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Quantitative analysis of spontaneous saccade-like rapid eye movements in C57BL/6 mice

Tomoya Sakatani [a,b,*], Tadashi Isa [a,b]

[a] Department of Developmental Physiology, National Institute for Physiological Sciences, Myodaiji, Okazaki 444-8585, Japan
[b] Graduate University for Advanced Studies (SOKENDAI), Hayama, Japan

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Abstract

Saccadic eye movement is a rapid shift of eye position to capture an object in the environment. In this study, we will describe the fundamental properties of spontaneously evoked saccade-like rapid eye movement (SLREM) in mice in order to establish the mouse experimental model for studying saccades. Spontaneous SLREM were recorded and analyzed in C57BL/6 mice in a quantitative manner, using high-speed video-oculography at a high temporal resolution (240 frames/s) under head-fixed conditions. Mice made spontaneous SLREMs in the dark with median amplitude of 14.3 ± 2.1°, mainly in the horizontal direction. The peak velocity of SLREM increased almost linearly against its amplitude with slope of 43.6 ± 6.1 (°/s)/° in the upward, 63.3 ± 18.0 (°/s)/° in the downward, 51.3 ± 3.9 (°/s)/° in the nasal, and 31.7 ± 3.2 (°/s)/° in the temporal direction. The duration of SLREM was 56.6 ± 23.3 ms in the upward, 57.3 ± 18.0 ms in the downward, 52.0 ± 5.0 ms in the nasal, and 69.3 ± 5.5 ms in the temporal direction. This study provides the basis for analyzing the neural and molecular mechanisms engaged in the control of saccadic eye movements in genetically-engineered mice.

Keywords: Saccade; Video-oculography; Head-restrained; Voluntary movement; Rodent

1. Introduction

Saccadic eye movement is a rapid shift of eye position to capture an object in the visual environment and is a well-controlled voluntary movement. When animals orient to a particular object of interest in the surrounding space, combined movements of eyes, head, trunk, and limbs are induced. Under head-fixed conditions, the ocular component of orienting movements can be observed as saccades. This is the situation where saccadic eye movements have been studied in cats, monkeys, and humans (Sparks, 1999). Studying saccadic eye movements to understand the neural mechanisms underlying the control of the accurate movements has several advantages. First, the mechanics of the oculomotor plant are relatively simple when compared to the limb movement controller. Therefore, quantification of movement is relatively easy. Second, electrical stimulation of a part of the related circuits can mimic naturally evoked movements. Finally, much knowledge has been accumulated on the properties of identified neuronal elements of the related circuits. Due to these facts, the neuronal circuitry underlying the generation of saccades has been intensively studied, especially in cats and primates (Moschovakis et al., 1996; Scudder et al., 2002; Sparks, 2002; Wurtz and Goldberg, 1989). Moreover, numerous theoretical models have been proposed for explaining the saccadic system, owing to the relative simplicity of the mechanical system to be controlled (Girard and Berthoz, 2005).

Recent advances in mouse molecular genetics offer a new approach to study the neural basis of behaviors (Steele et al., 1998). Previous studies on the oculomotor system in mice, however, have been performed from the viewpoint of motor learning, and concentrated on slow, reflexive eye movements such as the vestibulo-ocular reflex and optokinetic responses (Raymond, 1998). Primates and carnivores have been used as experimental animals in the studies of saccadic eye movements. Since rodents have poor retinal fovea, it has been believed that they are unlikely to use eye saccade for visual orientation.

* Corresponding author at: Department of Developmental Physiology, National Institute for Physiological Sciences, Myodaiji, Okazaki 444-8585, Japan. Tel.: +81 564 55 7761; fax: +81 564 55 7766.
E-mail addresses: sakatani-ns@umin.ac.jp, sakatani@nips.ac.jp (T. Sakatani).

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Thus, there is little knowledge about saccadic eye movements in rodents with laterally located eyes and less distinct fovea. Although the existence of saccadic eye movements has been reported (Balkema et al., 1984; Grusser-Cornehls and Bohm, 1988; Mitchiner et al., 1976), no previous report has described quantitative measurement of spontaneously evoked saccadic eye movements in mice except for a recent report on the vestibular nystagmus fast phase (Stahl, 2004). Our recent development of PC-based, high-speed (240 frames/s) video-oculography (Sakatani and Isa, 2004) enables us to investigate spontaneously evoked saccade in a quantitative manner. In this study, we will describe the fundamental properties of saccade-like rapid eye movement (SLREM) in mice, in order to establish a mouse experimental model for the study of saccades.

2. Materials and methods

All procedures for animal care and experimental protocols described below were carried out in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (1996), and were reviewed and approved by the Animal Experimentation Committee of the Okazaki National Research Institutes (Okazaki City, Aichi, Japan).

