THE CHROMATIC VISUAL EVOKED RESPONSE AS AN INDICATION OF VISUAL DEVELOPMENT

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SUMMARY

In an endeavour to provide further insight into the maturation of the cortical visual system in human infants, chromatic transient pattern reversal visual evoked potentials to red/green stimuli, were studied in a group of normal full term infants between the ages of 1 and 14 weeks post term in both cross sectional and longitudinal studies.

In order to produce stimuli in which luminance cues had been eliminated with an aim to eliciting a chromatic response, preliminary studies of isoluminance determination in adults and infants were undertaken using behavioural and electrophysiological techniques. The results showed close similarity between the isoluminant ratio for adults and infants and all values were close to photometric isoluminance.

Pattern reversal VEPs were recorded to stimuli of a range of red/green luminance ratios and an achromatic checkerboard. No transient VEP could be elicited with an isoluminant chromatic pattern reversal stimulus from any infant less than 7 weeks post term and similarly, all infants more than 7 weeks post term showed clear chromatic VEPs. The chromatic response first appeared at that age as a major positive component (P1) of long latency. This was delayed and reduced in comparison to the achromatic response. As the infant grew older, the latency of the P1 component decreased with the appearance of N1 and N2 by the 10th week post term. This finding was consistent throughout all infants assessed.

In a behavioural study, no infant less than 7 weeks post term demonstrated clear discrimination of the chromatic stimulus, while those infants older than 7 weeks could do so.

These findings are reviewed with respect to current neural models of visual development.

KEY WORDS: infants; subcortical vision; isoluminance; colour vision.

This thesis is dedicated to my mother and father

Marlene and Tom Rudduck

and

Julian

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Becky - for half the brain
Mum- for pouring over the drafts
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Vladimir : It's the start that's difficult

Estragon: You can start from anything

Vladimir: Yes, but you have to decide.

Waiting for Godot, Samuel Beckett.

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CHAPTER ONE
BACKGROUND TO STUDY AND RATIONALE FOR RESEARCH

1.1 Introduction

Rapid development occurs during the nine ante, and first six post natal months of an infant's life and this is particularly dramatic in the sense of vision. By six months of age, it is the most dominant of all the senses and is responsible for further perceptual, cognitive and social development (Atkinson 1984). Several theories have arisen to explain the developmental time course of the different visual functions.

1.2 Neural models of infant visual development

Bronson (1974) suggested that neonatal visual behaviour is mediated by a subcortical system and it is not until the second month of life that the cortex has matured enough to allow cortical function. This theory is based upon the assumption that, in humans, there exists two visual systems. The primary visual system comprises of lateral geniculate nucleus, striate cortex and and other visual cortical areas. It is thought particularly to subserve the fovea, analysing, encoding, identifying and recognising pattern information. This system allows the voluntary regulation of eye movement. The second visual system comprises of the superior colliculus and other motor nuclei of the mid brain and is assumed to be responsible for the supply of information regarding the location of a stimulus and interact with the primary visual system in controlling eye movements. Hence Atkinson (1984) proposed alternative names for the two systems; the 'what and 'where' systems. The presence of this dual system in higher vertebrates has also been proposed by several other investigators (For review see Salapatek 1975). The argument put forward by Bronson stated that, neonatal vision is mediated by the components of a phylogenetically older, subcortical system and by 2 months of age the cortical system begins to function allowing infants to begin encoding information and execute visual search patterns.

Much of Bronson's conceptual model was based on studies of eye movements and adults with cortical lesions. Dubowitz and co-workers (1986) reported that the visual function of very young infants, who had lesions at the thalamus, was more likely to be affected than those with lesions with substantial occipital involvement. Infants who would later become cortically blind retained basic visual function (tracking and pattern preference) until around 48 weeks post menstrual age (PMA). They suggested that, prior to this time, these visual capabilities were not dependent on cortical integrity but had subcortical mediation. Symmetrical VEPs could be recorded before 8 weeks post term from infants whose ultrasound revealed asymmetrical occipital lesions and these VEPs then became

asymmetrical at 2 months. There is agreement that visual tracking performance may be mediated subcortically by the superior colliculus (Stampalija 1986, Snyder et al. 1990). Hoffmann (1978) reported a shift in the locus of pattern VEP from a subcortical to cortical site between the ages of 6 to 10 weeks, demonstrated by a change in the scalp distribution of early (cortical) and late (possibly collicular) VEP components. The flash VEP waveform changes its morphology to become adult-like at 3 to 6 months and the emergence of this complexity implies increasing involvement of cortical function (Fielder and Evans 1988).

If Bronson's 'switch over' theory is correct, one would expect some discontinuity in visual development, as the reflexive subcortical system is superseded by the cortical system. This shift has been reported by some authors at around 6 weeks, with a change in visual preference, from size to quantity of elements in a stimulus, occurring at this time (Fantz and Fagan 1975). Pipp and Haith (1984) found no relationship however between age and number of elements. Patterns of hand and eye co-ordination during the first year, suggest cortical and subcortical systems follow a parallel developmental time course (McDonnell 1979).

The pattern VEP amplitude vs. check size function appears to be bi-modal between the ages of 30 and 40 days (Harter et al. 1977a, 1977b) with the amplitude of the first mode decreasing progressively from its peak of 20 minutes of arc between 10 and 30 days, disappearing completely by 40 days. The amplitude of the second mode increases progressively from 10 to 30 days to a peak above 50 minutes of arc. It is possible that the bi-modal function represents the activities of 2 groups of neurones tuned specifically to high and low spatial frequencies. If the first and second modes represent the activities of the subcortical and cortical neurones respectively, the apparent decrease in acuity in the second month could represent a point where the cortex becomes sufficiently mature to take over from the subcortical system.

Positron emission tomography (PET) of infants has been used to demonstrate the low activity of the calcarine cortex until about three months of age. PET activity increases even later in the visual association areas (Chugani et al. 1987) which is felt to provide additional indirect evidence that visual function in neonates is not mediated by actively functioning cortical areas.

X and Y cells are the two classes of ganglion cells found in the retina of the cat. The X cells fire in a sustained fashion throughout the presence of a stimulus whilst Y cells will fire transiently only when a stimulus is turned on and off. X cells tend to fire with a

longer latency responding better to small stimuli and high spatial frequencies while Y cells respond better to fast moving or flickering stimuli, to low spatial frequencies and large stimuli. X and Y cells in the cat and monkey retina project along separate pathways to areas 17 and 18 of the visual cortex via the lateral geniculate nucleus. Maurer and Lewis (1979) suggested that the infant at birth had a partially functioning cortex with an X cell input but no Y cell input having a Y pathway to the colliculus only. They proposed that, prior to 2 months, an infant should have difficulty with any task that is dependent on the Y pathway to the cortex. Their theory is based on the evidence of a few animal studies with the view that X cells subserve form vision while Y cells are responsible for motion detection and peripheral localisation. The functional roles of the X and Y systems remain uncertain however, and literature on their relative development is conflicting (Atkinson 1984).

Atkinson (1984) doubted the likelihood of Bronson's theory (since some cortical function is believed to be present at birth) and the wisdom of Maurer and Lewis's view and suggested an alternative hypothesis. During the first two postnatal months visual responses are largely determined by the subcortical system but some functional connections do exist between the eye and cortex. After 2 months , pathways between the subcortex and cortex mature to enable control of the responses in the former by the latter. This corresponds to the development of co-ordinated eye movements and the 'tuning up' of disparity detectors in the cortex leading to binocular vision. Karmel and Maisel (1975) had earlier proposed a similar, but less refined model. They suggested that prior to six weeks visual attention was mediated subcortically by a system that controlled general arousal and saccadic eye movements. Although an intact geniculostriate system was present at birth, it did not develop sufficiently to control behaviour until after 6 weeks. The maturation of an inhibitory pathway between area 18 and the superior colliculus was implicated in the subsequent development.

Atkinson (1992) has more recently proposed an updated model of visual development. In the adult visual system the input of visual cortex can be defined as two streams with different capabilities. The lateral geniculate body in man is made up of six layers composed of two types of morphologically and anatomically distinct ganglion cells. These are the magnocellular and parvocellular layers and it is from these that the two cortical pathways take their name. Each pathway projects to different areas of V1 (see figure 1.1). The parvocellular pathway is responsible for form and colour vision while magnocellular pathways process movement and stereopsis. It is the differential development of these two sub-systems on which the model is based (Lewis et al. 1989)

and the developmental time course of visual function, with reference to these models, will be reviewed in Chapter 3

1.3 Aims of the project

The emergence of visual capabilities related to cortical function may provide information on the development of the underlying mechanisms and the resulting normative data relating to this may well be of benefit clinically.

The visual evoked potential has been successfully used to assess the integrity of the visual system in adults (Crews et al. 1975, Thompson and Harding 1978, Harding 1982), children (Harding et al. 1982) and premature infants (Grose et al. 1989) providing valuable information regarding the temporal sequence of neural processing from receptor to cerebral cortex. The visual system of the neonate is in dynamic state of rapid development. Distortion or deprivation of vision during critical periods of visual development can result in permanent visual impairment, thus the intervention of early therapeutic treatment is crucial. The understanding of underlying processes of normal visual maturation is of interest in the future development of clinically reliable techniques for the investigation of infant vision. These techniques are essential in the early detection of visual defects and for the identification of aetiological factors that may lead to later neuro-behavioural visual impairment. The VEP reflects the structural maturation of the visual neural elements and their connections with the brain.

In the present study, visual evoked potentials are used to examine the developmental time course of one specific visual function, i.e. colour vision, using visual evoked potentials, with the aim of identifying the emergence of this cortical function. Pilot studies will be carried out to establish optimal recording parameters to produce a stimulus in which luminance cues have been eliminated. These findings will then be applied to a cross sectional and longitudinal study of the onset and maturation of the chromatic visual evoked response in a group of infants. This study should, in addition, provide useful developmental normative data for future clinical studies.

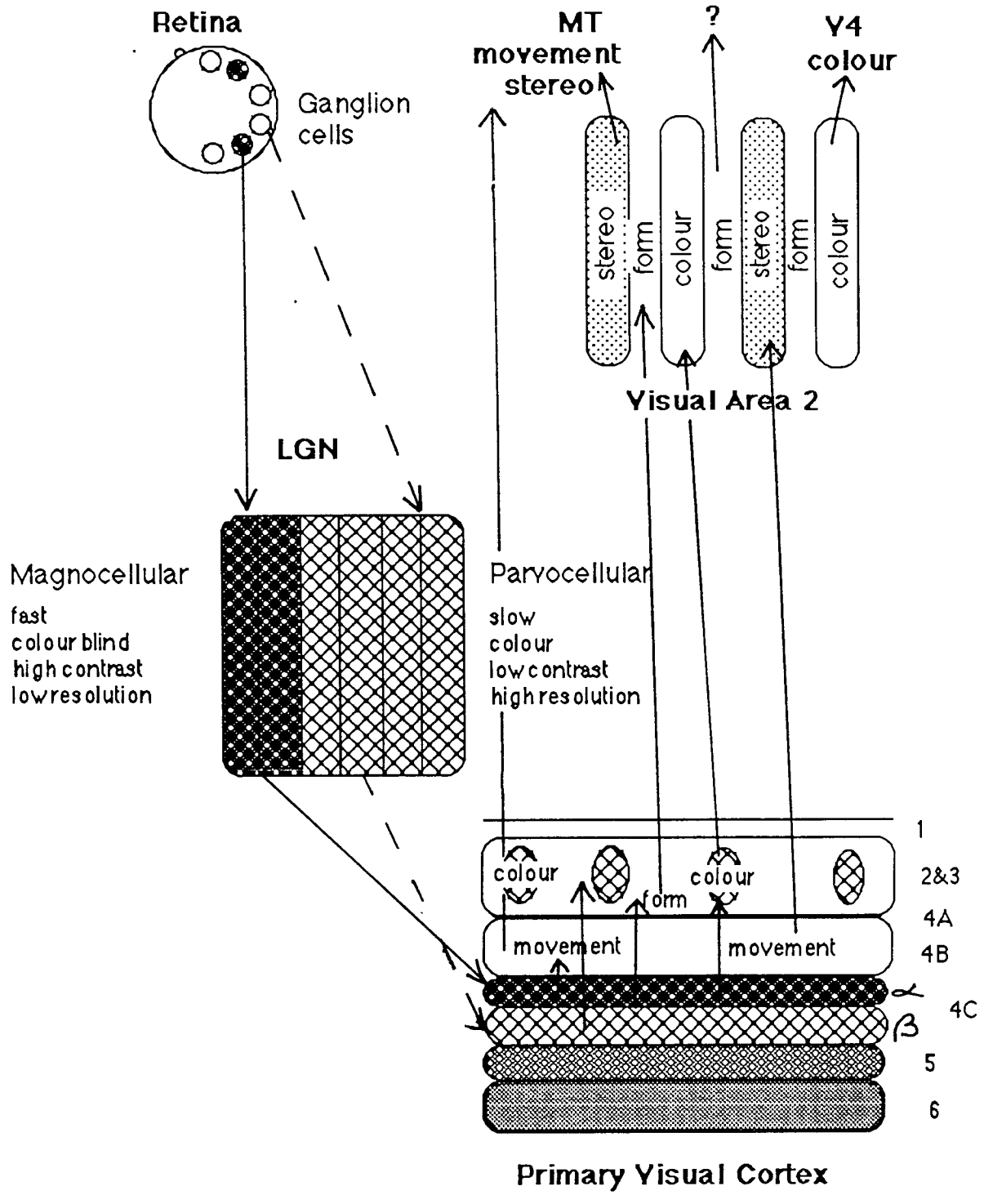

Figure 1.1 Schematic diagram of the functional separation of the primate visual system. **MT**, middle temporal lobe; **V4**, visual area 4; **LGN**, lateral geniculate body. **(After Livingstone and Hubel 1988)**

CHAPTER TWO

THE DEVELOPMENT OF THE HUMAN VISUAL SYSTEM

2.1 Introduction

The visual pathway in man consists of a primary projection from the retina to area 17 of the visual cortex, via the lateral geniculate nucleus. It is the embryological and postnatal development of this system that is presented below.

2.2 Formation of the gastrula and neural plate

Following fertilisation, the ovum subdivides progressively until, in about 72 hours, a small multicellular morula is formed and the uterus is reached. Blastocytation of the morula produces the trophoblast, which will serve as the embryonic support system, becoming associated with the uterine lining to form the placenta. Once implantation has occurred, gastrulation can begin. The cells within the blastocyte begin to flatten to form two layers,the future endoderm and ectoderm, which form the embryonic plate. Fluid enters the cell and the endoderm and ectoderm form hollow vesicles, with contact maintained at the embryonic pole. Newly differentiated cells split away from the underside of the ectoderm, filling the space between the trophoblast and inner cell mass with a jelly like mesoderm. Cells from this layer, form a midline, rope-like notochord and somites which are the precursors of muscles and bones. At about 16 days the overlying ectoderm begins to change structurally, forming the neural plate which is composed of multilayered newly differentiated cells. It is this plate that will become the source of the entire nervous system.

2.3 Development of the neural tube

A longitudinal neural groove appears along the middle of the neural plate, and on either side of this, the ectoderm becomes elevated to form two curved neural folds. These folds begin to converge as the groove deepens. Neural tube closure occurs at about 6 to 8 weeks gestation, beginning in the cerebral region but the anterior and posterior extremities remain open and are known as neuropores (Karfunkel 1974). A group of cells break off from the neural folds during tube formation and migrate laterally, to form a series of neural crest cell clusters, along the lengthening tube. These cells will form the posterior root ganglia, the sensory ganglia of the cranial nerves, the autonomic ganglia, Schwann cells and the basis of the pia, arachnoid and mesenchyme of the head. The walls of the neural tube will convert to form the various parts of the central nervous system (Weston 1970, Cowan 1979, Jacobsen 1978, Snell 1983).

At about the fourth week, segmentation of the mesoderm begins as the para-axial mesoderm becomes divided into segmental blocks, or somites, arranged in pairs. These will form the skeletal and musculature anatomy. The mesoderm however, remains unsegemented anteriorly and is the promordium of the skeletal coverings of the brain sclera, extraocular muscles and uveal tract.

2.4 Cellular Migration.

The cavity, or lumen, of the neural tube is lined with ectoderm or neuroepithelia. At about 4 weeks of age, these are found between the lumen and the outer limiting membrane and alternate in activity between cell mitosis and DNA synthesis. During the 5th week, the neuroepithelia differentiate into neuroblasts, which break their attachment and migrate away from the lumen, causing the neuroepithelial layer to reduce in size. The cells migrate away to form a new outer mantle, which will become the grey matter of the spinal cord and brain, and it is here that the neuroblasts will mature into neurons. The outward extension and migration of axons, from the developing neurons, form the marginal layer of the neural tube that will become white matter.

2.5 Cell Differentiation

Neuroglia, the cells that make up a very large part of the central nervous system, also originate from the neuroepithelial layer of the neural tube and undergo rapid miotic differentiation. At about the same time that the neuroblasts begin migration, the primitive glial cells (glioblasts) lengthen, while maintaining their attachment to the neural tube. These become arranged radially around the neural tube. As they mature, the majority become detached from the tube and the outer limiting membrane, differentiating into mature neuroglia; astrocytes, oliodencrocytes and ependymal cells.

2.6 Formation of the brain vesicles

By the end of the 4th week of gestation the neural folds fuse at their anterior ends initiating the closure of the anterior neuropore. The cranial end of the neural tube exhibits a series of swellings along its longitudinal axis, differentiating the dilated brain rudiment from the narrower spinal cord. Two transverse constrictions cause the future brain to form into three distinct spherical vesicles, the fore brain (prosencephalon), the mid brain (mesencephalon) and the hind brain (rhombencephalon). The fore brain and hind brain further subdivide and by the 5th week of gestation, five brain vesicles are apparent (figure 2.1). Whilst cell differentiation occurs in the neural tube, flexures begin to develop, the first occurring in the midbrain region of 3-4mm crown rump (CR) embryos. This produces a primitive head bend which accompanied by a cervical flexure, results in the whole head bending forward. Three brain flexures are apparent by the 6th week but

eventually two caudal flexures will re-straighten leaving only the cerebral hemispheres at an angle to to brain axis (Cowan 1979) .

2.7 The Mesencephalon

The lumen of the neural tube has a groove, down each side, along its length-the sulcans limitans, which separates the posterior alar plates from the anterior basal plate. The roof and floor plates lie superiorly and inferiorly to the lumen. Primitive neurocytes in the basal plates differentiate into neurons, which will form the nuclei of the III (oculomotor) and IV (trochlear) cranial nerves. The marginal layer of the basal plate enlarges and nerve fibres extend from the cerebral cortex, to lower centres of the pons and spinal cord to form the basis pedunculi. The alar and roof plates mature to form the tectum, which will bear sensory neurons of the superior and inferior colliculi. Fibres from the III cranial nerve emerge on the ventral surface, and fibres of the IV cranial nerve emerge on the dorsal surface of the midbrain.

2.8 The Rhombencephalon

The hindbrain divides into two parts to form the metencephalon (future pons and cerebellum) and the myelencephalon (medulla oblongata). The cavity of the hindbrain vesicle forms the fourth ventricle, which is continuous with the spinal cord and filled with cerebrospinal fluid. It is from the neurons of the basal plate that the pontine motor nucleus of the VI (abducent) cranial nerve originates with the V (trigeminal) arising from a large ganglion near the hind brain.

2.9 The Prosencephalon

The prosencephalon is important in the development of the visual system and rapidly divides into the two part tesencephalon and the diencephalon (Cowan 1979).

2.9.1 The Diencephalon

The cavity of the diencephalon forms the greater part of the third ventricle. In the lateral wall of the third ventricle, thalami arise as a thickening of the basal plate on each side. The thalamus is prominent at about 7 weeks gestation, and is responsible for information transfer from the various parts of the central nervous system to the neocortex. Posterior to the thalamus, the medial and lateral geniculate bodies arise as solid buds. The lateral geniculate body is the most important of the thalamic nuclei associated with vision. The nuclei of the hypothalamus are derived from the lower alar plates.

2.9.2 The Telencephalon.

The telencephalon forms the anterior end of the third ventricle, which is closed by the lamina terminalis (the original rostral end of the neural tube). The cerebral hemispheres bulge from the midline of the telencephalon during the fifth week of embryonic life. Their cavities (the lateral ventricles) reduce in size as they expand superiorly and the wall thickens. As development proceeds, the cerebral hemispheres grow rapidly, first anteriorly to form frontal lobes, then laterally and superiorly to form the parietal lobes. Finally enlarging inferiorly to form the occipital and temporal lobes. Due to this great expansion, the hemispheres cover the mid and hind brains.

At about 6 weeks, the neuroepithelium lining of the forebrain vesicle proliferates producing large numbers of neurocytes. These form the corpus striatum, which bulges into the lateral ventricle. Initially it is separated from the diencephalon by a deep groove, but as the hemispheres enlarge, its medial surface approaches the lateral surface of the latter. A thickening in the medial wall of the cerebral hemisphere, where it has invaginated to produce the choroid plexus, produces the hippocampus. This protrudes as a longitudinal elevation into the lateral vesicle. Nerve fibres pass through the corpus striatum, dividing it into the caudate and lentiform nuclei.

2.10 Formation of the fissures

The cortex initially develops as a smooth surfaced layer of cells. By the 6th month of life however, the rapidly expanding hemispheres must fit into the confining space of the cranium, and a multitude of convolutions, (gyri), separated by fissures, (sulci), become evident on its surface. The first two fissures to appear in the brain are the rhinal and hippocampal fissures developing in the 4th month. Around this time, the lateral fissure of Sylvius also forms. The central sulcus, the parieto occipital sulcus, the calcarine fissure and the collateral fissure are formed at six to seven months gestation (Jacobsen 1978). The cortex covering the lentiform nucleus, remains as a fixed area called the insula. Later this region becomes buried in the lateral fissure, as a result of overgrowth of the adjacent lobe.

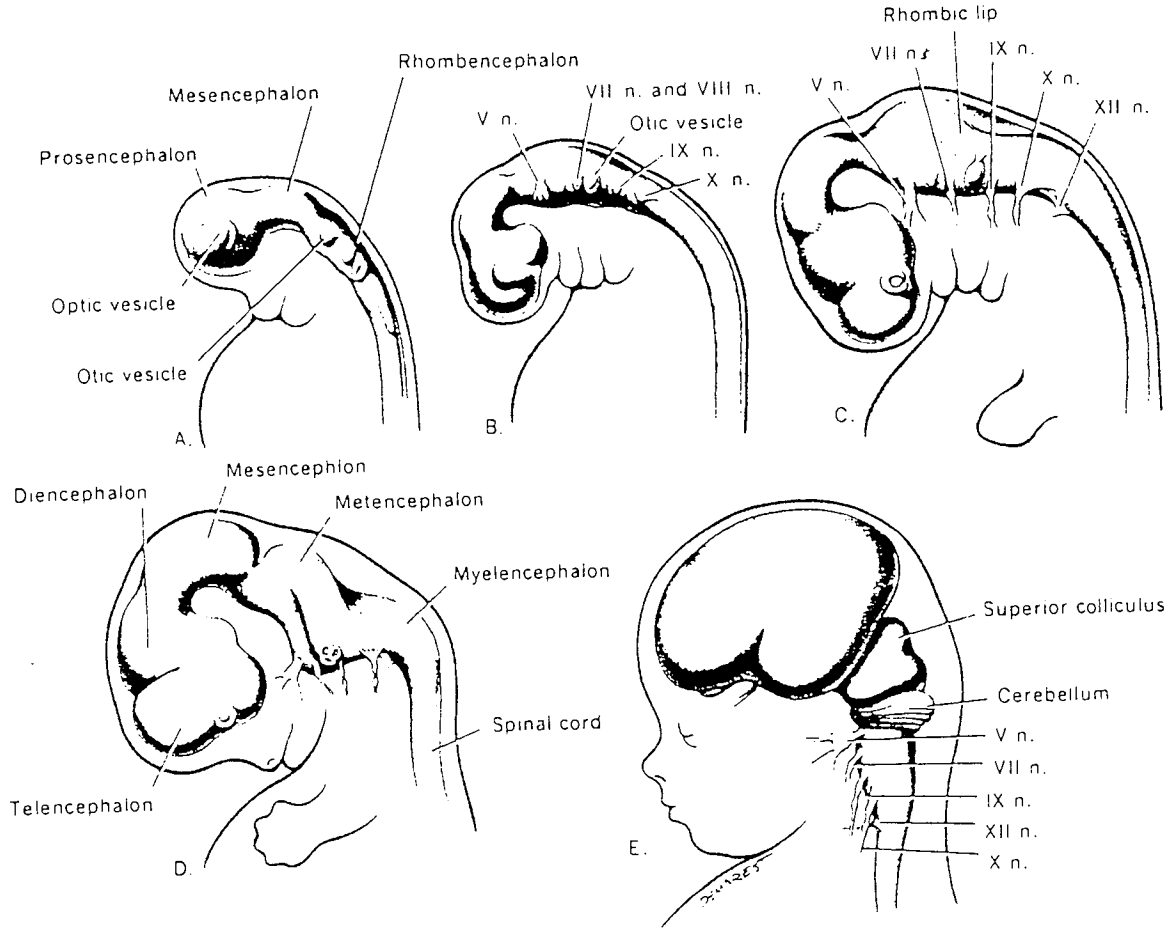

Figure 2.1. Formation of the brain vesicles (After Snell 1983)

2.11 The development of the commissures

The lamina terminalis forms a bridge between the two cerebral hemispheres. It is within this area that nerve fibres pass from one hemisphere to another (commissures). This connection enables co-ordination between different reflex centres, in both halves of the brain (Arey 1974). The anterior commissure, connecting the olfactory systems of both sides, is the first to develop. The second is the fornix, connecting the two hippocampi and the third is the largest and most important; the corpus callosum. This initially connects the frontal lobes, followed by the parietal lobes. As it grows, it arches back over the third ventricle. The lamina terminalis becomes stretched out to form a thin septum pellucidium. From the inferior part of the lamina terminilis, the optic chiasm is formed. This contains fibres from the medial half of the retinae, which join the optic tract on the opposite side, and pass to the lateral geniculate body and the superior colliculus (Snell 1983).

The neuroepithelial cells, that line the cavity of the hemispheres, produce large numbers of neuroblasts that migrate to form the cortical plate, which then becomes the neocortex. The neuroblasts are believed to migrate along the radial glial cells and fibres passing between the neocortex and the ventricular zone, to form an intermediate white matter zone (Lund 1978).

2.12 Stratification of the visual cortex

As the cerebral cortex forms, cell layers of varying densities appear. In the formation of the visual cortex, some of these layers are transient and will become integrated into the mature laminar formation. (Sauer et al 1983) The first zone to form is layer VI. Superficial cells migrate in waves through the deeper cortical cells to lie beneath layer I, (marginal zone), resulting in the formation of a dense zone S (Zilles et al 1981). Zone S is transient, becoming progressively flatter to form Layer II. This is the last layer to differentiate.

By 137 days, the cortical plate of area 17 can be seen to be stratified into 5 distinct zones of different cell densities, area 18 however, remains undifferentiated. Layers I,V and VI are present in area 17 with zone S, and a lighter band, zone P sandwiched between layers I and V (Sauer et al 1983). Between 160-170 days after conception, (DAC), zone P increases in width and subdivides into upper (E) and lower (D) zones. Zone D will further differentiate into 3 bands of different cell densities. After the 170th day, Area 18 begins to change with the appearance of layer III above zone S, and the formation of layer IV.

It is not until 180 DAC that the trilaminar layer IV of Area 17 will begin to emerge from the differentiation of zones D, and E. Sublamina IVa, IVb (line of Gennari) and IVc, will be formed by day 189. Lamina V and VI continue to decrease in width in Area 17 but not in 18, with zone S becoming less dense and narrowed as it converts to layer II. By 185 DAC all 6 layers of the cortex are visible in area 18 with area 17 attaining the laminar appearance of the adult cortex at 190 DAC once layer IV is formed. It is to layer IV that the majority of the cells of the LGB project.

Prior to birth, laminae V and VI of Area 17 decrease in width and cell density. Further postnatal development of the visual cortex will be discussed later in this chapter.

2.13 Myelination

Myelin acts as a nerve insulator, preventing the short circuiting of impulses between nerves. The speed of impulse conduction is enhanced by reduction of the mean capacity of the nerve per unit length. The rate of impulse conduction is related to the myelin thickness (Hodgkin 1964). Although complex behavioural activity can be carried out prior to myelination, there is a great improvement in co-ordinated behaviour following myelination (Langworthy 1933). Myelin is formed from oligodendrocytes. These develop from glioblasts, during both pre and post natal periods, producing membranous structures to wrap around the CNS neuronal axons. Peripheral nerves are myelinated by Schwann cells.

The pattern of myelination within the nervous system appears to follow the order of phylogenetic development (Langworthy 1933). The fibres of the basal ganglia in the brain begin to become myelinated in the sixth month of gestation, followed by the sensory nerves in the spinal cord. This is a slow process, and even at birth parts of the brain remain unmyelinated. It is not until after birth that the corticobulbar, corticospinal, corticopontocerebellar and tectospinal fibres myelinate. It is possible that some fibres remain unmyelinated until puberty (Snell 1983).

The upper visual pathways are among the first areas of the cerebral cortex to become myelinated at birth. There is no evidence of myelination of the optic tract at 24 weeks gestation, but by 32 weeks, some fibres will have begun to myelinate. By 36 weeks, nearly all the fibres of the intracranial nerve and tract show myelination, and by term, it can be seen in the orbital portion of the optic nerve, behind the globe.

2.14 Dendritic development

The development of dendrites can account for much of the increase in cell density and volume of the brain. The growth of the dendritic tree is affected only by the neuron itself, not its connections with other cells.

The formation of dendrites commences in the cortical neurones of area 17 at 20 weeks gestation. This begins at the base of the pyramidal cells, then branching, following the same order as the lamination of the cortex i.e. beginning at layer IV then layer III etc. The rate of increase in arborisation is maximal at 36-40 weeks gestation, slowing down in later weeks. After birth, branching will continue only in the apical dendrites, with maximum length of 1400μm achieved by 4 months post term.

The dendritic spine density in area 17 reaches adult values in the late foetal period and continues to increase reaching a maximum at 5 months post term. After this, the spine density decreases to adult values again, at 2 years. There is a change in the size and shape of the spines during this period. From 33 weeks gestation to 3-5 months post term, they change from hair like to 3-5x thicker with bulbous ends. After this time very little change occurs (Michel and Garey 1984).

Dendrites form the major proportion of the membrane surface for the integration of synaptic inputs. (Purapura 1975) and are the post synaptic targets for a variety of projects to the cortical neurones. It is the development of this system that is important in the synaptic function of the developing brain. A correlation between dendritic development and synaptic density is supported by the initial postnatal spine proliferation and consequential elimination.

The formation of synapses in the visual cortex begins after the migration of the cortical neurones. Synaptogenesis, in Area 17 of the visual cortex, spans from the third trimester of pregnancy to about 8 months postnatally (Garey and de Courten 1983). At 28 weeks, the synaptic density in layers IVb and IVc are relatively high in comparison to layer I. The overall number within area 17 increases from 2 to 17% of the adult number by term, reaching a maximum at 8 months postnatally. There is little increase in the synaptic density in layers IVb and IVc, resulting in a final lower density with more synapses in layers II-III than any others.

2.15 The development of the visual pathway

Growth cones develop at the end of retinal ganglion cell axons during ocular development and the nerves produced, from the accumulation of new material, grow into the CNS.

These nerves leave the optic stalk by 18 mm CR (crown rump)and pass into the marginal zone of the neural tube where by 22mm CR (7 weeks) they decussate to give rise to the optic chiasma. By the 11th week, uncrossed fibres appear in the chiasma and partial decussation is adult like by 80mm CR (13 weeks) (Sakamoto 1952).

Once the chiasma has been formed, the axons partially encircle the surface of the diencephalon and attach to a clump of cells on the dorso-lateral part of the thalamus. These will later differentiate to form the dorsal nucleus of the lateral geniculate body, LGB, (30mm CR) (Cooper 1945). It is not until 9 weeks that the ventral nucleus is apparent. In both the lateral geniculate nucleus and the superior colliculus (the major midbrain visual centre which receives substantial input from some classes of ganglion cell) optic nerve axons from both eyes are initially intermingled throughout the entire structure when they first invade early in gestation (Blakemore 1991). Formation of the cellular laminae of the LGB begins at the 22nd week and is complete by the 25th week (Hitchcock and Hickey 1980). The formation of the optic disc representation on the laminae 4 and 6 takes place during the same period. The laminae appear as 6 U shaped stripes and are classified according to the cell types found within them. There are two ventral magnocellular layers (1 and 2) and four dorsal parvocellular layers (3 to 6). Input from the ganglion cells in the retina of the contralateral eye pass to laminae 1,4,6,whereas 2,3,and 5 receive input from the ipsilateral eye (Garey 1984). The post natal development of the lateral geniculate body will be reviewed later in this chapter (see 2.29). Following innervation of the dorsal lateral geniculate, the ganglion cells reach the superior colliculus. This is also arranged in a laminar fashion but these are defined by the presence of fibre bundles interspersed by cell body fibres (Lund 1978).

2.16 Ocular Development

Ocular development begins at about 22 days gestation. As the neural ridges enlarge, optic grooves or pits, are formed on either side of the midline of the forebrain. The neural groove closes and the optic pits deepen. By the 24th day of gestation, two symmetrical diverticuli, the optic vesicles (figure 2.2), are visible (O'Rahilly 1975). The distance between the brain and surface ectoderm increases with development causing the optic vesicle to be separated by the optic stalk.

At about 28 days, the cells of the distal neural ectoderm lining the optic vesicle elongate to become columnar. Their nuclei migrate towards the cavity of the optic vesicle, leaving a marginal zone composed of cells without nuclei. The optic vesicle invaginates to form the two layered optic cup (figure 2.3). During this invagination, the distal wall comes into contact with the surface ectoderm causing a thickening- the lens placode. This will later

invaginate forming the lens vesicle. The inferior wall of the optic cup grows more slowly than the rest of the cup which produces an opening inferiorly, the foetal fissure (Mann 1964). The cup opening is gradually differentiated into a rounded portion, the primitive pupil.

2.17 Lens formation

The lens vesicle separates from the surface ectoderm at about 6 weeks gestation. This, in turn, induces the formation of the corneal epithelium in the ectoderm (Modak 1972). Cells in the posterior lens vesicle, that have been undergoing miotic division, change their metabolism to produce protein. The cells begin to elongate, eventually filling the vesicle. The development of the retinal cells is believed to play a part in this formation of lens fibres.

2.18 Corneal development

The first wave of mesoderm begins its migration from the edge of the optic cup and under the corneal epithelium at about 6 weeks. This will later become the corneal endothelium (Marshall and Grindle 1978). During the following weeks, the endothelium becomes a well defined two cell deep layer. A second wave of mesoderm migrates between the endothelium and epithelium forming the corneal stroma (Hay 1980).

2.19 Development of the vascular system

During the 6th week of gestation, a branch of the internal carotid artery grows through the foetal fissure, into the cavity of the optic cup (O'Rahilly 1975). As it enters, it is accompanied by some mesenchymal cells that are believed to form the primary vitreous (Balaz 1975). A branch leaves this hyaloid artery to form the tunica lentis and supply the posterior lens surface. At about 16 weeks gestation mesenchymal cells can be found near the hyaloid artery. These form solid cords, which become canalised to form a network of capillaries (Ashton 1970). The capillary network initially forms in the nerve fibre and ganglion cell layers growing centrifugally away from the optic nerve. The vessels then invade the deeper retinal layers, forming a second capillary system in the inner nuclear layer. The vascular system undergoes development and degeneration in different areas, as changes in size and function occur. This leads to a decreased uniformity of a less dense capillary bed. The retinal vessels reach the nasal ora serrata by the 7-8th month, while the temporal retina vascularises only to the equator at this time. General retinal vasculature is thought to be complete by 38 weeks (Ashton 1954,1957).

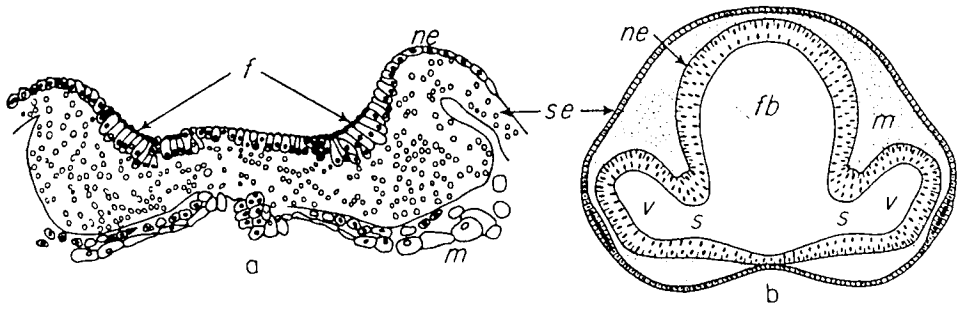

Figure 2.2. Formation of the optic vesicles. a) Cross section of frog neural tube before tube closure, b) Cross section of head of 4mm human embryo after closure.
f-fovealae opticae, fb-embryonic fore brain, m-mesoderm, ne-neural ectoderm, s-optic stalk, se- surface ectoderm, v-optic vesicle. **(After Walls 1991).**

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Figure 2.3. Formation of the optic cup. a,b,c diagrammatic models of optic vesicle and cup with surface ectoderm removed. a',b',c' optical sections through the stalk axis (dotted line). ef-embryonic fissure, g-groove(continuation of embryonic fissure), i-invagination of vesicle, il- inner layer (future retina), lp-lens placode, ol-outer layer (future pigment epithelium), s-stalk, se-surface ectoderm.
(Walls 1991)

2.20 Retinal development

Pigment appears in the columnar cell wall of the optic vesicle at about 5 weeks gestation. This will later develop into the retinal pigment epithelium. During the 5-6th week, differentiation of the thicker inner retinal wall into the neural retina commences. Cells in the germinal layer divide mitotically and migrate towards the vitreous, forming the inner and outer neuroblastic layers. Migration begins at the optic disc and forms a nucleus free zone, between the two layers (the transient layer of Chievitz) (Smelser et al 1973).

The inner neuroblastic layer produces spindle shaped Muller fibres adjacent to the inner limiting membrane. Their inner processes expand and their footplates spread eventually fusing with their limiting membrane (Spira and Hollenberg 1973, Maguire and Rodieck 1973). By the 6th week maximum thickness of the retinal wall has been achieved, and further growth produces increased retinal area. Contact between the inner and outer walls is maintained by membranous junctions and outer neuroblastic cilia, which penetrate the pigment cells (Hollenberg and Spira 1973).

Further cell differentiation in the inner neuroblastic layer takes place in the 9th week of gestation when the ganglion cell layer begins to form in the first of three stages (Provis et al 1985). Ganglion cells migrate towards the inner retinal surface, guided by the Muller fibres, forming a thin inner plexiform layer between the ganglion cell and inner neuroblastic layers. The ganglion cells produce long axons, which transverse the retinal layers by turning at right angles to reach the optic stalk (Barbar 1955).

Small clumps of glial cells are produced when the some of the retinal cells are cut off from the main body. This mass of cells is the cone shaped primitive papilla which is vasculated by the hyaloid artery and forms its sheath. When the hyaloid vessel disappears at birth, the papilla atrophies and it is the degree of atrophy that determines the depth of the physiological optic cup. Some parts of the papilla may persist in the glial cells of the arteries and retinal supports (Seefelder 1930).

The nerve fibres enter the optic stalk and pass rapidly towards the infero-nasal aspect of the brain. By 19mm CR the stalk is almost completely filled with fibres and by the 7th week these have decussated at the lateral angle of the optic recess on the underside of the forebrain in front of the pituitary. By the 11th week the uncrossed fibres appear at the chiasma and the 13th week sees partial decussation in an adult like pattern (Sakamoto 1952).

By the end of the 12th week, mitosis is occurring across the whole retinal surface. following the initial restriction to the central ganglion cell and internal plexiform layers. During the next few weeks of development, the Muller cells populate the inner plexiform layer, then migrate to the middle and outer layers (Provis et al.1985). The amacrine cells of the inner nuclear layer are formed from the remaining cells of the inner neuroblastic layer at about 10-15 weeks gestation. Their fibres synapse in the inner plexiform layers of the nerve fibres (Hollenberg and Spira 1973). Horizontal and bipolar cells migrate upwards from the outer neuroblastic layer, obliterating the transient layer of Chievitz (Smelser et al . 1973).

By 3 months, the inner and outer neuroblastic layers have extended as far as the pars ciliaris, and by the 4th month, ganglion cell layer has developed as far as the mid peripheral retina . Mitotic division has ceased in all layers by the 14-15th week of gestation and thus between 18-30 weeks, the ganglion cell population remains stable with a decline in mean cell density. The third stage of ganglion cell development commences at about 30 weeks, as the soma diameters of the temporal retinal ganglion cells increase. The conclusion of ganglion cell development occurs during the neonatal period, and is marked by the formation of the foveal depression and the maturation of the ganglion cell body size (Provis et al . 1985).

2.21 The development of the photoreceptors

The photoreceptors are the last component of the retina to be differentiated. They are probably derived from the ependymal layer that lines the primitive neural tube and optic vesicle (Mann 1964). The photoreceptor layer initially consists of an outer primitive cone layer with an number of nuclei lying more internally. These will eventually differentiate into rods (Spira and Hollenberg 1973).

Photoreceptor differentiation occurs initially at the macula region, but soon becomes retarded in that area, in comparison with all other retinal areas, and is the only area at birth not to have fully developed photoreceptors. Further development of the rods and cones is apparent at 20 weeks. Each cone has developed a synaptic process or pedicle and the narrower processes of the rods extend down between these, to the retinal pigment epithelium. Outer segment formation begins at 23 weeks, but prior to this synaptic connection has been made with the photoreceptors (Yamada and Ishikawa 1965). Outer segment formation is slower at the fovea , being only first detectable at 36 weeks, whereas the inner cone segments are developing at 24-26 weeks.

2.22 Development of Oculomotor Muscles and Adnexa

Oculomotor muscles are formed from the mesoderm that surrounds the optic cup. This begins at about 7 weeks gestation and at this time the foetal fissure fuses and the lids begin to develop (Gilbert 1957). The third and last wave of mesoderm migrates across the front of the lens at 26mm CR (8-9 weeks). This is highly vascularised and forms the anterior layers of the iris. Vessels from this mesodermal layer, contribute to the annular vessels around the optic cup, the major arterial circle of the iris (Duke-Elder and Cook 1963).

As the lens continues to grow and change shape, it is enveloped in an elastic capsule (Weale 1983) . It is the influence of the lens and increased intraocular pressure that causes the steepening of the cornea, and a distinct junction to form between the cornea and the sclera, the limbus (Hay 1980). The vascular choroid differentiates from the mesoderm around the optic cup with the outer sclera deriving from the same source.

2.23 General Ocular Development:3-4 months (gestational age)

By 3 months, the anterior margin of the optic cup has grown forward, to form the ciliary epithelium, sphincter and dilator pupillary muscles and the epithelial layers of the iris. At 60 mm CR, the lids begin to fuse and the obicularis oculi is visible (Mann 1964). By the 4th month, corneal differentiation has produced Bowmans layer (Hay 1980). The mesodermal parts of the ciliary body, including the Canal of Schlemm, ciliary processes and ciliary muscle, appear.

2.24 General Ocular Development:6-7 months (gestational age)

The extrinsic muscles develop insertions into the sclera at 200 mm CR. The final corneal layer (Descemets) develops, and the lids are fully formed, by the 6th month of gestation. By the 7th month, the eye has a diameter of 10-14mm and myelination of the optic nerve reaches the chiasma. The hyaloid artery becomes impermeable and begins to involute (Mann 1964).

2.25 General Ocular Development:9 months (gestational age)

The eye is now 16-18 mm in diameter and myelination of the optic nerve has reached the lamina cribrosa, but is not complete in the higher neural pathways. Atrophy of the mesoderm, that formed the pupillary membrane produces the pupil. The iris stroma in caucasians contains no pigment at birth, giving the iris a blue appearance.

2.26 Postnatal Development of the Visual System

At birth the pupil is relatively miotic. This may be due to the immaturity of the dilator muscle, which does not reach adult proportions until five years of age, or immaturity of the sympathetic innervation of the iris (Lind et al. 1971). Iris colour change is produced by pigment development in the iris stroma, as the infant becomes older. The cornea continues its development postnatally ,as the epithelium thickens and the stroma becomes less cellular and more fibrous.

The surface area of the retina increases at a rate of 10-15mm^2 per week, during gestation. This proceeds at a slower rate after birth. The increase in retinal area is thought to be due to maturation and growth of the cells, as cell division ceases at 30 weeks gestation.

2.27 Foveal development and differentiation

The foveal region is easily identifiable at 22 weeks gestation. It is the first region to cease cell division. A foveal pit appears by the 32nd week of gestation and is due to the peripheral migration of the ganglion cell layers. (Hendrickson and Yuodelis 1984, Yuodelis and Hendrickson 1986).

At birth, the peripheral retina is well developed and postnatal development in the retina is primarily concerned with differentiation of the macular region. The foveal depression is apparent but the inner retinal layers are still present across it and the outer and inner segments of the cones are still immature (figure 2.4). This suggests that the central retina is not fully functional at birth (Abramov et al. 1982). Originally, foveal development was thought to be complete by 4-6 months (Mann 1964), however the later work of Yuodelis and Hendrickson (1986) reveals that the developmental sequence is much longer.

The maturation of the fovea is thought to be marked by three main events. Firstly the inner retinal layers migrate peripherally to form the foveal depression, at 22-26 weeks gestation. This is not complete until 15 months post partum (Hendrickson and Yuodelis 1984). In order to maintain synaptic contact with the inner retina as it shifts, the foveal cones form basal axons, the fibres of Henle, which increase in length as the layers migrate peripherally. Secondly, there is a steady decrease in the diameter of the rod free zone, the foveola, from 1600μm wide at 22 weeks to 750μm, the adult diameter, between 15 and 45 months after birth.

There is substantial evidence to suggest that the limit of spatial resolution of the retina is set by the density of packing of the adult fovea (Hirsch and Haylton 1984). The elongation and central migration of cells, in the final stage of development, to form a

densely packed foveola, is thought to be of particular importance in visual acuity development. The packing and elongation of foveal cones produces a marked increase in cone density, but this does not reach adult levels until 15-45 months, post partum.

2.28 Myelination

Myelination of the human optic tract proceeds centrifugally towards the optic nerve from 32 weeks, and continues postnatally (Magoon and Robb 1981). Changes occur rapidly within the first 4 months, slowing down later to reach adult levels by 2 years (Friede and Hu 1967). Those visual pathways subserving subcortical vision, are fully myelinated by 3 months having started several months prenatally (Yakovlev and Lecours 1967). Myelination of other extrastriate visual areas and intracortical neurones takes much longer, continuing into mid childhood.

Figure 2.4 Shapes and dimensions (in micrometres) of neonatal and adult cones. (From Banks and Bennett 1988)

2.29 The lateral geniculate nucleus

There is a rapid increase in the volume of the lateral geniculate nucleus (LGN) between birth and six months of age. The LGN doubles in volume during this period then remains stable in size through adult life (Garey and de Courten 1983, Garey 1984). The cellular laminae begin to form by the 22nd week of gestation and this is complete by the 25th week.(Hitchcock and Hickey 1980).

There are four basic neurone types in the LGN of the adult; a) multipolar, b) bipolar, c) neurones with 'axon-like' dendrites and d) neurones with 'beaded' dendrites (Garey and de Courten 1983). The various neuronal types are recognisable in the LGN at birth, or even before, however they tend to be immature with smaller cell bodies and a smaller diameter of dendritic arbour (De Courten and Garey 1981,1982). The dendrites, however, tend to be longer as they are branched with more complexity (Leuba and Garey 1982). The immature dendrites and soma have large numbers of spines and hairlike processes. These are most abundant at 4 months post postnatally decreasing to adult values at 9 months. During this period there is an increase in soma size and dendritic spreading.

All the cells of the LGN are about 60% of their adult size at birth. Cells in the parvocellular layers show a rapid growth period from birth to six months of age reaching adult size by the end of the first year. However those cells in the magnocellular layers (1 and 2) continue their rapid growth until the end of the first year and reach adult size by the end of the second year (Hickey 1977).

2.30 Visual Cortex

Early work by Conel (1939-1963), demonstrated the relative variation in maturity between the visual areas and the visual cortex. Area 17, the striate cortex is the most mature at birth declining in maturity with an increase in anterior position. The order of relative maturity remains as area 17,18,19,21 and 8 throughout the first year of life. Several more recent studies have investigated the development of the human visual cortex.

The visual cortex increases four-fold in volume between 28 weeks gestation and birth. It then quadruples again to reach adult size by 4 months (Huttenlocher et al. 1982, Sauer et al. 1983). This increase in volume is accompanied by a growth in complexity of the cerebral convolutions (Garey 1984). Conel found a rapid change in the interconnectivity in the visual cortex between birth and three months of age.

2.31 Postnatal Synaptogenesis

There is a considerable growth in cortical volume between birth and 2 months, but little increase in the density of the synapses. The increase in number of synapses during this time is due to an expansion in volume. From 2 to 6 months however, there is an increase in cell size, synaptic density and interconnectivity (Atkinson 1984). Synaptic density and synaptogenesis reach a maximum in area 17 of the cortex relatively early compared to other areas and this is thought to reflect the difference in development time between cortical and association areas (Conel 1939, Yakovlev and Lecours 1967). In the superior colliculus of the rat, there is a rapid synaptic proliferation in the first four postnatal weeks (Lund and Lund 1972, Warton and McCart 1989).

2.32 Elimination of synapses

The postnatal maturation of the visual system involves both an increase in interconnectivity and an elimination of those synapses which become redundant. This elimination commences at about 8 months and continues until 11 years of age, when adult synaptic density is achieved. This will involve a 60% loss of synapses from the maximum value at 8 months. There is an equal loss of synapses from each layer of the visual cortex from early infancy to early childhood. This has been calculated to be a loss of 41% (Huttenlocher and de Courten 1987).

This reduction in synaptic density was originally believed to be due to neuronal loss but more recent work (De Courten et al. 1982, Leuba and Garey 1982) found no clear evidence to support this view and suggested it is due to a decrease in the number of synapses per neurone. The elimination of dendritic spines in the visual cortex occurs at similar rate to that of synaptic elimination (Michel and Garey 1984).

2.33 The plasticity of the visual system

The developing nervous system is greatly influenced by changes in its environment (Hickey 1981). Hubel and Wiesel (1970) showed that visual deprivation results in amblyopia in cat and monkey and called the period in which environmental factors have the greatest effect 'the critical period'. Clinical studies have shown the upper limit of this critical period to be as late as 7 years of age, in man (Assaf 1982) with the most sensitive period being the first two years of life. Investigations into the role of disruption of the visual environment in infants show that a critical period also exists in human development. Although behavioural studies can provide an estimate as to when the critical period in humans occurs, comparisons with animal studies must be made to determine the underlying neurological changes.

The structural changes due to deprivation can most easily be seen in the lateral geniculate nucleus. Monocular deprivation results in a shrinkage of those cells that receive input from the deprived eye. In cat and monkey, even short periods of deprivation during the critical period result in permanent changes of cell size. These changes parallel the physiological changes in the deprived visual pathway and the changes in the animals' capabilities (Hickey 1981). Geniculate cell size changes are often explained in terms of a competitive interaction that probably takes place in the visual cortex. Such interactions may involve a competition for synaptic space between the axon terminals of different lateral geniculate cells (Sherman 1979). In normal development the period in which the LGN cells develop maximally corresponds to the most sensitive time in the critical period and even short periods of deprivation during this time can produce marked cell changes (Hickey 1977, Kalil 1978).

There may be other anatomical changes taking place in the visual pathway, during the critical period. In early development, the afferent fibres of both eyes of the monkey are initially distributed diffusely in area IV of the cortex, prior to the formation of ocular dominance columns at 6 weeks (Hickey 1977). The progressive loss of synaptic connections, from one or other of the eyes, may produce the definition of these columns and this may also be the cause of dominance in man (Le Vay et al. 1978, Hitchcock and Hickey 1980). Layer IV cells are responsive to stimulation of only one eye whereas most other cells in the other cortical layers are binocular. The formation of the ocular dominance columns coincides with the most sensitive time of the critical period, but both this and the change in cell size of the LGN is complete before the critical period is at an end (Lund 1978).

Other morphological changes occurring during the critical period are as follows;
a) The over production of connections and subsequent elimination of synapses may impart plasticity into the developing visual system allowing adaptation to malformations. Recovery from dysfunction should be greatest during this period with a subsequent progressive reduction in elasticity as the neuronal system matures (Huttenlocher et al. 1982). The time course of synapse elimination in the striate visual cortex is compatible with the sensitive period in the human visual system. Clinically the upper limit of the sensitive period for the development of binocular vision is about 7 years with the most critical time within the first two years (Assaf 1982).
b) Quantitative studies on dendritic spine density in the visual cortex of the monkey show an initial rapid increase during the first two months of life followed by a slow reduction lasting more than 9 months (Boothe et al. 1979). This corresponds closely with the most sensitive part of the critical period.

c) In the human visual system there is a rapid growth of neurones in the parvocellular layers during the first 6 months with cells in the magnocellular layers growing rapidly throughout the first year of life (Hickey 1977). If the period of most rapid development corresponds to the most sensitive part of the critical period, this would be the first 6 months of life for those functions associated with parvocellular layers and the first year for magnocellular functions.

This last observation is in agreement with those behavioural studies that show the first year of life to be very important in visual development, and it is this development of visual function that will be reviewed in the next chapter.

CHAPTER THREE
THE DEVELOPMENT OF NORMAL VISUAL FUNCTION

3.1 Introduction

This chapter summarises current understanding regarding aspects of normal visual development especially during the first 6 months of life. It is during this period that an infant's visual system undergoes rapid improvement in function. The differential development of these visual functions is discussed with relation to neural models (See Table 3.1 for summary of visual function development).

3.2 Visual Acuity

Visual acuity in infants has been investigated using three different techniques; preferential looking, pattern visual evoked potentials (VEP) and optokinetic nystagmus (OKN). These methods will be reviewed in Chapter 4.

There is a rapid improvement in visual acuity from birth to 6 months and it is generally agreed that, using the different methods, the visual acuity of a three month old infant is approximately 3 cycles per degree (cpd) (Atkinson 1992) but estimates can vary by as much as 2 octaves at one month (Atkinson 1984). The generally accepted estimates of visual acuity for an achromatic stimulus are 1cpd at birth, 2-5cpd at 2-3 months and 6-20 cpd at 6 months (Atkinson 1991). Since absolute acuity differences exist between methods it is important to refer to them as VEP acuity, PL acuity and OKN acuity.

In pattern VEP studies of acuity, VEP amplitude as a function of spatial frequency extrapolated to zero microvolts is used to determine the visual acuity limit i.e. spatial frequency at which no VEP is recordable (Campbell and Maffei 1970). A number of adult studies have shown good correlation between this and the psychophysical threshold (Sokol 1978, Tyler et al . 1979). Higher levels of visual acuity are determined using the VEP technique than with behavioural studies and this method reveals a faster maturation course than preferential looking or OKN (Sokol 1990). VEP acuity levels increase from 4.5cpd during the first month to about 20cpd at 8 to 13 months. By eight months VEP grating acuity is not reliably different from adults examined using a similar procedure (Norcia and Tyler 1985). PL acuity, in comparison, does not reach adult levels until 36 months.

Table 3.1. Summary of developmental course of visual function. (For sources see 3.1 to 3.14)

	BIRTH	1 MONTH	2 MONTHS	3 MONTHS	6 MONTHS
Visual Acuity	poor 1cpd		2cpd	3cpd	6-20cpd
CSF	poor	7%		0.5%	adultlike
CFF					
(achromatic)	15Hz	41Hz	50Hz	51Hz	adultlike
(chromatic)	x	x	x	22Hz	
Orientation (VEP)	x	x	yes		
(behavioural)	yes				
Motion					
(VEP)	x	poor	poor		
(behavioural)	x	x	x	yes	
Pursuit	yes (slow targets)			yes (rapid targets)	
Saccades	yes	adultlike			
OKN (binoc)	yes				
MOKN					
(nasalward)	yes				
(temporalward)	x	x	x	yes	
Convergence	x	to near targets			yes
Accommodation		near accurate (≤ 75cm)		near accurate (150cm)	
Fusion	x	x	x	x	yes
Stereopsis	x	x	x	crossed	uncrossed
Stereoacuity	x	x	x	58'	1'
Visual Field		asymmetrical horizontally			adultlike
Colour	x	x	yes	R/G opponent	

Behavioural preferential looking data (Allen 1979) shows a steady increase in acuity with mean age whereas Atkinson and co-workers (1977,1979) suggested that the rate of improvement was not uniform, being greater between one and two months, than at any other time, and that this discontinuity may be taken as weak evidence of additional pathways or processes beginning to function. Sokol and co-workers (1992) determined VEP and PL acuity growth to be a decelerating function of age from 2-12 months and growth of PL acuity decelerates at twice the rate of VEP acuity.

Discrepancies in visual acuity assessment may be due to motivation, stimuli or scoring criteria, indeed Braddick and Atkinson (1988) found no difference in acuity levels using VEP and behavioural techniques when the criteria and stimuli were matched. At least part of the effect could be due to the higher criteria levels set for the threshold methods in behavioural techniques (Allen 1979) or the fact that PL acuity is subject to more constraints than VEP acuity (Sokol et al. 1992). VEP acuity is limited by structural and neural changes in the ocular media and visual pathway whereas behavioural acuity is limited also by attention and oculomotor development.

Birch (1985) investigated the ratio of monocular to binocular visual acuity of normal human infants using a method of constant stimuli preferential looking. He found there to be no significant difference below 6 months but after that age, binocular acuity became superior to monocular by 0.5 to 1 octave. Hamer and co-workers (1989) reported no superiority of binocular over monocular acuity.

3.3 Contrast Sensitivity

Whereas visual acuity represents the limits of spatial resolution at maximum contrast, contrast sensitivity gives an overall representation of visual functioning at different spatial frequencies. Contrast sensitivity is derived from the reciprocal of the lowest contrast at which a given spatial frequency can be perceived (Banks and Salapatek 1981). In adults, the contrast sensitivity function (CSF) is an inverted 'U' with a peak at intermediate spatial frequencies for a static stimulus.

