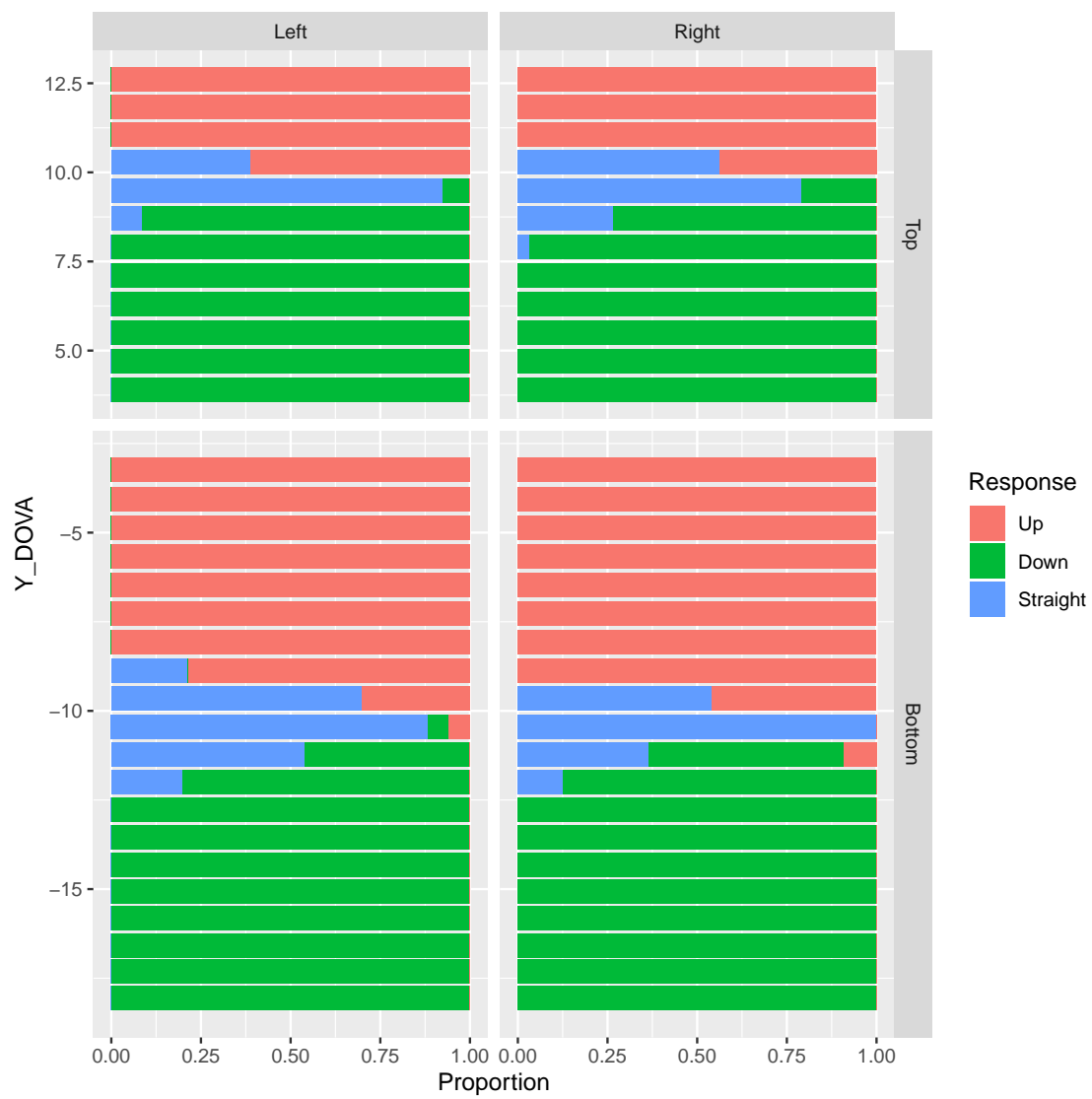
Figure 3.4 – Control Horizontal Alignment Responses
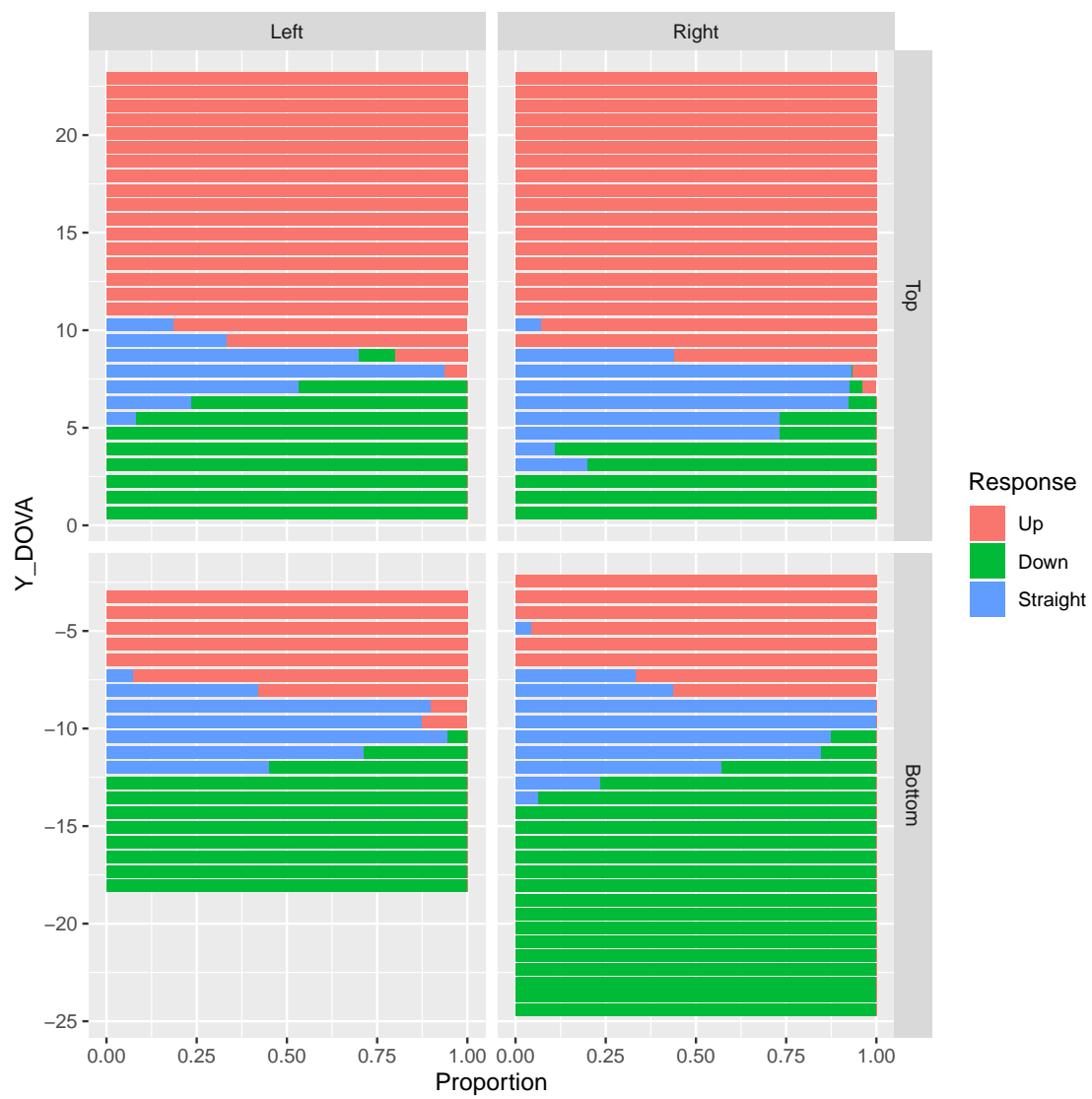
Figure 3.5 – POV Horizontal Alignment Responses
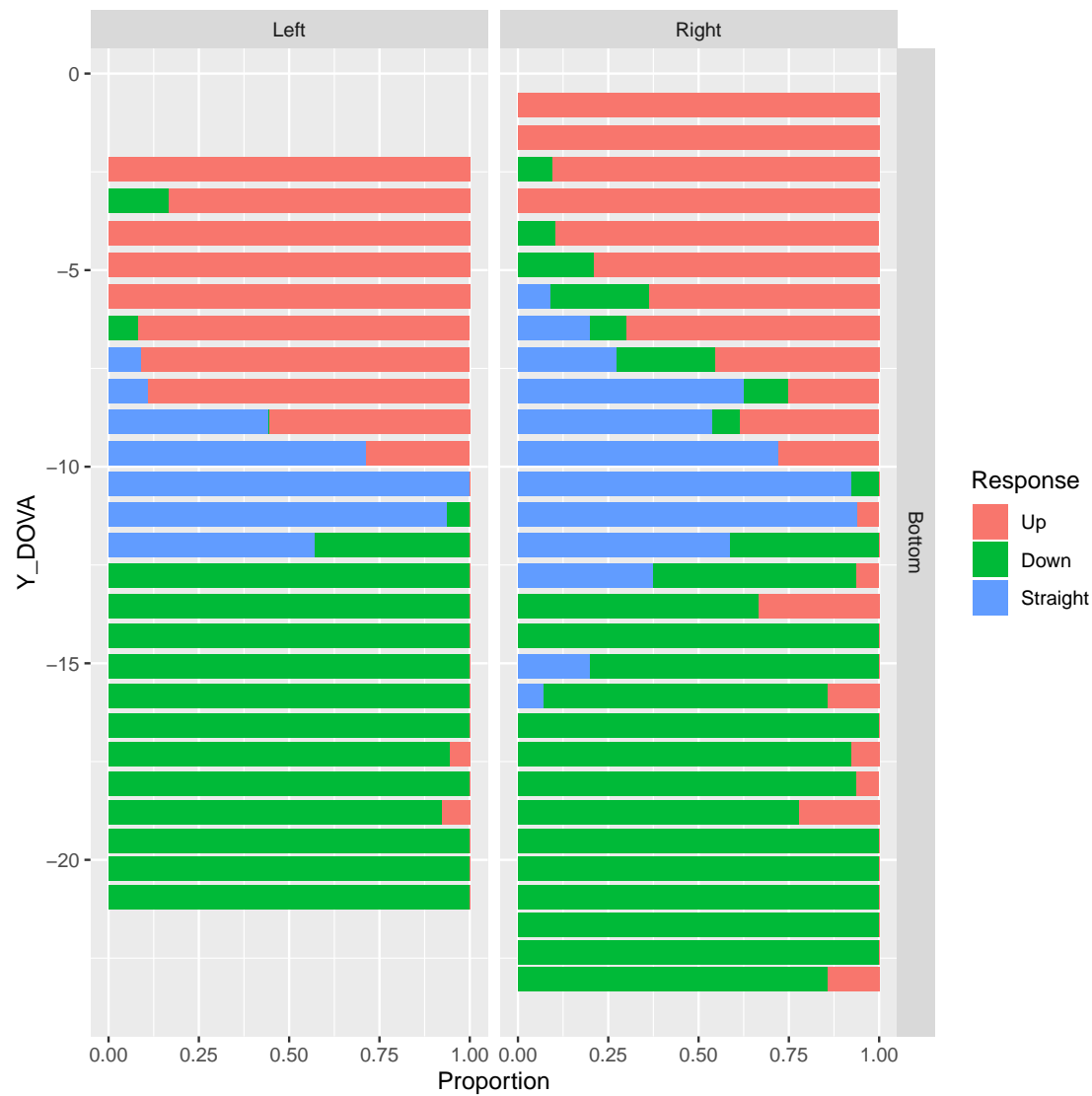
Figure 3.6 – PCA Case Horizontal Alignment Responses

Table 3.5 – Fisher p-values comparing LVF and RVF for POV

Y_{DOVA}	Fisher Test
10.28	p = 0.6015
9.5	p < 0.05
8.7	p = 0.0521
7.11	p < 0.01
6.31	p < 0.001
5.51	p < 0.01
4.7	p < 0.0001
3.89	p = 0.2176
3.08	p = 0.4737
-7.27	p = 0.0772
-8.86	p = 0.4895
-9.65	p = 0.2139
-10.44	p = 0.5909
-11.22	p = 0.6483
-12.0	p = 0.5377
-12.78	p < 0.05
-13.55	p = 0.3902

one finds a few heights at which significant differences between left and right hemifields do occur, and in particular for Y_{DOVA} between 4.7 and 9.5. Similarly, for the PCA subject, one has a couple of locations at which significant differences occur, although to a much lesser extent than for POV.

Table 3.6 – Fisher p-values comparing LVF and RVF for PCA

Y_{DOVA}	Fisher Test
-2.43	p = 0.5000
-3.24	p = 0.2400
-4.05	p = 0.4920
-4.86	p = 0.1050
-5.67	p < 0.05
-6.47	p = 0.4286
-7.27	p = 0.0817
-8.07	p < 0.01
-8.86	p = 0.8050
-11.22	p = 1.0000
-12.78	p = 0.0532
-13.55	p = 0.1038
-15.07	p = 0.1500
-15.83	p = 0.4831
-18.79	p = 0.5442

Next we produce tables with Fisher p-values comparing responses by a subject POV or PCA to those for control, at the same vertical locations in the LVF or RVF. The results show that for each subject and each side, there are vertical locations at which statistically significant differences arise between each subject and control. First the comparison of POV and Control on the left hemifield:

and then on the right hemifield.

Finally, we present the PCA subject vs Control comparisons on the left hemifield and on the right hemifield

Table 3.7 – **Fisher p-values comparing subjects POV and Control on the left hemifield**

Y_{DOVA}	Fisher Test
10.28	p = 0.2701
9.5	p < 0.001
8.7	p < 0.0001
7.91	p < 0.00001
7.11	p < 0.01
6.31	p = 0.1075
5.51	p = 0.4138
-7.27	p = 0.5216
-8.07	p < 0.01
-8.86	p < 0.0001
-9.65	p = 0.3402
-10.44	p = 0.7351
-11.22	p = 0.4401
-12.0	p = 0.1629

Table 3.8 – **Fisher p-values comparing subjects POV and Control on the right hemifield**

Y_{DOVA}	Fisher Test
10.28	p < 0.01
9.5	p < 0.00001
8.7	p < 0.00001
7.91	p < 0.00001
7.11	p < 0.00001
6.31	p < 0.00001
5.51	p < 0.00001
4.7	p < 0.00001
3.89	p = 0.2176
-7.27	p < 0.05
-8.07	p < 0.001
-8.86	p < 0.00001
-9.65	p < 0.001
-10.44	p = 0.4877
-11.22	p < 0.05
-12.0	p < 0.01
-12.78	p = 0.1026
-13.55	p = 0.4706

respectively.

Table 3.9 – **Fisher p-values comparing subjects PCA and Control on the left hemifield**

Y_{DOVA}	Fisher Test
-6.47	p = 0.3243
-7.27	p = 0.4074
-8.07	p = 0.3103
-8.86	p = 0.3630
-11.22	p < 0.05
-12.0	p = 0.0604

Table 3.10 – **Fisher p-values comparing subjects PCA and Control on the right hemifield**

Y_{DOVA}	Fisher Test
-4.05	p = 0.5195
-4.86	p = 0.1192
-5.67	p < 0.05
-6.47	p < 0.05
-7.27	p < 0.01
-8.07	p < 0.00001
-8.86	p < 0.01
-9.65	p = 0.3382
-11.22	p < 0.001
-12.0	p < 0.05
-12.78	p < 0.01
-13.55	p < 0.05
-15.07	p = 0.1630
-15.83	p = 0.0608
-18.06	p = 0.4706

3.2.2   Limitations of Horizontal Alignment Experiment

Testing was performed binocularly allowing potential accommodation and overlapping of the central visual fields of each eye. The monitor was 280mm from the observer, therefore, accommodation could have occurred. As shown above, an assumption of the size of the sprites being 2 DOVA was inaccurate by approximately 0.5 DOVA. By testing across the hemifield and with a control subject, the absolute size of the test sprites became irrelevant when it came to statistical testing.

3.3   Apparatus for novel neuropsychological experiments

3.3.1   Hardware

Due to the delays in acquiring the hardware for the laboratory set up, an "Intel NUC Kit D54250WYK" was required to begin initial testing. Experimental testing was started with the acknowledgement the monitor would need to be measured or calibrated again with a photometer once the final apparatus was set up. The

intended visual psychophysics experiments were all suprathreshold and were not timed. It is important to note at this stage that if the experiments were temporally, contrast or spectrometrically critical, the entire set up would have to be recalibrated and measured to ensure accuracy. Every apparatus should be tested for accuracy unless the equipment has been has been provided by a company that has specifically tested and calibrated it. Even then, rigorously testing the accuracy of the company's measurements is advisable to ensure the performance of the equipment in experimental conditions.

The Intel NUC Kit D54250WYK specifications are available at this website: https://ark.intel.com/content/www/us/en/ark/products/76977/intel-nuc-kit-d54250wyk.html The graphics card used for this configuration was "Intel (R) HD Graphics 5000".

The final experiments were performed using a "Dell Precision Tower 3420 XCTO BASE" with the "Windows 7 Professional 64bit" operating system and "6th Gen Intel® Core™ i5-6600 (Quad Core 3.3GHz, 3.9Ghz Turbo, 6MB, w/ HD Graphics 530)" processor. The graphics card was "AMD FirePro W4100 2GB (4 DP) Low Profile". This final apparatus enabled the ultra high definition capabilites of the NEC monitor. This allowed double the refresh rate both horizontally and vertically, see table 3.11.

3.3.2 Choice of display

Early vision scientist used a physical black screen and handheld visual stimuli. Technology and the use of computer graphics to present stimuli has been developed.

Traditionally, psychophysical and physiological studies of vision have used cathode ray tube (CRT) monitors to present stimuli. CRTs were considered the gold-standard for stimulus presentation in vision research. Manufacturers of CRT monitors have decreased their production of CRTs as liquid crystal display (LCD) and light emitting diode (LED) technology has improved. Researchers have begun to use LCD monitors as replacements for CRTs. OLED monitors are not being used for psychophysical and physiological testing at this stage as the technology is still being developed and there has not been much data comparing OLED against CRT or LCD monitors.

One of the most important differences between LCD and CRT monitors is LCD monitors present images continuously (hold type) whereas CRT monitors present images in a flash style (impulse type).

Flash type displays have the disadvantage that the onset of the flash may affect electrophysiological recordings. For flash type displays, the luminance of a stimulus remains relatively constant across display frames. For continuous display monitors, the luminance gradually changes across the inital frames.

Simulating flash display monitors with LCDs is possible by adding a blank frame after each frame to force the display to return to black. This method has been named "mimicked CRT" by Wang and Nikolic

[116]. The limitation of this approach is only half the refresh rate capacity can be obtained. For example, this "mimicked CRT" method can only display stimuli at 60 Hz if an LCD monitor has a maximal refresh rate of 120 Hz.

Liquid Crystal Display (LCD)

LCD monitors can be expensive when used in vision research. They also have limitations of slow refresh rates, which can result in motion blur when presenting moving stimuli. As more research is being performed using LCD monitors, there are more studies investigating the temporal and spatial characteristics of LCD monitors. One study suggests a consumer-grade LCD monitor could meet all the technical demands in vision research [117].

The advantages of LCD are: the high availablity in the consumer market, increased energy efficiency compared to CRTs, compact size and the ability to show no or little visual flicker.

The disadvantages of consumer LCD monitors are: they can be slow to respond which could produce motion blur, and they are unable to reach the same black levels of CRTs due to backlight leaking.

Organic Light-Emitting Diode Display (OLED)

These screens are capable of displaying deep black levels and a higher contrast ratio than LCD. They are thinner and lighter than LCD monitors. They could possibly be a high-quality replacement of CRT monitors, however, they are very costly and rare in the consumer market.

Display chosen for the appartus

NEC DISPLAY SpectraView® Reference 322UHD, Model SVRef322, Serial number 590501073TW (IPS Type TFT with W-LED backlight; screen size 31.5 inches; screen aspect ratio 16:9; pixel pitch 0.18mm; brightness 350cd/m^2; contrast ratio 1000:1; viewing angle 176 horizontal / 176 vertical degrees; response time 10ms (grey-to-grey), 24ms (12 white / black; 12 black / white); colours 1.074 billion (10-bit per colour); colour gamut size / coverage:101% / 99.2% Adobe RGB). This monitor has a synchronisation rate of 31.5-134kHz horizontal frequency and 24-120Hz vertical frequency. Optimum resolution is 3840 x 2160 at 60 Hz.

Calibration of NEC monitor

A photometer was used to measure detector-based luminance (cd/m^2). It was the commercially available Luminance Meter LMT L 1009 (manufacturer LMT Lichtmesstechnik GmbH, Berlin) which had the following specifications: selectable angular fields 3°, 1°, 20', 6'; display range 0.0001 cd/m2 (last digit) to 19 990 000

Table 3.11 – NEC monitor settings

Brightness	160cd/m²
ECO mode	OFF
Black	Min
Left/Right	50.0%
Down/Up	50.0%
Expansion	Aspect
Sharpness	0
UHD Upscaling	Off
RGB 1 Adobe RGB White 6500K	
Adjust	Hue
Red	0
Yellow	0
Green	0
Cyan	0
Blue	0
Magenta	0
Display Port (for both Intel NUC & Dell apparatus)	3840 x 2160
Intel NUC horizontal refresh rate 65.6kHz	Intel NUC vertical refresh rate 29.9Hz
Dell horizontal refresh rate 133.3Hz	Dell Vertical refresh rate 60.0Hz

cd/m2, measuring distance approx. 0.50 m to infinity; photometer head with Si-photoelement, fine V(λ)-approximation.

1. **Set up of photometer for measurements**. The photometer was secured on a tripod 1 metre from the LCD monitor. The LCD monitor was turned on and left for more than 30 minutes until the black readings stabilised. The LCD monitor settings were as for table 3.11 The angular field on the photometer was set to 3 degrees Psychtoolbox was used to create the following program to manually adjust the pixels in MATLAB

2. **Gamma curves from photometer measurements**. See Figures 3.7 - 3.10.

3. **Uniformity of monitor luminance**. Tested at [1024 1024 1024], 1 degree, handheld at 1 metre, a single measurements was made at each location on two separate days.

Day 1

137.9	170.5	134.3
152.4	170.7 (centre)	139.1
149.2	172.4	139.9

Day 2

131,3	168.3	137.4
140.3	171.6 (centre)	153.1
143.5	166.3	134.5
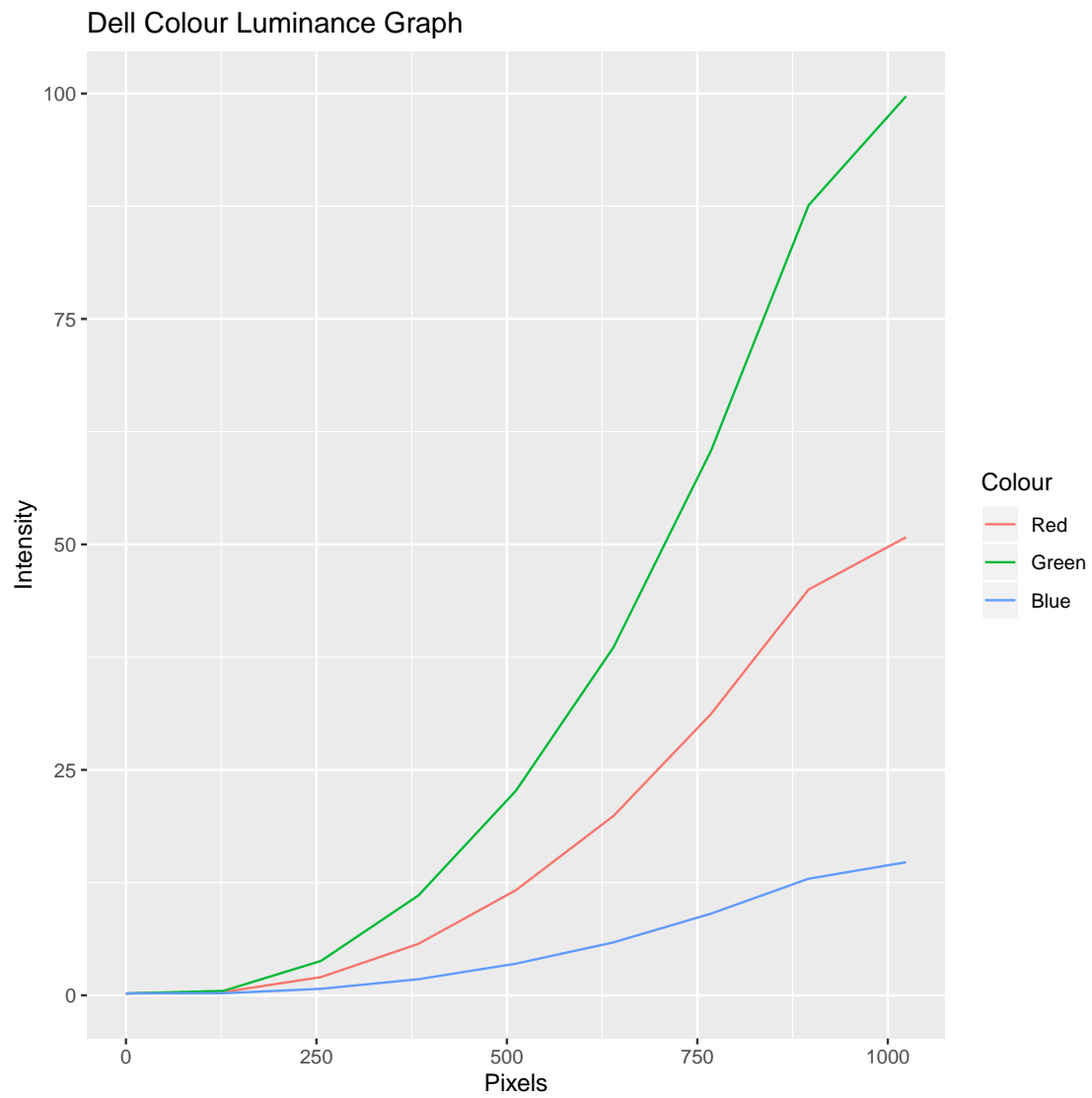
Figure 3.7 – Dell RGB Plot
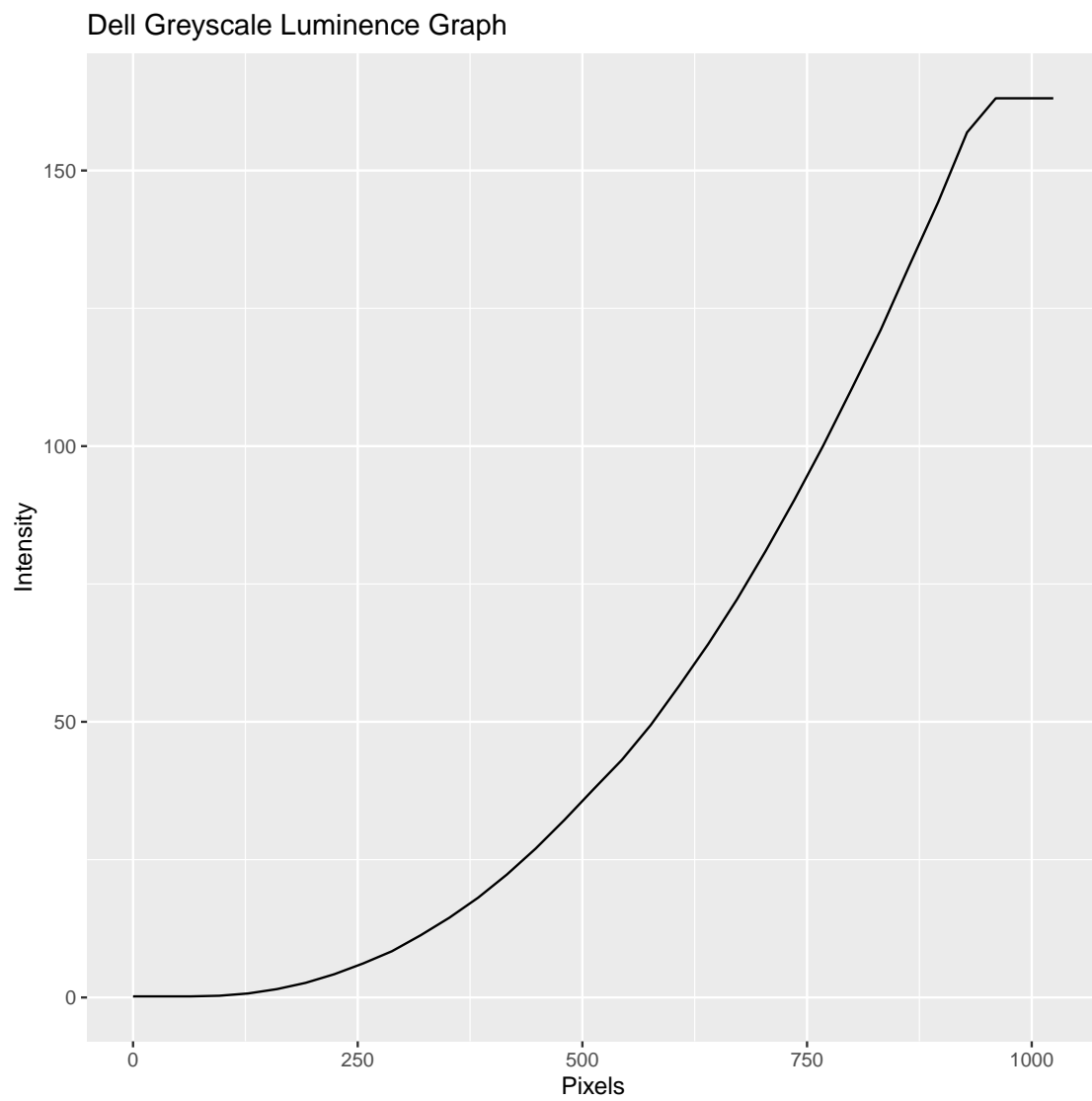
Figure 3.8 – Dell Grey Scale Plot
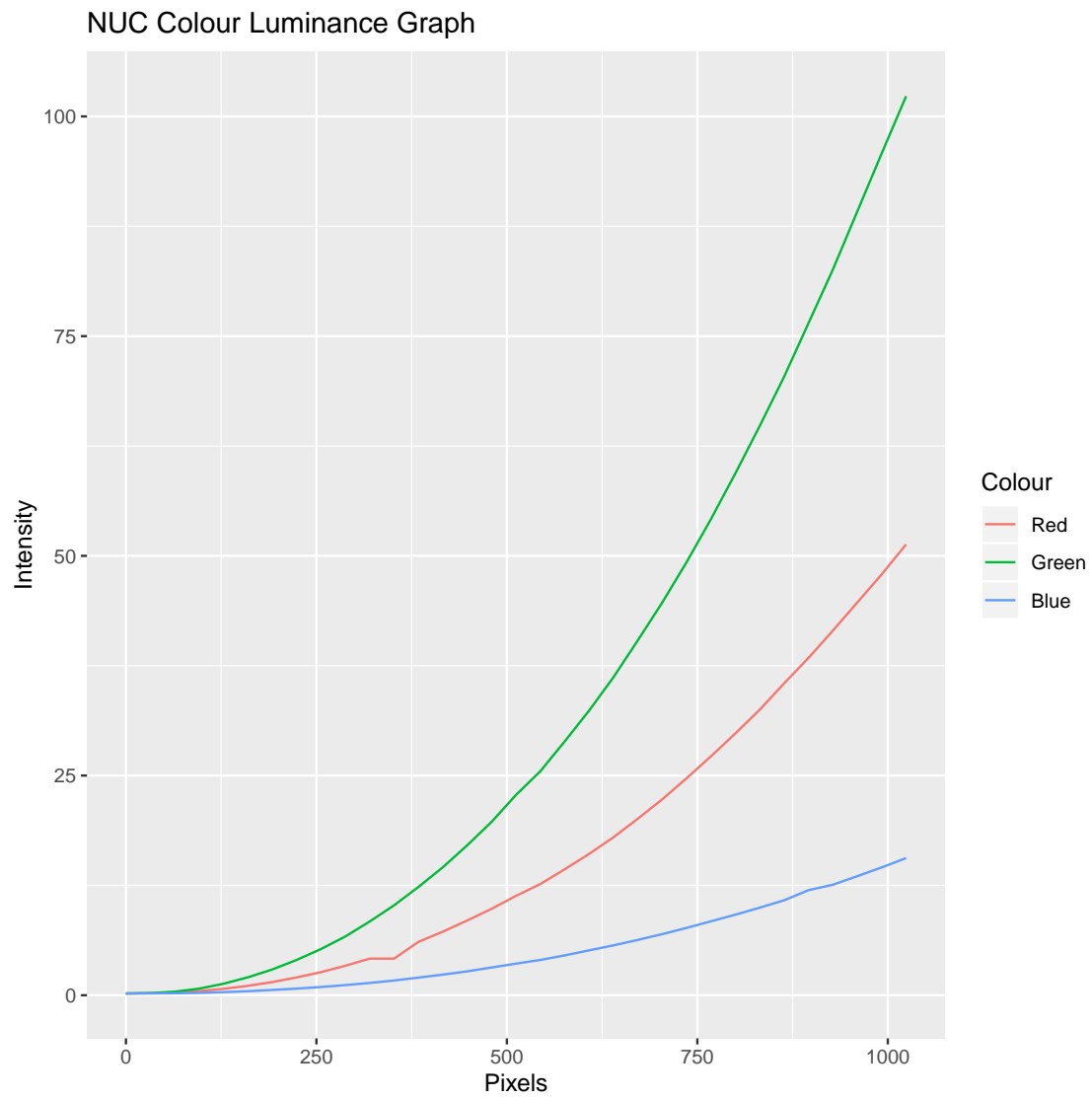
Figure 3.9 – **NUC RGB Plot**
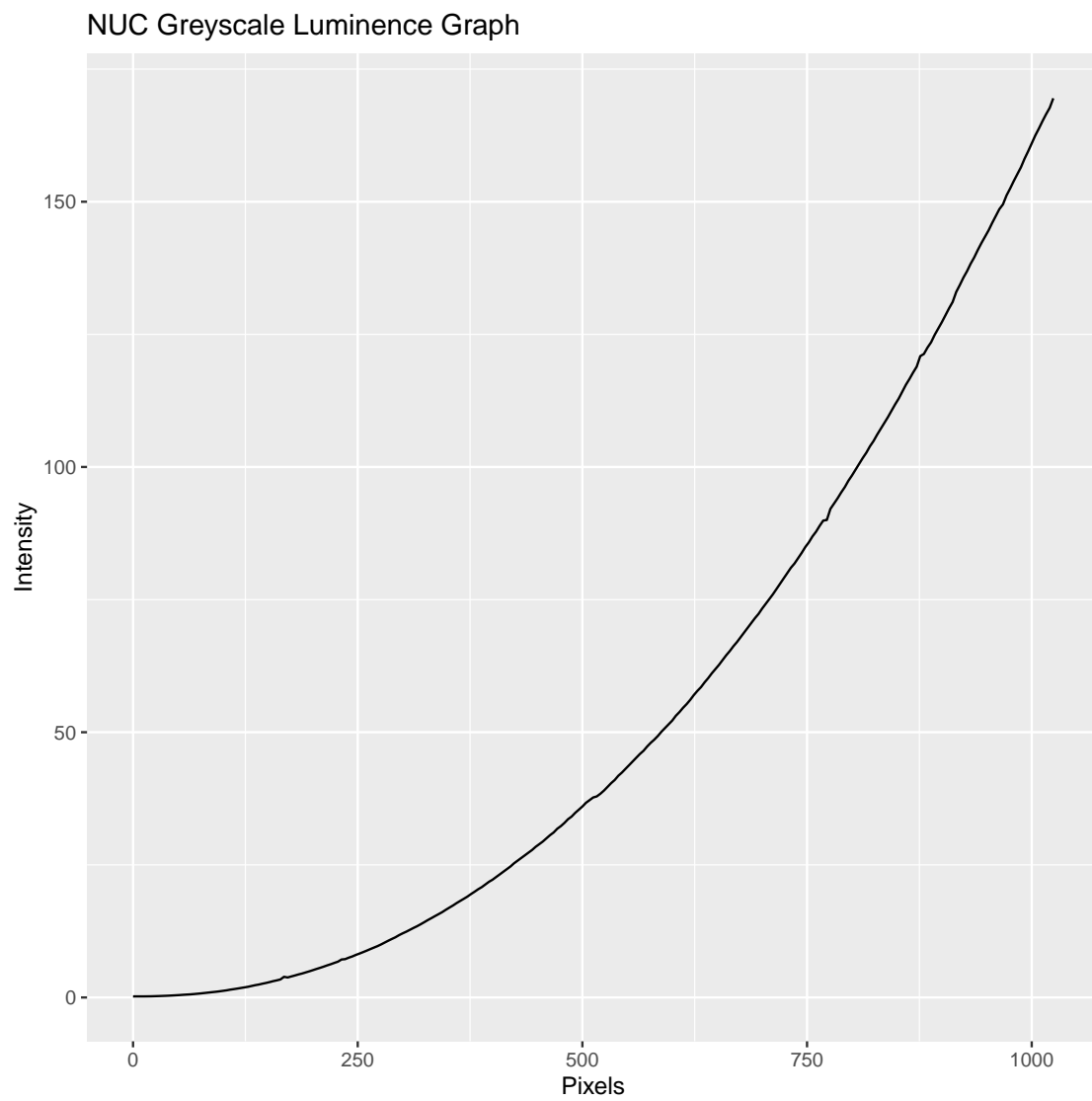
Figure 3.10 – NUC Grey Scale Plot

This demonstrates the variability of the monitor from the centre to the edges which is a limitation of LCD monitors. The luminance is greatest at the centre and decreases at the edges. This is important to recognise when luminance is being tested as threshold. For our experimentation, all stimuli were presented suprathreshold. Therefore, knowing what the exact luminance of the sprites presented at the edges of the screen should not change the percept.

