CASE REPORT

Decreased Ratio of Downward to Horizontal Smooth Pursuit Eye Movement Velocity in a Patient with Chiari I Malformation: Application in Early Detection of Vestibulocerebellar Malfunction

Makoto Kobayashi and Atsuhiko Sugiyama

Abstract

A 72-year-old man presented with dizziness and left hand muscle atrophy. Magnetic resonance imaging revealed a spinal cord cavity and descent of the cerebellar tonsils. His diagnosis was Chiari I malformation with syringomyelia. No cerebellar signs were observed on physical examination. The cause of dizziness was investigated using a video-based eye movement tracker, which revealed a downward smooth pursuit velocity gain significantly below normal when expressed relative to the horizontal pursuit velocity gain. Vestibulocerebellar damage can cause mild downward pursuit deficit. The downward to horizontal smooth pursuit velocity gain ratio may be a more sensitive means of detecting vestibulocerebellar damage early.

Key words: Chiari malformation, smooth pursuit eye movement, vestibulocerebellum

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Introduction

Chiari I malformation is an anomaly of the hindbrain in which the cerebellar tonsils are displaced caudally into the foramen magnum. It is usually detected by magnetic resonance imaging (MRI). However, such patients presenting with tonsillar herniation on MRI do not always exhibit overt neurological deficits, and the cerebellar tonsil descent spontaneously recovers in some cases (1). Therefore evaluation of cerebellar function may be important to determine the degree of impairment. Among the neurological signs of Chiari I malformation, downbeat nystagmus is well-known and has a significant diagnostic value (2), but the diagnostic value of impaired downward smooth pursuit eye movements (SPEMs) has not been investigated. We report the case of a patient with Chiari I malformation whose primary oculomotor abnormality was a mild deficit in selective downward SPEM that was significantly below the normal range when expressed as a ratio of the horizontal SPEM.

Case Report

A 72-year-old man with left hand muscle atrophy was referred to our hospital. His medical history was unremarkable except for hypertension, hepatitis C, and an aortic aneurysm that had been treated surgically. He experienced dizziness, described as a transient sense of unsteadiness when he moved his body abruptly. The sensation was exacerbated when he was in bad condition. His left hand muscle weakness had progressed slowly over the last thirty years and was most prominent in the left hypothenar muscle. Tendon reflexes were decreased in both upper extremities, but without sensory disturbances. On clinical examination, he showed no cerebellar signs; his speech, eye movements, and tandem gait were normal. There was no limb ataxia on the heel-to-knee and finger-to-nose tests and no abnormal body sway when standing with feet together and eyes opened or closed. Cervical spine MRI revealed cerebellar tonsil descent and a spinal cord cavity from the C3 to T5 vertebral level (Fig. 1A, 1B). The cavity was moderately off center to the left (Fig. 1C, 1D). Normal saccade, SPEM, and fixation

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without restriction of eye movements were observed on physical examination. Oculomotor investigation of dizziness was then performed using a video-based eye tracker. The methods of eye recording were adapted from previous studies (3, 4) and included recordings of eye movements, visually-guided saccades, SPEM (in response to a step-ramp stimulus), and fixation.

**Eye movement recordings:** Monocular recording at a 1,000-Hz sampling rate was performed using a video-based eye tracker system (EyeLink II, SR Research Ltd., Mississauga, Ontario, Canada). Each subject sat in a comfortable chair, and their head was immobilized by a chin rest and forehead-holding device. The visual stimulus was a white dot (0.5° in diameter) against a black background on a 24-inch monitor located 42 cm from the eye.

**Visually-guided saccade:** The target was placed in the center for 1,000-2,000 ms, removed for 200 ms, and then placed in another position. Horizontal and vertical saccades of various amplitudes (10° and 20° for horizontal saccades and 10° and 15° for vertical saccades) were recorded. The direction and amplitude between the first and second presentations were randomized. Twelve trials were performed for each direction and amplitude. The EyeLink II system detected saccades automatically with a 22/°s minimum velocity criterion. Saccade amplitude gain was calculated as the amplitude of the primary saccade divided by target displacement. Latency was defined as the interval from the second stimulus to saccade onset. Median values of latency, amplitude gain, and peak velocity were calculated.