Preferential looking and VEP have been used to assess development of contrast sensitivity with both procedures showing the CSF to be extremely immature near birth but developing substantially over the first few months of life (Norcia et al. 1990, Atkinson et al. 1977, Banks and Salapatek 1978, Pirchio et al. 1978). A qualitative change in the shape of the CSF occurs at 2 months with the appearance of a marked low frequency cut. At 2 to 3 months the shape of this function is similar to that of adults except it is shifted to lower spatial frequencies and lower sensitivities and the cut-off

frequencies are consistent with the grating acuity norms at the same age. One explanation of this low frequency cut may be a lack of lateral inhibition (Atkinson 1985) which does not appear until about 6 months (Morrone and Burr 1986). Retinal ganglion cells of kittens, have been shown to have weak surround responses (Rusoff and Dubin 1977, Hamasaki and Flynn 1977) and maturation and strengthening of these inhibitory processes would sharpen spatial selectivity of these cells. Banks and Salapatek (1978) showed a continuous smooth increase in sensitivity to intermediate and high spatial frequencies, whereas Atkinson and Braddick (1981a) showed the same pace of development as their acuity, between one and two months of age.

Using VEP, Norcia and co-workers (1990) calculated contrast threshold (zero voltage intercept of the initial rising portion of the CSF (Campbell and Maffei 1970)) to be 7% at 2-3 weeks increasing to 0.5% by 9 weeks. Photopic contrast sensitivity measured by VEP is 20x higher than that measured behaviourally and suggests that infant CSFs are near adult-like at 7 months. The differences between behavioural and VEP values of visual acuity have been discussed earlier and the same causes may be attributed to contrast sensitivity, however an alternative explanation has been offered in that the VEPs are generated from an early point within a visual system whose later stages are immature (Norcia et al. 1988).

Several reviewers (Atkinson 1984,1992, Banks and Bennett 1988, Atkinson and Braddick 1990, Chadna 1992) have considered the role of anatomical constraints on the development of visual acuity and contrast sensitivity. Possible limiting factors may be optical or neural and improvements in these may subsequently improve the transmission of spatial information.

The basic optical quality of the infant eye is good with no evidence of markedly greater aberration than the adult human eye (Atkinson and Braddick 1990). Refractive error studies show infants to make some errors of accommodation (see 3.10) but due to the small size of the eye the depth of focus compensates in such a way that any resulting defocus is not a limiting factor (Braddick et al. 1979, Banks 1980). Banks and Bennett (1988) utilised the concept of an ideal observer to determine the extent to which optics and photoreceptors of the neonatal eye limited acuity and contrast sensitivity. The ideal observer suggested that the optical quality of the newborn eye exceeded the resolution capability of the system and hence plays little part in limiting acuity.

As discussed in the previous chapter, the central retina is immature at birth (Yuodelis and Hendrickson 1986). The cone outer segments are broader, shorter and less densely

packed together in a lattice suggesting that the majority of incident quanta falling on the fovea, are not collected by infant cones (Banks and Bennett 1988). This will place a limit on the level of acuity and the fineness of detail that will be perceived. As the infant grows the cells become more closely packed within the fovea and this corresponds to an increase in acuity. Using the ideal observer model, contrast sensitivity functions were computed to reflect the influence imposed on spatial vision by this retinal immaturity. If the infants' visual system was identical to the adult, except for the observed differences in eye size and cone characteristics, one may expect the infant CSF to be shifted version of the adult CSF. Banks and Bennett produced contrast sensitivity functions based on this model (Figure 3.1) however, it could be seen that the ideal observer CSF did not completely match an infant CSF and hence, the influence of optical and photoreceptoral immaturies, could not fully account for the difference between actual infant and adult CSFs. Therefore, other post receptoral mechanisms most play some role in the limitation of infant visual function (Banks and Bennett 1988).

Work by Ikeda and Tremain (1978) demonstrated that individual neurons in the lateral geniculate nucleus of the cat undergo an improvement in their capacity to resolve gratings. This parallels the improvement in acuity assessed behaviourally and has also been observed in monkeys (Teller et al. 1978b, Boothe and Lee 1980). Single unit recordings from the dorsal LGN of monkeys show an increase in spatial resolution over the first 30 weeks postnatally from 5 to 35 cpd. These changes occur only in the central 2 degrees of the visual field, not the periphery and analogous development occurs in contrast sensitivity.

Myelination occurs progressively during the first few postnatal months (Magoon and Robb 1982) but prior to this neural transmission may be somewhat impaired. This could potentially limit the information transmitted to the cortex (Atkinson 1991). The infant striate cortex initially shows an increase in the population of spines and synaptic density during the first eight months followed by a decrease to reach adult levels (Garey and de Courten 1983). It is possible that this increase in interconnectivity produces a structure of receptive fields that can deal with fine detail and subtle contrast. The time course of anatomical and physiological changes that take place during the first 6 to 12 months of life appear to be directly related to the improvement of visual function during that period.

Figure 3.1 Empirically determined adult and infant's CSFs and the predicted loss of sensitivity caused by optical and receptoral factors (arrow indicate shift in CSF predicted by ideal observer model (Banks and Bennett 1988)

3.4 Temporal contrast sensitivity

Temporal contrast sensitivity function (CSF) represents an observer's sensitivity to flickering sinusoidal gratings over a range of spatial frequencies as a function of temporal frequency. In adults, at photopic luminances, sensitivity rises smoothly to a peak at about 10 Hz then falls smoothly to a high frequency cut off at about 60Hz (the critical flicker frequency or CFF). The CFF of infants have been estimated behaviourally and electrophysiologically with Heck and Zetterstorm (1958) and Horsten and Winkelmann (1961,1965) used electroretinograms (ERG) to assess the CFF of 1 and 2 month old infants. Horsten and Winkelmann observed nearly adult like values in all cases whereas Heck and Zetterstorm found CFF to increase from 15Hz at birth to adult like values at 2 months. The discrepancy between these two studies has been attributed to differences in methodology (Hartmann and Banks 1992).

Behavioural methods of CFF assessment have employed Forced Choice Preferential Looking or FPL (Regal 1981, Mercer and Adams 1989). Average estimates are 41 Hz at 1 month, 50Hz at 2 months and 51 Hz for 3 month olds. Adult values are typically 53 Hz. Regal concluded that CFF was adult like at 2 months but using chromatic stimuli Mercer and Adams contradict this with 3 month old infant values differing from adults at 22 Hz and 38 Hz respectively.

Swanson and Birch (1990) estimated the temporal CSF in 4-,6-, and 8-month old infants using FPL. The temporal contrast sensitivity of the infants investigated was found to be greatly reduced in comparison to adult values with best contrast thresholds of 20% at low temporal frequencies and 100% at frequencies of 8 and 17 Hz. Contrast thresholds improve to 10% by 8 months. Infants' high temporal frequency cut offs would appear to be comparable to adults while their sensitivities at lower temporal frequencies are one to two orders of magnitude below adults (Teller et al. 1992).

3.5 Orientation Detection

Slater and Sykes (1977) found the ability to detect changes in orientation of a stimulus to be present at birth, with newborns showing a preference for horizontal rather than vertical square wave gratings. This is in disagreement with several other authors (Braddick et al. 1986a, Cohen and Younger 1984, McKenzie and Day 1971, Maurer and Martello 1980) who showed no orientation discrimination until 6 weeks and this preference, demonstrated at birth, may be due to the astigmatism common in the horizontal and vertical meridians of the newborn eye or the tendency of newborns to predominately make horizontal eye movements (Slater et al. 1988).

The discrimination of mirror-like obliques is thought to be less susceptible to alternative interpretation (Atkinson and Braddick 1989). Steady state VEPs can be elicited in 6 week old infants when a grating at 45° is replaced by one at 135° (Braddick et al. 1986a) and this mechanism appears to have different orientation and temporal tuning curves at different ages. At 8 reversals per second (rps) between the two orientations, a response is only significant after 2 months whereas at 3rps the median age is 3 weeks (Braddick et al. 1989).

Infant habituation experiments have been used to assess the onset of orientation discrimination behaviourally (Atkinson et al. 1988a, 1988b, Slater et al. 1988). The infant is repeatedly shown a pattern and visual attention time decreases until visual habituation is achieved. If, after habituation, the infant shows a longer looking time to a novel rather than the familiar pattern, discrimination is said to have occurred. Discrimination to change in orientation is demonstrated behaviourally in newborns.

An explanation of this discrepancy between the onset of behavioural and VEP orientation discrimination suggests that VEP requires cortical function while behavioural discrimination functions via a simple pathway, possibly subcortical, or the mechanism for detecting static orientation (behavioural) is functioning at birth and a different mechanism is required for dynamic orientation (VEP). It has been suggested that parvocellular pathways are responsible for orientation at 6 weeks (Atkinson 1992).

3.6 Motion Detection

The onset of detection of motion in young human infants has been investigated using both behavioural and electrophysiological methods. Newborns are known to respond to movement across the visual field but motion will produce a temporal modulation i.e. flicker and it may be that stimulus that produces the response. Motion detection can only be said to be in operation if differential responses are produced to differential direction (Atkinson 1992).

Behavioural studies show infants under 2 months of age to have poor sensitivities to motion of all velocities(Kaufmann et al. 1985, Aslin et al. 1988, Wattam-Bell 1993). For rapid motion 1 and 3 month olds behave in the same manner with poorer sensitivites than adults. The VEP measurement technique defines a response as a component of the VEP that is synchronized with periodic up-down reversals in the random motion of a dot field. These direction reversals are embedded within a sequence of pattern changes in such a way that any signal of the correct frequency must be linked to change in direction of motion and not simply pattern reversal (Atkinson and Braddick 1990). Using VEP

techniques the onset of motion detection occurs by 10-12 weeks (Wattam-Bell 1991). Results suggest that the development of motion detection is paralleled by spatial vision, developing later than orientation (Braddick and Atkinson 1988) .

True directional detectors have not been demonstrated prior to 8 weeks. It is the magnocellular channel from cortical areas V1, V2, V3 and MT (area selective for the detection of motion of a stimulus (Dubner and Zeki 1971)).

3.7 Eye Movements

Using ultrasonography, episodic foetal eye movements have been measured from 16 weeks gestational age (Birnholz 1981, Precthl and Nijhius 1983). These are initially slow changes in eye position which become more rapid and by 36 weeks relate to foetal behaviour states.

3.7.1 Smooth Pursuit

Smooth pursuit movements were not generally thought to be present until 2 months and prior to that time, the infant would make a series of small saccades (Dayton and Jones 1964, Aslin 1981). Kremenitzer et al. (1979) and Roucoux et al. (1983) did however elicit small sections of smooth pursuit in newborn infants using a target of slow velocity and their findings have recently been reconfirmed (Shea and Aslin 1990). The slow and fast stages of OKN are present at birth and this would suggest the slow pursuit mechanism is functional (Dayton et al. 1964).

It is easier to elicit a smooth pursuit movement horizontally (Brazelton et al. 1966) and at high velocities this will breakdown into a series of saccades. The maximum velocity for smooth pursuit increases with age.

3.7.2 Saccades

Adults use small corrective eye movements or saccades to maintain fixation. Those may involve single eye movements or saccades and head movements. These are present in human infants from birth (Atkinson 1984). A newborn infant will direct it's eyes to a fixation target by a series of saccades that appear to be of a standard amplitude and not dictated by target distance. The latency of the initial saccade following target presentation is longer than in adults (Aslin and Salapatek 1975, Regal et al 1983).

Saccadic head and eye movements are adult like by one month and the change of fixation to an eccentric target with one saccade develops by one year. Prior to this two types of fixation movement may be undertaken: a succession of hypometric foveate like saccades

with small head movements or hypermetric afoveate like eye and head movements (Roucoux et al 1983).

3.7.3 Optokinetic Nystagmus (OKN)

Optokinetic nystagmus can be visually induced in infants from birth by moving large stripes through the visual field (McGinnis 1930). Slow and fast phases of OKN can be elicited in full term and a proportion of pre-term infants (Kiff and Lepard 1966) and this is used as an objective assessment of pattern perception (see chapter 4). The slow phase velocity is more restricted in infants than in adults (Kremenitzer et al. 1979) and the form of the response to vertical and horizontal stimuli are different (Boothe et al 1985). Downward stimuli do not elicit as strong an OKN response as that seen for upward moving stimuli. This asymmetry is present during the first month of life and gradually disappears over the following months (Hainline et al 1984).

In infants, under the age of 2 months, OKN can only be elicited monocularly (MOKN) in a temporal to nasal direction (Atkinson 1979, Atkinson and Braddick 1981b). MOKN can be elicited in either direction in older infants and adults but the nasalward MOKN remains more vigorous than the temporalward up to 5 months (Naegele and Held 1982). Monocular optokinetic after nystagmus (MOKAN) also displays this asymmetry, being only elicited by nasal to temporal movement until 4-5 months (Schor et al 1983).

The gain of MOKN response to a temporalward stimulus, increases steadily to equal that of nasalward motion by about the time of emergence of stereopsis. Some adults who have lacked binocularity since birth (amblyopes including strabismics) show the same asymmetry in MOKN (Schor, 1975, Schor and Levi 1980) and MOAKN (Schor and Westall 1984) as young infants.

There is good evidence to suggest that nasalward monocular OKN, present from birth, is subcortically mediated whereas a functioning cortex is required for temporalward response (Atkinson and Braddick 1981b). A route from the retina, via the binocular visual cortex, to the ipsilateral nucleus of the optic tract (NOT) is believed to be the pathway responsible for generating temporalward OKN. It is generally considered that this pathway is not functional in young infants thus accounting for the initial nasalward directional bias (Schor et al. 1983). In adults the cortical pursuit mechanism suppresses the subcortical OKN and it is this cortical system that may operate within the magnocellular system becoming functional later (Atkinson 1992).

3.7.4 Vestibulo Ocular Reflexes (VOR)

As the head rotates, the semicircular canals of the vestibular system sense a movement and initiate a reflex rotation of the eyes in the opposite direction. In adults, this vestibular oculo reflex provides about 60% of the eye velocity needed to compensate for the head velocity (Benson and Barnes 1978, Collewijn 1989). The movement of the visual world resulting from the head rotation elicits the visual optokinetic reflex (VOR) to help provide complete compensation (Finnocchio et al 1991).

The VOR is present at birth (Ornitz et al 1985). Before 10 days of age the ocular-cephalic ('doll's head') manoeuvre results in an ocular deviation to the opposite side to the head rotation (Paine 1963, Fielder 1985). At one month of age compensatory eye movements cancel out the effect of head movements and fixation is maintained. VOR is accurate before pursuit and OKN movements mature and would therefore appear to have an important role in stabilisation of the infant retinal image and visual world.

3.8 Pattern Discrimination

Three month old infants can readily discriminate patterns which differ in relative phase (Braddick et al. 1986b) and this is unaffected by contrast change. One month olds will not however, demonstrate pattern discrimination, even though they have the ability to process the individual components of the patterns.

This analysis of pattern by infants, can not be explained solely by the ability to process spatial information as two different patterns may contain the same frequency information but have different phase relationship. Thus an infants ability to discriminate patterns may reflect the maturation of channels which are selective for particular phase relationships (Atkinson 1991) and similar conclusions have been drawn from the work of Kleiner and Banks (1987). They found one month olds would demonstrate a preference for patterns comprising of components of the same spatial frequency as the components of a face like stimulus, even though their spatial relationship made them look unlike a face. Preference at 2 months however for a face-like pattern was due to the spatial relationship of the components. Slater and co-workers (1991) however suggested that infants have the ability to 'bind together' different visual features that occur at the same spatial location at birth.

The weight of opinion would suggest that young infants are aware of spatial pattern but do not process its configuration but by the 3rd month the system capable of processing spatial relationship information appears to be functional.

3.9 Convergence

Studies of the development of fusional accommodative vergence are reviewed by Aslin (1985). Convergence to near targets is present by one month but the quantitative precision improves rapidly with consistent demonstration by 2 months (Ling 1942,Aslin 1977, Aslin and Jackson 1979). Newborns show some degree of convergence (Hershenson 1964) and will alter the relative position of their eyes appropriately when presented with targets at 20, 10 inches but not at 5 inches (Slater and Findlay 1975b).

Studies of vergence eye movements (Ling 1942) as targets are moved towards and away from the infant, demonstrated no appropriate convergence until 7-8 weeks. More recent studies have elicited responses to a target moved along the midline from one month olds. Two to three month olds will converge by amounts compatible with bifoveal fixation but may still be using extra retinal loci (Aslin 1977).

Two mechanisms are involved in convergence; accommodative and disparity detecting. Both involve pathways between the cortex, colliculus and oculomotor control centres and immaturity in this pathway may underlie poor performance.

3.10 Accommodation

Early studies of accommodation (Haynes et al 1965) by dynamic retinoscopy suggested that newborn infants had a fixed focus of about 18cm and accommodative ability was absent. Braddick and co-workers (1979) demonstrated, using a photorefractive techniquethat newborn infants could achieve accurate focus over distances less than 75cm and by 2-3 months they could focus to 150cm. For large checks (60 min of arc) 2 to 4 month old infants can accommodate over a range of 9 dioptres, measured by VEPs, but for small checks 4-5 month olds cannot accommodate beyond 5 to 6 dioptres (Sokol et al. 1983). The presence of convergence during monocular viewing indicates the accommodation-convergence link to be present at 8 weeks (Aslin and Jackson 1979).

Large fluctuations in accommodation in very young infants may demonstrate a failure of control rather than muscular inability and achievement of accurate accommodation by the third month is probably due to improved neural control (Atkinson 1984).

3.11 Binocularity

Binocular function may be classified into three levels; bifoveal fixation, fusion and stereopsis and the presence, or otherwise of these functions can be used to define binocular function (Worth 1915). In adults, bifoveal fixation is a necessary pre-requisite of, but not a sufficent condition for, functional fusion and stereopsis. Aslin and Dumais

(1980) presented an extensive review of studies used to assess the level of binocular function in infants and its development.

3.11.1 Infant depth discrimination studies

Very early studies used multiple cues to assess the perception of depth e.g. visual cliff studies (Walk and Gibson 1961) and differential reaching (Cruikshank 1941). The results of these studies were confounded by the uncertainty over which cue provided the depth information. More recent studies have also failed to isolate monocular or binocular cues to depth. The results from these studies hence give no consistent information about the development of depth perception. Later studies of infants' responses to pictorial, binocular and kinetic depth cues (For review see Yonas and Granrud 1985) show reactions to all three cues by 6 months with sensitivity developing in the subsequent order of kinetic, binocular and then pictorial.

3.11.2 Bifoveal fixation studies

Adults who fail to align the two fovea perceive diplopia and inaccurate alignment results in degradation of stereopsis. If bifoveal fixation was absent in infants, then from the hierarchical model proposed earlier, fusion and stereopsis could not exist.

Several investigators working with the assumption that bifoveal fixation is a prerequisite of binocular function, have investigated the locus of the visual axes using corneal reflex photography. The opinion that bifoveal fixation is not present at birth has been supported by studies which found newborn infants to be divergent (Wickelgren 1967,1969). Slater and Findlay (1972, 1975a) cast doubt upon this conclusion with the finding that apparent divergence is an artefact of the large angle alpha of the neonatal eye causing the two eyes to appear optically divergent by approximately 17° when fixating binocularly. They suggested that newborns do show evidence of binocular fixation when correction for this artefact is made (Slater and Findlay 1975b).

Measurement of relative eye alignment for targets presented at various distances may provide an alternative method for determining an infants ability to bifoveally fixate. Two and three month olds converge by amounts compatible with bifoveal fixation although they may still be using an extra retinal locus to define the line of sight (Aslin 1977). Aslin and Dumais(1980) considered there to be no objective technique available to measure bifoveal fixation with sufficent accuracy (within adult Panum fusional area -15') to conclude bifoveal fixation is present.

3.11.3 Fusion

When a prism is placed before one eye of an adult observer, diplopia is induced as the retinal image is shifted off the fovea. By observing eye movements a compensatory refixation saccade can be seen to realign the visual axes and maintain fusion. This observation was utilised in the assessment of fusion of 3, 4.5 and 6 month old infants (Aslin 1977) with 2.5° and 5° prisms. Consistent realignment movements were not made until 6 months but the lack of fusional movement prior to that age could be accounted for by oculomotor immaturity, limited spatial resolution or experimental error (Aslin and Dumais 1980). These findings are however in agreement with later work which investigated the relative preference for fusable (binocularly identical) or rival (orthogonal, dissimilar stimuli) (Birch et al. 1985, Shimojo et al. 1986).

Shimojo and co-workers used a preferential looking paradigm with identical and non-identical stimuli to assess the development of fusion. At an average age of 3.5 months the infant showed a shift in preference from the dissimilar to the fusable pattern. The original preference for the interocularly orthogonal stimuli may be interpreted by the finding that grids are preferred to gratings in very young infants . The visual system may not selectively suppress prior to 3.5 months and the information received from each eye is combined regardless of orientation. This may be evidence of early lack of cortical inhibition.

Birch and co-workers (1985) undertook a similar investigation using random dot and checkerboard stimuli. None of the infants tested preferred rival stimuli at any age and by 6 months all showed preference for the fusable stimuli. The proportion of infants showing differential fixation to fusable stimuli increased between the ages of 2 and 6 months with mean age of onset at 11.7 weeks.

3.11.4 Binocular VEP summation

In normal adults the amplitude of pattern VEP recording is greater than the mean or larger of the monocular VEPs. Stereo-defective adults do not show this binocular facilitation (Amigo et al. 1978). Binocular VEP summation (BVS) is higher in 2 to 5 month old infants than those aged 6 to 10 months or adults (Shea et al. 1987, Leguire et al. 1991). This very high level of BVS occurs before the development of stereopsis and suggests two independent pools of monocularly driven neurons are sufficient for BVS. This would suggest that it is a poor index of functional binocularity.

3.11.5 Stereopsis

Stereoscopic discriminations requires detection by the visual system of correspondance of images from the two eyes. The onset of stereopsis in infants has been studied using a variety of methods with comparable results between studies.

a) Behavioural responses to line stereograms

Preferential looking may be utilised to assess stereo acuity using cross polarised line stereograms (Held et al.1980, Birch et al. 1982, 1983, 1985). Preference for stereograms over zero disparity fields is tested as infants will prefer to fixate a 3 dimensional object than an equivalent 2 dimensional picture (Fantz 1961).

Held and co-workers (1980) assessed stereopsis development with uncrossed (behind the plane of fixation) and crossed (in front of the plane of fixation) disparities and stereopsis developed earlier for crossed (12 weeks) than uncrossed at 17 weeks. These findings were confirmed (Birch et al. 1982) with no evidence of stereopsis before the 4th month. Stereoacuity develops very rapidly from 58' to1' of arc over a few weeks. Stereoacuity of 1' of arc was first demonstrated at 17 weeks for crossed and at 21 weeks for uncrossed disparities.

One criticism of these findings was that an negative binocularity result would be expected if it was dependent on convergence accuracy (Atkinson 1984) but Birch and co-workers (1983) reconfirmed the onset of binocularity using fields of 9°and 21° The large field allowed multiple opportunities for fusion even in the presence of vergence errors up to 25 prism diopters. This would support the conclusion that onset of responsiveness to disparity should be attributed to the development of sensory mechanisms rather than refinement of vergence control.

b) Random dot stereograms

Random dot stimuli have been used in both behavioural and electrophysiological studies of infant stereopsis. All monocular stimulus cues are removed as the random pattern contains no discernable information when viewed monocularly. When viewed binocularly an observer with stereopsis will perceive depth. This has been used in behavioural studies (Atkinson and Braddick 1976). Fox and co-workers (1980) observed visual tracking behaviour of young infants presented with a dynamic random dot display. Performance did not exceed chance at 4.5 months but did so at 6 months.

Any signal that is locked to the alternation between correlation and anti-correlation of a dynamic pattern must arise from neurons with a binocular input (Julesz et al. 1980) and

this is the basis of the random dot correlogram VEP. Presence of a random dot stereogram provides evidence of stereopsis. Both types of binocular VEP have been recorded from infants (Braddick et al. 1980,1983, Petrig et al. 1981) and the first VEPS can , on average be recorded at 3 to 4 months. Braddick and colleagues could elicit no VEP from neonates and it was not until 13 weeks that the recording became reliable. There are marked individual differences in the functional onset of binocular VEP between infants (Wattam-Bell et al. 1987) with individuals demonstrating a response at 2 months while others showed no response at 15 weeks.

3.11.6 Summary of binocular development

Objective techniques used to assess the presence of bifoveal fixation are not believed to be accurate enough to draw any definite conclusions (Aslin and Dumais 1980). Bifoveal fixation data does however indicate that a degree of binocular fixation i.e. consistent line of sight in the two eyes, may be present at birth (Slater and Findlay 1975b). Infants below the age of 2 months will make the appropriate vergence movements but the ability to alter convergence over a large range and maintain binocular fixation, especially for moving targets, improves with age (Ling 1942, Aslin 1977). By the third month of life, infants appear to be using an area of the retina close to the fovea for fixation and foveal alignment is fairly accurate. Even if bifoveal fixation was present it would not guarantee stereopsis and fusion.

The presence of cortical binocularity or stereopsis is not evident in infants below 2 months (Petrig et al. 1981, Braddick et al. 1983) except for one study which showed stereopsis at one month (Birch et al. 1985). It may be that prior to the development of stereopsis the visual system is incapable of interocular suppression (Shimojo et al.1986). The proportion of infants showing stereopsis increases steadily from 2 to 6 months and comparable data on this time course has been provided by electrophysiological and behavioural studies. The majority of infants will give some evidence of stereopsis by 4 to 5 months and virtually all do at 6 months (Fox et al. 1980, Held et al. 1980, Petrig et al. 1981,1982, Birch et al. 1982,1983,1985). Once stereopsis emerges the developmental time course for improvement in stereoacuity is very rapid, reaching values $\leq$ 1 minute of arc within 5 weeks of onset (Birch et al. 1982). Stereopsis for crossed disparity stimuli develops 4 to 5 weeks earlier than for uncrossed (Held et al. 1980, Birch et al. 1982).

The development of fusion follows a time course comparable to that for the emergence of sensory fusion (Birch et al. 1985) and is not limited by the development of vergence (Birch and Held 1983). Sensitivity to pictorial depth information does not develop until after 6 months (Yonas and Granrud 1985).

Binocular correlation is dependent on a cortical system as the first time the signals from the two eyes interact is at the cortex. Binocular responses can first be seen at around 4 to 5 months of age (Braddick et al. 1980, 1983, Petrig et al. 1981, Fox et al. 1980, Held et al. 1980, Braddick and Atkinson 1983,1988) and this would suggest that the onset of a functioning cortical binocular mechanism is postnatal.

3.12 Visual Fields

Neonates are capable of making saccades to fixate a peripheral stimulus. Both the central and peripheral retina appears functional at birth and although the fovea is immature no central scotoma is present (Lewis and Maurer 1980).

The visual field expands along the horizontal and vertical axes during the first year. Using kinetic perimetry, with a white ball on a black background, the nasal and temporal fields develop concomitantly from 2 to 12 months. This is not the case when using a grey stimulus which shows a delay in growth in the nasal, compared to the temporal, field (Mohn and Van Hof van Duin 1986). Changes in eye movements with growth can be said to have an effect on this method (Lewis and Maurer 1992). Using static perimetry (Lewis et al 1985), sensitivity to stimuli located at 20-30° along the horizontal meridian is substantially less in the nasal visual field than temporally for the first month.

The monocular visual field expands gradually during early infancy but the time course over which it achieves adult values is affected by experimental procedure:the presence or absence of a central competing stimulus. Lewis and Maurer (1992) proposed an adult like field was attained by 6 months (no central stimulus) whereas Mohn and Van Hof van Duin (1986) (central stimulus) did not find adult like values until after the first year. The development of responses to stimuli in the nasal field is slower than the temporal field with a large asymmetry between the hemi field sizes. Infants will respond to stimuli at 25 or 30° in the temporal retina but not to 20-25° nasally (Lewis and Maurer 1992).

Adults are more sensitive to stimuli temporally than nasally in the binocular visual field (Aulhorn and Harms 1972, Fahle and Schmidt 1988). The underlying causes of this are thought to be the higher number of receptors (Curcio et al 1990) and ganglion cells in the nasal retina (the area responsible for temporal vision) (Curcio and Allen 1990). This asymmetry can also be seen in the volume of layers of the LGN in an adult monkey (Gottlieb et al 1985) and its spatial resolution (Blakemore and Vital-Durand 1986). The asymmetry is much greater in infants and cannot be explained by an increased optical aberration or asymmetrical growth.

The underlying factors causing large infant field asymmetry are probably neural, indeed retinal ganglion cell development was believed to be asymmetrical with less rapid development temporally (Provis et al 1985) however this belief has been contested recently (Packer et al 1990). Within the LGN of monkeys there is no difference in cell spatial resolution between infants and adults (Blakemore and Vital-Durand 1986) and all cell layers grow at the same rate (Gottlieb et al 1985) suggesting that the cause for the asymmetry lies beyond the LGN. The uncrossed fibres within the visual pathway are nasal field detectors but they do not have a different developmental time course from the crossed fibres.

It is possible, that a delay in the development of cortical function would favour the detection of stimuli in the temporal visual field as the crossed axons direct retinal input from this area to the subcortically functioning superior colliculus (Lewis and Maurer 1992).

3.13 Spectral Sensitivity

The spectral sensitivity of the human eye has been studied using spectral luminous efficiency functions. Infant spectral sensitivity curves can give us information about the identity of underlying visual mechanisms. Forced Choice preferential looking has been used to measure spectral luminous efficiency in two ways. The first is the measurement of absolute threshold as a function of wavelength, while the second is similar to the adult heterochromic brightness matching paradigm. A test light is embedded within a field of standard light either on the left or the right with a dummy light, which matches the standard field in luminance and spectral composition, on the other side. The luminance of the test light is varied from trial to trial assuming that this will include a brightness match for the infant. This discrimination vs. luminance data can be used to generate a luminous efficiency curve by finding the test luminance at which minimum discrimination occurs for several test wavelengths. Discrimination is said to have occurred if minimum performance is significantly above chance. Visual evoked potentials have been used to measure luminance efficiency by equating the radiance of different wavelengths to give equal VEP amplitude or latency.

The luminous efficiency curves produced by Powers and co-workers (1981) at absolute threshold, were predominantly rod dominated , as were those of Werner and Wooten (1979) and Clavaldetscher and co-workers (1988). This suggests that rods may predominate in infant spectral sensitivity functions (Brown 1990). The functions of 2 month old infants determined by Dobson (1976), and of 1-3 month olds (Moskowitz-

Cook 1979, Varner et al.1985) differ from Werner in the short wavelength region of the spectrum even though they are similar in the long wavelengths. This has been explained by the fact that Dobson, Moskowitz-Cook and Varner, all light adapted their subjects to reduce rod contribution whereas Werner dark adapted before each experimental run (Brown 1990). Dobson and Moskowitz-Cook both showed an elevation of sensitivity to short wavelengths and in the older infants produced spectral luminous efficiency functions that were similar in shape to adult photopic luminous efficiency functions. Werner's spectral luminous efficiency curves for infants are similar in shape to the adult scotopic curve at wavelengths below 590nm. Above 590nm the function is complex and does not conform to photopic or scotopic curves.

The shape of the infant spectral luminous efficiency curves are evidence that at least one type of cone is functioning by the end of the second month of postnatal life. Pulos and co-workers (1980) measured the thresholds at 460nm and 560nm on a 1.5 log cdm^{-2} 'blue' and at 1.4 log cdm^{-2} 'yellow' adapting background. For most 2 month olds sensitivity was higher at 560nm than at 460nm on the blue background and lower at 560nm than at 460nm for the yellow background. This is a violation of the law of univariance so at least two receptor types with two different spectral sensitivities must have detected the lights (Brown 1990). Sensitivity for 460nm and 500nm was compared in 2-3 month old infants. A greater sensitivity to the 460nm test emerged at 3 months. Pulos et al. suggested that this indicated the appearance of a receptor mechanism with maximum sensitivity at less than 500nm, a short wavelength sensitive cone (SWS cone) at 2 months. Spectral sensitivity curves from white and 580nm adapting fields (Peeples and Teller 1975, Brown and Teller 1989 respectively) are of different shapes from each other and are too broad to be fitted with action spectra of any single visual pigment.

The spectral sensitivity functions of infants more than one month of age show a wide variation with technique and stimulus condition and thus more than one photoreceptor type must be functioning, one of which is the rods. Responses in the long wavelength section of the spectrum requires at least one receptor type in addition to rods to be functional there. As no other human photoreceptor is sensitive below 500nm, three month old infants probably have SWS cones as well. The weight of evidence would suggest that by 3 months of age infants are trichromatic.

As well as two photoreceptor types with different spectral sensitivities, the presence of colour vision requires at least two independent postreceptoral pathways with the capability to signal their response. Brown and Teller (1989) found a pronounced notch in

the spectral sensitivity curve of a 3 month old infant at the adapting wavelength. They interpreted this as evidence of a R-G opponent pathway at 3 months.

3.14 Colour Vision

The systematic investigation of the early development of human colour vision has a long history. Much of this research reflects that in adults, characteristics of specific colour vision abilities (e.g. spectral sensitivity, wavelength discrimination) reflect the activity of specific neural mechanisms (e.g. photoreceptors, post receptoral opponent processes, distinct cell types in layers of the LGN and visual cortex). Analysis of behavioural aspects of infants' colour vision allows one to speculate both about the functional maturity of the underlying neural mechanisms and the course of their development.

Most early investigations of infant colour vision (pre 1975) where flawed by the failure to control for the possibility that infants may discriminate between chromatic stimuli on the basis of brightness cues. The main criteria for colour vision is that an infant can discriminate between different wavelengths based solely on their spectral composition. Any luminance information must be eliminated and the methods employed to ensure this in colour vision studies are reviewed later (see Chapter 5).

Adams and co-workers (1986) demonstrated colour vision in newborn infants using a single stimulus looking method with infants' looking-time to grey and coloured checkerboards measured. The group average looking-time was longer for the pattern of grey and coloured checks than the uniform grey when the colours were red, yellow and green. There was no demonstrated increased looking time for a blue test stimulus. Following habituation, the procedure was repeated with the looking time for red being significantly longer. From this, they concluded that newborn infants have colour vision for long but not short wavelength stimuli. Using group averaged data makes the assumption that all infants would have the same luminance match point. If this is not the case (as in adults) enough infants may detect a luminance difference to make discrimination significant at all luminances even without colour vision. They have more recently (Adams et al. 1991) demonstrated a neutral zone between 470-480nm in neonates. These conclusions have since been questioned due to the limited range of luminances investigated which would allow the discriminations to be made by a rod monochromat (Brown 1990). A similar criticism can be made of the results of Schanel-Klitsch and Woodruff-Pak (1985) who also found neonates to be dichromats.

The emergence of colour vision between the ages of 1 to 3 months has been has been demonstrated using preferential looking and a wide range of spectral stimuli (see Table

3.2 for summary). Generally, the colour discrimination ability of 4 week old human infants is poor (Hamer et al 1982, Packer et al 1984, Varner et al 1985). For all wavelengths examined, no infant can perform better than chance at an individual radiance and do not discriminate a test colour from its surround. Clavadetscher et al. (1988) did demonstrate discrimination of long wavelengths by some one month olds but the spectral compostion of the red field used contained stray light from across the whole spectrum and differed from that wavelength which is predominantly red for adults. Subjects do not show colour vision at these ages because they do not behaviourally distinguish between lights on the basis of their spectral composition (Allen et al. 1988).

Over half 2 month olds demonstrate some chromatic discrimination by performing significantly better than chance in the discrimination of wavelength pairs. They reliably discriminate broadband red, orange, some greens, blue and some purples from white (Peeples and Teller 1975, Hamer et al. 1982, Clavadetscher et al. 1988, Allen et al 1988). They do however, exhibit a neutral zone running from short wavelenghts to yellow and green which contains colours that could not be differentiated from white (Teller et al. 1978a). Infants were tested over a wide range of luminances, including their brightness match, thus the luminance problem was not an explanation of the observed discrimination. The presence of functioning blue cones at 5 weeks was confirmed using a VEP technique (Volbrecht and Werner 1987). Hamer and co-workers, showed infants could discriminate broad band red and 550nm green from 589nm yellow and have at least 2 functional photopigment systems. The two month age is believed to be a transitional period with some infants discriminating more easily than others (Teller et al. 1978a). They found that stimuli with a dominant wavelength of 538nm and 561nm were particulary difficult to discriminate from white. For many stimulus combinations some two month olds will discriminate while others will not.

Almost all 3 month olds infants will successfully demonstrate chromatic discrimination (Hamer et al 1982, Packer et al. 1984, Allen et al.1988). Bornstein (1978) reported, that 3 month old infants discriminate stimuli of 490-500nm from white light. Thus most 3 month olds have some degree of colour vision but this cannot be taken as evidence of trichromacy and many will still fail to make some discriminations especially with small fields (Packer et al. 1984). Three month olds demonstrated Rayleigh discriminations with 2,4,and 8° targets but not with 1° targets. This finding may lead to the suggestion, that lack of colour vision could be attributed to immature spatial summation rather than a deficit in chromatic processing. Other theories on the development of colour vision will be reviewed below.

In summary: Most infants less than 3 months of age demonstrate some deficit in colour vision.

Two month old infants fail to discriminate five out of thirteen colours from white (Teller et al 1978a)

One and two month old infants fail to make Rayleigh discrimination (Hamer et al. 1982, Packer et al. 1984) and tritan discriminations (Varner et al. 1985).

Table 3.2 Summary of infant colour discrimination experiments **(Modified from Brown 1990)**

Study	Technique	Ages (weeks)	Test colours	Age with colour vision
Peeples & Teller (1975)	FPL	8	R	Some 8 week olds
Schaller (1975)	conditioned looking time	10	R	Most 12 week olds
Bornstein (1978)	habituated looking time	13	tungsten	Some 13 week olds
Teller at al (1978a)	FPL	8	Many broadband	Some 8 week olds
Hamer et al. (1982)	FPL	4,8,12	550nm R	Few 4 week olds Some 8 week olds Most 12 week olds
Packer et al. (1984)	FPL	4,12	650nm	No 4 week olds All 12 week olds
Varner et al. (1985)	FPL	4,5,7,8	417nm	No 4 week olds Some 5-8 week olds
Adams et al. (1986)	Spontaneous /habituated looking time	neonates	Several	At least some neonates
Allen et al. (1988)	FPL	4-16	B,G,R	Few 4 week olds Some 8 week olds Most 12-16 week olds
Clavadetscher et al. (1988)	FPL	3,7	417-650nm	Few 3 week olds Some 7 week olds
Adams (1989)	Habituated looking time	neonates	650,585, 454nm	Some neonates
Allen et al. (1990)	Sweep VEP	2-8	R,G	2 week olds
Morrone et al. (1990)	Sweep VEP	4-20	R,G	No 4 week olds Some 6-7 week olds

3.15 Theories of poor colour vision

There are several hypotheses (Brown 1989, 1990) to explain the reason why infants' under 2 months of age fail to make discriminations based solely on wavelength.

a) The Single Receptor Theory

Do infants only use one receptor type in colour vision investigations ?

One version of this theory suggests that the infant photopic luminance range may be restricted to a higher range than adults (Clavadetscher et al. 1988) and over the remaining range of luminances infants use only their rods, having no colour vision over moderate luminance ranges. In the work of Clavadetscher and co-workers (1988) no infant demonstrated wavelength discrimination below 540nm and luminance matches below this were scotopic. However, in studies were luminance levels were high, (Hamer et al 1982, Packer et al 1984, Varner et al. 1985) infants under 2 months of age still failed to make discriminations. The single receptor hypothesis may hold under some restricted experimental conditions but cannot be a general explanation of poor colour vision.

b) The Dichromat Theory

This suggests that infants lack one or more adult like cones and behave like a dichromat. Adult dichromats discriminate fewer colours and have a wider range of metameric matches than adult trichromats, as they have only 2 functioning cone types. The discrimination failures of infants do not, however, agree with those of dichromatic adults. When infants fail to make Rayleigh discriminations in the long wavelength section of the spectrum their brightness matches are not the same as the foveal brightness matches of adult protanopes and deutanopes (Hamer et al. 1982).

Adult tritanopes (blue cone dysfunction) demonstrate tritan pairs, which when properly balanced in luminance, are indistinguishable from white. The members of a luminance matched tritan pair yield equal quantum catches for MWS and LWS cones and hence a tritan discrimination cannot be made by a person with only MWS and LWS cones, thus tritan discrimination implies the presence of a functioning SWS cone. Three and four week old infants do not make tritan discriminations but will do so at 5 weeks (Varner et al. 1985). The ability of 7 week old infants to discriminate colour probably depends on the maturation of the mid-wavelength and long wavelength sensitive cones but colour deficiency in young infants is not due to a lack of one or more cone.

c) The Opponent Channel Deficiency Theory

Infants have no colour vision because they have no colour opponents channels.

The existence of colour vision is proof that at least two photoreceptors are sending information by at least 2 visual channels. If only one channel received the input from 2 cone types, no colour vision would occur. If a newborn possessed a luminance but no colour opponent channel, the emergence of this channel around 2 months would be responsible for the onset of colour vision.

Evidence of a colour opponent channel at 3 months comes from Brown and Teller (1989). The spectral sensitivity curve measured on a 580nm adapting field, shows a 'Sloan' notch at 580nm. This has been taken as evidence of a red/green colour opponent channel. No data exists for infants below 3 months of age. If newborns lack a colour opponent channel detection will occur via a luminance channel and the infants will have no colour vision (Maurer et al. 1989). Perhaps the synaptic connections for a chromatic opponency channel do not exist prior to 2 months.

d) The Visual Efficiency Theory (Large Weber Fraction Theory)

It has been proposed that infants have poor colour vision because their overall sensitivity is poor i.e. they have large Weber fractions. (Brown 1989, 1990, Banks and Bennett 1988). All the photoreceptors and postreceptoral channels are believed to be functioning but the photoreceptors are so immature that no isoluminant stimulus can exceed the threshold levels.

This theory is derived from the immaturity of the retinal photoreceptors at birth and as these mature, so does visual efficiency. Neonatal cones are broader and shorter than adults (Abramov et al. 1982, Yuodelis and Hendrickson 1986). The infant cones do not funnel light effectively. Any light that reflects off the inner walls of the cone segment at an acute angle cannot reach the outer segments and is lost. If the wavelength properties of the inner segment do not work, the effective aperture of the infant cone must be the outer segment itself. Banks and Bennett (1988) estimated that an infant's central foveal cone lattice would capture 350x less quanta than an adult's.

If the visual efficiency hypothesis is correct, maturation of luminance contrast sensitivity and chromatic contrast sensitivity would follow similar developmental time courses. If failure to discriminate colour, is due to a lack of functioning post-receptoral channels the ratio of chromatic sensitivity to luminance sensitivity would be greatest in the neonate and diminish with age as post receptoral channels become adult like.

Allen and co-workers (1990) undertook a study to measure luminance and chromatic contrast thresholds at different ages. Stimuli were sinusoidal red and green gratings that

were of equal contrast. These were added in spatial counterphase and modulated at 3 Hz to produce a sweep VEP. Varying the ratio of R/(R+G) (Mullen 1985) where R and G were the mean luminances of the red and green sinusoids respectively, ratios of 0, 0.5 and 1 produced black/green, red/green, and red/black sinusoids respectively. The sinusoids had a spatial frequency of 0.8cpd for the infant situation and 0.32 for the adults. A group of 14 infants aged between 2 and 8 weeks and 3 adult observers were tested. They also included 3 colour deficient adults. Sensitivity was found to greatest for the luminance gratings and least for the isoluminant gratings although the exact method of sensitivity calculation is not reported in the literature. Infants showed a reduced sensitivity for all stimuli compared to adults but the ratio of luminance to chromatic contrast sensitivity was found to be similar for infants and colour normal adults. Infants as young as 2 weeks of age were shown to demonstrate clear responses to isoluminant stimuli and Allen and colleagues suggested from this that human neonates appear to have functional MWS and LWS cones and postreceptoral mechanisms. They argue that the above findings are consistent with the visual efficiency hypothesis and a young infants inability to demonstrate colour discriminations is due to poor sensitivity. As luminance contrast sensitivity improves, so does, at the same rate, chromatic contrast sensitivity.

In a well documented concurrent study by Morrone and co-workers (Morrone et al. 1990, Burr et al. 1991) a similar technique was used to produce very different results. Sensitivity to plaid stimuli composed of the summation of horizontal and vertical gratings modulating in luminance or chromaticity was measured using steady state VEPs. The plaids reversed in contrast at a rate determined to elicit the maximum response (1.5Hz for the youngest infants, 5Hz for the oldest infants and adult observers). VEPs were recorded as a function of the proportion of red in a stimulus (Mullen 1985). A symmetrical curve of amplitude vs. red to green ratio about a minimum could be plotted and this minimum was taken to be isoluminance. This was very close to the red/green ratio of 0.5 for all colour normal adult and infant observers. For adult observers strong responses could be elicited for all colour ratios (Fiorentini et al 1991). For most of the infants no response could be elicited at or near isoluminant point before 7 weeks of age even at 100% contrast and the lowest spatial and temporal frequencies (0.05cpd, 1.5Hz) but at this age a luminance contrast of 20% could elicit a reliable VEP.

VEPs were recorded as a function of contrast and spatial frequency for both chromatic (isoluminant) and luminance (black/green) stimuli and the amplitude response curves fitted with a polynomial (3rd order). Extrapolation of this curve to zero gave an estimate of contrast threshold or spatial acuity (Campbell and Maffei 1970). For adults the extrapolated results were in agreement with those measured psychophysically. After 6

weeks infants' sensitivity to the isoluminant stimuli (at 0.1cpd) increased steadily with age to approach adult values by 18 weeks and acuity for the isoluminant stimuli also increased steadily with age from about 0.1cpd to around adult values of 8cpd at 30 weeks. This suggested that the chromatic visual system begins to develop at 5-7 weeks but at a different rate to the achromatic. Morrone and colleagues suggested that the symmetry of the amplitude curve about a minimum reinforced existing evidence that red and green stimuli that are equally effective for adults are equally effective for infants (Dobson 1976, Peeples and Teller 1975, Moskowitz-Cook 1979, Maurer et al. 1989).

As much evidence suggests the receptors with spectral sensitivities similar to MWS and LWS adult cones are functional by 2 months, Morrone and co-workers proposed that the differences in maturation rates of chromatic and achromatic spatial and temporal properties may reflect differential developmental rates of post-receptoral mechanisms.

e) The Chromatic Channel Deficiency Theory

Lack of a chromatic processing channel would imply that all colour information present at retinal level was lost upon transmission to the visual cortex. Alternatively, visual information before two months is processed by a system other than the visual cortex, that is insensitive to colour. Young infants have no access to colour vision and so will fail all colour discriminations (This is in agreement with the literature- see review 3.14) Visual evoked potentials would be expected to be absent when the stimuli were isoluminant (i.e. contained no luminance information) and VEPs would be solely dictated by the the luminance modulation of the stimuli. As chromatic channels develop, so should the sensitivity to isoluminant stimuli and the relative contrast sensitivity of luminance to colour should decrease with age.

Atkinson (1992) suggested that differential functional development is due to differential development of parvo and magnocellular pathways. Newborn visual mechanism is largely under subcortical control due to the evidence that specialised cortical detectors are not functioning. These do start to operate during the first few weeks of life allowing the discrimination of orientation and size. Separate parvo and magnocellular properties are hypothesized to account for these changes in visual capability over the first 6 months. The parvocellular system is functional before the magnocellular as orientation is functional before motion detection which is functional prior to disparity.

As parvo pathways are responsible for the processing of colour at what age does this cortical stream begin to function?

CHAPTER FOUR
METHODS OF VISUAL FUNCTION ASSESSMENT

4.1 Introduction

The objective methods, used to assess visual function in infants, fall into three main categories; optokinetic nystagmus (OKN), preferential looking (PL) and visual evoked potentials (VEP). All have been used to measure visual acuity, and absolute acuity differences do occur between methods. These methods have also been used to assess the development of other visual functions, e.g. contrast sensitivity, colour vision and stereoacuity (see chapter three for reviews of such studies).

Preferential looking (PL) has been designed specifically for use with infants, but can be applied to older children and adults with neurological impairment (Duckman and Selenow 1983, Birch and Bane 1991). OKN and VEP methods can be used over any age range, whereas operant PL techniques are most suitable for those infants over 6 months of age (Mayer and Dobson 1980, 1982, Birch et al. 1983b). This chapter reviews the variations of each method reported in infant visual development studies.

4.2 Optokinetic Nystagmus (OKN)

The earliest objective assessment of visual acuity was based on optokinetic nystagmus. The review of the literature by Pearson, still remains the most comprehensive account of that work done before 1973, (Pearson 1966,1973) as the use of OKN, as an objective assessment of visual function, appears to have fallen in popularity in recent years.

Pearson (1973) classifies variants of this technique, according to the particular reflex involved Thompson (1987) simplified this classification into the following categories:

a) method based on evoking oscillatory motion.
b) methods based on evoking optokinetic nystagmus.
c) methods based on termination of optokinetic nystagmus.
d) methods based on arresting optokinetic nystagmus.

Any of these methods can be assessed by observing the eye movements, or measurement with an electro-oculogram.

a) Method based on evoking oscillatory motion.

By moving a large object with pendulous movement before the eyes, a corresponding oscillatory motion of the eyes can be produced (Goldmann 1943). This movement will

not be induced unless the stimulus is perceived and has been used as an assessment of visual acuity, with progressively smaller stimuli or increased viewing distance. Goldmann (1943) first used this technique with a checkerboard target which would appear as an even grey if unresolvable. Visual acuity was estimated by measuring the maximum viewing distance at which eye movements could be induced.

In another estimation of visual acuity, pendular nystagmus was induced by steel wires, of various thickness, fitted to the arm of a metronome (Schwarting 1954). The smallest wire, moving across an illuminated field, to evoke a synchronous movement, was taken to be a measurement of visual acuity. A method widely used clinically , the Catford drum, (Catford and Oliver 1973) comprises of a motorised portable drum on which a black disc on a white background makes a slow phase across the field, followed by a quick return. The target measures minimum visible stimulus rather than minimum separable and is felt to overestimate visual acuity (Atkinson et al. 1981). The smallest stimulus on the drum cannot distinguish visual acuity of 6/6 from 6/24 and any interocular difference of this magnitude would go undetected.

b) Methods based on evoking optokinetic nystagmus.
When a series of objects move in one direction across the visual field, an involuntary, rhythmical conjugate movement of the eyes occurs. This consists of a slow phase, in pursuit of the moving stimulus and a fast recovery phase in the opposite direction and is known as OKN (see section 3.7.3). If a stimulus induces OKN, it must be resolvable by the subject and this has been taken as an estimate of visual acuity. This method was first reported by Gunther (1948) and has been utilised in a number of infant visual acuity studies (For review see Pearson 1973, Thompson 1987). Studies to determine isoluminance in infants have used this method, inducing OKN in humans and monkeys, when a stimulus is perceived as isoluminant (Chaudhuri and Albright 1990) (For review see Chapter 5).

c) Methods based on termination of optokinetic nystagmus.
As OKN could be induced by rotating a striped drum, the width of the stimulus elements could be decreased gradually until nystagmus ceased. Visual acuity could then be estimated from the visual angle subtended by one stripe (Adler 1950). The test comprised of the determination of the smallest stripe separation to sustain OKN.

Few infant visual acuity investigations have utilised this method but it produces comparable infant acuity assessment to preferential looking (Fantz et al. 1962). Another variation of this termination of nystagmus method has been used recently in the

determination of isoluminance for infants (Maurer et al. 1989, Teller and Lindsay 1989) and this will be reviewed later (section 5.4).

d) Methods based on arresting optokinetic nystagmus.
OKN can be suppressed, by placing a resolvable stationary object within a moving field and visual acuity can then be estimated from the smallest pattern to inhibit OKN. This method was the first objective method of visual acuity determination (Schumann 1952). OKN was induced by a rotating black and white drum, with the arresting stimulus appearing directly in front of the drum. Visual acuity was determined from the size and visual angle of the smallest stimulus to arrest OKN. This method has also been used to study the development of contrast sensitivity from birth to 38 weeks (Meijler and Van den Berg 1982). Pursuit eye movements, recorded by electro-oculography, were induced horizontally by a sinusoidally moving pattern and suppression of eye movements were determined statistically to indicate perception of the pattern.

A limitation of all the above variations on the method of optokinetic nystagmus when used objectively, to determine visual function, is that a failure to induce OKN may be a reflection of poor co-operation, on behalf of the subject and not an inability to resolve the stimulus. In the case of visual acuity determination, there is disagreement over whether resolution, or perception, is actually a pre-requisite of reflexive optokinetic nystagmus (Ruskell 1967).

4.3 Preferential Looking (PL)

Preferential looking depends upon the fact that infants will preferentially fixate, or track patterned stimuli, over a blank field (Fantz 1958). Demonstration of this preference for a particular pattern (spatial frequency) is evidence that an infant can detect such a pattern. It is this observation that has provided the basis for the preferential looking technique. Fantz estimated the duration of fixation of a grating pattern, by monitoring the amount of time the corneal reflex of the stimulus was located over the pupil. Acuity was designated, for a particular age group, to be the smallest stripe width, of a black and white striped stimulus, that produced a longer fixation time than a grey field in 75% of infants tested. Miranda (1970) demonstrated that this technique could be used to assess visual acuity in premature, as well as full term infants.

A modification of Fantz's 'looking time' procedure was introduced by Teller and colleagues in 1974. By combining it with a two-alternative forced choice psychophysical method (Blackwell 1953, Bush et al. 1963) they produced forced choice preferential looking (FPL). The position of the stimulus is unknown to the observer, who must make

a decision on its location based solely on the behaviour of the infant. The observer's response is scored as correct or incorrect. Feedback, as to the location of the grating, is given after each trial to aid the observer in determining the most reliable infant cues. A psychometric function can then be constructed, as a function of stimulus parameters, from the percentage of trials that the observer correctly chooses the side on which the pattern stimulus is displayed (Teller 1979).

Using the method of constant stimuli, repeated trials at a number of pre-selected stimulus levels are carried out. The observer aims to select about five stimuli that are equally spaced on the psychometric function from chance (50%) to 100%. Threshold is generally defined as 75% on this function. This method has been used in a variety of studies to investigate development of visual function; visual acuity (e.g.Teller et al. 1974, Dobson et al. 1978), stereoacuity (Held et al. 1980, Birch et al. 1982), colour vision (see table 3.2 for review), contrast sensitivity (e.g. Swanson and Birch 1990) and critical flicker fusion frequency (Regal 1981).

Working with infants presents a limit on the available testing time, and the method of constant stimuli requires up to 100 trials;on average 50 trials per hour are possible (Teller 1979). This makes the procedure too lengthy for clinical use. Atkinson and co-workers (1977a, 1977b) set a slightly lower criterion of 70% correct threshold, hence requiring fewer trials. Staircase procedures prove to be more efficient and less time consuming, requiring fewer stimulus presentations than the method of constant stimuli. Testing is concentrated near threshold and the stimulus to be presented is based on the previous stimulus, and the observers response. The initial stimulus is chosen to have a high probability of evoking a positive response, and for each successive positive response the stimulus is reduced in level (i.e. smaller stripe width) by a step (predetermined amount). A negative response will produce an increase by one step. The staircase is recommended to continue until 6 reversals are obtained (Wetherill and Levitt 1965) or a pre-determined number of trials has been completed (Cornsweet 1962). Threshold can be the mean value of a given number of stimuli, or the stimulus level above which 50% of the responses were positive.

A modification of this technique was reported by Atkinson and co-workers (1977a, 1977b, 1982) to obtain monocular and binocular visual acuities. Stimuli were presented in five trail blocks and if the observer made four or five correct choices in each block, the spatial frequency of the stimulus would be increased. Two or less correct choices resulted in a reduction in spatial frequency. The staircase was terminated after at least 20 trials had been run at two adjacent spatial frequencies with the proportion of correct

answers bracketing the 70% value. This criterion usually required 50 to 90 trials and acuity was taken as the interpolated 70% point. Manny (1983) used a microcomputer to generate stimulus patterns, record responses and determine the appropriate stimulus for staircase assessment. This system hence requires only a single operator.

McDonald et al. (1985) introduced the acuity card procedure as a clinical estimation of visual acuity to reduce the need for time consuming repeated trials. The observer is aware of the position of the stimulus, but not of the spatial frequency presented. The observer can then utilise more knowledgeable cues to determine the infants fixation preference and by relying on the subjective judgement, the procedure is thought to by-pass the statistical variability of the standard forced choice procedure requiring far fewer trials (McDonald et al. 1986).

Preferential looking techniques are most effective between 1 and 6 months of age but operant methods can be used to extend this age range. In this method, rewards, such as animated toys, are introduced to act as reinforcement and increase co-operation of older children may be used successfully (Mayer and Dobson 1980. 1982, Birch et al. 1983b).

4.4 Visual Evoked Potentials

The VEP is the electrical response of the nervous system, elicited by visual stimulation of the sensory nerves (Sphelmann 1985). These potentials have been used as an indication of the maturation of the infant visual system (Harding et al. 1982, Grose et al. 1989). VEPs elicited by flash and pattern stimuli are used commonly in the clinical assessment of brain function and the pattern VEP provides useful evidence of form vision in infants. VEP latency can provide an index of visual maturation (McCulloch and Skarf 1991).

The electroencephalogram (EEG) provides a record of continuous, spontaneous brain electrical activity and is probably a reflection of internal and biochemical events. It is however, unrelated to the incoming signal (Harding 1982). The transient VEP is a discrete signal in response to change in stimulus and is recorded as amplitude of response against time (Regan 1972). As it is time locked to the stimulus, it is possible to enhance the recording of the signal using a technique known as averaging. This entails the storage of an epoch of the incoming signal, which is subsequently added to the next incoming epoch. The time locked VEP signal will thus build up and the random background activity tends to cancel out. The signal to noise ratio is proportional to the square root of the number of sweeps averaged (Harding 1974). The signals must be presented with a sufficiently long inter stimulus interval (ISI) (1-2 Hz) to prevent successive responses from coalescing (Halliday 1982).

The morphology and latency of the pattern VEP varies according to the mode and nature of stimulus presentation. There are three basic modes of pattern presentation, flashed-on pattern, pattern onset and pattern reversal Different responses to each presentation may show differential rates of development (Orel-Bixler and Norcia 1987) making cross comparison difficult. The components of the transient VEP are analysed in terms of amplitude, latency and polarity.

