AN INVESTIGATION OF THE PRESACCADIC SPIKE POTENTIAL

HENRY ROSS DOIG

Doctor of Philosophy

THE UNIVERSITY OF ASTON IN BIRMINGHAM

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The University of Aston in Birmingham

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SUMMARY

A large negative spike potential, which is closely related to the onset of saccadic eye movements, can be recorded from electrodes adjacent to the orbits. This potential, the presaccadic spike potential, has often been regarded as an artefact related to eye movement recordings and little work has been performed to establish its normal waveform and parameters. A positive spike potential, exactly coincident with the frontal negative spike, has also been recorded from electrodes positioned over the posterior scalp and there has been some debate regarding any possible relationship between the two potentials. The frontal spike potential has been associated with motor unit activity in the extraocular muscles prior to the saccade. This thesis investigates both the large anterior and smaller posterior spike potentials and relates these recordings to the saccadic eye movements associated with them.

The anterior spike potential has been recorded from normal subjects to ascertain its normal latency and amplitude parameters for both horizontal and vertical saccades. A relationship between saccade size and spike potential amplitude is described, the spike potential amplitude reducing with smaller saccades. The potential amplitude also reduces with advancing age. Studying the topographical distribution of the spike potential across the scalp shows the posterior spike activity may arise from potential spread of the larger frontal spike potential.

Spike potential recordings from subjects with anomalous eye movements further implicate the extraocular muscles and their innervation in the generation of the spike potential. These recordings indicate that the spike potential may have some use as a clinical recording from patients with disease conditions affecting either their extraocular muscles or the innervational pathways to these muscles. Further recordings of the potential are necessary, however, to determine the exact nature of the changes which may occur with such conditions.

KEY WORDS:

Presaccadic spike potentials; saccades; extraocular muscles; ocular motoneurons; electrooculography.

ACKNOWLEDGEMENTS

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For My parents

Mr and Mrs J. Doig

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LIST OF ABBREVIATIONS

BNC	Balanced non-cephalic
ECG	Electrocardiogram
EEG	Electroencephalography
EMG	Electromyography
EOG	Electrooculography
EOM	Extraocular muscles
EOM	Extraocular muscles
FEF	Frontal eye fields
GR	Global region
IO	Inferior oblique
IR	Inferior rectus
LED	Light emitting diode
LR	Lateral rectus
MIC	Multiply innervated conducting
MINC	Multiply innervated non conducting
MR	Medial rectus
MRF	Mesencephalic reticular formation
MUAP	Motor unit action potential
MUAPT	Motor unit action potential train
OMN	Ocular motoneurons
OSL	Outer surface layer
PPRF	Paramedian pontine reticular formation
REM	Rapid eye movement
SC	Superior colliculus
SD	Standard deviation
SI	Singly innervated
SO	Superior oblique
SP	Spike potential
SR	Superior rectus
VOR	Vestibular ocular reflex

CHAPTER 1

A GENERAL INTRODUCTION TO THE THESIS

Fine control of eye movements is essential if the primate visual system is to operate at its maximum efficiency. Analysis of the visual world to the standards to which we are accustomed necessitates a practically stationary image of the visual scene to be sharply focussed on the retina, particularly the receptive cells at the fovea. Eye movements play a significant role in achieving this situation by first directing our eyes to the specific object of our attention and then maintaining accurate fixation at that point in space. If it were not possible to accurately direct the eyes in this manner it would be virtually impossible for the above requirements to occur, with a resultant decrease in the quality of our visual world.

Different types of eye movements are needed to achieve the goal of a stationary image on the fovea. The eyes must be able to move in such a way that they can track moving objects, e.g. keeping the image of a thrown ball located on the fovea. This is essential to allow the image to be analysed fully, as an object moving across the retina as slowly as one degree per second will suffer a degradation in image quality similar to the effect of nearly two diopters of myopia on grating resolution (Carpenter, 1988). Such tracking movements are achieved by the smooth pursuit system which depends upon the feedback of retinal slip to stabilise the retinal image (Figure 1.1).

The ability of eye movements to allow moving objects to appear stationary on the retina is also necessary when head movements are considered. If the eyes were unable to move independently of the head, these head movements would give rise to a dramatically reduced visual resolution as the image would slide across the retina every time the head was moved. To prevent such unwanted image slip, specific eye movement control systems have evolved primarily to isolate the eye position from the effect of head and body movements. The vestibulo ocular reflex (VOR), for example, utilises information from the motion sensors of the labyrinthine semi-circular canals to program eye movements that

counteract head rotations . A horizontal head rotation to the left will give rise to an equal eye rotation to the right and vice versa, so the image position in space will not change and the image stays fixed in place on the retina.

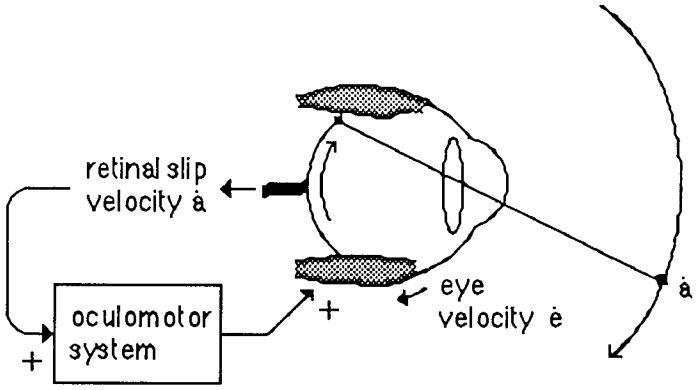


Figure 1.1 The feedback loop for retinal slip allowing the retinal image to be stabilised during both head movements and pursuit of a moving target. (After Carpenter,1988).

A different type of eye movement is needed to re-direct our eyes if our attention is suddenly attracted to an object in the peripheral visual field. It is clearly more preferable to rapidly move the eyes to fixate eccentric objects, than to be continually moving the head to enable different directions in space to be observed in rapid sequence. These fast eye movements are generally goal-directed movements serving to accurately locate a new object of regard at the fovea. The stimulus for a re-fixation movement may not only be visual however, and rapid eye movements are often observed to re-direct the eyes to auditory or tactile inputs. As well as locating new objects of regard on the fovea during visual scanning, rapid eye movements are used in other eye movement activities such as reading or the 'quick phases' of nystagmus. Most rapid eye movements belong to a specific group of eye movements produced by the saccade system. Saccadic eye movements will be the subject of the following Chapter.

The importance of eye movements in the processes of visual perception has been known for many years and eye movements have undergone intensive study by many workers. Various techniques have been developed to monitor and record eye movements, ranging from simple observational methods to electromagnetic techniques utilising magnetic coils

attached to the globe. Although it is not the purpose of this thesis to review all eye movement recording techniques, the technique of electrooculography which is used in this thesis will be discussed in Chapter 4. The reader eye is referred to Carpenter (1988) for an up to date review of eye movement recording techniques. The parameters of both fast and slow eye movements have been studied by many workers and the reaction times, durations and velocities of these movements have been accurately determined for a wide range of eye movement sizes and recording conditions and the latency, duration and velocity parameters of saccadic eye movements will be described in Chapter 2. Knowledge of normal values for these parameters and the effect that certain diseases have upon them, has encouraged eye movement recording to develop as a clinical tool for diagnosing or monitoring such conditions, particularly those involving the innervational pathways to the extraocular muscles producing the eye movements.

The innervation of all eye movement types has been studied by many workers and several structures within the brain have been implicated in the generation of eye movements. Although full details of all the neural structures involved in the generation of saccades are, as yet, still unknown, a pathway for the generation and control of saccadic eye movements can be proposed. This pathway is described in the Chapter 2, as are the six muscles attached to the eyes whose contraction and relaxation produce the eye movements.

The experimental work described in this thesis deals with one specific aspect of saccadic eye movements; the presaccadic spike potential. This is an electrophysiological potential associated with the onset of saccades and is a relatively recent recording related to saccades. The basic recording techniques necessary to record the potential will be introduced in Chapter 3, which will also review the relevant literature giving a full description of the spike potential and its known parameters and relationship to saccadic eye movements. The aspects of the potential which require further investigation and form the basis of the experimental work described in this thesis will be introduced in this review. Prior to any experimental work a suitable protocol for recording the potential had to be developed and this is detailed in Chapter 4. Once the technical details of the recording

technique had been finalised detailed experiments were performed to examine the spike potential. In initial experiments a set of normative data was recorded which allowed analysis of later experiments (Chapter 5). Further studies were performed to examine the spike potential under different recording conditions, e.g. different saccade sizes and directions and in subjects of different ages. These experiments and their results are described in Chapters 6-8. The results of these Chapters are discussed in relation to the present knowledge of the spike potential and its proposed origins.

It will be seen in Chapter 3 that the surface distribution of the spike potential has been the subject of some debate in the literature. The spike potential has been variously attributed with both an anterior and posterior origin, with different generator sites being proposed to explain these two possible origins of the potential. Knowledge of the spike origin is essential if the potential is to have any possible clinical use. A study of the topographical distribution of the potential to examine the location of the potential origin is described in Chapter 9.

Eye movement recordings have been used to diagnose and monitor various disease conditions and the presaccadic spike potential has been recorded in similar situations suggesting that it may have possible clinical uses. Chapter 10 describes further recordings of the spike potential from various subjects with eye movement anomalies and attempts to explain the results on the basis of the knowledge gained from the preceding Chapters and previously published data dealing with normal subjects.

The final Chapter of this thesis collates the information gained from the different experiments and gives an overall view of the presaccadic spike potential recording, both from the previously published knowledge and the results of the experimental work. The origin of the potential will be discussed in view of the experiments and suggestions for future studies will be given in this Chapter.

CHAPTER 2

THE SACCADIC EYE MOVEMENT SYSTEM

This Chapter will discuss saccadic eye movements and the anatomy and physiology of the saccade system. The function, nature and parameters of saccadic eye movements will be described and a relationship between saccade magnitude and its time course and velocity will be introduced. All eye movements, including saccades, are controlled by six extraocular muscles. The gross and histological anatomy of these muscles will be outlined, along with their innervation and actions. Finally a brief review of the neurological centres controlling saccades will be given.

2.1 SACCADIC EYE MOVEMENTS: A SYNOPSIS

2.1.1 THE FUNCTION AND NATURE OF SACCADES

During normal observation our attention is continuously drawn from one object of regard to another. During these attentional changes our eyes rapidly alter their point of fixation to the new object of interest. Such eye movements are goal-directed, i.e. acting to position the line of sight onto a specific point of the visual scene and are known as refixation eye movements (Feldon and Burde, 1987). Once the eye has reached the new position many small eye movements are performed to allow a full and detailed analysis of the visual scene. The majority of eye movements during such visual scanning involve rapid changes of fixation produced by flicking the eyes from one point to another. These rapid,or jerky, eye movements are known as saccades.

There is a copious volume of literature regarding saccades and, while it is inappropriate for this thesis to discuss all the experimental work regarding saccades, an attempt will be made to give a general picture of saccades and the saccade system. This will allow the

experimental work in this thesis to be readily appreciated without constant reference elsewhere for information on the saccade system.

The term saccade is derived from the French verb 'saquer', meaning to pull, which refers to the jerk of a horses head in response to the tug of the reins (Troost and Dell'Osso, 1979). This term has been used to describe rapid eye movements since the latter part of last century when Javal (1879) and Landolt (1891) used 'saccade' to describe rapid re-fixation movements in reading and voluntary changes of gaze. One of the earliest published descriptions of such eye movements was given by Dodge who, in 1903, described five types of eye movements in the horizontal plane. Although he did not call them saccades, Dodge (1903) was obviously referring to saccadic eye movements when he described the characteristics of the first type of eye movement as below:

> *1. Eye movements of the first type are fundamentally reactions to eccentric retinal stimulation, and are dependant on the tendency, developed during the first month of infancy, to move the eyes so that the point of interest will be seen with the visual centre of the retina.*
>
> *2. Their velocity is practically uninfluenced by voluntary effort. While their duration shows a slight individual variation under similar circumstances, it varies in direct proportion with the angle of movement.*
>
> *3. They are primarily not periods of perception, but rather interruptions of vision, whose sole function is to move the line of regard to an eccentric point of interest.*

Voluntary saccades in primates can be directly related to the presence within their visual system of a fovea. In normal emmetropic eyes objects are perceived most efficiently when focused on this point and saccades are performed to align the visual axis such that the incident rays from the object of regard fall upon the fovea. Afoveate animals, such as rabbits, do make saccades to bring previously unseen parts of the visual scene into the line of sight, but generally only in association with head movements. These eye

movements are assumed to re-orient the eyes quickly to the visual space into which the animal is turning and are not thought to aim at any specific point in space.

2.2 THE PARAMETERS OF SACCADIC EYE MOVEMENTS

2.2.1 SACCADE TIMING

The visual stimulus for saccadic eye movements is target displacement, with a resultant desire to move the eyes rapidly to fixate the eccentric object. During inspection of our visual surroundings we normally execute saccadic eye movements approximately every 3 seconds, or 173,000 saccades in each 16 hour day (Robinson, 1981). Between the appearance of a peripheral target and the resultant eye movement there is a small time delay of some 180-220 msec. This saccade reaction time, or saccade latency, represents the processing of the retinal image into an eye movement command and is dependent upon many variables.

Wheeless, Cohen and Boynton (1967) have indicated that saccade latency increases slightly as target luminance is decreased although the difference is small until the luminance falls below foveal threshold. Ciuffreda, Kenyon and Stark (1987a, 1987b) have found increased saccade latencies in amblyopic eyes. White, Eason and Bartlett (1962) and Bartz (1962) reported that saccade latency may depend upon the size of the eye movement required to bring the new object of regard to the fovea, with larger saccades having longer latencies. It is well documented that age affects the saccade latency which decreases during childhood development (Miller, 1969; Cohen and Ross, 1978; Groll and Ross, 1982), reaching a minimum in young adults and then increases again with advancing age (Henriksson, Pyykkö, Schalén and Wennmo, 1980; Spooner, Sakala and Baloh, 1980; Abel, Troost and Dell'Osso, 1983; Whitaker, Shoptaugh and Haywood, 1986; Sharpe and Zackon, 1987).

The increased saccade latencies with infants and young children has been associated with attentional factors by Kapoula (1984) and Hainline (1988). Young infants are less attentive than older children or adults and may, therefore, not respond as quickly to target changes, particularly if these are not of a dramatic nature. As the child's age increases, so too does its level of concentration with a coincident reduction in saccade latency.

The increasing saccade latency in elderly subjects has been attributed to normal ageing changes in the brain affecting the higher processes generating saccades (Hainline, 1988). The increased saccade latency with elderly subjects is also associated with a slightly greater degree of variability in their saccades when compared to those of younger subjects (Abel *et al.*, 1983). A more detailed review of the effect of age on saccade performance is given by Hainline (1988).

The influence of drugs on saccade latencies has been studied showing that ethyl alcohol causes an increase in latency (Abel and Hertle, 1988). This latency change is thought to result from the effect of alcohol on the cortical structures responsible for initiating the saccade (Fuster, Willey and Riley, 1985). Other psychoactive drugs, while affecting other saccade parameters, do not appear to affect saccade latencies (Abel and Hertle, 1988).

Although practice or extra voluntary effort by the subject do not alter saccade latency, the reaction time can appear to be dramatically reduced under certain conditions. If the subject knows exactly where and when the next stimulus will appear, e.g. after a few cycles of saccadic eye movements between two fixed targets with a short, fixed, inter-stimulus interval, he can produce saccades that are practically simultaneous with the stimulus signal (Westheimer, 1954; Fuchs, 1967). A similar observation is made when a warning signal is introduced into the triggering system (Ross and Ross, 1980). This warning may be as simple as extinguishing the fixation target a set latency before the new target is illuminated or more complicated such as fixation targets which change appearance shortly before the saccade. It is possible the reduced latency after a warning signal may be a reflection of a

general preparatory or alerting process affecting the subsequent processing of target information (Ross and Ross, 1980).

2.2.2 THE RELATIONSHIP BETWEEN SACCADE AMPLITUDE AND ITS VELOCITY AND DURATION CHARACTERISTICS

Human voluntary saccades can be performed over a wide range of angles. Haddad and Steinman (1973) have recorded voluntary saccades smaller than 5.7 minutes of arc, while Hyde (1959) has measured saccades as large as 90°. Such large saccades are not usually performed during normal eye movements and various reports have indicated that most naturally occurring saccades are less than 15° (Dodge and Cline, 1901; Lancaster, 1944; Bahill, Adler and Stark, 1975). For normal refixation movements greater than 15° the head usually moves in conjunction with the eyes limiting the size of eye movement required.

Over this large range of eye movements a relationship has been identified between the saccade amplitude and the peak velocity of the movement (Westheimer, 1954; Hyde, 1959; Boghen, Troost, Daroff, Dell'Osso and Birkett, 1974; Bahill, Clark and Stark, 1975). As the amplitude of the saccade increases, so too does the peak velocity with saccades of 90° reaching peak velocities greater than 700 deg/sec (Hyde, 1959). There is, however, a saturation in the peak velocity achieved with larger saccades. This is generally complete for saccades of 50° or more, although it may occur for movements as small as 20° in some subjects (Becker, 1989). The relationship between saccade size and peak velocity is illustrated in Figure 2.1.

When saccade peak velocity curves are plotted a characteristic pattern of rapid acceleration to a peak velocity followed by a slower deceleration until the eye reaches the new object of regard is found. With large saccades (e.g. 60° and 90°) the velocity curves can be highly skewed due to the prolonged deceleration of large saccades (Hyde, 1959).

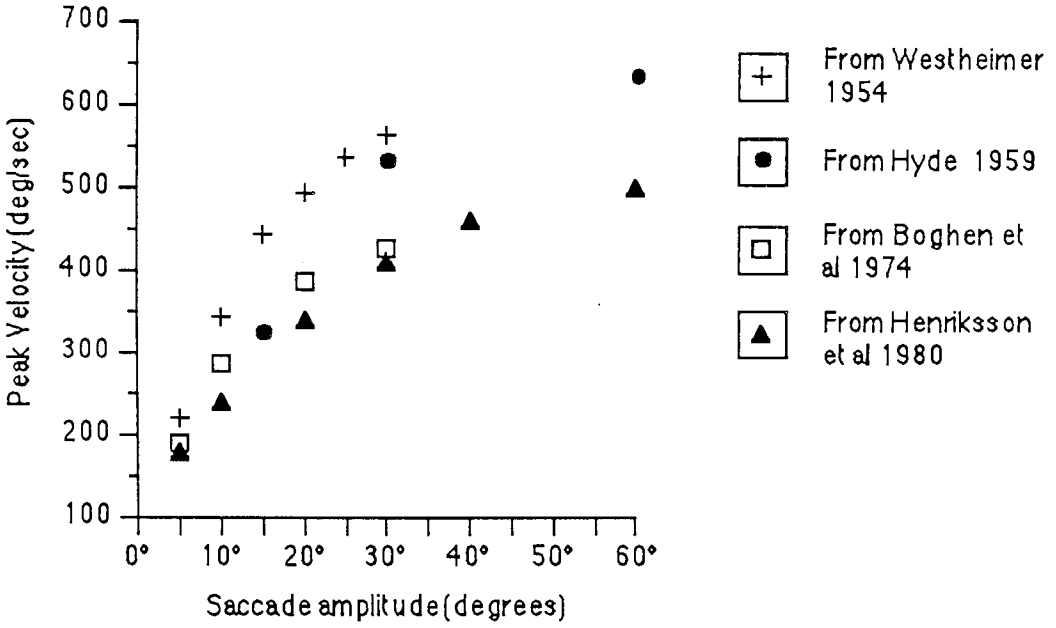


Figure 2.1 The relationship between peak saccade velocity and saccade size. Although the values are from different experiments and show the variations found with different eye movement recording methods, the underlying trend of a gradual increase in peak velocity is apparent in all the recordings.

Saccade peak velocity has also been examined for saccades of different directions and laterality with Abel, Dell'Osso, Daroff and Parker (1979) showing that centring saccades are significantly faster than eccentric saccades of identical size. The literature shows some debate as to whether abducting or adducting saccades are faster. Monocular electrooculography (EOG) measurements show adducting eye movements are faster (Boghen *et al.*, 1974; Bird and Leech, 1976), while infrared reflection techniques indicate the reverse with abducting saccades being faster (Hallett and Adams, 1980). Becker (1989) has suggested that the conflicting saccade velocity values reported for abducting and adducting saccades may be due to the different recording methods used and has shown that saccades recorded using the highly accurate scleral search coil exhibit little variation for different directions.

The relationship between saccade magnitude and the duration of the eye movement has been studied. The duration of a saccade can be determined in different ways. It may be defined as the period of time over which the eye velocity exceeds a specified threshold value or, alternatively, a direct measurement of the duration can be taken from eye

movement recordings showing the onset and offset of the eye movement. Dodge and Cline (1901), Hyde, (1959), White *et al.* (1962), Robinson (1964), Baloh, Sills, Kumley and Honrubia (1975) and Bahill, Brockenbrough and Troost (1981) have demonstrated that saccade duration increases as the saccade magnitude is increased.

If the full range of saccadic eye movements possible is considered the relationship between saccade size and duration is non-linear. If a more restricted range of saccade sizes is chosen, however, e.g. between 5° and 50°, an approximate linear function can be derived for the saccade duration where $D = D_O + d.A$ (Westheimer, 1989). In this equation 'd' represents the increment in duration per degree of amplitude, A is the amplitude of the eye movement and D_O is the intercept of the duration axis. The duration increment, d, has been calculated to be between 2 and 2.7 msec/degree, while the intercept value, D_O, ranges from 20-30 msec (Westheimer, 1989). This function is only an approximation and many saccades durations will fall outside these values. This relationship is shown graphically in Figure 2.2.

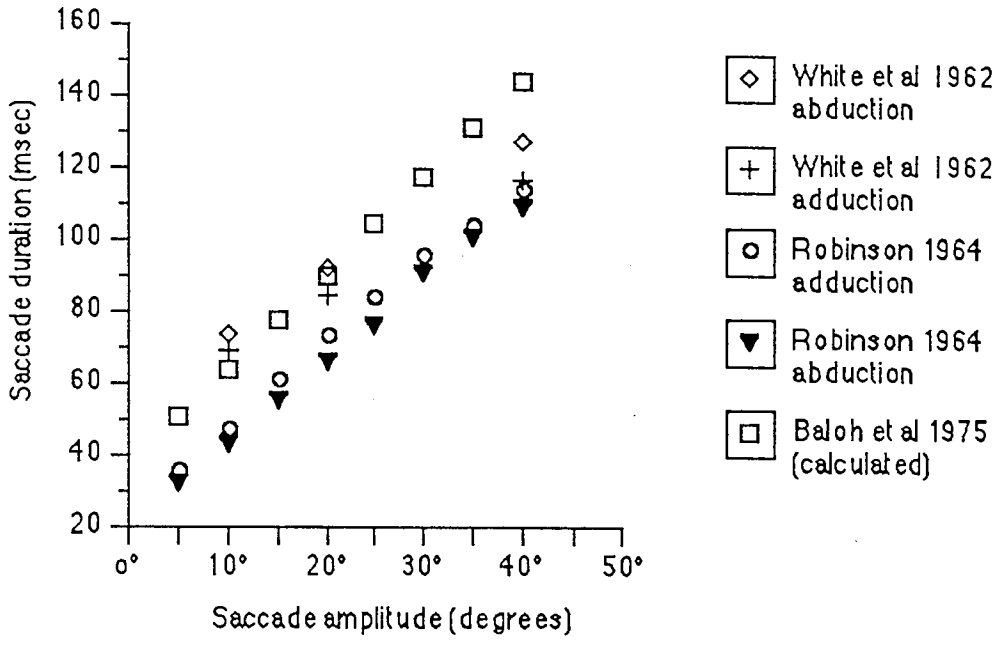


Figure 2.2 The relationship between saccade duration and saccade size. Abducting and adducting saccades have similar durations for each of the saccade sizes.

The majority of research regarding saccade parameters has been performed on horizontal saccades, interference from the eyelids making it difficult to accurately record vertical eye

movements (Yee, Schiller, Lim, Baloh and Honrubia, 1985). Experimental recordings of vertical and oblique saccades with search coils in animals has shown that vertical saccades have similar properties to horizontal saccades despite the different muscles involved (Evinger, Kaneko and Fuchs, 1981; Van Gisbergen, Van Opstal and Scheonmakers, 1985).

The relatively constant nature of the relationship between saccade size and its duration and velocity has prompted the development of a 'saccadic norm' against which unknown eye movements can be compared. This set of data, the 'main sequence' (Bahill *et al.*, 1975; Bahill *et al.*,1981), allows unknown eye movements to be identified as saccades if they fall within the limits of this relationship. Ron, Robinson and Skavenski (1972) compared the time courses and amplitude-duration relationships of saccades and the quick phases of nystagmus of monkeys to show that the quick phases fell into the same category of eye movements as voluntary saccades.

Saccades that lie outside the 'main sequence' can arise for a variety of reasons. Hainline, Turkel, Abramov, Lemerise and Harris (1984) examined the saccade peak velocity in infants and reported that, under certain conditions, these infants (14-151 days) produced slower saccades than adults. These authors attributed the reduced saccade velocities to the attentional nature of the saccade targets. The effect of increasing age has been studied with conflicting results. Spooner *et al.* (1980) reported that a normal group of elderly subjects (mean age 65 years) exhibited a peak velocity significantly lower than that of a young age group, while Henriksson *et al.* (1980) found no difference between young and old subjects for peak velocities. Abel *et al.* (1983) suggested that old age (mean age 72 years) may produce only a small, insignificant, reduction in velocity. More recently, Sharpe and Zackon (1987), in an older subject population than that used in earlier studies (mean age 77 years) have reported a significant reduction in velocities in elderly subjects

Saccades performed in the dark are generally slower than the main sequence (Becker and Fuchs, 1969; Riggs, Merton and Morton, 1974), and psychotic drugs can produce slowed

saccades (Abel and Hertle, 1988). Riggs *et al.* (1974), Bahill and Stark (1975) and Fuchs and Binder (1983) have recorded slowed saccades from fatigued subjects. Patients with an hemianopia execute slower saccades into their 'blind' half-field compared to saccades into their 'seeing' half-field (Körner, 1975).

Eye movements that appear to be faster than the main sequence would predict are also occasionally observed. These saccades generally occur, however, when the eye movement is interrupted in mid flight such that it does not reach its final destination. The saccade is therefore too small, this appearing to increase its peak velocity amplitude relationship when compared to a saccade of the correct magnitude (Leigh and Zee, 1983).

2.3 THE EXTRAOCULAR MUSCLES

2.3.1 INTRODUCTION

Movement of the eyes in humans is controlled by six extrinsic oculorotatory muscles. These muscles have been named according to their location with respect to the eyeball giving the superior, inferior, lateral and medial rectus muscles and the superior and inferior oblique muscles. A brief description of the gross anatomy of the extraocular muscles (EOM) will be given along with details of the innervation and actions of these muscles. The basic microscopic features of the EOM are similar to those of striated muscle elsewhere in the body, but there are histological differences which will be considered. There are many texts dealing with the general anatomy of the EOM and orbital contents and further details of this anatomy can be found in Duke-Elder (1961), Alpern (1969), Tunnacliffe (1984), Feldon and Burde (1987), and Spencer and Porter (1988).

2.3.2 THE ANATOMY OF THE EXTRAOCULAR MUSCLES

Five of the six extraocular muscles, the four recti and the superior oblique, originate at the apex of the orbit, the inferior oblique being the only muscle originating in the anterior orbit.

The four recti share a common tendinous origin enclosing the optic foramen and part of the inferior, medial end of the superior orbital fissure; the Common Annular Tendon of Zinn. The muscles arise from the portion of the ring corresponding with the location of their insertion on the globe and diverge as they proceed forward in the orbit away from the apex. This produces a 'muscle cone' enclosing connective tissue, motor nerves, blood vessels and fat as well as the optic nerve and the posterior part of the globe (Figure 2.3). The lengths and widths of their tendons and the respective distances of their insertions from the limbus are shown in Figure 2.4, while the gross anatomy described below can be better visualised by reference to Figure 2.3.

From its origin the lateral rectus (LR) muscle passes forwards close to the lateral wall of the orbit until it turns inwards and passes along the outer surface of the globe to penetrate Tenons capsule and insert into the sclera 7.0 mm from the lateral limbus. The insertion is 9.0 mm long and practically symmetrical above and below the horizontal meridian of the eye. The LR is 49 mm long and has a cross sectional area of 26 mm^2.

The medial rectus (MR) follows a route close to the medial wall of the orbit from its origin and, like the LR, inserts into the globe more or less symmetrically above and below the horizontal meridian of the eye. The MR is the largest of the EOM with a length of 40 mm, a width of 10.3 mm and a cross sectional area of 39 mm^2. The muscle tendon is 3.7 mm long and the line of insertion on the globe is 8.8 mm wide and 5.5 mm from the cornea.

The superior rectus (SR) originates in the superior part of the annulus medial to the globe and then runs forwards, upwards and outwards as it proceeds towards the eye. If a line is drawn connecting the middle of the SR origin and its insertion it is seen to make an angle of 23° to the medial wall of the orbit. The line of action of the muscle also therefore makes an angle of 23-25° to the line of sight in the straightforward position. The SR insertion is 10.8 mm wide and 7.7 mm from the limbus at its midpoint. The muscle is 41.8 mm long, 10.6 mm wide and has a tendon some 5.8 mm long.

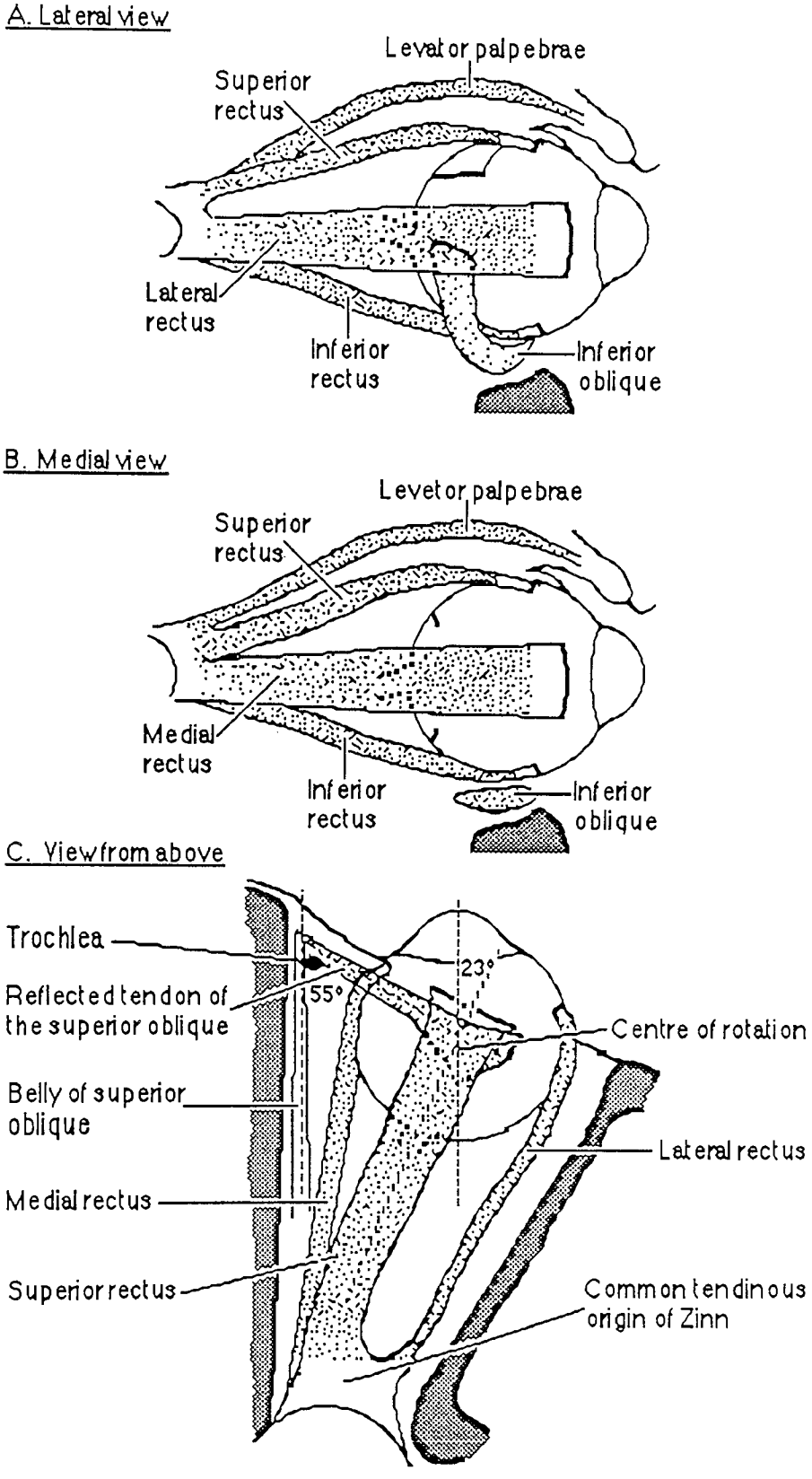


Figure 2.3 The gross anatomy of the extraocular muscles showing the 'muscle cone' produced by the divergence of the muscles from their origins. All the EOM can be seen to have broad insertions on the globe. In B. the SO is omitted for clarity, while in C. the IR follows a similar route to the SR.

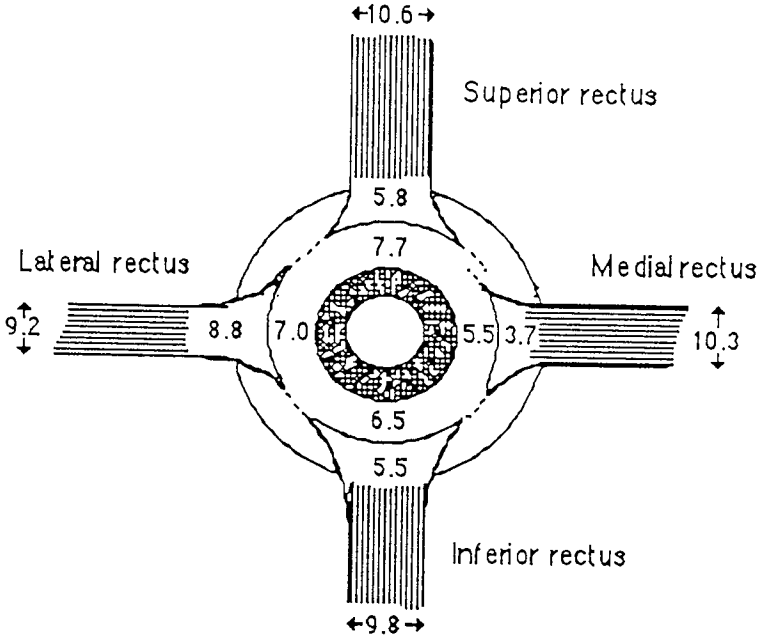


Figure 2.4 Schematic diagram of the anterior aspect of the globe to show the muscle insertions and mean tendon lengths, in millimetres, of the four rectus muscles. (Adapted from Feldon and Burde, 1987).

The inferior rectus (IR) originates at the annulus of Zinn medial to the globe and, like the SR, makes an angle of 23-25° to the line of sight as it passes forwards beneath the eye. The IR is 40 mm long, has a cross sectional area of 15.8 mm^2, a width of 9.8 mm and a tendon 5.5 mm long. It inserts into the eye 6.5 mm from the limbus with an insertion 9.8 to 10.3 mm wide.

There are two oblique muscles involved with eye movements; the superior and inferior obliques. Although they originate in different places their functional anatomy suggests an effective origin at the anterior medial corner of the orbit, the muscles passing back from here to the posterior part of the globe making an angle of 50-55° to the line of sight.

The superior oblique (SO) originates superiorly and medial to the optic foramen and passes forwards along tne angle between the roof and medial wall of the orbit until it reaches the orbital margin. The muscle, which is now tendinous, passes through the trochlea. This is a loop of fibro-cartilage attached to the frontal bone acting as a pulley to reflect the fibres back at an angle of 50-55° to their original direction. The SO tendon proceeds back to the globe above the eyeball and as it approaches the sclera, the fans out

to produce a wide (10.7 mm) insertion in the posterior, superio-lateral quadrant of the eye. The SO has a length of 60 mm, the tendon accounting for approximately half of this.

The inferior oblique (IO) differs from all the other EOM in that it originates at the anterior part of the orbit, just behind the lower orbital margin. From here the IO passes backwards, upwards and laterally to the eye at an angle of 51° to the line of sight. The insertion of the IO is 7-9.5 mm long. At 37 mm long the inferior oblique is the shortest of the EOM and the muscle is almost wholly muscular, the tendon being only 1-2 mm long.

2.3.3 THE ACTIONS OF THE EXTRAOCULAR MUSCLES

Although it is usual to consider the actions of the muscles individually it must be remembered that all eye movements are produced by the combined contraction and relaxation of two or more of the muscles. The EOM actions are detailed in Table 2.1 and shown schematically in Figure 2.5. Further details of the EOM actions can be found in Duke-Elder (1961), Alpern (1969b),Tunnacliffe (1984) and Feldon and Burde (1987).

MUSCLE	PRIMARY ACTION	SECONDARY ACTIONS
Lateral rectus	Abduction	Both LR and MR augment elevation and depression when eye already elevated or depressed
Medial rectus	Adduction	
Superior rectus	Elevation; maximal at 25° abduction	Adduction and intorsion increasing with adduction
Inferior rectus	Depression; maximal at 25° adduction	Adduction and extorsion increasing with adduction
Superior oblique	Depression; maximal at 51° adduction	Abduction and intorsion reducing to zero when eye 51° adducted
Inferior oblique	Elevation; maximal at 51° adduction	Abduction and extorsion reducing to zero when eye 51° adducted

Table 2.1 The primary and secondary actions of the six extraocular muscles showing the effect of different eye positions on these actions.

Table 2.1 shows that the individual muscles have both primary and secondary actions. The primary action is the main action of the muscle, e.g. the LR has the main action of abducting the globe. For the superior and inferior rectus and two oblique muscles this action can be seen to vary depending upon the position of the eye. In the straightforward position, for example, the oblique muscles exhibit a primary action of intorsion (SO) and extorsion (IO), although along their line of action the primary actions are depression and elevation (see Table 2.1). The secondary actions of the EOM also depend upon the position of the eye. Using the oblique muscles as an example again, the primary actions of depression and elevation when the eye is adducted become secondary actions when the eye is facing straight ahead.

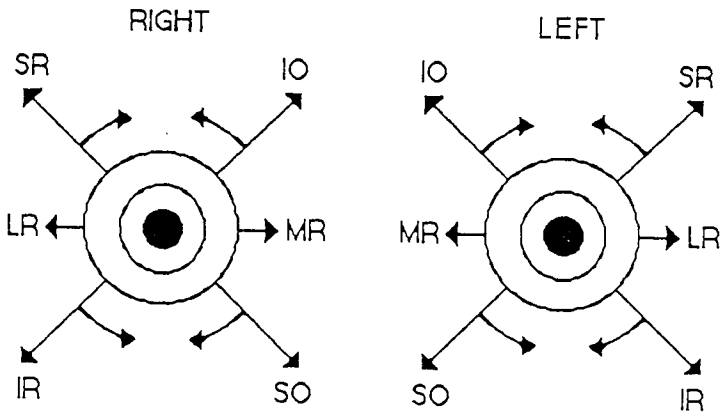


Figure 2.5 A diagrammatic representation of the primary and secondary actions of the six EOM. (After Tunnacliffe 1984).

2.3.4 INNERVATION OF THE EXTRAOCULAR MUSCLES

The eye movements produced by the EOM are dependent upon the contraction and relaxation of these six muscles. The nerves that control this activity are three of the twelve cranial nerves; the oculomotor (IIIrd), trochlear (IVth) and abducens (VIth) nerves. The fibres of these nerves are axons of the neurons having their cell bodies in the nuclei of the ocular motor nerves located in the brain stem. A summary of the functional anatomy of these nerves and their origins along with the course and distribution of the fibres will now be given and the reader is referred to Duke-Elder (1961), Alpern (1969), Feldon and Burde (1987) Carpenter (1988) and Spencer and Porter (1988) if greater detail is required.

The IIIrd nerve has two nuclei of origin, the motor nucleus and the Edinger-Westphal nucleus. The motor nucleus is situated on either side of the mid line anterior to the cerebral aqueduct at the level of the superior colliculi in the mid brain. This nucleus is inherently the most complex of the ocular motor nuclei because of the number of muscles controlled by the IIIrd nerve and there has been some debate as to the representation of the EOM within this nucleus (see Warwick, 1964). Somatic efferent fibres arise in the cells in the oculomotor nucleus to terminate in the SR, MR, IO and IR muscles. Of the muscles controlled by this nerve the SR is unique in having crossed innervation. The Edinger-Westphal nucleus innervates the intrinsic muscles of the eye controlling accommodation and pupil activity and is situated superiorly and slightly anteriorly to the somatic efferent complex.

From the motor nucleus and the Edinger-Westphal nucleus the fibres pass forwards, downward and laterally to the cavernous sinus where sympathetic fibres from the internal carotid plexus join the nerve. Just before the nerve enters the orbit it divides into two branches, a small superior branch innervating the SR and levator palpabrae muscles and a larger inferior division sending branches to the MR and IR muscles. The inferior branch also sends a branch to the ciliary ganglion where pre-ganglionic parasympathetic fibres synapse, the post-ganglionic fibres innervating the ciliary and sphincter pupillae muscles. The remaining fibres of the inferior division terminate in the IO near the front of the orbit.

As well as the somatic efferent and general visceral efferent fibres a third fibre type is present in the IIIrd nerve, this being general somatic afferent fibres proprioceptive from the above muscles. These afferent fibres leave the nerve in the cavernous sinus to join the ophthalmic division of the trigeminal nerve. Also in the cavernous sinus post-ganglionic sympathetic fibres from the internal carotid plexus join the third nerve for distribution to the dilator pupillae, blood vessels and other parts of the eyes and lids.

The nucleus of the IVth nerve is part of the somatic efferent column immediately inferior to the oculomotor nucleus in the midbrain, at the level of the inferior colliculi. Fibres pass

from the nucleus to emerge on the posterior aspect of the brain stem immediately inferior to the inferior colliculi. These fibres decussate in a plate of neural tissue, the superior medullary velum. The IVth nerve is the only oculo-rotatory nerve to decussate completely. From the decussation the nerve winds round the cerebral peduncle at the upper border of the pons to the cavernous sinus where it receives sympathetic fibres from the internal carotid plexus while sending fibres to the ophthalmic division of the trigeminal nerve. The IVth nerve enters the orbit through the superior orbital fissure to innervate the SO muscle.

Two types of nerve fibres are present in this nerve. Somatic efferent fibres arise in the trochlear nucleus of the midbrain to terminate solely in the SO muscle. Peripheral fibres of the nerve also contain proprioceptive and sympathetic nerve fibres like those of the IIIrd nerve.

The VIth nerve nucleus lies in the floor of the 4th ventricle in the caudal pons. The nerve fibres pass anteriorly from their origin to emerge at the lower anterior border of the pons. Two types of fibres are present in the VIth nerve. Somatic efferent fibres arise in the abducent nucleus of the pons to terminate in the LR muscle, while peripheral fibres of the nerve contain proprioceptive and sympathetic nerve fibres like those of the IIIrd nerve.

From their superficial origin the nerve fibres pass upwards between the pons and the anterior inferior cerebellar artery then curve forwards over the petrous part of the temporal bone to the cavernous sinus. Like the IIIrd and IVth nerves the abducent receives sympathetic fibres and sends a branch to the ophthalmic nerve before entering the orbit in the annulus of Zinn to innervate the LR muscle.

2.3.5 THE HISTOLOGICAL STRUCTURE OF THE EXTRAOCULAR MUSCLES

Skeletal muscle can be characterised by the presence of 3 or 4 different basic fibre types within a muscle which can be differentiated on the basis of their biochemical,

histochemical, ultrastructural and physiological properties. These fibre types are distributed throughout the muscles in a random fashion although the fibres in any one motor unit are usually of the same histochemical type (Spencer and Porter, 1988). The human EOM are specialised striated muscles with have certain features differentiating them from striated muscle elsewhere in the body. The histological and fibrous properties of the EOM have been described by many authors and a brief review is presented below. A comprehensive summary of the literature can be found in Peachey (1971), Bach-y-Rita (1975), Lennerstrand (1975), Feldon and Burde (1987)and Spencer and Porter (1988).

The four recti muscles have similar dimensions and consequently similar number of fibres with between 20-35,000 fibres each (Kato, 1938). The oblique muscles have less muscle fibres than the recti, each having approximately 15,000 muscle fibres. The diameter of these fibres is not constant varying from between 5μm to 40 - 50μm. Kato (1938) observed that the EOM are divided into two distinct regions; an outer, or peripheral, orbital surface layer (OSL) and an inner, or central, global region (GR). The muscle fibres are arranged in layers along the length of the muscle with a sheath of smaller diameter fibres covering the muscles peripheral surface forming the OSL. Below this lies the main body of the muscle, the global region which appears to consist of a mixture of both large and small fibres. It has proven difficult to determine accurately the distribution of fibres within the muscle because of the uncertainty regarding the length of the muscle fibres. Cooper and Daniel, (1949) suggested that the muscle fibres extend the full length of the muscle, tapering as they near the ends, while Alvarado and van Horn, (1975) have reported the smaller diameter fibres to be shorter than the muscle length and that large fibres may extend the full length of the muscle.

Fibre types within a muscle can be distinguished using many different criteria. In the extraocular muscles factors such as fibre diameter; position within the muscle; size and arrangement of the fibrils; number of mitochondria and the innervation of the fibres, along with others, have been used to differentiate the fibre types (Peachey, 1971). There has been much debate as to the nature and function of the different fibre types and although a

full review is outside the scope of this thesis the major proposals on this subject will be discussed below.

Classically the EOM have been described as having two fibre types, fast or twitch fibres and slow, tonic fibres (Hess, 1961; Hess and Pilar, 1963). This classification was based upon observations of frog muscles which have two fibre types. Some of the fibres in the muscle exhibited an 'all or nothing' response to electrical stimulation (twitch fibres), while other fibres showed a more sustained contraction to stimulation (slow tonic fibres). Peachey and Huxley (1962) showed that the activity of the muscles could be related to their morphological structure. The twitch fibres were generally larger with well developed sarcoplasmic reticulum and innervated by a large nerve fibre with large single endings on each fibre (en plaque), while the fibre itself conducted propagated action potentials. The slow fibres however, had smaller diameters and poorly developed sarcoplasmic reticulum and were supplied along their length by small diameter motor nerves with multiple (en grappe) endings with no action currents being propagated. The innervation pattern of the fast fibres means that these fibres will contract more or less simultaneously following an impulse from the motor nerve, while the tonic fibres, with their 'en grappe' endings spreading the innervational impulse across the muscle, will have a slower, more sustained, contraction. It was hypothesised that the two fibre types could explain the wide ranges of eye movements possible from very slow movements to extremely rapid saccades.

Later studies were to show, however, that the situation was not this simple. Peachey (1971), in a review of the literature, showed that the EOM could be divided into five different fibre types, while more recently it has been shown that there are six fibre types within the EOM (Spencer and Porter, 1988). These classifications were dependent upon the microscopic structures of the fibres, showing the typical twitch and slow fibres described by earlier studies with atypical fibres with varying characteristics lying in between these two groups. Similar fibre types to those proposed by Peachey (1971) were described by Alvarado and van Horn (1975).

As described above, the EOM consist of two layers of fibre types, the OSL and the GR. Within Peachey's (1971) and Spencer and Porter's (1988) classifications of the fibre types the OSL consists of two fibre types, both of small diameter, one showing multiple innervation, the other with focal innervation. The OSL singly innervated (SI) fibres are the predominant fibre type within this layer. The GR has been described as having four fibre types, all of which were of larger diameter than the OSL fibres (Spencer and Porter, 1988). Three of these fibre types are SI fibres, the other type multiply innervated (MI). A review of the histochemistry, ultrastructure, and motor innervation of these muscle fibres types is given by Spencer and Porter (1988). It is possible that the two fibre types in the OSL may correspond to the classic 'red muscle' type of fibre, high in mitochondrial content, whereas the four fibre types in the GR may correspond to 'white muscle' which is relatively low in mitochondrial content but high in galactic enzymes. This histochemical differentiation may help to explain the different types of muscle actions that are possible. Red muscle types, high in myoglobin, generally perform prolonged contractions (slow movements), whereas the muscle fibres with white fibre characteristics perform phase or twitch movements (fast movements). Kugelberg (1975) showed the histochemical reaction for myosin ATPase to be associated with contraction speed and mitochondrial oxidative activity to be associated with fatigue resistance. This implied the variety of enzyme types in the different fibre types permitted a wide range of speed and endurance specifications for the different fibres.

Although six different types of EOM fibres have been identified histochemically, only three functional types of fibres can be demonstrated using intracellular and extracellular recording methods. Lennerstrand (1975) has classified these fibres as follows; Singly Innervated (SI), Multiply Innervated Non Conducting (MINC), and Multiply Innervated Conducting (MIC) fibres.

The SI fibres are similar to mammalian twitch fibres with a resting potential of between -65 to -90 mV. Depolarisation to about -60 mV produces an action potential of 80 mV caused by rapid shifts of Na+. The end plate activity of these fibres exhibits both random miniature endplate potentials, triggered by single packets of Ach., and end plate potentials evoked

by neural impulses releasing large quantities of Ach. Depolarisation of these fibres results in a rapid contraction of the fibres, having a rise time of 5-8 msec and a decay time of 7 msec. The MINC fibres are tonic fibres which do not propagate action potentials. These fibres show a graded tension of a tonic or sustained nature to repetitive electrical stimulation. These fibres being innervated by small diameter nerve fibres. The MIC fibres have action potentials and were first described in 1966 by Bach-y-Rita and Ito. It is uncertain what percentage of EOM fibres are actually of this type. The MIC fibres conduct action potentials at a slower rate than the SI fibres and have a lower membrane potential of about 40 mV. The contraction time of these fibres is slower than the SI fibres and they are thinner in diameter.

The role of the different fibres in eye movements has been studied to determine their respective actions. It was suggested by Breinin (1971) that the constant tonic activity characteristic to the EOMs reflected the activity of slow fibres, but electromyography recordings of motor unit activity in tonic contraction showed propagated spikes and could not, therefore be arising from non propagated junction potentials of the slow fibres. The results obtained using electromyography suggest that it is too simplistic to say that fast twitch fibres are responsible for saccades and slow fibres responsible for vergence, pursuit and resting tone. It would appear that regardless of their contractile properties all types of EOM fibres may participate in all ocular movements (Chiarandini and Davidowitz, 1979). Collins and Scott (1973) and Scott and Collins (1973) have suggested that all fibre types are differentially recruited during eye movements on the basis of the amount of work the different fibres perform. It does seem likely though, that the mechanically slow fibre units are responsible for the majority of tonic activity in all gaze positions, and that singly innervated units generate most of the initial force necessary for saccades, as well as having a supportive role in fixation and pursuit.

Although these different fibre types have been identified within the EOM it is unlikely that, in normal muscles. the fibres will contract individually during a saccade. Instead, it is known that many small groups of fibres contract more or less simultaneously to produce the eye

movement. It has been shown that all the fibres within these groups are supplied by the terminal branches of the nerve fibre descending from a single motor neuron. This motor neuron, its axon, terminal branches and the muscle fibres innervated by these branches together constitute a 'motor unit'. As the muscle fibres within a motor unit contract almost simultaneously the motor unit is considered to be the smallest level of activity that can be voluntary innervated (Carusso, 1987).

The number of fibres within a motor unit varies depending upon the function and dimension of the muscle under consideration. In general, the smaller the muscle and the finer and smoother the movement it makes, the lower the number of muscle fibres it will contain, e.g. the muscles attached to the ossicles of the ear, the muscles of the larynx and, indeed, the EOM. Large, course acting muscles, on the other hand have large numbers of fibres within their motor units. The EOM are reported to contain fewer than 10 fibres per motor unit (Basmajian, 1978), while the gastrocnemius contains nearly 2000 fibres per motor unit (Feinstein, Lindergård, Nyman and Wolfhart, 1955).

When a motor unit is innervated an impulse from the motor neuron is sent to the myoneural junction where the axonal branches terminate on a muscle fibre. This impulse causes a wave of contraction to spread over the fibre giving rise to a brief twitch followed by a rapid and complete relaxation. The duration of the twitch and relaxation is dependant upon the fibre type (fast or slow) and can be only a few msec or as much as 0.2 seconds. During a saccade, or indeed any muscular activity, the motor units continuously contract and relax in response to this innervational impulse from the motor neuron. Normally the different motor units are activated in an asynchronous, but orderly manner giving a continuous shower of twitches which results in a smooth pull from the muscle. With certain muscular disturbances, however, the contractions may become synchronised resulting in a visible tremor (Basmajian, 1978). The motor unit activity of the EOM has been examined for saccadic eye movements with the technique of electromyography. This will be discussed in the following Chapter.

2.4 NEURAL STRUCTURES RELATED TO SACCADIC EYE MOVEMENTS

The neurophysiology of saccades has been examined by many different workers and while a full review of the literature is outside the scope of this thesis the pertinent points will be discussed below. For further information the interested reader is referred to Robinson (1981), Leigh and Zee (1983), Feldon and Burde (1987), Carpenter (1988) and Wurtz and Goldberg (1989). While considering any description of the neural activity related to saccades the information processing that is being performed should be remembered. For a visually triggered saccade to occur there has to be a retinal image of the new target position. This retinal picture is translated into a sensory image in the occipital cortex, the frontal eye fields and the superior colliculus. The saccade, however, is programmed in the brain stem by the prenuclear neurons, the duration of whose firing controls the duration and amplitude of the saccade. It follows, therefore, that there must be some spatial-temporal translation between the higher centres which encode the target location and the brain stem neurons which encode the saccade parameters.

2.4.1 THE PULSE-STEP PATTERN OF SACCADE INNERVATION

Saccades exist in a hierarchy of forms from simple involuntary quick phases of vestibular nystagmus to voluntary saccades to a specific command with the head held stationary. Although there are many different types of fast eye movements they all exhibit the same general trajectory of rapid acceleration to a peak velocity followed by deceleration until the eye reaches its new direction of gaze. All fast eye movements share the same basic problem of overcoming the viscous drag and elastic restoring forces of the orbital supporting tissues. To overcome these forces the extraocular muscles must initially exert a powerful and rapid contraction to start the eye movement. Once the eye has reached the new direction of gaze additional muscle activity is required to maintain this position against the elastic orbital forces that are trying to return the eye to the primary position. By looking at the innervation pattern sent to the extraocular muscles it has been possible to determine the motoneuron activity preceding and during saccades.

The neural signal that initiates saccadic eye movements consists of a burst of high frequency discharge to the agonist muscles with a corresponding period of inhibition to the antagonist muscles (Fuchs and Luschei, 1970; Robinson, 1970; Robinson and Keller, 1972). This phasic increase in the neural activity of the oculomotor nuclei is responsible for the initial rapid contraction of the EOM required to overcome the viscous orbital forces and is coordinated by the paramedian pontine reticular formation (PPRF) (Cohen and Henn, 1972; Keller, 1974). This burst of activity is the so-called *saccade pulse*. The duration and intensity of this saccade pulse determines the resultant saccade magnitude (Figure 2.6). Following the saccade an extra level of muscular activity is required to retain the eyes fixation at the new object of regard. This requires a sustained contraction of both the agonist and antagonist muscles to hold the eye position constant. This is produced by a new level of tonic neural activity; the step of innervation, or *saccade step*. This activity is produced by integration of the pulse signal in the PPRF (Keller, 1974). (Figure 2.6).

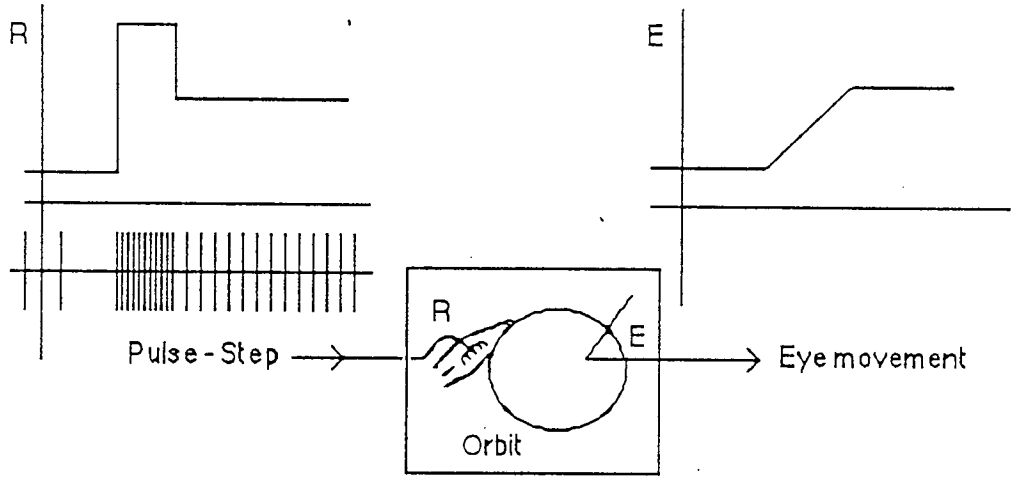


Figure 2.6 A representation of the neural signal generating a saccade. The left shows the neural activity, the vertical lines indicating the occurrence of action potentials. The graph shows the discharge rate (R) against time with the velocity command (pulse) and position command (step). The resultant eye movement is on the right where E is the eye position in the orbit against time. (After Leigh and Zee, 1983)

The saccade pulse itself is generated in the brain stem where information representing the desired change in the eye position to be achieved by the saccade is transformed into a pulse of the appropriate intensity and duration. This transformation is likely to be

controlled by a feedback loop so the activity of the pulse generator will persist as long as the actual eye displacement caused by that activity differs from the desired eye displacement. It is clearly essential that both these control signals are correctly matched for accurate saccades to be performed. Under certain conditions the pulse and step may become mismatched resulting in more complex saccadic trajectories (Bahill and Stark, 1979). For a fuller description of the pulse-step control of saccades the reader is referred to Van Gisbergen and Van Opstal (1989).

2.4.2 THE FINAL COMMON PATHWAY

There are many sensory routes through which saccadic eye movements can be initiated such as visual stimulation, the vestibular apparatus and nystagmoid eye movements. Regardless of the initial incentive to perform a saccadic eye movement however, the different sensory routes ultimately lead to innervation of the extraocular muscles. The initial contraction of the EOM is preceded by a burst of neural activity in the agonist motoneuron (Figure 2.6), with a corresponding cessation of activity in the antagonist motoneuron. At the end of the saccade there is a corresponding burst of activity in the antagonist motor neuron which may cause the antagonist muscle to act as a brake (Sindermann, Geiselmann and Fischler, 1978). This neural and muscle activity is identical for all fast eye movements and is known as the 'final common pathway' for fast eye movements.

2.4.3 THE ROLE OF THE BRAIN STEM IN SACCADE GENERATION

Foville (1858) demonstrated that the caudal pons of the brain stem is associated with the generation of horizontal saccadic eye movements while Spiller (1905) reported a similar relationship between the rostral mesencephalon and the generation of vertical saccades. Since these early studies three specific types of saccade related neurons as well as the ocular motoneurons have been identified within the PPRF. The three cell types mediating the supranuclear control of saccades are burst cells, pause cells and tonic cells (Hepp and

Henn, 1979; Van Gisbergen *et al.*, 1981). The activity of the different cell types is described below and the relationship between them can be seen in Figure 2.7.

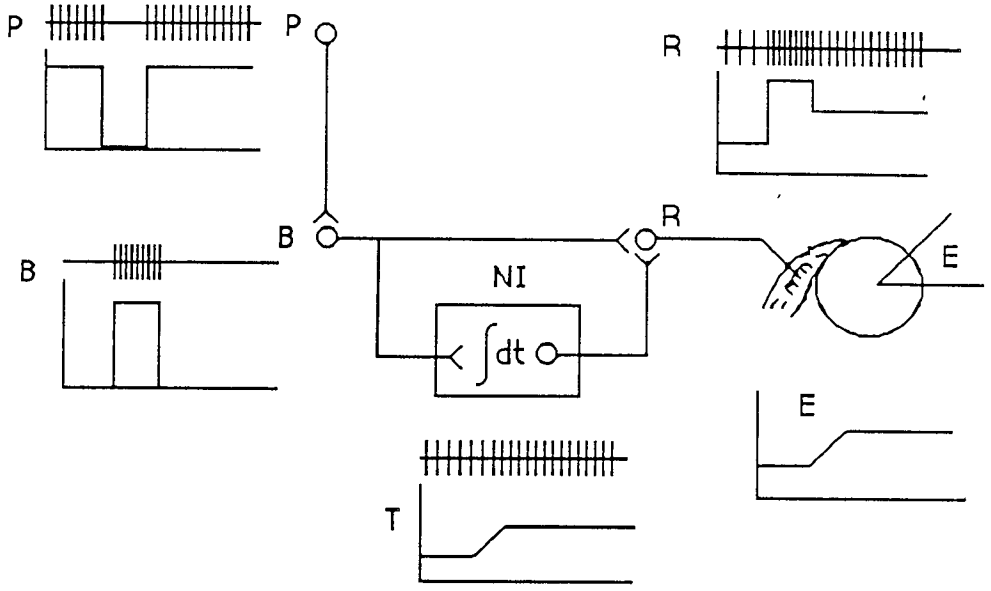


Figure 2.7 A schematic diagram of the relationship between pause (P), burst (B) and tonic (T) cells which are involved in the generation of the saccade pulse. Pause cells cease discharging just before the saccade, allowing the burst cells to generate the pulse. The neural integrator (NI) integrates this pulse to produce the step which is seen on the tonic neurons. The pulse and step combine to produce the innervational change (R) that produces the eye movement (E). (After Zee, 1980).

The ocular motoneurons (OMN) are the final link between the EOM and the pathways in the brain which initiate and program the eye movements produced by these muscles. Although differences have been shown between the different types of motoneurons innervating the muscles, these different motoneuron types are generally considered together when discussing their properties and relationship with the eye movements (Wurtz and Goldberg, 1989). Eye muscle motoneurons are situated in the nuclei of the EOM and the pathways for the axons of these neurons have been described previously.

The saccadic pulse-step of innervation has been previously described. This simple representation of motoneuron firing activity is typical of the OMN for saccades in their on-direction; an intense burst of activity (the pulse) initiating the eye movement followed by a sustained increase in activity (the step) to maintain the new line of fixation. The lead

time of single horizontal motor units is between 4-12 msec before the saccade onset (see Hepp *et al.*, 1989). The peak firing activity is reached at the onset of the saccade and the firing rate then decays during the course of the saccade. The fall off in firing activity is greater in smaller saccades than larger eye movements (Goldstein and Robinson, 1986).

For small saccades the average firing rate is approximately proportional to the saccade size, but with saccades greater than 10°-15° , however, the OMN firing pattern tends to saturate, the duration of the pulse increasing as the saccade size increases (Hepp *et al.*, 1989). The firing pattern of the OMN for the antagonist muscles is essentially a mirror image of the agonist OMN activity, although a small pulse of activity has been recorded at the end of the antagonist inhibition for small saccades (Van Gisbergen *et al.*, 1981; Sindermann *et al.*, 1978). Studies have been performed to equate the discharge patterns of the OMN with the direction and velocity of the resultant saccades. These have shown, for example, that the number of spikes in the horizontal component of an oblique saccade is essentially the same as that of a purely horizontal eye movement of the same horizontal magnitude, although the oblique saccade has a longer duration (Hepp *et al.*, 1989).

Saccade burst cells, or burst neurons, exist in two different forms; medium-lead and long-lead neurons. The medium-lead neurons contact the OMNs and exhibit a high frequency discharge commencing immediately prior and time locked to the horizontal component of all fast eye movements. The cells discharge preferentially for ipsilateral saccades and start firing some 4 msec before the the onset of the motoneuron burst. As these neurons discharge in close synchrony with the motoneuron burst and the saccade itself, they are assumed to produce the premotor command generating the saccade pulse (Leigh and Zee, 1983; Wirtschafter and Weingarden, 1988) (Figure 2.7). These neurons are known as excitatory neurons and are situated in the PPRF adjacent to the abducens nucleus. A second type of medium-lead burst neurons is also present, these being inhibitory cells. These cells create a pause in motoneuron firing for 'off direction' saccades, allowing reciprocal innervation to occur (Leigh and Zee, 1983; Wirtschafter and Weingarden, 1988). Both excitatory and inhibitory neurons project to the LR

motoneurons and the internuclear neurons. The internuclear neurons then project to the medial longitudinal fasciculus to innervate the contralateral MR motoneurons.

Medium-lead burst neurons associated with vertical saccades are in the mesencephalic reticular formation in the rostral interstitial nucleus of the medial longitudinal fasciculus (Büttner *et al.*, 1977; Büttner-Ennever and Büttner, 1978; King and Fuchs, 1979). These neurons code the vertical components of saccades in the same way as the burst neurons in the pons code the horizontal components. The vertical medium-lead neurons project directly to the vertical ocular motoneurons and the interstitial nucleus of Cajal (Büttner-Ennever, 1979).

Long-lead burst neurons, some of which discharge for horizontal saccades, others for vertical saccades exhibit irregular, low frequency, activity several hundred milliseconds before the saccade burst. It is possible that they may be active in encoding the saccade direction (Büttner-Ennever and Büttner, 1978). The long-lead neurons receive projections from the higher centres involved with saccades; the superior colliculus and the frontal eye fields (Leigh and Zee, 1983).

Pause neurons are located near the abducens nucleus and discharge continuously except immediately prior to a saccade when they pause, usually for the duration of the saccade (Zee and Robinson, 1979; Leigh and Zee, 1983). If pause cells are experimentally stimulated in the monkey the animal is rendered incapable of making fast eye movements in any direction although slow eye movements are unaffected (Westheimer and Blair, 1973). If these cells are stimulated during a saccade the movement is ceased (Keller, 1977). The activity of the pause cells led to the hypothesis that these cells tonically inhibit the burst cells until a saccade is initiated when the pause cells must themselves be inhibited to permit the burst cell to fire (Figure 2.7). This inhibition of the burst cells during fixation is obviously desirable to prevent unwanted saccadic pulses and ocular oscillations with opsoclonus and ocular flutter being attributed to abnormal control of saccadic burst neurons by pause cells.(Zee and Robinson, 1979).

Tonic neurons are also situated in the PPRF and are responsible for maintaining the eye position achieved at the end of a saccade (Robinson, 1975; Wirtschafter and Weingarden, 1988). It is possible that the tonic neuron discharge may be part of the neural integer that provides the step of innervation responsible for holding the eye in its new direction of regard following the saccade (Robinson, 1975) (Figure 2.7).

2.4.4 THE HIGHER CENTRES INVOLVED IN SACCADE GENERATION

The higher centres involved with the generation of saccades have been studied to try to determine the route with which the visual image of a targets position is transformed into a neural command to produce a saccadic eye movement. There are four higher centres involved in the generation of saccadic eye movements, the superior colliculus, the frontal eye fields, the parietal lobe and the cerebellum. A simplified schematic representation of the pathways from the visual input at the retina to the final output at the EOM is shown in Figure 2.8.

