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Characteristics of healthy school-age children's visual evoke potentials

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健康学龄儿童视觉诱发电位的研究

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摘要

目的:本文将对健康学龄儿童的闪光视觉诱发电位(FVEP)及图形诱发电位(PVEP)的特征进行总结概况,研究性别、年龄以及其他生理因素对视觉诱发电位结果的影响,并将两种诱发电位从方法到结果进行比较。

方法:选取101名健康儿童(5~14.4岁,平均8.27岁),分别进行FVEP及PVEP检查。应用SPSS 13.0软件对结果进行统计分析。

结果:PVEP诱发出的图形简单并且稳定,FVEP诱发出的图形变化较大。PVEP中女性儿童P100潜伏期较男性儿童的短,但不具备显著性差异。在FVEP中没有显示出性别差异。在左右眼对比中我们发现左眼P100波幅要比右眼波幅高,在FVEP研究中没有显示出左右眼的差异。在年龄指标上,PVEP及FVEP各项参数都没有显示与年龄具有相关性。最后FVEP与PVEP两种方法进行相关性比照,我们发现两者的相关性小。

结论:通过此次研究,我们发现性别、年龄等生理因素对儿童期视觉诱发电位影响不大。两种诱发电位的方法不具备内在联系,这与两者在大脑的应答区域不同相关。因此在视神经系统的检查上,两者应该互相补充。

关键词:儿童;闪光视觉诱发电位;图形诱发电位;特征;生理因素

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Abstract

• AIM: To conclude the characteristics of flash visual evoke potentials (FVEP), and pattern visual evoke potentials (PVEP) of the healthy school-age children. And to compare the two methods, in order to find the association of them, and to find the impact of sex, age, and the other biological variables.

• METHODS: A total of 101 healthy children were recruited (age from 5 to 14.4y, mean 8.27y). Each of them was underwent FVEP and PVEP examinations. Then the results were statistically analyzed by SPSS 13.0.

• RESULTS: The curves of PVEP are simple and stable, while FVEP waveforms are variable. The latency of P100 of females is shorter than males. However there was no significant difference for FVEP in sex control. To compare the parameters between the two hemispheres, the amplitude of P100 of left eyes were higher than the right side. FVEP showed no difference in the two hemispheres either. There was no significant difference for age-dependent decreased in neither PVEP nor FVEP. And in a regression analysis of the FVEP and PVEP, we could not find the inner connection of the two methods.

• CONCLUSION: Based on our research, there were no significant differences in age level or sex control in the period of school-age children. And there is no inner connection of the two methods. The differences between the PVEP and FVEP results might be due to the origin of these two responses. And these two stimuli should be used in a complementary manner not as alternative examinations.

• KEYWORDS: children; flash visual evoke potentials; pattern visual evoke potentials; characteristics; biological variables

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INTRODUCTION

Visual evoked potential (VEP) is a kind of potentials examining the visual pathway trough the optic nerve to the occipital cortex. And it is useful as an objective measurement for detecting lesions of visual pathways. VEP provide information on the integrity of visual system, and its results can be predictive of visual recovery in traumatic optic neuropathy[1-2].

VEP includes pattern evoke potentials and flash evoke potentials. As a dependable and noninvasive method, pattern

visual evoke potentials (PVEP) can offer information about the physiological functioning of the visual pathways from the retina, optic nerve, optic chiasm, and optic radiations to the occipital cortex[3]. The character waveform of PVEP is P100. P100 latency is sensitive to the effects of poor visual acuity, and was found superior to color vision and visual field in early stages of hydroxychloroquine maculopathy. Flash visual evoke potentials (FVEP) usually used on patients who cannot fixate on the screen, including coma patients and infants. Currently, the ISCEV standard generally recommends flash stimuli for patients who are unable or unwilling to cooperate for PVEP, and in cases where optical factors, such as media opacities, prevent the valid use of pattern stimuli[4]. In the following study we would exam the children with the two methods, and to find the characters of the waves of the school-age children. This study was conducted to gather the information of the two methods, and compared them with statistics methods. It is also anticipated that this study can provide information about the impact of sex, age, and the other biological variables.

