



Original article

Eye stabilization reflexes in traumatic and non-traumatic chronic neck pain patients



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ABSTRACT

Background: Many chronic neck pain patients experience problems with vision. These problems are possibly induced by deviations of the eye stabilization reflexes. It is not known whether these eye reflex alterations occur both in traumatic and non-traumatic neck pain patients.

Objective: To investigate if the cervico-ocular reflex (COR) and the vestibulo-ocular reflex (VOR) are changed in tertiary care patients with prolonged, chronic neck pain with various origin of complaints.

Design: Cross sectional study.

Methods: Ninety-one chronic neck pain patients were subdivided into three groups by origin of complaints, and compared with healthy controls. COR and VOR gains were measured with an infrared eye tracking device with the subject sitting on a rotating chair in a darkened room and with the head fixed. **Results:** Neck pain patients had a higher COR gain (median 0.41, IQR 0.289) compared with healthy controls (median 0.231, IQR 0.179). The mean COR gain did not differ between the three patient groups (Whiplash Associated Disorders 0.444 (SD 0.221); traumatic 0.397 (SD0.205); non-traumatic 0.468 (SD0.236)). There was no difference in VOR gain between the groups.

Conclusion: Chronic neck pain patients, who already received primary care, still have an elevated cervico-ocular reflex. The origin of complaints did not seem to be associated with this deviant oculomotor behavior.

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Introduction

Patients with chronic neck pain suffer from various complaints. Besides diminished range of motion, pain, headache and cognitive dysfunction (Curatolo et al., 2011; Treleaven, 2011; Anstey et al., 2016; Stenneberg et al., 2016), half of the patients report vision-related problems (e.g. concentration problems during reading, sensitivity to light and eye strain) (Wolff, 1996; Hülse, 1998; Treleaven and Takasaki, 2014). Especially in patients with Whiplash Associated Disorders (WAD) visual disturbances might be related to deficits in oculomotor control (Ischebeck et al., 2016). The

oculomotor system receives eye and body position information via eye stabilization reflexes using information from the eyes, the vestibulum and the cervical spine (Hikosaka and Maeda, 1973; Van Die and Collewyn, 1986). The vestibulo-ocular reflex (VOR) receives positional input from the vestibulum whereas the cervico-ocular reflex (COR) receives input from the muscle spindles and joint capsules in the (upper) cervical spine (Hikosaka and Maeda, 1973). The VOR and COR work in conjunction to stabilize the visual image on the retina during head and trunk movements in space. Previous studies showed that the synergy between the COR and VOR can be disturbed in neck pain patients, due to altered cervical sensory input (Kelders et al., 2005; Montfoort et al., 2006; de Vries et al., 2016). Patients' COR gain (that is, the amplitude of eye velocity fit compared to the stimulus velocity) is elevated without a compensatory decrease of the VOR gain, that is often observed in healthy

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Abbreviations

COR	cervico-ocular reflex
T group	traumatic neck pain group
NT group	non-traumatic neck pain group
VOR	vestibulo-ocular reflex
WAD	Whiplash associated disorders

individuals (Kelders et al., 2005; Montfoort et al., 2006; de Vries et al., 2016). The optokinetic reflex which receives information from the eyes, remains unchanged in patients with WAD (Montfoort et al., 2006). Despite the promising results of the studies of Kelders et al. and de Vries et al., their patient groups are diffuse with respect to duration of complaints, cause of complaints and previous treatments (Kelders et al., 2005; de Vries et al., 2016). In the present patient group the option of natural recovery is minimized by increasing the minimum duration of complaints to 6 months. It is unknown how long COR and VOR reflex deviations persist, or whether the reflexes might prove chronically maladjusted. To our knowledge, no information is available on eye stabilization reflexes in severely impaired chronic neck pain patients. Studying oculomotor function in this patient population is of particular interest, since these chronic patients still do report sensorimotor, visual and cognitive dysfunction, even after multiple treatments. Furthermore, in this study both traumatic and non-traumatic neck pain patients are included, with an extra subdivision of the traumatic group. Finally, in this study all patients received earlier, but unsuccessful treatment.

