



Letter to the Editor

Convergence paralysis caused by a localized cerebral infarction affecting the white matter underlying the right frontal eye field



Keywords:

Apraxia of eyelid opening
Convergence paralysis
Eye movements
Frontal eye field
Stroke

Dear Editor,

Conjugate eye movements are controlled by a number of areas in the cerebral cortex, including the frontal eye field (FEF) [1], supplementary eye field (SEF) [2], dorsolateral prefrontal cortex (DLPFC) [3], and parietal eye field (PEF), corresponding to the lateral intraparietal area in macaques [4]. Among these areas, the FEF plays an important role in triggering the intentional saccades [5]. The neuronal activities in the FEF are prepared in and projected from the other cortical areas [6].

Convergence eye movements are also associated with a number of cortical areas. Electrical microstimulation in the FEF of macaques has elicited convergence eye movements [7]. Another primate study has identified neuronal discharges in the SEF during vergence tracking [8]. Functional activation in the DLPFC for vergence has been observed on functional magnetic resonance imaging (MRI) [9]. Transcranial magnetic stimulation over the DLPFC has decreased the latency of the convergence made with saccades [10]. Moreover, another functional neuroimaging study has shown that predictive vergence eye movements activate many cortical areas including the FEF, SEF, DLPFC, and PEF [11]. However, the organization of these cortical areas for convergence eye movements has been much less studied than other conjugate eye movements, although the basic organization is believed to be comparable to that of saccades and pursuit [12]. Furthermore, convergence paralysis has never been reported as a symptom of a localized cerebral infarction. We report a case of convergence paralysis caused by a localized cerebral infarction affecting the white matter underlying the right FEF.

1. Case report

A 72-year-old, right-handed man was admitted for difficulty with opening his eyes and diplopia at near vision. Four days prior, the patient had experienced the sudden onset of an inability to open and close both eyelids voluntarily. He used his hands to open and close his eyelids. The next day, he developed diplopia at near vision. Before admission, his difficulty in eyelid opening and closure had gradually improved.

Abbreviations: AEO, apraxia of eyelid opening; DLPFC, dorsolateral prefrontal cortex; FEF, frontal eye field; MRI, magnetic resonance imaging; PEF, parietal eye field; SEF, supplementary eye field.

On examination, the patient was alert and well oriented. Corrected visual acuity at a distance was 20/13 in both eyes. Pupils were symmetric and equally reactive. Although ocular motility examination showed no limitation of conjugate eye movements, a severe convergence paralysis was observed (Fig. 1). An alternate prism cover test showed that the patient had exophoria of 1 prism diopter at distance and exotropia of 16 prism diopters at near vision. Pupillary constriction was observed on attempts to converge. The patient did not have monocular blurring at near vision, suggesting accommodation was not affected. Smooth pursuit eye movements were mildly saccadic in both directions, and the accuracy of horizontal saccadic eye movements was also mildly impaired, although the exact latency and velocity were not evaluated. He did not have nystagmus. Furthermore, he had difficulty with bilateral eyelid opening at will, despite contraction of the frontalis muscles. This eyelid-opening abnormality was not accompanied by visible contraction of the orbicularis oculi on clinical examination. The difficulty in opening the eyelids was not evident during spontaneous blinking. Eye closure was normal. He had no evidence of orobuccal, lingual, or limb apraxia. Muscle weakness was not apparent on admission, and his gait was stable without extrapyramidal symptoms.

Diffusion-weighted MRI of the brain showed a high-signal-intensity lesion extending from the lateral side of the right precentral knob to the white matter underlying the intersection between the right precentral sulcus and the right superior frontal sulcus, where the right FEF is most likely located (Fig. 2). There were no basal ganglia or thalamic lesions on MRI. He was diagnosed as having an acute cerebral infarction that caused apraxia of eyelid opening (AEO) and convergence paralysis. Although gradual improvement of the AEO was observed, convergence paralysis improved to a lesser extent and persisted 6 months after onset.

2. Discussion

This case suggests that disruption of the FEF can cause impaired convergence eye movements independently of other cortical areas. Previous studies have demonstrated that the FEF is related to the triggering of convergence eye movements, as with conjugate eye movements.