2.1. Animals and surgical procedures

Seven C57BL/6J Jms Slc male mice with black eyes (SLC; Hamamatsu, Shizuoka, Japan) were tested. Average body weight was 25.3 ± 1.6 g, and all animals were approximately 12 weeks of age at the time of the eye movement recordings. Animals were housed individually for at least 1 week before experiments under standard laboratory conditions with a 12-h day/night cycle; food and water were provided *ad libitum*. Under isoflurane anesthesia (induction dose: 3.5%; maintenance dose: 1.5–2.0% [FORANE; Abbott Laboratories, Abbott Park, IL, USA]), each mouse was placed in a stereotaxic apparatus (SR-6N; Narishige, Setagaya-ku, Tokyo, Japan). Stabilizing ear bars were inserted cautiously so as not to crush the bones. After an incision was made into the scalp, mounting hardware for the stereotaxic controls was attached to the mouse's skull with dental resin (SUPER-BOND; Sun Medical, Moriyama, Shiga, Japan). The mice were allowed to recover for at least 24 h after the procedure.

2.2. Eye movement recordings

Before the recording session began, each mouse was placed in a sound-attenuated chamber and allowed to habituate to darkness for 30 min. The animal's head was fixed painlessly to the stereotaxic platform (SR-6N; Narishige, Setagaya-ku, Tokyo, Japan), with a brass rod attached to the manipulator (SM-15; Narishige, Setagaya-ku, Tokyo, Japan). The position of the head was adjusted so that the elevation of the skull surface at both bregma and lambda was the same. Consequently, the nose pitched slightly down, so that the direction of the eyes at rest would be parallel to the earth/horizontal plane. The mouse's body was loosely restrained on a rubber sheet and the legs were extended out of the rubber sheet in the air, without further restraint or contact (Fig. 1A). Eye movement recordings were performed during the light period of the light–dark cycle.

Eye positions were recorded using a high-speed video-oculographic system, as previously described (Sakatani and Isa, 2004). Spontaneous movements of the right eye were monitored over a 30-min period with a high-speed CCD camera (CS3720; Toshiba TELI Corp., Hino, Tokyo, Japan) at a sampling rate of 240 frames/s; the camera was placed at an angle of 60° lateral to the body axis and 30° down from the horizontal plane (Fig. 1B). These coordinates define the arbitrary 0° position of the eye in the orbit. Infrared light-emitting diodes (HSDL4230; Agilent Technologies, Santa Clara, CA, USA) with wavelength of 880 nm were attached to the camera to illuminate the eye. The ambient background illumination was adjusted to 50–100 lx, so that the pupils were not overly enlarged, as this is not suitable for image processing of pupil movement detection. Captured images were processed online using custom-written software in LabVIEW and IMAQ Vision (National Instruments; Austin, TX, USA), which retrieved the center of the pupil by fitting a circular function to the pupil boundary and tracked the eye position continuously (Fig. 1C). Pupil displacement in the 2D video plane was geometrically converted to angular rotation of the eyeball by estimating its rotation center based on the anatomical eyeball model. Detailed procedures are presented in the article by Sakatani and Isa (2004).

2.3. Data analysis

Rapid eye movements with a velocity above the 100°/s threshold criteria were collected automatically. This high threshold was chosen to avoid accidental detection due to the higher level of video-oculography background noise. SLREMs smaller than 2° as well as small oscillatory eye movements observed after the end of SLREM were removed manually and excluded from the further analysis in this study. The movements were analyzed and displayed offline using custom-developed software written in LabVIEW and Matlab (Mathworks Inc., Natick, MA, USA). All SLREM traces were checked manually. Artifacts (ex. eye blinks) were removed from the dataset. The amplitude, duration, peak velocity, and direction were digitally computed for each saccade. For quantitative analysis, instantaneous eye velocity was determined by differentiating position signals. Eye velocity was computed with a two-point central difference algorithm as follows:

$$\dot{E}(i) = \frac{E(i+1) - E(i-1)}{2\mathrm{d}t}$$

where dt, the sampling interval, is 4.17 ms and i is the index for discrete time. $\dot{E}(i)$ is the eye velocity and $E(i)$ is the eye position at the time i, respectively. This differentiation algorithm had a cut-off frequency of 60 Hz (−20 dB). Data are reported as mean ± standard deviation unless otherwise stated. To test for

