

ELECTRICAL STIMULATION CAN RESTORE POSTURAL DISTURBANCE CAUSED BY VESTIBULAR DISORDERS

Byung Rim Park, Min Sun Kim, Moon Yong Lee, Kou Gyoum Kim, Seung Kwan Lim

Department of Physiology, Wonkwang University School of Medicine

Iksan 570-749, Korea

ABSTRACT

This study was proposed to evaluate the effect of electrical stimulation on restoration of postural disturbance following unilateral labyrinthectomy in rabbits. Electrical stimulation with 1-3 V, 0.1 ms, 100 Hz was applied to the lesioned vestibular system by means of gyrosensor. Vestibuloocular reflex, vestibulospinal reflex, and c-Fos protein expression in the medial vestibular nucleus were measured following left labyrinthectomy. Spontaneous nystagmus, head deviation, and flexion of lesion sided limbs occurred after labyrinthectomy. However, electrical stimulation to the lesioned vestibular system abolished spontaneous nystagmus and roll head tilt, and restored walking movement as well as eye movement induced by sinusoidal rotation. c-Fos protein expression showed significant increase in left medial vestibular nucleus than in right medial vestibular nucleus after 6 hours of labyrinthectomy, but electrical stimulation reduced asymmetry of c-Fos protein expression in the bilateral medial vestibular nucleus. These results indicate that electrical stimulation can restore postural disturbance caused by vestibular disorders and facilitate neuronal plasticity following injury.

Key words: electrical stimulation, vestibular symptom, c-Fos, neuronal plasticity

INTRODUCTION

Loss of unilateral vestibular function, as a result of unilateral labyrinthectomy (ULX), transection of the VIII nerve, or vestibular neuritis, causes an imbalance in resting electrical activity between the bilateral vestibular nuclei which results in vestibular symptoms including nausea, vomiting, vertigo, spontaneous nystagmus, head oscillation, and head deviation. However, over a period of a few days or weeks following ULX, some of these symptoms abate in a process of behavioral recovery known as vestibular compensation.¹⁾ Considering the main cause of vestibular symptom is deprivation of afferent signals from the unilateral vestibular receptors, restoration of the afferent signals from the lesioned vestibular receptors may recover from the vestibular symptoms. Electrical stimulation applied to the lesioned vestibular system may restore the afferent signals from the lesioned vestibular system and facilitate neuronal plasticity in the vestibular nuclei, since the electrical stimulation has a direct effect on the vestibular system as well as other metabolic effects.²⁾ In this study effects of electrical stimulation to the lesioned vestibular system on vestibular compensation were investigated by means of behavioral and immunohistochemical studies in unilateral labyrinthectomized rabbits.

METHODS

Nine rabbits weighing 2.0 - 2.5 kg with intact vestibular function were used in this study. Left labyrinthectomy was performed in this experiment. In order to apply electrical stimulation to the lesioned vestibular nerve, two teflon-coated stainless steel wires (0.1 mm in diameter) were implanted in the lesioned ampullary portion. Electrical stimulation was applied by 3 - 7 V, 1.0 ms, 100 Hz through the electrodes which were connected to the

stimulator with gyrosensor. The stimulator turns on when the head rotates toward the lesioned vestibular side and turns off when the head rotates toward the intact side. Horizontal eye movement was recorded by means of a DC amplifier. Head deviation was measured in roll head tilt which was defined as the angle of deviation between a line passing through the center of the animal's head in the coronal plane and gravitational vertical. In immunohistochemistry, number of c-Fos protein expression was measured in the vestibular nuclei by image analysis system.

RESULTS

1. Eye movement and head deviation

Persistent spontaneous nystagmus appeared following ULX and disappeared 4 days after. However, the nystagmus disappeared 3 days after ULX in electrical stimulated rabbits. Sinusoidal rotation of the whole body about vertical axis produced nystagmus, whose direction was consistent with the direction of rotation and the velocity was symmetrical by rotation on either side. However just after ULX, spontaneous nystagmus occurred only on sinusoidal rotation and the fast component of nystagmus was directed toward the intact labyrinthine side, even though the rotation imposed was toward the lesioned side. The direction of eye movement induced by sinusoidal rotation at 0.1 Hz did not show a normal pattern of the vestibuloocular reflex until 4 days after labyrinthectomy. Directional preponderance representing the symmetry of bilateral vestibular function was more than 100% until 4 days after ULX, which means severe asymmetry of bilateral vestibular functions. Electrical stimulation to the lesioned vestibular system during sinusoidal rotation following ULX produced the normal pattern of vestibuloocular reflex, even on rotation toward the lesioned side. In addition to the eye movement by rotation, spontaneous nystagmus and head deviation were abolished, and the rabbit could move just the same as an intact animal during electrical stimulation. Degree of roll head tilt was reduced by electrical stimulation (Fig. 1).

