

Interaction between Ocular Stabilization Reflexes in Patients with Whiplash Injury

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PURPOSE. In the past few decades, the automobile has become an increasingly more popular means of transport, which has led to an increasing number of rear-end collisions and consequently has resulted in more patients with whiplash-associated disorders (WADs). Recently, it was found that the gain of one of the ocular stabilization reflexes—the cervico-ocular reflex (COR)—is elevated in patients with whiplash injury. The COR responds to proprioceptive signals from the neck and acts in conjunction with the vestibulo-ocular reflex (VOR) and the optokinetic reflex (OKR) to preserve stable vision on the retina during head motion. Therefore, an investigation was conducted to determine whether the reported elevation of the COR in WADs is accompanied by changes in VOR or OKR.

METHODS. Eye movements of 13 patients and 18 age-matched healthy controls were recorded with an infrared eye-tracking device.

RESULTS. Analysis confirmed a significant increase in COR gain in whiplash patients. Meanwhile the VOR and OKR gains remained the same. No correlation was found between the gains of the reflexes in individual patients. This is in contrast to earlier observations in elderly subjects and subjects with labyrinthine defects, who showed increases in COR gain and decreases in VOR gain.

CONCLUSIONS. Impaired neck motion, altered proprioception of the neck, or disorganization in the process of VOR plasticity could explain the lack of change in VOR gain. (*Invest Ophthalmol Vis Sci.* 2006;47:2881–2884) DOI:10.1167/iovs.05-1561

In the past few decades, people have been using the automobile more often as a means of transport. As the grade of traffic increases, rear-end collisions occur more frequently and, as a result, whiplash-associated disorders (WADs) have become a common phenomenon in the western hemisphere. Especially since the introduction of the mandatory use of occupant-protecting seat belts, the incidence of WADs has increased.¹ The term WAD has been adopted by the Quebec Task Force (QTF) and refers to a variety of clinical manifestations, such as neck and head pain, but it also refers to visual disturbances,

tinnitus, dizziness, and fatigue.² The QTF defined whiplash as an acceleration-deceleration mechanism of energy transfer to the neck. Whiplash may result from rear-end or side-impact motor vehicle collision, but it can also occur during diving or other mishaps. The impact may result in bony or soft tissue injury.³ Although the mechanism seems clear, the variety of signs and symptoms makes it an extensive disorder. Furthermore, though in most patients the physical symptoms disappear in time, between 6% and 18% of the patients have permanent disability.⁴

Despite clear symptoms, it is difficult to find objective standards to produce evidence for the presence of the ailment in patients with WAD. However, Nederhand et al.⁵ found a decreased relaxation ability of the cervical trapezoid muscles, and Kelders et al.⁶ recently found that the gain of one of the ocular stabilization reflexes, the cervico-ocular reflex (COR), was elevated in patients with whiplash injury compared with an age-matched control group.

The COR acts in conjunction with the vestibulo-ocular reflex (VOR) and the optokinetic reflex (OKR) to preserve stable vision on the retina during head motion. It is elicited by rotation of the neck, thereby stimulating proprioceptive afferents from deep neck muscles and joint capsula from C1 to C3 to the vestibular nucleus,⁷ leading to eye movements that oppose the direction of the head movement.

The VOR can be subdivided into rotational and translational components induced by stimulation of the semicircular canals and the otolith organs, respectively. When the head is turned, the VOR moves the eyes in the opposite direction, responding optimally to high frequencies.⁸ The OKR is stimulated by visual motion and uses the relative velocity of the image on the peripheral retina to generate eye movements in the same direction. OKR and COR reflexes respond best at low head movement velocities.^{9–11} Gain values of the COR are increased over a broad range of velocities (1.2°–12.8° per second) in patients with whiplash injury, though the largest difference was found at lower velocities.⁶

In healthy persons, COR gain can be modified after 10 minutes of concurrent visual and cervical stimulation.¹² In patients with absent vestibular function, COR gain is also increased,^{13–16} as it is with age (older than 60 years¹¹). Meanwhile, in elderly persons, the gains of the VOR and OKR are decreased.^{17–19} Kelders et al.¹¹ reported a covariation between the gains of the COR and VOR in healthy persons—when the VOR is relatively high, the COR is low and vice versa.

Because the ocular stabilization reflexes work in parallel, we studied OKR, COR, and VOR in patients with WAD. We investigated whether the reported elevation of the COR in WAD was accompanied by changes in VOR, OKR, or both. This investigation of the stabilization reflexes helps to increase our understanding of the neuroanatomic basis of OKR, COR, and VOR characteristics and gives us a better understanding of motor control and of the mechanisms that underlie WAD.