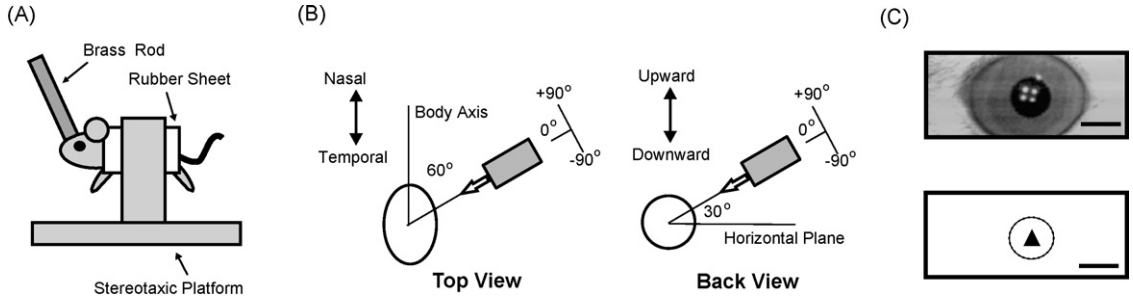

Fig. 1. Arrangement of the camera for measuring eye movements. (A) A mouse was loosely restrained with a rubber sheet and his head was fixed into place with a brass rod and a pedestal. (B) Top view (left), and back view (right) diagram of video coordinate system. Optical axis of camera is shown as a white arrow. The movements of right eye were monitored with a high-speed (240 frames/s) video camera. A CCD-camera (gray box) was set at an angle of 60° right against body axis and 30° down against horizontal plane. (C) Image processing software detected a boundary of the pupil (dotted circle in bottom panel) and its center (▲) online from a captured frame image (top panel). Angular eye positions were calculated based on an anatomical eyeball model (Sakatani and Isa, 2004). Scale bar in each panel represents 1 mm.

significance, one-way ANOVA and *post hoc* testing with the Tukey's test were performed. Statistical significance is assumed at a $p = 0.05$ level throughout. All statistical analyses were performed using commercially available software (KyPlot4.0; KyensLab Inc., Chiyoda-ku, Tokyo, Japan).

3. Results

3.1. Characteristics of SLREM in mice

A typical example of eye movement recordings is shown in Fig. 2. Arrowheads indicate the occurrence of SLREM (Fig. 2A top panel, Fig. 2C). The mouse made rapid shifts of eye position spontaneously in the dimly illuminated box. Horizontal and vertical eye position signals were then differentiated to obtain an estimate of horizontal and vertical eye velocity, respectively (Fig. 2A). Trajectories of SLREM were slightly curved (Fig. 2B), and mice had difficulty in holding the eye position at the end of SLREM. It is not shown in Fig. 2, but the eye often returned toward the central position by centripetal SLREM or drifted back slowly toward the center of the orbit after the SLREM. Thus, SLREM usually occurred from the center of the orbit. An averaged value for static eye position was $-9.6 \pm 6.8^\circ$ (horizontal position) and $-9.3 \pm 5.6^\circ$ (vertical position) relative to the camera axis (see Section 2).

3.2. Frequency of SLREM

Mice made spontaneous SLREM at a nearly constant rate under these recording conditions. On average, spontaneously evoked SLREM in all subjects occurred at a frequency of $7.5 \pm 4.7\ \text{min}^{-1}$ ($n = 7$). In order to investigate the effect of auditory and visual stimulus on the occurrence of SLREMs, an attempt was made to check the ability of these stimuli to induce these movements. Although mice responded with SLREM to novel stimuli (sound or light), they tended to be habituated to these stimuli quickly, and they were then almost unresponsive to repeated sound or visual stimuli.

3.3. Dominant direction of SLREM

Horizontal SLREMs, especially in the forward direction, were observed most often. The SLREM direction was defined as an angle of the SLREM vector on the polar coordinate. Nasal, upward, temporal, and downward SLREMs were defined as

