Vertical Saccades in Senescence

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Purpose. To determine the metrics of vertical saccades in elderly subjects for comparison in neurologic disease.

Methods. Sixteen elderly subjects, ten middle-aged subjects, and thirteen young subjects were examined using a magnetic search coil technique. Saccades were measured to predictable vertical target steps and maximal saccadic excursion was measured from primary position.

Results. Maximal upward voluntary excursion was reduced in the elderly (mean 32.9 degrees) compared to young subjects (mean 43.1 degrees). Maximal downward voluntary excursion was also reduced in the elderly (mean 32.8 degrees), compared to young subjects (mean 46.8 degrees). The limited ocular motor range of the elderly was not increased by oculocephalic maneuvers. Individual young subjects had significantly larger downward than upward excursions, but elderly subjects generally had symmetrical upward and downward excursions. Asymptotic peak velocities were not significantly slower in the elderly. Individual young subjects made faster upward than downward saccades. Vertical saccade latencies were significantly prolonged and saccadic accuracy was reduced in the elderly compared to the young subjects.

Conclusions. The range and accuracy of upward and downward saccades decrease, and their latency increases in senescence. This quantitative study provides norms for the detection of brain or orbital disease in young, middle-aged, and elderly subjects. Invest Ophthalmol Vis Sci. 1993;34:2588–2595.

Impairment of vertical gaze is a presumed but unquantified feature of senescence. In 1931, Critchley[1] described restriction of conjugate upward eye deviation as a common sign in the elderly. Forty years later, Chamberlain[2] observed the corneal reflection of light at different gaze angles, to estimate the upward deviation of the eye and found limitation of upward gaze with advancing age.

The effect of aging on horizontal saccades has been well documented. Horizontal saccades of elderly subjects have reduced peak velocities, hypometric amplitudes and prolonged latencies.[3-5] One study of vertical saccades to a 10-degree target in the elderly[6] found them to be slow and delayed, but accurate. The velocity, accuracy and range of vertical saccades to a spectrum of target amplitudes has not been reported.

Knowledge of the effect of aging on vertical saccades is required to provide diagnostic norms for elderly patients with brain or orbital disease and to identify functional defects of vertical gaze that accrue with normal aging. Vertical saccades were measured in young, middle-aged, and elderly subjects using a magnetic search coil technique.

METHODS

Three groups of normal volunteers were studied: 13 young subjects (aged 20–33 yr, mean 28.3 ± 4.6 yr, median 26.5 yr, 8 women); 10 middle-aged subjects

(aged 37–61 yr, mean 49.8 ± 9.0 yr, median 49 yr, 6 women) and 16 elderly subjects (aged 65–84 yr, mean 71.9 ± 5.5 yr, median 74.5 yr, 10 women). None of the subjects had neurologic disease and none was taking psychoactive medication. Our study followed the tenets of the Declaration of Helsinki and informed consent was obtained after the nature and possible consequences of the study were explained to the participants.

Eye movements were recorded by a magnetic search coil technique[7] using a silicone rubber scleral on one eye. Head position was recorded by a coil secured to the forehead. Analog direct current signals were recorded on a rectilinear ink jet polygraph and the eye position signals were digitized online at 200 samples/sec by a PDP 11/73 computer coil annulus (Skalar, The Netherlands). The amplitude of resolution in our system was 6 min of arc. Eye position signal was digitally differentiated to yield eye velocity using a 10-point moving window technique. For each eye movement with a velocity step greater than 20 degrees/sec, peak velocity was marked. For each selected peak velocity, the time when eye velocity surpassed or dropped below 5% of maximum velocity was taken as the beginning and the end of a saccade. Cursors then marked the beginning and end of saccades in the corresponding eye position channel. Only saccades occurring within a 70–600 msec interval *after* target movement were selected for analysis. For each subject at least 200 saccades were measured. To avoid fatigue, breaks approximately every 2 min for 1–3 min were allowed.

