



The influence of cervical movement on eye stabilization reflexes: a randomized trial

Britta K. Ischebeck^{1,2} · Jurryt de Vries^{1,3} · Jan Paul van Wingerden² · Gert Jan Kleinrensink¹ · Maarten A. Frens^{1,4} · Jos N. van der Geest¹

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Abstract

To investigate the influence of the amount of cervical movement on the cervico-ocular reflex (COR) and vestibulo-ocular reflex (VOR) in healthy individuals. Eye stabilization reflexes, especially the COR, are changed in neck pain patients. In healthy humans, the strength of the VOR and the COR are inversely related. In a cross-over trial the amplitude of the COR and VOR (measured with a rotational chair with eye tracking device) and the active cervical range of motion (CROM) was measured in 20 healthy participants (mean age 24.7). The parameters were tested before and after two different interventions (hyperkinesia: 20 min of extensive active neck movement; and hypokinesia: 60 min of wearing a stiff neck collar). In an additional replication experiment the effect of prolonged (120 min) hypokinesia on the eye reflexes were tested in 11 individuals. The COR did not change after 60 min of hypokinesia, but did increase after prolonged hypokinesia (median change 0.220; IQR 0.168, $p=0.017$). The VOR increased after 60 min of hypokinesia (median change 0.155, IQR 0.26, $p=0.003$), but this increase was gone after 120 min of hypokinesia. Both reflexes were unaffected by cervical hyperkinesia. Diminished neck movements influences both the COR and VOR, although on a different time scale. However, increased neck movements do not affect the reflexes. These findings suggest that diminished neck movements could cause the increased COR in patients with neck complaints.

Keywords Eye stabilization reflexes · Cervico-ocular reflex · Vestibulo-ocular reflex · Cervical range of motion · Neck pain patients · Oculomotor disturbances

Introduction

In patients with neck pain and Whiplash Associated Disorders (WAD) oculomotor disturbances have been described

(Heikkilä and Wenngren 1998; Kelders et al. 2005; Storaci et al. 2006; Montfoort et al. 2006, 2008; Treleaven et al. 2011; Ischebeck et al. 2016), which may be attributed to altered cervical functioning (Treleaven et al. 2006; Falla and Farina 2007; Kristjansson and Treleaven 2009; Hodges 2011). Here we studied the effects of neck (im-) mobilization on the eye stabilization reflexes as part of the oculomotor system in healthy subjects.

To guarantee clear vision the vestibulo-ocular reflex (VOR) and the cervico-ocular reflex (COR) work in conjunction to stabilize the visual image on the retina. The VOR receives input from the vestibulum, responding to movements of the head in space. The COR receives input from the mechanoreceptors, mainly the muscle spindles and joint sensors, of the upper cervical spine (Hikosaka and Maeda 1973). The COR responds to movements of the head relative to the trunk.

It is important that the reflexes are properly adjusted to each other, even in circumstances when one of them is

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✉ Jos N. van der Geest
j.vandergeest@erasmusmc.nl

¹ Department of Neuroscience, Erasmus MC, PO Box 2040, 3000 CA Rotterdam, The Netherlands

² Spine & Joint Centre, Noordsingel 113, Rotterdam 3035 EM, The Netherlands

³ Department of Physical Therapy, Rotterdam University of Applied Sciences, Rochussenstraat 198, 3015 EK Rotterdam, The Netherlands

⁴ Erasmus University College, Nieuwemarkt 1a, Rotterdam 3011 HP, The Netherlands

changed. Both reflexes are indeed quite plastic, in the sense that they adapt to perturbations and changes of input. In laboratory settings, it has been observed that the VOR and COR adapt to experimentally perturbed visual and vestibular input (Schweigart et al. 2002; Rijkaart et al. 2004; Montfoort et al. 2008; Yakushin et al. 2011). However, little is known about the adaption of the reflexes to perturbed cervical input.

The overall aim of the present study was to elucidate the effect of altered cervical input on COR and VOR. This latter reflex was not taken into account in our previous study (Montfoort et al. 2008). Here we will also investigate whether the synergy of reflexes is altered and whether the changes of reflexes are directly related to changes in active range of motion. The first objective is to assess the changes in COR and VOR gain in response to a temporary reduction of cervical proprioceptive output (hypokinesia), induced by passive immobilization of the neck. We first study if 1 h of neck immobilization is sufficient to observe changes in the eye stabilization reflexes. Then, we replicate our previous experiment using a 2-h immobilization period.

