The Relationship between Two Types of Upper Eyelid Movements: Saccades and Pursuit

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PURPOSE. To establish the relationship between upper eyelid saccades and upper eyelid pursuit movements

METHODS. Upper eyelid saccades and periodic sinusoidal upper eyelid pursuit movements were recorded in a sample of controls and patients with Graves upper eyelid retraction. A video-computerized system was used to register both types of movements that accompanied 60° of eye rotation across the upper and lower hemifields. The forced harmonic oscillator model was used to fit saccadic and pursuit movements.

RESULTS. Mean mid-pupil eyelid distance for the Graves patients (6.6 ± 1.1 mm) was significantly higher than for the controls (4.6 ± 0.8 mm; $t = 7.18$; $P < 0.00001$). Despite the difference in the upper eyelid resting position, saccades and pursuit eyelid movements of both groups were extremely well fitted by underdamped solutions and steady forced solutions of the harmonic oscillator model, respectively. For the controls, the amplitude of the pursuit movements was well correlated with the upward and downward saccades. The amplitude of the eyelid movements of the Graves patients (saccades and pursuit) was significantly reduced compared with that of the controls.

CONCLUSIONS. Saccadic and pursuit movements of the upper eyelid can be described by the harmonic oscillator model. In healthy subjects and Graves patients, the amplitude of pursuit lid movements is correlated to the saccade amplitude. Pursuit eyelid movements are more difficult to register than saccades, and their measurements do not allow clear separation of the relaxation and contraction properties of the upper eyelid retractors. (*Invest Ophthalmol Vis Sci.* 2008;49:2444–2448) DOI:10.1167/iovs.07-1308

W hen the eye looks up, the upper eyelid also moves after the rotation of the globe. Upward eyelid movement results from active forces generated by the contraction of the levator palpebral superioris (LPS) muscle. When eye fixation shifts rapidly to an object located in the inferior field of vision, the downward eyelid movement is entirely passive because of the relaxation of the stretched elastic components of the lid (tarsal plate, medial and lateral tendons, and Whitnal ligament).[1] These upper eyelid movements that accompany the vertical eye saccades have been well studied,[2,3] and we have recently demonstrated that they represent damped harmonic oscillations.[4] A different situation exists when the eye follows a target that moves slowly and periodically in the vertical meridian. Eye movement in this case (smooth pursuit) depends on the dynamics of the stimulus that is constantly imaged on the fovea.[5] Upper eyelid movements generated by eye pursuit movements have not been explored in clinical settings. In the present study, we measured upper eyelid saccades and pursuit movements in healthy subjects and in a sample of patients with Graves orbitopathy. Our results indicated that upper eyelid pursuit movements correspond to forced harmonic oscillations and are closely related to eyelid saccades dynamic properties.

SUBJECTS AND METHODS

Subjects

The research followed the tenets of the Declaration of Helsinki and was approved by the institutional human experimentation committee of the School of Medicine of Ribeirão Preto. Informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study.

Upper eyelid saccades and pursuit movements were monocularly recorded in two groups of subjects: a control group of 22 healthy adult subjects (11 females, 11 males; age range, 25–66 years; mean ± SD, 40.4 ± 12.96 years) and in 15 patients with Graves orbitopathy (13 females, 2 males; age range, 21–54 years; mean, 38.47 ± 9.2 years). Subjects in the control group had no systemic or ophthalmic diseases. All Graves patients were in the inactive phase of the disease. Eight patients were using antithyroid drugs, and seven were receiving thyroid hormones to control hypothyroidism secondary to hyperthyroidism therapy (thyroidectomy, thyroid irradiation, or both). No patient showed clinical evidence of lid lag (von Graefe sign), strabismus, diplopia, limitation of the vertical eye movements, or any previous eyelid or orbital surgery. Clinical data such as visual acuity, Hertel measurements, automatic perimetry, and orbital computed tomography were available for all patients.

