# Clinical Application of Saccade-Reflex Testing in Man

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**Computer-aided measurements of saccade-reflex reaction times, velocities, and accuracies have become important tools in the detection of central nervous system pathology. Because of improved knowledge of the reflex pathways in man, saccade testing can assist in differentiating between brain stem, cerebellar, or cerebral disorders and point toward unilateral lesions. Saccade-reflex testing is also useful in determining disability and measuring over time the course of central nervous system disorders. Further work, correlating lesions observed by high-resolution imaging techniques with abnormalities in reflexes, continues to improve the understanding of saccade mechanisms in man. Specific cases are used to show the effects of anatomic lesions on changes in saccade reflexes. The results from 100 consecutive patients evaluated for dizziness are provided in order to illustrate the prevalence of saccade abnormalities and the relationship between abnormalities in vestibular and slow and fast eye-movement reflexes. Patients complaining of disequilibrium and visual disturbances frequently have abnormalities in the saccade system, abnormalities which are often overlooked in present clinical testing of the dizzy patient.**

## INTRODUCTION

Rapid eye movements require an elaborate system of sensory perception, pathways to the cerebral visual cortex, and a complex effector system connected to most divisions of the central nervous system. The specific anatomic pathways responsible for this activity are now partly known. This paper reviews the known anatomic pathways, examines methods of measuring saccade reflexes, and describes how application of this simple physiologic test can aid in obtaining clinically useful information in patients complaining of disequilibrium or visual disturbances. Areas where additional research is needed are identified.

The application of digital computers to measurements of accuracy, velocity, and reaction times (latencies) in saccade reflexes coupled with accurate anatomic information from computed tomographic (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) scanning has produced major advances in knowledge about these reflexes and their function in man. Additional research with animals has helped clarify some of the specific neuronal mechanisms in saccades. Modeling of these mechanisms has produced a conceptual framework to further aid in understanding this system.

Patients experiencing dizziness rarely complain of true vertigo. Most commonly they complain of disequilibrium, of light-headedness, or of visual disturbances. They often seek evaluation and treatment of these symptoms from either the otologist, neurologist, or ophthalmologist. In such patients, saccade testing frequently detects abnormalities and aids in formulating an etiologic diagnosis. Failure to evaluate the saccade system in such patients may lead to the erroneous conclusion that the patient has no organic disorder.

### *Saccade Reflexes*

A saccade is defined as a rapid eye movement whose purpose is to fixate the gaze on a visual target. The purpose of a saccade is to fixate the fovea on new targets of interest or to make corrective "catch up" movements when a target escapes the more slowly tracking smooth-pursuit system. Volitional refixation in the dark is also considered a saccadic eye movement. The fast component of optokinetic and vestibular nystagmus reaches velocities similar to saccades and has the function of resetting the eyes in the orbit in a position which will allow further slow movements. Some authors would suggest that these fast movements are saccades as well. Although the slow eye movements of vestibular, optokinetic, and pursuit reflexes are largely related to the characteristics of the stimulus, saccades are ballistically preprogrammed by the central nervous system.

Because saccade pathways involve several regions of the cerebral cortex, the cerebellum, and brain stem, few disorders which alter central nervous system function escape detection when these reflexes are measured with precision. It is for these reasons that

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testing of saccade reflexes is such a powerful clinical tool for identifying the presence of central nervous system pathology. Although detection of saccade abnormalities is easy with presently available computer technologies, anatomic localization is much more difficult, since the saccade abnormality depends not only on the lesion but also on the extent of recovery. Present clinical testing concentrates on horizontal rapid eye movement.

### *History*

In 1830, Flourens[1] described slow and fast phases of nystagmus as a result of labyrinthine injury. In 1886, Ferrier[2] noted contralateral rapid eye movements after stimulation of the frontal cortex (area 8) in monkeys. It was after several observations of patients with altered fast components that Barany (1921)[3] proposed the brain stem as the area responsible for the generation of rapid eye movements. Lorente De No (1928)[4] concluded that the pontine reticular formation contained the mechanisms responsible for the generation of the fast component of nystagmus.

Since then, many experiments have extended the knowledge of the anatomy and physiology of these reflexes. Since this system has been greatly modified in higher primates, recent neurophysiological experiments have been done in awake monkeys and in man. These experiments have expanded current knowledge of the role of higher centers, including the superior colliculus, the midbrain, the cerebellum, and the cortex. Models of these systems have increased in complexity in order to incorporate new anatomic information and new experimental observations. A recent review by Van Gisbergen and Van Opstal[5] describes the current understanding of the saccade system.

### *Anatomy*

Visual information is transmitted from the retinal ganglion cells via the optic nerve, optic chiasm, and the optic tracts around the cerebral peduncles to the lateral geniculate body. The geniculocortical connections separate into a superior and inferior band; these project to the striate cortex of the occipital lobe (area 17)[6] (Fig. 1). This represents the sensory portion of the saccade reflex.