The second objective is to study reflex adaptation as result of temporary increased proprioceptive output (hyperkinesia), rather than immobilization.

The assessment of both reflexes in the same subjects under several neck (im-) mobilization conditions, allows us to assess the suggested interactions between the cervical and vestibular eye movement systems (Kelders et al. 2005; Montfoort et al. 2006). Adjustment of these reflexes is essential for optimal oculomotor control and will prevent vision problems. This study elucidates the synergy of eye stabilization reflexes and how changes in one reflex affect the other. This information is essential to enhance our understanding of oculomotor problems in neck pain patients.

Materials and methods

Participants

Twenty healthy adults [mean age 24.7 years (range 20–33), 12 male, 8 female] were recruited from the Erasmus MC to participate in the main experiment (hypokinesia and hyperkinesia). For the current replication experiment (prolonged hypokinesia) eleven healthy subjects [mean age 29.3 (22–48), 4 male, 7 female] were recruited (four of them also participated in the main experiment). All participants had no history of neck complaints (including no cervicogenic headache or dizziness) and no known neurological, visual or vestibular disorders. They all had normal or corrected-to-normal visual acuity and no one used any form of tranquilizing medication. The local ethical board of the Erasmus MC, which is in accordance with the Declaration of Helsinki

1975, revised Hong Kong 1989, approved this study and all participants gave prior written informed consent.

Intervention

In the main experiment, two types of intervention were applied in a cross-over design: hypokinesia and hyperkinesia. Directly before and after the intervention, the eye stabilization reflexes and the active range of motion were measured.

In the *hypokinesia* intervention, the neck was immobilized using a stiff neck collar (size 4, Laerdal Stifneck® Select™) for 1 h. In the *hyperkinesia* intervention, active neck movement in all possible directions of movement was evoked by having the participants move their neck excessively in all directions for 20 min. The participants were instructed to move their head as far as possible, following visual cues (left, right rotation, side bending, flexion, extension and combined movements). During the experiment they were motivated to keep moving their neck without rest.

Each participant of the main experiment received both interventions on two different days separated by 6 or 7 days. The order of the two interventions was pseudo-randomized and balanced across participants.

In the replication experiment, 11 participants wore the neck collar for 2 h (*prolonged hypokinesia*). This experiment took place 2 weeks after the end of the main experiment.

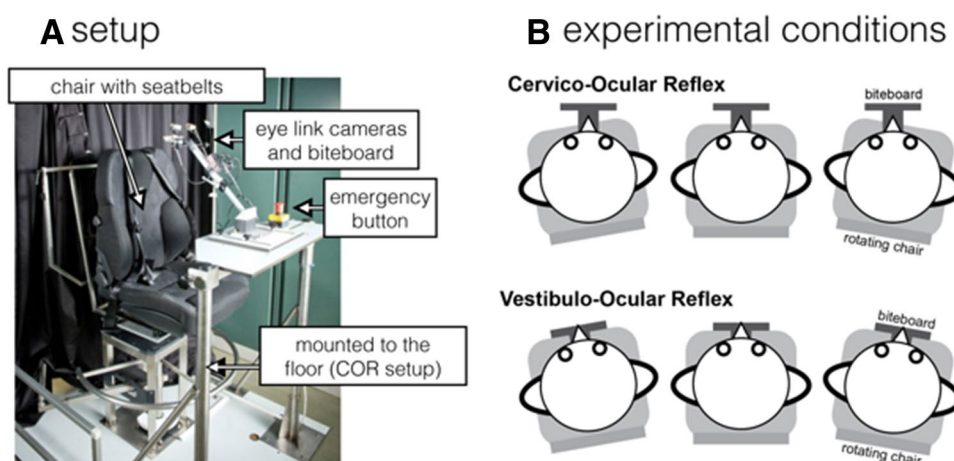
Experimental setup

Monocular (left) eye positions were recorded by infrared video-oculography (Eyelink 1, SMI, Germany; see van der Geest and Frens 2002) at a sample rate of 250 Hz. Eye position was calibrated using the built-in nine-point calibration routine.