THE SUPERIOR COLLICULUS

The information given below is a brief summary of the superior colliculus (SC) and its role in saccade generation. A fuller description of the SC and its role in the generation of saccadic eye movements can be found in Sparks and Hartwich-Young (1989) and Robinson and McClurkin (1989).

It is known that the SC receives an orderly projection of the retinal image such that the visual field can be mapped upon its surface. Apter (1946) reported that if the SC is electrically stimulated an eye movement is elicited which directs the eyes towards the point in the visual field corresponding to the retinal projection of the stimulated site. Pitts and McCullogh (1947) suggested that the SC acts to drive the eyes towards the new target so that when the target image reaches the fovea the saccade will end.

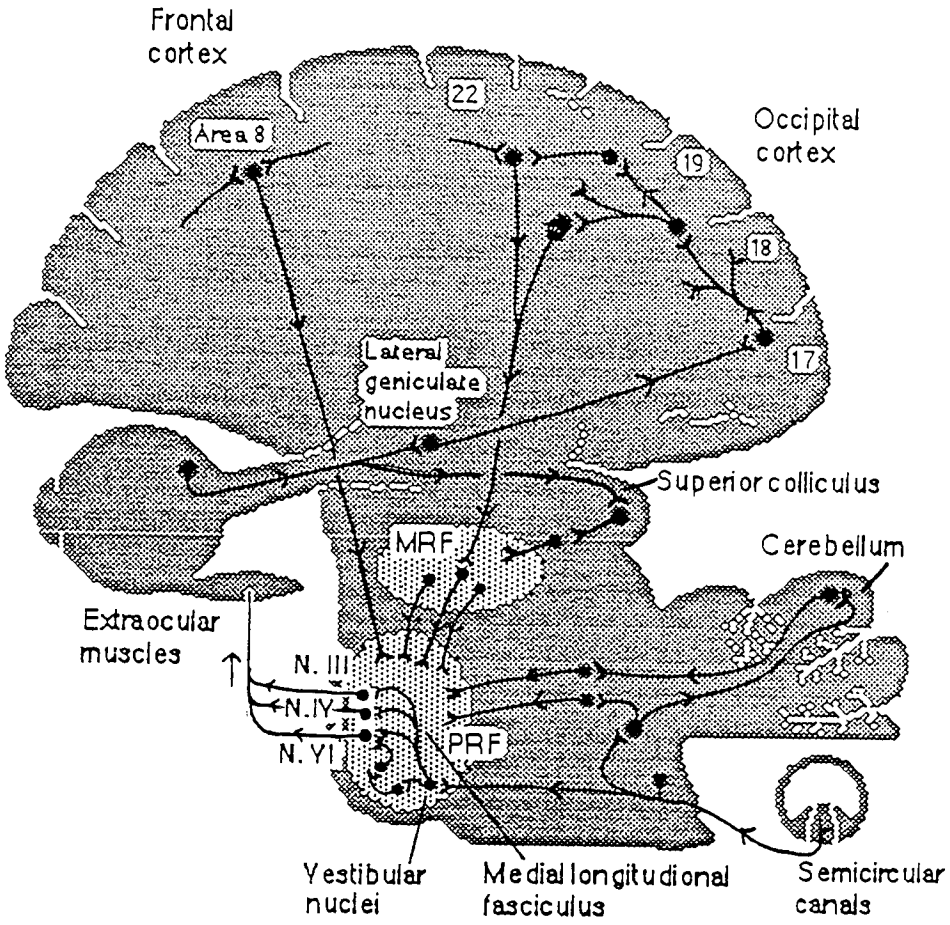


Figure 2.8 A diagrammatic representation of the neural centres involved in the generation of saccades and the interaction of these sites. The parietal and frontal cortices, frontal eye fields, superior colliculus, mesencephalic reticular formation (MRF) and pontine reticular formation (PRF) and motor nuclei are shown.

The SC consists anatomically of seven layers which are divided into dorsal (superficial) and ventral (deep) portions (Wurtz and Albano, 1980). The dorsal portion appears to play a sensory role receiving a direct retinal input and projecting to the lateral geniculate body and pulvinar. The ventral portion, however, appears to be a motor structure receiving its input from the striate cortex and projecting to motor areas within the subthalamus and brain stem. Harting *et al.* (1973) proposed that this anatomical organization suggests that the superficial SC is concerned with the visual processing while the deep SC is related to the movement of the head and eyes in response to a target. The functional anatomy of the SC, however, does not appear to be this simple, with Wurtz and Albano (1980) suggesting that the two regions can function independently of each other. Robinson (1972) and Schiller and Stryker (1972) reported the activity of the eyes to electrical stimulation of the

SC, with both vertical and horizontal saccades being elicited. The amplitude and direction of the saccade were dependent upon the location of the site of stimulation, not the electrical properties of the stimulus. Smallest saccades were recorded with stimulation of the anterolateral SC, while the largest were recorded from the posterior SC.

Single unit recordings of the visual receptive fields of collicular neurons have been made by Wurtz and Albano (1980). These receptive fields correspond to the sensory map suggested by anatomic studies of retino-tectal projections. The cells in the superficial layers of the SC respond to both stationary and moving targets, although most cells are not selective to the direction or velocity of the movement. The discharge of the superficial cells increases when the stimulus is the target for a saccade. Cells within the deep layers are more specific in their firing patterns, usually discharging before saccades made to a specific region of the visual field. The movement field of these cells is similar to the receptive field of the visual neurons in the superficial layers. Unlike the burst neurons in the brainstem, neither the duration or intensity of the cell discharge in the SC are related to the size or direction of the saccade (Leigh and Zee, 1983).

Trained monkeys have been used to study the effect of SC lesions on saccade performance (Wurtz and Goldberg, 1972). Saccade latencies are slightly increased and the saccade accuracy slightly reduced. If the SC lesion is coincident with lesions in other structures the role of the SC is further revealed. Lesions in the striate cortex, for example, produce a scotomata which makes it difficult to detect a target in that region of the visual field, resulting in increased saccade latency to that region (Mohler and Wurtz, 1977). The increased saccade latency does however diminish with practice. If the SC is then ablated, however, the original detection and latency deficits return. This implies the SC can provide the visual input necessary for accurate saccades even if the striate cortex is damaged. It is unknown if this capability exists in humans, although patients with hemianopias caused by striate lesions can make saccades towards targets presented in their blind side (Zihl, 1980)

THE FRONTAL EYE FIELDS

The frontal eye fields (FEF) have been associated with eye movements since Ferrier (1874) showed that stimulating the premotor cortical area 8 of monkeys elicited contralateral eye movements. More recently these eye movements have been identified as saccades (Wagman *et al.*, 1961; Robinson and Fuchs, 1969). The FEF have been shown to project to the basal ganglia, thalamus, pretectal region, SC and parts of the mesencephalic and pontine reticular formation (Künzle and Akert, 1977; Leichnetz 1981).

Robinson and Fuchs (1969) have shown the coding of neural activity within the FEF to be similar to that of the SC. Saccades of different directions and sizes are represented by neural activity in different anatomical locations. Like the SC, the intensity and duration of the stimulation has no bearing upon the eye movement once threshold is reached. Stimulation of one FEF will result in a contralateral saccade, usually with some vertical component. Purely vertical saccades are produced when both FEF are stimulated at corresponding sites so that the horizontal components cancel out. The latency from FEF stimulation to the resultant saccade onset is about 25 msec (Leigh and Zee, 1983).

The discharge rates of cells in the FEF were originally examined in untrained animals performing spontaneous saccades. Bizzi and Schiller (1970) recorded from cells discharging during saccades and quick phases of nystagmus, but no cells were found that discharged before rapid eye movements. Goldberg and Bushnell (1981) however, trained monkeys to perform saccades to specific targets. These authors were able to record from neurons in a restricted part of the FEF which had visual receptive fields and discharged before and specifically in relation to saccades elicited by a visual target. Bruce and Goldberg (1985) reported that 54% of cells in the FEF of monkeys discharged before visually guided saccades. These cells were further divided into three types based upon the relative strength of their presaccadic activity; visual, visuomovement and movement cells.

Visual cells were found to respond to visual stimuli but had no movement activity and did not discharge before learned saccades. Movement cells showed little response to visual stimuli, but discharge before and during learned saccades in darkness. These cells were found, however, not to discharge before spontaneous saccades. Visuomovement cells exhibit both visual and movement activity and discharge before visually guided saccades. Bruce and Goldberg (1985) also demonstrated the presence of cells which showed anticipatory activity, firing before saccades of a known direction and magnitude.

Damage to the frontal eye fields in monkeys produces only slight changes in saccade performance (Schiller, True and Conway, 1980). If the FEF alone are damaged the only abnormalities found are decreased frequency and size of saccades. If, however, both the FEF and SC are damaged an almost complete cessation of saccadic and voluntary eye movements results (Schiller *et al.* ,1980). In man, frontal lobe lesions are associated with difficulty in voluntarily looking contralaterally (Daroff and Hoyt, 1971) and suppression of unwanted saccades to contralateral visual stimulus (Guitton, Buchtal and Douglas,1982). The clinical and experimental evidence suggests that two parallel pathways produce visually guided saccades; one associated with the FEF concerned with voluntarily directing gaze and the second associated with the SC, concerned with reorienting gaze to visual stimulation. Both pathways project to a common brain stem saccadic pulse generator and can function independently of each other if one is damaged. Saccadic eye movement control is altered only if both structures are damaged (Leigh and Zee, 1983).

THE PARIETAL LOBE

A brief summary of the literature concerning the role of the posterior parietal cortex in the generation of saccades is given below. A more complete description of this region and its role in saccade generation is given by Anderson and Gnadt (1989).

Mountcastle, Lynch, Georgopoulos, Sakata and Acuna (1975) reported the presence of neurons in the posterior parietal cortex of alert monkeys (area 7a) that discharge before

and in association with saccades. These saccade cells were active when the animal made purposeful movements, but were absent when the monkey made spontaneous saccades (Mountcastle *et al.*, 1975). Robinson *et al.* (1978) later reported that many of the cells in area 7a also responded to visual or somatic stimuli. It was suggested that cells in area 7a were involved in sensory processes including selective attention.

Lesions of the parietal cortex produce eye movement defects with resultant difficulty in any visually guided task. Lynch and McLean (1982) found that parietal lobe lesions result in increased saccade latencies in the monkey, but there is little other data on the effects of posterior parietal cortex lesions on saccades. Anderson and Gnadt (1989) have shown the parietal lobe to have both motor-related and sensory-related responses indicating that the parietal cortex plays an intermediate role between sensory input and motor output in the processing of visually guided saccades acting in visuo-motor integration. This integration acts to transform retinotopic visual signals into spatial and motor coordinate information. This would help explain the deficits in spatial orientation following lesions to this region.

THE CEREBELLUM

Ferrier (1874) was amongst the earliest workers to stimulate the cerebellum and produce eye movements. It was not, however, until Cogan (1948) associated saccadic dysmetria with cerebellar lesions that control of saccades was associated with the cerebellum. Various studies have since examined the specific parts of the cerebellum associated with saccades (see Leigh and Zee, 1983) showing the cerebellum to be similar to both the SC and FEF with saccade direction coded by anatomic location in the cerebellum. Unlike these structures, however, saccades produced by cerebellar stimulation differ in that their amplitude is dependant upon stimulus intensity. The saccade amplitude depends upon the original position of the eye in the orbit as the end of the saccade tends to be at the same point in the orbit regardless of the starting position.

Lesions of the cerebellum or cerebellar disease have been shown to produce saccade dysmetria with over and under shooting saccades (Cogan, 1948; Sharpe and Fletcher, 1984). The cerebellum has therefore been implicated in compensating for non-linearities in the mechanical forces produced by the orbital contents and the EOM, the cerebellum appropriately changing the saccadic innervation to account for the position of the eye in the orbit.

Optican and Robinson (1980) showed that complete cerebellectomy in trained monkeys resulted in a saccadic dysmetria with no latency or velocity abnormalities. All the saccades were found to overshoot, this being caused by the saccadic pulse being too large. After the rapid, pulse portion of the saccade the eyes were seen to drift on for a few hundred milliseconds towards the final position of rest.

Human patients with cerebellar degeneration exhibit such saccadic pulse size dysmetria, but the specific pattern varies between patients. In general, more severe hypermetria is shown by patients with lesions involving the deep cerebellar nuclei (Selhorst, Stark, Ochs and Hoyt, 1976), while patients with cortical cerebellar lesions have mixed patterns of hypermetria and hypometria (Zee *et al.*, 1976). A greater discussion on the effect of cerebellar lesions on saccadic eye movements is given in Keller (1989).

2.5 SUMMARY

This Chapter has described the saccade system ranging from the parameters of these eye movements to the innervation of the saccades. It has been seen that saccades exist in a variety of forms, but these eye movements have the same general pattern of rapid acceleration from rest followed by a slow deceleration to the new position of regard. The peak velocity achieved during the eye movement is dependant upon the size of the eye movement, as is the duration of the saccade. The relationship between saccade size and its velocity and duration can be altered by external factors, many of which are described.

The functional anatomy and actions of the six extraocular muscles controlling the eye movements have been described as has the innervation of these muscles from the three cranial nerves involved with eye movements. The histological structure of the EOM is more complex than that of normal skeletal muscles and, although some attempt has been made to attribute different fibre types to specific actions, it appears that all fibre types are involved in both slow and fast eye movements.

Saccades are initiated by a 'pulse-step' pattern of firing activity in the ocular motoneurons, the frequency and duration of which alters with different saccade sizes. The saccade pulse acts to overcome the viscous drag of the orbital contents, while the step of activity maintains the eye at its new position of regard.

The neural structures related to saccade innervation have been outlined, from the ocular motoneurons in the brain stem to the higher centres involved in the generation of saccades. From experimental studies of the different centres involved in saccade generation a tentative pathway can be postulated for visually guided saccades which commences at the retina, goes to the striate, prestriate, parietal and frontal cortices, downward to the basal ganglia and superior colliculus. From here the saccade pathway passes to the mesencephalic and pontine reticular formations, the motor nuclei in the brainstem and, ultimately, the extraocular muscles. Such a pathway does not, unfortunately, consider all the centres involved in saccade generation and it may be many years before the full pathway of saccade generation is known.

CHAPTER 3

ELECTROPHYSIOLOGICAL RECORDINGS RELATED TO SACCADES

3.1 A REVIEW OF ELECTROPHYSIOLOGICAL RECORDING TECHNIQUES

Later sections of this Chapter will review the literature describing electrophysiological recordings related to saccades. It will be seen that there have been several different studies of this activity with different electrode types and montages. To fully understand the published results it is first necessary to consider the basic electrophysiological techniques involved. It is impossible for this thesis to give more than a general review of electrophysiological recording techniques and the interested reader is referred to Halliday (1982), Spehlman (1985) and Regan (1989) for further information on these topics.

3.1.1 ELECTRODES

In all electrophysiological recordings electrodes are used to transfer ionic potentials within the tissue adjacent to the electrode into electron flow within the recording amplifier circuitry. The main type of electrode used in recording presaccadic scalp activity has been the surface mounted electrode. Needle electrodes have also been used in studies related to all aspects of eye movements, including recording the EOM activity related to saccades. Surface electrodes are usually small, cupped metal discs positioned on the skin adjacent to the area to be recorded from. While they are preferable to needle electrodes in being non-invasive and causing less trauma for the subject, surface electrodes record over a much larger area than needle electrodes which can be inserted directly into individual muscles. Surface electrodes can be easily and repeatedly applied to the same recording site unlike needle electrodes where it is impossible to know exactly where the electrode tip is located. For eye movement recordings surface electrodes are preferable allowing recordings over a wider range of sizes. Sinderman *et al.* (1978) have found that needle electrodes are displaced with saccades greater than 20-25°

3.1.2 ELECTRODE LOCATIONS AND THE REFERENCE ELECTRODE

For any electrophysiological recording it is important to know exactly where the recording electrodes are situated. This knowledge allows one not only to determine the distribution of electrical activity, but also permits direct comparison with different subjects and ensures that accurate and repetitive studies can be performed. Knowledge of the electrode sites also means different studies in the literature can be compared. To standardize the location of scalp electrodes for electroencephalography (EEG) the '10-20 system' has been internationally adopted (Jasper, 1958). In this system each electrode is referred to constant anatomical features of the skull and located a set percentage (usually 10 or 20%) of the distance along the lines connecting these anatomical 'landmarks', e.g. inion to nasion. Each recording site is given a letter to identify the area of brain over which it is located and a number to indicate the right (even numbers) or the left (odd numbers) hemisphere (Figure 3.1).

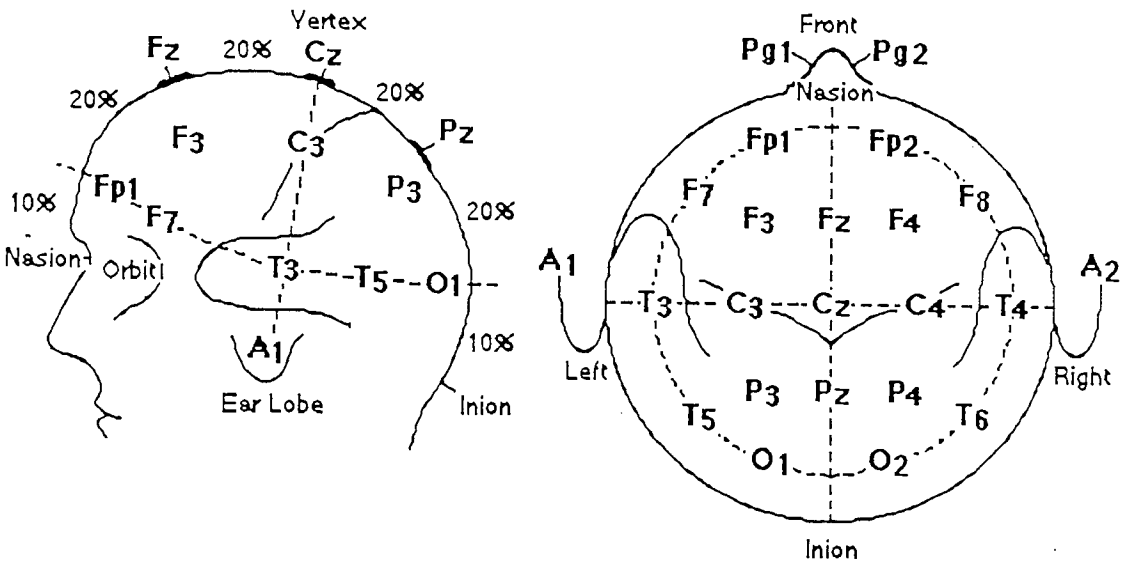


Figure 3.1 A schematic representation of the electrode placements in the 10-20 system in relation to the inion and nasion and the Rolandic and Sylvian fissures.

Some concern has been expressed about limitations of the 10-20 system, particularly regarding the lack of symmetry of the human skull (Binnie, 1987), and additional electrodes sites have been proposed to overcome these limitations. For the purposes of

this thesis, however, the 10-20 system will be used in its original manner as described by Jasper (1958), with additional electrodes located around the eyes to record the frontal activity.

Before any electrophysiological recordings can be made, the type and position of the reference electrode must be decided. Ideally electrophysiological recordings measure the potential difference between an active electrode located at or close to the source of the potential and a reference electrode distant from this point. Various possibilities are open to use for the reference electrode and common reference, bipolar, average reference and the balanced non-cephalic reference are techniques commonly used.

The simplest method of recording is common referencing, also known as monopolar or unipolar recording. In this technique each 'active' electrode in the montage is compared to a single common reference electrode, the difference between these electrodes being recorded. Common referencing generally assumes the reference site chosen is relatively inactive with respect to the activity at the recording electrodes, although ideally equipotential to the active electrodes with respect to myogenic activity, artefact or interference potentials. It should be noted, however, that no location on the body can be regarded as totally inactive in the sense that an evoked potential will be unaffected by the reference electrode (Regan, 1989).

With bipolar recording the electrodes are connected in a chain such that the first electrode is referred to the second, the second is referred to the third and so on. This method is useful to help determine the position of a locus of activity, this being indicated by a phase reversal in the waveform. The locus can be more accurately pinpointed if the phase reversal is recorded at an electrode common to two bipolar chains mutually at right angles.

Average referencing was first described by Offner (1950). By connecting all the electrodes together through high resistances and using the common junction as the reference he was able to show that if a large potential was recorded at one electrode it

would be recorded at the other electrodes with reversed polarity and reduced amplitude. The reference in this method, therefore, is an artificial reference obtained from the average of all the electrodes being used. In practice the average point is obtained by connecting each active electrode through a resistor of 1 or 2 MΩ to a common point. With this technique the maximum amplitude of the recorded activity is slightly less than that obtained with an unrelated reference electrode, the active electrode potential being reduced by the potential of the average reference. Care has to be taken with average references to avoid eye movement and muscle artefacts interfering with the average electrode potential and therefore giving false potentials at the other electrodes. This can be overcome by excluding from the reference any electrodes close to the eyes for example.

Regardless of the type or location of the reference electrode on the scalp there is always the problem of ensuring the relative inactivity of this electrode. Stephenson and Gibbs, (1951) attempted to overcome this problem by designing a reference electrode distant from the scalp; the balanced non-cephalic reference (BNC). One electrode is placed on the right sterno-clavicular joint and the other is placed on the spinous process of the seventh cervical vertebra, the vertebra prominens. The two electrodes are joined via two variable 20 KΩ potentiometers which can be adjusted to balance out the electrocardiogram (ECG), although complete elimination of the ECG can be time consuming.

3.1.3 AMPLIFYING, FILTERING AND AVERAGING THE RECORDING

Having recorded an evoked potential it is often difficult to observe the exact waveform of the potential against the random background electrical activity whether it is from the brain or muscular in origin. This problem has been overcome by the techniques of amplifying and filtering the response and averaging the waveforms to eliminate the background noise and therefore enhance the signal to noise ratio.

Averaging, introduced by Dawson (1954), allows any time-locked responses to be extracted from unrelated background activity by repeatedly adding each incoming epoch of activity to those already stored and dividing the resultant record by the total number of epochs recorded in the averaging process. This produces a final trace in which the time-locked activity has been enhanced and the random background activity diminished by cancelling itself out (Figure 3.2).

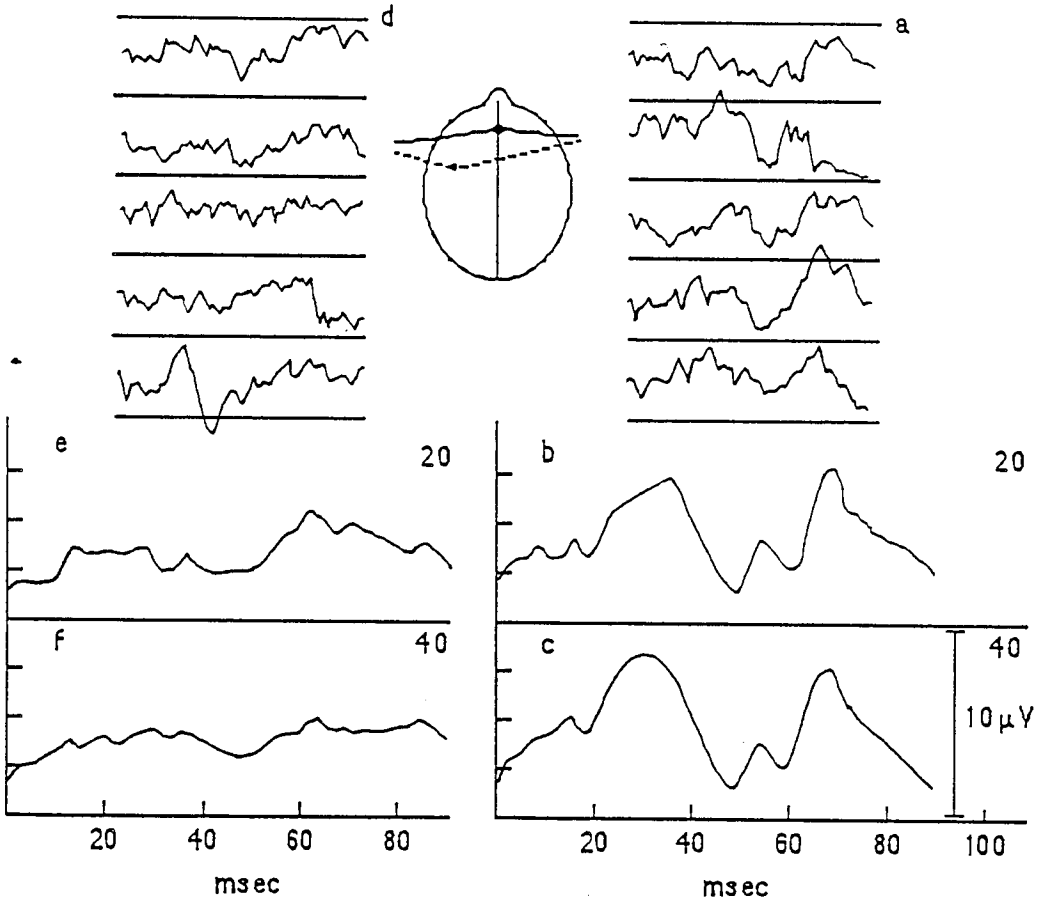


Figure 3.2 The principles of averaging as described by Dawson (1954). The right side of the figure shows the EEG data when a stimulus is applied to the right arm and recorded from the left scalp. In the top traces (a) the responses are not clear amongst random background activity. The bottom traces show the effect of 20 (b) and 40 (c) averages with the waveform clearly seen. For comparison the left side shows raw EEG data when no stimulus is applied (d) and 20 (e) and 40 (f) averages of this recording.

Averaging is used in most sensory recordings including visual, auditory and somatosensory and the number of epochs averaged is dependant upon the type of response being recorded. Large, easily distinguished potentials may be evident against

the background activity with only a few averages, whereas small, indistinct potentials may require many hundreds, or even thousands of epochs to produce a satisfactory waveform.

Before the response can be averaged however, it must first be amplified. The recordings made following each stimulation are fed into an amplifier which differentially amplifies the response. The procedure of differential amplification is designed to enhance the final waveform, the amplifier only amplifying the difference in potential between the two electrodes. This means that in-phase potentials, i.e. potentials that are common to both electrodes, will be ignored. The effectiveness with which the amplifier discriminates between in-phase and out-of-phase potentials is known as its common mode rejection ratio. Modern amplifiers aim to have a common mode rejection ratio of about 10,000 to 1, so that in-phase signals have to be 10,000 times larger than out-of-phase signals in order for them to be recorded as the same size. Differential amplification is useful to eliminate unwanted artefacts such as mains interference which will be common to both electrodes. Amplifiers can also be used to alter the size of the input signal (signal gain), this amplification being expressed as the ratio which indicates how many times larger the output signal is compared to the input signal.

A major technique used to obtain an ideal waveform is to filter the input signal in order to remove as much noise as possible without distorting the waveform morphology (Regan, 1989). Careful filtering can enhance the input signal such that fewer responses are required for averaging to produce a satisfactory waveform. Filters can be used to reduce both high and low frequency noise. A high frequency, or low pass filter, will remove frequencies above a set frequency, while a low frequency, high pass filter, will remove frequencies below a set level. The spectrum of frequencies within the upper and lower limits set by the filters, i.e. free to be amplified, is known as the bandpass, or bandwidth of the amplifier. By adjusting the bandwidth parameters the effects of undesired potentials such as low frequency EEG activity or high frequency myogenic activity can be minimised. Additional filters can be used to remove specific frequencies, these being 'notch' filters. Notch filters are most commonly used to remove mains interference (50 Hz in the UK).

Most responses are filtered before they are digitised for averaging and these filters are said to be analog filters. Digital filtering is also possible, having the advantage that it does not distort the time relationship of the signal as analog filtering can do.

An important feature of filters is that they do not abruptly exclude frequencies beyond their limits but instead progressively attenuate them, this attenuation commencing well before the 'cut-off point' of the filter. The 'cut-off point' is the frequency at which there is a predetermined attenuation with respect to the maximal amplitude of the frequencies passed expressed as a percentage of decibel ratio. This point is often defined as the the -3 dB point, i.e. the frequency at which a signal at the filter output is reduced by 3 dB or 30% of the maximal amplitude. Other common cut-off points are -2 dB (20% reduction) and -6 dB (50% reduction). The rate at which the amplitude declines for frequencies outside the bandwidth is known as the 'roll-off' of the filter. This is often 6 dB per octave, i.e. a 50% reduction in amplitude of the input frequency for every doubling or halving of the frequency at the upper or lower end of the bandwidth. Notch filters tend to have a much steeper roll-off than standard filters used to control the bandwidth characteristics.

An additional function found on averagers is that of smoothing the waveform. After averaging has been completed the waveform on the screen is a line drawn exactly through each data point in turn. A common type of smoothing is three point smoothing, where the average of three successive data points is taken and the line redrawn through this average point. Smoothing is, in effect, a further digital filtering and care should be taken to avoid secondary filtering, particularly reducing the amplitude of short waves (Spehlman, 1985).

3.1.4 SUMMARY

The above sections have described the basic techniques used in electrophysiological recordings, including the spike potential. The principles of averaging, filtering and amplifying the response have been described. The combination of the appropriate recording conditions (electrode locations and stimulus) followed by filtering, amplifying

and averaging the responses as described above will allow detailed studies of all aspects of electrophysiology to be performed. A description of the actual recording set up and electrode site preparation used in the experimental work in this thesis will be given in Chapter 4, as will a description of the eye movement monitoring technique used. Any individual variations in the recording set-up for different experiments will be given in the appropriate sections.

3.2 THE PRESACCADIC SPIKE POTENTIAL: AN HISTORICAL REVIEW

Although eye movements and electrophysiological potentials associated with them have undergone much intensive study over the years, the spike potential has only recently been recognised as a genuine recording related to saccades and their onset. For many years a small spike-like potential has been observed at the beginning of saccadic eye movements when recorded by electrophysiological techniques but this has generally been referred to as an artefact of eye muscle origin. Indeed, many clinical handbooks have described this potential in their artefact sections (see MacGillivray, 1974; Beaussart and Guieu, 1977; Binnie, Rowan and Gutter, 1982 and Halliday, 1982). The following sections will review the literature describing electrophysiological recordings related to saccadic eye movements.

3.2.1 ELECTROMYOGRAPHY OF THE EXTRAOCULAR MUSCLES DURING SACCADIC EYE MOVEMENTS

The presence within the EOM of motor units has been discussed in the previous Chapter. Electromyography (EMG) is used to study the electrical characteristics of such motor units, both individually and in relation to other motor units within the muscle. The electrical activity recorded by EMG is the motor unit action potential (MUAP). It has been observed previously that following the impulse to the fibres in a motor unit there is a resultant twitch of the muscle fibres. During this twitch a minute electrical potential of very short duration (less than 5 msec; Basmajian, 1978) is generated and dissipated into the surrounding

tissue. As the muscle fibres within a motor unit do not contract at exactly the same time the potential generated by the single twitch of all the fibres of the motor unit is prolonged to about 5-12 msec. This overlap in activity of the muscle fibres produces a resultant signal that is a spatial-temporal summation of the individual action potentials propagating on many muscle fibres; the MUAP. Obviously, in order to give a sustained contraction of the muscle the motor units must be repeatably activated. This requires a sequence of MUAPs; a motor unit action potential train (MUAPT). Needle electrodes inserted directly into the muscles can be used to record both individual action potentials and MUAP or MUAPTs. While surface mounted electrodes will also record this activity they give a more global recording of the muscle activity from a group of muscles (Basmajian 1978). The waveform and parameters of the potential recorded are therefore dependant upon the electrode type and recording site chosen.

The majority of EMG studies of the EOM have used needle electrodes inserted into the muscles to record the activity for different types of eye movements. Björk and Kugelberg (1953) recorded the motor unit activity of the levator palpebrae and the four recti muscles and found the frequency of motor unit firing increased with increasing voluntary contraction from about 50 discharges per second for weak contraction to 100 discharges per second for moderate contraction. The maximum discharge frequency was as high as 150 discharges per second in normal muscles. The firing duration of the motor units was about 1-2 msec and the amplitudes were about 110 μV (Björk and Kugelberg, 1953). These values can be compared to the average normal values for other skeletal motor units where the amplitude ranges from 100-3000 μV with a duration of some 5-10 msec and a frequency of 5-30 discharges per second (Breinin and Moldaver, 1955). Similar duration and firing frequencies to those previously reported by Björk and Kugelberg (1953) were found by Breinin and Moldaver (1955), but the amplitude values recorded by these authors were greater than those of Björk and Kugelberg (1953). Breinin and Moldaver (1955) suggested that the amplitude was very dependant upon the position of the electrode within the muscle with only small variations giving an increase of hundreds of microvolts.

Goodgold and Eberstein (1977) have described the action potentials of the normal EOM as having an amplitude of between 20 - 600 μV (mean amplitude 200 μV in the primary position), a duration of between 1-2 msec and a high frequency firing rate of several hundred discharges per minute. They also reported the ease with which reciprocal innervation can be shown using EMG if a pair of needles are inserted into direct or contralateral antagonists (Goodgold and Eberstein, 1977).

Electromyography has been used to study the motor unit activity of the EOM associated with saccades by several workers. Miller (1958) recorded the activity of four EOM to study the innervation of saccadic eye movements. This investigation showed saccades to be preceded by an initial burst of activity in the agonist with a corresponding inhibition of the antagonist. The duration of the initial burst varied from 3 msec for 2.5° saccades to 150 msec for 40° eye movements. Following the saccade the activity of both the agonist and antagonists reached a new and constant level for the duration of the recording.

Tamler, Marg, Jampolsky and Nawratzki (1959) performed a similar study recording activity from the LR, MR, SR and SO muscles during saccades. They found that during a saccade there was a burst of activity in the agonist, complete inhibition in the antagonist and coactivity of the auxiliary muscles. Following the saccade the activity of all the muscles returned to that which would be expected for the new line of regard. Tamler *et al.* (1959) did not agree with the results of Miller (1958) however, and suggested that the increased level of activity was present in the agonist for the complete duration of the saccade.

Sindermann, Geiselmann and Fischler (1978) used needle electrodes in the EOM to study the single motor unit activity during fixation and saccades from 8 subjects. The MR and LR muscles were studied for saccades up to 60°. The saccades were monitored using EOG recorded from standard skin electrodes. Sindermann *et al.* (1978) found that clear recordings could only be made for a limited range of saccade sizes as the needles became displaced from the motor units with saccades greater than 20-25° in amplitude. The activity of 14 motor units was studied and a characteristic pattern of motor unit activity was found

for saccadic eye movements. Regular firing before the saccade onset gave way to a burst of discharges immediately before and during the start of the eye movement for saccades in the 'on' direction of the muscle with corresponding silence for movements in the 'off' direction. The first saccade discharge usually preceded the onset of the eye movement by a few milliseconds, this latency having no dependence upon the saccade size. The instantaneous discharge rates of the motor units during the 'saccade burst' were found to increase as the saccade size increased, from 75-150 per second for saccades less than 5°, to 260-290 per second for larger saccades. With eye movements of 15° or more the discharge rate apparently saturated. Sindermann *et al.* (1978) also studied the activity of motor units in their 'off direction' during the saccade and showed that these motor units resumed firing shortly before the saccade offset at a higher rate than the post-saccadic discharge rate. It was presumed that this reactivation of the antagonist muscles helped to end the saccade movement by acting as a braking mechanism.

The burst of activity which can be recorded in the agonist can be likened to the saccade pulse, while the new level of sustained activity following the saccade is comparable to the saccade step required to maintain the eye's fixation in its new position of regard. The recordings of EMG activity associated with saccades would appear therefore, to confirm the known saccade pulse-step innervation pattern which has been identified at the oculomotor nuclei in the brain stem (see 2.1.2).

3.2.2 ANTERIOR SCALP ACTIVITY ASSOCIATED WITH SACCADIC EYE MOVEMENTS

The previous section has described the electrophysiological activity recorded from the EOM immediately prior too and during saccades. These eye movements have been shown to be preceded by a burst of muscle activity in the agonist and it is this activity that may be responsible for the small spike like potential which can be recorded at the onset of saccades from electrodes located round the orbits. It has been noted previously that the presence of anterior spike activity associated with saccades has been acknowledged for

many years, but it has generally been referred to as an artefact of eye muscle origin. Although considered by many as an artefact, some work has been performed to determine the origin of this anterior spike potential and a review of the literature concerned with this spike potential is given below.

In all mentions of the spike potential as an artefact, except that by Beaussart and Guieu (1977), the lateral rectus is proposed as an origin. Beaussart and Guieu (1977) considered that the large area around the orbits from which the spike could be recorded suggested that the orbicularis oculi muscle was a more probable site of origin. The association of the spike potential and LR can be traced back to Blinn (1955) who described a 'focal anterior temporal spike' related to eye movements recorded during EEG recordings. Blinn (1955) showed that frontal electrodes used in EEG recordings can record a spike like deflection at the onset of saccadic eye movements closely resembling an isolated muscle potential (Figure 3.3).

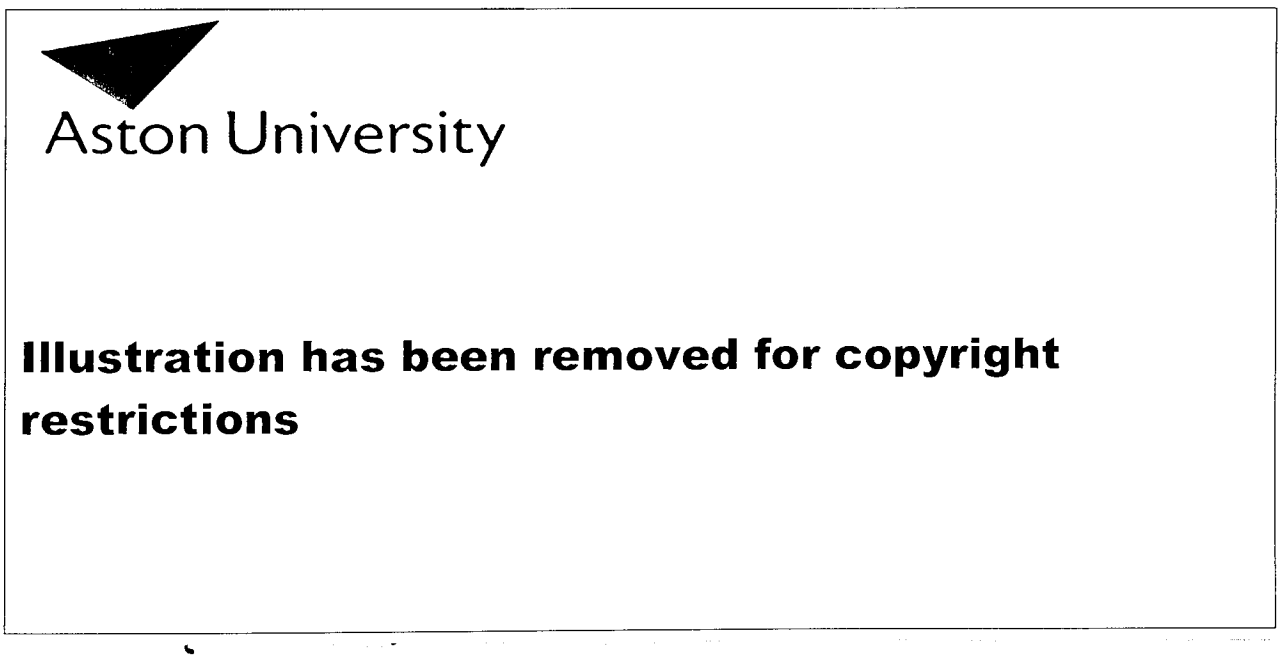


Figure 3.3 Bipolar leads positioned to emphasize phase reversals over the anterior temporal areas. An 'external rectus muscle spike' and its associated eye movement (ocular dipole) recording can be seen on the right side of the head (the rectus muscle spike is identified by the arrow). The left side shows only an ocular dipole potential. (From Blinn, 1955)

Using closely spaced electrodes on the scalp to map the distribution of this potential and correlating individual spikes with the eye movements generating them Blinn (1955) concluded the spike originated in the 'external rectus muscle'. The relatively wide spread over which this potential was recorded was thought to be due to the deep position of this muscle within the skull (Figure 3.4). Blinn (1955) considered the spike was generated by integral contractions of many motor units within the muscles.

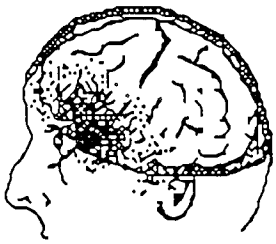


Figure 3.4 Amplitude distribution of 'focal anterior temporal spike' showing wide spread of the potential due to volume conduction through muscle, bone and skin (After Blinn, 1955).

Similar frontal spike potential activity has also been observed as an artefact of EOG traces. While using the EOG to study saccades under different conditions, Becker and Fuchs (1969) reported that all their eye movement records were preceded by a small, short duration (approximately 8 msec) potential in the opposite direction to the eye movement. The amplitude of the potential was equivalent to an eye movement of 2°. A similar spike had previously been described by Brockhurst and Lion (1951) as a small reversal in the direction of eye movement forming the initial part of a saccade.

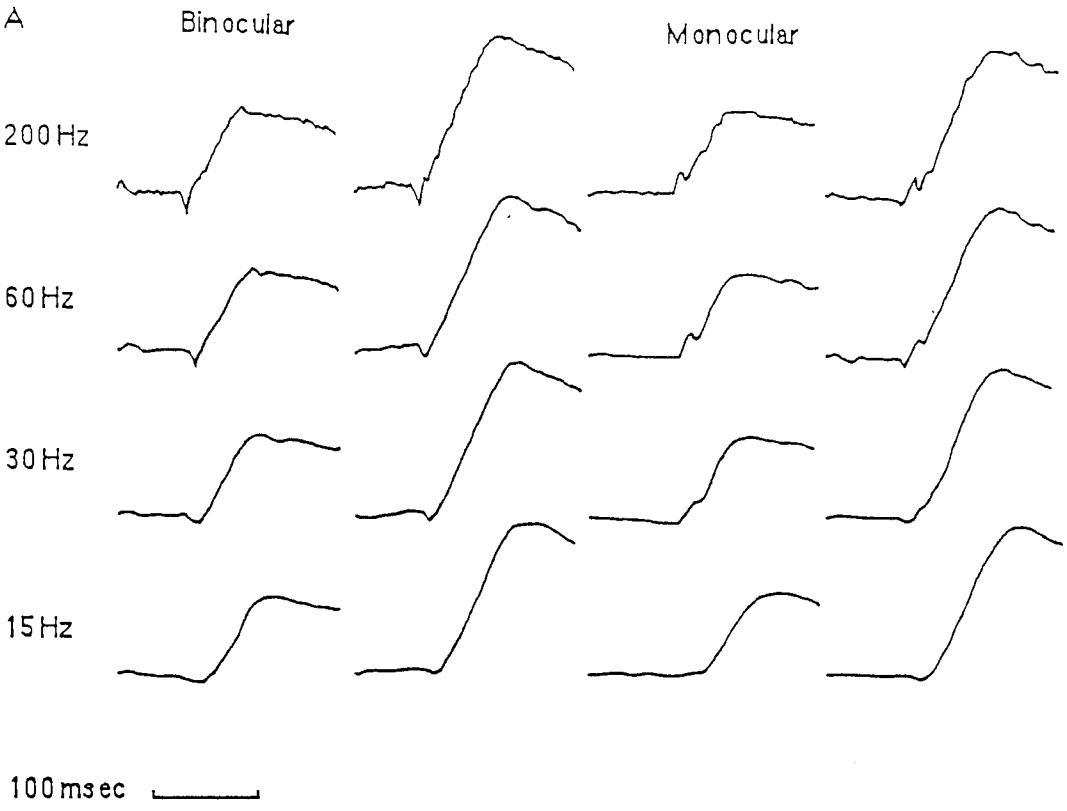
Lion and Powsner (1951) also reported a small negative spike (about 10 μV) at the onset of EOG recordings for both large decentring saccades and reading eye movements. They also suggested that this spike may be a retrograde eye movement of approximately 2° forming the initial part of the saccade, or possibly a minute muscle twitch connected with the onset of the eye movement.

The consistent nature of this spike led Becker and Fuchs (1969) to use it to aid identification of the saccade onset on EOG traces. They considered, however, that the spike represented an electrophysiological potential peculiar only to EOG recordings as opposed to a true eye movement.

Attention has recently been re-drawn to this spike deflection on EOG traces by Jäntti (1982), Jäntti, Aantaa,Lang, Schalén and Pyykkö (1983) and Jäntti and Häkkinen (1987) who have described a spike artefact associated with saccadic eye movements.

Jäntti (1982) performed a series of experiments to study the effects of different electrode sites and filters on the saccade spike. He was particularly interested in the effect the spike may have on automatic analysis of saccades. The spike was recorded from 22 patients with an electrode at the left outer canthus and another 3.5 cm temporal to this and a vertex electrode (C_Z, 10-20 system) was used as the reference. Saccades were initiated by two red LEDs, 25° apart, which lit alternately to trigger the saccades. A high cut-off filter of 30 Hz and a time constant of 2.5 second were used. Using this method Jäntti (1982) recorded spikes in all subjects for the more lateral electrode and 18 of the 22 subjects for the electrode at the outer canthus. The spike was found to occur very regularly with subjects showing spikes as often as 28 out of 30 recordings.

The effect of filtering the saccade spike was examined by recording the spike with a high frequency cut-off of 200 Hz and a low cut-off of 0.5 Hz. Following recordings the waveforms were digitally filtered with filters having high cut-off points of 15, 30 and 60 Hz. These filters were designed to simulate the effects of ordinary analog filters. Three subjects were used to record spikes from electrodes 15-20 mm from the outer canthi of both eyes for 24 saccades of 15 and 30° to the right of centre. The effects of the filters are shown in Figure 3.5a which indicates that the spike potential is clearly visible after filtering with the 30 Hz filter and a small deflection is just evident on the waveforms even after filtering with the 15 Hz filter.



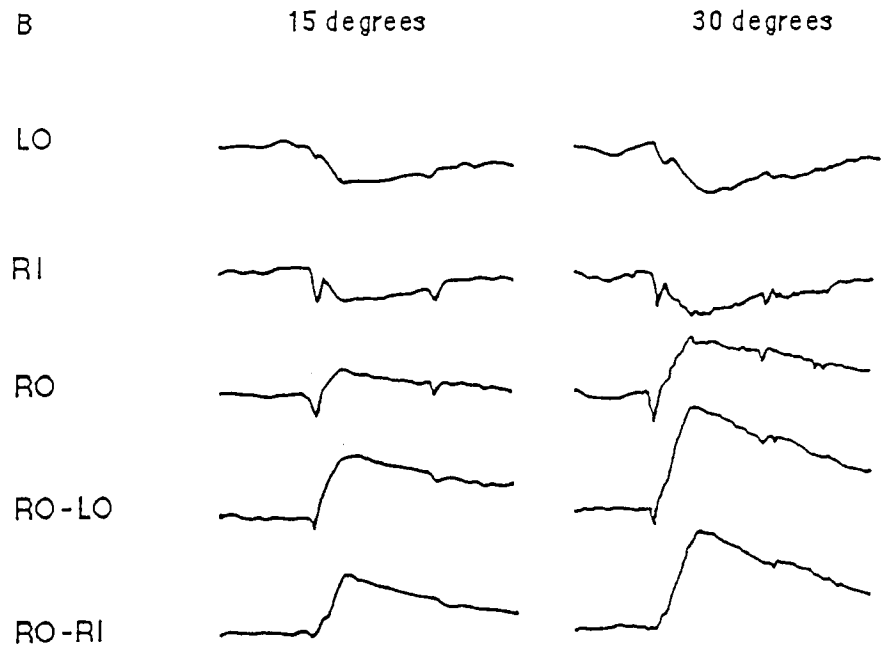


Figure 3.5a Effect of high frequency filtering on four saccades of 15° and 30° to the right. There is a polarity reversal in the saccade spike for binocularly recorded saccades.

Figure 3.5b The saccade spike recorded from the left outer canthus (LO), the right inner canthus (RI) and the right outer canthus (RO) with Cz as a reference electrode. The bottom two traces show the EOG activity recorded binocular (RO-LO) and monocular (RO-RI) where the SP activity is seen to be reduced (After Jäntti, 1982)

Jäntti (1982) used one subject to study the occurrence and shape of the saccade spike at three different electrode locations for monocular and binocular recordings. Electrodes were located at the left and right outer canthi and the right inner canthus with C_Z as the reference. The recordings were made with a high frequency cut-off of 200 Hz and a low cut-off of 0.5 Hz, and 24 saccades of 15° and 30° were recorded. The waveforms showed negative spikes for both the main saccades and later corrective saccades made by this subject (Figure 3.5b). Some waveforms were seen to be followed by a small burst of asynchronous activity similar to background EMG noise. When the spike was recorded with EOG electrodes the amplitude was reduced and, in cases where the spike was larger at the inner canthus, it had a positive potential in the EOG.

Jäntti (1982) concluded this study by expressing concern at the way in which the saccade spike can distort the onset of EOG recordings interfering with accurate quantitative eye movement analysis. In some cases the maximum saccade velocity appeared to coincide with the saccade onset but this was a measure of the shape of the spike rather than the saccade. This problem was reduced when 15 Hz high cut-off filters were used but these, unless digital, may also distort the saccade shape.

Jäntti (1982) suggested that the saccade spike resembled the compound action potential recorded from muscle after electrical stimulation of a peripheral nerve. Such stimulation generates a synchronous volley of action potentials in motor nerves causing near simultaneous activation of many muscle fibres. The potential resulting from this muscle activity shows a mainly negative component. Jäntti (1982) considered the spike in EOG records may arise from a synchronous volley of action potentials generated in the OMN in the brainstem (the saccade-pulse) causing a corresponding near simultaneous activation of muscle fibres in several motor units of the ocular muscles. His proposed origin of the saccade spike was the facial muscles due to the wide area over which it could be recorded, quoting Beaussart and Guieu (1977) who also suggested the orbicularis oculi muscle may produce the spike.

This origin for the spike potential was supported by Jäntti *et al.* (1983) when they repeated the earlier work performed by Jäntti (1982). Saccade spikes were recorded from electrodes at the inner and outer canthi. Different saccade sizes were examined and the saccade spike was recorded with closed eyes. A difference in the spike amplitude was reported for 40° and 5° saccades although no actual amplitude values are given. The spike was also recorded with the eye movements of rapid eye movement sleep. Jäntti and Häkkinen (1987), however, have since indicated that the saccade spike cannot, in fact, originate in the facial muscles. These authors have recorded saccade spikes with equal amplitudes from both sides of the face of a patient whose right facial nerve was cut in a tumour operation. Jäntti and Häkkinen (1987) concluded that the spike must actually be originating in the extraocular muscles.

The lateral rectus spike described by Blinn (1955) was later referred to in the work of Riggs *et al.* (1974). While examining saccadic suppression from subjects performing 20° saccades, spike-like potentials were recorded at the saccade onsets from electrodes over the posterior scalp. These spike potentials were exactly coincident with a much larger potential originating near the globe in close association with the eye movements; the lateral rectus spikes (Figure 3.6).

Figure 3.6 Simultaneously recorded 'Lateral rectus' spikes from the occiput and nasion during 20° saccades. The vertical voltage calibration bar represents 5 μV for the top trace, 20 μV for the middle and 200 μV for the bottom. (Waveforms from Riggs *et al.*, 1974).

Plots of potential distribution using chains of electrodes from the nasion to occiput over the vertex, or from the outer canthus to occiput round the side of the head above the ear, suggested that the smaller potential seen in posterior leads was the same potential as the lateral rectus spikes being recorded by passive spread with a phase reversal behind the vertex. Riggs *et al.* (1974) reported that the large anterior spike was also occured at the onset of rapid convergence eye movements as well as saccades.

The large anterior potential has recently been studied in a series of papers by Thickbroom and Mastaglia (1985b, 1986, 1987). In their initial study Thickbroom and Mastaglia (1985b) described a large amplitude short duration spike like potential preceding saccadic eye movements which was recorded across the scalp. As the origin of this potential was unknown Thickbroom and Mastaglia (1985b) studied the topography of the potential with multichannel recordings over the scalp and spatio temporal mapping of the results from a group of 10 normal subjects (aged 20-43 years). The generator site of the potential was predicted from dipole modelling and source derivation techniques. As well as the normal subjects, patients with a variety of pathological conditions affecting their eye movements were used to study the parameters and distribution of the spike potential.

It has been shown above that the spike potential is related to the onset of saccades (Blinn, 1955; Jäntti, 1982;Jäntti *et al.*, 1982; Riggs *et al.*, 1974) and it is known that this point is variable depending upon the reaction time of the subject (see 2.2.1). To allow the saccade onset to trigger the averaging, the eye movements must be recorded and the onset identified. Thickbroom and Mastaglia (1985b) monitored the saccades of each of their subjects with either EOG or infra-red movement detection. The saccade onset was determined from the eye movement record and used as the averaging trigger. Voluntary saccades between 10° and 40° were performed at a rate of 0.5-1 Hz from a central to peripheral target. The EEG activity was recorded from up to 30 sites over the head with a BNC reference electrode. The electrode sites used are shown in Figure 3.7. Filters with low frequency cut-offs 0.1 Hz and high frequency cut-offs of either 70 Hz or 10 Khz were

used, although in later experiments Thickbroom and Mastaglia used a high frequency cut-off of 500 Hz.

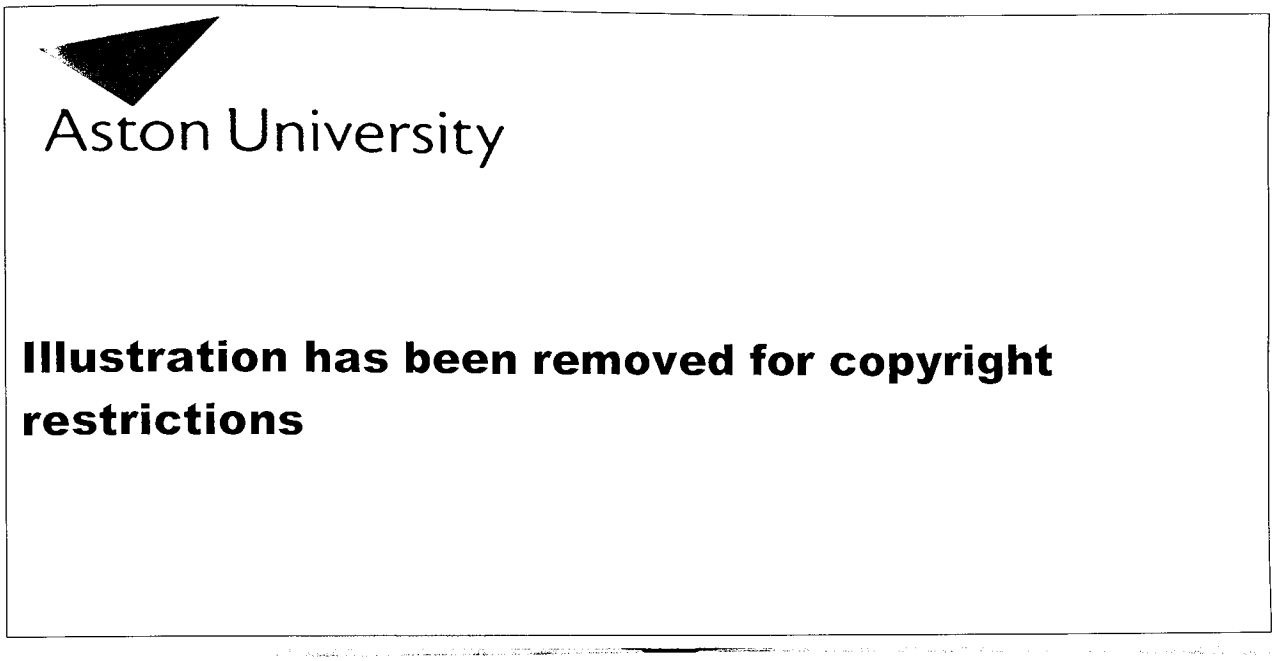


Figure 3.7 The location and nomenclature of the 30 cephalic recording sites used by Thickbroom and Mastaglia to monitor the EEG activity preceding saccades. (From Thickbroom and Mastaglia, 1985b).

The responses were back-averaged with automatic triggering of the averager from the eye movement onset. Thickbroom and Mastaglia (1985b) checked the accuracy of the automatic trigger by storing the individual EOG traces together with the EEG data for two subjects and using the EOG records to manually identify the saccade onset and average the EEG activity round this point. Although the results were similar it was found that the manual technique was advantageous in allowing poor saccade traces to be rejected. In addition to back-averaging the spike potential from the saccade onset Thickbroom and Mastaglia (1985b) also used, in some cases, the peak of the spike potential itself as the trigger for the averager, this point being identifiable in the individual eye movement traces.

The spike potential was found to be a very consistent recording, being present in each subject for all experiments and was described as a high amplitude potential appearing just prior to the eye movement (14-30 msec before the saccade; mean 18.7 msec), with a duration of 18-32 msec (mean 24.0 msec). The peak amplitude was recorded 7.5 msec before the saccade ranging from -4 to -22μV (mean -12.7μV) at the T_2 electrode to +3 to

+15μV, (mean 7.9μV) at the P_z electrode (Thickbroom and Mastaglia 1985b). The topography of the spike potential from the 30 electrode sites is shown in Figure 3.8.

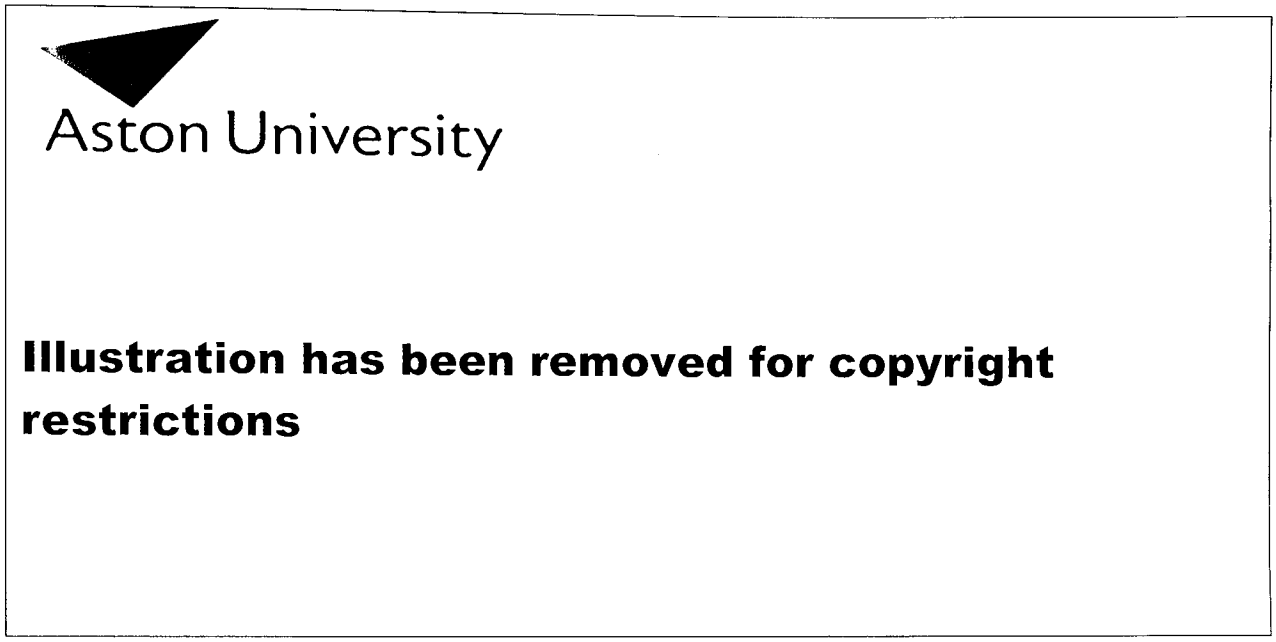


Figure 3.8 The topography of the spike potential recorded from the 30 electrode sites shown in Fig. 3.12 with horizontal saccades to the right. The spike is negative anteriorly on the right side with a more widespread positivity over the rest of the head. (Waveforms from Thickbroom and Mastaglia, 1985b)

The amplitude and latency of the waveform were unaffected by the magnitude of the saccade performed for saccades between 10° and 40° and no difference in the spike potential amplitude was found for equal horizontal saccades in different directions. Thickbroom and Mastaglia (1985b) also reported the spike potential to be unaltered for saccades recorded in darkness, or for voluntary or visually triggered eye movements. The spike potential was recorded with the same characteristics for saccades during reading and before fast phases of nystagmus.

Examination of the waveforms in Figure 3.8 shows that the SP had a maximum negative amplitude at the electrodes close to the right temple with a phase reversal immediately

behind this and widespread posterior positive activity. Thickbroom and Mastaglia (1985b) considered that this surface distribution for the spike potential suggested an origin close to the orbit so they performed a more detailed recording of the potential using ten electrodes around the eyes to record the spike potential. In this study the maximum amplitude of the spike potential for saccades to the right was recorded at the right inner canthus. No data is given for latency or amplitude values, nor is the reference electrode or trigger for the back-averaging known. The waveforms shown in Figure 3.9 are similar, however, to those reported by Jäntti (1982).

Figure 3.9 The distribution of the spike potential recorded from 10 electrodes near the orbits with horizontal saccades to the right in a normal subject. Electrodes 2 and 9 were at the inner canthi, electrodes 3 and 8 at the outer canthi of the eyes. The electrodes 1,4 and 5 were placed above, lateral to and below the left outer canthus at a distance equal to the distance between the inner and outer canthi. Electrodes 6, 7 and 10 were similarly placed for the right eye. (Waveforms from Thickbroom and Mastaglia 1985b).

Thickbroom and Mastaglia (1985b) also recorded the surface topography of the spike potential from subjects with different ocular motility and pathological conditions. To investigate the possibility of a cortical origin for the posterior positive spike activity a patient with a right hemispherectomy was examined. The subject was able to perform voluntary saccades in all directions and the spike potential was recorded from electrodes at the inner and outer canthi of both eyes and from multiple sites over the scalp with a BNC reference.

The potential was reported to have a similar topography over the cranium for both directions of gaze to that recorded from the normal subjects, suggesting that the posterior spike activity cannot be related to the cortical integrity of the subject.

To determine if a retinal or electrooculographic source may be responsible for the frontal spike potential Thickbroom and Mastaglia (1985b) recorded the spike from two subjects with unilateral ocular prosthesis. Movement of the normal eye was used to trigger the back-averaging. With both subjects a spike potential with normal distribution was found for horizontal saccades in both directions. This was thought to argue against a purely ocular origin for the spike, but it did not exclude a muscular origin for the potential as both subjects had residual functioning EOM attached to the prosthesis. When the spike was recorded from the subjects with the left lateral rectus palsies (one complete, one partial) the good eye was again used for the trigger of the averager. In the subject with the complete palsy the spike was normal for saccades to the right, but with saccades to the left an attenuated and broadened potential was recorded over the left inner canthus. No results are given for any attempt to record the potential over the left outer canthus. The subject with the incomplete palsy also showed normal spike potentials with saccades to the right but reduced amplitudes for eye movements to the left. Unfortunately, no latency or amplitude data or waveforms are presented for any of these patients.

The results of this study were similar to the earlier work of Riggs *et al.* (1974) and Jäntti (1982) and, like these authors, Thickbroom and Mastaglia (1985b) reported the presence of a large anterior spike potential ipsilateral to the direction of eye movement which was coincident with a smaller posterior positive spike potential. Thickbroom and Mastaglia (1985b) suggested that the posterior positivity was characteristic of current flow over the scalp from a more anterior source and argued against a cortical origin for the posterior activity by recording a spike of normal topography posteriorly for both saccade directions from a patient with a hemispherectomy. These authors concluded that results of their experiments indicated an extraocular muscle origin for the spike potential, agreeing with the hypothesis of Blinn (1955). Thickbroom and Mastaglia (1985b) considered, however,

that as well as the lateral rectus, the medial rectus muscle must also be involved in generation of the potential. Like Jäntti (1982), they speculated that the potential may be representative of the summated electrical activity generated by the near simultaneous recruitment of motor units by a highly synchronised motoneuron potential. This theory was supported by comparing the spike potential results to the known discharge pattern of motoneurons in the monkey abducens nucleus. For saccades greater than 5° these begin firing 5-7 msec before the saccade start, discharging at their maximum rate of 400 - 600 spike/second (Feldman and Cohen 1968). It was suggested that the maximum recruitment of all motoneurons for saccades of greater than 5° could explain the constant amplitude of the spike for saccades between 10° and 40° (Thickbroom and Mastaglia 1985b). An argument against this proposed origin of the potential is the fact that it does not persist for the duration of the saccade. Thickbroom and Mastaglia (1985b) attempted to explain this when they suggested that the rapid decline in the spike potential was due to the desynchronisation of the motor unit discharge following the initial recruiting burst.

Although this first report by Thickbroom and Mastaglia (1985b) was perhaps lacking in detail for the parameters of the potential and its waveform, particularly with regard to the subjects with anomalous eye movements, it never the less represented the first detailed study of this potential. In this paper Thickbroom and Mastaglia (1985b) referred to the anterior spike potential as the 'presaccadic spike potential' or 'SP' and this nomenclature shall be used from now to identify the anterior spike potential.

In a later paper Thickbroom and Mastaglia (1986) recorded the SP to determine if the vertical and oblique acting ocular muscles may also be involved in its generation. The potential was recorded from five subjects at four electrodes placed around the eyes (inner and outer canthi, above and below the eyes) for horizontal, vertical and 45° oblique saccades in each quadrant. P_z was chosen as a reference after their earlier mapping work had shown this site gave an enhanced SP waveform (Thickbroom and Mastaglia 1985b). The SP was also recorded from one subject for 30° and 60° oblique saccades. The filters were set with a time constant of 0.1 second and a high frequency cut-off of 500 Hz. The

saccadic eye movements were recorded with an infrared eye movement detector and this signal was differentiated to give an eye velocity measure, the saccade onset being determined automatically when the eye velocity passed a pre-determined threshold.

Forty saccades and SPs were recorded for self paced voluntary saccades between a central target and another placed 5° from this in the appropriate direction of gaze. Centring and decentring saccades were averaged separately. A time sweep of 150 msec was used, 25 msec before the eye movement and 125 msec after the saccade onset. In addition to using the eye movement trace to trigger the averaging, Thickbroom and Mastaglia (1986) also used the SP peak, manually cursoring this point in the single sweep waveforms. Re-averaging the waveforms about the SP peak was found to be useful as this was easily identified and the amplitude of the SP was unaffected by any trigger jitter introduced from using the eye movement trace. The disadvantage of using the SP peak as the trigger is that no latency data can be calculated for the SP onset and peak with respect to the saccade.