Visually guided saccades are programmed in the frontal cortex (area 8). In addition to retinal error perception (distance between foveal vision and the target), eye position information must be considered and a command issued to the oculomotor nuclei. The exact anatomic pathways of this sequence are not completely understood. Frontal eye fields direct movements to the contralateral side.[7] Neurons in the deeper layers of the frontal eye fields use the corpus callosum to connect with the superior colliculus neurons. In addition to direct pathways, a pathway using the pars reticulata area of substantia nigra to the

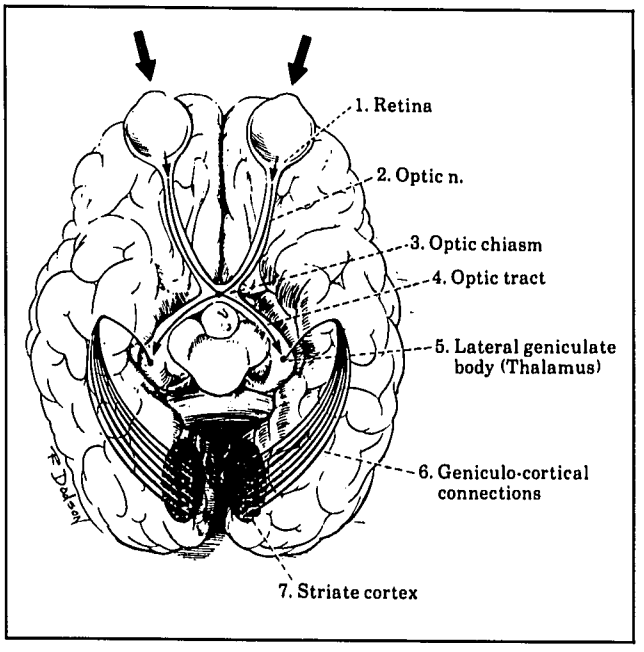


Fig. 1. The pathway from visual input to occipital cortex represents the sensory portion of the saccade reflex.

superior colliculus also appears to be present. Neurons from the superior colliculus connect with neurons in the mesencephalic reticular formation, and the output from this network innervates oculomotor neurons (Fig. 2). The parietal cortex is also part of this network when attention-directed saccades occur.

This area appears to contain a map of the visual field and targets directed eye movements to a new point of interest in that field.[8] This represents the motor portion in the saccade reflex. In addition to the information which targets the saccade, there is evidence for a local feedback system which monitors and integrates changing eye-position information into the reflex. The flocculus and nodules of the cerebellum also play an important part in these reflexes.[9] The cerebellar vermis is very important in the adaptation of eye movements, including saccades, by adjusting their gain.[10]

Much clinical information about saccade anatomy and physiology in man came from the computer analysis of eye movements which was developed in the 1970s.[11] Additions and improvements to these methods have been described in more recent publications, and there is now a strong attempt to improve standardization.

### *Physiology*

Saccade eye movements have specific characteristics dictated by the central connections and the mechanical properties of the eye muscles and the orbit. Since the neural activity from the oculomotor nuclei during a saccadic movement represents virtually a maximal output from the system, the velocity of the

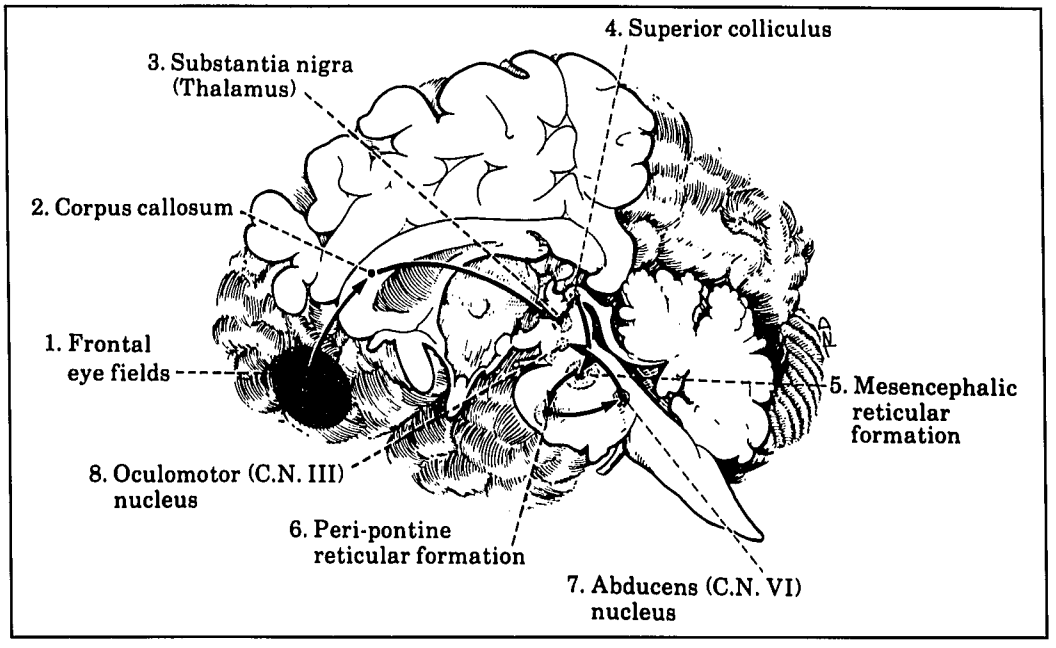


Fig. 2. The pathway from the frontal eye fields to the oculomotor nuclei represents the motor portion of the saccade reflex.

eye movement for saccades over 10° is determined by the duration of the burst of activity and the viscoelastic properties of the eye in the orbit. Therefore, eye velocities of 20° to 800° per second are achieved depending on the amplitude of the saccade. Most saccades fall slightly short of the target, and a second small corrective saccade completes placing the fovea on target. Because of the large pathway and large number of neural corrections involved in initiating a saccade after a target moves, there is a delay between the target movement and the subsequent eye movement (reaction time). Although this delay increases with advancing age, it is generally in the range of 180 to 220 msec (Fig. 3).

## MATERIALS AND METHODS

One hundred consecutive patients referred to the vestibular laboratory because of persistent dizziness were evaluated. Slightly more than half of these patients were referred by otolaryngologists—head and neck surgeons. Of the remainder, most referrals were from primary care physicians. In addition to these, cases with anatomically well-documented lesions were used to illustrate specific abnormalities in saccade reflexes.