3.3.3   Head mount

This was a chin and head rest from a slit-lamp setup.

3.4   Methodology of neuropsychological experiments investigating visual distortion

The author of this thesis was the only investigator who ran each experimental testing session. The experiments only test within each anatomical quadrant of the visual field. This is to minimise the likelihood of higher visual processing areas from influencing the results. If there are higher visual order processes occuring with visual perception, then one could assume these processes are equal as the stimuli are contained within this location of the the striate cortex. There is no crossing of stimuli beyond the calcarine sulcus nor the occipital hemispheres. However, the test stimuli are against the vertical meridian so there could be some cross over if the subjects eye is not maintaining fixation. Testing was performed monocularly to ensure no vergence eye movements. Vergence eye movements could cause an overlap of the homonymous scotoma to alter. The left temporal visual field was tested by covering the right eye using a standard occlusive eye patch, the right temporal visual field was tested by covering the left eye.

3.4.1   Subjects

Investigating visual perception in humans currently demands a conscious, co-operative, and intelligent subject. This subject must also express their experiences accurately and without bias. Visual psychophysical testing is subjective and not objective. There is currently no structural way or objective way to confirm what the subject experiences. The subject must be reliable for analysis of the collected data to proceed with reasonable confidence.

The investigations were performed on subjects who had homonymous paracentral scotomas. Despite their scotomas, these subjects are still able to fixate centrally or foveally. This prevents possible perceptual bias and instability induced by eccentric fixation. The proximity of the visual field defect to fixation allows the

analysis of scotoma-induced perceptual visual distortion. Patients were recruited if they had brain injuries affecting an occipital lobe. They were excluded if they had any other retinal or cortical pathology. After explanation of the nature and possible consequences of the study, the subjects gave their informed consent in accordance with the Declaration of Helsinki for research with human subjects.

1. POV Details of this subject are under the pilot experiment, see section 3.2.1.

2. DSS A 34-year-old right-handed man suffered a presumed vertebral artery dissection after a training session of Brazilian Jui Jitsu. He was initially incorrectly diagnosed with migraine after arriving via ambulance at the accident and emergency department of a London hospital in the United Kingdom. Initially, he had a CT brain which did not reveal any abnormality. He had a left paracentral homonymous scotoma which did not behave like a migrainous visual aura as it did not resolve spontaneously. On further investigation with MRI brain, he was diagnosed with a right V1 infarction caused by a presumed vertebral artery dissection. Fortunately, his homonymous paracentral scotoma improved with time and it did not impair his ability to read. He is not aware of his residual scotoma and fills-in the missing visual information.

Table 3.12 – Neuropsychological Testing

Test		POV	Comment	DSS	Comment
Age on test date		56		35	
WAIS-R	Verbal IQ	100	Average	116	High Average
	Performance IQ	117	Above Average	123	Superior
	Ravens Matrices	8/12 ss14	Above Average	-	-
Memory Tests	FCW	12	Above Average	14	Superior
	FCF	13	Above Average	7	Low Average
	Camden A	30/30	Above Average	26/30	Average
	Camden B	28/30	Above Average	-	-
	Famous Faces	12/12	Above Average	-	-
	AMIPB Visual Design			95% immediate and delayed recall	Superior
McKenna Graded Naming Test		28/30	Above Average	-	-
Baxter Spelling Test		23/30	Good	-	-
Jackson Arithmetic		7/24	Below Average	14/24	Good Average
Visual Acuity CORVIST	Shape Discrimination	-	-	8/8	
	Size Discrimination	-	-	2/2	
	Shape Detection	-	-	8/8	
	Hue Discrimination	-	-	4/4	

Continued from previous page					
Test		POV	Comment	DSS	Comment
	Form Perception	-	-	8/8	
Visual Acuity	Ffooks symbols	6/12	Good	6/9	
	TNO	120 degrees	Excellent		
Form Perception	Efron Squares	B2 20/20, B 20/20	Excellent		
	Shape Detection	20/20	Excellent		
Object Perception (VOSP)	Fragmented Letters	19/20	Excellent	20/20	
	Object Decision	19/20	Excellent	18/20	
	Silhouettes	26/30	Excellent	25/30	
	Progressive Silhouettes	14	Excellent		
Spatial Perception (VOSP)	Dot Counting	10/10	Excellent	10/10	
	Dot Centre	17/20	Good		
	Position Discrimination			20/20	
	Number Location			10/10	
	Cube Analysis			10/10	
Unilateral Neglect Tests	Cancellation	-	Excellent		
	Line Bisection Task	-	Mild displacement		
	Drawing - from memory	-	Excellent		
	Drawing - copying task	-	Excellent		
	Balloon Test	-	-	Right 9/10 Left 10/10	

WAIS-R = Wechsler Abbreviated Scale of Intelligence - Revised [118] VOSP = Visual Object and Spatial Recognition battery [114]

An age-matched control for DSS was also tested. This subject had no ocular, neurological or general medical history. They had a normal ophthalmic examination and visual field test.

3.4.2   MATLAB programming

Psychophysics Toolbox (PTB)

PTB was used to create the sprites and behavioural experiments within MATLAB [119]. PTB was chosen as it is an open-source resource which is extensively used in vision and neuroscience research.

Validating the sprite size in degrees of visual angle

MATLAB code was used to display the sprite in term of degrees of visual angle (DOVA). DOVA was calculated given the fixed distance of the subject from the tangent screen in millimeters, fixed dimensions of screen both height and width in millmetres, number of pixels in the screen both horizontally and vertically. The sprite displayed by the code was checked by manual measurements with a ruler to ensure the DOVA was correctly displayed by the program. The sprite dimensions were measure by hand with a ruler for several different distances from the tangent screeen for a fixed DOVA sprite size. The size of the sprite was also hand measured for different DOVA sprite sizes at a fixed distance from the tangent screen.

The following is the MATLAB expression that was used to calculate the number of pixels equivalent to one degree of visual angle:

```
oneDegPixels = 2*viewDistance*tan(pi*(1/180/2)).*[xMaxPixels yMaxPixels]./[xSize ySize];
```

where viewDistance is the manual measurement in millimetres of the subjects' eyes from the monitor, xMax-Pixels and yMaxPixels refer to the dimensions of the screen in pixels, and xSize and ySize refer to the dimensions of the screen in millimetres.

The above equation calculates the DOVA at the origin or centre or fixation or coordinates (0,0). DOVA was not adjusted for the tangent screen. Brightness of the sprite was not increased as it was displayed further into the peripheral vision as the luminance of each sprite was suprathreshold.

Head tilt

Two vertical bars presented before each run of experiments to ensure the subject's head is not tilted. The subject has to state the bars are straight before proceeding with the tests.

3.4.3 Response collection

Keyboard input was used to collect the subject's responses to visually displayed stimuli. They were asked to press different keys to indicate their responses. A computer keyboard was chosen as they are inexpensive, did not require any special hardware setup or programming. They also work with any computer hardware, operating system and standard software toolkit. To decrease the potential confusion or accidental pressing of other keys, the unused keys were removed from the keyboard. The keyboard used was a standard wired USB connection for the subject. The alternative would have been a button box or response box. There are certain advantages of a button box. Firstly, the buttons or interface is simpler and more ergonomic than a keyboard as there are fewer keys. Having fewer keys or buttons is useful in testing children or older

adults. Secondly, they can be designed to operate in special circumstances such as from the computer or in environments such as MRI machines. Thirdly, most button boxes have mechanisms to increase the accuracy of timing responses in relation to the presentation of the stimulus or from inputs of other devices.

Response times and accuracy define the speed-accuracy trade-off. This is a performance point in a trade-off between speed and accuracy. Response time is defined as the time elapsed between stimulus or task onset and a subject's response. There are possible substantial variations and biases in the measurements of response times using a computer keyhoard or mouse. More specialised button boxes must be used to obtain more accurate measurements. Regular keyboards or mice are designed for everyday use and are the result of low cost manufacturing. The sources of timing error in registering a keyboard or mouse response can add up to delays and uncertainties of between 20 and 70 ms.

3.4.4   Eye tracking

A formal eye tracker was not available due to funding and access restrictions.

3.4.5   Checking the accuracy of display timing

This was not performed due to the inavailability of equipment.

3.4.6   Randomisation of tests

The test runs were randomised to prevent subject learning and bias. Test points were specified in an array and randomised in the MATLAB code.

3.5   Experiment 1: Scotoma Mapping

The purpose of this experiment was to plot the scotoma, and define the area of testing in the visual field to ensure the stimulus square sprites are perceived as complete whilst using the new experimental apparatus. The aim is to investigate and map the size of the scotoma. This allows us to find a testing area for each subject where the stimuli will be presented. During this experiment, we are checking that the potential test stimuli are perceived as complete. For example, the test squares are perceived as a complete square and not as a rectangle or a diamond. All stimuli were presented at suprathreshold luminance. The subject fixates on a fixation target, then square stimuli of a suprathreshold luminence are presented on the monitor. The test stimulus is on the monitor until the subject responds. The subject has a USB keyboard and 3 responses are recorded: "Yes", the square is complete, "No" there is no square seen, and "Maybe" in which case the subject

is unsure whether a complete square is seen. A comparison between the two subjects POV and DSS would ideally be created. However, DSS's scotoma is much closer to fixation in the upper-hemifield whereas for POV, the opposite is demonstrated. POV's scotoma was closer to fixation in the lower hemifield. This led to creating the Aspect experiment in the upper hemifield for POV and lower hemifield for DSS.

3.6 Experiment 2: Visual distortion

The purpose of this experiment was to create a staircase behavioural test to investigate the perception of horizontal alignment across the scotoma. It was based on the pilot experiment, see section 3.2.1. This experiment was not successfully executed with the subjects. The subject was able to guess what response was correct which defeated the purpose of testing. This test was aborted and the Aspect experiment was created.

3.7 Experiment 3: Aspect

The purpose of this experiment was to investigate the acceptance of perceptual sizes considered to be the same sprite size horizontally across the scotoma. For each test demanding a single response, there are two sprites presented. The reference sprite is more centrally located in the visual field at a fixed distance from the test sprite. Both the reference and test sprites were constrained to a particular x-coordinate for each quadrant. During repetition of each test, the y-coordinates are varied, though constrained to be the same for the test and reference sprites. The size of the test sprite is varied, and the subject is asked whether they see the sprites as being the same size or different. A "same" response is recorded with a "1", and a "different" response as a "0". For each choice of x, y and test sprite size, the subject is asked to respond 10 times. These 10 test runs are occur in a randomised order so that from one instance the test to the next, both the reference and test sprites are changing their vertical location and the test sprite sizes are varying.

3.8 Experiment 4: Location

The purpose of this experiment was to investigate the accuracy of spatial orientation in each subject. A visual mask was used between displaying the two separate stimuli. The aim of this experiment is to investigate whether the subject had consistent spatial localisation. Testing occurred in the part of the visual field where they were able to see sprites (as determined by the scotoma mapping experiment). For example, if a sprite was presented in an area of their visual field and then a subsequent sprite was displayed on the same or

different location, how certain were they about whether the location of the first stimulus was the same as the second. As in the Scotoma Mapping exeeriment, the possible responses were "yes", "no" or "maybe".

3.9   Experiment 5: Filling-In

This experiment was created as a result of subjective observations POV made during Location experiment testing. It was created to investigate whether plasticity exists in the extrastriate cortex or higher visual processing areas when they are no longer receiving input from the striate cortex. This new experiment kept the basics of the Location program. The background luminance was changed to 50% of the maximum limit of the NEC monitor which was 100cd/m2. The luminance of the test sprites was set to 100cd/m2 +/- 50cd/m2. The stimulus size was kept the same as the Location experiment. However, the duration between the presentation of the first and second stimuli was varied. A visual mask was used between displaying the two separate stimuli.

3.10   Conclusion

Psychophysical testing of subjects has a heavy time burden. Experiments created from first priciples require an extensive design phase as well as initial testing phase. There are many hurdles encountered with psychophysical experimentation. Some novel experiments are destined to fail and be abandoned.

Chapter 4

Results

4.1 Preface

Damage to the striate cortex causes scotomas of the corresponding retinotopic map. The details of what happens to the surrounding healthy cortex is unknown. It is possible the remaining functional neurons reorganise structually leading to retinotopic remapping. Extensive psychophysical testing in subjects with small discrete lesions of V1 might reveal abnormal visual processing. The experiments in this thesis were designed to investigate whether there is any evidence of abnormal spatial visual perception surrounding homonymous paracentral scotomas. If visual perception is indeed different to normal, it could begin a journey into defining the general mechanisms governing the human visual system. Progress in this field has so far been slow given the heavy time burden in developing psychophysical experiments and recruiting appropriate subjects. Data demonstrating no spatial distortion could still be considered useful to guide future investigations into cortical plasticty. Evidence of abnormal spatial distortion after V1 damage could invigorate curiousity and encourage further research into the processes involved.

4.2 Experiment 1: Scotoma Mapping

The scotoma mapping experiment was not performed on the DSS age-matched control subject, as he had normal Humphrey visual field tests for both eyes. He did not have any ocular or neurological pathology.

The statistical program used was R [115]. The data is read in as 2 data frames `POVScoMapData` and `DSSScoMapData`, one for each subject. The following table gives the counts of the number of observations in each quadrant for each sprite size in DOVA.

We will plot the results for sprite sizes 2 and 3 DOVA for DSS, and all the data for POV. For DSS, all

Table 4.1 – Number of scotoma mapping observations

Subject	SpriteSize (DOVA)	Upper-Left	Upper-Right	Lower-Left	Lower-Right
POV	2.5	1364	1519	0	0
POV	5	192	552	192	336
DSS	0	99	99	0	0
DSS	2	60	0	0	0
DSS	3	1745	1746	13	0
DSS	4	13	0	0	0
DSS	6	0	0	13	0

the data (except for some columns which will not be used below) for sprite sizes 4 and 6 DOVA is given in Table 4.2. DSS's response counts when the sprite size is 0 (no sprite is presented) are given in Table 4.3, and indicates subject reliability.

Table 4.2 – All scotoma mapping data for sprite sizes 4 and 6 DOVA

FixationX	FixationY	VariableXDOVA	VariableYDOVA	SpriteSize	ResponseType
3276	2100	-29.5	2.5	4	0
3276	2100	-32.5	2.5	4	0
3276	2100	-35.5	2.5	4	2
3276	2100	-38.5	2.5	4	2
3276	2100	-41.5	2.5	4	2
3276	2100	-44.5	2.5	4	2
3276	2100	-47.5	2.5	4	2
3276	2100	-50.5	2.5	4	2
3276	2100	-53.5	2.5	4	2
3276	2100	-56.5	2.5	4	2
3276	2100	-59.5	2.5	4	2
3276	2100	-62.5	2.5	4	2
3276	2100	-65.5	2.5	4	2
3276	60	-29.5	-2.5	6	0
3276	60	-32.5	-5.5	6	0
3276	60	-35.5	-8.5	6	2
3276	60	-38.5	-11.5	6	2
3276	60	-41.5	-14.5	6	2
3276	60	-44.5	-17.5	6	2
3276	60	-47.5	-20.5	6	2
3276	60	-50.5	-23.5	6	2
3276	60	-53.5	-26.5	6	2
3276	60	-56.5	-29.5	6	2
3276	60	-59.5	-32.5	6	0
3276	60	-62.5	-35.5	6	0
3276	60	-65.5	-38.5	6	0

For a given subject and sprite size, the plots produced from the above code are scatter plots with box-shaped points and colours indicating the response. Each point was tested several times, and a number between 0 and 1 is computed as an average of the responses. For example, an average of 1 indicates the subject saw the sprite on all occasions and an average of 0 indicates the subject did not see the sprite on any occasion. For the purposes of this averaging of response types, the "Maybe" response contributions are

Table 4.3 – DSS response counts for sprite size 0 (reliability test)

Response	Count
Yes	0
No	194
Maybe	4

registered as 0.5. In the plots, the overall average for that particular test point is converted to a colour, with 1 mapped to yellow and 0 to black. The average is a number between 0 and 1 with the colour reflecting a mixture of these extremes.

The plots for DSS are given in Figures 4.1 and 4.2, and those for POV in Figures 4.3 and 4.4.

There was extra data for DSS which was split into left and right eye data sets. These are read into R, and plots are generated for sprite size 3 DOVA. The table of response counts for sprite size 0 DOVA, is as follows:

Table 4.4 – DSS response counts for sprite size 0 – extra data

Response	Count
Yes	2
No	71
Maybe	7

The plots of this extra data are given in Figures 4.5 and 4.6.

Residual vision inside POV's right-hemifield scotoma is noted for suprathreshold luminance stimuli. There are areas or instances where he has responded yes/maybe within his scotoma. This has been noted previously in other tests POV has performed and in a published research paper [120].
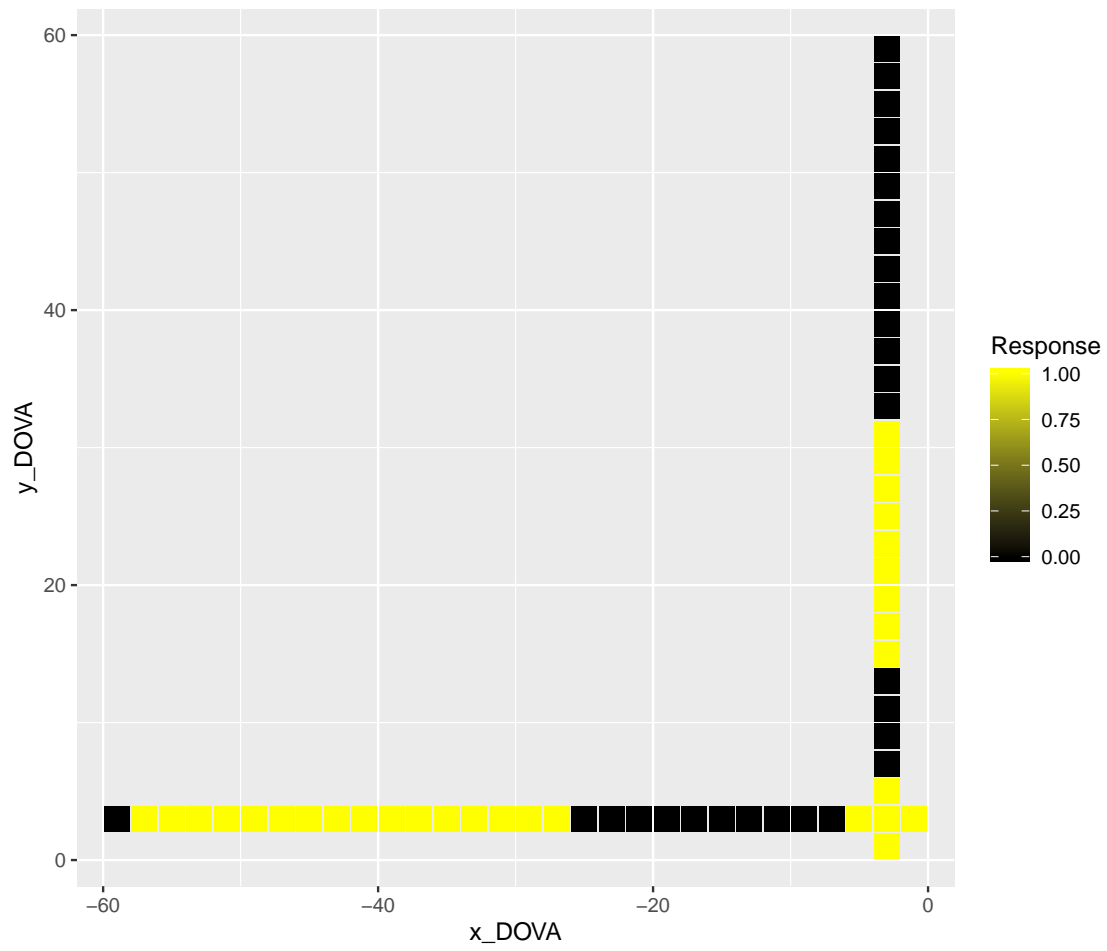
Figure 4.1 – DSS, Sprite Size = 2
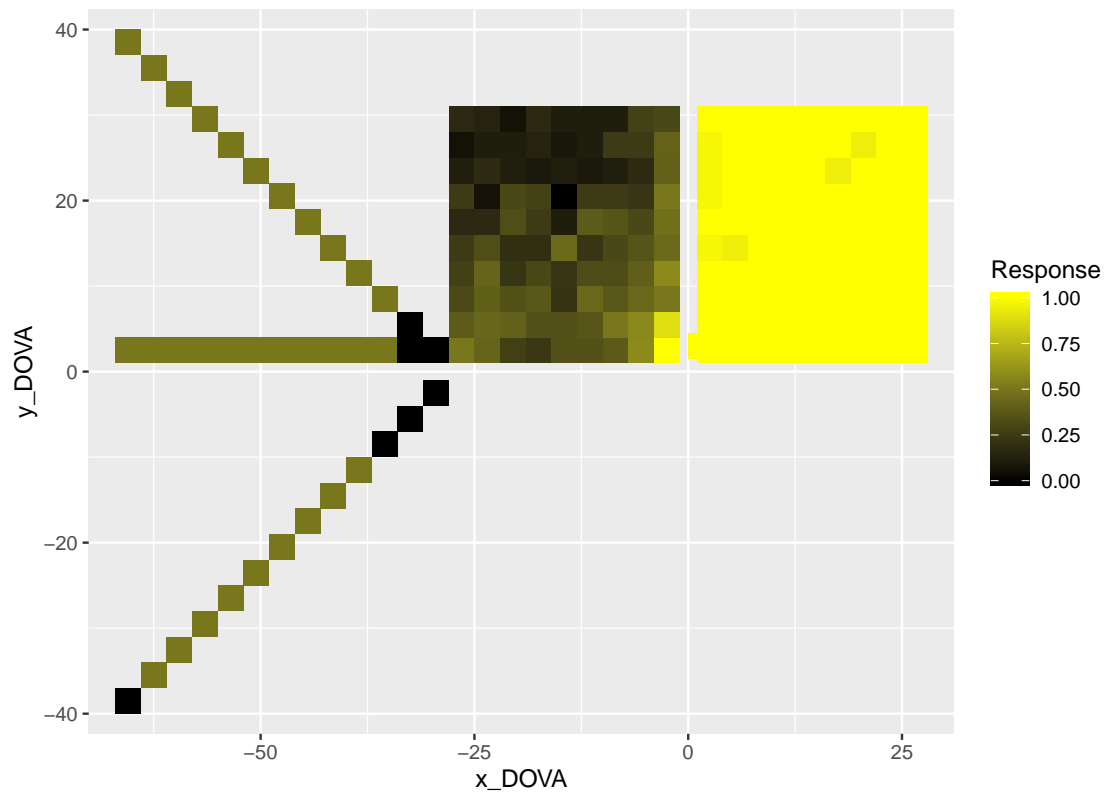
Figure 4.2 – DSS, Sprite Size = 3
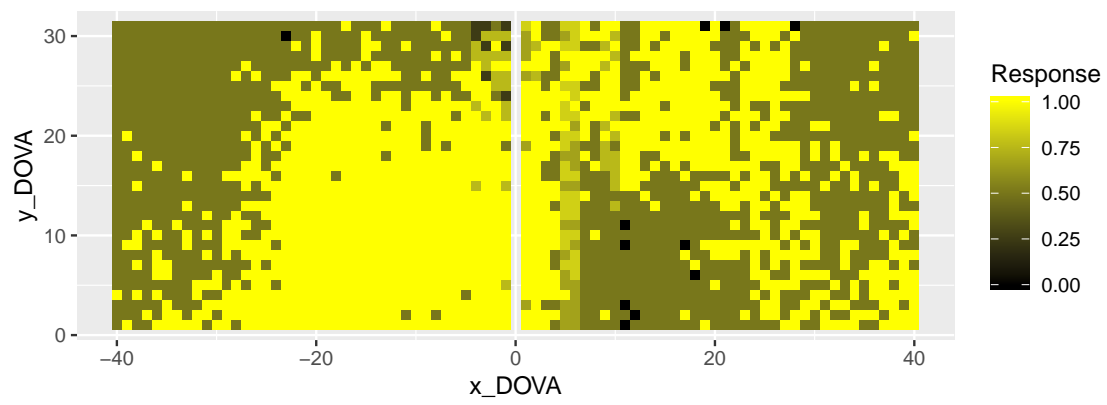
Figure 4.3 – POV, Sprite Size = 2.5
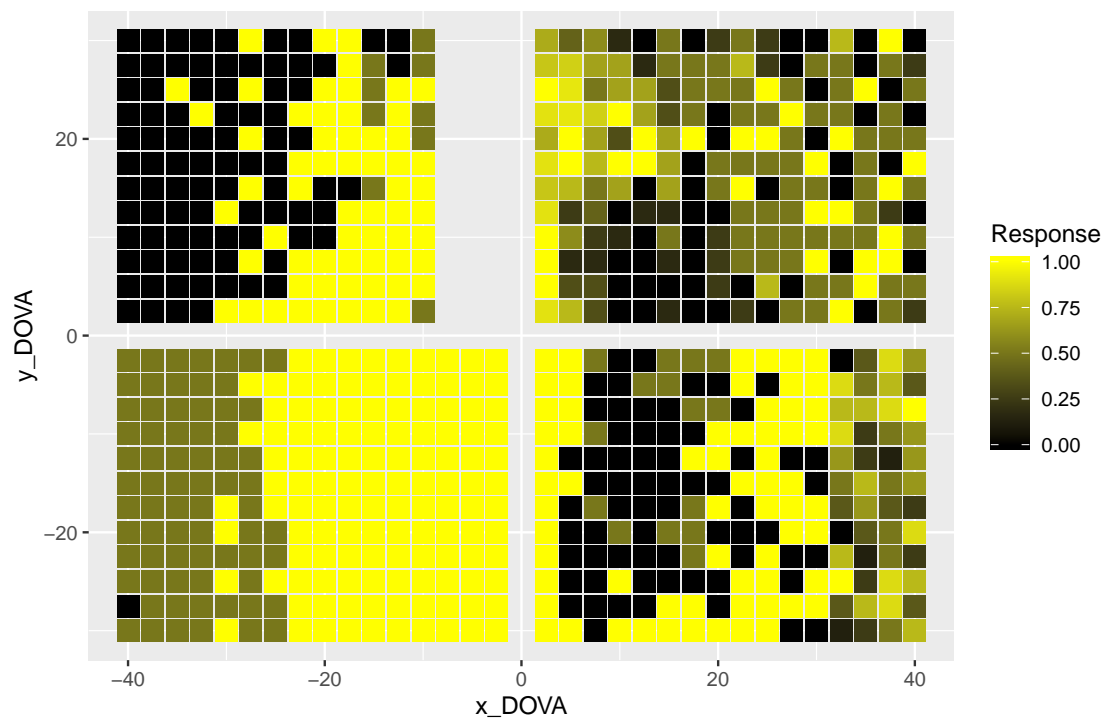
Figure 4.4 – POV, Sprite Size = 5
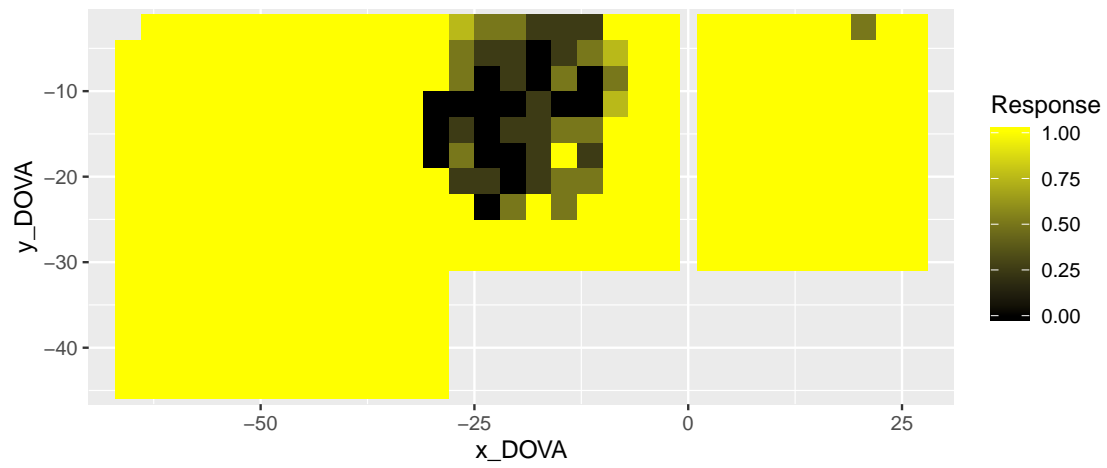
Figure 4.5 – DSS, extra data, left eye, sprite size = 3
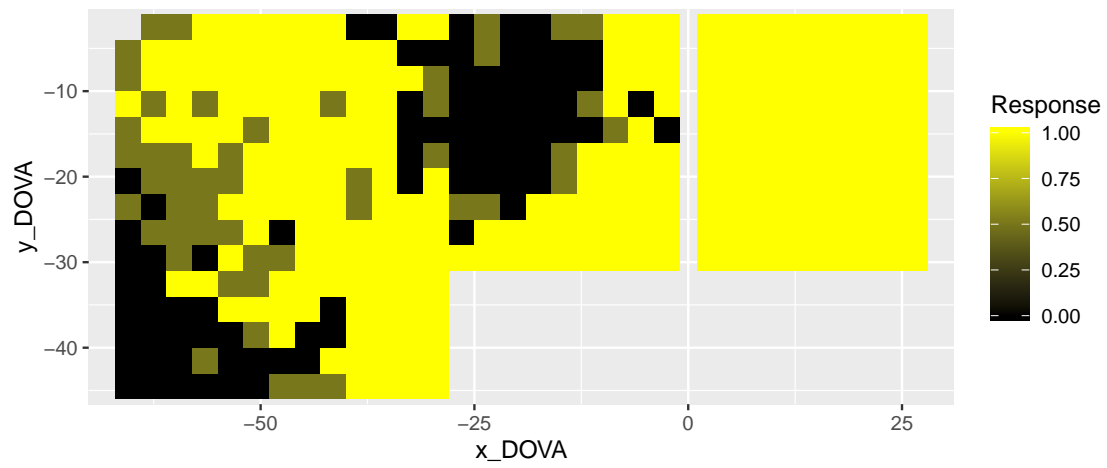
Figure 4.6 – DSS, extra data, right eye, sprite size = 3

4.3   Experiment 2: Visual distortion

This experiment was aborted as the subjects POV and DSS were able to predict or learn the correct response during each run. It was not possible to recreate this experiment to account for this bias. This led to the creation and development of the Aspect experiment.

4.4   Experiment 3: Aspect

4.4.1   Data

All sprite sizes are measured in DOVA **at the origin**. In these terms, all fixed square sprites are of 3 DOVA side-lengths, and the variable sprites are squares whose sizes vary between 1.5 and 7 DOVA in 0.5 DOVA increments. As explained below, as these square sprites are displayed peripherally from fixation, they are perceived as rectangles once they are projected onto the retina. The reduction in x and y side-lengths are functions of how displaced from fixation the sprites are displayed in the x and y directions. As explained in Appendix A.2.4, the true side-lengths and areas of the sprites have been calculated, and added to the data for further analysis.

The 3 Aspect data frames `POVAspData`, `DSSAspData` and `ControlAspData` have the following columns:

Table 4.5 – Columns for the Aspect data frames

Column name	Description
FixationX	x-coordinate of fixation point
FixationY	y-coordinate of fixation point
ReferenceXDOVA	x-coordinate of reference sprite
ReferenceYDOVA	y-coordinate of reference sprite
VariableXDOVA	x-coordinate of variable sprite
VariableYDOVA	y-coordinate of variable sprite
isTestHorizontalT	0 or 1, not needed
ReferenceSpriteSize	size of the reference sprite
VariableSpriteSize	size of the variable sprite
ResponseType	0 = "different", 1 = "same"

and they have the following numbers of observations in each quadrant and in total:

Table 4.6 – Number of observations for the Aspect experiment

Data frame	Upper-Left	Upper-Right	Lower-Left	Lower-Right	Total
POVAspData	2158	2278	18	0	4454
DSSAspData	0	0	1836	1872	3708
ControlAspData	1080	1080	1080	1080	4320

The data frame `AspectMaster`, which results from amalgamating these into one master data frame and adding columns for DOVA corrections, has 12464 observations of 18 variables. In particular the variable

`DiffAreas` gives a true measure of the difference between sprite sizes, obtained by taking the differences of the square roots of the true areas of the variable and reference sprites. Square roots were used here, because this leads to a distribution of observations in line with what was intended in the experiments. The meaning of different values of `DiffAreas` is described in Table 4.7.

Table 4.7 – Meaning of the Aspect DOVA-adjustment variable `DiffAreas`

Value of `DiffAreas`	Meaning
greater than 0	variable sprite is bigger than the reference sprite
less than 0	variable sprite is smaller than the reference sprite
(close to being) equal to 0	variable and reference sprites are the same size

Note that there are locations and sizes in which the variable sprite is bigger in one direction (ie in the x or y-direction) and smaller in the other. This is a defect of the experiment methodology, which could be overcome by making DOVA adjustments in the experiment itself, rather than in the analysis as we have performed here.