The waveforms and time course of the SPs recorded from the different electrode sites were found to be very similar for the different saccade directions although horizontal or oblique abducting saccades had greater amplitudes than adducting eye movements and upgoing vertical saccades had larger amplitudes than downgoing saccades. The mean onset to peak amplitude values for the five subjects at each electrode site are shown in Table 3.1. The small variation in the amplitudes for the different recording sites demonstrates a wide spread of the SP field, suggesting that the SP is a compound potential arising from potentials from all the EOM. Thickbroom and Mastaglia (1986) concluded that it was impossible to determine the relative contributions that individual muscles were making to the overall potential. The variations in the amplitude of the SP for different saccade directions which they recorded were considered to be due to a number of contributory factors. The maximum amplitude of the SP for upward saccades at the lower electrode may be arising due to the close proximity of this electrode to the inferior oblique which elevates the eye. This explanation however, could not account for the

maximum amplitude at the inner canthus electrode for downward saccades when the inferior rectus and superior oblique are involved.

Table 3.1 The SP onset to peak amplitudes (μV) at four electrode sites for horizontal, vertical and 45° oblique decentring saccades of 5° magnitude. The results are the mean values for five subjects (no SD values were given in the results. (From Thickbroom and Mastaglia 1986).

To provide support to their theory of the origin of the SP Thickbroom and Mastaglia (1987) have produced a computer model of this potential based upon motor unit recruitment patterns in the extraocular muscles. The model was based upon the discharge properties of motor units in the EOM and added credence to the hypothesis that the SP represents the summated electrical activity from the near synchronous activation of motor units within these muscles by the presaccadic burst of motoneuron activity. The model showed that a surface recorded ocular EMG, similar to the SP, could be produced by summing action potentials from a population of motor units and allowed the parameters of the discharge patterns of these motor units to be altered and the effect on the waveform determined. The parameters that were used to produce the model were the number of motor units (250), the action potential amplitude and duration, the mean and SD of the discharge frequencies for the population of motor units, and the dispersion in recruitment time amongst the units. Values were estimated for these parameters from the known properties of both the EOM and limb muscles and then altered to examine the effect on the SP waveform. It was found that increasing the recruitment dispersion of the motor units produced a reduction in the spike amplitude with a corresponding broadening of the potential (Figure 3.10a). If the discharge frequencies of the motor units were altered there

appeared to be little change in the SP amplitude and latency although increased secondary intrasaccadic potentials were generated with reduced discharge frequencies. Changing the amplitude of the second and subsequent action potentials in an 'action potential train' was seen to alter the peak to peak amplitude although the onset to peak amplitude of the SP was seen to change with no latency changes (Figure 3.10b). If the duration of the second component of the action potential was increased from 1-4 msec the SP amplitude increased by up to 120% with only a small latency change (Figure 3.10c).

Figure 3.10 Results of varying model parameters on modelled SP waveform. A: recruitment dispersion increased from ±2 msec to ±16 msec in 2 msec steps. B: reduction in amplitude of second and subsequent action potentials in a train. C: increase in duration of the second (+ve) component of action potential waveform from 1 msec to 4 msec in 1 msec jumps. (From Thickbroom and Mastaglia, 1987).

As these authors observed, the actual values for many of these parameters are unknown for human extraocular muscles, but they can be estimated from the information that is available for EOM and limb muscles. The changes they made to the model parameters were based upon this knowledge and helped to confirm that a potential similar to the SP can indeed be generated from the summation of muscle fibre action potentials. While this does not allow one to state with absolute certainty that the SP arises in the EOM motor units it does add more weight to this argument.

In their initial work Thickbroom and Mastaglia (1985b) recorded the SP for saccades of different magnitudes, reporting that the SP amplitude appeared to be consistent regardless of saccade size. Riemslag, Van Der Heijde and Van Dongen (1988) have examined the SP with abducting saccades from an electrode at the outer canthus over a range of horizontal saccade sizes to study if there is, indeed, a relationship between saccade size and SP amplitude. Five subjects, aged 21 - 54 years, were used to record saccades between 0.25° and 35°. Riemslag *et al.* (1988) were concerned about the trigger jitter introduced into the averaging process by the use of the EOG, and used an infrared scleral reflection technique to monitor the eye movements. The onset of saccades were detected automatically when the eye movement trace fell within upper and lower limits. A second possible source of error, according to these authors, is the presence of the corneo-retinal potential which produces a substantial artefact to the signal when the eyes are moving. An attempt was made in this study to remove this potential to try and determine more accurately the actual SP waveform. The SP activity was recorded from a silver/silver chloride electrode placed on the temporal bone at the outer canthus of the right eye with an electrode over the contralateral posterior parietal cortex, 3 cm up and 7 cm behind the auditory canal as the reference. No details as to why this reference site was chosen are given. The signals were filtered between 0.1 and 70 Hz with a pretrigger delay of 70 msec and a time sweep of 240 msec. Approximately 50 sweeps were averaged, although only abducting saccades were recorded.

Riemslag *et al.* (1988) attempted to remove the corneo-retinal potential from the SP trace by estimating the amplitude ratios of the EEG and eye position signals during the eye movements. The EEG signal is assumed to be the sum of the SP recording and the simultaneous eye movement signal. The eye movement artefact can be estimated from the infra-red record of the saccade and this can be removed by subtracting the eye position signal, multiplied by the ratio, from the EEG signal. The results of this technique are shown in Figure 3.11, which show that, although the technique does reduce the effect of the corneo-retinal potential on the SP waveform, the 'treated traces' still exhibit a

similar waveform for the initial onset to peak. Even after this point the waveform shape is similar, albeit with a reduced amplitude.

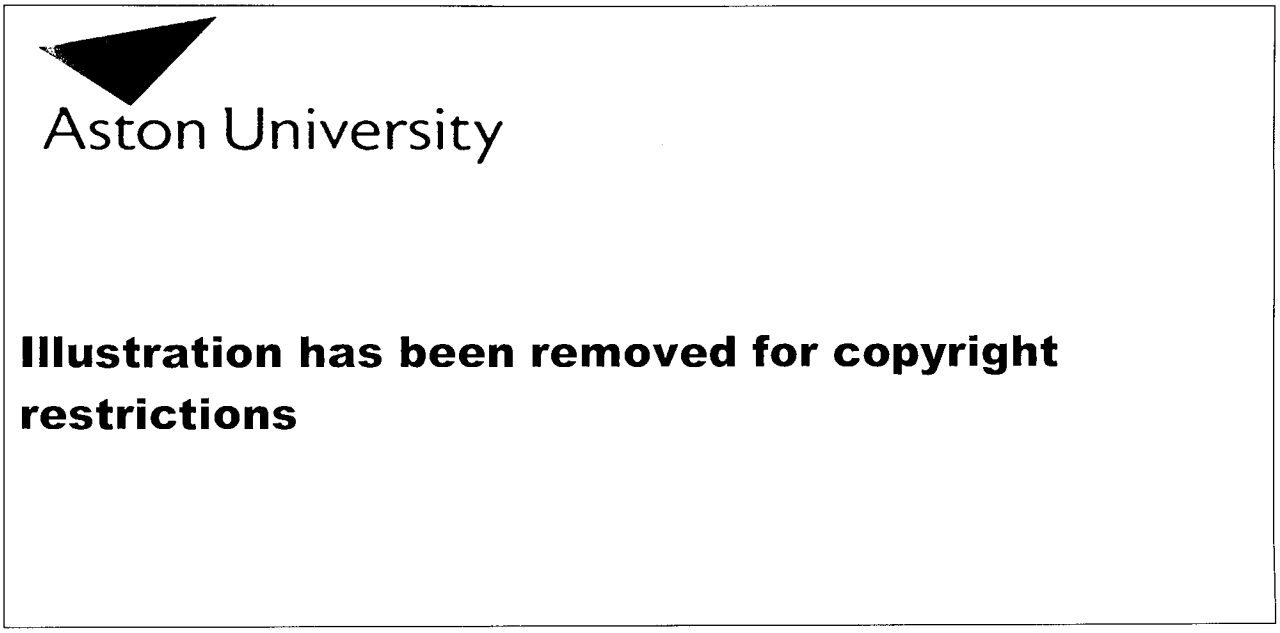


Figure 3.11 The uncorrected (top trace) and corrected (bottom trace) averaged signal showing the SP for 5° abducting saccades. (Waveforms from Riemslag *et al.*, 1988).

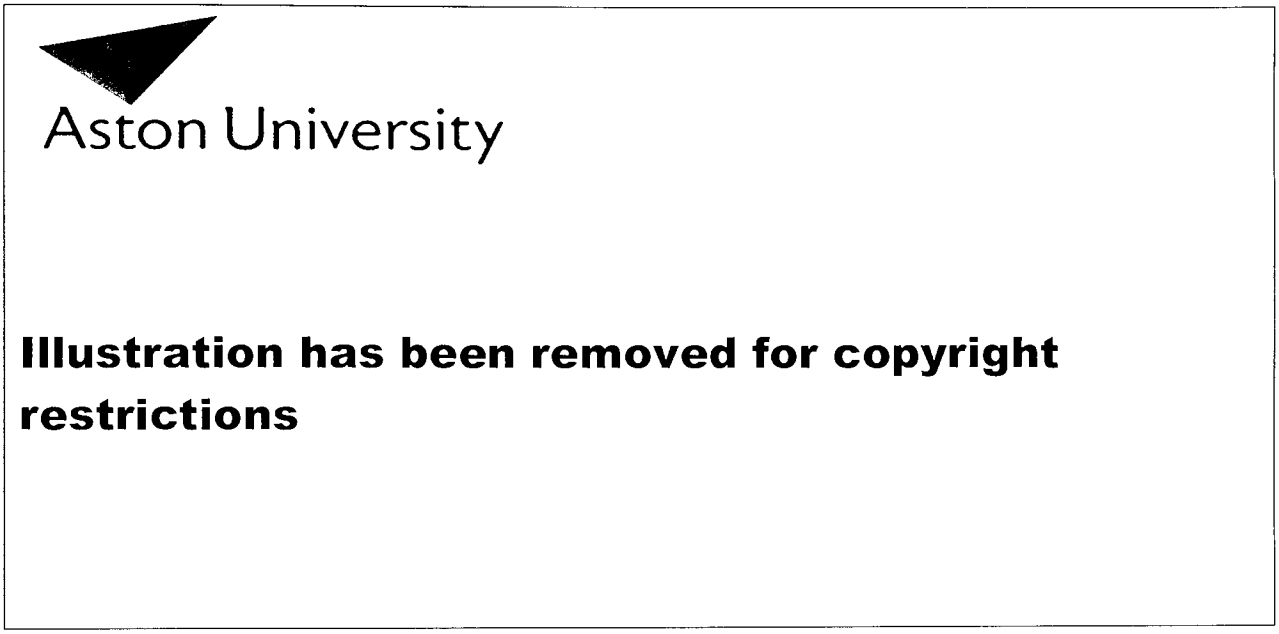
This process of artefact removal would further appear to have little role in SP recording when the other studies to date are examined. In all other papers the authors have concentrated on the initial onset to peak of the SP which is unaffected by the EOG activity and little, or no importance is placed on the following peak-to-peak activity.

When Riemslag *et al.* (1988) examined the effect of saccade size on the SP parameters they found that the onset to peak amplitude varied with saccade magnitude, increasing for saccades up to approximately 10°, but with little change beyond this (Figure 3.12).

Figure 3.12 The onset to peak amplitude of the SP as a function of saccade size. The rapid increase in the SP amplitude for saccades up to 10° can be seen, with little change after this. (From Riemslag *et al.*, 1988).

Riemslag *et al.* (1988) considered the increase in the SP amplitude for saccade size between 0.25-8° supported the proposed origin of the SP as synchronous firing of the motoneurons. These authors felt that if the origin of the potential was muscle unit activity then, based on the knowledge of saccade peak velocities with saccade size, a further increase in the SP amplitude would have been expected for larger saccades as the saccade velocity increased. They considered the SP waveform to be representative of a moving dipole source travelling along the oculomotor nerve, passing the recording electrode (Riemslag *et al* ., 1988).

A further possible origin for the spike potential has been proposed by Tsutsui, Ohnishi, Fukai and Matsudu (1987). While studying the spatio-temporal properties of cortical activity associated with saccades and the fast phases of optokinetic nystagmus, they observed all their subjects exhibited a large negative spike (between 8-10 μV) at electrodes F_{p1}, F_{p2}, F_7 and F_8 just before the eye movement onset (1-3 msec) (Figure 3.13).



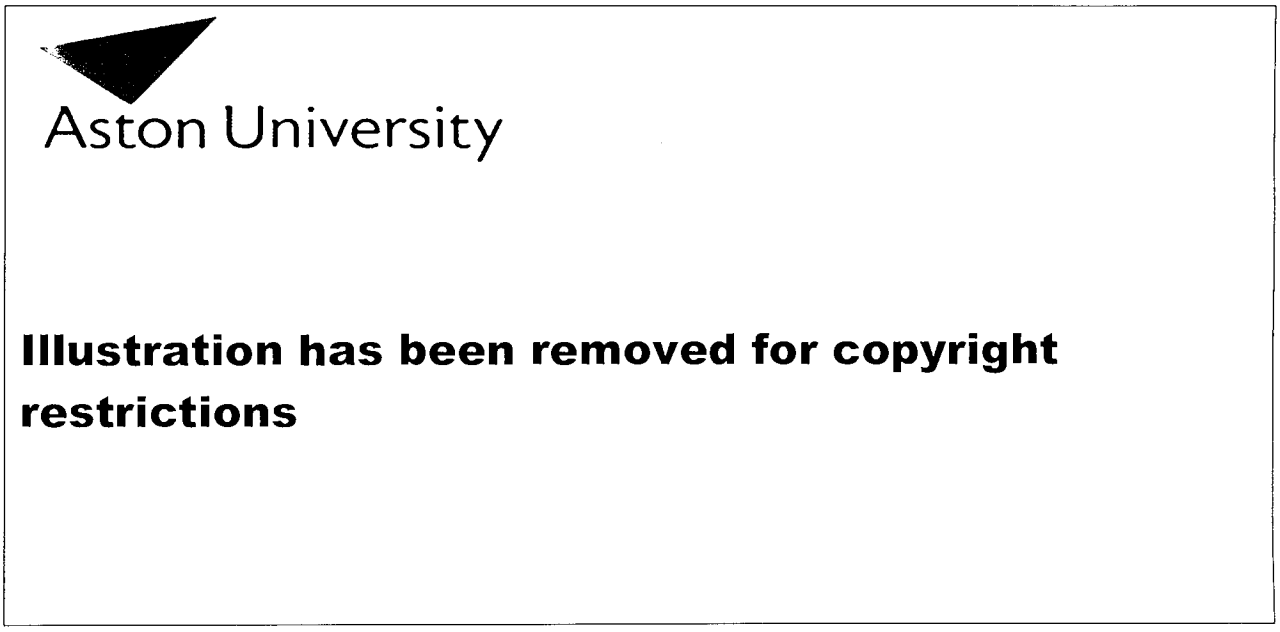


Figure 3.13 The group mean waveforms for 5 subjects performing saccades to the right (A) and left (B) showing the spike activity in relationship to the saccade onset. (Waveforms from Tsutsui *et al.*, 1987).

Tsutsui *et al.* (1987) considered this potential was caused by contraction of the supraciliary corrugator muscle just before the saccade. This muscle has been implicated in the production of sharp frontal negative spikes in another study. Ohnishi (1987) reported a spike between 12.0-0 msec before the saccade onset and, like Tsutsui *et al.* (1987), used

electromyography to show the potential originated in the supraciliary corrugator muscle. Although the EMG records presented in these papers do show some extra activity in the muscle at the onset of the saccade, it is unlikely that this small muscle is the origin of the large SP. These are the only papers suggesting this muscle may be responsible for the SP.

A similar distribution of EEG activity including a large negative spike in frontal leads has been reported by Niiyama, Shimizu, Abe and Hishikawa (1988) for the eye movements performed during rapid eye movement (REM) sleep. These authors found a similar frontal negative spike for both REM eye movements and voluntary saccades performed by alert subjects in a dark laboratory. Niiyama *et al.* (1988) considered the frontal spike to originate in the extraocular muscles prior to the eye movements. That the SP may be present at the onset of saccades during REM has also been suggested by Jäntti (personal communication, 1989) who proposed that this potential could be used to indicate the onset of such eye movements.

3.2.3 CORTICAL ACTIVITY ASSOCIATED WITH SACCADIC EYE MOVEMENTS

It has been seen in the above review of the anterior scalp presaccadic spike potential that posterior scalp activity coincident with the frontal SP can be clearly recorded. Both Thickbroom and Mastaglia (1985b) and Tsutsui *et al.* (1987) have published waveforms showing a large negative spike potential, with corresponding widespread positive spike like activity over the posterior scalp. Thickbroom and Mastaglia (1985b) did suggest that the posterior activity may have arisen due to current flow over the scalp from the large anterior spike potential.

There have been several studies of cortical activity related to many human motor actions, including eye movements and three potentials are known to precede saccades The first potential related to saccades is a negative ramp-like potential beginning up to 1 second

before the eye movement onset and centred over the vertex (Becker, Ottomar, Katsuhiko and Kornhuber, 1972; Kurtzberg and Vaughan, 1973, 1980, 1982; Armington, 1977, 1978). This premotor negativity is similar to the readiness potential preceding voluntary movements of the extremities and is thought to reflect preparatory activity in the cerebral cortex prior to the forthcoming movement (Deecke, Grozinger and Kornhuber, 1976; Shibasaki, Barrett, Halliday and Halliday, 1980; Shibasaki, 1982). The second potential before the eye movement is a positive ramp potential about 100-150 msec prior to the saccade (Armington, 1977, 1978; Kurtzberg and Vaughan, 1980, 1982). This potential, which is localised to the precentral region contralateral to the movement (Shibasaki, 1982), is known as the premotor-positivity and is associated with the formulation of the motor plan (Deecke *et al.*, 1976). The third potential before rapid eye movements is a sharp spike like potential which, unlike the other cortical potentials, does not have a correlate in movement of the extremities (Thickbroom and Mastaglia, 1985a). While this spike potential has been studied in some detail by several workers, as will be seen below, not all of these authors have considered the possibility that the posterior scalp activity may be related to frontal SP activity.

Becker *et al.* (1972) used time reversed EEG data to record the scalp potentials related to human saccadic eye movements and reported a sharp positive spike was recorded from electrodes on the posterior cortex at the onset of the eye movement. This positive potential was presumably the same positive potential as that found by Thickbroom and Mastaglia (1985b). Becker *et al.* (1972) used bipolar recordings in a symmetrical line through the chin, nasion, mid frontal, vertex and neck to study the sharp positive cortical potential in more detail. With this montage they showed a potential reversal at the nasion with another diffuse reversal between the mid frontal and neck (Figure 3.14). The phase reversal at the nasion led Becker *et al.* (1972) to conclude that the potential was being generated intraorbitally, probably of an eye muscle origin.

Figure 3.14 Investigation of the oculomyogenic potential using bipolar recordings in a sagittal line from the chin (A), nasion (B), mid-frontal (C), vertex (D) and neck (E). The waveforms from Becker *et al.* (1972) show a potential reversal at the nasion with another more diffuse reversal between the vertex and the neck suggesting an intraorbital origin of the sharp oculomyogenic potential.

Kurtzberg and Vaughan (1973), while discussing the electrocortical activity related to eye movements described a similar potential to that recorded by Becker *et al.* (1972). Kurtzberg and Vaughan (1973) identified a brief sharp wave corresponding closely to the onset of eye movement in the anterior frontal region of the head, which they also considered to be of eye muscle origin. In discussion with these authors, Kornhuber (1973) further described this eye muscle potential, showing that, due to potential spread, it could be traced as a spike artefact all around the head. Kornhuber (1973) expressed concern that the spread of the eye muscle potential may lead to confusion with cortical activity associated with saccades. We are reminded of the hypothesis of potential spread across the scalp causing confusion between posterior and anterior activity when the later work of Thickbroom and Mastaglia (1985b) is remembered. These authors also indicated that the anterior and posterior spike potential activity may be related.

In a later study, Kurtzberg and Vaughan (1980), used 12 electrodes to examine the activity over the cortex from the mid-frontal (P_z) to the occipital region (O_z). No details of the

reference electrode were given. Different saccade directions and types (voluntary and visually triggered) and hand movements were examined to study the topography of eye movement potentials with these different conditions. In the results of this study Kurtzberg and Vaughan (1980) again mentioned the sharp positive deflection related to the onset of the saccade. This sharp potential was reported as being present at all recording sites in all conditions with a maximum amplitude over the parietal region and a fall off to less than 40% at F_z (Figure 3.15) (Kurtzberg and Vaughan, 1980). No further information regarding this potential was given for the different recording conditions, nor was any possible origin proposed.

Figure 3.15 The group mean eye movement potentials found by Kurtzberg and Vaughan (1980) associated with visually triggered and return saccades showing the fall off in the spike amplitude across the scalp.

While the above workers have recorded the cortical activity for saccades of varying sizes only Armington (1977,1978) has recorded this activity with microsaccades. A

photoelectric recording system utilising a mirror mounted on a contact lens was used to record microsaccades of up to 81 minutes of arc, this eye movement record being used to trigger recordings from electrodes attached to the vertex and the occipital midline. The joined earlobes were used as a reference. The waveforms found in this study showed the typical cortical presaccadic spike activity described in the previous papers (Figure 3.16).

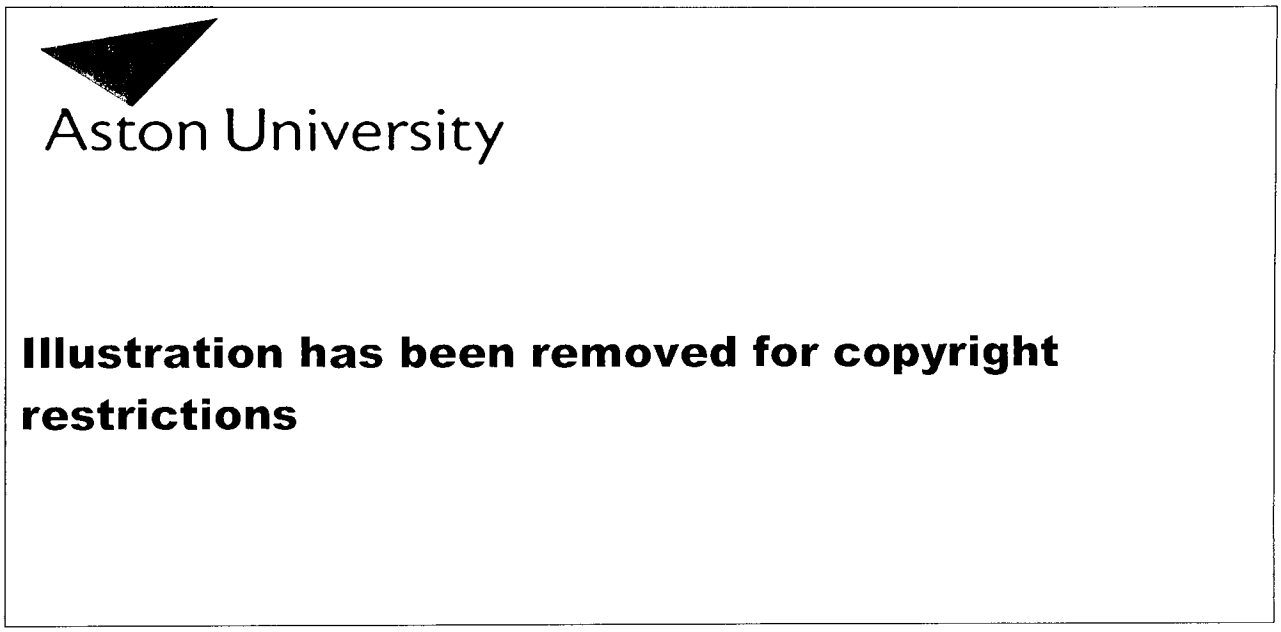


Figure 3.16 Cortically spike potentials recorded from an electrode on the midline 3 cm anterior to the inion. Right and left saccades of several amplitudes were recorded. (Waveforms from Armington, 1978)

Armington (1977,1978) examined the effect of saccade size on the positive cortical spike for microsaccades up to 81 minutes of arc and found the amplitude of the spike varied with the size of the eye movement, reaching a maximum of about 10 μV for saccades of 75 minutes and above. Armington (1978) also demonstrated the presence of the spike with vertical saccades using a vertex electrode referred to the ears. Armington concluded his studies by suggesting that the spike cannot be an electroocular artefact as it does not change polarity with the direction of eye movement. He considered that it may be partly related to muscle tensing prior to the saccade, although the apparent maximum spike amplitude for microsaccades of 75 minutes suggested that it may not be simply a muscle

tensing as this activity would be expected to increase with larger saccades (Armington, 1977, 1978).

Weinstein, Williams, Drack, Stank and Balaban (1984) have examined the cortical potentials preceding voluntary saccadic eye movements. The posterior spike potential activity was studied from two patients with progressive supranuclear palsy and two patients with congenital ocular motor apraxia as well as 20 normal subjects. Electrodes were placed at P_3 and P_4 with linked ears as the reference. No reasons are given for the choice of P_3 and P_4 as the recording sites.The differentiated EOG signal was used to trigger the averaging process and, in general, 100 saccades were required to produce satisfactory waveforms. In some cases however, up to 250 saccades had to be performed to give a recognizable waveform.

The normal subjects showed a clear waveform over both parietal lobes for 10° saccades to the left and right of centre. The amplitude of the potential varied from 5.4-7.1 μV, but unfortunately no information was given for the latency of the spike with regard to the saccade onset. In this study the two patients with progressive supranuclear palsy were unable to perform refixation movements greater than 5°-10° without using multiple hypometric saccades to perform the desired refixation. In both these cases no definite SP was recorded over either parietal lobe, with just a broad positive wave over the parietal lobe in one. Of the two patients with congenital motor apraxia, one was able to perform saccades to either side of between 8°-10° and a sharp SP was recorded over both parietal lobes with rightward and leftward saccades. The second subject was unable to perform saccades greater than 7° and showed only a broad peak of presaccadic activity with no definite spike like waveform. The EOG traces and spike potential waveforms for the different subjects described above are shown in Figure 3.17.

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Figure 3.17 The EOG traces and eye movement potentials in a normal subject and four patients (see text). For each subject the top two traces are right parietal and the bottom two are left parietal. The saccade onset is indicated by an arrow. (Waveforms from Weinstein *et al.*, 1984).

While discussing the results, Weinstein *et al.* (1984) suggested that the spike potential may be representative of the discharge of a population of saccade related neurons in the posterior parietal area of the cortex. The lack of a definite SP recording from the patients with progressive supranuclear palsy was attributed to a "disruption to the eye-movement related ascending pathways to the parietal cortex". It was considered that the spike potential may be affected by trigger jitter introduced by the variability of the saccades in these subjects, particularly in the patients with the poorer saccades. They found, however, that even in the patient with the most heterogeneous saccades, the averaging

trigger occurred within a 9 msec window compared to 5 msec for their normal subjects. It was felt unlikely that this small difference in trigger latency could account for the broadened spike recorded from that patient.

Balaban and Weinstein (1985) used the same electrode sites (P_3 and P_4) and reference (linked ears) as Weinstein *et al.* (1984) to examine the effects of the visual target, saccade direction, electrode laterality and instructions to perform saccades upon the posterior saccade spike potential. Balaban and Weinstein (1985) recorded and averaged 100 spontaneous saccades from a subject who had received no instructions to perform specific eye movements. The averaging was triggered automatically from the eye movement record. This recording showed little evidence of the saccade spike (Figure 3.18), particularly when compared to the prominent spike recorded after instructing the same subject to perform self-paced saccades between two LEDs 10° apart.

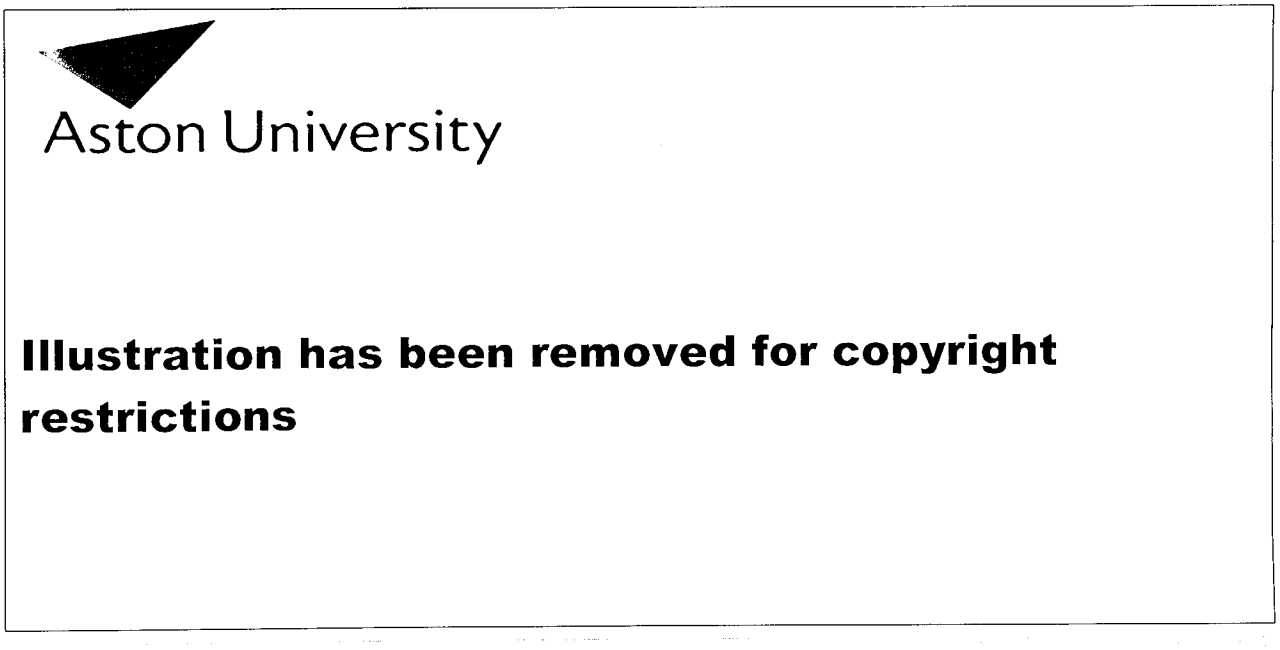

Figure 3.18 Saccadic eye movement potentials recorded from a naive subject performing spontaneous saccades in a lit room. No well-defined spike can be seen at P_3 or P_4 for saccades to the right or left. The saccade onset is indicated by the arrow. (Waveforms from Balaban and Weinstein, 1985).

In this study the spike potentials recorded under different conditions were found to show some variability in the amplitude for the different recording sites with leftward and rightward saccades. Balaban and Weinstein (1985) attempted to determine if there was any correlation between the spike potential laterality and the eye movement direction. Three-way analysis of variance showed a significant ($p<0.001$) interaction between the cortical laterality and the saccade direction with the saccade spike appearing to be greater over the contralateral parietal recording site, although this was only true for saccades to the right when they were performed in the dark.

The reduced or absent spike with spontaneous saccades was said to indicate that the presence of the SP requires the subject to be motivated to perform saccades and Balaban and Weinstein (1985) considered that this was consistent with the disappearance of presaccadic discharges from area 7 from monkeys performing spontaneous saccades with no reward. Some consideration was given to the effect that varying saccade amplitudes may have on the averaged spike potential, but this was not considered to be a possible cause for the changes in the potential. This led Balaban and Weinstein (1985) to suggest that the electrical activity of the parietal cortex reflected the performance of motivated, but not spontaneous saccades. The presence of the spike with saccades performed in the dark suggested that visual input was not necessary for the generation of the SP. When the apparent directional indices shown in the group averages were studied in individual subjects it became apparent that there was a large degree of intersubject variation, with statistical analysis suggesting that individual subjects demonstrate larger spikes at P_3 and P_4 for saccades in one direction rather than for contralateral saccades.

A further study of the cortical spike potential and the effect of saccade size and direction was carried out by Weinstein, Drack, VerHoeve and Balaban (1988) who recorded the spike from 18 normal subjects. Electrodes at P_3 and P_4 were used with a linked earlobe reference. An infra-red monitoring technique was used to monitor the eye movement, this record giving the trigger for averaging. Saccades of 2.5°, 5°, 10° and 20° to the right or left of centre were averaged, the subjects performing the eye movement at their own pace

and 100 recordings were averaged for each saccade size. When the results were analysed Weinstein *et al.* (1988) found that the spike amplitude increased for saccades between 2.5°-10°, but there was little apparent change for larger eye movements, indeed the amplitude was found to decrease significantly for 20° saccades to the right at both electrodes. The relationship between the saccade direction and the recording site laterality was also examined by these authors who showed that, although the simultaneous pattern of spike activity at P_3 and P_4 was different for leftward and rightward saccades, the mean spike amplitude was greatest for leftward saccades at P_4 for all eye movement sizes. The variation between the electrode sites was said to indicate that the spatial distribution of the spike activity contained information about the saccade direction for the eye movement to be performed. The latency of the spike onset recorded in this study was 10.5± 2.00 msec before the eye movement start with no change in this value for the different saccade sizes. The spike potential duration was also found to remain constant across the range of eye movements.

Weinstein *et al.* (1988) have argued against an eye muscle potential or brainstem generator for the spike potential from the results of this study. The absence of an increase in the amplitude for saccades of 20° and the uniform duration of the potential for the different saccade sizes was considered inconsistent with an electro-myographic origin, while the duration of firing of the brainstem presaccadic neurons is known to increase with saccade size. It was also argued that a single source for the potential was unlikely because of the many cortical sites that exhibit similar discharge patterns. Weinstein *et al.* (1988) concluded that it was more likely that the cortical spike represented activity at multiple sites within a neural network concerned with the programming of rapid eye movements.

3.3 SUMMARY

The literature review given in this Chapter has shown the electrophysiological activity that can be recorded, using different recording techniques, prior to saccades from the extraocular muscles, frontal electrodes placed around the eyes and the scalp. There

appears to be some similarities in the activity that is recorded with these techniques, mainly the 'spike potential' which is a sharp 'burst' of activity recorded immediately before the saccade onset. This potential can be demonstrated at all levels of recordings from intracellular, intramuscular and with superficial surface recordings. The spike potential has undergone some study with regard to its distribution and parameters with these different recording techniques, but there is no detailed information for the normal values and waveform of the spike. There still also exists some confusion as to the exact origins and relationship between the anterior and posterior recordings. Several workers have recorded both the posterior and anterior spike activity and have suggested that the posterior spike activity may be related to the anterior spike potential (Becker *et al.*, 1972; Kornhuber, 1973; Kurtzberg and Vaughan, 1973; Armington, 1977,1978; Thickbroom and Mastaglia, 1985b). This, clearly, is an area of debate which must be considered in this thesis if the SP is to be fully examined.

A possible relationship between the both the anterior and posterior potentials and the saccade size has been suggested by several authors. Armington (1977, 1978) has recorded the posterior scalp spike potential for microsaccades up to 81 minutes of arc, while Thickbroom and Mastaglia (1985b) have recorded the SP for saccades between 10° and 40°. Riemslag *et al.* (1988) have recorded the SP for a range of saccade sizes which encompasses the range of eye movements recorded by Armington (1977,1978) and Thickbroom and Mastaglia (1985b). Riemslag *et al.* (1988) reported a growth in the SP amplitude for saccades between 0.25° and 8-10° with little change in amplitude for saccades greater than this. The results of Riemslag *et al.* (1988) disagree with the extrapolation of SP amplitudes made by Thickbroom and Mastaglia (1985b) who reported no difference in the amplitude for 10° saccades compared to microsaccades of 77 minutes of arc recorded by Armington (1977, 1978). This relationship between SP amplitude and saccade size is also an aspect of the SP which should be addressed in this thesis.

Although Thickbroom and Mastaglia (1985b, 1986) and Riemslag *et al.* (1988) have both used posterior scalp locations for the reference electrode, the choice of a reference

electrode on the posterior scalp can be considered totally correct only if the posterior and anterior SP activity are directly related. Clearly, if the posterior and anterior spike potentials are totally separate recordings it would be incorrect to use P_z as the reference site due to any possible influence activity near the reference may have on the SP recording. If, on the other hand, the frontal and posterior activity are related, it is quite valid and correct to use a reference placed at e.g. P_z to enhance the recording.

Recordings from superficial electrodes, both anteriorly and posteriorly, have been performed on subjects with anomalous eye movements indicating that the SP may undergo some changes in these conditions. This suggests that the recording should be examined in more detail to ascertain if it may have any clinical implications or, as suggested by some authors, if the SP can be considered no more than an artefact related to saccades. The following Chapters will describe the experimental work that has been performed in this thesis to attempt to answer these questions.

CHAPTER 4

EXPERIMENTAL RECORDING METHODS

4.1 INTRODUCTION

The literature review in the previous Chapters has indicated the interest shown in the presaccadic spike potential, both recently and with early recordings of eye movement potentials. The studies presented have demonstrated that two spike like potentials related to saccades can be recorded from the scalp, one anteriorly and one posteriorly. Although some attempt has been made to examine the relationship between these potentials it is still uncertain whether they are two separate recordings or are more closely linked with each other (see 3.2.2; 3.2.3).

The posterior spike potential has been recorded by different workers for a number of recording conditions. Much of this work, however, has concentrated on two electrode sites only, these being P_3 and P_4, with linked ears as a reference. In these studies little detail is given as to why these electrode sites were chosen nor, apparently, is any consideration given to the known widespread distribution of the potential. Various workers have implied that the positive posterior potential may actually be arising as a result of potential spread from the anterior negative recording (see 3.2.2, 3.2.3).

The anterior SP has also been examined for different recording conditions and is reported to be a large, consistent potential time locked to the onset of saccadic eye movements. Recordings of this potential have, however, failed to identify the exact origin of the SP although different sites have been proposed. One hypothesis is that the frontal SP may be related to motor unit activity in the extraocular muscles preceding saccades. This origin gains support from the EMG activity which can be recorded from these muscles with needle electrodes (see 3.2.1). EMG recordings clearly demonstrate the pulse-step innervation of saccades and it is conceivable that the SP may be a surface recording of this

motor unit activity. Alternatively, it has been suggested that the SP may be representative of the motor impulse travelling along the oculomotor nerves to the EOM. Other facial muscles around the eyes have been implicated in the generation of the potential, such as the orbicularis oculi and supraciliary corrugator muscles (see 3.2.3). Although it is possible that these muscles are involved to some extent in generating the waveform it is unlikely that they are the sole origin.

If the anterior SP is indeed related to muscular activity, particularly that of the EOM, it is conceivable that it may be useful as an indication of anomalies in this activity and some workers have shown this may be the case (see 3.2.3). The posterior spike potential has, in some studies, been tentatively linked to the coincident anterior activity and it would appear to be of little benefit examining the posterior activity without first studying the large frontal SP in more detail. For these reasons it is primarily the frontal SP that is examined in this thesis, although some consideration will be given to the posterior activity.

Although several workers have reported the presence of the spike potential in their recordings, there has been relatively little work performed to determine normative data for the potential under different recording conditions. For any electrophysiological potential to have possible use in a clinical environment it is important to have normal data against which one can compare recordings from a range of subjects, both normal and abnormal. For a potential associated with saccadic eye movements it is obvious that any normal data must include information for a range of saccade sizes and different saccade directions with the potential recorded from different recording sites around the two eyes.

A normative study of any potential related to saccades should include information about the effect of age upon the potential as increasing age has been shown to alter certain parameters of saccades (see 2.2.2) and there are known muscle changes with increasing age (Miller, 1975). The published papers have shown little regard for this factor with large variations in the age of subjects used in the experiments by these authors.

Although some of the published reports do include limited latency and amplitude values for the SP, there is no indication of the consistency of these values. If pathological conditions which affect saccadic eye movements are to be considered more information of the normal values is required. The few reported recordings of the SP from patients with anomalous saccades have been lacking in detailed information regarding the changes in the waveform and SP parameters associated with such pathology. This information is of particular importance if the SP is to have any clinical use and should therefore be included in such studies.

It is obvious that there are aspects of the SP which have not been examined and further detail is required for much of the experimental work previously performed. The experiments in this thesis will attempt to provide some of this information in such a way that any future studies of the SP should not have to repeat the basic experimental work before attempting to examine the potential in more diverse conditions. The experiments will, in some cases, be repeating earlier work performed by other workers, but in a more detailed manner with regard to both the experimental conditions and the data analysis. A brief outline of the experiments performed in this research project will be presented below so the rationale for performing each experiment can be seen. In many cases the work follows on from the preceding recordings allowing a wider knowledge of the SP to be developed as more aspects of the potential are studied.

Experiment 1. A study of the spike potential for 20° horizontal saccades recorded from different electrodes around the eyes

This experiment, the initial investigation of the SP, was designed to study the ease of recording the potential and to determine the best recording montage. During this study the SP was recorded from different electrode sites for 20° horizontal saccades to provide initial data against which other experiments could be compared. Four electrode sites around both eyes were compared and abducting and adducting saccades were examined separately. The latency of the onset and peak of the SP were measured along with the

amplitude of the potential. A group of subjects then took part in a repeat study of the SP to examine the consistency and repeatability of the recording.

Experiment 2. The effect of saccade size on spike potential parameters

The initial experiment was repeated for a range of different sized horizontal saccades. The previous experiment had shown that the four electrode sites recorded an equal potential and the two eyes had identical SPs, so a reduced number of electrodes was used to examine six sizes of saccade. It was seen in Chapter 2 that there are well documented changes in saccade latency, duration and velocity parameters with different saccade sizes and it was felt important to ascertain if the SP also shows such variance.

Experiment 3. The effect of age on spike potential parameters

This experiment was designed to determine if the SP is affected by known aging changes in saccade performance and the extraocular muscles. A group of elderly subjects was used to record the SP for a range of four saccade sizes using the same experimental procedure for the above studies. The potential was also recorded from a second, middle aged group, to determine the rate of any change in the potential with increasing age.

Experiment 4. The spike potential recorded with vertical saccades

In this experiment the SP was recorded with vertical eye movements to determine if any changes occur in the potential with these eye movements. Vertical saccade recording has inherent difficulties compared to horizontal saccade recording, mainly due to eyelid activity and a different group of muscles is involved in producing the eye movement. It was considered useful to determine if the SP is changed under these different recording conditions. Like the initial study four electrodes around the eyes were used to record the SP and normal waveforms and parameters were calculated.

Experiment 5. The topographical distribution of the spike potential

The previous Chapter has described the controversy that exists with regard to the cortically and frontally recorded SPs. This problem was addressed in this experiment and the distribution of the SP across the scalp was examined. The potential was recorded from 16 electrodes on the scalp with average and non-cephalic references and the distribution from these waveforms compared.

Experiment 6. The spike potential recorded from subjects with known ocular motor anomalies

The above studies were all performed on subjects with no known ophthalmological or neurological anomalies which would interfere with their saccadic eye movements. There have been some attempts to record the SP from subjects with conditions known to affect their saccade performance but the information gained from these has been limited. It was decided to record the SP from such subjects using the same procedure as for the normal subjects in the earlier experiments.

A subject with a congenital lateral rectus palsy was examined to assess if the SP is altered in the presence of a muscle palsy. In any EOM palsy the saccadic eye movements are affected in the direction of the palsied muscle so it is important to ascertain the affect on the SP recording. It is also important to determine if the SP may give additional information about the ocular motor performance of the subject. Further recordings were also made on a subject with multiple sclerosis and a patient with an enucleated eye, again to determine if the SP can give any additional information regarding the saccade performance of such patients. The results from the pathological studies were compared to these of the normal studies. These comparisons were considered in light of the suggested origin of the SP to determine if these results could help confirm this origin of the potential. The results of such studies on anomalous eye movements may also give an indication of any usefulness the SP could have in the early detection of such conditions.

4.1.1 THE SUBJECT POPULATION

All normative studies of the SP were performed on adult subjects with no known ophthalmological or neurological defects. The research was carried out in the Vision Sciences Department of Aston University giving an easily accessible pool of undergraduate and postgraduate students from which subjects were obtained. The undergraduate teaching clinics of the Optometry Department also provided a ready source of elderly subjects who were used in the age related study. The middle aged group in this study was obtained from members of academic and non-academic staff within the Department. Subjects with eye movement disorders came from the undergraduate teaching clinics and referral from an optometrist in private practice. All undergraduate subjects and the elderly and external patients were financially rewarded for participating in the experiments. Prior to all recordings the experimental procedure was explained to each subject and their informed consent to act as a subject was obtained.

4.2 THE RECORDING SYSTEM

Throughout the research project the recording equipment and technique remained essentially unaltered for the different experiments. For all recordings a Nicolet Pathfinder II was used to record the SP and monitor the eye position using electrooculography. Electrooculography is basically an electrical technique which utilises the presence in the eye of a permanent standing potential between the cornea and the posterior pole, the cornea being positive with respect to the retina. The standing potential of the eye was first demonstrated by du Bois-Reymond (1849) and it is generally accepted to reflect the metabolic activity of the retina (Galloway,1981). In the normal eye the potential difference between the cornea and the fundus is about 6 mV, the cornea being positive with respect to the fundus (Arden, Barrada and Kelsey, 1962). This standing potential causes the eye to act as a miniature dipole, the axis of which changes as the eye rotates and changes in the dipole orientation can be detected by surface electrodes placed around the eyes allowing eye movements to be monitored (Figure 4.1).

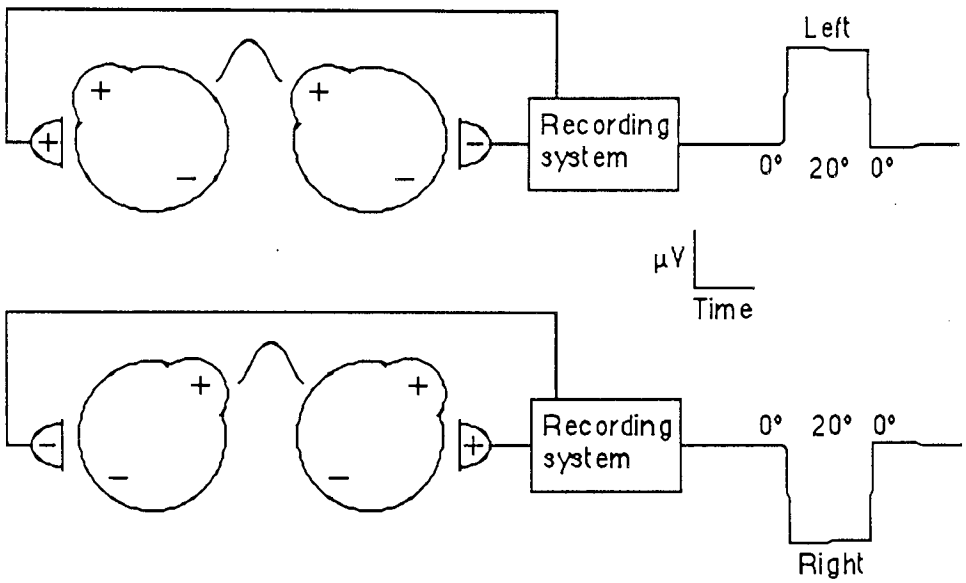

Figure 4.1 The principles of electrooculography. The eye acts as a miniature dipole and as it rotates the poles come closer to the respective electrodes attached to the adjacent skin. The resultant changes in potential are recorded and the angle of rotation can be determined. (After Shackel 1967).

The origin of the standing potential in the retina has allowed the EOG to be developed as a diagnostic technique to assess the retinal integrity in certain disease conditions. The standing potential of the eye alters when the retinal illumination is altered, reducing in darkness and increasing in bright illumination and Arden *et al.* (1962) have described how this variation in EOG magnitude can be used as a clinical test. There are many reviews of the development and use of the EOG and the reader is referred to Marg (1951), Shackel (1967), Crickmar (1969) and Boylan (1990) for more information on this technique.

The EOG was used to monitor the eye movements for the experimental work in this thesis as it is easily recorded for a wide range of eye movements and allowed the same electrodes to be used for recording the EOG and SP activity. Thickbroom and Mastaglia (1985b) also monitored the saccades for their SP recordings by the EOG and using the same technique allows the results in this thesis to be compared to earlier studies.

There are no standard programs written for recording the SP so a program was specifically developed to allow the SP to be recorded and averaged with the Pathfinder. During recordings the Pathfinder automatically triggered a wall mounted array of red, light emitting

diodes (LEDs) which provided a visual stimulus for the saccades. The subjects were seated with their heads held steady by a chin and forehead rest and the eye not being recorded from was occluded with an occluder suspended from the forehead rest. In most experiments forty saccades were recorded (20 abducting and 20 adducting for horizontal recordings; 20 upward and 20 downward for vertical recordings). The inter-saccade interval was fixed at approximately seven seconds. To avoid changes in the EOG the background lighting was kept constant, the subjects adapting to the illumination while the electrode sites were prepared. The LEDs were arranged in a horizontal strip of eight lights, four either side of the midline. These were positioned so as to subtend 20°,15°,10° and 5° at the subject when seated one metre away (10°,7.5°,5° and 2.5° either side of centre). For larger or smaller saccade than these the subject were seated nearer or further away as required. An identical LED display was mounted vertically to provide the trigger for vertical saccades although only saccades of 20° were recorded in this direction.

In Chapter 3 the different electrode types which have been used to record SP activity were described. The electrodes used in this thesis were small (approximately 10 mm diameter) silver/silver chloride cup electrodes to which an electrode lead was soldered. These were usually attached to the skin with strips of adhesive tape (Blenderm), although a fast drying adhesive, collodion, could be used where the tape did not provide a secure contact. To improve the skin/electrode contact the electrode sites were first prepared. A mildly abrasive paste (Omniprep, D.O. Weaver & Co., 585-C Nucla Way, Aurora, CO. 80011 USA) was used to scarify the skin at the electrode site and, once the electrode was positioned, electrode jelly was inserted into the cup using a blunt, disposable needle. This procedure ensured the electrode contact impedance was 5 kΩ or less before the recording started. If this was not the case, or if the electrodes had different impedences, the blunt needle was used to gentiy abrade the skin further until the same impedance was measured at all the recording sites. The use of sticky tape to locate the electrodes meant that following the recording sessions the electrodes round the eyes could be easily removed without the use of acetone.

4.2.1 AVERAGING THE SPIKE POTENTIAL WAVEFORM

The SP has been shown to be time-locked to the start of saccadic eye movements (see 3.2.2), but, as has been shown in 2.2.1, saccadic latency is an unknown variable. The variability in saccade latency, and therefore the SP onset, makes it difficult to average the SP using standard averaging techniques averaging round the trigger onset. To overcome this a similar program to that used by Thickbroom and Mastaglia (1985b, 1986) was developed to record an eye movement trace simultaneously with the SP recordings on separate channels of the Pathfinder. With this eye movement record the onset of the saccade can be determined and the SP averaged round this point. Like Thickbroom and Mastaglia (1985b) electrooculography was used to monitor the eye position with electrodes at the inner and outer canthi being used for horizontal saccades and electrodes above and below the eyes for vertical eye movements.

During recording sessions the individual eye movement and SP traces were stored on hard disc and, following the recordings, the traces obtained for each individual saccade were recalled and the onset of the saccade identified manually using the Pathfinder's internal cursor. This visual inspection of the eye position data allowed accurate identification of the EOG deflection and hence the beginning of the saccade; if this point could not be clearly identified the data was rejected. It was, however, very seldom that traces had to be rejected and every attempt was made to ensure that no 'bias' was introduced into the back-averaging. The computer then back-averaged the SP recordings from the saccade start. For display purposes the onset of the saccades were aligned at a predetermined and fixed latency (256 msec for the 500 msec time sweep, 512 msec for the 1000 msec time sweep). Abducting and adducting saccades and upward and downward saccades were averaged separately.

This averaging technique allowed the onset and peak latencies of the SP to be determined relative to the start of the eye movement. Manually locating the saccade onset reduced any possible trigger jitter that may have been introduced into the averaging

system with automatic identification of the saccade onset, artefacts such as blinking for example being recognised as such and rejected when necessary. It has been argued that the use of manual identification of the saccade onset, particularly with EOG records may be a possible source of error, but Weinstein *et al.* (1984) have shown that even with patients who have grossly abnormal eye movements, the maximum trigger window was 9 msec compared to 5 msec for normal subjects. This technique was also used by Thickbroom and Mastaglia (1985b) who showed the SP averaged with such a manual trigger did not differ from that averaged automatically.

For all recordings, following averaging, the Pathfinder's internal cursor was used to measure the latencies of the onset and peak with respect to the start of the saccade. Where the SP had secondary peaks only the first was considered. These points are identified in Figure 4.2. To avoid unwieldy numbers and confusion with saccade latencies, the numerical value zero was allocated to the preset latency at which the traces were aligned. Hence, when recording SP onset and peak latency values, a negative value indicates a latency before the eye movement and a positive value a latency after the saccade start. This notation is constant for all recordings, allowing easy comparison between different experiments. The onset-peak amplitude of the SP waveform was also measured with the Pathfinder's internal cursor following averaging (Figure 4.2).

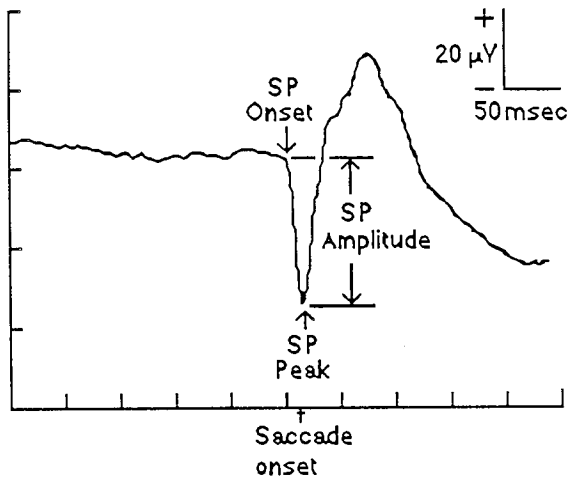

Figure 4.2 A schematic diagram of the SP waveform showing the SP onset and peak and the onset-peak amplitude measurements.

4.2.2 THE CHOICE OF FILTERS TO RECORD THE SPIKE POTENTIAL

During the development of the computer program the filter settings to be used in the experiments were determined. The SP was recorded from one subject and the input filtered with four different high pass filters (25, 50, 100 and 400 Hz). The waveforms from this recording are shown in Figure 4.3 and are comparable to the waveforms of Jäntti (1982) shown in Figure 3.5a. Figure 4.3 shows that a high cut-off of 100 Hz gives a clear waveform with minimal noise and a distinct spike onset and peak. This value compares to those used by Thickbroom and Mastaglia (1985b, 1986) (10, 70 and 500 Hz) and Riemslag *et al.* (1988) (70 Hz). The low cut-off filter was chosen on the basis of the filters used by previous workers. Thickbroom and Mastaglia (1985b, 1986) and Riemslag *et al.* (1988) used a 0.1 Hz low cut-off while Jäntti (1982) and Jäntti *et al.* (1983) used a 0.5 Hz low cut-off filter. For this thesis a low cut-off of 0.50 Hz and a high cut-off of 100 Hz (roll-off 12 dB per octave) were used and these values were written into the recording program. Each individual recording epoch commenced immediately on the Pathfinder triggering the LED, and a choice of two time sweeps was available, 500 msec or 1 second.

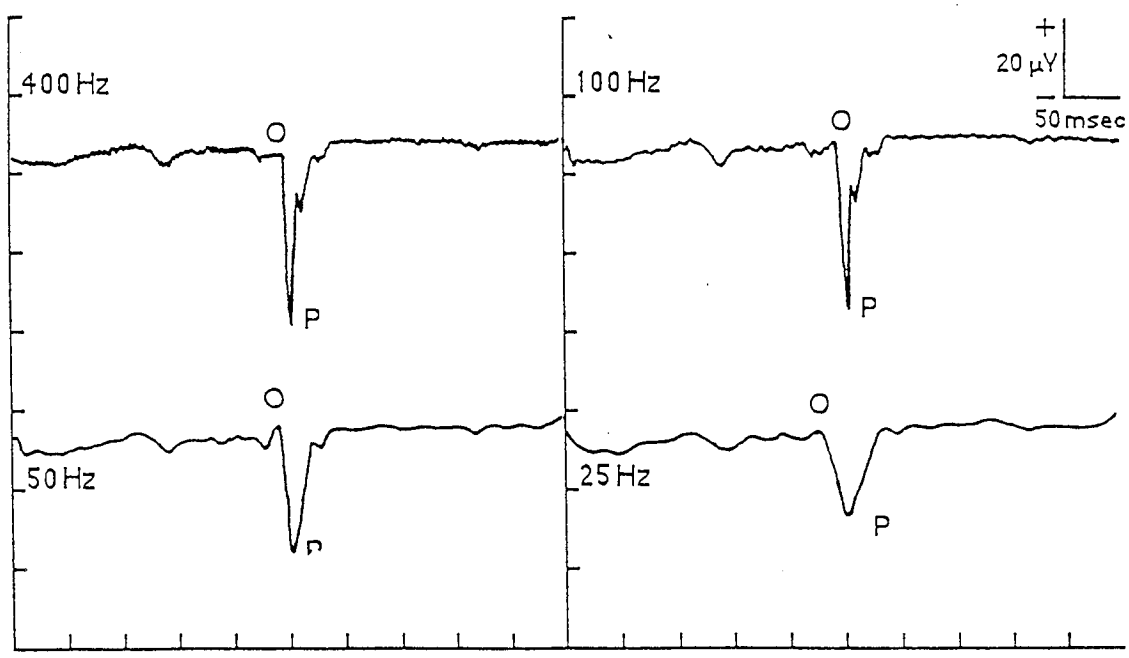

Figure 4.3 The effect of four different high pass filters (400, 100, 50 and 25 Hz) on the SP. The onset (O) and peak (P) of the SP are also shown, these being the points between which the SP amplitude is measured.

4.2.3 THE CHOICE OF REFERENCE ELECTRODE SITE TO RECORD THE SPIKE POTENTIAL

The choice of electrode locations around the eyes was based upon the earlier work of Thickbroom and Mastaglia (1985b, 1986), Jäntti (1982), Jäntti *et al.* (1983) and Riemslag *et al.* (1988). The recording set-ups used by these authors differed, however, in the choice of reference electrode location. Thickbroom and Mastaglia (1985b) reported a maximum SP with the reference electrode at P_z, and used this site in a later study (Thickbroom and Mastaglia 1986), while Jäntti (1982), Jäntti *et al.* (1983) and Jäntti and Häkkinen (1987) used C_z as the reference site. Riemslag *et al.* (1988) positioned electrodes over the poster parietal cortex as the reference, while linked ears have been used in recordings of both the anterior and posterior spike potential (see 3.2.2, 3.2.3). The position of the reference electrode is of considerable importance due to the controversy regarding the origin of the frontal and posterior spike potentials. If, as suggested by Weinstein *et al.* (1984), Balaban and Weinstein (1985) and Weinstein *et al.* (1988), the posterior spike potential is independent from the anterior SP, the choice of an electrode on the posterior scalp is not ideal for examining the frontal SP as the waveforms may be artificially altered by activity at the reference electrode. If, on the other hand, the frontal and posterior spike potential are directly related, as suggested by Becker *et al.* (1972), Kurtzberg and Vaughan (1973), Armington (1977, 1978) and Thickbroom and Mastaglia (1985b, 1986), the choice a reference on the posterior scalp may be beneficial in enhancing the SP amplitude. The lack of a specific recording montage for the SP, particularly regarding the reference site, indicated that it would be beneficial to initially record the SP using different reference sites to determine which should be used for the main experimental work.

Two subjects were used to record the SP with an electrode at the inner canthus of one eye with P_z, C_z, P_3, P_4 and linked ears as the reference sites. The filter settings described above were used and the EOG was recorded from the electrodes at the inner canthus and outer canthus. Saccades of 20° amplitude were recorded. All electrode sites were

prepared as described previously. The SP was easily recorded from all the reference sites. The averaged waveforms for the different reference locations are shown in Figures 4.4 and 4.5 and the latency and amplitude values are given in Table 4.1.

Reference	Pz			Cz			P3			P4			Linked ears		
Abduction	On	Pe	Amp	On	Pe	Amp	On	Pe	Amp	On	Pe	Amp	On	Pe	Amp
CN	-6	11	49.0	-3	11	29.7	-3	11	40.6	-2	11	37.6	-3	11	26.7
JR	-6	5	61.6	-8	5	58.6	-6	7	45.0	-8	6	40.1	-7	4	42.9
Adduction															
CN	-13	-2	45.6	-8	-1	24.3	-10	-2	36.5	-10	-1	30.9	-8	-1	15.4
JR	-12	0	75.5	-12	0	59.4	-12	0	65.7	-11	0	67.1	-11	1	46.3

Table 4.1 The spike potential onset (On) and peak (Pe) latencies and onset-peak amplitudes (Amp) for the SP recorded from the inner canthus to a reference electrode located at five different sites on the scalp.

The traces in Figures 4.4 and 4.5 show the SP waveform appears to be little affected by the choice of reference site, the only waveforms showing an obvious difference being those recorded with the linked ears reference. In this case the SP amplitude appears reduced, this being confirmed by the amplitude values in Table 4.1. The latency values in Table 4.1 show the SP onset and peak to vary little with the different references, although it should be remembered that these values are only for two subjects. Table 4.1 shows the greatest amplitude values were recorded with the reference at P_z, confirming the earlier findings of Thickbroom and Mastaglia (1985b). The smallest amplitude was recorded with the linked ears, suggesting this is not the most appropriate reference location to record the SP, particularly for smaller saccade sizes where there may be increased noise compared to SP activity.

It has been shown in the previous Chapter that the presaccadic spike potential can be recorded with a widespread distribution across the scalp. The possible influence that saccade direction may have upon the waveform recorded from scalp electrodes, particularly P_3 and P_4 has also been highlighted (see 3.2.2). Although the waveforms shown in Figures 4.4 and 4.5 do not appear to differ greatly for these two electrode locations, the possible effect that saccade direction may have on the recordings implies that a centrally located reference electrode may be more suitable.

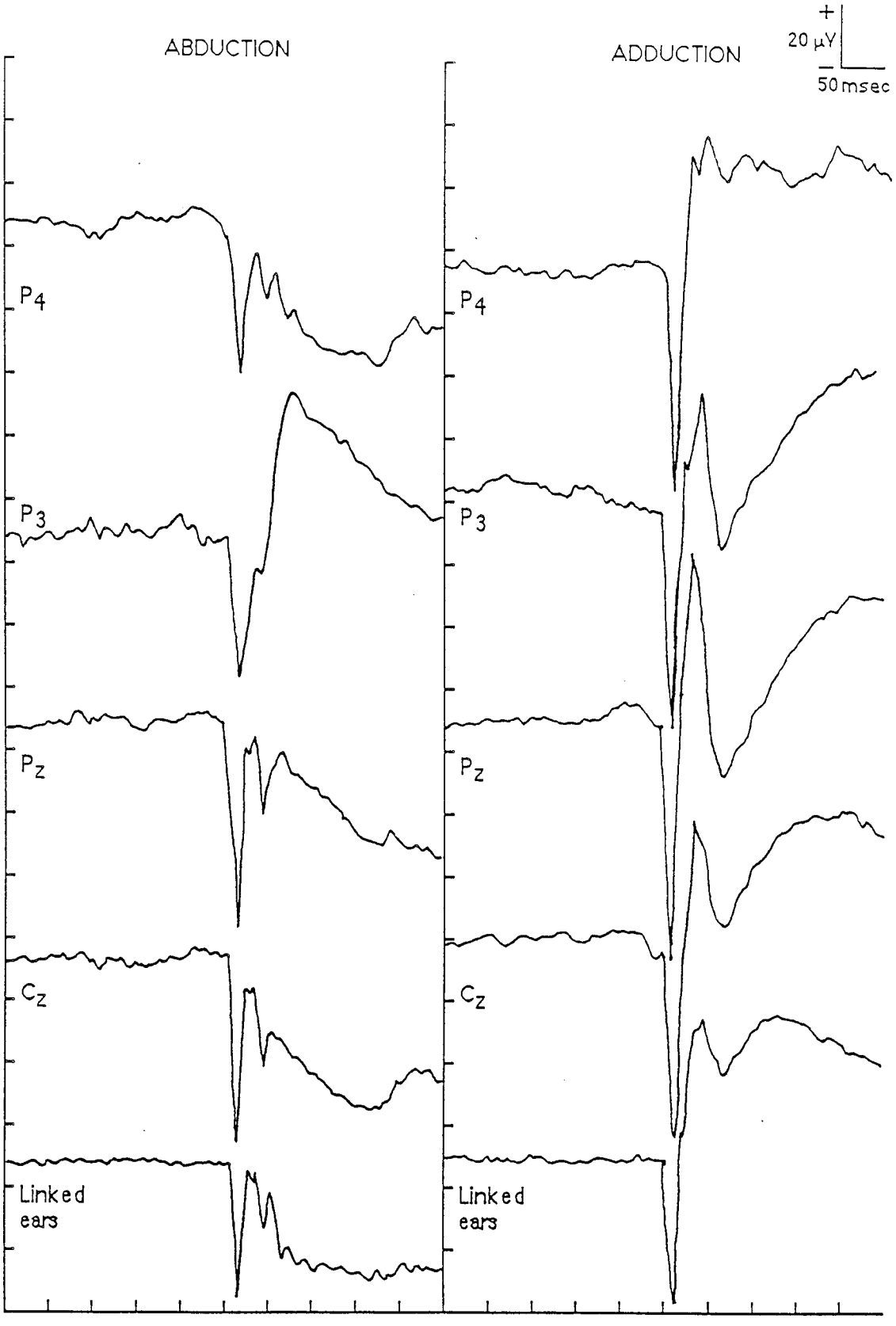

Figure 4.4 The SP waveform recorded from the inner canthus of the left eye to five reference electrode sites. The waveform shape is very similar in all the recordings for all reference sites (subject JR).