Participants were seated in a comfortable rotatable chair (Fig. 1a). The trunk of the participant was fixed to the chair at shoulder level by a double-belt system. The chair was attached to a motor (Harmonic Drive, Germany) which induced continuous sinusoidal chair rotations around the vertical axis without any backlash. A sensor connected to the chair recorded chair position, which was stored on the computer along with eye positions.

The subjects head was fixed by means of a custom-made bite board, which was positioned with the axis of chair rotation under the midpoint of the inter-aural line. The bite board could be fixed to the floor or to the chair (Fig. 1b). During the COR stimulation, the bite board, mounted to the floor, fixed the position of the head in space. Measurements took place in complete darkness inducing pure cervical stimulation, which elicits the COR in isolation. During this stimulation, the chair rotated for 134 s with an amplitude of 5.0° and a frequency of 0.04 Hz. This yielded five full sinusoidal

Fig. 1 **a** A photograph of the chair and the position of the cameras and the bite board in the COR setup. **b** The measurement of the vestibular ocular reflex (VOR) with the bite board attached to the chair, and the cervico-ocular reflex (COR) with the bite board attached to the floor, whilst the chair is rotating back and forth



rotations of the chair with peak velocity of $1.26^\circ/\text{s}$. When the bite board was mounted to the chair, rotation of the chair in complete darkness induced pure vestibular stimulation, eliciting the VOR in isolation. During the VOR stimulation, the chair rotated for 33 s with an amplitude of 5.0° and a frequency of 0.16 Hz. This yielded five full sinusoidal rotations of the chair with peak velocity of $5.03^\circ/\text{s}$. In both eye movement stimulations participants were instructed to look at a position directly in front of the set-up. This position was briefly indicated by means of a laser dot in the completely darkened room.

The amount of the active cervical range of motion (CROM) in both the horizontal and vertical planes was also measured before and after an intervention using the CROM measurement device (Performance Attainments Associates, USA; <http://www.spineproducts.com/>) (Williams et al. 2012). The CROM device consists of two gravity dependent goniometers and one compass dial on a head-mounted frame allowing measurement of ROM in three planes. A magnetic yoke consisting of two bar magnets held anteriorly and posteriorly is supplied to reduce the influence of thorax rotation. Participants have to rotate their head in all directions (left, right rotation, side bending, flexion, extension and combined movements) as far as possible. The range of motion is measured in 2° increments.

Data analysis

Eye movement reflexes were analyzed by looking at the eye velocity relative to the chair or stimulus velocity. The phase was not detected. All data processing was done with custom-written scripts in Matlab R2013a (The MathWorks Inc., Natick, MA, USA). The same analysis was used for all interventions. Eye velocity was calculated by taking the derivative of the horizontal eye position signal. After removal of blinks, saccades and fast phases (using a 20° -per-second threshold), a sine wave was fitted through the eye

velocity signal data. The gain of the response was defined as the amplitude of the eye velocity fit divided by the peak velocity of the chair rotation (COR $1.26^\circ/\text{s}$; VOR $5.03^\circ/\text{s}$).

A gain of 1 thus reflects that the peak velocity of the eye was the same as the peak velocity of the stimulus. Gain changes were defined as the difference in gain before and after the intervention.

Statistical analyses were done using SPSS 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics were computed for the gains of the two eye movement reflexes and the cervical range of motion before and after the interventions. Since the number of subjects was low, and data was not distributed normally (Shapiro–Wilk test: $p < 0.05$), non-parametric statistics were applied. For each intervention the changes in COR and VOR gains, and changes of the cervical ranges of motion (horizontal and vertical) were statistically assessed using the Wilcoxon signed rank test. The differences in the changes between the two interventions were assessed using as well the Wilcoxon signed rank test. A correlation analysis (Spearman-rho) was performed to determine any correlation between the five variables.

An alpha level of $p < 0.05$ was considered significant for all statistical tests. Reported values are medians and inter-quartile ranges.