4.4.1 Flashed-on pattern VEPs

The first report of infant pattern VEP used a checkerboard superimposed on a flash stimulus to elicit VEPs from infants between the ages of 30 and 156 days (Harter and Suitt 1970). Interpretation of these results was difficult as it was not possible to subtract the flash VEP to isolate the pattern response, due to the non liner summation of the two responses (Regan 1972). Harter and co-workers (1977b) used a similar protocol to extensively study pattern VEP development in ten infants aged 6 to 45 days.

a) Morphology of the flashed-on pattern VEP

The most consistent flashed on pattern VEP response from infants is triphasic. This comprises of a positive peak (P2) at 130-160 msec, a negative (N3) at 190-210 msec and a second positive peak (P3) at 300-400 msec (Harter and Suitt 1970, Harter et al. 1977b). The latency of the P2 and N3 components show a linear decrease with age, while amplitudes increase curvilinearly to a maximum at 65 days, before decreasing again.

b) Scalp topography of flashed-on pattern VEP

Hoffmann (1978) investigated the distribution of the flashed-on pattern VEP over the scalp and its change with development. Using checks of different sizes (40', 1° 10', 5°) the responses at O_Z, C_Z, P_Z and T_4 (reference electrode on right ear) were recorded. Two major components were recorded in all subjects,at all ages (28-96 days). These were a large positive component at 100-250 msec and a late negative component at about 617-878 msec. The latency of the positive component was found to be related to age.

Similar topographical findings have been reported in cat VEPs and it has been suggested that the early positive wave reflects cortical activity while the late negative is due to superior colliculus activity (Rose and Lindsley 1968). Hoffmann suggested that this data may represent a change in physiological locus of visual control from a subcortical to a cortical level at 6-10 weeks.

4.4.2 Pattern onset-offset VEP

In order to remove the contamination of the flash response, it is necessary to maintain a constant overall luminance level; the response then produced would represent a specific pattern response. This constant luminous flux is maintained by using pattern onset-offset or pattern reversal stimulus. Clinically it is the pattern reversal stimulus that is most frequently used as it has been shown to be less variable than the pattern onset-offset stimulus (Drasdo 1980, Wright et al. 1985). For use with young infants however, a brief pattern appearance, followed by a long disappearance, is believed to be effective, as it does not require prolonged periods of accommodative effort (Spekreijse 1983)

a) Morphology of the pattern onset-offset VEP

In adults, the pattern onset-offset VEP has two main complexes. The onset response takes a P-N-P form and its components are generally referred to as CI, CII and CIII respectively (Kulikowski 1971). The positive (CI) has a latency of 80 msec; negative CII has a mean latency of 120 msec and a positive wave (CIII) arises around 130 msec. CI tends to reflect local luminance change, CII is contour or edge specific and CIII is favoured by binocular conditions (Spekreijse et al. 1977). CI is believed to arise from the striate cortex whereas the other two components may originate from the association areas (Jeffreys and Axford 1972a, 1972b).

The morphology of the infant onset pattern VEP was found to be much simpler, consisting only of a positive wave at 190 msec at 2 months (Spekreijse 1978). This positive peak may consist of two components possibly CI and CIII (Apakarian et al. 1984). The latency of the positive wave reduces with age to reach 160 msec by the fifth month, but the implicit time of the beginning of the wave remains unaltered (Spekreijse 1978). It was suggested that the 'sluggish' shape of the VEP may be a reflection of immature cortical myelination producing a high dispersion in velocities. Infants less than ten months of age do not show a CII component with only 40% of infants demonstrating a CII at 20 months. It is not until 100 months of age that all infants will display a CII (De Vries-Khoe and Spekreijse 1982). The pattern onset wave form becomes more distinct with age, becoming sharper and smaller. There is a change of dominance from the initial positive peak to the negative CII (De Vries-Khoe and Spekreijse 1982) and it is the growth of this component that splits the positive component into CI and CIII, which attain adult-like latencies at puberty.

4.4.3 Pattern Reversal VEP

A pattern reversal stimulus maintains constant luminance flux, therefore overall luminance information in the response is minimised.

a) Morphology of the pattern reversal VEP

The adult pattern reversal VEP to a checkerboard consists of a N-P-N wave form, but in infants it has a simpler morphology consisting of a single, slow rising positive peak (P1) (Sokol and Jones 1979, Moskowitz and Sokol 1983). The positive component is preceded by a negative component (N1) by 8-14 weeks (Sokol and Jones 1979) with the emergence of a N2 component by 2 months (Moskowitz and Sokol 1983, Grose et al. 1989). The P1 component is reported to be the most reliable component of the infant VEP, and has been demonstrated in infants as young as 30.5 weeks post menstrual age (PMA) (Grose et al. 1989).

b) Development of the pattern reversal VEP

Relatively large checks are required to elicit successful VEP responses from neonates. Pattern reversal VEPs at one month of age can only be recorded to checks of 30' of arc or larger (Sokol and Jones 1979, Moskowitz and Sokol 1983, Porciatti et al. 1982) with the first measurable VEP, to a check of 15' of arc, only appearing at 8-10 weeks (Sokol and Jones 1979, Moskowitz and Sokol 1983). Both of these studies used a TV system to generate black and white checkerboards, of a range of check sizes (7.5' to 240' min of arc). By three months, a late positive wave is present in the infant VEP to large checks and to small checks at 9 months. Harding et al. (1989) and Grose et al. 1989) found clear responses in pre-terms with 2^0 checks and reported maturation of VEP to have an almost linear rate, with responses to large check sizes maturing at a faster rate than smaller checks. Latencies for pre-term and full term infants were comparable when a correction is made for gestational age.

Odom et al. (1983) recorded VEPs and ERGs simultaneously to reversing square wave gratings, in an attempt to investigate the relationship between pattern ERG and pattern VEP visual acuity in infants. Using transient VEPs, the second harmonic of the VEP was the response measure and visual acuity was estimated by extrapolation of the amplitude versus spatial frequency function. This gave an acuity of 8.5 cpd, but Fiorentini (1984) criticised the Fourier analysis of transient responses as inappropriate. The maturation of the pattern reversal response to checkerboards has been compared to square wave gratings, and for large pattern components, 30-240' of arc, no P1 latency difference was noted. However, smaller pattern sizes (7.5' and 15' of arc) produced a significantly longer P1 latency for checks than for stripes (Moskowitz and Sokol 1983). Fourier analysis shows checks to have a higher spatial frequency than equivalent width stripes (Kelly 1976) and expressing the data in terms of fundamental frequency shows no difference in the maturation of the two responses.

The smallest check sizes will, as in adults, give the longest pattern reversal latency (Sokol and Jones 1979) with the latency for large checks maturing faster than for small. The latency for large checks (60' of arc) decreases linearly at a rate of between 1 msec (Porciatti 1984) and 2 msec per day (Sokol and Jones 1979, Moskowitz and Sokol 1983).The P1 component for checks of 30' min of arc, or larger, reaches adult like latency at 16 weeks. Latency for smaller checks has a much longer developmental time course, decreasing from birth to 6-7 years (15' of arc checks) (Sokol and Jones 1979) or 13 years (7.5' of arc checks) (Wenzl and Brandl 1984). This differential rate of development, in relation to check size, has been suggested to reflect the differences in maturation of the transient and sustained cells of the visual system. The transient or Y system is thought to detect movement or gross pattern, the sustained or X system, being responsible for the discrimination of fine pattern (Moskowitz and Sokol 1983).

c) Steady state pattern reversal VEPs

If the reversal rate of a checkerboard is increased to about 8 reversals per second (rps) or more, the adult VEP will take on a sinusoidal wave form. This is the steady state visual evoked potential (Regan 1966) and is analysed in terms of amplitude and phase (Regan 1978). If the response wave form to a sine wave temporal stimulus, is not a sine wave the system is said to be non linear. This distorted response can be broken up into a series of sine waves, each harmonically related to the stimulus wave form. Infant responses become sinusoidal at about 4 rps (Porciatti 1984) and will diminish at temporal frequencies about 16 rps. These temporal tuning characteristics of the infant pattern VEP vary with check size, being maximal for large checks (48' of arc) at 4 rps at 2 months. Adult levels of 8-10 rps are reached by 4 months of age and this shift is thought to reflect the development of the underlying luminance pathways (Moskowitz and Sokol 1983). Temporal tuning functions for small checks are bi-modal in form for infants older than 4 months of age. There are two peaks, one at 4 rps and a second a 10-12 rps.The low temporal frequency peak becomes more prominent with smaller check sizes and increased age with the peak still occurring at 4 rps at 3 to 5 years of age.

The gradient of the phase characteristic of the fundamental harmonic of a steady state VEP is proportional to the latency of the transient response (Spekreijse et al. 1977) and is much steeper in infants than in adults (Porciatti 1984). This is in agreement with the latencies of the transient response.

4.4.4 Assessment of visual acuity by pattern VEP

An inverted 'U' shaped function of amplitude and check size has been demonstrated for various modes of pattern presentation in adults (Campbell and Maffei 1970). Visual

acuity estimates can be made by extrapolating the descending limb of this function to zero amplitude. This represents the smallest check size to elicit a VEP and can be used with both transient (Harter and Suit 1970, Harter et al. 1977, Orel-Bixler and Norcia 1987) and steady state VEPs and this technique has also been used by several workers to assess the development of contrast sensitivity in infants (for review see section 3.3)

The main disadvantage of estimating visual acuity by extrapolation, from the amplitude versus spatial frequency function, is that as progressively smaller pattern elements are used, the area of stimulation changes from a parafoveal to a foveal site. This may result in wave form variation or even polarity reversal of responses as the cortical regions relating to the fovea are positioned more posterior than the parafovea (Spekreijse 1978, 1980). The slope of the curve of amplitude versus check size is dependent on the contrast level used (Campbell and Maffei 1970) and this may account for some variability between studies.

Norcia and Tyler (1985) introduced a rapid sweep method of VEP recording to estimate visual acuity. Sinusoidal gratings were reversed at 12 rps and swept simultaneously in spatial frequency, with each sweep lasting 10 seconds. The amplitude and phase of the second harmonic was derived by discrete Fourier Transformation (DFT). Plots of VEP amplitude and spatial frequency showed narrowly tuned peaks at one or more frequencies, and acuity was estimated by linear extrapolation to zero amplitude of the highest spatial frequency peak in the function. This rapid method of VEP recording is of particular advantage in infants, due to the speed of execution offering a possibility to make 12-20 visual acuity estimates in one session (Norcia and Tyler 1985).

4.4.5. Visual evoked potentials to chromatic pattern stimuli in adults

Visual evoked potentials to pattern stimuli composed of red and green checks or gratings have been elicited in adults using pattern onset-offset and pattern reversal. Regan (1973) recorded visual evoked potentials to checkerboards, that reversed in colour contrast or luminance contrast, with maximum amplitudes being recorded at a reversal rate of 6 to 8 Hz. The response to both luminance and chromatic stimuli fell to a minimum above the rate of 12 to 16 Hz, and the topographical distribution of both chromatic and luminance responses were found to be similar. Regan and Spekreijse (1974) used both methods of presentation for red and green checkerboards (12' of arc checks). The relative luminance of the red to the green was subjectively equated (isoluminant) using heterochromic flicker photometry and VEPs to red/black, red/green and black/green stimuli were compared. Transient and steady state VEPs were recorded from adults with normal colour vision and deutranopes. No difference in response morphology could be detected for the chromatic

and luminance stimuli for the colour normals, however, the deutranopes gave no recorded response to the chromatic stimulus.

The finding for colour normal adults is in agreement with the work of Carden et al. (1985) and Murray et al. (1987) and Kulikowski and Parry (1987), who, when using pattern reversal stimuli found no difference between the morphology of the chromatic and achromatic VEP. However using a pattern onset gratings of 1 cpd, at a range of red/green ratios, a small negative component could be seen at isoluminance to replace the usual positivity. This effect was still observable with pattern onset checkerboards but using a higher spatial frequency of 4 cpd the effect was even clearer and would remain as long as the red/green ratio was within 6% of isoluminance. Murray and co-workers eliminated chromatic aberration, contrast or stimulus size as the possible causes of this change in morphology. Kulikowski and Parry (1987) suggested that the morphological change was due to the contribution of a non transient mechanism to the achromatic and chromatic response. They proposed that the negativity, seen in the chromatic response was due to parvocellular activity which would also be present in an achromatic checkerboards VEP (due to the very high spatial frequencies). If the achromatic stimulus was of low spatial frequency, it would be processed by the magnocellular system and produce a positive response. Thompson and Drasdo (1992a) found that, at low contrast levels, the achromatic pattern reversal stimulus is a monophasic positive peak with a negative component appearing at contrast levels above 10%, while the isoluminant reversal stimulus showed a negativity for transient stimuli, (in disagreement with previous work -see above). They also found the amplitude of the positive pattern onset VEP to chromatic stimuli decreased as isoluminance was approached while the succeeding negativity increased (Thompson and Drasdo 1992b). Thus controversy exists over the morphology of the adult chromatic VEP which may be attributed to different electrode montage.

Using sweep VEPS to checkerboards and gratings, Bach and Gerling (1992) demonstrated equiluminance tuning curves, with the amplitude of the response falling to about 13% of the achromatic response at isoluminance. This is in agreement with the findings of Regan (1970) and Burr and co-workers (1990) and this amplitude minimum has been used as a measure of isoluminance in subsequent work (Morrone et al. 1990, Fiorentini et al. 1991). Burr and co-workers (Burr et al.1990; Fiorentini et al 1991) estimated the latency of the chromatic VEP from the slope of the phase vs. temporal frequency curves and found it to be delayed, with respect to the achromatic response. In a study of the temporal properties of the chromatic system (Fiorentini et al. 1991) steady state isoluminant VEPs were recorded at a range of contrasts. Amplitude vs. contrast functions for luminance stimuli showed a shallow limb at low contrasts followed by a steeper limb at higher contrasts. This bi-modal function may indicate the contribution of

two neural systems to luminance processing i.e. magnocellular and parvocellular, while the isoluminant chromatic function was linearly steep, suggesting only parvocellular processing.

4.4.6 Visual evoked potentials to chromatic pattern stimuli in infants

Visual evoked potentials to chromatic stimuli in infants have been used to assess the development of colour vision. Dobson (1976) measured the implicit time and amplitude of flash VEPs to monochromatic light, and plotted implicit time as a function of the log energy of the stimulus. From this a spectral sensitivity curve for 2 month old infants was constructed. Moskowitz-Cook (1979) undertook similar investigation for infants between the ages of 3 and 22 weeks. Using a pattern reversal stimulus, with an alternation rate of 4 Hz (8 reversals per second), i.e. steady-state, checkerboards composed of 45' black and coloured checks were used to elicit monopolar VEPs. Ten wavelengths were investigated over a range of radiance levels and clear responses were obtainable from all stimuli in infants above 7 weeks of age. Again, implicit times of the negative component (N1) were plotted as a function of wavelength. This data was then transformed to produce a spectral sensitivity function (see section 3.13).

Allen and co-workers (1990) used sweep VEPs with sinusoidal red/green gratings to study luminance and chromatic contrast thresholds in infants. Clear responses to isoluminant stimuli could be recorded in all infants investigated , including a 2 week old infant, with clear performance minima at isoluminance. Morrone and colleagues (1990) used the same technique as that used to record chromatic VEPs in adults (Fiorentini et al.1991) to study the characteristics of the chromatic VEP in infants. Stimuli were composed of the summation of horizontal and vertical sinusoidal gratings (of 0.1cpd) to form plaids. VEPs to these were recorded as a function of the proportion of red in the stimulus (Mullen 1985).A performance minimum could again be seen at around photometric isoluminance, and this was taken as subjective isoluminance for the subjects.

One aim of this present research project is to assess the development of the transient chromatic visual evoked potential and ascertain its presence and morphology in young infants. Development of this response may go some way to give further evidence to the developmental time course of the chromatic or cortical system. As controversy surrounds the age of onset of chromatic function in infancy, we aim to carry out a both a cross-sectional and longitudinal study to clarify the earliest age at which isoluminant stimuli can elicit a transient VEP. The use of chromatic patterns is ideal for activating a localised region of the visual cortex assuming the human visual pathway is organised in a similar way to the macaque monkey (Murray et al. 1987). In the macaque, chromatic patterns

stimulate mainly opponent-type (tonic) cells with thin axons which project to the parvocellular layers of the lateral geniculate nucleus (Gouras 1968). These LGN cells project to specific locations in the visual cortex (Livingstone and Hubel 1984). If infants function subcortically via a tectal pathway which is insensitive to colour then they should be insensitive to chromatic stimulation until visual function is subserved via a geniculostriate pathway which is colour sensitive. Findings and conclusions with respect to this and other hypotheses are discussed later (See chapter 10).

CHAPTER FIVE
THE DETERMINATION OF ISOLUMINANCE

5.1 Introduction

Any assessment of the chromatic system of an infant requires a stimulus in which luminance cues have been eliminated. Isoluminant stimuli i.e. stimuli in which each chromatic component is perceived as having equal luminance, have been used in adults to study the relative contributions of colour and luminance based pathways in visual processing. The selective luminance and chromatic stimulation of the visual system has lead to psychophysical evidence for some of the functional differences between the two principal geniculostriate pathways i.e. the magno and parvocellular streams (Livingstone and Hubel 1988).

5.2 The "brightness problem"

In previous studies of the infant chromatic system, three ways of overcoming the problem of luminance cues within a chromatic stimulus have been utilised. These are summarised below: (For review see Teller and Bornstein 1987).

a) The most basic method is the use of an adult brightness match, assuming that this will be an adequate match for infants (Chase 1937). Unfortunately, infants are still capable of tracking stimuli across a field even if the brightness difference between the stimuli and field is less than 0.1 log unit (Peeples and Teller 1975). If their isoluminant point was more than 0.1 log unit away from an adult match, this estimation would not be sufficient to eliminate brightness cues (see 5.2c).

The second and third techniques are essentially similar with the same basic principles. By varying the relative luminances of two chromatic stimuli over a range that is distributed around and includes the adult brightness match, the infant should, at some point, be presented with a brightness pairing close to their own brightness match. Thus for at least one stimulus presentation, luminance cues will be eliminated.

b) Using the second technique, Schaller (1975) initially reinforced a particular colour for an individual by the use of auditory, tactile and food rewards, finding that an infant was more likely to stare at a reinforced colour that a non reinforced one. The relative luminances of the two colours were then varied in an unsystematic fashion around the adult brightness match. If the infant could then demonstrate systematic fixation of the reinforced colour, irrespective of the brightness difference between the two stimuli it was showing evidence of colour discrimination.

c) The third technique has been used extensively by Teller and colleagues (e.g.Peeples and Teller 1975, Hamer et al. 1982, Packer et al. 1984 ,Clavadetscher et al. 1988). Systematic variation of the luminance ratio around the first approximation (adult brightness match) must at some point encompass the infant's brightness match. The separation of each brightness pairing from the next must be small enough so that the actual infant brightness match falls close enough to one pairing and is not missed. Peeples and Teller (1975) demonstrated that an infant could distinguish brightness differences of less than 0.1 log unit. They then calculated that if chromatic stimuli were presented at a series of brightness differences,each separated from the next by 0.08 log units, the infant brightness match, or isoluminant point, should fall close to one of these pairings. Hence luminance cues should be eliminated on at least on presentation. Using preferential looking, wavelength discrimination was taken as above chance performance at all brightness pairs presented. Any fall to below chance for a brightness pair would indicate no discrimination on the sole basis of wavelength.

Several methods have been used to determine the adult brightness match. These are reviewed below.

5.3 Determination of adult isoluminance

Isoluminance, the point at which two components of different wavelengths are subjectively equated for luminance, has been assessed in adults in a number of ways.

Direct comparison of the brightness of two lights can easily be made as long as the chromaticity between them is not too different. The accuracy of this method of direct heterochromic photometry (or brightness matching) decreases with increasing chromaticity difference and there is an extended brightness range over which equal brightness decisions are not easily made (Wagner and Boynton 1972). Heterochromic flicker photometry utilises the perception of flicker produced when two fields of different wavelengths are alternated at a frequency greater than 10 Hz (Ives 1912). Observers are required to adjust the luminance of one of the components until the sensation of flicker is minimised. The field should then take on the appearance of an intermediate colour. A variation of this method is 'Complex Image Counter Flicker Photometry'. Using an image on a background, the fore and background colours are interchanged at about 25 to 30 Hz and as long as there remains a luminance difference between the two colours the stimulus pattern will be visible, becoming less so with decreasing luminance difference to eventually disappear at isoluminance. This has been suggested for use with children (Troscianko and Low 1985).

In the Minimally Distinct Border technique, subjects are required to adjust the luminance of one field until the border between itself and a second field of different chromaticity is minimally distinct. There is however,no brightness match at which the border between a red and green field will completely disappear. Although both this technique and flicker photometry are felt to be superior to the method of brightness comparison, responses from both methods rely upon perceptual judgements (Wagner and Boynton 1972). Whereas well trained observers give reliable and reproducible results, the task is hard to explain to a naive observer and a training period is required.

In Heterochromic Modulation Photometry, the luminance of a test and comparison fields are fixed and it is the depth of modulation of the pair that is reduced until no flicker is perceived by the observer (Pokorny et al. 1989).This threshold depth of modulation is determined for a series of test/ comparison luminance ratios and the minimum of the V shaped sensitivity function produced is taken to represent isoluminance.

In 1983, Anstis and Cavanagh introduced the Minimum Motion Technique for the determination of isoluminance. Red and green gratings were alternated with dark yellow/light yellow gratings displaced by 0.25 cycles to the right in a four stroke cycle. The grating appeared to jump to the left if the green bars were lighter and to the right if the red bars were lighter. The four stroke cycle thus produced apparent motion in the direction of the lighter bars with no motion at isoluminance. Appropriate adjustments could be made in the relative luminances of the bars to approach isoluminance. This technique was found to give highly comparable results to flicker photometry for the same stimulus. It has been used with monkeys and children (see below) and used extensively to assess the effect of spatial and temporal frequency on isoluminance (Cavanagh et al. 1987). The amplitude of luminance of the green component required to null the motion of the stimulus varied little over the spatial frequency range of 0.5cpd to 10 cpd but this amplitude increased by about 8% over the temporal frequency range of 0.5 to 7.5 Hz. This finding for spatial frequency, although in agreement with Kelly (1983) is contradicted by Mullen (1985) who found the efficiency of red to increase with spatial frequency with respect to green. This may be the effect of spatial frequency but Mullen corrected for this.

5.4 Determination of infant and monkey isoluminance

One major drawback of the traditional methods of isoluminance determination is the requirement of the observer to make informed and trained judgements. This subjective decision making is obviously not viable in infants and animals and although some techniques may be of use in older children, an objective assessment is required for the very young .

Maurer and co-workers (1989) showed that using the Minimum Motion Technique any apparent luminance within the stimulus would induce an OKN response in infants. They presented the stimulus at five red/ green luminance ratios bracketing the normal adult isoluminance ratio and the isoluminant point of the infant was taken as the red/green luminance ratio at which OKN was observed equally as often in the red and green directions. This was determined by interpolating between the two tested values that bracketed this 50% point. Isoluminant points for infants were similar to those of their mothers, with a shift towards increased green in the isoluminant ratio of a deutranopic mother and her son. There was no sex difference and no obvious developmental change. Control experiments were undertaken to assess the effect of macular pigment and inaccurate accommodation. Adult observers viewed the display with the central 10° blanked out and no difference in isoluminance was found using the peripheral retina only. It was suggested that using such a large field (64°) macular cones did not appear to determine the isoluminant point. For red and green gratings at the spatial frequency used (0.25 cpd) moderate misfocus of 2 to 3.00D did not alter the result significantly with a misfocus of 4 to 8.00D having only moderate effect. From their results they concluded that the contribution of the red and green cones to the achromatic pathway is the same in infants as normal adult trichromats. Limitations on infant colour vision during the first months of life are not caused by an absence of red or green cones or an abnormality in the achromatic pathway, rather they may be due to a deficiency in cone input to opponent colour channels or the preservation of information within that pathway.

Teller and Lindsey (1989) confirmed that spectral efficiency curves derived from motion nulling techniques are similar in infants and adults. Infant spectral sensitivity curves have previously been shown to differ from adults with an increased short to mid wavelength sensitivity (Clavadetscher et al. 1988) and Teller and Lindsey suggested that the adult and infant similarity using the minimum motion technique was due to the effects of the large field used which caused a peripheral photopic luminance dominated result not seen in earlier infant spectral sensitivity estimations.

Logothetis and Charles (1990) used the same technique with monkeys and found no statistically significant variation over a spatial frequency range of 0.5 to 2.2cpd. However, as temporal frequency increased from 1 to 7.5 Hz there was a change in the isoluminant point of about 10% and this is consistent with the findings of Cavanagh et al. (1987). Chaudhuri and Albright (1990) presented an alternative to the Minimum Motion technique. In this method, motion was only perceived as the luminance ratio of the component stimuli approached isoluminance. At this point they demonstrated OKN in

monkeys and found OKN to disappear at luminances 10% above and below isoluminance.

Isoluminance has been determined in both adults and infants using steady state VEPs. Amplitude of response is recorded as a function of the luminance ratio and the minimum amplitude is taken to be isoluminance. The investigation of development of colour contrast and acuity by Morrone and co-workers is based on this method (Morrone et al. 1990, Fiorentini et al. 1991).

5.5 Determination of isoluminance: Pilot study

In an attempt to determine the stimulus parameters to be used in the study of the chromatic VEP, it was initially felt that isoluminance should be assessed for the infants taking part, in order to reduce luminance cues within a chromatic stimulus. Standard adult isoluminant techniques are impractical for use with infants and as the author had no experience of the minimum motion technique, a psychophysical technique was developed to determine isoluminance. The applicability of this was first assessed in an adult pilot study.

5.5.1 Equipment

All stimuli were presented with a Venus Neuroscientific stimulator controlled by application software written in Microsoft C. This has independent control of the red, green and blue guns and a refresh rate of 119Hz. The stimuli were displayed on a standard colour CRT monitor (CIE x and y co-ordinates, 0.591,0.373 for red and 0.297,0.596 for green). The display subtended an 8° square when viewed at 1.25 metres.

5.5.2 Subjects

A preliminary study was undertaken on a group of 9 adults (mean age 25.6± 2.73), all staff and students at Aston University . All subjects were optically corrected for the working distance and determined to be red/green normal by Ishihara screening plates. The non-dominant eye was occluded.

5.5.3 Stimulus

Horizontal chromatic sinusoidal gratings of 1 cycle per degree (cpd) were produced on the CRT, by removing the output of the blue gun and presenting the output of the red and green guns 180° out of phase spatially. The mean luminance of the red/green stimulus was maintained at 10 cdm^{-2} as measured by a Nikon photometer but the individual

luminances of the red and green gratings could be varied relative to one another. At a red/green luminance ratio of 1.0 both gratings were of equal objective luminance.

The individual gratings were made to counterphase 180° out of phase in a sinusoidal manner at a temporal frequency of 16Hz. Since luminance contrast sensitivity at such high temporal frequencies exceeds chromatic sensitivity (the basis of flicker photometry) the detection of this temporal modulation is dominated by any residual luminance information in the stimulus. The stimulus was presented randomly in the upper or lower half screen with the other half screen containing a uniform stationary field composed of the same mean luminance and chromaticity as the grating. This would thus tend to be of a brown/yellow colour.

5.5.4 Procedure

Sensitivity to the flickering stimulus was determined at several photometrically determined red/green luminance ratios distributed with logarithmic equality around a value of 1.0. A two forced choice staircase technique was used to determine thresholds. Each staircase commenced at a suprathreshold chromatic contrast level (amplitude of modulation of the gratings) with the grating appearing randomly in the upper or lower half screen and the observer was required to make a decision on its position. Incorrect identification of the flickering half screen led to an increase in amplitude of modulation of the red and green gratings by a step, thus making the flicker more apparent. Two successive correct responses were required before the amplitude of modulation was reduced. The thresholds for up to five different red/green ratios could be determined at the same time with stimuli randomly presented. Modulation threshold was determined as an average of six reversals in the staircase procedure.

5.5.5 Treatment of data

Flicker will reduce to a minimum when there is no luminance difference between the two gratings. A plot of sensitivity against log red/green ratio revealed a distinct minimum and the red/green ratio at which this occurred was taken to be the observer's isoluminant point. The position of the minimum was found by interpolating between the data points using 4th order polynomial functions.

Figure 5.1 demonstrates the method by which the isoluminant ratio of the individual, CN, was calculated. Interpolation of the minimum point of this function gives a log R:G ratio of - 0.018 (isoluminant R:G ratio of 0.96) for this observer. A similar technique, heterochromic modulation photometry has previously been described (Porkorny et al. 1989).

5.5.6 Results

The isoluminant red/green ratio for each of the nine adult observers assessed using this technique are shown in Table 5.1. The mean isoluminant point for this group of individuals using a spatial frequency of 1cpd is 1.004 ± 0.045.

Table 5.1 The isoluminant point of each individual using a stimulus of spatial frequency 1cpd, as determined for interpolation of the 4th order polynomial function of contrast sensitivity against log red green luminance ratio.

SUBJECT	AGE	LOG R:G RATIO	R:G RATIO
GR	24	- 0.083	0.98
RD	24	- 0.007	0.98
VV	29	- 0.014	0.97
CH	28	0.027	1.06
CN	25	- 0.018	0.96
JP	27	0.02	1.05
GB	24	- 0.013	0.97
DW	29	0.033	1.08
GH	21	- 0.004	0.99

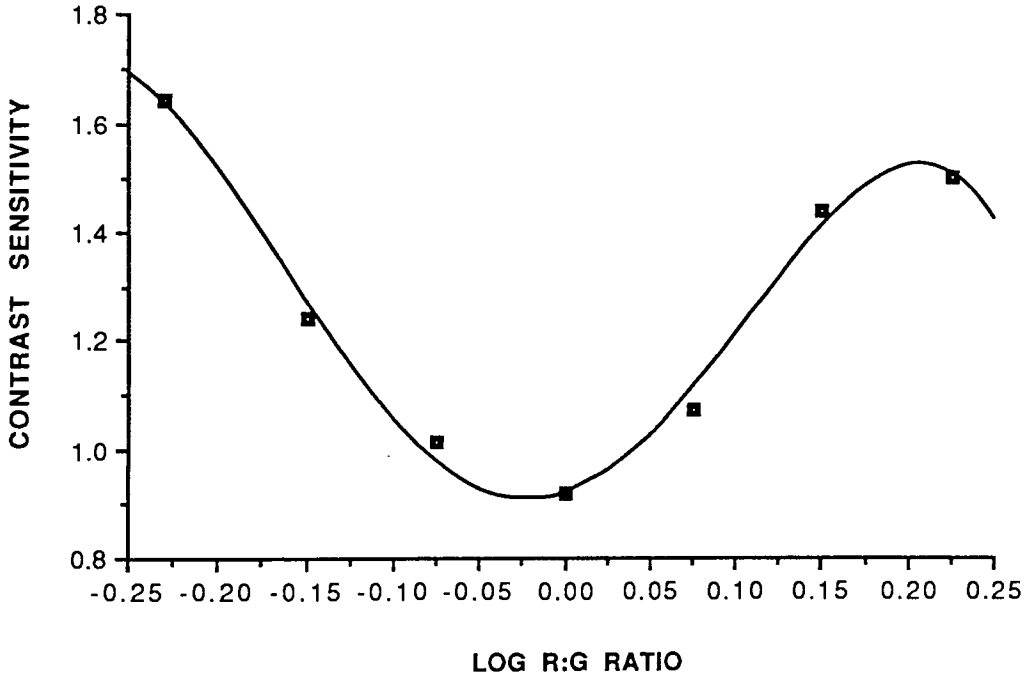


Figure 5.1 Plot of sensitivity thresholds at seven red/green ratios obtained using a two forced choice staircase procedure for an adult observer CN. ($r^2 = 0.989$).

5.5.7 The effect of defocus on the isoluminance

As refractive correction of the infants taking part in the main studies may have proved impractical, a study was carried out into the possible effects of incorrect refraction. The effect of defocus on the isoluminant point for red/green stimuli was investigated using four experienced observers. Having already been fully corrected for the viewing distance of 1.25 metres and isoluminance of a 1cpd grating determined as above, additional lenses of +1.00, +0.50, -0.50 and -1.00 dioptres were incorporated and the isoluminant point re-determined for each condition. A second spatial frequency of 4 cpd was also used.

Figures 5.2 and 5.3 show the effective change in isoluminant red/green ratio that was produced when the refractive error of the individual was changed over a 2.00 dioptre range. It can be seen that isoluminance varied significantly over the range of 2 dioptres tested here, when the spatial frequency of the stimulus was 4 cpd ($p < 0.0008$). The effective change with a low spatial frequency of 1 cpd was less but still reaches significance ($p < 0.05$). In agreement with these findings, Maurer et al. (1989) using the minimum motion technique to determine the effect of misfocus in adults found no effect produced by 2.00 to 3.00 dioptres of blur with a stimulus of spatial frequency 0.25 cpd. With larger amounts of misfocus of 4 to 8.00 dioptres only a slight change in isoluminance was produced. The findings here would thus support the view that the isoluminant point is more susceptible to blur as the spatial frequency increases which is in agreement with the knowledge of spatial degradation with increasing blur.

5.5.8 The effect of spatial frequency on isoluminance

Three experienced observers were used to assess any change in the red/green isoluminant point with change of spatial frequency. All the observers were again corrected for the viewing distance of 1.25 m and the procedure was repeated using additional spatial frequencies of 0.5 and 2 cpd to produce a total of four spatial frequency conditions. Figure 5.4 shows the relative change in isoluminant point for 3 adult observers, DW, GR and RD at the four spatial frequencies used. For all observers, the correlation between increasing spatial frequency and increasing green luminance within the stimulus to produce luminance match was significant (DW $r = 0.945, p < 0.05$; GR $r = 0.963$, $p < 0.04$; RD $r = 0.993$, $p < 0.01$). This shows isoluminance to be affected by change of spatial frequency with an increase in relative red luminance efficiency with increasing spatial frequency.

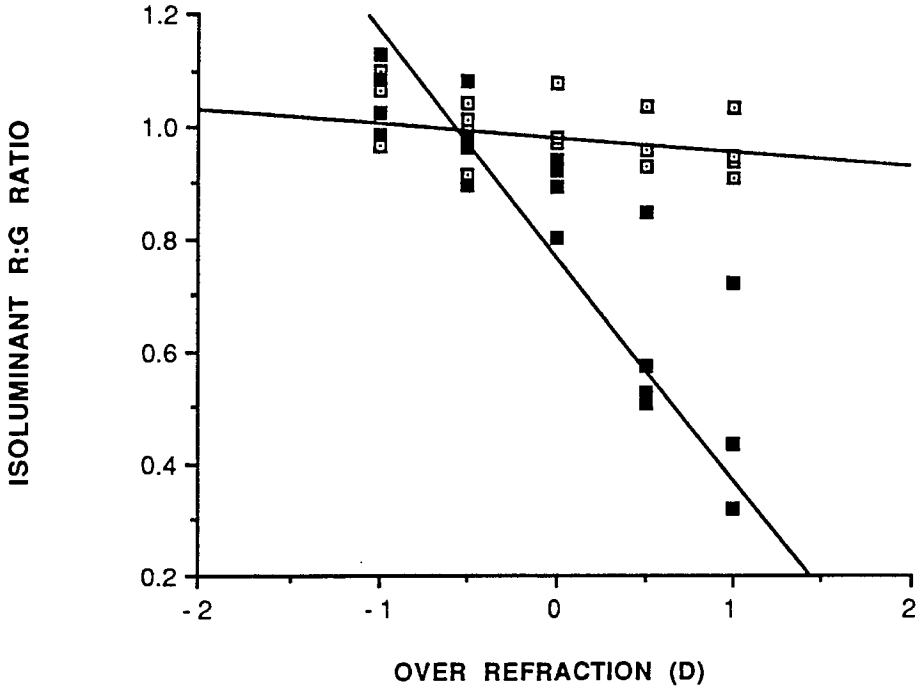


Figure 5.2 Distribution of change of isoluminant red/green ratio for four adult observers over a 2.00 dioptre power change in over refraction. Isoluminant points with a grating of spatial frequency 1cpd are shown as shown as dotted squares while isoluminant points for a 4cpd grating are shown as filled squares. The formula of the regression line for 1cpd is $y = 0.988 - 0.02x$; $r = 0.445$; $p < 0.05$; D.F. 19 The formula of the regression line for 4cpd is $y + 0.776 - 0.4x$; $r = 0.0.882$; $p < 0.0008$; D.F. 19.

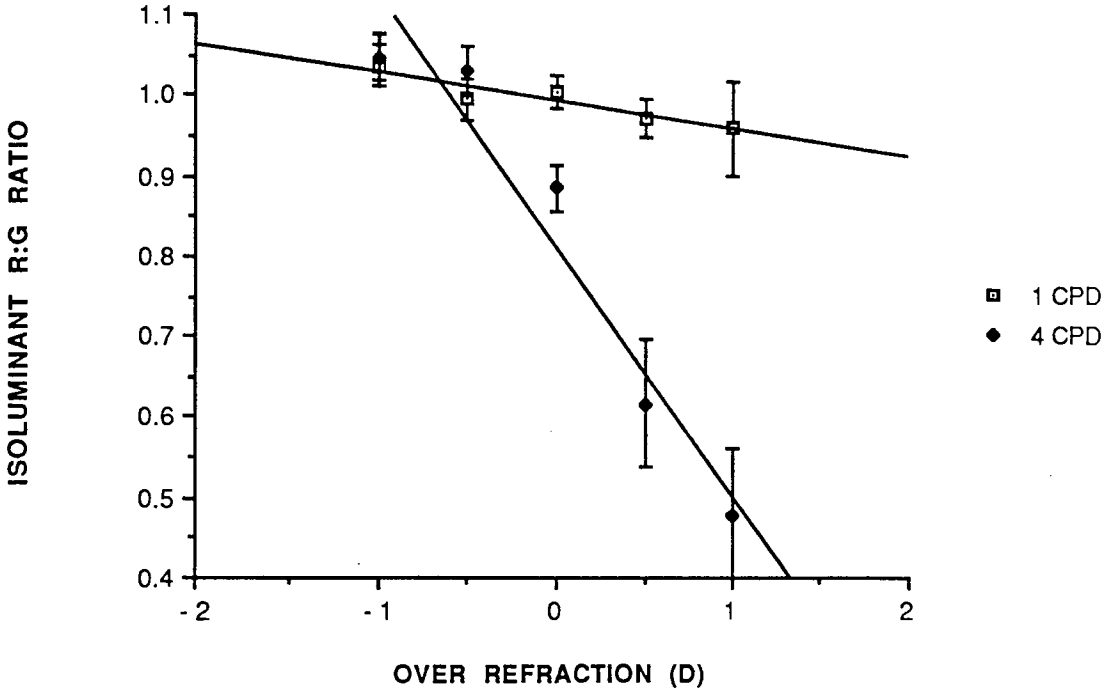


Figure 5.3 Distribution of mean change of isoluminant red/green ratio for four adult observers over a 2.00 dioptre power change in over refraction. Mean isoluminant points with a grating of spatial frequency 1cpd are shown as dotted squares while isoluminant points for a 4 cpd grating are shown as filled squares.Error bars show standard errors. The formula of the regression line for 1cpd is $y = 1.0 - 0.032x$; $r = 0.924$; $p < 0.03$; D.F. 4. The formula of the regression line for 4 cpd is $y = 0.85 - 0.311x$; $r = 0.965$; $p < 0.008$; D.F. 4.

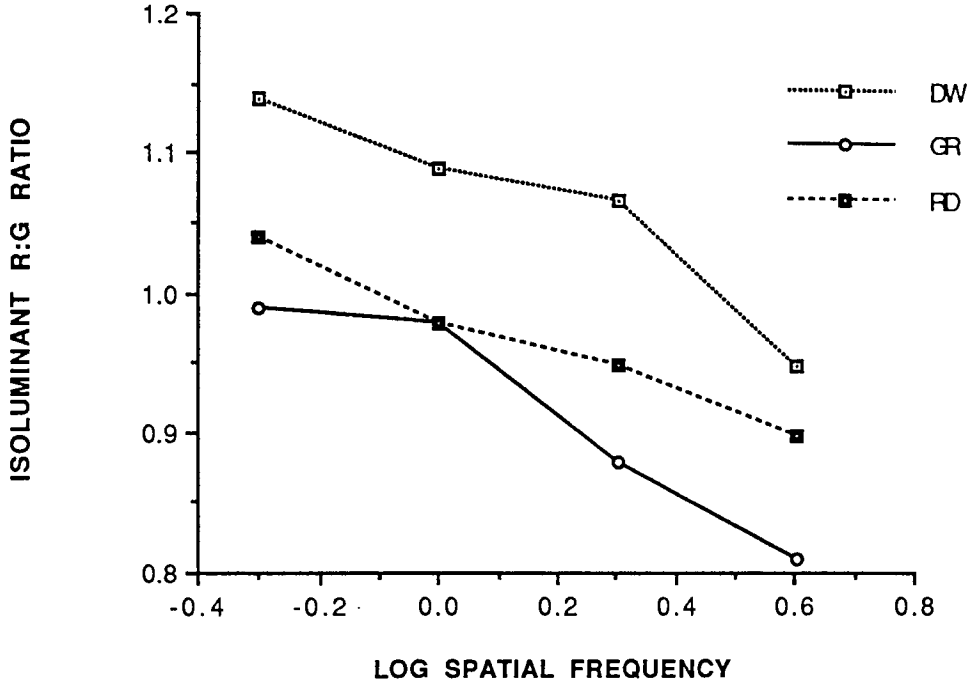


Figure 5.4 Line plot to show change of isoluminant points with respect to spatial frequency (in cpd) for 3 adult observers.

5.5.9 Discussion

Using the above technique, the isoluminant point of young, colour normal, adult observers varies little from that determined photometrically, under the spatial frequency condition of 1cpd .

The effect of blur on isoluminance was found to be greater at the higher spatial frequency of 4 cpd with less effect at a lower spatial frequency of 1cpd. However the effect over a 2 dioptre range for 1cpd was still significant. Previous authors (Maurer et al. 1989) have shown this change in power to have minimal effect at lower spatial frequency of 0.25 cpd. It would thus appear that blur within a range of 2.00 dioptre has a greater effect as spatial frequency is increased.

The efficiency of the luminance response to red increased as spatial frequency was increased, leading to a relative increase in the required luminance of the green grating, to produce a luminance match. These results are in agreement with the findings of Mullen (1985) but not with those of Kelly (1983) and Cavanagh et al. (1987) who demonstrated no effect on isoluminance with spatial frequency change. The effect demonstrated in the present study, may be the result of chromatic aberration but Mullen (1985) could still demonstrate an increase in the efficiency of the luminous response to red at high spatial frequencies in experiments where chromatic aberration was corrected. Alternatively, it has been suggested (Cavanagh et al. 1987) that this spatial frequency effect may be due to an inequality in the size of the receptive fields of the red and green Wiesel and Hubel (1966) Type I cells. This would cause a change in spectral sensitivity of the luminance channel with spatial frequency.

These effects of change in isoluminance with blur at higher spatial frequencies and with increasing spatial frequency must be taken into account in the design of any isoluminant stimuli. The relevance of these findings will be discussed below with respect to the stimuli used in the sequential studies.

5.6 Determination of isoluminance : Main study

5.6.1 Review of parameters

The above technique used in the pilot study in adults was adapted to assess the isoluminant red/green ratio for a sample group of infants. Before this was possible several factors known to affect isoluminance had to be taken into account in the stimulus design. As demonstrated above, blur and spatial frequency have an effect on the isoluminant point. The component gratings of the stimulus for the infants were selected to be of a spatial frequency that is known to be resolvable at all of the ages to be assessed

(visual acuity development is reviewed in section 3.2). Changing spatial frequency was demonstrated to change the isoluminant point of the adult observers assessed. It was thus thought necessary to determine isoluminance for subjects with the proposed spatial frequency that would be used in later studies . In studies of the chromatic visual evoked potential, Morrone and co-workers found that very low spatial frequencies (0.1 cpd) were required to elicit responses in infants below 8 weeks of age and by 9 weeks of age, responses to 0.4cpd stimuli could be obtained. In view of these findings it was proposed that isoluminance in infants should be determined with stimuli of 0.1 and 0.4 cpd.

Blur of 1.00 to 2.00 dioptres (D) has been demonstrated to have an effect on isoluminance with stimuli of spatial frequencies of 4cpd and above and blurring of 4.00 to 8.00D affects isoluminance at lower spatial frequencies (Maurer et al. 1989). It would thus be desirable to have a working distance for the infants that would produce minimum blur, to avoid the need to refractively correct every individual infant in all studies.

5.6.2 Development of refractive error

The refractive error of any individual will have a large effect on the quality of retinal image if uncorrected. A variety of techniques have been used to determine the refractive error of infants e.g.ophthalmoscopy, retinoscopy and photorefraction and a range of spherical equivalent refractions (SER) are found in neonates (See Banks 1980, Thompson 1987 for review) with Banks (1980) concluding that the average SER at birth is +2.00D (SD 2.00). The incidence of neonatal myopia, in studies that have excluded premature infants, vary from 0 to 25% with values typically around 10%. Mohindra and Held (1981) noted a higher incidence of neonatal myopia with a mean SER of -0.6D during the first month of life. This may be due to the use of 'near retinoscopy'; a technique which does not require cycloplegia (Mohindra 1975, 1977b). Myopia is the most common finding in pre term infants but the degree of ametropia varies widely between authors ranging from 17% (Fledelius 1976) to 100% (Fletcher and Brandon 1955) and the average amount of ametropia estimated spans from + 0.76D (Fledelius 1976) to between - 10 and -20D (Fletcher and Brandon 1955).

Opinion differs on the change in hypermetropia in full term infants over the first few months of life. Traditionally a decrease in hypermetropia with age was accepted but work by Brown (1936) and Slataper (1950) showed an increase. This may however have been due to the proportionally high number of subjects who later developed squints causing an artifact in results. Santonastaso (1930) noted an increase in hypermetropia immediately following birth followed by a decline over the first year while later studies have reported decreases in hypermetropia between birth and 3 months (Akiba 1969).

5.6.3 Refractive error study

As few authors have published the refractive findings of one month old infants it was decided to undertake a pilot study of refraction. This was used in conjunction with baby clinics at Newtown Health Centre, Birmingham as a refractive screening test for those infants taking part. All findings of refractions were given to the infants' General Practitioner for information.

a) Subjects

Thirty-five infants from Newtown Health Centre were refracted. All infants were full term and healthy as assessed by the health visitors or doctor. Mothers were approached by the health visitors or G.P. and informed consent was received prior to examination. Any family history of strabismus or ocular abnormality served to exclude infants from the study although refraction was still carried out as information for the G.P. Six infants in the youngest group were refracted at home following an explanation of the technique and introduction of the refractionist by the health visitor. All the other infants were refracted in a dark room at the health centre. The total number of infants finally included in the study was thirty-two.

b) Method

Retinoscopy is the standard method of objective refraction used routinely by refractionists. It is essentially a nulling method in which trial lenses are positioned before the subject's eye in order to neutralise movement of a reflex seen within the pupil. Detailed descriptions of the optical principles and clinical use of this technique are discussed in various standard texts (Borisch 1970, Bennett and Rabbetts 1984), A thorough description of this technique and possible sources of error are provided by Thompson (1987). Experienced use of the technique can provide estimates of refraction within 0.5 D of either principal meridian and within 15° on the astigmatic axis (Bennett and Rabbetts 1984)

To achieve an accurate retinoscopy result, accommodation must be controlled. This is achieved in adults by instructing them to fixate a distant object and adding plus power to the eye not under examination. In infants, however, temporary paralysis of the ciliary muscle may be achieved by instillation of cycloplegic agents. Cyclopentolate Hydrochloride is an antimuscarinic commonly employed (O'Connor-Davies 1981). An alternative to cycloplegia is Mohindra's Near Retinoscopy Technique (1977a, 1977b) but as the author has no experience of this, cycloplegic streak retinoscopy using 0.5% Cyclopentolate HCl was used. This antimuscarinic was considered to be a suitable

cycloplegic agent with the minimal risk of adverse systemic effects (O'Connor-Davies 1981).

One drop of 0.5% Cyclopentolate HCl was instilled into the conjunctival sac of each eye. Instillation was performed whilst the infant reclined on the mother's lap or on a changing mat in the testing room and the infants returned to the main baby clinic to allow the cycloplegic agent to take effect. All examinations were performed at least 30 minutes after instillation to allow adequate cycloplegia (Vale and Cox 1978) with an average delay before retinoscopy of 37.62 minutes (SD 6.12) for all infants.

Retinoscopy was conducted with the infant sitting on the mother's lap in a darkened room. A working distance of 50cm was maintained by means of a piece of string attached to the retinoscope head (Thompson 1987). Full aperture spherical trial lenses were used to neutralise the reflex and these were held in front of the infant's eyes. Pairs of lenses, one in front of each eye, were introduced where practically possible. Refractions were recorded in sphero-cylindrical form before and after correction for working distance.

Alert babies were calmer and easier to refract if sucking a dummy but problems arose if the infants were asleep. There is a tendency for the eye to roll upwards and outwards on lid closure (Bell's Phenomenon) and the examiner had to rely on occasional downward drifts to the central position when the lid where retracted against the orbital rim by an assistant. During this, care was taken not to artificially induce astigmatism by excess pressure on the globe (Graham and Gray 1963).

c) Treatment of data

Adjustment to the spherical component of the refraction was made in accordance with the working distance used (i.e. -2.00D) but no adjustment was made for tonus (O'Connor-Davies 1981). The spherical equivalent refractions (SERs) of the astigmatic infant were calculated by adding one half of the cylindrical correction to the spherical component. Any anisometropia was calculated from the difference of the SERs of the right and left eyes and each eye was analysed separately. Combining right and left eye data has previously been shown to yield spurious levels of significance (Ray and O'Day 1985).

d) Results

The infants were grouped into three age classifications (see Table 5.2). Of the thirty two infants in the study the refractive findings of one infant was not included in the data analysis due to incomplete cycloplegia at the time of refraction.

The range of spherical equivalent refractive finding encountered in the whole of the sample group (N=31) varied between+1.00 and +4.75 for the right and left eyes. The frequency distribution of these SERs are summarised in figures 5.5 and 5.6 for the three age groups. Spherical equivalent refractive errors for thirty-one individuals are shown in Figure 5.7 as a function of age (weeks) . Averaged data is presented in Table 5.3 and plotted in Figure 5.8.

Table 5.2 Details of weekly and monthly age categories

Age group (months)	Age Group (weeks)	Allowed range (days)
NEONATES	1	4 ≤ 10
	2	11 ≤ 17
1	3	18 ≤ 24
	4	25 ≤ 31
	5	32 ≤ 38
	6	39 ≤ 45
2	7	46 ≤ 52
	8	53 ≤ 59
	9	60 ≤ 66
	10	67 ≤ 73
3	11	74 ≤ 80
	12	81 ≤ 87
	13	88 ≤ 94
4	14	95 ≤ 101
	15	102 ≤ 108
	16	109 ≤ 115

Table 5.3 Averaged refractive findings (in dioptres) of sample age groups between one and three months. (Mean and standard errors are given)

Age Group	n	R SER	L SER	ANISO	R CYL	L CYL
1 month	10	3.30 (0.33)	3.27 (0.37)	0.17 (0.09)	0.66 (0.09)	0.62 (0.08)
2 months	11	2.88 (0.24)	2.86 (0.25)	0.53 (0.10)	1.33 (0.31)	0.96 (0.22)
3 months	10	3.48 (0.21)	3.52 (0.21)	0.41 (0.04)	0.8 (0.13)	1.0 (0.07)

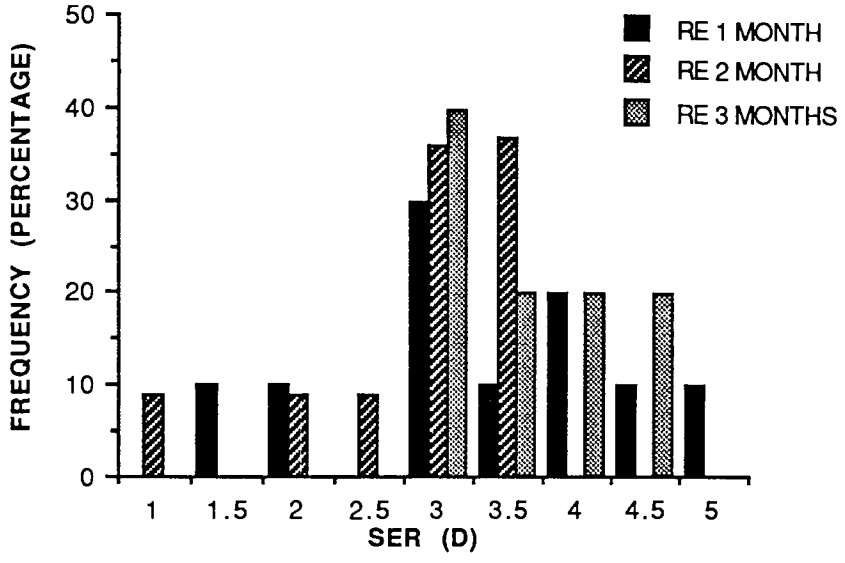


Figure 5.5 Frequency histogram illustrating the distribution of spherical equivalent error findings (SER) amongst the three sample age groups right eyes. (Three month sample n= 10, two month sample n = 11, one month sample n = 10)

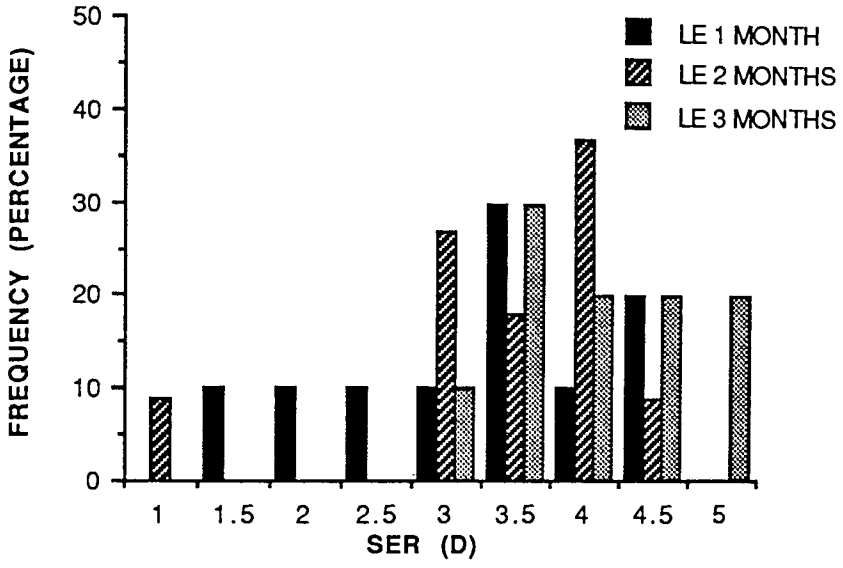


Figure 5.6 Frequency histogram illustrating the distribution of spherical equivalent error findings (SER) amongst the three sample age groups left eyes. (Three month sample n= 10, two month sample n = 11, one month sample n = 10)

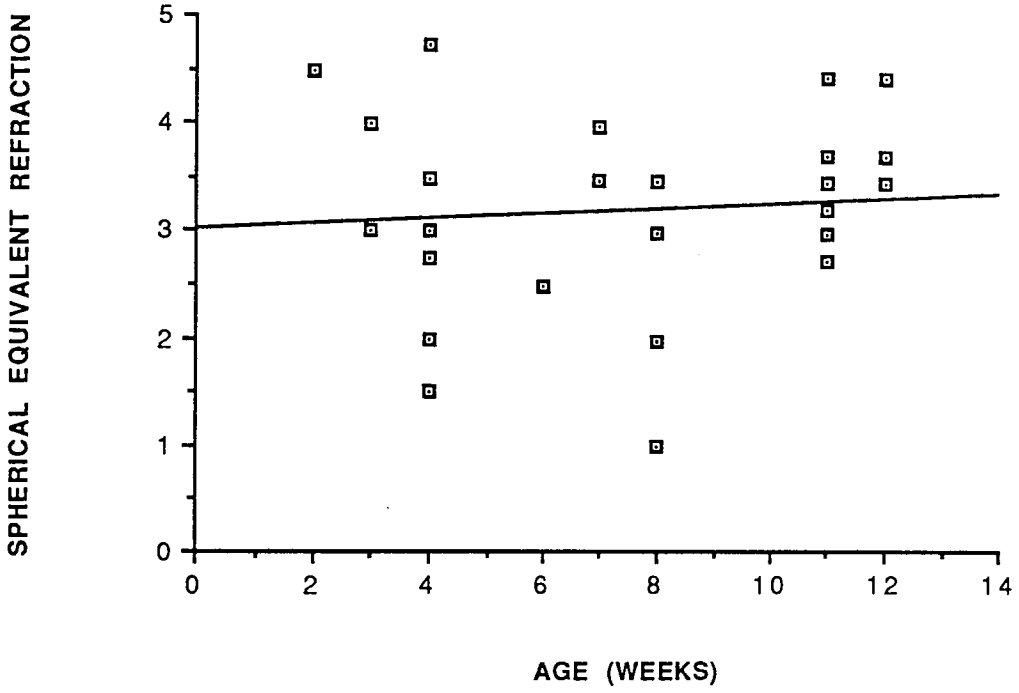


Figure 5.7 Scatterplot of infant spherical equivalent refraction data versus age (weeks). Data is from the right eyes of thirty one infants. No significant correlation was found between these two variables.

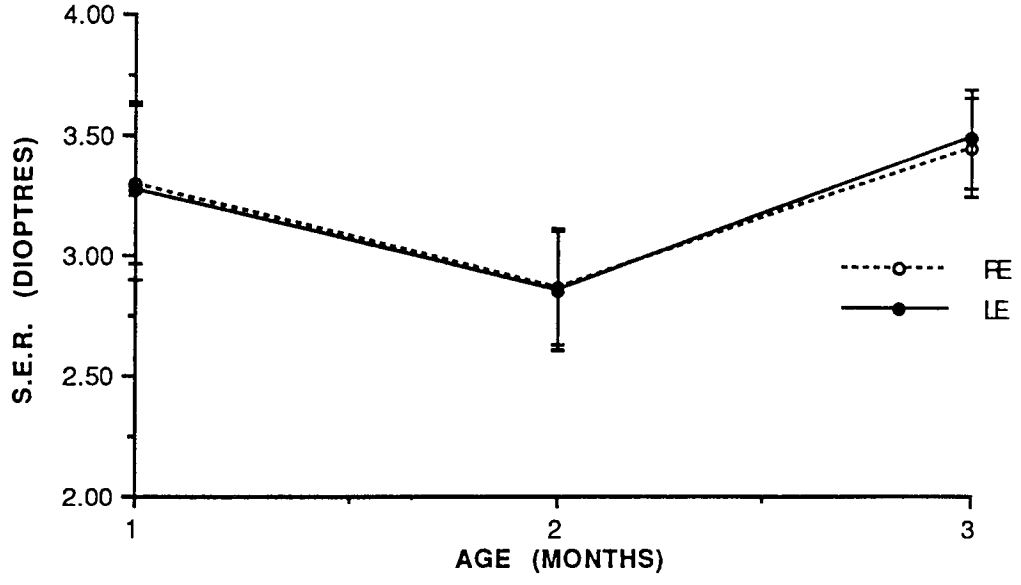


Figure 5.8 Group averaged spherical equivalent refractive findings of right (RE) and left eyes (LE) between 1 and 3 months. Vertical error bars represent standard errors. Numerical values are given in Table 5.3.