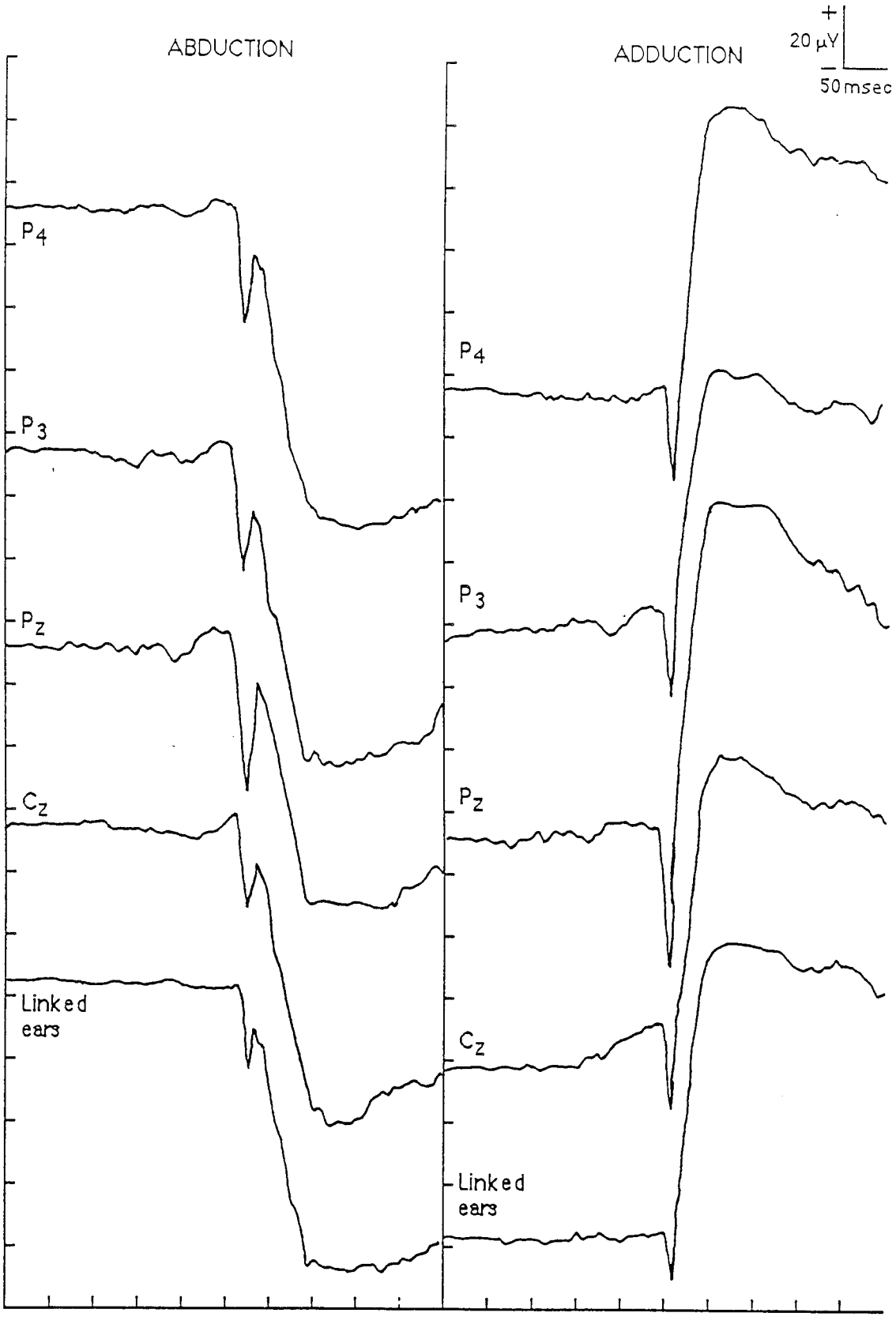

Figure 4.5 The SP waveform recorded from the inner canthus of the right eye to five reference electrode sites. The waveform shape is very similar in all the recordings for for all reference sites (subject CN).

From the literature it would appear that P_Z or C_Z will be least affected by any directional influences upon the recording as these are centrally located on the scalp. Although the latency values in Table 4.1 were very similar for these two references, the amplitude recorded with C_Z was smaller than that of P_Z. The recordings from these two subjects implied that P_Z may be the most appropriate reference electrode site to record the SP with the maximum amplitude as long as it is assumed that the posterior and anterior spike potentials are related. As this location had been used previously by Thickbroom and Mastaglia (1985b, 1986) for the reference it was decided to use P_Z as the reference location for the experiments in this thesis.

The electrodes around the eyes were situated at the inner and outer canthi in accordance with earlier studies, being located on the bony edge of the orbit at the outer canthus and as close to the inner canthus as was possible. These electrodes were both horizontally in line with the pupil. Additional electrodes, when required, were placed above and below the eyes, vertically in line with the pupil centre, again located on the bony edge of the orbit. These electrode positions were chosen because as well as allowing the activity from all round the globe to be recorded they also allowed the same electrodes to be used for recording the SP and EOG. For the experiment in which the distribution of the potential was recorded 14 electrodes were placed on the scalp in accordance with the 10-20 system with two located below the eyes. Both an average reference and a balanced non-cephalic reference were used in this study.

The duration of the recording sessions was dependent upon the nature of the experiment and the number of recording conditions, but as a general guide recording the SP from one electrode site for one saccade size took approximately 20 minutes. This time included positioning the electrodes and the actual recording and averaging of the potential. For the longer experiments, e.g. the different saccade sizes and mapping the distribution, the total recording time was over two hours. Regular breaks were taken during these recording sessions to avoid fatiguing the subjects.

4.3 ANALYSIS OF RESULTS

Following the recording sessions the individual waveforms were hard-copied with the Pathfinder's X-Y plotter, the latencies and amplitudes being determined with the averager's internal cursor as described above. The Pathfinder was also used to calculate group average waveforms for the different recording conditions and, unless otherwise stated, the waveforms shown in this thesis are group means although examples of individual waveforms and the raw data are given in the appendices.

An Apple Macintosh computer was used to store the data in spread sheet form (Microsoft Works) allowing the means and standard deviations to be updated automatically as new subjects were studied. This computer was also used to plot the graphs (using Cricket Graph) of the data shown in this thesis. Statistical analysis of the raw data was performed with either the Apple Macintosh, or with programs written specifically for a Research Machines 380Z computer. The different statistical tests used for the various experiments will be given in the appropriate sections.

The experimental design used in this thesis has been based upon the previously published work describing the SP. The literature review presented in the preceding Chapter has shown that all the recording systems used have followed the same basic principles. These principles have been adapted for use in this theses although the exact set-up will obviously differ due to the different apparatus available. The general recording conditions were consistent for all the experimental work in this thesis with only small variations relating to individual experiments. These changes will be described in detail in the following Chapters dealing with the experimental work.

CHAPTER 5

A STUDY OF THE PRESACCADIC SPIKE POTENTIAL RECORDED WITH 20° HORIZONTAL SACCADES

5.1 INTRODUCTION

The previous Chapters have described the SP parameters and waveforms recorded by earlier workers. It has been seen that the SP has often been regarded as no more than an eye movement artefact and, as such, there has been little research into its normal parameters and waveform. Although the data is limited, the the workers who have studied the SP have found similar SP onset and peak latencies. Some debate exists, however, regarding the SP amplitude values that can be recorded. This lack of normal SP data is a problem which must clearly be addressed before the SP can be studied with abnormal eye movements.

This initial experiment was designed to provide a set of normative SP data by recording the potential from different electrode sites around the eyes in a group of normal subjects. Normal SP data should include information regarding the onset and peak latency of the potential with regard to the saccade start and the normal onset-peak amplitude. The literature shows no single montage to be ideal for recording the SP, so different electrode sites should be used to examine the effect this may have on the potential. This knowledge will help determine the most suitable recording set-up for further experiments.

Many previous studies of the SP have used small numbers of subjects. Ideally, the mean parameters and waveforms should be calculated for a larger number of subjects if further studies, particularly involving abnormal saccades, are to be compared to normal results. Much of the published work regarding the SP also shows little analysis of the results, with scarce details of the variance of the data and little comparison of SP parameters for

different recording sites and saccade directions. Appropriate statistical analysis should be performed to examine any relationship between the SP and saccadic eye movements.

5.2 METHODS

The technical details of the Pathfinder and the averaging program used in the experiments have been described previously and only the specific features pertinent to this study will be given below (see 4.2.1). A time sweep of 500 msec was used and the bandpass filters were set at 0.5 and 100 Hz. The recording technique was designed to allow comparison with earlier published work (Thickbroom and Mastaglia, 1985b,1986; Riemslag *et al.*, 1988).

The SP was recorded from twenty normal subjects; 10 male (mean age 25.0±2.3 years) and 10 female (mean age 23.6±4.0 years) who had no known ophthalmological or neurological defects. The subjects were seated one metre away from the LEDs which were positioned so as to subtend 20° at the subject, 10° either side of centre. The height of the chin rest was adjusted until the subjects eyes were the same height as the LEDs. This ensured that purely horizontal eye movements were being recorded.

Prior to the recordings the electrode sites round the eyes and on the scalp were prepared (see 4.2) and all electrode resistances were 5 KΩ or below. Eight electrodes, four around both eyes, were used to record the SP. These were located at the inner and outer canthi and above and below the two eyes and were positioned on the bony margins of the orbit, in line with the pupil centres. Following the initial recordings described in 4.2.3, and the early work of Thickbroom and Mastaglia (1985b,1986), an electrode at P_z was used as the reference electrode and an electrode on the forehead acted as a ground.

Forty horizontal saccades of 20° magnitude (20 abducting and 20 adducting) were recorded with the corresponding spike potentials from each electrode site. During recordings subjects were instructed to keep their heads as still as possible, the chin and

forehead rest reducing head movements. The recording program allowed only two eye movement traces and SP waveforms to be recorded at any one time, so to record the SP from all eight electrodes required a recording session lasting approximately $2^1/_2$ hours. Subjects were encouraged to rest between recordings from each electrode site and verbal encouragement was given to ensure concentration and accurate saccades. To avoid any effect of fatigue on the recordings the order in which the eight electrode sites were used was randomised for each subject.

The individual SP and eye movement (EOG) waveforms were stored on hard disc during recordings and, following the recording, averaged using the program previously described. From the averaged waveforms the onset and peak latencies and onset-peak amplitudes were measured with the averager's internal cursor (see Figure 4.2) and this data was used to calculate group means and standard deviations (SDs) for these parameters at each electrode site. The Pathfinder was used to calculate group average waveforms for each recording condition. It should be remembered that the group average waveforms will show some smoothing when compared to waveforms for individual subjects as the SP did not always occur at exactly the same latency before the saccade onset for each subject.

5.3 RESULTS

A clear SP was recorded from each subject for all electrode sites with both abducting and adducting saccades. The waveforms were characterised by a large, negative spike like deflection beginning shortly before the onset of the saccade and peaking at, or just after the start of the eye movement. The waveforms from the different electrode sites had a similar appearance and compare well with those found in earlier studies of the SP. The group average waveforms for each electrode site are shown in Figures 5.1 and 5.2 while examples of waveforms recorded from single subjects are given in Appendix 1.3.

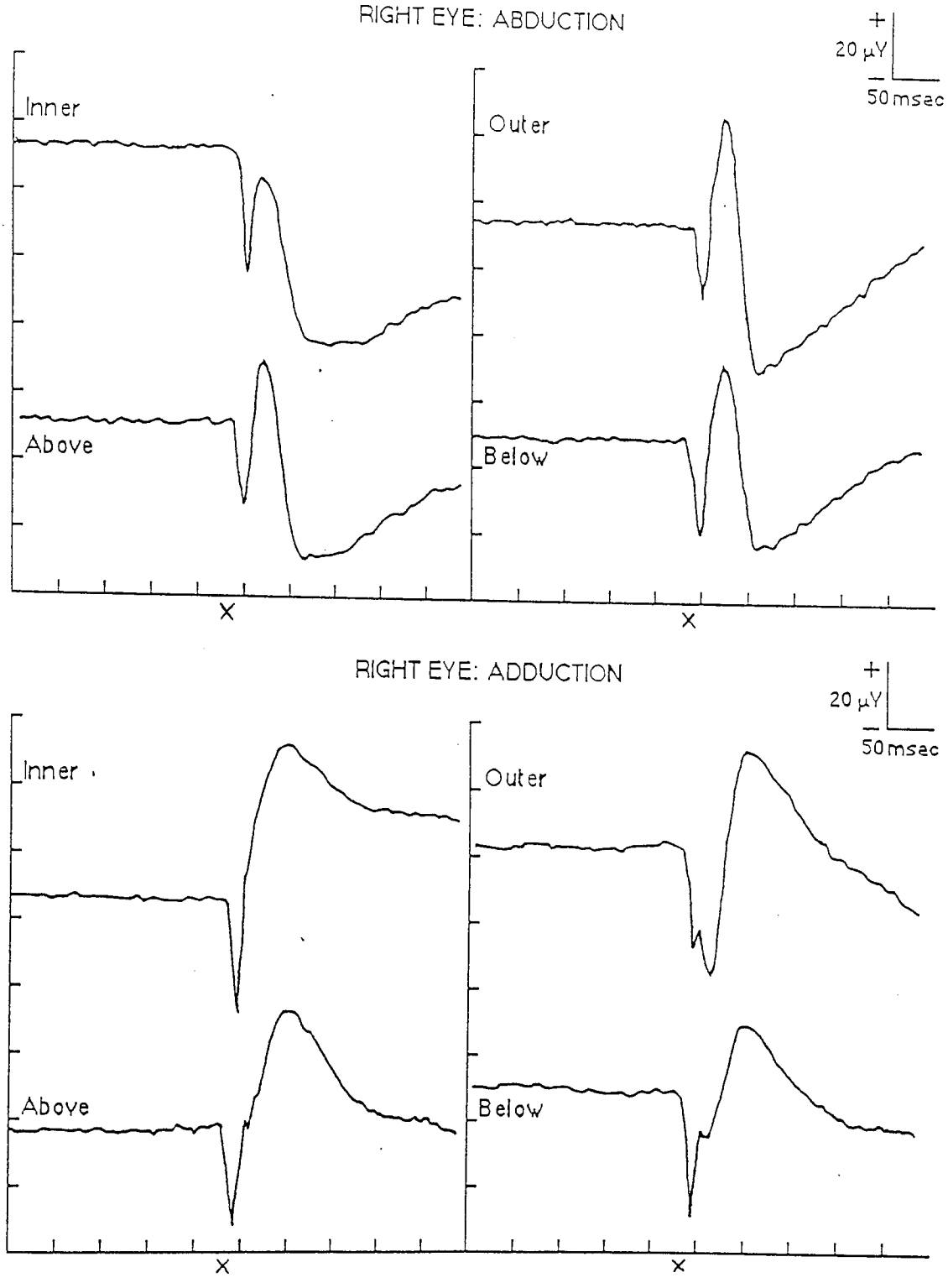

Figure 5.1 The group average spike potential waveforms for the right eye of 20 subjects performing abducting and adducting saccades. The saccade onset is indicated by the cross. The results of recordings from four electrode sites around the eye are shown.

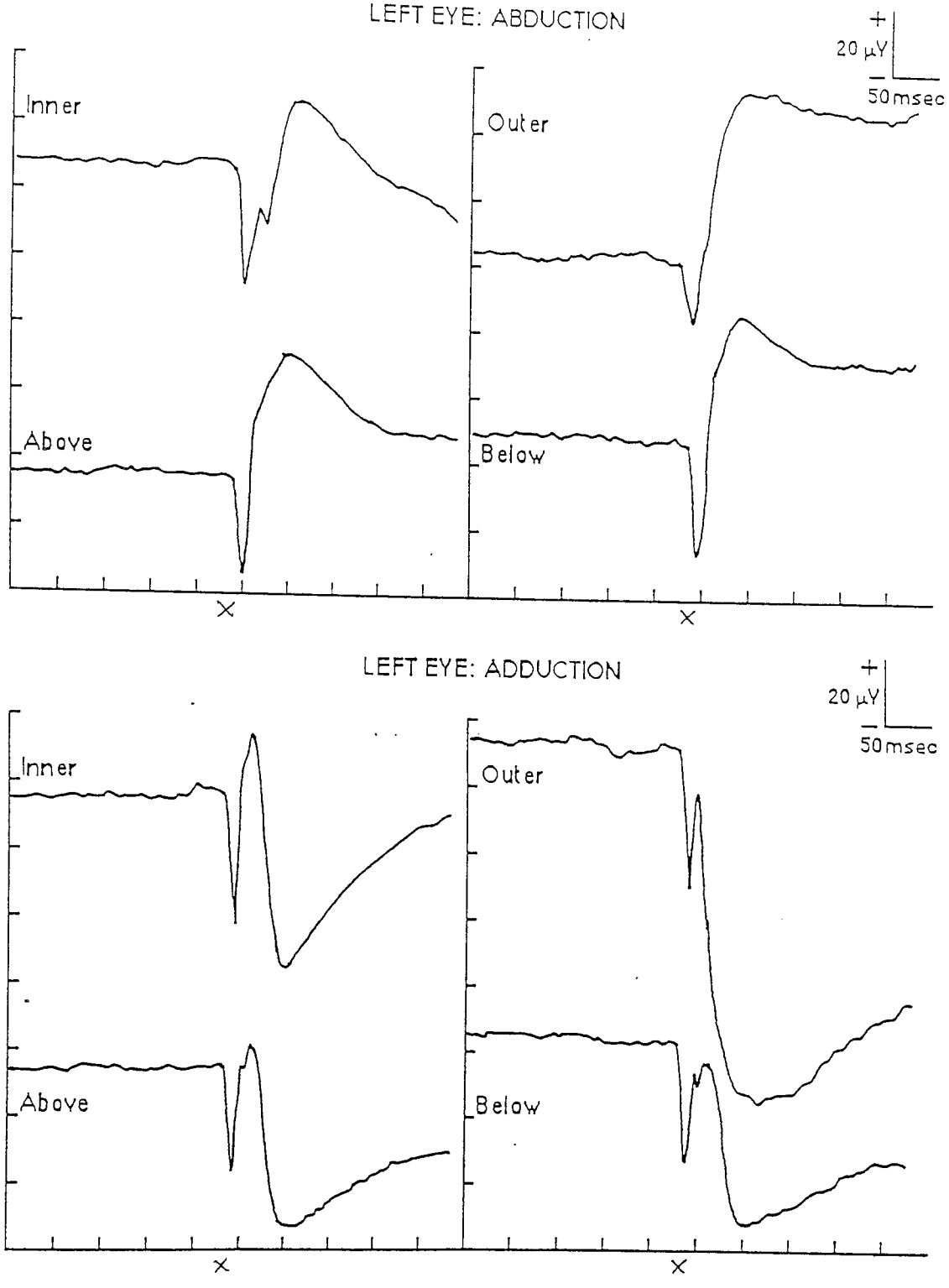

Figure 5.2 The group average spike potential waveforms for the left eye of 20 subjects performing abducting and adducting saccades. The saccade onset is indicated by the cross. The results of recordings from four electrode sites around the eye are shown.

5.3.1 ONSET AND PEAK LATENCIES FOR 20° SACCADES AND THEIR RELATION TO SACCADE DIRECTION

The individual SP onset and peak latencies were used to calculate group average values for these parameters. The convention discussed earlier (4.2.1) was used such that positive values indicate a latency after the saccade onset and negative values indicate a latency before the saccade onset. The average SP onset at the eight electrode sites for the twenty subjects was between -4.1 to -11.0 msec (mean -7.8±2.4 msec) before the start of the eye movement. The average SP peak at the eight electrode sites was between -0.1 msec before the saccade start to 8.1 msec after the saccade onset (mean 3.8±3.2 msec) The onset and peak latency raw data is given in Appendix 1.1.

Table 5.1 shows the mean latency values and standard deviations (SD) for the eight electrode sites and two saccade directions recorded from twenty subjects. The Table indicates that adducting saccades exhibited earlier SP onset and peak latencies than the SPs recorded with abducting saccades for all eight electrode sites. The Table also shows the consistency of the SP latencies when recorded from different sites around the eyes.

		ELECTRODE SITE							
		INNER		OUTER		ABOVE		BELOW	
		Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak
RIGHT ABD	Mean	-5.3	7.9	-5.7	6.6	-4.1	8.1	-5.7	6.8
	SD	3.6	3.1	3.2	4.2	3.9	4.0	3.6	4.3
LEFT ABD	Mean	-6.9	6.2	-6.3	6.8	-5.0	5.9	-6.2	6.8
	SD	3.4	3.1	3.6	3.1	3.5	3.2	3.1	2.9
RIGHT ADD	Mean	-9.8	-0.1	-11.0	1.4	-11.0	0.5	-10.0	0.3
	SD	2.7	2.6	3.8	4.5	4.1	3.6	3.4	4.0
LEFT ADD	Mean	-9.9	0.8	-10.0	1.0	-9.3	1.2	-9.8	1.2
	SD	3.1	4.1	3.5	4.4	4.8	5.0	5.2	6.0

Table 5.1 The mean and standard deviation (SD) SP onset and peak latencies (msec) for twenty subjects at four electrode sites round both eyes for 20° abducting (ABD) and adducting (ADD) saccades.

Analysis of the latency data was performed in two ways. Initially the results from the two eyes were analysed to determine if these were comparable. During this comparison the

two saccade directions were considered separately. Following this, the two saccade directions were considered, in this case the eyes were treated separately.

Two-way analysis of variance (ANOVA) was performed on the raw data to compare the two eyes with the eye recorded from (right eye, left eye) as one treatment and the electrode site (inner canthus, outer canthus, above the eye, below the eye) as the second. Abducting and adducting saccades were examined separately. No statistically significant differences were found between the right and left eyes for the onset or peak values or the electrode sites for both saccade directions (Table 5.2).

	Right vs Left eye	Electrode sites
Abduction onset	$F_{1,19}$=3.22; NS	$F_{3,57}$ =0.56; NS
Abduction peak	$F_{1,19}$=3.26; NS	$F_{3,57}$ =0.12; NS
Adduction onset	$F_{1,19}$=1.54; NS	$F_{3,57}$ =0.31; NS
Adduction peak	$F_{1,19}$=1.37; NS	$F_{3,57}$ =0.42; NS

Table 5.2 ANOVA results comparing the two eyes and electrode sites for the SP onset and peak latencies with abducting and adducting saccades.

To examine the relationship between saccade direction and the SP onset and peak values the two eyes were considered separately. The saccade direction (abduction, adduction) was one treatment and the electrode site (inner canthus, outer canthus, above the eye, below the eye) the second. The SP onset and peak latencies were both statistically significantly earlier with adducting saccades than abducting saccades, but no statistically significant differences were found for the latency values at the electrode sites (Table 5.3).

	Saccade direction	Electrode sites
Right eye onset	$F_{1,19}$=49.98; p<o.001	$F_{3,57}$ =0.85; NS
Left eye onset	$F_{1,19}$=23.79; p<0.001	$F_{3,57}$ =0.55; NS
Right eye peak	$F_{1,19}$=29.88; p<0.001	$F_{3,57}$ =0.1.11; NS
Left eye peak	$F_{1,19}$=35.39; p<0.001	$F_{3,57}$ =0.40; NS

Table 5.3 ANOVA results comparing the two saccade directions and electrode sites for the SP onset and peak latencies.

5.3.2 AMPLITUDE VALUES FOR 20° SACCADES AND THEIR RELATION TO SACCADE DIRECTION

The onset-peak SP amplitudes were measured with the Pathfinder's internal cursor for each subject. Group average amplitude values were calculated for each electrode site and saccade direction. Table 5.4 shows similar amplitude were recorded at all electrode sites, ranging between 35.5 and 48.5 μV (mean 40.9±3.4 μV). The amplitude raw data are given in Appendix 1.2.

		ELECTRODE SITE			
		INNER	OUTER	ABOVE	BELOW
RIGHT ABD	Mean	42.0	35.5	37.1	39.1
	SD	14.1	14.2	13.6	14.2
LEFT ABD	Mean	38.8	38.4	39.1	40.3
	SD	12.2	10.8	10.6	11.0
RIGHT ADD	Mean	41.3	39.2	40.8	42.4
	SD	17.0	12.2	13.4	13.4
LEFT ADD	Mean	47.8	42.7	41.7	48.5
	SD	19.0	17.0	16.0	15.8

Table 5.4 The mean and standard deviation (SD) SP amplitudes (μV) for twenty subjects at four electrode sites for 20° abducting (ABD) and adducting (ADD) saccades.

Like the latency values, the amplitude results were first analysed to compare the two eyes. ANOVA of the amplitudes was performed with the eye recorded from as one treatment and the electrode site the second with abducting and adducting saccades considered separately. No statistically significant differences were found between the right and left eyes or the electrode sites for the amplitudes of both saccade directions (Table 5.5)

	Right vs Left	Electrode sites
Abduction	$F_{1,19}$=0.103; NS	$F_{3,57}$ =1.67; NS
Adduction	$F_{1,19}$=4.13; NS	$F_{3,57}$ =1.77; NS

Table 5.5 ANOVA results comparing the two eyes and electrode sites for the SP onset-peak amplitudes with abducting and adducting saccades.

The relationship between saccade direction and the SP amplitudes was then examined with the two eyes studied separately. The saccade direction was one treatment and the

electrode site the second. No significant differences were found in SP amplitudes for abducting and adducting saccades or the electrode sites for both eyes (Table 5.6).

	Abd vs Add	Electrode sites
Right eye	$F_{1,19}$=0.101; NS	$F_{3,57}$ =1.59; NS
Left eye	$F_{1,19}$=4.16; NS	$F_{3,57}$ =1.89; NS

Table 5.6 ANOVA results comparing the two saccade directions and electrode sites for the SP onset-peak amplitudes from both eyes.

5.4 DISCUSSION

The results of this experiment show that a clear SP can be recorded from several electrode sites around both eyes with abducting and adducting saccades having equally clear SP waveforms. The mean SP onset is between -11.0 to -4.1 msec before the saccade start and the SP peak is between -0.1 msec before to 8.1 msec after the saccade onset. A significant difference between abducting and adducting saccade spike potentials exists, with adducting saccade SPs having earlier onset and peak latencies than abducting saccade SPs. The mean onset-peak amplitude of the SP is between 35.5-48.5 μV but there are no significant differences in the amplitude values for the two saccade directions or electrode sites.

In this experiment the SP was back-averaged around a pre-defined point; the saccade onset. Thickbroom and Mastaglia (1985b,1986) used a similar technique in their studies of the SP, although they did also use the peak of the SP as an averaging trigger. Riemslag *et al.* (1988), similarly, used the saccade onset as the averaging trigger, but these authors monitored the saccades with infra-red reflectometry. Riemslag *et al.* (1988) expressed some concern regarding potential errors that may be introduced into the averaging process when using EOG traces to determine the saccade onset (see 3.2.2). While the EOG may not be as accurate as infra-red recording techniques, for example, this did not appear to cause problems with trigger jitter in the present experiment. When the individual eye movement records were examined for each subject there was little difficulty in

determining the saccade onset on the EOG trace and clear SPs were averaged round this point. As described in 4.2.1, if the saccade onset was not be readily recognisable on the EOG waveform that epoch was rejected from the average. The group average waveforms shown in Figures 5.1 and 5.2 can be compared to those in earlier studies (Jäntti *et al.*, 1982; Thickbroom and Mastaglia 1985b,1986; Riemslag *et al.*, 1988; see 3.2.2) and indicate that the present technique allows successful recording of the presaccadic spike potential.

The latency values in this study give a more accurate representation of the SP onset and peak than previously reported by Thickbroom and Mastaglia (1985b,1986) and Riemslag *et al.* (1988). Thickbroom and Mastaglia (1985b,1986) did, in some cases, use the SP peak as the trigger for the averaging which does not allow an accurate identification of the SP onset with regard to the saccade start. To determine the relationship between the saccade and SP onset the waveforms must be averaged accurately around the beginning of the saccade. Choosing components of the SP as the averaging trigger does not allow this information to be calculated. Riemslag *et al.* (1988), in their study of the spike potential, did average the potential round the saccade onset, but they did not consider adducting saccades and therefore give no latency values for these eye movements.

The amplitude values found by Thickbroom and Mastaglia (1986) differ from the values found in the present study, their waveforms generally having larger amplitudes than those recorded in this experiment. This, again, may possibly be due to their choice of the SP peak as the averaging trigger. Using the peak of the SP as the point round which the waveforms are to be averaged will enhance the amplitude of the potential and it should be noted that the amplitude values reported by Thickbroom and Mastaglia (1986) for 5° saccades often exceed the values found in the present experiment for 20° saccades. Unfortunately, there is no information given by Thickbroom and Mastaglia (1985b, 1986) of the variability of the amplitude values they recorded.

The finding of a significant difference in the onset and peak latencies with saccade direction is a previously unreported observation. Why this should occur, particularly at all electrode sites, is uncertain. It is possible that the SP recording may be a reflection of activity in different muscle groups involved in the saccade activity. With simple horizontal eye movements both the lateral and medial recti are the primary muscles acting to move the eyes. It has been suggested previously that the SP may be a reflection of activity in the muscles responsible for the eye movements (see 3.2.2). The main muscles controlling horizontal saccades (MR, LR) receive their innervation from different nerves and nuclei (medial rectus,IIIrd nerve, oculomotor nucleus; lateral rectus, VIth nerve, abducent nucleus; see 2.5.1). If the SP does represent activity of the motoneurons of the EOM a difference in SP latencies with different saccade directions could be explained if the innervational activity in the oculomotor nucleus and the abducent nucleus differed in their latencies. Sindermann *et al.* (1978) have recorded the innervational pulse in motor units of both the medial and lateral rectus muscles but, unfortunately, they give no information as to whether the activity in the respective motor units occurs at different latencies prior to the saccade onset in the two muscles. Until further information is known regarding the activity of motoneurons for the different muscles it is difficult to explain the differences in SP latency with saccade direction.

The waveforms and statistical analysis reveal no significant changes in SP latency and amplitude parameters with the different electrode sites chosen providing saccades in the same direction are compared. This, unfortunately, suggests that it may be difficult to isolate the role of individual extraocular muscles in the generation of the potential. It is known that the individual EOM exhibit different levels of activity depending upon the eye movement direction, but it does not appear that the electrodes nearest the muscle controlling the eye movement (i.e. inner canthus for the MR with adduction and outer canthus for the LR with abduction) record different levels of SP activity compared to the other electrodes around the orbit. This implies that the potential may be a compound potential resulting from combined activity of the different muscle groups involved in the

saccadic eye movement and that the SP may be incapable of isolating activity from the individual muscles.

This experiment shows, however, that it is unnecessary to record the SP from a large number of electrode sites to obtain comprehensive and accurate information about the potential waveform and parameters. The results show the SP latency and amplitude parameters do not alter when recorded from either eye and the SP waveforms from both eyes are consistent for saccades to the left and right. Although Figures 5.1 and 5.2 show the SP can be clearly recorded from all electrode sites, the latency values were most consistent when recorded from the electrodes at the inner canthus and below the eyes. For most recordings the maximum SP amplitudes were also recorded at these two sites. This suggests the optimum sites for SP recording may be the inner canthus and below the eye.

5.5 RELIABILITY OF THE SPIKE POTENTIAL RECORDING

5.5.1 INTRODUCTION

With any electrophysiological recording it is important to know how consistent the potential is over a period of time. There have been no studies in the literature of the reproducibility of the SP recording. While the initial study has shown the SP can be easily recorded from individual subjects, this does not indicate the consistency of the recording. Knowledge of how the SP varies with time is essential if the potential is to be recorded on more than one occasion. It is essential to know if any differences observed in the SP in subsequent recordings are normal changes, or due, for example, to disease conditions affecting the EOM.

It was also anticipated that knowledge of the reproducibility of the SP would confirm the suitability of the averaging trigger used in these experiments. If the repeat recordings did not differ from the original traces in terms of both amplitude and latencies, this would help

resolve any concern that the eye movement trigger may be introducing random jitter into the averaging process. To assess the reliability of the SP recording therefore, the potential was recorded from a group of subjects on two separate occasions.

5.5.2 METHODS

The experimental set-up was identical to the earlier study, with 20° saccades again being recorded. The initial experiment revealed the similarity of the SP recorded from four electrode sites around the two eyes performing horizontal saccades. These results suggested that it would be possible to perform fewer recordings for each subject yet still collect enough information about the SP to allow accurate analysis of the results and comparisons with different recording conditions. The initial recordings showed electrodes placed at the inner canthus and below the eyes gave the best overall recordings and these electrode sites were therefore used to record the SP from eight subjects (mean age 23.5±3.5; 3 males, 5 females). The eye to be recorded from was chosen on a random basis although equal numbers of right and left eyes were used.

The electrode sites were prepared as usual (see 4.2.1) and the impedences were all 5 KΩ or below. The SP was recorded from each subject on two occasions, the same SPs being recorded at each session. The interval between recordings ranged from between one week to several months for the different subjects.

5.5.3 RESULTS

A clear SP was recorded from all subjects showing the characteristic negative spike immediately prior to the saccade onset. Following recordings group average waveforms for the original and repeat recordings were calculated. These waveforms are shown in Figure 5.3. The latency and amplitude values at the two electrode sites for the eight subjects were determined as before and these values are shown in Tables 5.7 and 5.8. It

is evident from the Tables that the SP is very consistent with some subjects (KD, HO and BE in particular) showing very similar latency and amplitude values for the two recordings.

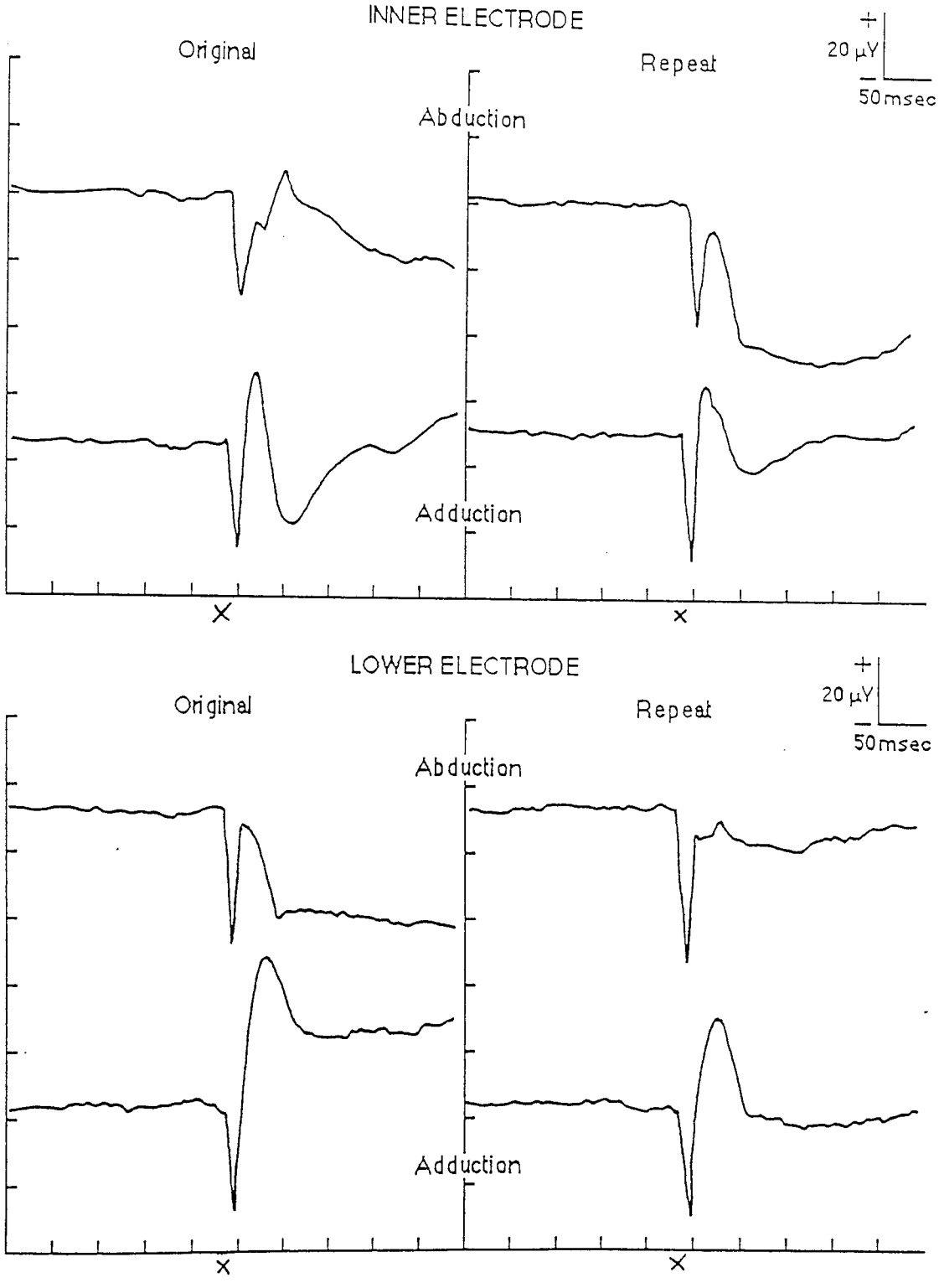

Figure 5.3 The group average waveforms for eight subjects comparing original and repeat recordings of the SP from two electrode sites. The saccade onset is indicated by the cross.

	Inner electrode: Abduction					
	Original			Repeat		
Subject	Onset	Peak	Amplitude	Onset	Peak	Amplitude
BE le	-3	12	57.7	-3	8	60.8
CN le	-8	12	50.4	-3	13	57.1
DT le	-2	10	66.8	-6	12	50.0
HO re	-4	5	66.8	-4	5	66.3
KD re	-9	4	53.1	-9	5	48.2
MD re	-5	4	40.5	-7	8	33.4
MH re	-1	11	56.9	-1	14	48.5
RD le	-10	7	40.4	-10	10	32.9
	Inner electrode: Adduction					
BE le	-12	-1	60.8	-11	0	57.6
CN le	-11	-2	46.4	-11	-2	33.4
DT le	-9	4	21.2	-9	3	35.0
HO re	-10	-1	47.0	-8	0	51.4
KD re	-9	-1	59.6	-9	-1	60.5
MD re	-10	-2	36.6	-9	-1	36.6
MH re	-11	-2	19.3	-11	-2	19.1
RD le	-10	0	45.2	-10	0	53.6

Table 5.7 The SP onset and peak latencies and amplitude recorded from an electrode at the inner canthus

	Lower electrode: Abduction					
	Original			Repeat		
Subject	Onset	Peak	Amplitude	Onset	Peak	Amplitude
BE le	-3	9	42.1	-5	7	41.6
CN le	-3	10	44.5	-1	13	39.6
DT le	-2	11	42.3	-2	9	46.5
HO re	-4	5	64.5	-4	4	56.4
KD re	-7	5	49.1	-7	4	46.0
MD re	-7	3	39.3	-4	4	36.4
MH re	-3	12	52.7	0	12	48.5
RD le	-9	5	29.8	-7	6	37.1
	Lower electrode: Adduction					
BE le	-14	-1	60.7	-12	-1	64.5
CN le	-12	-3	58.0	-12	-3	54.5
DT le	-13	-3	33.4	-15	-3	36.5
HO re	-9	-1	46.4	-10	-1	49.5
KD re	-10	-4	65.6	-11	-1	54.2
MD re	-9	1	45.3	-10	-2	49.5
MH re	-14	-3	46.6	-13	-3	30.8
RD le	-12	0	66.1	-11	0	57.8

Table 5.8 The SP onset and peak latencies and amplitude recorded from an electrode located below the eye.

The waveforms shown in Figure 5.3 and the latency and amplitude values given in Tables 5.7 and 5.8 show the SP to be a very reproducible recording. Visually examining the traces and raw data does not, however, indicate if the recordings can be considered statistically similar. To confirm the repeatability of the SP recording an index of reliability was calculated using the technique adopted by Millodot (1981). Pearson's correlation coefficient (r) was calculated for the twelve recording conditions along with the probability

(P) and these values were used to show the reliability and reproducibility of the recordings by comparing the original and repeat recordings (Table 5.9).

Factor	Group mean (SD) Original	Repeat	Correlation Coefficient (r)	Probability (P)
Inner abduction				
onset	-5.25 (3.3)	-5.38 (3.2)	0.80	0.016
peak	8.13 (3.5)	9.38 (3.4)	0.75	0.034
amplitude	54.1 (10.2)	49.9 (12.3)	0.78	0.022
Inner adduction				
onset	-10.3 (1.0)	-9.75 (1.2)	0.77	0.025
peak	-0.01 (2.1)	-0.40 (1.6)	0.79	0.019
amplitude	42.0 (15.5)	43.4 (14.5)	0.92	0.029
Below abduction				
onset	-4.75 (2.5)	-3.75 (2.6)	0.76	0.027
peak	7.50 (3.4)	7.38 (3.6)	0.88	0.004
amplitude	45.6 (10.2)	44.0 (6.7)	0.90	0.002
Below adduction				
onset	-11.6 (2.1)	-11.8 (1.7)	0.76	0.030
peak	-1.80 (1.7)	-1.80 (1.2)	0.80	0.016
amplitude	52.7 (11.6)	49.7 (11.1)	0.76	0.029

Table 5.9 The correlation coefficient (r) and probability (p) as a reliability index for repeat recordings of the SP from eight subjects at two electrode sites.

5.5.4 DISCUSSION

This study confirms the ease with which the SP can be recorded but, unfortunately, gives no further clues as to the specific origin of the SP. The results clearly show that the SP is a consistent recording, the correlation between the original and repeat recordings demonstrating, for all parameters, that the SP can be reliably recorded at more than one session with a high degree of confidence that the results will be the same for each recording. This knowledge is important as it allows one to say that any changes over time are probably due to changes in the generation of the potential as opposed to an unreliable recording technique.

The similarity in the latencies of the repeat values confirm the validity of the recording technique used in this thesis. If, as has been suggested by some authors, EOG recordings did not allow an accurate identification of the saccade onset, it would be fair to

expect a greater spread of latency and amplitude values than shown in the present studies. This would be particularly true for repeated recordings where a lower level of correlation would be expected if the averaging trigger suffered from random and variable jitter at each recording session. The results do not show such a spread of values and it can be concluded, therefore, that the technique is satisfactory with regard to the accuracy of the averaging trigger determined from the EOG records. Thickbroom and Mastaglia (1985b) have also averaged the SP around the saccade onset as determined from EOG records and suggested that this technique is better than automatic techniques, for example, in allowing rejection of poor recordings from the averaged recordings (see 3.2.2).

5.6 SUMMARY

The experiments in this Chapter have contributed further to the knowledge of the SP recording waveform and parameters from normal subjects. The technique used has been based upon techniques reported previously in the literature. This allows some comparisons to be drawn between the present work and previously published studies. The results of the experiments have confirmed the anterior SP recording to be a large negative spike potential commencing shortly before the saccade onset. The reliability of the recording has been established and the normal waveform and parameters for this saccade size determined.

A previously unknown difference in the latency for adducting and abducting saccades has been found, with adducting saccades having earlier SP onset and peak values than abducting eye movements. Unfortunately, it is difficult to account for this difference. It appears that different electrode sites are unable to differentiate between the individual muscles involved in producing saccades and the related SPs. From the known firing patterns of the EOM motor units it can be assumed that the antagonist muscle will be playing only a small role in both saccade and SP generation. It can be hypothesised that the MR and LR muscles may receive their innervational pulse from the respective

motoneuron at different latencies before the saccade onset. It this were the case, the difference in SP latency with different saccade directions may be accounted for by the innervation of the EOM. Unfortunately, as has been described above, such information regarding different innervational patterns and onset latencies for different muscles is unknown and one can only postulate that this may account for the SP latency differences.

The amplitude of the SP recording for 20° saccades is between 35.5 and 48.5 μV. While these amplitudes are smaller than the values found by Thickbroom and Mastaglia (1986) for 5° saccades this is to be expected when it is remembered that these authors used the SP peak as the trigger for averaging. Riemslag *et al.* (1988) did not give any specific amplitude data, but an amplitude of approximately 20 μV for 20° saccades can be calculated from their graphs. This amplitude value was for 5 subjects performing abducting saccades only, with a reference electrode over the parietal cortex. Despite the differences in technique in the present study and the earlier work, the results are similar and show that the SP can be recorded with a variety of methods.

The SP waveform has been determined for normal young subjects for this saccade size and the following Chapters will describe the experiments to determine if any changes occur with different recording conditions. The latency and amplitude values given in this Chapter will be used as the basis for comparison with these studies of the potential. The waveform and parameters have been shown to be consistent between the two eyes and different recording sites and it has been decided to concentrate further studies on a modified recording set-up with less electrodes per subject to reduce the recording time, and hence subject fatigue which may result in reduced saccade accuracy.

CHAPTER 6

THE EFFECT OF SACCADE SIZE ON THE SPIKE POTENTIAL

6.1 INTRODUCTION

In Chapter 5 the SP was shown to be an easily recorded potential for 20° saccades with well defined latency and amplitude values and a distinctive waveform consistent with earlier published recordings of this potential. The initial study detailed in Chapter 5, however, only gave data for spike potential recordings with 20° saccades with no information about the possible effect that changing saccade size may have on the SP waveform and parameters.

The relationship between saccade size and the its duration and velocity was discussed in Chapter 2. Both the velocity and durations of larger saccades are greater than those of smaller movements (2.2.2). The literature shows the innervation pattern to saccades of different magnitudes also alters with saccade size. The initial innervational impulse to the EOM prior to a saccade is the 'saccade-pulse'. This pulse of activity determines the direction and size of the movement and helps overcome the viscous drag of the orbit. The firing patterns of the ocular motoneurons generating the pulse differ with changing saccade size. With saccades of less than 15° the firing rate varies with saccade size, but with movements larger than this the motoneuron firing rate saturates. With larger saccades the duration of the saccade pulse is related to the size of the eye movement (2.4.2).

It has been suggested that the SP may be related to motor unit activity within the EOM (3.2.2). Knowledge of how the SP changes with saccade size is important as this may give a further indication to the possible origin of the potential. If a similar pattern of amplitude changes to that of the ocular motoneurons can be demonstrated for SP recordings, for example, this may suggest that the SP is indeed related to the activity of these structures.

Although the saccade-pulse parameters are known to vary with saccade size, little information is forthcoming about the effect of saccade size upon SP recordings. Thickbroom and Mastaglia (1985b) found the SP amplitude remained constant for saccades between 10-40°, while Riemslag *et al.* (1988), reported the SP amplitude changed for saccades up to 8-10° in size with little subsequent change for saccades larger than this. In both studies the information given regarding the parameters of the SP was sparse and there was no statistical analysis of the data to support the findings. Only a small number of subjects were used in the two experiments and neither Thickbroom and Mastaglia (1985b) or Riemslag *et al.* (1988) considered the effect that age may have on the SP recording, the two subject groups showing a wide spread of ages. The results of these studies cannot therefore be accurately compared with the normal values found for 20° saccades in the initial experiment of this thesis described in the preceding Chapter.

The lack of detailed information gained from earlier studies prompted a fuller investigation into the effect of saccade size on the SP. This Chapter describes experiments performed to study any latency and amplitude changes that occur in the SP with varying saccade size. The results are discussed in light of proposed origins of the SP and compared to earlier studies of the potential with different sized saccades.

6.1.1 METHODS

Following the results of the initial recordings which had shown the SP to be recorded most consistently at the inner canthi and below the eyes, the SP was recorded from electrodes placed at these sites for horizontal saccades of 20°,10°,7.5°,5° and 2.5°. The recording apparatus and set-up were as before (see Chapter 4). The SP was averaged separately for each saccade size and direction. Group mean and SD latency and amplitude values were calculated for the abducting and adducting values for each saccade size and the Pathfinder was used to produce group average waveforms for the different saccade sizes and directions.

Recordings were made from ten normal subjects aged 23-30 years old (mean age 25.6±3.5). Twenty abducting and twenty adducting saccades were back-averaged for each saccade size. The recordings were performed in two recording sessions, one per electrode, each session lasting between $1^1/_2$ and $1^3/_4$ hours. The initial recordings had emphasised the lack of any difference in the SP recording between the two eyes so it was decided that one eye could be be used per subject. The eye to be used was chosen using random number tables to give five right and five left eyes. The eye not being recorded from was occluded and the head held steady with the chin and forehead rest. For the 7.5° and 2.5° saccade sizes the subjects were seated two metres from the array of LEDs and the 15° and 5° targets used as appropriate. The remaining sizes were recorded with the subjects one metre from the LEDs.

6.2 RESULTS

A clear SP waveform was recorded from each subject for all saccade sizes and both electrode sites. With the smaller saccades (2.5° and 5°) there was an increase in noise relative to both the EOG and SP signal and some EOG traces had to be rejected from the averages for these saccade sizes. The latency and amplitude raw data for this experiment is given in Appendix 2.1 while the group mean values are given in Tables 6.1 and 6.4. Group mean waveforms are shown in Figures 6.3 and 6.4.

6.2.1 THE SPIKE POTENTIAL ONSET AND PEAK LATENCIES WITH DIFFERENT SACCADE SIZES

The group mean SP onset and peak latencies for the different saccade sizes are given in Table 6.1. When these onset and peak latencies are plotted against saccade size a clear trend can be seen involving the saccade direction and the SP latencies (Figure 6.1). For all saccade sizes, the SP onset and peak appears to occur earlier with adducting saccades than with abducting eye movements.

	Saccade Size				
	20°	10°	7.5°	5°	2.5°
Inner Electrode					
Abd onset	-8.1 (3.6)	-6.1 (3.0)	-5.4 (3.3)	-4.6 (4.2)	-5.9 (6.7)
Abd peak	7.4 (3.5)	6.1 (3.0)	6.6 (2.9)	7.7 (2.7)	3.2 (7.2)
Add onset	-10 (1.9)	-10 (3.2)	-11 (2.1)	-10 (4.1)	-11 (4.5)
Add peak	0.3 (2.3)	0.2 (3.9)	0.2 (3.9)	0.1 (3.9)	-1.8 (4.7)
Lower Electrode					
Abd onset	-9 (4.8)	-7.6 (1.8)	-5.8 (2.7)	-6.4 (2.6)	-9.5 (5.7)
Abd peak	4.7 (5.9)	5.0 (2.6)	5.1 (3.2)	6.1 (3.6)	0.5 (5.6)
Add onset	-11 (4.3)	-11 (3.6)	-9.5 (3.3)	-11 (5.6)	-12 (4.8)
Add peak	0.2 (4.6)	0.2 (4.2)	0.9 (4.0)	-0.5 (5.1)	-0.7 (3.9)

Table 6.1 The group mean and standard deviation (in brackets) SP onset and peak latencies with respect to the saccade start for ten subjects performing five saccade sizes.

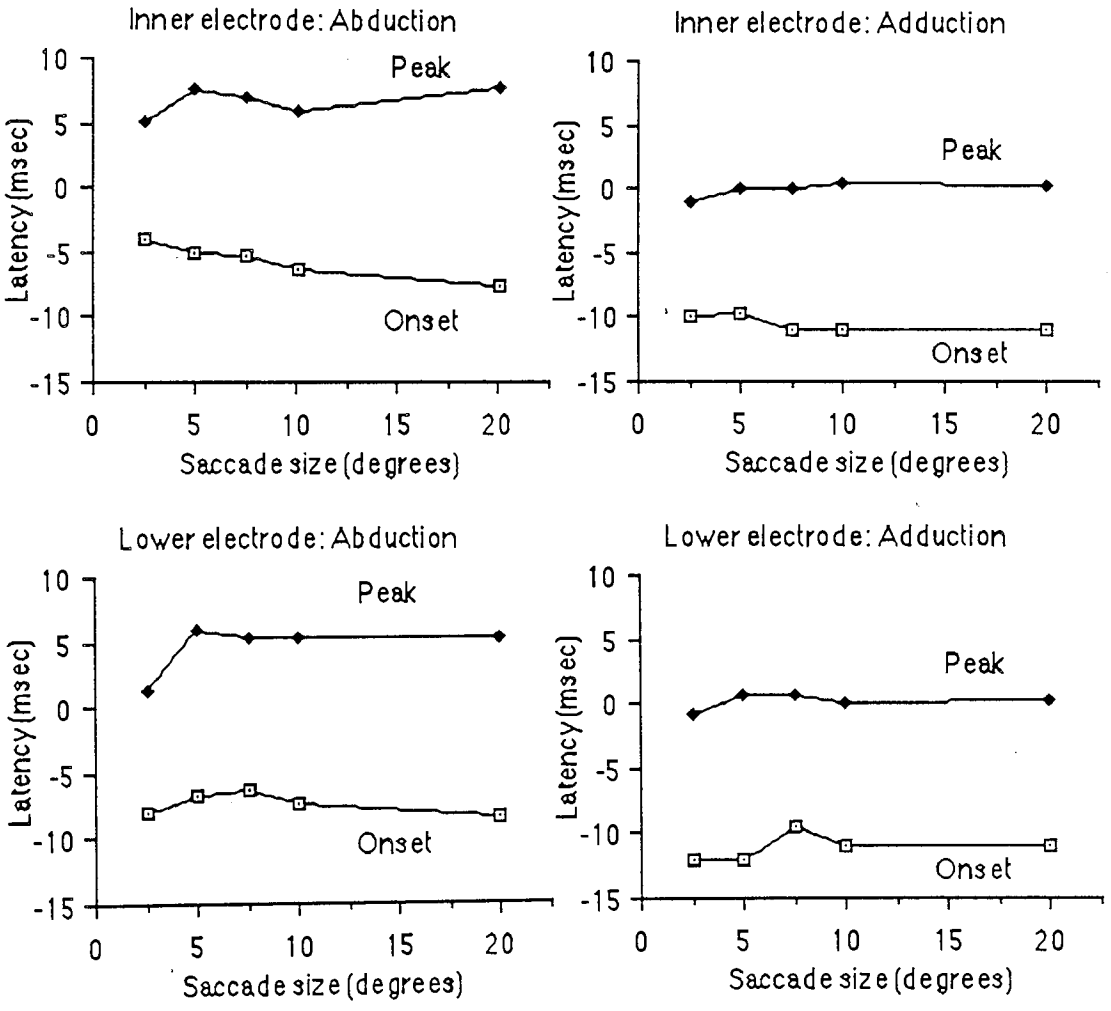

Figure 6.1 The mean SP onset and peak latencies plotted against saccade size for ten subjects. The SP onset and peak occur earlier with adduction than abduction across the range of saccade sizes.

It is known that the SP onset and peak latencies occur sooner with adducting saccades than with abducting saccades for 20° saccades (5.3.1). To determine if this relationship was true for the smaller saccade sizes two-way ANOVA was performed on the latency data for each saccade size with saccade direction (abduction, adduction) as the first treatment and the electrode site the second. Adducting SP onsets were significantly earlier than abducting SP onsets with all except 20° saccades, while the SP peak latencies were significantly earlier with adducting saccades at all except 2.5° saccades (Table 6.2). No significant differences were found between the electrode sites for any saccade size.

Saccade size	Abd vs Add onset	Abd vs Add peak
20°	$F_{1,9}$=2.17; NS	$F_{1,9}$=16.31, p<0.01
10°	$F_{1,9}$=23.16; p<0.001	$F_{1,9}$=20.12, p<0.01
7.5°	$F_{1,9}$=42.88; p<0.001	$F_{1,9}$=19.9, p<0.01
5°	$F_{1,9}$=8.42; p<0.025	$F_{1,9}$=44.74, p<0.001
2.5°	$F_{1,9}$=7.88; p<0.025	$F_{1,9}$ = 4.70, NS

Table 6.2 ANOVA results comparing abducting (Abd) and adducting (Add) SP onset and peak latencies for five saccade sizes.

From Table 6.1 and Figure 6.1, it appears that the SP latencies change little for the different saccade sizes. Table 6.1 shows the variance of the latency data did not remain constant with the different saccade sizes. To determine if there were any statistically significant differences in the latency values with the different saccade sizes therefore required the use of a non-parametric test. A Wilcoxin T test was used to compare the latency values for abducting and adducting saccades at both electrode sites with the SP latency values for each saccade size being compared to the equivalent latency for all the other saccade sizes (i.e. 20° vs 10°; 20° vs 7.5°; 20° vs 5°; 20° vs 2.5°; 10° vs 7.5°;10° vs 5°; 10° vs 2.5°; 7.5° vs 5°, 7.5° vs 2.5°, 5° vs 2.5°).

This analysis revealed that, in the majority of cases, there were no significant differences in the SP onset and peak latency values for the different saccade sizes at the two electrode sites. Table 6.3 shows only the comparisons where the Wilcoxin T-test did reveal a significant difference between the SP latencies when the different saccade sizes were compared.

Saccade sizes	SP Latency	Electrode site	Wilcoxin T test result
10° vs 2.5°	Abduction SP peak	Lower	n=9, T=6.5; p<0.05
7.5° vs 2.5°	Abduction SP peak	Lower	n=8, T=0; p<0.01
5° vs 2.5°	Abduction SP peak	Lower	n=9, T=0; p<0.01
10° vs 2.5°	Adduction SP peak	Inner	n=8, T=0; p<0.01
7.5° vs 2.5°	Adduction SP peak	Inner	n=8, T=3; p<0.05
5° vs 2.5°	Adduction SP peak	Inner	n=6, T=0; p<0.01
10° vs 7.5°	Adduction SP onset	Lower	n=10, T=7; p<0.05
20° vs 2.5°	Adduction SP peak	Lower	n=8, T=3; p<0.05
10° vs 2.5°	Adduction SP peak	Lower	n=9, T=4.5; p<0.05
7.5° vs 2.5°	Adduction SP peak	Lower	n=8, T=0; p<0.01

Table 6.3 Statistically significant results for the Wilcoxin T test comparing the SP onset and peak latencies for abducting and adducting saccades of different sizes at two electrode sites.

6.2.2 THE SPIKE POTENTIAL ONSET-PEAK AMPLITUDE WITH DIFFERENT SACCADE SIZES

The group mean SP onset-peak amplitudes are given in Table 6.4. Plotting the onset-peak amplitudes against saccade size revealed an apparent relationship between the two parameters with the SP amplitude increasing with saccade size up to saccades of 10° at both electrodes with abduction and adduction (Figure 6.2). There was little apparent change in the amplitude with the larger saccades of 20° except at the lower electrode with adduction.

	Saccade Size				
	20°	10°	7.5°	5°	2.5°
Inner Electrode					
Abduction	36.4 (9.8)	36.0 (9.2)	34.5 (11.9)	23.2 (9.1)	12.6 (7.1)
Adduction	34.9 (13.4)	33.5 (14.7)	30.2 (15.5)	28.3 (11.6)	17.0 (8.5)
Lower Electrode					
Abduction	32.4 (9.8)	33.9 (9.6)	28.3 (11.2)	19.1 (7.0)	14.8 (7.6)
Adduction	44.0 (17.8)	35.2 (16.4)	32.7 (13.4)	23.4 (13.9)	19.0 (9.0)

Table 6.4 The group mean and standard deviation (in brackets) SP onset-peak amplitudes for ten subjects performing five saccade sizes.

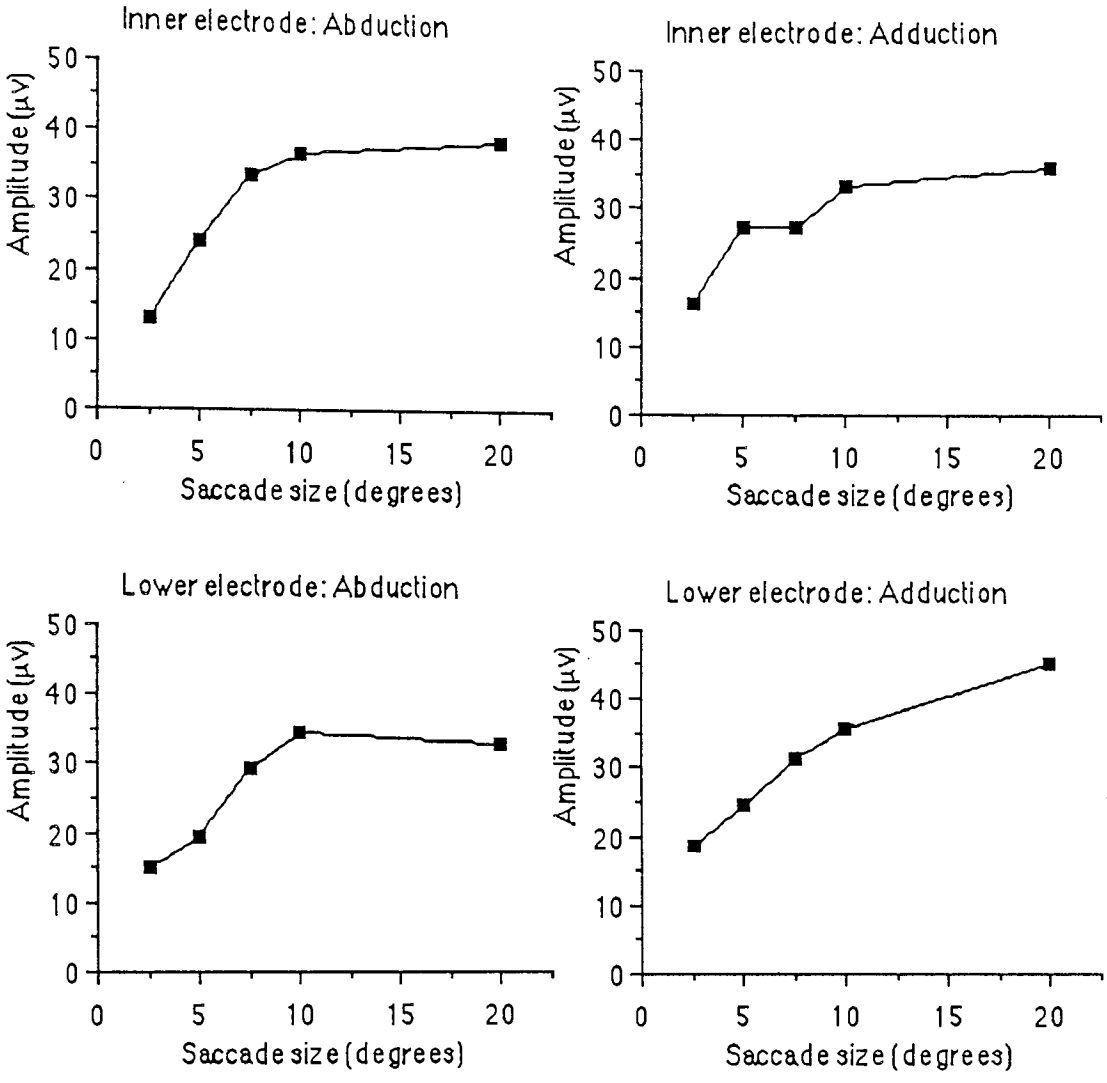

Figure 6.2 The onset-peak amplitude of the SP plotted against saccade saccade size. The SP amplitude increases with saccade size up to 10° but there is little change from 10° to 20° except at the lower electrode with adduction.

To investigate the amplitude changes with saccade size statistically required the use of a non-parametric test since the variance of the data changed with saccade size (see Table 6.4). A Wilcoxin T-test was therefore used to compare the amplitude data for the different saccade magnitudes at both electrode sites with abduction and adduction saccades. The amplitude values were compared as the latency values had been (see 6.2.1) and Table 6.5 shows the comparisons where the Wilcoxin T-test did reveal a significant difference between the spike potential onset-peak amplitudes when the different saccade sizes were compared.

Saccade sizes	SP Direction	Electrode site	Wilcoxin T test result
20° vs 5°	Abduction	Inner	n=10, T=0.0; p<0.01
20° vs 2.5°	Abduction	Inner	n=10, T=0.0; p<0.01
10° vs 5°	Abduction	Inner	n=10, T=1.0; p<0.01
10° vs 2.5°	Abduction	Inner	n=10, T=0.0; p<0.01
7.5° vs 5°	Abduction	Inner	n=10, T=5.0; p<0.05
7.5° vs 2.5°	Abduction	Inner	n=10, T=0.0; p<0.01
5° vs 2.5°	Abduction	Inner	n=10, T=0.0; p<0.01
20° vs 5°	Abduction	Lower	n=10, T=0.0; p<0.01
20° vs 2.5°	Abduction	Lower	n=10, T=0.0; p<0.01
10° vs 5°	Abduction	Lower	n=10, T=1.0; p<0.01
10° vs 2.5°	Abduction	Lower	n=10, T=0.0; p<0.01
7.5° vs 5°	Abduction	Lower	n=10, T=9.0; p<0.05
7.5° vs 2.5°	Abduction	Lower	n=10, T=2.0; p<0.01
20° vs 2.5°	Adduction	Inner	n=10, T=0.0; p<0.01
10° vs 2.5°	Adduction	Inner	n=10, T=0.0; p<0.01
7.5° vs 2.5°	Adduction	Inner	n=10, T=4.0; p<0.01
5° vs 2.5°	Adduction	Inner	n=10, T=4.0; p<0.01
20° vs 7.5°	Adduction	Lower	n=10, T=6.0; p<0.05
20° vs 5°	Adduction	Lower	n=10, T=0.0; p<0.01
20° vs 2.5°	Adduction	Lower	n=10, T=0.0; p<0.01
10° vs 5°	Adduction	Lower	n=10, T=0.0; p<0.01
10° vs 2.5°	Adduction	Lower	n=10, T=0.0; p<0.01
7.5° vs 5°	Adduction	Lower	n=10, T=10.0; p<0.05
7.5° vs 2.5°	Adduction	Lower	n=10, T=0.0; p<0.01
7.5° vs 2.5°	Adduction	Lower	n=10, T=0.0; p<0.01

Table 6.5 Statistically significant results for the Wilcoxin T test comparing the SP onset-peak amplitudes for abducting and adducting saccades of different sizes at two electrode sites.

Table 6.5 shows that there were no significant differences between the 20° and 10° spike potentials with any electrode site or saccade direction, and only the lower electrode with adducting eye movements shows a significant difference between the 20° and 7.5° spike potentials. Comparing the smaller saccade sizes, however, reveals a significant difference for most comparisons indicating a more rapid reduction in SP amplitude with the smaller saccades.

The reduction in SP amplitude with saccade size is evident in the group mean waveforms (Figures 6.3 and 6.4). The SP waveform is constant throughout the recordings with reducing saccade size and the change is simply one of amplitude reduction.

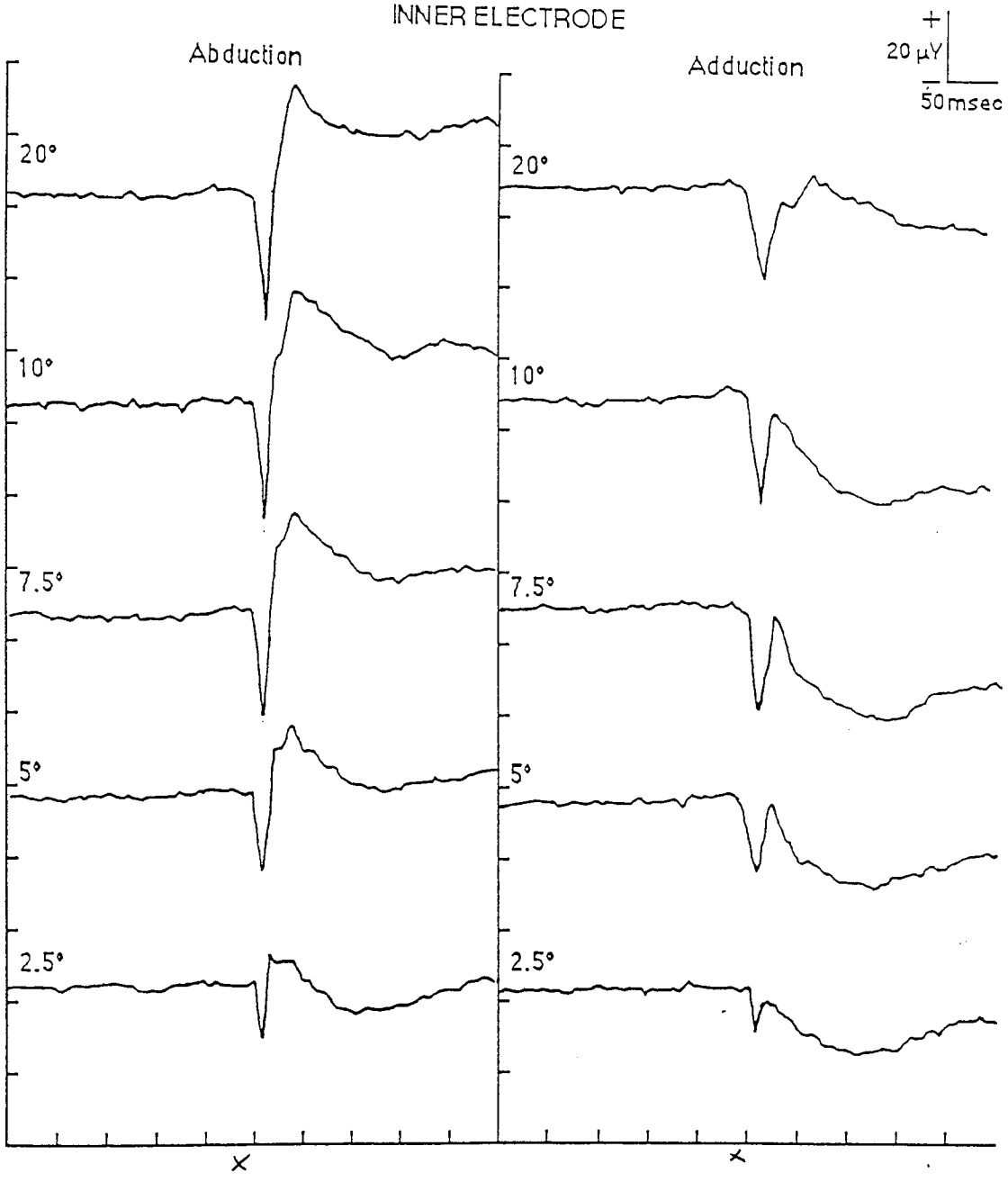

Figure 6.3 The group mean SPs of ten subjects recorded from an electrode at the inner canthus during adduction and abduction for progressively smaller saccades. The onset and peak latencies are relatively unaltered for the different saccade sizes but the amplitude clearly reduces with decreasing saccade size. The saccade onset is indicated by the cross.