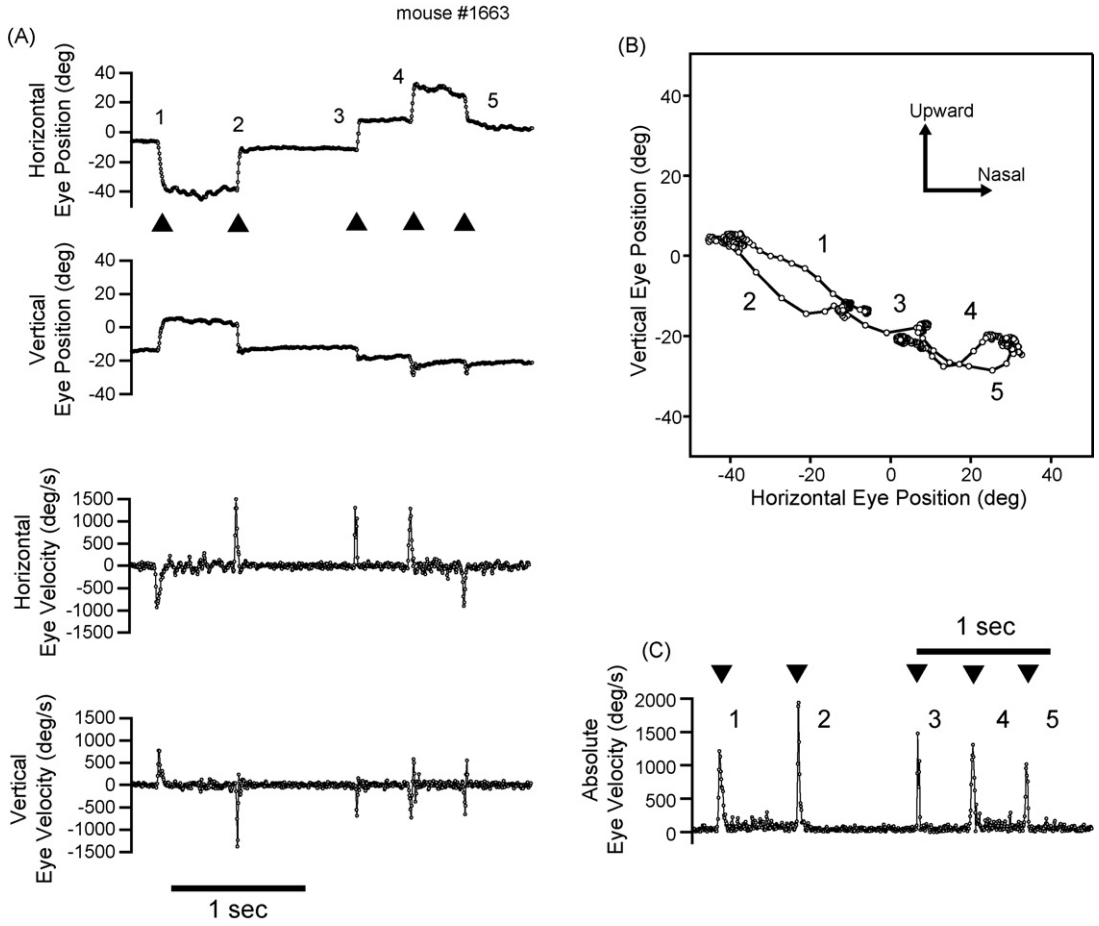

Fig. 2. An example of recorded eye positions and instantaneous velocities. (A) Horizontal and vertical eye positions, with corresponding eye velocities. Positive positions are nasal and upwards. (B) Eye trajectories in an *X*–*Y* plane during the same recording period in A. White circles represent instantaneous eye positions. Each number represents the corresponding SLREM shown in A. (C) An absolute eye velocity was calculated from horizontal and vertical eye velocity. Rapid eye movements having a velocity of above 100°/s were defined as SLREM. Small oscillatory eye movements observed after the end of SLREM were removed manually and excluded for further analysis in this study.

SLREMs where the angle of SLREM vector was within the range of −45 to +45°, +45 to +135°, +135 to +225°, and +225 to +315°, respectively. It should be noted that these coordinates largely depend on the way in which the mouse heads were fixed. There was a significant difference among the relative frequency of SLREMs in the different directions (ANOVA; $p < 0.001$, $F_{(3,24)} = 103.7$). The difference between any two directions was significant ($p < 0.01$), except for that between upward and downward ($p = 0.27$). For all subjects, the preferred SLREM direction was horizontal.

3.4. Amplitude of SLREM and the oculomotor range

Distribution of SLREM amplitudes during the 30-min recording period with velocity thresholds of 100°/s was analyzed. Although most spontaneous SLREM were smaller than 20° in amplitude, large SLREM over 40° were also observed. The average value of the median amplitude was 14.3 ± 2.1° ($n = 7$).

The distribution of the end position of the spontaneous SLREM relative to the central position was also examined. Among the subjects ($n = 7$), the observed maximum oculomotor ranges were 66.7–99.6° (mean: 79.5 ± 13.1°) for the horizontal direction and 39.8–59.8° (mean: 48.6 ± 7.2°) for the vertical direction.

3.5. Main sequence relationship

Kinematics of saccadic eye movements can be defined on the basis of velocity–amplitude characteristics (Bahill et al., 1975). Fig. 3A shows a single subject's velocity profiles of SLREM with four different amplitudes. The velocity profile of SLREM with different amplitudes exhibited a characteristic appearance, with approximately symmetrical and typical bell-shaped velocity profiles. The amplitude and peak velocity of SLREM exhibited virtually linear correlation across the observed amplitude range of 2–50°. Fig. 4A shows an example of the relationship between amplitude and the peak velocity in a single mouse. This relationship showed nearly linear correlation (correlation coefficient: 0.99 in the upward, 0.95 in the downward, 0.92 in the nasal, and 0.92 in the temporal direction) and could be well fitted to the linear regression line. Peak velocity increased almost linearly with a slope of 37.4 (°/s)/° in the upward, 61.5 (°/s)/° in the downward, 52.2 (°/s)/° in the nasal, and 34.7 (°/s)/° in the temporal direction. SLREM amplitude and peak velocity were found to be linearly correlated in all the seven subjects (correlation coefficient: 0.94 ± 0.08 in the upward, 0.92 ± 0.06 in the downward, 0.91 ± 0.03 in the nasal, and 0.85 ± 0.07 in the temporal direction), with a mean slope of 43.6 ± 6.1 (°/s)/° in the upward, 63.3 ± 18.0 (°/s)/° in the downward, 51.3 ± 3.9 (°/s)/° in the nasal, and 31.7 ± 3.2 (°/s)/° in the temporal direction (Table 1). There was a significant difference among the slope of the fitted line in the different directions (ANOVA; $p < 0.001$, $F_{(3,24)} = 12.8$). The differences between upward versus downward, downward versus temporal, and nasal versus temporal are significant (p value; <0.01, <0.001, <0.01, respectively). It should be noted that SLREM smaller than 2° were not measured in the present experiment due to the limitation of the recording method.