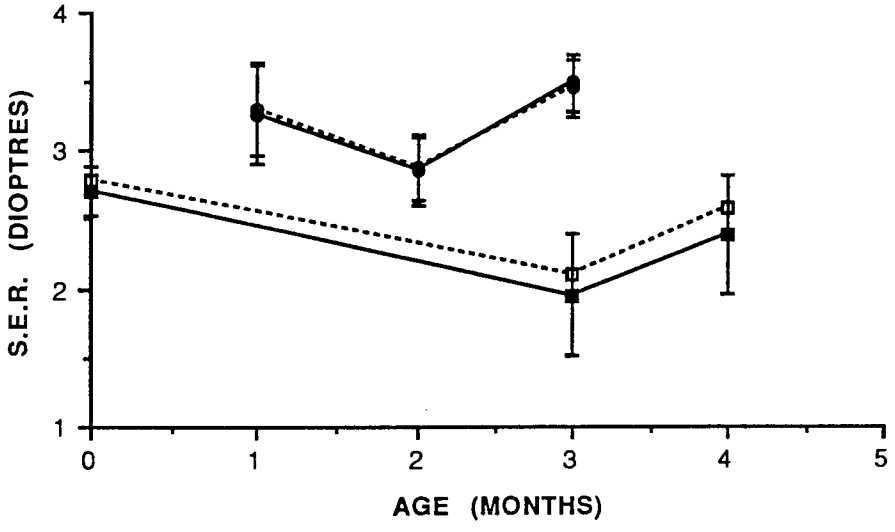


Figure 5.9 Group averaged spherical equivalent refractive findings of right and left eyes of the present study (open and closed circles respectively) compared to those SER findings of Thompson (1987) (right eye-open squares, left eye-closed squares). Vertical error bars represent standard errors.

Table 5.4 Statistical significance for age related SER power changes. Independent t - tests. Mean data for the relevant groups can be found in Table 5.3.

Age Groups compared	Comparison of mean SER power findings t-stat.	d.f.	significance
R SER			
1 v 2	1.027	19	p> 0.1
1 v 3	- 0.512	18	p> 0.1
2 v 3	- 1.944	19	p> 0.1
L SER			
1 v 2	0.968	19	p> 0.1
1 v 3	- 0.603	18	p> 0.1
2 v 3	- 1.980	19	p> 0.1

e) Discussion

Individual and group averaged refractive error (SER) showed no significant alteration between the ages of 1 and 3 months. This is in agreement with the pattern of development found by other workers. Wood and Hodi (1992) have recently reported that refractive error changes from near emetropia at one month of age to an average of +1.50 dioptres at 3 months of age in a sample of 120 infants but this view differs significantly from the work of Banks (1980) and Thompson (1987). Thompson (1987) demonstrated a monotonic decrease from around 2.75 dioptres of hypermetropia at birth to an average of 0.86 dioptres at one year, with alterations between birth and 3 months showing no statistical significance. The findings of this previous study are plotted here with those of the present study (Figure 5.9) for direct comparison. Higher levels of hypermetropia have been found in the present study than in any other study using a cycloplegic. Near retinoscopy techniques have revealed even lower levels e.g. +0.75 D at 2 months (Kohl et al. 1986). The present results may be due to the the author's inexperience with infant refraction producing variable working distances leading to erroneous results. It is possible that due to the method of recruitment, subjects with a family history of hypermetropia or amblyopia may be more likely to have been volunteered, hence inducing a bias within the group of which we were unaware at the time of refraction. The aim of the refraction study was to ascertain the level of misfocus at 1 to 3 months of age and the precautions taken with respect to this and other factors are discussed below.

5.6.4 Discussion of parameters to be used in infant studies

In any study of visual function it is desirable to have a stimulus that would produce minimum blur for the subjects. This is important in the present study, as it was felt to be

impractical to refract and correct each individual. The following summary describes the factors taken into account:-

a) As discussed previously, inaccurate refractive correction can produce a significant change in isoluminance with a high spatial frequency of 4 cpd with the effect reducing but remaining significant at 1 cpd. At very low spatial frequencies (0.25 cpd) the effect is eliminated over a 2 dioptre range but present at incorrect refraction of the order of 4 to 8 dioptres.

b) Newborns are capable of adjusting their accommodation and do so most accurately for close targets (75cm) (Braddick et al. 1979). Accommodation increases in accuracy with age and can be demonstrated over a large range of target distances by three to four months.

c) Isoluminance may change with spatial frequency thus it is important to equate the intensities of the colours under the appropriate spatial conditions to be used later (Mullen 1990).

d) In work on the development of chromatic VEPs in infants (Morrone et al. 1990) very low spatial frequencies (0.1cpd) were required to elicit responses at an early age (< 8 weeks). As this present study is aimed to assess those parameters to be used in the main study of chromatic visual function this finding should be taken into account.

In summary, taking all of the above into account, employing a short viewing distance (i.e. 50cm from the stimulus) and very low spatial frequencies (e.g.0.1 and 0.4 cpd) the effects of blur on isoluminance induced by inaccurate accommodation and refractive error should be negligible.

5.7 Study to determine of isoluminance in infants

5.7.1 Introduction

In an attempt to determine isoluminance in young infants, in order to produce chromatic stimuli for further studies of the visual system, the above procedure as described for adults, was adapted to utilise the method of forced choice preferential looking (Teller et al.1974, Teller 1979). The adult study required the determination of chromatic contrast threshold at a range of red/green luminance ratios using a two forced choice staircase design. From this, interpolation of a 4th order polynomial function revealed the red/green ratio at which chromatic contrast sensitivity was minimum (maximum contrast

threshold). This method required all staircases to be completed to produce a function from which isoluminance could be determined (see Figure 5.1).

Due to the limited time available in which young infants remain attentive and co-operative, an alternative, less time consuming method for use with infants was sought. With reference to the sensitivity function produced to determine adult isoluminance, an alternative testing protocol was devised. . In the adult study, red/green lumiance ratios were constant with amplitude of modualtion varied to determine threshold values whereas in the new method, amplitude of modulation of the stimulus (chromatic contrast) was kept constant and red/green luminance ratio was varied in a staircase design. The infant model required two staircases (indicated by the horizontal arrows on Figure 5.10) at each contrast level to describe the function and the treatment of these staircase end points is discussed later. Forced choice preferential looking has been widely used in the area of infant visual assessment (see section 4.3) and it was this method that we have utilised in a staircase manner, to determine the isoluminant point of 1 to 3 month old infants using a flickering stimulus.

5.7.2 Stimulus

Stimuli were again produced by a Venus stimulator (Neuroscientific) controlled by application software. This has a 119 Hz frame rate and independent control of the red, green and blue guns. The output of the blue gun was removed. As the Venus system is unable to drive two separate monitors in colour, it was necessary to present both of the preferential looking stimuli on one screen. The display was presented on a standard CRT colour monitor with the stimulus split in half vertically and a pattern appearing randomly in the left or right half screen.

The pattern was composed of sinusoidal red and green horizontal gratings presented 180° out of phase with each other. The individual red and green constituent gratings were made to counterphase 180° out of phase in a sinusoidal manner at a temporal frequency of 16 Hz. At high temporal frequencies the detection of the temporal modulation, i.e. flicker, is dominated by any residual luminance information in the stimulus. Flicker will thus reduce to a minimum when there is minimum luminance difference between the two gratings. The mean luminance of the pattern was maintained at 10 cdm^{-2} but the individual luminances of the gratings could be varied relative to one another to produce different ratios of red to green. At a red /green ratio of 1.0 both the gratings were of equal objective luminance, measured photometrically. The other half of the screen contained a uniform field having the same mixture of red and green and the same luminance as the gratings producing a neutral brown-yellow appearance. For the infant assessment, the observer

and the stimulus generator were hidden by a black screen with two apertures, one for the screen and one for observing the infants' reactions. The edges of the stimulus and the central division of the pattern were masked to produce two panels of visual angle 20°x 9° separated by 0.6° when viewed at 50 cm. The separation of the two half fields was small but as screen separation has been shown to have no effect on the estimation of visual acuity (Atkinson et al. 1983) it was assumed that its effect in the present study may also be negligible. The small separation used was a limitation imposed by the Venus system which will not simultaneously drive two monitors in colour.

The spatial frequency of the gratings in the stimulus were chosen to be of a size appropriate for infant visual acuity (see 5.6.4)

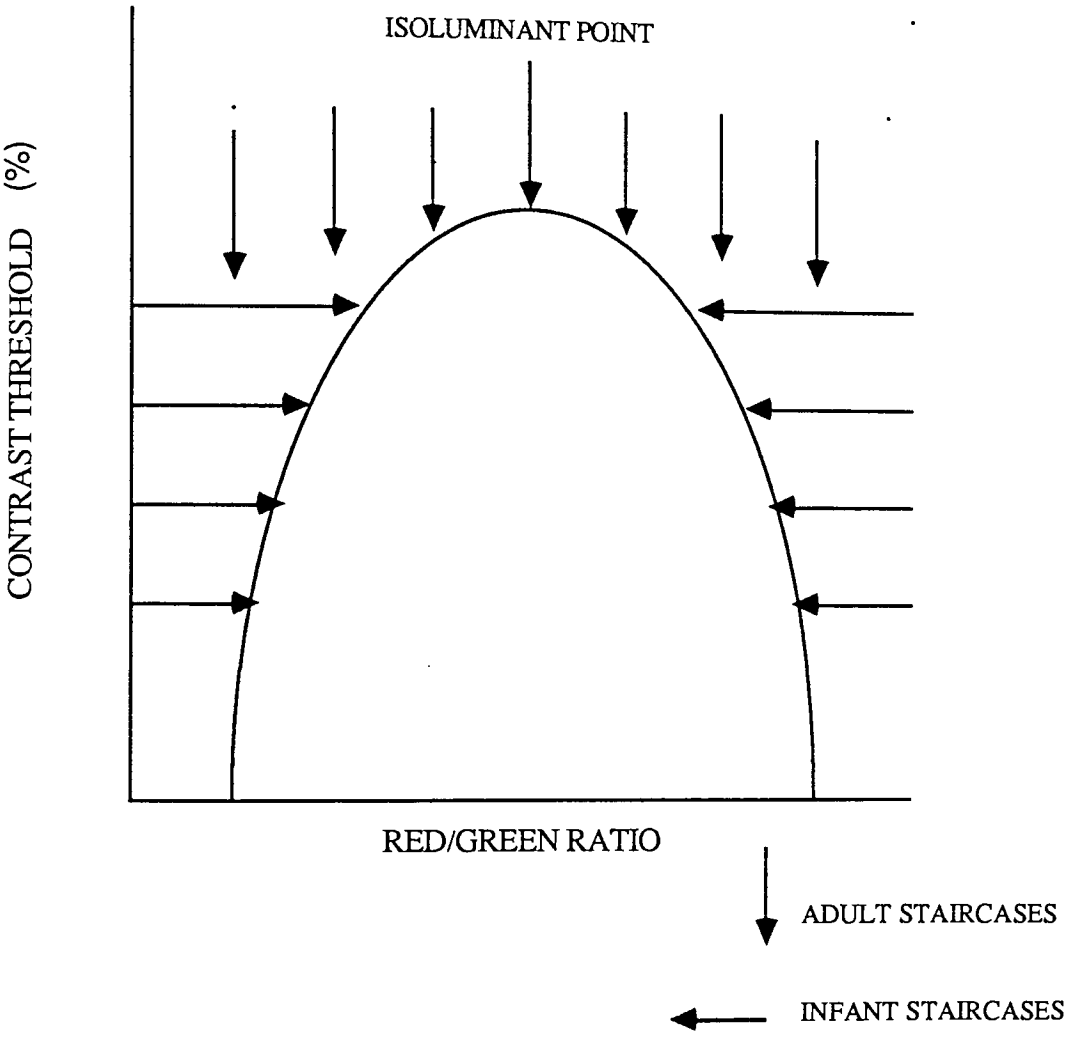


Figure 5.10 Schematic diagram to show the difference between the two procedures used to determine isoluminance in adults and infants as described in the text.

5.7.3 Subject recruitment

Subject recruitment for all parts of this study proved to be a very time consuming and sometimes very unproductive task. Infants were initially recruited for this isoluminance study through the heath visitors at Aston Health centre, Birmingham. Details were received of infants whose parents had expressed an interest in participating in the study after initial contact with the health visitor. Further information and provisional appointments were sent to those parents with maps of the departmental location and offers of transport assistance. Through this system 60 infants were sent appointments with 23 infants attending. Due to the 63% failure rate of this method, it was that attendance rate might improve if the author made personal contact with the mothers. The author therefore attended weekly baby clinics at two health centres in Birmingham. Following routine health and developmental assessment by health visitors or a doctor, the study and procedure was explained to the parent. Mutually convenient appointments were made with those parents wishing to participate in the study. A written summary of the study was given and the parents were encouraged to contact the department if they had any further queries or worries. Where necessary arrangements were made to supply a free taxi service to collect and return the family. Appointments were always reconfirmed by the author in writing and/or by phone. This change in recruitment method reduced failure to attend appointments rate to 30%.

5.7.4 Subjects

Twenty-six infants attended the Vision Sciences department, Aston University. Of these, five infants attended for two visits, separated by four weeks, one three month old attending twice within two weeks, the other 19 attending only once (N= 31). All the babies were full term by maternal report (gestation age $\geq$ 38 weeks and birth weight $\geq$ 2500g). Table 5.5 shows the distribution of infants in each sample group. It was accepted that male infants were more likely to be colour deficient than female infants and although more female than male subjects participated in this study (17 females, 8 males) it was considered impractical to exclude males considering the difficulty of recruitment (see above). However any family history of colour deficiency served as one of the exclusion criteria from this and the main study (see section 7.3 for summary).

The study was approved by both the University and Health District Ethical Committees. Informed consent was obtained from the mothers after the technique had been fully explained.

Table 5.5 Sample age groups showing mean age in weeks and days (with standard deviations)

Sample group	n	Mean age (weeks)	Mean age (days)
1 month	5	4.60 (0.89)	34.00 (6.78)
2 months	13	8.16 (0.83)	57.58 (6.47)
3 months	13	12.0 (0.95)	85.75 (6.00)

5.7.5 Procedure

The test was carried out in a windowless room with each infant sitting on the holder's (usually the mother's) lap (see Plate 5.1). Infants were allowed to bottle feed or suck a dummy during the test. The distance between the screen and the infants' eyes was checked against a tape measure attached to the screen to ensure a 50 centimetre viewing distance was maintained. This distance is within the accommodative range of young infants (Braddick et al. 1979, Banks 1980) The observer could not see the stimulus or the holder's face and the holder was instructed to keep the baby facing the centre of the screen. To attract attention the observer tapped on the back of the screen prior to grating presentation.

After these preparations, the room lights were extinguished. The observer selected a spatial frequency (initially 0.1 cpd) and a chromatic modulation contrast (amplitude of modulation) for the gratings. Each staircase commenced from any one of five red/green luminance ratios randomly selected from one of two ratio ranges (0.6 -0.72) and (1.32-1.58). Two staircases were carried out at each chromatic contrast level one starting from each ratio range, with no relationship between the two starting points which were randomly varied between chromatic contrast levels and infants.

The stimulus was presented twice at the starting red/green luminance ratio with a screen of mean luminance and chromaticity between trials. If the observer correctly identified the position of the grating on two successive trials, or presentations, by interpretation of the infant's looking behaviour, the red/green luminance ratio was changed to be nearer to 1.0 and further trials were carried out at the next ratio. This change in ratio was ±0.015 log units (1 step) for the first in any staircase and then ±0.03 (2 steps) for the subsequent changes. If the observer made an incorrect response within the first two trials, the procedure was interrupted and a new starting ratio chosen which was further away from 1.0. Whenever an incorrect response was made within a sequence the observer reversed the staircase by three steps and then continued the sequence until a further incorrect response. This three step change was required to allow re-test of the ratios previously presented. This procedure was repeated until the staircase reversed at least three times (four incorrect responses) or at least four trials were carried out at luminance ratios around

the point of reversal. A written record of the observer's score at each ratio was made and from this percentage correct scores at each ratio presented could be calculated (an example of the scoring procedure is given in Appendix I). The end point of the staircase was taken as the red/green ratio closest to 1.0 at which the observer's percentage correct score was ≥ 75%. This staircase procedure was repeated for starting points on either side of photometric isoluminance and up to six contrast levels distributed with logarithmic equality between 94 and 63% were assessed (100% was the maximum chromatic contrast available). At the highest contrast levels (94%) the observer correctly estimated the position of the grating for all red/green luminance ratios presented on repeated trials to the 2 and 3 month old infants. This was noted and hence for six contrast levels assessed only five sets of no preference points for an individual were obtained.

All infants were initially assessed at the spatial frequency of 0.1 cpd and if the infant remained alert and co-operative, the procedure was repeated at 0.4 cpd. Due to the large numbers of trials required at each contrast level to determine end points for each of the two staircases and the time required to allow the infant to settle or sleep, many sessions took up to 2 hours.

5.7.6 Treatment of results

Completed data sets consisted of two staircase end points, one on either side of isoluminance, at each contrast level. The red/green ratio, midway between these end points was calculated at each contrast level and the mean of these midpoints was accepted as the final isoluminant point for an individual.

5.7.7 Results

Of the 31 infants assessed at separate sessions, a total of 29 sets of completed data for 0.1 cpd were collected at separate visits, with only 2 infants becoming too sleepy for the recording to be continued. In addition, where infants were co-operative and attentive we repeated the procedure for 0.4 cpd. Complete sets of data were collected from all thirteen of the infants tested at 0.4 cpd. All of these infants were between two and three months of age. No assessment at 0.4 cpd was possible with the youngest infants due to uncooperation following the initial trials. Table 5.6 shows the estimated isoluminant points of the 29 infants successfully assessed using this technique and Table 5.7 shows the mean isoluminant point of each sample group.

Isoluminant points were not significantly different between the three sample groups (see Table 5.8 for results of independent t-tests).The distribution of isoluminant points with age for a spatial frequency of 0.1 cpd can be seen in Figures 5.11 and 5.12. Isoluminant

points for thirteen infants assessed with both spatial frequency conditions (0.1 and 0.4 cpd) were not significantly different.

Table 5.6. Estimated isoluminant points of the sample group of 29 infants assessed using the preferential looking technique.

Infant	Age (Weeks)	Age (Days)	Isoluminant R:G ratio 0.1 cpd	0.4 cpd
LP	13	94	0.99	0.98
NC	13	93	1.04	1.03
NH	13	92	0.98	
RE	13	92	1.03	1.03
PP	13	90	0.97	1.04
RC	12	85	0.99	
CR	12	83	1.04	1.03
YH	11	81	1.00	
GM	11	81	1.06	
NJ	11	80	0.98	1.06
AR	11	80	0.97	0.99
LP	11	78	1.0	1.04
JS	9	66	1.07	1.02
MUA	9	66	1.01	1.06
NC	9	65	1.04	0.99
SMc	9	63	1.02	
LH	9	62	1.06	
MA	8	58	1.03	
SA	8	54	1.02	
MI	8	53	0.98	
RK	8	53	1.06	1.0
AR	7	51	1.00	1.04
SB	7	51	1.00	
CR	7	49	1.02	
SF	5	38	0.99	
LH	5	38	1.02	
MD	5	36	1.00	
MUA	5	36	1.01	
TE	3	22	1.03	

Plate 5.1 Infant participating in preferential looking test to determine isoluminance.

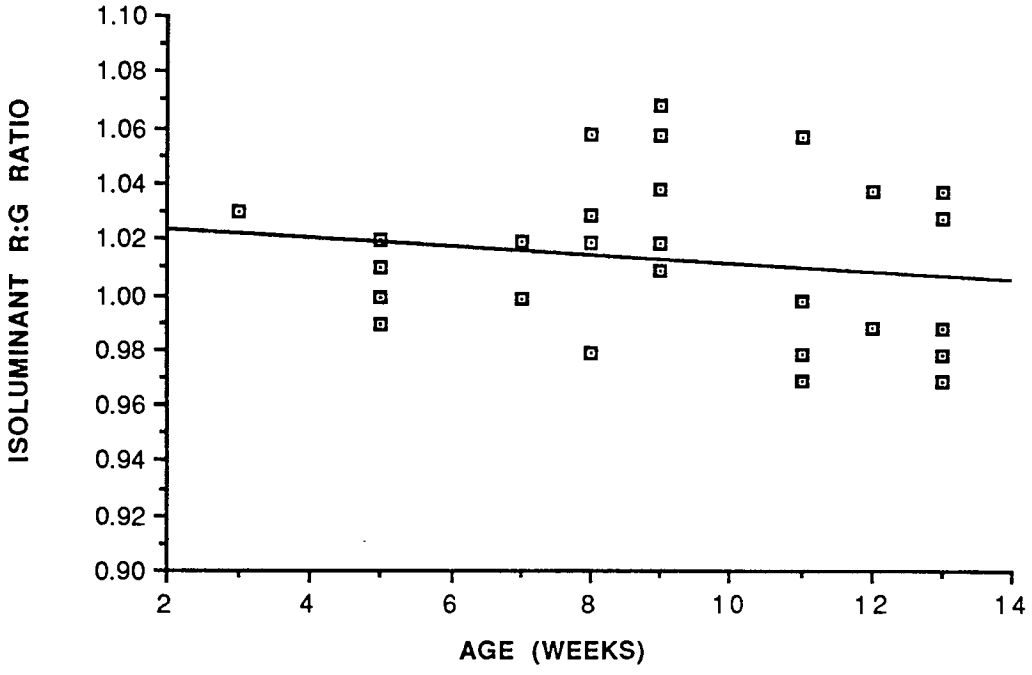


Figure 5.11 Scatterplot of isoluminant points versus post natal age (weeks).Data is from all infants (N=29) for a spatial frequency of 0.1 cpd. The equation of the regression line is y= -0.0012x + 1.026 (r = 0.129; d.f. 28; p > 0.1)

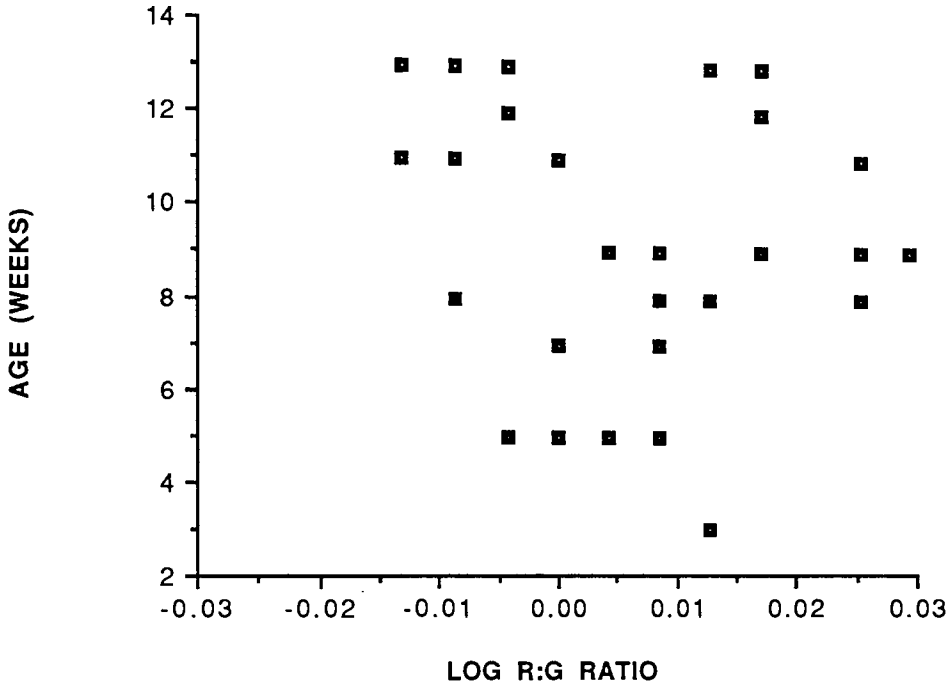


Figure 5.12 Scatterplot of log red to green luminance ratios estimated to be isoluminant at 0.1 cpd for a sample of 29 infants at age of assessment (in weeks).

Table 5.7 The mean isoluminant red/ green ratio (and standard deviation) of sample groups for spatial frequencies of 0.1 cpd and 0.4 cpd.

Sample group	Isoluminant R:G Ratio			
	n	0.1 cpd	n	0.4 cpd
1 month	5	1.01 (0.02)	0	No result
2 months	12	1.03 (0.03)	5	1.03 (0.03)
3 months	12	1.00 (0.03)	8	1.03 (0.03)

Table 5.8 Statistical significance for age related isoluminant point changes. Independent t-test. Mean data for these groups is shown in Table 5.7.

Age Groups compared	Comparison of isoluminant points		
	t-stat.	d.f.	significance
1 v 2	1.195	15	p>0.1
1 v 3	- 0.399	15	p>0.1
2 v 3	- 1.826	22	p>0.1

5.7.8 Discussion of infant preferential looking isoluminant results

The method presented here has been used to estimate the isoluminant point of human infants between 1 and 3 months of age using forced choice preferential looking . With a spatial frequency of 0.1 cpd, it was possible to determine a distinct isoluminant point for 29 of the 31 infants investigated. The other two infants became too unco-operative to allow complete data collection. The infant (LP) who attended twice within two weeks allowed us to assess the repeatability of the technique. All end point estimations varied by two steps, or less, between visits and final isoluminant points for this infant were 1.00 and 0.99.

The distribution of log isoluminant points with age for 0.1 cpd (Figure 5.12), reveals that the red to green luminance ratio that is isoluminant for a human infant, does not vary significantly between the ages of one to three months and isoluminant points determined for the infants using this technique are highly comparable to those findings for adults using the original method (see section 5.5.6). This finding is in agreement with other studies, which have used large fields to determine the isoluminant ratio by the minimum

motion technique, in infants and adults (Maurer et al. 1989), however, this similarity has been attributed to the contribution of the peripheral retina and hence does not reflect the difference found between adult and infant spectral sensitivity curves (Teller and Lindsey 1989). In order to achieve the appropriate spatial frequency at a distance at which the procedure could be reliably undertaken, the stimulus in the present study subtended a visual angle of 20°. Due to the large size of this stimulus, it was accepted that the similarity between our findings for both adults and infants may also be due to large peripheral retinal contribution. The isoluminant point of all subjects varied by less than 0.1 log unit from the objective measurement of isoluminance and due this small variation, it was presumed that all infants examined had no colour deficiency, since this has been shown to shift the isoluminant point in adults (Maurer et al. 1989).

All of the infants, who remained alert enough to be assessed at a spatial frequency of 0.4 cpd (N=13), fell into the age range of 2 to 3 months. No isoluminant point could be determined for the remaining infants, as they had become unco-operative or sleepy due to the time taken to assess the initial spatial frequency. The isoluminant point determined from these infants at 0.4 cpd is very similar to that at 0.1 cpd and would suggest that isoluminance is not affected by change of low spatial frequency in agreement with Mullen (1985).

Luminance contrast sensitivity is more robust than chromatic sensitivity at high temporal frequencies in adults (Wis ›waty 1981), thus any residual flicker within a stimulus alternating between two chromaticities at a rate of 16 Hz must be due to the luminance difference between the chromatic components. Flicker will reduce to a minimum when this luminance difference is minimal i.e. at isoluminance and this is the basis of flicker photometry (Ives 1912). For this reason, a temporal frequency of 16 Hz was used for the determination of isoluminance in the adult study and this was then arbitrarily selected for use in the infant study. Recent work, however, suggests that although this flicker rate is below the critical flicker frequency of a 1 to 3 month old human infants (41-52 Hz, Regal 1981) contrast thresholds at 1 to 3 months of age are near 100% at 8 to 17 Hz (Swanson and Birch 1990) with a maximum contrast sensitivity of 20-30% at a temporal frequency of 5 Hz for a 6 week old (Hartmann and Banks 1992). If the contrast sensitivity of 1 to 3 month old infants is as poor as described at the temporal frequency used, one may expect all the staircase end points to merely be a function of the starting points due to the sub-threshold testing conditions (Nachimas 1982). However, correlation co-efficients of the regression plotted between start and end points for all staircases completed are extremely poor (see Figures 5.13 and 5.14) suggesting little bias of resulting end points due to chosen start points in this present study. This would thus suggest that the end points were

not determined simply by chance and one may presume that they are true representations of the infants' performance. This would, of course be in contrast to the findings of Hartmann and Banks (1992).

Although the above technique produces comparable results to previous workers (Maurer et al. 1989, Teller and Lindsey 1989), it is extremely time consuming and fatiguing for any infant and hence, an alternative method of isoluminance determination was sought.

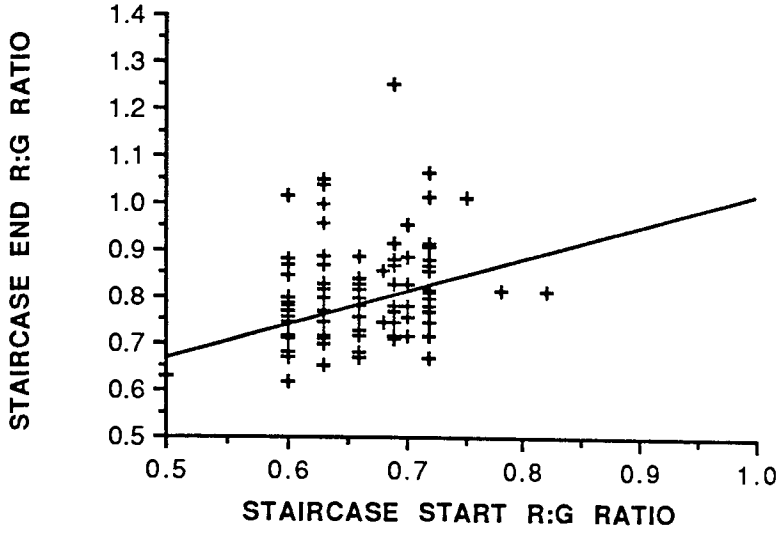


Figure 5.13. Scatterplot of preferential looking staircase end points with respect to starting points for all staircases completed by a group of 29 infants. Data shown is for those starting points falling within the red/green luminance ratio range of 0.5 to 1.0. The equation of the regression line is $y = 0.723x + 0.305$ ($r = 0.332$; d.f 141 ; $p < 0.05$)

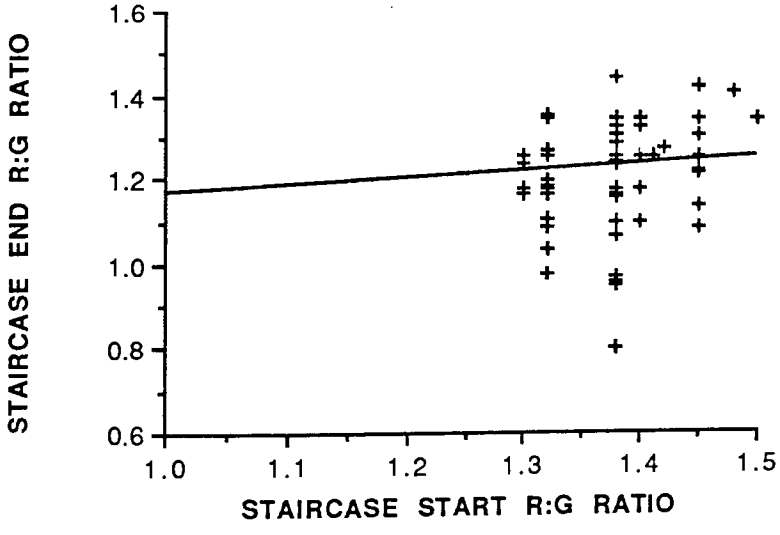


Figure 5.14. Scatterplot of preferential looking staircase end points with respect to starting points for all staircases completed by a group of 29 infants. Data shown is for those starting points falling within the red/green luminance ratio range of 1.0 to 1.5. The equation of the regression line is $y = 0.172x + 0.996$ ($r = 0.123$; d.f 141 ; $p < 0.05$)

5.8 Electrophysiological determination of isoluminance

Due to the time consuming nature of the above preferential looking technique, an alternative procedure was sought. As previously discussed (see section 5.4) some workers have demonstrated a minimum amplitude steady state VEP to a stimulus of one particular red/green luminance ratio, in a range of luminance ratios, and this was taken to be isoluminance (Morrone et al 1990, Fiorentini et al. 1991, Bach and Gerling 1992). As the main aim of this present project was to examine the chromatic response using electrophysiology, it was felt that isoluminance determination using a similar experimental set-up immediately prior to this would be highly beneficial in reducing testing time and increasing patient co-operation for the main study. Due to the author's inexperience with recording steady-state VEPs, a pilot study was undertaken to determine optimum recording parameters.

5.8.1 Subjects

Seven infants (five male, two female) were recruited from the sources previously described (see section 5.7.3). Table 5.9 gives details of post term (PTA) and chronological age (CA) (post natal) age at time of assessment. Two infants, RE and TN, returned for a second, follow-up visit 1 to 2 weeks after the first.

Table 5.9 Subjects taking part in pilot study

Infant	Sex	CA (weeks)	PTA (weeks)
VE	M	8	7
RE	M	7,9	7,9
TN	M	7,8	7,8
CH	F	8	8
PA	F	8	7
TI	M	6	6
ES	M	7	7

5.8.2 Stimulus

The stimulus used was the Neuroscientific Venus system and this was maintained throughout the project (refer to sections 6.3 and 7.5 for full descriptions of this equipment). Previous investigations have shown low chromatic acuity in infants (Morrone et al. 1990) and the effect of chromatic aberration is negligible at low spatial frequencies (Flitcroft 1989). For these reasons, the stimuli used were composed of sinusoidal horizontal red and green gratings of a spatial frequency of 0.5cpd presented

180° out of phase and temporally modulated at 2 to 4 Hz. Five red/green luminance ratios, symmetrically distributed around and including the first approximation to an infant's brightness match (R:G =1.0) were chosen i.e. 0.8, 0.9, 1.0, 1.1, 1.2. Mean luminance was maintained at the maximum available of $10cdm^{-2}$ and amplitude of modulation of the gratings was 100%. A black/white sinusoidal grating (mean luminance:$10cdm^{-2}$), of 90% contrast, was used initially for all subjects to assess presence and quality of the achromatic steady-state visual evoked potentials.

5.8.3 Averaging

Thirty responses were averaged by the Biologic Traveller, as this number was found to be adequate to record the response and there was no significant improvement if more than 30 responses were averaged. Three runs were recorded for each stimulus in order to estimate the reliability of the response and where possible, stimulus runs were compared to non-stimulus runs. Each response was amplified 24,000 times with band pass filters of 0.3 to 30 Hz.

5.8.4 Electrode Montage

Pattern reversal VEPs were recorded using silver-silver chloride electrodes, filled with electrode gel, which were positioned in accordance with the international 10-20 system. Two channel recordings were made from *O2 (active) referenced to C4 and O1 (active)* referenced to C3. Cz was used as the earth. (See Figure 6.1).

5.8.5 Reversal Rate

Porciatti (1984) demonstrated a peak in the neonates achromatic temporal tuning curve at 4 reversals per second (rps) for large checks. In order to assess the temporal characteristics of the chromatic system, to determine the optimum reversal rate for use in this study, tuning curves were determined for four of the infants at temporal frequencies of 2, 3 and 4 Hz with a photometric isoluminant stimulus (i.e. R:G = 1.0).

5.8.6 Procedure

The infant sat at 37 cm from the screen on a holder's lap and at this distance the stimulus subtended 32° x 32°. Stimulus runs were recorded in a random order with repeat runs also randomly distributed. Non-stimulus runs were distributed throughout each session and data was stored on disk to allow analysis at a later occasion. Averaging could be interrupted at any time if the infant failed to fixate the screen.

5.8.7 Treatment of data

The amplitude of each response was measured using the Biologic Atlas system and from this the mean and standard deviation of three runs was calculated to allow assessment of variability. The quality of the response between runs and stimulus conditions i.e. temporal frequency or luminance ratios, was subjectively compared.

5.8.8 Results-Temporal Tuning

Peak amplitudes of the steady state response at the red/green ratio of 1.0 decreased by an average of 6μV if the temporal frequency of the sinusoidal gratings was increased from 2 to 3 Hz (i.e. from 4 to 6 rps) and decreased a further 3μV with an increase to 4 Hz. However, one of the sample showed an increase of 2 μV with a temporal frequency change from 3 to 4 Hz (Figure 5.15). It can be seen that, for this sample of 7 to 8 week old infants,the response amplitude is maximal at a temporal frequency of 2 Hz (4 rps) for the chromatic stimulus used. Figure 5.16 shows a comparison of achromatic and chromatic tuning curves for an week old infant RE2. The chromatic steady state VEP appears to show a peak at a lower temporal frequency than the achromatic, i.e. at 4 rps (2 Hz) and 6 rps (3 Hz) respectively.

The maximum amplitude response for this sample of four infants to a chromatic stimulus appears to occur at a temporal frequency of 2 Hz. This is comparable to the achromatic findings of Porciatti (1984) and would indicate the use of a stimulus of 2 Hz temporal frequency in infant chromatic steady-state VEP studies. However, in a comparison of quality, repeatability and ease of amplitude measurement of the response, stimulus reversal rate of 3 Hz demonstrated a consistently clearer result in all cases. Figure 5.17 shows examples of stimulus runs at each temporal frequency. In view of this, a 3 Hz stimulus reversal rate was adopted for the remainder of this pilot study.

5.8.9 Results - Isoluminance determination

Full data sets (i.e at least three stimulus runs with one black/white and five red/green stimuli) were acquired for six of the sample at one visit and again, from two of these, at a further follow-up visit. Recording for the other infant, TI, had to be terminated prematurely due to lack of infant co-operation. Mean amplitude and standard deviations of response for each stimulus were calculated for each infant and these are plotted as a function of luminance ratio in figures 5.18 and 5.19. In only one case did the amplitude of the response fall to noise at one or more luminance ratios and this was for a 6 week old infant ES at a luminance ratio of 0.9 . For each of the other infants, there is no one luminance ratio at which a clear minimum amplitude is demonstrated. Standard deviations

from the mean show a wide variability of amplitude between runs, making the determination of a minimum even harder.

5.8.10 Discussion

In previous studies, that have used this steady-state technique to isolate the isoluminant point, an amplitude difference between maximum and minimum values in the order of 2μV (Fiorentini et al 1991) or even 1μV (Bach and Gerling 1992) has been considered significant in adults and 3μV is considered significant in infants (Morrone et al. 1990) over a comparable range of luminance ratios to those used here. In the present study, maximum to minimum amplitude differences are much higher (10μV) however it can be seen from Figures 5.18 and 5.19 that variation of the amplitudes between runs is wide with no distinct minimum amplitude response to any particular stimulus, in contrast to other workers. The studies of these previous workers examined amplitudes to red/green luminance ratios over a much wider range than the one used in this pilot study and it is possible that by increasing the number and range of red/green stimuli assessed a more clearly defined minimum amplitude response would become apparent. However, as the aim of this pilot study was to determine the accuracy and efficiency of this technique, the variability of response amplitude and the need to extend the stimuli to make it a viable assessment prior to the recordings required from the main study, suggest it to be unsuitable for use in this project.

It is interesting however, that the response amplitude of a six week old infant ES consistently fell to zero for a luminance ratio close to photometric isoluminance, whereas all other infants assessed with chromatic stimuli produced clear responses at all luminance ratios. This would appear to be in agreement with Morrone and co-workers and will be discussed later (see section 7.14).

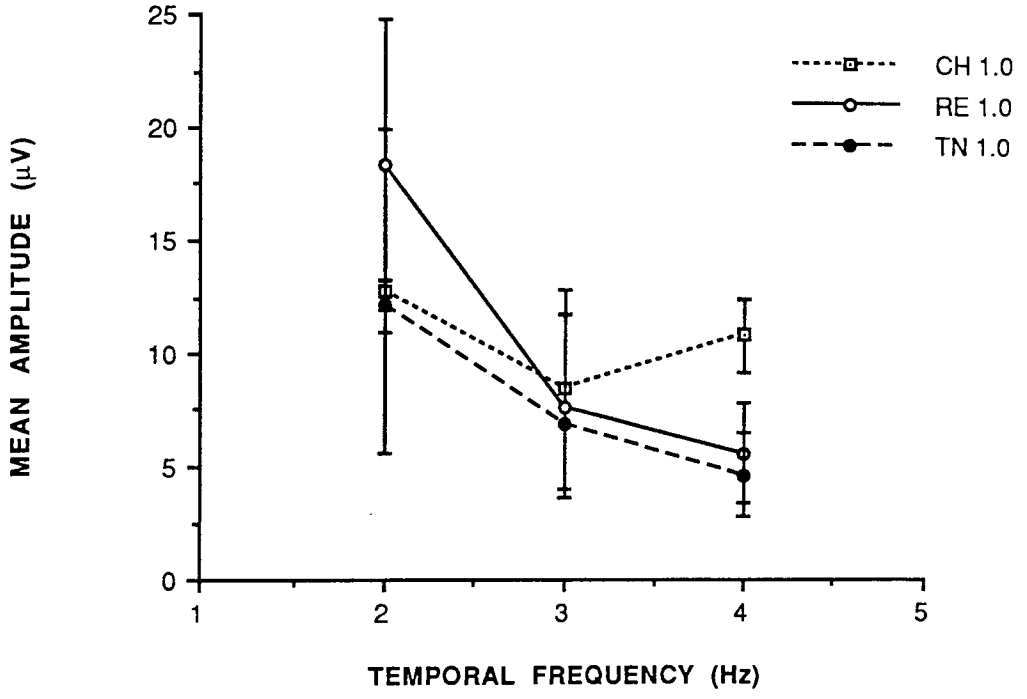


Figure 5.15 Line plot to show change of mean amplitude of steady-state VEP response with change of stimulus temporal frequency for three 7 to 8 week old infants CH, RE and TN for a red/green stimulus of luminance ratio 1.0. Error bars show standard deviation.

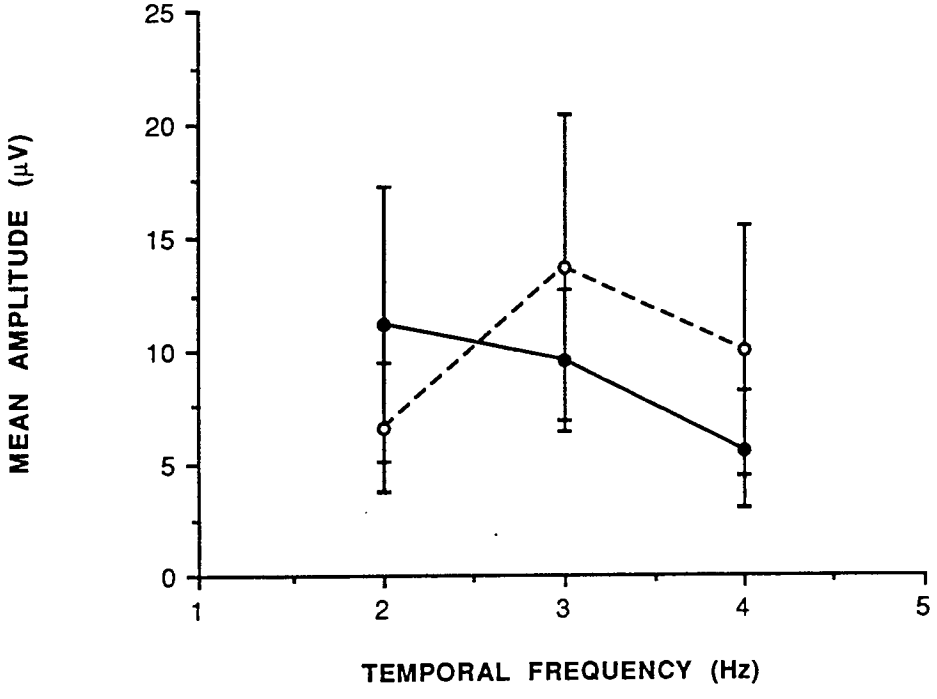


Figure 5.16 Line plot to show change of mean amplitude of steady-state VEP response with change of stimulus temporal frequency for a 9 week old infant RE2 for a red/green stimulus of luminance ratio 1.0 (filled circles) and a black/white stimulus (open circles). Error bars show standard deviation.

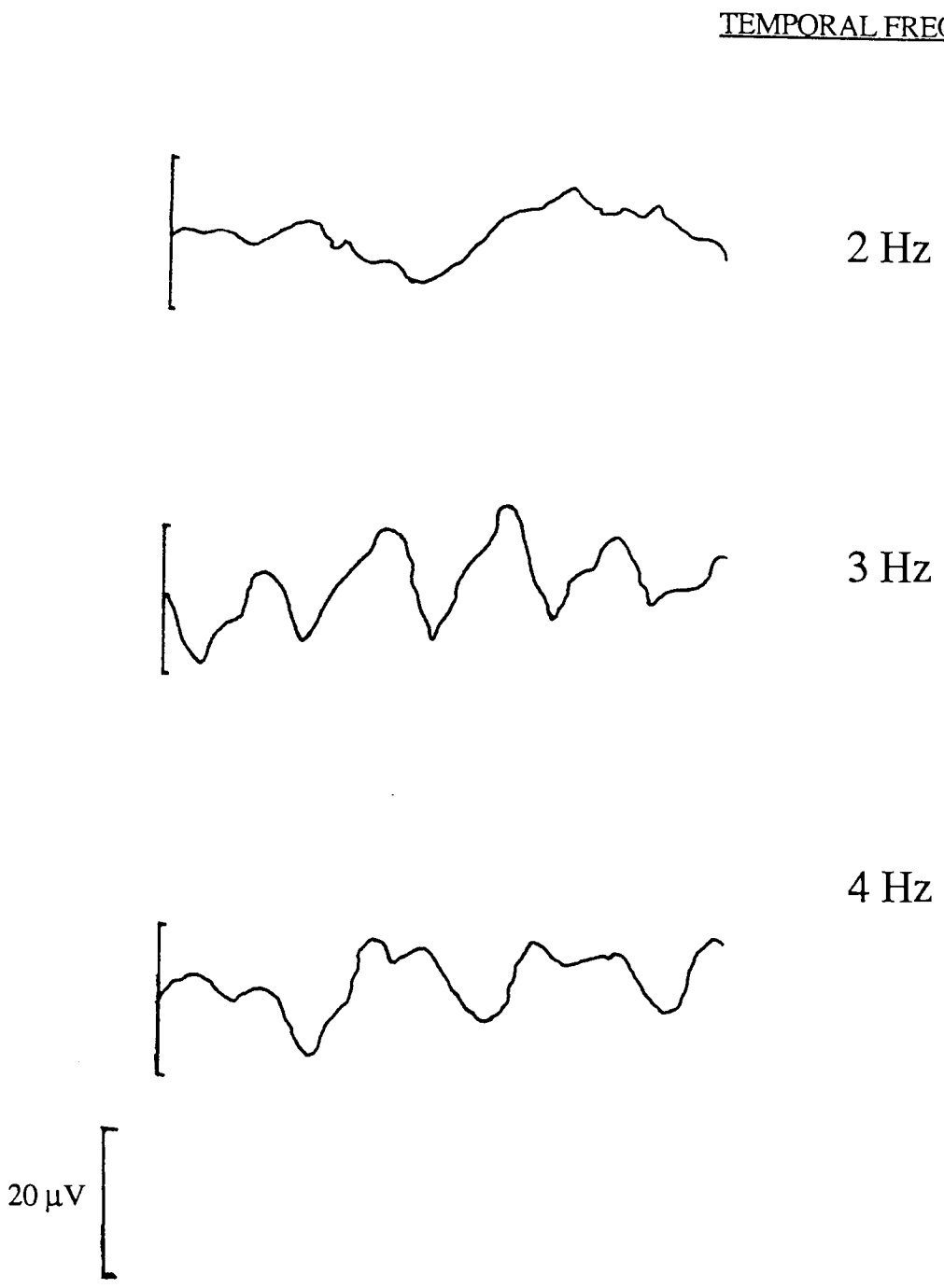
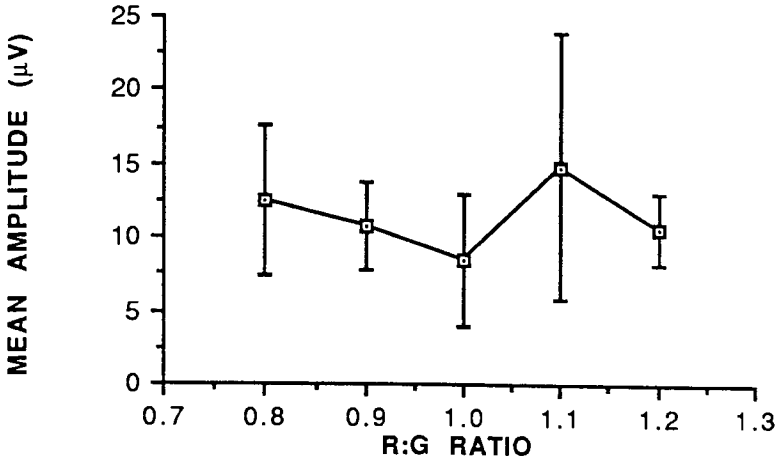
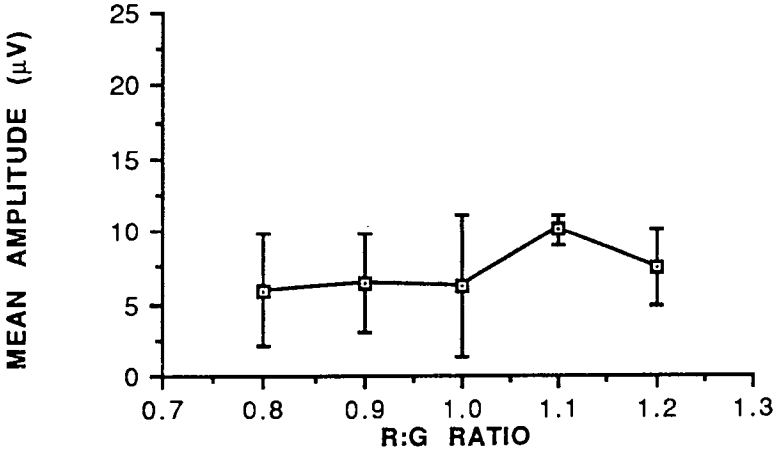


Figure 5.17 Steady-state visual evoked potentials to a red/green 0.5 cpd grating of luminance ratio, 1.0 reversing at 2, 3 and 4 Hz recorded from an 8 week old infant CH, demonstrating quality of response at each temporal frequency.

Infant CH



Infant PA



Infant VE

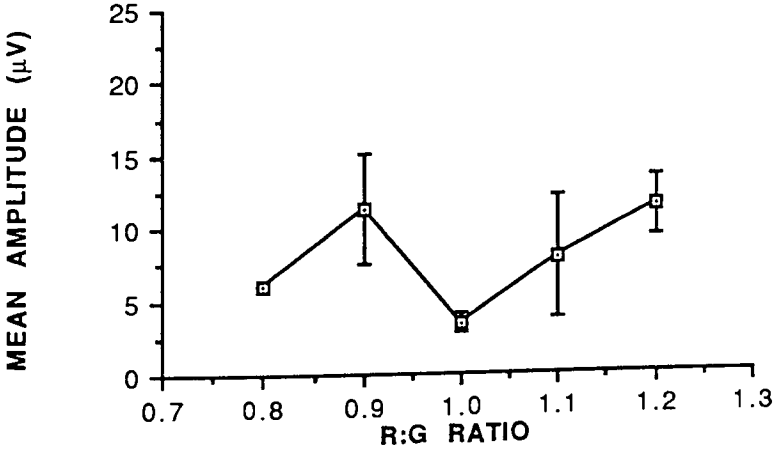
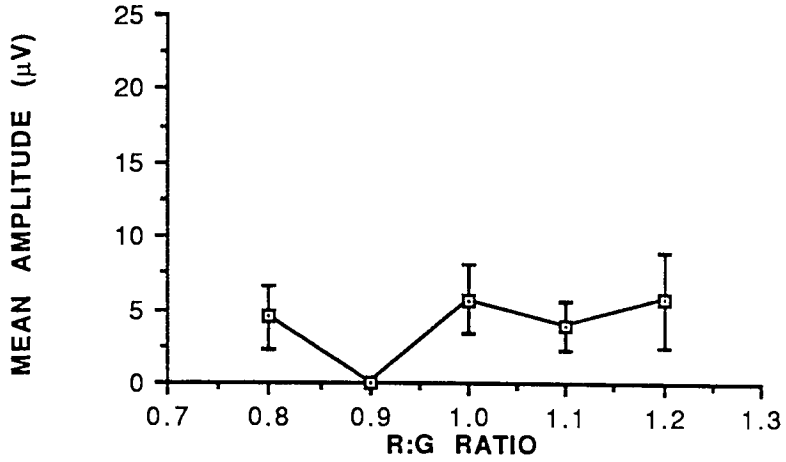
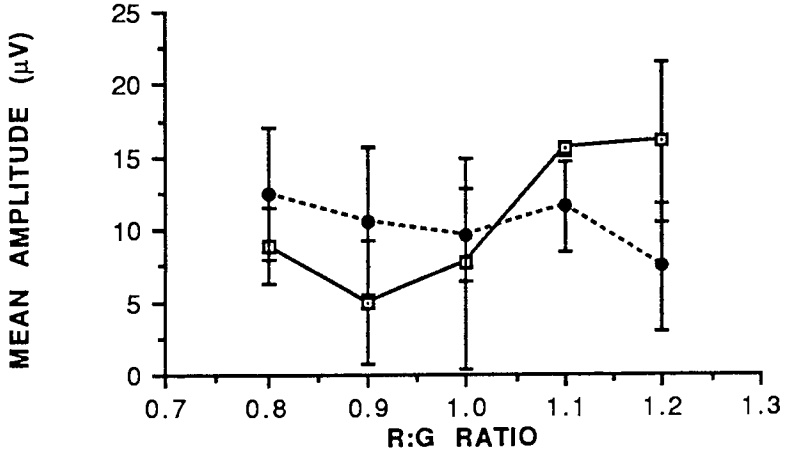


Figure 5.18 Line plots showing change of mean amplitude steady-state VEPs with red to green luminance ratio of stimulus components for three infants. Error bars show standard deviations.

Infant ES



Infant RE



Infant TN

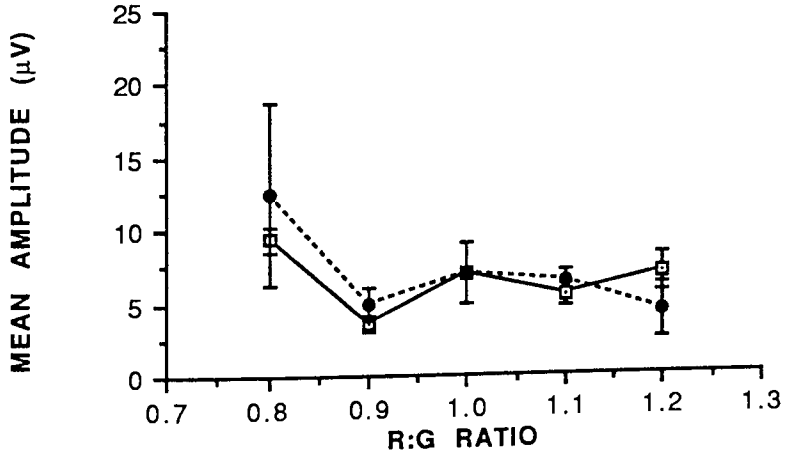


Figure 5.19 Line plots showing change of mean amplitude steady-state VEPs with red to green luminance ratio of stimulus components for three infants. Infant ES,demonstrates a minimum amplitude of zero at a luminance ratio of 0.9. Plots for infants RE and TN show results for two visits (visit one - squares, visit two - filled circles). Error bars show standard deviations.

5.9 Discussion of isoluminance determination methods

Using forced choice preferential looking as a behavioural assessment of isoluminance, yielded results which showed infant isoluminance between one and three months of age to be highly similar to adult isoluminance determined under comparable conditions. This calculated luminance ratio was close to photometric isoluminance and did not vary significantly over the age range tested or between individuals. Infant isoluminance was comparable for stimuli of both 0.1cpd and 0.4 cpd. Although the results reported here are in agreement with those of Maurer and co-workers (1989), who used the minimum motion technique and showed similar isoluminant points for infants and their mothers, the procedure used in the present project to determine a behavioural estimate of infant isoluminance was extremely time consuming and, for this reason, considered unsuitable for use as a clinical estimation of isoluminance in individuals.

In the study of an alternative method of isoluminance determination, an electrophysiological technique, as used by Morrone and colleagues (Burr et al. 1990, Morrone et al. 1990, Fiorentini et al. 1991),was assessed. Although previously reported to demonstrate clear amplitude minima at isoluminance in infants (Morrone et al. 1990), the results from the present study showed wide variability in amplitude and over the range of stimulus luminance ratios used, no minimum amplitude response was apparent. From the results of this pilot study, the clinical use of this method of isoluminance determination did not appear to be viable.

In addition, isoluminance has been demonstrated to change with temporal frequency (Cavanagh et al. 1987) as well as spatial frequency and it has thus been recommended that any brightness match must be made and utilised under the same temporal and spatial frequency conditions (Mullen 1990). The initial aim of determining isoluminance for any subject was to produce stimuli that would then be used to elicit chromatic transient visual evoked potentials. As transient VEPs require temporal frequencies of about 1 Hz, an isoluminant match determined at 16Hz (in the behavioural study) or even 3 Hz (in the steady state study) may not suffice. In view of the shortcomings of the two techniques assessed, an alternative method to overcome the presence of luminance information within a chromatic stimulus was sought. A protocol was designed that dispensed with the need to determine isoluminance for every subject and thus also cut down testing time.