The target was a rear-projected laser spot with a luminance of 42.1 cd/m² subtending 0.25 degrees of visual angle, projected on a featureless screen 1 m from the subject's cornea. The target center (zero position) was set at eye level. Subjects viewed the target with both eyes while they held their head in the erect position. The target was stepped at 3-sec intervals from center to ± 10, ±20, and ±30 degrees; both timing and amplitude were predictable. Subjects were instructed to keep their eyes on the target. Anticipatory saccades from predicting the next target position were rejected as noted above. All 10-degree steps were presented first, followed by 20- and 30-degree target steps. To elicit saccades greater than 30 degrees from primary position, the target stepped between 20 degrees up and 20 degrees down, and 25 degrees up and 25 degrees down, while subjects bent or extended the head 20 or 25 degrees above and below the erect position; this pitch of the head maintained gaze within the linear range of the magnetic search coil system. For example, when a target stepped from 25 degrees down to 25 degrees up, subjects with the head bent down 25 degrees, performed 50 degrees upward saccades, above primary eye position in the orbit, which had

been established with the head erect. Stability of head position was monitored by the head search coil.

The range of maximal voluntary vertical excursion of the eyes in the orbit (the ocular motor range) was measured by instructing the subjects to look as far as possible upward or downward from the primary position. For each subject the single largest upward and downward excursion was selected from 4 or 5 trials. We measured the vertical ocular motor range in 13 elderly subjects, 3 middle-aged, and 10 young subjects. We attempted to increase the ocular motor range during maximal voluntary vertical saccadic excursion by using oculocephalic maneuvers to stimulate the vestibulo-ocular reflex in four subjects who had low amplitude vertical excursion. While they attempted to fixate a target at maximal upward and downward voluntary excursion, with the head in an initial erect position, we manually flexed and extended the subjects' head in pitch about 20–30 degrees.

The peak velocity amplitude relationship of saccades for each subject was computed from scatter plots of individual saccades that were fitted to an exponential curve of the form $PV = V[1-\exp(-A/C)]$ where PV is peak velocity at any point of the curve, V is the peak velocity at the asymptote, A is saccade amplitude and C is a constant. Group mean V values were compared. Comparisons were also made of the peak velocities for upward and downward saccades grouped in 9–11-degree amplitude bins for each age group. In addition, the asymptotic peak velocities (V) of saccades to centrifugal 40- and 50-degree target steps were compared to V values of saccades to 40- and 50-degree centripetal target steps for each age group.

Latency, defined as the interval between target step and the onset of the saccade, was determined for each target amplitude.

The accuracy of saccades was expressed by saccadic gain, the ratio of the amplitudes of initial saccades to the target amplitude.

Statistical Analyses

Student's two-tailed t tests were used to compare centrifugal to centripetal saccade peak velocities in each age group. t tests were also used to compare saccadic gain between the young and elderly groups. Individual subject differences between maximal upward and downward excursion in each group were tested against zero, using paired sample t tests. Individual differences between upward and downward asymptotic peak velocities in each group were also examined by the same method. Age groups means for maximal excursion, peak velocity, latency and accuracy were compared by analysis of variance using the Statistical Analysis System program (version 6.04). Analysis of variance identified that the means either did not differ significantly or that at least one mean was different. If
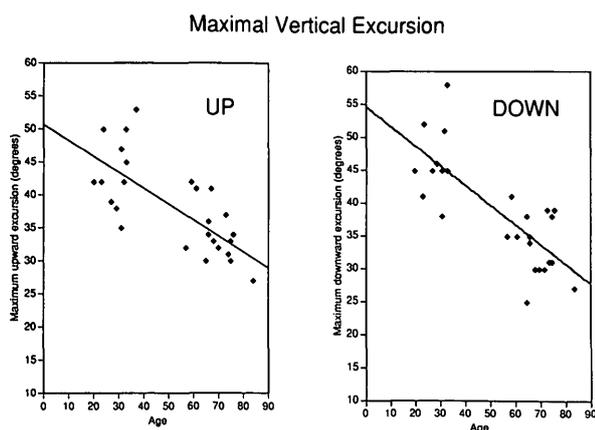
Maximal Vertical Excursion