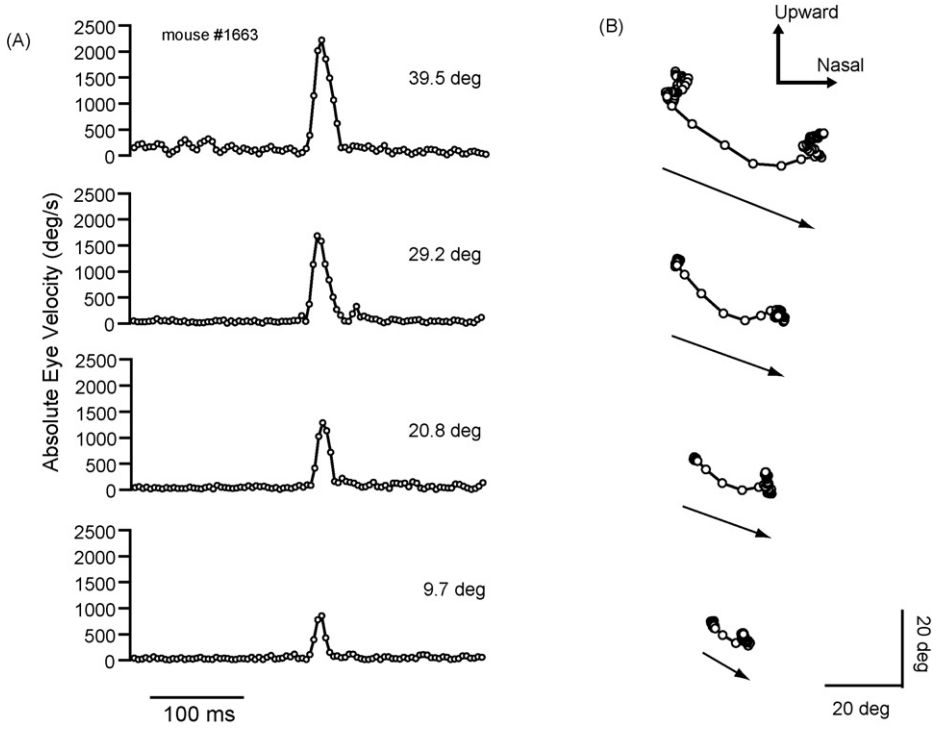

Fig. 3. Velocity profiles of the spontaneous SLREMs in mice. (A) Examples of velocity profiles of SLREM of different sizes and velocities. Each velocity trace is aligned with the SLREM onset determined by velocity threshold above 100°/s. Corresponding eye trajectories are represented in (B). The amplitude of spontaneous SLREM was 39.5, 29.2, 20.8, and 9.7° from top to bottom, respectively. The peak velocity was 2222, 1685, 1284, and 851°/s, respectively.