Results

In the main experiment, COR recording failed in two participants, and VOR recording failed in another participant, in both interventions due to technical reasons. In one participant the COR and VOR recording failed in the hyperkinesia condition and in one other participant, VOR recording failed in the hyperkinesia condition. Statistical analyses were done on the remaining participants. The results of the main experiment are summarized in Table 1 and shown in Fig. 3.

Table 1 Gains of the eye reflexes and cervical range of motion recorded before and after the two interventions, the change of gain/range of motion (including *p* value) and the correlation (including *p* value) between the two recordings

Intervention	Hypokinesia						Hyperkinesia					
	<i>n</i>	Before Median (IQR)	After Median (IQR)	Change Median (IQR)	<i>p</i> value	Correlation <i>r</i>	<i>n</i>	Before Median (IQR)	After Median (IQR)	Change Median (IQR)	<i>p</i> value	Correlation <i>r</i>
COR (gain)	14	0.214 (0.216)	0.307 (0.178)	0.049 (0.263)	0.397	0.03	17	0.257 (0.522)	0.403 (0.448)	0.052 (0.365)	0.435	0.35
VOR (gain)	15	0.568 (0.21)	0.736 (0.275)	0.155 (0.26)	0.003	0.45	16	0.672 (0.245)	0.686 (0.192)	−0.011 (0.23)	0.642	0.32
CROM horizontal (degrees)	16	141° (10°)	140° (18°)	−5.5° (14°)	0.005	0.77	19	140° (14°)	148° (10°)	1 (8°)	0.208	0.75
CROM vertical (degrees)	16	144.5° (24°)	132.5° (16°)	−8° (17°)	0.044	0.71	19	138° (32°)	150° (28°)	2 (25°)	0.198	0.75
												<0.001

COR gain of cervico-ocular reflex, *VOR* gain of vestibulo-ocular reflex (gain=eye velocity divided by stimulus velocity), *CROM* horizontal active range of movement of the neck in the horizontal plane in degrees, *CROM* vertical active range of movement of the neck in the vertical plane in degrees

Hypokinesia

Sixty minutes of wearing the stiff neck collar did not influence the COR gain, but it increased VOR gain by 29.6%. The cervical range of motion decreased slightly in the horizontal plane and in the vertical plane. The gains of the reflexes before and after the intervention were not correlated. The cervical ranges of motion before and after the intervention did correlate.

Hyperkinesia

Twenty minutes of intensified neck movements did not change COR, or VOR gains. The cervical ranges of motions were also not affected. Both COR gains and VOR gains were not correlated before and after the intervention. The cervical ranges of motion were correlated.

Hypokinesia versus hyperkinesia

A direct comparison of the hypokinesia and hyperkinesia interventions in the sixteen participants who performed both interventions successfully, shows that the COR gain changes were not different between the two interventions (difference in gain change: -0.059 median ± 0.56 IQR, $p=0.463$). The increase in VOR gain after wearing a neck collar for an hour was different from the decrease in VOR gain in the hyperkinesia intervention (0.105 ± 0.33 , $p=0.039$). The changes in cervical ranges of motion were significant in both planes (horizontal $-6^\circ \pm 17^\circ$, $p=0.004$, vertical $-12^\circ \pm 29^\circ$, $p=0.025$).

Prolonged hypokinesia

In the replication experiment, 11 participants wore the stiff neck collar for 2 h. In one subject both the COR and VOR recordings failed and in one other subject the VOR recording failed. The results are shown in Table 2. In Fig. 2 exemplary eye movement velocity traces of the VOR and COR of different subjects before and after the hypokinesia interventions are shown (sections a–h).

COR gain increased after prolonged neck immobilization by 81.8%, while VOR gain and the cervical ranges of motion did not change. The cervical ranges of motion did not change significantly in both the horizontal ($-5^\circ \pm 12^\circ$, $p=0.294$) and vertical planes ($-8^\circ \pm 20^\circ$, $p=0.79$). The before and after measurements were not correlated for the COR, but they were for the range of motion and the VOR. A between group-comparison of the hypokinesia and prolonged hypokinesia interventions showed that COR and VOR gain changes differ between the two interventions (difference in COR gain change 0.124 ± 0.228 , $p=0.048$ and the VOR gain change 0.092 ± 0.224 , $p=0.003$, Fig. 3).