4.4.2 Coloured scatter plots

In the coloured scatter plots, for each sprite size, each point that was tested is marked with a square dot. The colour of this square dot has been designated on a sliding scale from black to yellow. Pure black indicates that for all trials at that point for the given sprite size, the subject indicated that the reference and test sprites were different sizes. Pure yellow indicates that on all trials the sprites were thought to be the same size. The colour is on a sliding scale, so for instance, a colour mixture of three-quarters black and one-quarter yellow indicates that at the point and for the given test sprite size, on three-quarters of the trials the subject indicated that the test and reference sprites were different sizes. Each plot contains a range of DOVA-adjusted relative sprite sizes and locations for each subject: POV, DSS and Control. Note that Control is age-matched for DSS, but not for POV – there is at least a 40 year difference between POV and Control.

Using these DOVA-adjusted relative sprite sizes as measured by `DiffAreas` (the difference between the areas of the fixed and variable sprites), introduces an added complication. Since `DiffAreas` is a continuous variable, for these plots we need to decide how to divide its range of values into intervals. That is, we needed to decide what the width of these intervals should be. After some analytical trial and error, it was felt that interval width of 0.45 was optimal, in that the distribution of observations among different intervals was the most evenly spread.

Figures 4.7-4.11 compare the subject DSS with his age-matched control for the various sprite and location ranges. Figures 4.12-4.16 do the same for the subject POV.
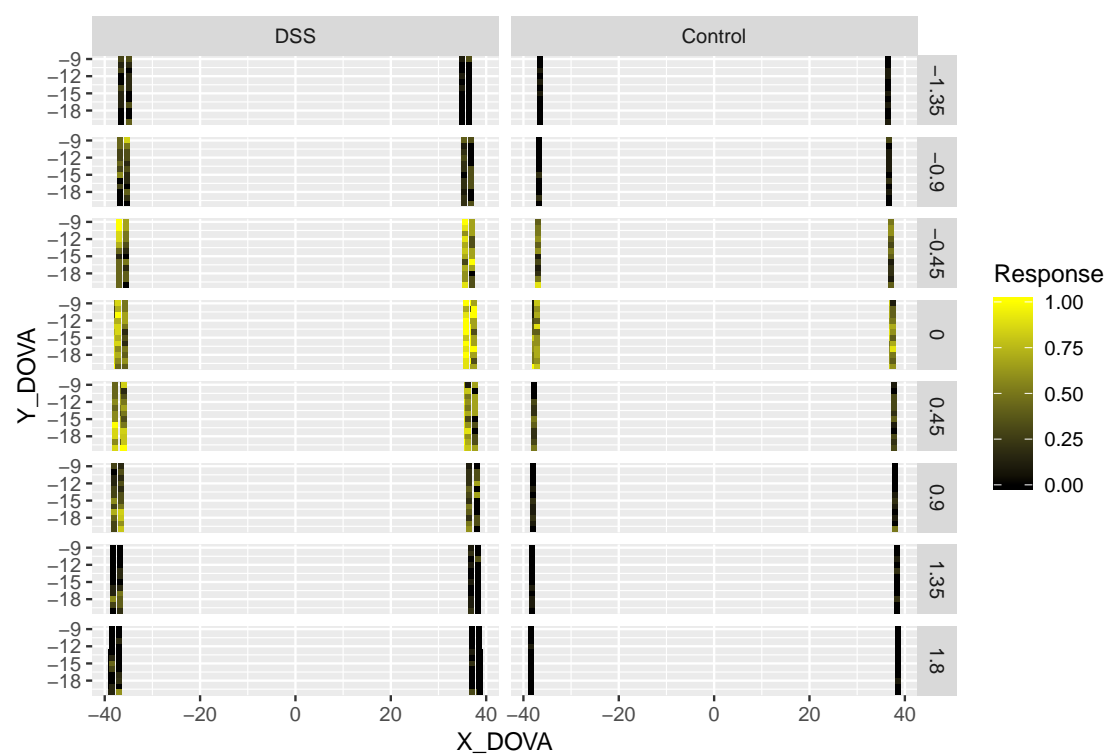
Figure 4.7 – **Aspect coloured scatter plot: DSS vs Control – All comparable data**
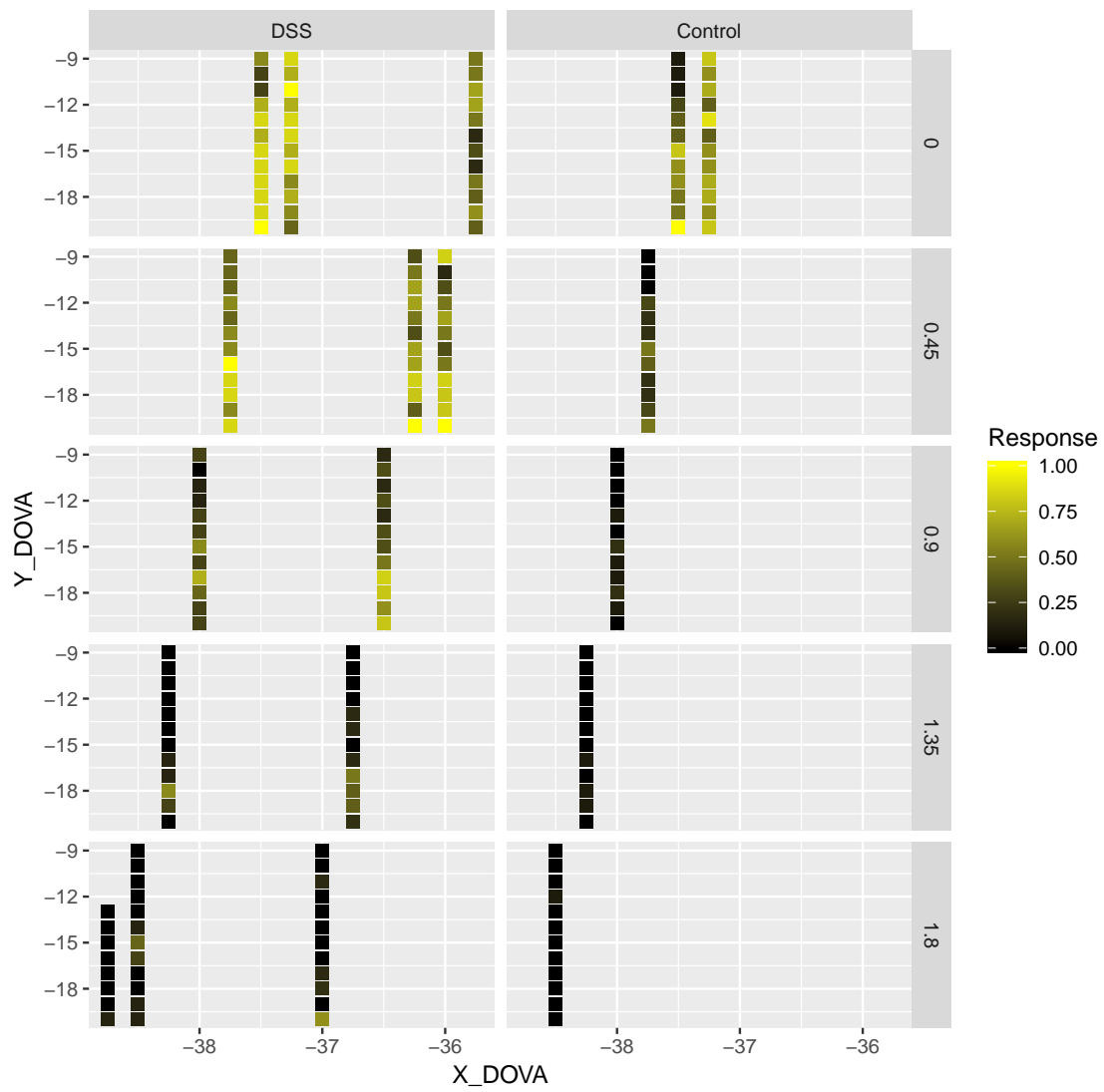
Figure 4.8 – Aspect coloured scatter plot: DSS vs Control – LVF big sprites
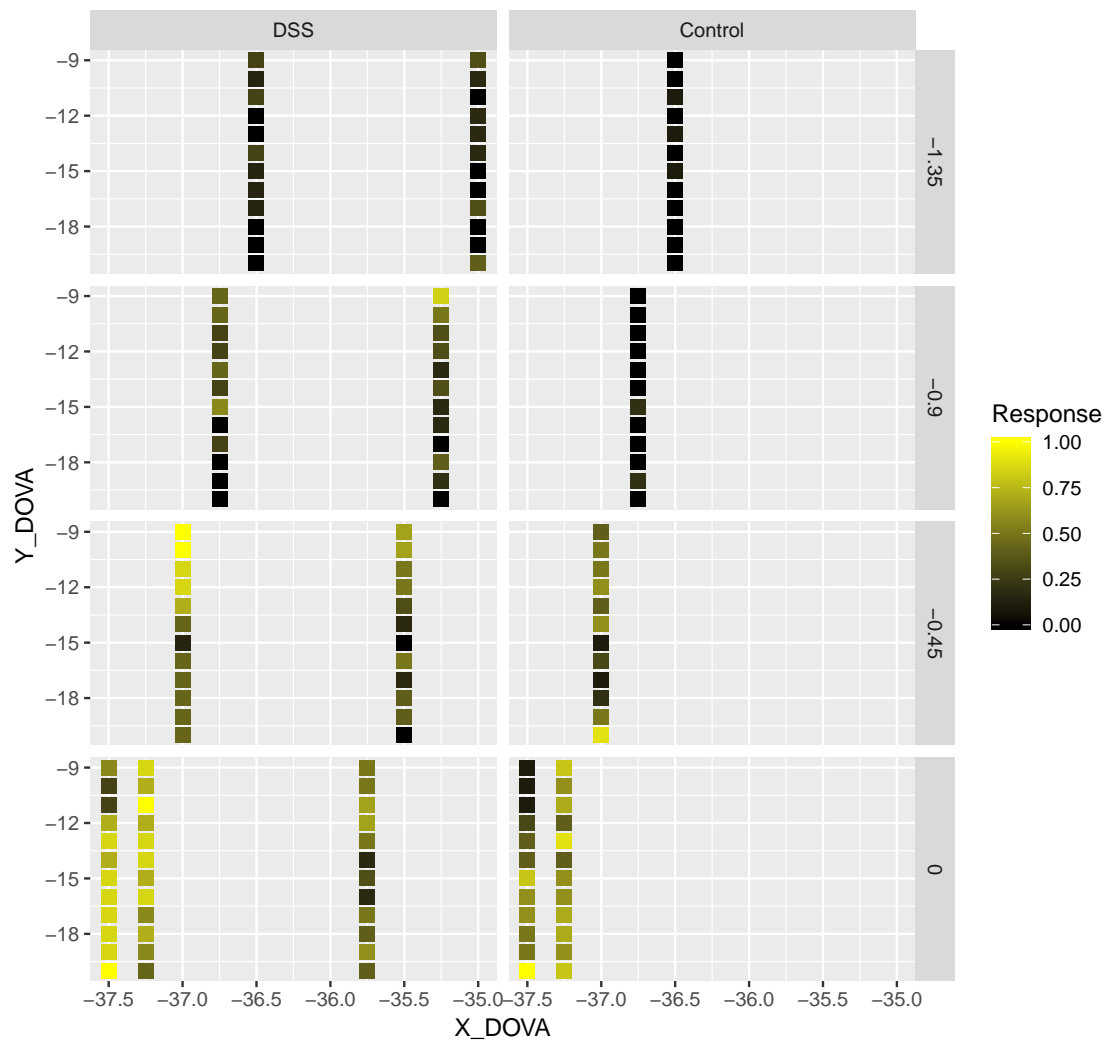
Figure 4.9 – Aspect coloured scatter plot: DSS vs Control – LVF small sprites
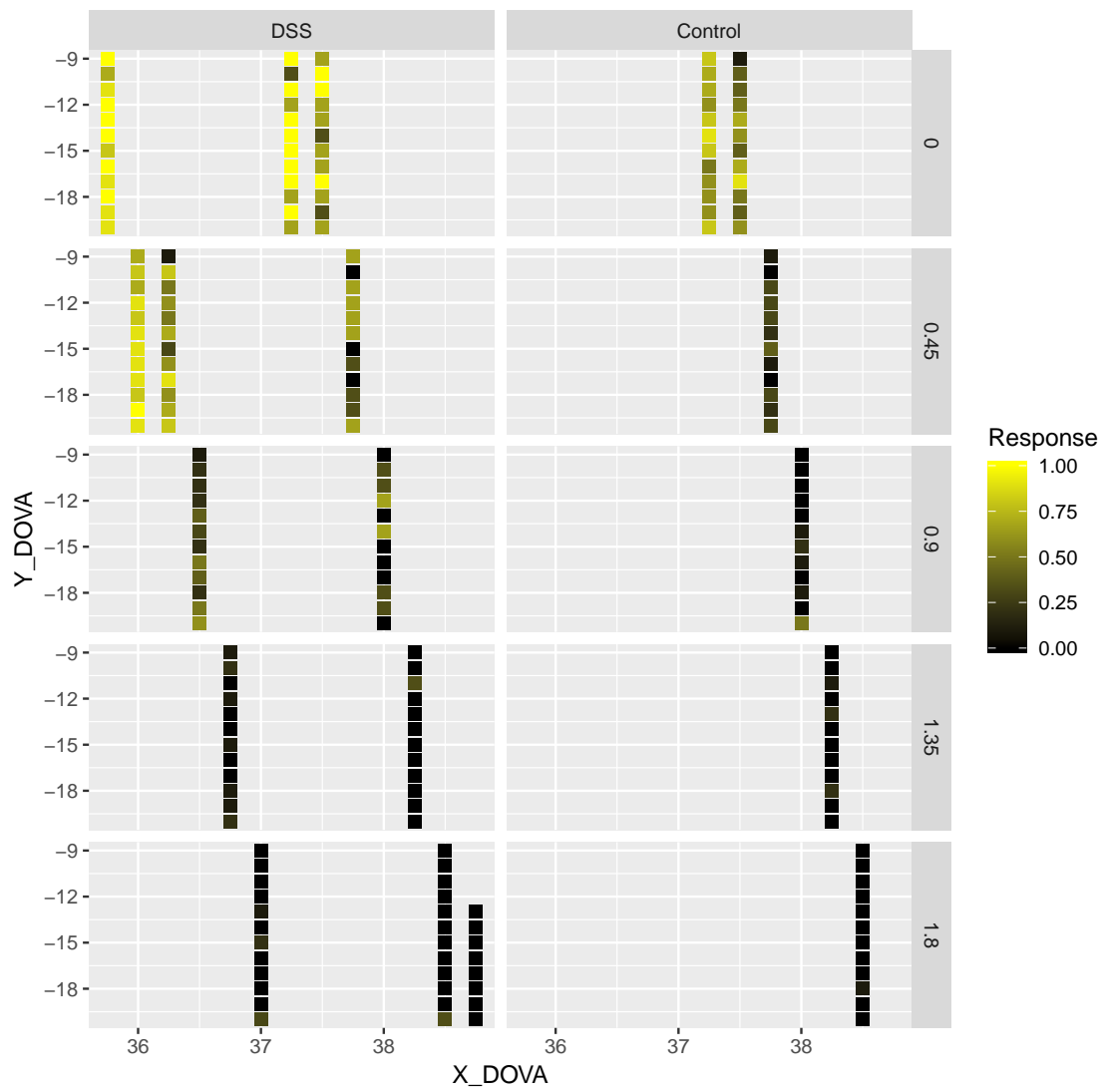
Figure 4.10 – Aspect coloured scatter plot: DSS vs Control – RVF big sprites
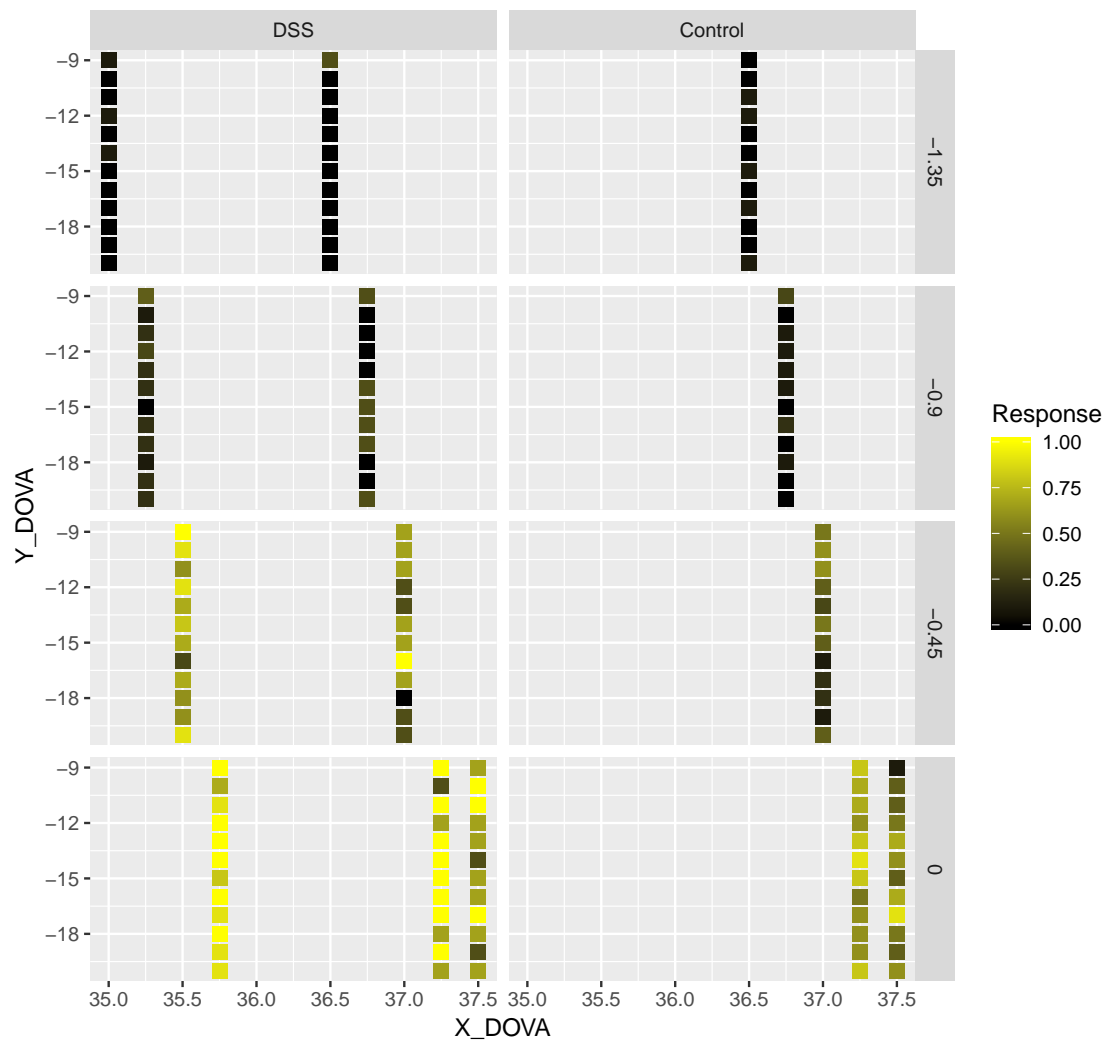
Figure 4.11 – **Aspect coloured scatter plot: DSS vs Control – RVF small sprites**
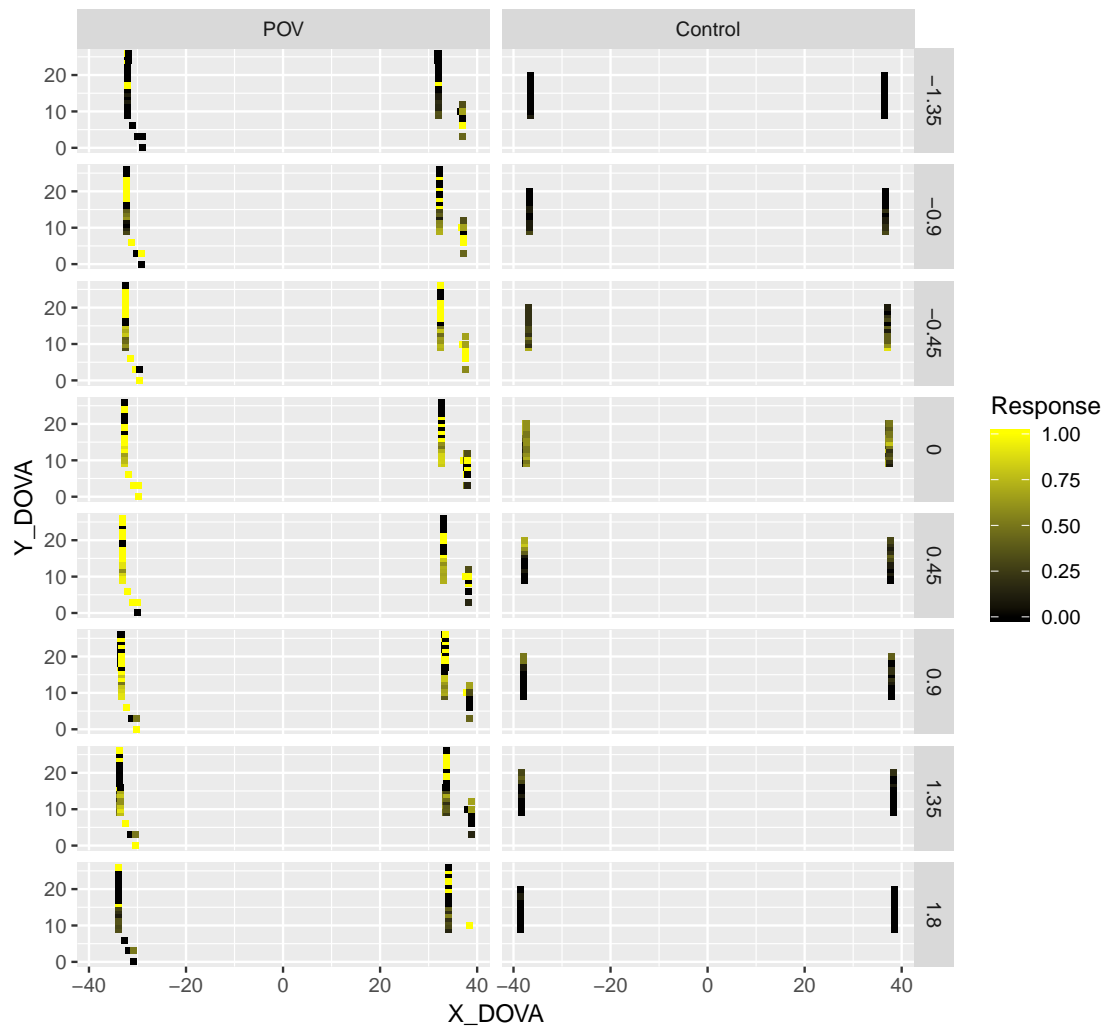
Figure 4.12 – **Aspect coloured scatter plot: POV vs Control – All comparable data**
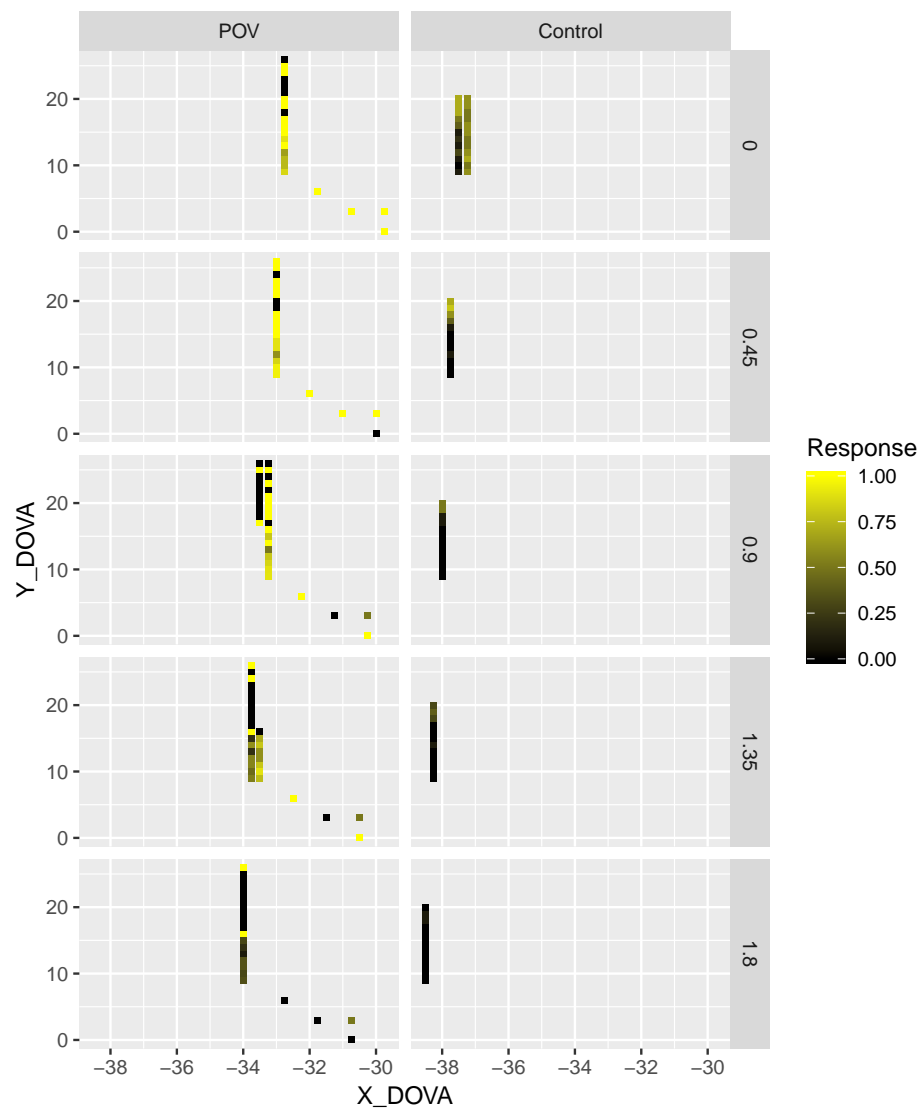
Figure 4.13 – **Aspect coloured scatter plot: POV vs Control – LVF big sprites**
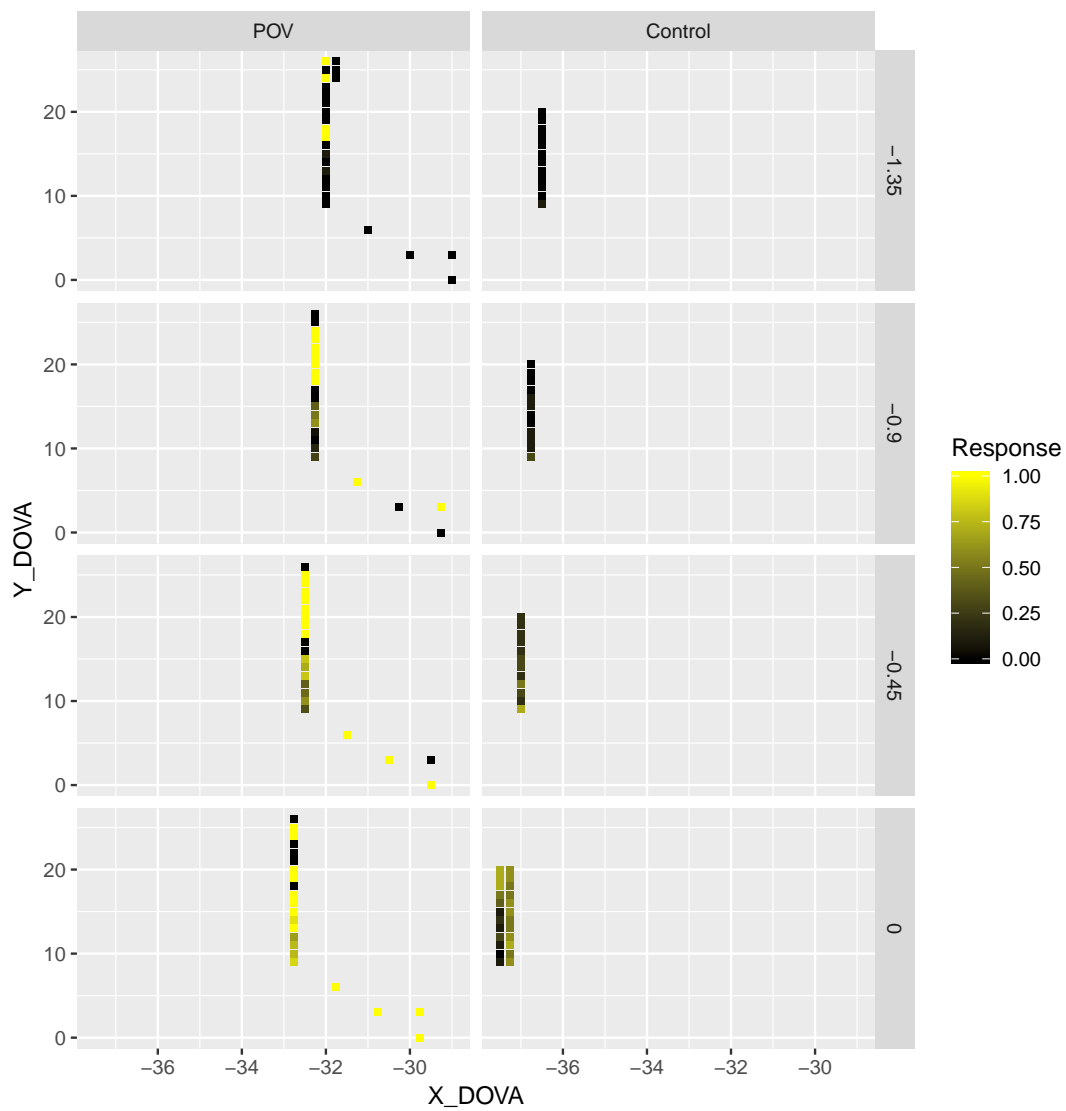
Figure 4.14 – Aspect coloured scatter plot: POV vs Control – LVF small sprites
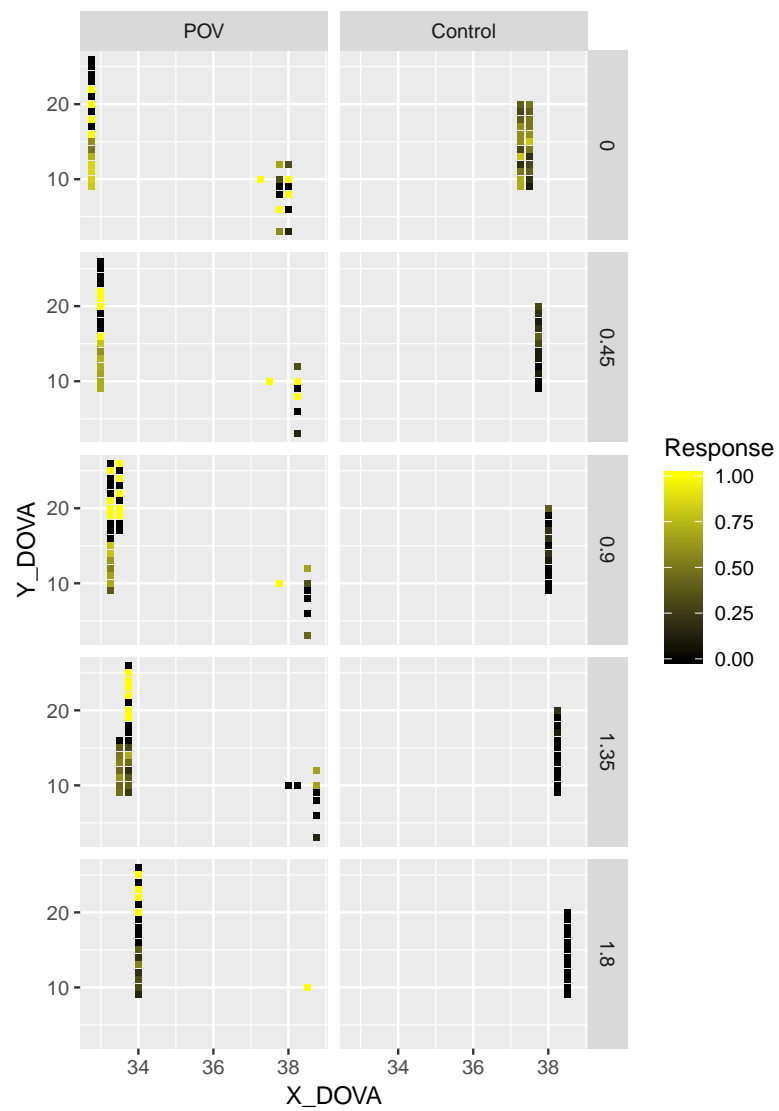
Figure 4.15 – Aspect coloured scatter plot: POV vs Control – RVF big sprites
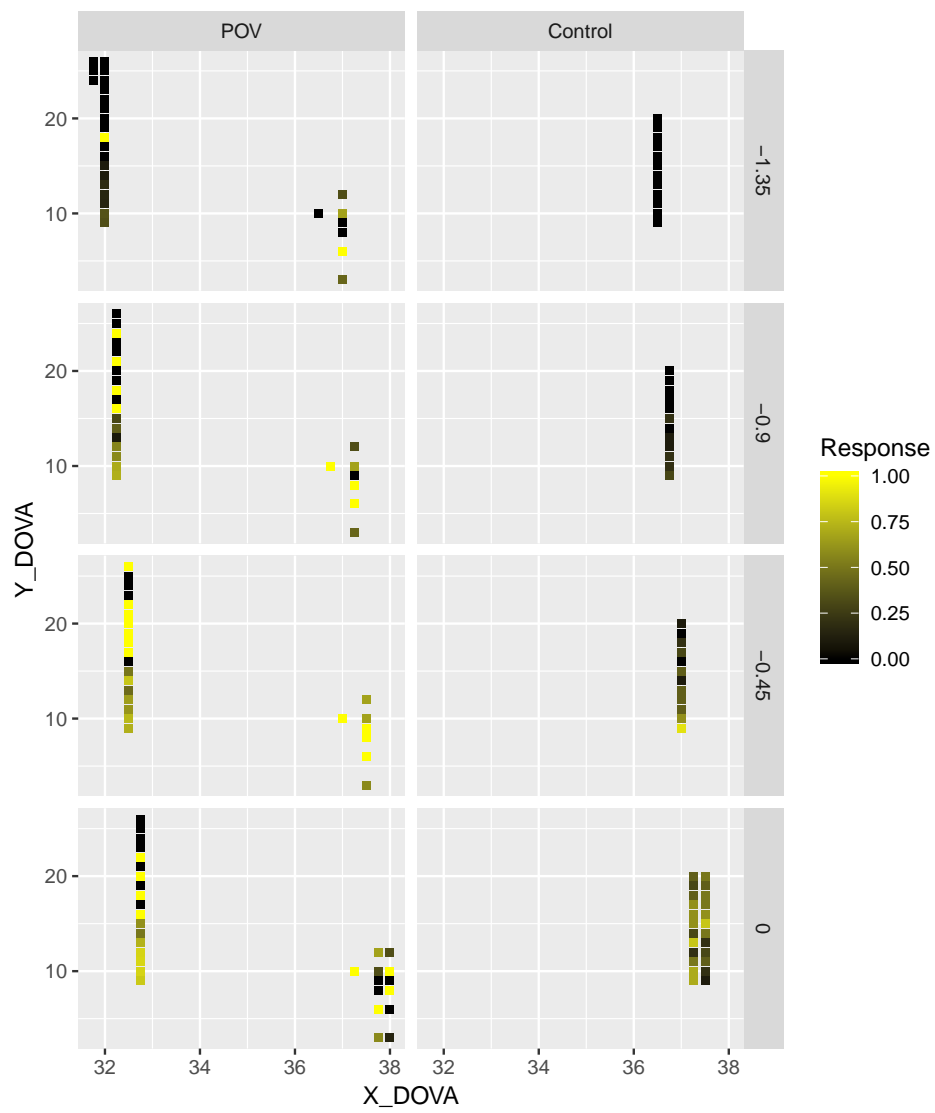
Figure 4.16 – Aspect coloured scatter plot: POV vs Control – RVF small sprites

4.4.3   Response vs sprite size

For each location of variable sprite and for each subject, we will consider the distribution of the number of same responses against the DOVA-adjusted relative sprite size. First we will produce histograms at each location and for each subject.