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MATERIALS AND METHODS

Subjects

Thirteen patients (mean age, 40 years; range, 26–60 years) who visited the Emergency Department of the Erasmus MC with symptoms of isolated whiplash injury (WAD grades 1 and 2 according to Spitzer et al.³) after head-to-tail automobile collision were included. Patients with a history of vestibular problems, recent use of tranquilizing medication, fractures or dislocations of bones of the neck, or cervical arthrosis were excluded. All patients were interviewed for factors concerning the crash, such as velocity at impact, anticipation of the crash, signs and symptoms, and use of seatbelt, headrests and airbag. Eighteen age-matched healthy controls (mean age, 36 years; range, 23–64 years) were asked to participate in the trial. For age stratification, the control group used in Kelders et al.⁶ was extended by 10 control subjects. All participants had clear vision, and no one used any form of tranquilizing or vestibular sedative medication. Every subject gave informed consent. In accordance with the ethical standards laid down in the 1964 Declaration of Helsinki, the experiments were approved by the medical ethics committee of the Erasmus MC.

Experimental Setup

A projection screen and a custom-made rotating chair were used to record COR, VOR, and OKR responses. Details of the experimental setup are described in Kelders et al.¹¹

COR Recordings

By passively rotating the body while fixating the subject's head (trunk-to-head rotation), isolated COR responses were recorded in the absence of visual or vestibular input. The subject's head was fixed in space by means of a custom-made bite board (Dental Techno Benelux, Rotterdam, The Netherlands), and the trunk was fixed to the chair by a double-belt system at shoulder level. A cervical range-of-motion device was used to demonstrate that the head was sufficiently stabilized in space, with negligible head movement induced by chair motion.

VOR Recordings

In contrast to the setup used for the recordings of the COR responses, the bite board was attached to the chair so the trunk and the head moved passively together. As in COR recordings, the room was totally darkened.

OKR Recordings

The stimulus was generated by a personal computer (Matlab 6.1; Mathworks Inc., Natick, MA) and consisted of 50 sinusoidally moving white dots with a diameter of 0.8° in a 60°-wide and 45°-high field. The dots were projected on a 235-cm broad and 170-cm wide translucent screen through a data projector (InFocus LP 335; GroupComm Systems, Newton, MA). This projector back-projected the image onto the screen with the use of a mirror, attached to a step motor (model number 6900; Cambridge Technology, Cambridge, MA), for reflection. The dots were homogeneously distributed over the screen and had a limited lifetime of 50 msec to prevent foveal pursuit of single dots. No dots were shown in the central area of 6°. Rotations of the mirror induced the motion of the dots. Subjects were instructed to keep fixating at the center of the dots-free area to prevent visual motion in the (peri)foveal region while their heads were also fixed with the help of the bite-board.

Chair location, mirror position, and eye position data were stored on hard disc. Eye movements were recorded with the use of an infrared eye-tracking device (EyeLink; SMI, Berlin, Germany) assembled to the same construction as the bite board, with a resolution of 20 sec arc and a sampling frequency of 250 Hz.²⁰ The positions of the eyes relative to the cameras were constantly observed to ensure stabilization of the subject's head during recordings.

Stimulus Paradigms

For optokinetic and cervical or vestibular stimulation, the mirror and chair, respectively, were rotated at four different frequencies (0.1, 0.08, 0.06, and 0.04 Hz) with an amplitude of 5° about the vertical axis. For COR and VOR recordings, subjects were instructed to focus on an imaginary target located straight ahead on the screen, briefly indicated in advance by a laser dot.

