Experimental Research of Flash Visual Evoked Potential of Chinese White Rabbit after Optic Nerve Injury

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Abstract: Objective: To investigate the changes of the Flash visual evoked potential (F-VEP) in China rabbit after the optic nerve injury. Methods: Changes of F-VEP in normal China rabbits and those after optic nerve injury were detected using TEC automatic visual electric physiological system. Results: Compared with that of the normal rabbits, the latency of F-VEP in optic nerve incomplete injury rats increased significantly, but the amplitude of F-VEP decreased significantly. "Silent pattern" waveform of F-VEP was found in optic nerve transected China rabbits. Conclusion: The model of China rabbits with optic nerve injury can be used for the investigation of the neuroprotective effect of optic nerves. Detection of the changes of F-VEP is an objective, reliable, and effective method for the examination of optic nerve functions.

Keywords: China rabbits; Flash visual evoked potential

1. Introduction
The China White Rabbit in recent years were used more for scientific research of ophthalmology, but their normal visual electrophysiological properties is not clear, rarely reported in the literature (Cai, 2009). We studied the Chinese White Rabbit flash visual evoked potential (F-VEP), to establish the range of normal value and the feature after optic nerve injury, with purpose to lay a foundation of further optic nerve damage repair research.

2. Materials and Methods
2.1 Experimental animals
Chinese white rabbits, male half and female half, a total of 20 (Zhengzhou University Experimental Animal Center), body weight 250 to 260 g. Record the F-VEP of left eye, establish the normal value of latent time and the amplitude of Chinese White Rabbit F-VEP. The choice of which recorded in the 18 animals was chosen to record F-VEP 1 h after incomplete transection of the right optic nerve; F-VEP was recorded in the remaining two after optic nerve transection, in order to monitor the status of the optic nerve function after acute optic nerve injury.

2.2 Animal models of optic nerve injury
10% chloral hydrate was used to anesthetize rabbits by ear vein, fixed on the operating table with prone position. According to the position of the optic nerve of the rabbit eye, get close to the optic nerve from above the surface of the eye. Cut the bulbar conjunctiva in the 10:00–14:00 position of the cornea edge of the upper right eye, blunt separation of the bulbar conjunctiva to the rear ball, pull superior rectus to the below with a self tractor, expose and cut the superior rectus muscle, careful use of mosquito-clamp clamping 10 s at 2 mm after the ball and make injury by optic nerve crush. Optic nerve transection model as above, expose the superior rectus muscle, cut the cord-like optic nerve with bent-shaped tissue scissors, result in optic nerve transaction (Yan, 2012).

2.3 Recording method of F-VEP and stimulus parameters
Electrophysiological examination with reference to international clinical visual electrophysiological criteria, Chongqing Tektronix automatic visual electrophysiology system was used. Anesthetized animals fixed on the bench, homemade silver needle electrode (adapted from acupuncture needles) was used to guide the electrode inserted into the external occipital tuberosity below the periosteum from the midpoint of two ears attachment, reference electrode inserted into the forehead, below the periosteum at the midpoint of two eyes attachment, the ground electrode behind the right ear, recorded F-VEP after 15min of dark adaptation. White flash stimulus of full vision stimulator was used with colorless background, the pass-band low-frequency 75 Hz, high-frequency 0.1 Hz, stimulation pattern for single stimulation, frequency 2Hz, flash intensity 3.556e-3cd.s/m², to stimulate 50 times, magnification of 100,000 times, each sampling time 500 ms, waveform overlay of 100 times, consecutive measurements at least five times, each
interval of 30min. Each animal recorded stable waveforms three times. Each animal inspection one eye, using self-made opaque black patch completely cover the contralateral eye.

2.4 The observed indicators
Harding nomenclature was used. The experiment recorded relatively stable N-P-N waveform of the F-VEP waveform, records of each animal: N1 wave, P1 wave, N2 wave latency (ms) and N1-P1, P1-N2, wave amplitude (v). Measurement method: N1 peak latencies is from the start to N1 peak, P1peak latencies is from the start to the bottom of P1, and so on; N1- P1 amplitude is from the peak of the N1 to the bottom of P1, and so on. Each index value of computer automatic measurement, taking the average of three times to register.

2.5 Statistical analysis
The the SPSS 11.0 was used, t test was used for comparison among groups.

### Table 1. Normal rabbit F-VEP amplitude

<table>
<thead>
<tr>
<th>F-VEP</th>
<th>N1</th>
<th>P1</th>
<th>N2</th>
<th>N1-P1</th>
<th>P1-P2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>26.13</td>
<td>46.10</td>
<td>95.10</td>
<td>15.10</td>
<td>35.10</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>8.70</td>
<td>10.40</td>
<td>21.41</td>
<td>5.4</td>
<td>14.50</td>
</tr>
</tbody>
</table>

3. Results

#### 3.1 normal white rabbit F-VEP
A typical N-P-N waveforms was seen in each rabbit, measured the average and calculated the variability index standard deviation and range. The results shown in Table 1.

