Journal of Gerontology: MEDICAL SCIENCES
2001, Vol. 56A, No. 6, M386–M390

Effect of Age on Ocular Microtremor Activity

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Background. Ocular microtremor (OMT) is a high-frequency tremor of the eyes. It is present in all individuals and is related to brainstem activity. The OMT signal appears as an irregular oscillatory movement with intermittent burst-like components. The clinical interest in OMT has centered on its use in the assessment of the comatose patient, with broad agreement among authors of its prognostic value. The purpose of this study was to examine the changes in OMT activity related to aging.

Methods. OMT was recorded from 72 normal healthy subjects using the piezoelectric strain gauge technique. The subjects ranged in age from 21 to 88 years (54.22 ± 20.43 years, mean ± *SD*).

Results. Our results show that the overall frequency and frequency content of the bursts falls with age ($p < .002$ and $p < .001$, respectively). There is a highly significant drop in all three frequency parameters of OMT ($p < .0001$) in subjects older than 60 years of age.

Conclusions. These results suggest that different values of normality should operate for subjects over 60 years of age when considering the clinical application of OMT.

MANY physiological processes change with aging. Changes in physiological parameters of nervous-system activity accompanying aging are well documented; these include slower motor responses (1), sensory responses (2), and cognition (3). Thus, it is not surprising that histological changes in extra-ocular muscle, such as the altered staining of mitochondria, disruption of fibers, and an increased collagen content, also occur with age (4). Age-related changes in eye movements have been documented. These include prolonged horizontal latency (3), decreased amplitude of saccades (5), slower saccades (6), reduced accuracy of perceptual motor performance (7), and eye–hand coordination (8). Thus, normal accepted values for commonly applied physiological measurements of visual and ocular function, such as the visual evoked response and vestibulocular reflex, are different for young and older subjects (9).

Ocular microtremor is a small, high-frequency tremor of the eyes that is present even when the eyes are at rest. It was first described fully in 1934 by Alder and Fleigelman (10) as one of three fixational eye movements—the other two being drifts and microsaccades. This tremor is caused by high-frequency extra-ocular muscle stimulation, which originates in the brainstem from the oculomotor neurones (11). The mean extent of the ocular microtremor (OMT) amplitude is 6 seconds of arc (12), and the peak-to-peak rotation involves a displacement of the surface of the eye of between approximately 150 and 2000 nm (13). The OMT signal appears as an irregular oscillatory movement with intermittent burst-like components. These bursts have near-sinusoidal oscillation (range 75–155 Hz), are generally of greater amplitude than the rest of the microtremor, and possess a packet-like appearance being clearly defined against the background tremor (11). The period between the bursts is termed the baseline. The clinical interest in OMT has centered on its use in the assessment of the comatose patient, with broad agreement among authors of its prognostic value (14,15).

Recent research by Bolger and colleagues measured the OMT activity in 105 normal healthy adults and found the mean peak frequency to be 83.68 ± 5.78 Hz (mean ± *SD*) (16). However, a significant difference was noted when comparing the mean peak frequency in subjects younger and older than 70 years of age [i.e., the mean peak frequency fell in the subjects older than 70 ($p < .008$)]. A previous study by Coakley (17) also compared OMT activity in 26 young adults and 15 subjects over 70 years of age. He could find no significant change in OMT frequency associated with age.

Many neurological conditions to which the recording of OMT may be applied are common only to elderly subjects (e.g., Parkinson's disease). It could be erroneous to apply OMT recording and the assessment of normality to these subjects on the basis of a normal population of young adults. The purpose of this study was to examine possible changes in the frequency or pattern of OMT records relating to age, using the piezoelectric strain gauge transducer technique, in the normal population.

Methods

Subjects

A total of 72 normal healthy subjects were recruited for study. Informed consent was obtained from all subjects.

Subjects under 21 years of age were not studied because of concern regarding informed consent as defined by the Hospital Ethics Committee. All subjects underwent a full history and clinical examination. Exclusion criteria were any evidence or a history of neurological or ocular disease or trauma. All subjects were free of medication. The subjects were 54.22 ± 2.41 years of age (mean ± *SD*), with a range of 21 to 88 years. The median was 54.50 years, and the mode was 23 years. The subjects were divided by age into seven groups: 21 to 30 years, 31 to 40 years, 41 to 50 years, 51 to 60 years, 61 to 70 years, 71 to 80 years, and over 80 years. Each group contained 10 subjects except for groups 31 to 40 years and 51 to 60 years, which contained 11 subjects each.