Peeples and Teller (1975) discovered that infants can distinguish less than a 0.1 log unit brightness difference between two components of a stimulus. Although the variation of isoluminant ratios across the whole sample of 29 infants tested in the preferential looking study, is less than 0.1 log units it was felt to be unsound to assume that the brightness

match for one individual infant will be sufficient for another, thus isoluminance must be determined for each individual infant. Alternatively, the photometric or adult value of isoluminance might be used with the provision of a range of brightness matches < 0.1 log units on either side of the initial approximation. as already utilised by Teller and colleagues (e.g. Peeples and Teller 1975, Hamer et al. 1982, Clavadetscher et al. 1988). This makes the assumption, that any individual's brightness match must fall less than 0.1 log units away from one of these approximations. It is this protocol that has been utilised in the subsequent electrophysiological studies presented here and Chapters 6 to 8 provide further details of the protocol and experimental design employed.

CHAPTER SIX
DEVELOPMENT OF THE CHROMATIC VISUAL EVOKED POTENTIAL: PILOT STUDY

6.1 Introduction

The development of the transient chromatic pattern reversal VEP has not previously been reported, however, as previously discussed (see section 3.14) the development of the steady-state chromatic VEP is controversial with disagreement on the age of onset. The aim of the present study is to investigate of the age of onset and morphology of the transient chromatic pattern reversal VEP and provide normative data.

6.2 Protocol

Due to the problems that present with isoluminance determination (see chapter 5) the paradigm of the brightness control developed by Peeples and Teller (1975) was adopted for use in the study of the transient VEP. This previous study used FPL to demonstrate red-white discrimination in 2 month old infants and found that a white bar presented on a white screen was indistinguishable over a brightness difference range of 0.1 log units for the infant. From this, they concluded that infants are insensitive to brightness differences of less than 0.1 log units. They then tested at 0.08 log units brightness difference intervals, centred around an adult brightness match, for red-white discrimination and as the infants discriminated the red bar from the white background at every luminance step, this demonstrated colour perception.

Systematic variation of luminance around an approximation to an infant brightness match should present the infant, at some point, with luminances of red and green that differ indiscriminately (Teller and Bornstein 1987) therefore, if a visual evoked potential can be elicited for all the relative luminances of red to green one may assume that the visual system of the infant is capable of processing chromatic information.

In this present study, the first order approximation to infant brightness match was taken as objective photometric isoluminance (i.e. 1.0). The preceding study had demonstrated behaviourally that all the sample of 29 infants all had isoluminant points that fell less than 0.1 log units away from this point. Stimuli of seven red/green luminance ratios, symmetrically distributed around and including this first match approximation of 1.0 were chosen. Five of these points were separated by less than 0.1 log units with the overall brightness difference range covering 0.5 log units. The red to green luminance ratios arbitrarily selected were; 0.5, 0.8, 0.9, 1.0, 1.1, 1.2, 1.5.

6.3 Stimulus

Pattern reversal checkerboards were produced by the Neuroscientific Venus system. This was controlled by application software, which allowed the independent control of the red, green and blue guns and the output of the blue gun was removed for the red/green chromatic stimuli.

In view of the reported variability of the pattern onset-offset response (Wright et al. 1985) a pattern reversal stimulus was the stimulus of first choice used to record pattern VEPs in this study. The quality of the infant chromatic transient pattern reversal response was unknown prior to this study and pattern onset stimuli were designed as a 'back up' stimulation if the pattern reversal checkerboard yielded poor responses under all conditions. These pattern onset stimuli were however, not required in any study.

Large checks have been shown to elicit clear pattern reversal VEPs to achromatic stimuli in infants as young as 30.5 weeks post menstrual age (Harding et al. 1989). Previous investigation of the steady state VEP to chromatic stimuli have shown low chromatic acuity in infants (Morrone et al. 1990) and the effects of chromatic aberration is negligible at low spatial frequencies (Flitcroft 1989). For these reasons,checkerboards composed of checks of 2° angular subtense (0.25cpd) were chosen to record the pattern reversal VEP.

Independent control of the red and green guns enabled the production of a series of checkerboard stimuli at a range of red/green luminance ratios. These were programmed and stored on disk for instant retrieval and presentation. The mean luminance of the chromatic stimulus was constant at the maximum available for the monitor used (10 cdm^{-2}) but relative red to green luminances could be adjusted to produce a series of red/ green luminance ratios. Human cones have broad spectral sensitivities which overlap. The long wave sensitive cones (LWS) will respond maximally to the red component of the stimulus but will also have some response to the green component at a reduced level. The LWS cone modulation to each of the two components of the red/green stimulus cancel out to some degree and the overall modulation is smaller. The inverse will also apply to medium wave sensitive cones (MWS) (Banks and Bennett 1988). This serves to reduce the effective contrast of the stimulus in relationship to an achromatic stimulus, by a factor of 4 to 5 in an adult (Mullen 1985), thus a high chromatic contrast (amplitude of modulation) level of 90% was used. This could be further increased up to 100% in the cases where no response could be elicited to a chromatic stimulus.

A black/white checkerboard of 90% contrast and mean luminance 10$cdm^{-2,}$ was included throughout the recording sessions to assess the presence, quality and repeatability of the

pattern reversal response. The pattern reversed at a rate of 1 cycle per second (1Hz or 2 reversal per second) and a trigger pulse was developed at the beginning of each cycle to initiate the averaging procedure.

6.4 Averaging

Thirty responses (fifty for the adult pilot study) were averaged by the Biologic Traveller. Each response was amplified 24,000 times with band pass filters of 0.3 to 30 Hz. Thirty sweeps were averaged for the infants as this was found to be adequate to record the response. There was no significant improvement, if more than 30 responses were averaged, and as this prolonged the recording time the infants were apt to lose interest. The analysis time window used was 800 msec as this allowed complete development of the response with an interstimulus interval of 1 second. Two to three runs were recorded for each stimulus in order to estimate the reliability of the response and where possible, stimulus runs were compared to non-stimulus runs. Averages were stored on disk with an allocated record number. Due to the random nature of presentation of the stimuli, previously designed in the form of a 'look-up' table, each stimulus and run was assigned a record number which bore no relationship to the luminance ratio of the stimulus. Averages could then be analysed with no reference to the stimulus to which they related. This was felt particularly to be of benefit with an aim to removing any bias toward determining the presence or absence of a particular response. Only once the analysis of the response had taken place, were the appropriate ratios reunited with the responses elicited by them. The Biologic equipment has an artefact rejection facility that was utilised. Averaging caused timelocked responses to increase while random noise reduced. Signal to noise ratio was $\sqrt{}$number of samples.

6.5 Electrode Montage

Pattern reversal VEPs were recorded using silver-silver chloride electrodes, filled with electrode gel, which were positioned in accordance with the international 10-20 system (Jasper 1958). Two channel recordings were made from O2 (active) referenced to C4 and O1 (active) referenced to C3. Cz was used as the earth. (See figure 6.1). These references were chosen in preference to Fz due to the susceptibility of this position to eye movements.

In order to reduce skin resistances, Omniprep™ was applied to the electrode position prior to electrode placement. Resistances of 5K ohms or less were always possible and once the electrodes were allowed to settle on the scalp, resistances tended to decrease further. Electrodes were initially held in place by Blenderm tape, but where recording sessions were prolonged, the electrodes tended to slip. To prevent this, collodion glue was applied to the tape and the electrode re-placed.

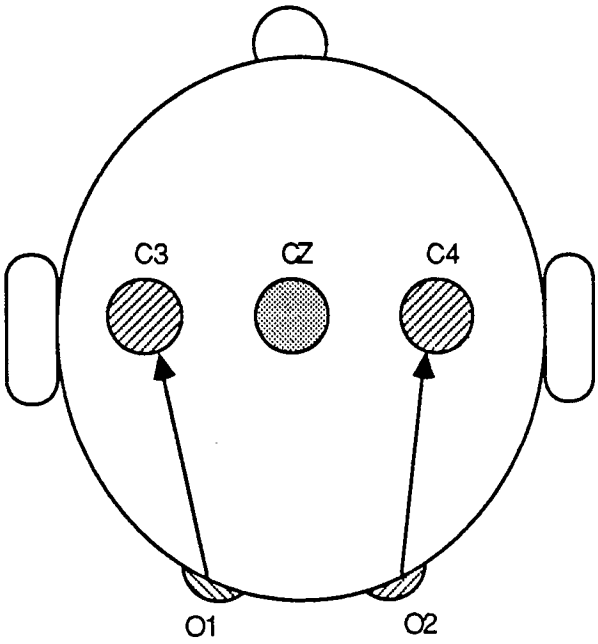


Figure 6.1 Schematic diagram of electrode montage used throughout the visual evoked potential studies

6.6 Adult pilot study

In order to assess the quality and morphology of the transient chromatic VEP response to a pattern reversal stimulus, a pilot study was undertaken on a sample group of adults. Ethical approval was obtained for this and the following studies from both the University and Health District Ethical Committees.

6.6.1 Subjects

Ten adult subjects, all staff and students at Aston University, with mean age 25.1± 2.1 years, took part in the pilot study. Of these, eight were female and two male. All were emmetropic or wore appropriate optical corrections and had Snellen visual acuity of 6/6 or better. All ten subjects were determined to be colour normal by Ishihara screening plates.

6.6.2 Procedure

Each subject binocularly viewed the stimulus at 63 cm, giving an overall stimulus subtense of 16° x 16°. All subjects were initially assessed with the black/white stimulus followed by the seven red/green stimuli presented in a random order. Fifty samples were averaged within a 500 msec time window. All averages were stored on floppy disk to enable data analysis to be carried out on a later occasion.

6.6.3 Results

Response morphology was analysed and traces printed out using the Biologic Brain Atlas. Latency and amplitude of the major components of the response could be measured using the EP program of this system. Repeated averages for any one stimulus were averaged together, which produced a record of 150 averages for each stimulus and from these averages, the mean latency and amplitude of the major components were calculated. Figure 6.2 shows the averaged visual evoked potential of 150 sweeps for an adult observer KE using a black/white checkerboard and seven red/green checkerboards at a range of red/green luminance ratios.

The achromatic VEP can be seen to have the standard morphology of the N-P-N (negative, positive negative) complex and the mean latencies and amplitudes of these major components for the sample of 10 adult subjects are given in Table 6.1 i.e. 72, 105 and 140 msec respectively. These findings are in close agreement with the averaged reported latencies of 75, 100 and 135 msec respectively (Halliday et al. 1977) hence the terms N75, P100 and N135 are applied.

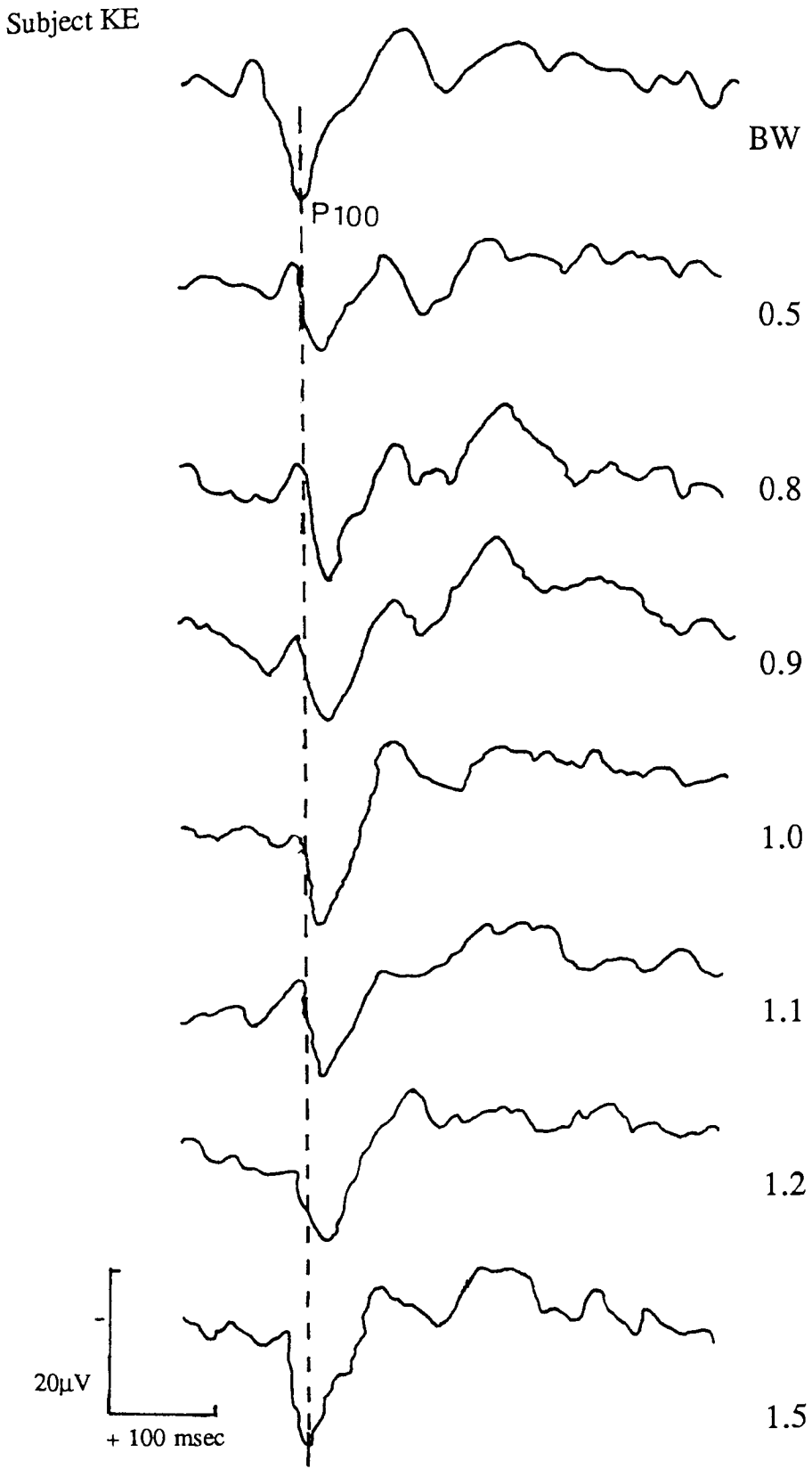


Figure 6.2 Averaged responses to 150 sweeps for an adult observer KE to pattern reversal achromatic and chromatic stimuli of seven different red/green luminance ratios.

The chromatic pattern reversal VEP shows a similar morphology to the achromatic in agreement with other workers (Regan and Spekreijse 1974, Carden et al 1985, Murray et al. 1987- for review see section 4.4.5) The mean latencies and amplitudes of the N75, P100 and N75 components for the chromatic stimulus at photometric isoluminance of the group of ten subjects is given in Table 6.1.

Table 6.1 Averaged latencies and amplitudes of major components of pattern reversal VEP to achromatic and chromatic 2° checks for a sample group of 10 adults. (Mean and standard deviation are given).

	Stimulus Type			
	Achromatic		Chromatic	
Component	Latency (msec)	Amplitude (μV)	Latency (msec)	Amplitude (μV)
N75	72 ± 7.9	3.1 ± 3.2	96 ± 8.8	3.5 ± 1.9
P100	105 ± 4.8	11.6 ± 4.2	118 ± 6.0	5.1 ± 2.5
N135	140 ± 15.8	8.4 ± 4.7	171 ± 17.1	8.6 ± 3.2

Mean latencies and amplitudes are plotted for achromatic and chromatic stimuli with a R:G ratio of 1.0 in Figure 6.3. From this it can be seen that the chromatic pattern reversal VEP shows a morphology of reduced amplitude and increased latency in comparison to the achromatic VEP. The mean amplitude of the P100 component of the chromatic response is reduced by 56% of the mean P100 achromatic component amplitude with a relative increase in latency of 13 msec. This delay and reduction is statistically significant for the sample group ($p<0.0001$)This change in morphology is in agreement with the findings of workers who used a steady state stimulus (Regan 1970, Burr et al. 1990, Bach and Gerling 1992).

The P100 component of the pattern reversal VEP has been shown to be the most consistent component of that response in infants (Sokol and Jones 1979, Moskowitz and Sokol 1983). It has been successfully demonstrated in infants as young as 30 weeks post menstrual age (Grose et al. 1989). The preceding N1 component is not apparent until 8-14 weeks post natal age (Sokol and Jones 1979) with the emergence of the N2 component by 2-3 months of age (Moskowitz and Sokol 1983, Grose et al. 1989). The morphology and development of the chromatic transient pattern reversal VEP is unknown but due to the reliability of the P100 component in infancy, analysis of the chromatic VEP in this pilot study was based upon the P1 (P100 in adults) component.

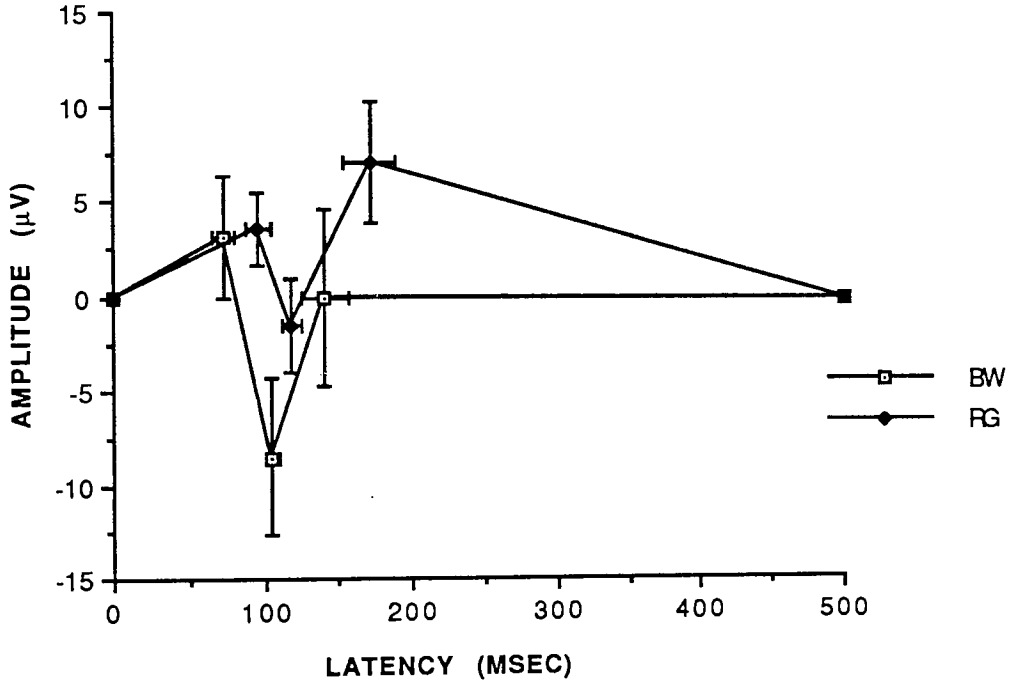


Figure 6.3 Morphology with respect to mean amplitude and latency of the major components (N75-P100-N135) of the achromatic (BW) and chromatic (RG) pattern reversal VEP. Horizontal error bars show standard deviation of latency, vertical error bars show standard deviation of amplitude. Sample group means calculated from O2 referenced to C4 for a sample of 10 adults.

6.6.4 Reliability of the chromatic VEP in adults

The differences between the latency and amplitudes of separate runs for each stimulus were measured in order to provide an indication as to the variability of the chromatic component. The variability of the P100 latency of the chromatic stimuli was very small and ranged from 0-8 msec for any one observer with a mean difference between runs of 5 msec. Amplitude of the P100 component between successive runs for the same stimulus varied by a mean of 7 μV for the sample group.

6.6.5 Relationship between chromatic pattern VEP and luminance ratio

Latency and amplitude of the P100 component for all the subjects were analysed as a function of red/green luminance ratio of the stimulus. The variability of the latency of the P100 component of the response over the chromatic stimuli range of seven red/green luminance ratios for any one subject was small and ranged from 0-12 msec and average maximum mean difference in peak latencies between all red/green ratios, was only 7 msec (± 3.8). The maximum amplitude difference for any individual to chromatic stimuli across all luminance ratios ranged from 1-6 μV across the sample group with mean maximum difference in P100 amplitude between stimuli of 3.5 μV (± 1.7).

Although overall change in amplitude between maximum and minimum P100 response over the range of red/green luminance ratios used was small, eight of the adult observers demonstrated a minimum amplitude response at or close to photometric isoluminance. This decrease in amplitude corresponded with an increased latency of the same component. One observer, RD, demonstrated an increased latency at a red/green ratio of 1.0 but amplitude of the P1 response was unchanged for this subject, over the ratio range of 0.8 to 1.5, whilst another FF demonstrated a clear amplitude reduction as photometric isoluminance was approached but P100 latency remained constant for all ratios. The change of amplitude and latency of the P100 component with respect to luminance red/green ratio for a sample of four observers are plotted on Figures 6.4 and 6.5 respectively.

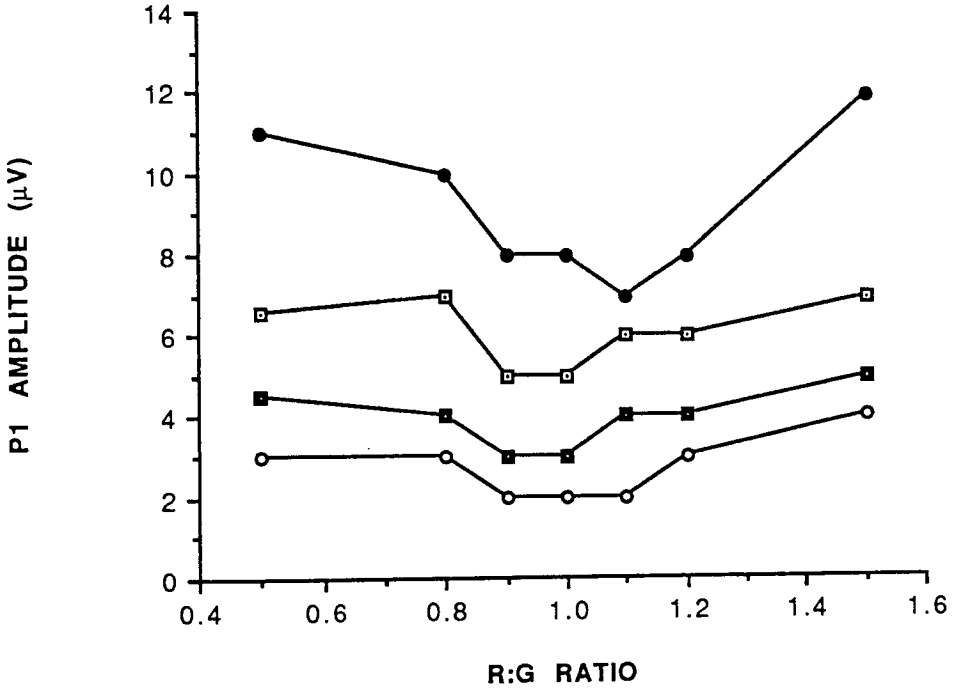


Figure 6.4 Graph to show the change of amplitude of the pattern reversal P100 component over a range of seven red/green luminance ratios for four adult observers demonstrating a reduction in amplitude at or close to a red/green luminance ratio of 1.0.

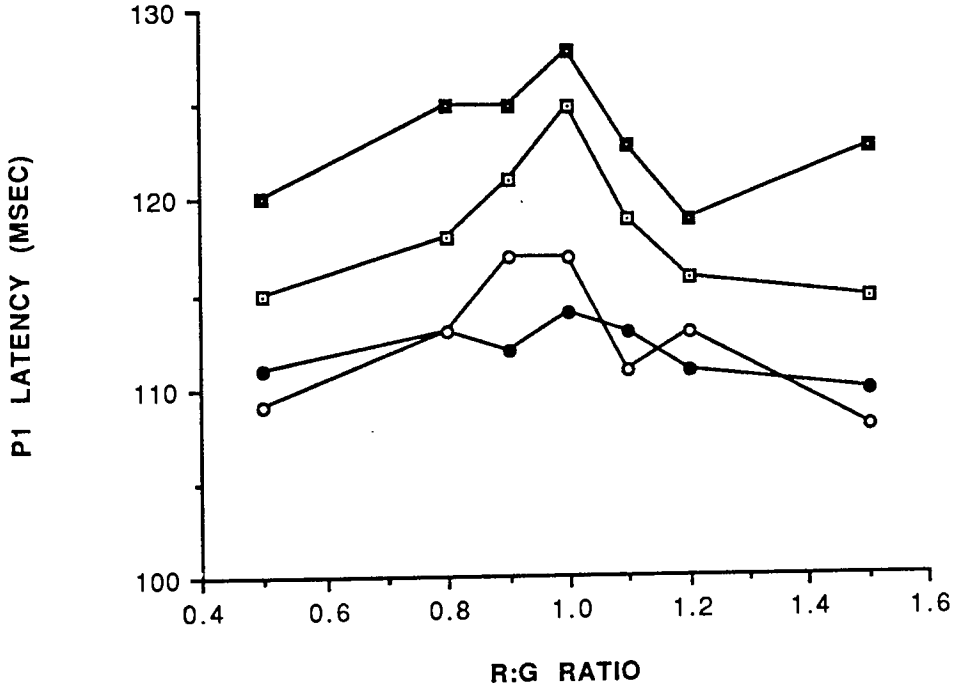


Figure 6.5 Graph to show the change of latency of the pattern reversal P100 component over a range of seven red/green luminance ratios for four adult observers demonstrating an increase in latency at or close to a red/green luminance ratio of 1.0.

6.7 Discussion of pilot study results

The pilot study on a sample group of adults showed the achromatic and chromatic pattern reversal VEP to be highly similar with both demonstrating a N-P-N morphology. This is in agreement with the findings of previous workers (for review see 4.4.5). The chromatic P100 component shows an increased latency and reduced amplitude with respect to the achromatic response and this change is seen to be dependent on the luminance ratio of the red and green component checks. As photometric isoluminance is approached the amplitude decreases and latency is seen to increase, however the size of this change varied between subjects with a mean change from maximum to minimum amplitude of only 3.5μV and a mean maximum latency increase of 7 msec.

Several other workers have reported such changes in amplitude of chromatic pattern reversal VEPs when using steady state stimulation and have reported amplitude decreases in the order of 2μV to be significant (Fiorentini et al. 1991, Bach and Gerling 1992). In fact, it is this reduction in amplitude that has been used in such work to determine isoluminance.

The stimuli in this pilot study have been seen to produce clear, repeatable transient pattern reversal VEPs and over the range of red/green ratios used, appear to be adequate to demonstrate an almost symmetrical decrease in latency and increase in amplitude of the P100 component on either side of isoluminance as the luminance information within the stimulus is increased. The chromatic response at isoluminance is delayed significantly in comparison to the achromatic for the whole sample group.

Due to the clarity of response and the consistency of change of response over the luminance ratio range used for the sample of ten adults, the same protocol and stimuli were adopted for the study of transient chromatic visual evoked potentials in infants. The final recording parameters and protocol chosen for the main study are summarised in chapter 7.

CHAPTER SEVEN
DEVELOPMENT OF THE CHROMATIC VISUAL EVOKED POTENTIAL: MAIN STUDY

7.1 Introduction

The processing of chromatic information is believed to be a cortical function via the parvocellular system (Livingstone and Hubel 1988). With a view to assessing the presence of cortical function a study of the presence of the chromatic VEP in infants was undertaken.

7.2 Subject recruitment

Subjects were recruited by personal contact with the author at routine developmental clinics at Aston and Newtown health centres, Birmingham. The procedure and aim of the study was explained at the time of recruitment and a written summary of this given to the parent, with a contact phone number for any further queries. In many cases it was necessary to provide a free taxi service for the infant and their family and this provision appeared to reduce the failure to attend rate from 50% (no taxi service offered) to 32% (taxi service). The appointment to attend Aston University was reconfirmed by the author in writing or by telephone.

7.3 Exclusion criteria

1. Infants living outside of the catchment area of Newtown or Aston health centres.
2. Significant congenital abnormality.
3. Gestational age at birth $\leq$ 36 weeks.
4. Family history of colour deficiency or other congenital abnormality.

7.4 Subjects

Forty infants between 5 and 13 weeks postnatal age, were recruited into the study and written consent was obtained from the parents of all infants.(See Table 7.1 for details of infants taking part in main study). Twenty-three of the infants were male and although this group has a higher probability of colour deficiency, it was felt to be impratical to exclude these infants from the study.

As visual development is more closely related to post conceptional rather than post natal age (van-Hof van-Duin et al. 1983) and development of preterm infants is equivalent to that of full term infants when matched for post conceptional age (Foreman et al. 1991), each infant was classified in terms of calculated post term age rather than post natal age. This makes the assumption that full term was 40 weeks post menstrual age. The age

distribution of the 40 infants (post term) taking part in the main study is shown in Figure 7.1.

Table 7.1 Subjects participating in the main study

Infant	Sex	CA (weeks)	PTA (weeks)
AJ	M	7	7
SON	F	8	7
JAD	F	7	7
AR	M	5	5
MID	F	13	13
SF	M	10	10
JD	M	10	10
NF	F	10	10
SPL	M	10	10
JM	M	7	9
TE	F	9	9
NH	F	9	9
MHE	M	8	8
CW	F	8	8
KBK	M	7	8
DJ	M	7	7
NHB	M	7	8
DW	M	7	4
RJ	F	5	1
RM	M	7	7
GH	M	6	6
WM*	M	8	4
TM*	M	8	4

Infant	Sex	CA (weeks)	PTA (weeks)
SH	M	7	7
LL	M	7	5
MD	M	5	5
KYB	F	9	7
KL	M	7	7
MB	M	8	8
CK	F	9	8
LH	F	8	8
MF	M	7	7
AG	F	7	7
KB	M	6	7
GEMH	F	6	6
LS	F	6	4
RG	F	6	6
CA	F	7	7
CP	M	6	6
MFA	F	7	7

KEY TO SYMBOLS:
CA - Chronological age
PTA - Post term age
* - Twin.

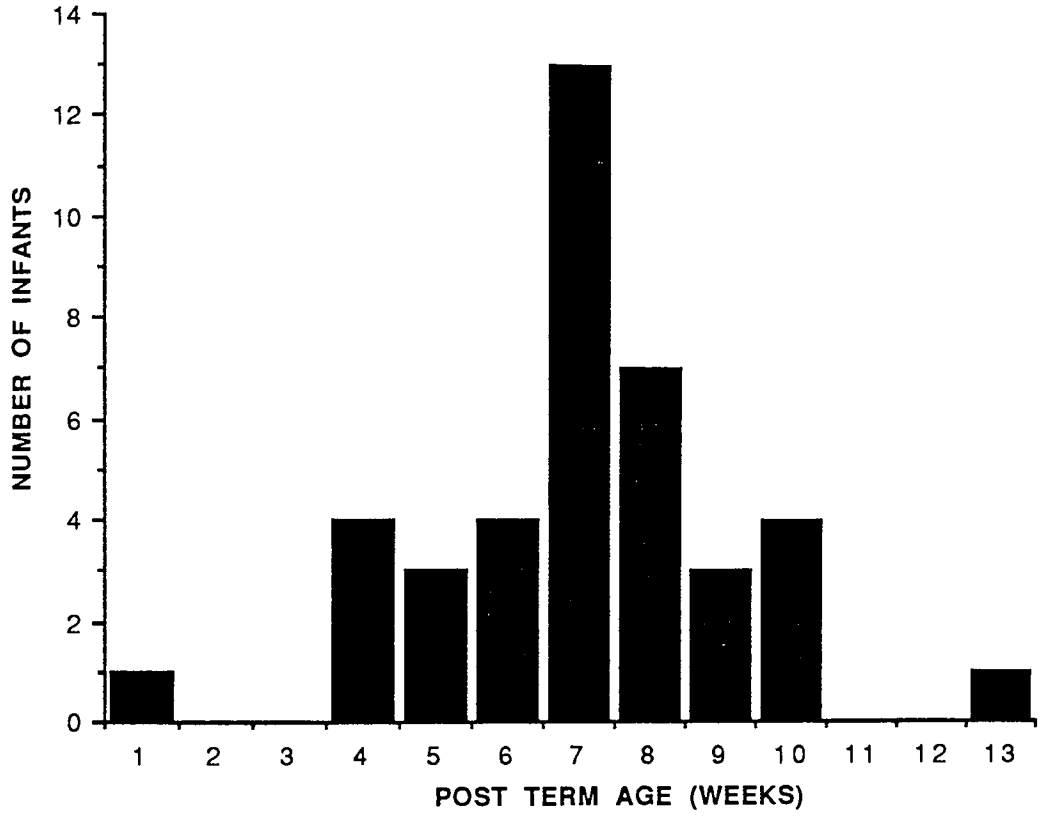


Figure 7.1 Frequency distribution of ages of 40 subjects taking part in main study as classified by post term age in weeks

7.5 Parameters used in main study

The achromatic (black/white) stimulus was always used first followed by the chromatic (red/ green) stimuli in random order.

Electrode montage: O1 referenced to C3, O2 referenced to C4. Earth Cz (see figure 6.1).

Stimulus: Checkerboard reversal at 37 cm from the eyes.

a) Achromatic:Colour of checks ;Black/white.
Angular subtense of checks; 2°
Mean luminance of checks ; 10 cdm^{-2}
Contrast : 90%

b) Chromatic: Colour of checks;Red/green.
Angular subtense of checks;2°
Mean luminance of checks ; 10 cdm^{-2}
Contrast : 90-100%
Luminance ratios of red to green checks ; 0.5, 0.8, 0.9, 1.0, 1.1, 1.2,1.5.

Stimulus size: 32 x 32 degrees.

Reversal rate: 1 Hz

Recording Parameters

Trigger rate: 1 per second.

Number of sweeps averaged: 30.

Band pass: 1-30 Hz. (-3db downpoint) Reject facility of 95% of full scale deflection.

Analysis time: 800 msec.

The recording set-up is illustrated in Plate 7.1.

7.6 Recording success rate

All infants were initially assessed with the achromatic stimulus and only if a clear response could be obtained from this stimulus was recording continued with chromatic stimuli. As much of a young infant's time is spent sleeping, some recording sessions had to be interrupted to allow for this. Recording by the averager could also be interrupted during a run if the corneal reflection of the stimulus was not centred on the infant's pupil. This was observed throughout the recording sessions by a separate observer who also aided in keeping the infant's attention on the screen. In cases where recording was interrupted, a minimum of three different chromatic stimuli (2 to 3 averages for each) was accepted as a completed data set but where infant co-operation allowed, up to seven chromatic stimuli were used. The distribution of number of chromatic stimuli assessed for the sample of 40 infants is shown in Figure 7.2. The number of successful red/green ratios assessed was not statistically correlated with age at time of recording ($r = 0.116$, $p>0.1$). Data collection not was possible with only one infant TM and this was due to sleepiness following the recording time with twin WM.

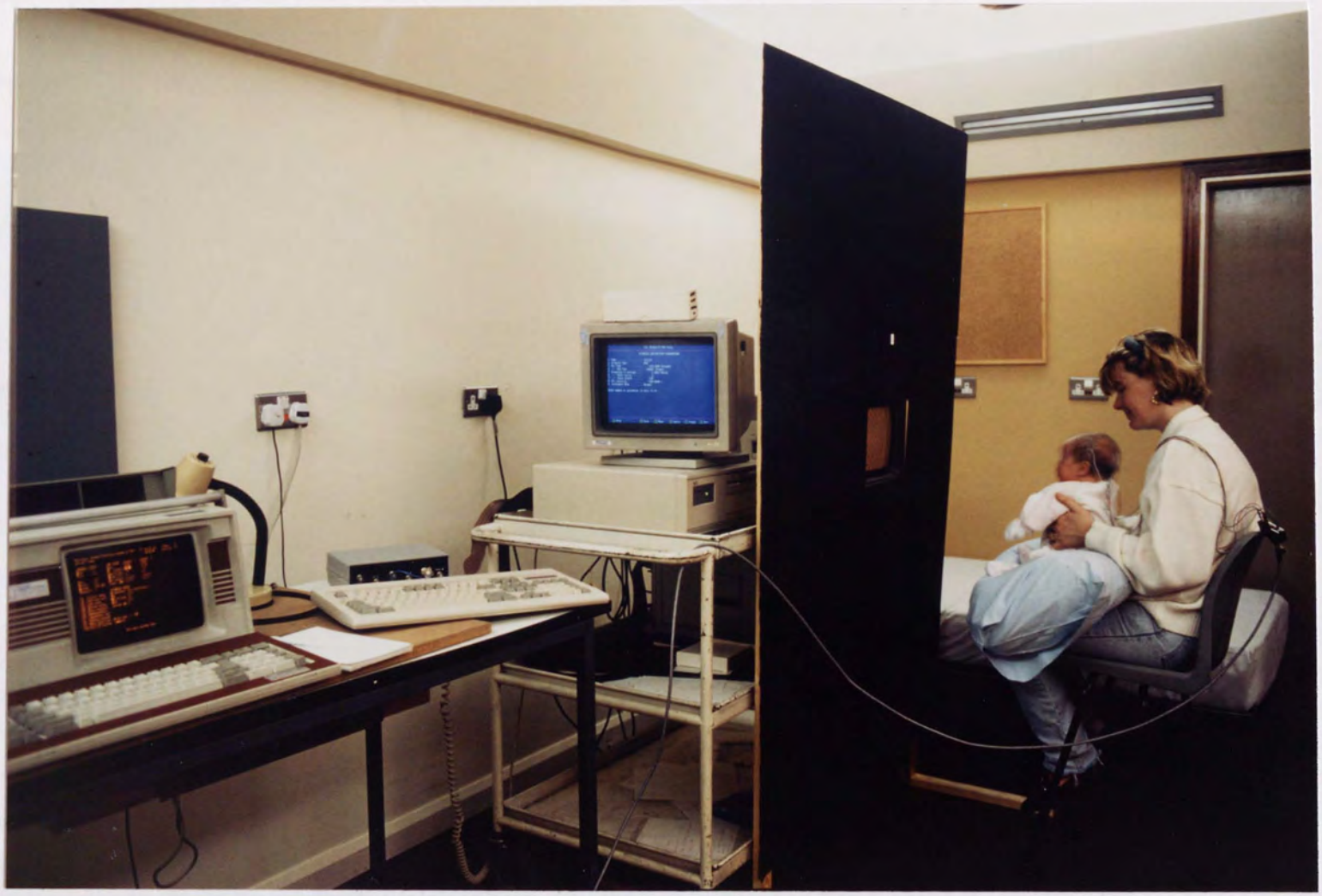


Plate 7.1 Experimental set-up for infant visual evoked potential study

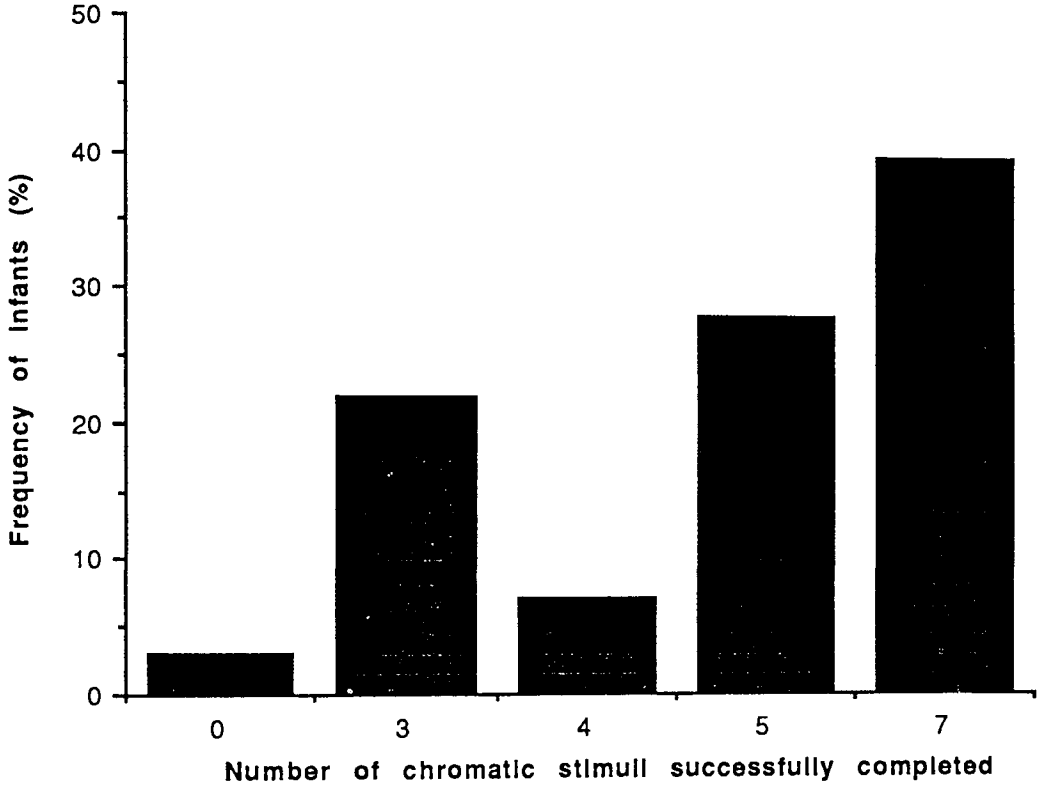


Figure 7.2 Frequency distribution showing number of chromatic stimuli assessed at one recording session for 40 infants.

7.7 Morphology of the achromatic pattern reversal VEP

The adult pattern reversal VEP to a checkerboard consists of a N-P-N waveform but in the youngest infants, it took a simpler morphology consisting of a single positive peak (P1). In adults, the positive component, P1, occurs at about 100 msec and is often referred to as P100, however, the latency of the P1 was considerably longer in young infants with a mean latency of 254 msec in the first month of life (1-5 weeks) (for age classifications see Table 5.2). With increasing age, this P1 component became more sharply defined.

The morphology increased in complexity with age (Figure 7.3) and the P1 component was preceded by an initial negative wave (N1) from 6-7 weeks of age. The presence of an N2 component following the P1 wave was noted in all infants above 9 weeks of age. Despite an increase in complexity of the achromatic pattern reversal VEP, the P1 component was found to be the most consistent component of the pattern reversal VEP over the age range studied. The development of morphology of the achromatic response is schematically represented in Figures 7.4 to 7.6 with the mean latency and amplitude for each major component of the response is given in Table 7.2.

Table 7.2 Mean latencies (in msec) and amplitudes (in μV) (with standard deviations) of the main components of the achromatic VEP for sample groups as defined by post term age (in weeks)

Age	N	N1		P1		N2	
		Lat.	Amp.	Lat.	Amp.	Lat.	Amp.
1	1	-	-	262	10	-	-
4	3	-	-	276±71	10±4	-	-
5	3	-	-	222±24	7±2	-	-
6	4	118±13	4±3	206±17	13±4	-	-
7	13	124±22	4±3	214±30	13±5	-	-
8	7	123±23	3±2	210±25	12.5±6	-	-
9	3	117±24	2.6±2	198±25	15±4	-	-
10	4	95±22	4±2	146±25	14±11	233±25	18±11
13	1	80	11	123	18	200	28

7.8 Reliability of the achromatic pattern reversal VEP

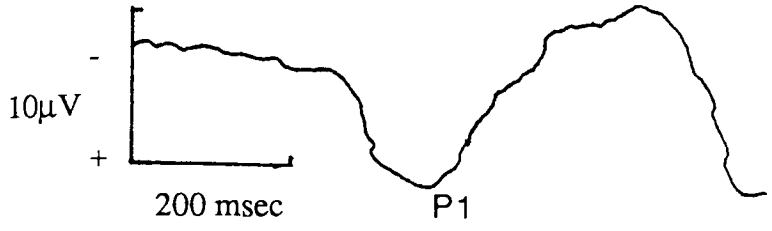
For each infant, two to three runs for each stimulus were recorded. A non-stimulus run was included for comparison to assess the random noise level. Figure 7.7 shows two stimulus runs and a non-stimulus run for an achromatic stimulus.

The mean latency and amplitude of the P1 components and the differences between separate runs were calculated to give an indication as to the variablity of the P1 component. The variablity of the latency was small and ranged from 0-40 msec, the maximum difference between peak latencies was, on average, 18msec. The difference in amplitude of the achromatic response varied from 0-17μV over the sample group. There was no relationship between the variability of the achromatic pattern reversal response and post term age.

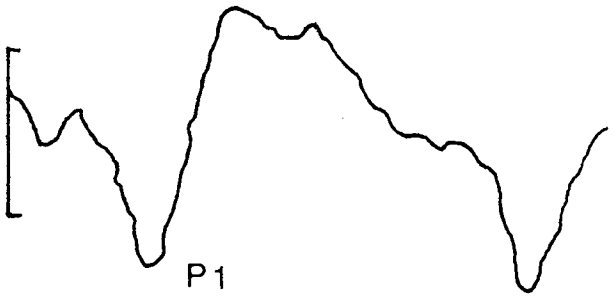
7.9 Relationship between the achromatic pattern reversal VEP and post term age

The latency of the P1 component for the sample of 39 infants decreased from around 260 msec in the first four weeks post term to 123 msec at 13 weeks post term. The latency of the P1 component was found to be negatively correlated with post term age at the time of recording ($r = 0.658$, $p < 0.001$) (Figure 7.8). A poor correlation was found to exist between the amplitude of the P1 component which tended to increase with post term age but this was not statistically significant (Figure 7.9).

Infant WM - 4 weeks PTA



Infant AJ - 7 weeks PTA



Infant NH - 9 weeks PTA

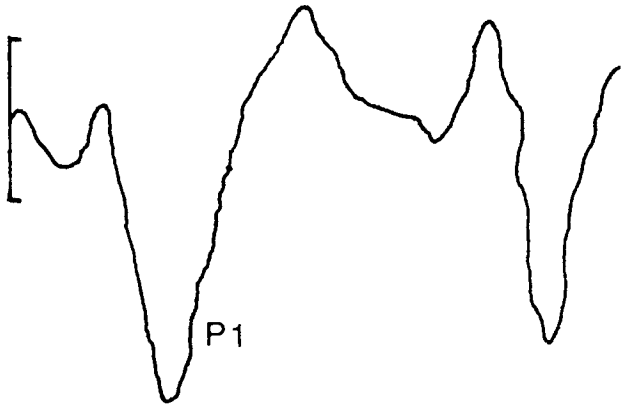


Figure 7.3 Achromatic pattern reversal VEP from three infants to show an increase in complexity of morphology with post term age (PTA).

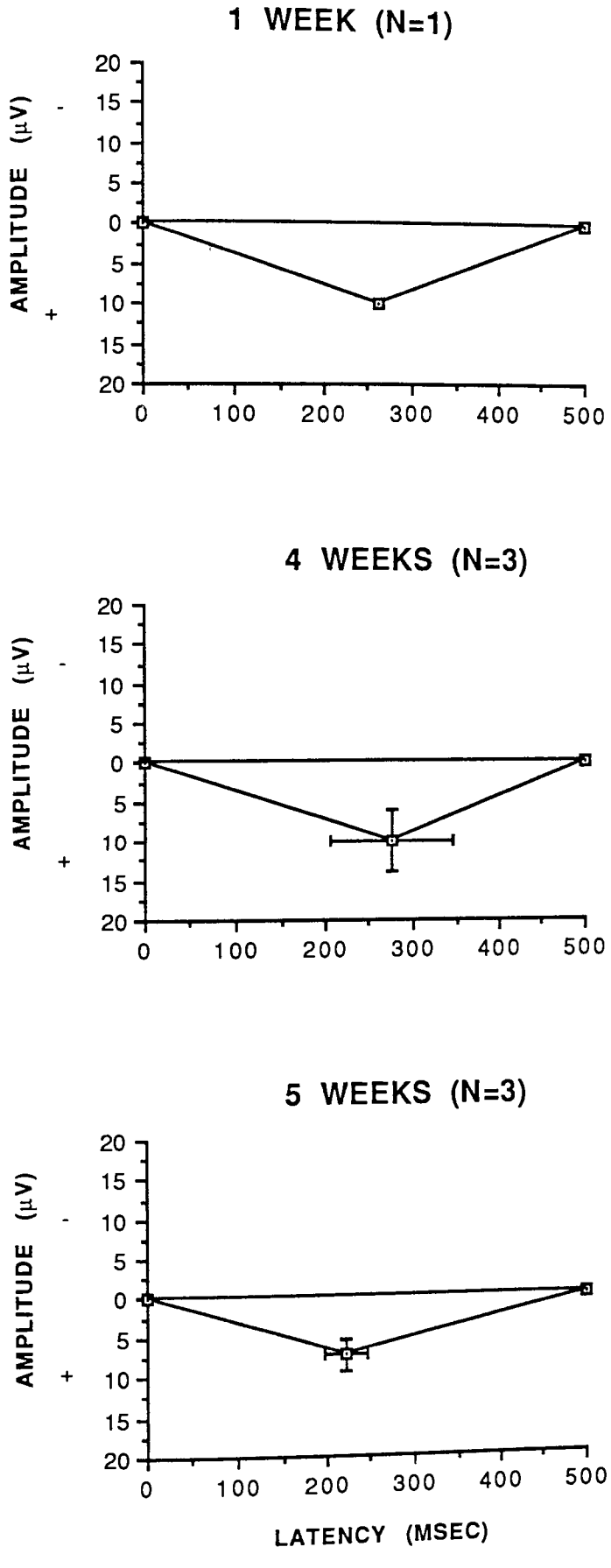


Figure 7.4 Schematic representation of mean VEP responses to achromatic stimuli for 1 to 5 week old sample groups. Error bars show standard deviation.

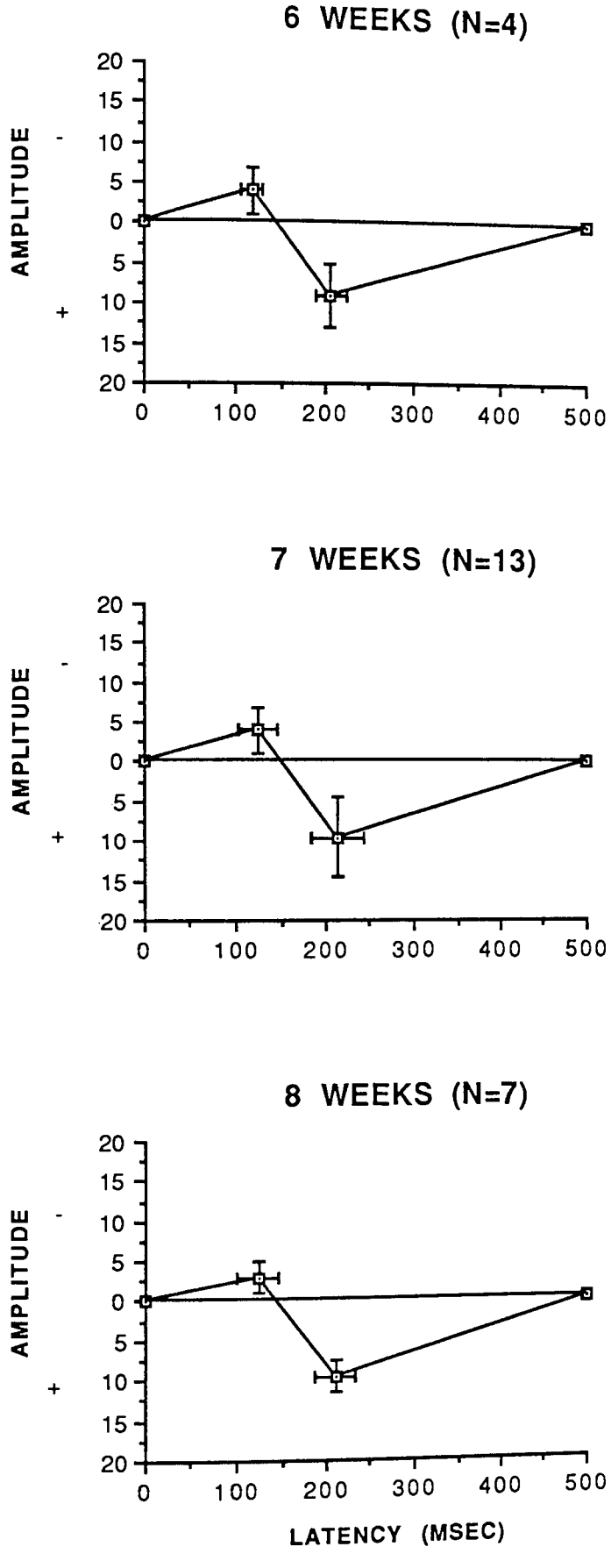


Figure 7.5 Schematic representation of mean VEP responses to achromatic stimuli for 6 to 8 week old sample groups. Error bars show standard deviation.

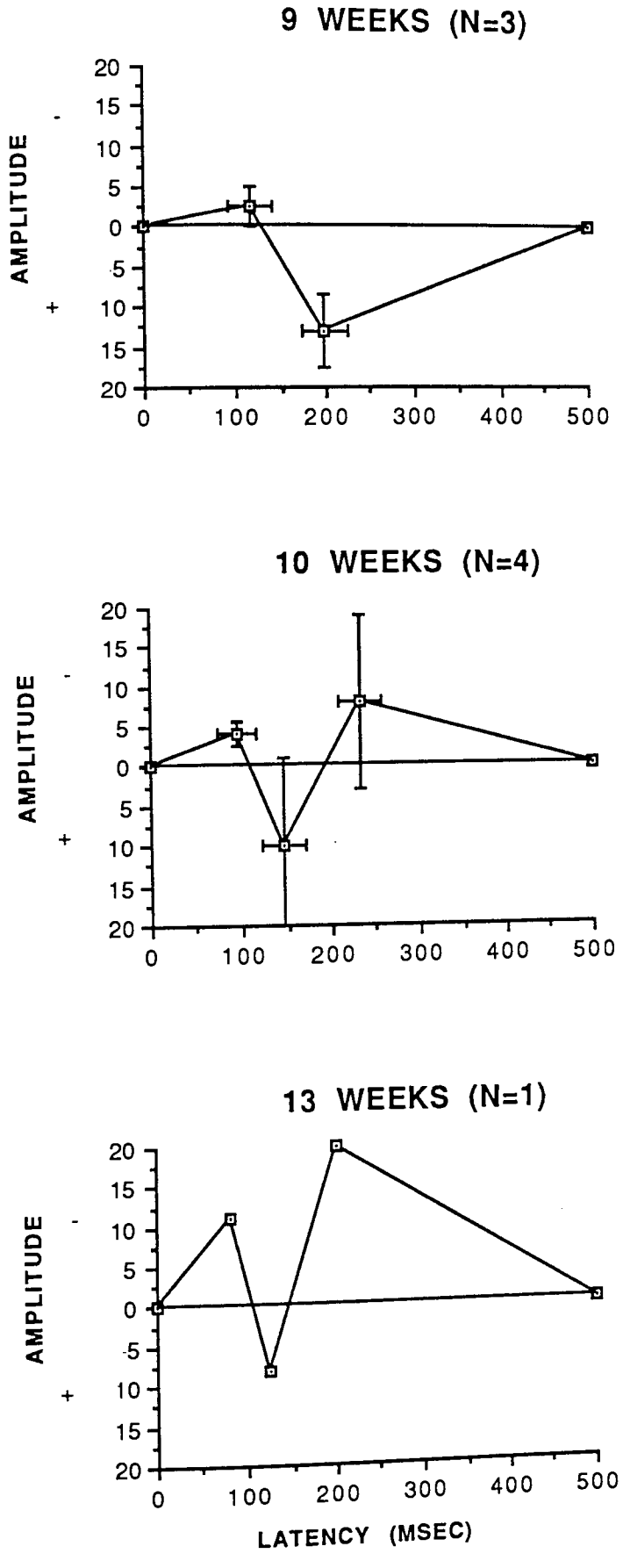


Figure 7.6 Schematic representation of mean VEP responses to achromatic stimuli for 9 to 13 week old sample groups. Error bars show standard deviation.