Methods

The resting position of the upper eyelid was measured for all subjects on photographic images of the palpebral fissure with the public domain software ImageJ, version 1.38, available at http://rsb.info.nih.gov/ij/.

Eyelid saccades and pursuit movements were recorded with a charge-coupled device camera connected to a computer by a frame grabber, as previously described.[4] The camera's temporal resolution was the standard NTSC (30 Hz or 30 frames/s). Motion recording was performed with software that tracked, in real time, the center of a blue spot in each frame. This spot, which provided the localizing signal for the software, was a small piece of blue paper (0.01 g) attached to the eyelashes of the central portion of the upper eyelid.

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Procedures

With the head stabilized on a chin rest, each subject was first photographed in primary position of gaze. To permit pixel per millimeter conversion, a detail of known dimensions was always introduced in the image. These fissure images were transferred to a computer, and the mid-pupil eyelid margin distance was measured with the ImageJ software. The subjects then faced a computer screen located at a distance of 20 cm. Two red spots 30° above and below a central white spot were generated on the screen. To produce saccadic lid movements, the subject's visual axis in the primary position of gaze was aligned with the central mark. The subject was then instructed to change his or her fixation, looking down or up from one red spot to the other (60° of eye rotation across the upper and lower hemifields). To generate pursuit movements, the white spot was converted to a moving stimulus, and the position changed with time in a sinusoidal pattern with an amplitude of 30°. One entire cycle was programmed to have a period of 6 seconds, corresponding to a frequency of approximately 0.17 Hz.

Data Collection and Analysis

The data points recorded in saccadic movements were fitted using the underdamped solutions of the harmonic oscillator.[4] For the pursuit movements, a sinusoidal function was adjusted to the experimental data according to a forced oscillator model driven by a sinusoidal external force.

Harmonic Oscillator Model

In a previous study, we showed that eyelid saccades can be modeled using the underdamped solutions of the damped harmonic oscillator, with an appropriate choice of initial conditions.[4] In the present study, we demonstrated that both saccadic and slow pursuit movements can be described with the more general harmonic oscillator model that includes, besides elastic restoration and dissipative forces, an external force acting on the eyelid.

Forces acting on the upper eyelid are modeled by a linear restoration force, mainly because of the activity of the LPS, and by a linear dissipative force arising from the friction between the lid and the eyeball and from other friction between the elements of the system. In addition to these forces, when the eye follows a target, an external force also acts on the upper eyelid. This comes from the neural stimuli that drive the movement of the globe and are transmitted to the eyelid by the LPS muscle. Although the restoration force is proportional to the eyelid displacement, the dissipative force is proportional to the velocity of the eyelid. As a consequence, the upper eyelid position is given by a function of time that satisfies the linear, second-order differential equation

$$\frac{d^2Y(t)}{dt^2} + 2g\frac{dY(t)}{dt} + \zeta^2 Y(t) = F(t). \qquad (1)$$

where g is the damping coefficient, ζ is the natural angular frequency related to the strength of the restoration force and to the inertia of the eyelid, and $F(t)$ denotes the external force per unit of mass.

Saccadic movements along the vertical meridian lead to eyelid movements that can be described by assuming that, when the eye suddenly changes its fixation target, the external force per unit of mass acting on the upper eyelid is a constant force, that is $F(t) = F_0$ for $t \geq$ 0. In this case, we can redefine the origin from which the position of the eyelid is measured such that $Z(t) = Y(t) - F_0/\zeta^2$ and, because the time derivatives of $Y(t)$ and $Z(t)$ are equal, $Z(t)$ satisfies the homogeneous equation associated with equation 1, that is, the equation whose right-hand side equals zero. In other words, a harmonic oscillator pushed externally by a constant force is equivalent to a damped harmonic oscillator with a displaced equilibrium position. The underdamped solutions of this homogeneous equation, which correspond to an oscillatory part enveloped by a decaying exponential function, describe adequately the eyelid saccadic movements.[4]

Now, when the target moves up-down in a periodically repeated manner, the globe performs a periodic pursuit movement, and, thus, a periodic external force acts on the upper eyelid. Therefore, the position of the upper eyelid that accompanies a periodic pursuit eye movement on the vertical meridian must satisfy equation 1 with a periodic force per unit of mass in the right-hand side.