**Smooth pursuit eye movement:** The target was placed 3° horizontally or 3° vertically from the center, then moved at a constant velocity (15°/s) either in the same direction as the step (foveofugal ramp) or in the opposite direction (foveopetal ramp). For each direction, 10 foveopetal ramps and two foveofugal ramps were performed in random order with the foveofugal ramps interspersed for unpredictability. Duration of fixation before each trial was varied from 1,500 to 2,000 ms. Analyses were performed using the LabChart 7 software (AD Instruments Pty Ltd., Bella Vista, NSW, Australia) and a custom-made program. For open loop phase analysis, the eye position variable (plotted against time) was smoothed by a Gaussian filter, and initial eye acceleration was computed by linear regression of the velocity trace over the subsequent period of 60 ms. The linear regression started when eye velocity exceeded the standard deviation (SD) of 3.2 during fixation (100 ms from the target presentation). The onset of smooth pursuit was defined by the intersection of the regression line with the mean eye velocity during the fixation. Latency was defined as the interval from target presentation to onset of smooth pursuit. For closed loop phase analysis, saccades were removed and mean eye velocity was measured at intervals of 200 ms, starting at 400, 600, and 800 ms after the onset of target presentation. Velocity gain was defined as the maximum value of all three sections divided by the target velocity. Median latency, initial acceleration, and velocity gain were calculated.

**Fixation:** Nystagmus was examined during 30-s fixations on central, eccentric 15° vertical, and eccentric 25° horizontal points.

**Statistical analysis:** The results were compared with control subjects (n=14) in the seventh decade of life with no neurological diseases or medication histories that would affect the central nervous system. The normal (control) range was defined as ±2 SDs of the mean when values were normally distributed as determined by the Shapiro-Wilk test or as the range from the minimum to maximum when values were
Table 1. Visually-guided Saccade

<table>
<thead>
<tr>
<th></th>
<th>Horizontal</th>
<th>Upward</th>
<th>Downward</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10°</td>
<td>20°</td>
<td>10°</td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>Patient</td>
<td>177.3</td>
<td>197.3</td>
</tr>
<tr>
<td></td>
<td>NC</td>
<td>183.6 ± 24.2</td>
<td>208.7 ± 21.9</td>
</tr>
<tr>
<td>Amplitude gain</td>
<td>Patient</td>
<td>0.99</td>
<td>0.83</td>
</tr>
<tr>
<td></td>
<td>NC</td>
<td>0.95 ± 0.10</td>
<td>0.91 ± 0.05</td>
</tr>
<tr>
<td>Peak velocity (deg/s)</td>
<td>Patient</td>
<td>391.7</td>
<td>427.1</td>
</tr>
<tr>
<td></td>
<td>NC</td>
<td>364.6 ± 50.9</td>
<td>413.1 ± 58.1</td>
</tr>
</tbody>
</table>

The results of visually-guided saccades are shown in detail. The parameters (latency, amplitude gain, and peak velocity) were within normal ranges.

NC: Normal control. Values of normal controls are presented as mean ± standard deviation.

Table 2. Smooth Pursuit Eye Movement

<table>
<thead>
<tr>
<th></th>
<th>Horizontal</th>
<th>Upward</th>
<th>Downward</th>
<th>U/H</th>
<th>D/H</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency (ms)</td>
<td>Patient</td>
<td>199.7</td>
<td>190.2</td>
<td>239.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NC</td>
<td>174.0 ± 31.7</td>
<td>175.8 ± 27.1</td>
<td>206.7 ± 39.5</td>
<td></td>
</tr>
<tr>
<td>Acceleration (deg/s/s)</td>
<td>Patient</td>
<td>40.0</td>
<td>25.9</td>
<td>32.8</td>
<td>0.66</td>
</tr>
<tr>
<td></td>
<td>NC</td>
<td>42.9 ± 18.3</td>
<td>47.9 ± 18.3</td>
<td>28.2 (13.6–74.5)</td>
<td>0.99 (0.53–3.46)</td>
</tr>
<tr>
<td>Velocity gain</td>
<td>Patient</td>
<td>0.70</td>
<td>0.66</td>
<td>0.30</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>NC</td>
<td>0.61 ± 0.15</td>
<td>0.65 ± 0.22</td>
<td>0.53 ± 0.13</td>
<td>1.08 ± 0.31</td>
</tr>
</tbody>
</table>

Latency, initial acceleration, and velocity gain of smooth pursuit eye movements (SPEMs) in each direction are shown, as well as the ratios of upward to horizontal SPEM (U/H) and downward to horizontal SPEM (D/H). Horizontal, upward, and downward SPEM parameters (latency, initial acceleration, and velocity gain) were normal, but downward velocity gain was near the lower limit for normal individuals. The ratio of downward to horizontal velocity gain was significantly below the normal range. NC: Normal control; U/H: Upward/Horizontal; D/H: Downward/Horizontal. Values of normal controls are presented as mean ± standard deviation or median (range). An abnormal value is indicated in boldface.

were not normally distributed. In the control subjects, correlation analyses between SPEM parameters (initial accelerations and velocity gains) measured during different eye movement directions were performed using R version 2.13.1 software. Pearson’s correlation analysis was performed for normally distributed data, and Spearman’s rank test was used for data that was not normally distributed. A probability of <0.05 was considered significant.

Ethics approval: Ethical approval was granted by the Ethics Committee of Asahi General Hospital, Chiba, Japan.