The mean age was 54.7 years with a range from 11 to 96. Sixty-four of these patients were 50 years or older with a peak at the 7th decade. Seventy of the patients were women and 30 men. All were evaluated and a history and head and neck examination were performed including an examination of cranial nerves, cerebellar function, posture, and gait. Only patients thought to have abnormalities of the vestibular end organs or of the eye-movement control system on clinical grounds were sent for a computer-aided evaluation of these systems. The evaluation included an examination for spontaneous and gaze nystagmus with eyes open and eyes closed, for positional nystagmus, and Hallpike tests. Smooth pursuit was tested at 22° and 44° per second, sinusoidally. Optokinetic responses were elicited using full-field stimulation at 30° per second sinusoidally. Caloric tests were performed by irrigating each ear with 30° and 44° water for 40 seconds.

For smooth pursuit and saccade tests, the stimulus was generated by the computer on a strip of light emitting diodes 1 m from the subject. Five silver/silver chloride electrodes and electro-oculography were used to measure eye movements. Movements of each eye were recorded separately by using inner and outer canthus electrodes. A digital computer sampled the amplified signal and generated integer values which were used to calculate eye position. From these, gain, phase, velocity, accuracy, and reaction time were calculated. Subjects were repeatedly alerted during the test procedures.

During each saccade test, the computer moved the target back and forth at random time intervals (1 to 4 seconds) to different randomly selected positions on the target display (deflection ranging from 5° to 36° angular movement). Each test contained 30 such jumps. As the digitized eye position was processed through the saccade-identifying routine, the data were treated with a low-pass digital filter with a bandwidth of 30 Hz (Hanning Window) to remove spurious high-frequency fluctuations and smooth the data. Saccades were identified by determining the point in time that the peak eye velocity occurred, then searching backward through the eye-velocity array until a point in time is reached where the instantaneous eye velocity dropped below a preset minimum. Latency (reaction time) was determined by measuring the time interval between this minimum and the movement of the target. The computer calculates the amplitude, velocity, accuracy, and latency (reaction time) of each saccade. Patients were scored abnormal if their test values were outside a 95% confidence limit.

### *Normal Values*

Normal values used in this study are supplied; however, it is recommended that each laboratory obtain their

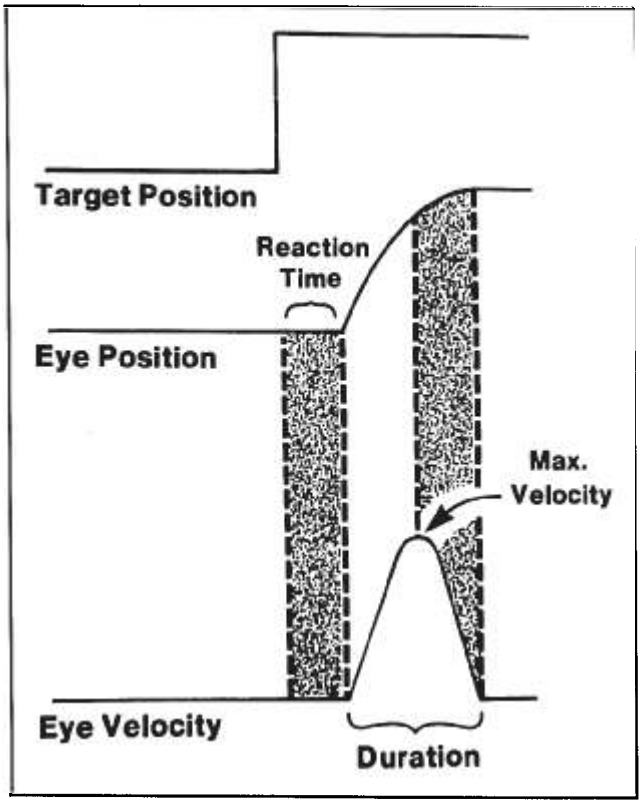


Fig. 3. Diagrammatic plot showing target movement and the corresponding saccadic eye movement. Eye position and velocity are plotted separately.

own values. The actual values depend to some extent on the equipment and programs used, on the instructions to the subject, on the technician, and on the environment of the testing laboratory. Normal values should be obtained on a group of subjects who by history as well as clinical evaluation have no disorders affecting vision or central nervous system function and who are on no medications. The normal values used in this study are given in Table I.

### *Age*

In order to understand disorders affecting the saccade system, this system's normal activity and its normal variations must first be evaluated. One variable that alters saccade parameters is age. Hainline, *et al.*[12] found that, even in infants a few weeks old, saccades with normal velocities and amplitudes were performed. Although there were also slower saccades, these were thought to be related to difficulty with attention, calibration, and recording methodology.

Children with a mean age of 8.5 years seem to have saccade characteristics similar to adults.[13] It is only with advancing age that saccade parameters seem to change. Most authors report increased reaction time with advancing age.[14–17] Saccade amplitude and accuracy are not affected by age. The changes in saccade reaction time noted by most experimenters suggest that age has an effect on the sensory portion of the saccade reflex (Fig. 1). The brain stem reticular formation, which is primarily responsible for saccade velocity and amplitude, does not seem to be affected as much.

TABLE I.
Normal Values.

| | | |
|---|---|---|
| 1. | Smooth pursuit gain at .2 Hz | >.60 |
| | at .4 Hz | >.50 |
| 2. | Optokinetic gain: | >.70 |
| 3. | Calorics: directional preponderance | <25% |
| | unilateral weakness | <20% |
| 4. | VOR: gain at .05 Hz | >.60 |
| | VOR: gain asymmetry | <10% |
| 5. | Saccade: | |
| | Interval age 10.60 | <220 msec |
| | Over age 60 | <250 msec |
| | Peak velocity | >420°/sec |
| | Accuracy | >80%; <110% |

### *Drugs*

Aschoff[18] in 1968 first described the use of saccade measurements to evaluate the effect of centrally active drugs. Since saccades once initiated are not under voluntary control, and saccade tests are noninvasive, quick, and not uncomfortable, these tests are attractive for the evaluation of the alteration of neurophysiologic function due to drugs. As saccade velocity is largely related to brain stem function, while saccade accuracy and reaction time is related to higher central functions, these tests can also be used to obtain information about the general anatomic location of the action of drugs and to make inferences about possible neuronal transmitters at various anatomic locations in the saccade reflex. Several classes of drugs have been studied in man, a few quite extensively.