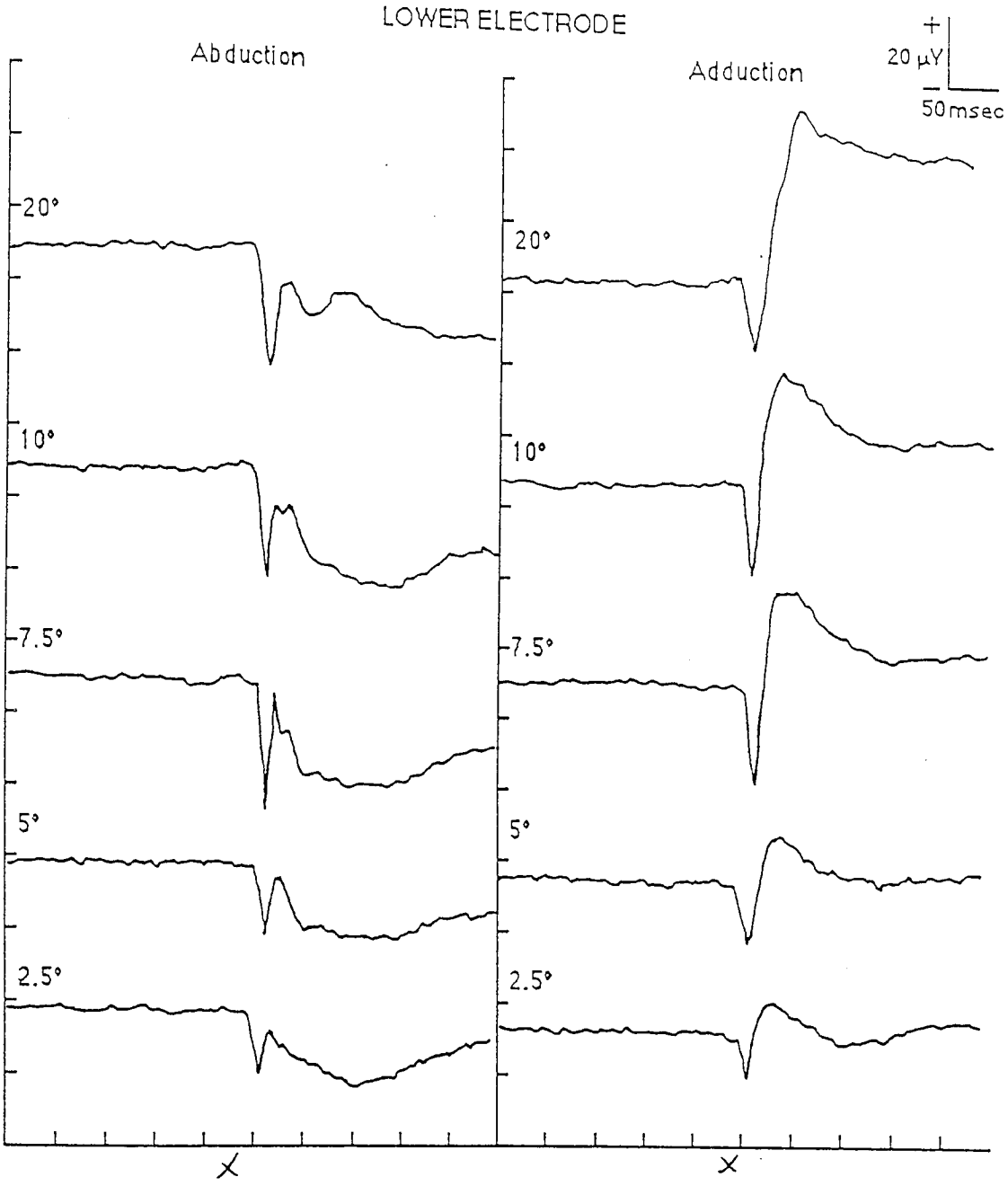

Figure 6.4 The group mean SPs of ten subjects recorded from an electrode the below the eye during adduction and abduction for progressively smaller saccades. The onset and peak latencies are relatively unaltered for the different saccade sizes but the amplitude clearly reduces with decreasing saccade size. The saccade onset is indicated by the cross.

6.3 DISCUSSION AND CONCLUSIONS

This study has examined the SP recorded with five different saccade sizes. The mean SP onset and peak latencies given in Table 6.1 and the graphs in Figure 6.2 suggest that the SP latencies do not differ greatly over the range of saccades studied. When the results

were analysed statistically no significant differences were found when the large saccade SP latencies were compared to the smaller eye movements except at the lower electrode with the adduction peak latency. When the smaller saccades were directly compared, however, some significant differences were found (Table 6.3). It has been noted that increased noise levels with the smaller saccades necessitated the removal of some recording epochs from the average for the small saccades (6.2). It is conceivable that the apparent variation in SP latencies with smaller saccades may simply be due to less accurate averaging of the potential in the presence of higher noise levels.

Further examination of the latency data reveals that the onset and peak latencies were earlier with adducting saccades than abducting eye movements for all recordings. The statistical analysis of the results, however, shows that this is not always a significant finding over the range of saccades. Although examination of the latency values has revealed some changes with saccade size, these do not follow any specific pattern and must, therefore, be considered with some caution.

The parameter that does vary consistently with saccade size is the SP onset-peak amplitude. The amplitude increases with ascending saccade size from 2.5° to 10° with little change beyond this. The limited variation in the SP amplitude for saccades greater than 10° is confirmed by the Wilcoxin T-test which shows no significant differences in SP amplitudes between 20° and 10° saccades, or even 20° and 7.5° except with the lower electrode with adducting saccades. The greatest rate of change in the SP amplitude is seen with the smaller saccade sizes. The results from the inner electrode show the most consistent relationship between saccade size and SP amplitude, the lower electrode site showing a greater variation in the SP amplitude with increasing saccade sizes.

The results of this study are similar to those of Riemslag *et al.* (1988), who recorded the SP for saccade sizes up to 40°. They reported an increase in the SP onset-peak amplitude for saccades up to approximately 10° with little change in amplitude beyond that. Riemslag *et al.* (1988) used one electrode and only abducting saccades were recorded. The

amplitude values in this study are, however, larger than the amplitudes found by Riemslag *et al.* (1988). The mean maximum amplitude reported by Riemslag *et al.* (1988) was approximately 20 μV, compared to over 45 μV in the present study.

A possible explanation for the difference between the present work and that of Riemslag *et al.* (1988) can be found in the choice of electrode locations used in the two experiments. Riemslag *et al.* (1988) used an electrode 3 cm up and 7 cm behind the auditory canal as the reference site compared to P_z in the present recordings. P_z was chosen as the reference site after the work of Thickbroom and Mastaglia (1985b, 1986), who reported the maximum SP amplitude to be recorded with this reference, and our initial recordings described in 4.2.3. These recordings found the maximum SP amplitude was recorded with the reference at P_z, while smaller amplitude values were recorded with the reference at P_3 and P_4. It is possible that the differences in SP amplitudes between this study and that of Riemslag *et al.* (1988) may simply be due to the choice of reference site.

The finding of an increase in the SP amplitude with saccade size up to approximately 10° can be used to suggest a possible origin of this potential. If the results of this study are compared to the known activity in the EOM that precedes saccades a tentative relationship can be seen between the two sets of activity. The work of Sindermann *et al.* (1978) has been discussed in 3.2.1. Using electromyography to record the activity of ocular motoneurons from single motor units in the MR and LR muscles during saccades, Sindermann *et al.* (1978) reported the first discharge of the motor units preceded the saccade by a few milliseconds. The initial latency of the onset of firing was constant for all saccade sizes. The first phase of the firing pattern of the motor units consisted of a burst of rapid discharges, the peak frequency of which occurred at the the onset saccade. Sindermann *et al.* (1978) reported that this peak frequency was found to increase with increasing saccade size up to about 15° with a saturation in the discharge rate after this.

It can be hypothesised from these recordings that the origin of the SP may lie in the motor units of the EOM; the SP latency reflecting the onset of the motor unit activity preceding

the saccade, while the amplitude may reflect the amplitude of this motor unit activity at the onset of the burst. The rapid decline in the SP after the onset of the saccade for all saccade sizes has been hypothesised as being due to a progressive desynchronisation of the motor unit discharge following the initial recruitment burst, or to a state of relative refractoriness and reduced excitability of the muscle fibres during a tetanic contraction of the EOM (Thickbroom and Mastaglia 1985).

6.4 THE SPIKE POTENTIAL RECORDED WITH LARGE HORIZONTAL EYE MOVEMENTS

6.4.1 INTRODUCTION

The SP has been shown to exhibit an increase in the onset-peak amplitude as the magnitude of the saccade increases up to approximately 10°. This finding agrees with earlier work which has examined the SP parameters over a range of saccade sizes (Thickbroom and Mastaglia 1985, Riemslag *et al.* 1988). Both these studies examined the SP for saccades not only up to 20° in size, but also for eye movements as large as 40°. Thickbroom and Mastaglia (1985b) and Riemslag *et al.* (1988) found the SP amplitude did not appear to increase with saccades greater than 10°, although there are limitations in both studies which must be considered.

In their study, Thickbroom and Mastaglia (1985b) recorded the SP from electrodes placed all around the scalp with a sternoclavicular reference but no details are given as to which electrodes were used when different sized saccades were being recorded. Furthermore, no actual values are given for the amplitudes measured for the saccade sizes, nor are any statistical analysis of the results described.

Riemslag *et al.* (1988) have recorded the SP for saccades of up to 40°, but only from one electrode (outer canthus) with an electrode over the contralateral posterior parietal cortex as a reference. Five subjects were used in this study and the SPs with abducting

saccades only were examined. Riemslag *et al.* (1988) found the SP amplitude did not appear to increase for the larger 40° saccades. When the results of this study are considered, however, it must be remembered that Riemslag *et al.* (1988) attempted to remove the EOG artefact from the SP waveform and it is conceivable that this may have influenced the final amplitude values. Riemslag *et al.* (1988) felt that if the SP were related to muscle unit activity then the SP amplitude should increase for saccades of all sizes because of the relationship between saccade peak velocity and saccade size.

The limited information that could be gained from these these two studies suggested that they should be repeated using the recording technique developed in this thesis which is known to provide consistent and reliable results. Such recordings would provide a more detailed analysis of the effect that large saccades may have on the parameters of the spike potential and perhaps help determine the possible origin of the potential.

6.4.2 METHODS

The spike potential was recorded from electrodes at the inner canthus and below the eye of ten normal subjects aged 22-30 years (mean 25.8±2.3). The eye to be examined was chosen on a random basis to give five left and five right eyes. P_z was used as the reference electrode site and the electrode sites were prepared in the usual manner (see Chapter 4). Recordings took place in a single recording session lasting approximately $1^1/_4$ hours and saccades of 5°, 10°, 20° and 40° were recorded. For the 40° saccades the subjects were seated 50 cm from the LEDs and the 20° targets used. Saccades of 40° are not usually performed during normal viewing; a refixation of this size generally being accompanied by a head movement in the respective direction and the importance of ensuring no head movements was emphasised to all subjects.

Forty saccades and SPs were recorded for each eye movement size (20 abducting, 20 adducting) and the saccade onset identified from the EOG trace as usual. Following the recordings the waveforms were averaged as before and the onset and peak latencies and

onset-peak amplitude measured as usual. Group average waveforms and latency and amplitude values were calculated for each saccade size.

6.4.3 RESULTS

In all subjects a clear SP was recorded from both electrode sites for all saccade sizes. Tables 6.6 and 6.7 show the mean SP latency and amplitude values for these saccade sizes, while Figure 6.7 shows the group averaged SP waveforms recorded from the ten subjects. The latency and amplitude raw data are given in Appendices 2.2.

	Saccade Size			
	40°	20°	10°	5°
Inner Electrode				
Abd onset	-5.1 (3.8)	-8.3 (3.1)	-5.3 (2.2)	-4.7 (4.2)
Abd peak	8.0 (4.6)	8.0 (2.4)	7.3 (2.9)	8.3 (2.7)
Add onset	-9.9 (2.8)	-10 (1.6)	-10 (3.5)	-9.6 (4.0)
Add peak	0.3 (3.4)	0.4 (2.1)	0.4 (3.7)	0.0 (3.9)
Lower Electrode				
Abd onset	-5.3 (4.2)	-8.3 (5.3)	-7.2 (1.4)	-6.8 (2.5)
Abd peak	7.6 (3.1)	6.8 (6.9)	5.5 (3.2)	5.6 (2.9)
Add onset	-9.9 (3.2)	-9.7 (4.4)	-11 (3.5)	-12 (6.0)
Add peak	0.2 (3.7)	1.4 (5.1)	1.1 (3.8)	-1.9 (5.8)

Table 6.6 The group mean and standard deviation (in brackets) SP onset and peak latencies with respect to the saccade start for ten subjects performing four saccade sizes.

	Saccade Size			
	40°	20°	10°	5°
Inner Electrode				
Abduction	56.9 (20.0)	37.1 (9.4)	37.5 (7.9)	25.5 (8.3)
Adduction	57.7 (15.3)	40.6 (14.4)	38.0 (13.0)	28.7 (10.2)
Lower Electrode				
Abduction	47.0 (16.1)	31.5 (7.6)	31.8 (8.3)	19.3 (5.2)
Adduction	59.2 (15.4)	48.3 (14.3)	37.8 (14.7)	24.6 (13.5)

Table 6.7 The group mean and standard deviation (in brackets) SP onset-peak amplitudes for ten subjects performing five saccade sizes.

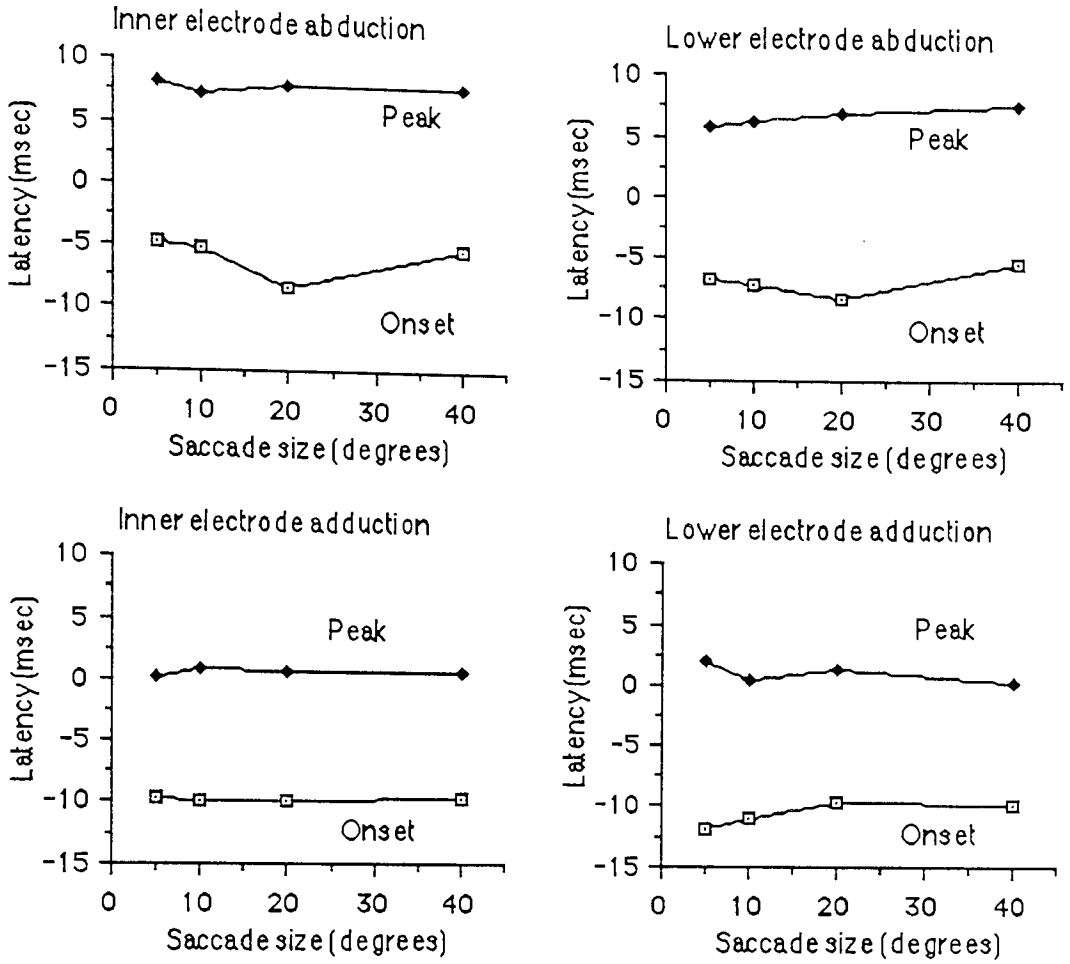

Figure 6.5 The mean spike potential onset and peak latencies for ten subjects performing abducting and adducting saccades of four different sizes. The results for the SP recorded from two electrode sites are shown.

The relationship between saccade direction and SP onset and peak latencies has been examined for horizontal saccades up to 20° showing a trend for adducting SP latencies to occur earlier (6.3.1). This trend continues for saccades up to 40° (Table 6.5, Figure 6.5) and to examine the latency values statistically two-way ANOVA was performed on the raw data in the same manner as used previously. The ANOVA results are given in Table 6.8.

Saccade size	Abd vs Add onset	Abd vs Add peak
40°	$F_{1,9}$=8.46; p<0.025	$F_{1,9}$=23.24, p<0.01
20°	$F_{1,9}$=1.69; NS	$F_{1,9}$=13.13, p<0.01
10°	$F_{1,9}$=24.46; p<0.001	$F_{1,9}$=27.67, p<0.01
5°	$F_{1,9}$=6.94; NS	$F_{1,9}$=44.77, p<0.001

Table 6.8 ANOVA results comparing abducting (Abd) and adducting (Add) SP onset and peak latencies for four saccade sizes.

The SP onset and peak latencies for the different saccade sizes were compared with a Wilcoxin T-test as before. Only two statistically significant differences were found, both at the inner canthus; when the SP onset for 20° abducting saccades was compared to that of 10° abducting saccades (n=9, T=1; $p<0.01$) and when the SP onset for 20° abducting saccades was compared to that of 5° abducting saccades (n=9, T=7; $p<0.05$).

The group mean SP onset-peak amplitudes for these recordings are given in Table 6.7. Plotting the onset-peak amplitudes against saccade size revealed the expected increase in SP amplitude between 5° and 10° with little change between 10° and 20°. With the 40° saccades, however, the SP amplitude increased again (Figure 6.6).

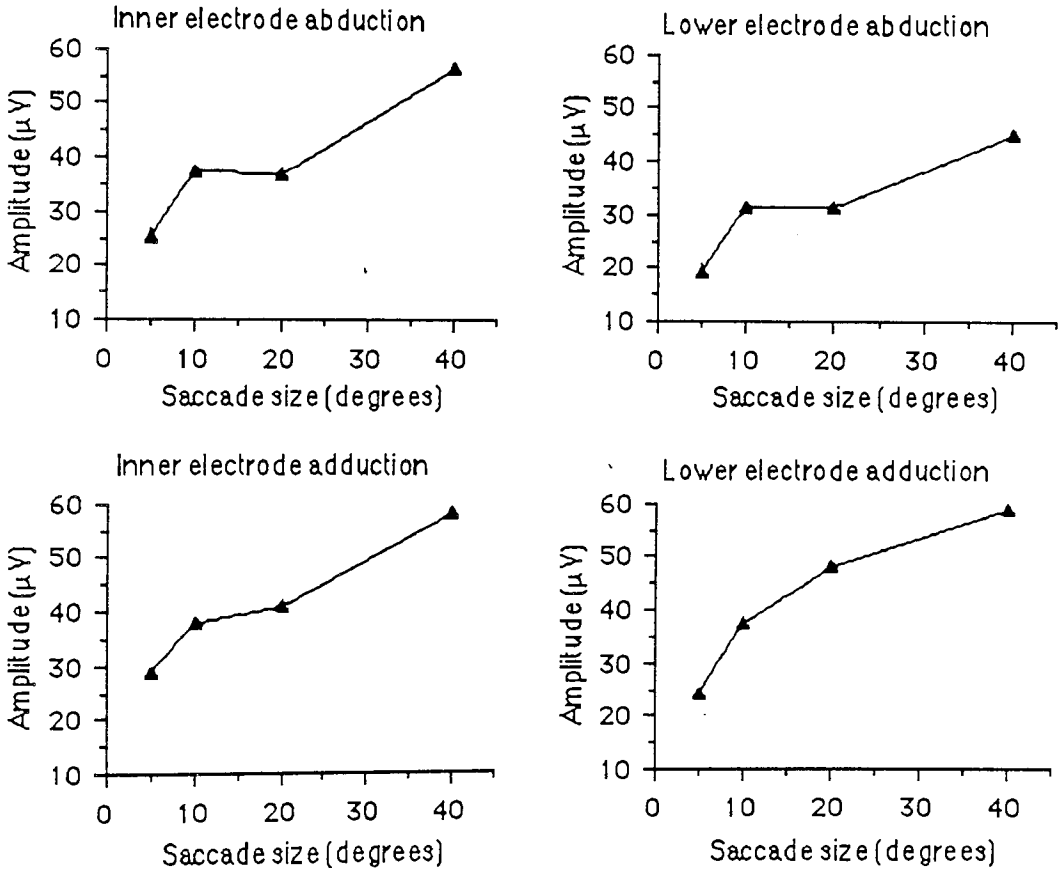

Figure 6.6 The SP onset-peak amplitude for ten subjects performing saccades of between 5° and 40° in magnitude. The results for abducting and adducting saccades recorded from two electrode sites are shown.

A Wilcoxin T-test was used to compare the amplitude data for the four saccade sizes as before and Table 6.9 shows where the Wilcoxin T-test revealed a significant difference between the amplitudes when the different saccade sizes were compared.

Saccade sizes	SP Direction	Electrode site	Wilcoxin T test result
40° vs 20°	Abduction	Inner	n=10, T=1.0; p<0.01
40° vs 10°	Abduction	Inner	n=10, T=2.0; p<0.01
40° vs 5°	Abduction	Inner	n=9, T=0.0; p<0.01
10° vs 2.5°	Abduction	Inner	n=10, T=0.0; p<0.01
20° vs 5°	Abduction	Inner	n=10, T=3.0; p<0.05
10° vs 5°	Abduction	Inner	n=10, T=1.0; p<0.01
40° vs 20°	Abduction	Lower	n=10, T=6.0; p<0.05
40° vs 10°	Abduction	Lower	n=10, T=6.0; p<0.05
40° vs 5°	Abduction	Lower	n=10, T=0.0; p<0.01
20° vs 5°	Abduction	Lower	n=10, T=0.0; p<0.01
10° vs 5°	Abduction	Lower	n=10, T=1.0; p<0.01
40° vs 20°	Adduction	Inner	n=10, T=2.0; p<0.01
40° vs 10°	Adduction	Inner	n=10, T=1.0; p<0.01
40° vs 5°	Adduction	Inner	n=10, T=0.0; p<0.01
20° vs 5°	Adduction	Inner	n=10, T=7.5; p<0.05
40° vs 20°	Adduction	Lower	n=10, T=5.0; p<0.05
40° vs 10°	Adduction	Lower	n=10, T=1.0; p<0.01
40° vs 5°	Adduction	Lower	n=10, T=1.0; p<0.01
20° vs 10°	Adduction	Lower	n=10, T=5.0; p<0.05
20° vs 5°	Adduction	Lower	n=10, T=0.0; p<0.01
10° vs 5°	Adduction	Lower	n=10, T=0.0; p<0.01
10° vs 2.5°	Adduction	Lower	n=10, T=0.0; p<0.01

Table 6.9 Statistically significant results for the Wilcoxin T test comparing the SP onset-peak amplitudes for abducting and adducting saccades of different sizes at two electrode sites.

Examining Table 6.9 shows a significant difference between the 40° and 20° saccades with both electrode sites and saccade directions. There was no significant difference between the 20° and 10° saccades except at the lower electrode with adduction. Comparing the 20° and 10° saccades to the 5° eye movements reveals a significant difference for most comparisons indicating a reduction in SP amplitude with the smaller saccades as before. The reduction in SP amplitude with these saccade size is evident in the group mean waveforms (Figures 6.7). The SP waveform is constant throughout the recordings with reducing saccade size and the change is simply one of amplitude reduction.

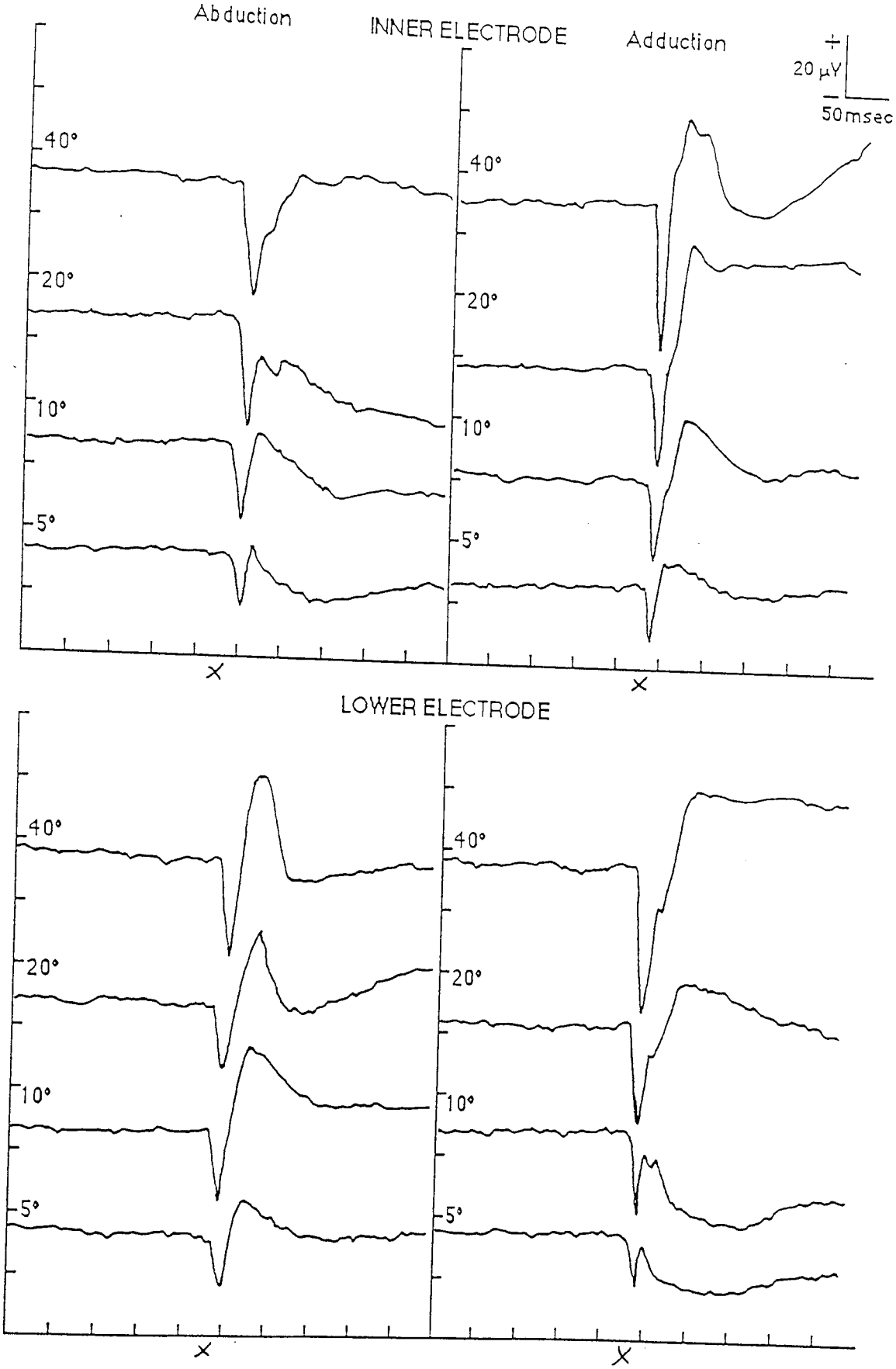

Figure 6.7 The group mean SP waveform recorded from ten subjects for saccades of 40°, 20°, 10° and 5° with an electrode at the inner canthus and below the eye referred to P_Z. The SP waveform remains constant for all saccade sizes except for an increase in amplitude with larger saccades. The saccade onset is indicated by the cross.

The statistical analysis of the results shows that the SP onset-peak amplitude was significantly larger with 40° saccades than the smaller saccade sizes (20°, 10° and 5°) in both saccade directions. With the smaller saccades there was no significant difference between 20° saccades and 10° eye movements but the 5° saccades were significantly smaller than the 20° eye movements. This confirms the results discussed in the previous section.

6.4.4 DISCUSSION

Recording the SP with large eye movements has demonstrated that the SP onset and peak latencies show little variation with large saccade sizes and the usual pattern of adducting saccades having earlier onset and peaks than abducting saccades was repeated with these larger eye movements. From the graphs in Figures 6.4 and 6.5, and the waveforms in Figure 6.7, it can also be seen that the duration of the SP onset to peak remains constant with increasing saccade size.

The SP onset-peak amplitude, on the other hand, does vary with changing eye movement size. The increase in SP amplitude for saccades up to 10°-20° confirms the amplitude values found in the previous experiment (6.2.2). The continued increase in the onset-peak amplitude for saccades greater than this is, however, a new finding. The graphs in Figure 6.6 show that the SP amplitude increased dramatically at all electrode sites for saccades between 5° and 10° then, at all except the lower electrode with adduction, the amplitude values tended to level off between 10° and 20°.

This is a similar pattern of activity to that shown in the preceding experiment for saccades smaller than and up to 20° in magnitude. With the larger saccades of 40°, however, the amplitude was seen to again increase. This contradicts the earlier work of Thickbroom and Mastaglia (1985b) and Riemslag *et al.* (1988) who found no difference in the SP amplitude for saccades larger than 10°. The difference in the results of these experiments needs to be explained.

Thickbroom and Mastaglia (1985b), in their initial experiment which examined different saccade sizes, used a different recording montage to that in the study presented above. Thickbroom and Mastaglia (1985b) were primarily examining the distribution of the potential across the scalp and used 30 electrodes on the head and a sternoclavicular reference to record the EEG activity. The amplitude values found at the different electrode sites ranged from between -22 μV to +15 μV depending upon the electrode site under study, with no change for saccades between 10° and 40°. In a later study Thickbroom and Mastaglia (1986), however, using electrodes round the eyes referred to P_z, recorded onset-peak amplitudes as large as 64.4 μV for 5° saccades. This amplitude value is greater than that recorded by Riemslag *et al.* (1988) for all their saccade sizes and is also greater than the mean values found in this experiment for saccades of 40°. The amplitude values found by Thickbroom and Mastaglia (1986) in their second study do not agree with the values they gave in their initial report of the SP (Thickbroom and Mastaglia, 1985b), where maximum amplitudes of 22 μV recorded from an electrode at T_2 referred to a sternoclavicular reference were reported.

An explanation for this may be found when the averaging technique used by Thickbroom and Mastaglia (1986) is examined. In this paper, rather than using the saccade onset as the averaging trigger, these authors used the spike potential peak as the trigger. While the choice of the SP peak as the point around which the potential is averaged does not allow information to be gained regarding the latency of the SP with respect to the saccade onset, it will tend to enhance the amplitude of the potential. This may account for the large difference in the SP amplitude found by Thickbroom and Mastaglia (1986) in their second experiment compared to both their earlier paper (Thickbroom and Mastaglia, 1985b) and the work of Riemslag *et al.* (1988) who found smaller amplitude values. This is also true of the present study where the saccade onset was used as the trigger for averaging and smaller SP amplitudes were recorded for larger saccades.

While the differences in amplitude between the present work and that of Thickbroom and Mastaglia (1985b, 1986) can be explained on the basis of the averaging trigger, this does

not account for the discrepancy between the present work and that of Riemslag *et al.* (1988). These authors recorded the SP for saccades up to 40° in size yet found no increase in amplitude for saccades greater than approximately 10°. Like the present study, Riemslag *et al.* (1988) used the onset of the saccade as the averaging trigger, although they did use infra-red reflectometry to monitor the saccade movement. The maximum amplitude found by these workers can be estimated to be approximately 20 μV from the graphs given in their paper, compared to a maximum of 59.2 μV for 40° saccades in the present experiment. This difference in amplitude values needs to be explained.

The experimental procedure and electrode locations used by Riemslag *et al.* (1988) have been described earlier (6.3). These authors used one electrode to record the SP with abducting saccades only and an electrode 3 cm up and 7 cm behind the auditory canal as the reference. The possible effect that the reference site may have on the recorded amplitudes has also been described previously (6.3.3).

The other major difference in the experimental procedure of Riemslag *et al.* (1988) and the present study is the attempt by Riemslag *et al.* (1988) to remove the artefact caused by the eye movement on the latter half of the SP trace. Riemslag *et al.* (1988) considered that the corneo-retinal potential introduces a substantial artefact to the SP recording and, while they acknowledge the SP should not be influenced by EOG activity as the SP occurs before the saccade, they did attempt to remove this artefact. The technique they used utilised the infra-red recording of the eye movement to identify the saccade activity which was then removed from the SP trace by estimating the proportion of the SP waveform due to the original signal and that due to the EOG activity.

The procedure used by Riemslag *et al.* (1988) does make some basic assumptions about the EOG activity. It is assumed that the EOG activity remains constant during the saccade and that this activity increases linearly with the size of the saccade. While the EOG activity may remain constant for the relatively short time over which the SP activity is being recorded, the second consideration is, however, not true. The EOG has been shown to

have an upper limit of linearity with saccades no greater than 30° (Shackel 1960). Riemslag *et al.* (1988) also assumed that the EOG activity recorded with a reference at the back of the head can be estimated from knowledge only of the eye movement and that the effect of volume conduction of the EOG activity in the head and orbit was constant for all saccade sizes. The lack of certainty about the EOG parameters casts some doubt on the accuracy of using infra-red recording of the eye movement to indicate the extent of EOG activity in the SP recording. The uncertainty regarding the accuracy of the artefact removal technique suggests that it may not be appropriate to perform such techniques on the SP waveform.

Although the SP peak often occurs before the saccade start, in many cases the two events are simultaneous, or the peak may occur after the saccade start. In these situations, removal of the EOG artefact will affect the waveform after the start of the saccade and may therefore possibly reduce the amplitude of the potential. Riemslag *et al.* (1988) assumed that the infra-red recording of the eye movement activity gave a good indication of the expected EOG waveform for that eye movement. It is probable, however, that the infra-red eye movement actually activity becomes less closely linked to EOG activity with larger saccades due to the non-linearity of the EOG with eye movement size. This suggests that the estimated effect of EOG activity on the spike potential waveform may be considerably different from the actual effect that it has. If this is the case, the amplitude values reported by Riemslag *et al.* (1988) may have been artificially reduced by the attempt to remove the eye movement activity from the SP waveform. Some caution must be shown, therefore, when comparing the results of Riemslag *et al.* (1988) to the present work.

The continued increase in the SP amplitude for saccades of 40° found in this experiment stills has to be accounted for. Both Thickbroom and Mastaglia (1985b) and Riemslag *et al.* (1988) reported no increase in the SP amplitude for saccades greater than 20°. Riemslag *et al.* (1988) did expect to find increased amplitudes for these saccade sizes if the SP is related to muscle activity. This assumption was based upon the known velocity patterns of

saccades which show increasing velocity with increasing saccade size. Riemslag *et al.* (1988) hypothesised that the SP activity would increase in line with increasing muscle activity for the larger movements.

The previous experiment suggested that the SP may be related to activity in the extraocular motoneurons which shows a saturation in activity for saccades larger than 10-15° (6.3.3). This, clearly, is not true of the presaccadic spike potential which shows increasing activity with larger saccades than the saturation level of the motoneurons. Thickbroom and Mastaglia (1985b, 1986) have suggested that the SP may be representative of motor unit activity in the six extraocular muscle. The motor unit action potentials and the resultant motor unit action potential trains of skeletal muscles during sustained contractions are described in Chapter 3 (3.2.1). Thickbroom and Mastaglia (1987) have produced a computer model of the motor unit activity in the EOM to help explain the generation of the SP in these muscles (see 3.2.2). In this model different factors of the motor unit activity could be altered and the resultant effect on the SP waveform determined. In the model the waveform of motor unit action potentials were assumed to be bi-phasic with an initial negative phase followed by a positive phase. The amplitude of the SP was seen to alter under two conditions. If the second and subsequent action potentials in a train of action potentials were increased from 0% to 100% of the initial action potential amplitude, the onset-peak SP amplitude increased by 20%, with no change in SP duration. Alternatively, if the duration of the second positive component of the action potential was increased from 1 msec to 4 msec, the SP amplitude increased by 120%, with a slight increase in duration.

While the exact details of motor unit activity in the EOM is unknown, the computer model does give a possible explanation for the increase in SP amplitude with saccade size. It can be hypothesised that during larger saccades the motor unit activity may change in either one, or perhaps a combination, of the two ways suggested above. The amplitude values for 40° saccades recorded in the present experiments, while considerably larger than those for 5° saccades, are not 120% larger than the amplitude for the smaller saccades,

nor does the duration of the potential alter for the different saccades sizes. The first suggestion of increasing amplitude of the second and subsequent action potentials appears to be a more suitable alternative, as the duration remains constant and the amplitude change is of a similar magnitude to that found in this thesis. Unfortunately details of motor unit activity in the EOM are not available to determine which, if either, of these two changes may occur with larger saccades.

6.5 SUMMARY

This Chapter has described the experimental work performed to examine the effect of increasing saccade size on the presaccadic spike potential parameters and waveform. Earlier studies have demonstrated that the SP amplitude does alter with saccade size, increasing with increasing saccade amplitude up to saccades of about 10-15°. The duration and latency of the potential were unaffected by the increased size of the eye movement (see 3.2.2).

In Chapter 5, a relationship was described between the onset and peak latencies of the SP and the eye movement direction, with adducting saccades having earlier SP onset and peak latencies than abducting eye movements. This latency difference has been shown to continue for all sizes of saccades studied in this Chapter, although the difference is not always statistically significant. While this difference in SP onset and peak values is generally recorded, it is unlikely that the absence of a statistical difference can be considered to be representative of an abnormal SP recording.

The results of the experiments with different saccade sizes up to 40° have confirmed the previous finding of an increase in SP onset-peak amplitude for eye movements up to 10°, but they also indicate that the amplitude continues to increase for eye movements larger than this. The increase in amplitude for saccades of 40° is a previously unreported finding and an attempt has been made to explain this on the basis of possible changes in motor unit activity of the EOM with larger saccades. The activity of the EOM motor units have

been modelled on a computer and altering the parameters of the motor unit activity can affect the amplitude of the SP (Thickbroom and Mastaglia, 1987).

The information gained from this Chapter does not, unfortunately, allow a more definite location of the origin of the SP, but it does indicate that the potential is closely linked to the magnitude of the eye movement being performed. The possibility that the SP may originate from the activity of the motor units of the EOM is confirmed by the computer model of this activity and while this cannot be stated with absolute certainty to be the origin of the SP, it is likely that the potential is related to this muscle activity.

CHAPTER 7

THE EFFECT OF AGE ON THE PRESACCADIC SPIKE POTENTIAL

7.1 INTRODUCTION

Until now the experimental work in this thesis has used young subjects and the results compare favourably with previously published SP recordings. Some caution must be shown, however, when making such comparisons as the subject ages used in previous studies differ from the present work. In their initial study, for example, Thickbroom and Mastaglia (1985b) recorded the SP from subjects aged between 20-43, while Riemslag *et al.* (1988) used subjects between 21-54 years old. The variation in subject ages for these studies gives rise to some concern when the effects of age on saccades are considered.

Chapter 2 showed the major change affecting saccades with old age is increased latency (2.2.1), but increasing age also leads to a reduction in saccade accuracy and reduced saccade peak velocity (2.2.2). As well as changes in saccade performance there are also changes in the EOM associated with increased age. These include degeneration, loss of fibres and an increase in fibrous tissue (Miller, 1975). While age changes occur in saccade parameters it is unknown if these changes affect the SP. Knowledge of changes to the SP with advancing age is important if the potential is to be used to examine EOM activity. It must be known if the ageing changes in the muscles affect the SP recording and, if so, how the potential is altered.

7.2 METHODS

Before starting recordings the amount of information required from elderly subjects was considered. Older subjects could not cooperate for the periods of time necessary to record the SP from all electrode sites used previously, so it was decided to record the SP from one electrode placed below the eye with an electrode at P_z as the reference. The

eye from which the SP was recorded was chosen randomly such that six right eyes and four left eyes were used. The filter settings and time sweep were as before and the recording site preparation and data analysis following recordings was as usual.

The SPs for 20 abducting 20 adducting saccades were recorded from 10 elderly subjects (5 male, 5 female) aged between 73-85 (mean 77.1±4.7) years old. Where glasses were required to see the targets clearly it was checked that the frame did not obscure the LEDs. Four saccade sizes were examined; 2.5°, 5°, 10°, and 20°. The eye not being recorded from was occluded and the head held steady with the chin and forehead rest. The recordings took place in one session lasting about $1^1/_2$ hours; subjects were encouraged to rest as often as wanted. All subjects were financially rewarded for their cooperation.

7.3 RESULTS

A clear SP was recorded from all subjects and the onset and peak were easily recognised. As with the young subjects in the previous Chapter, there was increased noise with the smallest saccade size (2.5°) but this did not appear to interfere with the SP waveform. The latency and amplitude raw data is given in Appendix 3.1. The mean and standard deviation SP onset and peak latencies for the elderly subjects are given in Table 7.1. These latency values are compared to the corresponding results for the young age group in Figure 7.1.

	Saccade Size			
	20°	10°	5°	2.5°
Lower Electrode				
Abd onset	-7.8 (7.8)	-9.0 (5.3)	-7.6 (2.5)	-8.8 (4.4)
Abd peak	3.3 (6.7)	1.8 (6.0)	4.2 (3.2)	-0.1 (4.3)
Add onset	-10.4 (4.3)	-10.7 (5.9)	-13.2 (2.6)	-12.1 (1.5)
Add peak	-0.8 (5.6)	-2.4 (4.5)	-2.8 (2.8)	-3.0 (1.9)

Table 7.1 The group mean and standard deviation (in brackets) onset and peak latencies of the SP with respect to the saccade start for ten elderly subjects performing four saccade sizes.

Figure 7.1 shows the old subjects adducting SPs onset and peak latencies were earlier than abducting SPs. Two-way ANOVA was performed on the latency data to determine if there were any significant differences between the age groups. Each saccade size was

examined separately and the age group was the first treatment and the saccade direction the second. The results of this analysis are given in Table 7.2

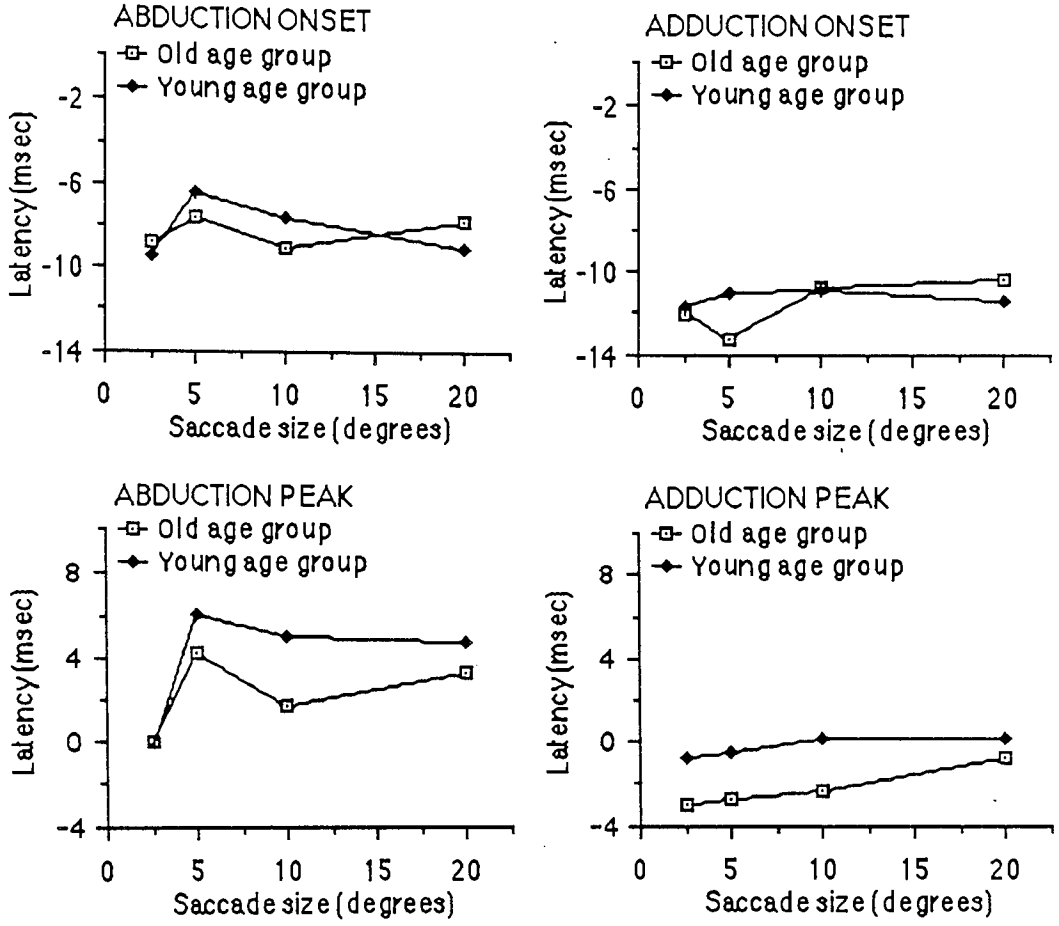

Figure 7.1 The mean onset and peak SP latencies recorded from an electrode below the eyes of elderly and young subjects performing four sizes of saccades.

	OLD vs YOUNG		ABD vs ADD	
	Onset	Peak	Onset	Peak
20°	$F_{1,8}$=0.29; NS	$F_{1,8}$=0.30; NS	$F_{1,8}$=2.67; NS	$F_{1,8}$=8.1; p<0.01
10°	$F_{1,8}$=0.10; NS	$F_{1,8}$=2.61; NS	$F_{1,8}$=11.24; p<0.01	$F_{1,8}$=20.52; p<0.001
5°	$F_{1,8}$=1.51; NS	$F_{1,8}$=2.96; NS	$F_{1,8}$=35.52; p<0.001	$F_{1,8}$=23.7; p<0.001
2.5°	$F_{1,8}$=0.02; NS	$F_{1,8}$=2.53; NS	$F_{1,8}$=2.33; NS	$F_{1,8}$=0.95; NS

Table 7.2 ANOVA results comparing the SP latencies for old and young subjects and abducting and adducting saccades for four saccade sizes

The mean and standard deviation SP onset-peak amplitudes for the elderly subjects are given in Table 7.3. The amplitude of the SP recorded with the four saccade sizes exhibits the previously documented changes with increasing saccade size. These amplitude values are compared to the corresponding results for the young age group in Figure 7.2.

Lower Electrode	Saccade Size 20°	10°	5°	2.5°
Abduction	22.8 (11.5)	26.8 (11.4)	12.5 (7.5)	8.1 (6.3)
Adduction	19.8 (10.0)	20.75 (13.2)	15.4 (11.8)	9.2 (7.5)

Table 7.3 The group mean and standard deviation (in brackets) onset-peak amplitudes of the SP with respect to the saccade start for ten elderly subjects performing four saccade sizes.

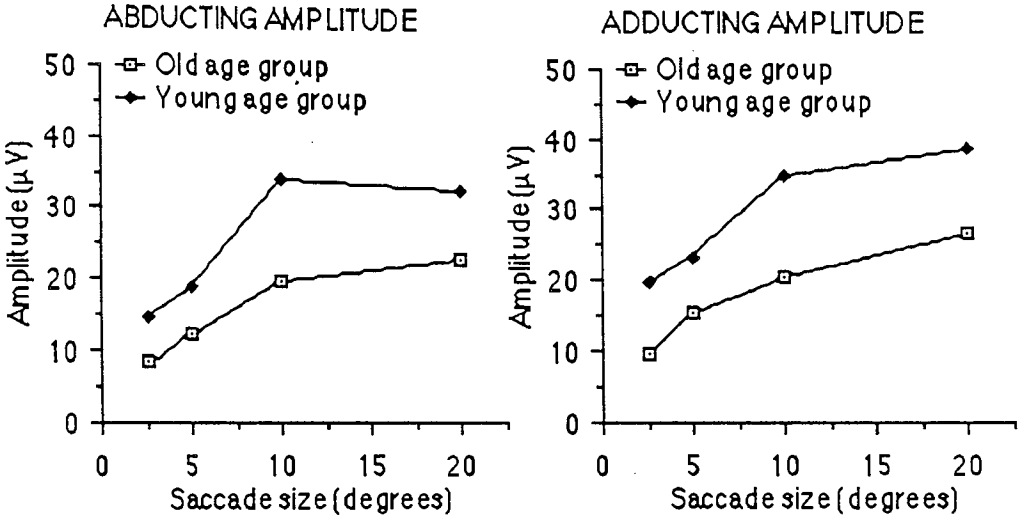

Figure 7.2 The mean SP onset-peak amplitude recorded from an electrode below the eyes of elderly and young subjects performing four sizes of saccades.

To study the relationship between the SP amplitude and the old and young subjects two-way ANOVA was performed on the amplitude raw data. The two age groups were used as one treatment and the saccade direction was the second. Each saccade size was considered separately. The results of this ANOVA are shown in Table 7.4.

	OLD vs YOUNG	ABD vs ADD
20°	$F_{1,18}$= 5.24; p<0.05	$F_{1,18}$= 2.31; NS
10°	$F_{1,18}$= 8.99; p<0.01	$F_{1,18}$= 0.12; NS
5°	$F_{1,18}$= 2.91; NS	$F_{1,18}$= 2.58; NS
2.5°	$F_{1,18}$= 6,45; p<0.025	$F_{1,18}$= 1.02; NS

Table 7.4 ANOVA results comparing the SP onset-peak amplitudes for old and young subjects and for abducting and adducting saccades for four saccade sizes.

The group average waveforms for the four saccade sizes recorded from the elderly subjects are shown in Figure 7.3.

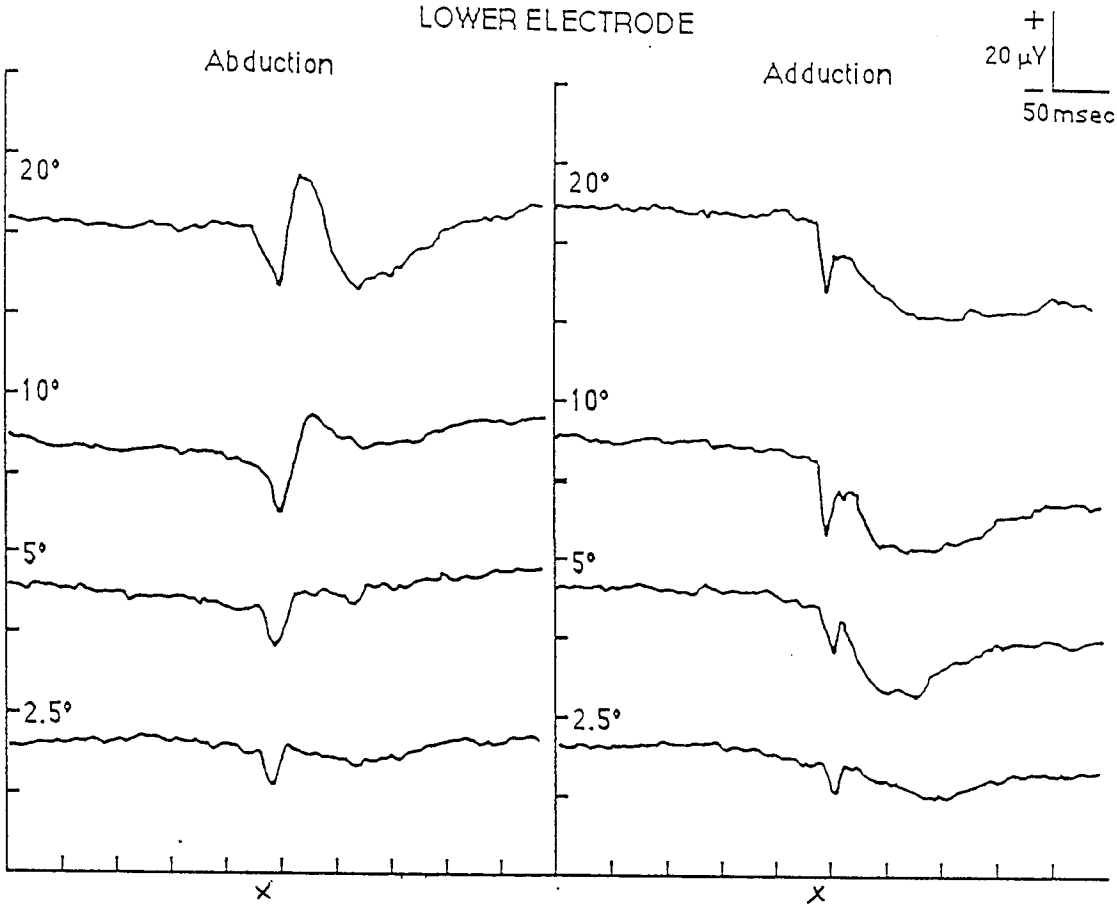

Figure 7.3 The group mean SP waveforms for four saccade sizes recorded from an electrode below the eye from ten elderly subjects. Abducting and adducting saccades are shown, and it can be seen that the waveform remains constant although the onset-peak amplitude decreases. The saccade onset is indicated by the cross.

7.4 THE PRESACCADIC SPIKE POTENTIAL IN MIDDLE AGED SUBJECTS

The reduction in SP amplitude with age is a previously unreported aspect of the recording. While the results discussed above describe the change in SP amplitude with old age, they gives no clues to the rate of amplitude change with age. It was decided, therefore, to record the SP from middle aged subjects to examine the rate of change in SP amplitude.

7.4.1 METHODS

The SP was recorded from a group of ten (five male, five female),'middle-aged' subjects (mean age 44.0±1.7 years). These subjects were mainly from the academic staff of the Vision Sciences Department. The recording conditions were identical to those used

previously and the same electrode locations (below the eye and P_z reference) were used. Unfortunately the members of staff were unable to act as subjects for as long as the other subjects so only one saccade size was recorded. Twenty abducting and twenty adducting saccades of 20° magnitude were recorded with their corresponding spike potentials.

7.4.2 RESULTS

Clear SPs were recorded from all the subjects. The raw data for the SP latencies and amplitudes are given in Appendix 3.2 while the group mean values and standard deviations are given in Table 7.5. The group mean SP waveforms for the ten middle aged subjects are shown in Figure 7.4.

	Onset	Peak	Amplitude
Abduction	-6.88 (5.6)	6.25 (3.6)	32.8 (7.3)
Adduction	-9.25 (3.4)	-0.12 (2.4)	40.0 (12.4)

Table 7.5 Group mean and standard deviation (in brackets) SP onset and peak latencies and onset-peak amplitudes for abducting and adducting 20° saccades recorded from an electrode below the eye of ten middle aged subjects.

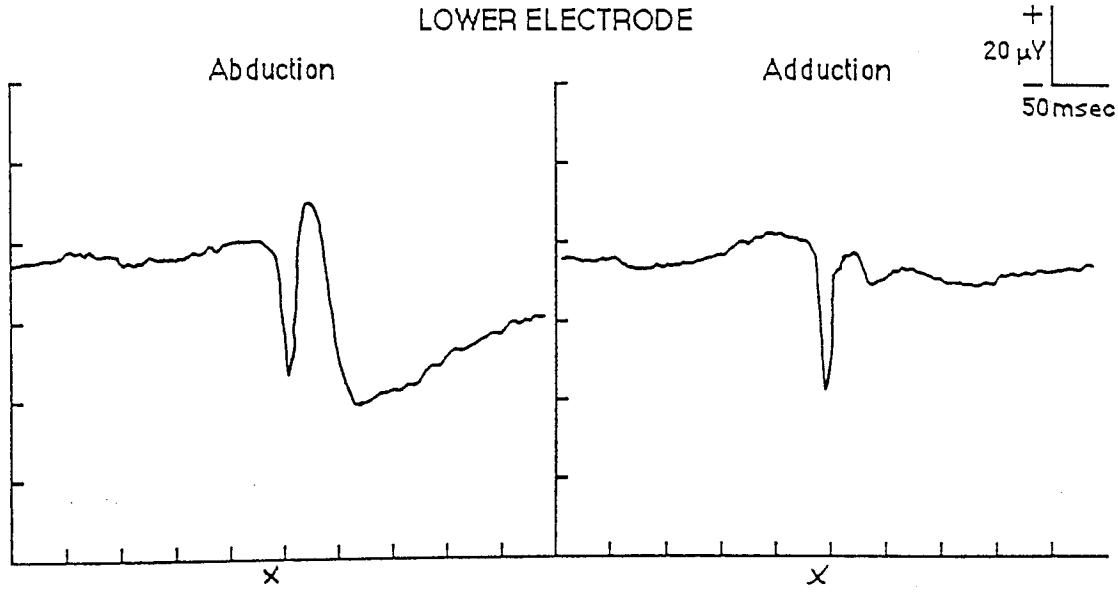

Figure 7.4 The group mean SP waveform recorded from ten middle aged subjects for abducting and adducting saccades from an electrode below the eye. The saccade onset is indicated by the cross.

The SP onset and peak latencies and onset-peak amplitude values for the old, middle and young age groups are compared in Figure 7.5.

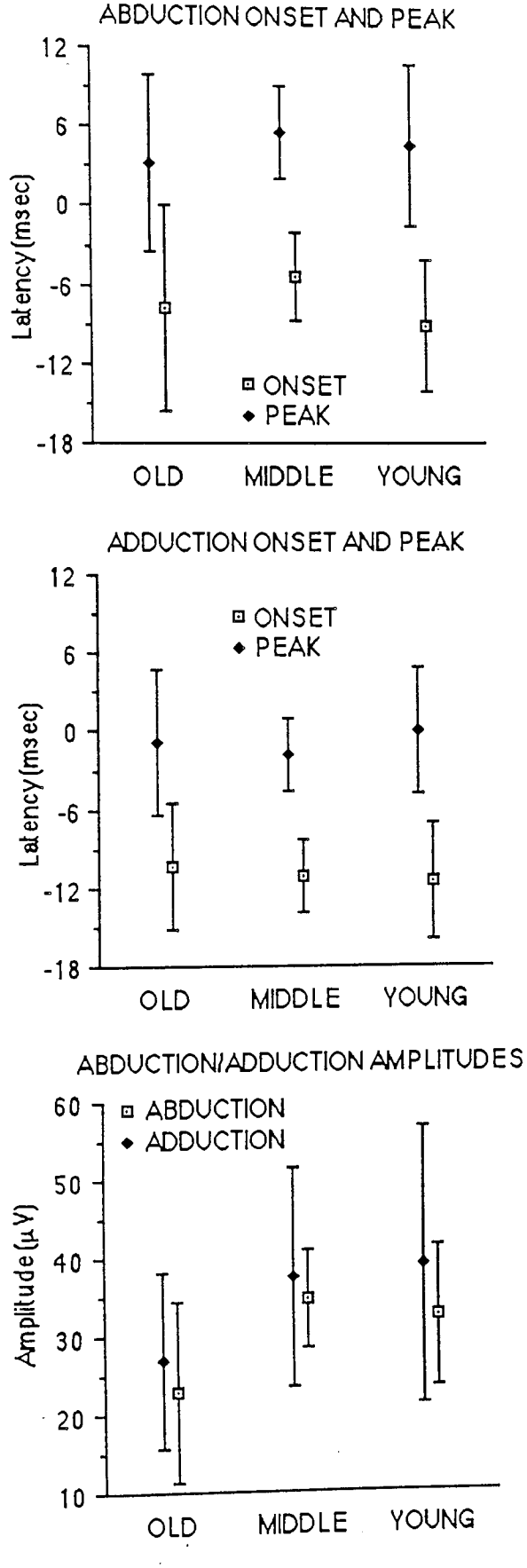

Figure 7.5 The SP onset and peak latencies and SP onset-peak amplitudes for 20° saccades recorded from an electrode below the eyes of old, middle aged and young subjects. The SP onset and peak latencies are similar for the three subject groups, but the amplitude is smaller with the elderly subjects.

Figure 7.5 shows the SP onset and peak remains quite constant for the three age groups and the latency difference between abducting and adducting saccades is present for all ages. While the SP amplitude is smaller for the old subjects, there is little obvious difference in the amplitude for the middle aged and young subjects. To examine the relationship between the subject age and the latency parameters two-way analysis of variance of the SP latency parameters was performed. The subject age (old, middle, young) was the first treatment while the saccade direction (abduction, adduction) was the second. The results of this analysis are given in Table 7.6.

	Subject Age	Abduction vs Adduction
Onset	$F_{2,27}$= 7.62; NS	$F_{2,27}$= 11.47; p<0.01
Peak	$F_{2,27}$= 0.19; NS	$F_{2,27}$= 25.45; p<0.01

Table 7.6 ANOVA results comparing the SP onset and peak latencies for three subject ages and two saccade directions.

To examine the relationship between SP amplitude and subject age for the three age groups a Wilcoxin T-test was used to compare the old, middle aged and young subjects SP amplitudes. The results of the comparisons are given in Table 7.7.

Subject ages	SP Direction	Wilcoxin T test result
Old vs Middle	Abduction	n=10, T=5, p<0.05
Old vs Young	Abduction	n=10, T=9, p<0.05
Middle vs Young	Abduction	n=10, T=23, NS
Old vs Middle	Adduction	n=10, T=12, NS
Old vs Young	Adduction	n=10, T=9, p<0.05
Middle vs Young	Adduction	n=10, T=12, NS

Table 7.7 Results of a Wilcoxin T test comparing the abducting and adducting SP onset-peak amplitudes for three subject age groups.

The statistical analysis of the latency data for the three age groups shows that there was no significant differences for the SP onset and peak latencies with the different subject ages. Analysis of the amplitude data, however, reveals that the SP amplitude was significantly smaller with the old age subjects than with the young with both saccade directions. The

old age group SP amplitude was also smaller than the middle age group for abducting saccades. There was no significant differences in the amplitudes for the middle aged and young subjects.

7.5 DISCUSSION

While previous studies of the potential have stated that it can be recorded from subjects up to 54 years of age (Riemslag *et al.*, 1988), there has been no reported recording of the potential with subjects older than this. The recordings described in this Chapter demonstrate that the SP can be easily and successfully recorded from subjects of all ages. The waveform of the SP remains constant for older subjects and the relationship between saccade size and SP onset-peak amplitude remains true for the elderly subjects. This Chapter demonstrates that the main change to the SP with advancing age is a reduction of the onset-peak amplitude, the SP onset and peak latencies changing little with subject age. The experiments show the amplitude reduction is only apparent with old subjects, middle age subjects showing no reduction in the onset-peak amplitude compared to young subjects.

The lack of any definite pattern of SP latency changes with subject age is perhaps unexpected when the known saccade latency changes with old age are considered. It is well documented that saccade latency increases with increasing age (Henriksson *et al.*, 1980; Spooner *et al.*, 1980; Abel *et al.*, 1983; Whitaker *et al.*, 1986; Sharpe and Zackon, 1987), yet the SP latency remains consistent. This would imply that, although the time interval between the stimulus onset and the start of the eye movement is prolonged in old age, the relationship between the SP onset and the saccade start remains constant. This consistency of the SP latency may be explained by the theory that the SP is linked to the brain-stem saccadic generator which is unaffected by age, while the higher centres involved in programming the saccades may deteriorate with advancing age (Abel *et al.*, 1983). If the SP is related to brain-stem activity producing the saccade it is clear that the potential will retain the same relative latency to the saccade onset although both may be

delayed relative to the onset of the eye movement trigger due to slower cognitive processing (Whitaker *et al.*, 1986).

The reduction in SP amplitude found in the recordings described above cannot, unfortunately, be fully explained from the knowledge we have of the SP recording and the behaviour of the extraocular motoneurons. It is known that age related changes occur in the extraocular muscles, including degeneration, loss of fibres and increased fibrous tissue (Miller, 1975). It is possible that these muscle changes may have a direct bearing on the SP recording if it is linked to the motor unit action potentials of the EOM. Unfortunately, there do not appear to be any reports in the literature of the effect of age on the action potentials of not only the EOM, but any skeletal muscles within the body.

The computer model of SP generation within the EOM proposed by Thickbroom and Mastaglia (1987) provides a possible clue to the changes which occur with increasing age. In this model the SP amplitude is dependent upon the recruitment dispersion rate of the motor units within the muscles. If the recruitment dispersion rate is increased, the amplitude of the SP reduces. Increasing the recruitment dispersion rate is equivalent to reducing the synchronicity with which the the motor units fire. It is conceivable that there is an increased desynchronisation of motor unit activity with increasing age, resulting in a reduced SP amplitude. Until further information is available regarding the synchronicity of motor unit activity with different ages, however, this hypothesis can only remain as such and the true cause of the SP amplitude reduction with age will remain unknown.