Fig. 1. Ocular movements. (A) Eye positions at far vision; (B) eye positions at near vision.

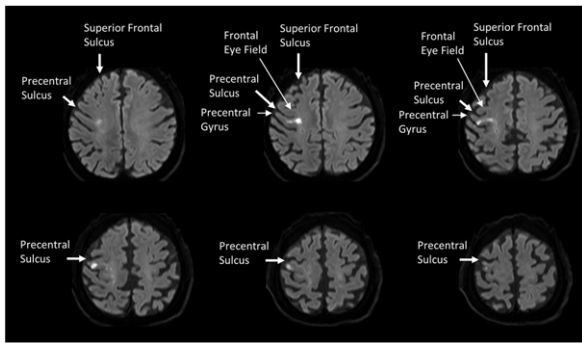


Fig. 2. Magnetic resonance imaging of the brain. Diffusion-weighted magnetic resonance imaging of the brain shows a high signal intensity lesion extending from the lateral side of the right precentral knob to the white matter underlying the intersection between the right precentral sulcus and the right superior frontal sulcus, where the right frontal eye field is most likely located.

Electrical stimulation of the FEF, in a patient with epilepsy and in macaques, induced disconjugate contraversive horizontal eye movements and convergence eye movements, respectively [7,13]. Moreover, other cortical areas (i.e., SEF and DLPFC) are also associated with controlling convergence [12]. However, hierarchical organization of these cortical areas has never been studied in detail. Except for the FEF, the above-mentioned brain regions responsible for convergence eye movements were not affected in the present patient. The severity of convergence impairment in our case was equivalent to that of conjugate impairment caused by a lesion affecting the FEF in the previous report [14]. As the organization of the cortical areas for convergence eye movements is believed to be comparable to that of conjugate eye movements, our case suggests that a damaged FEF can lead to insufficient convergence eye movements, independent of other cortical areas.

Furthermore, this case suggests that anatomical and functional differences within the FEF may exist, which reflect the dual responsibility for convergence and conjugate eye movements, because a discrepancy between the degree of impairment of convergence and conjugate eye movements was observed in the present patient. This is consistent with previous neuroimaging studies of humans and a single-cell study of macaques, which demonstrated that a convergence-related region is located anterior to a saccade-related region in the FEF [7,9]. The precise relationship between these two regions needs to be elucidated in future studies.

Finally, the FEF and the middle part of the precentral gyrus may be involved in the pathogenesis of AEO. AEO is caused by contraction of the pretarsal portion of the orbicularis oculi muscles, absent contraction of the levator palpebrae superioris muscles, or both [15]. The precise neuroanatomical basis of AEO is still unclear, probably because of variation in the underlying mechanism, despite similar phenotypes. However, neuroimaging studies have reported that the responsible cortical areas for voluntary blinking include the FEF, SEF, and precentral gyrus [16]. In our patient, the white matter underlying the right FEF and the middle part of the right precentral gyrus were affected. We suggest that these two areas contribute to the pathogenesis of AEO and probably participate in the control of voluntary blinking.

In conclusion, this case suggests that disruption of the FEF can cause impaired convergence eye movements independently of other cortical areas. Furthermore, a cerebral infarction affecting the unilateral FEF should be raised as part of the differential diagnosis for acute onset of convergence paralysis, even without conjugate impairment.

Conflicts of interest

None.

Study funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical standard

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of the Graduate School and Faculty of Medicine at Kyoto University and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from the patient.