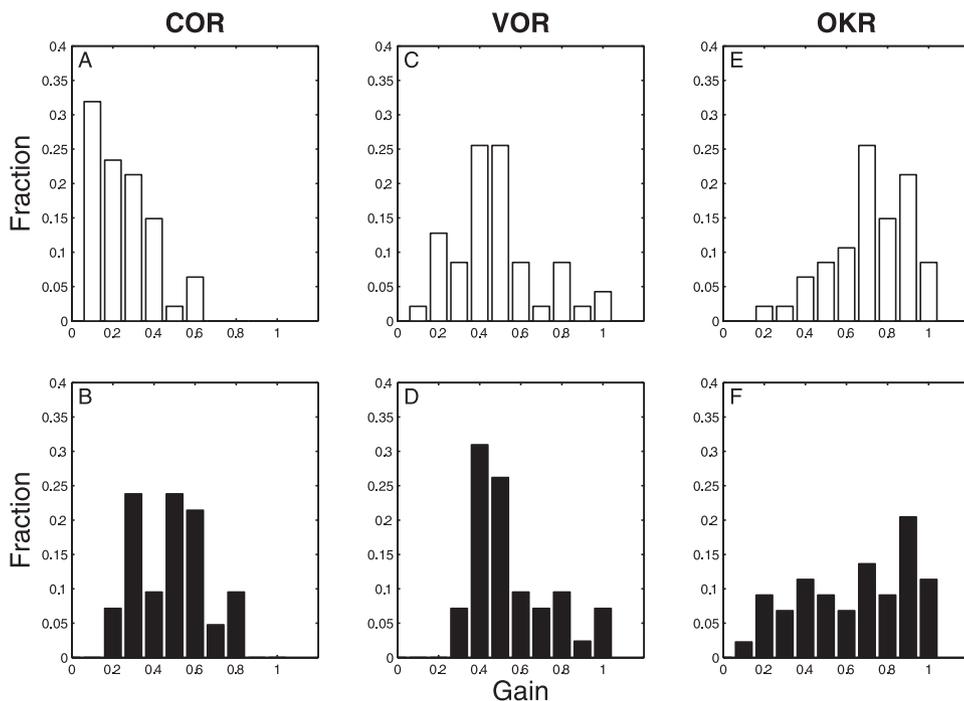


FIGURE 1. Fractions of COR, VOR, and OKR gains pooled for the whole range of stimulus peak velocities. Results of the age-matched healthy controls (A, C, E) and whiplash patients (B, D, F) are plotted.

Analysis

Eye velocity was calculated by taking the derivative of the horizontal eye position signal, identical with what was done in earlier experiments by Kelders et al.¹¹ Although the eye reflexes were never perfectly symmetrical in both groups, resulting in small drift toward the left or the right, no differences in symmetry were found between the whiplash patients and healthy subjects. After removal of blinks, saccades, and fast phases using a 20 degree per second threshold, a sine wave was fitted to the velocity signal. The gain of the response was defined as the amplitude of the eye velocity fit divided by the V_{max} of the chair. Outliers were removed. Further analyses were performed with Kolmogorov-Smirnov tests and linear regression (Matlab 6.1; Mathworks Inc.).

RESULTS

Gain values were independent of stimulus frequencies within the range that we presented, as was also described in Kelders et al.¹¹ Therefore, data were pooled over all frequencies.

The three reflex-gain values of the age-matched subjects at all frequencies are plotted in Figure 1 (controls A, C, E; patients B, D, F). Recently, Kelders et al.¹¹ found an increased COR gain in elderly patients (older than 60 years) and in patients with whiplash injury.⁶ In addition, in this study, a higher COR gain was found in WAD patients than in healthy controls (Figs. 1A, 1B; Kolmogorov-Smirnov test, $P = 2.9 \times 10^{-6}$). OKR and VOR gains do not show a significant change (VOR gain, $P = 0.27$; OKR gain, $P = 0.25$). Gain values of patients remained consistent with those of healthy controls (Figs. 1C-F). Previously, Kelders et al.¹¹ also found a negative correlation between COR gain and VOR gain in healthy controls. Figure 2A shows a similar correlation for healthy participants ($r = -0.38$, $P = 0.01$), but not for patients ($r = 0.01$, $P = 0.95$). Furthermore neither reflex was significantly correlated with the OKR in controls ($r = 0.26$, $P = 0.08$; $r = -0.02$, $P = 0.9$ respectively, Fig. 2B), or patients ($r = 0.09$, $P = 0.05$, $r = 0.16$, $P = 0.31$ respectively, Fig. 2C). Although the COR gain increases with age in controls ($r = 0.32$, $P < 0.02$), such a difference does not appear in patients ($r = -0.05$, $P > 0.7$; Fig. 3).

DISCUSSION

COR gain values in patients with WAD are significantly increased compared with those in healthy controls. An age-related increase was not seen in patients, which could indicate that the whiplash injury cancels out this age-related effect. After stratifying for age, values remained higher, similar to what was seen in Kelders et al.⁶ In addition, in contrast to what was found in healthy controls, no synergy was found between COR and VOR in the patient group. Furthermore, no correlation was found between the remaining eye reflex combinations in patients or in controls. However, age-related decay in VOR and OKR in healthy subjects has been reported.¹⁷⁻¹⁹ The