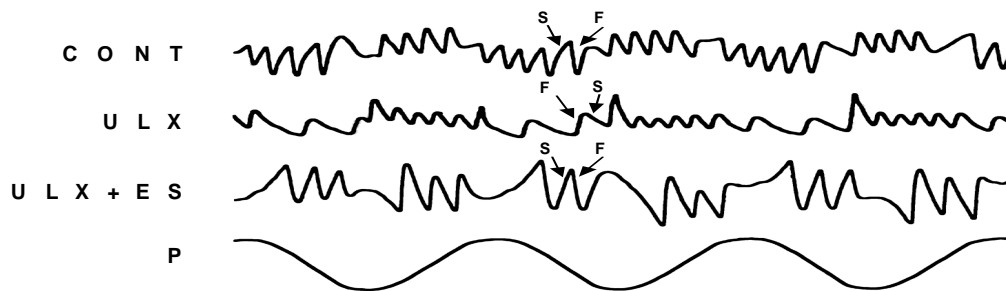


Fig. 1. Effect of electrical stimulation on vestibuloocular reflex induced by sinusoidal rotation of the whole body in a left labyrinthectomized rabbit. CON, right-beating nystagmus by rightward rotation and left-beating nystagmus by leftward rotation in intact labyrinth; ULX, right-beating nystagmus by right- or leftward rotation following left ULX; ULX+ES, normal pattern of eye movement was restored by electrical stimulation of left vestibular system; P, position curve of rotation; F, fast component of nystagmus; S, slow component.

2. Expression of c-Fos protein

In rabbits without ULX, few of c-Fos protein neurons appeared in some brain stem nuclei including MVN and inferior olivary nuclei. Compared to labyrinthine intact rabbits, ULX produced marked induction of c-Fos protein neurons in the bilateral MVN, prepositus hypoglossi, and beta nuclei of inferior olivary nuclei 2 hours after ULX. This induction was asymmetrical in that the number of c-Fos protein neurons contralateral MVN were much higher than ipsilateral MVN to the lesioned side ($p < 0.05$). Six hours after ULX, there was a significant reduction of c-Fos protein neurons in contralateral MVN than that in ipsilateral

MVN so that the number of c-Fos protein neurons was slightly higher in ipsilateral MVN than contralateral MVN. Asymmetric c-Fos protein expression between ipsilateral MVN and contralateral MVN was also observed up to 24 hours after ULX and disappeared 72 hours after ULX. However, electrical stimulation after ULX reduced asymmetry in c-Fos protein expression. Number of c-Fos protein neurons was higher in contralateral MVN than ipsilateral one 2 hours after ULX and higher in ipsilateral MVN than contralateral one 6 hours after ULX, but there was no significant difference between the bilateral MVN 12 hours after ULX (Fig. 2).

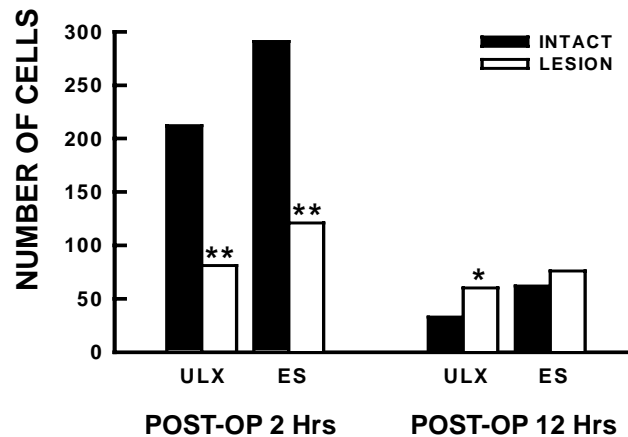


Fig. 2. Effect of electrical stimulation on c-Fos protein expression in medial vestibular nuclei (MVN) following ULX. ULX, unilateral labyrinthectomy; ULX+ES, unilateral labyrinthectomy with electrical stimulation; INTACT, MVN in intact labyrinthine side; LESION, MVN in lesioned labyrinthine side. *compared with INTACT (* $p < 0.05$, ** $p < 0.01$).