OMT was recorded using the piezoelectric transducer technique. The OMT signal is not a completely deterministic signal but has random elements (18). The piezoelectric transducer technique is described in detail elsewhere (13) and provides a reliable estimate of OMT activity (19). Briefly, the piezoelectric element is mounted in a Perspex rod and its tip is coated with silicone rubber. The subject lies supine in a normally lit room looking straight ahead. The subject is advised to keep their eyes fixating straight ahead at a point on the ceiling throughout the recording. Movements of the head can represent a source of noise, and this problem is overcome by mounting the transducer onto the head by means of a headset (13). The subject is advised to keep their head still throughout the recording, but no means of restraint are used.

The scleral surface is anesthetized with 0.5% proxymethacaine hydrochloride solution topically. The eyelids are retracted with adhesive tape. The rubber-tipped piezoelectric probe is lowered so that the probe is just touching the scleral surface. Probe placement is judged by visual inspection and by listening to the signal being recorded, using headphones. All records were obtained by a single operator, and a recording of between 30 seconds and 1 minute of activity was taken (16). An example of a normal recording is given in Figure 1.

The signal from each probe is passed to a conditioning unit and amplifier with a 40-dB common mode rejection ratio. The signal is then stored on audio tape using an adapted Sony Walkman without automatic gain control. The tape is later played back and analyzed on an ECG tape analyzer (Reynolds Medical Pathfinder 3 and a Reynolds Medical Thermal Printer).

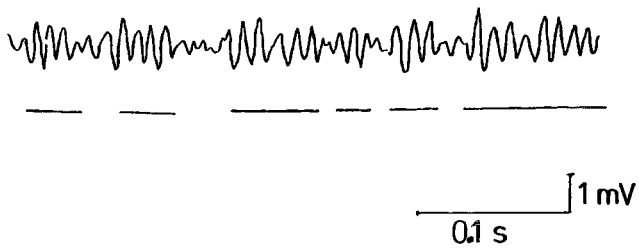

Figure 1. Example of a normal ocular microtremor record. Bursts, which are identified visually from the record during analysis, are underlined. The period between the bursts is the baseline.

This system shows a frequency response between 20 and 150 Hz, which deviates less than 2 dB from peak response. The system filters out inputs below 20 Hz, in particular any drift movements. Microsaccades cannot be dealt with as easily because the frequency content of microsaccades overlaps that of OMT (12). Microsaccades occur only intermittently. They are excluded by examining the intervening record during analysis. The system has a signal-to-noise ratio of >23 dB, and the resolution is less than 1% of the dynamic range, or 12 nm.

Record Analysis

The peaks occurring per unit time on a printed record are counted. This provides a good estimate of the high-frequency component of any random signal (20), particularly OMT (13).

Peak counting is also the method of obtaining frequency information favored by Coakley (17) who, to date, has published the largest series on OMT.

The parameters measured were (Figure 1):

1. The overall frequency (Hz)
2. The number of bursts occurring per second, calculated by counting the number of bursts in the record and dividing by the record duration.
3. The duration of bursts (milliseconds), calculated by estimating the total duration of record occupied by bursts and dividing by the number of bursts.
4. The percentage of record occupied by baseline (%), calculated as the total duration of baseline divided by the record duration × 100.
5. The frequency content of bursts (Hz), calculated by peak counting over the total duration of bursts in a record.
6. The duration of baseline (milliseconds), calculated by taking the total duration of baseline and dividing by the number of baseline segments in any given record.
7. The frequency content of baseline (Hz), calculated by peak counting over the total duration of baseline segments (16).

A least-squares linear regression correlation coefficient was calculated for each parameter. A further comparison was made between subjects younger than 60 years of age and those older than 60 years of age.

RESULTS

Linear Regression

The values for linear regression correlation coefficient and age are given in Table 1, which shows that two parame-

Table 1. Linear Regression Coefficient (*r*) for 7 Parameters of Ocular Microtremor Activity and Age in 72 Subjects

Parameter	*r* Value	*t* Value	*p* Value
Frequency, Hz	−.36	−3.26	.002
Baseline, %	−.087	−.728	.469
Frequency baseline, Hz	−.225	−1.934	.057
Number of bursts	0	0	1
Frequency of bursts, Hz	−.534	−.528	.00
Duration of bursts, ms	.162	1.37	.17
Duration of baseline, ms	−.004	−.365	.72