γ-aminobutyric acid (GABA) appears to be a commonly occurring central nervous system neurotransmitter, and there are specific benzodiazepine binding sites in areas of the brain stem known to be involved in oculomotor control.[19] Benzodiazepines appear to facilitate GABA-mediated inhibition. In this way, benzodiazepines appear to exert an inhibitory effect on the burst neurons whose firing controls saccade velocity.

Studies by Rothenberg and Selkoe[20] show decreasing saccade velocities with increasing doses of benzodiazepines without much change in saccade accuracy or reaction time. These studies concur with studies by Coale, *et al.*[21] using oral diazepam.

The effect of opiates[22] seems to be to reduce saccade accuracy and increase saccade reaction time. Rothenberg and Selkoe found decreased saccade accuracy and increased saccade reaction time with oral doses of methadone (5 mg). Saccade velocity, however, was not affected. This suggests that opiates affect the sensory side of the saccade reflex or the activity in the visual cortex or frontal eye fields. Because the accuracy of larger saccades is affected more than small saccades, mechanisms responsible for visual encoding are likely to be affected by opiates. Peripheral retinal projections directly to the superior colliculus could be the mechanism affected.

Amphetamines do not appear to affect saccade movements after oral administration. After intravenous administration, however, Tedeschi, *et al.*[23] noted reduced reaction time and an abolition of the effect of fatigue on saccade velocity. The anatomic location of this effect is conjectural, but it may be due to a general alerting effect.

Fig. 4. Patient 1. Magnetic resonance image (MRI) scan showing many small lesions within the periventricular areas and in the left corpus callosum region. This patient had prolonged saccade reaction times particularly for right-going saccades.

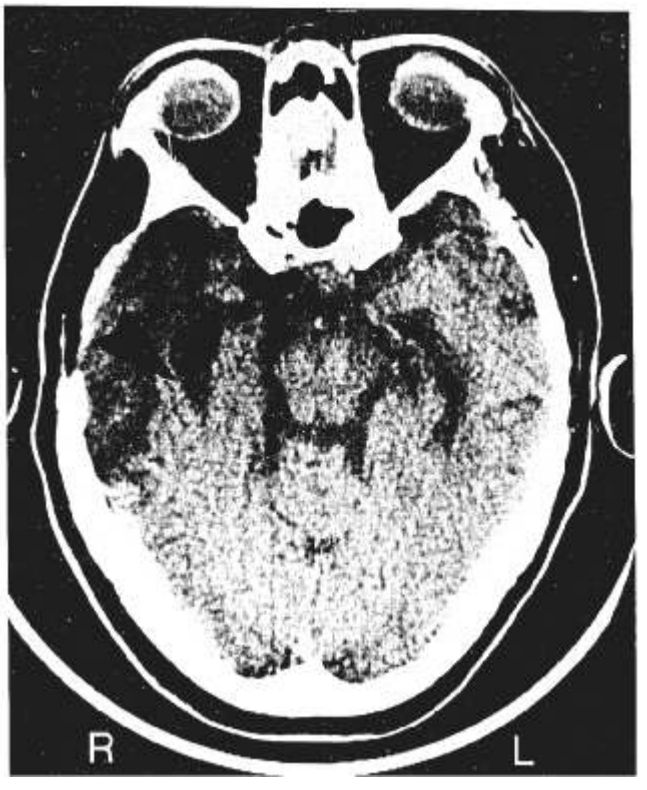


Fig. 5. Patient 2. Computed tomography (CT) scan showing a radiolucent area in the right superficial and deep frontoparietal area. The patient had severe prolongation of left-going saccade reaction time.

Jantti, *et al.*[24] in a study on alcohol and saccades, noted that saccade velocity decreased and saccade reaction time increased with the intravenous infusion of ethanol. The changes best correlated with the subjective feeling of drunkenness rather than with serum alcohol levels.

More surprising is an increase in saccade reaction time in response to the common antihistamine chlorpheniramine (Chlor-Trimeton®). Alerting mental exercises were used during these tests as with all others, and no change in alertness was noted.[25] Most likely, histamine is involved in neuronal transmission in these reflexes.

## PATIENT REPORTS AND DISORDERS AFFECTING SACCADE REFLEXES

### *Multiple Sclerosis*

Multiple sclerosis is a disorder in which the myelin surrounding nerve fibers is damaged. In 20 patients with early multiple sclerosis followed over a 5-year period, the saccade test was the most commonly abnormal of a series of tests of central function.[26] (Tests included audiogram; auditory reflexes; auditory-evoked response; visual-evoked response; and rotational vestibulo-oculomotor, smooth pursuit, and optokinetic reflexes and saccade tests.) The most common abnormality was an increase in saccade reaction time. This suggests that multiple sclerosis affects the transmission velocity of central neural pathways or interrupts direct pathways requiring the participation of alternate, less direct, routes.