#### 3.2 Chinese white rabbits of the F-VEP after optic nerve incomplete injury
measured the average and calculated the variability index standard deviation. Table 2 shows that the waveform change low and wide after optic nerve incompletely damage. The incubation period of N1, P1, N2 prolonged significantly, peak N1-P1, P1-N2 amplitudes were reduced, and have significant difference from the normal (P <0.01).

<table>
<thead>
<tr>
<th>F-VEP</th>
<th>N1</th>
<th>P1</th>
<th>N2</th>
<th>N1-P1</th>
<th>P1-P2</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORMAL</td>
<td>26.13±8.7</td>
<td>46.10±10.4</td>
<td>95.10±21.41</td>
<td>15.10±5.4</td>
<td>35.10±14.5</td>
</tr>
<tr>
<td>CRUSHED</td>
<td>66.73±19.63</td>
<td>131.2±30.22</td>
<td>191.30±55.28</td>
<td>8.1±3.5</td>
<td>8.9±2.2</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

4. Discussion
Visual evoked potentials is a bunch of electrical signals in the cerebral cortex to visual stimuli react, also known as visual evoked cortical potentials (VECP) or visual evoked response (VER) (Holmes, 2004). VEP with other visual electrophysiology can provide important diagnostic information on whether the function of the visual system is intact. F-VEP is a more mature and effective noninvasive method of visual function status between the normal state and the disease process(Heiduschka,2005). Stimulation and recording methods between different laboratories, the F-VEP peak polarity, latency, amplitude is very different, yet there is no single standard value. Variability index standard deviation of the experiment is larger, indicating that the Chinese White Rabbit F-VEP variability and volatility is larger, the F-VEP in certain individual differences. We studied the F-VEP of Chinese White Rabbit, to establish the normal range and depending on the variation after the injury, to lay an experimental foundation for further clinical diagnosis and prognosis. Experiment to detect the F-VEP of normal and post optic nerve damage of China White Rabbit, leads to good reproducibility of the waveform, the F- VEP latency and amplitude of normal and post optic nerve damage of China White Rabbit was achieved. There are incomplete injury and complete injury types of traumatic optic nerve injury model. Complete injury include the myelin sheath damage of the optic nerve damage and no damage to the myelin sheath of the optic nerve. Incomplete optic nerve injury method is optic canal crush injury, optic indirect good, clamp contusion, crush injury, draw-off injury etc. Incomplete optic nerve injury is clinical common, we have established the most common and recognized more accurate optic nerve injury model to simulate the process of clinical optic nerve injury. 1h after optic nerve r injury F-VEP was measured with the contrast to normal eye. The results showed that the waveform becomes low and broad in incomplete optic nerve injury, the incubation period of N1, P1, N2, was significantly prolonged, peak of N1-P1, P1-N2 decreased significantly compared with the normal eye, there are significant differences. Experiments establish optic nerve transection model, Chinese White Rabbit F-VEP waveform basic after optic nerve transection was extinguished type, no significant peaks appear. The optic nerve injury is a
common type of ocular trauma, After the injury in time to understand vision is important index for guiding therapy and prognosis judgment, but the subjective visual inspection is often affected by many factors, and patients often accompanied with coma caused by brain trauma, therefore, F - VEP inspection as an objective index, is of great significance to guide the clinical treatment of ocular trauma. Zhu Yu et al. found through experimental and clinical research, application of the F-VEP in orbital surgery is reliable for optic nerve conduction function monitoring and can reduce the accident rate of blindness of the optic nerve injury, so that the surgical procedure from clinical experience anatomy to functional anatomy. F-VEP abnormalities reveals a high degree of optic nerve dysfunction, and can predict the size of the possibility of recovery. F-VEP is sensitive to the degree of response to optic nerve damage, in severe optic nerve damage the rate of decline of the F-VEP amplitude can be as a judgment of the visual acuity after injury and a prognosis of objective indicators. Record of this experiment to the normal Chinese White Rabbit typical F-VEP waveform, the peak of the optic nerve injury model significantly reduced, indicating that this animal model can be used to further observe the optic nerve protective effect of the study, and the F-VEP waveform changes in the optic nerve damage consistent with the visual information and is of great value for the understanding of the injury to the conduction of the visual cortex. With the continuous improvement and development of the F-VEP detection technology, it will be more valuable in the clinical application(Zhu,2011).

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