FIGURE 1. Maximum voluntary upward and downward excursions of individual subjects plotted against age. Correlation coefficient for upward excursion is r = −0.70 (P < 0.0001) and for downward excursion is r = −0.80 (P < 0.0001).

at least one mean differed, we used the Bonnferoni test of inequality to determine what pair(s) demonstrated significant differences and their corresponding probability value. A P value of < 0.05 was considered statistically significant.

RESULTS

Range of Vertical Gaze

We correlated the ocular motor range with age (Figure 1). Ranges diminished with increasing age for both upward (r = −0.70; P < 0.0001), and downward excursions (r = −0.80; P < 0.0001). Maximum upward excursion in elderly subjects was significantly reduced compared to the subjects in the young and middle-aged groups (Table 1). Maximum downward excursion was similarly limited in the elderly when compared to young subjects (Table 1). The maximal upward excursion minus maximal downward excursion of individual subjects revealed asymmetric characteristics (Table 1). Individual young subjects made significantly larger downward than upward excursions.

No increase in maximal upward and downward excursion of the eyes was elicited by vestibular smooth eye movements stimulated with oculocephalic maneuvers while subjects attempted maximal fixation.

No centripetal drift or end-point nystagmus[8] was recorded in the elderly group at maximum vertical excursion, but we did not instruct subjects to maintain eccentric gaze for more than a few seconds (Figure 2).

Peak Velocity

There were no significant differences in group mean asymptotic peak velocities between the three age

groups for either upward or downward saccades (Table 2). There was no significant difference between upward and downward group mean V values within each age group, but individual young subjects made significantly faster upward than downward saccades (individual V_{up} minus V_{down} by paired sample t tests; Table 2). Mean intrasubject differences between up and down of the three age groups were significantly different between elderly and young subjects (analysis of variance, Table 2). Group mean peak velocities for 9–11-degree saccades bins (upward or downward) did not differ between groups. We found no significant differences between asymptotic peak velocities of centripetal versus centrifugal saccades in any group (Table 3).

Latency

Reaction times were longer in the elderly group than in the young group for all target displacements and were significant for 10- and 20-degree downward target steps (P < 0.01) and for 30 (P < 0.01), 40 (up P < 0.005, down P < 0.01), and 50 (up P < 0.05, down P < 0.005) degrees target steps (Fig. 3).

Accuracy

Mean amplitudes of saccades to targets within their ocular motor range were significantly reduced in the elderly group compared to young subjects for target steps of 10 degrees downward, 20 degrees upward and

TABLE 1. Maximal Vertical Voluntary Saccadic Excursion

	Elderly (E)	Middle Aged (M)	Young (Y)
Up mean	32.9 (3.6)	42.0 (8.6)	43.1 (5.3)
Min	27.0	32.0	35.0
Max	41.0	53.0	50.0
Down mean	32.8 (4.7)	47.0 (3.5)	46.8 (6.0)
Min	25.0	35.0	38.0
Max	39.0	41.0	58.0
Up minus down mean	−0.8 (4.2)*	+1.3 (4.5)*	−4.9 (5.4)†

Mean signifies group means (±1 SD), and min and max are minimum and maximum single values of an individual subject. Maximal upward excursion E < M (P < 0.025), E < Y (P < 0.005). Maximal downward excursion E < Y (P < 0.005), E < M (P < 0.01), analysis of variance. Differences between maximal upward and downward excursion of individual subjects in each age group were compared using paired sample t-tests, and significance values are shown next to each value.
* Not significant by paired sample t-test.
† P < 0.025.

FIGURE 2. Maximal vertical upward excursion in an elderly subject with limited ocular motor range (32 degrees). Endpoint nystagmus and centripetal drift are absent.