Since this disease is characterized by scattered lesions in the nervous system, it is not surprising that a test which measures a reflex with extensive central connections is so often abnormal. Furthermore, multiple sclerosis frequently produces lesions in the white matter around the lateral ventricles and the corpus callosum. These are areas where the descending connections from the frontal eye fields and parietal cortex are located (*cf.* patient report 1.) Increased transmission time in the afferent pathways may also play a role in increased latencies.[27]

### *Patient Report 1*

Patient 1 is a 25-year-old woman with severe chronic disequilibrium, a constant floating feeling, and progressive difficulties with reading and walking. Saccade reaction time was severely prolonged particularly for right-moving saccades. The MRI scan shows many lesions within the periventricular areas of the cerebrum and with a predominance of lesions in the left corpus callosum region (Fig. 4). Since multiple sclerosis can interrupt pathways anywhere in the central nervous system, other changes in saccade responses can also occur depending on the site of the lesion.

Saccade-reflex testing is useful in detecting a central nervous system abnormality in patients where multiple sclerosis is suspected on clinical grounds.

### *Head Injury*

In a series of patients complaining of disequilibrium after a head injury, saccade abnormalities were common (11 of 20). In all 11 patients, there was an increase in reaction time which was usually asymmetrical but did not always correlate with the side of impact to the head. In addition, if patients with post–head-injury disequilibrium had evi-

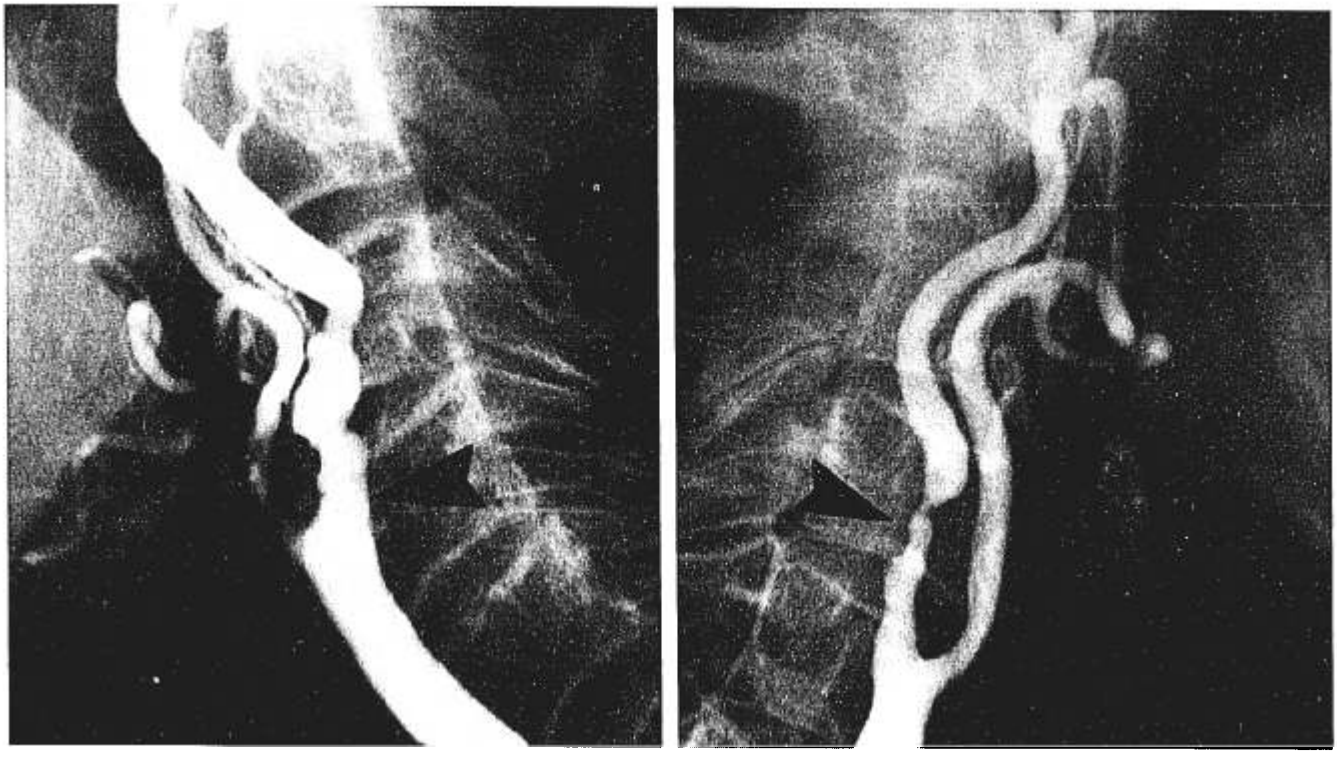

Fig. 6. Patient 3. Arteriogram showing 90% right internal carotid occlusion and 50% left internal carotid occlusion. Increased saccade reaction times occurred for left-going saccades.

dence of both labyrinthine (by caloric or rotational vestibular testing) and saccade-reflex testing, their probability of recovery and resumption of previous employment was unlikely (35%).

### *Patient Report 2*

A 36-year-old woman received severe head injuries during a motor vehicle accident. Following recovery, she had a left hemiparesis and difficulty reading. She had severe increases in left-going saccade reaction time but normal saccade velocity and amplitude. The CT scan shows that radiolucent areas involved both superficial and deep frontoparietal regions on the right side (Fig. 5).

Saccade testing is a useful part of the work-up of patients with post–head-injury disequilibrium, and saccade abnormalities predict the reduced probability of a return to previous employment.

### *Cerebrovascular Disease*

In a group of patients with internal carotid artery disease who also complained of disequilibrium, saccadic eye movements contralateral to the side of the major carotid obstruction were delayed.[28] In two patients who were tested after endarterectomy and an improvement of disequilibrium, the saccade-reaction time had returned to normal.

