

Visual Function with Acupuncture Tested by Visual Evoked Potential

YOSHIKO SAGARA, NOBUO FUSE, MOTOHIKO SEIMIYA, SYUNJI YOKOKURA,
KEI WATANABE, TORU NAKAZAWA, MASAYUKI KURUSU,¹ TAKASHI SEKI¹
and MAKOTO TAMAI²

Department of Ophthalmology, Tohoku University Hospital, ¹Department of Geriatric and Complementary Medicine, Tohoku University Graduate School of Medicine, and

²Department of Biofunctional Science, Tohoku University Biomedical Engineering Research Organization, Sendai, Japan

SAGARA, Y., FUSE, N., SEIMIYA, M., YOKOKURA, S., WATANABE, K., NAKAZAWA, T., KURUSU, M., SEKI, T. and TAMAI, M. *Visual Function with Acupuncture Tested by Visual Evoked Potential*. Tohoku J. Exp. Med., 2006, **209** (3), 235-241 — Visual evoked potential (VEP) testing is used frequently and is an important ophthalmologic physiological test to examine visual functions objectively. The VEP is a complicated waveform consisting of negative waveform named N75 and N135, and positive waveform named P100. Delayed P100 latency and greatly attenuated amplitude on VEP are known characteristics for diagnosing optic nerve disease. Acupuncture has been used to treat wide clinical symptoms with minimal side effects. The confirmation of the efficacy of acupuncture generally relies on subjective symptoms. There is not much scientific evidence supporting the acupuncture treatments for eye diseases up to today. However, the VEP test can evaluate objectively and numerically the efficacy of the treatment by the acupuncture. We analyzed 19 healthy subjects (38 eyes). The P100 latencies in the group of less than 101.7 msec (total average) before acupuncture stimulations were not different than those after treatment (98.2 ± 3.0 msec, 98.2 ± 4.0 msec, respectively, $p = 0.88$, $n = 17$), but the latencies in those subjects with longer or equal to 101.7 msec were statistically different after acupuncture (104.6 ± 2.8 msec, 101.9 ± 3.7 msec, respectively, $p = 0.006$, $n = 21$). These results show that the acupuncture stimulation contributes to the P100 latencies of pattern reversal (PR)-VEP to some subjects who have delayed latencies, and this electrophysiological method is a valuable technique in monitoring the effectiveness of acupuncture therapy in the improvements of visual functions. The purpose of this study is to evaluate the physiological effects by acupuncture stimulations using PR-VEP in normal subjects. ——— VEP; acupuncture; visual function; alternative medicine

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Correspondence: Nobuo Fuse, Department of Ophthalmology, Tohoku University Hospital, 1-1 Seiryomachi, Aoba-ku, Sendai 980-8574, Japan.

e-mail: fusen@oph.med.tohoku.ac.jp

The methods of ophthalmologic diagnosis and treatments have developed remarkably in recent years. However, oriental medical treatments of traditional Chinese medicine, acupuncture stimulations are now being recognized and used to accompany preventive medicine by the increase of the aged population, and the chronic and modern diseases where the treatment is not established. In 1999, the American Academy of Ophthalmology task force acknowledged that acupuncture may be useful as an adjunctive therapy or an acceptable alternative to conventional treatment for certain ocular conditions (Astbury 2001).

Some patients seek complementary or alternative medicine (CAM) to supplement their regular treatments (Rhee et al. 2001), and the effects of acupuncture have been described and handed down empirically for centuries. However there is not much scientific evidence supporting the acupuncture treatments for eye diseases (Astbury 2001; Rhee et al. 2001; Siedentopf et al. 2002; Kurusu et al. 2005).

Visual evoked potential (VEP) reflects the function of visual pathway from photoreceptor cells, which lie in the central retina to visual cortex (Negishi et al. 2001). Mature luminance flash VEP is a complicated waveform consisting of negative waveform named N75 and positive waveform named P100. Optic nerve diseases like optic neuritis, optic neuropathy (Adachi-Usami et al. 1972; Takasoh et al. 2000), multiple sclerosis (Halliday et al. 1973; Asselman et al. 1975), diabetic retinopathy (Puvanendran et al. 1983; Anastasi et al. 1985; Khardori et al. 1986; Moreo et al. 1995), and Wilson diseases (Satishchandra and Ravishankar Naik 2000) show delayed P100 latency. The purpose of the present study is to evaluate the physiological effects by acupuncture stimulations and to access the selective possibility as a treatment for ocular diseases. We acupunctured normal subjects and evaluated the visual functions before and after acupuncture stimulation using pattern reversal (PR)-VEP.