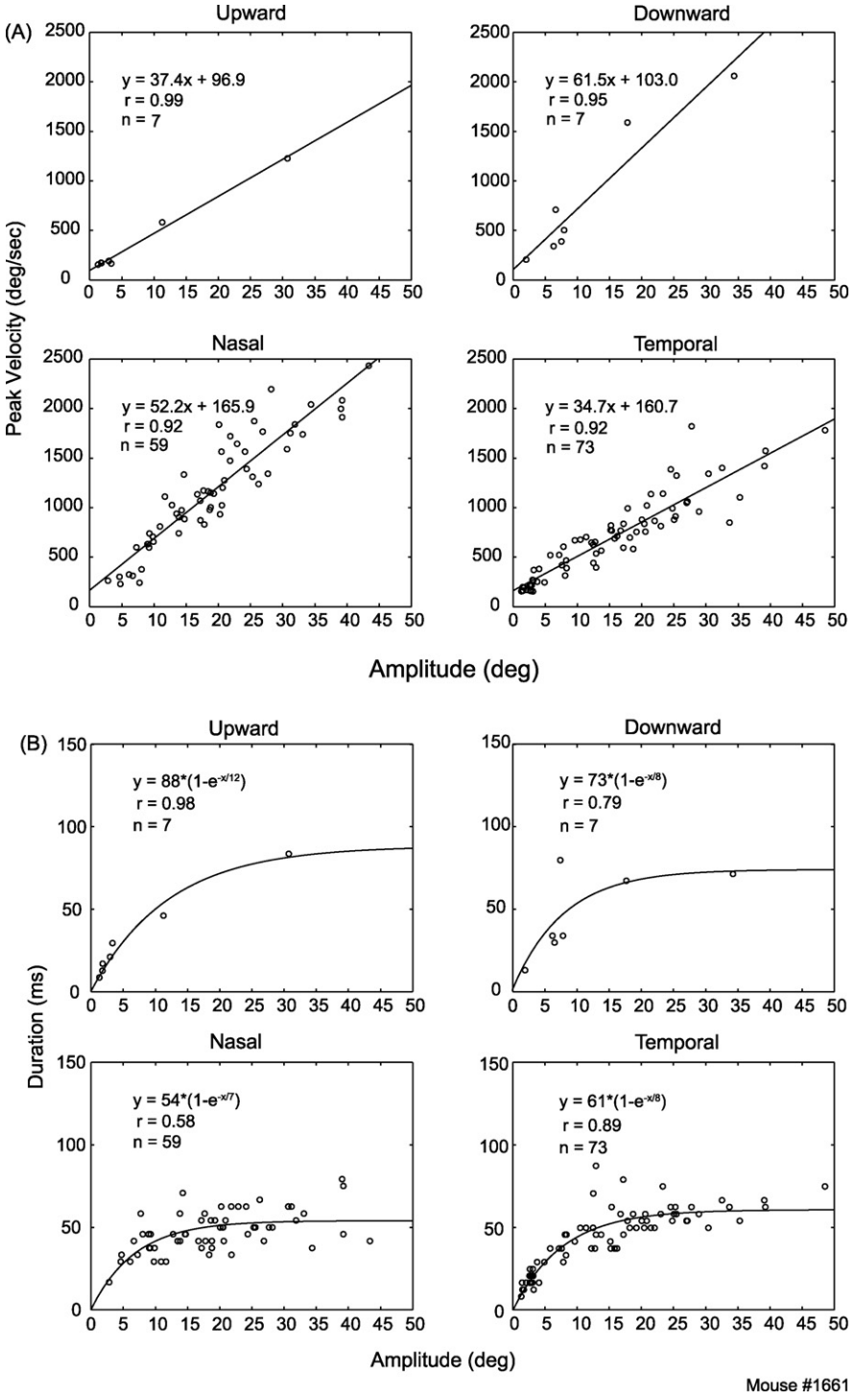

Fig. 4. The main sequence relationship of spontaneous SLREM in mice. (A) An example of peak velocity vs. SLREM amplitude plot in a single mouse. The solid line indicates the linear regression line. (B) An example of duration vs. SLREM amplitude plot in the same animal as in (A). The solid line indicates the fitted line.

The duration of SLREMs also increased with amplitude, although it was highly variable (Fig. 4B). Duration tended to be saturated for larger SLREM amplitude. Therefore, a nonlinear regression was used to fit the data in the following model. SLREM amplitude and duration had a nonlinear relationship that was fit by an exponential equation by least-square optimization. An exponential curve of the form:

$$D = K(1 - e^{-A/\tau}),$$

where D = SLREM duration, A = SLREM amplitude, and K and τ = constants returned by the curve-fitting program. The correlation coefficients were 0.98 in the upward, 0.79 in the

Table 1
Peak velocity–amplitude relationship

Subject	Upward				Downward				Nasal				Temporal			
	Slope	Intercept	*n*	*r*	Slope	Intercept	*n*	*r*	Slope	Intercept	*n*	*r*	Slope	Intercept	*n*	*r*
1660	49.6	88.6	2	1	51	135.6	13	0.89	51.7	83.8	47	0.92	29.9	269.6	36	0.74
1661	37.4	96.9	7	1	61.5	103	7	0.95	52.2	165.9	59	0.92	34.7	160	73	0.92
1662	42.7	92.9	2	1	65.4	121.6	13	0.8	54	105.9	216	0.9	37.6	129.5	168	0.88
1663	36.7	112.1	16	0.94	91.1	−10.1	18	0.95	54.3	88.2	218	0.96	29.1	194.7	165	0.93
1664	53.4	−25.1	3	0.9	54.7	142	11	0.96	49.3	213.9	57	0.87	30.3	209.6	32	0.84
1665	43.3	86.5	12	0.96	38.4	199.5	19	0.96	43.4	118.4	56	0.87	31.5	188.1	38	0.87
1666	42	67.9	17	0.79	81.2	17.2	49	0.92	54.1	217.4	132	0.9	29	249	88	0.78
Mean	43.6	74.3	8.4	0.9	63.3	101.3	18.6	0.9	51.3	141.9	112.1	0.9	31.7	200.1	85.7	0.9
S.D.	6.08	45.8	6.6	0.1	18.0	73.5	14.0	0.1	3.9	57.1	77.1	0.0	3.2	48.4	59.0	0.1

Linear regression line was fitted against peak velocity vs. amplitude plot. Slope and *y*-intercept of the fitted line are shown for each SLREM direction. *n*: number of SLREM observed in each direction. *r*: correlation coefficient of the regression line.