### *Patient Report 3*

Patient 3 is a 68-year-old man with progressive difficulty in walking, difficulty in reading, and chronic disequilibrium. An ophthalmologic examination showed no visual abnormalities to explain his reading difficulties. Saccade reaction time was severely prolonged bilaterally but more so for left-going saccades. The patient's arteriogram showed fairly normal vertebral circulation but a 90% right internal carotid occlusion and a 50% left internal carotid occlusion (Fig. 6). The saccade abnormalities not only reflect the cerebrovascular occlusive disease but also point to the side of the greater stenosis (contralateral).

In patients with risk factors for cerebrovascular disease and prolonged reaction times, carotid artery arteriosclerosis should be considered in the differential diagnosis. Both symmetric and asymmetric prolongation in saccade reaction time is observed in this disease. In the past, vertebral artery occlusive disease in patients with disequilibrium was considered. It is now clear that the carotid cerebral circulation in these patients must also be evaluated, since decreased blood flow or infarctions of the cerebral eye-movement control areas can result in the symptoms of disequilibrium.

### *Huntington's Disease*

Huntington's disease appears to involve the basal ganglia and the substantia nigra pars reticularis. In a series of 20 patients with early Huntington's disease tested by Lasker, *et al.*,[29] there were significant increases in saccade reaction times. This was particularly true for volitional saccades and less so for reflexive saccades, suggesting that the caudate and substantia nigra mediate volitional saccades.

### *Parkinsonism*

Parkinsonism appears to be a disorder of dopamine neurotransmission in the basal ganglia and substantia

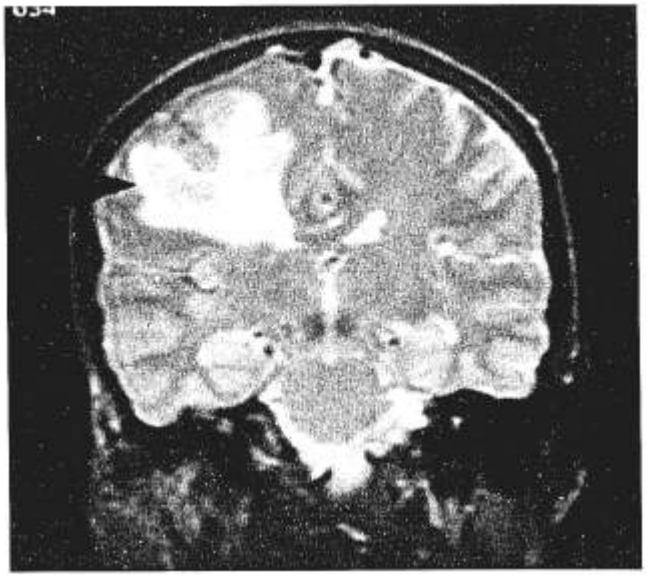

Fig. 7. Patient 4. MRI scan showing a right parietal neoplasm with surrounding edema. The patient had increased left-going saccade reaction times which improved after treatment with systemic steroids.

nigra. Increased saccade reaction time and decreased saccade velocities and accuracies were reported in patients with idiopathic Parkinsonism as well as in patients and monkeys in whom Parkinsonism was due to the toxic effects of N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine.[30,31] These changes were reversed by dopamine, a neurotransmitter thought to act on basal ganglia and substantia nigra. A postmortem examination on the monkeys showed decreased cell numbers in substantia nigra.

### *Cortex Disorders Affecting Saccade Reflexes*

Since the occipital, parietal, and frontal cortex are all involved in saccade reflexes, disorders affecting the cerebral cortex can alter these reflexes. The frontal cortex is the command center which initiates a saccade. Lesions of the frontal cortex result in a contralateral increase of reaction time (*cf.* patient report 1). Since the ipsilateral frontal cortex is able to take over this function in time, the differences in saccade reaction time between saccades contralateral and ipsilateral to the lesion gradually diminish. Large hemispheric deficits, such as appear in response to an occlusion of the internal carotid artery, result in a severe increase in contralateral saccade reaction time. This is reversed in some patients following carotid endarterectomy.[28]

Studies using gamma cameras to image local blood-flow increases in response to neuronal activity confirm the frontal and temporo-occipital areas as areas associated with saccade activity in man.[32] Studies in hemidecorticated monkeys showed that contralateral voluntary and reflexive saccades were damaged by decortication, but spontaneous saccades and the quick phase of nystagmus were not. One year after decortication, there was some recovery, but saccade reaction time was still increased.[33] Sharp, *et al.*[34] also found increased contralateral saccade reaction times in five hemidecorticated patients. Guitton, *et al.*,[35] in patients where the frontal cortex was removed for the treatment of epilepsy, found impairment in the suppression of unwanted reflexive contralateral saccades and in triggering volitional saccades.

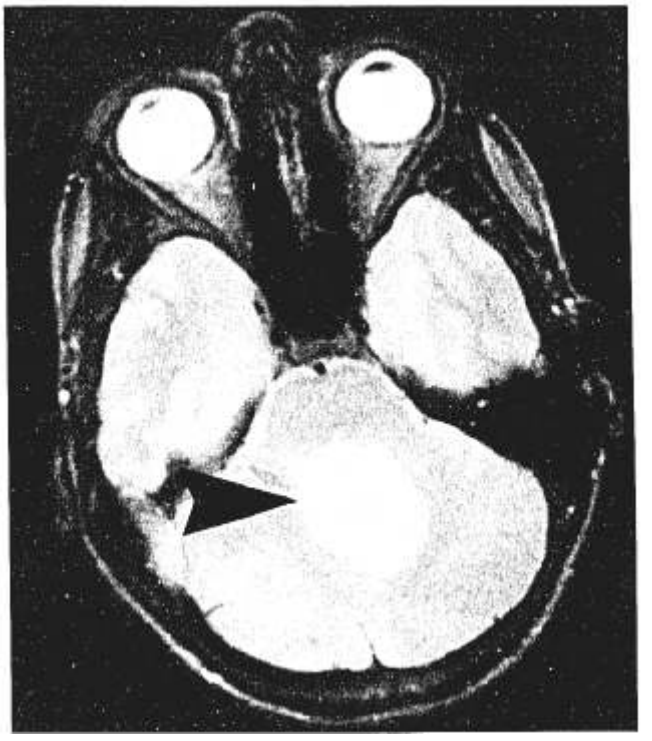

Fig. 8. Patient 5. MRI scan showing a central cerebellar tumor. The patient had bilateral saccade overshoots and large alternating saccades during attempts at fixation.