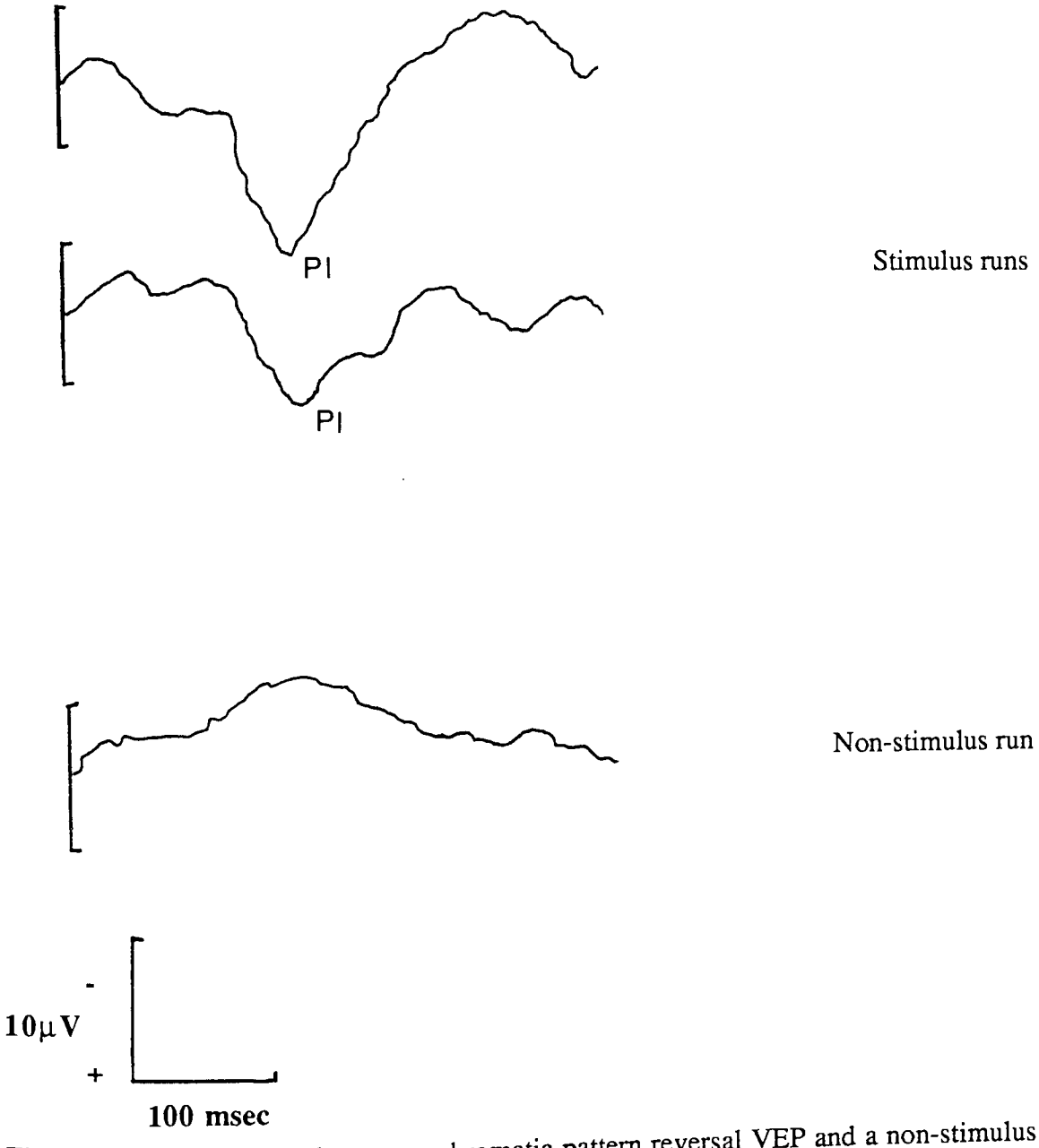


Figure 7.7 Comparison between achromatic pattern reversal VEP and a non-stimulus run

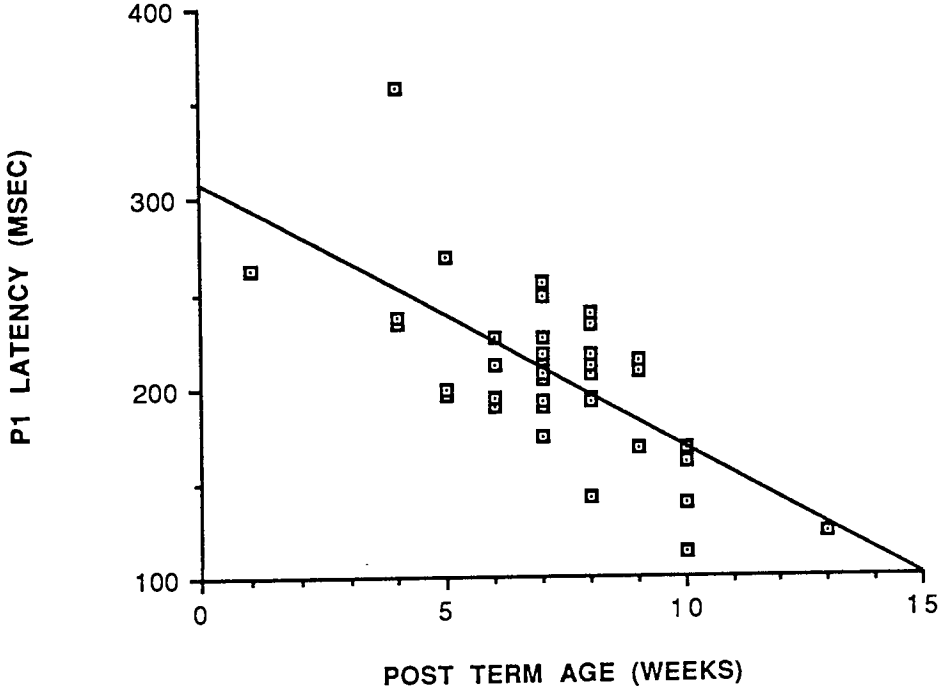


Figure 7.8 Graph to show relationship between latency of achromatic pattern reversal P1 component and post term age. The formula for the regression line is $y = -13.861x + 307.49$: $r = 0.658$: $p < 0.001$; d.f. 38.

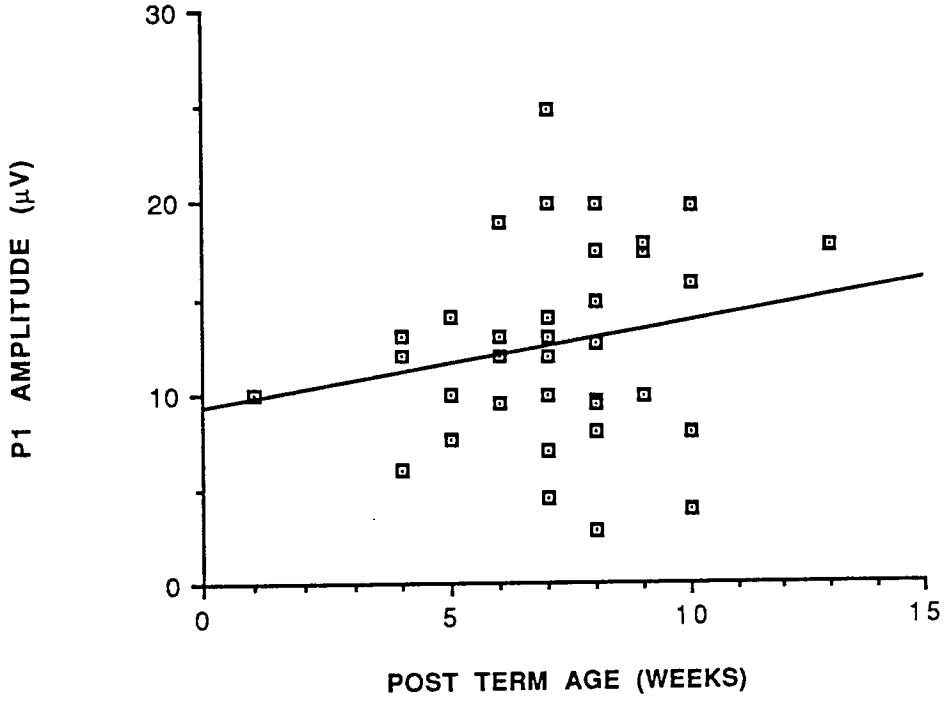


Figure 7.9 Graph to show relationship between amplitude of achromatic pattern reversal P1 component and post term age. The formula for the regression line is y = 0.417x + 9.265: r = 0.178; p> 0.1; d.f. 38.

7.10 The chromatic pattern reversal VEP

In the youngest infants, the waveform of the non isoluminant chromatic response showed a simple morphology of a major positive component (P1) comparable to the achromatic response. These responses were symmetrical across both channels and all non-isoluminant chromatic responses were delayed and reduced in comparison to the achromatic response. As the chromatic luminance ratio approached 1.0 the response became progressively delayed and reduced to eventually disappear at , or close to, the luminance ratio of 1.0 (i.e. isoluminance). Figures 7.10 to 7.12 show averaged responses from three infants demonstrating this. The corresponding latency and amplitude of the P1 component with respect to luminance ratio for these infants are plotted in Figures 7.13 to 7.15.

Nineteen, of the thirty-nine infants assessed, demonstrated no recordable response at isoluminance although clear responses could be elicited with other chromatic stimuli. Where this occurred, increasing the amplitude of modulation of the stimulus from 90 to 100% had no effect. The distribution of these infants with respect to post natal (chronological) and post term age is shown in figure 7.16. It can be seen that if a correction is made for post term age, all nineteen infants are less than 8 weeks of age. The other twenty infants showed responses to all chromatic stimuli, although again the positive component demonstrated a significant delay ($p< 0.001$) and reduction ($p< 0.0001$) at isoluminance in comparison to the black/white response. Figures 7.17 and 7.18 show averaged responses from two of these infants, with P1 latency and amplitude change demonstrated in Figures 7.19 and 7.20. The age distribution of this group of twenty infants is shown in Figure 7.21. Again, making a correction for post term age demonstrates a clear onset age of the chromatic response at 7 to 8 weeks. Figure 7.22 shows the distribution of infants with and without a transient chromatic VEP for the whole sample group as defined by post term age.

7.11 Reliabilty of the chromatic reversal VEP

The variability of the latency of the P1 component for any one chromatic stimulus, ranged from 0-30msec between runs with a mean of 13msec. Amplitude of P1 between successive runs for any one stimulus ranged from 0-10μV across the sample group with a mean difference of maximum amplitude of only 3μV.

Stimulus runs were compared to non-stimulus runs and this was of particular value when determining the presence or absence of a response. Figure 7.23 shows two stimulus runs and a non-stimulus run demonstrating the presence and absence of a response to chromatic stimuli. Identification of each response was checked by an individual observer who was blind to subject and stimulus parameters.

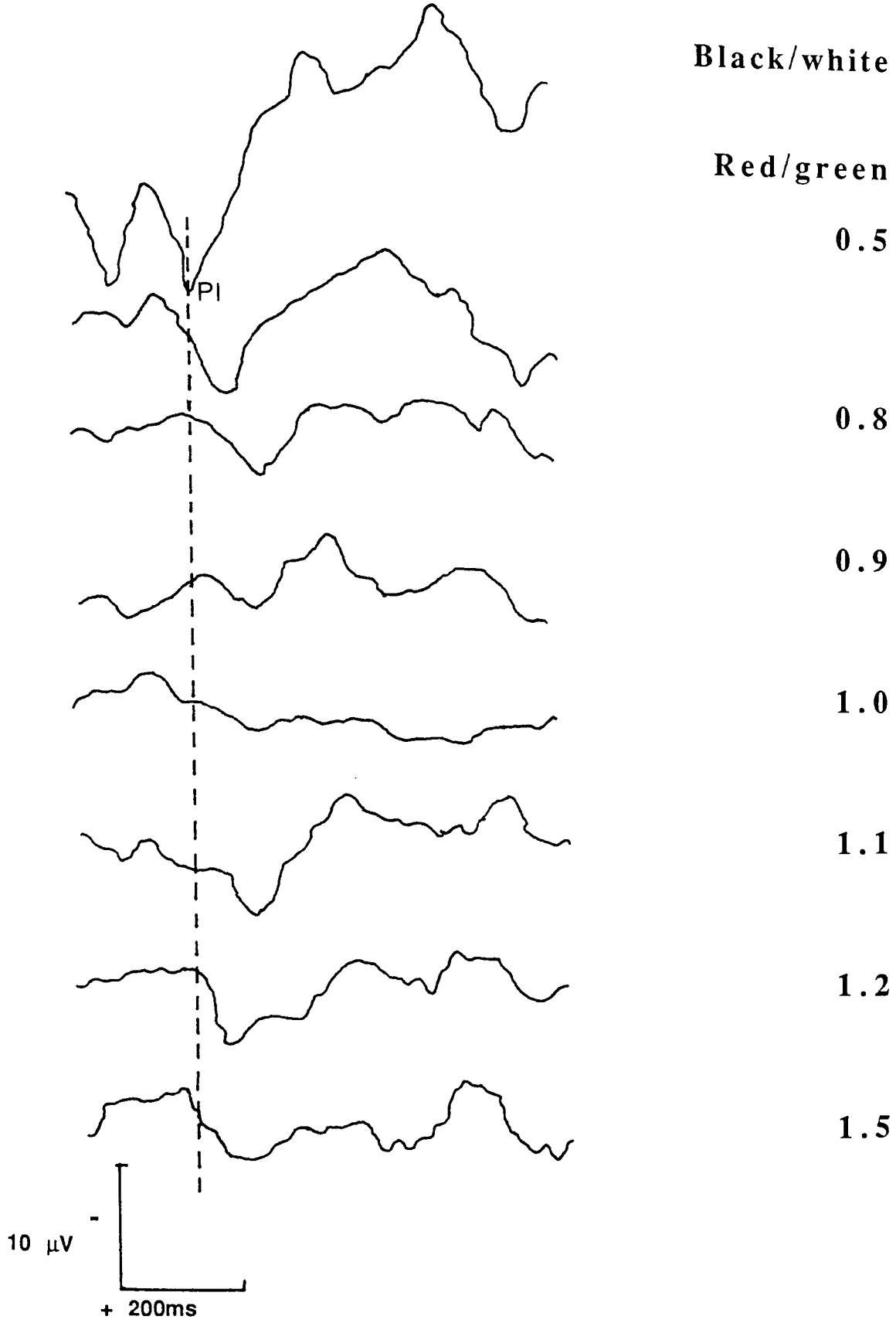


Figure 7.10 Change in morphology of chromatic VEP with change of R:G ratio for a 6 week old infant RG. The achromatic response is shown above for comparison. (Latency and amplitude of the P1 component are plotted in Figure 7.13)

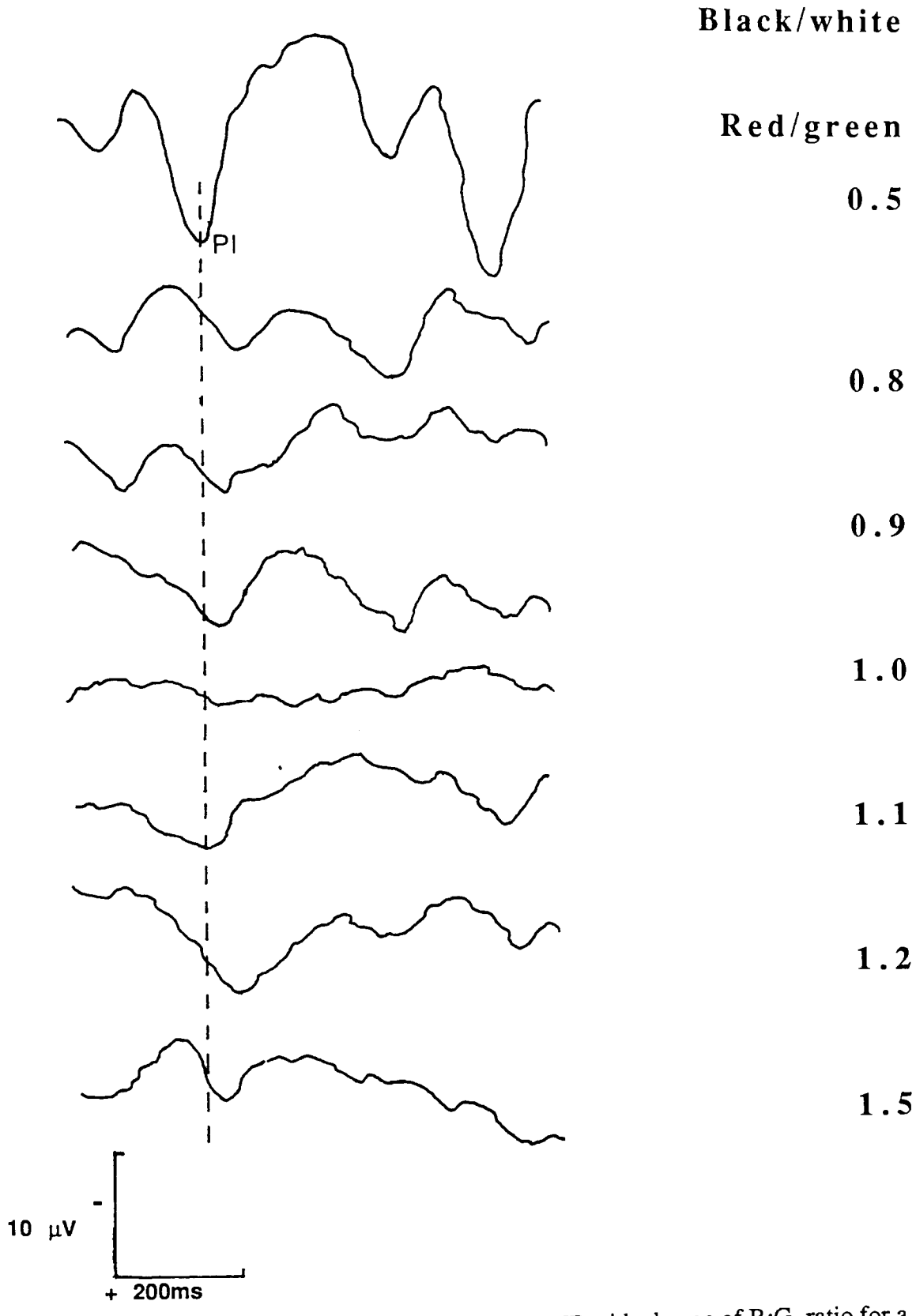


Figure 7.11 Change in morphology of chromatic VEP with change of R:G ratio for a 7 week old infant JAD. The achromatic response is shown above for comparison. (Latency and amplitude of the P1 component are plotted in Figure 7.14)

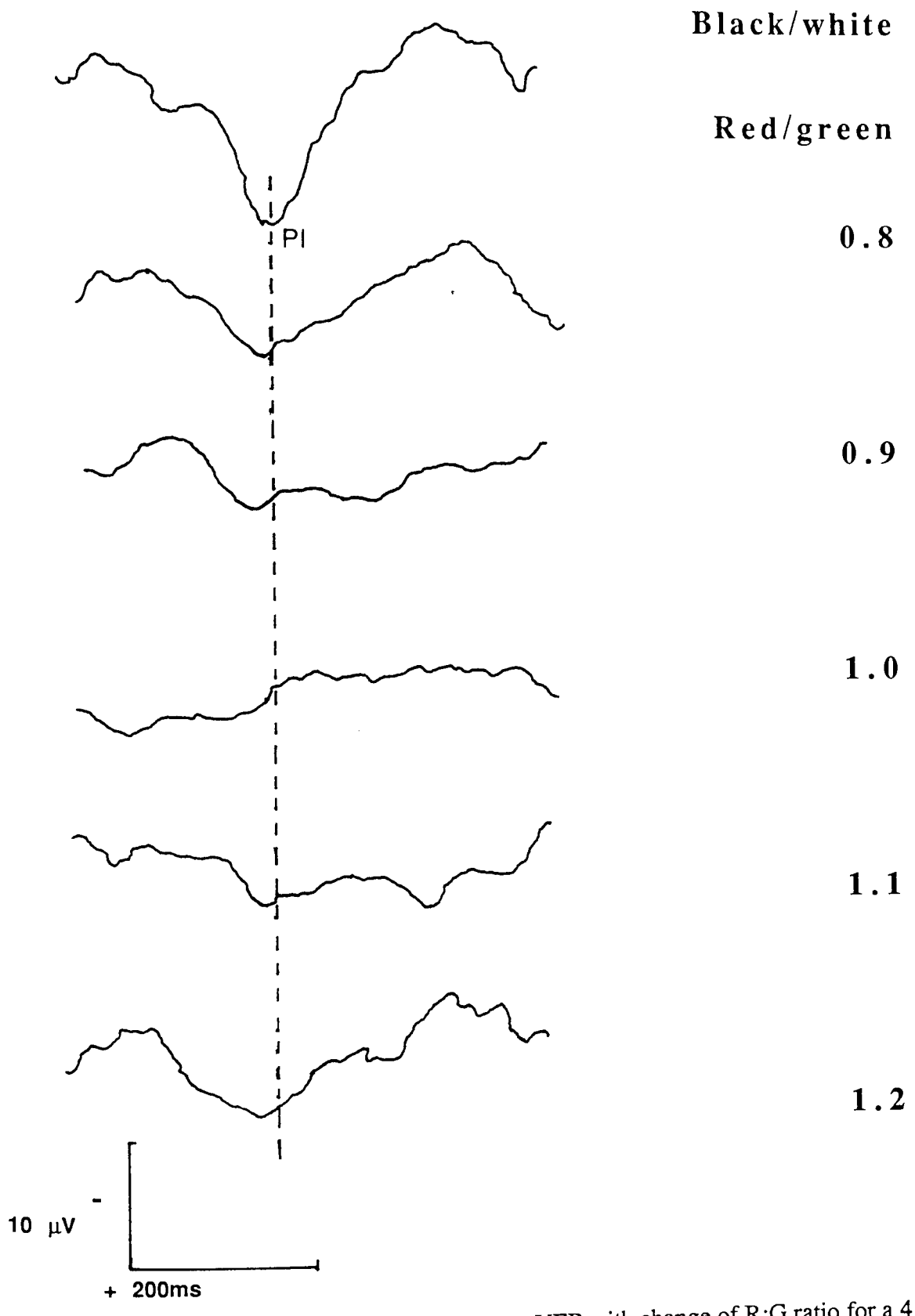


Figure 7.12 Change in morphology of chromatic VEP with change of R:G ratio for a 4 week old PTA (CA= 7 weeks) infant DW. The achromatic response is shown above for comparison. (latency and amplitude of the P1 component are plotted in Figure 7.15)

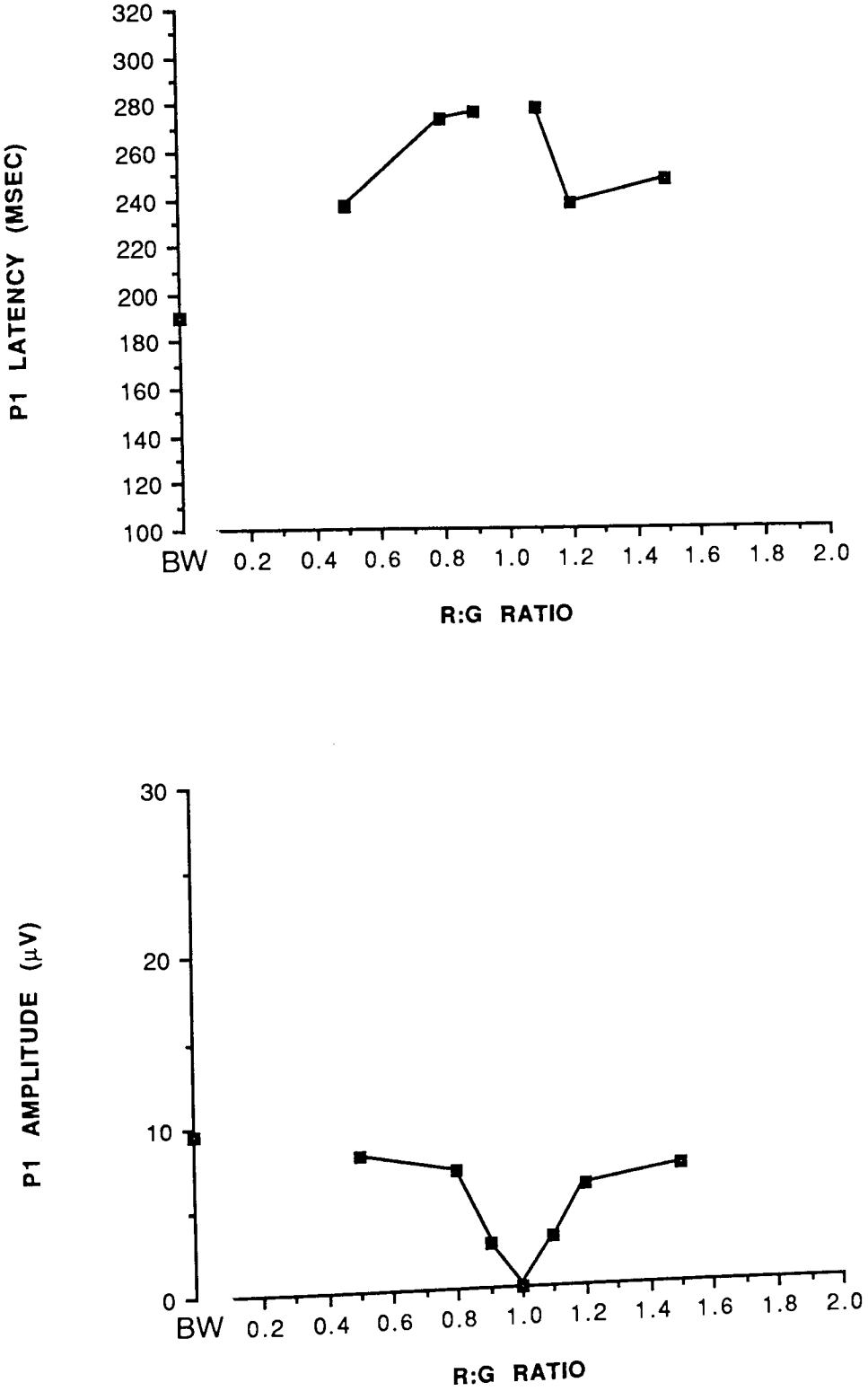
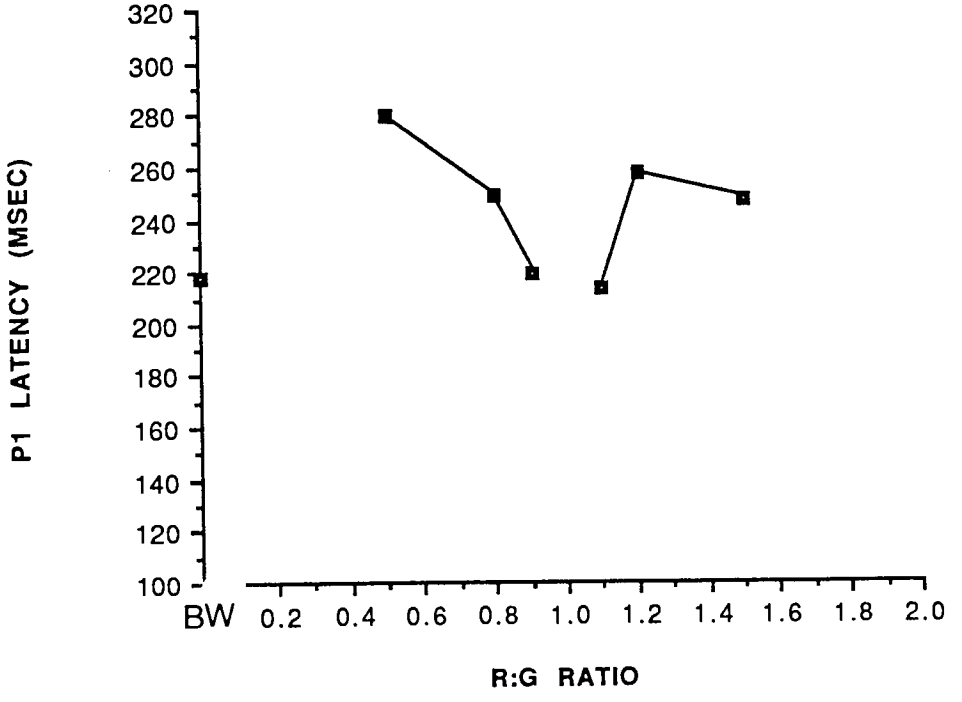


Figure 7.13 Line plot to show latency and amplitude of P1 component of the chromatic VEP to stimuli of different red/green ratio of 6 week old infant RG. The black/white (BW) response is included for comparison.



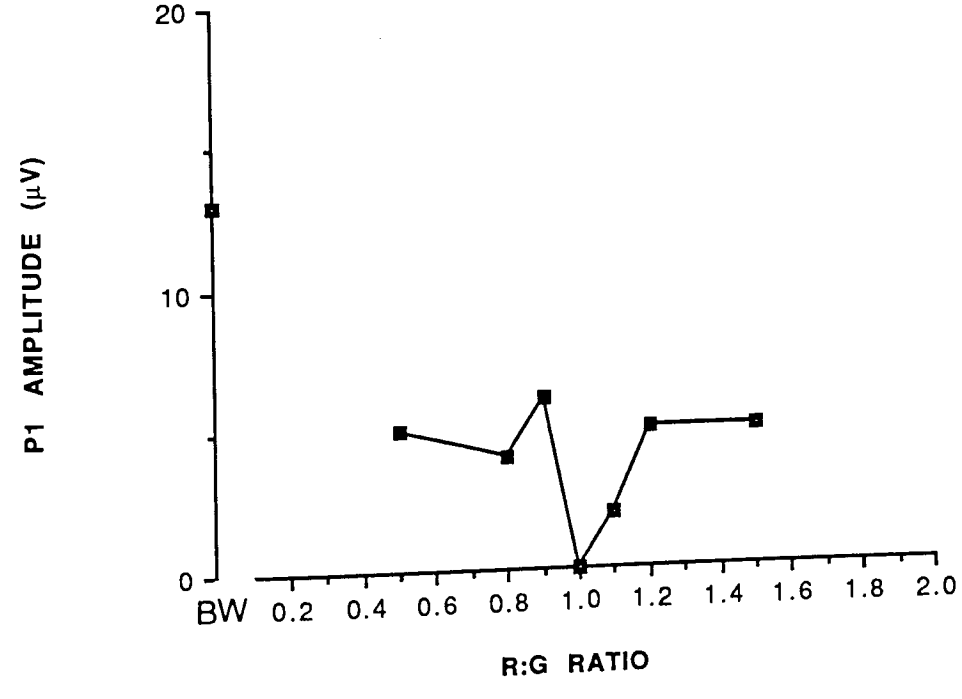
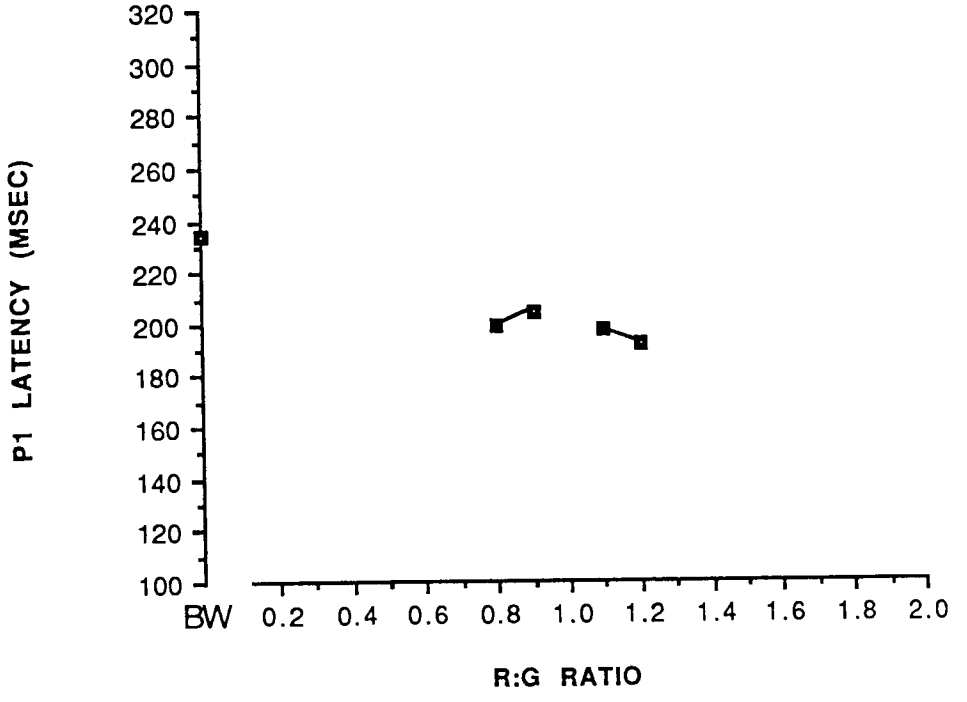


Figure 7.14 Line plot to show latency and amplitude of P1 component of the chromatic VEP to stimuli of different red/greeen ratio of 7 week old infant JAD. The black/white (BW) response is included for comparison.



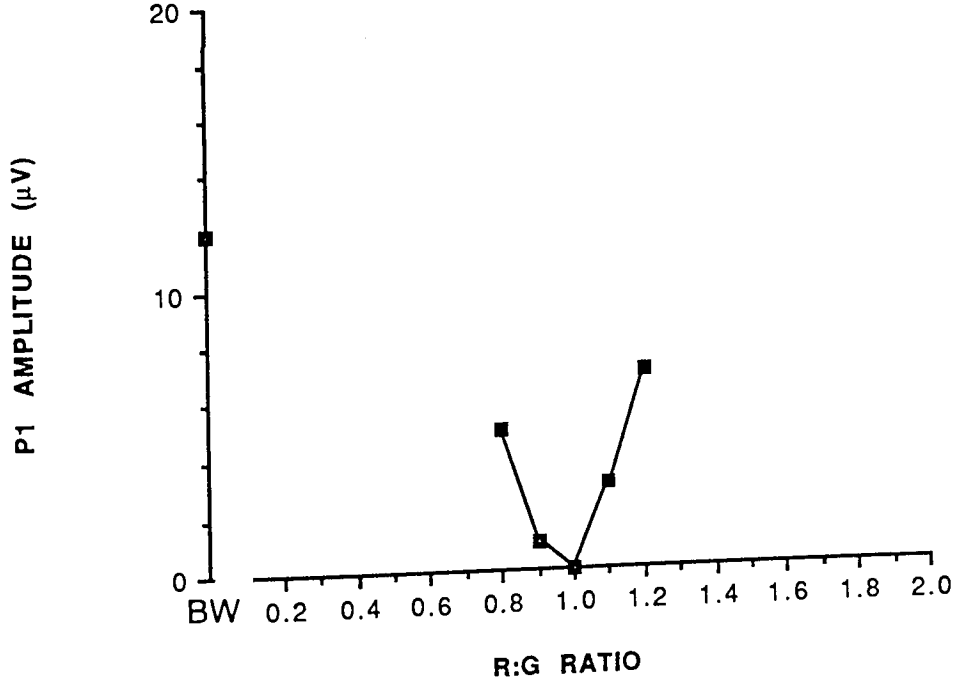


Figure 7.15 Line plot to show latency and amplitude of P1 component of the chromatic VEP to stimuli of different red/greeen ratio of 4 week old infant DW. The black/white (BW) response is included for comparison.

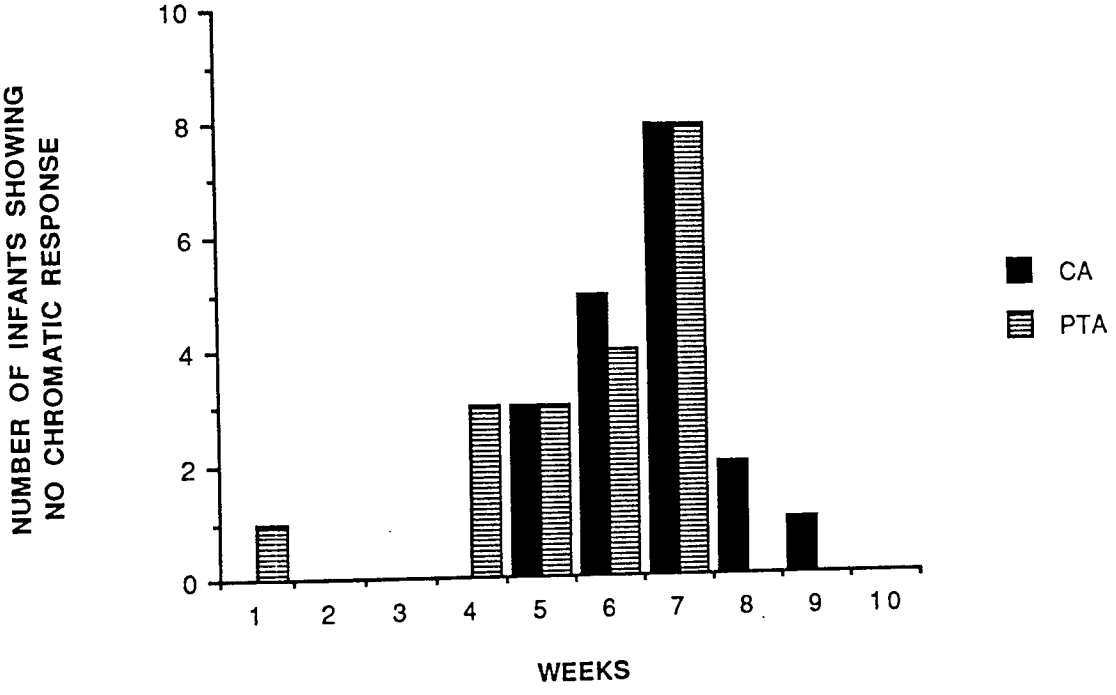


Figure 7.16 Distribution of chronological age, CA (solid bars) and post term age, PTA (striped bars) in weeks, of those infants showing no response to isoluminant chromatic stimuli.

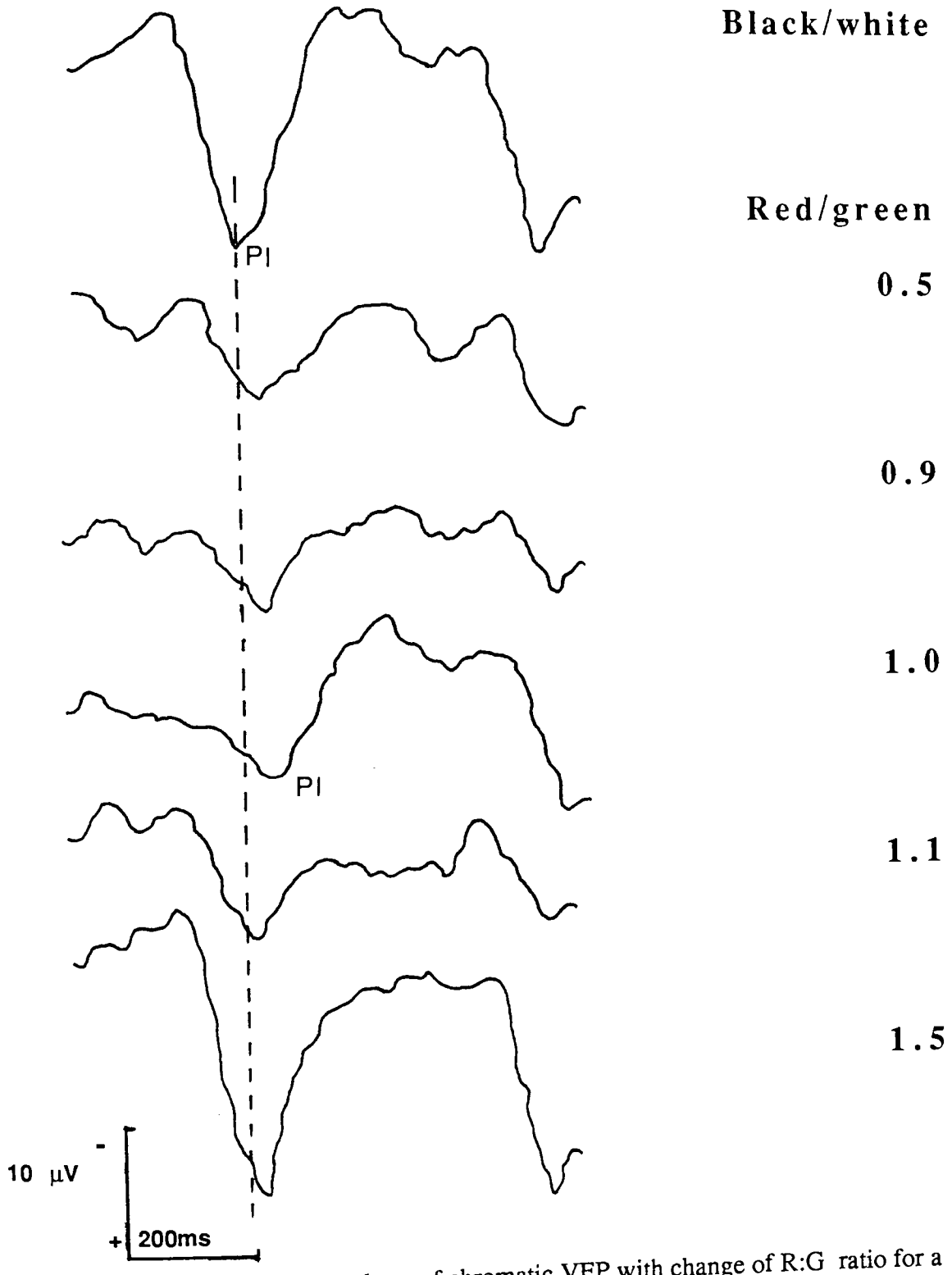


Figure 7.17 Change in morphology of chromatic VEP with change of R:G ratio for a 7 week old infant KB. The achromatic response is shown above for comparison. (Latency and amplitude of P1 are plotted in Figure 7.19)

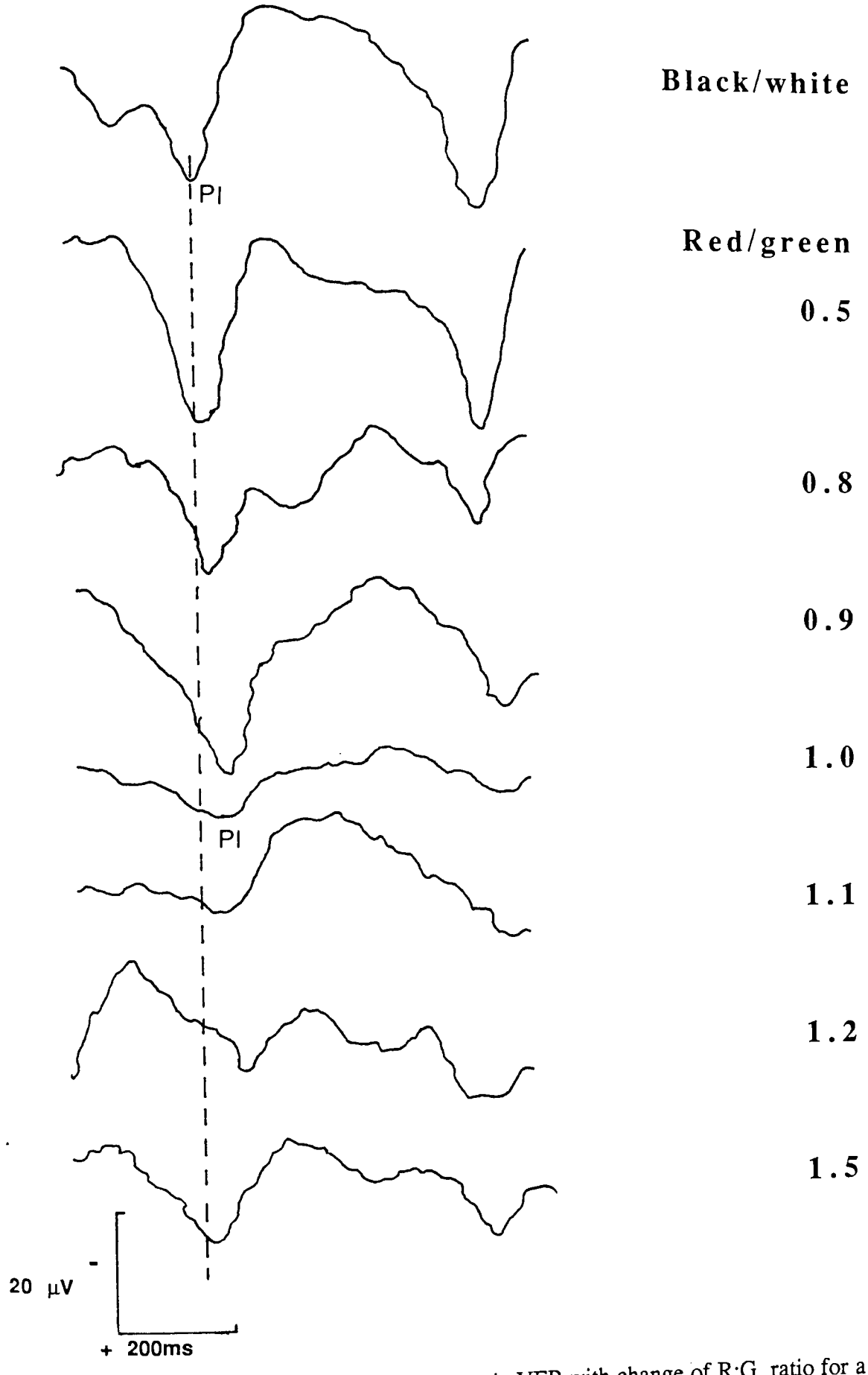


Figure 7.18 Change in morphology of chromatic VEP with change of R:G ratio for a 7 week old infant AG. The achromatic response is shown above for comparison. (Latency and amplitude of P1 are plotted in figure 7.20)

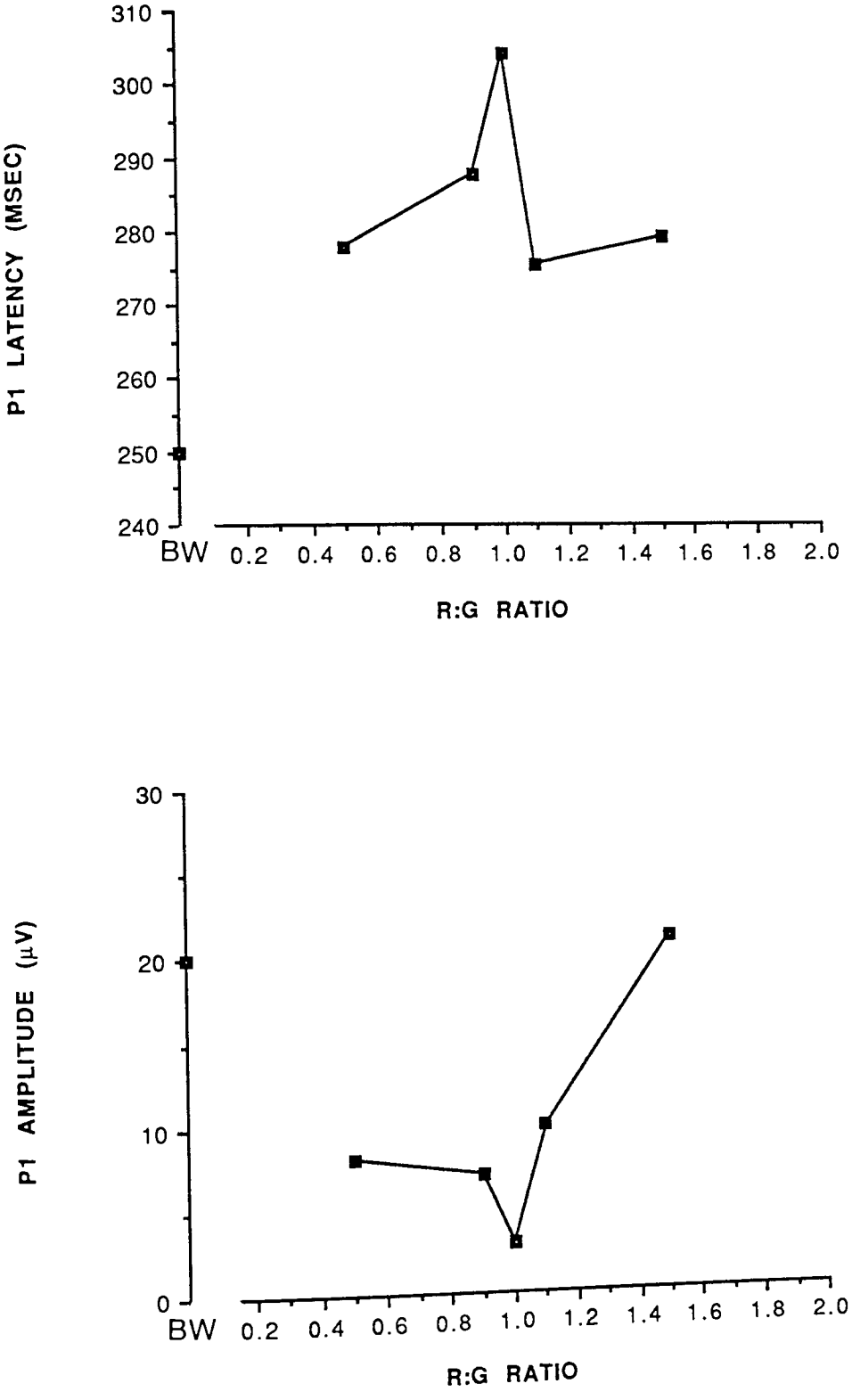


Figure 7.19 Line plot to show latency and amplitude of the P1 component of the chromatic VEP to stimuli of different red/green luminance ratios for a seven week old infant (KB). The achromatic response is included for comparison.

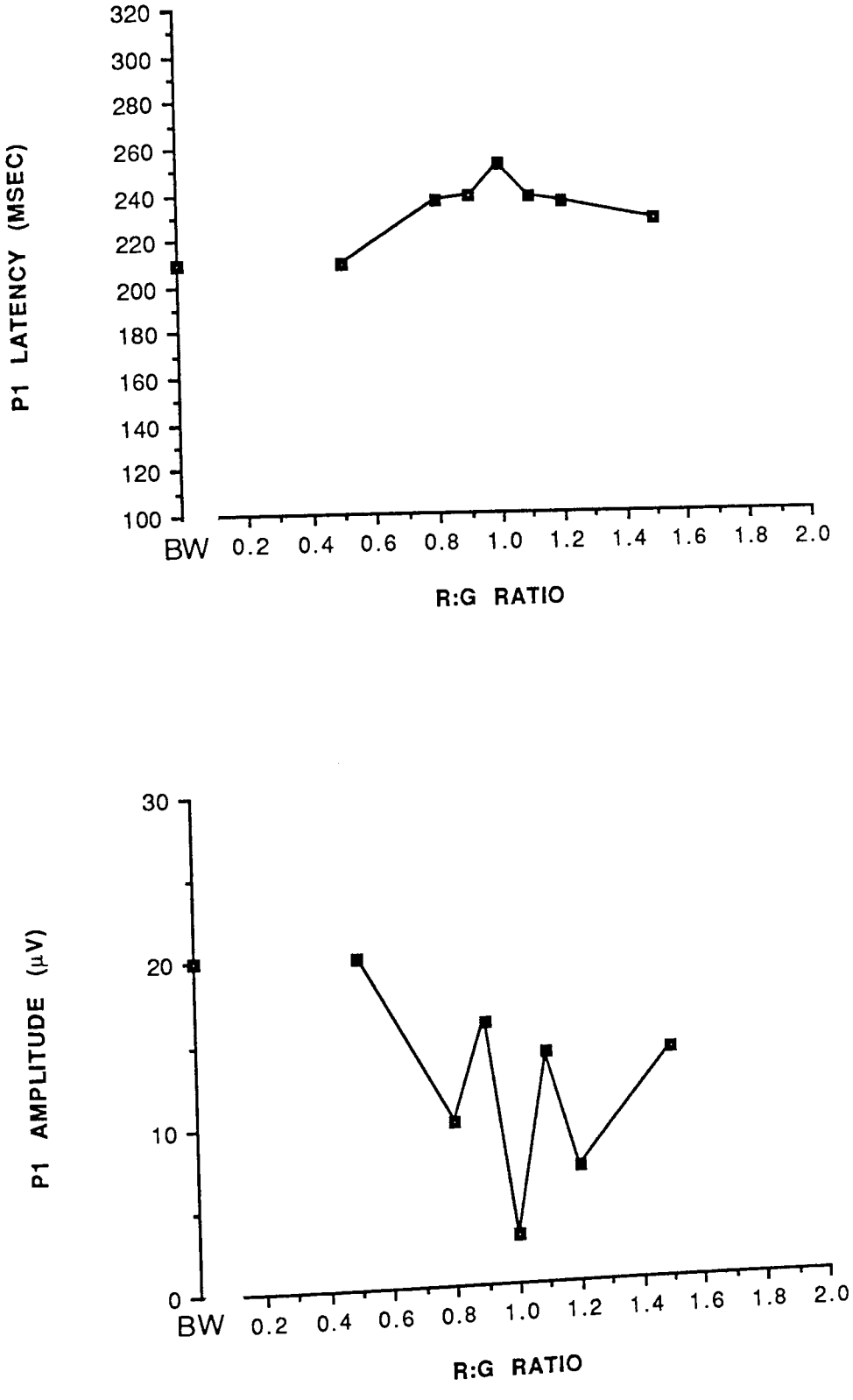


Figure 7.20 Line plot to show latency and amplitude of the P1 component of the chromatic VEP to stimuli of different red/green luminance ratios for a seven week old infant (AG). The achromatic response is included for comparison.

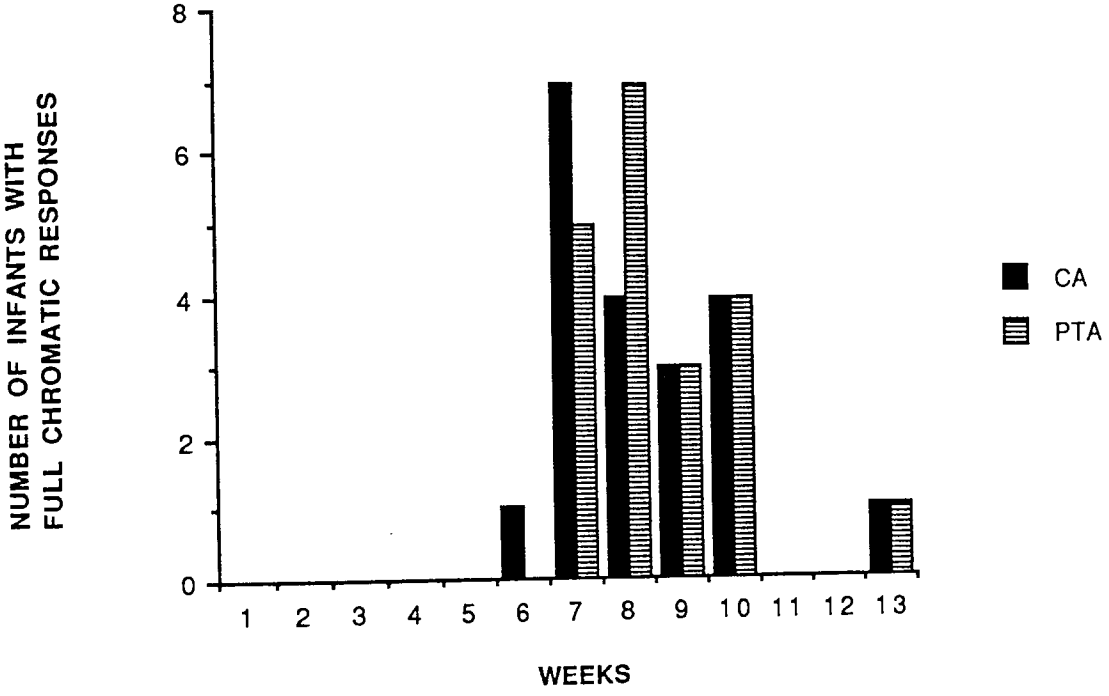


Figure 7.21 Distribution of chronological age, CA (solid bars) and post term age, PTA (striped bars) in weeks, of those infants showing clear responses to all chromatic stimuli.

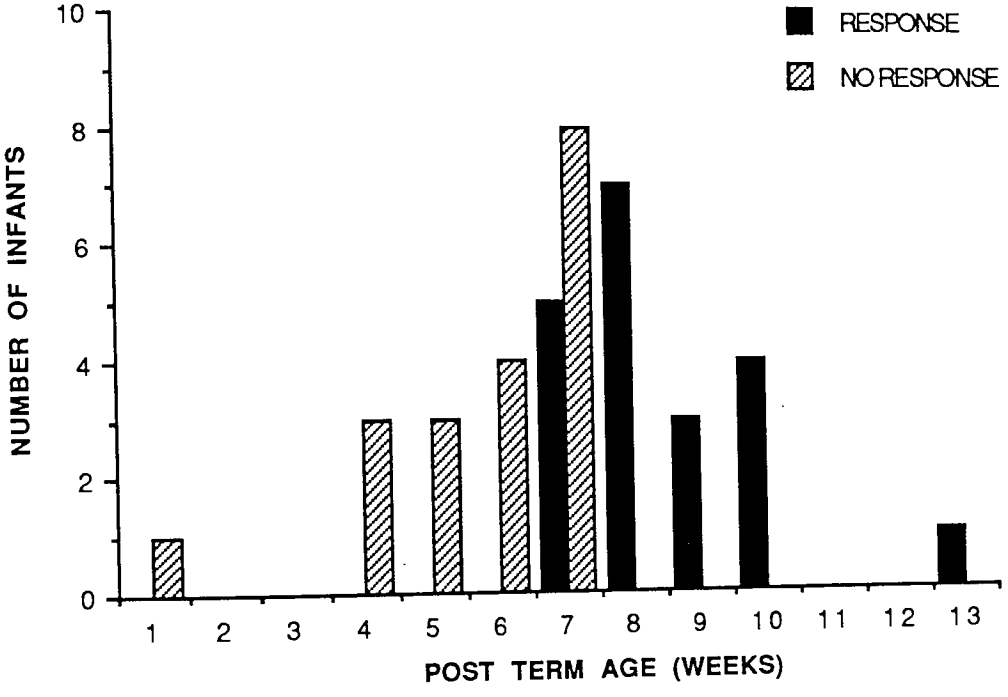


Figure 7.22 Distribution with age (PTA in weeks) of those infants showing responses to all chromatic stimuli presented (solid columns) (N = 20) and those who failed to show a response at one or more red/green luminance ratios (striped columns) (N = 19).

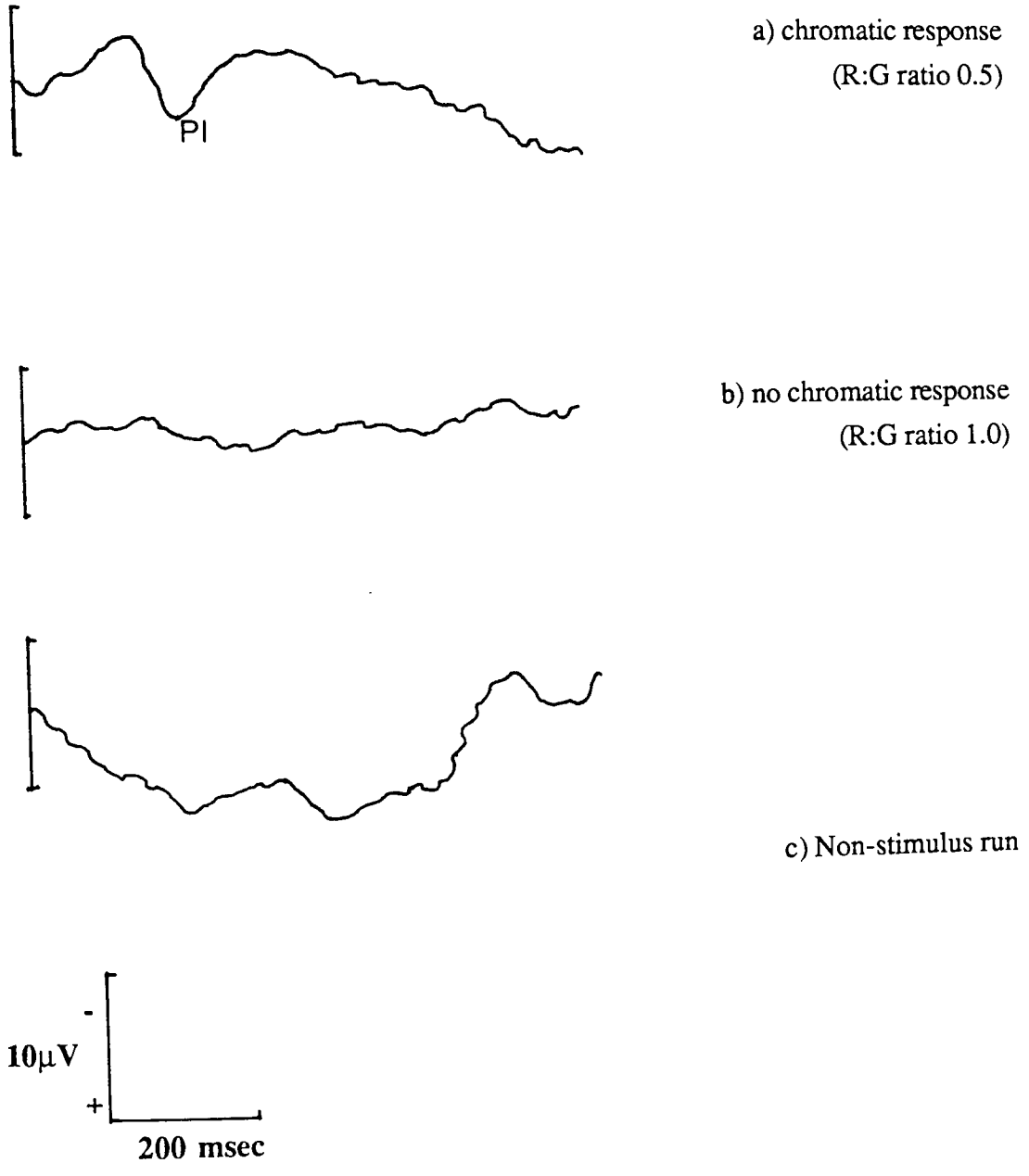


Figure 7.23 Comparison of chromatic stimulus runs producing a) a pattern reversal VEP b) no response and c) a non-stimulus run.