30 degrees both upward and downward (Fig. 4). We analyzed the strategy of making saccades by young and elderly individuals to targets beyond their vertical ocular motor range by determining initial saccade amplitudes as a percent of the ocular motor range in individual young and elderly subjects. Initial saccade amplitudes were approximately 80% of the ocular motor ranges in the young and elderly (Figure 5), regardless of the amplitude of large target steps ($\geq$ 40 degrees).

DISCUSSION

Limited Vertical Excursion

Elderly subjects have a lower range of voluntary upward deviations, and smaller initial saccades to upward target steps. The ocular motor range in the elderly averaged 33 degrees upward, whereas in the young group it averaged 43 degrees upward. Vertical range had not been previously quantified. Electro-oculography (EOG) or infrared reflection oculography do not reliably record vertical eye movements.[9] By observing the corneal reflex of a target light moved along a perimeter, Chamberlain[2] found an average upward excursion of 22 degrees for subjects between 65 and 74 yr and 17 degrees for those between 75 and 84 yr. The elderly subjects in our study were similar in age, but even the individual with the most limited upward excursion performed better than Chamberlain's reported average.[2] Using the magnetic search coil technique, the most precise method available for measuring vertical eye movements, we affirmed the clinical aphorism that upgaze is limited in senescence.

We also identified a previously unrecognized reduction in downward excursion in the elderly. The downward range of voluntary gaze among the elderly averaged 33 degrees compared to 47 degrees in young subjects.

The vertical range is quite variable in the young and elderly. This may reduce the value of measuring excursion in a single patient for the early recognition of disorders such as thyroid orbitopathy or progressive supranuclear palsy. Our data indicate that a normal elderly subject could lose up to 37% of his normal ability to look up and still remain within the lower limit of normal range. In other words, the subject with a maximal upward excursion of 41 degrees (see Table 1) could have a reduction to 25.7 degrees (the normal group mean upward excursion minus 2 SD) from brain or orbital disease, before being recognized as abnormal.

The mechanism of limited vertical excursion is uncertain. Because we did not record an increase in range with oculocephalic maneuvers, we conclude that limitation occurs at a level below the convergence of vertical vestibulo-ocular and saccadic commands to motor neurons. Abnormal centripetal drift was not observed in the elderly after maximal saccadic excursion indicating appropriate matching of the pulse and step of innervation that is required for accurate saccades. For vertical saccades, the pulse is generated in the paramedian pontine reticular formation[10] and the rostral interstitial nucleus of the medial longitudinal fasciculus[11] and the step of tonic innervation is probably generated in the vestibular nuclei[12,13] and the interstitial nucleus of Cajal.[13] This lack of pulse-step mismatch implies integrity of neurons that carry the position command to ocular motor neurons. Normal peak velocities of vertical saccades signified that burst neurons in the rostral interstitial nucleus of the medial

TABLE 2. Asymptotic Peak Saccade Velocity (V)

	Elderly (E)	Middle Aged (M)	Young (Y)
Up	390.0 (93.7)	411.0 (64.0)	467.8 (76.7)
Down	421.2 (78.0)	409.0 (92.3)	398.9 (86.7)
V_{up} minus V_{down}	−30.6 (85.0)*	+2.0 (51.4)*	+56.5 (77.0)†

Values are group means in deg/sec (± 1 SD). Differences between the age group means for either upward or downward peak velocities (V) values were not significant (analysis of variance). The differences between upward and downward peak velocities of individual subjects ($V_{up} > V_{down}$) were significant E < Y ($P < 0.01$; analysis of variance). Positive (+) indicated $V_{up} > V_{down}$. Negative (−) indicated $V_{down} > V_{up}$. Individual young subjects made significantly faster upward saccades than downward saccades; significance level is shown next to data.
* Not signficant by paired sample t-test.
† $P < 0.05$.