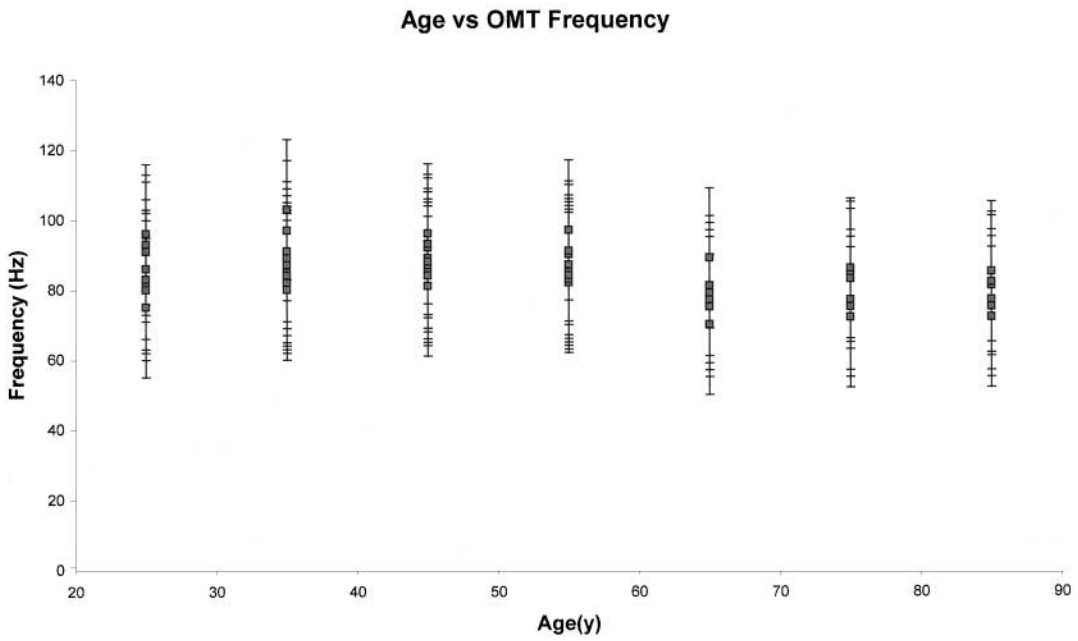

Figure 2. Age versus ocular microtremor frequency (Hz).

ters of OMT activity are significantly correlated with age. The overall frequency of OMT is negatively correlated with age, tending to fall in older age groups. Although the correlation coefficient is small at −0.36, it is highly significant ($p < .002$) (Figure 2).

The strongest correlation is that between the frequency content of bursts and age. Once again the correlation is negative, with the frequency tending to fall with age. The value of r is −0.53 and is highly significant ($p < .001$) (Figure 3). All of the remaining parameters except duration of bursts are negatively correlated with age, but not significantly.

None of the mean values for each parameter for each age group differed significantly from each other (multiple group comparison and ANOVA). However, there was a tendency for the overall frequency, baseline frequency, and frequency content of burst to fall with age.

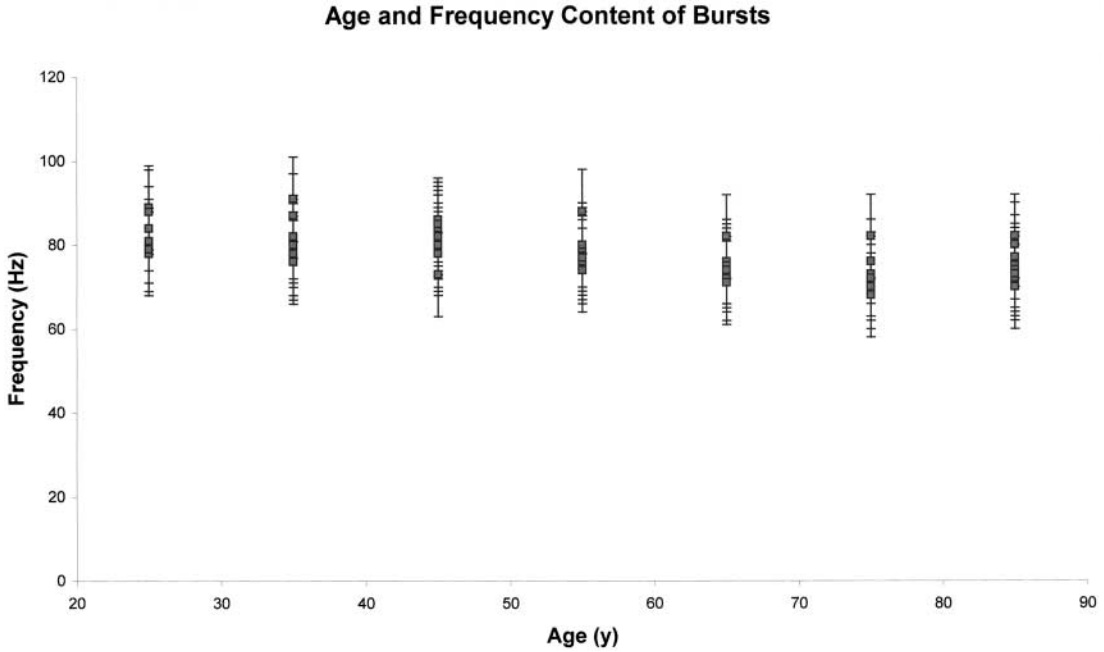

Figure 3. Age and frequency content of bursts (Hz).