Table 2 Gains of the eye reflexes and cervical range of motion recorded before and after the prolonged hypokinesia intervention, the change of gain/range of motion (including *p* value) and the correlation between the two recordings (including *p* value)

Prolonged hypokinesia	<i>n</i>	Before Median (IQR)	After Median (IQR)	Change Median (IQR)	<i>p</i> value	correlation <i>r</i>	<i>p</i> value
COR (gain)	10	0.242 (0.375)	0.440 (0.349)	0.220 (0.168)	0.017	0.52	0.128
VOR (gain)	9	0.733 (0.209)	0.709 (0.278)	−0.031 (0.215)	0.314	0.68	0.042
CROM horizontal (°)	11	142° (24°)	134° (24°)	−2° (18°)	0.383	0.73	0.011
CROM vertical (°)	11	138° (32°)	130° (30°)	−8° (25°)	0.305	0.88	0.001

COR gain of cervico-ocular reflex, *VOR* gain of vestibulo-ocular reflex (gain=eye velocity divided by stimulus velocity), *CROM horizontal* active range of movement of the neck in the horizontal plane in degrees, *CROM vertical* active range of movement of the neck in the vertical plane in degrees

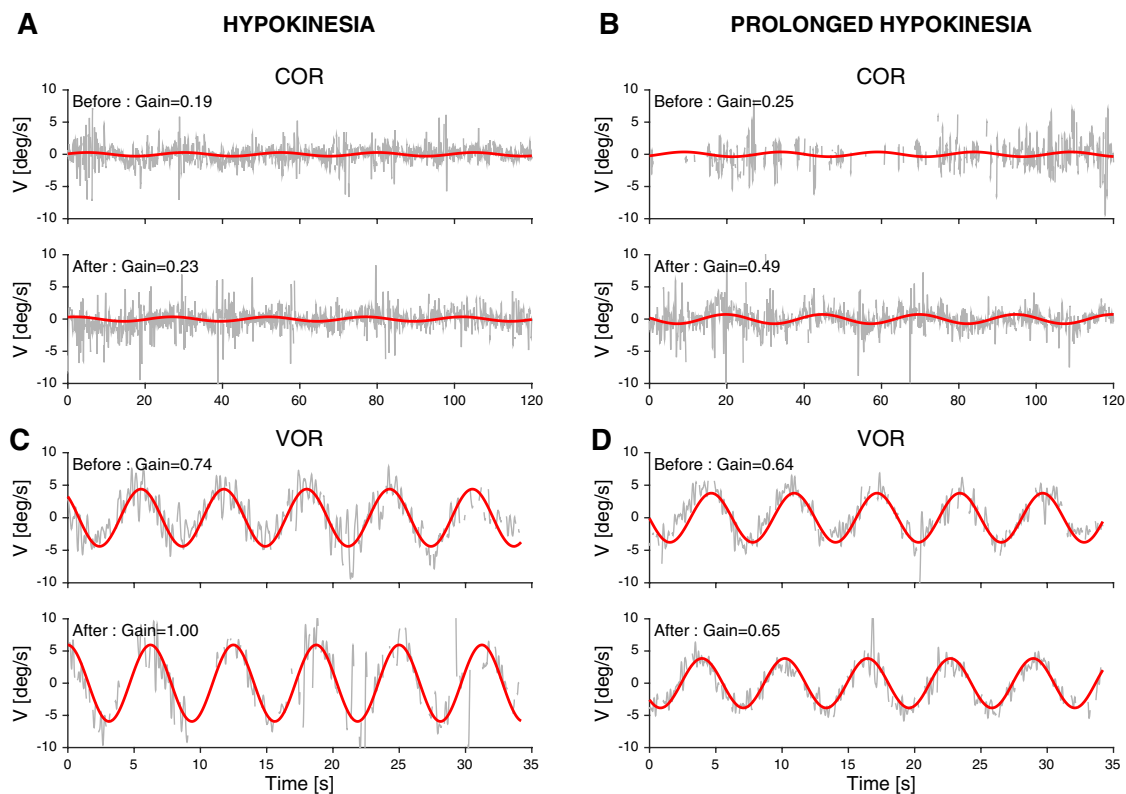


Fig. 2 Exemplary eye movement velocity traces of the VOR and COR before and after 60 or 120 min (prolonged) hypokinesia (of different subjects). Red line=the fit through the raw eye movement velocities (grey line). **a** COR traces before and after hypokinesia; **b**