MATERIALS AND METHODS

Setting

Tohoku University Hospital, Department of Ophthalmology and the Department of Geriatric and Complementary Medicine Sendai, Japan.

Ethical approval was given by the ethics committee of the Tohoku University School of Medicine. The experiments were performed to conform to the tenets of the Declaration of Helsinki.

Subjects

Nineteen healthy subjects between the age's 22 and 49 (males 14, females 5, mean age 30.9 ± 6.8 years old) without eye disease were recruited from hospital and laboratory staff with informed consent, and were given acupuncture stimulation and recorded PR-VEP. All subjects had a corrected visual acuity of 20/20 or better.

Methods

The 19 healthy subjects were given acupuncture stimulation and tested PR-VEP before and after the treatment. They were administered acupuncture at 10 needles points, LR3 (taichong) (R, L), SP6 (sanyinjiao) (R, L), GB20 (fengchi) (R, L), GV20 (baihui), EX-HN2 (yintang) and BL2 (cuanzhu) (R, L) for 15 min. We performed PR-VEP and recorded the amplitude and latency of the cortical electric responses.

Recording of PR-VEP

PR-VEP was recorded using Neuropack Four mini manufactured by Nihon Kodan Co. Ltd. (Tokyo). PR-VEP was recorded and the recording electrodes were placed according to the standard methods (Odom et al. 2004). The recording electrodes were placed at Oz point, the reference electrode at Fz point, the ground electrode connected to an ear. We examined PR-VEP to 2 rev/sec stimulation consisting of a black and white checker board with central stimulus of 0 to 16 degrees radius (Fig. 1) under monocular condition with the best-corrected visual acuity. The pupils were not dilated. The checker board has a 100% contrast with 515 cd/m² of a white space luminance. Responses to 100 reversals were averaged. The latency of P100 was measured as the time from stimulus to the peak, and amplitude was from the trough of the preceding N75 to the peak of P100 (Fig. 2).

Acupuncture stimulation

The disposable stainless steel needles (0.16 mm in diameter, 40 mm in length, Seirin Co. Ltd., Shizuoka)

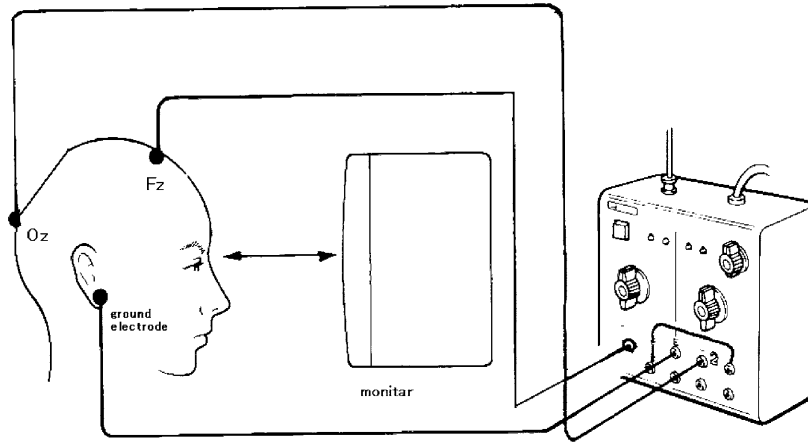


Fig. 1. Examination method of PR-VEP:

PR-VEP was recorded using a Neuropack Four mini manufactured by Nihon Kodan Co., Ltd. (Tokyo).

Oz is the recording electrode. Fz is the reference and the ear is the ground electrode. Monitor shows white and black checkerboard.

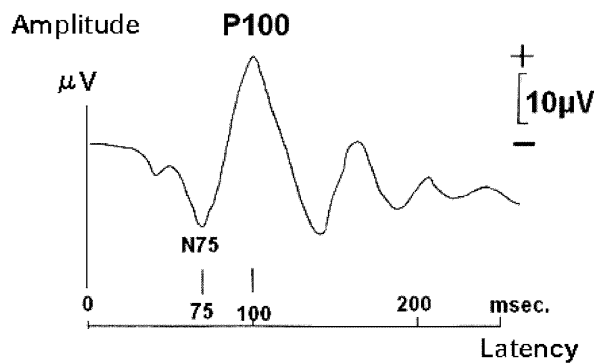


Fig. 2. The wave pattern of PR-VEP:

This chart shows the amplitude and latency of N 75 and P 100.

Seventy five msec is the trough latency named N 75. 100 msec is the peak latency named p100.