Table 2
Duration–amplitude relationship

Subject	Upward				Downward				Nasal				Temporal			
	K	τ	*n*	*r*	*K*	τ	*n*	*r*	*K*	τ	*n*	*r*	*K*	τ	*n*	*r*
1660	38	3	2	1	54	4	13	0.44	55	6	47	0.64	71	10	36	0.76
1661	88	12	7	0.98	73	8	7	0.77	54	7	59	0.58	61	8	73	0.88
1662	31	2	2	1	41	4	13	0.65	54	8	216	0.58	74	12	168	0.81
1663	73	8	16	0.87	47	3	18	0.51	52	6	218	0.67	72	10	165	0.84
1664	81	11	3	0.89	89	15	11	0.66	48	4	57	0.5	71	9	32	0.63
1665	45	5	12	0.79	57	6	19	0.72	58	8	56	0.59	74	11	38	0.72
1666	40	3	17	0.81	40	3	49	0.24	43	4	132	0.44	62	8	88	0.75
Mean	56.6	6.3	8.4	0.9	57.3	6.1	18.6	0.6	52.0	6.1	112.1	0.6	69.3	9.7	85.7	0.8
S.D.	23.3	4.1	6.6	0.1	18.0	4.3	14.0	0.2	5.0	1.7	77.1	0.1	5.5	1.5	59.0	0.1

An exponential curve of the form: $D = K(1 - e^{-A/\tau})$ was fitted against duration vs. amplitude plot. *D*, duration of SLREM; *A*, amplitude of SLREM; *K* and τ, constant. *K* and τ are shown in this table for each SLREM direction. *n*: number of SLREM observed in each direction. *r*: correlation coefficient of the regression line.

downward, 0.58 in the nasal, and 0.89 in the temporal direction for the data in Fig. 4B. The averaged correlation coefficients for all subjects were 0.91 ± 0.08 in the upward, 0.58 ± 0.18 in the downward, 0.58 ± 0.08 in the nasal, and 0.78 ± 0.09 in the temporal direction (Table 2). The average *K* values were 56.6 ± 23.3 ms in the upward, 57.3 ± 18.0 ms in the downward, 52.0 ± 5.0 ms in the nasal, and 69.3 ± 5.5 ms in the temporal direction. Average τ values were $6.3 \pm 4.1/^\circ$ in the upward, $6.1 \pm 4.3/^\circ$ in the downward, $6.1 \pm 1.7/^\circ$ in the nasal, and $9.7 \pm 1.5/^\circ$ in the temporal direction. There was no significant difference among the values for *D* in these fitted lines in the different directions (ANOVA; $p = 0.20$, $F_{(3,24)} = 1.65$) and among the values of τ in the different directions (one-way ANOVA; $p = 0.11$, $F_{(3,24)} = 2.17$). For all mice, most SLREMs ended within approximately 70 ms.

4. Discussions

4.1. General observations of the spontaneous SLREM in mice

This is the first quantitative study of spontaneous SLREM in mice. It was found that most of spontaneous SLREM were made in the horizontal direction. The mice preferred to make SLREM in the nasal direction rather than the temporal, and downward rather than upward. A similar tendency was also observed in the monkey, which made saccades mostly down and in the nasal direction under dark conditions (Snodderly, 1987). Significant higher peak velocity of nasal SLREMs than that of temporal SLREMs may explain our frequent counting of SLREMs in the nasal direction. Though we roughly observed conjugated SLREMs using an additional video camera (30 frames/s), we could not completely exclude the possibility that some of SLREMs were monocular or "binocular and disconjugate" eye movements. Whether mouse SLREMs are completely conjugate or not, will be solved by our future study of quantitative simultaneous recording of binocular eye movements. In the present study, only a few vertical SLREM were observed. These results suggest the possibility that, although both horizontal and vertical saccade generators exist, horizontal eye movements are developed in particular in this lateral-eyed animal species. It is generally believed that mice use head movements for orienting and do not use saccadic eye movements because of poor foveal specialization. We interpret these results to indicate that mice might use both eyes and head for orientation in the natural condition; however, because the head was restrained in the present experiment, we could observe ocular saccades. To know how the ocular saccade is used in the natural environment, it would be necessary to measure both eye and head movements under conditions where the head could move freely.

We often observed a tendency for the mouse's eye to return quickly to the primary position after SLREMs in an apparently reflexive manner. Other cases were found where the eye drifted back slowly to the center of orbit. These observations were consistent with previous reports in mice. Several explanations can be made for these results. It has been conceptually suggested that the eye position signal is generated by the putative neuronal integrator, which integrates the velocity signal from the saccadic command generator. If this neuronal integrator is leaky in the mathematical sense, it is difficult to keep holding an eye position and likely to drift back to the primary eye position. A study by van Alphen et al. (2001) reported that the time constant of the velocity-to-position integrator could be measured to be 2.1 ± 0.7 s in mice, which is very low compared to that in cat and monkey. It has also been reported that in darkness it is difficult to keep an eye stable and the eyes tend to drift, bringing the eye towards the primary position (Becker and Klein, 1973). In addition, because mice are nocturnal animal and have poor visual acuity (Dräger, 1975), they might be unable to control saccadic eye movements precisely.