SUBJECTS AND METHODS

A total of 101 children were recruited from Women and Children's Medical center, aged from 5.8y to 14.5y. They are composed of 58 males and 43 females, no ophthalmologic disorders or refractive errors, no neurological or developmental disorder, no medication, birth weight ≥2500 g and gestation duration ≥37wk. This study was approved by the Ethics Committee of Guangzhou Women and Children's Medical Center. This study was approved by the Ethics Committees of all three participating hospitals. Written informed consent was obtained from the legal guardians of the patients.

VEP were examined using Nicolet Viking Quest equipment. According to the international 10/20 electrode placement system, the reference electrode was placed on the frontal scalp (Fp), the recording electrode was placed on the middle of occipital region (Oz), and the ground electrode was placed at the mastoid (A1/A2). Impedance for each electrode usually was less than 5 KΩ. And 100 responses were averaged in each test.

PVEP using TCL-L172SE monitor (17 inch, luminance of 50 cd/m2 and contrast 400/1), black - and - white checkerboard patterns with a spatial frequency of 1.9 Hz were delivered monocularly. From a distance of 50-60 cm in the dimly lit room, the participants were required to fixate a small red dot located in the center of the screen, and were recorded separately for each eye (left eye would be performed initially).

When the patients finished the PVEP test, they were required to be performed with FVEP subsequently. In FVEP test the patient is fitted with a pair of LED goggles, and the flash stimulates each eye independently (left eye would be performed initially).

In test PVEP, we can record the NPN patterns (Figure 1), the positive peak that occurs at approximately 100ms is named P100. And the preceding negative peak is the N75, and the negative peak following the P100 is the N145. On the country the cortical potentials of FVEP are more variable and more diffusively distributed. We can record six or seven peaks in the first 250 ms usually (Figure 2), and we name them N1, P1, N2, P2, N3, P3, N4 sequentially (N for negative, P for positive).

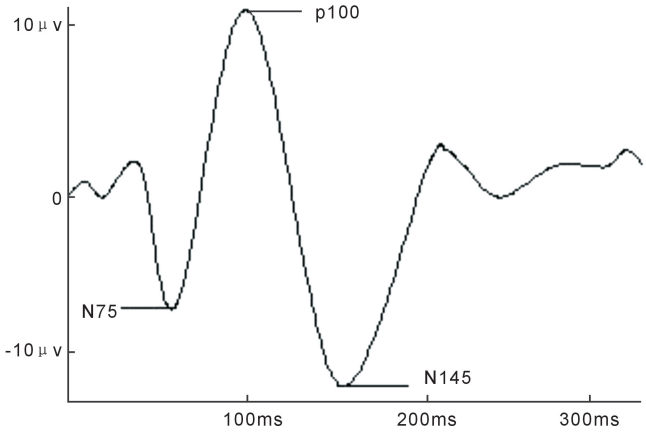

Figure 1 The dramatic drawing of PVEP. There are three major parameters, N75, P100 and N145.

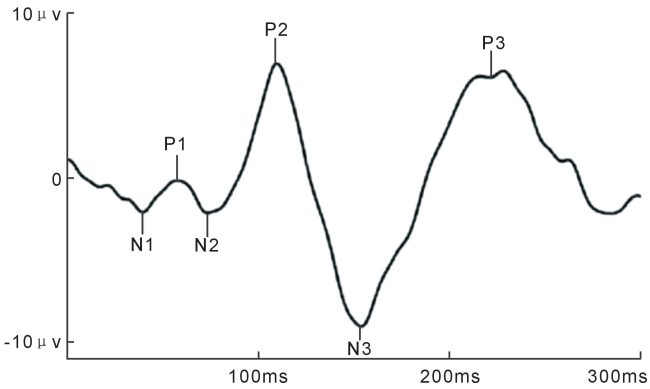

Figure 2 The dramatic drawing of FVEP. The parameters of FVEP include N1, P1, N2, P2, N3, P3 and N4.