The first aim of the present study is to investigate the eye stabilization reflexes in a group of unsuccessfully treated patients with long-lasting neck pain and compare these outcomes with a group of healthy controls.

The second aim is to determine whether there are differences in eye stabilization reflexes in patients with comparable history, but different origin of complaints, i.e. traumatic versus non-traumatic. In order to specify if a certain traumatic impact is determinative for alteration of eye stabilization reflexes, the traumatic group will be divided into a whiplash associated disorders (WAD) group as defined by Spitzer et al. and patients with a traumatic impact, but no whiplash acceleration-deceleration mechanism of energy transfer to the neck (Spitzer et al., 1995). Most of the patients in the WAD group have had a car accident with a whiplash mechanism, associated with or without blunt trauma to the head. The patients of the traumatic group have had no direct trauma to the neck or the head.

Right now, the underlying mechanisms of eye reflex alterations are still unknown. It can be argued that patients with WAD have, due to the high traumatic impact on the cervical spine, a more distinct reflex alteration than non-WAD and non-traumatic neck pain patients. However, eye stabilization reflexes may be, besides due to anatomical damage, also altered due to sensorimotor changes or behavioral factors (Montfoort et al., 2006; Curatolo et al., 2011). It is worthwhile to investigate this influence as it may aid in diagnosis and assessing the effectiveness of treatments.

Methods

Participants

Patients with chronic neck pain were included from the population of the Spine & Joint Centre Rotterdam, a Dutch

rehabilitation centre for patients with chronic neck complaints. All patients took part of the study prior to their rehabilitation. Participants with neck pain were included if they 1) were referred to the Spine & Joint Centre with the diagnosis of chronic neck pain (pain primarily in the neck for more than six months); 2) had received primary care physiotherapy more than 9 times without benefit (actual intervention not specified); 3) were between the age of 18 and 65 years; 4) were able to understand and speak the Dutch language and 5) were physically able to undergo COR and VOR measurements (which involved sitting immobilized in a chair for 30 min).

The participants with neck pain were divided into three groups: Group 1. patients with WAD grade 2 or 3 (Spitzer et al. 1995) (WAD group); Group 2. patients with a traumatic origin of the complaints, but no motor vehicle accident and no direct impact on the neck (e.g. falling of a horse or bicycle, traumatic delivery) (Traumatic neck pain group [T]); Group 3. patients with a non-traumatic origin of complaints (Non-traumatic neck pain group [NT]).

Participants in the healthy control group were recruited among co-workers and students and had no personal or legal relationship with the investigator. The inclusion criteria were 1) aged between 18 and 65; 2) able to understand and speak the Dutch language; 3) without any complaints of the cervical spine (including cervicogenic headache and dizziness) in the last 5 years; and 4) without any history of neck trauma. Exclusion criteria were 1) suffering from any neurological disorder, or vestibular or visual problems prior to the neck pain; and 2) having fractures or surgery in the cervical spine, temporomandibular joint or head in the past.

All participants were without any ocular abnormalities that could not be corrected by wearing glasses or contact lenses. They were recruited and tested between January 2012 and January 2015. The study was approved by the local ethical board of the Erasmus MC and all participants gave prior written informed consent.

Experimental setup

The experimental setup was identical to the setup described in an earlier study (de Vries et al., 2016). In short, infrared video-oculography [Eyelink 1, SMI, Germany (van der Geest and Frens, 2002)] at a sample rate of 250 Hz was used for the recording of monocular (left) eye positions while people were rotated using a motor driven rotatable chair (Harmonic Drive, Germany). The motor induced continuous sinusoidal chair rotations around the vertical axis without any backlash. The position of the chair was recorded with sensors and stored on the computer.

The trunk was fixed to the chair at shoulder level by a double-belt system (Fig. 1a). Head position was fixed by means of a custom-made bite board. The bite board was positioned with the axis of chair rotation under the midpoint of the inter-aural line and fixed to the floor to guarantee a fixed head position. In this case, rotation of the chair in complete darkness induced pure cervical stimulation, which elicits the COR in isolation (Fig. 1b). In the COR 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 rotations of the chair with peak velocity of 1.26°/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 (Fig. 1b). In 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°/s.