Next we will regard these as probability distributions, which we call the "Subjective Distribution" for the given subject at the given location. The mean of the subjective distribution is a natural measure of what the subject perceives as the 'same', in units in which 0 corresponds with the fixed and variable sprites being the same size in reality, and positive (resp. negative) values corresponding to when the variable sprite is larger (resp. smaller). In other works, the mean of the subjective distribution has been called the "Point of Subjective Equality" (PSE). The variance and coefficient of skewness of the subjective distribution are also meaningful. The variance measures how uncertain the subject is, and the skewness measures the tendency for perception errors to be biased depending on whether the variable sprite is larger or smaller.

The response vs relative sprite size histograms for POV vs Control are given in Figures 4.17 and 4.18, and those for DSS vs Control are given in Figures 4.19 and 4.20. It should be kept in mind the Control was 40 years younger in age than POV.
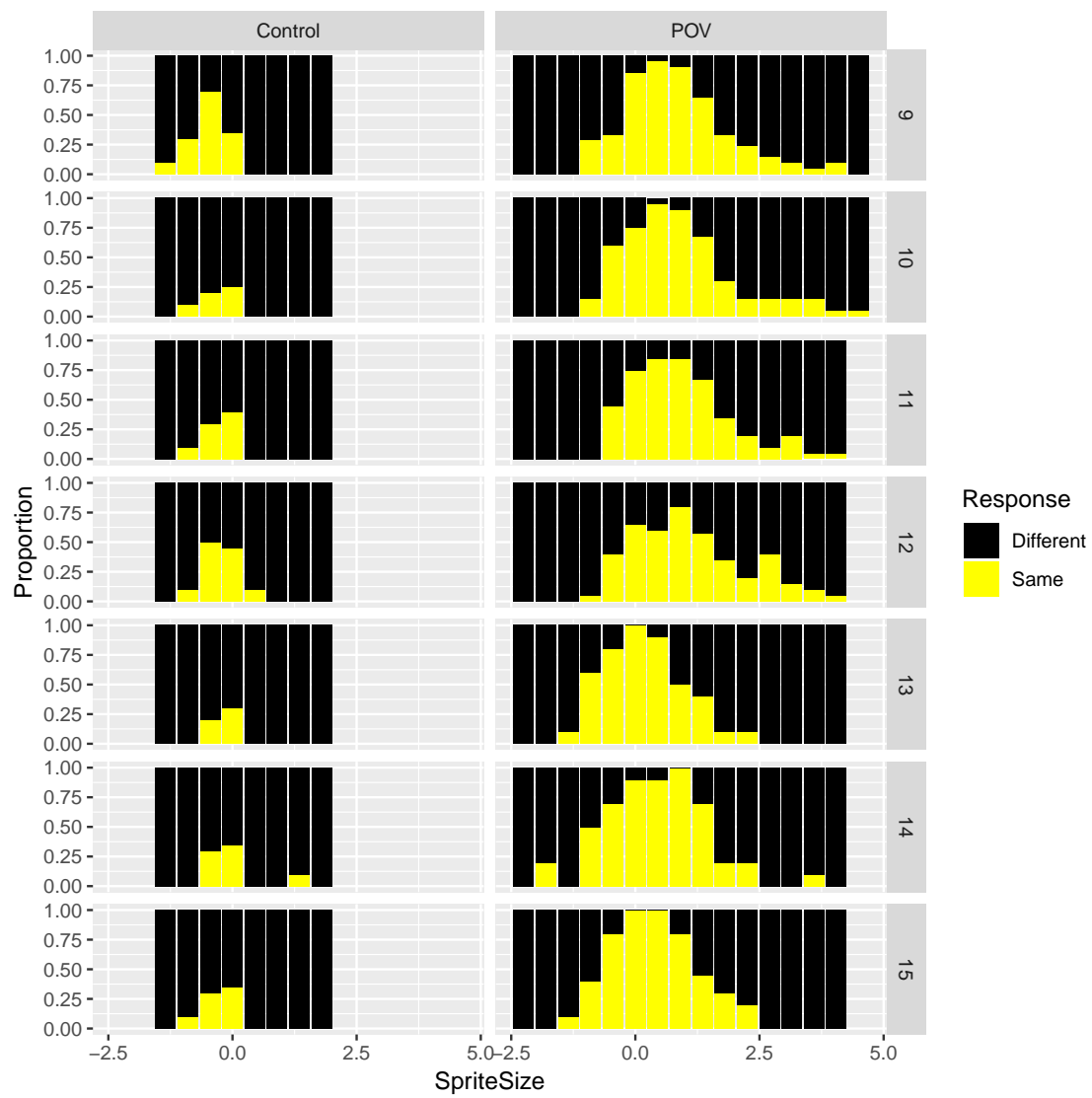
Figure 4.17 – POV vs Control, LVF, response vs relative sprite size
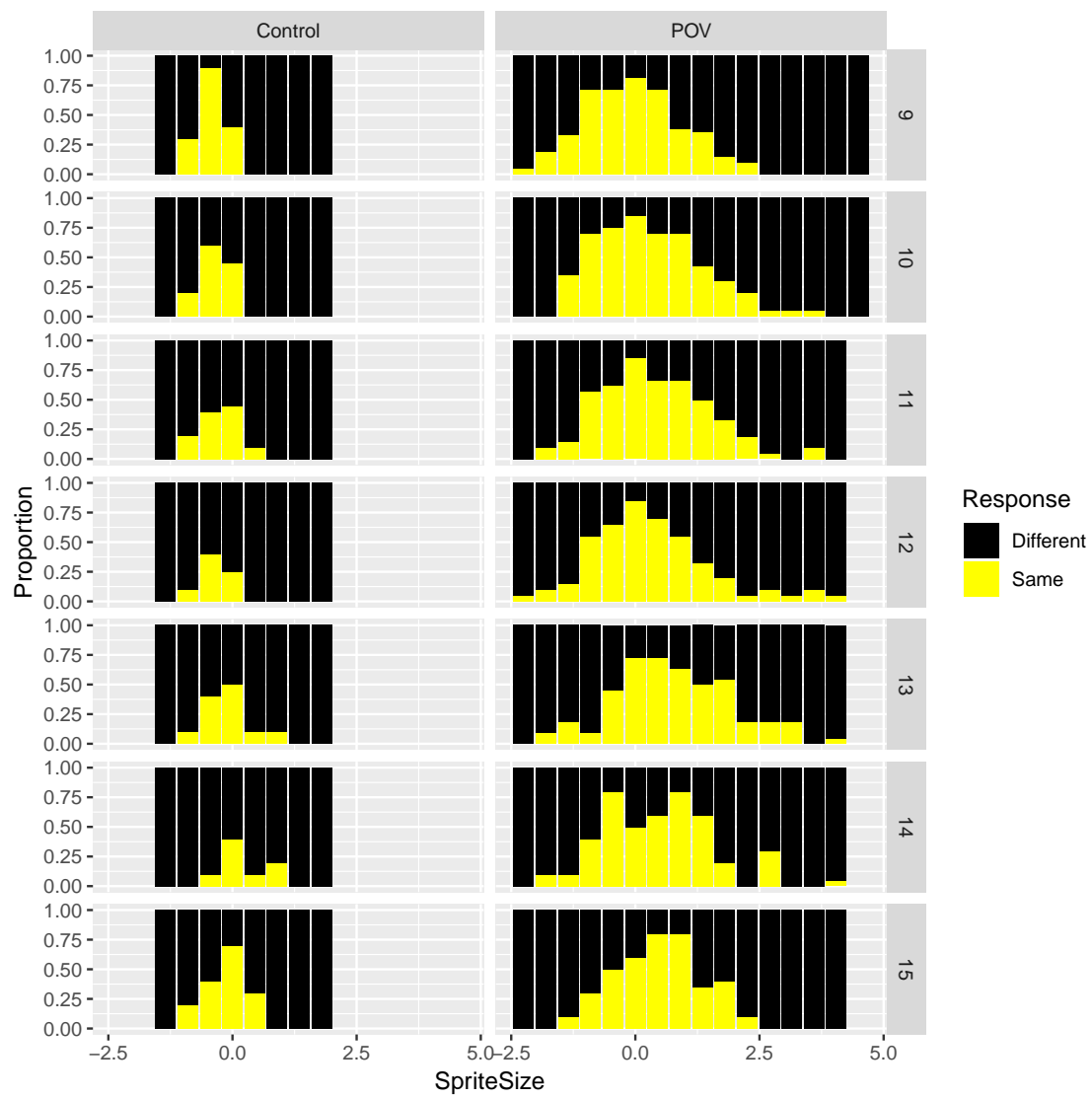
Figure 4.18 – POV vs Control, RVF, response vs relative sprite size
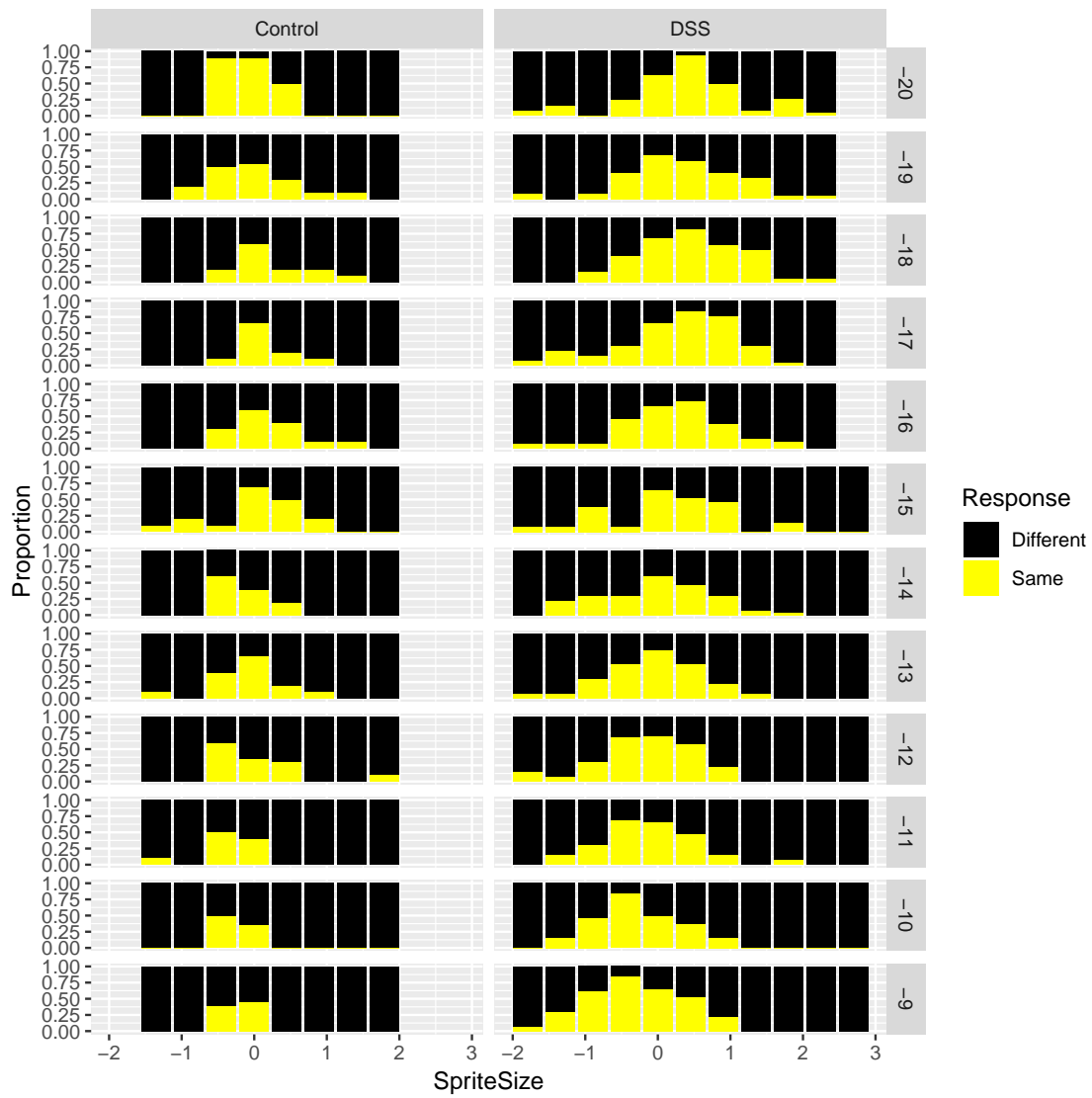
Figure 4.19 – DSS vs Control, LVF, response vs relative sprite size
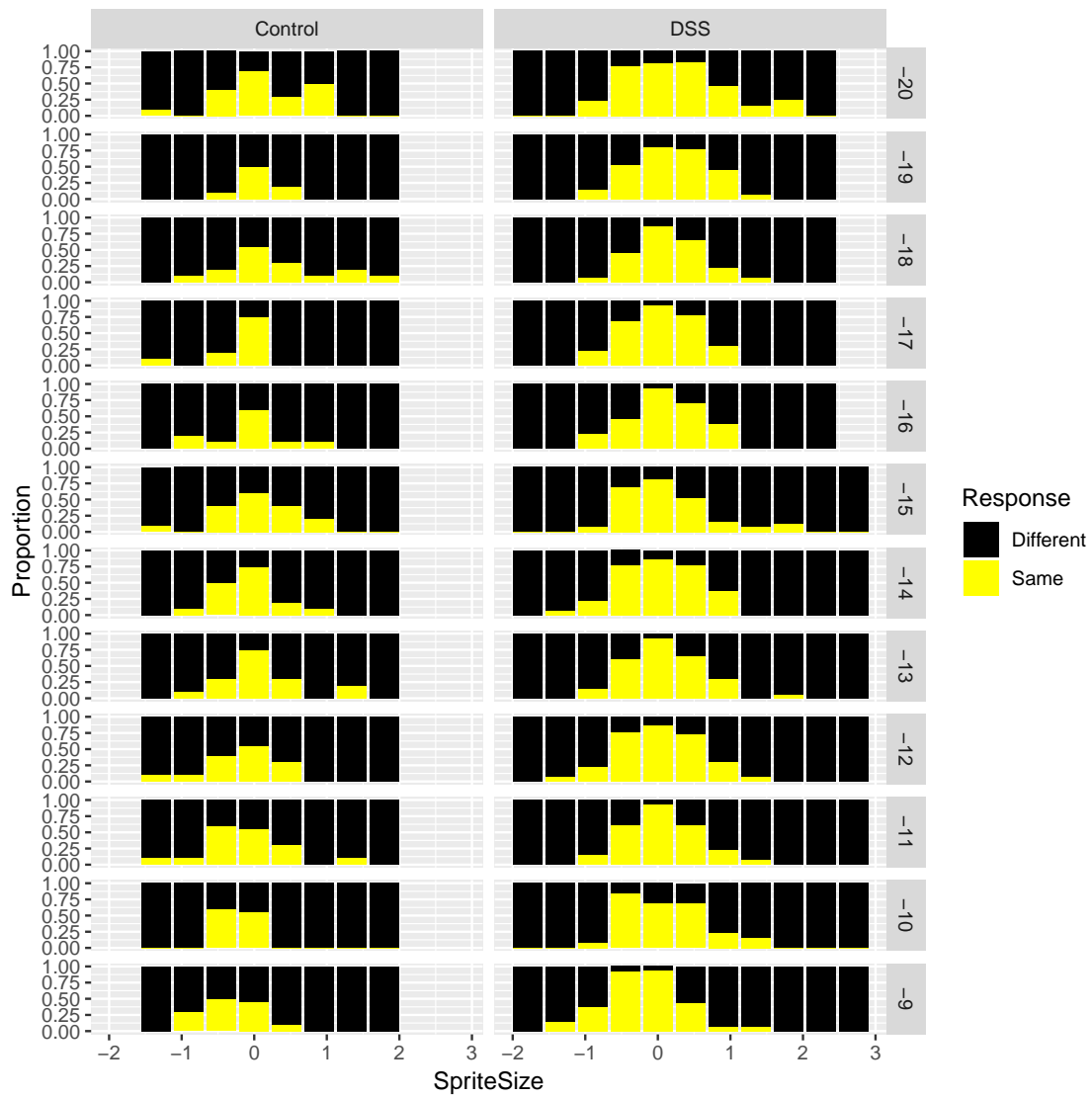
Figure 4.20 – DSS vs Control, RVF, response vs relative sprite size

Here we record the mean, variance and skewness coefficients for the subjective distributions. In the first table, we compare these statistics for POV and Control in the LVF.

Table 4.8 – Comparing the POV and Control LVF Subjective Distributions

Y	ControlMean	POVMean	ControlVar	POVVar	ControlSkew	POVSkew
9	-0.5	0.83	0.14	1.11	-0.49	0.82
10	-0.33	0.89	0.11	1.3	-0.49	0.99
11	-0.28	0.93	0.1	1.01	-0.66	0.88
12	-0.23	1.1	0.12	1.25	0.07	0.55
13	-0.18	0.17	0.05	0.63	-0.41	0.41
14	0.0	0.42	0.32	1.01	1.58	0.31
15	-0.3	0.38	0.1	0.71	-0.56	0.27

Next we do the same for the RVF.

Table 4.9 – Comparing the POV and Control RVF Subjective Distributions

Y	ControlMean	POVMean	ControlVar	POVVar	ControlSkew	POVSkew
9	-0.42	-0.05	0.09	0.94	-0.07	0.19
10	-0.36	0.3	0.1	1.15	-0.29	0.58
11	-0.27	0.4	0.15	1.17	-0.06	0.47
12	-0.36	0.32	0.09	1.43	-0.23	0.82
13	-0.11	0.77	0.21	1.37	0.52	0.23
14	0.23	0.48	0.2	1.23	0.38	0.48
15	-0.14	0.47	0.17	0.73	-0.32	-0.02

The last two tables give the same comparisons for DSS vs Control, the first for the LVF:

Table 4.10 – Comparing the DSS and Control LVF Subjective Distributions

Y	ControlMean	DSSMean	ControlVar	DSSVar	ControlSkew	DSSSkew
-9	-0.21	-0.32	0.05	0.44	-0.12	-0.02
-10	-0.26	-0.28	0.05	0.33	0.36	0.23
-11	-0.36	-0.12	0.15	0.44	-1.3	0.47
-12	0.03	-0.18	0.37	0.45	1.64	-0.55
-13	-0.09	-0.08	0.26	0.45	-0.46	-0.28
-14	-0.15	-0.02	0.11	0.59	0.63	0.0
-15	0.03	0.12	0.35	0.68	-0.69	-0.21
-16	0.18	0.2	0.24	0.55	0.73	-0.32
-17	0.13	0.25	0.12	0.64	0.74	-0.67
-18	0.24	0.44	0.27	0.48	0.66	0.13
-19	-0.03	0.33	0.33	0.61	0.59	-0.14
-20	-0.08	0.37	0.12	0.71	0.3	-0.32

and the second for the RVF:

4.4.4 Fisher tests

For a given subject, quadrant, and (relative) sprite size range, one can consider the number of "same" and "different" responses. For a given sprite size range, the response counts form a contingency table when one takes either

Table 4.11 – Comparing the DSS and Control RVF Subjective Distributions

Y	ControlMean	DSSMean	ControlVar	DSSVar	ControlSkew	DSSSkew
-9	-0.33	-0.2	0.16	0.32	0.11	0.26
-10	-0.23	0.1	0.05	0.3	0.09	0.5
-11	-0.13	0.06	0.34	0.26	0.38	0.31
-12	-0.19	0.02	0.24	0.33	-0.69	-0.0
-13	0.11	0.1	0.33	0.3	0.75	0.55
-14	-0.08	0.01	0.18	0.31	0.37	-0.21
-15	0.03	0.13	0.3	0.38	-0.51	1.02
-16	-0.08	0.09	0.25	0.26	-0.03	-0.17
-17	-0.21	0.04	0.17	0.25	-1.99	-0.05
-18	0.32	0.14	0.51	0.24	0.48	0.27
-19	0.06	0.17	0.07	0.29	-0.05	-0.01
-20	0.14	0.25	0.35	0.5	-0.43	0.5

1. A pair of subjects for a given quadrant, or

2. A pair of quadrants for a given subject.

As explained in Section 3.2.1, a rejection of the null hypothesis by either the chi-square or Fisher exact test in the case of (1), gives evidence that the two subjects' responses are different for the given quadrant and sprite size range; and in the case of (2), gives evidence that the given individual subject's responses are different for the two quadrants being considered and the given sprite size range.

All of this can be carried out for unadjusted sprite size lengths, and for DOVA-adjusted relative sprite sizes. So here we just report on tests involving the latter. In general, chi-square p-values and Fisher p-values measure the same thing, the former being an approximation (which is sometimes better behaved numerically) of the latter. For us, there is almost no difference in the p-values obtained for these different tests, and so here we just report the Fisher test statistics.

We now provide tables with columns: Subject, LBound (ie lower bound of the relative sprite size range), UBound (ie upper bound of the relative sprite size range), Verticality, and results of the Fisher test. Significance indicates that the given subject's responses are different for the LVF and RVF. The results indicate that there is no evidence of such a difference for Control, but there are sprite size ranges for which such a difference is statistically significant for both POV and DSS. First we use a fairly wide relative sprite size interval to get an overview:

Next we use the relative sprite size interval of 0.45 that resulted in the most even distribution of observations, for a more complete picture.

Table 4.12 – Fisher test: LVF vs RVF, Aspect, Overview

Subject	LBound	UBound	Verticality	Fisher Test
Control	-2.25	-0.75	Superior	p = 0.8200
Control	-2.25	-0.75	Inferior	p = 0.1248
Control	-0.75	0.75	Superior	p = 0.9461
Control	-0.75	0.75	Inferior	p = 0.8966
Control	0.75	2.25	Superior	p = 0.0986
Control	0.75	2.25	Inferior	p = 0.5638
POV	-2.25	-0.75	Superior	p < 0.00001
POV	-0.75	0.75	Superior	p < 0.05
POV	0.75	2.25	Superior	p < 0.001
POV	2.25	3.75	Superior	p = 0.0712
POV	3.75	5.25	Superior	p = 0.3827
DSS	-2.25	-0.75	Inferior	p < 0.0001
DSS	-0.75	0.75	Inferior	p < 0.00001
DSS	0.75	2.25	Inferior	p < 0.01
DSS	2.25	3.75	Inferior	p = 0.4951

Now we tabulate the outcome of Fisher tests for subject ("POV" or "DSS") vs Control, over a range of relative sprite sizes. The results indicate highly significant differences between subject and Control for all quadrants and almost all sprite size ranges. Each table refers to one quadrant and one affected subject, and provides Fisher p-values for intervals of relative sprite sizes. So the columns of these tables will be `LBound` and `UBound` to give the interval of relative sprite sizes to which a row refers, and the result of the Fisher test.

First we give the comparison for POV on the left side.

Now we give the comparison table for POV on the right.

The next two blocks give the comparison tables for DSS for the left and right sides respectively.

4.5   Experiment 4: Location

For POV there were 1650 observations in the Location data set. Table 4.18 indicates a lack of consistent spatial localisation for this subject. During this experiment, POV expressed he had difficulty making his decision as a "ghost" square would appear and stay fleetingly. The ghost square was perceived after several runs of the experiment. POV stated he knew the ghost square was not part of the experiment as its appearance was not in keeping with what he had experienced and learnt during the first runs. POV has experienced a visual hallucination usually after a nap. When he wakes up from his nap, one of his grandsons appears to be walking to the peripheral of the right side of his vision. It is always the same grandson and he appears to be always the same age, around 15-years-old. POV explained he used to spend lots of time with this grandson at this age.

The ghost square continued to appear even when testing was confined to his normal hemifield without the scotoma. POV thought the ghost square was appearing in part of his scotoma. The reference sprite also

Table 4.13 – **Fisher test: LVF vs RVF, Aspect, Full picture**

Subject	LBound	UBound	Verticality	Fisher Test
Control	-1.575	-1.125	Superior	p = 1.0000
Control	-1.575	-1.125	Inferior	p = 0.7219
Control	-1.125	-0.675	Superior	p = 0.6336
Control	-1.125	-0.675	Inferior	p = 0.1666
Control	-0.675	-0.225	Superior	p = 0.7791
Control	-0.675	-0.225	Inferior	p = 0.3546
Control	-0.225	0.225	Superior	p = 0.7833
Control	-0.225	0.225	Inferior	p = 0.2294
Control	0.225	0.675	Superior	p = 0.1854
Control	0.225	0.675	Inferior	p = 0.7558
Control	0.675	1.125	Superior	p = 1.0000
Control	0.675	1.125	Inferior	p = 0.8072
Control	1.125	1.575	Superior	p = 0.0503
Control	1.125	1.575	Inferior	p = 0.7219
Control	1.575	2.025	Superior	p = 0.4979
Control	1.575	2.025	Inferior	p = 1.0000
POV	-2.475	-2.025	Superior	p < 0.05
POV	-2.025	-1.575	Superior	p < 0.001
POV	-1.575	-1.125	Superior	p < 0.0001
POV	-1.125	-0.675	Superior	p < 0.0001
POV	-0.675	-0.225	Superior	p = 0.0798
POV	-0.225	0.225	Superior	p < 0.05
POV	0.225	0.675	Superior	p < 0.0001
POV	0.675	1.125	Superior	p < 0.001
POV	1.125	1.575	Superior	p < 0.001
POV	1.575	2.025	Superior	p = 0.8898
POV	2.025	2.475	Superior	p = 0.7342
POV	2.475	2.925	Superior	p = 0.8470
POV	2.925	3.375	Superior	p = 0.0681
POV	3.375	3.825	Superior	p = 0.7858
POV	3.825	4.275	Superior	p = 0.5427
POV	4.275	4.725	Superior	p = 1.0000
DSS	-2.025	-1.575	Inferior	p < 0.01
DSS	-1.575	-1.125	Inferior	p < 0.001
DSS	-1.125	-0.675	Inferior	p = 0.1028
DSS	-0.675	-0.225	Inferior	p < 0.001
DSS	-0.225	0.225	Inferior	p < 0.00001
DSS	0.225	0.675	Inferior	p = 0.1303
DSS	0.675	1.125	Inferior	p = 0.2263
DSS	1.125	1.575	Inferior	p = 0.0806
DSS	1.575	2.025	Inferior	p = 0.1903
DSS	2.025	2.475	Inferior	p = 0.1155
DSS	2.475	2.925	Inferior	p = 1.0000

Table 4.14 – Fisher test: POV vs Control, Aspect, LVF

LBound	UBound	Fisher Test
-1.575	-1.125	p = 0.1218
-1.125	-0.675	p < 0.0001
-0.675	-0.225	p < 0.0001
-0.225	0.225	p < 0.00001
0.225	0.675	p < 0.00001
0.675	1.125	p < 0.00001
1.125	1.575	p < 0.00001
1.575	2.025	p < 0.00001

Table 4.15 – Fisher test: POV vs Control, Aspect, RVF

LBound	UBound	Fisher Test
-1.575	-1.125	p < 0.00001
-1.125	-0.675	p < 0.00001
-0.675	-0.225	p < 0.00001
-0.225	0.225	p < 0.0001
0.225	0.675	p < 0.00001
0.675	1.125	p < 0.00001
1.125	1.575	p < 0.00001
1.575	2.025	p < 0.00001

Table 4.16 – Fisher test: DSS vs Control, Aspect, LVF

LBound	UBound	Fisher Test
-1.575	-1.125	p < 0.01
-1.125	-0.675	p < 0.00001
-0.675	-0.225	p = 0.3281
-0.225	0.225	p < 0.05
0.225	0.675	p < 0.00001
0.675	1.125	p < 0.00001
1.125	1.575	p < 0.01
1.575	2.025	p < 0.01

Table 4.17 – Fisher test: DSS vs Control, Aspect, RVF

LBound	UBound	Fisher Test
-1.575	-1.125	p = 0.5087
-1.125	-0.675	p < 0.05
-0.675	-0.225	p < 0.00001
-0.225	0.225	p < 0.00001
0.225	0.675	p < 0.00001
0.675	1.125	p < 0.00001
1.125	1.575	p = 0.5937
1.575	2.025	p = 0.1507

appeared to shift into where he thought his scotoma was. His experience in many psychophysical experiments was valuable as he was able to unreservedly describe his visual perceptions.

Table 4.18 – **POV consistency of spatial localisation**

Quadrant	Accuracy Same	Accuracy Different
Upper Left	0.6666667	0.425
Upper Right	0.4777778	0.5744444

DSS's data contains only 16 observations. So we list it all in Table 4.19. There was insufficient time to perform further experiment runs. His response was correct in 15/16 trials suggesting he had quite accurate spatial localisation.

Table 4.19 – **DSS Location data**

X	Y	BackLuminence	MaskTiming	RefTiming	VarTiming	Response
3	-6	0.56	0.75	3	3	1
-3	-6	0.9	0.75	3	6	1
3	-6	0.56	0.75	3	6	1
3	-6	0.56	0.75	3	4	1
-3	-6	0.9	0.75	3	3	1
-3	-6	0.56	0.75	3	4	1
-3	-6	0.9	0.75	3	4	1
3	-6	0.9	0.75	3	5	1
-3	-6	0.56	0.75	3	6	1
-3	-6	0.56	0.75	3	3	1
3	-6	0.9	0.75	3	3	1
3	-6	0.9	0.75	3	6	1
-3	-6	0.9	0.75	3	5	1
3	-6	0.56	0.75	3	5	1
-3	-6	0.56	0.75	3	5	1
3	-6	0.9	0.75	3	4	0

4.6   Experiment 5: Filling-In

The Filling-in experiment was created after POV described the sprite closest to fixation had appeared to move eccentrically during the Location experiment. This means the reference sprite was now perceived inside of what he felt was his scotoma. Repeated trials were created to replicate the same conditions as his intial observation in the Location experiment.

Unfortunately, POV also developed an after-image which occurred on immediate presentation of the experiment reference sprite. A prolonged duration of an initial black screen presentation, a visual mask and increased duration between trials was used to try to counter the occurrence of the after-image. However, all attempts to create experimental conditions which could negate the after-image or shift of the reference sprite failed. This included resting POV for 3 months between experiment runs. After resting POV for 3

months, the after-image or ghost sprite would appear on the fixation screen even before the reference sprite. This could be an example of cortical reorganisation in the higher visual areas extrapolating visual data to predict the visual scene rather than relying on what is immediately perceived. Eventually, POV was unable to tell the difference between the reference sprite and the ghost image. Therefore, all testing was ceased at this stage for POV.

The Filling-in experiment was not performed for DSS due to time contraints. With specific questioning, he did not volunteer he was experiencing a "ghost" or after-image during any of the experiments he had participated in.

4.7 Conclusion

Analyses of the results of the "Aspect" experiment demonstrate a statistically significant difference between the two subjects with homonymous paracentral scotomas and the control, both around the scotoma and in the opposite unaffected hemifield. A comparison between the two hemifields in each subject also revealed a statistically significant difference (not observed in the control subject).

For subject POV, results in the left upper quadrant demonstrate uncertainty with larger sprites perceived as being the same size compared to control. In the right upper quadrant, testing across POV's scotoma demonstrates further uncertainty with even larger sprite sizes being perceived as the same. The distribution of this uncertainty decreases with increasing eccentricity after 15 DOVA on the vertical axis.

For subject DSS, results in the right inferior quadrant demonstrate uncertainty compared to control. Both smaller and larger sprites are perceived as the same size in DSS's quadrant which is not affected by the scotoma. In DSS's left inferior quadrant affected by his scotoma, there is even greater perceptual size uncertainty compared to his right inferior quadrant and control. Smaller sized sprites closer to fixation are perceived to be the same size for DSS compared to control. With eccentricity beyond 14 DOVA, larger sprites are perceived to be the same size. Also, the distribution spread increases with eccentricity in the left inferior quadrant.

These results suggests there is a visual perceptual spatial distortion surrounding each of the two subjects' scotomas. The results differ for subjects POV and DSS. Testing was performed in the superior hemifield for POV and the inferior hemifield for DSS. There may be different visual processes occurring for visual information presented above or below the horizontal meridian; and within or beyond 15 DOVA. DSS results suggest visual information presented in the inferior hemifield within 15 DOVA may be strengthened or amplified. POV results in the superior hemifield suggest larger sprites are perceived to be the same size. However, beyond 15 DOVA of eccentricity, the distribution spread of uncertainty is narrowed.

Furthermore, there were statistically significant differences between the two hemifields within each of the subjects. However, there was no statistically significant difference between the two hemifields for the normal Control. For each subject, the hemifield without the scotoma also demonstrated a statistically significant difference compared with the Control data. This suggests visual perception is potentially distorted in the hemifield without the scotoma and visual processing is affected on the side contralateral to the cortical lesion. For DSS, responses in the inferior right quadrant unaffected by the scotoma demonstrate a spread either side of 0 with size difference. Both smaller and larger sprites were perceived to be the same size for DSS. For POV, testing in the superior left quadrant unaffected by the scotoma demonstrates a distribution of responses suggesting larger sprites are perceived to be the same size.

The observations voiced during the "Location" experiment gave rise to a novel finding for subject POV. The consistent visual hallucinations reported by the subject may reflect cortical plasticity with regards to learning through experience or exposure to repeated conditions. The development of these persistent hallucinations raises the possibility of manipulating structural cortical reorganisation to modify visual function in impaired individuals.

Chapter 5

General discussion

5.1 Preface

The literature review, case series and experimental data presented in this thesis do not strongly demonstrate retinotopic remapping as the explanation for metamorphopsia after occipital lobe damage. For both the literature review and case series, the timing of onset of visual symptoms after the central visual pathway lesion is difficult to determine. Also, there are confounding factors of simultaneous injuries of other cortical areas apart from V1. Although a geometric distortion of visual spatial perception is less likely as the cause of the visual symptoms suffered by the cases in the literature, the experimental data for both subjects and normal control suggest modifications in visual processing does occur after injury to V1.

Interestingly, visual spatial perception was changed in the visual field not affected by the scotoma for both subjects POV and DSS. Also, the results suggest different visual processing occurs when visual information is presented above or below the horizontal meridian; and centrally or peripherally.

The general mechanisms of the normal human visual system are not yet fully understood. The experimental data presented in this thesis suggest single human case studies with specific isolated lesions of V1 still play a role in further investigating normal and abnormal visual processing.

5.2 Normal human vision

An explanation for how humans consciously see has not yet been determined and is not really understood. For a review on the consciousness of sight, see article by Zeman [121]. Contrast sensitivity and spatial resolution underlie the processing of all visual stimuli. The identification and mapping of the human visual cortex was a slow process involving anatomical, physiological and clinical observations. The accumulation of

evidence led to the conclusion that vision is mapped in an orderly fashion in the occipital lobes. Observations were made from visual psychophysical testing in patients who had suffered injuries to their visual processing areas. Tatsuji Inouye was a Japanese ophthalmologist who trained in Tokyo before the outbreak of the Russo-Japanese war from 1904-1905 [122, 123]. As an army physician, he observed patients who were injured by bullets from a Russian rifle, Mosin-Nagant Model 91. This rifle deployed a bullet with high velocity, resulting in complete wound penetration without widespread damage to the surrounding tissue. The soldiers were able to survive this type of head wound and the edges of the injury were well demarcated. Inouye studied and plotted the visual fields of 29 patients. He correlated the respective lesions by drawing the defects into an introduced coordinate system. He also observed macular sparing in soldiers who had suffered extensive cortical damage. During World War I (1914-1918), Lister and Holmes conducted research in military hospitals in France based on the same principles as Inouye [124].