COR traces before and after prolonged hypokinesia; **c** VOR traces before and after hypokinesia; **d** VOR traces before and after prolonged hypokinesia

Correlations

When we collapsed all data across all interventions, changes in the reflexes (COR and VOR) were not correlated (Table 3). Subjects who moved their head more in the horizontal plane, also did so in the vertical plane. As well subjects who tended to move their heads more in the horizontal plan tended to exhibit smaller changes in VOR gains.

Discussion

The present study aimed to elucidate the role of neck movements in the adaptive mechanisms of the cervico-ocular reflex (COR) and the vestibulo-ocular reflex (VOR). Thereto we temporarily immobilized the head relative to the trunk (hypokinesia) or asked participants to move their neck extensively (hyperkinesia). While COR gain does not adapt after 1 h hypokinesia or after hyperkinesia, it increases after

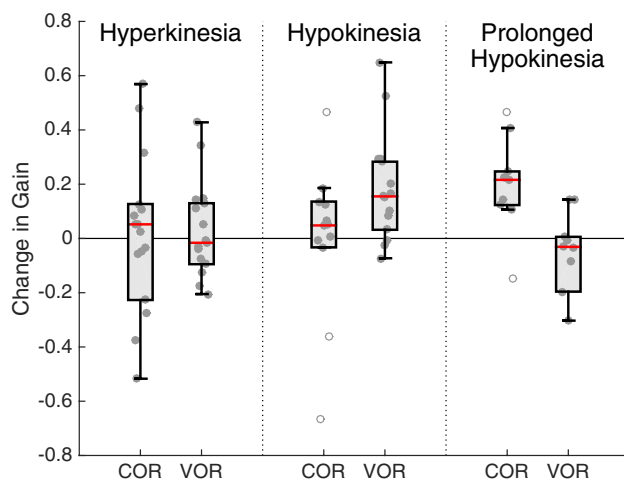


Fig. 3 Boxplot of the changes in COR and VOR gains following the three different interventions. Red line = median; grey box = IQR, grey dots = individual gain values; open circles = outliers

Table 3 Correlations (correlation coefficient r and p value) between the gains of COR and VOR and the range of motion in the horizontal and vertical planes

	VOR	CROM horizontal	CROM vertical
COR	0.081 (0.638)	0.015 (0.927)	−0.02 (0.904)
VOR		−0.369 (0.019)	0.005 (0.975)
CROM horizontal			0.537 (0.000)

2 h of hypokinesia. VOR gain increases slightly after 1 h hypokinesia, but was not changed after 2 h hypokinesia nor after hyperkinesia. The influence of the maximal range of cervical motion on the eye stabilization reflexes seems to be negligible.

The changes in COR reflex are in line with the ‘upregulation theory’: if the output of the vestibulum and the neck is reduced by minimizing the movement of the head and spine, reflex responsiveness is increased to receive enough information which is needed to stabilize the posture (Schweigart et al. 2002; Montfoort et al. 2008). While the COR did not adapt after a shorter period of time, we replicated our previous findings of an increase in COR gains after 2 h of hypokinesia (Montfoort et al. 2008). This finding suggests that the COR adapts rather gradually to changed circumstances. In general, the exact time course of sensory adaptation following a stimulus change depends on the availability of sensory vestibular, visual and proprioceptive information and on the amplitude of the stimulus and the response. For instance, proprioceptive systems adapt slower to diminished sensory stimuli and faster to increased sensory stimuli (Jeka et al. 2008).