On general grounds, the solution of equation 1 can be written as the sum of the solution of the homogeneous equation, $Y_h(t)$, with a particular solution of the inhomogeneous equation 1, $Y_i(t)$. The function $Y_h(t)$ always dies out exponentially in time, whereas the solution $Y_i(t)$ remains with a steady oscillatory behavior driven by the periodic external excitation. This then is the solution of interest here, to describe eyelid pursuit movement. One expects to find the steady solution profile similar to that of the external force $F(t)$.

The simplest case corresponds to a sinusoidal external stimulus, which can be expressed in the form $F(t) = C \cos(\omega t + \theta)$. In this case, the steady state solution of equation 1 is

$$Y_i(t) = A \sin(\omega t + \theta + \beta), \qquad (2)$$

where the amplitude A and the phase angle β are given by[6]

$$A = \frac{C}{\sqrt{(\zeta^2 - \omega^2)^2 + 4g^2\omega^2}}, \quad \beta = \arctan\left(\frac{\zeta^2 - \omega^2}{2g\omega}\right). \qquad (3)$$

In the more general case, where $F(t)$ is an arbitrary periodic function of time, we proceed by using Fourier analysis. Any periodic $F(t)$ such that $F(t + T) = F(t)$ can be written as a sum of sinusoidal function in the form

$$F(t) = \sum_{n=1}^{\infty} C_n \cos(\omega_n t + \theta_n) \qquad (4)$$

with $\omega_n = 2\pi n/T$ and with C_n and θ_n constants that depend on the function $F(t)$.

An interesting aspect of equation 1 is that it satisfies the principle of superposition, that is, if $Y_1(t)$ and $Y_2(t)$ are solutions of equation 2 with stimuli $F_1(t)$ and $F_2(t)$, respectively, then $Y_1(t) + Y_2(t)$ is a solution of equation 2 with the inhomogeneous term $F_1(t) + F_2(t)$. This permits us to write the steady state solution for the case of the general periodic stimulus as

$$Y_i(t) = \sum_{n=0}^{\infty} \frac{C_n}{\sqrt{(\zeta^2 - \omega_n^2)^2 + 4g^2\omega_n^2}} \sin(\omega_n t + \theta_n + \beta_n), \qquad (5)$$

which represents the superposition of the solutions associated with each parcel of equation 5 separately.