Neuroanatomical and neurophysiological studies investigating visual processing have been performed in humans and the macaque monkey. Brodmann area 17, known also as the striate cortex or V1, performs multiple visual processing tasks. For example, blobs rich in cytochrome oxidase specialise in processing colour. Between these blobs, there are further separate visual information streams for motion, depth and form. Surrounding V1, there are more than 30 further visual maps of the visual world. Brodmann area 18, also referred to as V2 or Visual Association Area, is involved in feature extraction. Brodmann area 19 is also referred to as extrastriate or peristriate cortex and includes V3, V4, V5 and V6. These areas are thought to process tasks involved in determining feature, shape, attention and visual information integration. There are many models of visual processing with the most popular models being functionally specialised or modular.
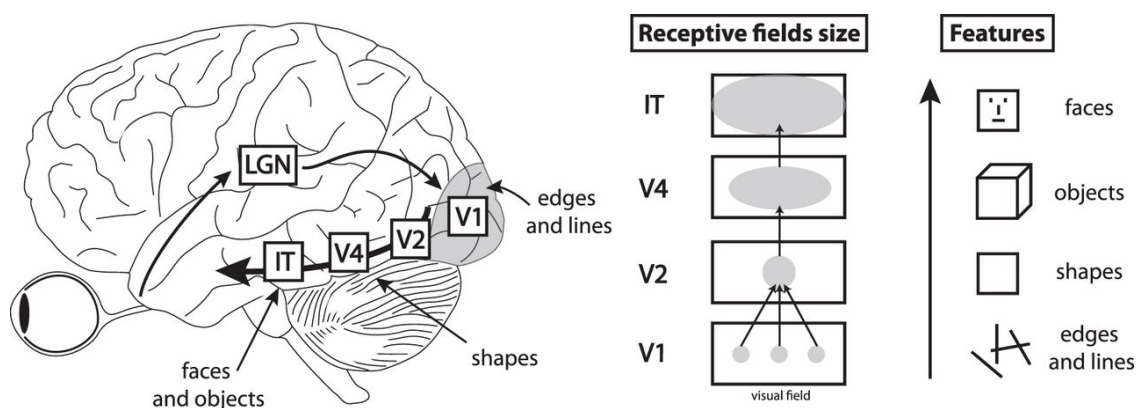
Figure 5.1 – **Hierarchical, feedforward visual processing, taken from [125]**

Impaired visual perception can be due to a lesion at any location along the visual pathway. The lesion results in disintegration of neuronal networks. Intact neurones may discharge uninhibited by normal interactions with surrounding damaged neurones. Insights into visual disturbances due to injury have been

provided by patients who are able to described their experiences in detail. For example, a neurology professor suffering from a right hemianopia provided an excellent description of his visual experiences [126]. Cole described his visual hallucinations and illusions after a left occipital infarction affecting both banks of the calcarine fissure. He had undergone surgery for aortic valve replacement with a St Jude valve, as well as a double coronary artery bypass graft. He discovered he had a dense right hemianopia in the recovery room after his surgery. He was also unaware of his hemianopia: "unless I attend to it or strike things on my right side. I may start a line of writing on the wrong line above if the left side of the line is blank, since I may be unaware of writing on the right side of the line." In this thesis, the subjects POV and DSS suffered from discrete lesions of the occipital lobes. These lesions resulted in homonymous paracentral scotomas and visual spatial perception was investigated in the visual field surrounding the scotomas. Analysis of the experimental data suggest there is distortion of visual spatial perception surrounding the scotoma which could represent cortical reorganisation.

5.3 Cortical plasticity

Cortical plasticity is the functional and structural changes of the cerebral cortex. Plasticity of the cortex occurs during normal learning to improve cognitive performance. It can also occur during recovery following an injury to the nervous system. Balance or homeostasis is a general rule that governs cortical circuits. Cortical stability of neural networks is also necessary. There is a tendency to keep neuronal activity within normal bounds, for a review see [127]. Cortical activity prefers no chaos or amplification. Cortical circuits prefer dampening, otherwise there would be uncontrolled neural activity. A cortical circuit that perpetuates constant firing of neurons leads to epilepsy and a dysfunctional organism. An excessively plastic circuit may disrupt the function of the network.

Adult visual cortical plasticity must exist as experience dependent changes in perception require the visual cortex to be capable of encoding new information, see review article [128]. There are various forms of visual cortical plasticity including declarative memory, encoding information about places, faces and events. There is also a form of implicit memory known as perceptual learning. Perceptual learning is the improvement in ability to detect or discriminate visual stimuli resulting from repeated practice.

Cortical circuitry enables V1 neurons to integrate information over larger parts of the visual field. The circuitry also allows selectivity for more complex visual stimulus configurations. Cortical pyramidal cells create a plexus of connections which extend a long distance parallel to the cortical surface [129, 130, 131, 132]. These cells are thought to be partially responsible for higher-order visual properties. They enable neurons to integrate information over large parts of the visual field and given neurons selectivity for stimulus context.

If one considers more complex stimuli of multiple line segments, the neural responses to a stimulus placed in the receptive field are modified by the global context, for a review see [133]. The distinction between the "classical" and "nonclassical" receptive fields was formed due to contextual influences modulating a neuron's respose by stimuli " outside" the receptive field. Both facilitatory or inhibitory influences flanking the receptive field can modulate neural responses. Neurons rely upon the global characteristics of image components far outside their core receptive fields as well as the local features within the receptive field centre. Contour integration and saliency are influenced by contextual modulation and relate to the specificity in perceptual learning. Alterations in contextual interactions denote specificity for the configuration of discriminated stimuli [134].

The contextual interactions in V1 are in keeping with the Gestalt rules of perceptual grouping [135]. These rules include proximity, similarity and good continuation. The rules allow the linkage of components of extended contours in complex visual scenes. Our human visual system simplifies the problem of linking contour elements by taking into account the statistical properties of scene contours. This simplification follows the priciples of collinearity and cocircularity [136, 137]. The association field is the framework underlying these interactions in perceptual grouping and at the level of cortical receptive fields [138]. The contours that are salient are contour elements we perceptually group together that lie along smooth contours. This is called "good continuation" and these contours tend to pop-out in complex visual environments.

The receptive fields in V1 reflect the association field. Orientation selectivity is a local property of the receptive fields and is demonstrated by the response of neurons to a simple stimulus such as a single, oriented line segment. Contour integration is the correponding property in intermediate level vision. In monkeys, there is selectivity of V1 neurons' responses for the properties of extended contours with complex geometries. The neurons' responses are faciliatated by collinear interactions. A line placed outside the receptive field will not elicit a response. However, this line outside the receptive field can faciliate a neuron's response several fold when placed in conjunction with a collinear line segment within the receptive field [139, 140]. In monkeys, if the continuity is blocked by a perpendicular line between the two collinear line segments, facilitation is eliminated. However, perceived continuity and facilitatory interaction is restored by moving the perpendicular line segment into a different depth plane from the two collinear line segments [141].

The intrinsic circuity of V1 is responsible for the properties of natural scene contours, the perceptual strategies involved in linking contour elements and contextual interactions. An important part of this intrinsic V1 circuity is the plexus of long-range horizontal connections. In normal cortex, these connections play a modulatory role and allow propagation of information across the visual map. These long-range connections allow neurons to integrate inputs from larger areas of the visual field than their classical receptive fields. The circuity underlying lateral interactions in V1 is thought to mediate the linkage of elements in a visual

scene into global contours [128].

Studies have investigated the mechanism of cortical plasticity at the levels of receptive field properties, changes in circuitry and the molecular mechanisms involved in reorganisation of the cortical topography after retinal lesions, see review article [58]. The lesion projection zone (LPZ) in V1 is the retinotopic region corresponding to the the focal binocular retinal lesions. During recovery, the neurons within the LPZ regain responsiveness to visual input from the intact retina surrounding the lesion. Reorganisation of V1 retinotopic map has been documented with fMRI in patients with macular degeneration and in stroke patients with partially damaged input to V1 [142, 143]. The reorganisation in cortical topography is mediated by long-range horizontal connections. Following retinal lesions, these connections become strengthened. They enable neurons in cortical regions surrounding the LPZ to drive activity within the LPZ to spiking levels. This accounts for the shifting receptive fields of LPZ neurons to the locations outside the retinal lesion. Long-range horizontal connections are thought to be the ideal candidate for the source of visual input into LP. The extent of recovery of visual driven activity in the LPZ is approximately the same as the long-range horizontal connections in postmortem analysis, 8mm in length [57]. This has also been observed in vivo in the macaque primary visual cortex with the use of two-photon imaging [144]. It should be noted that these observations may represent functional reorganisation rather than strutural reorganisation as it examines individual axonal boutons and dendritic spines. Also, it would be unethical to perform two-photon imaging in human subjects due to its invasiveness. If illusionary transformations occur with prolonged fixation on the object, the visual distortion is not likely due to long-term remapping. These transformations could be cellular, neuronal or receptive field plasticity; or higher-order processing plasticity.

In 1956, three authors subjected themselves to six days of perceptual isolation in a monotonous sensory environment [145]. All three observers experienced visual hallucinations after their first day of isolation. After they were released from isolation, they experienced the distortion of shapes. There was a tendency for straight edges or lines to appear curved. Flat surfaces in the region around the fixation point appeard to bulge outwards. In one observer, the visual distortion lasted more than 24 hours. A visual psychophysical experiment was performed in which "a standard disc was presented 2ft. in front of the subject and he was required to select a figure of the same size from a graduated row of discs 12 ft. in front of him, the experimental subjects consistently chose larger discs than did a comparable group of controls". The change in size constancy after visual sensory deprivation could be due to cortical reorganisation resulting in tighter or closer horizontal connections. The visual information could have become more spatially integrated, therefore, causing objects to appear smaller than their actual size.

Systematic human psychophysical studies investigating visual processing are difficult to perform. There are usually a small number of affected cases with a specific visual disturbance or anatomical lesion, the visual

symptoms are often transient, patients may not volunteer their symptoms, often the changes are subtle and difficult to describe by the patient. Later during recovery from their injury, patients might describe visual changes they thought to be part of the "normal" healing process. Therefore, it is difficult to detect whether a patient is experiencing changes in their visual perception unless they are specifically questioned at the appropriate time. This leads to missed opportunities in recruiting subjects for psychophysical testing during their symptomatic phase.

Metamorphopsia due to lesions of suprachiasmatic origin is identical in both eyes. An attempt in this thesis was made to investigate cortical reorganisation of the occipital lobes after a lesion of V1. Both subjects POV and DSS had stable, healed or scarred lesions of V1 with no other cortical lesions to limit potentially confounding parameters that could influence the psychophysical testing results. Adaptation and plasticity occur concurrently in cortical networks, posing a challenge in isolating specific functions or dysfunctions. Since POV and DSS have a scotoma in one hemifield across the vertical meridian, they have their own control field which is their normal hemifield. Comparisons can be made across the two vertical hermifields when the same experiments are performed in both hemifields.

5.4   Aspect experiment results

Analysis of the data for the DSS age-matched control did not demonstrate a significant difference between the left and right visual hemifields. The control perceives the same range of square sprite sizes to be equal in each hemifield. This result was expected as the control had no neurological or ophthalmological pathology. It was predicted that the normal control would not have a difference between the two hemifields.

There was a statistically significant difference between the results for the two subject with homonymous paracentral scotomas (POV and DSS) and the control. This difference was demonstrated both around the scotoma and in the opposite unaffected hemifield.

For subject POV, testing was performed above the horizontal meridian, in the upper visual field. His scotoma affected his right upper visual field. When the aspect experiment was performed in the left upper quarterfield, larger square sprites were perceived to be the same size compared to the control. In the right upper quarterfield, even larger square sprites presented eccentrically to the scotoma were perceived as the same. Beyond 15 DOVA on the vertical axis, uncertainty of the sprite size decreased, as demonstrated by a smaller distribution spread. These results could suggest that in the superior hemifield, visual information within 15 DOVA from fixation is more important than information presented further eccentrically. Beyond 15 DOVA superiorly, visual processing mechanisms may discard information, in favour of central vision. There may be down-regulation of the importance of visual information beyond central vision in the superior

hemifield.

There is early crossing over of visual information in the corpus callosum. This could account for an unexpected finding of a statistically significant difference in POV's left upper quarterfield without the scotoma compared to control. Higher-order processing could have been influenced by the remaining healthy tissue in the occipital lobe surrounding the damaged area which then crosses over in the corpus callosum and influence processing of the visual field without the scotoma. The visual system could be trying to normalise the entire visual field and not just the affected hemifield. Therefore, changes in the visual spatial perception appear to influences both hemifields after damage to V1. There was a similar result for DSS, the lower quarterfield without the scotoma demonstrated statistically different responses compared to the same quarterfield in the control.

In general, there is more relevant visual information across the horizontal compared to the vertical dimension. One paper investigated 12 cases with V1 damage to test the hypothesis unilateral cortex lesions produce bilateral visual deficits [146]. They found unilateral visual cortex lesions were associated with visual processing deficits outside the fields of the classically defined scotoma and extending into the normal hemifield. The paper discussed possible underlying mechanisms and proposed damage between V1 and other areas. Damage to several connectional systems, such as callosal and feedback might explain their observations. A more recent article reviews animal models and human studies regarding the physiology of visual interhemispheric connections [147].

The results of testing in the lower hemifield for DSS were different than for POV. For DSS, his scotoma was present in his left visual hemifield. The results in his right lower quarterfield without the scotoma revealed that both smaller and larger sprite sizes were perceived as the same. In his left lower quarterfield, both smaller and larger sprite sizes were perceived to be the same when presented eccentric to his scotoma. Beyond 14 DOVA inferiorly from fixation, larger sprites were perceived to be the same. There was greater uncertainty the further away from fixation the sprite was preseented. However, within 14 DOVA inferiorly from fixation, smaller sprites were perceived to be the same. This may reflect changes in visual processing where information is pulled into the scotoma when the presented within the central field. If smaller sprites are perceived to be the same, the interactions between receptive fields could be more integrated or the area each receptive field represents could be narrower. These changes could represent reorganisation of the point-to-point retinotopic map in the inferior half of the central visual field.

The "Aspect" experiment results suggest there is a visual perceptual spatial distortion surrounding each of the two subjects' scotomas. Cortical processing of central vision and the inferior visual field may take priority over the superior visual field and the peripheral visual field. The results also raise questions whether inferior visual information processing preceeds that presented in the superior visual field; and whether information

in the superior field tends to be ignored with the inferior visual field information strengthened. In analysing these results and planning further neuropsychological experiments, it should be taken into account that central vision has more cortical volume dedicated to visual processing compared to peripheral vision.

The first study to provide psychophysical evidence for higher spatial resolution in the lower versus the upper vertical meridian, was by Talgar and Carrasco in 2002 [148]. The study also demonstrated the extent to which resolution declines is greater in the upper than in the lower vertical meridian. These findings were consistent with a previous paper by Cameron, Talgar and Carrasco [149]. These papers proposed that the spatial resolution differences along the vertical meridian could reflect ecology. They argue that in most circumstances, there is more visual information in the lower than in the upper half of the human visual field. It is possible that the inferior visual field is more important for survival. It has been proposed that the upper and lower visual fields are functionally specialised for far and near vision [150]. From the results of the "Aspect" experiment, vertical asymmetry may play a prominent role in tasks that require high resolution. Experiments performed across the horizontal meridian could pose a confounding variable for studies presenting stimuli at different locations in the visual field [148].

5.5   Location and filling-in experiment results

During the "Location" experiment testing, POV voiced unexpected observations. He experienced difficulty making his response decision as a "ghost" square would appear and stay fleetingly during each test. The ghost square was first perceived after several runs of the "Location" experiment. POV stated he knew the ghost square was not part of the experiment as he had not experienced it during the first experimental runs. The ghost square continued to appear even when tesing was performed in his normal hemifield. POV expressed he percevied the ghost square in part of his scotoma. Interestingly, the reference sprite was perceived to shift into where he though his scotoma was. These changes in his visual perception during the experiment may reflect cortical plasticity through perceptual learning. The visual hallucination that POV developed could have developed from the square test sprites creating a "memory" of a "ghost square" in his scotoma. POV has experienced a visual hallucination usually after he has a nap. When he awakes, he hallucinates one of his grandsons walking to the right side of his vision. The visual hallucination always involves the same grandson who appears to be around 15-years-old. POV explained he used to spend lots of time with this grandson at this age. Unfortunately, due to the persistence of the hallucinatory square, all further experiments with POV were ceased after the "Filling-in" experiment was attempted.

It is not clear whether DSS would have developed an after-image or hallucination square with extensive testing. DSS is a relatively young subject compared to POV with excellent stamina for performing neu-

ropsychological experiments. Exciting novel experiments that could be created and tested with DSS are ones that investigate shifting of the sprite into the scotoma and one that triggers a square hallucination after repeated trials. These experiments could investigate whether cortical plasticity from perceptual learning drives a visual percept when the subject is presented with a repeated familiar visual environment. It could be possible to investigate whether the visual system has learnt an expectation and modulates visual input accordingly.

Visual filling-in occurs rapidly and imperceptibly. The process could be due to perceptual learning from past experiences. Given a particular visual scene, the information presented might create a cognitive 'short cut' or 'best guess'. This process might be in place to reduce the burden in processing the vast amount of information presented to the visual system. Perceptual learning could be responsible for POV's ghost square or hallucinatory perseveration during the "Filling-in" experiment.

5.6 Strengths of this research

The emphasis of this thesis was to intensively investigate an early component of the human visual system in select cases with an isolated and specific cortical lesion. The investigation was performed in context and in relation to other parts of the visual system, given that the final outcome of human visual perception is to enable better interactions with the outside environment. The holism method is in contrast to the purely analytical, where attempts are made to understand entire systems by dividing them into smaller and smaller elements.

In acquired bilateral retinal disease, structural plasticity seems to be limited [151]. Robust fMRI evidence for reorganisation of the adult visual cortex is lacking. Also, fMRI studies lack spatial precision. The slow measurement timescale of fMRI obscures faster neural processes [151].

Subjects POV and DSS were extensively tested. Each subject contributed a large dataset for a small region of their visual field affected by lesions of only V1. Also, psychophysical testing did not cross left or right hemispheres, or the calcarine sulcus of each V1. This method of testing decreased other potential confounding cognitive processes in the human visual system or at least one could argue that the same processes were acting simultaneously. Therefore, the other subconscious processes could theoretically cancel each other out during the analysis of the data.

The utilisation of animal psychophysical studies to investigate visual processing is a difficult and lengthy process. The conclusions made from these studies are inferred from the behaviour of the animal that it has conscious awareness. This takes many months of work to develop and refine the methodology for experiments. It also leaves the investigators open to challenges regarding their conclusions. This thesis used

human subjects who were consciously able to express their perceptions.

5.7   Limitations of this research

As with previous research into human visual processing, this thesis is unable to establish specific mechanisms involved in cortical plasticity. Due to the small sample size, the analysis of the results has little epidemiological validity. Recruitment is difficult as it is rare to find subjects with isolated V1 lesions resulting in relatively small paracentral homonymous scotomas. Futhermore, there is difficulty finding reliable subjects for neurophysiological experiments. The creation and execution of the neuropsychological experiments performed in this thesis was time-intensive. All experimental conditions were adjusted for each subject by the author of this thesis. The validity of the results could be questioned as there was potential for subject fatigue. Response times were not recorded that could indicate potentially unreliable data. A larger response time could have flagged subject fatigue and these results could have been excluded from the analysis. The experiments were not performed in all four quadrants of the subjects POV and DSS due to time constraints. Subject POV could have had gliosis from his neurosurgery and this could have been an iatrogenic cause of his distorted visual perception. However, subject DSS had no external injury the normal healing and recovery was allowed to occur without iatrogenic interference.

Visual psychophysical equipment is highly specialised. Each piece of equipment potentially requires calibration every time it is integrated into a new experimental apparatus. To prevent goal or target directed eye movements, about 250ms are needed for a saccade to occur [152]. Unfortunately, funding was not available to purchase a dedicated eye tracker that could be integrated into experiments. Nor could one be borrowed from other groups involved in visual psychophysic experiments. Validation of the dataset could be achieved by running the behavioural experiments in an established visual psychophysics laboratory.

5.8   Translational outcomes

The results in this thesis have no direct implications for improving clinical practice for patients suffering from damage to their posterior visual pathway. The development of a screening test for visual perceptual distortion may be useful in patients who describe vague visual disturbances after occipital lobe injury. This could encourage patients to express any changes in their vision and initiate further investigations into their condition.

The article [153] contains a review of the literature on rehabilitation after acquired visual field defects. After acquiring a visual field defect, spontaneous visual behaviour modification can occur with oculomotor

strategies to compensate for the decreased visual field. The rehabilitative approaches with the most success are those aimed at transferring the maximal amount of visual scene information onto the healthy visual field. They are based upon learning to create large ocular movements towards the blind visual field. These rehabilitative methods do not enhance or restore functional vision. They also required active voluntary creation of these movements which are not useful or do not allow the individual to compensate in automatic situations. Once the presence and extent of cortical plasticity is determined, it may become possible to develop rehabilitative and restorative interventions to improve a patient's visual function and quality-of-life after suffering from lesions of the posterior visual pathway. These interventions could be tailored for the individual depending on the pathophysiology of their specific defect.

Chapter 6

Conclusion

The literature review of cerebral metamorphopsia as well as the clinical cases were not highly suggestive structural cortical reorganisation of the occipital lobes caused visual distortion due to retinotopic remapping. A theory explaining human visual consciousness has remained unobtainable despite the many avenues of research attempted by various groups world-wide from multiple disciplines. The general mechanism of the human visual system remain mysterious and enticing to discover. Without an understanding of the normal visual cortical processes, there is much difficulty in explaining the abnormalities that arise within the visual system. Meticulous methodology in experimental design as well as robust and reproducible results are the foundations for unlocking the mysteries of visual cortical processing. As more is understood about a single element of the visual system, the opportunity expands for further systematic exploration. This could lead to refinement of current theories and consensus regarding conclusions made from results of studies into this single element. It is tempting to be caught up in the current excitement regarding 'big data'. However, misguided experimentation and the resultant 'data mining' are unnecessarily costly.

In this thesis, there is sufficient data to draw preliminary conclusions and plan the next investigative steps into structual reorganisation of the visual cortex. The results from the neuropsychological experiments demonstrate there could be visual perceptual distortion after damage to the primary visual cortex. The visual perceptual distortion appears to be pulling space outwards from the defect in the upper half of the visual field, above the horizontal meridian. The distortion below the horizontal meridian appears to be pulled towards fixation. This could represent receptive fields becoming closer together in the remaining undamaged brain representing the upper half of the visual field or the higher-visual processing areas are disregarding this information. The distortion below the horizontal meridian may be caused by structural neuronal reorganisation which increases the importance of the visual information surrouding the defect,

therefore, driving the stimuli to be pulled towards fixation. It is possible, for both the distortion above and below the horizontal meridian, there is structural reorganisation of the opposite normal hemifield influencing the abnormal visual perception. It is also possible the visual distortion represents the influences of higher visual processing areas due to a lack of positive feedback from the damaged area of brain.

When designing further studies investigating visual processes, it must be kept in mind each quadrant of the visual field is subject to modulation from higher-visual processing from both within that particular hemifield as well as across it. In otherwords, there are influences from the same half of the cortical hemisphere as well as the other hemisphere. Robust conclusions cannot be made from results when experimental methodology does not take into account these variabilities.

Chapter 7

Future directions

The experimental methodology could be improved upon. The experiments could be coded to present the sprites with automatic size compensation depending on the eccentricity of its presentation from fixation. Eye tracking or monitoring during experimental testing would improve subject reliablity and accuracy of results. The availability of the subjects POV and DSS limited the extent of the experiments. If there was increased availability, testing could have been performed in all four quadrantfields, and one could then analyse how each quadrantfield differs within and between each subject.

The unexpected visual distortion detected in the hemifield without the scotoma, could be due to higher order processing. To uncover the visual spatial distortion created in the damaged V1, the data in the hemifield without the scotoma could be subtracted from the data in the opposite hemifield.

A screening test of both retinal and cerebral causes of metamorphopsia, could be invaluable. It could also be given to patients suffering from brain-damage to uncover any occult visual distortion. The test could also be part of an outreach education website informing patients suffering from metamorphopsia. This website could also be used to recruit patients for research studies. The screening test could better identify subjects for more detailed experimentation. An online profile on the website could allow them to perform screening or psychophysical testing on their own device. The results from the testing could be compiled in an online open-access database. Having a greater number of human subjects contributing to visual research could decrease and potentially cease the need for non-human primates in neuroscience research [154].

In the 2008 paper by Mavrakanas, two cases suffered from right inferior homonymous paracentral scotomas [155]. The neuropsychological testing in the paper crossed the calcarine sulcus in V1. Therefore, the visual stimulus activated neurons above and below the calcarine sulcus. These two cases could be tested using the novel experiments created in this thesis. There could be two internal controls within each subject as only

one quadrant is affected by the scotoma: 1. A mirror image test across the vertical meridian; 2. A mirror image test across the horizontal meridian. Open-source access to the code used to create my experiments could be used by these investigators to replicate my experiments with these cases and future subjects.

A cognitive neuropsychological approach could be integrated with new techniques in neuroscience. Also, the 'big data' approach could be used. However, it is important to recognise what can (and cannot) be found with these new analytical methods. New neuroimaging techniques, including functional MRI, could be performed while subjects are undergoing neuropsychophysical experiments. The focus of neuroimaging and analysis could occur in areas found to be of theoretical importance from the behavioural testing in this thesis. In particular, the subject DSS could participate in such studies, since he is relatively young and very willing to participate. He also has a lesion that is unlikely to change with time, and he is otherwise fit and healthy.

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Appendix A

Code to generate experiments and analyse results

A.1 MATLAB code

A.1.1 Acknowledgement

The code in this section generated the visual field testing experiments using the MATLAB PsychToolBox library. I am grateful to Pak Ming Wan for producing this code.

A.1.2 Scripts and Functions

For the distinction between scripts and functions, see this help page. In our situation

- `VDExperimentLauncher.m` is a script

- `VDLaunchTest.m` is a function.

A.1.3 Overview of `VDExperimentLauncher.m`

Setup of Experiment

Clear workspace, precision, setup speech object, and initialise the results matrix.

```
clear;
digits(32);

if ispc
```

213

```
    NET.addAssembly('System.Speech');
    obj = System.Speech.Synthesis.SpeechSynthesizer;
    obj.Volume = 100;
else
    obj = 1; %identify, just a placeholder
end


allResults = [];
```

Setup of Psych Toolbox

`SkipSyncTests` currently sets the timing tests off, and `VisualDebugLevel` sets the debugging level of PsychToolbox. For more on the debugging level, see this wiki.

```
Screen('Preference', 'SkipSyncTests', 1);
Screen('Preference','VisualDebugLevel', 0);
```

Select screen to run experiment (if applicable, in multi screen issue).

```
% Initialise Psych Toolbox
[screens, screenNumber] = VDInitScreen;

% force init on Other screen
[window, windowRect, screenXpixels, screenYpixels, xCenter, yCenter]
= VDBackgroundInit(screenNumber);
```

Vary `xMaxPixels` and `yMaxPixels` for testing of dynamic scaling. Otherwise set them to `screenXpixels` and `screenYpixels`.

```
xMaxPixels = screenXpixels;
yMaxPixels = screenYpixels;
```

Set the monitor size and viewing distance (`xSize`, `ySize` and `viewDistance`, all in the same units millimetres). Calculate one degree of visual angle, based on monitor size and viewing distance. `VODA!` used to calculate size of reference and variable sprites in `VDLaunchTest`.

```
xSize = 697;
ySize = 392;
viewDistance = 780;
oneDegPixels = VODACalcOneDegree(xMaxPixels, yMaxPixels, xSize,
                                 ySize, viewDistance);
```

Show Vertical lines

```
SaySomething(obj, 'Please_align_your_screen_to_these_lines');
VDDrawVertLine(window, windowRect, [1 1 1], xCenter, yCenter, oneDegPixels);
Screen('Flip', window);
    beep;
    [secs, keyCode, deltaSecs] = KbStrokeWait;
```

Read experiment runs from spreadsheet

Note that with different versions of Excel, True and False (versus 1 and 0) may be different. Recommend using 1 and 0.

```
inputConfig = xlsread('VisualDistortionExperimentConfig.xlsx');
```

Run experiment and collect results

Loop over the number of rows in the spreadsheet

```
60  for i = 1:size(inputConfig,1)
61      runConfig = inputConfig(i,:);
62      fixTargetX = runConfig(1);
63      fixTargetY = runConfig(2);
64      refSpriteDOVAX = runConfig(3);
65      refSpriteDOVAY = runConfig(4);
66      variableInputDOVAX = runConfig(5);
67      variableInputDOVAY = runConfig(6);
68      testIsHorizontal = runConfig(7);
69      refSpriteSizeDOVA = runConfig(8);
70      varSpriteSizeDOVA = runConfig(9);
71      tempResults = VDLaunchTest(window, windowRect, screenXpixels,
72                                  screenYpixels, xCenter, yCenter,
73                                  oneDegPixels, fixTargetX, fixTargetY,
74                                  refSpriteDOVAX, refSpriteDOVAY,
75                                  variableInputDOVAX, variableInputDOVAY,
76                                  testIsHorizontal, refSpriteSizeDOVA,
77                                  varSpriteSizeDOVA, obj, xSize, ySize,
78                                  viewDistance);
79      tempConfig = [fixTargetX fixTargetY refSpriteDOVAX refSpriteDOVAY
80                      variableInputDOVAX variableInputDOVAY testIsHorizontal
81                      refSpriteSizeDOVA varSpriteSizeDOVA];
82      tempConfig2 = repmat(tempConfig, [size(tempResults,1) 1]);
83      tempAllResults = horzcat(tempConfig2, tempResults);
84      allResults = [allResults; tempAllResults];
85  end
```

Lines 60-70 assign input variables from the spreadsheet into temporary variables. Lines 71-78 call `VDLaunchTest`
to perform an experiment run. Lines 79-84 append results onto results variable. For more on Matlab indexing
see this help page.

Write results and close PsychToolbox

```
VDSaveExperimentResults ( allResults );
sca;
```

A.1.4 Overview of `VDLaunchTest.m`

Function signature

```
function VDResults = VDLaunchTest (window, windowRect, screenXpixels,
                                   screenYpixels, xCenter, yCenter,
                                   oneDegPixels, fixTargetX, fixTargetY,
                                   refSpriteDOVAX, refSpriteDOVAY,
                                   variableInputDOVAX, variableInputDOVAY,
                                   testIsHorizontal, refSpriteSizeDOVA,
                                   varSpriteSizeDOVA, obj, xSize, ySize,
                                   viewDistance)
```

Setup of the experiment run

Set up reference and variable sprite rectangles based on size input to function (potential improvement:
calculate degrees of visual angle). Set up of colours (RGB) of reference and variable sprite.

```
refStimuliRect = [0  0  oneDegPixels (1)* refSpriteSizeDOVA
                  oneDegPixels (2)* refSpriteSizeDOVA ];
varStimuliRect = [0  0  oneDegPixels (1)* varSpriteSizeDOVA
                  oneDegPixels (2)* varSpriteSizeDOVA ];
stimuliColour = [0.9  0.9  0.9]; % colour of moving target
stimuliColour2 = [0.9  0.9  0.9]; % color of reference target
```

Coordinate system fix: reverse Y axis as Psychtoolbox works in the reverse direction. Set maximum number
of loops (or trials until it terminates automatically).

```
refSpriteDOVAYFix = −refSpriteDOVAY ;
variableInputDOVAYFix = −variableInputDOVAY ;
loopNum = 10;
```

Calculate DOVA in Pixels based on reference sprite position.

```
[refSpriteX, refSpriteY] = DOVAToPixels(viewDistance, screenXpixels,
                                        screenYpixels, xSize, ySize,
                                        refSpriteDOVAX, refSpriteDOVAYFix);
```

Calculate the initial staircase starting offset based on the DOVA offset input to the function.

```
if testIsHorizontal
  [tempVarStartPixels, ~] =
  DOVAToPixels(viewDistance, screenXpixels, screenYpixels,
              xSize, ySize, variableInputDOVAX, 0);
    staircaseInitErr = tempVarStartPixels-refSpriteX;
else
  [~, tempVarStartPixels] =
  DOVAToPixels(viewDistance, screenXpixels, screenYpixels,
              xSize, ySize,  0, variableInputDOVAYFix);
    staircaseInitErr = tempVarStartPixels-refSpriteY;
end
```

Initialise the variables used in the loop. Of note, it is the `staircaseCurrErr` that stores the current offset to draw the variable sprite (either up/down or left/right from the reference sprite).

```
staircaseCurrErr = abs(staircaseInitErr); %here to set current error,
                                         % initerr must have correct sign
isConverged = false; % toggle random error factors
tempResults = [];
resultType = 0;
```

Show reference stimuli

Draws background, fixation, and reference sprite, then flips the screen. Awaits a keyboard entry before proceeding.

```
VDDrawBackground(window, [0 0 screenXpixels screenYpixels], [0 0 0], xCenter, yCenter);
VDDrawFixTarget(window, stimuliColour, fixTargetX, fixTargetY);
VDDrawRectangleSafe(window, windowRect, refStimuliRect, stimuliColour2,
                    fixTargetX+refSpriteX, fixTargetY+refSpriteY);
Screen('Flip', window);
beep;
[~, keyCode, ~] = KbStrokeWait;

% start experiment
if testIsHorizontal
    %SaySomething(obj,'Horizontal test starting.');
else
    %SaySomething(obj,'Vertical test starting.');
end
```

First part of main loop to handle the variable sprite

Redraw background, fixation, and reference sprite.

```
for i = 1:loopNum


    % Reset black background
    VDDrawBackground(window, [0 0 screenXpixels screenYpixels],
                      [0 0 0], xCenter, yCenter);
    Screen('Flip', window);


    % Draw first stimuli
    VDDrawFixTarget(window, stimuliColour, fixTargetX, fixTargetY);
    Screen('Flip', window);
    beep;
    [~, keyCode, ~] = KbStrokeWait;



    % Draw fixation and reference target
    VDDrawFixTarget(window, stimuliColour, fixTargetX, fixTargetY);
    VDDrawRectangleSafe(window, windowRect, refStimuliRect, stimuliColour2,
                        fixTargetX+refSpriteX, fixTargetY+refSpriteY);
```

Draw variable sprite and await keyboard entry (either above/below or left/right or on).

```
93   % Calculate horizontal of vertical reference offset and add variable movement
94   % ramdomise approach to zero
95   tempSign = randSign();
96
97   % output staircase currerr
98
99   % NOTE: delta variables are always relative to fixation
100
101  % draw variable sprite
102  if i == 1
103      % variable sprite different on first loop
104      %[variableInputDOVAX, variableInputDOVAYFix] % for debugging
105    [tempDOVAOutX, tempDOVAOutY] =
106    DOVAToPixels(viewDistance, screenXpixels, screenYpixels, xSize, ySize,
107              variableInputDOVAX, variableInputDOVAYFix);
108      if testIsHorizontal
109          % vertical offset, variable horizontal movement
110          xDelta = staircaseInitErr
111          yOffset = tempDOVAOutY;
112          tempSign = sign(xDelta);
113          [varRealX, varRealY] =
114          VDDrawRectangleSafe(window, windowRect, varStimuliRect, stimuliColour,
115                          fixTargetX+tempDOVAOutX, fixTargetY+tempDOVAOutY)
116          xDelta = refSpriteX−varRealX; %override with real value
```

```matlab
117        else
118            % horizontal offset , variable vertical movement
119            yDelta = staircaseInitErr
120            xOffset = tempDOVAOutX;
121            tempSign = sign(yDelta);
122            [varRealX, varRealY] =
123            VDDrawRectangleSafe(window, windowRect, varStimuliRect, stimuliColour,
124                            fixTargetX+tempDOVAOutX, fixTargetY+tempDOVAOutY)
125            yDelta = varRealY−fixTargetY−refSpriteY; %override with real value / hack
126        end
127    else
128        % variable sprite for subsequent loops
129        [tempDOVAOutX, tempDOVAOutY] =
130        DOVAToPixels(viewDistance , screenXpixels , screenYpixels , xSize , ySize ,
131                    variableInputDOVAX , variableInputDOVAYFix );
132        if testIsHorizontal
133            % vertical offset , variable horizontal movement
134
135            %oneDegreeX = tempDOVAOutX; % unused
136            yOffset = tempDOVAOutY;
137            xDelta = (tempSign∗staircaseCurrErr );
138            [varRealX, varRealY] =
139            VDDrawRectangleSafe(window, windowRect, varStimuliRect, stimuliColour,
140                            fixTargetX+refSpriteX+xDelta, fixTargetY+yOffset );
141            xDelta = varRealX−refSpriteX−fixTargetX; %fix xDelta if off
142                        %screen , in theory should be the same otherwise
143        else
144            % horizontal offset , variable vertical movement
145            xOffset = tempDOVAOutX;
146            %oneDegreeY = tempDOVAOutY; %unused
147            yDelta = (tempSign∗staircaseCurrErr ); %sign change
148            [varRealX, varRealY] =
149            VDDrawRectangleSafe(window, windowRect, varStimuliRect, stimuliColour,
150                            fixTargetX+xOffset, fixTargetY+refSpriteY+yDelta);
151            yDelta = varRealY−refSpriteY−fixTargetY; %fix yDelta if off
152                        %screen , in theory should be the same otherwise
153        end
154    end
155
156    Screen('Flip', window);
157    beep;
158    [~, keyCode, ~] = KbStrokeWait;
159
160    % random convergence factor between 1−5
161    convFact = round(3∗rand)+2; %minimum of 1 required
```

Line 95: randomise approach direction – `randSign()` will return either -1 or 1. Lines 102-127: the first run is performed separately as the first position of the variable sprite as defined to the function. Line 105 is

to ensure that we have covered that location. Lines 128-155: draw the variable sprite based on the current staircase error. Line 162: calculate a random convergence factor between 2 and 5. The number of runs and this convergence formula are linked.