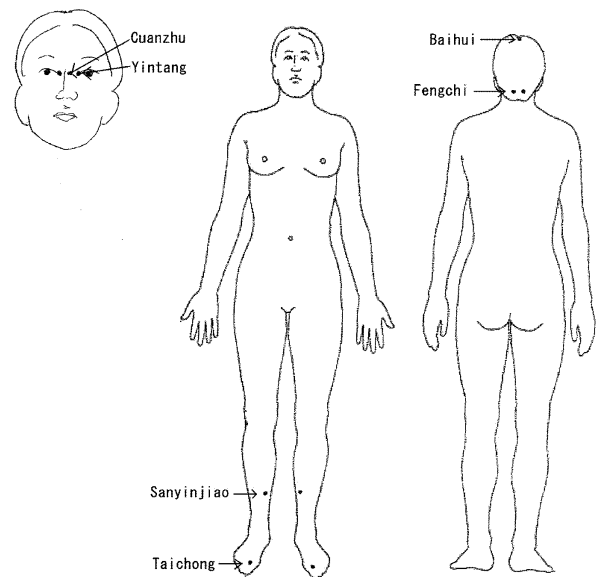


Fig. 3. Acupuncture points.

Acupoints used in the prone and supine positions.

Cuanzhu, on the bridge of the nose; Yintang, on the sides of the nose; Sanyinjiao, on both shins; Taichong, base of big toes; Baihui, top of head; Fengchi, base of head.

were inserted to the depth of 2 mm to 20 mm depending on acupoints.

We acupunctured GV20 (baihui), EX-HN2 (yintang), and bilateral GB20 (fengchi) (R, L), BL2 (cuanzhu) (R, L), LR3 (taichong) (R, L), SP6 (sanyinjiao) (R, L) for 15 minutes at the Department of Geriatric and Complementary Medicine. These acupoints are ineffective to eye diseases. According to the principles of traditional Chinese medicine (TCM) (Maciocia 1989), selection of the acupoints and methods of acupuncture are generally based on the TCM diagnosis. The licensed

acupuncturist and the physician-acupuncturist administered the acupuncture in this study. Acupuncture points were localized in the head, face and legs (Fig. 3).

Statistics

Statistical analysis was performed using the paired *t*-test for multiple comparisons of means. All data were expressed as the mean \pm s.d. $P < 0.05$ was considered statistically significant.

RESULTS

P100 latency

N75 trough and P100 peak were identifiable clearly in all recordings. Table 1 shows P100 latency and the values from N75 to P100 (N75-to-P100) of PR-VEP before and after acupuncture in all subjects. Those two values are routinely measured covariates in ophthalmic field. We could not calculate the differences between males and females because the numbers of females were small. The total average of the P100 latencies before acupuncture stimulations were 101.7 ± 4.3 msec and after 100.2 ± 4.2 msec ($p = 0.01$, $n = 38$; Fig. 4). We divided the subjects into two groups, whose P100 latencies were more than (group 1) and less than (group 2) average (Table 2). The P100 latencies of the group 1 were

(before) 104.6 ± 2.8 msec and (after) 101.9 ± 3.7 msec. There was a statistical difference on a level of $p = 0.006$ ($n = 21$, Fig. 5). On the contrary, the P100 latencies in the group 2 were not different than those after treatment (98.2 ± 3.0 msec, 98.2 ± 4.0 msec, $p = 0.88$, $n = 17$; Table 2). Fig. 6 shows that the more latency (before) the subject has, the more different between the latencies before and after acupuncture. The latency was in mild proportional with the difference at $R^2 = 0.225$.

N75-to-P100 amplitude

The total average of the N75-to-P100 amplitude before acupuncture stimulation was 7.7 ± 2.6 μ V and after 7.8 ± 2.4 μ V on a nonsignificant level of $p = 0.74$ ($n = 38$). Concerning N75-to-P100 amplitude, total average was not changed, and there were no statistical differences between before and after acupuncture stimulation, and even divided into two groups; group 1 and group 2. The reaction of the N75-to-P100 amplitude was not coincident with that of the latency.