Although the exact cause of the reduction in SP amplitude with increasing age is unknown, the presence of this reduction in amplitude with older subjects does have important implications with regard to SP recordings. The raw data shows that, for all recording conditions, the elderly subjects exhibited SP amplitudes smaller than the corresponding mean SP amplitude for young subjects in all but one case. Of greater concern, however, is the fact that when two standard deviations were added to the individual old subject group amplitudes, nearly one quarter of these subjects exhibited SP

amplitudes plus two standard deviations which were smaller than the corresponding mean amplitude values for the young age group. As it is common practice to use two standard deviations either side of the mean to represent the upper and lower limits of a normal population this clearly indicates that comparing young amplitude values to the mean old amplitude values would give rise to many false positive identification of abnormal amplitude values. It is obviously important, therefore, that experiments involving recording the SP must use age matched subjects at all times.

7.6 SUMMARY

This Chapter describes the recordings performed to examine the effect of age on the SP recording. Many previously published papers describing the SP have used subjects of varying ages in their experiments with little regard for possible changes that may occur in the potential with advancing age (Thickbroom and Mastaglia, 1985b; 1986; Riemslag *et al.*, 1988). The previous experiments in this thesis have used age matched subjects, but this does not give any information about the SP with different aged subjects.

The SP was recorded from elderly subjects for four saccade sizes. The onset and peak latencies of the potential did not alter with age but a significant reduction in the onset-peak amplitude was found for the older subjects. To examine the rate of change in the SP amplitude the SP was recorded from middle aged subjects. These subjects did not show the same reduction in amplitude, suggesting that the changes in amplitude may only be associated with later life.

A possible explanation for the reduced SP amplitude can be hypothesised from a computer model of the spike potential which shows the amplitude of the potential reduces as the motor units fire less synchronously. Although it is not certain that this is the cause of the amplitude reduction, it is obvious from this Chapter that it is quite unsatisfactory to directly compare SP amplitude values recorded from old and young subjects, and every effort should be made to use age matched subjects in recordings of the potential.

CHAPTER 8

THE PRESACCADIC SPIKE POTENTIAL WITH VERTICAL SACCADES

8.1 INTRODUCTION

The previous Chapters have described the SP recorded immediately prior to horizontal saccades from electrodes around the eyes. Although the SP has a very consistent waveform and parameters for horizontal saccades, only one paper has described the SP with vertical eye movements. In this study Thickbroom and Mastaglia (1986) recorded the SP for 5° vertical saccades from electrodes placed round the right eye of five subjects. While these authors found similar waveforms for vertical and horizontal saccades, only limited information was given regarding the latencies and amplitudes of the potential.

Recording the SP with horizontal saccades does not, unfortunately, give a complete picture of the EOM activity during eye movements as different muscles are used to move the eyes vertically compared to horizontally. Four extraocular muscles are involved in moving the eyes vertically, the superior and inferior oblique muscles and the superior and inferior rectus muscles. The combined actions of these muscles are inherently more complex than the muscles actions of horizontal saccades where only the lateral rectus and medial rectus are directly involved in moving the eye.

Knowledge of human vertical saccade parameters is less detailed than that for horizontal saccades, mainly due to problems from lid interference with eye movement recordings (Yee, Schiller, Lim, Baloh, Baloh and Honrubia, 1985; Becker, 1989). Although the parameters of vertical saccades are similar to those of horizontal movements, with vertical saccades showing the familiar relationship between peak velocities and saccades size (Becker, 1989), there has been some debate regarding the respective velocities of upward and downward saccades. Using electrooculography, Rosenbaum, Carlson and Gaffney (1977) reported that downward saccades were slightly faster than upward

movements, while Yee *et al.* (1985), also using the EOG, found upward saccades to be faster than downward. In the same study, Yee *et al.* (1985) also recorded vertical saccades with infrared limbus tracking and a magnetic search coil and found the infrared technique recorded faster downward saccades while the search coil demonstrated no difference in the two saccade direction velocities. This apparent anomaly in the saccade velocities was explained on the basis of variations in the recording techniques giving conflicting results.

The innervation for vertical saccades differs slightly from that of horizontal saccades. It was seen in Chapter 2 that the brainstem plays an essential role in the innervation of both horizontal and vertical movements (2.4.3), but where horizontal saccades are generated within the PPRF, vertical saccades rely upon the rostral interstitial mesencephalic formation (RIMF) for innervation (Büttner and Büttner-Ennever, 1988). From the RIMF, however, the saccade commands are directed to the PPRF and the pause and burst cells controlling the impulses from the oculomotor neurons to the EOM. The innervation for vertical saccades, therefore, shares the same 'final common pathway' previously described for horizontal eye movements (2.4.2).

Recording vertical saccades has been recognised as a useful clinical tool in the early diagnosis of certain disease conditions exhibiting slowing of vertical saccades amongst their first oculomotor signs (Becker, 1989). Progressive supranuclear palsy, for example, shows impairment of vertical saccades as the initial ocular motor defect (Leigh and Zee, 1983). Obviously, it is unknown if the SP would show any differences in these disease conditions, but for the SP to have any clinical use it is essential to know the normal parameters for both horizontal and vertical saccades.

It is conceivable that the different muscles groups and different innervational processes involved in the control of vertical saccadic eye movements may cause the SP parameters or waveform to differ for vertical saccades. This Chapter will describe experimental work performed to repeat the earlier work of Thickbroom and Mastaglia (1986) with a larger number of subjects and greater analysis of the results in an attempt to more fully determine

the nature of the SP with vertical saccades. The experiments were performed primarily to confirm the ability to record the SP with saccades other than horizontal and this Chapter does not attempt to describe the relationship between the SP and vertical saccades as fully as has been done with horizontal eye movements.

8.2 METHODS

The SP was recorded from 10 young age matched subjects (mean age 25.2±2.8 years). Recordings were made from both eyes using the recording system previously described for horizontal saccades. Electrodes were placed symmetrically at the inner and outer canthi and above and below both eyes with P_Z was as the reference. The trigger for the vertical saccades differed only in the orientation of the LEDs which were positioned so as to subtend 20° vertically; 10° above and below the horizontal centre. Forty saccades (20 upwards and 20 downwards) were recorded along with their respective SPs.

8.3 RESULTS

Clear SPs were recorded from all subjects at each electrode site for both upward and downward saccades. The waveforms showed the characteristic negative spike which has been recorded with horizontal saccades. The group average traces for the two eyes are shown in Figures 8.1 and 8.2. The latency and amplitude raw data are given in Appendix 4.1.

The SP began between -17.3 and -6.8 msec before the saccade start and peaked between -3.4 msec before to 5.2 msec after the saccade start. The onset-peak amplitude was between 15.9 to 42.3 μV. At most electrode sites the onset and peak latencies were earlier with downward saccades. The electrodes placed below the eyes recorded a larger amplitude for upward saccades than the other electrodes for this saccade direction. Table 8.1 shows the mean and standard deviation SP onset and peak latency values while the mean amplitudes and standard deviations are shown in Table 8.2.

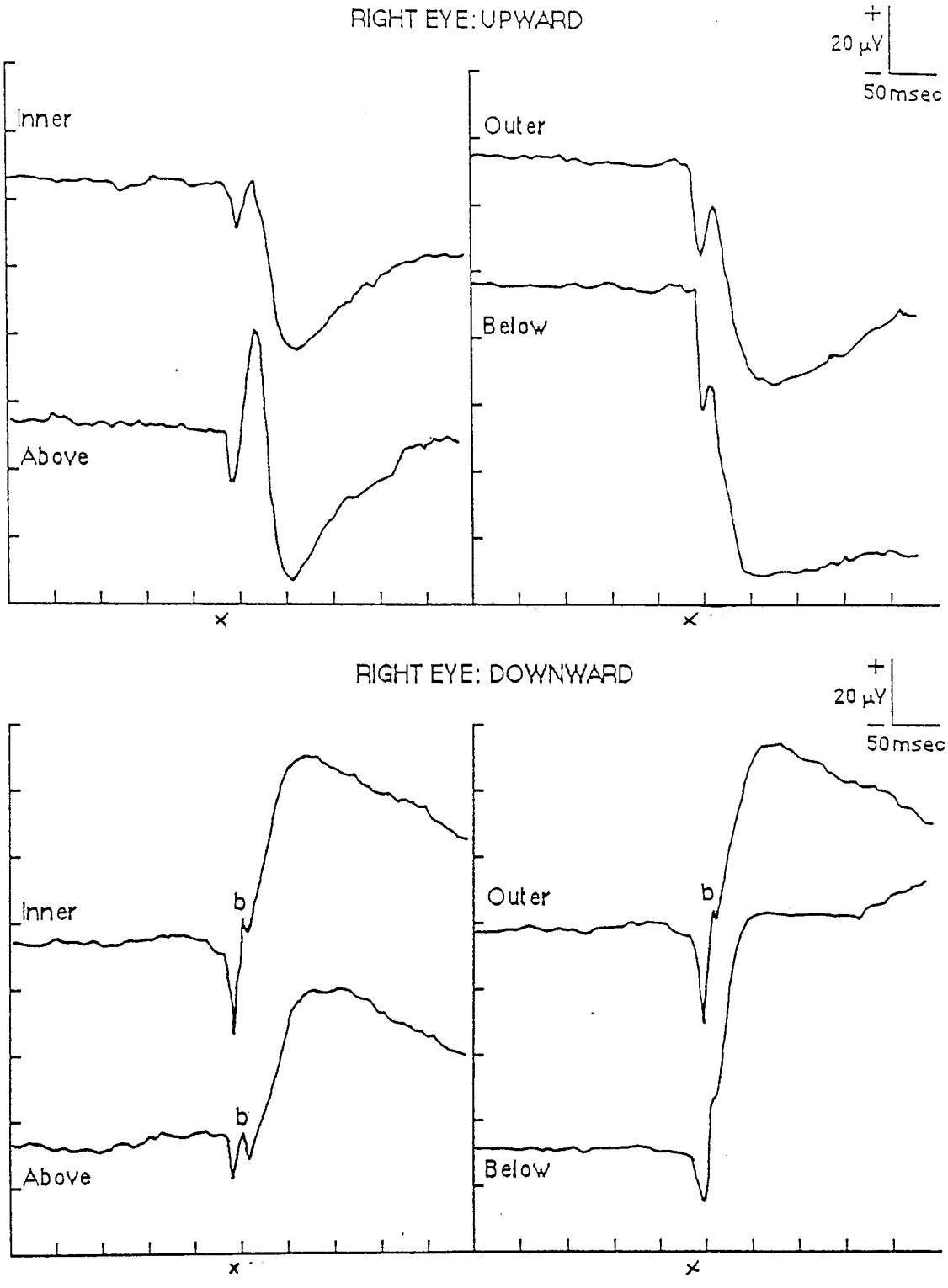

Figure 8.1 The group average spike potential waveforms for the right eye of ten subjects performing upward and downward saccades. The traces from four electrode sites are shown. A second component of the SP waveform (labelled b) can be clearly seen. The saccade onset is indicated by the cross.

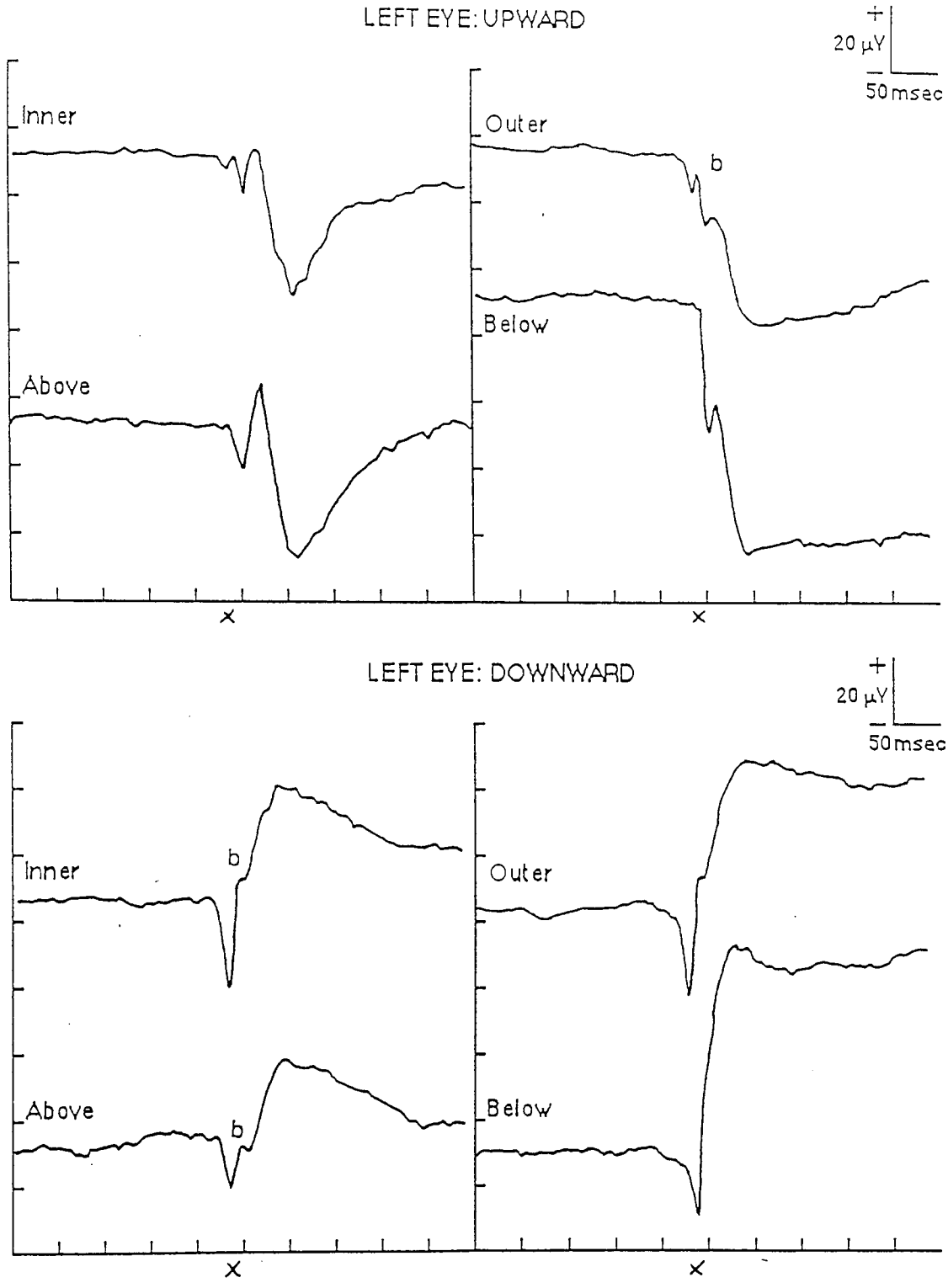

Figure 8.2 The group average spike potential waveforms for the left eye of ten subjects performing upward and downward saccades. The traces from four electrode sites are shown. A second component of the SP waveform (labelled b) can be clearly seen. The saccade onset is indicated by the cross.

		ELECTRODE SITE							
		INNER		OUTER		ABOVE		BELOW	
		Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak
RIGHT UP	Mean	-9.7	0.1	-9.2	3.7	-6.8	5.2	-7.4	5.0
	SD	6.6	6.8	7.7	8.0	6.2	7.3	6.9	7.1
LEFT UP	Mean	-12.7	-1.9	-12.1	-2.7	-13.6	-1.8	-15.1	-2.7
	SD	6.9	7.8	4.9	3.5	6.0	4.8	5.8	3.4
RIGHT DOWN	Mean	-10.7	2.8	-10.0	2.4	-10.9	-1.4	-12.2	0.8
	SD	6.7	7.3	9.9	10.6	10.7	10.9	10.0	11.2
LEFT DOWN	Mean	-12.4	-2.4	-13.4	-1.3	-17.3	-3.4	-16.4	-3.3
	SD	6.6	6.7	4.8	1.9	6.6	6.1	4.0	1.9

Table 8.1 The mean and standard deviation (SD) SP onset and peak latencies (msec) for ten subjects at four electrode sites. 20° upward (UP) and downward (DOWN) saccades are compared from the two eyes.

		ELECTRODE SITE			
		INNER	OUTER	ABOVE	BELOW
RIGHT UP	Mean	20.8	33.1	21.0	42.3
	SD	12.5	11.5	12.0	21.0
LEFT UP	Mean	18.8	28.2	21.3	38.7
	SD	10.8	10.4	11.9	19.4
RIGHT DOWN	Mean	30.1	26.8	20.6	15.9
	SD	15.0	12.8	9.4	9.6
LEFT DOWN	Mean	27.7	27.5	21.0	21.8
	SD	11,9	10.9	11.7	10.8

Table 8.2 The mean and standard deviation (SD) SP amplitudes (μV) for ten subjects at four electrode sites. 20° upward (UP) and downward (DOWN) saccades are compared.

Two-way analysis of variance was performed on the latency and amplitude raw data using the saccade direction (upward, downward) as one treatment and the electrode position (inner canthus,outer canthus, above the eye and below the eye) as the second. Although the SP onset was earlier with downward saccades, this was found to be statistically significant only for the right eye (right eye $F_{1,9}=7.37$, $p<0.025$, left eye $F_{1,9}=2.38$, NS). The SP peak was also statistically significantly earlier for only the right eye results (right eye $F_{1,9}=9.92$ $p<0.025$, left eye $F_{1,9}=2.01$, NS).

In both eyes no significant difference between upward and downward saccades was found for the SP amplitude. On examining the different electrode sites however, a statistically significant difference was found with regard to the amplitude recordings (right

eye $F_{3,27}=4.07$, $p<0.05$, left eye $F_{3,27}=4.51$, $p<0.025$). This can be understood when the mean amplitude results are examined (Table 8.2). The amplitude recorded from the lower electrode with upward saccades was considerably larger than that recorded from the other electrodes for the same eye movement

8.4 DISCUSSION AND CONCLUSIONS

The results of this study confirm the SP can be easily recorded with vertical saccades. While the latency values for the vertical SP compare well with earlier studies of the SP with horizontal saccades recorded from the same electrode sites, there does appear to be a greater degree of variation in the results with the vertical eye movements.

The amplitude values recorded in the present study do, however, appear to differ from those of horizontal saccades. The amplitudes are generally reduced for vertical eye movements although this varies with the electrode position. For upward saccades the largest amplitude was recorded at the lower electrode while for downward saccades the largest amplitude was recorded at the inner canthus. These findings agree with amplitude changes found by Thickbroom and Mastaglia (1986) who recorded maximum amplitudes for these saccade directions at the same electrode sites. Thickbroom and Mastaglia (1986) hypothesised that the increase in the amplitude for upward saccades at the lower electrode site may be due to the proximity of this electrode to the muscle belly of the inferior oblique muscle which acts as an elevator of the eye. The difference in the SP amplitude for downward saccades, with a maximum at the inner canthus, may be explained by the proximity of this electrode to the trochlea over which the superior oblique muscle passes as it heads towards the eye.

The waveforms recorded for the vertical eye movements are similar to those found for horizontal saccades but many of the traces display a distinct secondary component (Figures 8.1, 8.2). While it is possible that the more complex SP waveform recorded with vertical saccades may be a reflection of the different muscle activity involved in this type of

eye movement, an alternative explanation of this component with vertical saccades can be found if one considers the activity of the eyelids during these eye movements. Barry and Jones (1965) have recorded the activity of the eyeball and eyelids during vertical saccades and examined the effect of this activity on EOG records. They found that with both upward and downward saccades the eyelids start to move simultaneously with the eyeball, this lid movement producing an artefact on the EOG trace due to the eyelids acting as sliding electrodes. Although the artefact did not interfere with the EOG record until the end of the saccade it must be remembered that the SP is a considerably smaller potential than the EOG record and it is possible that lid activity which commences with the eye movement may contaminate SP traces earlier than EOG traces.

Although the SP has been shown to be recorded with both horizontal and vertical saccades its precise origin is still uncertain. It is generally considered that the SP is linked with the innervation of the EOM motor units and the parameters and waveform of the potential with both horizontal and vertical saccades in normal subjects have now been well documented. It would appear from the the preceding Chapters that the SP does not allow the isolation of activity in separate muscles involved in horizontal saccades. Although it is likely that this is also true of vertical eye movements, this cannot be said with absolute certainty. Rosenbaum *et al.* (1977) recorded the saccade parameters for vertical saccades with the eye both facing straight ahead and abducted and adducted. This was performed to allow some isolation of the activity of the vertical rectus and oblique muscles. The present study has only recorded the SP with vertical saccades in the straight ahead position which are produced by the co-contraction of both the oblique and vertical rectus muscles. The resultant SP was obviously generated by activity in both these muscle groups, perhaps also accounting for the more complex waveform.

The results of this study suggest that future studies of the SP with vertical saccades will have to consider carefully the choice of electrode sites used. Electrodes placed above the eyes show the most consistent amplitude values while those below the eye appear a poor choice due to greater variability in recordings. Indeed, the increased variability of the

SP parameters with vertical saccades may preclude the recording of the SP for vertical saccades in patients with ocular motor anomalies, the results of this and earlier studies indicating that SPs recorded with horizontal saccades are much less variable.

8.5 SUMMARY

This Chapter has described the SP which can be recorded with vertical saccadic eye movements. The waveform and latency parameters of the potential did not appear to differ from those of horizontal saccades although the SP onset-peak amplitude was smaller with vertical eye movements than with the corresponding horizontal saccades. The SP latency values did show slightly less consistency with vertical saccades, but it is known that vertical eye movements recordings are hampered by eyelid activity which may interfere with the ability to recognise the saccade onset.

The SP waveform recorded with vertical saccades frequently shows a second peak following the initial deflection. Although, as discussed by Riemslag *et al.* (1988), the actual SP waveform is masked to some extent by the EOG activity, it has been hypothesised that the more complex waveform may be indicative of the inherently more complex muscle activity associated with vertical saccades. A further factor which may influence the SP waveform, particularly with vertical saccades, is the eyelid activity associated with the eye movements.

This study indicates that, although the SP can be recorded for vertical saccades, there is little to be gained with this recording compared to horizontal eye movements, at least with normal subjects. The latency values appear to be less reliable than those recorded for horizontal saccades, and the amplitude values are reduced. It also appears that if the SP is to be recorded with vertical saccades, some care must be taken in choosing the electrode site to record the SP with vertical saccades as the electrodes located below the eyes show a greater degree of variability than the other sites, especially the electrode above the eyes.

CHAPTER 9

A STUDY OF THE TOPOGRAPHICAL DISTRIBUTION OF THE PRESACCADIC SPIKE POTENTIAL

9.1 INTRODUCTION

In Chapter 3 it was observed that electrophysiological activity related to motor actions, including eye movements can be recorded from electrodes placed on the scalp. Three potentials are known to precede saccades; the readiness potential (Becker *et al.*, 1972; Deecke *et al.*, 1976; Shibasaki *et al.*, 1980; Kurtzberg and Vaughan, 1980, 1982), the pre-motor positivity (Deecke *et al.*, 1976) and the presaccadic spike potential (Thickbroom and Mastaglia, 1985a,b). This third potential has been the topic of study in this thesis and has been recorded from electrodes around the eyes to a reference electrode located at P_z for different saccade directions and sizes.

The literature has indicated that there is some debate as to the exact origin of the SP and the distribution with which it can be recorded across the head. Some workers (Kurtzberg and Vaughan, 1973, 1980; Weinstein *et al.*, 1984; Balaban and Weinstein, 1985; Weinstein *et al.*, 1988; see 3.2.2) have recorded the spike potential as a positive cortical potential, perhaps representing activity of multiple sites involved with programming rapid eye movements (Weinstein *et al.*, 1988). The posterior positive potential has a widespread distribution across the scalp with a maximum amplitude over the parietal region falling to less than half at frontal electrodes (Kurtzberg and Vaughan, 1980).

The papers describing the posterior potential do not, however, appear to consider the alternative suggested origin of the potential. Many authors have found that the spike potential can be recorded, as in this thesis, as a large negative frontal potential from electrodes close to the eyes (Blinn, 1955; Becker *et al.*, 1972; Riggs *et al.*, 1974; Beaussart and Guieu, 1977; Jäntti, 1982; Jäntti *et al.*, 1983; Jäntti and Häkkinen,

1987;Thickbroom and Mastaglia, 1985b, 1986, 1987). Although uncertain of the exact origin of the potential, these authors agree that it is probably muscular in origin, possibly from the extraocular muscles.

Several reports have indicated that the large anterior negative potential is coincident with the smaller positive posterior spike (Becker *et al.*, 1972; Kurtzberg and Vaughan, 1973; Kornhuber, 1973; Deecke and Kornhuber, 1977; Thickbroom and Mastaglia, 1985b, 1986). Indeed, it has been implied by Becker *et al.* (1972), Kornhuber (1973), Deecke and Kornhuber (1977) and Thickbroom and Mastaglia (1985b, 1986) that the posterior potential may actually arise as a result of potential spread of the large anterior potential. If the posterior potential is related to the anterior activity, some doubt must be cast upon the conclusions reached from recordings of the posterior spike activity. Weinstein *et al.* (1984), Balaban and Weinstein (1985) and Weinstein *et al.* (1988) have all recorded the posterior spike activity from electrodes at P_3 and P_4 with linked earlobes as the reference. These authors have performed detailed analysis of the recordings from the two electrode sites, comparing the SP parameters to the eye movement directions and laterality of the recording electrode. Unfortunately, in all these studies, no consideration appears to have been given to the widespread nature of the posterior activity and no other electrode sites are used to support the results of recordings from P_3 and P_4.

The distribution of the SP across the head has been examined using electrodes placed over the scalp to record the activity related to saccades. Blinn (1955) found the sharp spike potential appeared to originate in the orbital region, more specifically in the lateral rectus muscle (3.2.2), while Becker *et al.* (1972), using bipolar electrodes in a chain from the chin to inion, confirmed an orbital origin. Thickbroom and Mastaglia (1985b), in a more comprehensive study, used 30 electrodes on the scalp to record the distribution of presaccadic cortical activity. These authors found the SP to originate in the orbital region with a maximum negative amplitude at the frontal electrodes and a reversal in the potential polarity at electrodes located on the posterior scalp. Thickbroom and Mastaglia (1985b)

indicated that current flow across the scalp from the anterior activity could account for the surface distribution of presaccadic activity, including the posterior positive potential.

The debate over the origin of the spike potential is clearly an important question to answer if the potential is to be fully understood. If the posterior activity is related to the frontal spike potential, the recordings by Weinstein *et al.* (1984), Balaban and Weinstein (1985) and Weinstein *et al.* (1988) may be considered as superfluous. Although Thickbroom and Mastaglia (1985b) have shown the SP to be widely distributed across the scalp, it was felt that the recordings should be repeated to confirm these findings and examine the distribution with the recording set-up used for the other experiments in this thesis.

9.2 THE PRESACCADIC SPIKE POTENTIAL DISTRIBUTION RECORDED WITH AN AVERAGE REFERENCE

The recording program used in earlier experiments only allowed the SP to be recorded from one electrode at a time. Obviously this was not suitable for recording the SP from several electrodes on the scalp as the recording session would be extremely long, leading to patient fatigue and poor cooperation. A separate program was therefore developed for the Pathfinder to simultaneously record the SP from 16 channels, thus allowing the topography to be more accurately determined. Unfortunately, due to memory limitations of the Pathfinder, it was impossible to perform simultaneous back-averaging of 16 channels so all recordings in this experiment are single sweep recordings.

Before any recordings could be made, the choice of reference had to be made. Many studies of scalp activity use an average reference to record potential distribution as this technique is well suited to these type of recordings. No additional electrodes are required as the electrodes positioned on the scalp for the recordings are also used for the reference. When using a single reference electrode it is essential to ensure that the electrode site is relatively inactive with respect to the recording sites. This is not necessary when using an average reference as, generally, the activity at all the recordings sites is used in the reference. The fact that all electrode sites are included in the reference can,

however, cause problems in interpretation of results as large potentials in some channels may appear inverted in the other channels. This problem can be minimised if electrodes which are known to record large signals are excluded from the average reference.

9.2.1 METHODS

The SP was recorded from 14 electrodes on the scalp (F_7, F_8, F_4, F_3, P_z, F_z, C_3, C_4, T_5, T_6, P_3, P_4, O_1, O_2 with an average reference; International 10-20 system, see Figure 3.1). Two additional electrodes were located below the eyes to record the SP activity immediately adjacent to the orbits. The electrode locations were chosen to give a wide coverage of the scalp and include the electrodes used by previous authors to record SP activity. Three normal subjects (DS, aged 27; PF, aged 32 and SJH, aged 24) were used.

The electrode sites were prepared in the usual manner and the electrodes were attached with Blenderm tape although in some cases it was necessary to use collodion glue to ensure satisfactory contact. All electrode sites had an impedance of 5KΩ or below. The SP is known to be recorded as a large negative spike potential around the orbits and it was felt that the electrodes below the eyes could be a possible source of error if included in the reference. For this reason, these electrodes were discounted from the average. The scalp spike activity was recorded for either rightward or leftward horizontal saccades of 20°. The LEDs used previously were used to trigger the saccades and the same filters and time sweep as before were used (low cut-off 0.50 Hz, high cut-off 100 Hz, time sweep 500 msec). The Pathfinder was programmed to commence recording coincidentally with triggering the LEDs so the latency values for the SP onset are given with respect to the eye movement trigger.

9.2.2 RESULTS

Waveforms for the presaccadic scalp activity are shown in Figures 9.1-9.3. These recordings clearly show the large frontal negative potential and coincident smaller,

widespread posterior positivity. The waveforms are, in some cases, more noisy than the traces usually recorded for the spike potential, but it should be remembered that all the results in this experiment are single sweep recordings.

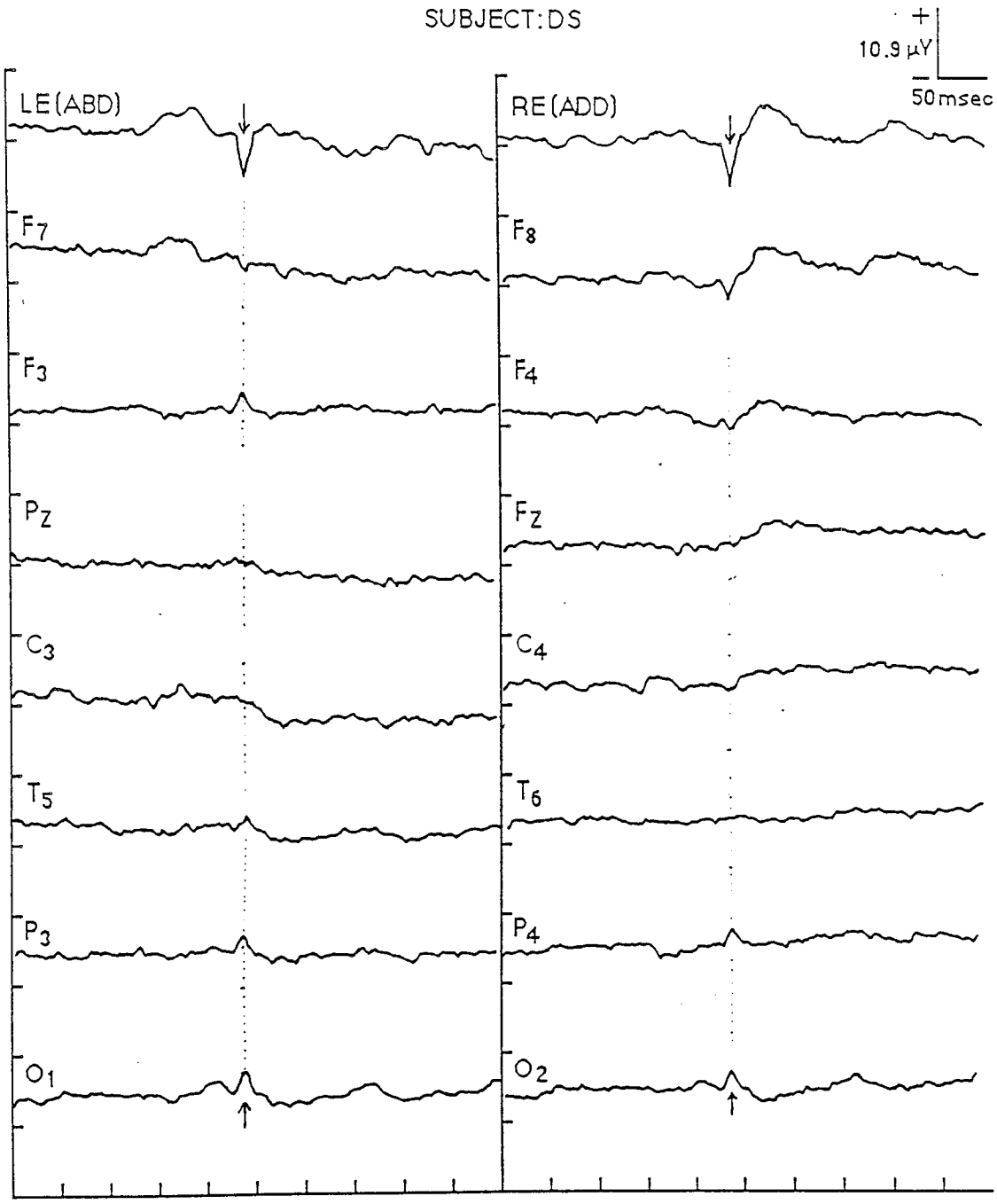

Figure 9.1 Single sweep recording of the presaccadic spike potential activity from 14 electrodes across the scalp and two electrodes below the eyes (top two traces) with an average reference. The electrodes below the eyes were not included in the average. The SP is indicated by the arrow. A large frontal negative spike potential can be clearly seen with corresponding smaller posterior positive spike activity. (Subject DS, right to left saccade).

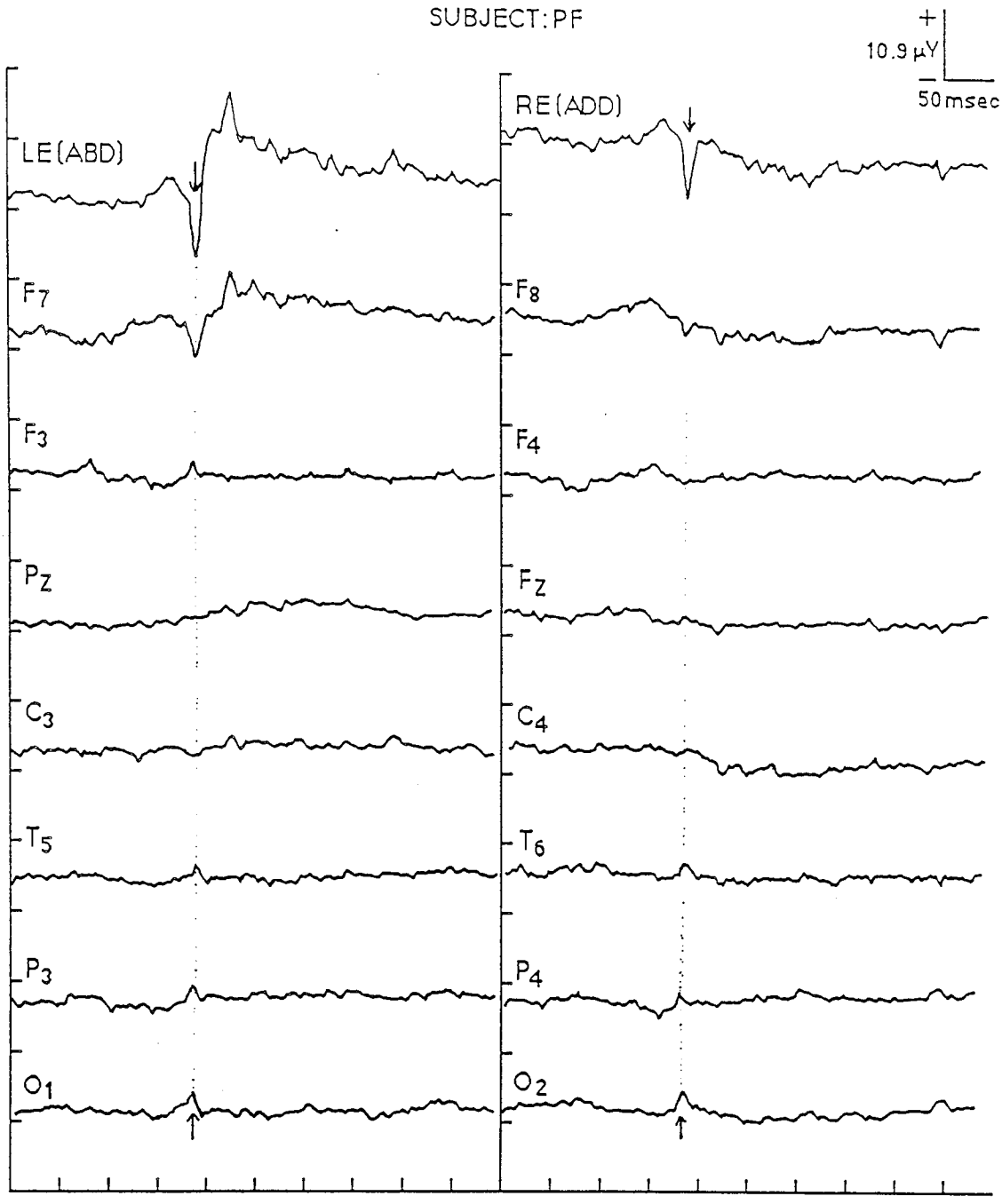

Figure 9.2 Single sweep recording of the presaccadic spike potential activity from 14 electrodes across the scalp and two electrodes below the eyes (top two traces) with an average reference. The electrodes below the eyes were not included in the average. The SP is indicated by the arrow. A large frontal negative spike potential can be clearly seen with corresponding smaller posterior positive spike activity. (Subject PF, right to left saccade).

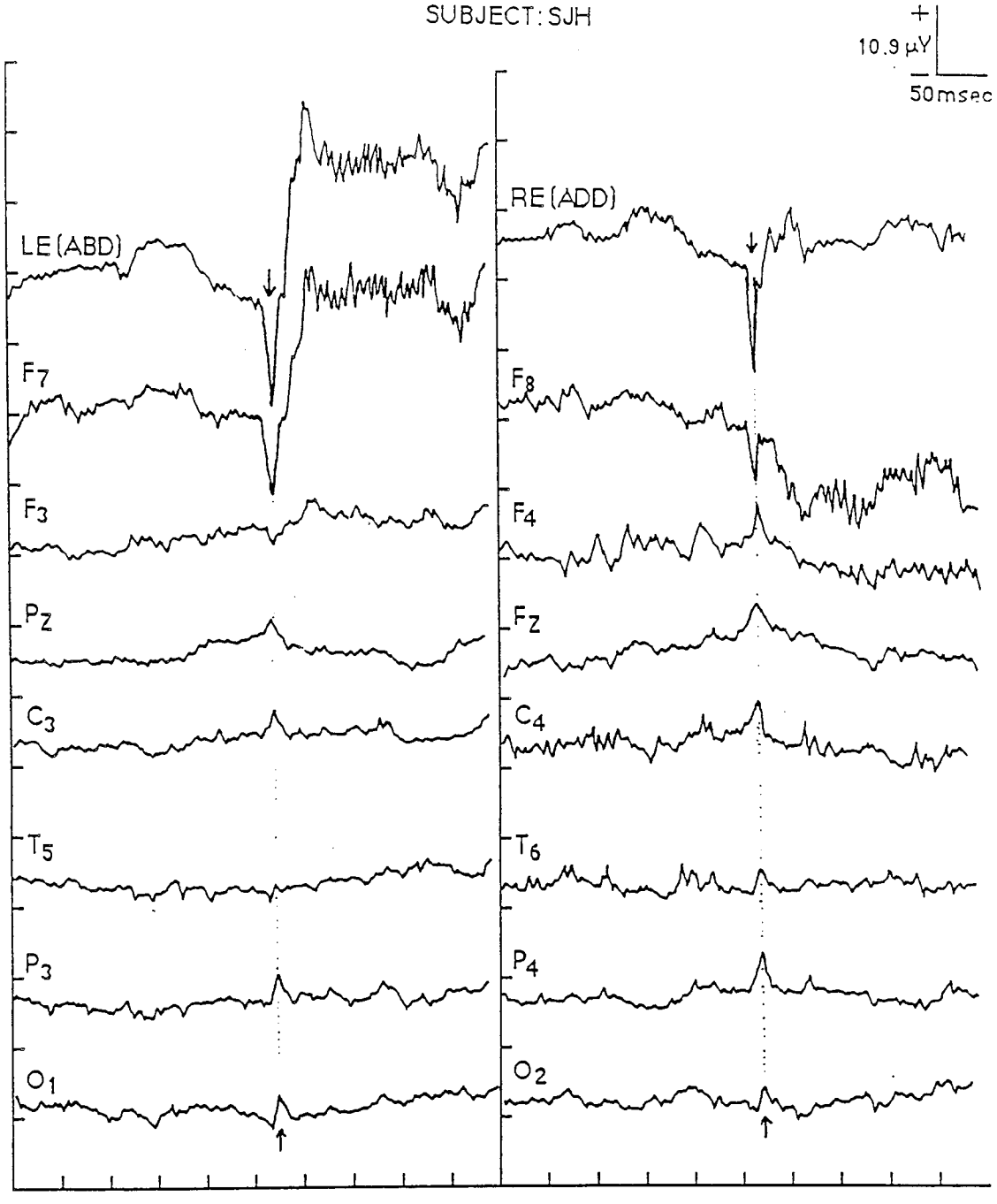

Figure 9.3 Single sweep recording of the presaccadic spike potential activity from 14 electrodes across the scalp and two electrodes below the eyes (top two traces) with an average reference. The electrodes below the eyes were not included in the average. The SP is indicated by the arrow. A large frontal negative spike potential can be clearly seen with corresponding smaller posterior positive spike activity. (Subject SJH, right to left saccade).

The waveforms confirm that the frontal negative SP has corresponding posterior positive activity. This posterior activity is widespread with a distinct potential visible at many electrode sites (Figures 9.1-9.3). The frontal electrodes (F_7, F_8, F_4, F_3) show a

well-defined negative deflection in nearly all cases. Many of the posterior electrodes (T_5, T_6, P_3, P_4, O_1, O_2) show clear positive spike activity at the same latency as the larger frontal spike, although with a much reduced amplitude. The remaining electrodes (P_z, F_z, C_3, C_4) appear, in general, to exhibit relatively little spike potential activity although subject SJH shows some positive activity coincident with the frontal spike at all electrodes posterior to F_7 and F_8. The posterior and anterior spike latencies were compared by measuring each spike peak latency with the Pathfinder's internal cursor (Table 9.1). It should be remembered that the latency values are relative to the saccade trigger.

	Electrode Site															
	Re	Le	F_3	F_4	F_6	F_7	F_z	P_z	C_3	C_4	T_5	T_6	P_3	P_4	O_1	O_2
DS	248	249	249	249	249	249	—	248	—	249	249	—	249	249	249	248
PF	194	194	195	195	195	195	—	—	194	194	194	195	194	194	193	194
SJH	287	287	286	287	287	287	287	287	287	288	—	286	287	287	288	287

Table 9.1 The SP peak latencies (msec) after the saccade trigger recorded from electrodes below the right (Re) and left (Le) eyes and 14 electrodes across the scalp with an average reference. The latencies are different for the three subjects, but show little variation for the different electrode sites for each subject. Where no value is given there was no definite spike on the waveform.

Unfortunately, the waveforms in these Figures can not, by themselves, be used to confirm or deny any relationship between frontal and posterior positive activity because they were recorded with an average reference. Although the two channels below the eyes were removed from the reference, the electrodes at F_7 and F_8 did still record greater negative activity compared to the other electrodes on the scalp. It could be argued that any posterior positive activity may be an artefact due to the large frontal negativity influencing the average reference. The posterior electrodes, where there may have been no activity, would appear to be positive with respect to the artificial average reference value, resulting in an upward (positive) deflection for these electrode sites. Average reference recording was not, therefore, the ideal technique to give a definite indication of SP distribution.

9.3 THE PRESACCADIC SPIKE POTENTIAL DISTRIBUTION RECORDED WITH A BALANCED NON-CEPHALIC REFERENCE

The limitations of recording with an average reference prompted further recordings of the scalp activity but with a balanced non-cephalic reference (BNC). This reference was chosen as it would be unaffected by large variations of activity on the scalp and would give a more accurate representation of the distribution of the spike potential.

9.3.1 METHODS

Two normal subjects (CN, aged 23, HRD aged 24) were used to record the SP from 16 electrodes across the scalp with electrodes on the sterno-clavicular joint and the vertebra prominens acting as the reference. The impedences of all electrodes were maintained at 5 KΩ or below. To reduce ECG activity the subjects were supine and the LEDs, mounted on a board, were held one metre above their head. As before, the scalp activity was recorded for 20° horizontal saccades. A slightly different electrode montage was used to examine the posterior activity with the BNC reference, the electrodes at F_7 and F8 being replaced by electrodes at T_3 and T_4 (montage: F_4, F_3, P_z, F_z, C_3, C_4, T_3, T_4, T_5, T_6, P_3, P_4, O_1, O_2). It was hoped that this would indicate any differences in the activity recorded from electrodes near the ears compared to the parietal cortex.

9.3.2 RESULTS

The waveforms recorded with the balanced noncephalic reference are shown in Figures 9.4 - 9.8. In some cases the ECG was included in the waveforms to allow comparison between the two potentials but this has been clearly identified to avoid any confusion between the two potentials.

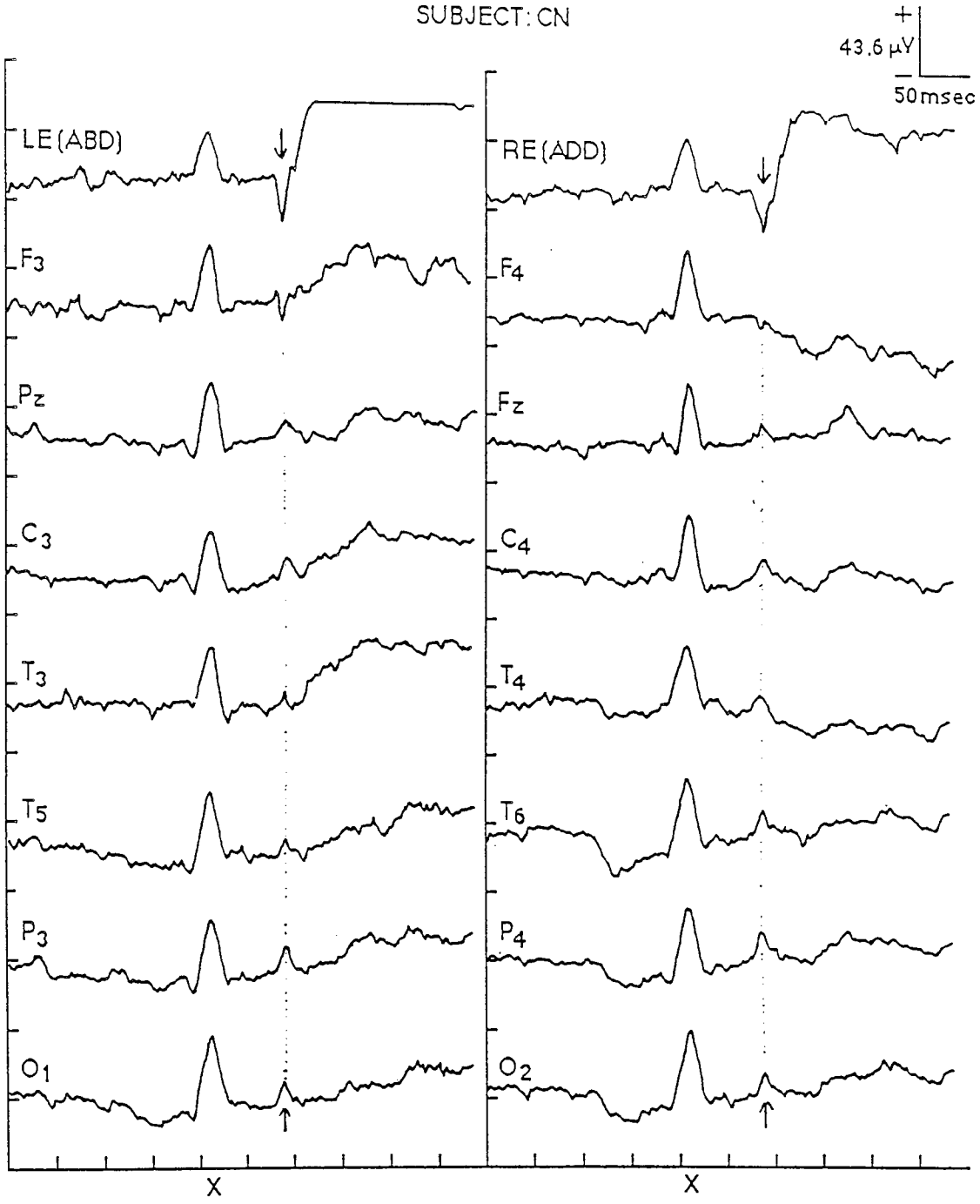

Figure 9.4 Single sweep recording of the presaccadic spike potential activity from 14 electrodes across the scalp and two electrodes below the eyes (top two traces) recorded with a balanced non-cephalic reference. The SP onset is indicated by the arrow. A large frontal negative spike potential can be seen with corresponding smaller posterior positive spike activity. To allow comparison of the SP and the ECG, the ECG has also been recorded in these traces (indicated by the cross). (Subject CN, right to left saccade).

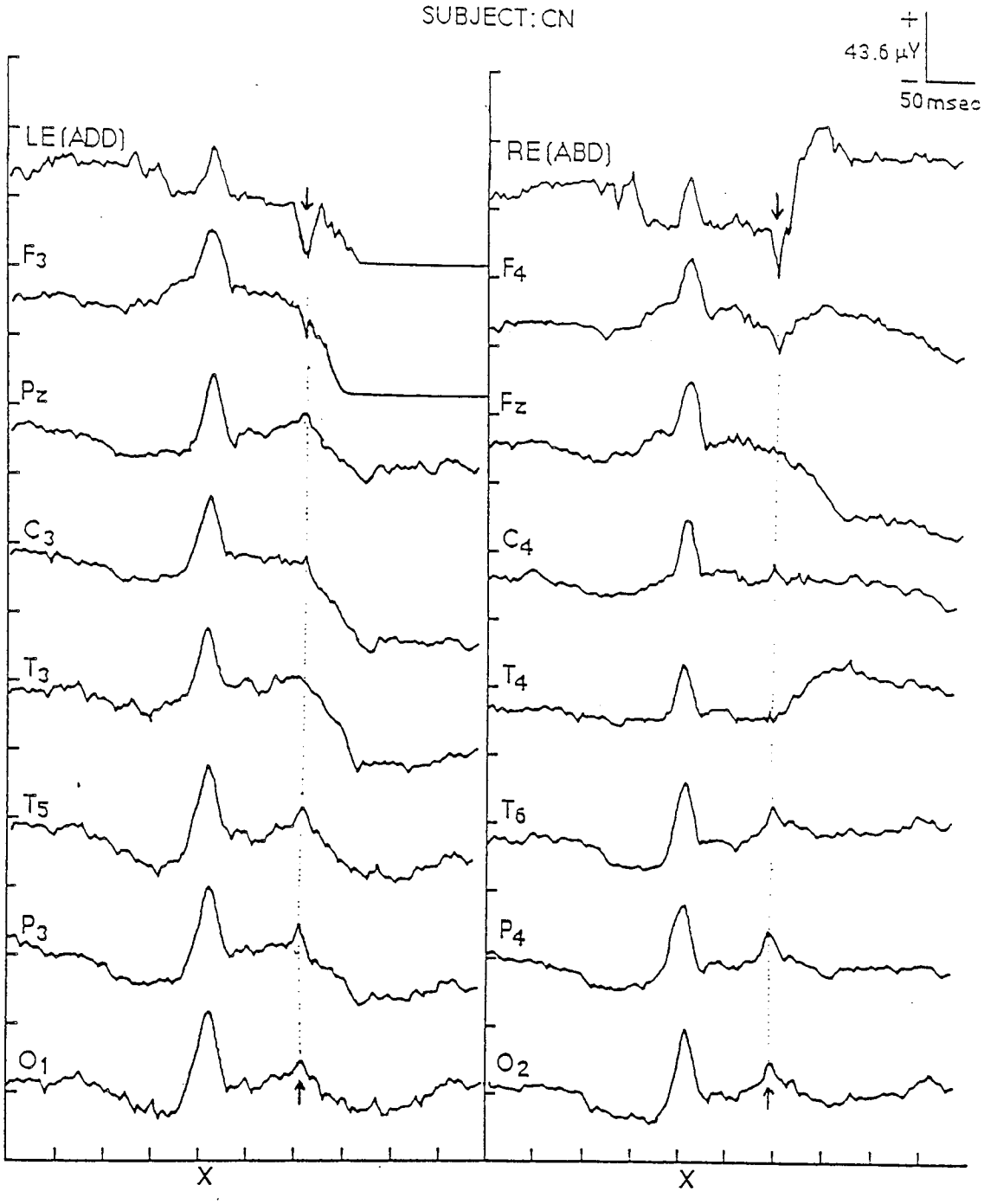

Figure 9.5 Single sweep recording of the presaccadic spike potential activity from 14 electrodes across the scalp and two electrodes below the eyes (top two traces) recorded with a balanced non-cephalic reference. The SP onset is indicated by the arrow. A large frontal negative spike potential can be seen with corresponding smaller posterior positive spike activity. To allow comparison of the SP and the ECG, the ECG has also been recorded in these traces (indicated by the cross). (Subject CN, left to right saccade).

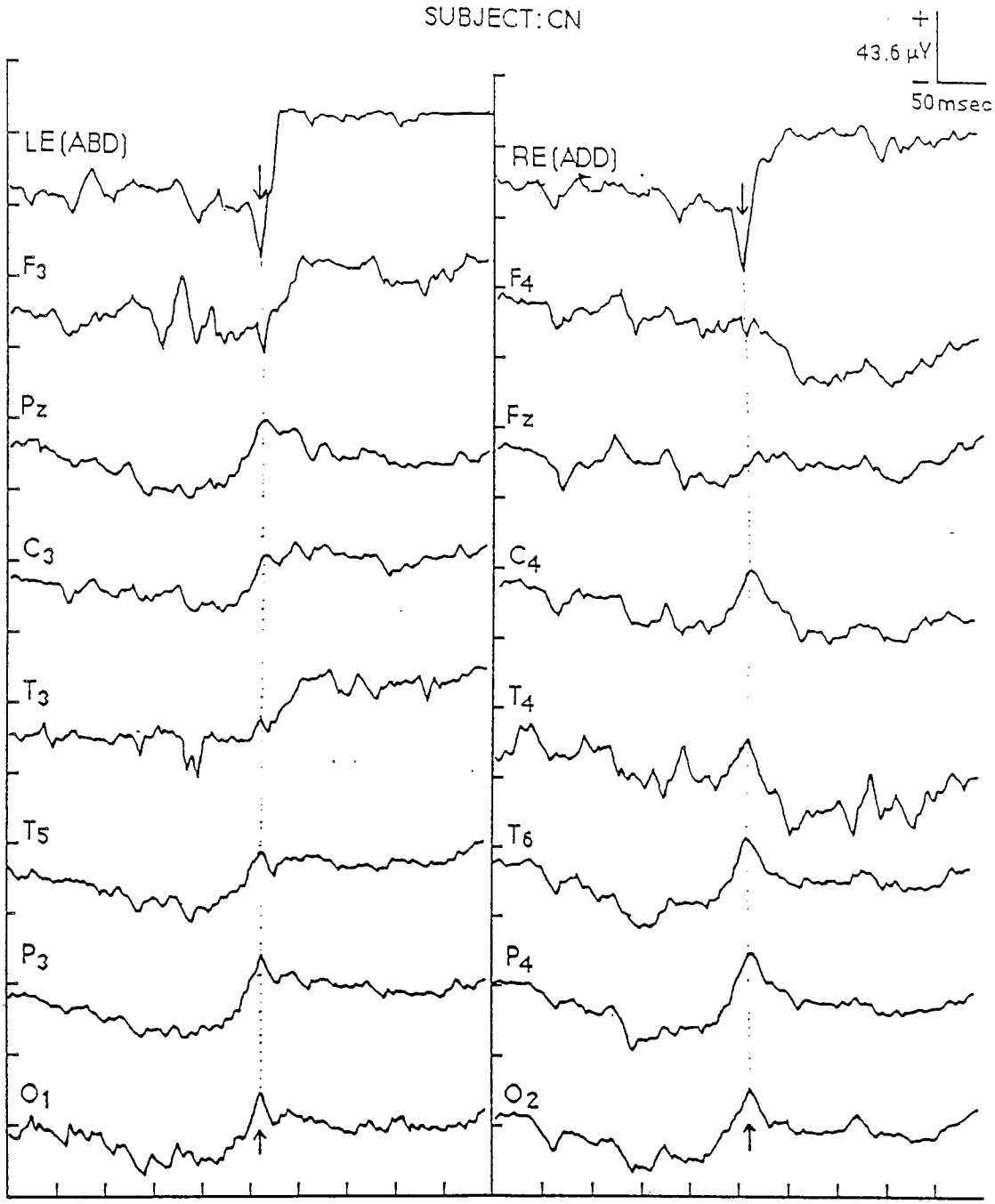

Figure 9.6 Single sweep recording of the presaccadic spike potential activity from 14 electrodes across the scalp and two electrodes below the eyes (top two traces) recorded with a balanced non-cephalic reference. The SP onset is indicated by the arrow. A large frontal negative spike potential can be seen with corresponding smaller posterior positive spike activity. No ECG was recorded in these traces. (Subject CN, right to left saccade).

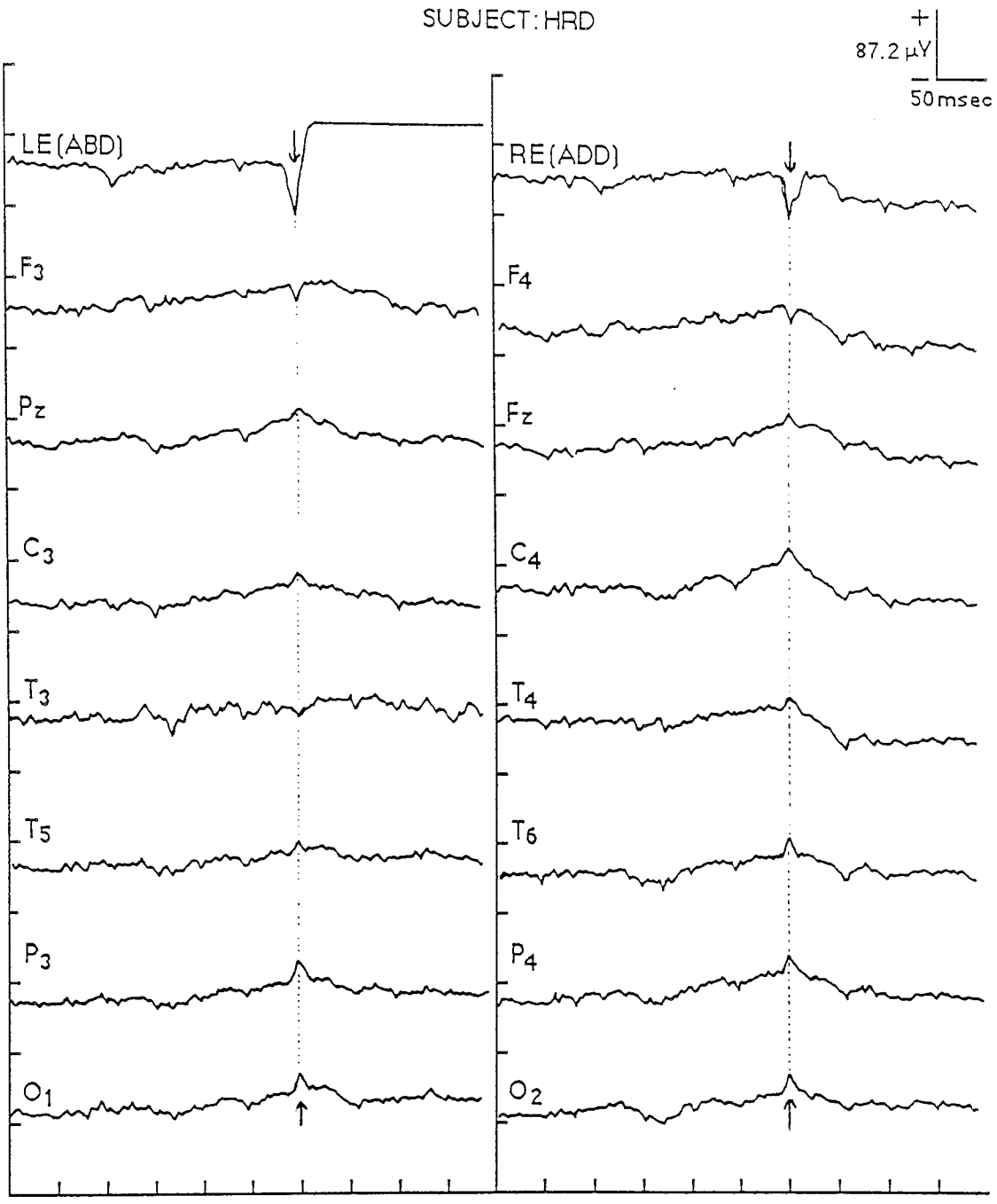

Figure 9.7 Single sweep recording of the presaccadic spike potential activity from 14 electrodes across the scalp and two electrodes below the eyes (top two traces) recorded with a balanced non-cephalic reference. The SP onset is indicated by the arrow. A large frontal negative spike potential can be seen with corresponding smaller posterior positive spike activity. No ECG was recorded in these traces. (Subject HRD, right to left saccade).

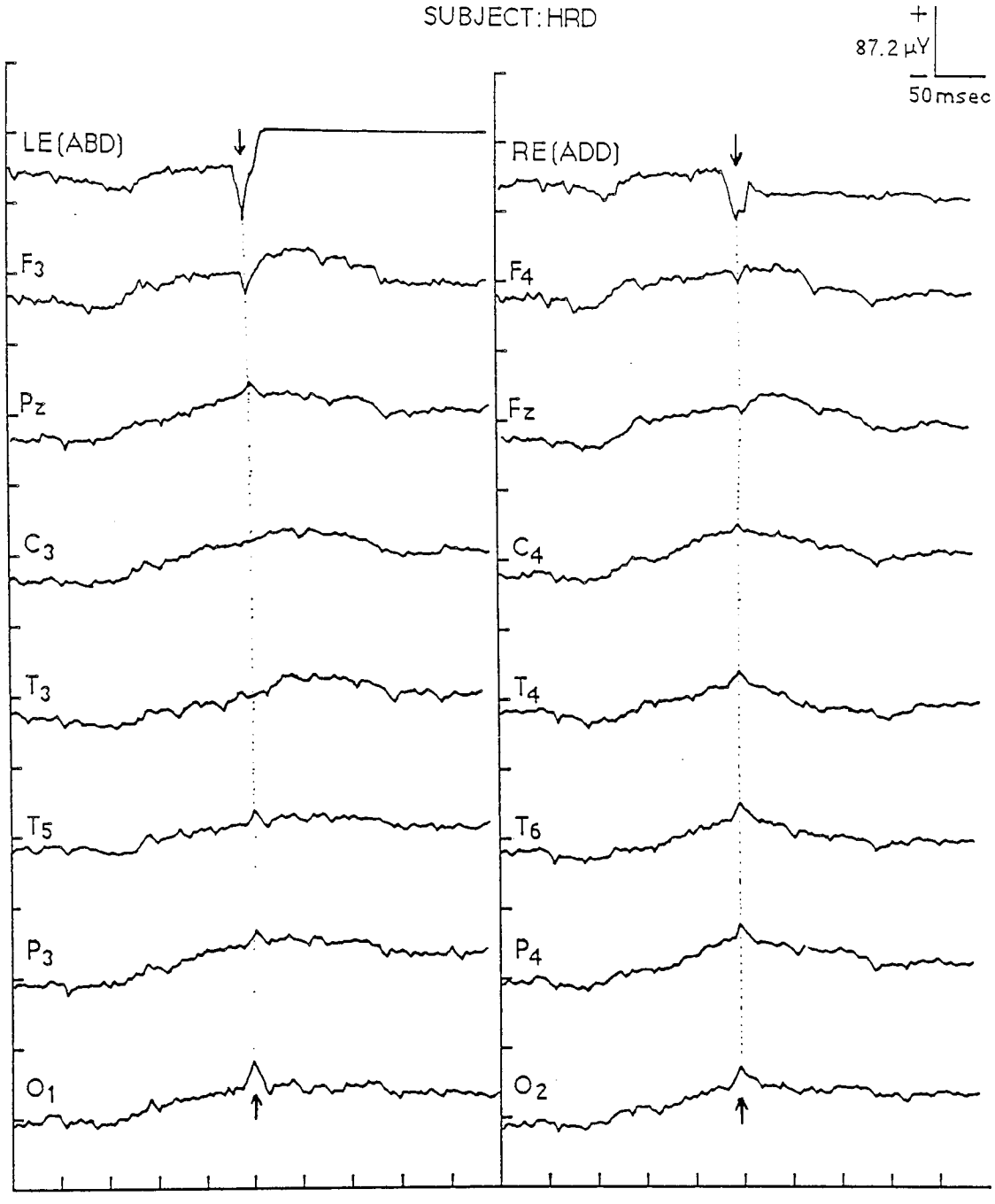

Figure 9.8 Single sweep recording of the presaccadic spike potential activity from 14 electrodes across the scalp and two electrodes below the eyes (top two traces) recorded with a balanced non-cephalic reference. The SP onset is indicated by the arrow. A large frontal negative spike potential can be seen with corresponding smaller posterior positive spike activity. No ECG was recorded in these traces. (Subject HRD, right to left saccade).

A similar pattern of activity to that recorded with the average reference can be seen, with a large frontal negative spike with simultaneous, smaller positive posterior spike activity. In all the recordings the positive spike recorded from the posterior electrodes was much smaller than the frontal negative potential. Like the average reference recordings, the spike potential activity was seen to reduce for electrodes located near the centre of the scalp. The latency values for the SP peaks at each of the recording sites are given in Table 9.2. The latencies given in Table 9.2 are again relative to the eye movement trigger and are therefore dependant upon the saccade latency.

	Electrode Site															
	Re	Le	F_3	F_4	P_z	F_z	C_3	C_4	T_3	T_4	T_5	T_6	P_3	P_4	O_1	O_2
CN	307	306	307	—	307	306	306	305	308	307	307	307	307	306	307	305
CN	317	315	—	316	317	—	316	—	317	315	317	316	317	316	318	315
CN	264	264	—	—	264	—	—	264	264	264	264	264	264	264	264	264
HRD	313	312	313	312	312	313	312	313	—	—	313	312	312	312	313	313
HRD	257	257	257	257	—	—	—	257	—	257	256	257	256	256	257	257

Table 9.2 The SP peak latencies (msec) after the saccade trigger for activity recorded from electrodes below the two eyes (Re, Le) and 14 electrodes across the scalp. A balanced non-cephalic reference electrode was used. Where no latency value is shown indicates no definite spike was evident in the waveforms for that electrode site.