The visually-guided saccade parameters (latency, amplitude gain, and peak velocity) measured in the study patient were within the normal range as established by age-matched control subjects (Table 1). The SPEM parameters (latency, initial acceleration, and velocity gain) were also within normal limits, but the ratio of downward to horizontal SPEM velocity gain was significantly below (Table 2) the range of the control group. Horizontal and upward SPEM velocity gains were preserved, but the downward SPEM velocity gain was near the lower limit of 2 SDs below the mean (Fig. 2A). In normal control subjects, the initial accelerations measured during the different eye movement directions (horizontal, upward, and downward) were not significantly correlated, but velocity gains between horizontal and vertical (upward/downward) directions were significantly correlated (Fig. 3A, 3B). To reveal directional deficits in the study patient, the ratios of upward and downward SPEM relative to horizontal SPEM (U/H and D/H) were calculated for initial acceleration and velocity gain. The ratios of initial acceleration were within normal ranges, but the ratio of downward to horizontal velocity gain was below the normal range (Table 2, Fig. 2B). Illustrative upward and downward SPEMs are shown in Fig. 4. The patient showed no signs of nystagmus in the fixation study.

Discussion

Patients with Chiari I malformation present with neurologic deficits caused by cranial neuropathies, brainstem compression, cerebellar dysfunction, or syringomyelia. Patients with syringomyelia often present with signs related to the location of the spinal damage. The classical clinical picture includes weakness of the upper limbs and segmental suspended sensory loss (5). The present case had no obvious sensory disturbances probably because the spinal cavity was left-sided and relatively small (Fig. 1C, 1D). Various ocular deficits have been reported in Chiari I malformation patients including spontaneous nystagmus (horizontal, upbeat, and downbeat), impaired SPEM, positional nystagmus, and saccadic dysmetria (1, 2). A downward SPEM defect has al-
The vestibulocerebellum (floccular/parafloccular lobe and cerebellar tonsils herniate through the foramen magnum, and has been emphasized. In patients with Chiari I malformation, the mus (6), but its significance as a diagnostic sign has not already been reported in association with downbeat nystagmus (6), but its significance as a diagnostic sign has not been emphasized. In patients with Chiari I malformation, the cerebellar tonsils herniate through the foramen magnum, and the vestibulocerebellum (floccular/parafloccular lobe and nodulus/uvula) is damaged (1, 2). The downward SPEM was shown to be more severely impaired than other directions in both monkeys (7) and humans (8) with a damaged nodulus/uvula. The parafloccular lobe also has an important role in the SPEMs of monkeys (9) and in the SPEMs of humans in the downward direction (10, 11). Thus, the downward SPEM is considered as an important measure for evaluating the cerebellar function in patients with Chiari I malformation. However, the functional integrity of the SPEM system varies considerably among individuals and is affected by age, attention, and medications (12). These variables can result in baseline variations that make mild abnormalities in SPEM difficult to detect.

In our study, the normal control subjects were in their seventies and their SPEMs varied widely probably due to the effects of age, but horizontal SPEM velocity gain was significantly correlated with both upward and downward SPEM velocity gains. In other words, the vertical SPEM velocity gain increased linearly with the horizontal SPEM velocity gain (Fig. 3A, 3B). Although factoring in the intercepts of the regression lines in Fig. 3 could allow for more precise SPEM measurements, simple division (upward/horizontal and downward/horizontal) was performed for convenience. The ratio may detect more subtle directional differences by considering individual differences in SPEM com-

Figure 2. Results of smooth pursuit eye movement (SPEM). A: Horizontal and upward SPEM velocity gains are within the ranges of control subjects (normal), but downward SPEM velocity gain is near the lower limit of control subjects. B: The ratio of upward to horizontal SPEM velocity gain is normal in the present patient, but the ratio of downward SPEM is clearly below the normal control range. NC: normal control

Figure 3. Correlations of different direction smooth pursuit eye movement velocity gains in normal control subjects. A: Upward velocity gain is moderately correlated with horizontal velocity gain. B: Downward velocity gain is strongly correlated with horizontal velocity gain. NC: normal control

Figure 4. Illustrative upward and downward smooth pursuit eye movements (SPEMs) are shown. Contaminated with saccades, the slope is gentler for downward than for upward SPEMs.
petency rather than velocity gain by itself.

In the case presented here, the downward SPEM velocity gain was low but still within the normal range, whereas the ratio of the downward SPEM velocity gain to the horizontal SPEM velocity gain was significantly below the normal range of control subjects. In other words, this patient had mildly reduced downward SPEM velocity gain with well-preserved horizontal SPEM velocity gain. This D/H ratio may enable earlier and more precise detection of vestibulocerebellar dysfunction in patients with mild Chiari I malformations. Larger scale studies are needed to corroborate these findings and validate the usefulness of the D/H for early detection of vestibulocerebellar dysfunction.

The authors state that they have no Conflict of Interest (COI).

References