DISCUSSION

Asymmetry of electrical activity in the bilateral vestibular nuclei is considered as a main cause of vestibular symptoms resulting from loss of unilateral vestibular function. Electrical activity in ipsilateral vestibular nuclei to the lesioned side is suppressed by commissural connections and deprivation of afferent signals since ULX deprives peripheral receptors of their afferent signals. This asymmetry of electrical activity after ULX has the same effect as excitation of contralateral vestibular system and inhibition of ipsilateral vestibular system. The direction of spontaneous nystagmus and head deviation after ULX was corresponded to the response induced by electrical stimulation of contralateral vestibular system. c-Fos protein, one of the immediate early gene products, can be expressed by a variety of stimuli in neurons of CNS, considers as a useful marker for detecting changes in neuronal activity.³⁾ Recent studies have shown the induction of c-Fos protein in the vestibular nuclei in response to otolith stimulation, ULX, or vestibulocerebellectomy.⁴⁻⁷⁾ Considering that the induction of c-Fos protein expression in neurons occurred within 20 minutes by transsynaptic depolarization³⁾ a lot of c-Fos protein neurons in the bilateral MVN 2 hours after ULX may result from transsynaptic excitation of CNS connecting with vestibular nuclei. And reduction of c-Fos protein neurons in contralateral MVN may be caused by inhibitory synaptic input from vestibulocerebellum and long term depression within contralateral MVN itself.

Electrical stimulation of the lesioned side vestibular system activates the ipsilateral vestibular nuclei which was suppressed by labyrinthectomy, and inhibits contralateral vestibular nuclei by way of the inhibitory interneuron from the ipsilateral side.⁸⁾ Disappearance of ULX induced- spontaneous nystagmus and head deviation during electrical stimulation suggests that electrical stimulation has a very potent effect on acute vestibular

symptoms caused by loss of peripheral vestibular system.⁹⁾ Electrical stimulation reduced asymmetry in c-Fos protein expression of the bilateral MVN after ULX. This immunohistochemical result also suggests that electrical stimulation facilitates vestibular compensation. Underlying mechanism of electrical stimulation on vestibular compensation could have several explanations, such as unmasking of existing connections, functioning blind axonal endings, supersensitivity and up-regulation of receptors for neurotransmitters in vestibular nuclei. In summary, electrical stimulation to the lesioned vestibular system after ULX facilitated recovery of acute vestibular symptoms as well as neuronal plasticity by activation of the lesioned vestibular nuclei, vestibulocerebellum or other CNS.
(Supported by Braintech 97-N1-02-03-A-01)

REFERENCES

1. Smith PF, Curthoys IS: Mechanisms of recovery following unilateral labyrinthectomy: a review. *Brain Res Rev* 14: 155-180, 1989
2. Altman TJ, Hudlicka O, Tyler KR: Long term effects of tetanic stimulation on blood flow, metabolism, and performance of fast skeletal muscle. *J Physiol* 296: 36-50, 1979
3. Morgan JJ, Curran T: Stimulus-transcription coupling in the nervous system: involvement of the inducible proto-oncogenes Fos and Jun. *Ann Rev Neurosci* 14: 421-451, 1991
4. Darlington CL, Lawlor P, Smith PF, Dragunow M: Temporal relationship between the expression of fos, jun and krox-24 in the guinea pig vestibular nuclei during the development of vestibular compensation for unilateral vestibular deafferentation. *Brain Res* 735: 173-176, 1996
5. Kaufman GD: Activation of immediate early genes by vestibular stimulation. *Ann NY Acad Sci* 781: 437-442, 1996
6. Park BR, Kim MS, Lee MY, Kim OJ: Significance of c-Fos immunoreactive cells in the medial vestibular nuclei during vestibular compensation. *J Vest Res* 6: S11, 1996
7. Kim MS, Jin BK, Chun SW, Lee MY, Lee SH, Kim JH, Park BR: Effect of MK801 on cFos-like protein expression in the medial vestibular nucleus at early stage of vestibular compensation in uvulonodullectomized rats. *Neurosci Lett* 231: 147-150, 1996
8. Precht W, Shimazu H, Markham C: A mechanism of central compensation of vestibular function following hemilabyrinthectomy. *J Neurophysiol* 29: 996-1010, 1966
9. Park BR, Suh JS, Kim MS, Jeong JY, Chun SW, Lee JH: Effect of sensory deprivation or electrical stimulation on acute vestibular symptoms following labyrinthectomy in rabbit. *Acta Otolaryngol (Stockh) Suppl* 519: 162-167