In both eye movement stimulations, which were ran in complete darkness, participants were instructed to look at a position directly in front of the set-up which was briefly indicated by means of a laser dot.

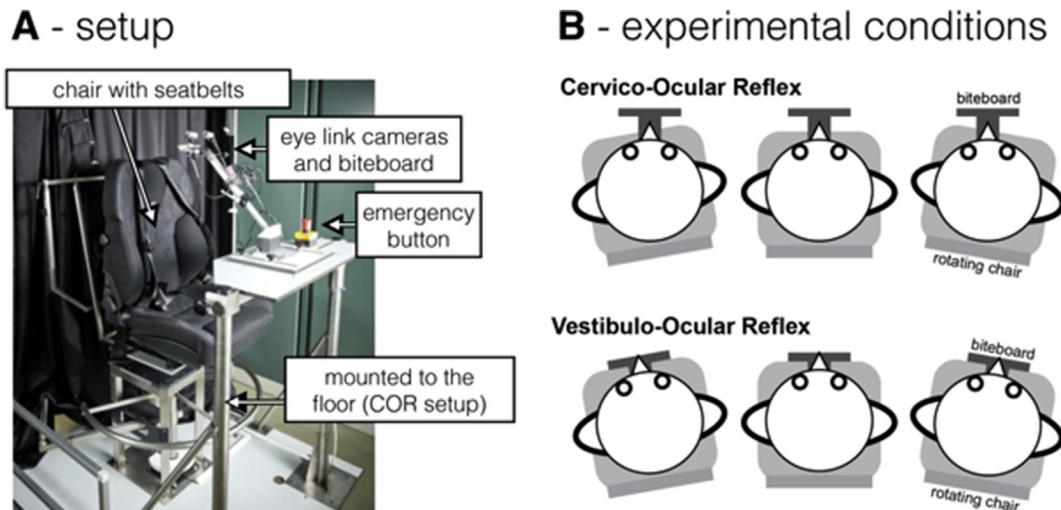


Fig. 1. Panel A shows a photograph of the chair and the position of the cameras and the bite board in the COR setup. Panel B shows the measurement of the vestibular ocular reflex (VOR) with the bite board attached to the chair, and the cervico-ocular reflex (COR) with the bite board attached to the floor,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

Data analysis

All data processing was done with custom-written scripts in Matlab R2013a (The MathWorks Inc., Natick, MA). Eye movement reflexes were analyzed by looking at the eye velocity relative to the chair or stimulus velocity, referred to as the gain of the eye movement. Eye velocity was calculated by taking the derivative of the horizontal eye position signal. Blinks, saccades and fast phases were removed (using a 20 degrees-per-second threshold) and 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: $1.26^\circ/s$; VOR: $5.03^\circ/s$). A gain of 1 thus reflects that the peak velocity of the eye was the same as the peak velocity of the stimulus.

Statistical analysis

Differences in the eye stabilization reflexes between patients with chronic neck pain and healthy controls were statistically assessed by non-parametric statistics using Mann-Whitney tests. Correlations between the gains of the COR and VOR, as well as between these gains and age and gender, were statistically assessed using Spearman's correlations.

To assess the effect of the origins of complaints, we compared the eye stabilization reflexes between the three groups (WAD, T and NT) with the Kruskal-Wallis test.

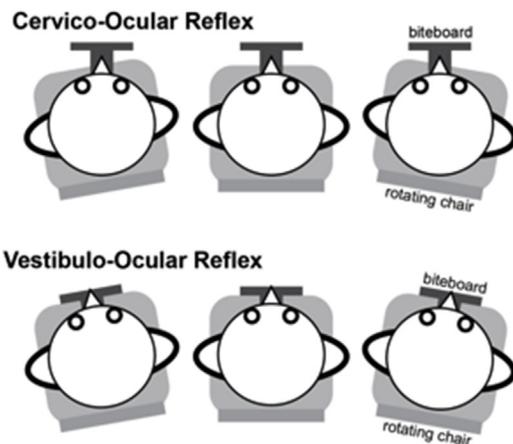
An alpha level of $p < 0.05$ was considered significant for all statistical tests. The data was analyzed with IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, NY).