- See the Excel spreadsheet `RandomConvergenceEstimator` to see how the number of pixel offset will coverge over the number of runs.

- An arbitrary selection of 10 runs has been selected based on this random convergence factor.

Collect input and prepare for the next run

Here we collect keyboard input, store the input result, and update the variables for next run of the experiment (or exit the loop in the case the user thinks it is equal). First check that the keystroke press is a valid entry. Press 0 on the keyboard to abort the test.

```
if keyInputIsGood(keyCode, testIsHorizontal)
    % This is the break scenario
    if keyCode(45) == 1
        resultType = 0;
        disp(sprintf('Test aborted.'));
        break;
    end
```

If the test is horizontal:

- lines 166-180: if it is not converged, and the user selects the right location, converge the error by the random convergence factor and set the resultType = 2. If the staircase error is zero, then set the isConverged flag to true.

- lines 181-185: if it is converged, and the user thinks it is still left / right, record `resultType=3`.

- lines 186-192: if it is converged and the user thinks it is converged, record `resultType=1`, and break the loop.

- lines 193-199: if it is not converged and and user it is converged, record `resultType=5`, and break the loop.

- lines 200-206: otherwise, it is incorrect, record `resultType=4`, and stay with the same staircase error and rerun the experiment.

- lines 207-210: update the delta variable for next loop and covert delta to DOVA.

```matlab
164        if testIsHorizontal
165  % vertical offset, horizontal converging variable
166          if ~isConverged && (((tempSign == -1) && (keyCode(37) == 1))
167                              ||
168                              ((tempSign == 1) && (keyCode(39) == 1)))
169              if abs(staircaseCurrErr) > 0
170                  staircaseCurrErr = floor(abs(staircaseCurrErr) / convFact);
171              end
172              % need separate if condition, next loop will pass to next
173              % elseif block
174              if staircaseCurrErr == 0
175                  isConverged = true;
176              end
177              resultType = 2;
178              disp(sprintf('Vertical_Offset_Test:_%d', 'Response:_%s',
179                          'Current_Error:_%d', 'Convergence_Factor:_%d', i,
180                          'Correct_/_Converging', xDelta, convFact));
181          elseif isConverged && ((keyCode(37) == 1) || (keyCode(39) == 1))
182              resultType = 3;
183              disp(sprintf('Vertical_Offset_Test:_%d', 'Response:_%s',
184                          'Current_Error:_%d', i,
185                          'Incorrect_/_Already_Converged', xDelta));
186          elseif isConverged && (keyCode(12) == 1)
187              % if correct and converged, then end test
188            disp(sprintf('Vertical_Offset_Test:_%d', 'Response:_%s',
189                          'Current_Error:_%d', i, 'Correct_/_Converged',
190                          xDelta));
191              resultType = 1;
192              break;
193          elseif ~isConverged && (keyCode(12) == 1)
194              % if correct and converged, then end test
195            disp(sprintf('Vertical_Offset_Test:_%d', 'Response:_%s',
196                          'Current_Error:_%d', i, 'Incorrect_/_Not_Converged',
197                          xDelta));
198              resultType = 5;
199              break;
200          else
201              % if incorrect, keep same error
202              resultType = 4;
203              disp(sprintf('Vertical_Offset_Test:_%d', 'Response:_%s',
204                          'Current_Error:_%d', i, 'Incorrect_/_Stay_Same',
205                          xDelta));
206          end
207          resultDelta = xDelta;
208          [resultDeltaDOVA, ~] =
209          PixelsToDOVA(viewDistance, screenXpixels, screenYpixels,
210                      xSize, ySize, xDelta, 0);
```

If the test is vertical, proceed similarly to the horizontal case.

```matlab
else
    % horizontal offset, vertical converging variable
  if ~isConverged && (((tempSign == -1) && (keyCode(38) == 1)) ||
                      ((tempSign == 1) && (keyCode(40) == 1)))
        if abs(staircaseCurrErr) > 0
            staircaseCurrErr = floor(abs(staircaseCurrErr) / convFact);
        end
        % need separate if condition, next loop will pass to next
        % elseif block
        if staircaseCurrErr == 0
            isConverged = true;
        end
        disp(sprintf('Horizontal_Offset_Test:_%d', 'Response:_%s',
                    'Current_Error:_%d', 'Convergence_Factor:_%d', i,
                    'Correct_/_Converging', yDelta, convFact));
        resultType = 2;
    elseif isConverged && ((keyCode(38) == 1) || (keyCode(40) == 1))
      disp(sprintf('Horizontal_Offset_Test:_%d', 'Response:_%s',
                  'Current_Error:_%d', i, 'Incorrect_/_Already_Converged',
                  yDelta));
        resultType = 3;
    elseif isConverged && (keyCode(12) == 1)
        % if correct and converged, then end test
      disp(sprintf('Horizontal_Offset_Test:_%d', 'Response:_%s',
                  'Current_Error:_%d', i, 'Correct_/_Converged', yDelta));
        resultType = 1;
        break;
    elseif ~isConverged && (keyCode(12) == 1)
        % if correct and converged, then end test
      disp(sprintf('Horizontal_Offset_Test:_%d', 'Response:_%s',
                  'Current_Error:_%d', i, 'Incorrect_/_Not_Converged',
                  yDelta));
        resultType = 5;
        break;
    else
        % if incorrect, keep same error
      disp(sprintf('Horizontal_Offset_Test:_%d', 'Response:_%s',
                  'Current_Error:_%d', i, 'Incorrect_/_Stay_Same', yDelta));
        resultType = 4;
    end
    resultDelta = yDelta;
    [~, resultDeltaDOVA] =
    PixelsToDOVA(viewDistance, screenXpixels, screenYpixels,
                xSize, ySize, 0, yDelta);
end
```

Save results from run (for both vertical and horizontal cases).

```
[dDovaX, dDovaY] = PixelsToDOVA(viewDistance, screenXpixels,
                            screenYpixels, xSize, ySize,
                            varRealX-fixTargetX, varRealY-fixTargetY);
tempResults = [tempResults; resultType -resultDelta
            -resultDeltaDOVA dDovaX -dDovaY]; %change of sign
```

If the user pressed an incorrect key, then tell the user they pressed the wrong key.

```
    else
        % redo experiment if wrong button press
        i = i - 1;

        if testIsHorizontal
          SaySomething(obj,
                       'Press the left, right, or equal buttons only.',
                       'The test will restart.');
        else
          SaySomething(obj,
                       'Press the up, down, or equal buttons only.',
                       'The test will restart.');
        end
        disp(sprintf('Wrong keypress. Restarting experiment'));

    end

end
```

In the case where the loop exits early, this appends the results.

```
if resultType == 1 || resultType == 5 || resultType == 0
  [dDovaX, dDovaY] =
  PixelsToDOVA(viewDistance, screenXpixels, screenYpixels,
               xSize, ySize, varRealX-fixTargetX,
               varRealY-fixTargetY);
    if testIsHorizontal
        resultDelta = xDelta;
        [resultDeltaDOVA, ~] =
        PixelsToDOVA(viewDistance, screenXpixels, screenYpixels,
                     xSize, ySize, xDelta, 0);
                            % needs to be added here because of the break
    else
        resultDelta = yDelta;
        [~, resultDeltaDOVA] =
        PixelsToDOVA(viewDistance, screenXpixels, screenYpixels,
                     xSize, ySize, 0, yDelta);
    end
    tempResults =
    [tempResults; resultType -resultDelta -resultDeltaDOVA
```

```
        dDovaX −dDovaY]; % change of sign

    end
```

Set the results to the output variable and indicate to the user if the test is aborted or ended.

```
    VDResults = tempResults;

    if resultType == 0
        SaySomething(obj,'Test aborted.');
    else
        SaySomething(obj,'Test ended.');
    end
```

A.2   R code

A.2.1   Acknowledgement

The code in this section helped to organise the data of the results of the experiments, and to perform statistical tests and generate plots from this data. It was written in the statistical programming language R. I am grateful to Mark Weber for producing this code.

A.2.2   Horizontal alignment tests

Initial data processing

In the original data, the X and Y coordinates were recorded in pixels. The following function is used for conversion to DOVA.

```
    convertToDOVA <− function(spriteCoord, fixCoord, XY, pixelSize = 0.396875,
                              distToScreen = 280){
      EXP <− ifelse(XY == "X", 0, 1)
      (−1)^EXP * 180/pi * atan(pixelSize * ((spriteCoord − fixCoord)) / distToScreen)}
```

The data itself is read into R in the following block and concatenated into one big data frame called `HAlignMaster`. Prior to running this block, we organised the data into nicely-named csv files.

```
    ## initializations
    initColNames <− c("Response", "X", "Y")
    subjects <− c("Control", "PCA", "POV")
    quadrants <− c("BL", "BR", "TL", "TR")
    dataFrameList <− NULL
```

```
## Reading in the data
for (S in subjects) {
  for (Q in quadrants) {
    stringName <- paste(S, "HAlign", Q, sep = "")
    assign(stringName, read.csv(paste("../PhD-Data/", S, "/HAlign",
                                       Q, ".csv", sep = ""),
                                col.names = initColNames))
    numRows <- do.call(nrow, list(as.name(stringName)))
    assign(stringName, cbind(get(stringName), "Quadrant" = rep(Q, numRows)))
    assign(stringName, cbind(get(stringName), "Subject" = rep(S, numRows)))
    dataFrameList <- c(dataFrameList, list(as.name(stringName)))}}


## Concatenating the data
HAlignMaster <- do.call(rbind, dataFrameList)
```

Next we do some house keeping: the responses are given more meaningful names, the DOVA conversions are carried out, and unneeded columns are discarded.

```
HAlignMaster$Response <- sapply(HAlignMaster$Response,
                                function(x){
                                  switch(as.character(x),
                                         "AA" = "Up", "BB" = "Down",
                                         "CC" = "Straight")})
yFix <- c(308, 308, 100, 100)
HAlignMaster$Y_DOVA <- mapply(function(y, q){
  switch(as.character(q), "TL" = convertToDOVA(y, yFix[1], "Y"),
         "TR" = convertToDOVA(y, yFix[2], "Y"),
         "BL" = convertToDOVA(y, yFix[3], "Y"),
         "BR" = convertToDOVA(y, yFix[4], "Y"))},
  HAlignMaster$Y, HAlignMaster$Quadrant)
HAlignMaster <- subset(HAlignMaster, select = -c(X, Y))
```

Data wrangling for plotting

We need to arrange the data in the form appropriate for ggplot to create stacked histograms. First we produce an intermediate data frame `HAlignProps` containing the proportions of Up, Down and Straight responses.

```
HAlignProps <- do.call(data.frame,
                       aggregate(. ~ Quadrant + Subject + Y_DOVA,
                                 data = HAlignMaster,
                                 FUN = function(x){
                                   c(sum("Up" == x)/length(x),
                                     sum("Down" == x)/length(x),
                                     sum("Straight" == x)/length(x))}))
names(HAlignProps)[4:6] <- c("Up", "Down", "Straight")
```

This data frame is not yet in the form required by `ggplot2`'s plotting function. This is rectified in the following block, resulting in the data frame `HAlignPlotData`.

```r
## Put data into the form for plotting
HAlignProps_Up <- subset(HAlignProps, select = c(c(Quadrant, Subject, Y_DOVA), Up))
HAlignProps_Up <- cbind(HAlignProps_Up, Response = rep("Up", nrow(HAlignProps_Up)))
names(HAlignProps_Up)[4] <- "Proportion"
HAlignProps_Down <- subset(HAlignProps,
                          select = c(c(Quadrant, Subject, Y_DOVA), Down))
HAlignProps_Down <- cbind(HAlignProps_Down,
                          Response = rep("Down", nrow(HAlignProps_Down)))
names(HAlignProps_Down)[4] <- "Proportion"
HAlignProps_Straight <- subset(HAlignProps,
                              select = c(c(Quadrant, Subject, Y_DOVA), Straight))
HAlignProps_Straight <- cbind(HAlignProps_Straight,
                              Response = rep("Straight",
                                            nrow(HAlignProps_Straight)))
names(HAlignProps_Straight)[4] <- "Proportion"
HAlignPlotData <- rbind(HAlignProps_Up, HAlignProps_Down, HAlignProps_Straight)
## Break up Quadrant column into Vertical and Horizontal for faceting
## and order these correctly
HAlignPlotData$Vertical <- factor(sapply(HAlignPlotData$Quadrant,
                                        function(x){
                                            strsplit(as.character(x),
                                                    split = "")[[1]][1]}),
                                   levels = c("T", "B"),
                                   labels = c("Top", "Bottom"))
HAlignPlotData$Horizontal <- factor(sapply(HAlignPlotData$Quadrant,
                                        function(x){
                                            strsplit(as.character(x),
                                                    split = "")[[1]][2]}),
                                   levels = c("L", "R"),
                                   labels = c("Left", "Right"))
HAlignPlotData <- subset(HAlignPlotData, select = -c(Quadrant))
```

This data frame has 687 observations and the following columns.

Column Name	Description
$ Subject	Factor w/ 3 levels "Control","PCA Case",..
$ Y_{DOVA}	num -24.4 -23.7 -23 -23 -22.3 …
$ Proportion	num 0 0 0.143 0 0 …
$ Response	Factor w/ 3 levels "Up","Down","Straight"
$ Vertical	Factor w/ 2 levels "Top","Bottom"
$ Horizontal	Factor w/ 2 levels "Left","Right"

Plotting function

Our plotting function `HAlignHist` takes a data frame and an output file path, and prints the response histogram to a PDF file with the given file name. In practice the data frame will be subsetted from `HAlignPlotData` by `Subject`.

```
HAlignHist <- function(DATA, OUTPATH){
  HIST <- ggplot(data = DATA, aes(x = Y_DOVA, y = Proportion, fill = Response))
  HIST <- HIST + geom_bar(stat = "identity")
  HIST <- HIST + coord_flip()
  HIST <- HIST + facet_grid(DATA$Vertical ~ DATA$Horizontal,
                            scales = "free_y", space = "free")
  pdf(file = OUTPATH)
  print(HIST)
  dev.off()}
```

The plots contained in Figures 3.4-3.6, are produced by our function via the following code.

```
lapply(c("Control", "POV", "PCA"),
       function(S){HAlignHist(subset(HAlignPlotData, Subject == S),
                              paste("../Plots/", S, "HorAlign.pdf", sep = ""))})
```

Producing contingency tables for statistical tests

For the sake of producing contingency tables easily, we'll use a variant of the `HAlignProps` data frame in which proportions are replaced by counts, which we call `HAlignCTable`.

```
HAlignCTable <- do.call(data.frame,
                        aggregate(. ~ Quadrant + Subject + Y_DOVA,
                                  data = HAlignMaster,
                                  FUN = function(x){
                                    c(sum("Up" == x),
                                      sum("Down" == x),
                                      sum("Straight" == x))}))
names(HAlignCTable)[4:6] <- c("Up", "Down", "Straight")
HAlignCTable$Side <- sapply(HAlignCTable$Quadrant,
                            function(x){
                              strsplit(as.character(x),
                                       split = "")[[1]][2]})
HAlignCTable <- subset(HAlignCTable, select = -c(Quadrant))
```

Next we provide the function `RespCount` which carries out the response counts, and `RespTable` which produces contingency tables in all the cases of interest. The contingency tables are output as matrices with rows and columns labelled in the appropriate way, this being the required input form for R's contingency table testing functions.

```r
RespCount <- function(RESPONSE, SUBJECT, YMIN, YMAX, SIDE){
  sum(subset(HAlignCTable,
             Subject == SUBJECT & Y_DOVA >= YMIN & Y_DOVA <= YMAX & Side == SIDE,
             c(RESPONSE)))}
RespTable <- function(SUBJECT1, SIDE1, SUBJECT2, SIDE2, YMIN, YMAX){
  Responses <- c("Up", "Down", "Straight")
  CT <- matrix(c(sapply(Responses,
                        function(R){
                          RespCount(R, SUBJECT1, YMIN, YMAX, SIDE1)},
                        USE.NAMES = FALSE),
                 sapply(Responses,
                        function(R){
                          RespCount(R, SUBJECT2, YMIN, YMAX, SIDE2)},
                        USE.NAMES = FALSE)),
               ncol = 2)
  rownames(CT) <- Responses
  if (SUBJECT1 == SUBJECT2) {colnames(CT) <- c(SIDE1, SIDE2)}
  else {colnames(CT) <- c(SUBJECT1, SUBJECT2)}
  CT}
```

Statistical tests

The function `LeftRightFisher` produces tables with Fisher p-values comparing LVF and RVF for individual subjects. The output is a table giving Fisher p-values for each height, whenever there is data in both the LVF and RVF, and whenever this p-value is strictly less than 1.

```r
SigOutput <- function(p){
  if (p < 0.00001) {"p < 0.00001"}
  else {
    if (p < 0.0001) {"p < 0.0001"}
    else {
      if (p < 0.001) {"p < 0.001"}
      else {
        if (p < 0.01) {"p < 0.01"}
        else {
          if (p < 0.05) {"p < 0.05"}
          else {
            if (p == 0.05) {"p = 0.05"}
            else {paste("p = ",
                        as.character(formatC(p, digits = 4, format = "f"))
                        )}}}}}}
LeftRightFisher <- function(SUBJECT){
  TABLE <- data.frame(UnformattedY = unique(
                        intersect(
                          subset(HAlignCTable, Subject == SUBJECT
                                 & Side == "L")$Y_DOVA,
```

```
                              subset(HAlignCTable, Subject == SUBJECT
                                   & Side == "R")$Y_DOVA)))
    TABLE$Y_DOVA <- sapply(TABLE$UnformattedY,
                              function(y){formatC(y, digits = 2, format = "f")})
    TABLE$Fisher.p.value <- sapply(TABLE$UnformattedY,
                                   function(Y){
                                        fisher.test(
                                           RespTable(SUBJECT, "L", SUBJECT, "R", Y, Y)
                                        )$p.value},
                                   USE.NAMES = FALSE)
    TABLE$"Fisher_Test" <- sapply(TABLE$Fisher.p.value, SigOutput,
                                   USE.NAMES = FALSE)
    subset(TABLE, Fisher.p.value < 1, -c(UnformattedY, Fisher.p.value))}
```

The next block provides the general function `SubConFisher` for producing similar tables of Fisher p-values for subject vs control tests.

```
SubConFisher <- function(SUBJECT, SIDE){
    TABLE <- data.frame(UnformattedY = intersect(
                              unique(subset(HAlignCTable, Subject == "Control"
                                   & Side == SIDE)$Y_DOVA),
                              unique(subset(HAlignCTable, Subject == SUBJECT
                                   & Side == SIDE)$Y_DOVA)))
    TABLE$Y_DOVA <- sapply(TABLE$UnformattedY,
                              function(y){
                                 formatC(y, digits = 2, format = "f")})
    TABLE$Fisher.p.value <- sapply(TABLE$UnformattedY,
                                   function(Y){
                                        fisher.test(
                                           RespTable("Control", SIDE, SUBJECT,
                                                       SIDE, Y, Y))$p.value},
                                   USE.NAMES = FALSE)
    TABLE$"Fisher_Test" <- sapply(TABLE$Fisher.p.value, SigOutput,
                                   USE.NAMES = FALSE)
    subset(TABLE, Fisher.p.value < 1, -c(UnformattedY, Fisher.p.value))}
```

A.2.3   Scotoma mapping

The raw data is read in as 2 data frames `POVScoMapData` and `DSSScoMapData`, one for each subject. The code in this section produces plots of the scotomas from this data. First we provide the function `ScoMapWrangle`, which outputs the input data frame for plotting. This data frame has 3 columns – the `x` and `y` degrees of visual angle, and the proportion of responses indicating that the sprite was seen (computed as the mean of the (`0, 0.5, 1`) responses at each location).

```
DSSRespFunc <- function(N){ifelse(N != 2, N, 0.5)}
POVRespFunc <- function(N){ifelse(N != 1, DSSRespFunc(2-N), N)}
ScoMapWrangle <- function(DATA, RESPFUNC, SPRITESIZE){
  RD <- DATA[DATA$SpriteSize == SPRITESIZE, c(3,4,6)]
  RD$ResponseType <- vapply(RD$ResponseType, RESPFUNC,
                             FUN.VALUE = numeric(1))
  GI <- aggregate(RD, list(RD$VariableXDOVA, RD$VariableYDOVA), mean)[3:5]
  names(GI) <- c("x_DOVA", "y_DOVA", "Response")
  GI}
```

Next we provide the plotting function. Each call of this function produces a PDF containing a plot which maps a subject's scotoma.

```
ScoMapPlot <- function(DATA, RESPFUNC, SPRITESIZE, BOXSIZE, OUTPATH){
  library(ggplot2)
  InDATA <- ScoMapWrangle(DATA, RESPFUNC, SPRITESIZE)
  PLOT <- ggplot(InDATA, aes(x=x_DOVA, y=y_DOVA, colour=Response))
  PLOT <- PLOT + geom_point(shape=15, size=BOXSIZE)
  PLOT <- PLOT + scale_colour_gradient(low="black", high="yellow")
  PLOT <- PLOT + coord_fixed(ratio = 1)
  pdf(file = OUTPATH)
  print(PLOT)
  dev.off()}
```

This function is then applied to the previously entered data in the following way.

```
ScoMapPlot(POVScoMapData, POVRespFunc, 2.5, 1.75,
           "../Plots/POVScoMap-2.5.pdf")
ScoMapPlot(POVScoMapData, POVRespFunc, 5, 4.5,
           "../Plots/POVScoMap-5.pdf")
ScoMapPlot(DSSScoMapData, DSSRespFunc, 2, 5,
           "../Plots/DSSScoMap-2.pdf")
ScoMapPlot(SSScoMapData, DSSRespFunc, 3, 5,
           "../Plots/DSSScoMap-3.pdf")
```

A.2.4   Aspect

Calculation of perceived sprite sizes

The usual mathematical transformation between rectangular and angular-based coordinates is the polar transformation. Here

$$r = \text{length of the vector}$$

$$\theta = \text{angle in the x-y plane}$$

$$\psi = \text{angle over the x-y plane}$$

The polar-to-rectangular transformation is:

$$(r, \theta, \psi) \mapsto (r\cos(\theta)\cos(\psi),\ r\sin(\theta)\cos(\psi),\ r\sin(\psi))$$

and its inverse transformation is:

$$(x, y, z) \mapsto \left(\sqrt{x^2 + y^2 + z^2},\ \arcsin(\frac{y}{\sqrt{x^2+y^2}}),\ \arctan(\frac{z}{\sqrt{x^2+y^2}}) \right)$$

and is valid when $(x, y) \neq (0, 0)$. The conversion between rectangular coordinates and coordinates expressed in degrees of visual angle (DOVA) is different to this, and is simpler.

In terms of visual field experiments, one of the three coordinates, let's say z, measures the (minimal) distance between the observer and the screen, and the points on the screen are referenced by the other coordinates (x, y) together. We will use the acronymn "ROVA" for the units of "radians of visual angle". Transforming from ROVA to rectangular coordinates is done as follows:

$$(x_{\text{ROVA}},\ y_{\text{ROVA}},\ z) \quad \mapsto \quad (z\tan(x_{\text{ROVA}}),\ z\tan(y_{\text{ROVA}}),\ z)$$

and the inverse transformation

$$(x,\ y,\ z) \quad \mapsto \quad (\arctan(\tfrac{x}{z}),\ \arctan(\tfrac{y}{z}),\ z)$$

is valid when $z \neq 0$. Converting between ROVA and DOVA is just a matter of converting between radians and degrees:

$$\text{ROVA} = \tfrac{\pi}{180} \cdot \text{DOVA} \qquad \text{DOVA} = \tfrac{180}{\pi} \cdot \text{ROVA}.$$

Putting this together, the transformation from DOVA to rectangular coordinates is given by

$$(x_{\text{DOVA}},\ y_{\text{DOVA}},\ z) \quad \mapsto \quad (z\tan(\tfrac{\pi}{180} \cdot x_{\text{DOVA}}),\ z\tan(\tfrac{\pi}{180} \cdot y_{\text{DOVA}}),\ z)$$

and the inverse transformation (valid for $z \neq 0$) is given by

$$(x,\ y,\ z) \quad \mapsto \quad \left(\tfrac{180}{\pi}\arctan(\tfrac{x}{z}),\ \tfrac{180}{\pi}\arctan(\tfrac{y}{z}),\ z \right).$$

Our basic correction starts with the DOVA coordinates and the origin-based size of one sprite. Let (c_x, c_y) be the DOVA-coordinates (at the centre of the sprite), d be the distance between the observer and

the screen (from eye to fixation point), and s be the side-length of the square sprite (at the origin). For convenience, we denote the function τ by $\tau(t) = \tan(\frac{\pi}{180}t)$, which is the tan function with angles measured in degrees.

Each point of the sprite whose true area we wish to determine is calculated as follows. Take a point (p, q) of the square centred at $(0, 0)$ of side length s, these coordinates and the length s being in DOVA. So p and q are both in the interval $[-\frac{s}{2}, \frac{s}{2}]$ on the real number line. Now we transform to rectangular. This gives $(d\tau(p), d\tau(q))$. Then we translate, which amounts to addition by the vector $(d\tau(c_x), d\tau(c_y))$, so this translated vector is

$$d \cdot (\tau(c_x) + \tau(p), \tau(c_y) + \tau(q))$$

which is then transformed back into DOVA. We denote the result of doing so as

$$f(p, q) := \frac{180}{\pi} \cdot (\arctan(\tau(c_x) + \tau(p)), \arctan(\tau(c_y) + \tau(q))) := (f_1(p), f_2(q))$$

Let's denote by S the original square at the origin, which as a subset of $\mathbb{R}^2$ is $[-\frac{s}{2}, \frac{s}{2}] \times [-\frac{s}{2}, \frac{s}{2}]$. Let us denote by T the result of transforming S in the manner just described. In other words, T is the sprite whose area we want, with its points expressed in DOVA coordinates. So in terms of our notation $T = f(S)$, that is to say $T = \{f(p, q) : (p, q) \in S\}$. Since $f(p, q)$ is of the form $(f_1(p), f_2(q))$, and both f_1 and f_2 are monotone increasing, T is a rectangle whose sides are parallel to the coordinate axes, and the vertices of T are the result of applying f to the corresponding vertices of S. Thus its side-length in the x-direction (in DOVA) is

$$\frac{180}{\pi} \cdot \left(\arctan\left(\tau(c_x) + \tau(\frac{s}{2}) \right) - \arctan\left(\tau(c_x) - \tau(\frac{s}{2}) \right) \right)$$

and its length in the y-direction is

$$\frac{180}{\pi} \cdot \left(\arctan\left(\tau(c_y) + \tau(\frac{s}{2}) \right) - \arctan\left(\tau(c_y) - \tau(\frac{s}{2}) \right) \right)$$

and so its area is the product of these last two quantities. Next, we turn to the expression of this adjustment into R code.

Adding true lengths and areas to the data

Here we express the algebraic expressions for true area and length derived above, in terms of R code, giving functions `TrueLength` and `TrueArea` which will be used below. `TrueLength` takes a given sprite size and a given coordinate (which could be an x or a y-coordinate), and produces the DOVA-corrected side-length

of the sprite (in the x or y-direction as the case may be). `TrueArea` provides the corresponding sprite area correction.

```
tanDEG <- function(t){tan((pi * t)/180)}
TrueLength <- function(SPRITESIZE, COORD){
   (180/pi) * (atan(tanDEG(COORD) + tanDEG(SPRITESIZE/2))
     - atan(tanDEG(COORD) - tanDEG(SPRITESIZE/2)))}
TrueArea <- function(SPRITESIZE, XCOORD, YCOORD){
   TrueLength(SPRITESIZE, XCOORD) * TrueLength(SPRITESIZE, YCOORD)}
```

In the following block, the initial Aspect data frames `POVAspData`, `DSSAspData` and `ControlAspData` were amalgamated, and extra columns for DOVA sprite size corrections were added.

```
AspectMaster_P <- cbind(POVAspData,
                        Subject = rep("POV", length.out = nrow(POVAspData)))
AspectMaster_D <- cbind(DSSAspData,
                        Subject = rep("DSS", length.out = nrow(DSSAspData)))
AspectMaster_C <- cbind(ControlAspData,
                        Subject = rep("Control", length.out = nrow(ControlAspData)))
AspectMaster <- rbind(AspectMaster_P, AspectMaster_D, AspectMaster_C)
AspectMaster$TrueRX <- TrueLength(AspectMaster$ReferenceSpriteSize,
                                  AspectMaster$ReferenceXDOVA)
AspectMaster$TrueRY <- TrueLength(AspectMaster$ReferenceSpriteSize,
                                  AspectMaster$ReferenceYDOVA)
AspectMaster$TrueRA <- TrueArea(AspectMaster$ReferenceSpriteSize,
                                AspectMaster$ReferenceXDOVA,
                                AspectMaster$ReferenceYDOVA)
AspectMaster$TrueVX <- TrueLength(AspectMaster$VariableSpriteSize,
                                  AspectMaster$VariableXDOVA)
AspectMaster$TrueVY <- TrueLength(AspectMaster$VariableSpriteSize,
                                  AspectMaster$VariableYDOVA)
AspectMaster$TrueVA <- TrueArea(AspectMaster$VariableSpriteSize,
                                AspectMaster$VariableXDOVA,
                                AspectMaster$VariableYDOVA)
AspectMaster$DiffAreas <- sqrt(AspectMaster$TrueVA) - sqrt(AspectMaster$TrueRA)
```

Data wrangling for coloured scatter plots

The following code block produces the data frames `POVModAspForPlot` and `DSSModAspForPlot` appropriate for feeding into the plotting function which produces the coloured scatter plots. The first part of this block adds an extra column `DACat` to `AspectMaster` which is a version of `DiffAreas` made categorical by being broken up into intervals of width 0.45 (as discussed in the main body of the thesis).

```
AspectMaster$DACat <- as.character(cut(AspectMaster$DiffAreas,
                                       breaks = centredSeq(-2.5, 5, 0.45)))
MidPtTable <- data.frame(interval = levels(as.factor(AspectMaster$DACat)),
```

```
                    midpoint = c(0.00, -0.45, -0.90, -1.35, -1.80,
                                 -2.25, 0.45, 0.90, 1.35, 1.80, 2.25,
                                 2.71, 3.16, 3.61, 4.05, 4.50))
MidPtFunc <- function(INTERVAL){MidPtTable[MidPtTable$interval == INTERVAL, 2]}
AspectMaster$DACat <- sapply(AspectMaster$DACat, MidPtFunc, USE.NAMES = FALSE)
RedModPOVAsp <- droplevels(subset(AspectMaster,
                           Subject != "DSS" & ReferenceYDOVA >= 0,
                           select = c("VariableXDOVA", "VariableYDOVA",
                                        "DACat", "ResponseType",
                                        "Subject")))
POVModAspForPlot <- do.call(data.frame,
                           aggregate(. ~ VariableXDOVA + VariableYDOVA +
                                         DACat + Subject,
                                     data = RedModPOVAsp, FUN = mean))
names(POVModAspForPlot) <- c("X_DOVA", "Y_DOVA", "SpriteSize",
                             "Subject", "Response")
RedModDSSAsp <- droplevels(subset(AspectMaster,
                           Subject != "POV" & ReferenceYDOVA <= 0,
                           select = c("VariableXDOVA", "VariableYDOVA",
                                        "DACat", "ResponseType", "Subject")))
DSSModAspForPlot <- do.call(data.frame,
                           aggregate(. ~ VariableXDOVA + VariableYDOVA +
                                         DACat + Subject,
                                     data = RedModDSSAsp, FUN = mean))
names(DSSModAspForPlot) <- c("X_DOVA", "Y_DOVA", "SpriteSize",
                             "Subject", "Response")
```

Plotting function for coloured scatter plots

These plots are implemented by a function `AspPlot`, which creates the PDF containing the plot. The variable of interest is a number between 0 and 1 measuring the response (1 means all instances the sprites were seen as the same size, 0 means that the sprites were seen as being of different sizes). This response variable is indicated on the graph by colour, with yellow corresponding to 1, black to 0, and numbers strictly between 0 and 1 to an appropriate mixture of these colours (as discussed above).

```
AspPlot <- function(DATA, BOXSIZE, YXRATIO, OUTPATH){
  library(ggplot2)
  PLOT <- ggplot(DATA, aes(x=X_DOVA, y=Y_DOVA, colour=Response))
  PLOT <- PLOT + geom_point(shape=15, size=BOXSIZE)
  PLOT <- PLOT + scale_colour_gradient(low="black", high="yellow", limits=c(0,1))
  PLOT <- PLOT + coord_fixed(ratio = YXRATIO)
  PLOT <- PLOT + facet_grid(DATA$SpriteSize ~ DATA$Subject)
  pdf(file = OUTPATH)
  print(PLOT)
  dev.off()}
```

For example, the following code produces a plot of the comparison between POV and Control, for variable sprite sizes between 2 and 6, and on the left visual field.

```
AspPlot(POVAspForPlot[POVAspForPlot$"Sprite_Size" >= 2
                      & POVAspForPlot$"Sprite_Size" <= 6
                      & POVAspForPlot$X_DOVA < 0, ],
        1, 0.2, "../Plots/POVAspOverlap-left.pdf")
```