TABLE 3. Centrifugal Versus Centripetal Asymptotic Peak Velocities

	Elderly	Middle	Young
Up			
Centrifugal	398.2 (127.9)	543.3 (106.9)	458.3 (190.7)
Centripetal	396.4 (134.3)	593.3 (110.1)	513.3 (105.7)
Petal minus fugal	−1.8 (122.0)	−5.0 (148.0)	55.0 (150.0)
Down			
Centrifugal	402.7 (115.9)	463.3 (75.7)	335.0 (31.5)
Centripetal	419.1 (120.2)	400.0 (96.4)	400.0 (133.0)
Petal minus fugal	16.4 (95.2)	−60.0 (27.1)	65.0 (125.3)

Asymptotic peak velocities (V) of saccades to centrifugal and centripetal 40° and 50° target steps. Values are age group means in deg/sec (±1 SD). No significant differences were found between centrifugal and centripetal V values in any age group by t-tests. V value age group means were not significantly different (analysis of variance). The difference between centripetal and centrifugal V values of individual subjects in each age group (petal minus fugal) were compared by paired sample t-tests and were not significant.

longitudinal fasciculus and paramedian pontine reticular formation are largely preserved in senescence.

All ocular motor neurons participate in each class of eye movements, and the amplitude of excursion is determined by the discharge rate of a population of motor neurons active for a specified excursion. All motor neurons are recruited when the eyes move in their on direction more than several degrees from primary position.[14] Loss of a fraction of motor neurons might not limit excursion, provided the remaining motor neurons can discharge at a rate appropriate for the eccentric gaze range. Histologic studies have not identified motor neuron loss associated with aging in the oculomotor nuclei,[15] trochlear,[16] or abducens nuclei,[17] but subtle neuronal loss may have been undetected. Reports indicate nerve fiber loss with increasing age in the human optic nerve[18] and vestibular

nerve[19] but no studies have identified nerve fiber loss within ocular motor nerves.

Degeneration of extra-ocular muscles is a feature of senescence.[20] Either decreased action of the agonist muscles or restriction of their antagonists might lead to limitation of upward or downward excursion, and explain restriction of vertical gaze in the elderly. Forced duction testing might confirm restriction of antagonist muscles as a mechanism contributing to the reduced ocular motor ranges that we recorded. Forced duction testing is a gross qualitative maneuver that cannot detect small amounts of restriction.[21] Although instruments have been developed to quantify forced ductions,[21,22] variability in recordings makes in-
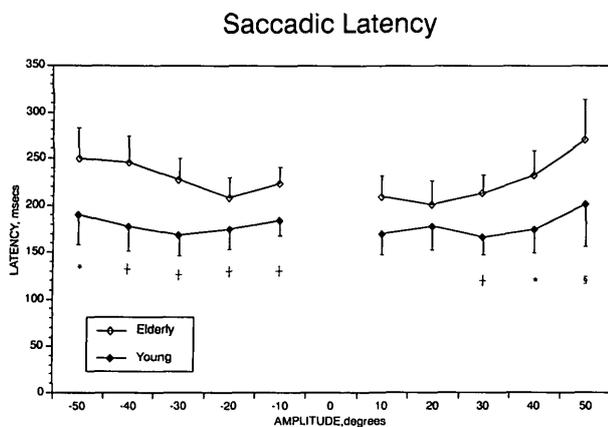
Saccadic Latency

FIGURE 3. Latency of vertical saccades in elderly subjects (◊) and young subjects (♦). Differences were significant between the young and elderly groups for saccades to 10 degrees and 20 degrees downward and 30, 40, and 50-degree target steps both upward and downward. *$P < 0.005$; †$P < 0.01$; §$P < 0.05$.
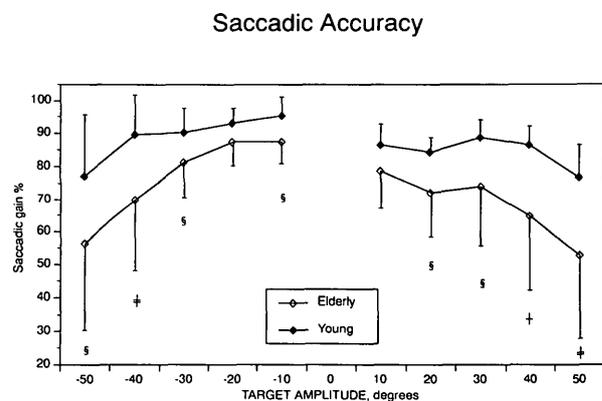
Saccadic Accuracy