Results

117 participants completed the measurements successfully. The VOR measurement of three patients ($2 \times$ WAD; $1 \times$ NT) and one healthy control were discarded due to technical errors.

The comparison of eye stabilization reflexes between 91 patients with chronic neck pain [45 male, 84 female; median age 42 (IQR 19); median VAS pain 56 (min-max: 11-90; IQR 39)] and 30 healthy controls [(16 male, 14 female; median age 25 (IQR 6))] are summarized in Table 1 and Fig. 2. The COR gain of patients with chronic neck pain was significantly higher than the COR gain of healthy controls, but the VOR gain did not differ between the two groups.

B - experimental conditions



In both groups no correlations between the eye stabilization reflexes and age or gender were found (Table 2).

We observed no effect of the origin of the neck pain when we compared the three different patient groups (Table 3 and Fig. 3). Both the COR and VOR gains were similar between patients with WAD, with a traumatic origin and with a non-traumatic origin.

In the WAD group and in the traumatic group, the gain of the COR was moderately correlated with age. There was no correlation between COR and age in the non-traumatic group (Table 4).

Discussion

The current study aimed at the question whether eye stabilization reflexes are altered in unsuccessfully treated chronic neck pain patients and whether there are differences in eye stabilization reflexes between traumatic and non-traumatic patients. The results of this study show that chronic neck pain patients have an elevated COR and an unchanged VOR gain compared with healthy controls. Furthermore, traumatic and non-traumatic neck pain patients have similar COR and VOR gains. Apparently, changes in eye stabilization reflexes are not predominantly caused by a traumatic physical impact.

Chronic neck pain patients who experience neck pain for at least six months, still show an elevated COR and an unchanged VOR. Apparently, COR does not diminish automatically in chronic neck pain patients even when they receive paramedical treatment. It appears that in this severely impaired patient group (with a median reported VAS pain of 56) the persistence of altered reflexes depends on other -non temporary-factors. Studies show that chronic neck pain patients demonstrate irregular cervical movement strategies and diminished cervical range of motion (Sjölander et al., 2008; Stenneberg et al., 2016). Sensorimotor impairment is suggested as underlying cause for these specific motion patterns (Sjölander et al., 2008; Kristjansson and Treleaven, 2009; Baydal-Bertomeu et al., 2011). It is hypothesized that this specific motion characteristic may lead to altered reflexes (Röjjezon et al., 2015). Consequently, the COR remains augmented as long as cervical afferent information is hampered by this sensorimotor impairment. Cervical sensorimotor impairment includes disturbed mechanisms of muscle control (altered activation pattern of muscles) and changed muscle properties (e.g. fatty degeneration of the cervical extensor muscles) (Elliott et al., 2006; Treleaven et al., 2006; Falla and Farina, 2007; Sjölander et al., 2008; Kristjansson and Treleaven, 2009; Baydal-

Table 1

Eye stabilization reflexes in patients and healthy controls. VOR = vestibulo-ocular reflex; COR = cervico-ocular reflex; IQR = interquartile range.

	Patients	Controls	Mann-Whitney-test
n	91	30	
Age (median, IQR)	42 (19)	25 (6)	U = 605.5, Z = -5.856, p < 0.001
Gender	65% female	46% female	U = 1578.0, Z = -1.866, p = 0.062
VOR (median, IQR)	0.7 (0.302)	0.7 (0.255)	U = 1399.5, Z = -0.041, p = 0.968
COR (median, IQR)	0.41 (0.289)	0.231 (0.179)	U = 659.5, Z = -4.235, p < 0.001

Bertomeu et al., 2011; Hodges, 2011; Karlsson et al., 2016). It would be of high clinical relevance to determine if eye stabilization reflexes regulate themselves after diminishing of this sensorimotor

disturbances. This could be studied by measuring the effect of specific sensorimotor training on altered eye stabilization reflexes (Kristjansson and Treleaven, 2009; Clark et al., 2015; Røijezon et al., 2015).