9.4 GENERAL DISCUSSION AND CONCLUSIONS

The recordings presented above demonstrate that the SP is an extremely robust potential, being readily visible even in single sweep recordings of the scalp activity preceding saccades. This is not unexpected when one considers the relatively small numbers of SP recordings required in earlier experiments to produce averaged recordings of the potential from electrodes around the eyes. The recording techniques used in this study can be readily compared to the earlier work of Thickbroom and Mastaglia (1985b). These authors used several electrodes across the scalp to examine the surface distribution of the SP. Although slightly different montages were used with the two reference types in the present study, the waveforms show a similar distribution of activity

over the scalp with a maximum negative spike recorded at the electrodes below the eyes and on the frontal scalp (F_7, F_8, F_4, F_3 with the average reference; F_4, F_3 with the BNC reference) and a corresponding simultaneous widespread positive spike at the electrodes on the posterior scalp (C_3, C_4, T_5, T_6, P_3, P_4, O_1, O_2 with both references). The remaining electrodes on the scalp (P_z, F_z, C_3, C_4 with the average reference; P_z, F_z, C_3, C_4, T_3, T_4 with the BNC reference) exhibited little, or no specific spike activity for any of the recordings. This distribution of spike activity is similar to that reported by Thickbroom and Mastaglia (1985b) who also recorded a maximum negative potential anteriorly with a widespread synchronous posterior positivity. These authors reported that the potential distribution exhibited a polarity reversal along a line extending from the nasion to the ipsilateral temporal region for the eye movement direction, suggesting that the surface topography was dependant upon the saccade direction (Thickbroom and Mastaglia, 1985b). While the SP waveforms recorded in the present study do not appear to alter for different saccade directions, they do exhibit a similar pattern of polarity reversal at the electrodes located on, or near, the mid-line of the scalp (F_z, T_3, T_4,C_3, C_4).

While the waveforms recorded in this study exhibit the characteristic SP waveform they do show, in some cases, a more variable waveform than that recorded in the earlier work. Earlier SP recordings have shown the waveform to occasionally exhibit secondary components, but these were often masked by the eye movement activity. In the present study, the waveforms were less affected by eye movement activity and secondary components of the SP are more readily seen in some of the recordings. These may be genuine components of the SP waveform, or perhaps artefacts due to the single sweep recordings of the scalp activity which would be lost with averaging.

An important observation from this experiment was the effect of the different reference types upon scalp recordings of presaccadic spike potentials. With both the average and BNC reference a distinct frontal SP was recorded from the electrodes round the eyes and on the anterior scalp. With both reference types the posterior electrodes also recorded spike activity, but with an opposite polarity. The posterior spike potential recordings were

more obvious when recorded with the average reference than the when recorded with the BNC reference. This apparent difference in the magnitude of posterior scalp spike activity can be attributed to the reference types. With the average reference, although the two channels below the eyes were omitted from the reference, the large frontal activity will have biased the reference. The large frontal negative potential will have caused the reference to enhance posterior activity if it was positive, or minify the activity if it was negative. As the posterior spike activity has a positive polarity, it will have been enhanced by the average reference montage, as is shown in the waveforms presented in Figures 9.1-9.3. The BNC reference, on the other hand, was not influenced by the magnitude of activity on the scalp and therefore gave a more accurate representation of the respective magnitudes of activity at the different electrode sites. With the BNC reference the posterior spike activity, although having the same distribution, was seen to be smaller in amplitude than that recorded with the average reference.

Examining the waveforms recorded from the different electrode sites, for both reference types, shows the latency of the negative and positive spike potentials to be very consistent. The widespread and diffuse posterior scalp activity is consistent with a far-field recording of frontal activity originating from a specific source, possibly in this case, muscular in origin. This supposition agrees with the earlier work of Tsutsui *et al.* (1987) who suggested that the posterior spike potential shows a far-field potential distribution on the posterior scalp due to strong negative activity anteriorly arising from the supraciliary corrugator muscle. This explanation is flawed, however, when the work of Sato (1968) is considered. In a study of the facial muscles of 620 cadavers Sato (1968) noted that the supraciliary corrugator muscle was completely absent in approximately 18% of the population. While the present study has not examined the SP from as many subjects as Sato (1986), the SP has been successfully recorded in many subjects (>60 in total) with no normal subjects exhibiting an absence of the potential. If the supraciliary corrugator was responsible for the potential it would be expected that the SP would be absent or altered in some subjects, which is not the case. It is more likely, as indicated by other workers (Blinn, 1955; Becker *et al.*, 1972; Riggs *et al.*, 1974; Jäntti and Häkkinen, 1987;

Thickbroom and Mastaglia, 1985b, 1986, 1987) that the frontal SP arises in the extraocular muscles rather than the smaller supraciliary corrugator muscle.

The recordings performed in this study were made for both rightward and leftward saccades to examine the SP latency with the different saccade directions. The latencies of the spike recorded at the different electrode sites can be seen to be very consistent with no apparent latencies difference for spikes recorded from the different electrode sites (Tables 9.1 and 9.2). To allow as many channels of scalp recordings as possible, no specific eye movement trace was recorded in this experiment. It is impossible, therefore, to determine the latencies of the spikes at the different electrode sites with respect to the eye movement start and no analysis can be made of the respective latencies with regard to abducting and adducting saccades.

The latency values and waveforms show the similarity of the frontal and posterior spike potential peaks, confirming the hypothesis that the two may be related to each other. If, as has been suggested, the posterior potential is representative of different cortical centres programming the saccadic eye movement (Weinstein *et al.*, 1988), one would expect the cortical activity to precede the frontal spike potential. This, however, has been shown not to be the case, with identical latencies for the posterior and frontal spike potentials. The similarity of the latencies at all electrode sites and the widespread distribution of the posterior activity both suggest the positive cortical activity is likely to be a far-field recording of the larger frontal negative activity and not a separate posterior spike potential.

The recordings in this experiment confirm the distribution of scalp activity preceding saccades found by Kurtzberg and Vaughan (1980), Thickbroom and Mastaglia (1985b), Tsutsui *et al.* (1987) and Niiyama *et al.* (1988) who have all recorded the scalp distribution of the spike potential. While Thickbroom and Mastaglia (1985b) and Niiyama *et al.* (1988) considered the frontal activity to originate in the extraocular muscles, Tsutsui *et al.* (1987) suggested the supraciliary corrugator muscle. It has been shown that the supraciliary

corrugator is unlikely to be the origin of the SP and it is more likely that activity in the extraocular muscles is responsible for the large frontal negative spike potential.

The widespread distribution of the posterior activity casts some doubt upon the validity of the work of Weinstein *et al.* (1984), Balaban and Weinstein (1985) and Weinstein *et al.* (1988). In their experiments these authors have recorded the posterior scalp activity from two electrodes (P_3 and P_4) and suggested that the posterior spike potential at P_3 and P_4 was representative of programming activity for the saccade. Unfortunately, they apparently gave no consideration to the larger negative anterior spike activity, or the general posterior positivity which can be recorded from electrodes across the whole of the posterior cortex. While it is known that positive activity preceding saccades can be recorded over the posterior scalp, this is the premotor positivity (PMP) occurring some 100 msec before the movement and related to the formulation of the motor plan (Deecke *et al.*, 1976, Thickbroom and Mastaglia,1985a). The positive activity found by Weinstein *et al.* (1984), Balaban and Weinstein (1985) and Weinstein *et al.* (1988) was a sharp, positive, spike potential immediately before the saccade onset. This potential was clearly different to the PMP, and is more likely to have been related to the frontal activity in the manner described above. While it is impossible to say with absolute certainty that the anterior potential is responsible for the posterior positive potential, it would appear that Weinstein *et al.* (1984), Balaban and Weinstein (1985) and Weinstein *et al.* (1988) were incorrect to use only two electrode sites to record the posterior activity and the conclusions from their work, therefore, cannot be totally relied upon.

The recordings in this study, when considered with the earlier work of Thickbroom and Mastaglia (1985b), would suggest that the posterior presaccadic spike potential may not actually exist as a specific potential, but may simply be an artefact due to potential spread of the large frontal negative spike activity. Thickbroom and Mastaglia (1985b) have given more evidence for a non-cortical origin of the posterior spike potential by recording the SP from a patient whose cortical grey matter had been removed from the right cerebral hemisphere. The SP was recorded as having a normal distribution over the cranium for

both saccades to the right and left, arguing against a cortical origin for the potential. If the posterior scalp activity is a far-field recording of the frontal activity this does, however, suggest that the SP may be limited in its potential uses. It has been seen that the SP does not appear to be able to differentiate between different muscles controlling the eye movements and the posterior activity is similar regardless of the electrode sites chosen to record it from. The widespread of the potential across the scalp also implies that there is likely to be cross talk between the two eyes, indicating again that it may be impossible to isolate individual muscle activity with the SP.

9.5 SUMMARY

In this Chapter the distribution of the presaccadic spike potential across the scalp has been examined. The potential has been recorded from a total of sixteen electrodes across the scalp with two different reference electrode configurations. In the initial recordings an average reference was used with the two electrodes directly below the eyes not included in the average. This montage exhibited a distinct frontal spike potential with corresponding posterior spike activity from the electrodes across the scalp. The magnitude of the posterior activity was greater than that recorded when a balanced non-cephalic reference was used. The waveforms recorded were all single sweep recordings as it was impossible to back-average the sixteen channels of spike activity recorded in each recording sweep.

Although the latency of the SP could not be determined with respect to the saccadic eye movement, it was obvious that the posterior and anterior activity shared the same peak latencies with respect to each other (see Tables 9.1, 9.2). This, and the surface distribution of the spike waveform over the scalp, confirms the earlier findings of a maximum negative potential at the anterior scalp with a smaller, simultaneous, positive posterior potential. The polarity reversal of the waveforms, just behind the orbits, indicates that the origin of the potential may indeed be located within the orbital region confirming the suggested origin of the SP as the extraocular muscles.

The widespread distribution of the potential across the posterior scalp is similar to the expected distribution of a far-field recording of an anterior potential and it is obvious that recordings of posterior scalp activity must be made with the larger anterior negative potential borne in mind. This, unfortunately, has not always been the case and earlier studies of posterior presaccadic scalp activity must be treated with caution.

The results of this study, and the earlier work to examine the topography of the SP, indicate that the posterior and anterior spike potentials are probably the same potential, the smaller posterior spike arising due to potential spread across the scalp. The widespread nature of the SP may, however, limit any clinical applications which the recording may have and the following Chapter will describe recordings of the SP from subjects with known eye movement anomalies to determine the effect these have on the SP recording.

CHAPTER 10

THE SPIKE POTENTIAL RECORDED FROM SUBJECTS WITH ANOMALOUS EYE MOVEMENTS

10.1 INTRODUCTION

The previous Chapters in this thesis have described the presaccadic spike potential (SP) when recorded from electrodes around the eyes in normal subjects. This negative spike has been shown to have similar waveforms when recorded from electrodes at the inner canthus, outer canthus, above the eye and below the eye and has an onset between -30.0 to -4.4 msec before the beginning of a saccade, peaking at between -7.8 msec before and 7.8 msec after the beginning of the saccade. At all electrode sites the latencies for adduction movements are earlier than those for abduction movements, although this is not always statistically significant. The onset-peak amplitude has been found to increase with the size of the eye movement for saccades up to 40° in magnitude although the change is not linear.

The SP is thought to originate in the extraocular muscles; from the muscle units or ocular motoneurons that innervate these units (Thickbroom and Mastaglia 1985b, 1986, 1987; Riemslag *et al.*, 1988). The majority of work has involved the examination of normal subjects and the behaviour of the SP parameters in such subjects has been used to support the proposed origin of the potential (Thickbroom and Mastaglia 1985b; Riemslag *et al.*, 1988). In addition, a computer model based upon motor unit recruitment patterns has supported the theory that the SP arises from the burst of motoneuron activity that precedes saccades (Thickbroom and Mastaglia 1987).

Recording the SP in subjects with known extraocular muscle defects may give additional information regarding the behaviour of the SP and how it reflects motoneuron activity but recordings in such patients are limited. Thickbroom and Mastaglia (1985b), for example,

have recorded the SP from two subjects with lateral rectus palsies, two patients with ocular prosthetics and a single patient with an exenterated orbit. In the case of the two lateral rectus palsies, SPs were recorded from the palsied eye using the normal eye for fixation. Thickbroom and Mastaglia (1985b) reported that normal SPs were recorded when the palsied eye adducted but with abduction the waveform was markedly attenuated and broadened with the attenuation less severe in the presence of a partial rather than a complete palsy. Unfortunately no waveforms or SP data were given for comparison purposes.

The information given regarding the two subjects with prosthetic eyes is also very limited. Although Thickbroom and Mastaglia (1985b) reported a normal SP distribution was found for horizontal saccades in both directions, they did not indicate where this distribution was recorded from. If the electrodes were placed only around the remaining eye, a normal SP distribution would be expected. When the patient with a right extenerated orbit was discussed Thickbroom and Mastaglia (1985b) indicated that a normal SP was recorded from electrodes at the left inner and outer canthus with saccades to the left, while with saccades to the right an attenuated SP was recorded, having a maximum amplitude at the left inner canthus. No details of any recordings made round the right eye were given. It would be particularly useful in all these studies to have been given more details of not only the SP waveform and parameters from the normal eye, but also to compare the results to those obtained from recordings round the abnormal eye.

Having recorded the SP from many normal subjects under a variety of recording conditions, it was felt that it would be beneficial for this research project to also record the SP from subjects with eye movement disorders. This would allow the SP to be more fully assessed in such conditions and allow a comparison of the SP parameters and waveforms for these subjects with the known normal values. Such a comparison may give information as to any possible clinical uses which the SP may have in monitoring the electrophysiological activity of the EOM.

10.2 THE PRESACCADIC SPIKE POTENTIAL RECORDED FROM A PATIENT WITH A LEFT LATERAL RECTUS PALSY

In their earlier study, Thickbroom and Mastaglia (1985b) recorded the SP from two subjects with left lateral rectus palsies. Thickbroom and Mastaglia (1985b) unfortunately gave very little information of the recording conditions used to monitor the SP activity from these subjects. The size of eye movements performed is unknown and no details of the recording electrode sites were given.

Recording the SP from a subject with a lateral rectus palsy may be useful because the lateral rectus is unusual when compared to most of the other EOM in that it is singly innervated from one cranial nerve, the VIth nerve. This one-to-one ratio of innervation implies that if the SP is related to muscle activity, any observed changes in SP activity must result from changes in the lateral rectus only. While the results of recordings in the previous Chapters imply that it may be difficult to isolate SP activity specific to individual muscles recording the SP from patient with a lateral rectus palsy may show that the SP does alter with changing activity of specific muscles.

Lateral rectus palsies are the most common form of ocular muscle paresis, the long and vulnerable course of the VIth nerve making it particularly susceptible to damage (Duke-Elder 1973). Patients with a unilateral lateral rectus palsy often exhibit a compensatory head tilt towards the affected side in an attempt to maintain binocular fixation (Duke-Elder 1973).

10.2.1 SUBJECT DETAILS AND METHODS

The SP was recorded from a 22 year old male student with a left lateral rectus palsy which, as far as could be ascertained, had been present from birth. The subject had undergone regular ophthalmological examination until 10 years of age but had had no orthoptic or surgical treatment. There was no history of birth trauma, no family history of ocular

problems and no other ophthalmological or neurological defects. Unaided visual acuities were 6/5 in both eyes and, with the head in its habitual position, there was no strabismus at distance or near. The subject did have a slight compensatory head turn to the left and, with his head in the straight ahead position, a small angle strabismus was evident. Motility of the right eye was full, as was left eye adduction, but abduction of the left eye was weak. Saccadic movements to the left could however be attempted by the left eye.

Spike potentials were recorded using the usual system described in Chapter 4, with an electrode below the eyes recording the SP activity and a P_Z reference. The eye position was monitored by electrodes at the inner and outer canthi of both eyes and the SPs for 20° saccades were recorded. The reduced ability of the left eye to perform abducting saccades meant that the saccade records for eye movements in this direction did not always exhibit a distinct saccade onset. To examine the effect that this may have on the averaging procedure the SPs were averaged using both the fixating eye and the non-fixating eye EOG records to determine the saccade onset. Recordings were made, therefore, in four different conditions; from the right eye with the right eye fixating, from the right eye with the left eye fixating, from the left eye with the left eye fixating and from the left eye with the right eye fixating. In each case the non-fixating eye was occluded.

The individual saccadic traces and the SPs were recorded as before, on separate channels of the Pathfinder with a time sweep of 500 msec and a bandpass filter with a low cut off of 0.50 Hz and a high cut off of 100 Hz. The SP latencies and onset-peak amplitudes were measured as usual.

10.2.2 RESULTS

The waveforms obtained in each recording condition are shown in Figures 10.1 and 10.2 and the results obtained with each recording situation will be considered in turn.

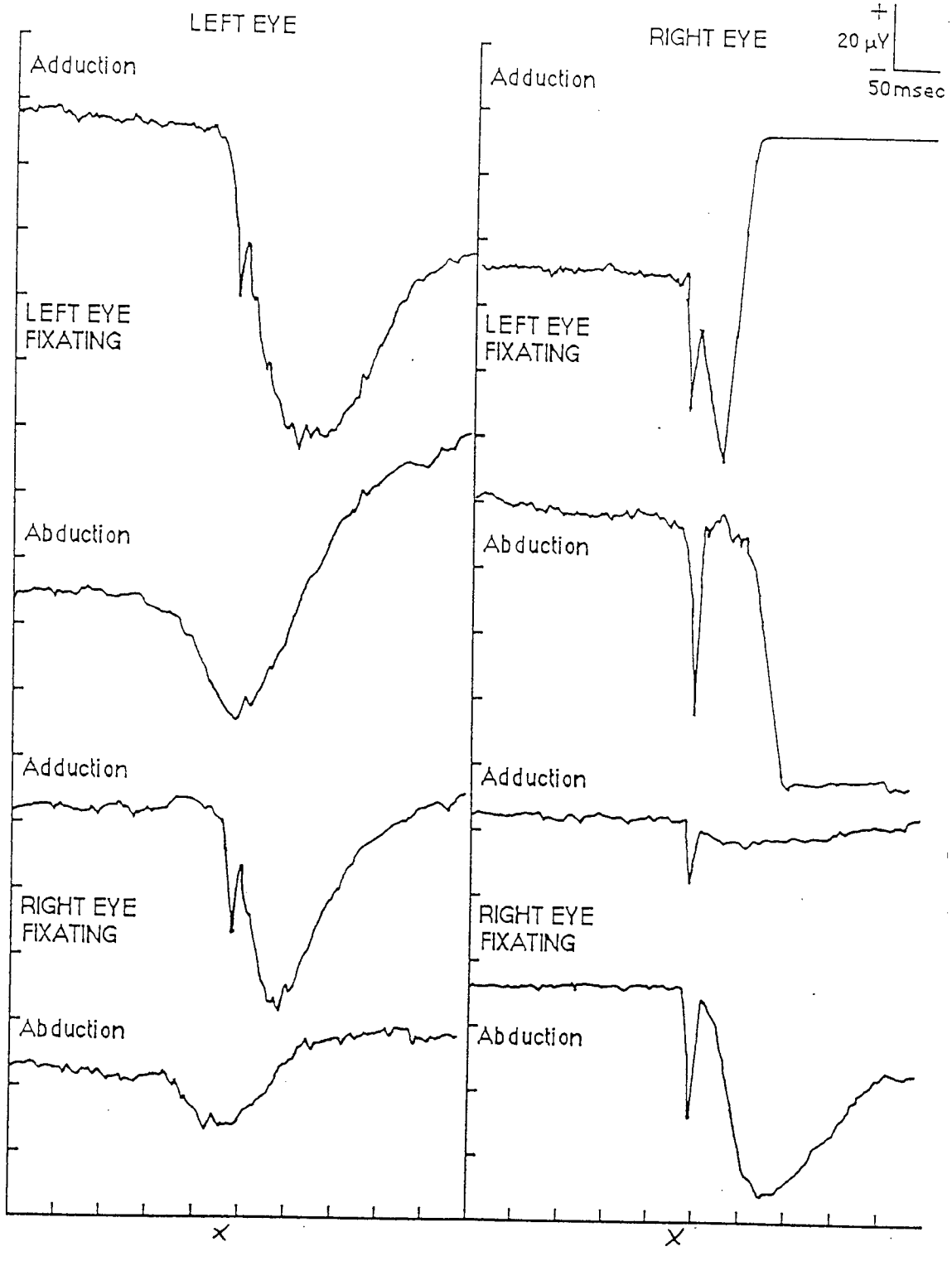

Figure 10.1 The spike potential recorded from the left and right eyes with each eye fixating for 20° horizontal saccades. In each case the direction of movement given (abduction or adduction) refers to the direction of movement of the eye from which the SP was recorded as indicated by the top titles. The eye position was monitored in the eye from which the SPs were recorded. The waveforms recorded from the left eye with abduction show little SP activity, while those recorded with right eye adduction were of reduced amplitude. The saccade onset is indicated by the cross.

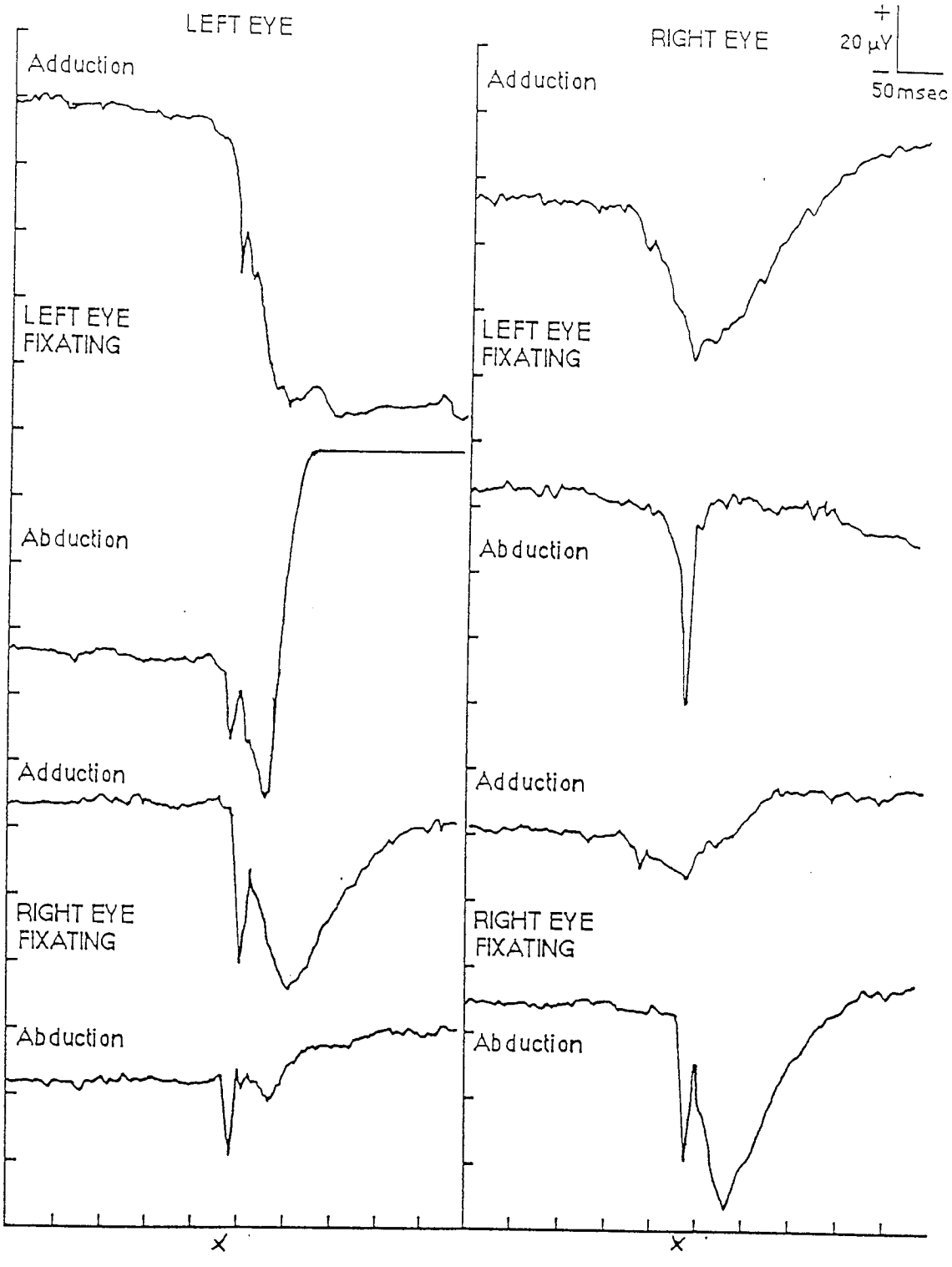

Figure 10.2 The spike potential recorded from the left and right eyes with each eye fixating for 20° horizontal saccades. In each case the direction of movement given (abduction or adduction) refers to the direction of movement of the eye from which the SP was recorded as indicated by the top titles. In these recordings the eye position was monitored in the eye from which the SPs were not recorded. An SP was recorded from the left eye with abduction although it was smaller in amplitude than that recorded adduction. The SP recorded with right eye adduction were poorly formed in these recordings. The saccade onset is indicated by the cross.

Recordings from the right eye with the right eye fixating showed a normal SP waveform with an onset -7.0 msec before the saccade start with abduction and -9.0 msec before the saccade start with adduction. The peak occurred -3.0 msec before the saccade onset with adduction and 4.0 msec after the saccade onset with abduction. The onset-peak amplitude was greater with abduction (43.2 μv) than adduction (20.3 μv) (Figure 10.1).

Recordings from the left eye with the left eye fixating showed a clear spike with adduction (onset -16.0 msec, peak -6.0 msec before the saccade start; amplitude 42.2 μV). With abducting saccades, however, no clear spike potential was seen (Figure 10.1).

Recordings from the left eye with the right eye fixating also showed a clear spike with left eye adduction, (onset -17.0 msec, peak -5.0 msec before the saccade start; amplitude 37.4 μv), but there was no definite SP with abduction (Figure 10.1).

Recordings from the right eye with the left eye fixating showed a clear spike with abduction (onset 8.0 msec before the saccade start, peak 1.0 msec after the saccade start; amplitude 61.8 μv) and a smaller amplitude spike with adduction (onset -13.0 msec, peak -4.0 msec before the saccade start; amplitude 48.6 μV) (Figure 10.1).

Figure 10.2 shows the second set of recordings made when eye position was monitored in the eye from which the spikes were not recorded. These recordings were performed to establish any effect that poorly defined saccades may have had on the SP averaging procedure. Recordings from the right eye with the right eye fixating showed a clear spike on abduction (onset -20.0 msec, peak -6.0 msec before the saccade start; amplitude 47.4 μv). Only a very low amplitude deflection was found on adduction.

Recordings from the left eye with the left eye fixating showed a high amplitude spike on adduction (onset -18.0 msec before the saccade start, peak 1.0 msec after the saccade

start; amplitude 42.6 μv). On abduction a lower amplitude spike was recorded (onset -14.0 msec, peak -3.0 msec before the saccade start; amplitude 21.8μv) (Figure 10.2).

Recordings from the left eye with the right eye fixating also showed a high amplitude spike on adduction (onset -10.0 msec, peak -2.0 msec before the saccade start; amplitude 50.9μv). On abduction a lower amplitude spike was found (onset -13.0 msec, peak -3.0 msec before the saccade start; amplitude 25.1 μv) (Figure 10.2).

Recordings from the right eye with the left eye fixating showed a clear spike on abduction (onset -17.0 msec, -peak 6.0 msec before the saccade start; amplitude 47.9 μv) but only a broad negative deflection on adduction (Figure 10.2).

10.2.3 DISCUSSION AND CONCLUSIONS

With the initial recordings shown in Figure 10.1, a poorly formed spike was recorded with left eye abduction compared to right eye abduction suggesting that there may have been changes in the SP activity with attempted left abduction. The later recordings shown in Figure 10.2, however, reveal that relatively normal SPs were recorded with left eye abduction when the eye position was monitored in the right eye. The most likely reason for this can be related to the use of the eye movement record to trigger the onset of the back-averaging. When the left eye was fixating and attempted abducting saccades, these eye movements would not have the rapid acceleration phase found in a normal saccadic movement. Consequently, although it was possible to identify the beginning of the eye movement on the EOG trace its position would be subject to slight variance leading to errors in the back-averaging process. This problem was further shown in the recordings from the right eye during adduction with the left eye fixating. If eye position is monitored in the right eye (Figure 10.1) clear SPs are recorded but if the left eye is used (Figure 10.2) only a poorly formed spike remains.

Considering the conditions where clear spikes were recorded from both eyes, it was

apparent that the SPs recorded from the left eye on abduction were of reduced amplitude compared to those of both left eye adduction and right eye abduction. A similar situation was also seen in the spike recorded during right eye adduction which had a much reduced amplitude compared to that recorded during right eye abduction and left eye adduction. The previous studies in this thesis have shown that, in normal subjects, there are no statistically significant differences in SP amplitudes with abduction and adduction although there is a trend for adduction spikes to be of greater amplitude. The findings in the subject are in contrast with these results and suggest that changes may have occurred within the motor system to reduce the amplitude of the spike. These changes not only occur during left eye abduction but also during right eye adduction suggesting that alterations may have occurred in the recruitment pattern to the extraocular muscles of this eye during adduction when the eye is moving into the field of action of the defective left lateral rectus.

A possible explanation for these amplitude reductions may be found in the results obtained in Thickbroom and Mastaglia's computer simulation of motor unit activity that precedes saccades (Thickbroom and Mastaglia 1987). Within this model, Thickbroom and Mastaglia observed that changes to the model parameters cause variations in the SP amplitude. The SP amplitude could be made to reduce by increasing the recruitment dispersion of the motor units (see Figure 3.15a). Alternatively, if the duration of the second, positive, component of the action potential waveform was decreased, the amplitude of the SP decreased.

It could be hypothesised that the innervation to the palsied muscle (left LR) of this subject has altered such that the motor units are not recruited as simultaneously as those of the normal muscles, leading to a reduced SP amplitude. The reduction in SP amplitude for right eye adduction may be caused by secondary changes to the innervation to the contralateral agonist (right MR) to avoid over action of this muscle when looking to the left. While the exact nature of the reduction in SP amplitude is unknown, the above recordings did indicate that the potential may be affected by different levels of muscle activity when

the eye is moved into the 'on-direction' of muscles which are receiving some form of anomalous innervation compared to normal muscles.

The SP recordings from this subject clearly demonstrate the effect of trigger jitter on the back-averaging procedure. The recordings which were back-averaged using the left eye abducting EOG traces to locate the saccade onset exhibited grossly abnormal SP waveforms due to the lack of an accurate eye movement onset for the averaging trigger. While this indicates that care must be taken to ensure that the saccade is accurately identified, it does also, however, confirm the accuracy of this method of back-averaging the SP under normal conditions. The result of SP recordings from this patient suggest that the SP may alter with changing muscle activity and this should be confirmed by further recordings from patients with different conditions affecting the EOM to discover the exact changes which occur in such conditions.

10.3 THE PRESACCADIC SPIKE POTENTIAL RECORDED FROM A PATIENT WITH MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a chronic disabling disease which attacks the Central Nervous System (CNS) causing severe and permanent demyelination of nerve axons. Multiple sclerosis accounts for some 228,000 consultations to GPs annually and the prevalence of the disease has been variously estimated to be between 50,000 to 100,000 people within the UK (O'Brien, 1987). The uncertainty over the number of people affected by the condition in the UK can be attributed to the fact that a definitive diagnosis of MS can only be made from the pathological findings of a postmortem examination (O'Brien, 1987).

The symptoms of MS have been well documented and one of the earliest symptoms in approximately 15-20% of cases is optic neuritis (ON) (Shibaski, McDonald and Kuroiwa, 1981; O'Brien, 1987), while approximately 50% of all multple sclerosis patients will have a clinical attack of ON during the course of the disease (McAlpine, Lumsden and Acheson, 1972). That MS should affect the optic nerves can be understood when it is remembered

that these nerves are part of the CNS. MS causes a transient blurring of the vision in one, or both eyes,usually worsening over 1-2 weeks, persisting for 2-3 weeks, with a subsequent reduction in the blurring over a period of 2-3 months (O'Brien, 1987). This remission over time is characteristic of MS, both when affecting the eyes and other parts of the CNS, although it is also usual to have subsequent relapses in the condition.

The other symptom of MS which is of interest with regard to the eyes and in particular this thesis, is the effect that this condition has upon eye movements due to lesions of the medial longitudional fasciculus (MLF). The MLF plays an important role in the innervation of horizontal saccades by allowing the transfer of horizontal eye movement commands from abducent internuclear neurons to the medial rectus subdivision of the contralateral oculomotor nucleus (Leigh and Zee, 1983) (see Figure 2.8). If the MLF suffers a lesion this will interfere with the innervation of eye movements, the effect on the movements depending upon the nature of the lesion. Internuclear Ophthalmoplegia (INO) is the condition resulting from lesions of the MLF and this is often observed in MS patients.

Unilateral INO lesions result in weakness of the ipsilateral MR, ranging from a complete inability to adduct the affected eye resulting in transient diplopia, to a minimal reduction in adducting saccade peak velocity with little or no other ocular symptoms. In the contralateral eye to the MLF lesion it is usual to observe nystagmus on abduction of that eye and various proposals have been given to account for this. It has been suggested that the nystagmus may be due to factors such as impaired inhibition to the contralateral MR; adaptation to the contralateral MR undershoot or interruption to the descending fibres to the contralateral abducent nucleus (see Leigh and Zee, 1983). Bilateral INO causes bilateral adduction weakness and bilateral abduction nystagmus (Leigh and Zee, 1983)

While MS does not directly affect the extraocular muscles, the innervation to these muscles is clearly altered in the presence of this disease. There have been no reported attempts to record the SP in conditions such as MS and it would be interesting to observe if any changes occur in the SP recording with this condition. If, as has been suggested,

the SP is representative of the motor impulse to the EOM, it could be supposed that the SP recorded from subjects with this condition may exhibit changes related to the anomalous eye movement control signals being sent to the EOM.

10.3.1 SUBJECT DETAILS AND METHODS

The subject, Mr AF (D.o.B. 24/9/52), was referred to Aston by an optometrist in private practice who was interested in spike potential recordings. Mr AF had been diagnosed as suffering from MS approximately 10-15 years ago and presented with classic signs of the condition. As well as the ocular signs described below, Mr AF also exhibited difficulty walking, reduced strength and some numbness of his limbs.

Gross examination of his ocular motility revealed limited activity of both eyes with adduction and nystagmus of the contralateral, abducting eye. The near point of convergence of the patient was poor (approximately 15 cm) and there was a small near exophoria (approximately 5 Δ). The corrected vision of this patient was RE 6/9, LE 6/12.

The spike potential was recorded using the standard recording technique from electrodes at the inner and outer canthi of both eyes and above and below the eyes. The electrode sites were prepared in the usual manner and P_z was the reference electrode site. A well known sign of MS is increased saccade latency (Mastaglia, Black and Collins, 1979), so the longer time sweep of 1000 msec was used during recordings of the SP. The electrodes at the inner and outer canthi were also used to record the latency, peak velocity and magnitude of the saccades.

10.3.2 RESULTS

It should be noted that throughout all the recordings from this patient a definite saccadic eye movement with a distinct onset was recorded from the electrodes at the inner and outer canthi of the respective eyes. This information is important because the presence of

a definite saccade onset has been shown to be an essential factor in the accurate back-averaging of the SP (see 10.2.4). The spike potential itself, however, was not always obvious when compared to the eye movement to which it was related. The SP waveforms from the eight electrodes sites and the two saccade directions are shown in Figures 10.3 and 10.4. The waveforms given in these figures indicate that the SP from the left eye did not appear to be greatly affected in the presence of MS. With the right eye, however, differences can be seen between the abducting and adducting recordings. There are also some differences between the waveforms from the two eyes.

If the traces for the right eye are considered for abducting and adducting saccade SPs, it can be seen that no definite SP can be seen with adducting saccades for all electrode sites (Figure 10.3).

The SP amplitude values for the right eye recorded with abducting saccades were between 25.9-40.5 μV, (inner canthus 40.5; outer canthus 25.9; above the eye 33.8; below the eye 27.8) while no amplitude values could be recorded for the adducting saccades. The latency of the SP onset was between -11 to -12 msec before the saccade start for the abducting saccades (inner canthus -11; outer canthus -11; above the eye -11; below the eye -12).

When the waveforms for the left eye were considered, however, it was seen that clear SPs were recorded from all electrode sites with both saccade directions. The amplitude values for left eye abducting saccades were between 16.1-20.5 μV, (inner canthus 20.5; outer canthus 16.9; above the eye 17.9; below the eye 18.3) while the amplitudes for adducting saccades were between 16.1-28.1 μV, (inner canthus 16.1; outer canthus 26.7; above the eye 18.4; below the eye 28.1). The adducting SP onset was -12 msec at all electrodes except below the eye where the onset was -10 msec before the saccade start. With abducting saccades the SP onset was -10 msec at all electrode sites.

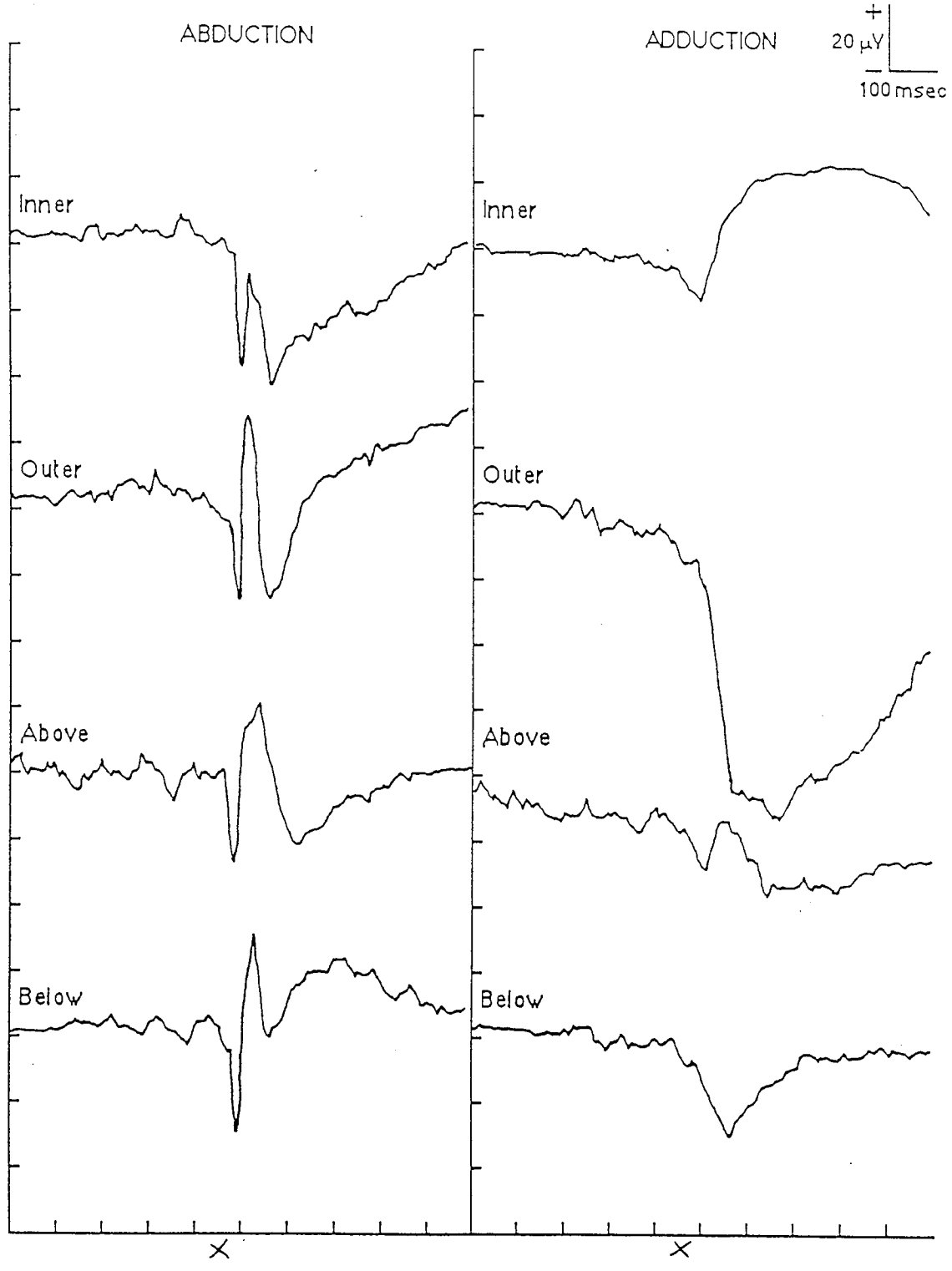

Figure 10.3 The spike potential recorded at four electrodes around the right eye from a patient suffering from multiple sclerosis. Both abducting and adducting saccade spike potentials are shown. The saccade onset is indicated by the cross.

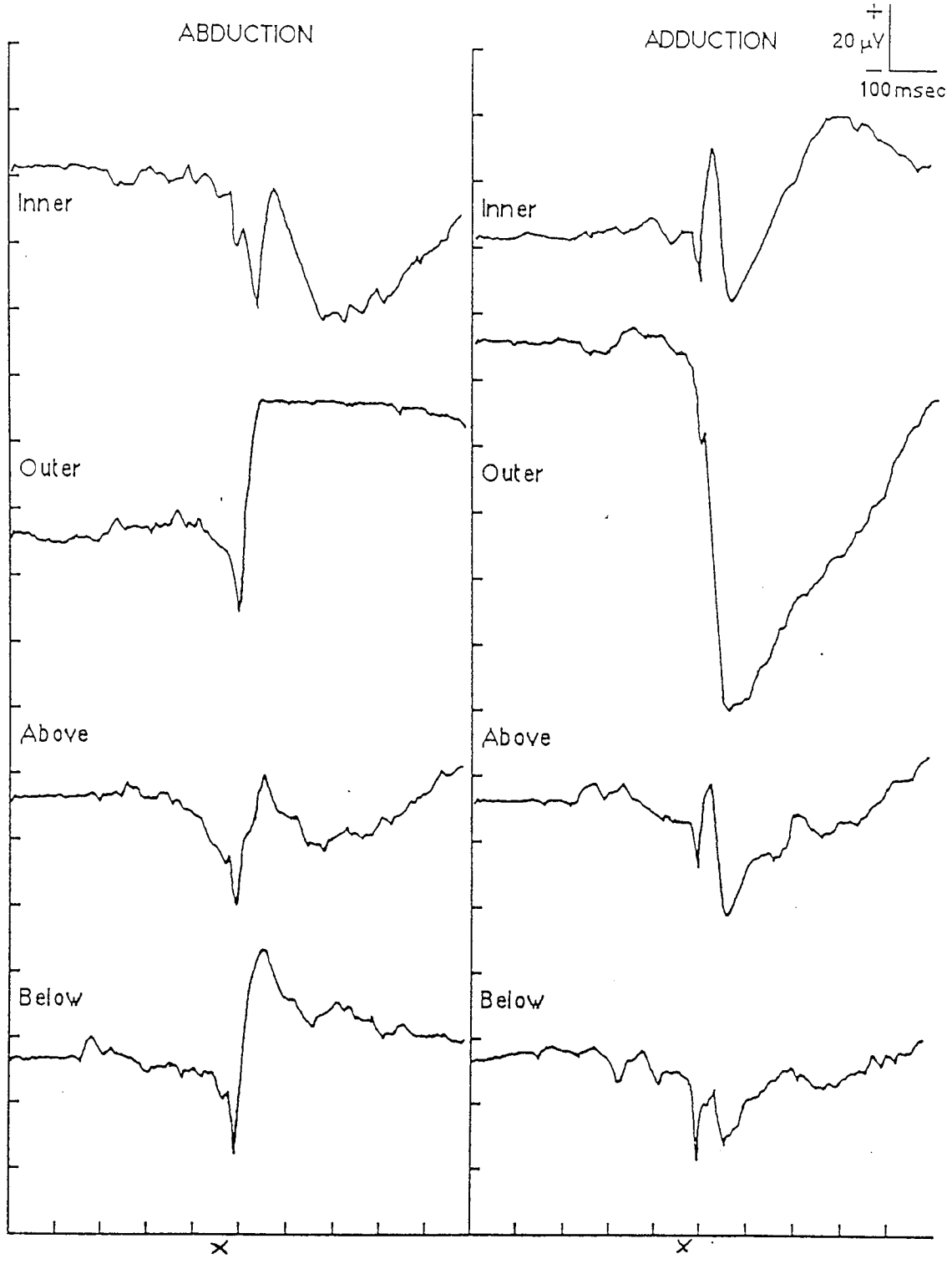

Figure 10.4 The spike potential recorded at four electrodes around the left eye from a patient suffering from multiple sclerosis. Both abducting and adducting saccade spike potentials are shown. The saccade onset is indicated by the cross.

In addition to recording the SP from this subject, the electrodes at the inner and outer canthi of both eyes were used to record the EOG to examine the saccade parameters. A separate program, developed for routine clinical analysis of saccadic eye movements, was used to examine the saccades of this patient. Eight saccades were averaged (4 abducting and 4 adducting) for the two eyes. The Pathfinder was set with a high cut-off of 70 Hz, a DC low cut-off and a time sweep of 1000 msec. Following recordings the saccade onsets and offsets were identified with the averager's cursor allowing the saccade latency, peak velocity, duration and peak acceleration to be calculated. The respective values for these components are shown in Table 10.1.along with the normal values recorded with this program and apparatus. It is clear from Table 10.1 that many saccade parameters recorded from the subject with MS differed from the mean normal values, but of greater importance is the observation that several parameters differed from the normal values by more than two standard deviations. These are identified by an asterisk in the Table.

	LATENCY	DURATION	ACCELERATION	VELOCITY
LE abd	292.0* (212.7)	74.5 (62.6)	14861.4 (17167.5)	448.4 (451.8)
LE add	363.0* (231.8)	59.0 (55.3)	18387.9 (22108.0)	448.4 (572.4)
RE add	316.0* (208.7)	66.0 (54.3)	9403.8* (15716.7)	325.4* (568.6)
RE abd	302.0* (217.6)	55.5 (65.5)	16624.6 (19458.3)	578.7* (436.6)

Table 10.1 The saccade latencies (msec), duration (msec), acceleration (deg/sec^2) and peak velocities (deg/sec) for saccades to the right and left (Subject AF). The figures in brackets to the right of each column are the normal values for the same saccade parameters.

10.3.3 DISCUSSION

The saccade latency values given in Table 10.1 are not unusual for a patient suffering from multiple sclerosis as Mastaglia *et al* . (1979) have reported that saccade latencies are increased in patients suffering from this condition. Likewise, reduced adducting saccade peak velocity is a common finding in patients with INO (Metz, 1976; Baloh, Yee and Honrubia, 1978; Bradford, 1981), and it has been observed that INO is a common feature of patients with MS (Leigh and Zee, 1983). While these saccade findings are to be

expected, there has been no previous report of the SP recorded from a patient with MS. The reduced right eye adduction and coincident left nystagmus with abduction, along with the abnormal saccade parameters shown in Table 10.1 suggest that this subject may have unilateral INO affecting the right eye.

In Figure 10.3, the SP waveforms recorded from the right eye show a large and distinct SP waveform for right eye abduction at all the electrode sites, but with adducting saccades there is a more general deflection with no specific onset or peak. Indeed, at many of the electrodes round the eye no SP can be seen in the waveforms recorded during right adduction. The left eye, on the other hand, shows clear SP waveforms for both saccade directions, albeit with a general reduction in the onset-peak amplitudes. The presaccadic spike potentials presented in Figures 10.3 and 10.4 may be explained on the basis of this interpretation of the eye movement parameters of this subject.

A tentative relationship can be drawn between the SP waveforms and the saccade parameters given in Table 10.1. The reduced peak velocity of the right adducting eye movements and abnormal SP recorded with right eye adducting saccades may possibly be related, while the larger SP recorded for right abducting saccades may be associated with the faster abducting saccade peak velocity. For the left eye, where the SP waveforms and parameters were more consistent, the saccade parameters are more closely related to the normal values except for the prolonged latency and slightly reduced left adduction peak velocity (see Table 10.1).

The known changes in saccade parameters has prompted the use of eye movement recording as an additional tool in the diagnosis of INO. In the present study the saccade parameters would confirm the presence of changes to the saccade innervation in this subject. The SP waveforms also exhibit differences from the waveforms recorded from normal subjects. Unfortunately, it is difficult to attribute the SP differences to a single specific cause. The apparent relationship between the reduced right adduction saccade velocity and the abnormal SP recorded with these eye movements must be explained. It is

possible that the reduced SP may simply be a reflection of the reduced muscle activity associated with the slower saccades or alternatively, the abnormal SP activity may be more closely linked with the anomalous innervation resulting from the INO. The fact that the SP amplitude is larger for the abducting saccades which were dramatically faster than the adducting eye movements of the right eye and both saccade directions of the left eye suggests that the former hypothesis may be the correct suggestion.

A relationship between SP activity and saccade velocity has been implied previously in this thesis during the recordings of the SP with different saccade sizes and different age groups. It was seen in Chapter 2 that saccade peak velocity increases with increasing saccade size (2.2.2) and decreases slightly with advancing age (2.2.2). When the SP was recorded for smaller saccade sizes, it was observed that the amplitude of the potential decreased compared to that for larger saccades. During these recordings no measurements of the saccade peak velocities for the different eye movement sizes were recorded or calculated, but the literature implies that the smaller saccades were slower than the larger eye movements (2.2.2). The SP amplitude has also been shown to fall when the potential is recorded from elderly subjects with little change between middle aged and young subjects. Although it is less definite that saccade peak velocity falls with advancing age the literature implies that there may be a reduction in peak velocities with older as opposed to middle ages subjects (2.2.2).

The changes in the SP waveform with the right eye adducting are not simply a reduction in amplitude, however, and while a decrease in SP amplitude can possibly be explained in terms of changes in saccade velocity, this does not account for the absent or broadened SP waveform. For a possible explanation of this we must re-consider the computer model of SP activity proposed by Thickbroom and Mastaglia (1987). These authors found the SP amplitude was reduced and the waveform broadened when the recruitment dispersion of the motor units within the EOM was increased (3.2.3). The waveforms found when the recruitment rate was increased are not dissimilar to those given in Figure 10.3 for the right

eye adducting and it can be hypothesised that the abnormal SP recorded with adduction may have occurred as a result of changes to the innervation of the right medial rectus

Unfortunately, there is no evidence in the literature that the recruitment rate of EOM motor units does alter in MS although this could be expected with the reduced velocity of the action potentials found in this disease. It is conceivable that the reduced action potential velocities in MS may lead to a less synchronous activation of motor units in the EOM than would be found in normal subjects. A reduced synchronicity of the motor unit activation can be considered the same as an increased dispersion of recruitment rate of the motor units. It is evident from the present study that further studies are required of both the SP recording in MS and the motor unit activation of the EOM in normal and abnormal subjects.

10.4 THE SPIKE POTENTIAL RECORDED FROM A PATIENT WITH AN ENUCLEATED EYE

It was shown by Thickbroom and Mastaglia (1985b), that the SP could be recorded with a normal distribution for saccades in both horizontal directions from a patient with an artificial eye. Thickbroom and Mastaglia (1985b) suggested that the SP recorded at electrodes round the prosthetic eye argued against a purely ocular, i.e. retinal or electrooculographic, origin of the potential, but they could not discount a muscular origin as both their subjects with prosthetic eyes did have some functioning EOM remnants attached to the prothesis.

The only way to be certain that there can be no muscle activity after orbital surgery is when the orbit is totally cleared of all ocular and muscular tissue; an extenerated orbit. Unfortunately we were unable to obtain a subject with an extenerated orbit, but we did obtain a patient with a recently enucleated eye fitted with a prosthesis. This subject also had some muscle tissue still present which was attached to the prosthetic eye, so we could only repeat the earlier work of Thickbroom and Mastaglia (1985b) with the aim of providing more comprehensive results for this recording condition.

10.4.1 SUBJECT DETAILS AND METHODS

The subject, Mrs LH (D.o.B. 2/6/15) was originally seen in the undergraduate teaching clinic of the Vision Sciences Department in November 1988 after noticing a reduction in the vision of her right eye. Following this examination she was referred for further tests to the Birmingham and Midlands Eye Hospital where a malignant melanoma in her right eye was confirmed. This eye was subsequently enucleated in February 1989 and a prosthesis fitted. During the enucleation the EOM were not totally removed and the muscle remnants allowed some movement of the prosthetic eye. Examination of Mrs LH's left eye revealed unaided vision of 6/60, correctable to 6/6 with spectacles. Motility of her left eye was normal and the prosthetic eye followed the movement of the left to a moderate extent, although there was slight discomfort with rapid eye movements.

To minify the discomfort to the patient the SP was recorded from only three electrodes round each orbit (inner and outer canthi and below the eyes) using the normal SP recording apparatus and technique (Chapter 4). The saccade trace recorded from the left eye was used as the trigger for all back-averaging, including the potentials recorded from electrodes round the right eye.

10.4.2 RESULTS

As with the preceding experiments the SP was easily recorded form this subject although she had no previous experience of participating in such recordings. A clear SP was recorded from all the recording sites, including those round the right orbit, for both saccade directions and the waveforms are shown in Figures 10.5 and 10.6. The waveforms shown in the two Figures indicate that the SPs recorded from electrodes round the right orbit were smaller in amplitude than those recorded from around the left orbit. This difference in SP amplitudes is shown in more detail in Table 10.2 which also lists the onset and peak latencies for these recordings.

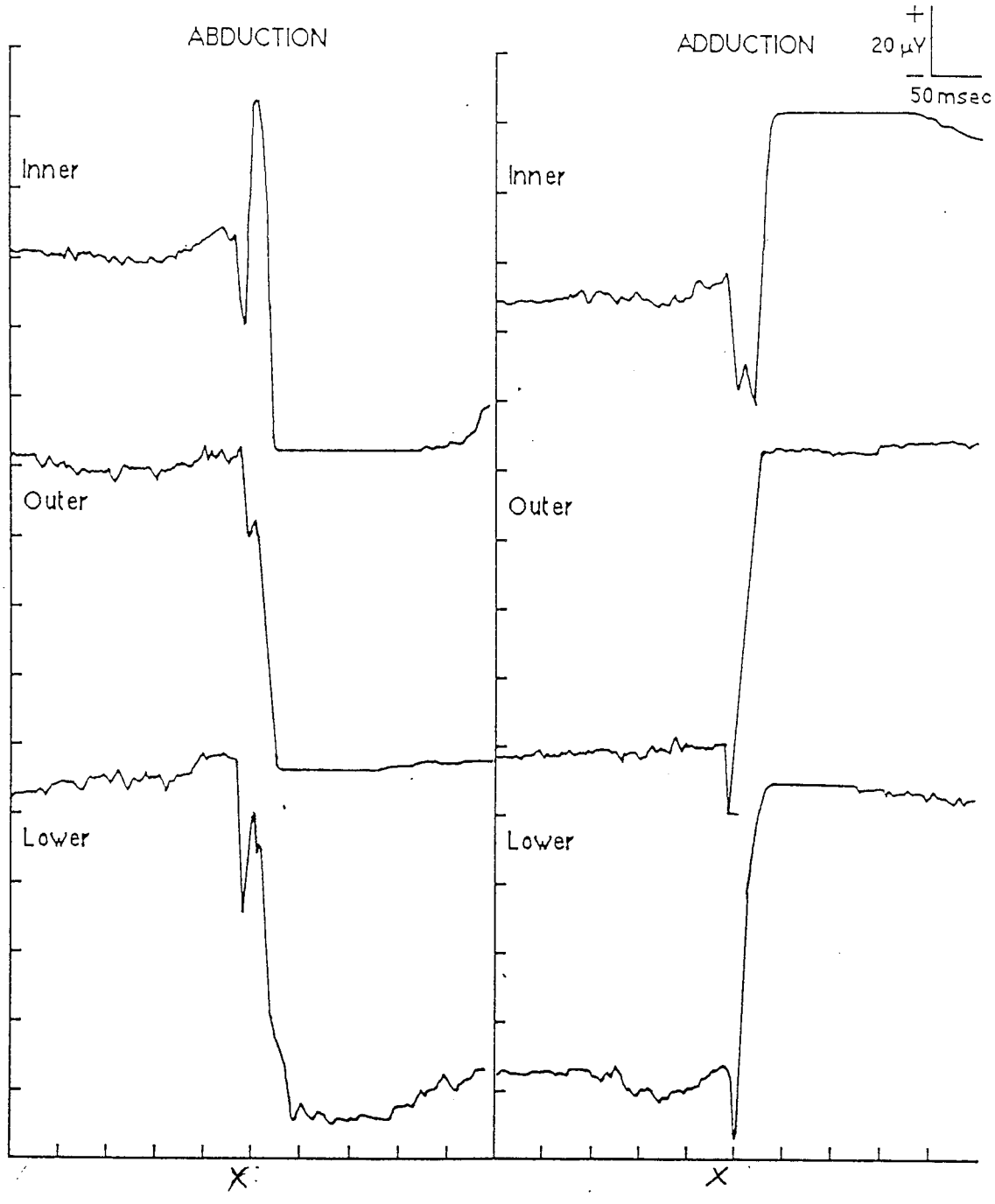

Figure 10.5 The presaccadic spike potential recorded from three electrode sites around the left orbit of a patient with a right eye enucleation. The saccade onset is indicated by the cross.

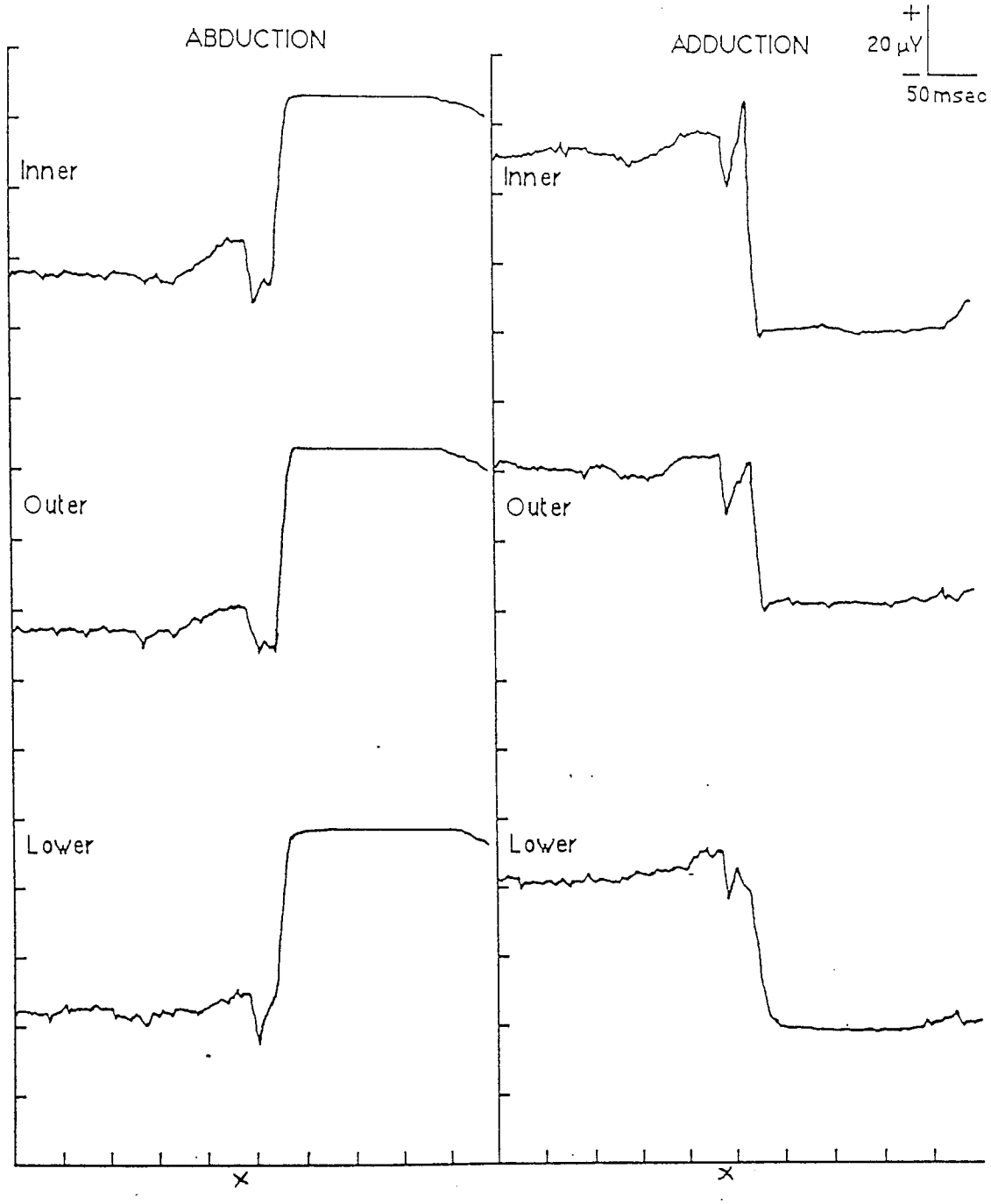

Figure 10.6 The presaccadic spike potential recorded from three electrode sites around the right orbit of a patient with a right eye enucleation. The saccade onset is indicated by the cross.

		INNER			OUTER			LOWER		
		Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
RE	Abd	-6	11	20.5	-3	8	12.1	-4	7	16.8
	Add	-12	-3	13.4	-12	-4	13.0	-12	-3	16.2
LE	Abd	-3	4	27.6	-6	3	26.4	-7	6	35.8
	Add	-15	-3	40.2	-13	-2	23.9	-10	-1	29.6

Table 10.2 The spike potential onset and peak latencies (msec) and onset-peak amplitudes (Amp) (μV) for abducting (Abd) and adducting (Add) saccades when recorded from three electrode sites around the right (RE) and left (LE) orbits.

10.4.3 DISCUSSION

The waveforms given in Figures 10.5 and 10.6 indicate, once again, the ease with which the SP can be recorded from untrained subjects. The SPs recorded from this patient show the characteristic waveform with the sharp negative deflection shortly before the saccade start evident at all the electrode sites. The presence of a SP from the electrodes round the right eye may, at first, seem surprising if the suggested origin of the potential in the EOM is correct. When considering the recordings from this patient, however, it must be remembered that the right prosthetic eye did have some remnants of the extraocular muscles attached to it. The waveforms recorded from around the right eye could therefore presumably be a reflection of activity within these muscle remnants.

The onset and peak latencies of the above SPs are similar to the normal values which have been determined from earlier experiments and there does not appear to be any difference between the two eyes (see Table 10.2). This was expected as the innervation to the EOM of the two eyes would still be the same as for two normal eyes. The SP amplitudes for the different electrode sites and saccade directions did, however, show a difference between the two eyes. The SP amplitude recorded from the electrodes at the left eye was between 26.4-35.8 μV for abduction and 23.9-40.5 μV for abduction, while for the right, prosthetic, eye the amplitudes varied between 12.1-20.5 μV for abduction and 13.0-16.2 μV for adducting saccades (see Table 10.2). The difference in SP amplitude between the eyes

may be related to the reduced muscle activity of the right eye extraocular muscles, these muscles being smaller than those of the left eye.

Although the SP recordings from electrodes around the prosthetic eye do not give us any further information regarding the origin of the potential, it is obvious from these recordings that the presence of a healthy eye is not essential for the potential to be generated, a point which was previously noted by Thickbroom and Mastaglia (1985b). There is, however, little else that can be concluded from the results of this study regarding the origin of the SP. It has been observed that the only way that no muscle activity can be recorded from electrodes round the orbit is when the complete orbital contents have been removed, i.e. an extenerated orbit. As this was not the case in either the present study or the earlier work of Thickbroom and Mastaglia (1985b), it cannot be assumed that the muscle remnants of the right eye were not generating some spike potential activity.

A further possible source of a spike potential recording from the side of the prosthetic eye is 'cross-talk' of the potential between the two orbits. The previous Chapter has described the far-field nature of the SP when it is recorded from electrodes across the posterior scalp and it is possible that there may also be some spread of the potential in the frontal part of the head. If this is indeed the case it is conceivable that this may also affect recordings of the SP in normal subjects. It would be advantageous, therefore, to repeat the above recordings on patients with a totally extenerated orbit as this would give more information regarding the spread of the spike potential between the two eyes.

10.5 SUMMARY

This Chapter has described the recording of the SP from three subjects with different eye movement anomalies. The first section describes the SP when recorded from a subject with a left lateral rectus palsy. The SP was found to be reduced in amplitude for left eye abduction and also right eye adduction. The reduction in SP amplitude were attributed to changes in the innervational patterns being sent to the left lateral rectus due to the palsy

and the right medial rectus. If the innervation to the right medial rectus had remained unaltered, this would have resulted in over action of this muscle. It was not unexpected, therefore that the innervation to this muscle may have been reduced and it is possible that the reduced SP activity may be a reflection of this.

The recordings in this study also gave some information regarding the effect of trigger jitter on the averaging of the SP. When the saccade traces from the left eye, especially with left eye abduction, were used to determine the onset of the eye movement and therefore the averaging trigger, it was noted that the SP waveforms were broadened and had smaller amplitudes normal. When the right eye saccade traces were used to determine the saccade onset, however, the SP waveforms for the same electrode sites had normal waveforms albeit with reduced amplitudes. The difference in waveforms was considered to be due to trigger jitter introduced into the averaging process by using the poorer saccade waveforms from the eye with the muscle palsy. This experiment indicated, therefore, the importance of correct averaging of the waveforms which is obviously dependant upon a clear and accurately determined saccade onset.

The effect that trigger jitter has on the SP averaging is of some concern when the second patient in this study, who suffers from multiple sclerosis, is considered. Both the SP and the saccadic eye movements were recorded and averaged in the normal manner.

Clear saccade were recorded for both saccade directions at both eyes, so any changes in the SP could not be due to poor averaging. It was noted that adducting SP amplitudes were smaller than those of abducting saccades and that adducting saccades were slower than abducting eye movements and the waveform was broadened with no definite spike potential. The reduction in adducting saccade velocity is known to occur in MS following innervational changes to the medial rectus muscles due to internuclear ophthalmoplegia. The reduced SP amplitude may be a reflection of the reduced innervation rates to these slower saccades. The abnormal SP waveform could not, however, be explained by reduced saccade velocity and it was considered that this may have been due to changes

in the innervational pattern of the muscles. The computer model of SP activity proposed by Thickbroom and Mastaglia (1987) has shown that the SP amplitude was reduced and the waveform broadened when the recruitment dispersion of the motor units within the EOM was increased. It was considered that the abnormal SP recorded with adduction may have been due to changes in the recruitment rate of the motor units in the right medial rectus. While the exact cause of the altered SP amplitude is unknown, the results did indicate that changes in the SP characteristics can be related to variations in the saccade performance of the eye movement producing the spike potential.