Considering the importance of proper interaction of COR and VOR in relation to vision, we set out to measure the response of the VOR in response to hypokinesia as well. We observed that after 1 h of hypokinesia the VOR was increased (while the COR was not altered). However, after 2 h of neck immobility the VOR was no longer affected (while at this time we did observe an increased COR). The different time-courses could be explained by a non-linear reaction of the VOR. When the COR is not adapted yet to the immobilization of the neck, the VOR adapts to improve oculomotor control. However, when after a longer period the COR finally does adapt, the change in VOR is no longer required. This shows that it takes some time for the two reflexes to balance out their interaction in response to changes in the environment. A similar effect is found in postural control experiments (Peterka 2002; Jeka et al. 2008). In our view, the results of the hypokinesia and prolonged hypokinesia experiment can be explained by the experience that the COR as a low gain reflex needs more time to adapt than the high gain VOR. However, it should be noted that in the present study the two reflexes were evoked at different frequencies. Therefore, the idea of compensatory interactions between the COR and the VOR needs to be examined further in a more elaborate experiment which uses a broader range of frequencies.

From a clinical point of view this study helps to comprehend the frequently diffuse and confusing symptoms of neck pain patients. Neck pain patients show sensorimotor disturbances that are often related to pain, diminished range of motion, quality of movement, and oculomotor disturbances (Storaci et al. 2006; Treleaven 2008; Kristjansson and Treleaven 2009; Bexander and Hodges 2012; Kristjansson et al. 2016; Stenneberg et al. 2016). These oculomotor disturbances can provoke blurred vision, dizziness and the need to concentrate more than usual when reading (Treleaven and Takasaki 2014). Part of these problems could be attributed to disturbed eye stabilization reflexes (Kelders et al. 2005; Montfoort et al. 2006). In patients with WAD and in chronic idiopathic neck pain patients the normally weak COR is found to be increased (Kelders et al. 2005; Montfoort et al. 2006; de Vries et al. 2016; Ischebeck et al. 2017). Based on the findings in this study, it can be speculated that reflex alterations are not completely dependent on the origin of complaints, but do also depend on the amount of movement. From our studies we can conclude that in healthy controls limitation of neck motion affects the COR (Montfoort et al. 2008). If a patient decreases neck motion due to, e.g., disturbed motor control, pain, illness perceptions of fear of motion, the oculomotor system has to deal with reduced afferent sensory information from the cervical spine. In healthy controls the temporary increase of the COR is reversible (Montfoort et al. 2008); it is unknown if altered

reflexes are reversible in patients also. It will be crucial to understand how patients with disturbed eye reflexes, i.e., an increased COR gain, will react to augmented neck motion. From a therapeutic perspective it would be exciting if improved quality and increased neck motion would help to normalize COR gain and reduce visual problems of neck pain patients.

An alternative explanation for the diversity of whiplash disorders, such as oculomotor disturbances, is tissue damage of diverse structures due to the traumatic origin of complaints (Curatolo et al. 2011). However, we recently observed that eye reflex alterations are also found in non-traumatic neck pain patients (de Vries et al. 2016; Ischebeck et al. 2017), making a lesion based explanation for eye reflex alterations in whiplash patients less likely. This, however, needs to be further explored.

Another finding in the current study is that excessive movement of the neck did not change the gain of the reflexes. However, we have to keep in mind that there is a timing difference between the hypokinesia and hyperkinesia condition. Possibly, 20 min was not enough for reflex adaptation. The result of the hyperkinesia condition implies that an increase of afferent somatosensory input of proprioceptors does not affect a properly functioning system. This is confirmed by a study of Peterka (2002) who found saturation behavior to increased proprioceptive stimuli in subjects with normal sensory function. The conclusion for the clinical practice is that with respect to eye reflexes, proprioceptive training of a properly working system may have little surplus value.

In the present study, the COR and VOR altered after an intervention. However, the gain was highly variable. Due to the complex nature of the measurement equipment not all data could be recorded and analyzed in this study, resulting in missing data. To elucidate this variability, replication of this experiment in a bigger population can be considered.

Conclusion

The amount of cervical movement influenced the gain of the eye stabilization reflexes as a part of the oculomotor system. The gain of the reflexes increased after temporary immobilization. However, the opposite strategy, intensification of movement, did not affect the oculomotor system. These findings suggest that neck immobility may indeed play a role in the oculomotor disturbances observed in patients with neck complaints.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent The local ethical board of the Erasmus MC approved this study and all participants gave prior written informed consent.

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