Statistical Analysis

Depending on the nature of the variables (dependent or independent), group comparison was performed by paired or unpaired *t*-tests. Linear correlations were determined using least squares regression and expressed by the Pearson (*r*) coefficient of correlation. The goodness-of-fit for the nonlinear models used in the study was measured by the calculation of coefficient of determination (R^2). Variability was indicated by the symbol $\pm$ and always expressed standard deviations of the mean.
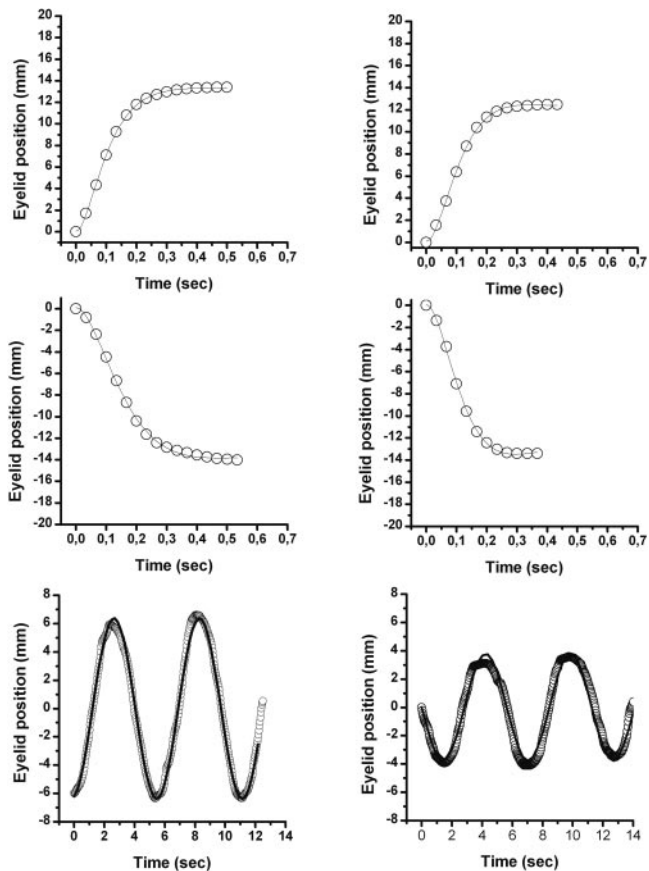
FIGURE 1. Typical plots of saccades and pursuit upper eyelid movements. *Left*: control subjects. *Right*: Graves patients. *Top*: upward saccades. *Middle*: downward saccades. *Bottom*: pursuit.
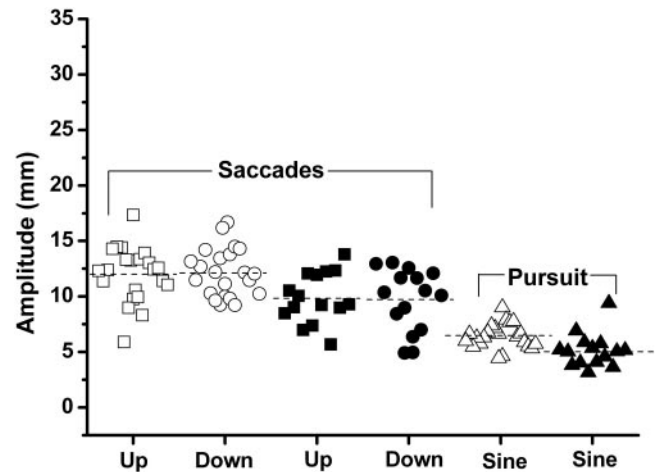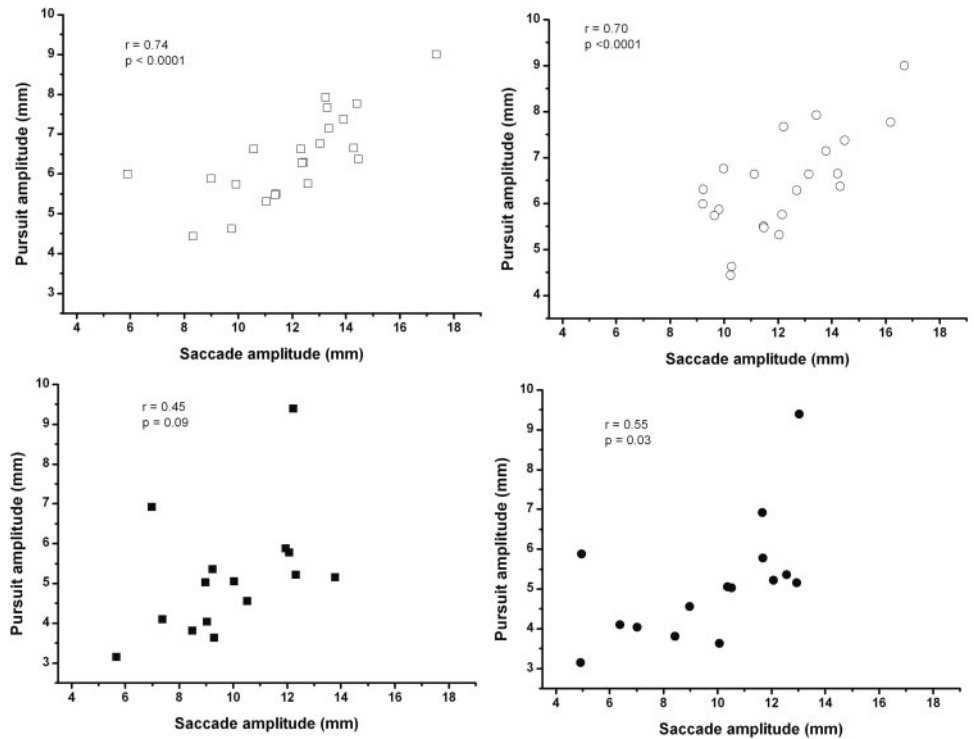