Static eye position was measured in mice and revealed to be $-9.6 \pm 6.8^\circ$ in the horizontal coordinate and $-9.3 \pm 5.6^\circ$ in the vertical coordinate relative to the camera's optical axis (placed at an angle of 60° laterally from the body axis and 30° down from the earth plane; see Fig. 1). The static eye position, in particular the horizontal eye position at rest, roughly agreed with Dräger's description (Dräger, 1975) that the optic disk projected roughly 60° lateral to the animal's midline and 40° above the horizontal in anesthetized mice. The vertical eye position at rest was also consistent with previous work in which static eye elevation was reported to range from 11 to 30° from the earth plane in alert mice (Stahl, 2004).

4.2. Oculomotor range

Mice had an oculomotor deviation of about 80° (range: 66.7–99.6°) on average in the horizontal direction and 50° (range: 39.8–59.8°) in the vertical direction. The observed maximum oculomotor range of 80° in the horizontal direction in mice is unexpectedly larger than that in cats (50°) (Guitton et al., 1980) and in rabbits (30°) (Collewijn, 1970), and is close to the oculomotor range in humans (110°) (Guitton and Volle, 1987). Our observation was inconsistent with the previous report by van Alphen et al. (2001), in which only small spontaneous gaze-shifting eye movements were observed, and it was suggested that the mouse appeared to restrict eye eccentricity to a relatively limited range (generally eye-in-orbit positions remained within ±7°). One possible explanation for this inconsistency is that their use of a search coil for the eye movement recording slightly affects ocular motility. It should be noted that there could be a possibility that the maximum range of eye movements was overestimated, due to an error in eye position tracking at the periphery of the orbit in the present recording system.

4.3. The main sequence relationship

The peak velocity of SLREM increases against its amplitude in mice, similar to other mammals such as human, monkey, and cat. Even though there is similar tendency among these mammals, mice showed some differences in the following points. The peak velocity did not saturate in the range of observation. The peak velocity of SLREM in mice increased almost linearly as a function of amplitude, with an average slope of 43.6 ± 6.1 (°/s)/° in the upward direction, 63.3 ± 18.0 (°/s)/° in the downward direction, 51.3 ± 3.9 (°/s)/° in the nasal direction, and 31.7 ± 3.2 (°/s)/° in the temporal direction. These values are much higher than seen in other mammals, with human (20 (°/s)/°) (Boghen et al., 1974), monkey (40 (°/s)/°) (Fuchs, 1967), cat (10 (°/s)/°) (Evinger and Fuchs, 1978), rabbit (13 (°/s)/°) (Collewijn, 1970), and rat (20–40 (°/s)/°) (Fuller, 1985; Hikosaka and Sakamoto, 1987) all presenting with much lower ranges. On the other hand, for SLREMs of over 15°, the duration of SLREM saturated at 60 ms. This was in contrast to previous findings in cats, monkeys, and humans, where peak eye velocities were saturated relative to amplitude, while the duration was scaled linearly to amplitude. Thus, the mice may have saccade generator circuits which share common properties with those in cats, monkeys, and humans; however, there might also be some different properties related to the control of saccade duration, which should be a subject of future studies.

Differences in the slope of the peak velocity versus amplitude relationship among the different SLREM directions were observed in this study. In humans, it has been reported that kinematics of centrifugal saccadic eye movements are different from that of centripetal saccades (Pelisson and Prablanc, 1988). In a recent study on the vestibulo-ocular reflex in mice, Stahl (2004) described that abducting fast phases of nystagmus tended to be slower than adducting fast phase, although the reported values of the slopes (abduction [temporal]: 23.9 ± 1.5/s, adduction [nasal]: 27.1 ± 1.3 (°/s)/°) were much slower than those seen in spontaneous saccade. This discrepancy between the slope of fast phase nystagmus and that of the spontaneous SLREM might be partially explained by a previous report that in humans the quick phases of optokinetic nystagmus had a significantly lower peak velocity compared to saccades (Garbutt et al., 2001).

With the present recording system, because the angular positions of the eyes were calculated from pixel images on the screen, there is a potential risk that the error in estimation of angular eye position would become large at larger angles. However, because the duration of SLREM appeared to saturate already in the range of 15–20°, where the error should be small (Fig. 4B), it is not likely that the methodology of our eye position recording system was the major reason why the relationships between SLREM velocity, duration, and amplitude in mice was different from those described in other species. In the future, further improvements in both time and spatial resolution of video-oculography would be necessary to enable us to perform more accurate measurements of saccadic eye movement in mice.

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