FIGURE 4. Accuracy of vertical saccades in elderly (◊) and young subjects (♦) to target steps from center (zero position) to ± 10, 20, 30, 40, and 50 degrees. Accuracy is the ratio of the initial saccade amplitude (saccadic gain) to target amplitude expressed as a percentage. Differences were significant between the young and elderly groups for saccades to 10 degrees downward, 20 degrees upward, and 30, 40, and 50-degree target steps both upward and downward. Downward is negative and upward is positive on abscissa. †$P < 0.01$; ‡$P < 0.025$; §$P < 0.05$.
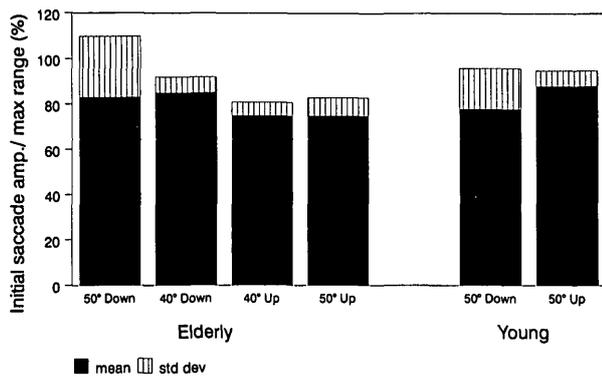
FIGURE 5. Ratio of initial saccadic amplitude to maximum vertical range (%), for 40- and 50-degree targets that were beyond the ocular motor range of elderly subjects and for 50-degree targets that were beyond the ocular motor range of young subjects. The four left columns represent the elderly group and the two right columns represent the young group. Both young and elderly subjects used about 80% of their maximal range for their initial saccades.

terpretation difficult. Although failure of forced ductions to further elevate or depress the eye would support restriction by tight antagonist muscles, a full range of ductions would not exclude mild restriction and would also be consistent with weak agonist muscles.

We cannot attribute the vertical limits of gaze to restriction of the scleral search coil by either the superior or inferior fornix of the conjunctiva. If the coil were restricted at the fornix, coil slippage would be apparent by a change in calibration position when the eye returned to the orbital midposition. Trials for maximal upward and downward excursion were begun from center followed by saccadic return to the center position; no change was detected in the calibrated eye position after maximal excursion. Moreover restriction of the scleral anulus would not explain the differences in ocular motor range between the age groups. The fornices are not known to change in senescence. The coil anulus extends approximately 4 mm from the limbus and is unlikely to be impeded by the superior or inferior fornices, which measure 8–10 mm from the limbus.[23] The fornices are easily distensible and deepen when the levator palpebrae and recti muscles contract[23] during vertical gaze.

Peak Velocity

No significant slowing in peak velocities was recorded in the elderly subjects. One study[6] of vertical saccadic velocity in normal young and elderly subjects and patients with dementia, found significant reduction of peak velocities for 10 degree targets in the elderly. An electro-oculography study,[24] comparing normal young and elderly subjects to patients with brain stem dis-

orders reported that upward saccades were faster than downward saccades in normal subjects, but vertical saccades were not significantly slower in the elderly. The preserved peak saccadic velocities that we recorded, imply that burst neurons that generate vertical saccades are unaffected by age, in agreement with histologic examination of senescent brains that have not identified neuronal degeneration in the midbrain or pontine reticular formation.[15] In a previous study,[25] normal elderly subjects but not patients with dementia, demonstrated an increase in horizontal saccade velocity with unpredictable targets, relative to predictable targets. If in response to unpredictable target steps, young subjects increased their saccade velocities more than elderly subjects then saccadic slowing might have been observed in our elderly subjects. However our study, using only predictable steps, would not detect such differences in peak velocities.