FIGURE 2. Distributions and mean values (*horizontal line*) of saccades and pursuit sinusoidal movements. *Open symbols*: control subjects. *Filled symbols*: Graves patients.

RESULTS

As expected the mean resting position of the upper eyelid of the Graves patients (6.6 ± 1.1 mm) was significantly higher than that of the controls (4.6 ± 0.8 mm; $t = 7.18$; $P < 0.00001$).

Eyelid movements for both groups were extremely well fitted by the underdamped solution of the harmonic oscillator (saccades) and by the forced harmonic oscillator (pursuit), with coefficients of determination ranging from 0.99 to 1.0 (saccades) and 0.81 to 0.99 (pursuit). Figure 1 displays typical plots of saccades and pursuit movements recorded in one subject of each group.

Table 1 presents the mean values of the model's parameters, ζ and g, for upward and downward saccades. For both groups of subjects, the mean damping coefficient of upward saccades was higher than of downward movements. Paired *t*-tests indicated that this difference was significant only for the controls ($t = 2.52$; $P = 0.02$).

Distributions of the amplitudes of the saccades and pursuit movements of the controls and patients with Graves disease are shown in Figure 2. For both groups, there was no difference between mean upward and mean downward amplitude saccades (controls upward = 12.02 ± 2.48, downward = 12.18 ± 2.18 mm; Graves upward = 9.87 ± 2.28, downward = 9.71 ± 2.81 mm). However, the mean Graves saccades were significantly smaller than those of the control subjects (upward $t = 2.67$, $P = 0.01$; downward $t = 3.01$, $P = 0.005$). The difference between control subjects and Graves patients was also verified when pursuit movements were compared (mean controls = 6.42. ± 1.10 mm, Graves = 5.13 ± 1.53 mm; $t = 2.96$, $P = 0.05$).

For control subjects and Graves patients, the amplitude of the pursuit movements was almost half the amplitude of the saccades. Ratios between pursuit (sine) and saccades were as follows: controls, sine/upward = 0.55 ± 0.12, sine/downward = 0.53 ± 0.08; Graves, sine/upward 0.55 ± 0.16, sine/downward = 0.56 ± 0.20. In addition, for the controls, the amplitudes of the pursuit movements were well correlated with the upward and downward saccades. For the Graves patients, this correlation was poor and not significant (Fig. 3). Finally, the well-known linear correlation between saccade amplitude and velocity was verified for both groups (controls, $r = 0.85$) though the correlation was slightly worse for the Graves patients ($r = 0.64$), reflecting the inhomogeneous nature of this population.