Pierrot-Deseilligny, *et al.*[36] found increased saccade reaction time only in some patients with frontal lesions, specifically in patients where the deeper and posterior regions of the frontal cortex and regions near the corpus callosum were damaged. They theorize that in these patients the damage is to the efferent pathways descending from the frontal eye fields. In Alzheimer's disease, saccade reaction time is increased and velocity decreased[37] when using saccade presentations which are unpredictable. When subjects engage in saccadic movement back and forth between two targets of known location, there is no significant alteration of saccade parameters.

### *Parietal Lesion*

Anders Sundqvist[38] studied six patients with primarily posterior parietal lesions and found increased saccade reaction time for contralateral saccades. In two of these patients, treatment with betamethasone resulted in a reduction of edema surrounding the lesion, and the saccade reaction time asymmetry disappeared. Contralateral voluntary saccade reaction time is increased in these patients.

### *Patient Report 4*

This patient had a right parietal neoplasm with edema of the deeper white matter. The patient had difficulty producing left-going saccades on command and had increased saccade reaction times to the left (Fig. 7).

### *Cerebellum*

Although the nodulus and flocculus (lateral cerebellum) are clearly implicated in visual-vestibular interac-

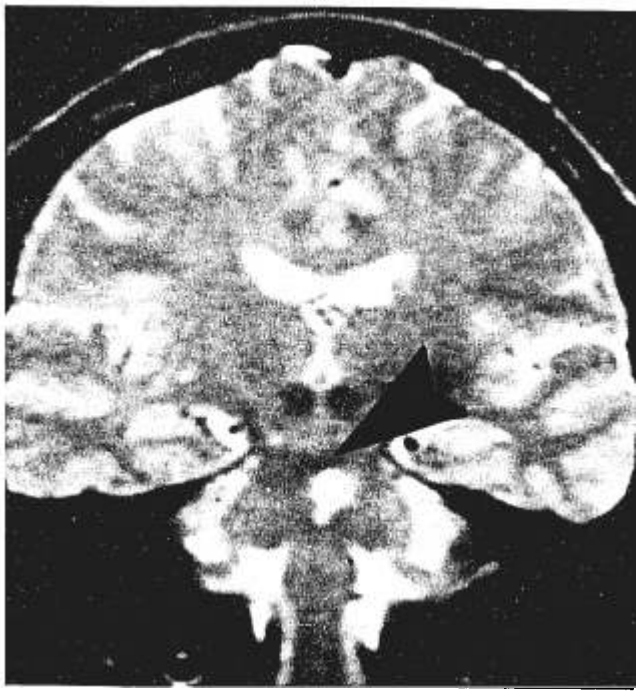

Fig. 9. Patient 6. MRI scan showing several lucent white lesions in the brain stem. The patient had left-moving gaze paralysis.

tions, the role of the cerebellum in saccadic eye movements has not been as well-established in man. Patients with cerebellar degeneration do have abnormalities in saccades. Ranalli and Sharpe[39] found hypometria for ipsilateral saccades and hypermetria for contralateral saccades in a patient with a unilateral rostral cerebellar lesion. Selhorst, *et al.*[40,41] describe saccadic overshoots and macrosaccadic oscillations in their patients with cerebellar vermis lesions. The lesions in the Ranalli and Selhorst reports are somewhat more circumscribed and suggest two basic functions for the cerebellum. This is also suggested by the work in monkeys by Ritchie,[42] Optican and Robinson,[43] and Vilis and Hore.[44] The cerebellar vermis, primarily lobule VII, acts to continuously adjust the gain of the saccadic eye-control system. It also allows the subject to compensate for disorders affecting the saccade system or visual changes which would alter the saccade stimulus. The system is primarily ipsilateral. Since cerebellar control appears to act from outside the direct saccadic pathways, lesions of the cerebellum have no effect on saccade reaction time.

### *Patient Report 5*

This patient had a central cerebellar lesion. In addition to general ataxia, the patient had saccadic overshoot and large alternating saccades during attempts at fixation (Fig. 8).

### *Brainstem Lesion*

Lesions of the brain stem usually produce paralysis of the eye movements when an oculomotor nucleus is involved. Isolated nuclear lesions are seen in patients with diabetes mellitus and multiple sclerosis. These disorders frequently interrupt the pathways between the nuclei or between right and left side interrupting ocular adduction.[45] Vascular lesions affecting eye movements at the brain stem level usually involve other pathways and important vital functions, and can usually be diagnosed on the basis of the altered findings on neurological examinations.[46] Lesions of the immediate supranuclear brain stem (tegmentum of pons) also cause profound alterations in eye movements (paralysis of ipsilateral gaze)[47] and do not require computer-aided measurements in order to show an abnormality.