Because saccades toward primary position are generated by elastic muscle forces in addition to a pulse of innervation to agonist muscles and a pulse of inhibition to antagonist muscles, centripetal saccades might be faster than centrifugal saccades. No significant differences between the asymptotic peak velocities of centrifugal and centripetal saccades in any age group were recorded.

Latency

Saccades to predictable target steps were delayed in the elderly subjects. One report[6] found prolongation of latency to unpredictably timed vertical target steps of 3–15 degrees. Slowing skeletal motor reaction time is a well-documented phenomenon in aging.[26] The major component in the slowing of reaction time is the time of central processing.[26] Central processing for saccades involves several cerebral cortical areas. Prolongation of saccadic latencies are reported in patients with lesions of the frontal lobes,[27] posterior parietal lobe,[28] dorsolateral prefrontal cortex,[29] and superior colliculus.[30] Cerebral neuronal degeneration identified in the aging brain[31] can explain the saccadic delay in the elderly.

Accuracy

Vertical saccadic accuracy was reduced in this study's elderly subjects. One study[6] found vertical saccadic accuracy in the elderly, to be no different than young subjects when targets steps were small (10 degrees). Motor commands that generate saccades, constitute the difference between desired position and actual eye position, called motor error.[32] The command is transmitted from cerebral cortex to burst neurons in the paramedian pontine reticular formation. Frontal eye field lesions transiently decrease the accuracy to ran-

dom and predictable timed targets in monkeys[33] and humans.[27] Posterior parietal cortex and dorsolateral frontal cortex lesions in humans reduce the accuracy of memory guided saccades.[29] The dorsal cerebellar vermis[34] and underlying fastigial nucleus[34,35] are involved in producing accurate saccades. Hypometric saccades are a feature of both cerebral hemispheric and cerebellar disease. Loss of cerebral cortical neurons[31] or cerebellar Purkinje cells[36] or both, in the aging brain can explain hypometric saccades in the elderly.

For large target steps beyond the ocular motor range, both young and elderly subjects used approximately 80% of their maximal range for their initial saccades, regardless of the amplitude of the target step (see Figure 5). This strategy of undershooting the target is similar to the behavior of saccades to large amplitude targets within the ocular motor range.[4,38] Similar strategies were used by subjects[37] to make horizontal saccades to targets outside the ocular motor range. On average subjects made 45-degree gaze shifts (mean horizontal range 55 degrees) or approximately 85% of their total horizontal ocular motor range.[37]

Vertical Versus Horizontal Senescent Saccades

Maximal vertical excursions are smaller (mean 45 degrees up and 47 degrees down; see Table 1) than the reported maximal horizontal ocular motor range of 53 degrees reported in young subjects.[37]

We compared vertical saccade metrics in our elderly subjects to the results of an infrared oculographic study of horizontal saccades[4] performed in our laboratory. Although vertical saccadic peak velocities were slower than horizontal peak velocities, the differences were not significant. Another study[39] using a magnetic search coil method found no differences between the peak velocities of horizontal and vertical saccades. We found delay of saccades to both vertical and horizontal target steps in the elderly. Saccadic accuracy in the elderly was reduced for 20-degree target steps, both vertical and horizontal, compared to young or middle-aged subjects.

We conclude that upward and downward saccadic range and accuracy are reduced and latency is prolonged in senescence. These results quantify and confirm the clinical impression of limited upgaze in the elderly and provides evidence, for the first time, that downward excursion is similarly reduced. These quantitative data provide diagnostic norms for the assessment disordered vertical saccades in the young, middle-aged, and elderly.

Key Words

saccades, aging, eye movements, vertical, saccadic delay

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