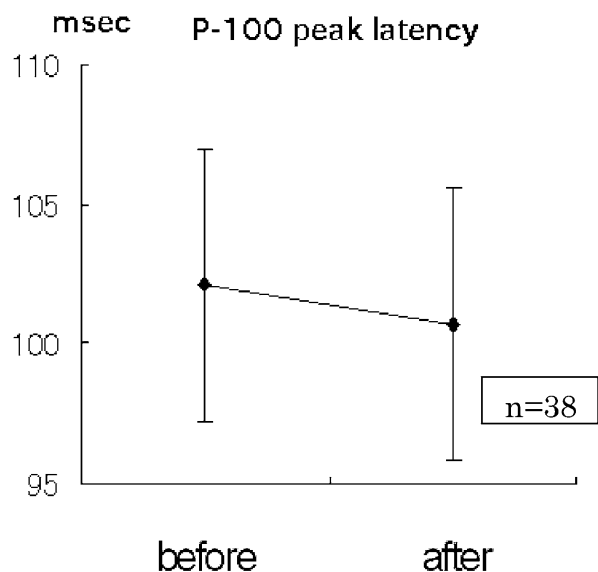


Fig. 4. The total average of the P100 latencies before and after acupuncture.

The total average (before) of all subjects was 101.7 ± 4.3 msec, and (after) 100.2 ± 4.2 msec. The standard deviation was shown as \pm s.d.

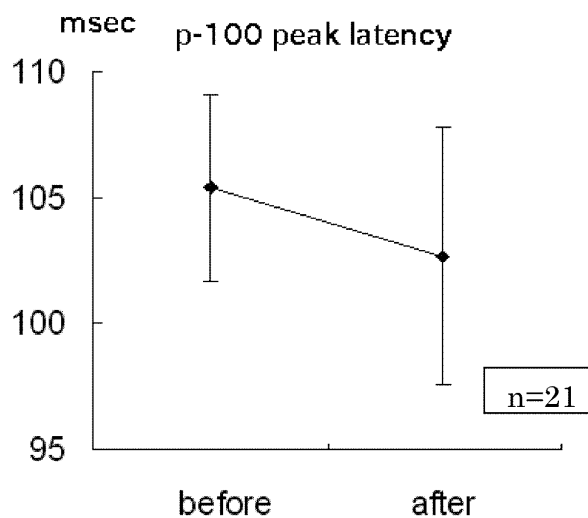


Fig. 5. The total average of the P100 latency before and after acupuncture in the cases of P100 latency of more than 101.7 msec.

The P100 latencies in cases of more than 101.7 msec before acupuncture was 104.6 ± 2.8 msec and that of after acupuncture was 101.9 ± 3.7 msec. Standard deviation was shown as \pm s.d.

TABLE 1. P100 latency and N75-to-P100 amplitude values of PR-VEP before and after acupuncture.

No	Gender	Age	Eye	P-100 latency		N-75-P100 amplitude	
				Before	After	Before	After
1	Male	33	OD	102	100	4.7	6.47
			OS	107	105	4.33	3.21
2	Male	27	OD	100	100	7.36	6.44
			OS	108	98.4	5.07	6.59
3	Male	45	OD	100	102	7.95	8.63
			OS	103	105	8.34	8.75
4	Male	32	OD	102	97.2	9.38	9.58
			OS	100	102	10.5	9.45
5	Male	32	OD	107	102	5.03	5.44
			OS	102	105	4.7	3.68
6	Female	49	OD	99.6	100	11	10.1
			OS	100	99.6	8.77	8.42
7	Male	24	OD	101	102	5.97	5.8
			OS	103	101	4.95	4.77
8	Male	33	OD	97.2	97.8	12.6	11.7
			OS	99.6	96.6	10.5	12.7
9	Male	24	OD	103	104	11.3	10.9
			OS	102	102	10.6	10.7
10	Male	30	OD	103	96	3.17	3.47
			OS	111	102	3.58	4.27
11	Female	27	OD	106	103	10.8	10.8
			OS	106	103	9.8	8.63
12	Female	25	OD	100	98.4	6.07	8.15
			OS	102	94.2	5.28	7.25
13	Female	22	OD	90	91.8	5.66	7.53
			OS	93.6	90.6	7.69	7.02
14	Male	32	OD	103	97.8	7.33	8.57
			OS	101	99	6.44	7.97
15	Male	34	OD	110	106	10.5	8.39
			OS	106	102	12.3	7.88
16	Male	34	OD	103	108	5.85	6.63
			OS	105	108	7.15	5.08
17	Female	26	OD	95.4	96.6	9.58	9.59
			OS	97.2	101	9.93	9.82
18	Male	29	OD	100	104	4.28	4.29
			OS	102	100	7.7	7.8
19	Male	29	OD	96	91.2	7.85	8.7
			OS	99.6	96	8.81	10.4

OD, right eye; OS, left eye.

TABLE 2. P-100 latency and N75-to-P100 amplitude.