In the current study besides the COR, also the VOR was measured. It is yet unclear why the VOR does not adapt in neck pain patients and we can only speculate about the cause. In healthy individuals, age dependent decrease of the VOR is caused by degeneration of the vestibular system (Paige, 1994). The COR adapts to this alteration with increased gain. However, in neck pain patients not the vestibular system, but the cervical system changes (Kelders et al., 2005; Montfoort et al., 2006). This change affects the COR without an effect on the VOR, thereby changing the correlation between the two reflexes. Apparently, while VOR gain seems conditional for COR gain, this does not automatically imply that COR gain is also conditional for VOR gain.

The second result of this study is that the three groups of chronic neck pain patients with traumatic and non-traumatic origin of complaints have comparable gains of the eye stabilization reflexes.

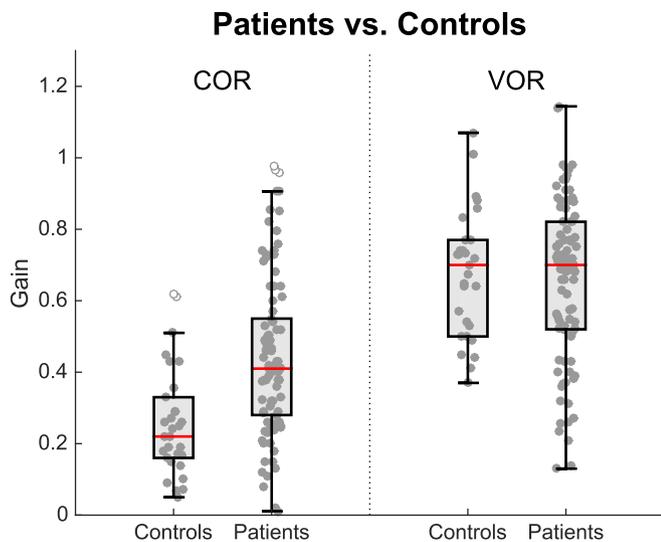


Fig. 2. Boxplot of COR and VOR gain in patients and healthy control group. Thick horizontal line in the grey box line = median; grey box = IQR, grey dots = individual gain values; open circles = outliers. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2

Correlations (correlation coefficient and p-value) between the different variables (gain of the COR and VOR, age and gender) for the two groups (PT = patients; CT = controls).

	VOR	Age	Gender
COR	CT: -0.014 (p = 0.944)	CT: -0.052 (p = 0.786)	CT: 0.154 (p = 0.415)
	PT: -0.054 (p = 0.617)	PT: 0.002 (p = 0.984)	PT: 0.144 (p = 0.173)
VOR		CT: -0.019 (p = 0.923)	CT: -0.07 (p = 0.716)
		PT: 0.186 (p = 0.083)	PT: -0.036 (p = 0.742)
Age			CT: -0.077 (p = 0.684)
			PT: 0.025 (p = 0.814)

Table 3

Eye stabilization reflexes in the three different patient groups. VOR = vestibulo-ocular reflex; COR = cervico-ocular reflex; WAD= Whiplash group; T = traumatic group; NT = non-traumatic group; IQR = interquartile range.

	WAD	T	NT	Kruskal-Wallis
n	28	16	47	
Age (median, IQR)	40; 21	42; 22	44; 17	H(2) = 6.604, p = 0.037
Gender	59% female	65% female	68% female	H(2) = 4.603, p = 0.100
VOR (median, IQR)	0.695; 0.386	0.680; 0.397	0.712; 0.299	H(2) = 0.351, p = 0.839
COR (median, IQR)	0.420; 0.372	0.395; 0.182	0.468; 0.330	H(2) = 0.903, p = 0.637