7.12 Development of morphology of the chromatic response

In the adult study, the chromatic pattern reversal VEP was comparable to the achromatic response with an N-P-N waveform (see section 6.6). The latency of the P1 component increased as the luminance ratio of the red and green component checks was reduced towards photometric isoluminance and there was comparable decrease in amplitude of this component over the same luminance ratio range.

In the present study, no isoluminant chromatic VEP could be elicited prior to 7 weeks post term. The response was present in five of the infants at 7 weeks of age appearing as a broad positive wave (P1). The response increased in complexity with age with the P1 component being preceded by a negative (N1) wave by 10 weeks. The presence of a following negative wave (N2) was noted in the isoluminant response of all infants of 10 weeks PTA or above. The mean latencies and amplitudes of the major components, at each age, are given in Table 7.3. The P1 wave was, as in the achromatic response, the most consistent component of the chromatic pattern reversal VEP over the age range examined and the development of the mean chromatic isoluminant response is shown in Figures 7.24 and 7.25.

Table 7.3 Mean latencies (in msec) and amplitudes (in μV) (with standard deviations) of the main components of the isoluminant chromatic VEP for sample groups as defined by post term age (in weeks)

Age	N	N1		P1		N2	
		Lat.	Amp.	Lat.	Amp.	Lat.	Amp.
1	1	-	-	-	-	-	-
4	3	-	-	-	-	-	-
5	3	-	-	-	-	-	-
6	4	-	-	-	-	-	-
7	5	-	-	286±53	1.7±3	-	-
8	7	-	-	214±21	5.5±2	-	-
9	3	-	-	232±59	6.5±5	-	-
10	4	101±8	2.2±3	176±11	9±3	288±45	10±3
13	1	78	2	156	15	206	20

7.13 Relationship between the chromatic VEP and post term age

As shown, no infant less than 7 weeks PTA demonstrated an isoluminant chromatic response at chromatic contrast levels of 90-100%. Five of the thirteen 7 week olds demonstrated a broad P1 of average latency 286 msec and the latency of this decreased with age, across the group, to around 156 msec at 13 weeks. The latency of this P1 component was found to be negatively correlated with post term age at time of recording (

r = 0.654; p< 0.002) (Figure 7.26). Amplitude of the P1 component showed a progressive increase with age from about 3μV at 7 weeks to 16μV at 13 weeks. This change was positively correlated with age (r = 0.76; p< 0.0001) (Figure 7.27). The delay of the chromatic P1 component compared to the achromatic response was not significantly correlated with post term age (r = 0.159;p< 0.50). This was also the case for the relative reduction chromatic P1 amplitude in comparison to the achromatic (r = 0.25; p<0.142).

7.14 Discussion of transient VEP findings

The morphology of the achromatic pattern reversal VEP in adults is generally acknowledged as consisting of a N-P-N complex (Halliday et al. 1977), however, in the youngest infants it is of a much simpler morphology, comparable to that reported by Sokol and Jones (1979) and Moskowitz and Sokol (1983). Initially consisting of only a broad positive wave, P1, seen in premature infants as young as 30 weeks post menstrual age (Grose et al. 1989), the achromatic response becomes more complex as the infant grows older, with the N1 emerging at 6-7 weeks post term and a N2 component after 9 weeks. Similar studies have reported the appearance of N1 at, on average, 8-14 weeks post term (Sokol and Jones 1979) and the emergence of an N2 component at about 2 months (Moskowitz and Sokol 1983).

The morphology of the isoluminant chromatic pattern reversal VEP in adults was similar to that of the achromatic response, i.e. N-P-N (in agreement with other authors; Regan and Spekreijse 1974, Carden et al. 1985, Murray et al. 1987), however, the P100 component shows significant delay and reduction when compared to the achromatic response, again consistent with previous reported findings (Burr et al. 1990, Fiorentini et al. 1991). In the present study, chromatic pattern reversal VEPs could not be elicited from any of the infants younger than 7 weeks of age post term at time of recording with transient chromatic VEPs making a dramatic appearance, around the 7th post term week, throughout the whole sample group. Viewing age of onset in terms of chronological age, the age range of emergence is widened only slightly with again, no infant less than 6 weeks of age demonstrating a chromatic VEP.

The transient chromatic pattern reversal response first appeared at 7-8 weeks post term as a broad positive, P1. The P1, or P100, component is generally recognised as being the most consistent component of the pattern reversal VEP in adults (Halliday et al. 1977) and both full term and premature infants (Sokol and Jones 1979, Moskowitz and Sokol 1983, Wenzl and Brandl 1984, Grose et al 1989) and remained the most consistent component throughout the chromatic studies presented here. An increase in complexity

of the chromatic response occured at about 10 weeks post term with the appearance of, first the N1, then the N2 components and the pattern reversal response became more sharply defined with age. An increase in amplitude of the P1 component was accompanied by a decrease in latency but this component retained a significant delay and reduction in comparison to the achromatic response. This was in agreement with the adult chromatic VEP findings and was, in part, due to the reduced contrast sensitivity of the chromatic system in comparison to the achromatic. Human cones have broad spectral sensitivities which overlap. The long wave sensitive (LWS) cones respond maximally to the red in the stimulus but will also have some response to the green component at a reduced level. The LWS cone modulation to each of the two components of the red/green stimulus will thus cancel out to some degree, producing a smaller overall modulation. The inverse will apply to the medium wave sensitive cones (MWS) (Banks and Bennett 1988). This will serve to reduce the effective contrast of the chromatic stimulus, in relation to the achromatic stimulus, by a factor of 4 to 5 in adults (Mullen 1985) and we may assume it to have a similar effect in those infants whose red/green colour opponent channels are functioning. Reduced contrast of a stimulus is known to increase the latency and reduce the amplitude of the pattern reversal VEP and it is this second observation that has been utilised to determine contrast sensitivity in infants (see section 3.3 for review).

The morphology and development of the chromatic transient pattern reversal VEP in infants has not previously been reported, however, its apparent absence prior to seven weeks post term, is in close agreement with the work of Morrone and colleagues (1990) using steady state stimulation. In line with their work, the amplitude of the VEP fell to zero at , or close to photometric isoluminance for all infants less than 7 weeks post term. Increasing the amplitude of modulation of the red and green component checks to a maximum of 100% at this point did not produce a response. In the pilot study, carried out to assess the technique of isoluminance determination using steady state VEPs, one of the sample, a six week old infant, demonstrated no response at a luminance ratio close to photometric isoluminance while all other stimuli elicited clear responses from this infant. All other infants in this sample group showed clear steady-state responses to all stimuli. Obviously it is difficult to draw firm conclusions from this pilot study alone but this infant was the youngest of the sample (6 weeks post term) and in view of the transient VEP findings, it is perhaps not surprising that this type of result was acquired from this infant using steady-state stimulation.

Both the results of the present study and those reported by Morrone and co-workers (1990,1993) are in contrast to the work of Allen and co-workers (1990,1993) who reported the presence of chromatic steady state VEPs in infants of 2 weeks of age. This

VEP, however may be the result of chromatic aberration producing luminance contrast within a stimulus that is thought to be isoluminant. The longitudinal chromatic aberration of the eye produces different points of foci within the eye for different colours, leading to an inequality in the amount of accommodation required to focus each component of the stimulus. Thus causes differential defocus of the red and green checks or bars, affecting the relative contrast of the chromatic components and hence inducing a luminance contrast artefact. The effect of chromatic aberration increases with spatial frequency and the stimuli of Allen et al. were slightly higher (0.8 cpd) than those of the present or Morrone's study (0.175and 0.1 cpd respectively). Although, in adults, a spatial frequency of 0.8 cpd may be considered low enough to make the effect of chromatic aberration negligible (Flitcroft 1989), it may be that for an infant, the aberrations are larger and thus effective at this spatial frequency. This would thus produce artefactual luminance responses to what is considered a chromatic stimulus. The present study and that of Morrone et al. (1990, 1993) used very low spatial frequencies with a view to overcoming this chromatic aberration artefact and it may thus appear that, where no response could be recorded one could be certain of no occurrence of luminance artefacts.

In order to confirm the results of the cross sectional study and the morphological development of the chromatic response, a longitudinal study of a sample group of infants was undertaken.

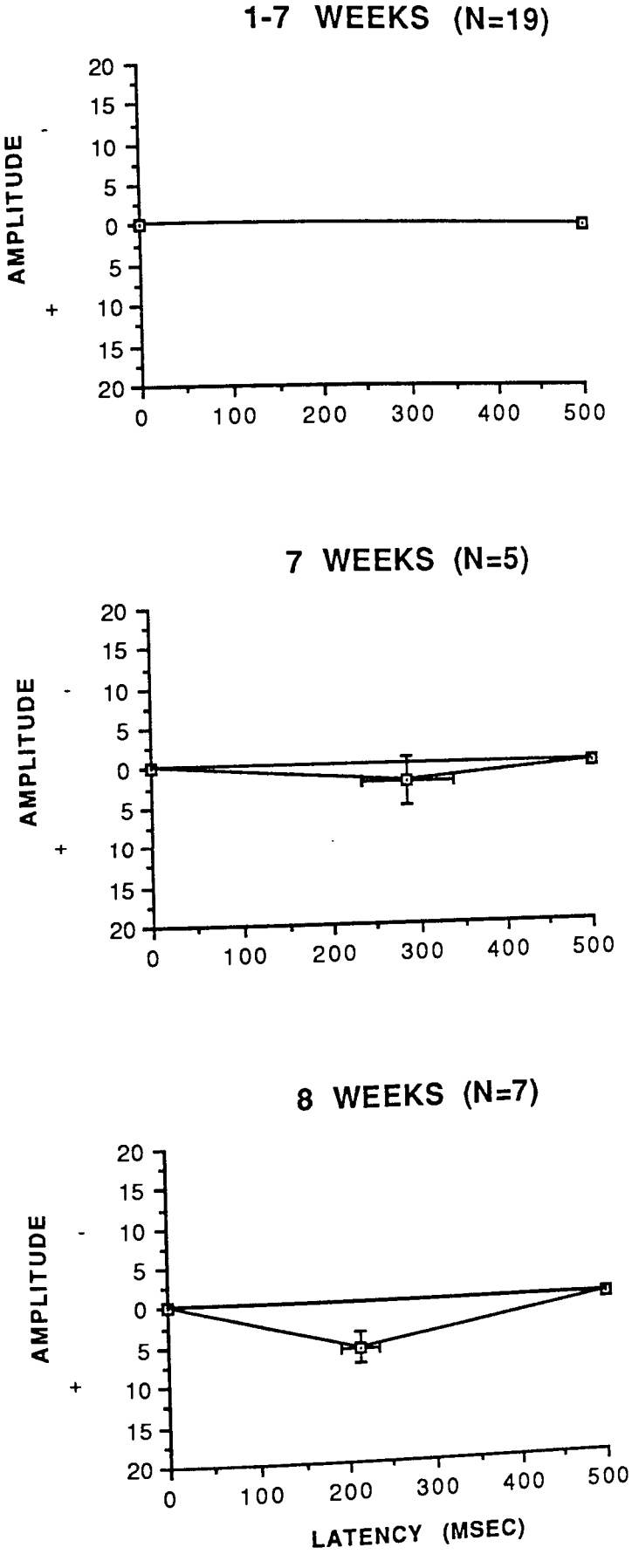


Figure 7.24 Schematic representation of mean VEP responses to isoluminant chromatic stimuli for 1 to 8 week old sample groups

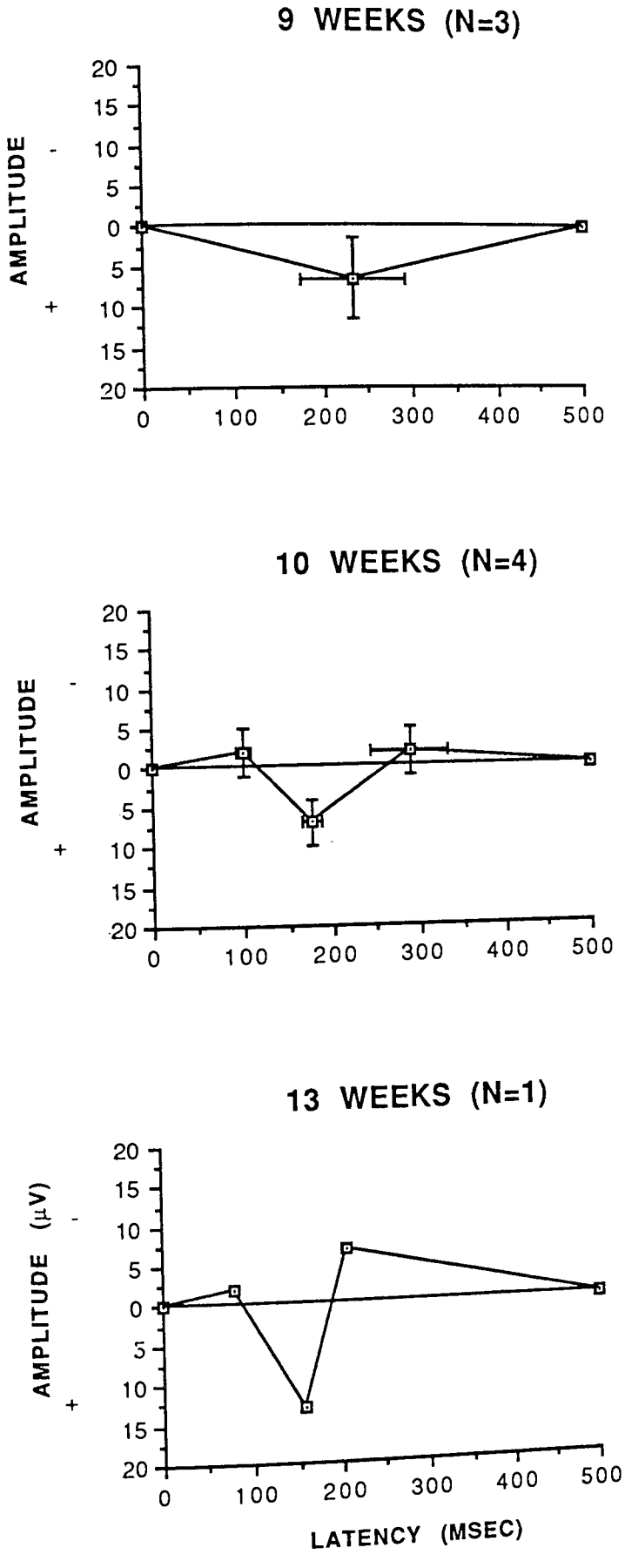


Figure 7.25 Schematic representation of mean VEP responses to isoluminant chromatic stimuli for 9 to 13 week old sample groups

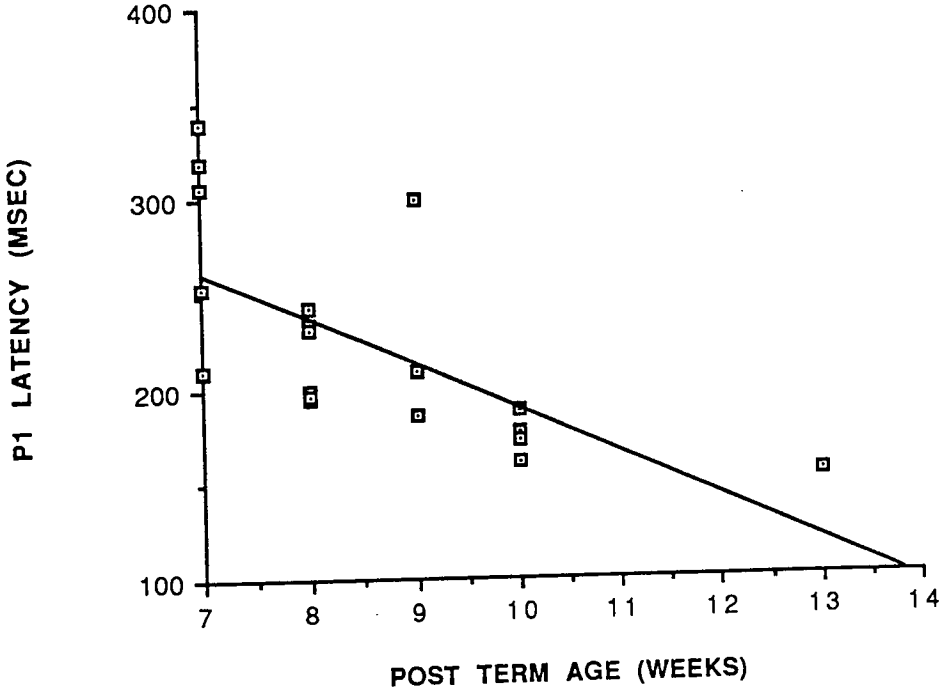


Figure 7.26 Graph to show relationship between latency of the chromatic pattern reversal P1 component and post term age. The formula for the regression line is $y = -23.57x + 425$; $r = 0.654$; $p < 0.002$; d.f. 19.

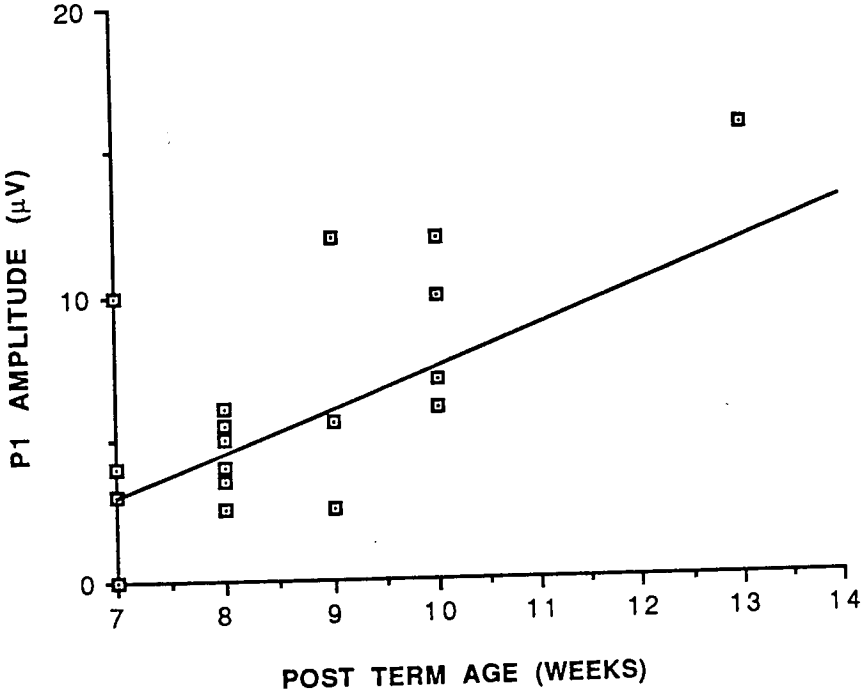


Figure 7.27 Graph to show relationship between amplitude of the chromatic pattern reversal P1 component and post term age. The formula for the regression line is $y = -1.49x - 7.49$; $r = 0.76$; $p < 0.0001$; d.f. 38.

CHAPTER EIGHT
DEVELOPMENT OF THE CHROMATIC VISUAL EVOKED POTENTIAL: LONGITUDINAL STUDY

8.1 Introduction

In the previous study isoluminant chromatic VEPs were found to show a sudden onset at 7-8 weeks post term. In order to assess the validity of this finding a longitudinal study was undertaken. This also allowed the investigation of development of morphology of the response.

8.2 Subjects

Infants who had initially taken part in the main study and were 7 weeks post term age (PTA) or less at the time of recording were invited to return for one to two follow-up visits at two weekly intervals. The same transport arrangements were provided and all fourteen families approached agreed to take part in this follow-up study. Infants taking part and the ages at which they were seen are given in Table 8.1. In summary, three infants attended for a total of two visits and the other eleven attended three times.

Table 8.1 Subjects participating in the longitudinal study

Infant	Sex	CA (weeks)	PTA (weeks)
LS	F	6,8,10	4,6,8
LL	M	7,9,11	5,7,9
GEMH	F	6,8,10	6,8,10
CP	M	6,8,11	6,8,11
RG	F	6,8,11	6,8,11
RM	M	7,9,11	7,9,11
MFA	F	7,9,14	7,9,14
KYB	F	9,11,16	7,9,14
CA	F	7,9,13	7,9,13
KL	M	7,9,16	7,9,16
SON	F	8,10,16	7,9,15
MD	M	5,12	5,12
DJ	M	7,9	7,9
SH	M	7,9	7,9

8.3 Recording parameters

Recording parameters and protocol were identical to those used in the main study (see section 7.5).

8.4 Longitudinal development of the achromatic pattern reversal VEP

As in the main study, the achromatic response of the youngest infants took the morphology of a single major positive component (see section 7.7). By 7-8 weeks of age, the preceding negative (N1) began to emerge and the P1 component became more clearly defined. The presence of an N2 component was noted in four of the infants by nine weeks PTA with only one infant not demonstrating this component by 14 weeks. Figure 8.1 shows the development of the achromatic pattern reversal response for one infant. The latency of the consistent P1 component decreased with age and for each infant in the present study this change was found to be significantly correlated with age. The amplitude of the same component tended to increase with age across the whole sample group.

8.5 Longitudinal development of the chromatic pattern reversal VEP

As demonstrated in the previous study, the chromatic response showed an increased latency and reduced amplitude with respect to the achromatic response. This change in morphology increased as the luminance ratio of the component red and green checks approached photometric isoluminance (i.e. R:G = 1.0).

For all of those infants less than 7 weeks PTA at time of recording, no VEP could be produced with a red/green stimulus at a luminance ratio of, or close to 1.0. Under these circumstances, the amplitude of modulation (chromatic contrast) of the stimulus was increased to 100% with no apparent difference in response. However, once these infants had passed their 7th week, all demonstrated clear and repeatable responses to all chromatic stimuli used. Figures 8.2 and 8.3 show the development of the averaged response to an isoluminant stimulus for two infants with Figures 8.4 and 8.5 showing the corresponding change in latency and amplitude of the P1 component with R:G ratio and age at 3 separate visits. Latency of the P1 component showed an increase, with corresponding amplitude decrease, as the luminance information in the stimulus was reduced. It can be clearly seen that prior to the 8th post term week, no response can be recorded at isoluminance producing a corresponding zero amplitude.The P1 latency decreased, and amplitude increased with post term age.

Two of the fourteen infants showed clear repeatable responses to all of the red/green stimuli used during their 7th week PTA and all infants older than this showed clear

responses to all stimuli. Figure 8.6 shows the distribution of the presence of an isoluminance chromatic response with age. It can be seen that no response to isoluminant chromatic stimuli could be recorded from any of this group prior to the 7th post term week and all infants demonstrated chromatic responses after this age.

8.6 Development of morphology of the chromatic response

The isoluminant chromatic response initially appeared in all infants older that 7 weeks PTA, as a broad positive wave (P1) with latencies of between 200 and 300 msec. The P1 became more defined with age and a negative component was present in two of the infants by the 11th week PTA. Two other infants demonstrated the emergence of a following negative wave (N2) at 14 weeks, however this was not consistent in all infants by this age with one continuing to show a response of only a simple positive waveform. These changes in morphology are consistent with those reported in the previous chapter.

8.7 Discussion of longitudinal transient VEP findings

All infants taking part in this longitudinal study demonstrated comparable achromatic and chromatic pattern reversal transient VEPs to those previously reported in the preceding chapter. Again, achromatic responses in the youngest infants showed a simple broad positive morphology with an increase in complexity with age as both early and late negative components (N1 and N2) begin to emerge by 7-8 weeks and 9 weeks respectively. These findings are in close agreement with the reported literature (Sokol and Jones 1979, Moskowitz and Sokol 1983).In the study of the chromatic response, no chromatic VEP could be elicited from twelve of the fourteen infants at or before their 7th week of life using isoluminant stimuli. This result is in agreement with the previous study and the reported of Morrone and co-workers (1990,1993). All fourteen infants demonstrated clear, repeatable chromatic responses after the 7th post term week. Viewing the presence of the chromatic response in terms of chronological age still shows the age of onset to be spread over a slightly wider age of 7-10 weeks.

The emergence of a chromatic VEP at 2 months of age appears to be consistent with the ability of infants to discriminate broadband red and 550 nm green from yellow as demonstrated behaviourally by Hamer and co-workers (1982). Visual performance, measured electrophysiologically, is usually higher than that measured behaviourally (e.g contrast sensitivity, visual acuity). This is possibly due to the visual evoked potential being solely a reflection of activity within the cortex whereas behavioural measures also depend on the visual and motor areas, thus being a truer representation of what the infant actually responds to. This implies that information in the visual cortex is lost in the higher cortical areas. It is perhaps more likely however, that response criteria and

motivation are uncontrollable in infants and this may reduce the apparent infant sensitivity if measured behaviourally.

In order to determine whether discrimination of our chromatic stimulus could be demonstrated behaviourally at 2 months, a further study was undertaken.

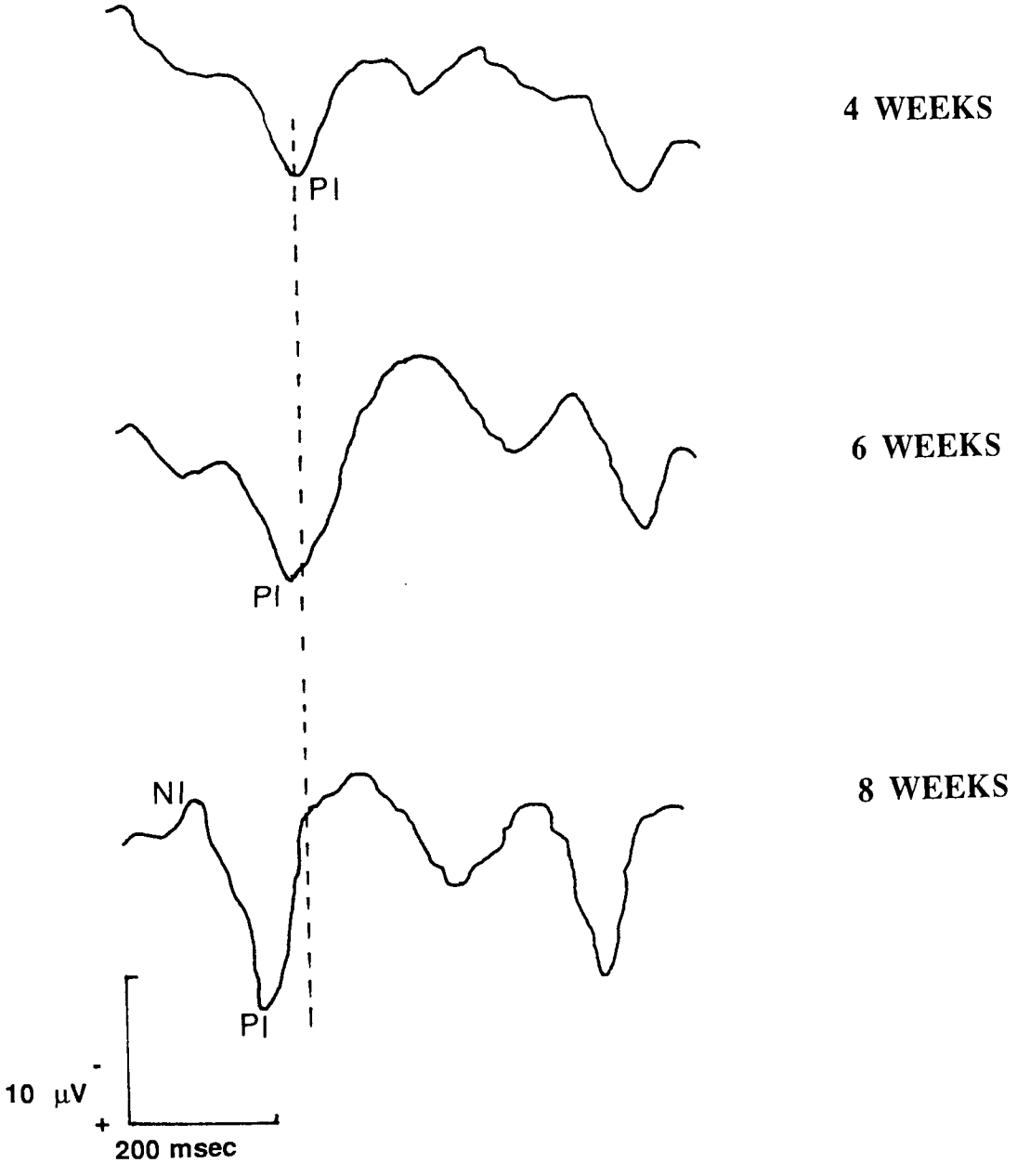


Figure 8.1 Development of the achromatic pattern reversal response of infant LS over a four week period. (Corresponding P1 latency and amplitude of the achromatic response are shown in Figure 8.4)

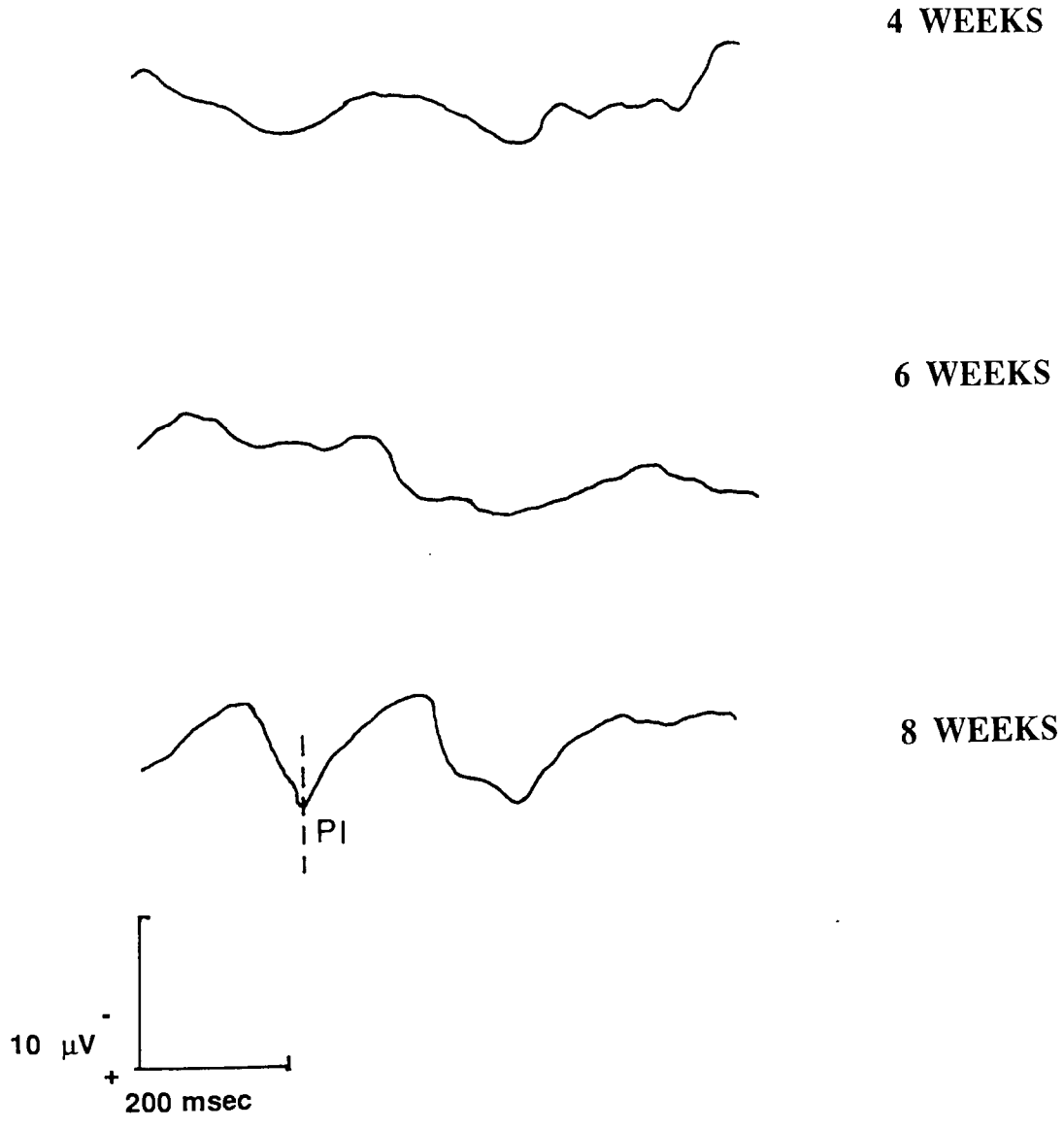


Figure 8.2 Development of the chromatic pattern reversal response of infant LS over a four week period. (Corresponding P1 latency and amplitude of the chromatic responses are shown in Figure 8.4)

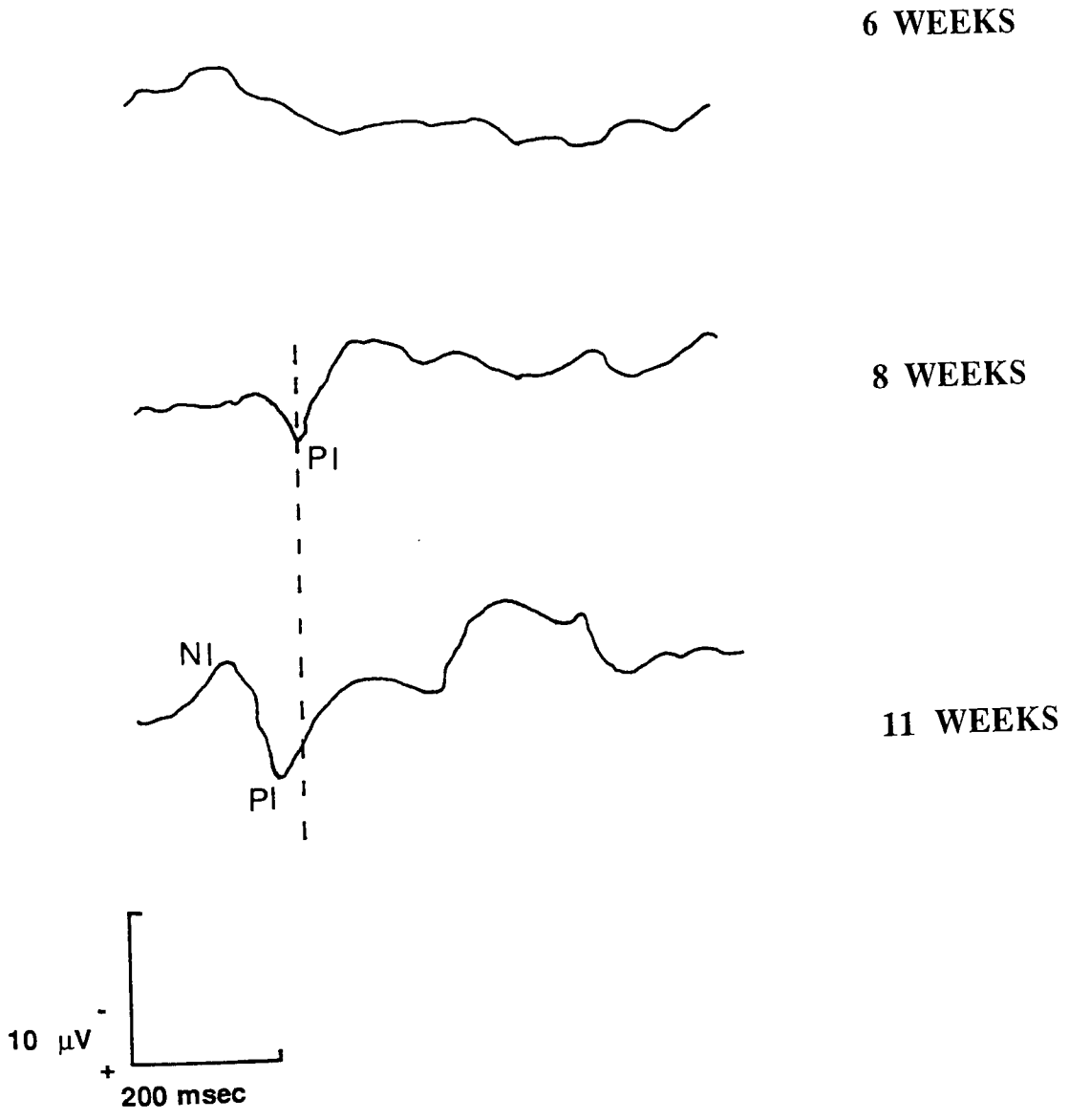


Figure 8.3 Development of the chromatic pattern reversal response of infant RG over a four week period. (Corresponding P1 latency and amplitude of the chromatic responses are shown in Figure 8.5)

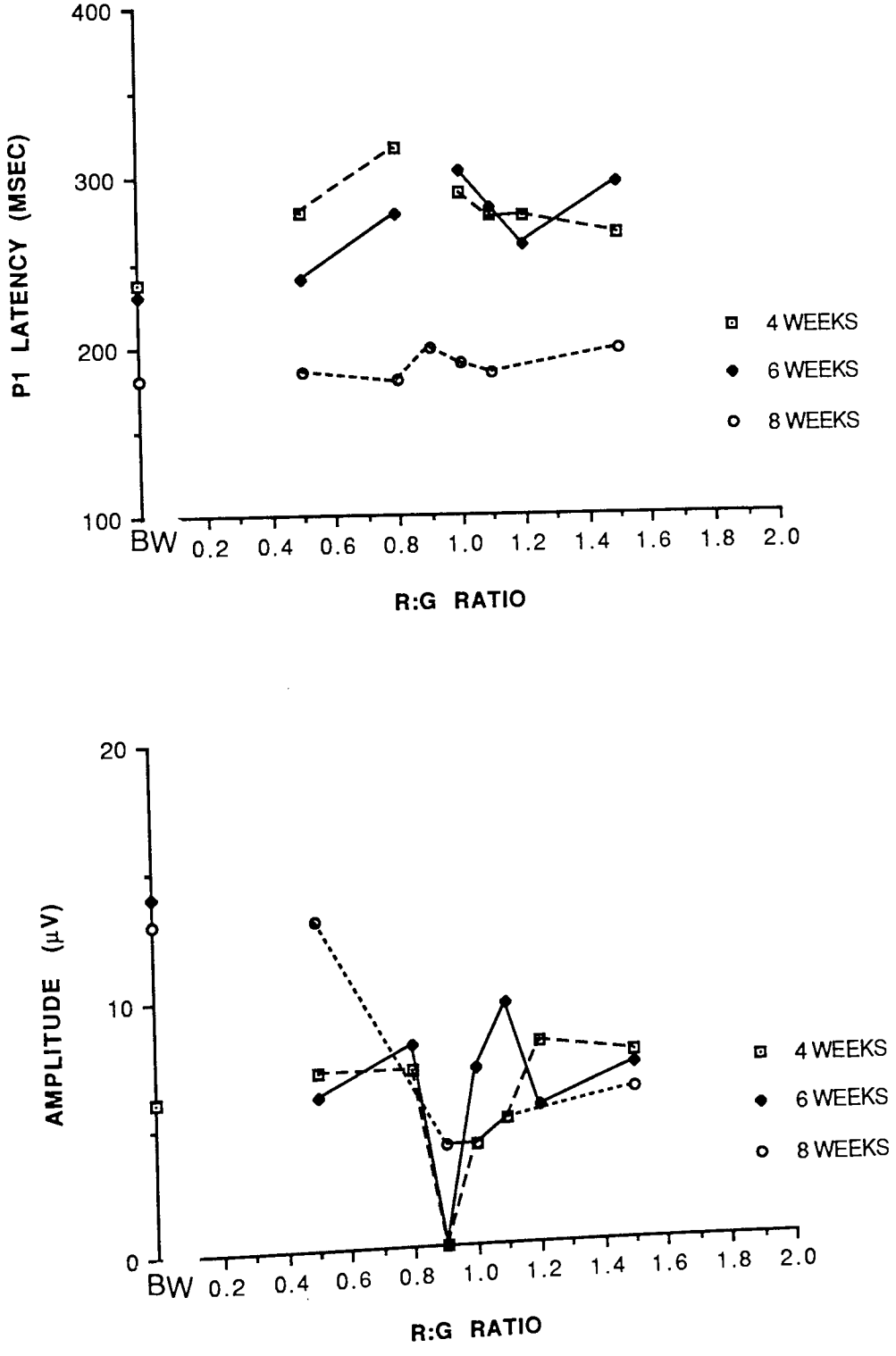
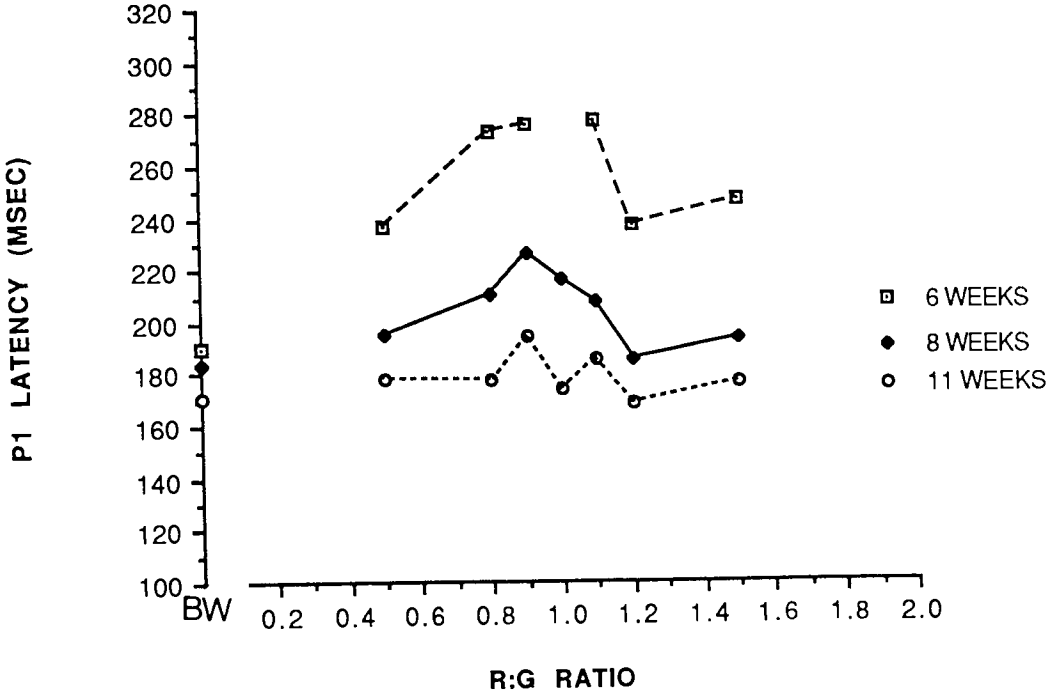


Figure 8.4 Development of the latency and amplitude of the P1 component of the chromatic response for one infant LS at three separate visits. The achromatic P1 component latency is included for comparison



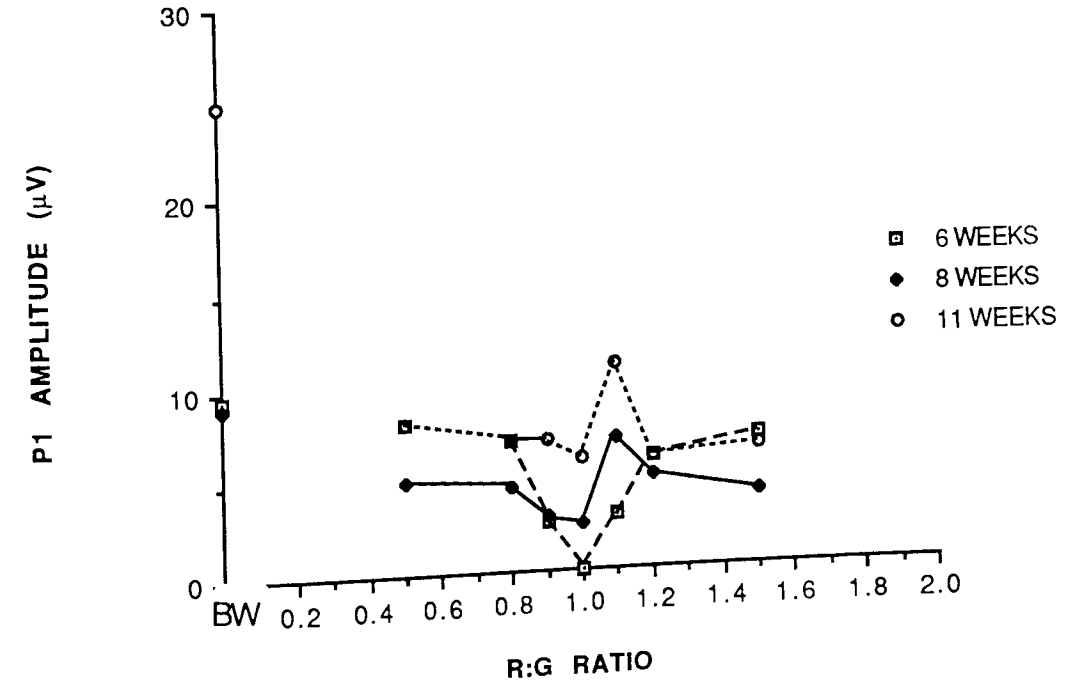


Figure 8.5 Development of the latency and amplitude of the P1 component of the chromatic response for one infant RG at three separate visits. The achromatic P1 component latency is included for comparison

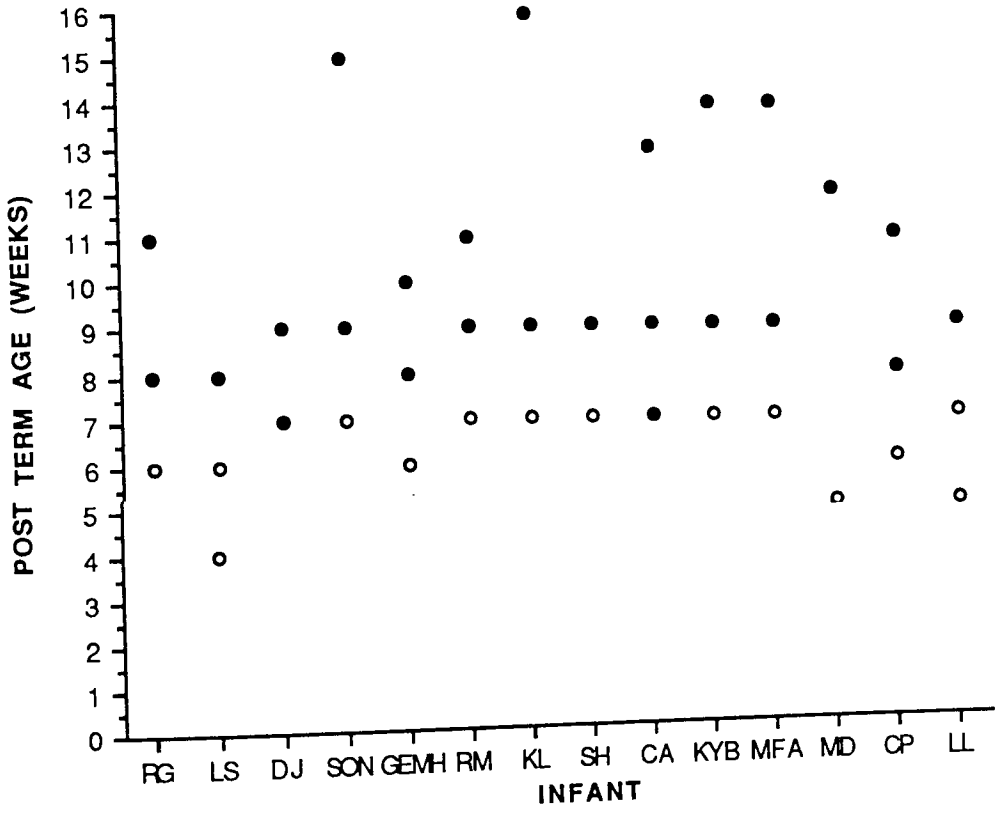


Figure 8.6 The distribution of absence (open circles) or presence (filled circles) of isoluminant chromatic responses at post term age (weeks) of assessment for sample of 14 infants.

CHAPTER NINE
BEHAVIOURAL STUDY

9.1 Introduction

The transient chromatic pattern reversal VEP appears to demonstrate a dramatically defined age of onset at 7 weeks post term and this may be indicative of a sudden onset of chromatic discrimination. In a follow-up study, the age at which discrimination of the chromatic stimulus could be demonstrated was assessed behaviourally.

9.2 Subjects

Seven subjects (five male,two female) were recruited from the sources previously described (see section 7.2) and two of these infants were seen for one further follow-up appointment. The exclusion critieria described in section 7.3 applied. Table 9.1 gives details of post term (PTA) and chronological age (CA) (post natal) age at time of assessment.

Table 9.1 Subjects taking part in behavioural study

Infant	Sex	CA (weeks)	PTA (weeks)
AS	M	8	7
JC	M	6	7
MER	F	8	8
CFW	M	6	6
GMC	F	6	8
KS	M	7,9	6,8
DP	M	7,8	7,8

9.3 Stimulus

Stimuli were produced by the Venus system as previously described (see section 5.5.1). The stimulus subtended a visual angle of 32° x 32° when viewed at 37 cm. This was split in half vertically to produce two screens of 32° x 14° separated by 2°. The patterned stimuli were composed of red and green horizontal sinusoidal gratings presented 180° out of phase with no temporal modulation. Each grating had a spatial frequency of 0.25cpd and hence each bar subtended 2° when viewed at 37 cm. The amplitude of modulation of the gratings was constant at 100% and the mean luminance of the screen was maintained at 10 cdm^{-2}. The individual luminances of the red and green bars could be varied relative to one another to give five stimuli of a range of R:G ratios as used in the previous studies

(i.e. 0.8,0.9,1.0,1.1,1.2). The other half of the screen was composed of a uniform field of the same luminance and chromatic composition as the gratings, producing a neutral orange appearance. The stimulus generator and observer were hidden behind a large black screen with two apertures, one for the stimulus and one for the observation of the infant.

9.4 Procedure

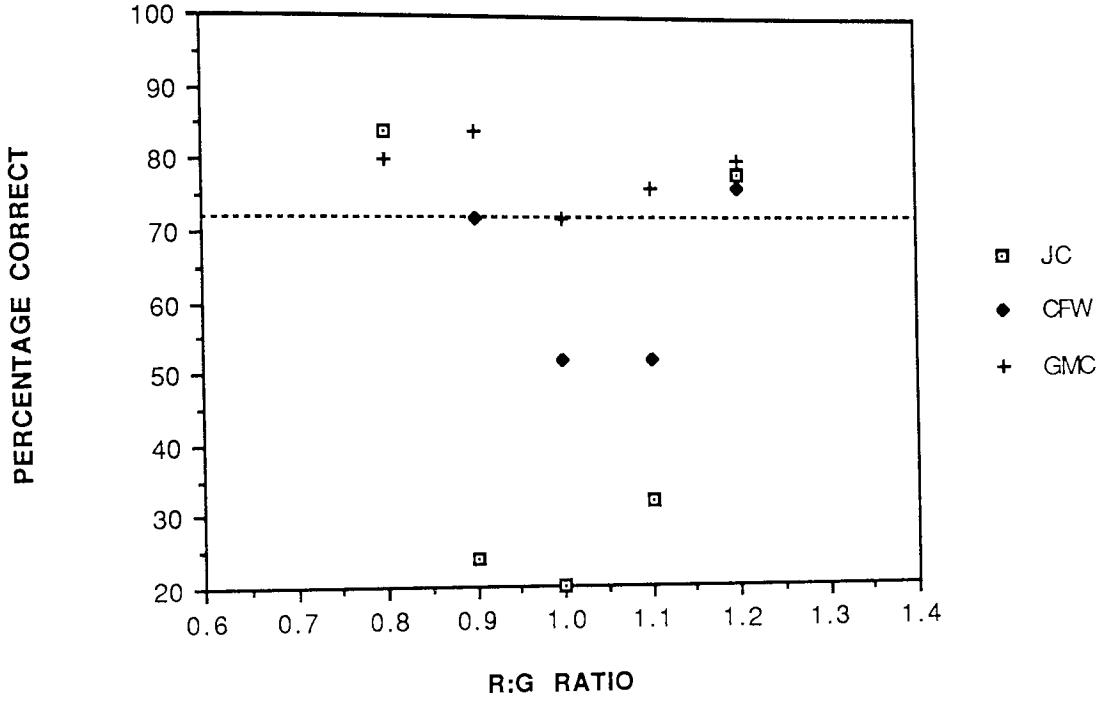
In order to assess the discrimination of a chromatic stimulus, a method of constant stimuli preferential looking technique was employed (Teller 1979). All sessions took place in a darkened room. The infants sat 37 cm away from the screen on a holder's lap. The observer could not see the stimulus or the holder's face. The holder was instructed to keep the infant facing the centre of the screen throughout the test and the infants' attention was attracted to the centre of the screen by a moving target and tapping on the screen prior to the presentation of each stimulus.

The grating appeared randomly on the left or right half screen. The observer was required to estimate the position of the grating based solely on the behaviour of the infant, i.e. head and eye movements and fixation. Twenty-five trials were carried out for each of up to five of the red/green luminance ratios. All infants were initially assessed with the photometric isoluminant grating (i.e.R:G =1.0) then with the other four stimuli in random order. The number of correct position determinations by the observer were scored as a percentage and recorded.

9.5 Results

Scores for 25 trials at each of five R:G luminance ratios were successfully acquired from three of the five infants who attended for one visit. The other two infants, attending once, completed four luminance ratios. Infant KS completed four luminance ratios and infant DP completed five ratios at both visits. The time taken to achieve a full data set varied considerably between infants with some sessions lasting up to three hours. Allowing the infants to bottle feed whilst watching the screen was beneficial but this produced a short time window in which to carry out testing. Due to the slightly higher number of trials used in this study than those of Teller and colleagues (Peeples and Teller 1975, Teller 1979) a criterion of $\geq$ 72% was accepted as the minimum level of discrimination. The percentage correct scores for the five infants seen on one occasion are shown in Figure 9.1. It can be seen that the percentage score falls below the limit of 72% for infants JC, CFW and AS, whereas infants MER and GMC score at above chance for all luminance ratios presented.

A.



B.

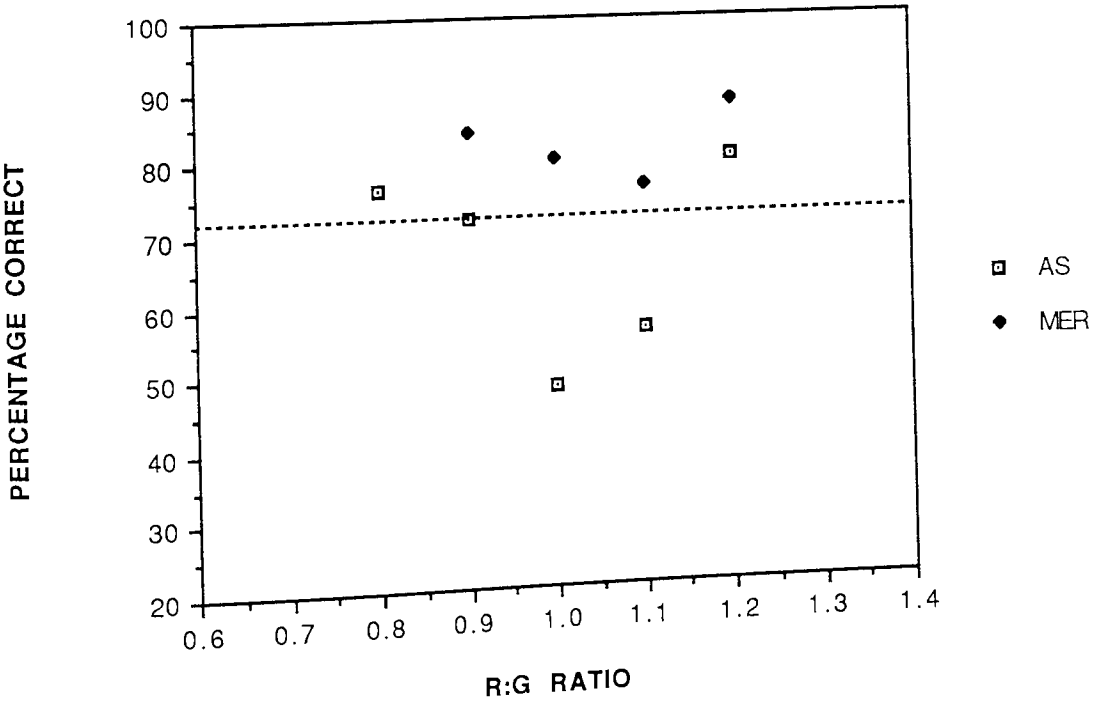


Figure 9.1 Percentage correct preferential looking scores for stimuli of different red/green luminance ratios for A) infants JC, CFW and GMC and B) infants AS and MER ; each assessed on one occasion. The dotted line indicates the minimum score accepted as detection of the stimulus.

9.6 Follow-up study

Two of the infants whose scores fell below chance for two or more luminance ratios on the initial visit returned for a second appointment one to two weeks later. The percentage correct scores for the infants seen on two occasions are shown in Figure 9.2. It can be seen that both infants scored at chance for two or more stimuli at the first visit and the scores improved to above chance for all stimuli at the second visit.

9.7 Discussion

Peeples and Teller (1975) developed the procedure used in the present study and utilised it to determine the discrimination of a red light from a white screen by young infants. They assumed that because the brightness difference between the background and stimulus was varied in steps less than 0.1 log units that the infant must at some point be presented with a brightness pairing in which luminance cues had been eliminated. This was due to the infant's insensitivity to < 0.1 log unit brightness differences. If the infant behaved at above chance for all brightness pairings then it must be making discriminations based solely on the wavelength information i.e.demonstrating the ability to discriminate colour.