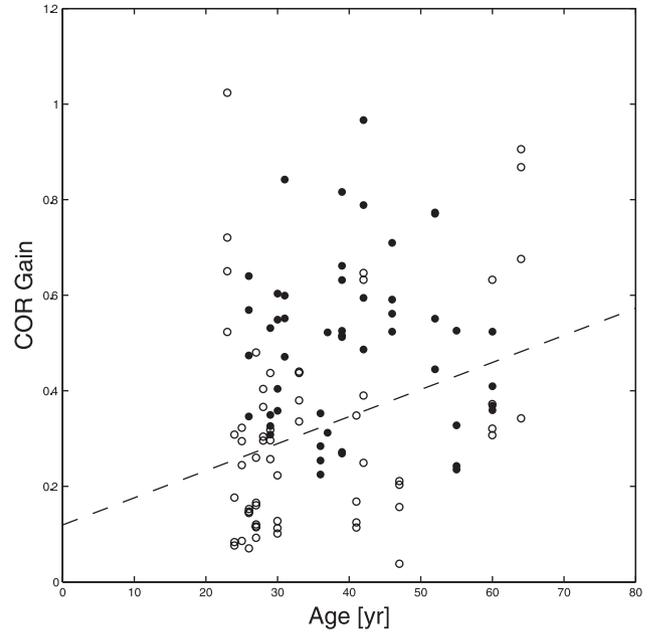


FIGURE 3. Correlation between COR gain and age. Whiplash patients (closed circles) and controls (open circles). Dotted line is fitted through the data of the healthy subjects by means of linear regression (slope = 0.0057 yr^{-1})

increase in COR gain in elderly patients might be an adjustment for the decline in VOR gain. Moreover, in persons with bilateral labyrinthine defects, the COR partly takes over for the diminished VOR by increasing^{13,15,21} and decreasing after restoration of the vestibular apparatus.¹⁴ In earlier experiments, Rijkaart et al.¹² showed that the COR is able to adapt after only 10 minutes of incongruent simultaneous visual and cervical stimulation.

A decrease in VOR gain might have been responsible for an increase in COR gain in our whiplash patients, as seen in elderly subjects¹¹ and in those with labyrinthine defects.¹³⁻¹⁶ However, a higher COR gain could also be the cause of a decline in VOR gain. Earlier experiments showed that the VOR gain could be adapted in 1 hour by noncorresponding vestibular and visual information.²²⁻²⁵ Contrary to the latter theory, the COR gain was elevated with no decline in the VOR gain in WAD patients.

Three hypotheses can provide an explanation for this lack of synergy in patients with whiplash injury:

First, it may be that decreased mobility of the neck leads to alteration in proprioception of the neck, which in turn results in an augmented gain of the COR without any problems in the VOR pathway.

Second, it may be that adaptation of the VOR requires sufficient head motion, and, because of impaired neck motion,

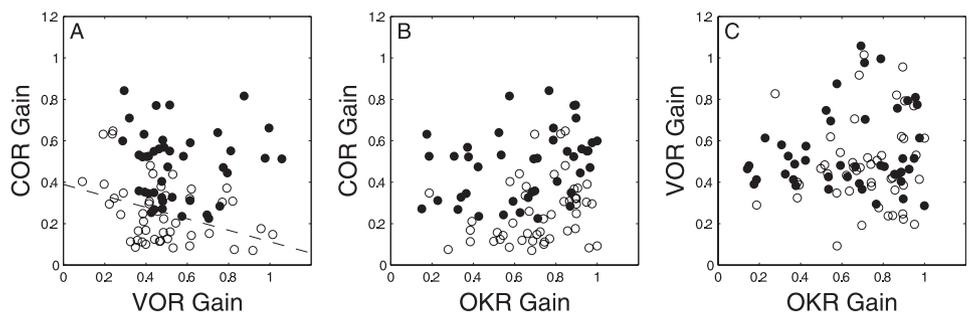


FIGURE 2. Correlations between the reflex gains (A-C). Whiplash patients (closed circles) and controls (open circles). (A) Dotted line is an orthogonal fit through the data of the healthy subjects (slope = -0.4581). In the remaining data, no significant correlation could be found; therefore, no fitting line is shown.

the patient has too little adaptive input for the VOR to induce a negative adaptation in VOR gain. It is known that the VOR responds best at high velocities, whereas the COR is most responsive at low frequencies. This could explain the lack of decrease in VOR gain.

Third, it may be that there is a disorganization in the process of VOR plasticity because of microtrauma in the VOR pathway, such as in the flocculonodular area of the cerebellum. The latter hypothesis will be subject to more research in the near future when we perform VOR adaptation experiments in patients with whiplash injury.

Although a variety of symptoms such as head and neck pain, visual disturbances, tinnitus, dizziness, and fatigue are associated with whiplash injury,² it can be speculated to what degree abnormalities in COR gain are responsible for the reported signs and symptoms. Although the correlation between them is striking, correlation does not prove causation. However, the results might explain some symptoms. Improperly tuned VOR and COR may lead to symptoms such as dizziness and to visual problems such as reading impairment. The absence of synergy between COR and VOR combined with head and neck pain may induce symptoms of fatigue.

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