	Latency \pm s.D. (msec)		<i>t</i> -test	<i>n</i>	Amplitude \pm s.D. (μ V)		<i>t</i> -test
	Before	After	<i>p</i>		Before	After	<i>p</i>
Total	101.7 \pm 4.3	100.2 \pm 4.2	0.01*	38	7.7 \pm 2.6	7.8 \pm 2.4	0.74
Group 1	104.6 \pm 2.8	101.9 \pm 3.7	0.006*	21	7.2 \pm 2.8	7.1 \pm 2.4	0.66
Group 2	98.2 \pm 3.0	98.2 \pm 4.0	0.88	17	8.3 \pm 2.2	8.6 \pm 2.1	0.24

Group 1: more than 101.7 msec of before acupuncture.

Group 2: less than 101.7 msec of before acupuncture.

P, probability; n, number.

Results are expressed as the mean \pm standard deviation.

Statistical analysis was performed using paired *t*-test.

**p* < 0.05 is considered statistically significant difference.

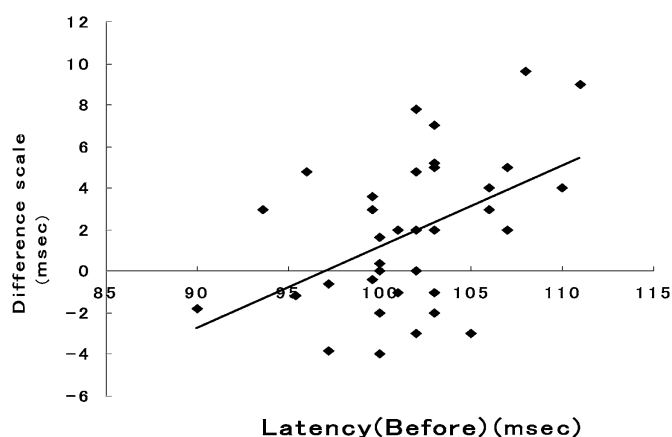


Fig. 6. Correlation between the change of the P100 latency before and after acupuncture and initial P100 latency.

Horizontal line shows the initial P100 latency before acupuncture treatment (msec).

The vertical line is the differences of P100 latencies in cases of (before) and (after) the treatment (msec).

There was a mild proportional correlation between P100 latency (before) and the difference in cases (before) and (after) at $R^2 = 0.225$. Total number = 38.

DISCUSSION

Acupuncture can improve vision by several mechanisms, the blood flow in the eye may be improved and sympathetic nerve activity suppressed. In cases in which normal subjects were acupunctured at Goukoku (the acupoint of hands), the choroidal blood flow improved as measured by the Heidelberg retina flowmeter even after removing the needles (Naruse et al. 2000). Also, parasympathetic nerve activity was increased and acupuncture contributed to the improvement of the choroidal blood flow (Yamaguchi 1995).

Acupuncture stimulation induced excitation of afferent fibers of the nerve, and involved a reflex response of pupil dilation through the third cranial parasympathetic efferent nerve. Thus, the beneficial effects on the eyes can be achieved by several mechanisms. These articles suggest that the improvement of choroidal blood flow and autonomic nervous system balance by acupuncture treatment were effective to optic function.

Our results showed that there was a positive correlation between the PR-VEP test and the response of the acupuncture treatments. Because PR-VEP reflected the optic nerve functions, this

electrophysiological method could check the improvements of visual functions after acupuncture treatment in the cases that have prolonged P100 latencies; longer or equal to 101.7 msec. Usually, the patients with optic nerve disease have prolonged P100 latencies more than 100 msec. We suggest that a PR-VEP examination could be a very useful method to identify the improvement of visual functions. Following the acupuncture, subjects who initially had prolonged P100 latencies got the reduced latency, and reported that they could see more clearly and easily.

It is necessary to test acupuncture and placebo groups in order to evaluate the efficacy of acupuncture treatments. There are some articles in which no difference was detected between the acupuncture and the placebo acupuncture, while there was a statistical significant difference between the acupuncture groups compared with no acupuncture group (Linde et al. 2005). We have started to use the double blind acupuncture stimulation including 3 placebo treatments on a trial basis for glaucoma subjects, which show optic neuropathy. In general, the effects of acupuncture tended to weaken as time passed, and the subjects' conditions returned close to those before acupuncture after 3 or 4 days intervals. It is also necessary to study whether continuous acupuncture is desirable to maintain the effects of acupuncture.

In conclusion, the present study suggests that acupuncture has the possibility to supplement conventional study for disease of the optic nerve without major adverse effects. To clarify further the role of acupuncture in controlling PR-VEP, more study including patients with optic nerve disease will be needed in the future.

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