Applied to the present study, five of the infants tested, showed below chance performance for at least two of the red/green luminance ratios used, whereas the other four demonstrated above chance performance at all luminance ratios. Indeed, the two infants who returned for a follow-up visit demonstrated above chance performance at the second session when they had not done so on the first session. Above chance performance is accepted as the infants' ability to detect the stimulus even when presented with a brightness match, when luminance cues should be eliminated and we can thus presume that the infant is able to detect the stimulus based purely on the chromatic information within it. In the cases where the score of correct trials falls to chance, it would appear that the infant fails to detect the stimulus when presented with a brightness match i.e. if luminance cues have been removed.

Figures 9.3 and 9.4 show the distribution of those infants scoring above chance at all red/green luminance ratios and those failing to detect the stimulus for at least one red/green ratio with respect to chronological and post term age in weeks. If an above chance score is taken as the ability to process chromatic information within the stimulus, i.e. the presence of some chromatic discrimination, it can be seen from this sample study that only one of the infants demonstrated this ability at 6 weeks post natal age and only one infant failed this task at 8 weeks. If adjustments are made for post term age, all

infants of 7 weeks or less fail to detect the stimulus whereas all infants above this age show chromatic discrimination using this technique.

Making the adjustment for gestational age produces a post term age plot (Figure 9.4B) which supports the results of the previous electrophysiological studies. Seven weeks post term again appears to be a transitional age at which the ability to process wavelength information emerges. However, the use of such a small sample of infants may cast doubt upon the validity of this study. The narrow age range studied allows no indication of the chromatic performance of infants older and younger than this range. Although being in support of the our previous findings, it does not produce substantial evidence of onset of chromatic discrimination in its own right. It is however in line with the numerous studies on the development of colour vision in infants by Teller and colleagues (for review see section 3.14).

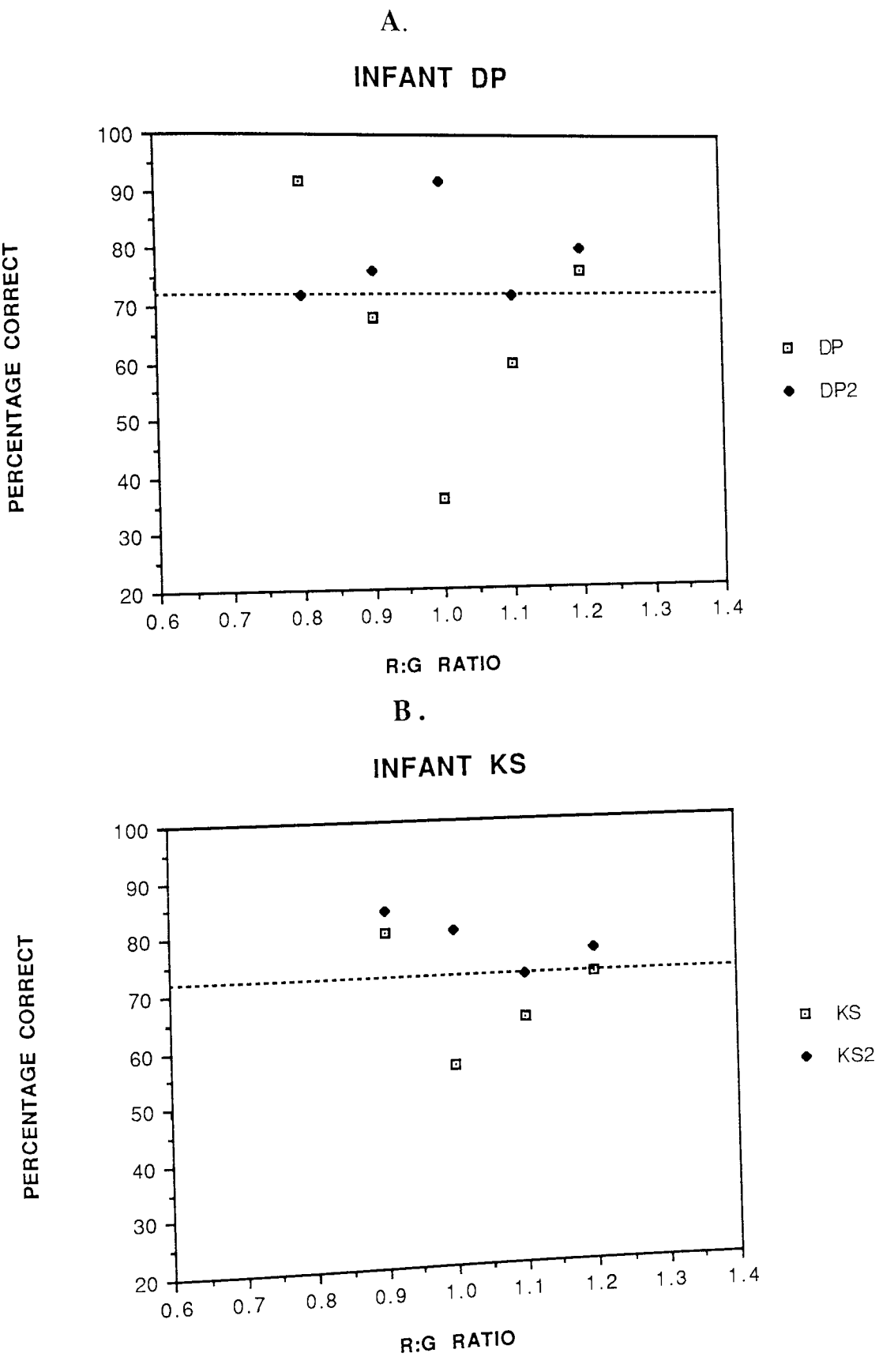
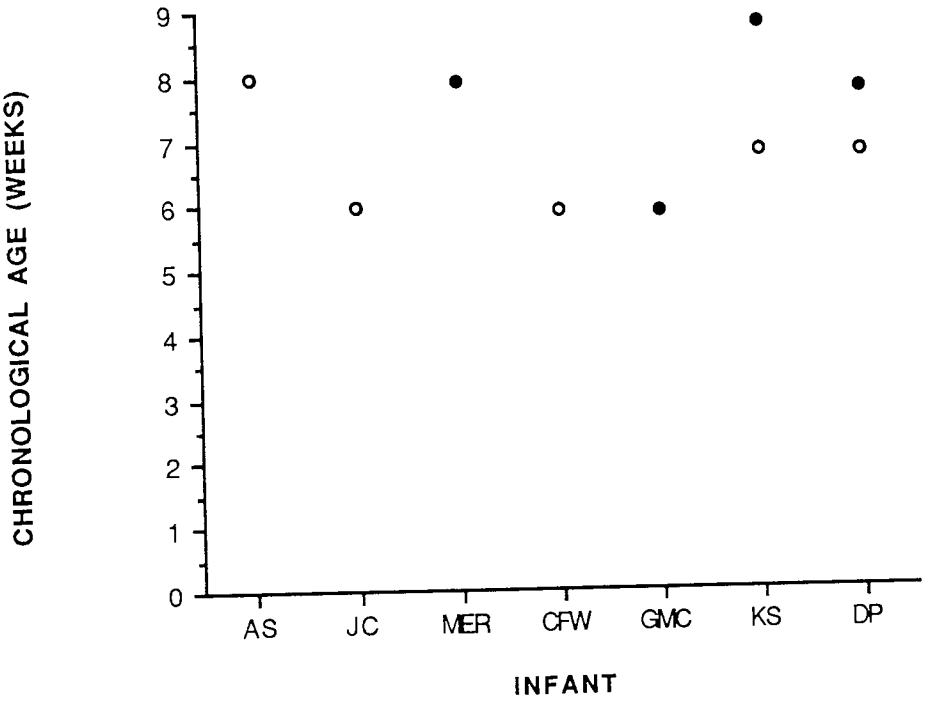


Figure 9.2 Percentage correct preferential looking scores for two infants A) DP and B) KS seen on two separate occasions (DP:visit 1; DP2: visit 2; KS:visit 1; KS2: visit 2).

A.



B.

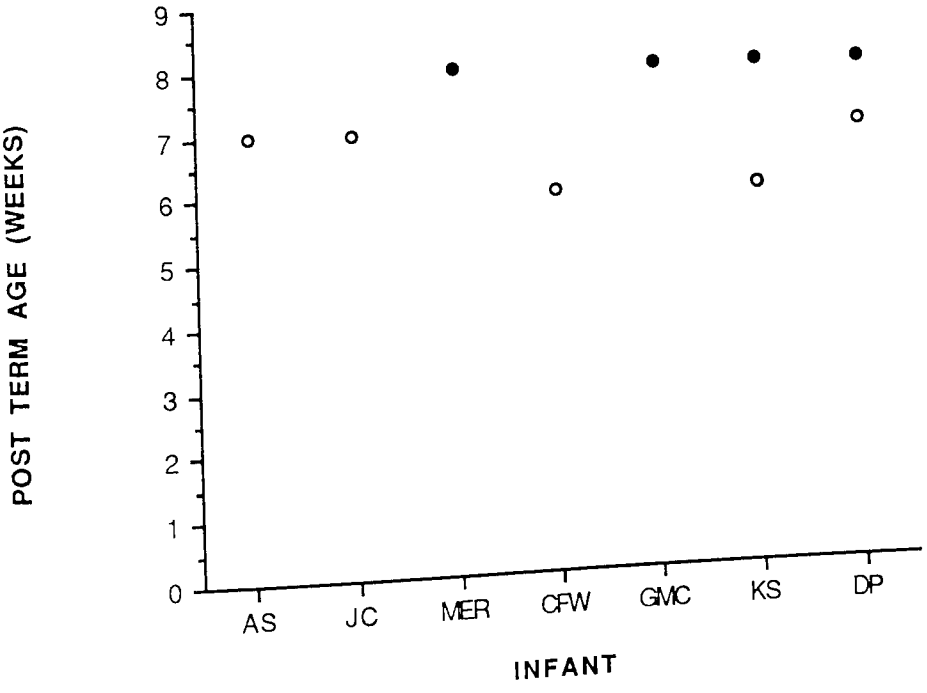
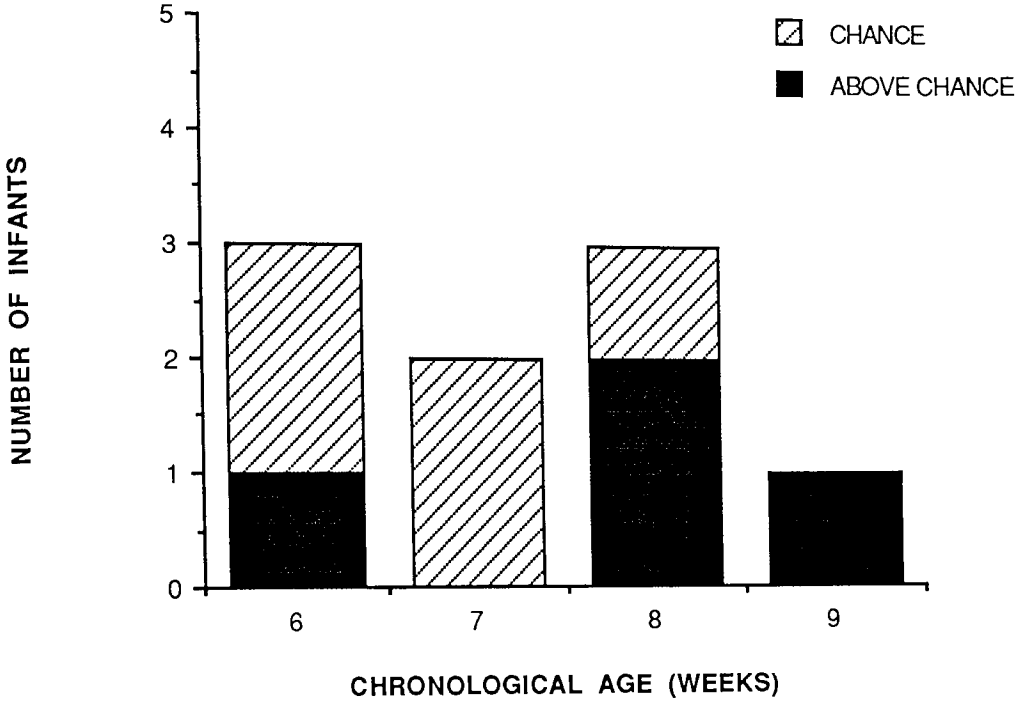


Figure 9.3 Visits showing performances above (filled circles) and at chance (open circles) for two or more red/green ratios in terms of A) chronological age (weeks) and B) post term age (weeks) for sample group of 7 infants.

A.



B.

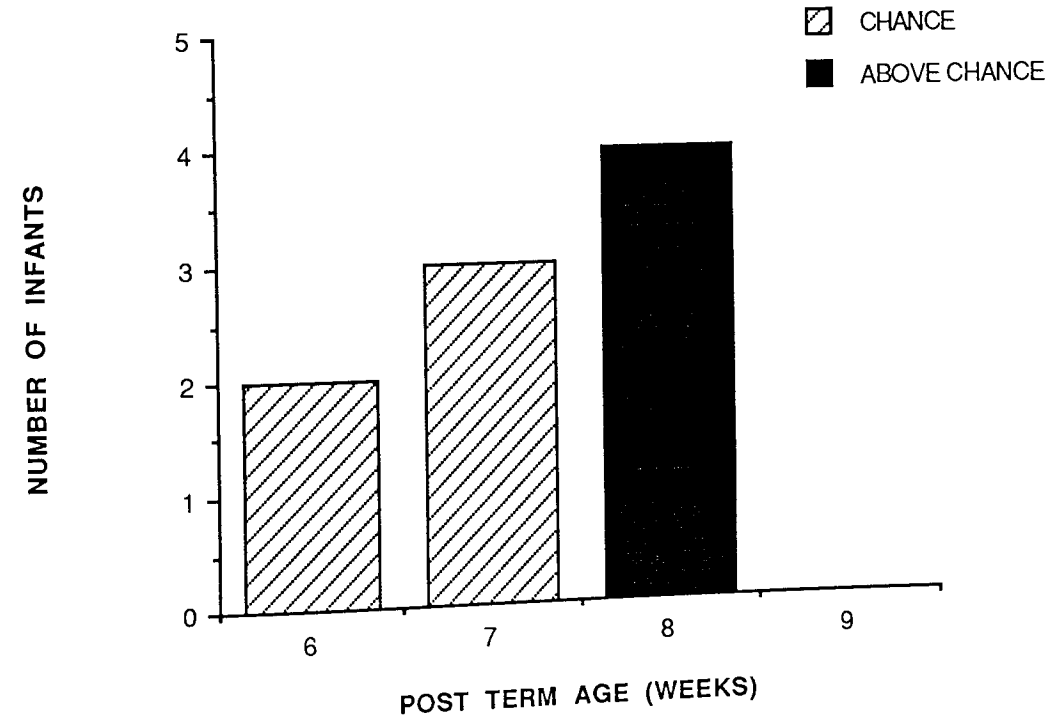


Figure 9.4 Distribution of infants performing at chance (striped columns) or above chance (solid columns) for two or more red/green ratios with respect to A) chronological age and B) post term age (in weeks).

CHAPTER TEN
GENERAL DISCUSSION

10.1 Summary of major findings

1. The mean isoluminant ratio for a red/green grating of 1cpd for a group of nine colour normal adult observers was found to be 1.00 ± 0.05. This is equivalent to the photometric isoluminant ratio and varied little for all observers. This result was highly similar to that determined using a method of preferential looking to determine the isoluminant ratio of a red/green grating of 0.1cpd, for individual 1 to 3 month old infants. Isoluminance did not vary significantly between the sample groups of 1, 2 and 3 months. With a stimulus of higher spatial frequency (0.4 cpd), isoluminant ratios for individuals were again close to and distributed about the red/green luminance ratio of 1.0 and were not significantly different between 2 and 3 months of age.

2. The development of the chromatic transient visual evoked potential has not previously been reported In this study,using isoluminant red/green stimuli, no response could be recorded from any infant younger than 7 weeks post term at the time of recording. This response first appeared at 7 weeks or above, as a broad positive , P1, with the appearance of N1 and N2 components at about 10 weeks post term. The latency of the P1 component was correlated with post term age at time of recording decreasing in latency as the infant grows and the amplitude of this component increased with post term age. By 10-11 weeks, this response had a similar morphology to the adult chromatic transient response. In a behavioural study, infants less than 7 weeks post term failed to demonstrate discrimination of a red/green grating from a uniform field, if the component bars were of equal luminance.

3. The adult chromatic transient visual evoked potential at a red/green ratio of 1.0, i.e. photometric isoluminance, showed a similar morphology to the achromatic response i.e. N-P-N. The mean latencies of these components were 96±9, 118±6 and 171±17 msec respectively and the P100 component was found to show a delay ($p<0.0001$) and reduction in amplitude ($p<0.0001$) in comparison to the achromatic response. As the luminance information within the chromatic stimulus reduced to approach photometric isoluminance, the P100 component of this response became progressively delayed and reduced.

10.2 General Discussion

This project was undertaken to investigate the presence of chromatic processing within the infant visual system, with a view to determining the developmental time course of the

underlying mechanism. Chromatic processing is believed to be solely a function of the parvocellular system projecting from layers within the lateral geniculate nucleus to the primary visual cortex (Livingstone and Hubel 1988, Kaplan et al.1991). The presence or emergence of the ability to process colour should hence be a reflection of the development or function of this system.

Prior to this study, controversy has existed over the presence of a chromatic visual evoked potential in very young infants. Using a sweep VEP technique to assess chromatic contrast sensitivity, Allen and co-workers (1993) have reported the presence of a chromatic VEP to sinusoidal red/green gratings at, and around, photometric isoluminance in 2 week old infants. Their results showed that chromatic contrast sensitivity is reduced in comparison to luminance sensitivity by the same factor in infants and adults. The luminance contrast sensitivity of young infants is known to be poor (Atkinson et al. 1977, Banks and Salapatek 1978) and Allen and co-workers suggested that it is the very poor chromatic sensitivity of young infants that had caused them to fail the behavioural discrimination of colour in previous studies. If this was the case and cone contrast was the sole limiting factor, using the ideal observer model (Banks and Bennett 1988, Geisler 1989) one would expect cone contrast sensitivity at isoluminance to be 20% of the luminance sensitivity of any individual. Norcia and co-workers (1990) calculated luminance contrast thresholds to be 7% at 2-3 weeks improving to 0.5% by 9 weeks using sweep VEPs and one may thus expect a 2-3 week old infant's chromatic contrast threshold to be five times below this level. A chromatic stimulus of 100% contrast should then be well above this threshold and thus, if poor chromatic contrast sensitivity is the sole limiting factor on chromatic discrimination, the stimuli contrast of 90-100% used in the present study study should be capable of eliciting a VEP. However, this was not the case and no response could be elicited from any infant less than 7 weeks of age even at maximum chromatic contrast. This finding is in agreement with the results of a steady state VEP study reported by Morrone and colleagues (1990, 1993) and would thus suggest that chromatic contrast cannot be the only limiting factor of chromatic discrimination before 7 weeks of age.

Both the Allen et al.(1993) and Morrone et al.(1993) used steady-state stimulation to investigate chromatic VEPs in infants. The steady state method of recording has not been shown to have any significant advantage over transient recording techniques (Harding 1988). It can, however only yield information in terms of amplitude and phase whilst delivering no indication of developmental morphology or latency information. Amplitude measures of the VEP response can be highly variable both within and between subjects and, for this reason, latency is a more reliable index of visual maturation (Sokol and

Jones 1979). Transient evoked potentials have been widely used in the electrophysiological investigation of infant development (For review see section 4.4) and the developmental morphology of the pattern reversal VEP has been reported from infants as young as 32 weeks post menstrual age (Grose et al. 1989, Harding et al. 1989). The use of transient stimulation in the present study was advantageous in providing information of the longitudinal development of chromatic processing in terms of morphology and allowed direct comparison to the development of the achromatic response.

The results presented here show that neither chromatic VEPs nor behavioural chromatic discrimination could be demonstrated by any infant below 7 weeks post term, implying that young infants do not have the ability to process chromatic information until the second month of life. Allen et al.(1993) suggest that infants as young as 2 weeks of age have the ability to process chromatic information, demonstrated by the presence of a sweep VEP to all chromatic stimuli presented to them. It would appear however, that only one infant at this youngest age was assessed, although no precise details of this are given. By extrapolation from the figures within the text of their paper, one may presume that all other infants were 5 weeks of age or older (chronological age) at the time of recording. Although their paper states that all infants were within 2 weeks of their due date, no correction is made for post term age and hence any reported chronological age may be post term age +/- 2 weeks. As demonstrated in the studies presented within this thesis, making the appropriate correction and analysing the presence of chromatic responses with reference to post term age has a marked effect on the distribution of the chromatic VEP with age. No infant in any study revealed a chromatic response prior to 7 weeks post term and all infants showed chromatic processing by 8 weeks post term age. If no correction is made, infants younger than 6 weeks of age will undoubtedly demonstrate chromatic responses by both behavioural and electrophysiological means as their true post term age may be 2 weeks older (i.e.8 weeks PTA). Firm evidence of chromatic discrimination at 2 weeks (+/- 2 weeks) post term age is difficult to accept on the basis of only one subject but it is possible that if corrections for post term age are made for all other infants, the results of Allen et al. (1993), no longer contradict but are, in fact, in agreement with the present study. It is, perhaps, unfortunate that the Morrone et al. study fails to specify if any correction or exclusion criteria have been utilised with respect to chronological or post term age but, regardless of this, their results would appear to be in agreement with our own.

As previously discussed (see section 3.15) several hypotheses relating to the lack of chromatic processing in early life can be discounted. At retinal level, all cones are present although immature (Yuodelis and Hendrickson 1986) and will thus capture less quanta than adult cones. It is of interest to note that the mean luminance of the screen used in the present study was higher than that reported to elicit chromatic VEPs in the Allen et al. study (1993) as was the luminance of the screen used in the steady state VEP study of Morrone et al. (1993). The production of chromatic VEPs by Allen and colleagues could not then be due to the use of brighter stimuli. As previously discussed (see section 7.14) the presence of a response to stimuli that are believed to be purely chromatic may the result of spurious luminance artefacts within the stimulus. The phosphors of the screen used in the present series of studies, presented within this thesis, were closely matched in terms of CIE co-ordinates i.e. Red 0.591,0.373 Green 0.297,0.596 as were those of Morrone and co-workers (Red 0.618,0.373 Green 0.28,0.605). The screen phosphors in the Allen et al. work, although being within the Rayleigh region, were slightly less well matched (Red 0.65,0.34 Green 0.42,0.57) and one may speculate that this discrepancy associated with the effect of chromatic aberration may be enough to produce a luminance artefact at all chromatic ratios hence revealing a luminance response in those youngest infants who do not actually have any true chromatc response. Chromatic aberrations are negligible at low spatial frequencies in adults (Flitcroft 1989) but may be apparent in the infant eye at the spatial frequency used by Allen and co-workers whilst absent in the studies in which chromatic stimuli failed to elicit a VEP. Both the present study and that of Morrone and colleagues used very low spatial frequencies (i.e. 0.175 and 0.1 cpd respectively).

If cone immaturity, producing poor cone contrast was the sole limiting factor of chromatic vision one would expect luminance and chromatic contrast sensitivity to develop at the same rate with chromatic contrast sensitivity showing a reduction by a constant factor in comparison to the luminance contrast sensitivity throughout life. This is not the case in the work of Morrone and colleagues and cannot explain the absence of the chromatic potential at 100% chromatic contrast reported here, in those infants whose luminance threshold is far greater than 20% (the ratio of luminance/chromatic contrast sensitivity for most spatial frequencies is about 5 (Mullen 1985)).

If retinal immaturity does not account for the lack of chromatic processing, chromatic information must be lost at a level beyond the retina. Bronson (1974) proposed a neural modal to explain neonatal visual behaviour suggesting that it is mediated by a

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APPENDIX I

Example of preferential looking score procedure

Step	1	2	3	4	5	6	7	8
R:G ratio	0.69	0.71	0.74	0.76	0.79	0.82	0.85	0.88
log.	-0.16	-0.145	-0.13	-0.115	-0.10	-0.085	-0.07	-0.055
Trials	1 1	1 1		1 1		1 0*		
			1 1	1 1		1 1		0 *
					1 1	1 1		1 0 *
					1 1	1 0*		
Score	2/2	2/2	2/2	4/4	4/4	6/8		1/3
Score (%)	100	100	100	100	100	75		33
End point						**0.82**		

Key : 1 - correct
0 - incorrect
* - reversal

TABLE A1.1 Refraction study

INFANT	PTA	INSTILL	R SER	LSER	ANISO	R ASTIG	L ASTIG
MR	5	38	2.75	3.25	0.50	0.50	0.50
NJ	4	30	3.00	2.50	0.50	1.00	-
RE	5	40	2.00	2.00	-	-	-
PP	5	43	1.50	1.50	-	-	-
ME	3	30	4.00	4.0	-	-	1.00
MMc	2	37	4.5	5.00	-	-	-
NMc	3	35	3.00	3.00	-	-	-
SH	5	42	3.5	3.50	-	-	-
MM	4	40	4.75	4.75	-	0.50	0.50
YH	4	46	4.00	3.25	0.75	-	0.50
UG	7	39	3.00	3.50	0.50	-	-
LG	9	49	1.00	1.00	-	-	-
UK	9	38	3.50	3.25	0.25	-	0.50
NK	8	35	3.00	3.00	-	-	-
JE	9	32	3.50	3.50	-	-	-
LS	8	35	3.50	2.25	1.25	2.50	1.50
RR	9	38	2.50	2.25	0.25	-	0.50
LB	7	37	3.00	3.25	0.25	-	0.25
RS	9	39	3.50	3.00	0.50	-	1.00
LB2	7	33	2.00	2.50	0.50	1.00	-
DF	9	29	3.25	4.00	0.75	0.50	-
RB	11	43	INCOM	PLETE	CYCLO	-	-
AE	11	40	3.00	2.50	0.50	1.00	-
JB	11	32	4.50	4.50	-	-	-
FE	11	41	3.00	3.00	-	-	-
AC	11	39	3.75	3.50	0.25	0.50	-
SF	12	35	3.75	4.00	0.25	0.50	-
MP	11	53	2.75	3.00	0.25	0.50	0.75
JR	12	25	4.50	4.50	-	-	-
HT	11	36	3.50	4.0	0.50	-	-
TS	12	30	3.50	3.00	0.50	-	1.00
ES	11	45	2.75	3.25	0.25	0.50	1.25

KEY PTA : Post Term Age (weeks)
INSTILL : Time between instillation and refraction (minutes)
SER : Spherical Equivalent Refraction (dioptres)
ASTIG : Astigmatism
ANISO : Anisometropia
R : Right eye
L : Left eye

TABLE A1.2 STEADY STATE VEPS: MEAN AMPLITUDES (μV)

Standard deviations in brackets

				RED/ GREEN RATIOS				
INFANT	**CA**	**PTA**	**Achromatic**	**0.8**	**0.9**	**1.0**	**1.1**	**1.2**
VE	8	7	-	6.09 (0.1)	11.38 (3.7)	3.5 (0.7)	8.0 (4.24)	11.5 (2.1)
RE	7	7	21.5 (3.5)	8.9 (2.6)	5.0 (4.2)	7.74 (7.29)	15.65 (0.5)	16.27 (5.6)
RE2	9	9	13.8 (16.8)	12.52 (4.6)	10.54 (5.1)	9.64 (3.2)	11.66 (3.1)	7.52 (4.5)
TN	7	7	9.0 (4.2)	9.4 (0.8)	3.56 (0.6)	7.0 (0)	5.5 (0.7)	7.0 (1.41)
TN2	8	8	20.34 (7.2)	12.43 (6.3)	4.93 (1.1)	7.04 (2.06)	6.5 (0.7)	4.35 (1.91)
CH	8	8	34.75 (3.8)	4.48 (2.2)	0	5.7 (2.4)	3.9 (1.7)	5.79 (3.4)
ES	7	7	8.09 (2.2)	12.46 (5.1)	10.79 (3.0)	8.48 (4.5)	14.99 (9.2)	10.86 (2.5)
TI	6	6	4.13 (1.05)	-	-	-	-	-
PA	8	7	11.79 (5.6)	5.93 (3.8)	6.49 (3.4)	6.19 (4.9)	10.15 (1.08)	7.56 (2.7)

TABLE A1.3 TEMPORAL TUNING:MEAN AMPLITUDES (μV)

Standard deviations in brackets

				TEMPORAL FREQUENCIES		
INFANT	**CA**	**PTA**	**STIMULUS**	**2 HZ**	**3 HZ**	**4 HZ**
CH	8	8	R:G 1.0	12.83 (7.16)	8.48 (4.5)	10.93 (1.68)
RE	7	7	R:G 1.0	18.43 (6.46)	7.74 (4.11)	5.66 (2.3)
RE2	9	9	ACHROMATIC	6.61 (2.88)	13.8 (6.8)	10.15 (5.6)
RE2	9	9	R:G 1.0	11.21 (6.1)	9.64 (3.2)	5.65 (2.65)
TN	7	7	R:G 1.0	12.14 (1.21)	7.0	4.67 (1.88)

APPENDIX II

TABLE A2.1 P100 LATENCIES (MSEC)

ADULT R:G RATIO	RD	KE	EW	RS	NE	NAT	FF	LW	CH	GB
B/W	104	107	102	99	105	107	113	113	101	101
0.5	112	115	125	118	111	113	132	120	109	113
0.8	111	118	127	117	113	122	132	125	113	113
0.9	112	121	125	115	112	117	132	125	117	115
1.0	113	125	125	115	114	121	132	128	117	113
1.1	113	119	120	115	113	117	132	123	111	115
1.2	110	116	124	118	111	117	132	119	113	113
1.5	108	115	132	115	110	113	132	123	108	109

TABLE A2.2 P100 AMPLITUDES (μV)

ADULT R:G RATIO	RD	KE	EW	RS	NE	NAT	FF	LW	CH	GB
B/W	15	9	17.5	7	16	17	8	9	9	8
0.5	8	6.5	10	4	11	9	8	4.5	3	5
0.8	10	7	10	2	10	8	5	4	3	6
0.9	10	5	8	2	8	6	5	3	2	3
1.0	10	5	10	6	8	4	4	3	2	3
1.1	10	6	7.5	4	7	6	5	4	2	5
1.2	9.5	6	6.5	4	8	5	6	4	3	4
1.5	10	7	4	4	12	7	8	5	4	4

TABLE A2.3 MAJOR COMPONENT LATENCY (ACHROMATIC AND ISOLUMINANT CHROMATIC) (MSEC)

	ACHROMATIC			CHROMATIC		
	N75	P100	N135	N75	P100	N135
RD	78	104	133	100	113	166
KE	66	107	133	100	125	166
EW	66	102	146	93	125	180
RS	62	99	133	98	115	173
NE	66	105	193	100	114	180
NAT	80	107	166	100	121	206
FF	67	113	120	92	132	193
LW	89	113	140	106	128	160
CH	80	101	126	99	117	146
GB	74	101	133	100	113	173

TABLE A2.4 MAJOR COMPONENT AMPLITUDE (ACHROMATIC AND ISOLUMINANT CHROMATIC) (μV)

	ACHROMATIC			CHROMATIC		
	N75	P100	N135	N75	P100	N135
RD	3	15	7	6	10	11
KE	3	9	5	2	5	7
EW	2	17.5	6	4	10	10
RS	2	7	5	2	6	6
NE	2	16	20	2	8	10
NAT	5	17	16	3	4	
FF	3	8	4	8	4	7
LW	2	9	9	2	3	11
CH	4	9	5	5	2	4
GB	?	8	7	2	3	5

APPENDIX III

TABLE A3.1 P1 COMPONENT LATENCY (MSEC)

				RED/GREEN RATIOS						
INFANT	**CA**	**PTA**	**BW**	**0.5**	**0.8**	**0.9**	**1.0**	**1.1**	**1.2**	**1.5**
MID	13	13	123	126	156	-	156	-	156	132
SF	10	10	113	-	169	-	189	-	164	
JD	10	10	140	175	203	175	175	178	180	175
NF	10	10	169	-	183	171	173	175	171	-
SPL	10	10	162	190	-	160	162	162	-	190
JM	7	9	210	228	-	203	210	203	-	228
TE	9	9	169	201	177	-	187	-	189	177
NH	9	9	215	240	-	300	256	220	-	231
MHE	8	8	218	-	-	189	200	189	-	-
CW	8	8	193	-	-	190	196	190	196	-
MB	8	8	212	-	-	210	232	210	230	-
CK	9	8	209	-	-	196	196	230	-	-
LH	8	8	234	-	210	244	206	210	230	-
KBK	7	8	240	-	-	220	234	230	-	-
NHB	7	8	165	160	162	180	195	170	162	160
MF	7	7	228	230	-	212	340	212	225	
AG	7	7	209	210	237	240	253	240	237	230
KB	6	7	250	278	-	290	306	278	-	290
DJ	7	7	256	270	293	300	320	280	293	253
CA	7	7	175	196	209	209	210	-	200	196

TABLE A3.1 Cont. P1 COMPONENT LATENCY (MSEC)

				RED/GREEN RATIOS						
INFANT	**CA**	**PTA**	**BW**	**0.5**	**0.8**	**0.9**	**1.0**	**1.1**	**1.2**	**1.5**
AJ	7	7	193			193	*	193	-	-
SON	8	7	143	190	260	306	*	310	225	210
JAD	7	7	218	280	250	220	*	215	260	250
AR	5	5	196	234	-	228	*	228	-	215
DW	7	4	234	-	200	205	*	199	193	-
RJ	5	1	262	300	-	-	*	-	-	300
RM	7	7	228	246	253	*	*	296	260	235
GH	6	6	228	231	212	*	200	-	212	231
WM	8	4	359	380	-	*	*	*	-	-
LL	7	5	200	221	-	-	*	-	-	221
MD	5	5	270	-	-	-	*	305	310	-
KYB	9	7	215	215	209	*	200	206	209	200
SH	7	7	215	195	265	406	*	*	300	220
KL	7	7	206	187	215	300	220	*	210	187
GEMH	6	6	212	230	228	270	280	*	228	240
LS	6	4	237	280	320	*	280	293	280	270
RG	6	6	190	237	275	278	*	280	240	250
CP	6	6	195	280	-	*	230	-	-	256
MFA	7	7	190	209	-	*	212	-	-	209

* DENOTES RESPONSES OF ZERO AMPLITUDE

TABLE A3.2 P1 COMPONENT AMPLITUDE (μV)

				RED/GREEN RATIO						
INFANT	**CA**	**PTA**	**BW**	**0.5**	**0.8**	**0.9**	**1.0**	**1.1**	**1.2**	**1.5**
MID	13	13	18	20	16	-	15	-	16	16
SF	10	10	16	-	4	-	12	-	15	-
JD	10	10	30	16	8	6	7	5	7	15
NF	10	10	4	-	2	7	10	14	9	-
SPL	10	10	8	6	-	5	6	7	-	6
JM	7	9	10	9	-	5	2.5	17	-	8
TE	9	9	18	10	6	-	12	-	10.5	10.5
NH	9	9	17.5	7	-	5	5.6	7	-	9.5
MHE	8	8	2.8	-	-	2	2.5	2	-	-
CW	8	8	17.5	-	-	10	5.5	8	5.7	-
MB	8	8	15	-	5	6	3.5	6	4	-
CK	9	8	13	-	-	5	8.8	4	-	-
LH	8	8	10	-	7	8	5	8	3	-
KBK	7	8	9.5	-	-	6	6	5	-	-
NHB	7	8	20	10	5	4	4	3	6	5
MF	7	7	12	6	-	6	3	7	-	9
AG	7	7	20	20	10	16	3	14	7	14
KB	6	7	20	8	-	7	4	10	-	21
DJ	7	7	10	8	7.5	6	3	5	7	5
CA	7	7	25	7.5	8	9	10	-	11	8

TABLE A3.2 Cont. P1 COMPONENT AMPLITUDE (μV)

				RED/GREEN RATIOS						
INFANT	CA	PTA	BW	0.5	0.8	0.9	1.0	1.1	1.2	1.5
AJ	7	7	4.5	-	2	5	0	3	4	-
SON	8	7	20	8.5	5	3	0	5	5	7
JAD	7	7	13	5	4	6	0	2	5	5
AR	5	5	10	8	-	9	0	7	-	11
DW	7	4	12	-	5	1	0	3	7	-
RJ	5	1	10	7	-	-	0	-	-	7
RM	7	7	14	11	9	0	0	8	5	8
GH	6	6	19	6	-	0	7	-	11	7
WM	8	4	13	7	-	0	0	0	-	-
LL	7	5	7.6	5	-	-	0	-	-	5
MD	5	5	14	-	-	3	0	2	9	-
KYB	9	7	13	10	11	0	5	6	4	6
SH	7	7	12	5	6	4	0	0	5	4
KL	7	7	10	5	3	5	6	0	-	5
GEMH	6	6	12	12	9	7	7	0	5	7
LS	6	4	6	7	7	0	4	5.2	8	7.5
RG	6	6	9.5	8	7	2.6	0	3	6	7
CP	6	6	13	10	-	0	5	-	-	10
MFA	7	7	6.7	6	-	0	2.5	-	-	4

TABLE A3.3 MAJOR COMPONENT LATENCIES (msec)

			ACHROMATIC			CHROMATIC (R:G =1.0)		
INFANT	**CA**	**PTA**	**N1**	**P1**	**N2**	**N1**	**P1**	**N2**
MID	13	13	80	123	200	78	156	206
SF	10	10	85	113	200	96	189	-
JD	10	10	100	140	230	-	175	-
NF	10	10	125	169	243	107	173	256
SPL	10	10	72	162	260	-	162	320
JM	7	9	-	210	-	-	210	-
TE	9	9	100	169	-	-	187	-
NH	9	9	134	215	-	-	256	-
MHE	8	8	-	218	-	-	200	-
CW	8	8	109	193	-	-	196	-
MB	8	8	-	212	-	-	232	-
CK	9	8	125	209	260	130	196	-
LH	8	8	140	234	-	-	206	-
KBK	7	8	150	240	-	-	234	-
NHB	7	8	93	165	220	-	195	-
MF	7	7	130	228	-	-	340	-
AG	7	7	-	209	-	-	253	-
KB	6	7	143	250	-	-	306	-
DJ	7	7	-	256	-	-	320	-
CA	7	7	-	175	-	-	210	-

TABLE A 3.4 MAJOR COMPONENT AMPLITUDES (μV)

			ACHROMATIC			CHROMATIC (R:G =1.0)		
INFANT	**CA**	**PTA**	**N1**	**P1**	**N2**	**N1**	**P1**	**N2**
MID	13	13	11	18	28	2	15	20
SF	10	10	5	16	11	6	12	-
JD	10	10	5	30	35	-	7	-
NF	10	10	2.8	4	10	3	10	7.5
SPL	10	10	2	8	17	-	6	12
JM	7	9	-	10	-	-	2.5	-
TE	9	9	3	18	-	-	12	-
NH	9	9	5	17.5	-	-	5.6	-
MHE	8	8	-	2.8	-	-	2.5	-
CW	8	8	5	17.5	-	-	5.5	-
MB	8	8	-	15	-	-	3.5	-
CK	9	8	5	13	10	5	8.8	-
LH	8	8	3	10	-	-	5	-
KBK	7	8	5	9.5	-	-	6	-
NHB	7	8	3	20	32	-	4	-
MF	7	7	2	12	-	-	3	-
AG	7	7	-	20	-	-	3	-
KB	6	7	5	20	-	-	4	-
DJ	7	7	-	10	-	-	3	-
CA	7	7	-	25	-	-	10	-

TABLE A3.5 MAJOR COMPONENT LATENCIES AND AMPLITUDES

(For infants with no chromatic response)

			ACHROMATIC AMPLITUDE (μV)			ACHROMATIC LATENCY (msec)		
INFANT	**CA**	**PTA**	**N1**	**P1**	**N2**	**N1**	**P1**	**N2**
AJ	7	7	2	4.5	-	120	193	-
SON	8	7	13	20	-	84	143	-
JAD	7	7	5	13	-	118	218	-
AR	5	5	-	10	-	-	196	-
DW	7	4	-	12	-	-	234	-
RJ	5	1	-	10	-	-	262	-
RM	7	7	3	14	-	162	228	-
GH	6	6	-	19	-	-	228	-
WM	8	4	-	13	-	-	359	-
LL	7	5	-	7.6	-	-	200	-
MD	5	5	-	14	-	-	270	-
KYB	9	7	-	13	-	-	215	-
SH	7	7	5	12	-	112	215	-
KL	7	7	4	10	-	137	206	-
GEMH	6	6	7	12	-	109	212	-
LS	6	4	-	6	-	-	237	-
RG	6	6	5	9.5	-	128	190	-
CP	6	6	-	13	-	-	195	--
MFA	7	7	3	6.7	-	118	190	

APPENDIX IV

TABLE A4.1 P1 COMPONENT LATENCIES (MSEC)

INFANT	CA	PTA	BW	0.5	0.8	0.9	1.0	1.1	1.2	1.5
LL	7	5	200	221	-	-	*	-	-	221
LL2	9	7	156	178	190	-	*	-	190	168
LL3	11	9	143	159	180	-	231	-	150	150
CP	6	6	195	280	-	*	230	-	-	256
CP2	8	8	173	185	-	180	195	180	-	185
CP3	11	11	137	140	165	153	156	153	165	160
MD	5	5	270	-	-	-	*	305	310	-
MD2	12	12	171	143	-	-	200	-	-	143
MFA	7	7	190	209	-	*	212	-	-	209
MFA2	9	9	190	-	-	-	203	-	-	200
MFA3	14	14	156	178	-	253	178	165	168	162
KYB	9	7	215	215	209	*	200	206	209	200
KYB2	11	9	175	178	175	175	196	178	178	175
KYB3	16	14	115	135	143	139	148	135	129	129
CA	7	7	175	196	209	209	210	-	200	196
CA2	9	9	162	190	181	203	200	200	208	196
CA3	13	13	107	128	131	145	154	137	143	139
SH	7	7	215	195	265	406	*	*	300	220
SH2	9	9	175	-	210	228	246	235	220	205

INFANT	CA	PTA	BW	0.5	0.8	0.9	1.0	1.1	1.2	1.5
KL	7	7	206	187	215	300	220	*	210	187
KL2	9	9	184	190	200	200	205	180	181	190
KL3	16	16	170	140	-	180	180	150	-	140
GEMH	6	6	212	230	228	270	280	*	228	240
GEMH2	8	8	160	175	175	210	220	225	190	175
GEMH3	10	10	140	162	171	-	171	171	171	165
RM	7	7	228	246	253	*	*	296	250	230
RM2	9	9	180	193	200	193	190	190	196	193
RM3	11	11	171	171	178	188	193	180	195	171
SON	8	7	143	190	260	306	*	310	225	143
SON2	10	9	123	123	140	143	153	137	150	123
SON3	16	15	150	154	176	190	173	188	157	150
DJ	7	7	256	296	293	300	*	280	293	256
DJ2	9	9	200	235	240	265	283	281	240	200
LS	6	4	237	280	320	*	280	293	280	237
LS2	8	6	230	270	240	*	284	306	262	230
LS3	10	8	181	200	181	190	190	185	-	181
RG	6	6	190	237	275	278	*	280	240	190
RG2	8	8	184	196	212	228	218	210	187	84
RG3	11	11	171	178	178	196	175	187	170	171

* DENOTES ZERO AMPLITUDE RESPONSE

TABLE A4.2 P1 COMPONENT AMPLITUDES (μV)

INFANT	CA	PTA	BW	0.5	0.8	0.9	1.0	1.1	1.2	1.5
LL	7	5	7.6	5	-	-	0	-	-	5
LL2	9	7	9	10	6.5	-	0	-	3	5.6
LL3	11	9	7.3	11	7.5	-	4	-	3	4
CP	6	6	13	10	-	0	5	-	-	10
CP2	8	8	25	16	-	2	2	2	-	11
CP3	11	11	15	10	6	2	5	6	6	8
MD	5	5	14	-	-	3	0	2	9	-
MD2	12	12	15	10	-	4	4	4	-	7
MFA	7	7	6.7	6	-	0	2.5	-	-	4
MFA2	9	9	5	-	-	5	7	-	-	6
MFA3	14	14	5	3	-	7	8	5.5	3	3.7
KYB	9	7	13	10	11	0	5	6	4	6
KYB2	11	9	12	9	6.5	5.6	10	5.5	10	6.5
KYB3	16	14	31	15	7	5	13	13	10	8
CA	7	7	25	7.5	8	9	10	6	11	8
CA2	9	9	40	35	20	8	10	10	6	9
CA3	13	13	60	30	6.5	23	9	31	12	14
SH	7	7	12	5	6	4	0	0	5	4
SH2	9	9	15	-	8	10	3	7	8	10

INFANT	CA	PTA	BW	0.5	0.8	0.9	1.0	1.1	1.2	1.5
KL	7	7	10	5	3	5	6	0	-	5
KL2	9	9	8	7	5	6	6	4	7.5	8
KL3	16	16	31	4	-	8	5	6	-	4
GEMH	6	6	12	12	9	7	7	-	5	7
GEMH2	8	8	15	8	4	4	8	13	7	7
GEMH3	10	10	18	13	8	-	3	6	4	4
RM	7	7	14	6	9	0	0	8	5	6
RM2	9	9	8	13	7	2.7	3	5	4	8
RM3	11	11	12	13	12	5	6	5	-	10
SON	8	7	20	8.5	5	3	0	5	5	7
SON2	10	9	20	4	4	5	10	9	5	4
SON3	16	15	6	2	4	5	4	4	8	3
DJ	7	7	10	8	7	6	3	4	7	5
DJ2	9	9	30	17	19	8	10	8	12	14
LS	6	4	6	7	7	0	4	5	8	7.5
LS2	8	6	14	6	8	0	7	9.6	5.5	7
LS3	10	8	13	13	-	4	4	5	-	6
RG	6	6	9.9	8	7	2.6	0	3	6	7
RG2	8	8	19	5	4.6	3	3	7	5	4
RG3	11	11	12.5	8	7	7	6	11	6	6.5

APPENDIX V

TABLE A 5.1 PREFERENTIAL LOOKING PERCENTAGE SCORES

			RED/GREEN RATIOS				
INFANT	CA (weeks)	PTA (weeks)	0.8	0.9	1.0	1.1	1.2
AS	8	7	76	72	48	56	80
KS	7	6	-	80	56	64	72
KS2	9	8	-	84	80	72	76
DP	7	7	92	68	36	60	76
DP2	8	8	72	76	92	72	80
JC	6	7	84	24	20	32	78
MER	8	8	-	84	80	76	88
CFW	6	6	-	72	52	52	76
GMC	6	8	80	84	72	80	80

APPENDIX VI STATISTICAL ANALYSIS OF DATA

Statistical analysis of data was performed by the Apple Macintosh Statworks program. The regression lines were calculated by the method of least squares and the p values for the correlation co-efficients were calculated form the t values. A students t test was used to compare other mean values.

APPENDIX VII SUPPORTING PUBLICATIONS

1. Rudduck, G.A., Whitaker, D. and Harding, G.F.A. (1992)
Use of preferential looking to determine isoluminance in infants.
Invest. Ophthalmol. Vis. Sci.. (suppl)33 :112.

2. Rudduck, G.A., Harding, G.F.A. and Whitaker, D. (1993)
Determination of isoluminance in infants by preferential looking, using a computer generated stimulus.
Ophthalmol. Physiol. Opt. 13:107

3. Rudduck,G.A. and Harding, G.F.A.
Visual electrophysiology to achromatic and chromatic stimuli in premature and full term infants.
First International Meeting on Advanced Methods in Visual Psychophysiology and Electrodiagnosis
Bristol, U.K. Paper presentation. (March 23rd-25th 1993)

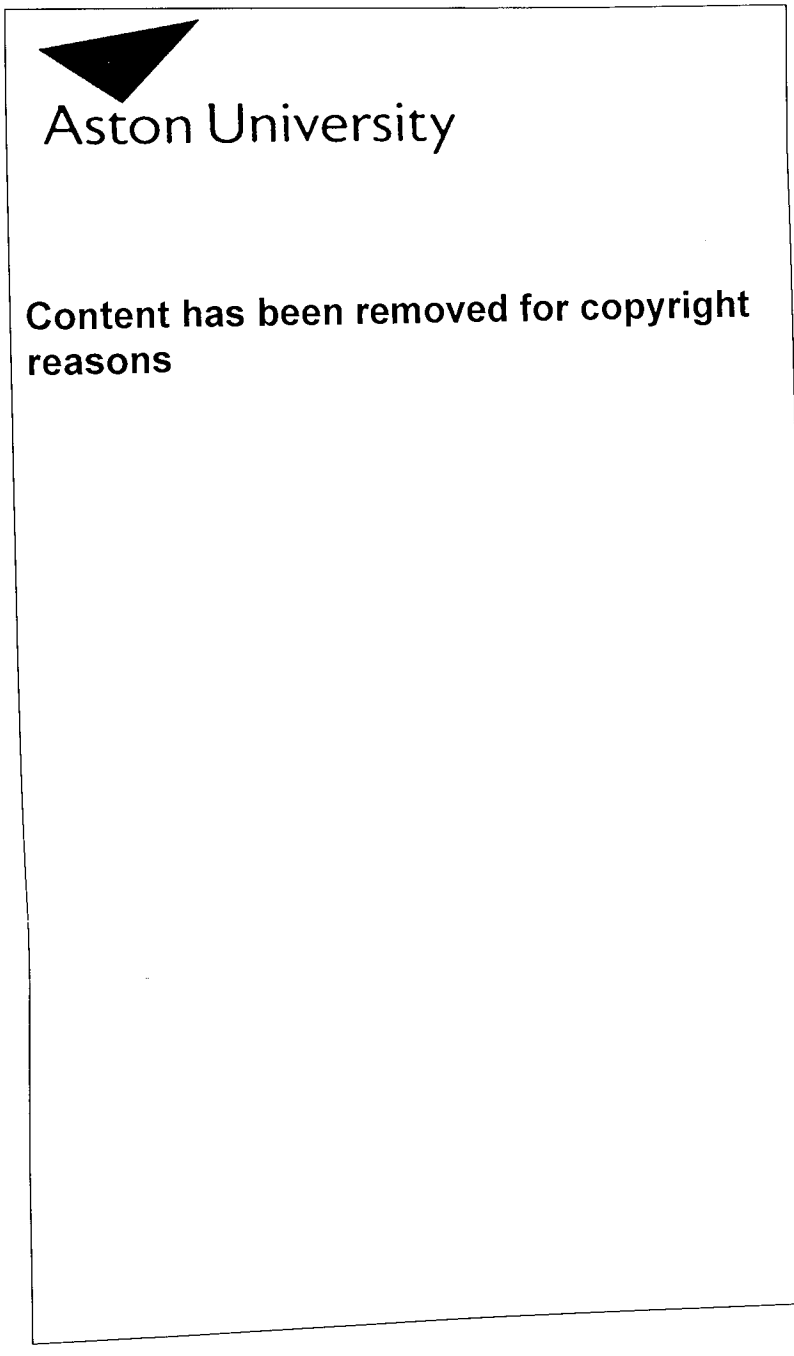
4. Rudduck,G.A. and Harding, G.F.A. (1993)
Visual electrophysiology to achromatic and chromatic stimuli in premature and full term infants.
Int. J. Psychophy. Accepted in press

5. Rudduck, G.A. and Harding, G.F.A. (1993)
The development of the transient chromatic VEP
Invest. Ophthalmol. Vis. Sci. 34 (suppl.) :3228

6. Rudduck, G.A. and Harding, G.F.A.
The absence of chromatic VEPs in human infants below 7 weeks of age.
Meeting of the Society for the Promotion of Visual Sciences 1993
Cardiff, U.K. Paper presentation (July 5th - 8th 1993)

7.Rudduck, G.A. and Harding, G.F.A. (1993)
Human infants' VEPs to chromatic pattern reversal stimuli.
Sixteenth European Conference on Visual Perception.
Edinburgh, U.K. Accepted as poster presentation (August 25- 29th)
Abstract to be published in *Perception* (1993).

1. *Invest. Ophthalmol. Vis. Sci.*. 33 (suppl) :112 (1992)



2. *Ophthalmol. Physiol. Opt.* 13:107 (1993)

Determination of isoluminance in infants by preferential looking, using a computer generated stimulus.

Gillian A. Rudduck, Graham F.A. Harding and David Whitaker.

Department of Vision Sciences,
Aston University,
Birmingham B4 7ET, U.K.

3. Abstract of paper presented at the First International Meeting on Advanced Methods in Visual Psychophysiology and Electrodiagnosis.Bristol, U.K. (March 23rd-25th 1993)

VISUAL ELECTROPHYSIOLOGY TO ACHROMATIC AND CHROMATIC STIMULI IN PREMATURE AND FULL TERM INFANTS

Gillian A. Rudduck and Graham F.A.Harding
Department of Vision Sciences, Aston University, Birmingham B4 7ET

4.Paper submitted to the International Journal of Psychophysics. Accepted in press (1993)

VISUAL ELECTROPHYSIOLOGY TO ACHROMATIC AND CHROMATIC STIMULI IN PREMATURE AND FULL TERM INFANTS

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Aston University,
Birmingham,
B4 7ET
U.K.

Summary

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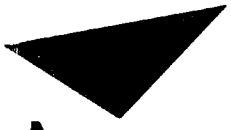

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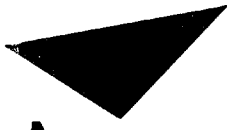

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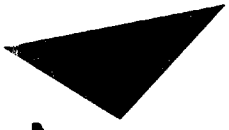

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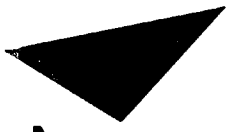

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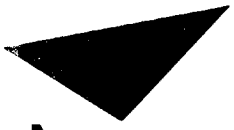

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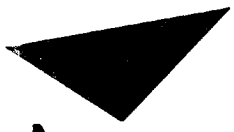

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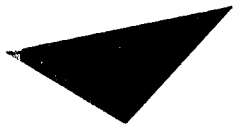

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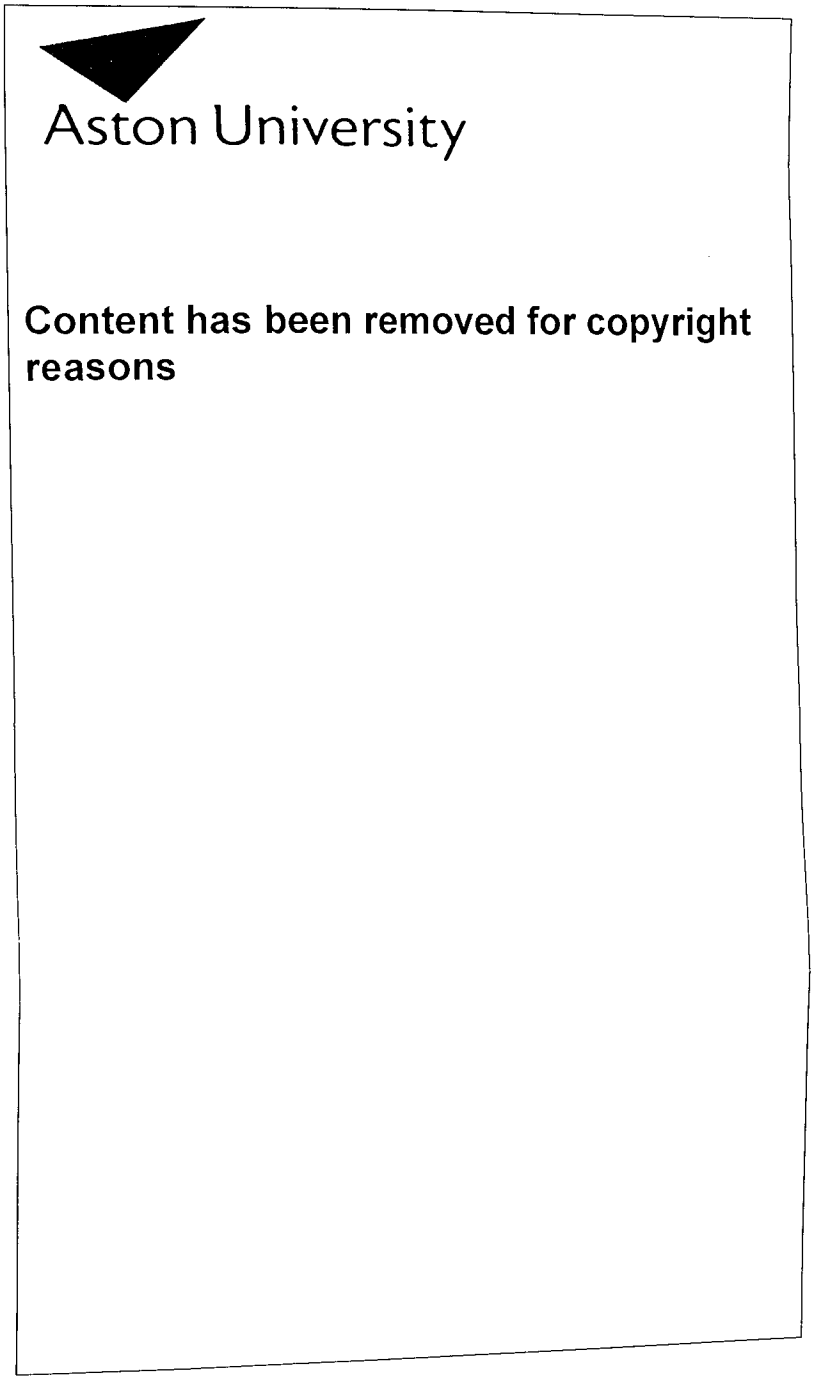
5.*Invest. Ophthalmol. Vis. Sci.* 34 (suppl.) :3228 (1993)



6. Abstract of paper presented at Meeting of the Society for the Promotion of Visual Sciences 1993, Cardiff, U.K (July 5th - 8th 1993)

THE ABSENCE OF CHROMATIC VEPS IN HUMAN INFANTS BELOW SEVEN WEEKS OF AGE

Gillian A. Rudduck and Graham F.A.Harding
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7. Abstract of poster presented at Sixteenth European Conference on Visual Perception.,Edinburgh, U.K. (August 25- 29th) Abstract to be published in *Perception* (1993).

Human infants' VEPs to chromatic pattern reversal stimuli

G.A. Rudduck and G.F.A.Harding. (Department of Vision Sciences, Aston University, Birmingham , B4 7ET, UK)