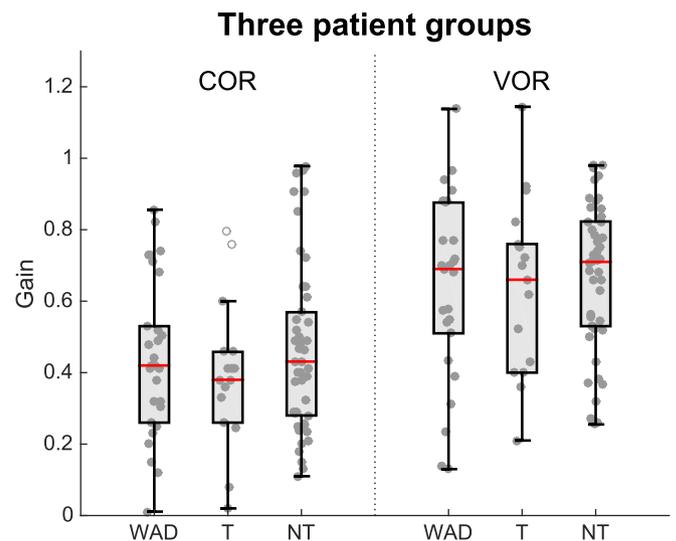


Fig. 3. Boxplot of COR and VOR gain in the three patient groups. Thick horizontal line in the grey box line = median; grey box = IQR, grey dots = individual gain values; open circles = outliers. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 4
Correlations (correlation coefficient and p-value) between the different variables for the three different patient groups.

	VOR	Age	Gender
COR	WAD: -0.099 (p = 0.631) T: -0.185 (p = 0.494) NT: -0.03 (p = 0.843)	WAD: 0.561 (p = 0.002) T: -0.615 (p = 0.011) NT: -0.118 (p = 0.429)	WAD: 0.097 (p = 0.622) T: -0.14 (p = 0.604) NT: 0.255 (p = 0.083)
VOR		WAD: 0.148 (p = 0.470) T: 0.156 (p = 0.565) NT: 0.172 (p = 0.254)	WAD: -0.139 (p = 0.5) T: 0.098 (p = 0.718) NT: -0.047 (p = 0.758)
Age			WAD: -0.186 (p = 0.343) T: 0.24 (p = 0.371) NT: -0.077 (p = 0.605)

A whiplash trauma seems to be no prerequisite for the development of oculomotor disorders. Thus, in the studied population, the origin of complaints, whether traumatic or non-traumatic do not determine alteration of reflexes and can no longer be seen as negative predictive factor for the development of altered eye stabilization reflexes. This implies that the alteration is dependent of other, presently unknown, factors which can possibly be changed by treatment. These factors are not explored in the current study. To get more insight into the underlying mechanisms of changed reflexes, it would be useful to study the influence of a variety of patient characteristics (sensorimotor function, degree of disability and pain, duration of complaints, cervical range of motion) and behavioral factors, like e.g. fear avoidance behavior, fatigue and stress on eye stabilization reflexes.

With respect to possible confounding in the current study, we paid attention to influence of age on reflex gain. In this study there is a significant age difference between patients and healthy controls (the healthy control group was younger than the patient group). Nevertheless, the impact of age on the COR seems to be negligible. Age dependent increase of the COR is only seen in healthy individuals of 60 years and older (Kelders et al., 2003). In the current study the correlation between the COR gain and age differs in the two traumatic groups. The correlation in the WAD group is positive and in the traumatic group negative (Table 4). We can only speculate about this reversed correlation between COR and age between the groups. It could be related to differences in patient characteristics between the groups, e.g., in neck mobility and in duration of the complaints.

It is point of discussion whether a negative correlation exists between the VOR- and the COR gain in healthy individuals. Two studies report a moderate negative relationship between COR and VOR gain (Kelders et al., 2003; Montfoort et al., 2006), but in the present study and in the study of de Vries et al. this correlation could not be confirmed (de Vries et al., 2016).

Conclusion

Severely impaired chronic neck pain patients have an elevated COR and an unchanged VOR compared to healthy controls. This elevation seems to be independent of the traumatic or non-traumatic origin of complaints. The group of neck pain patients with altered eye stabilization reflexes is thereby bigger than suspected. Maybe persistent sensorimotor disorders of the cervical spine are a perpetuating factor for eye reflex alteration.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.msksp.2017.03.004>.

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