In practice the values of box-size and yx-ratio were set by trial and error. As another example, the following code produces plots for each sprite size individually, comparing DSS and Control, for the right visual field.

```
for (i in seq(2,6,0.5)) {
  AspPlot(DSSAspForPlot[DSSAspForPlot$"Sprite_Size" == i
                        & DSSAspForPlot$X_DOVA > 0, ],
          14.5, 0.3,
          paste("../Plots/DSSAsp-right-", as.character(i), ".pdf", sep = ""))}
```

Response vs sprite size histograms

As with other plotting code, we first prepare the data so that it is in a form to be received by the plotting function. This is the content of the following block, which culminates in the function `StackedHistWrangle` which produces an R data frame of the appropriate form for a single subject.

```
VectorsToFunction <- function(INPUT, OUTPUT){
  TABLE <- data.frame(input = INPUT, output = OUTPUT)
  function(x) {TABLE[x,2]}}
MidPoints <- function(LOWER, UPPER, STEP){
  SEQ <- centredSeq(LOWER, UPPER, STEP)
  VectorsToFunction(1:(length(SEQ)-1), seq(min(SEQ) + STEP/2, max(SEQ), STEP))}
RespSizeSpreadWrangle <- function(SUBJECT, WIDTH, AGGFUN){
  RD <- subset(AspectMaster, Subject == SUBJECT ,
               c(ReferenceXDOVA, ReferenceYDOVA, ResponseType, DiffAreas))
  RD$DACat <- findInterval(RD$DiffAreas, centredSeq(-2.5, 5, WIDTH))
  RD$DACat <- MidPoints(-2.5, 5, WIDTH)(RD$DACat)
  RD <- subset(RD, , -c(DiffAreas))
  FINDATA <- do.call(data.frame,
                     aggregate(. ~ ReferenceXDOVA + ReferenceYDOVA + DACat,
                               data = RD, FUN = AGGFUN))
  names(FINDATA) <- c("X_DOVA", "Y_DOVA", "SpriteSize", "Response")
  FINDATA}
StackedHistWrangle <- function(SUBJECT, WIDTH){
  SameDATA <- RespSizeSpreadWrangle(SUBJECT, WIDTH, mean)
  names(SameDATA)[4] <- "Proportion"
  DiffDATA <- SameDATA
  DiffDATA$Proportion <- 1-DiffDATA$Proportion
  SameDATA$Response <- rep("Same", nrow(SameDATA))
```

```
DiffDATA$Response <- rep("Different", nrow(DiffDATA))
rbind(SameDATA, DiffDATA)}
```

The plots themselves are produced by the following code block. The function `StackedComparisonPlot` first combines the data for the two subjects being compared, and then produces a PDF containing the plot.

```
StackedComparisonPlot <- function(CDATA, SDATA, SNAME, LeftRight){
  DATA_C <- subset(CDATA, select = -c(X_DOVA))
  DATA_C$Subject <- rep("Control", nrow(DATA_C))
  DATA_S <- subset(SDATA, select = -c(X_DOVA))
  DATA_S$Subject <- rep(SNAME, nrow(DATA_S))
  DATA <- rbind(DATA_C, DATA_S)
  PLOT <- ggplot(data = DATA,
                   aes(x = SpriteSize, y = Proportion,
                       fill = Response))
  PLOT <- PLOT + geom_bar(stat = "identity")
  PLOT <- PLOT + facet_grid(DATA$Y_DOVA ~ DATA$Subject)
  PLOT <- PLOT + scale_fill_manual(values=c("black","yellow"))
  pdf(file = paste("../Plots/AspectStacked-", SNAME,
                     "Control-", LeftRight, ".pdf", sep = ""))
  print(PLOT)
  dev.off()}
## POV vs Control stacked histogram on the left
StackedComparisonPlot(subset(StackedHistWrangle("Control", 0.45),
                             X_DOVA <= 0 & Y_DOVA >= 9 & Y_DOVA <= 15),
                      subset(StackedHistWrangle("POV", 0.45),
                             X_DOVA <= 0 & Y_DOVA >= 9 & Y_DOVA <= 15),
                      "POV", "Left")
## POV vs Control stacked histogram on the right
StackedComparisonPlot(subset(StackedHistWrangle("Control", 0.45),
                             X_DOVA == 3 & Y_DOVA >= 9 & Y_DOVA <= 15),
                      subset(StackedHistWrangle("POV", 0.45),
                             X_DOVA == 3 & Y_DOVA >= 9 & Y_DOVA <= 15),
                      "POV", "Right")
## DSS vs Control stacked histogram on the left
StackedComparisonPlot(subset(StackedHistWrangle("Control", 0.45),
                             X_DOVA <= 0 & Y_DOVA <= 0),
                      subset(StackedHistWrangle("DSS", 0.45),
                             X_DOVA <= 0),
                      "DSS", "Left")
## DSS vs Control stacked histogram on the right
StackedComparisonPlot(subset(StackedHistWrangle("Control", 0.45),
                             X_DOVA >= 0 & Y_DOVA <= 0),
                      subset(StackedHistWrangle("DSS", 0.45),
                             X_DOVA >= 0),
                      "DSS", "Right")
```

Producing contingency tables for statistical tests

The following code block culminates in the function `SRTable` which produces contingency tables, as appropriately labelled 2-by-2 matrices, in all the situations of interest. It is quite general, being applicable whether one is using unadjusted sprite sizes or DOVA-adjusted sprite sizes.

```r
DiffAreaInt <- function(LBOUND, UBOUND){
  AspectMaster$DiffAreas <= UBOUND
  & AspectMaster$DiffAreas >= LBOUND}

SpriteSizeRange <- function(LBOUND, UBOUND){
  AspectMaster$VariableSpriteSize <= UBOUND
  & AspectMaster$VariableSpriteSize >= LBOUND}

NarrowResp <- function(SUBJECT, TB, LR, SSRDAI, LBOUND, UBOUND){
  SUBVECT <- AspectMaster$Subject == SUBJECT
  if (TB == "Top" || TB == "Superior") {
    TBVECT <- AspectMaster$ReferenceYDOVA >= 0}
  else {TBVECT <- AspectMaster$ReferenceYDOVA <= 0}
  if (LR == "Left") {
    LRVECT <- AspectMaster$ReferenceXDOVA <= 0}
  else {LRVECT <- AspectMaster$ReferenceXDOVA >= 0}
  if (SSRDAI == "SSR") {
    SIZEVECT <- SpriteSizeRange(LBOUND, UBOUND)
    COLS <- c("VariableXDOVA", "VariableYDOVA",
              "VariableSpriteSize", "ResponseType")}
  else {
               SIZEVECT <- DiffAreaInt(LBOUND, UBOUND)
               COLS <- c("VariableXDOVA", "VariableYDOVA",
                         "DiffAreas", "ResponseType", "Subject")}
  RDATA <- AspectMaster[SUBVECT & TBVECT & LRVECT & SIZEVECT, COLS]
  RDATA}

SameResponses <- function(SUBJECT, TB, LR, SSRDAI, LBOUND, UBOUND){
  DATA <- NarrowResp(SUBJECT, TB, LR, SSRDAI, LBOUND, UBOUND)
  sum(DATA$ResponseType)}

DifferentResponses <- function(SUBJECT, TB, LR,
                                     SSRDAI, LBOUND, UBOUND){
  DATA <- NarrowResp(SUBJECT, TB, LR, SSRDAI, LBOUND, UBOUND)
  nrow(DATA) - sum(DATA$ResponseType)}

SRTable <- function(SUBJECT1, TB1, LR1, SUBJECT2, TB2, LR2,
                      SSRDAI, LBOUND, UBOUND){
  CT <- matrix(c(SameResponses(SUBJECT1, TB1, LR1, SSRDAI, LBOUND, UBOUND),
                 SameResponses(SUBJECT2, TB2, LR2, SSRDAI, LBOUND, UBOUND),
                 DifferentResponses(SUBJECT1, TB1, LR1, SSRDAI, LBOUND, UBOUND),
```

```
                    DifferentResponses(SUBJECT2, TB2, LR2, SSRDAI, LBOUND, UBOUND)),
              nrow = 2)
  if (SUBJECT1 != SUBJECT2) {rownames(CT) <- c(SUBJECT1, SUBJECT2)}
  else {rownames(CT) <- c(paste(TB1, LR1), paste(TB2, LR2))}
  colnames(CT) <- c("Same", "Different")
  CT}
```

Here is an example of this code in action. The following function call

```
SRTable("DSS", "Bottom", "Left",
        "DSS", "Bottom", "Right",
        "DAI", -0.45, 0.45)
```

generates the contingency table

	Same	Different
Bottom Left	195	111
Bottom Right	269	43

which compares the responses for DSS in the bottom left and bottom right quadrants, for a given DOVA-adjusted relative sprite size range (-0.45 to 0.45). The "DAI" parameter tells `SRTable` to use DOVA-adjusted relative sprite sizes.

Statistical tests

In this section we provide functions which are used to give tables of Fisher test p-values. The first of these for the case of individual subject tests, is `DOVAAdjustedIndSubTests`, which has an argument for the width of the adjusted sprite size intervals being examined.

```
SubjectIntervals <- function(SUBJECT, STEP){
  DATA <- subset(AspectMaster, Subject == SUBJECT)
  do.call(centredSeq, list(min(DATA$DiffArea) - STEP,
                           max(DATA$DiffArea) + STEP, STEP))}


DOVAAdjustedIndSubTests <- function(STEP){
  ControlInt <- SubjectIntervals("Control", STEP)
  POVInt <- SubjectIntervals("POV", STEP)
  DSSInt <- SubjectIntervals("DSS", STEP)
  TABLE <- data.frame(Subject = c(rep("Control",
                                      2 * (length(ControlInt)-1)),
                                  rep("POV", length(POVInt)-1),
                                  rep("DSS", length(DSSInt)-1)))
  TABLE$LBound <- c(as.vector(sapply(
    ControlInt[-length(ControlInt)], function(x) rep(x,2))),
    POVInt[-length(POVInt)], DSSInt[-length(DSSInt)])
  TABLE$UBound <- c(as.vector(sapply(ControlInt[-1],
```

```
                                    function(x) rep(x,2))),
                   POVInt[−1], DSSInt[−1])
  TABLE$Verticality <− c(rep(c("Superior", "Inferior"),
                          length(ControlInt)−1),
                       rep("Superior", length(POVInt)−1),
                       rep("Inferior", length(DSSInt)−1))
  TABLE$Fisher.p.value <− mapply(function(S, V, L, U){
    fisher.test(SRTable(S, V, "Left", S, V, "Right",
                        "DAI", L, U))$p.value},
    TABLE$Subject, TABLE$Verticality, TABLE$LBound, TABLE$UBound)
  TABLE$"Fisher_Test" <− sapply(TABLE$Fisher.p.value,
                                 SigOutput, USE.NAMES = FALSE)
  subset(TABLE, select = −c(Fisher.p.value))}
```

For the case of subject vs control tests, function `DOVAAdjustedSubControlTests` produces the desired tables.

It is defined in the following block.

```
IntForComparison <− function(SUBJECT, TB, LR, STEP){
  InitSubDATA <− NarrowResp(SUBJECT, TB, LR, "DAI", LBOUND = −10, UBOUND = 10)
  InitConDATA <− NarrowResp("Control", TB, LR, "DAI", LBOUND = −10, UBOUND = 10)
  MinDA <− max(min(InitSubDATA$DiffAreas), min(InitConDATA$DiffAreas))
  MaxDA <− min(max(InitSubDATA$DiffAreas), max(InitConDATA$DiffAreas))
  do.call(centredSeq, list(MinDA − STEP, MaxDA + STEP, STEP))}


DOVAAdjustedSubControlTests <− function(SUBJECT, TB, LR, STEP){
  EndPoints <− IntForComparison(SUBJECT, TB, LR, STEP)
  TABLE <− data.frame(LBound = EndPoints[−length(EndPoints)],
                      UBound = EndPoints[−1])
  TABLE$Fisher.p.value <− mapply(function(L,U){
    fisher.test(SRTable(SUBJECT, TB, LR, "Control", TB, LR, "DAI", L, U))$p.value},
    TABLE$LBound, TABLE$UBound)
  TABLE$"Fisher_Test" <− sapply(TABLE$Fisher.p.value, SigOutput, USE.NAMES = FALSE)
  subset(TABLE, select = −c(Fisher.p.value))}
```

Appendix B

Aspect coloured scatter plots without DOVA-corrections

The coloured scatter plots for the Aspect experiment were produced allowing for DOVA-corrections as described above. Similar plots without DOVA-correction were also produced, and are included here. Thus, in the following plots, the sprite sizes are just recorded as the side-length of the sprite measured at fixation. As before, each plot contains a range of variable sprite sizes and locations, for the control and one of either POV or DSS. The data wrangling code is simpler than in the DOVA-adjusted case discussed above, so we omit it.

Figures B.1-B.5 compare the patient DSS with control for various sprite and location ranges. Figures B.6-B.10 do the same for the patient POV.
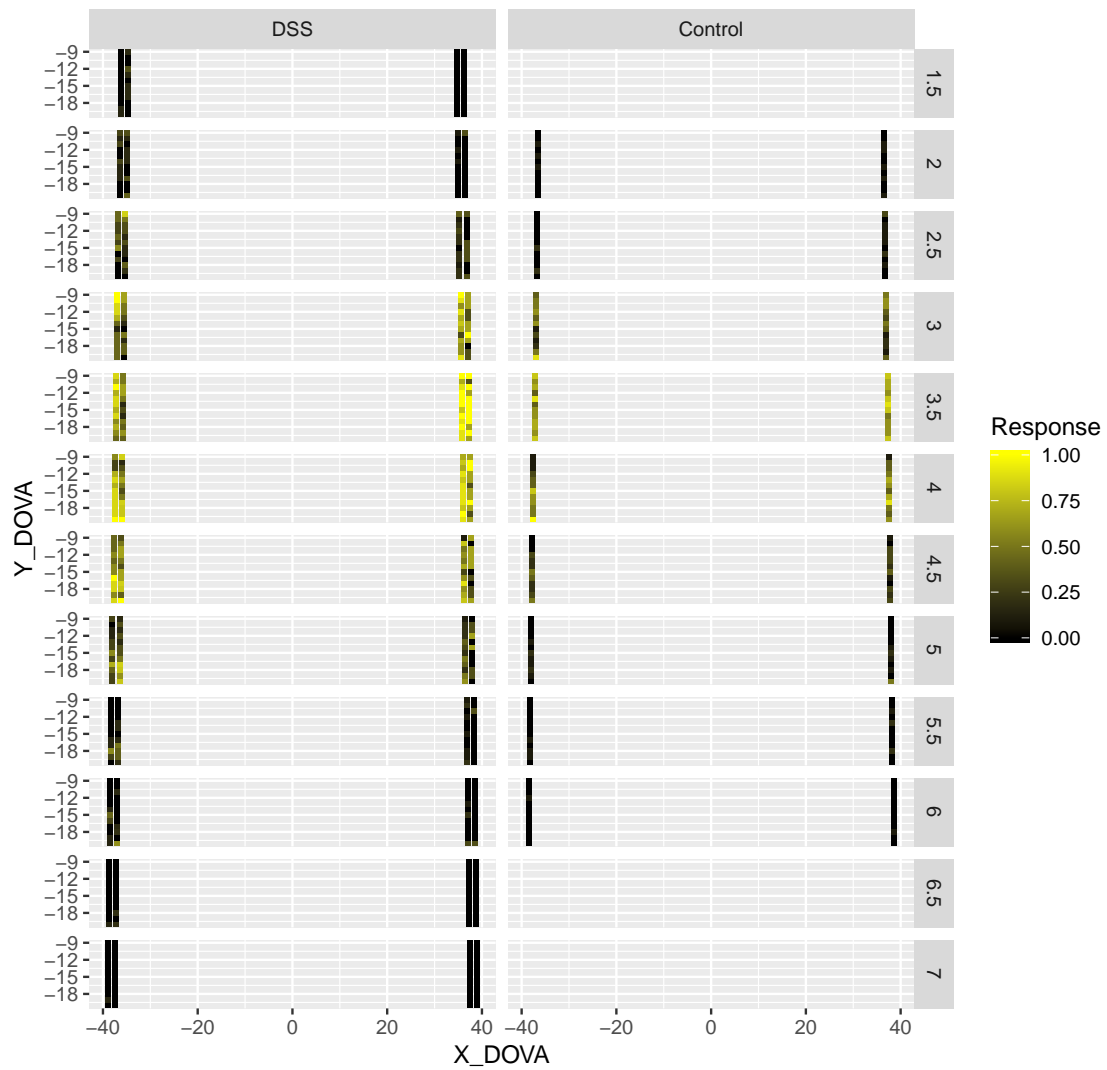
Figure B.1 – **DOVA-unadjusted Aspect scatter plot: DSS vs Control − All data**
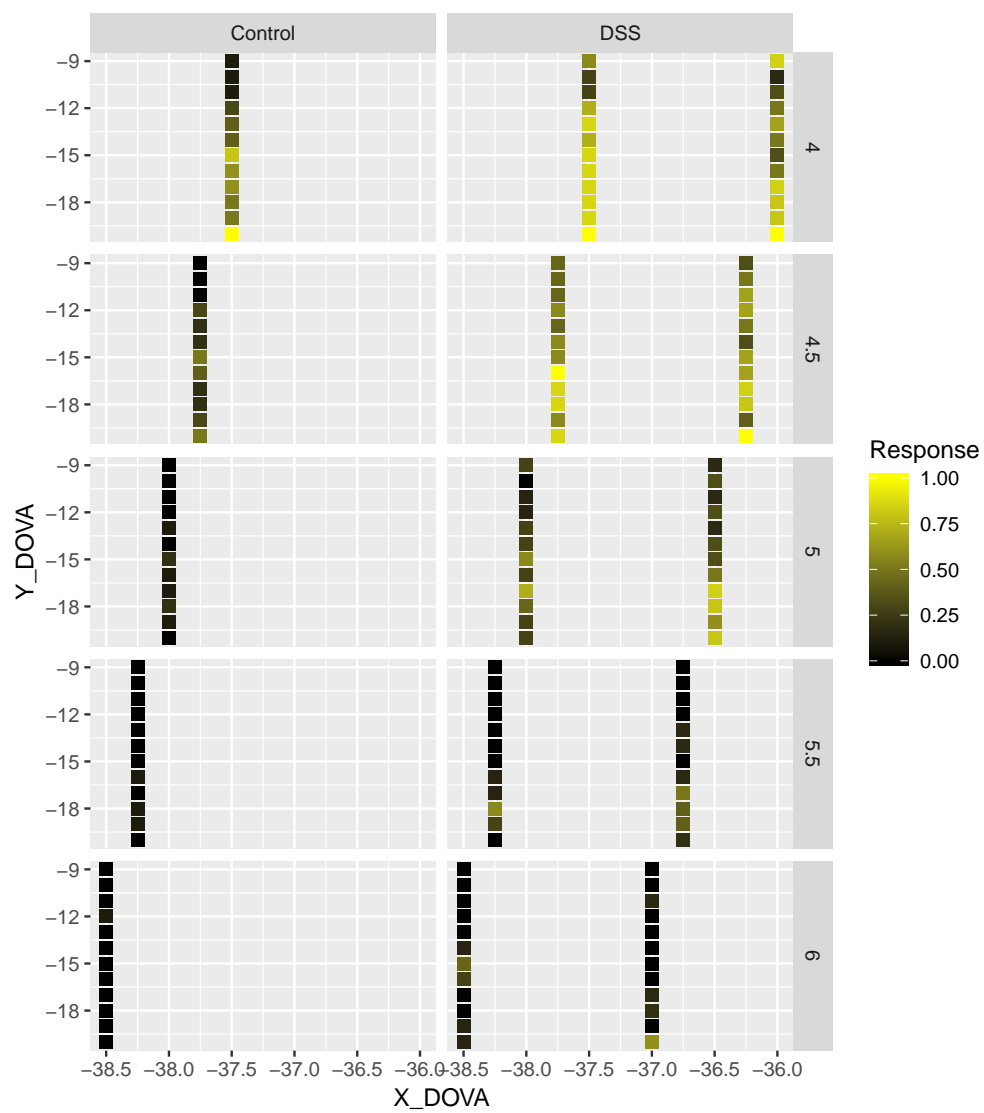
Figure B.2 – DOVA-unadjusted Aspect scatter plot: DSS vs Control – LVF big sprites
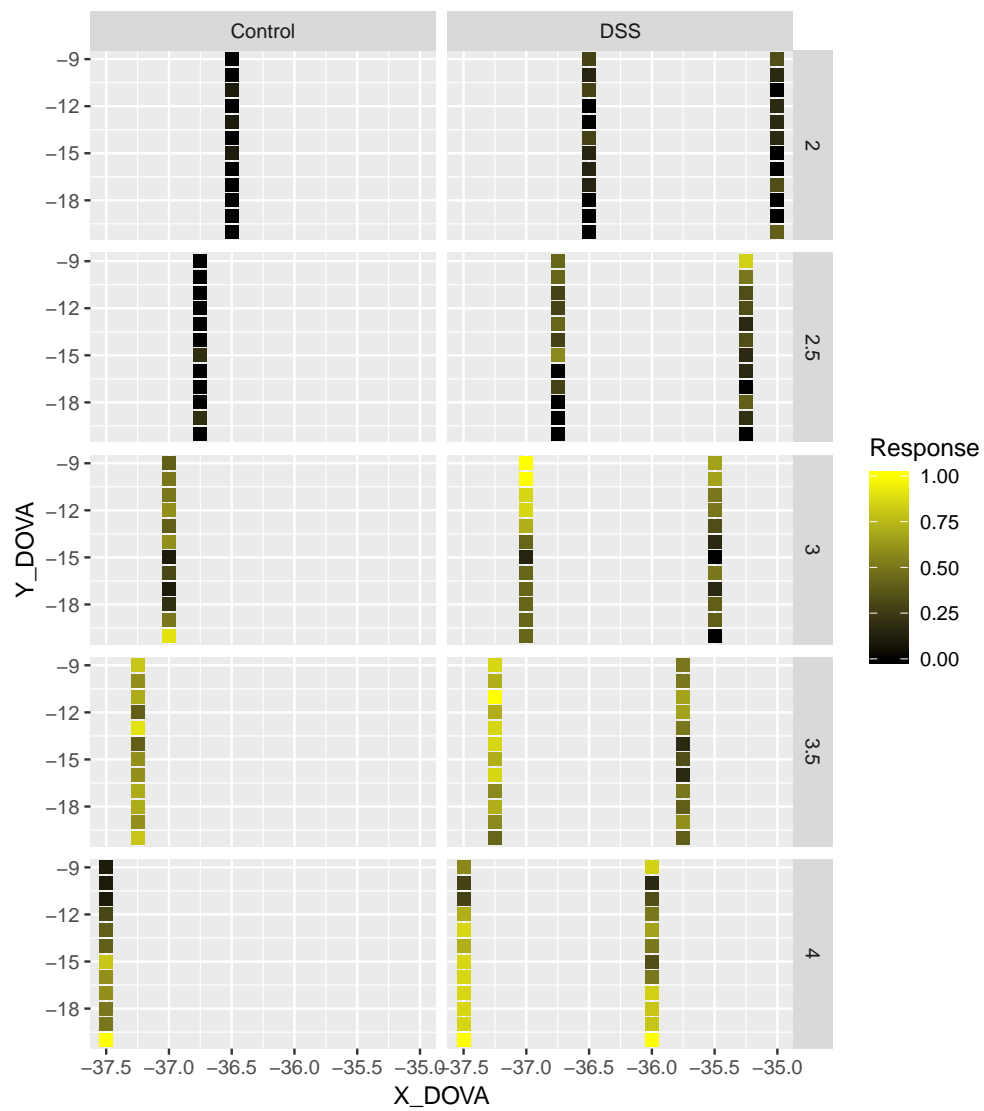
Figure B.3 – **DOVA-unadjusted Aspect scatter plot: DSS vs Control − LVF small sprites**
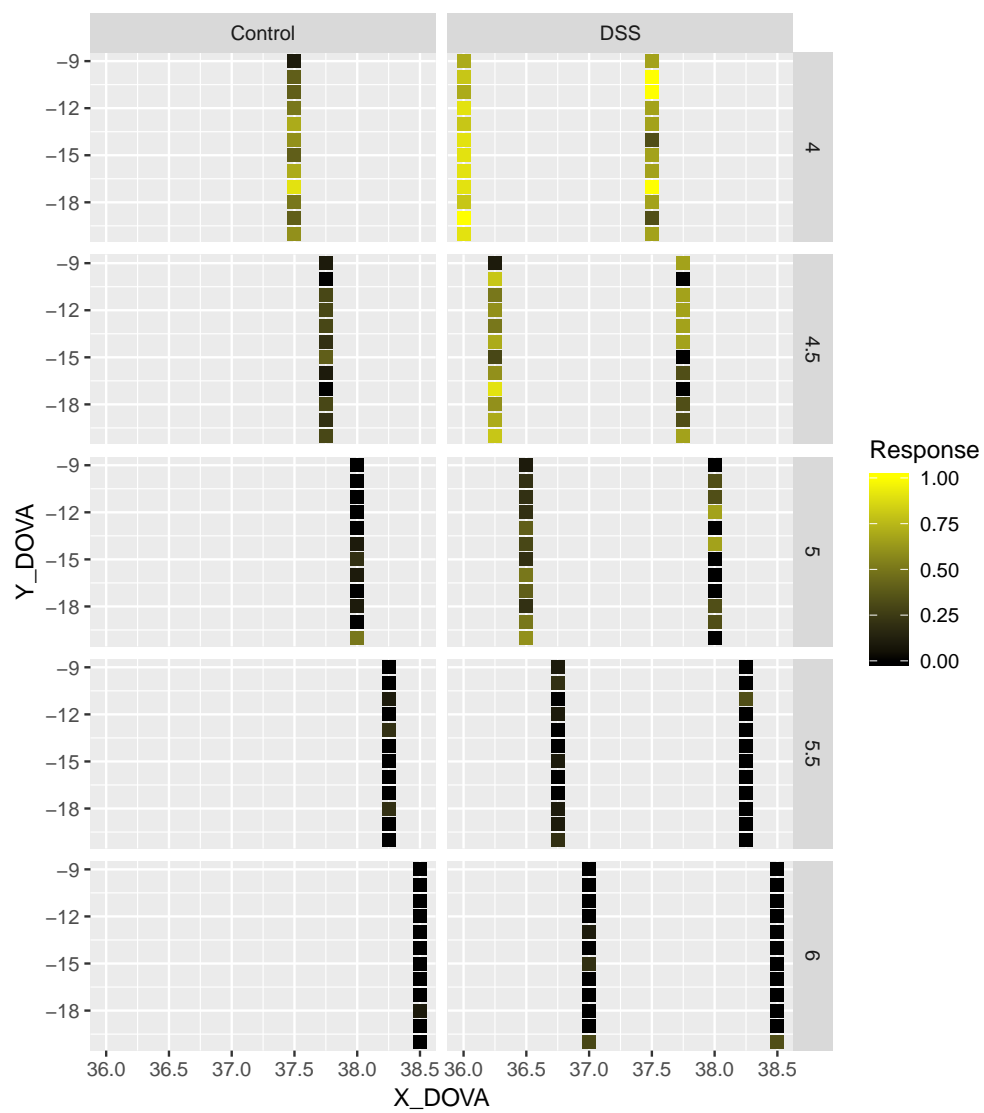
Figure B.4 – DOVA-unadjusted Aspect scatter plot: DSS vs Control – RVF big sprites
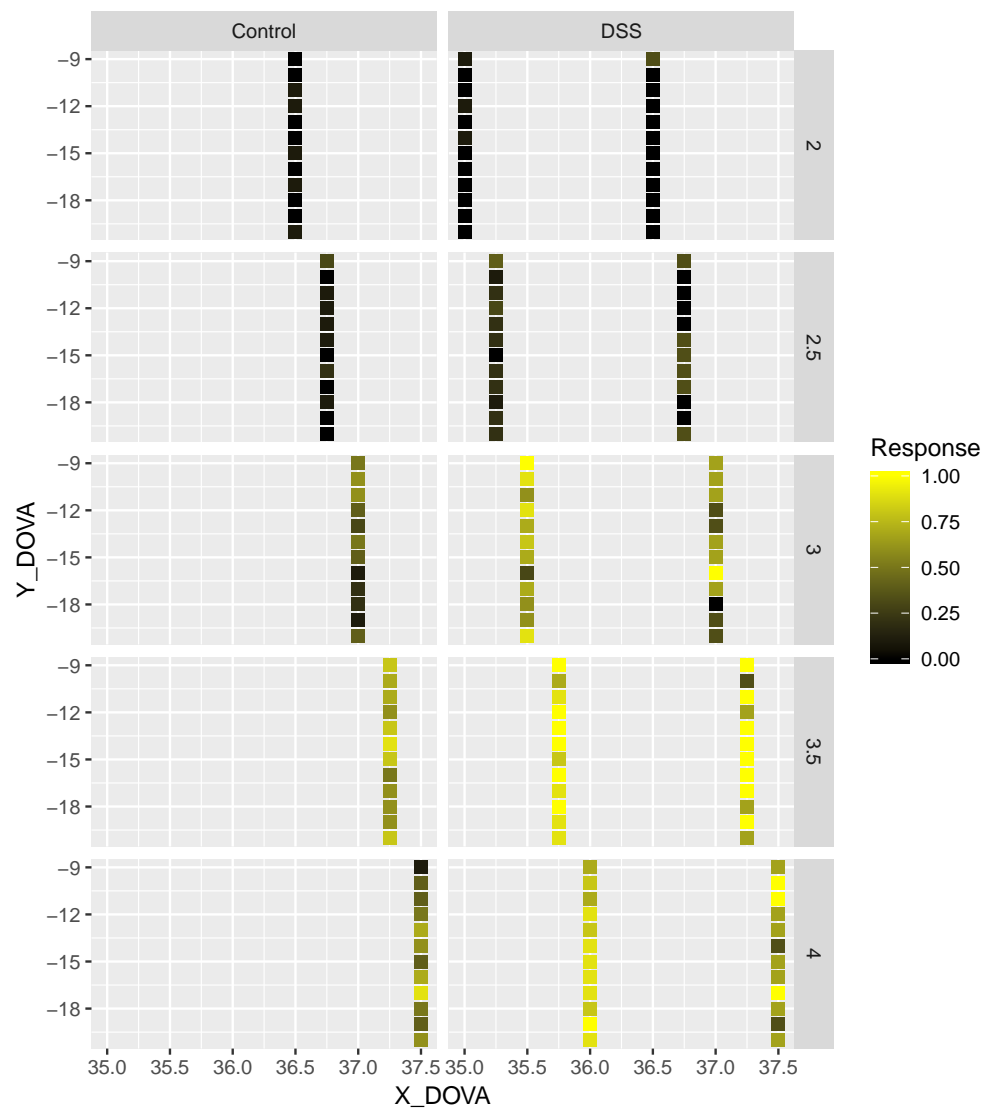
Figure B.5 – DOVA-unadjusted Aspect scatter plot: DSS vs Control – RVF small sprites
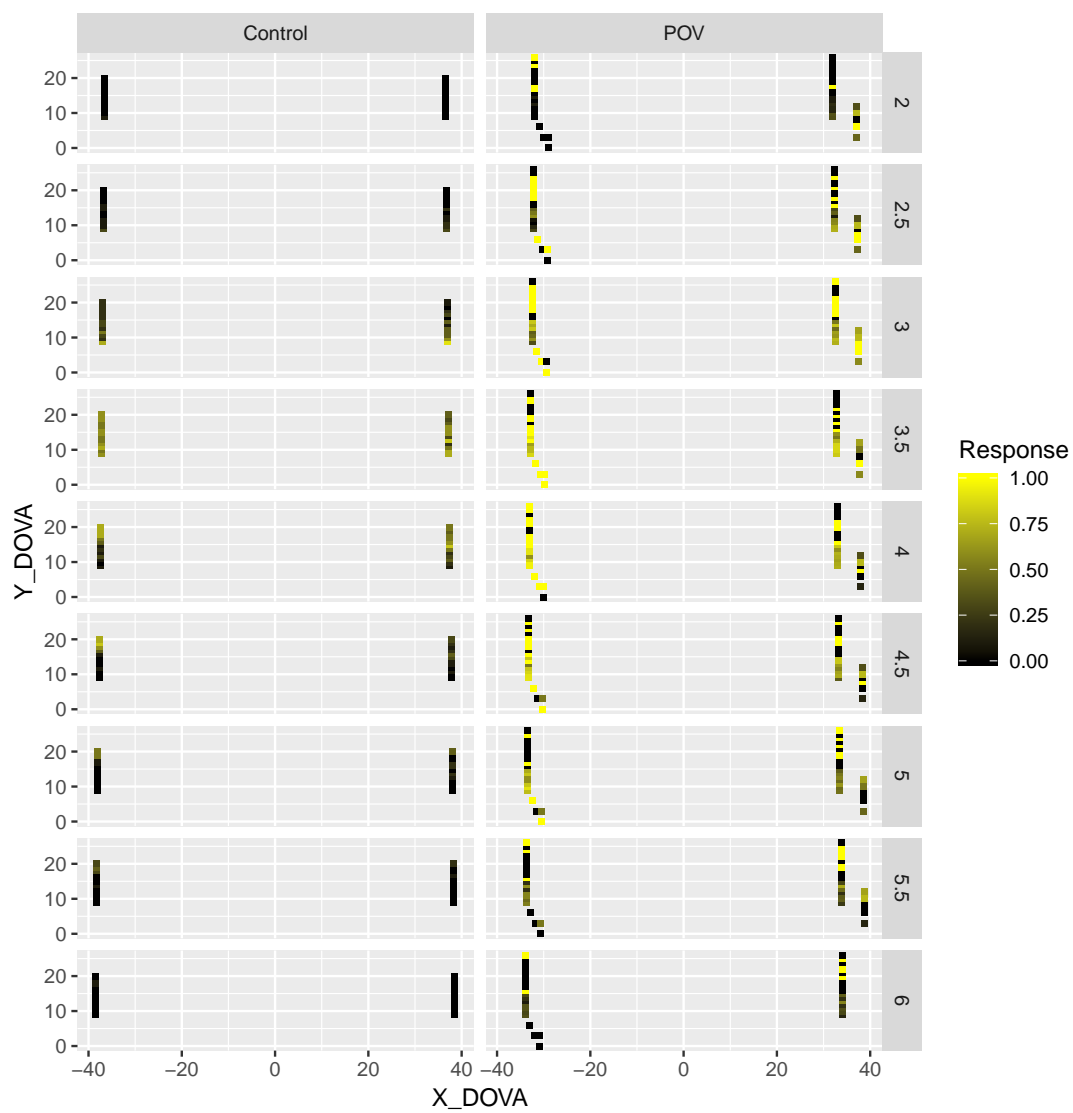
Figure B.6 – **DOVA-unadjusted Aspect scatter plot: POV vs Control − All comparable data**
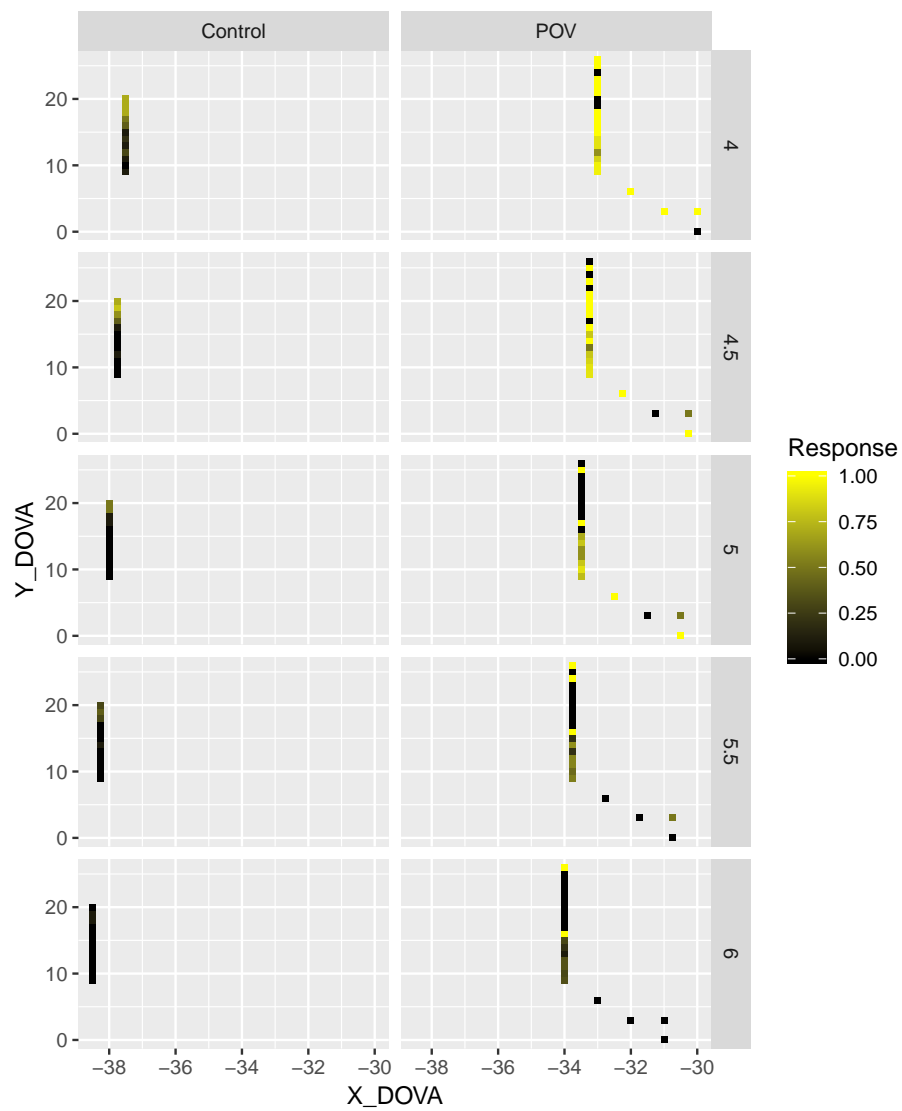
Figure B.7 – **DOVA-unadjusted Aspect scatter plot: POV vs Control − LVF big sprites**
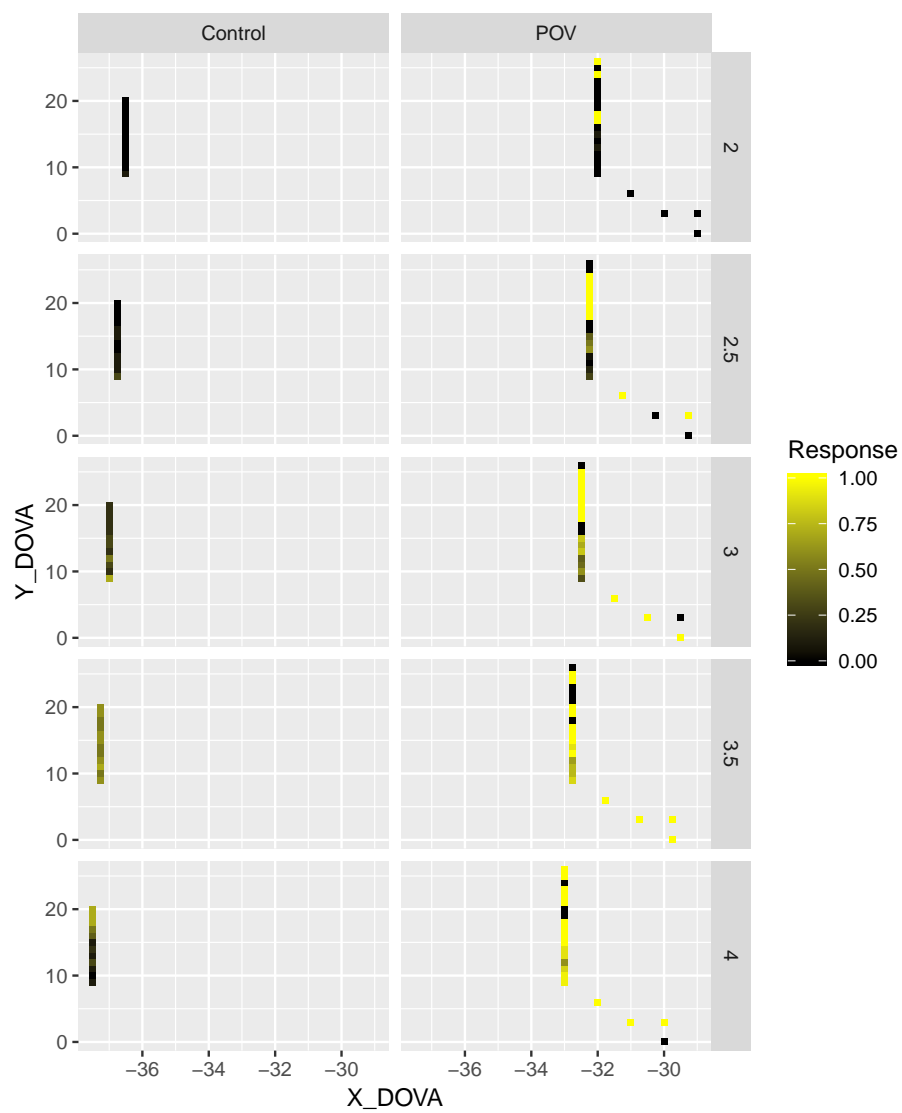
Figure B.8 – DOVA-unadjusted Aspect scatter plot: POV vs Control – LVF small sprites
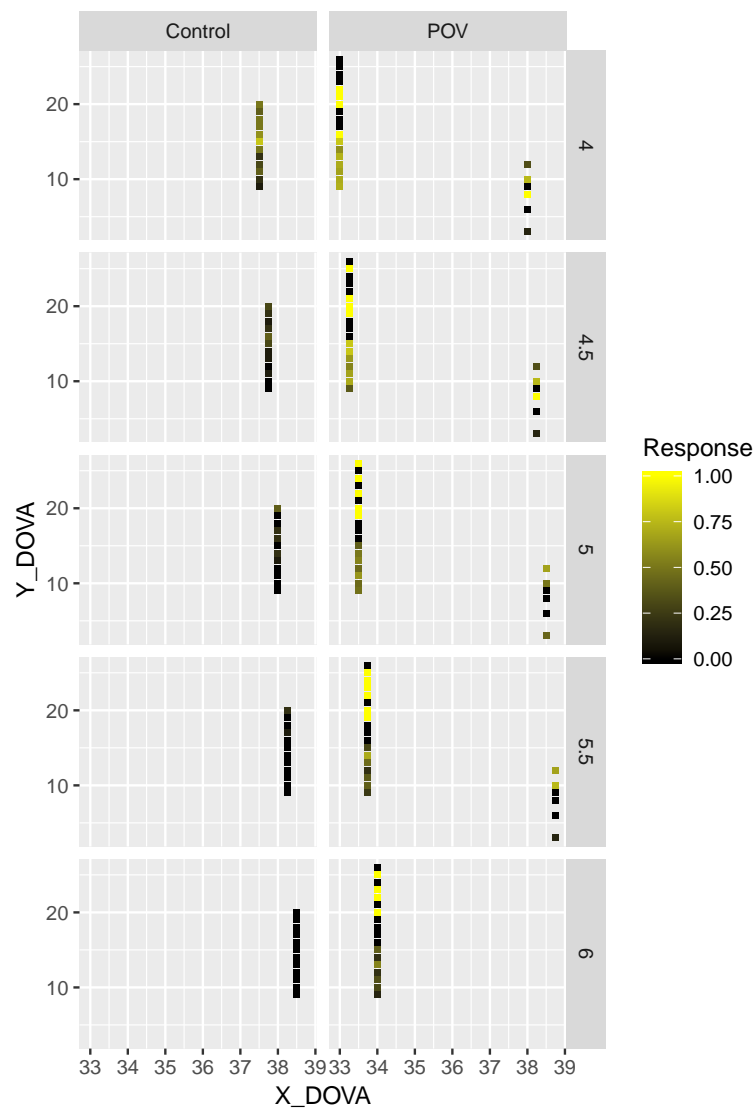
**Figure B.9** – **DOVA-unadjusted Aspect scatter plot: POV vs Control − RVF big sprites**
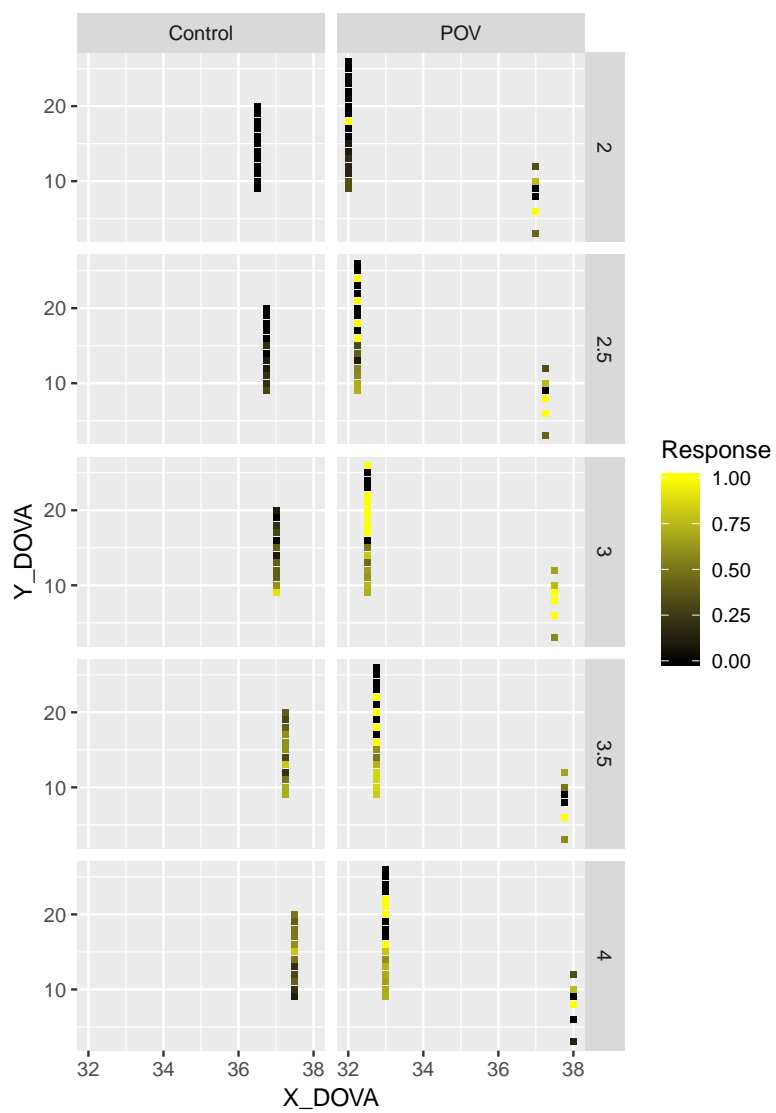
Figure B.10 – DOVA-unadjusted Aspect scatter plot: POV vs Control – RVF small sprites