References

- [1] O. Blanke, M. Seeck, Direction of saccadic and smooth eye movements induced by electrical stimulation of the human frontal eye field: effect of orbital position, *Exp. Brain Res.* 150 (2003) 174–183.
- [2] M. Isoda, J. Tanji, Cellular activity in the supplementary eye field during sequential performance of multiple saccades, *J. Neurophysiol.* 88 (2002) 3541–3545.
- [3] T. Nyffeler, C. Pierrot-Deseilligny, J. Felblinger, U.P. Mosimann, C.W. Hess, R.M. Müri, Time-dependent hierarchical organization of spatial working memory: a transcranial magnetic stimulation study, *Eur. J. Neurosci.* 16 (2002) 1823–1827.
- [4] J.W. Bisley, M.E. Goldberg, Neuronal activity in the lateral intraparietal area and spatial attention, *Science* 299 (2003) 81–86.
- [5] E.C. Dias, M.A. Segraves, Muscimol-induced inactivation of monkey frontal eye field: effects on visually and memory-guided saccades, *J. Neurophysiol.* 81 (1999) 2191–2214.
- [6] P. Pouget, The cortex is in overall control of 'voluntary' eye movement, *Eye* 29 (2015) 241–245.
- [7] P.D. Gamlin, K. Yoon, An area for vergence eye movement in primate frontal cortex, *Nature* 407 (2000) 1003–1007.
- [8] J. Fukushima, T. Akao, N. Takeichi, S. Kurkin, C.R. Kaneko, K. Fukushima, Pursuit-related neurons in the supplementary eye fields: discharge during pursuit and passive whole body rotation, *J. Neurophysiol.* 91 (2004) 2809–2825.
- [9] Y. Alkan, B.B. Biswal, T.L. Alvarez, Differentiation between vergence and saccadic functional activity within the human frontal eye fields and midbrain revealed through fMRI, *PLoS One* 6 (2011), e25866.
- [10] O. Coubar, Z. Kapoula, R. Müri, S. Rivaud-Pécho, Effects of TMS over the right prefrontal cortex on latency of saccades and convergence, *Invest. Ophthalmol. Vis. Sci.* 44 (2003) 600–609.
- [11] T.L. Alvarez, Y. Alkan, S. Gohel, B. Douglas Ward, B.B. Biswal, Functional anatomy of predictive vergence and saccade eye movements in humans: a functional MRI investigation, *Vis. Res.* 50 (2010) 2163–2175.
- [12] R.J. Leigh, D.S. Zee, *The Neurology of Eye Movements*, fifth ed. Oxford University Press, New York, 2015.
- [13] M.J. Thurtell, A. Mohamed, H.O. Lüders, R.J. Leigh, Evidence for three-dimensional cortical control of gaze from epileptic patients, *J. Neurol. Neurosurg. Psychiatry* 80 (2009) 683–685.
- [14] H. Tanaka, M. Arai, J. Kubo, K. Hirata, Conjugate eye deviation with head version due to a cortical infarction of the frontal eye field, *Stroke* 33 (2002) 642–643.
- [15] M. Aramideh, B.W. Ongerboer de Visser, J.H. Koelman, J.D. Speelman, Motor persistence of orbicularis oculi muscle in eyelid-opening disorders, *Neurology* 45 (1995) 897–902.
- [16] D. Bristow, C. Frith, G. Rees, Two distinct neural effects of blinking on human visual processing, *NeuroImage* 27 (2005) 136–145.

Hisanori Kinoshita
Takakuni Maki*

Department of Neurology, Kyoto University Graduate School of Medicine,
54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan

*Corresponding author.

E-mail addresses: hkino@kuhp.kyoto-u.ac.jp (H. Kinoshita),
harutoma@kuhp.kyoto-u.ac.jp (T. Maki).

Masayuki Hata

Department of Ophthalmology and Visual Sciences, Kyoto University,
Graduate School of Medicine, 54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto,
606-8507, Japan

E-mail address: trj74h6@kuhp.kyoto-u.ac.jp.

Yoichi Nakayama
Hirofumi Yamashita

*Department of Neurology, Kyoto University Graduate School of Medicine,
54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan*

Nobukatsu Sawamoto

*Department of Human Health Sciences, Kyoto University, Graduate School
of Medicine, 54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan*

Akio Ikeda

*Department of Epilepsy, Movement Disorders and Physiology, Kyoto
University, Graduate School of Medicine, 54 Shogoin-Kawahara-cho,
Sakyo-ku, Kyoto 606-8507, Japan*

Ryosuke Takahashi

*Department of Neurology, Kyoto University Graduate School of Medicine,
54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan*

20 October 2016