Table 2. Mean Values for 7 Parameters of Ocular Microtremor Activity in Subjects Younger and Older Than 60 Years of Age

Parameter	>60 Years of Age	<60 Years of Age	*t* Value	*p* Value
Frequency, Hz	80.5 ± 4.7	86.8 ± 5.5	4.7	.0001
Baseline, %	52.3 ± 11.6	52.4 ± 11	.012	.99
Frequency Baseline, Hz	85.3 ± 6.8	94.4 ± 10.6	3.64	.0001
Number of Bursts	8 ± 1.4	8.2 ± 1.4	.376	.7
Frequency of Bursts, Hz	75.3 ± 4.2	80.5 ± 4.1	4.9	.0001
Duration of Bursts, ms	59.1 ± 6.7	58.2 ± 7.9	.44	.64
Duration of Baseline, ms	71.3 ± 27.9	69 ± 28.4	.31	.76

Subjects Younger and Older Than 60 Years of Age

Table 2 gives the mean value for each parameter for each group. There is a highly significant drop in the overall frequency, the frequency content of the baseline, and the frequency content of the bursts in subjects older than 60 years of age ($p < .0001$). There is no significant change in the other parameters.

Discussion

These results indicate a tendency for two of the three frequency parameters of OMT (i.e., the overall frequency and the frequency content of the bursts) to fall with advancing age. Although the strength of the correlation for overall frequency is small ($r = -0.36$), it remains significant ($p < .002$). The negative correlation between the frequency content of the burst and age is stronger ($r = -0.534$). In subjects older than 60 years of age there is a significant fall in all three frequency parameters of OMT activity (i.e., the overall frequency, the frequency content of the baseline, and the frequency content of the bursts). In each case the difference is small, about 5.3 Hz for overall frequency, 9.1 Hz for baseline frequency, and 5.2 Hz for frequency content of bursts. However, all these differences are significant.

However, a previous study by Coakley (17) compared OMT in 26 young adults and 15 subjects older than 70 years of age. He could find no significant change in OMT frequency associated with age. This could be explained by the small number of subjects studied. The analysis of the microtremor record in this study was based on velocity rather than on displacement waveforms, as in our study. Velocity against time analysis will enhance the contribution of higher-frequency components to the overall measured frequency.

A significant change in frequency of either bursts or the baseline will have a concurrent effect on overall frequency, as we have seen. However, the other parameters studied are also affected by age, although not significantly. This would suggest that the overall pattern of OMT activity is not affected significantly by age but that the firing frequency of the extraocular motor neurones that lead to bursts are. These findings are consistent with other noted changes in the aging ocular motor system. Increases in saccadic eye movement latency are well documented (3,8). Changes in the saccadic system are presumed to be due to age-related changes in the ability to process sensory input. In the case of OMT, however, the frequency of activity is not dependent on sensory input (21). Studies by Shimada and colleagues (22) looked at age-related changes in brain size in the SAM-R/1 mouse model. They found age-related atrophy only in a restricted part of the cerebral cortex, mainly in the parietal region. Neural activity from the inferior parietal cortex is known to impinge on the oculomotor nuclei (23). It may be that a loss of cells in this area (or decrease in function) with age could therefore reduce neural activity.

Interestingly, elderly subjects show a decreased frequency of nystagmus as stimulated through the vestibular system (9). Thus, physiological changes are not confined to the sensory input level alone. Histological changes in extraocular muscle with age (4) may account for a changing response to neuronal input in elderly persons. The disturbance of orderly fiber alignment and direction of the muscles themselves would tend to reduce the frequency of movement for any given input. Furthermore, increases in muscle collagen content would tend to decrease the compliance of the globe, altering resonance, and could also be responsible for a reduction in OMT frequency, if the neuromechanical model of OMT is accepted (18).

In latter years it has been recognized that recording OMT may be of value in clinical situations, particularly as a method of assessing brain-stem function (11). Studies have shown that OMT activity is reduced in comatose patients and could have prognostic value (14,15). More recently, our group has shown that OMT activity is absent in subjects who are clinically diagnosed as being brain-stem dead (24). Studies have also shown that OMT activity is affected by anesthetic agents and propose that monitoring OMT may have a role in assessing the depth of anesthesia (11). In relation to the clinical application of OMT, these results are important. They suggest that different values of normality should operate for subjects older than 60 years of age, at least for frequency parameters. They also suggest that age matching of subjects in controlled trials of OMT is essential if valid conclusions are to be drawn from study results.

Acknowledgments

This research was supported by the Health Research Board, Ireland.

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Received December 1, 2000
Accepted December 5, 2000
Decision Editor: William B. Ershler, MD