TABLE II.
Causes of Abnormal Saccade Test Results.

| |
|---|
| Increased saccade latency unilateral: |
| contralateral frontal or parietal lesion |
| contralateral parietal lesions preferentially affect voluntary saccades |
| contralateral internal carotid vascular disease |
| contralateral superior colliculus lesions |
| Increased saccade latency bilateral: |
| centrally depressive medications |
| cerebral anoxia |
| centrally active metabolic disorder |
| diffuse central degeneration |
| hydrocephalus |
| Saccade overshoots: |
| lateral cerebellar lesions (ipsilateral) |
| Bilateral hypermetric saccades: |
| cerebellar vermis lesions |
| Saccadic glissades: |
| cerebellar degeneration |
| Decreased saccade velocity: |
| brain stem lesion (usually ipsilateral) |

### *Patient Report 6*

This 40-year-old woman had developed left-moving gaze paralysis. She later had an evaluation and MRI scan which suggested multiple sclerosis (Fig. 9). This case is included to complete an illustration of specific common lesions along the pathway of saccade generation.

### *Compensation*

The saccadic system, like most other major control systems in the brain, has both redundancy and elasticity. The cortex may be able to shift some functions between the frontal and parietal areas, and descending pathways may have both direct and indirect pathways at least through the substantia nigra to superior colliculus. There may even be pathways which go directly from the frontal eye fields to the mesencephalic reticular formation without stopping in the superior colliculus. In addition, there is evidence that the ipsilateral brain stem may be able to take over some functions usually served by the contralateral side. Age, the state of the remaining central nervous system, and the integrity of other sensory systems may also play a role in compensation. Exercise may also change the rate of compensation. For this reason, clinical interpretation of saccade abnormalities must be viewed in terms of the history of onset, the duration of the disturbance, and the general state of health of the individual.

For clinical interpretation of the test, Table II lists common abnormalities found in saccade testing and the anatomic lesion responsible for this change.

TABLE III.
Abnormal Findings in 100 Patients.

| Variable | Percentage Abnormal |
|---|---|
| Saccade delay | 62 |
| VOR | 53 |
| Positional | 44 |
| Smooth pursuit | 39 |
| Caloric | 38 |
| Optokinetic | 27 |
| Saccade velocity | 13 |
| Saccade accuracy | 3 |

## FINDINGS AND RESULTS: SACCADE ABNORMALITIES IN 100 CONSECUTIVE PATIENTS WITH DISEQUILIBRIUM

The predominance of women referred for evaluation was surprising. The chance occurrence of this rate (70 women, 30 men) had a $P$ value of .0039. The age distribution is skewed toward advancing age. Increased saccade reaction time was the most common abnormal finding. Abnormal vestibulo-ocular reflex (VOR) gain and phase were second most common, and positional nystagmus was third in the frequency of abnormal findings (Table III). Caloric tests were abnormal in only 38% of the patients. Since saccade reaction-time increases are due to abnormalities of the central eye-movement control system, this group of patients exhibits a higher frequency of central abnormalities than abnormalities in the labyrinthine sensors. This suggests that central findings are more commonly associated with disequilibrium than abnormality associated with sensory organ disease.

When applying Pearson correlation coefficients to evaluate the relations between abnormal findings and age, several correlations appear significant. Age is significantly correlated with abnormal saccade reaction time ($P<.0001$), smooth-pursuit gain ($P<.0001$), and optokinetic nystagmus (OKN) gain ($P<.001$). Correlations between variables are significant for VOR with caloric abnormalities ($P<.0001$), between smooth-pursuit gain and OKN gain ($P<.0001$), saccade reaction time and smooth-pursuit gain ($P<.0001$), and saccade reaction time and OKN gain ($P<.0001$). Saccade reaction time and saccade velocity abnormality were also highly correlated ($P<.0001$).

This suggests that diseases of aging primarily affect central processing systems (eye-movement control) rather than labyrinthine receptors (caloric abnormalities, $P<.88$) or positional nystagmus, a finding not localized to central or labyrinthine structures ($P<.70$). Significant correlation between VOR and caloric abnormalities is expected since both tests evaluate the same sensor and similar pathways. Significant correlations between abnormal saccade reaction time and smooth-pursuit gain, and saccade reaction time and OKN gain, suggest that disorders affect both the slow and fast eye-movement reflexes in the same individuals. Significant correlations between smooth-pursuit gain and OKN gain are not surprising since these systems share some of their pathways. One of the important points in this study is the finding that abnormalities of the saccadic system are very common in patients with disequilibrium.

## DISCUSSION AND CONCLUSION

The clinical evaluation of patients with dizziness, vertigo, and visual complaints is aided by several laboratory and imaging methods. Recently, computer-aided measurements of eye movements have improved the ability to obtain quantitative localizing information about the structure and function of the eye-movement control system in these patients. Although imaging methods are superior in locating lesions in the brain, an evaluation of function is still critical in determining disability and in following the course of the disease process including compensation. Imaging techniques are also more expensive, and eye-tracking tests are completely noninvasive and without exposure to ionizing radiation. Saccade testing has become particularly useful in detecting evidence for central nervous system disease in these patients, since the saccade reflex requires so many areas within the central nervous system in order to function properly. By combining information from saccade testing and fine-resolution imaging in the same individual, more can be learned about the anatomic pathways involved in these reflexes in man.

The evolution of this system has been so profound in recent phylogeny that only advanced mammals and primates have systems analogous to man. A highly specialized fovea and forward-directed binocular vision required the development of these complex neural mechanisms. This makes it difficult to draw inferences about anatomy from less advanced (nonfoveate) animals. Several disease processes, including neoplasms, vascular accidents, and multiple sclerosis, can lead to small, well-circumscribed lesions in the central nervous system which can be identified with high-resolution MRI imaging. Cataloging these lesions and evaluating the subsequent changes in saccade reflexes will not only improve the knowledge of central architecture but also make the saccade test a more precise anatomic localizing test in the future. Evaluating changes in these reflexes caused by pharmacologic agents with known actions can also point to possible neuronal transmitters active in these reflexes and improve the general knowledge of brain function.

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