Appendix C

Cerebral Metamorphopsia Literature Review

Table C.1 – Summary of Published Cerebral Metamorphopsia Cases

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Poppel-reuther 1917 [62]	Left occipital lobe gunshot wound	Cortical irritation, epileptic discharge, deafferenta-tion	Occipital	Left	Two perimacular scotomas	Wave-like distortion of objects	Objects would dance paroxysmally and appeared elevated so he would have to look up. There was a wave-like distortion of objects. After he experienced the distortion, his wound would hurt.	Dyschromatopsia, Illusion of movement	Persistent for nine months, no follow-up after this period	Left occipital gunshot wound. Probable involvement of parietal/temporal lobes.
Riddoch 1917 [79]	Right occipital shrapnel bullet wound	Epileptic discharge, cortical irritation, deafferenta-tion	Occipital	Right (from left frontal vertex)	Left homony-mous hemianopia with partial inferior quadrant recovery	Not geometric	Loss of stereoscopic vision, no depth perception	Post-craniotomy seizures, visual spatial disorientation, transient right hand motor, loss of sensation right upper limb	Persistent	Right occipital lobe shrapnel bullet damage, entry wound left front vertex, craniotomy performed to remove bullet and abscess
Potzl 1928 Case 1 [63]	Left or midline occipital gunshot wound	Cortical irritation, epileptic discharge, deafferenta-tion	Occipital	Left (mid-line)	Right hemianopia (possibly incomplete)	Vertical lines appear bent	Lines would appear "geknickt" (bent/broken/fragmented) like a branch stuck into the water ("wie ein ins Wasser gesteckter Stab")	Vertigo, Diplopia	Unknown	Left or midline occipital gunshot wound

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Potzl 1928 Case 2 [63]	Left occipital lobe lesion from shrapnel	Cortical irritation, epileptic discharge, deafferenta-tion	Occipital	Left	Right paracentral scotoma	Visual distortion of contours	Visual distortion of contours	Depth perception problems (shallow appearance), Illusion of movement of the right side of objects	Unknown	Left occipital lesion from shrapnel, possible parietal lobe involvement
Hoff 1935 case 1	Right parietal depressed skull fracture	Cortical irritation, epileptic discharge, deafferenta-tion	Parietal	Right	Slight bilateral temporal and nasal restriction	Wave-like distortion	"portion of the opposite wall of the room arched like an alcove; to the right and the left the wall appeared flat", fo other objects affected. He oberved the roof of the opposide house was distorted in a wavy manner, both the edge of the roof as well as its steeply inclind surface. Distortion apparent in the whole visual field. The wavy contours were in the centre of the visual field, larger towards the outside and overal corresponded to irregular arches.	Paralysis of left arm during surgical excision and exploration of the wound, Post-operative: mild left faceial paresis, spastic left hemiparesis, sensations were more unpleasant and stronger on the entire left half of the body.	8 days, sponta-neously resolved	Fluctuating ischaemia and oedema of the right parietal lobe after surgical exploration of the wound
Hoff 1935 case 2	Bilateral (mostly right) occipital hy-poperfusion	Deafferentation	Occipital	Bilateral (mostly right)	Right monocular severe upper left (nasal) defect, at times he had concentric constric-tion, (3 years previously, bilateral concentric constricted visual fields)	Lines and contours distorted	Lines were wavy vertically > horizontally. Desk appeared arched more so on the left: convex or concave, [Previous episode: tools appeared too short or obscured, table looked convex, straight lines became especially bent after he focused on something]	Depth perception problems, Optokinetic nystagmus more pronouced to the right	Current episode: persistent 8 months after first symptoms,; Previous episode: unknown duration	Bilateral (mostly right) occipital lobe or posterior cortical artery hypoperfusion
Brain 1947 [70]	Malignant hyperten-sion, right posterior cortical artery hy-poperfusion	Epileptogenic discharge, deafferenta-tion	Occipital	Right	Transient left homony-mous hemianopia	Prosopo-meta-morphopsia, objects appeared wrong size and distorted	Objects appeared the wrong size and distorted, the seemed too large or too small, the faces of people approaching her appeared too large and sometimes grotesquely distorted especially if they came up fo her from her left side, she found it very terrifying.	Micropsia, macropsia, simple and complex hallucinations, hyperacuisis and sounds synaesthetically aroused visual hallucinations	One episode, post-sympathectom (fluctuating blood pressure)	Malignant hypertension, right posterior cortical artery hypoperfusion

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Bodamer 1948 case 3 [105]	Left occipital shrapnel wound	Cortical irritation, epileptic discharge, deafferentation	Occipital	Left	Right hemianopia	Hemi-prosopo-meta-morphopsia	Pure hemi-prosopometa-morphopsia: distorted, oblique or strange	No other objects distorted	Unknown	Left occipital shrapnel wound. Possible other visual areas affected by injury, oedema or scarring.
Bodamer 1948 case 1 [105]	Left parieto-occipital gunshot wound	Cortical irritation	Parieto-occipital	Left	Bilateral paracentral scotomas	Prosopo-meta-morphopsia	Blurred outlines, prosopometamorphopsia,	Illusion of movement, achromatopsia	Episodic, unknown long-term outcome	Left parieto-occipital gunshot wound
Critchley 1949 (quoted)	Right middle cerebral artery thrombosis	Deafferentation	Parietal	Right	Unknown	Tilted	"all the mats were crooked"	Unknown	Unknown	Right middle cerebral artery thrombosis
Critchley 1949 (quoted)	Left parieto-occipital glioma	Epileptogenic	Parieto-occipital	Left	Unknown	Rotated objects	"The furniture seemed to be turned around"	Unknown	Unknown	Left parieto-occipital glioma
Critchley 1949 (quoted)	Right temporo-parieto-occipital glioblastoma	Epileptogenic	Temporo-parietal	Right	Unknown	Micropsia	"Things for a minute or so seem smaller than they actually are"	Unknown	Minute or so, presumed episodic	Right temporo-parieto-occipital glioblastoma
Critchley 1949 (quoted)	Right parietal area puerperal venous thrombosis	Epileptogenic, deafferentation	Parietal	Right	Unknown	Blurred objects, macropsia	"Objects looked different and blurred. Her husband seemed too big, and yet unduly far away"	Teleopsia	Unknown	Right parietal area puerperal venous thrombosis
Critchley 1949 (quoted)	Post-encephalitis	Epileptogenic, cortical irritation	Post-encephalitis	Unknown	Unknown	Vision altered	"lower part of objects looked obscured while the upper portions were seen with greatly exaggerated detail"	"recurring oculogyric crises in which her eyeballs would involuntarily become deviated to the right"	Unknown	Post-encephalitis
Critchley 1949 (quoted)	Left-sided rapidly growing cerebral tumour	Epileptogenic	Cerebral	Left	Unknown	Distortion of sight	"Objects to her right side looked more distant and larger than to the left, while objects to to the left side appeared diffuse, distorted, and smaller than usual."	Unknown	Unknown	Left-sided rapidly growing tumour
Chavany 1959	N/A	N/A	Unknown	Unknown	Unknown	Distortion of faces and objects	acute onset of newspaper text going from black to white. A few hours later, he noticed distortions of faces and other objects. The objects also appeared rotated.	Unknown	Unknown	Unknown
Hecaen 1962 case 3	Right parieto-occipital meningioma excision	Epileptogenic discharge, focal cortical irritation, deafferentation	Parieto-occipital	Right	Unknown	Prosopo-meta-morphopsia	Bizarre, non-geometric distortion of faces	Unknown	Unknown	Right parieto-occipital meningioma excision

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Geyer 1963	Right parieto-occipital glioma		Parieto-occipital	Right	Unknown	Hemi-macropsia	hemi-metamorphopsia, shimmering outlines of objects	Headaches, vertigo, nausea	Two days pre-craniotomy, patient died shortly after operation	Right parieto-occipital glioma
Geyer 1963	Left optic radiation aneursym	Subarachnoid haemorrhage, cortical irritation	Optic Radia-tion	Left	Right homony-mous quadran-tanopia (?superi-or/inferior)	Hemi-macropsia	Hemi-metamorphopsia, left side of his face appeared deformed, left side of his head appeared grotesquely elongated, left side of all the objects in the room appeared to be stretched vertically.	Vertigo	Four days after sub-arachnoid haemor-rhage. Sponta-neously resolved.	Lesion of the left optic pathway immediately posterior to the chiasm or the optic radiation and subarachnoid haemorrhage
Mooney 1965	Left parasagittal parieto-occipital meningioma	Cortical irritation, epileptic discharge, deafferenta-tion	Parieto-occipital	Left	Complete right lower quadran-tanopia with macular sparing and incomplete right upper homony-mous quadrants with wide macular sparing	Prosopo-meta-morphopsia, distort	"Everything about every person became grotesque." Two types, eyes open and eyes closed.	Palinopsia, simple and complex visual hallucinations, dyschromatopsia, dysmetropsia, illusion of movement	Postoperative recovery from craniotomy and partial excision of menin-gioma. Controlled with pheno-barbitone. Returned to work four months later with no recurrence of visual symptoms.	Left parasagittal parieto-occipital meningioma
Bender 1968 case 2	Right occipital meningioma	Epileptic discharge, deafferenta-tion	Occipital	Right	Left homony-mous superior quadran-tanopsia	Macropsia, micropsia	The examiner's finger appeared "broadened" and "increased in size" when in her left upper quadrant. A white disc would appear "larger and larger" if held in the same position for fifteen seconds.	Palinopsia, cerebral polyopia	Intermittent, increased frequency over time	Right occipital meningioma on angiofram, clinical symptoms of seizure
Bender 1968 case 4	Seizure of unknown aetiology	Epileptic discharge, deafferenta-tion	Bilateral occipito-temporal	Bilateral	Transient, homony-mous field defects	Meta-morphopsia	"All the doctors in the room had green beards"	Cerebral polyopia, palinopsia, dysmetropsia, complex visual hallucinations, dyschromatopsia, not oriented to time/place, unable to perform simple calculations	Spontaneously resolution over six weeks	Normal angiogram, EEG: bilateral occipito-temporal spikes
Gloning 1968	See other table									

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Lance 1976 Case 7	Right occipital infarction, vertebrobasilar insufficiency	Epileptic discharge, deafferentation	Occipital	Right	Dense left homonymous hemianopia spitting the macula	Non-geometric meta-morphopsia	"fingers became thicker and thinner, shorter then fatter"	Palinospia, cerebral polyopia, simple and complex visual hallucinations	Spontaneously resolution over five weeks	Isotope brain scan demonstrated a "wedge of intensely increased uptake in the medial occipital lobe on the right side". Vertebral angiogram showed "some stenosis of the proximal part of the right posterior cerebral artery". The brain scan returned to normal after three months, however, his left homonymous hemianopia persisted.
Lance 1976 Case 8	Right parietal infarction	Epileptic discharge, deafferentation	Parietal	Right	Dense left homonymous hemianopia which resolved over one week	Alice-in-Wonderland Syndrome, Micropsia	She perceived herself as a "tiny figure, two feet long, wrapped in a green bundle on the floor. Subsequently her room appeared very small, like a tiny caravan with the walls close to her."	Simple and complex visual hallucinations, left hemiplegia with anosognosia which resolved after hours	Spontaneous resolution in five days	Brain scan demonstrated "diffusely increased uptake in the right parietal area"
Lance 1976 Case 9	Right occipital infarction (vertebrobasilar insufficiency)	Epileptic discharge, deafferentation	Occipital	Right	Left homonymous hemianopia	Movement of the visual scene	"room seemed to rock backwards and forwards and she had to hang on to furniture to retain her balance"	Palinopsia, cerebral polyopia, illusion of movement, transient left hemiparesis during the original episode	Resolved with carbamazepine	Brain scan demonstrated increased uptake in the right occipital area which resolved over a period of three months
Brust 1977 case 2 [95]	Right occipito-temporal infarction	Epileptic discharge, deafferentation	Occipito-temporal	Right	Large left homonymous paracentral hemianopic scotomas, splitting the macula and sparing peripheral vision	Hemi-prosopo-meta-morphopsia	Right half of people's faces seemed to transiently melt "like clocks in a Dail painting" and took on a yellow or violet colours. The distortion only affect faces and was sharply demarcated to only one half of the face.	Palinopsia, dyschromatopsia, simple and complex visual hallucinations	Episodic, 18 months, resolved with phenytoin	Right occipito-temporal epileptogenic discharge from infarction. EEG during typical hallucinations, frequent sharp forms right posterior temporo-occipital area with decreased amplitude of alpha rhythm on that side.
Lazaro 1983	Right occipital glioblastoma	Epileptogenic discharge, cortical irritation, deafferentation	Occipital	Right	Subtle left homonymous hemianopia	Prosopo-meta-morphopsia	People's faces appeared similar to a man he saw earlier, including his wife. Faces appeared wavy, flat and with a tan complexion, their eyes looked tired.	Palinopsia	One episode lasting several minutes	Right occipital glioblastoma causing epileptogenic discharge, focal cortical irritation, or deafferentation

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Brau 1986 [90]	Bilateral occipital ischaemia from multiple intracranial artery spasm	Epileptogenic discharge, deafferentation	Occipital	Bilateral	Developed cortical blindness	Micropsia	The ceiling light appear to rotate 180 degrees intermittently, the rotated lights appeared farther away, people appeared consistently shorter and sometimes upside-down, sometimes only the upper-half of the person appeared upside-down	Teleopsia, inversion of vision, depth perception issues, simple and complex hallucinations	Day 1-7 after posterior fossa craniec-tomy, before cortical blindness	Bilateral occipital lobe ischaemia from multiple intracranial artery spasm
Young 1989	Right parietal astrocytoma	Epileptic discharge, deafferentation	Parietal	Right	none		Micropsia, prosopometamorphopsia	Bilateral prosopo-metamorphopsia, Unilateral palinopsia, Polyopia, dysmetropsia/Micropsia, Dyschromotopsia, Seizures, Spatial disorientation, Loss of depth perception, visual hallucinations	Episodic coinciding with PLEDs on EEG.	Right parietal astrocytoma, PLEDs
Ebata 1991 [99]	Right retrosplenial lesion	Deafferentation	Retro-splenial	Right	None	Hemi-prosopo-meta-morphopsia	Left hemi-prosopometamorphopsia	None	Five weeks, resolved spontaneously	Small haematoma in the right retrospelenial region
Lindgren 1992	Right occipito-parietal infarction	Deafferentation	Occipito-parietal	Right	Left homony-mous hemianopia	Distortion of spatial vision.	Feeling of distorted or oblique vision, square room looked like a pentagon with a the triangular apex far away in the centre of the visual field, when he shifted gaze from a door opening to a flat wall, the apex fold moved along and deformed the appearance of the wall. When reaching for a plate at the kitchen table, the plate seemed to be far away, the peripheral part of his right arm and hand look abnormally long.	Acute severe transient sensory deficit of his left arm, Simultangnosia, Environmental orientation deficit, Depth perception issues, Complex hallucinations, Anisocoria	Several hours	Right occipito-parietal infarction
Tohgi 1994 [108]	Right occipito-temporal infarction	Epileptogenic discharge, deafferentation	Occipito-temporal	Right	Left upper quadranop-sia in the right eye		Prosopometamorphopsia; Prosopagnosia			Right parieto-occipital infarction
Seron 1995 [85]	Right occipito-temporal haemorrhage	Epileptogenic discharge, deafferentation, focal cortical irritation	Occipito-temporal	Right	None	Familiar faces and objects distorted	Prosopometamorphopsia; faces appeared more pleasant	None	Transient	Right occipito-temporal haemorrage due to sub-cortical metastasis

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Imai 1995 [104]	Left retrosplenial infarction	Deafferentation	Retro-splenial	Left	None	Hemi-prosopo-meta-morphopsia	Visual hemifield blurring	Right margin of all object in her visual field appeared blurry	Unknown	Left spotty infarct lesion between retrosplenium and cingulate gyrus
Hoksbergen 1996 [109]	Right occipito-temporal hypoperfu-sion	Epileptogenic discharge, deafferenta-tion	Occipito-temporal	Right	None	Hemi-prosopo-meta-morphopsia	Partial form distortions of faces strictly confined to the person's right facial side with associated loss of colour perception	Dyschromatopsia, achromatopsia, subjective blurring in left visual hemifield, simple moving hallucinations	One episode, resolved with ticlopidine 250mg twice daily	Right occipito-temporal hypoperfusion, occlusion of right posterior cerebral artery on cerebral angiogram
Shiga 1996 [66]	Left putaminal haemorrhage	?cortical irritation, deafferenta-tion	Optic Radia-tion	Left	Transient right homony-mous hemianopia	Hemi-field distortion of face and hand	Right visual hemifield objects and faces distortion: stretched, tortuous, missing fingers on a hand;	Right inferior facial palsy and right hemiparesis without sensory involvement, Visual hallucinations in right hemifield	Four days after onset of right hemiparesis and after right homony-mous hemianopia resolved, visual symptoms 3-4 days	Left putaminal haemorrhage on CT brain
Satoh 1997 [74]			Occipital	Left			Prosopometamorphopsia; distortion of objects		Episodic, 10 minutes	Left occipital lesion probably epileptogenic; Marked increase in cerebral blood flow of left occipital pole during symptoms and marked decrease in cerebral blood flow after symptoms disappeared
Werring 1999	Left occipito-parietal tuberculous granuloma	Focal cortical irritation	Occipito-parietal	Left	None	Unsure whether meta-morphopsia was perceived	Unsure	Simple hallucinations, palinopsia	Episodic over 2 months, resolved with anti-tuberculous medica-tions, symptom free after 2 years	left occipito-parietal tuberculoma, focal cortical irritation
McElvanney 1999	CJD, spongioform encephalopa-thy		Occipital	Right	Left incongruous homony-mous scotoma		Fragmentation and illusion of movement	Increased intensity of colours	Progressive, improved with intravenous diazepam	Spongioform encephalopathy CJD, particularly right occipital lobe. Spongiform change was noted in the basal ganglia, thalamus and hypothalamus.

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Frassinetti 1999 [67]			Occipital	Right			Left hemi-micropsia; Shrunk and Distorted	Reading was difficult due to letters appearing to overlap one another, and the lines of the text were not properly aligned	Persistent, More than a month	Old lesion left inferior parietal lobe (BA39 and BA40) and superior parietal lobe (BA5 and BA6); Recent inferior lateral right occipital lobe including BA18 and BA19; When correlated to recent functional maps based on functional MRI in humans, the presumptive location of the lesion was posterior to area MT (V5) involving ventral V4 (V4V) and part of the lateral occipital area.
Werring 1999			Occipito-parietal	Left	?	?	No distortion of objects	Coloured positive visual symptoms, Palinopsia	Episodic, resolved with antitu-berculous medications	left occipito-parietal tuberculoma
Heo 2004 [75]			Temporo-occipital	Right			Prosopometamorphopsia; No distortion of other objects	Unformed visual hallucinations, Pelopsia, Teleopsia, Illusion of movement	Episodic, Resolved with valproate and dialysis for renal failure	Epileptogenic focus right temporo-occipital adjacent to cerebromalacia from previous hypertensive haemorrhage in right occipital region
Sun 2004 [86]	Right occipital and left temporal hypoperfu-sion	Epileptogenic discharge, deafferenta-tion	Temporal (Left), Occipi-tal (right)	Left (right occipi-tal)	Transient dense left homony-mous hemianopia	Tilted, geometric	The left edge of her bed tilted downward and the left railing of the bed became distant to her. She felt she was going to fall down from the left side. Her quilt became triangular and she tried to fold it back as a square	Transient visual hemifield perseveration before distortion commenced	12 hours, sponta-neously resolved	Right occipital and left temporal hypoperfusion from untreated hypertension
Miwa 2007 [96]	Right temporal brain abscess	Cortical irritation	Temporal	Right	None	Hemi-prosopo-meta-morphopsia	Right half of a person in front of him appeared swollen, particularly affected the lower half of the face, consistently the right side of faces in front of him and only when the face was rounded. The distortion did not affect other objects or if the face was thin	None	Episodically for over 4 years, anti-epileptic medication did not improve the meta-morphopsia and no epileptic seizure activity during these episodes	Right temporal abscess and damage from aspiration

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Kamibuko 2008	Right temporo-occipital infarction	Epileptic discharge, deafferenta-tion	Temporo-occipital	Right	Left homony-mous hemianopia	Hemi-prosopo-meta-morphopsia	"Left half of the faces of people walking on the street in the opposite direction appeared distorted; they looked like monsters"	None	Persisted for over 3 years	Right temporo-occipital infarction
Abert 2010	HPPD/trazadc	Diffuse neuro-transmitter/rece changes	Diffuse	Diffuse	None	Lines known to be parallel are not	Two parallel walls comprising the doorway would change size in a teeter-totter fashion	Palinopsia, halos	40 years after LSD use	LSD use, possibly exaccerbated by multiple head traumas and trazodone
Gonazalez 2011	Right occipital intra-parenchymal haemorrhage	Epileptogenic discharge, focal cortical irritation, deafferenta-tion	Occipital	Right	None	Dysmetrops	Constant variations in the shape of objects and people. They appeared extremely long and thin, short, wide, etc.	Dyschromatopsia, optical allesthesia	36 hours, resolved within 24 hours of commenc-ing levetirac-etam 1000mg.day	Right occipital intraparenchymal haemorrhage
Anabrasan 2013	Relapsing-remitting multiple sclerosis	Active demeylination in left temporo-occipital region	Temporo-occipital	Left	-	Hemi-prosopo-meta-morphopsia	Distorted faces in her right field of vision. When looking at any face, the left side of the face she percived in her right visual field appeared distorted or elongated. People's eye appeared stretched outin an almost ovoid shape on thie side of their face. No distortion of other objects	Palinopsia	Improved sponta-neously after a few weeks, episodically occurred without identifiable triggers	Multiple sclerosis, demyelienation left temporo-occipital region
Tanaka 2015	Bilateral occipital lobe lymphoma		Occipital	Bilateral	Unknown	Meta-morphopsia	Metamorphopsia, no other description or definition	Right facial nerve palsy	Unknown	Lymphomatoid granulomatosis, Brain MRI T2-weighted high-intensity lesions in both occipital lobes
Orjuela-Rojas 2015	Right temporo-parieto-occipital epilepsy		Parieto-temporo-occipital	Right		Meta-morphopsia	Distortion of objects	Left hemi-asomatognosia; unformed, formed and experiential visual hallucinations	Episodic, improved frequency with anti-epileptic medication	Right temporo-parieto-occipital epilepsy due to right temporo-occipital neurocystocercosis
de Souza 2017	Bilateral temporo-occipital hypoperfu-sion after cardiac arrest	Epileptogenic discharge, deafferenta-tion	Temporo-occipital	Bilateral	Transient acute visual loss in both eyes (visual field normal in 10 days)	Distortion of straight lines	Straight lines or fluorescent tube lights appeared curved when viewed directly, 3 days after the acute visual loss	Transient bilateral visual loss (revovered in 1 month)	Unsure, probably between days 3-10 after acute visual loss	Bilateral temporo-occipital hypoperfusion after cardiac arrest
McCarty 2017			Splenial	Left			Other people's mouths only	Prosopoagnosia, Alexia without agraphia, Distortion of Amsler grid R>L	Unknown	T2-weighted brain MRI revealed late subacute infarct within the left splenium of the corpus callosum, just medial to the occipital horn.

Table C.1 – continued

Reference	Primary Aetiology	Mechanism	Location of Lesion	Side of Lesion	Visual Field Defect	Type of Visual Distortion	Description of Visual Distortion	Other visual symptoms signs	Duration of meta-morphopsia	Pathology
Nass 1985 [72]	Right parieto-temporo-occipital arteriove-nous malforma-tion	Epileptogenic discharge	Parieto-temporo-occipital	Right	None	Faces looked older, shapes of objects were distorted	Distortion of objects, Prosopometamorphopsia	Faces appear older, dyschromatopsia, depth Perception issues	Episodic, resolved with partial excision and carba-mazepine	Epileptogenic discharges from arteriovenous malformation
?????			Unknown				32 M wallpaper pattern disappears, doctors' faces distorted or oblique with an enlarged nose	Objects appear distant; illusion or dreamy experience where scenery and people around him appear ancient or like in the mountains. Possible hemineglect or hemianopia of the hallucinating visual field.	Unknown	epileptic aura, absence and generalised seizures