The final section of this Chapter detailed the recording of the SP from a lady with a right enucleated eye. Spike potentials were recorded from electrodes around both the normal and the prosthetic eye and the waveforms were considered. Although the right globe had been removed, there were still remnants of the right EOM attached to the prosthetic eye. The presence of these muscles may have accounted for the fact that a SP was recorded from the electrodes at both the normal eye and the artificial eye. A further possible source for the SP recorded round the enucleated eye was considered to be potential spread from the normal muscles of the left eye. This, unfortunately, cannot be examined unless the SP is recorded from a subject with a totally extenerated orbit.

While the recordings from the three subjects in this Chapter do give some additional information of the SP recording, they are only initial recordings of the potential from subjects with anomalous eye movements. An important observation which should be made from these recordings is the ease with which the SP can be recorded from relatively 'naive' subjects. All three subjects used in the above recordings had had no previous experience of SP recordings, and only the patient with MS had any experience of eye movement recordings, yet the SP was readily recorded from all subjects. The ease with which the SP can be repeatedly recorded is an important consideration if the potential is to be used clinically. SP recordings could easily be added to normal electrophysiological recording set-ups with little extra time or effort on the patients part, particularly if the EOG is already used to monitor saccadic eye movements. The recordings presented above have

shown, however, that future studies must ensure SP recording conditions optimise the back-averaging of the spikes by ensuring that eye position is monitored carefully so the beginning of the eye movement is sharp and can be easily identified, otherwise abnormal spike waveforms may result and be misinterpreted.

While no definite conclusions can be drawn regarding the significance of the changes in the SP with the above subjects, the results are sufficient to suggest that further recordings should be made to show if the changes in the potential are a consistent finding with extraocular muscle palsies and multiple sclerosis for example. The SP should also be recorded from further patients with different conditions affecting saccadic eye movements to examine the effect they may have on the potential.

A further factor which should be considered with all the above studies is the location of the reference electrode and the effect this may have on the recorded waveforms. It was shown in the previous chapter that positive spike activity coincident with the anterior spike can be recorded from electrodes positioned over much of the posterior scalp. It is quite conceivable that the spike potential recorded in the present 'clinical' studies may be arising from the decision to use a scalp electrode as the reference. If the anterior scalp has little, or no activity compared to the posterior positivity, this will result in a downward (negative) deflection of the trace when anterior electrodes are compared to a posterior reference. This could, possibly, be overcome by using a non-cephalic reference site for these recordings and this should be confirmed before any further clinical recordings are undertaken.

CHAPTER 11

SUMMARY AND CONCLUSIONS

11.1 THE PRESACCADIC SPIKE POTENTIAL: A RÉSUMÉ

A large negative spike potential (SP) can be recorded at the onset of saccadic eye movements from electrodes round the orbits. This potential has been associated with muscle activity immediately before the saccade onset (Blinn, 1955; Lion and Powsner, 1951; Riggs *et al.*, 1974; Thickbroom and Mastaglia, 1985b, 1986, 1987; Jäntti *et al.*, 1982; Jäntti and Häkkinen, 1987; Tsutsui *et al.*, 1987; Riemslag *et al.*, 1988; Niiyama *et al.*, 1988) and is known as the presaccadic spike potential (Thickbroom and Mastaglia 1985b). The presence of the spike potential has been acknowledged by many workers but it has often been considered as no more than an artefact related to saccadic eye movements (MacGillivary, 1974; Beaussart and Guieu, 1977, Binnie *et al.*, 1982; Halliday, 1982).

Although several workers have recorded the spike potential its exact origin is, as yet, unknown. Both the facial muscles (Jäntti *et al.*, 1982) and the extraocular muscles (EOM) (Blinn, 1955; Lion and Powsner, 1951; Riggs *et al.*, 1974; Thickbroom and Mastaglia, 1985b, 1986, 1987; Jäntti and Häkkinen, 1987; Riemslag *et al.*, 1988; Niiyama *et al.*, 1988) have been suggested as the site of the potential origin, while some workers have been more specific and implicated the supraciliary corrugator as the actual muscle giving rise to the potential (Ohnishi, 1987; Tsutsui *et al.*, 1987). An origin of the SP in the facial muscles has, however, been discredited by Jäntti and Häkkinen (1987) who recorded the SP from a patient whose facial nerve had been severed. Likewise, there is considerable doubt regarding the possible origin of the potential in the supraciliary corrugator muscle as this muscle is absent in some 18% of the population (Sato, 1968). It appears likely, therefore, that the EOM are the most probable site for generation of the spike potential.

The SP waveform can been likened to the motor unit action potential recorded from the EOM following an innervational impulse from the ocular motoneurons in the brain stem. Examination of the pattern of innervation to drive saccades reveals a characteristic pulse of motoneuron activity immediately before the saccade followed by a new level of tonic neural activity to hold the eye at its new position of regard (2.4.1). The SP can be tentatively identified as originating from motor unit activity in the EOM following the saccade pulse, and a model of SP activity based upon the discharge of the EOM motor units has been produced to confirm this relationship (Thickbroom and Mastaglia, 1987).

The SP waveform is characterised by a sharp negative deflection occurring just before the saccade and peaking at, or just after, the start of the eye movement. The SP has a widespread distribution across both the frontal and posterior scalp, with a phase reversal about the midline (Thickbroom and Mastaglia, 1985b). The waveforms recorded by Thickbroom and Mastaglia (1985b) over the posterior scalp correspond to a far-field recording of frontal activity with a source close to the orbits. A similar spread of low amplitude, widespread spike activity over the posterior scalp was reported by Deecke and Kornhuber (1977). There have been some reports in the literature of a small, positive 'presaccadic spike potential' which can be recorded from electrodes at P_3 and P_4 and several studies have examined the relationships between this posterior spike potential and the saccade direction and size (Kurtzberg and Vaughan, 1973, 1980, 1982; Armington, 1977, 1988; Weinstein *et al.*, 1984; Balaban and Weinstein, 1985; Weinstein *et al.*, 1988). The posterior spike potential has an identical relationship between its onset latency and the saccade start to the frontal SP and shows some variation in amplitude with different saccade sizes (3.2.2). It has been suggested that this posterior potential may be related to presaccadic activity in the different neural centres involved in the generation of saccades (Weinstein *et al.*, 1988). Unfortunately, in all studies examining the posterior spike potential there does not appear to have been any acknowledgement of the larger, coincident, frontal spike potential with its widespread distribution across the head. This must be borne in mind when considering the results of these recordings.

There have been a few studies of the frontal SP recorded from surface mounted electrodes located around the eyes for different saccadic eye movements and sizes, but most of these experiments were lacking in subject numbers and full analysis of the results. Thickbroom and Mastaglia (1985b, 1986) described the normal SP waveform recorded from a group of ten subjects but gave only limited information for the latency and amplitude parameters of the potential. A relationship between saccade size and SP amplitude has been identified by Riemslag *et al.* (1988) but this study only examined the SP from five subjects and one saccade direction with a single electrode at the outer canthus. An attempt was also made by Riemslag *et al.* (1988) to remove the eye movement potential which follows the SP peak from the SP waveform, but there did not appear to be much to be gained from this procedure. The frontal SP has been the main area of study in this thesis and the experiments performed in the thesis will be summarised and discussed below.

11.2 A SUMMARY OF THE EXPERIMENTAL RECORDINGS

Prior to this study of the SP there had been little work performed to ascertain the normal parameters and waveform of the spike potential. For any potential to be used, either clinically or in a research study, it is essential that a set of normal values is known. In Chapter 5 the initial experiment to determine this normal data-base is described. Using an experimental set-up based upon those of the previously published studies the SP was recorded from 20 normal subjects for 20° horizontal saccades and the average waveform and latency and amplitude parameters were determined.

The results of these recordings revealed a previously unknown, statistically significant difference in the latency for adducting and abducting saccades, with adducting saccades having earlier SP onset and peak values than abducting movements (5.3.1). A possible explanation for the difference between abducting and adducting saccades was based upon the premiss that there may be differences in the latencies before a saccade at which the medial rectus and lateral rectus receive their innervational pulse from their respective

motoneurons. Unfortunately, there is no information in the literature regarding this so the hypothesis can be neither confirmed or denied. The amplitude of the SP recording for 20° saccades was between 35.5 and 48.5 μV; this being similar to earlier studies.

These initial recordings confirmed the anterior SP recording to be a large negative spike potential commencing shortly before the saccade onset and allowed the normal waveform and parameters, for 20° saccades, to be determined. It was observed that the SP could be recorded equally from electrodes placed all round the globe and it appeared, at least from this study, that the SP was a compound potential derived from activity in all the EOM concerned with horizontal saccades.

Following recordings of the SP for 20° saccades, the potential was recorded for different saccade sizes to observe any changes which may occur in the potential with different eye movement sizes. Initially the saccades ranged between 2.5° and 20° and, although it was found that there was no statistically significant difference between the 20° and 10° saccade SP amplitudes, there was a significant difference between these saccade sizes and the smaller eye movements (6.2.2). The lack of change in SP amplitude between 10° and 20° saccades was attributed to the fact that ocular motoneuron activity saturates for saccades greater than 15°. (Sindermann *et al.*, 1978) and it was considered that the SP may be a reflection of this activity.

Later recordings of the spike potential with larger saccades revealed, however, that the amplitude did increase significantly for eye movements up to 40° (6.4.3). The computer program of motor unit activity proposed by Thickbroom and Mastaglia (1987) was used to explain this increased SP amplitude. The model indicated that an increased spike potential amplitude will arise when the second and subsequent action potentials in an action potential train are increased in amplitude from 0% to 100% of the initial action potential amplitude. Larger saccades require greater innervational inputs to the EOM and, as a result of this higher level of muscle activity, have greater peak velocities than smaller

eye movements. Changes in the SP amplitude may be a reflection of the changing muscle activity required for the larger, faster eye movements.

Many previously published papers describing the SP have used subjects of varying ages in their experiments with little regard for any possible changes that may occur in the potential with advancing age (Thickbroom and Mastaglia, 1985b; 1986; Riemslag *et al.*, 1988). The majority of the experiments in this thesis have used young, age matched, subjects but this does not give any information about the SP with different aged subjects.

In Chapter 7, recordings of the SP from elderly and middle aged subjects are described. The recording procedure was identical to that used for the young subjects, so the results could be compared. Although the onset and peak latencies of the potential remained constant with the old age group compared to the young subjects, a statistically significant reduction in the onset-peak amplitude was found for the older subjects (7.3.2). This reduction in SP amplitude was not, however, evident when the SP was recorded from the middle aged subjects, suggesting that the changes in amplitude may only be associated with later life (7.4.2).

The results from the initial experiments previously described may shed some light upon the changes which occur in the SP amplitude with elderly subjects. The literature has shown that peak saccade velocities are reduced in elderly subjects (2.2.2). If the SP amplitude is a reflection of the different levels of muscle activity necessary to produce saccades of varying sizes, and therefore velocities, it could be expected that the SP amplitude should be smaller for older subjects who have slower saccades due to reduced levels of muscle activity. An alternative explanation for the reduced SP amplitude can also be hypothesised from a computer model of the spike potential, which has shown that the amplitude of the potential reduces as the motor units fire less synchronously, a change which may occur in the EOM with advancing age. Although the cause of the amplitude reduction remains uncertain, it is obviously unsatisfactory to directly compare SP amplitude values recorded from old and young subjects.

The majority of studies of eye movements concentrate only on horizontal saccades because of interference with the eye movement recording from eyelid activity in vertical saccades. Recording the SP with vertical saccades was considered to be of interest, however, as the main muscles involved in moving the eyes vertically are different from those needed to move the eye in a horizontal direction and the innervational pathways differ slightly between the two eye movement directions. This different muscle activity may be reflected in the SP recorded with vertical saccades.

Recordings of the SP with vertical eye movements are described in Chapter 8, where it can be seen that the waveform and latency parameters of the potential were similar to those of horizontal saccades. The onset-peak amplitude was smaller with vertical eye movements than the corresponding horizontal SP amplitude (8.3). The SP waveform with vertical saccades often exhibited a second peak following the initial deflection. While it can be hypothesised that the more complex SP waveform may be indicative of the inherently more elaborate muscle activity associated with vertical saccades, a second possible factor causing this second deflection on the SP waveform, particularly with vertical saccades, may be eyelid activity associated with these eye movements.

Although recording the SP with vertical saccades did not reveal any new findings regarding the waveform or SP parameters, it should be remembered that this was only an initial study to determine if the potential could, in fact, be recorded with different saccade directions. It is evident from the recordings in Chapter 8 that the normal problems associated with vertical saccade recordings do not appear to affect the SP recording to any great extent and, if the SP has any clinical application, it may be of some benefit in the analysis of vertical saccades

In Chapter 3, it was observed that there has been some confusion regarding the distribution of the SP across the scalp. Several workers have recorded posterior spike activity which is coincident with the larger frontal activity but they do not appear to have considered that recordings from the posterior scalp activity may be influenced by the

frontal SP activity. In order to examine the distribution of the presaccadic spike potential across the scalp the potential was recorded from sixteen electrodes across the scalp with two different reference electrode configurations (Chapter 9). Both an average and a balanced non-cephalic reference were used. The traces recorded with both montages revealed a distinct frontal SP with a corresponding posterior spike activity from the electrodes across the scalp (9.2.2; 9.3.2). The magnitude of the posterior activity was greater with the average reference than when recorded with the non-cephalic reference.

With these recordings it was impossible to determine the latency of the SP onset with respect to the saccadic eye movement, but it was clear that the posterior and anterior activity shared the same peak latencies with respect to each other. The surface distribution of the spike waveform over the scalp, the similarity of the latency values and the polarity reversal of the waveforms just behind the orbits, suggested that the origin of the SP may be located in the orbital region, while the posterior spike activity is probably a far field recording of the frontal activity. This implies that any studies of posterior SP activity should ideally not confine themselves to only two electrode sites, and no conclusions regarding a posterior origin of the potential can be made from such recordings.

The last experimental Chapter of this thesis describes recordings of the SP from subjects with anomalous eye movements to examine the effect of these conditions on the SP recording. The first subject in Chapter 10 had a left lateral rectus palsy and the SP amplitude reduced for left eye abduction and right eye adduction. This amplitude reduction was attributed to changes in the innervation of the left lateral rectus and the right medial rectus due to the palsy. Perhaps of greater importance from these recordings, however, was the effect of trigger jitter on the averaging of the SP. It was observed that the SP waveforms were altered when saccade traces on which a distinct eye movement onset was less obvious were used to determine the trigger for the back-averaging. The difference in waveforms was considered to be due to trigger jitter introduced into the averaging process by using the poorer saccade waveforms from the eye with the muscle

palsy. This indicated the importance of correct averaging of the waveforms which is dependant upon a clear and accurately determined saccade onset.

The second patient in Chapter 10 had multiple sclerosis (MS) and, for this subject, both the SP and saccade traces were recorded. Adducting SP amplitudes were smaller than abducting amplitudes and adducting saccades were slower than abducting saccades and there was no definite spike recorded from the right eye with adducting saccades. A reduced adduction velocity is expected in MS due to innervation changes to the medial rectus caused by internuclear ophthalmoplegia. The reduction in SP amplitude and the abnormal waveform may have arisen from this altered innervation. The computer model of SP activity of Thickbroom and Mastaglia (1987) has shown that SP amplitude is reduced and the waveform broadened when the recruitment dispersion of the motor units within the EOM is increased. It is conceivable that the abnormal SP recorded with adduction may be due to changes in the recruitment rate of the motor units in the right medial rectus.

The final patient described in Chapter 10 was a lady with a prosthetic right eye which had remnants of the EOM attached providing some movement. When the SP was recorded from electrodes around both eyes, an SP waveform was observed round both eyes. The muscles remnants attached to the artificial eye may explain the SP recorded from around the artificial eye, but an additional possible source for the SP at the enucleated eye may be potential spread from the normal muscles of the left eye. This, unfortunately, cannot be examined unless the SP is recorded from a subject with a totally exenterated orbit.

11.3 CONCLUSIONS AND PROPOSALS FOR FUTURE STUDIES

The presaccadic spike potential is known to accompany the onset of saccadic eye movements and can be easily and repeatedly recorded from both trained and naive subjects. The potential is assumed to arise from motor unit activity in the EOM following the burst of innervation from the extraocular motoneurons; the saccade pulse. While there have been several reports of the potential in the literature, there has been no

serious attempt to examine the normal parameters and waveform of the potential under different recording conditions. This thesis describes a comprehensive study of the potential for both normal subjects and patients with abnormal eye movements and the results of these recordings lend some support to the proposed origin of the potential.

The SP was easily recorded from all subjects, including those with anomalous eye movements and its waveform and parameters were consistent both between subjects and over a period of time between repeat recordings (5.5). The single sweep recordings shown in Chapter 9 indicate the robustness of the potential particularly well. The ease with which the SP can be recorded suggests that it may be useful, not only as an experimental recording, but also in clinical recordings. The possible clinical usefulness of the SP is given further backing when the results of the recordings from patients with pathology are considered. These have shown that the SP parameters, particularly the amplitude, can be affected in some pathological conditions.

If the SP is used clinically the effect of subject age and saccade size must be remembered. It has been shown that advancing age is associated with a reduction in SP amplitude so it is essential that recordings from elderly pathological subjects are compared only to normal values for the same age group. The respective saccade sizes must also be considered as comparing SP amplitudes for eye movements of different sizes may give rise to possible confusion due to the amplitude reduction with smaller saccades.

While the experiments in this thesis have examined many aspects of the SP, there are some proposals for further work which may give a fuller understanding of the recording:

1. The SP recorded from electrodes round an exenterated orbit.

An important recording that should ideally be performed before any further recordings are made is to record the SP from a subject who has no muscle activity at all in one orbit, i.e. an exenterated orbit. Although a patient with an enucleated eye has been a subject in this

thesis, there was still muscle activity from the artificial eye and it was impossible, therefore to determine the effect of potential spread from one orbit to the other. Recording the potential from electrodes round an exenterated orbit would allow the effect of potential spread between the orbits to be determined.

2. The SP recorded with oblique saccades and with the eyes abducted or adducted.

The normal parameters of the SP have been accurately determined for horizontal and vertical saccades. It would be interesting to attempt to isolate different muscles more fully by recording the SP with the eyes abducted or adducted, or with different saccade directions so different muscle actions could be isolated. If the potential alters with such recordings this would imply that some isolation of individual muscle activity is possible.

3. The SP recorded from further subjects with pathological conditions affecting their saccadic eye movements.

If the above recordings reveal that the SP can be isolated to one orbit and possibly individual muscles, further recordings could be made from subjects with pathological conditions affecting both the muscles and neural centres controlling saccades. It has been seen that the back-averaging used to record the SP is dependant upon the presence of a distinct saccade onset. It is possible that if the SP is recorded from subjects with anomalous eye movements a clear saccade onset may not be obvious. It may be necessary, therefore, to back-average the SP from the potential itself as opposed to the saccade start. Studies should be performed to examine any difference which this has on the SP waveform and amplitude. The SP should also be recorded from further patients with both definite and possible MS to ascertain how sensitive the SP is to such disease conditions. Further studies of the SP from patients with different conditions affecting their eye movements may reveal a clinical use for the potential, perhaps as an alternative to the invasive technique of electromyography.

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APPENDIX A: RAW DATA AND WAVEFORMS

APPENDIX 1.1

The onset and peak latencies and onset - peak amplitudes for 20 subjects performing 20° saccades. The SP was recorded from four electrodes around the right eye.

RIGHT EYE ABDUCTION

ELECTRODE SITE

	INNER			OUTER			ABOVE			BELOW		
Subject	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
CB 30	-12	6	27.0	-3	12	18.0	-6	10	25.7	-11	11	27.3
AJH 30	-9	1	28.9	-10	-1	39.2	2	8	28.8	-8	0	34.6
DET 18	-9	-8	35.0	-8	0	17.0	-14	4	28.9	-7	3	30.0
EP 23	-3	8	42.6	-4	7	30.7	-3	6	33.9	-4	6	36.7
DD 27	-9	7	42.8	-7	3	46.2	-7	4	46.8	-7	5	58.9
JR 26	-8	6	49.0	-8	7	38.5	-7	7	36.5	-7	8	36.6
MCD 26	-7	8	33.4	-9	4	27.6	-3	5	19.8	-7	3	29.3
RB 25	-6	14	56.5	-5	13	32.0	3	14	52.3	-2	12	47.4
RD 23	-11	5	29.1	-8	2	26.9	-9	4	39.1	-8	10	25.8
VV 25	-4	8	32.5	-9	7	21.5	-1	18	15.8	-8	9	21.0
VMH 18	-4	4	79.0	-9	2	78.2	-8	4	57.0	-7	4	74.6
NP 28	-4	7	32.7	-5	7	26.2	-4	5	34.8	-4	7	35.2
TS 23	-1	9	37.2	0	10	36.9	-1	8	28.4	-3	6	35.9
SP 23	-3	10	52.1	-4	8	38.8	-7	9	59.2	-2	9	53.6
EL 25	-1	12	58.9	-7	9	30.9	0	14	22.5	-1	14	43.9
CD 23	0	13	18.8	0	14	26.3	0	8	21.5	-15	-4	12.2
BE 28	-3	6	40.2	-5	6	36.2	0	10	53.8	-3	9	43.5
DC 23	-6	8	36.2	-8	5	33.9	-5	5	40.0	-5	5	40.1
JH 21	0	11	55.3	0	12	57.5	0	13	57.7	0	12	54.8
KD 21	-6	7	53.1	-4	5	47.8	-5	6	38.7	-4	6	41.3

RIGHT EYE ADDUCTION

ELECTRODE SITE

	INNER			OUTER			ABOVE			BELOW		
Subject	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
CB 30	-7	-1	34.6	-11	-1	27.0	-15	-2	44.1	-14	-3	44.3
AJH 30	-12	-4	24.4	-13	-2	27.0	-8	0	18.2	-12	-4	10.3
DET 18	-10	-1	79.2	-13	-2	57.8	-11	-2	55.5	-13	-2	60.2
EP 23	-7	2	37.2	-5	5	22.2	-12	0	32.0	-11	-1	60.9
RD 27	-11	0	16.6	-11	1	40.0	-9	1	52.5	-9	0	49.8
JR 26	-11	1	69.0	-9	0	48.1	-10	1	29.3	-11	1	49.8
MCD 26	-11	2	36.6	-9	3	33.1	-12	0	21.2	-9	1	45.3
RB 25	-10	1	46.9	-12	1	48.9	-8	0	42.8	-10	-1	37.7
DD 23	-9	1	44.8	-11	2	33.1	-12	1	45.3	-12	1	28.5
VV 25	-10	-1	29.7	-20	12	43.0	-1	12	32.4	-2	13	53.1
VMH 18	-8	2	67.5	-8	3	61.4	-15	2	57.0	-8	4	52.6
NP 28	-9	0	22.3	-10	3	29.0	-14	-1	27.5	-10	0	25.1
TS 23	-1	8	12.0	-1	9	47.1	0	8	39.2	-1	8	32.9
SP 23	-11	-1	50.0	-11	-2	40.4	-14	-2	43.7	-12	-1	45.4
EL 25	-11	-2	43.8	-16	-4	22.6	-14	-3	64.0	-12	-3	29.6
CD 23	-14	-3	21.8	-11	-2	22.1	-14	-3	19.5	-15	-4	23.2
BE 28	-11	0	44.6	-13	-2	41.0	-10	-1	41.8	-10	0	44.8
DC 23	-11	0	44.8	-11	-1	38.0	-9	0	50.2	-12	-1	55.7
JH 21	-13	-4	42.7	-14	-3	57.9	-11	-2	58.9	-11	-1	47.8
KD 21	-9	-1	58.4	-11	-1	44.7	-11	-2	58.9	-11	-1	47.8

The onset and peak latencies and onset–peak amplitudes for 20 subjects performing 20° saccades. The SP was recorded from four electrodes around the left eye.

LEFT EYE ABDUCTION

ELECTRODE SITE

	INNER			OUTER			ABOVE			BELOW		
Subject	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
CB 30	-10	7	44.4	-9	7	19.5	-1	1	31.0	-8	9	23.5
AJH 30	-12	3	35.8	-7	1	30.8	2	11	22.3	-8	1	28.5
DET 18	-9	1	29.0	-7	13	53.0	-8	5	48.2	-8	4	53.2
EP 23	-7	6	63.0	-4	2	18.7	-11	0	40.3	-6	5	45.6
DD 27	-10	7	40.4	-9	4	26.2	-6	4	26.4	-9	5	29.8
JR 26	-8	7	44.9	-10	5	25.6	-7	6	40.5	-9	5	29.8
MCD 26	-6	5	53.0	-9	5	33.4	-5	5	33.1	1	11	39.8
RB 25	-1	14	51.0	-9	10	33.6	-5	11	46.4	-7	6	47.8
RD 23	-10	8	26.0	-7	4	33.2	-7	4	33.2	-9	4	37.2
VV 25	-8	8	23.1	-3	10	45.2	-1	9	25.5	-5	9	37.6
VMH 18	-6	2	50.0	-6	7	46.8	-8	8	40.2	-9	7	46.6
NP 28	-1	6	28.1	-14	5	34.6	-4	5	48.3	-3	6	36.9
TS 23	-2	8	42.1	0	7	38.9	0	8	44.7	-2	8	55.1
SP 23	-3	10	61.9	-2	10	57.3	-5	9	51.1	-4	11	58.2
EL 25	-4	8	27.9	-1	11	58.4	-1	10	44.8	-2	10	37.7
CD 23	-8	6	20.2	-6	-7	24.9	-3	6	18.0	-10	6	15.5
BE 28	-4	9	36.6	-1	8	34.6	-5	6	25.5	-2	9	42.1
DC 23	-12	3	32.0	-4	5	42.5	-10	4	45.3	-7	4	47.8
JH 21	-8	2	24.4	-10	9	46.8	-9	1	53.9	-9	12	45.1
KD 21	-9	4	53.1	-7	-6	44.9	-5	5	54.1	-7	5	49.8

LEFT EYE ADDUCTION

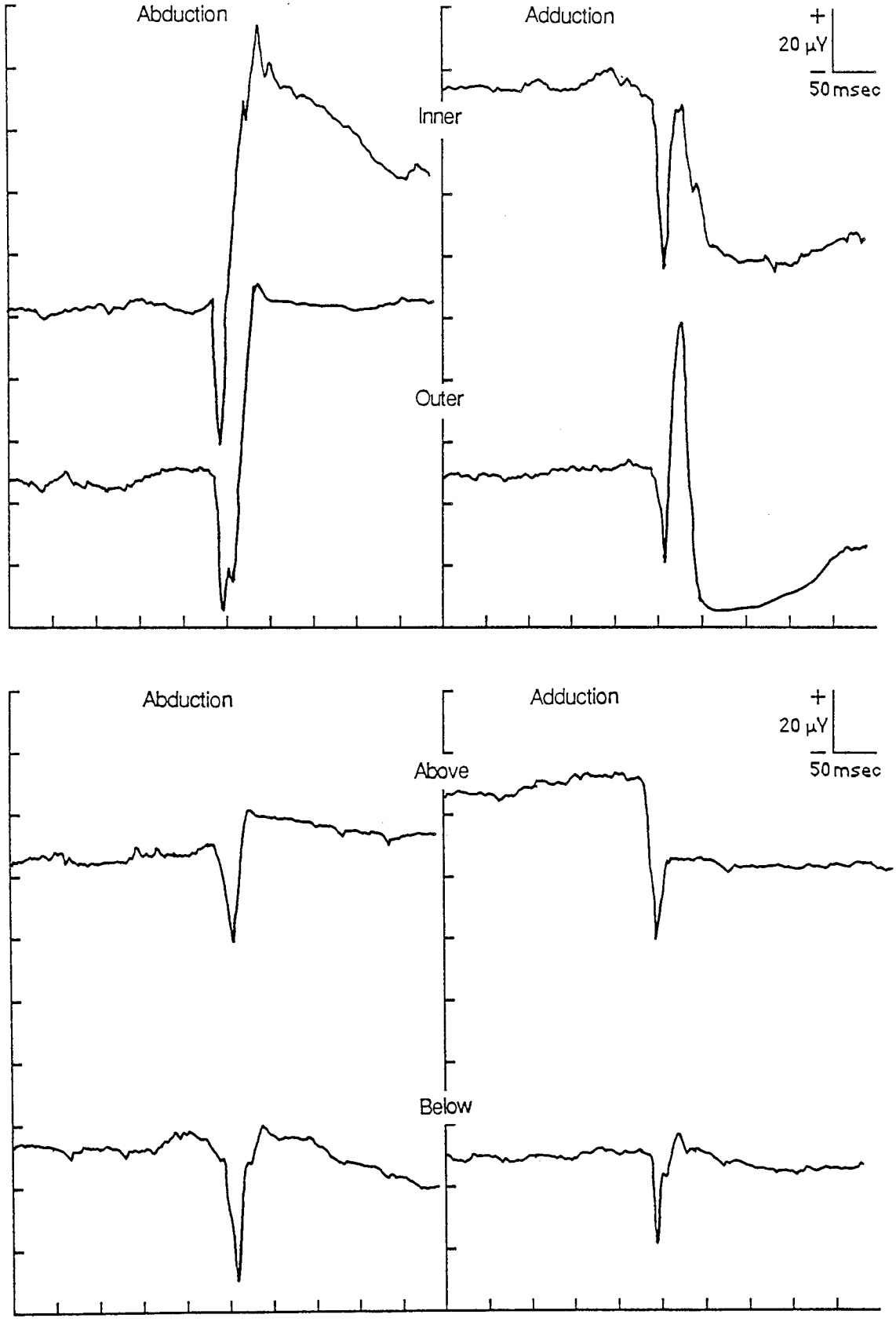
ELECTRODE SITE

	INNER			OUTER			ABOVE			BELOW		
Subject	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
CB 30	-12	-2	41.2	-14	-2	46.2	-13	-3	34.3	-12	-3	47.8
AJH 29	-13	-3	34.4	-11	-2	31.8	2	12	37.2	-12	-3	47.8
DET 18	-13	-1	63.6	-10	0	66.3	-11	-2	56.5	-12	-1	61.0
EP 23	-11	0	64.6	-12	0	25.1	-10	-1	45.9	-17	-9	25.0
DD 27	-10	0	45.2	-13	0	46.2	-11	0	46.9	-12	-1	66.1
JR 26	-10	1	67.9	-11	1	55.2	-12	0	59.9	-11	1	71.6
MCD 26	-7	5	23.1	-9	5	33.6	-10	0	12.3	-12	0	19.5
RB 25	-10	0	27.6	-12	-1	67.7	-12	-1	45.4	-19	-2	47.0
RD 23	-8	0	38.1	-9	1	32.3	-7	1	47.8	-8	1	55.1
VV 25	-11	13	44.2	-4	11	17.3	-1	12	33.6	0	12	38.9
VMH 18	-6	3	78.3	-4	10	56.1	-4	8	27.4	-2	8	41.2
NP 28	-9	0	19.5	-12	-3	19.9	-13	-2	17.9	-8	12	21.9
TS 23	0	10	11.7	0	10	21.5	0	10	21.6	0	11	35.1
SP 23	-11	-1	69.0	-12	-1	53.9	-13	-2	62.7	-12	-2	65.8
EL 25	-10	-2	38.2	-14	-4	56.4	-15	-3	58.0	-13	-3	66.3
CD 23	-10	-2	37.9	-12	-2	12.7	-10	-2	15.0	-11	-1	38.1
BE 28	-12	-1	60.8	-11	0	53.9	-13	-1	44.1	-2	9	42.1
DC 23	-13	-2	64.2	-10	-2	47.1	-11	-2	58.9	-11	-2	61.6
JH 21	-13	0	66.1	-10	1	54.1	-11	2	56.1	-12	0	51.7
KD 21	-9	-1	59.6	-11	-2	56.9	-11	-2	51.6	-10	-4	65.6

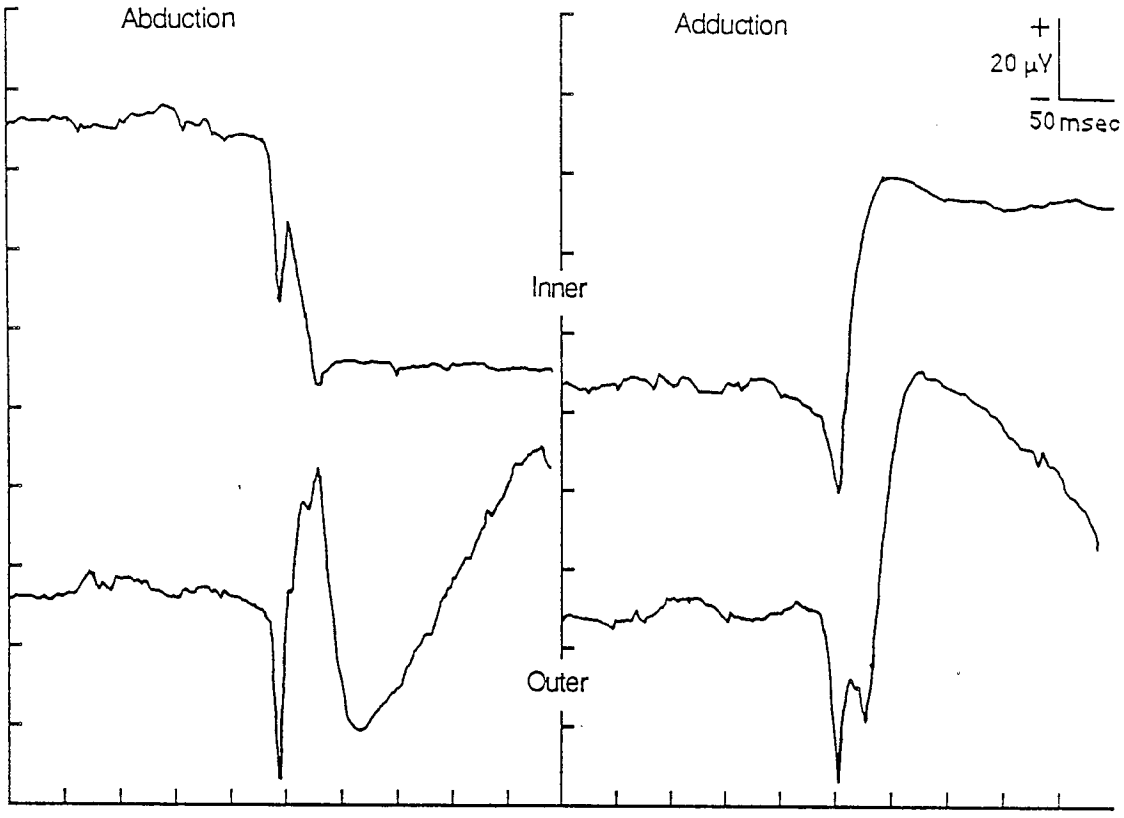
APPENDIX 1.2

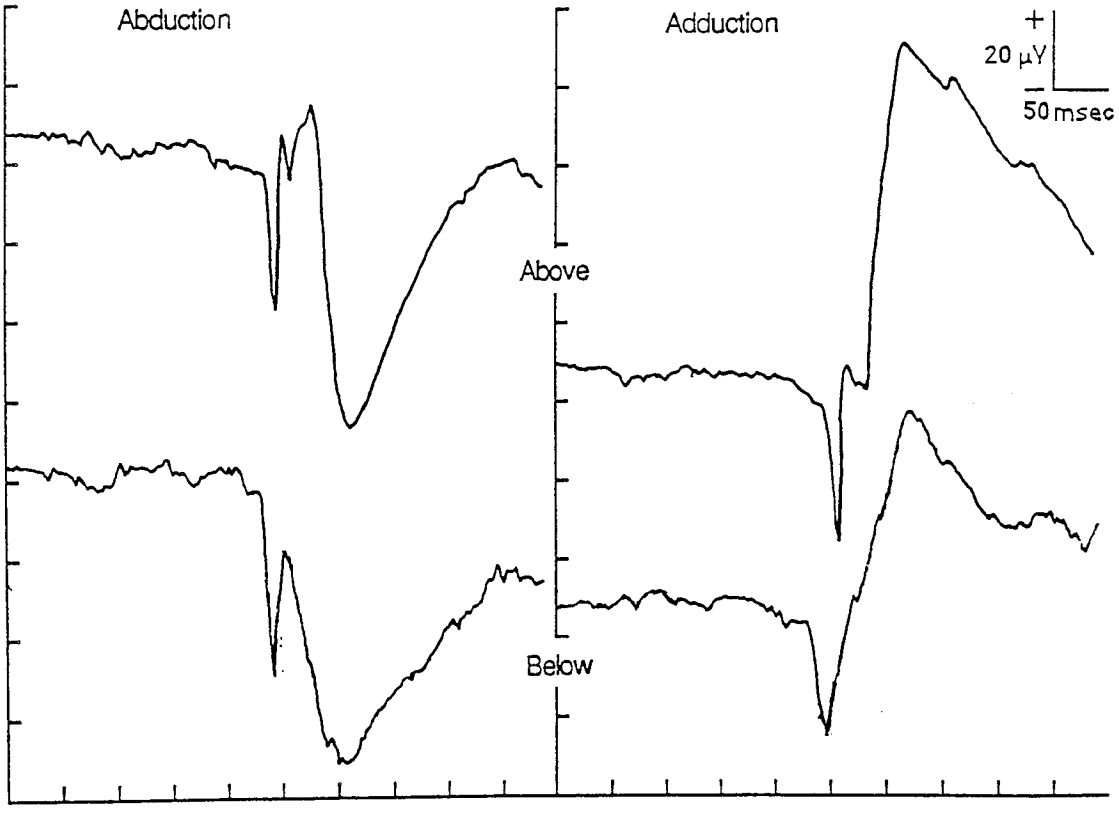
Spike Potential waveforms recorded from single subjects for 20° saccades. The SP was recorded from four electrodes round the eye.

Subject RB: Right eye.

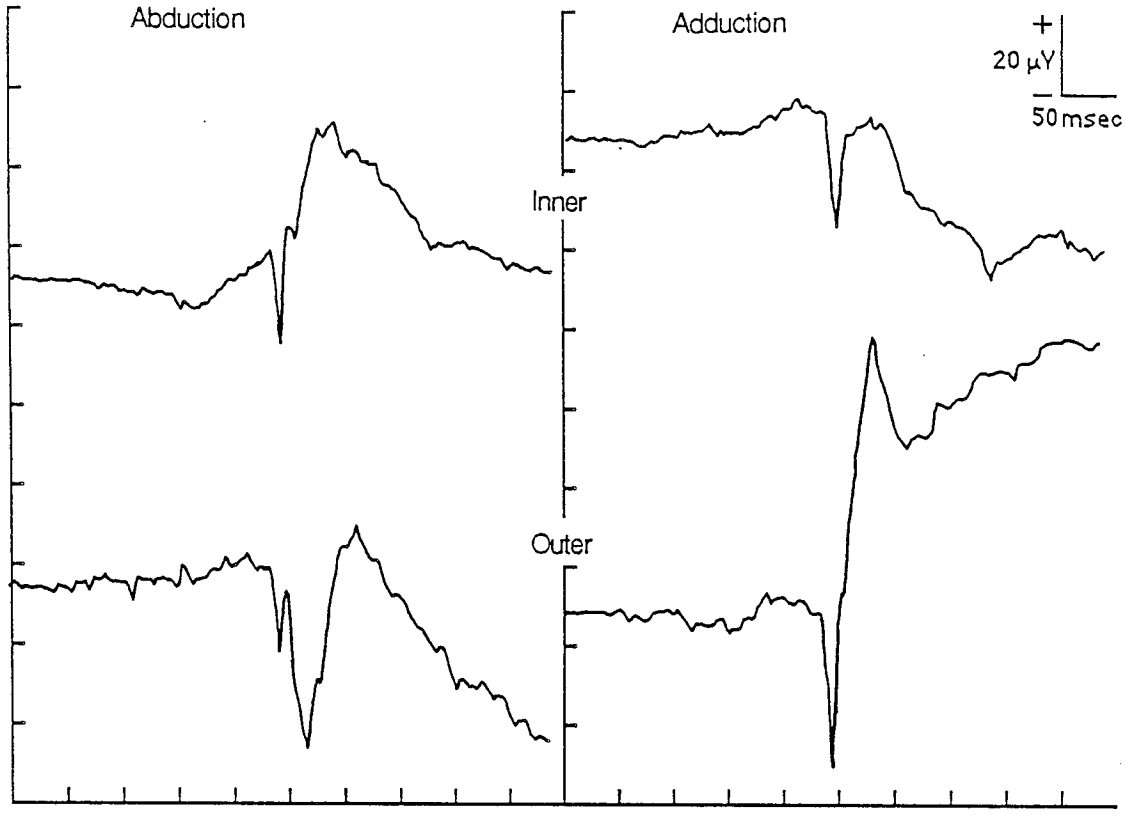


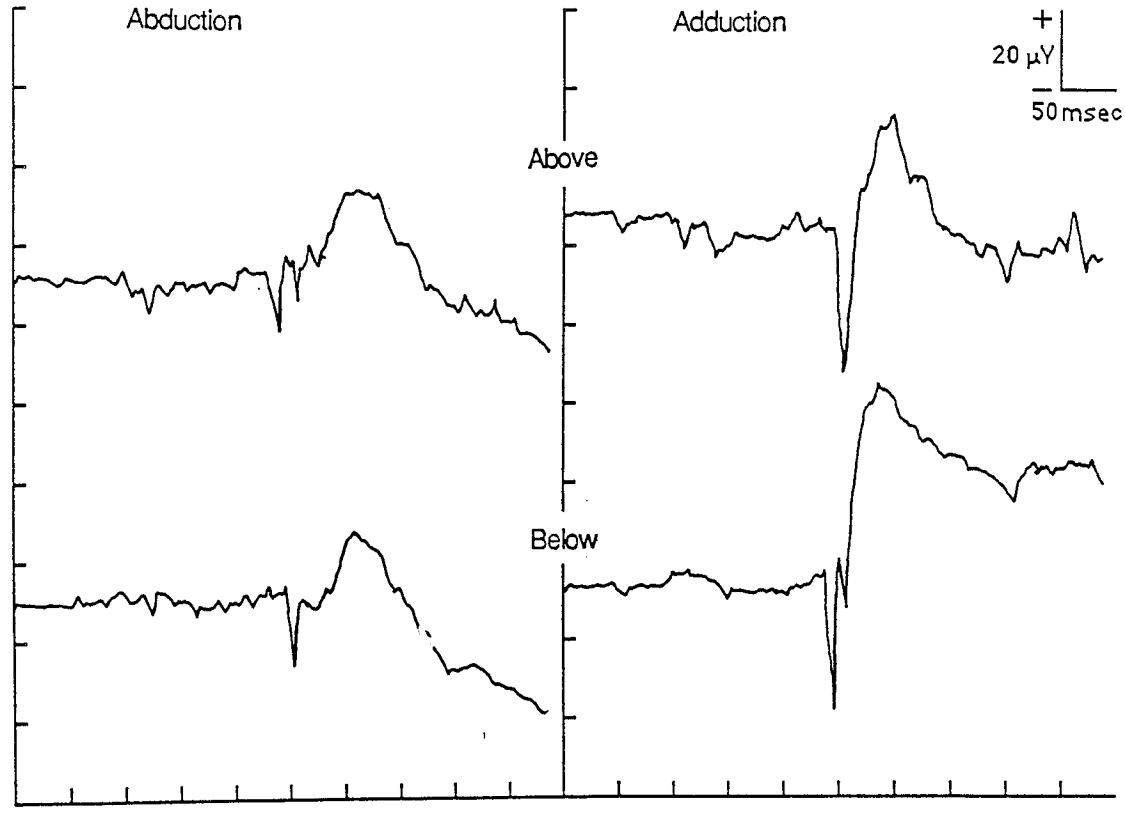
SUBJECT CB: LEFT EYE.



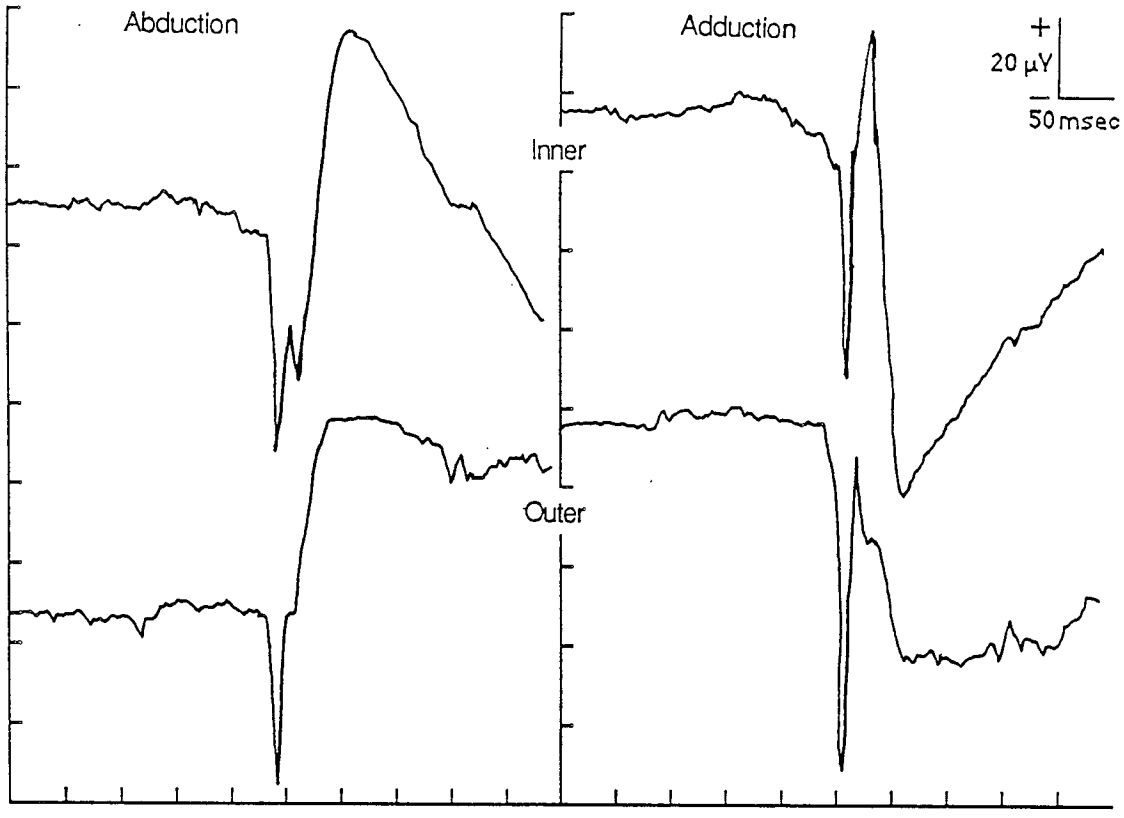


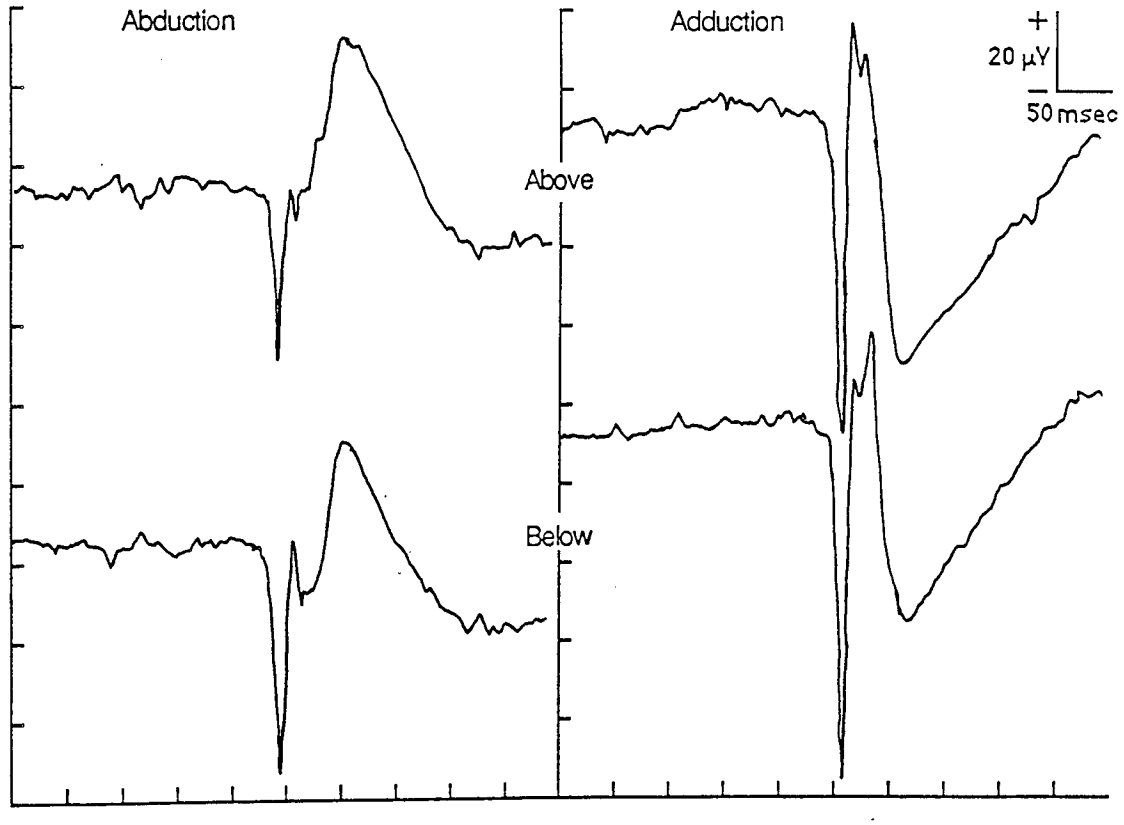
SUBJECT AJH: RIGHT EYE.





SUBJECT JH: RIGHT EYE.





APPENDIX 2.1

The onset and peak latencies for 10 subjects performing five differently sized abducting saccades recorded from electrode at the inner canthus and below the eye.

INNER CANTHUS
SACCADE SIZE

	20°		10°		7.5°		5°		2.5°	
Subject	Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak
AJH 30	-9	1	-11	0	-6	4	-1	7	-6	4
CMS 24	-14	4	-5	6	-4	4	-6	4	-2	8
CN 22	-8	12	-8	8	-2	10	-4	10	-2	9
DT 29	-6	12	-4	10	-3	11	-1	9	-4	9
RD 23	-10	7	-7	6	-4	7	-16	5	-16	10
JR 25	-8	6	-6	5	-4	8	-4	8	0	9
MCD 26	-7	8	-8	3	-8	3	-4	5	-5	3
RB 25	-1	14	-6	7	-8	7	-4	6	-3	5
DD 27	-10	8	-6	5	-13	4	-6	11	-4	5
VV 25	-4	8	-2	11	0	12	-4	13	2	10

LOWER ELECTRODE
SACCADE SIZE

	20°		10°		7.5°		5°		2.5°	
Subject	Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak
AJH 30	-8	0	-11	-1	-8	3	-7	4	-5	3
CMS 24	-22	-10	-8	4	-10	-1	-5	3	-11	-2
CN 22	-6	18	-7	9	-9	8	-9	4	-7	-2
DT 29	-2	11	-8	7	-4	9	-2	7	-9	5
RD 23	-9	5	-6	7	-8	6	-6	4	-5	4
JR 25	-7	8	-6	7	-5	4	-11	9	-17	-6
MCD 26	-7	3	-8	3	-8	3	-6	4	-5	3
RB 25	-7	6	-7	7	-5	7	-3	13	-10	-1
DD 27	-9	4	-9	3	-6	4	-10	1	-11	0
VV 25	-8	9	-4	8	0	11	-8	11	-1	10

The onset and peak latencies for 10 subjects performing five differently sized adducting saccades recorded from electrode at the inner canthus and below the eye.

INNER CANTHUS
SACCADE SIZE

	20°		10°		7.5°		5°		2.5°	
Subject	Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak
AJH 30	-14	-4	-12	-4	-8	-2	-12	-4	-12	-4
CMS 24	-12	4	-13	-1	-16	-5	-12	-1	-12	-4
CN 22	-12	-2	-15	-1	-11	-3	-10	-4	-15	-4
DT 29	-9	4	-12	-2	-10	0	-10	0	-10	-4
RD 23	-10	0	-13	0	-11	0	-12	-1	-11	-1
JR 25	-11	0	-9	0	-10	0	-11	0	-11	-1
MCD 26	-11	2	-11	1	-11	-1	-11	-1	-12	-1
RB 25	-10	0	-12	-1	-11	-1	-11	0	-10	-1
DD 27	-8	0	-8	1	-8	1	-8	1	-11	0
VV 25	-11	-2	-2	11	-12	11	1	11	-1	9

LOWER ELECTRODE
SACCADE SIZE

	20°		10°		7.5°		5°		2.5°	
Subject	Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak	Onset	Peak
AJH 30	-12	-4	-15	-5	-12	-3	-13	-6	-15	-4
CMS 24	-11	-2	-12	-1	-8	5	-21	-7	-11	-2
CN 22	-12	-3	-13	-3	-12	-2	-18	7	-16	-4
DT 29	-16	-3	-13	-4	-10	-3	-10	0	-20	-5
RD 23	-12	0	-11	0	-10	0	-9	3	-11	-1
JR 25	-11	1	-12	1	-11	1	-12	0	-10	0
MCD 26	-9	1	-13	0	-11	-1	-13	1	-17	-1
RB 25	-19	-2	-11	-1	-12	-1	-12	-1	-10	-1
DD 27	-8	1	-9	3	-10	1	-10	-3	-9	0
VV 25	-2	13	-1	11	0	11	2	12	-1	10

The onset to peak amplitudes for the SP recorded with five different saccade sizes from electrodes at the inner canthus and below the eye. The amplitudes for both abductiong (Abd) and adducting (Add) saccades are shown.

INNER CANTHUS
SACCADE SIZE

	20°		10°		7.5°		5°		2.5°	
Subject	Abd	Add	Abd	Add	Abd	Add	Abd	Add	Abd	Add
AJH 30	28.9	22.7	24.3	7.3	31.2	11.0	15.2	6.4	14.4	4.1
CMS 24	25.5	25.5	30.1	19.7	9.4	3.3	21.6	26.0	7.5	4.7
CN 22	50.4	46.4	41.5	38.6	23.2	10.9	23.5	12.4	17.9	8.3
DT 29	50.0	21.2	44.2	16.8	46.5	24.7	45.2	32.6	32.6	6.1
RD 23	40.4	45.2	35.4	42.9	44.3	42.8	20.1	20.3	8.8	23.4
JR 25	49.0	69.0	41.8	56.7	34.3	52.0	29.2	47.7	9.4	26.2
MCD 26	33.4	36.6	31.9	32.3	30.7	26.4	19.6	25.2	9.1	21.8
RB 25	51.0	27.6	56.3	51.7	49.4	46.1	28.6	39.9	13.0	26.8
DD 27	26.0	38.1	23.8	35.6	22.5	39.9	12.2	21.4	6.3	20.1
VV 25	32.5	28.5	37.6	31.9	45.9	16.5	25.2	21.4	10.4	22.3

LOWER ELECTRODE
SACCADE SIZE

	20°		10°		7.5°		5°		2.5°	
Subject	Abd	Add	Abd	Add	Abd	Add	Abd	Add	Abd	Add
AJH 30	34.6	10.3	50.2	14.7	21.4	24.9	5.7	10.1	5.6	06.2
CMS 24	18.7	16.0	24.8	12.5	10.2	8.4	16.2	12.3	7.0	6.4
CN 22	31.3	58.0	27.9	46.7	30.6	22.8	16.2	19.2	10.2	9.4
DT 29	42.3	36.5	39.3	22.2	43.4	21.9	23.0	13.4	19.2	15.9
RD 23	29.8	66.1	41.6	37.3	36.8	40.8	11.2	21.1	24.4	28.9
JR 25	36.0	66.1	38.4	64.3	25.8	57.1	29.8	46.1	8.1	35.9
MCD 26	29.3	45.3	27.9	34.5	30.7	24.3	23.9	26.4	9.1	13.0
RB 25	47.3	47.0	44.7	52.2	43.7	49.3	26.3	35.7	26.8	22.7
DD 27	37.2	55.1	22.7	22.7	16.1	34.6	23.3	12.6	20.1	20.3
VV 25	21.0	53.1	28.8	51.2	36.7	30.0	18.0	46.7	19.5	25.8

APPENDIX 3.1

The onset (On) and peak latencies and onset-peak amplitudes (Amp) for the SP recorded from ten elderly subjects performing four sizes of abducting saccades.

	LOWER ELECTRODE SACCADE SIZE											
	20°			10°			5°			2.5°		
Subject	On	Peak	Amp	On	Peak	Amp	On	Peak	Amp	On	Peak	Amp
EB 73	-15	-2	25.2	-12	-2	17.5	-11	-4	13.6	-3	4	9.2
EB 73	-2	6	17.8	-7	3	8.5	-4	2	21.0	-15	-5	22.3
OC 73	-1	10	46.9	-1	13	33.6	-6	7	12.1	-8	-3	12.6
SH 84	0	11	25.0	0	9	15.8	-9	3	10.8	-10	2	3.7
WH 77	-12	0	30.4	-10	3	36.1	-8	9	27.8	-6	2	13.6
AL 73	-13	-6	18.9	-15	-6	21.5	-7	9	15.5	-14	-4	4.9
WF 81	-21	-8	19.1	-12	0	8.4	-9	1	9.7	-7	-3	3.4
KM 78	-13	7	5.8	-15	-4	11.9	-11	3	3.4	-11	-1	3.6
MM 74	-3	7	10.1	-12	-3	15.5	-7	4	4.7	-12	-2	4.1
HS 85	2	8	28.9	-9	5	29.4	-4	8	6.4	-2	9	3.8

The onset (On) and peak latencies and onset-peak amplitudes (Amp) for the SP recorded from ten elderly subjects performing four sizes of adducting saccades.

	LOWER ELECTRODE SACCADE SIZE											
	20°			10°			5°			2.5°		
Subject	On	Peak	Amp	On	Peak	Amp	On	Peak	Amp	On	Peak	Amp
EB 73	-11	-1	31.0	-12	-2	23.1	-9	-2	19.4	-10	-3	4.5
EB 73	-7	5	28.6	-2	-3	14.8	-10	4	19.6	-10	-1	19.6
OC 73	-11	-2	25.2	-9	-2	18.9	-10	-5	11.1	-13	-4	5.7
SH 84	0	12	22.9	0	9	15.8	-14	-3	16.5	-13	-6	10.4
WH 77	-12	-4	54.1	-10	-3	53.7	-15	-3	44.4	-12	-2	24.0
AL 73	-13	-4	23.3	-18	-6	21.0	-13	-6	9.8	-13	-6	5.1
WF 81	-13	-4	18.5	-13	-5	13.3	-14	-3	3.1	-13	-1	2.1
KM 78	-16	-8	12.7	-14	-3	10.4	-16	-5	6.3	-13	-4	2.7
MM 74	-12	-2	18.6	-18	-8	6.9	-15	-4	5.8	-10	-2	5.2
HS 85	-9	0	33.5	-11	-1	29.6	-16	-1	18.7	-14	-1	13.6

The onset and peak latencies and onset-peak amplitudes (Amp) for the SP recorded from ten middle-aged subjects performing 20° abducting and adducting saccades.

	LOWER ELECTRODE					
	Abducting			Adducting		
Subject	Onset	Peak	Amp	Onset	Peak	Amp
DB 43	-5	7	31.1	-8	-1	24.3
HY 43	-8	9	42.0	-12	0	36.4
CF 42	0	11	34.4	-7	-1	24.8
BG 41	-6	4	44.0	-10	-1	45.3
BB 44	-5	5	31.9	-12	-1	41.9
EB 45	-5	3	25.3	-10	0	28.2
AH 46	-12	-2	37.2	-17	-9	13.5
PC 45	-6	8	43.3	-12	-2	61.3
PR 47	-3	5	43.7	-11	-1	62.4
CW 42	-2	6	63.2	-8	0	57.5

APPENDIX 4.1

The onset and peak latencies and onset - peak amplitudes for 10 subjects performing 20° vertical saccades. The SP was recorded from four electrodes around the right eye.

RIGHT EYE UPWARD

ELECTRODE SITE

	INNER			OUTER			ABOVE			BELOW		
Subject	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
AS 23	-11	2	20.0	-3	12	18.0	-9	2	20.0	-11	11	27.3
BE 26	-5	1	28.9	-10	-1	39.2	-5	4	48.1	-8	0	34.6
CB 30	-2	-8	35.0	-8	0	17.0	-7	1	11.7	-7	3	30.0
CN 22	-2	8	42.6	-4	7	30.7	-17	-2	11.7	-4	6	36.7
DS 24	-2	7	42.8	-7	3	46.2	-1	7	20.5	-7	5	58.9
HO 30	-20	6	49.0	-8	7	38.5	-25	-17	21.1	-7	8	36.6
JR 25	-1	8	33.4	-9	4	27.6	-5	0	12.6	-7	3	29.3
MD 26	-1	14	56.5	-5	13	32.0	-5	8	18.8	-2	12	47.4
RD 23	-18	5	29.1	-8	2	26.9	-13	-5	7.6	-8	10	25.8
SP 23	-11	8	32.5	-9	7	21.5	-10	3	37.8	-8	9	21.0

RIGHT EYE DOWNWARD

ELECTRODE SITE

	INNER			OUTER			ABOVE			BELOW		
Subject	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
AS 23	-15	-4	29.3	-15	-5	26.4	-18	-3	47.8	-20	-4	51.4
BE 26	-8	0	31.9	-8	0	34.8	-12	-1	35.4	-12	-2	33.2
CB 30	-18	-8	8.4	-10	0	7.2	-13	-7	5.7	-13	-5	7.7
CN 22	0	13	19.4	-5	1	3.3	1	11	19.9	-2	6	24.2
DS 24	-10	-1	11.0	-7	0	10.8	-12	-1	6.8	-10	-1	14.1
HO 30	-28	-18	20.7	-20	-8	15.8	-19	-5	36.0	-26	-5	32.8
JR 25	-11	-2	20.6	-12	-2	14.6	-9	0	41.4	-14	-2	34.8
MD 26	-9	7	5.1	-21	-10	5.1	-20	-7	20.2	-16	-8	8.5
RD 23	-14	-2	33.2	-11	-2	16.9	-15	-2	47.8	-16	-3	30.8
SP 23	-14	-4	26.6	-12	-1	24.1	-19	-3	40.1	-16	-3	30.2

The onset and peak latencies and onset - peak amplitudes for 10 subjects performing 20° vertical saccades. The SP was recorded from four electrodes around the left eye.

LEFT EYE UPWARD

ELECTRODE SITE

	INNER			OUTER			ABOVE			BELOW		
Subject	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
AS 23	-11	2	20.0	-3	12	18.0	-9	2	20.0	-11	11	27.3
BE 26	-5	1	28.9	-10	-1	39.2	-5	4	48.1	-8	0	34.6
CB 30	-2	-8	35.0	-8	0	17.0	-7	1	11.7	-7	3	30.0
CN 22	-2	8	42.6	-4	7	30.7	-17	-2	11.7	-4	6	36.7
DS 24	-2	7	42.8	-7	3	46.2	-1	7	20.5	-7	5	58.9
HO 30	-20	6	49.0	-8	7	38.5	-25	-17	21.1	-7	8	36.6
JR 25	-1	8	33.4	-9	4	27.6	-5	0	12.6	-7	3	29.3
MD 26	-1	14	56.5	-5	13	32.0	-5	8	18.8	-2	12	47.4
RD 23	-18	5	29.1	-8	2	26.9	-13	-5	7.6	-8	10	25.8
SP 23	-11	8	32.5	-9	7	21.5	-10	3	37.8	-8	9	21.0

LEFT EYE DOWNWARD

ELECTRODE SITE

	INNER			OUTER			ABOVE			BELOW		
Subject	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp	Onset	Peak	Amp
AS 23	-15	-4	29.3	-15	-5	26.4	-18	-3	47.8	-20	-4	51.4
BE 26	-8	0	31.9	-8	0	34.8	-12	-1	35.4	-12	-2	33.2
CB 30	-18	-8	8.4	-10	0	7.2	-13	-7	5.7	-13	-5	7.7
CN 22	0	13	19.4	-5	1	3.3	1	11	19.9	-2	6	24.2
DS 24	-10	-1	11.0	-7	0	10.8	-12	-1	6.8	-10	-1	14.1
HO 30	-28	-18	20.7	-20	-8	15.8	-19	-5	36.0	-26	-5	32.8
JR 25	-11	-2	20.6	-12	-2	14.6	-9	0	41.4	-14	-2	34.8
MD 26	-9	7	5.1	-21	-10	5.1	-20	-7	20.2	-16	-8	8.5
RD 23	-14	-2	33.2	-11	-2	16.9	-15	-2	47.8	-16	-3	30.8
SP 23	-14	-4	26.6	-12	-1	24.1	-19	-3	40.1	-16	-3	30.2

APPENDIX B: SUPPORTING PUBLICATIONS

C. Boylan and **H. R. Doig** (1988) Presaccadic spike potential to horizontal eye movements. *Electroenceph. Clin. Neuro.*, 70: 559-562.

H. R. Doig and C. Boylan (1989) The pre-saccadic spike potential. *Ophthal. Physiol. Opt.*, 9: 100.

H. R. Doig and C. Boylan (1989) Presaccadic spike potential with large horizontal eye movements. *Electroenceph. Clin. Neuro.*, 73: 260-263.

C. Boylan and **H. R. Doig** (1989) Presaccadic spike potential with congenital lateral rectus palsy. *Electroenceph. Clin. Neuro.*, 73: 264-267.

H. R. Doig and C. Boylan (1989) Changes in the presaccadic spike potential with age. *Electroenceph. Clin. Neuro.*, 73: 549-551.

C. Boylan and **H. R. Doig** (1989) Effect of saccade size on presaccadic spike potential amplitude. *Invest. Ophthalmol.*, 30: 2521-2527.

H. R. Doig, C.J. Nesfield and C. Boylan (1990) Presaccadic spike potential with vertical saccades. *Ophthal. Physiol. Opt.*, 10: 182-185.

H. R. Doig, L.Jones and C. Boylan (1990) The presaccadic spike potential in multiple sclerosis. In press.

Electroencephalography and clinical Neurophysiology, 1988, 70: 559–562
Elsevier Scientific Publishers Ireland, Ltd.

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Short communication

Presaccadic spike potential to horizontal eye movements

C. Boylan and H.R. Doig

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

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Presaccadic spike potentials with large horizontal eye movements

H.R. Doig and C. Boylan

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

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Presaccadic spike potential with congenital lateral rectus palsy

Christine Boylan and H. Ross Doig

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

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Changes in the presaccadic spike potential with age

H. Ross Doig and Christine Boylan

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

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Effect of Saccade Size on Presaccadic Spike Potential Amplitude

Christine Boylon and Henry Ross Doig