DISCUSSION

Quantification of the upper eyelid saccades movements offers interesting possibilities to study the elastic properties of the retractor elements of the lid. The video system we have used is

TABLE 1. Mean Values of the Model's Parameters

| Group | Upward (s⁻¹) | | Downward (s⁻¹) | |
	Natural Angular Frequency	Damping Coefficient	Natural Angular Frequency	Damping Coefficient
Control subjects	15.5 ± 2.27	14.7 ± 2.81	14.3 ± 3.22	11.8 ± 4.16
Graves patients	15.4 ± 4.26	14.07 ± 4.70	16.2 ± 4.66	12.28 ± 6.25

FIGURE 3. Scatterplots between saccade and pursuit amplitude in control subjects (*top*) and patients with Graves orbitopathy (*bottom*). *Squares*: upward. *Circles*: downward.

simple and can be easily used in clinical settings. Because the time interval between two2 frames is 0.033 seconds, the system is adequate to record large movements.

The upward phase of the lid saccades is dependent on the contraction of the LPS muscle and thus reflects an active force generation. The downward phase, on the other hand, is attributed to the relaxation of LPS only. It is thus the expression of the passive forces generated by the stretch of the elastic components of the lid.[1] Mathematically, both movements follow a forced harmonic oscillator model. For the saccades, a suddenly established constant force acts on the eyelid that is equivalent to an unforced harmonic oscillator with a displaced equilibrium position. As we demonstrated in a previous work, the lid saccades are well described as underdamped harmonic oscillations.[4] For the pursuit movements, the eye continuously fixates a slowly moving target. When the eye movement is periodic, the external force that acts on the upper eyelid is also periodic. In the case of a sinusoidal eye movement, the resultant eyelid movement is also sinusoidal.

In the eyelid pursuits, as the elastic relaxation of the downward phase and the active contraction of the upward movement are slowly induced by the stimulus, the amplitude of the movement is smaller than the saccades. Although smaller, the pursuit eyelid movements are correlated with the saccade amplitude. One disadvantage of the use of pursuit eyelid movements in clinical settings is the relative difficulty in obtaining the eye pursuit. In fact, a significant number of patients considered it difficult to follow the periodic pattern of stimulus movement on the screen.

Upper eyelid retraction, one of the most characteristic and frequent signs of Graves orbitopathy, is present in more than 90% of the patients with the disease.[7] The retraction is clearly multifactorial, and distinct neural and restrictive factors have been implicated in the genesis of the retraction.[8] A well-known neural mechanism is LPS overaction associated with inferior rectus muscle restriction. Because the LPS action is linked to the superior rectus muscle activity, any

effort to obtain vertical eye alignment in the presence of inferior rectus muscle restriction will cause an increased innervation of the superior and LPS muscles.[9] This type of retraction is not associated with intrinsic abnormalities within the LPS muscle and is corrected with squint surgery. Another cause of retraction that is not associated with LPS abnormalities is Müller muscle hyperaction. This mechanism appears to operate on selected patients with retractions that are highly variable and fully corrected with the use of guanethidine drops.[8] In other cases, eyelid retraction is clearly associated with LPS enlargement[10] and lid motion restriction on down gaze (the so-called von Graefe sign).

Our results show that pursuit and saccades of eyelids with Graves retraction are well modeled by the harmonic oscillator model. The biological meaning of the model's parameters is a matter open to investigation. In the present study, no difference was seen between controls and patients when the mean values of the parameters were compared. Theoretically, intrinsic levator muscle elastic abnormalities, which are believed to be the cause of the lid lag, should be manifest as high values of the damping coefficient on downward saccades. The lack of difference between controls and patients with respect to the damping coefficient may point out that, in our sample of patients, retraction resulted from abnormal Müller muscle modulation of the eyelid resting position. Further testing of the model in different types of patients is necessary to clearly ascertain the biological value of quantifying the model's parameters.

Although no subject displayed a clear von Graefe sign, a subset of patients showed reduced saccade and pursuit amplitude, whereas for others these movements were normal. We think that eyelid saccade recording is a sensitive way to demonstrate abnormalities of the elastic properties of the LPS and thus to identify subtypes of upper eyelid retraction. Saccades are easier to record, and measurement of saccade amplitude should be encouraged in clinical practice.

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