Each patient was tested with the two methods, and the traces were averaged 100 times. Latency was defined as the time from the stimulus onset to the dominant peak, and the amplitude of the wave was defined by the voltage difference between the dominant positive peak and the preceding negative peak. Finally, all the parameters for the two eye in each subject was used for statistical analysis. And statistical comparisons were performed by SPSS software 13.0 for Windows. As P-value less than 0.05 was considered to be statistically significant.

RESULTS

The Results of Healthy Children's PVEPs The means and standard deviations of the parameters were shown in Table 1. First, the wave N75, P100, and N145 could be recorded clearly and the occurrence rate of them was 100%. Second, the dispersion of N75, P100 and the amplitude of P100 was in a relatively small area. It meant the differences of those parameters among the children are small. Table 2 showed the results of the differences in amplitudes and latencies between

Table 1 The average of the parameters of the PVEPs and FVEPs

Parameters	No.	Frequency of occurrence (%)	Minimum	Maximum	Mean	Std. deviation
N75 (PL) (ms)	101	100	64.00	89.80	77.58	5.03
P100 (PL) (ms)	101	100	102.00	131.00	111.71	5.34
N145 (PL) (ms)	101	100	132.00	201.00	160.76	13.39
P100 (AMP) (uV)	101	100	2.78	44.60	18.86	8.57
N75-N145 (IPL) (ms)	101	100	53.00	163.50	83.88	15.93
N1 (PL) (ms)	76	75.25	20.00	48.50	39.83	4.79
P1 (PL) (ms)	76	75.25	35.00	63.50	52.35	4.86
N2 (PL) (ms)	101	100	60.50	86.50	72.30	5.01
P2 (PL) (ms)	101	100	84.00	142.00	115.09	13.62
N3 (PL) (ms)	101	100	99.50	254.00	168.29	27.87
P3 (PL) (ms)	83	85.15	141.00	251.00	203.94	30.13
N4 (PL) (ms)	87	86.14	168.00	328.00	254.31	38.23
P1 (AMP) (uV)	76	75.25	0.07	14.60	3.61	2.66
P2 (AMP) (uV)	101	100	3.10	44.50	20.20	8.92
P3 (AMP) (uV)	83	82.17	0.44	33.90	12.58	8.18
N1-N2 (IPL) (ms)	76	75.25	18.50	57.50	32.70	7.29
N2-N3 (IPL) (ms)	99	98.02	36.00	178.00	98.96	26.02
N1-N3 (IPL) (ms)	76	75.25	60.00	194.50	130.09	26.44
N2-N4 (IPL) (ms)	87	86.14	93.00	257.50	182.28	38.65

PVEP: Pattern visual evoke potentials; FVEP: Flash visual evoke potentials; PL: Peak latent; IPL: Inter peak latency; AMP: Amplitude.

the two hemispheres. We found that there was no significant difference in latencies between the two hemispheres, but the amplitudes of P100 of left eyes were higher than the right eyes ($P<0.001$).

In the contrast research of PVEPs (Table 3), we compared the parameters of VEPs between males and females. Females showed shorter latencies of N75, P100 and N145, and larger amplitudes of P100 than males. Furthermore the latencies of P100 showed the significant difference ($P<0.05$).

In the study of the age-related changes in the VEPs (Table 5), we found all regression fits were not statistically significant except for a small increase in latency of P100 ($r=0.324$) and decrease in latency of N1 ($r=-0.369$). Nevertheless there was only weak correlation.

The Results of Healthy Children's FVEP The means and standard deviations of the parameters are shown in Table 1. Table 1 shows that, the frequency of waves N2, P2 and N3 could be recorded 100%, meanwhile the frequency of waves N1 and P1 is 75.25%, and the frequency of waves P3 is 85.15%, N4 is 86.14%. The low frequency of occurrence means the waves of FVEP were not stable, they were absent or were difficult to be recognized sometimes.

In the contrast research of FVEPs (Table 2), we compare the parameters of VEPs between males and females. While we could not find sex-related difference between the males and females.

In the paired-samples t-test for differences in amplitudes and latencies between hemispheres (Table 3), there was no significant difference in latencies between the two hemispheres.

And final we made a regression analysis of the FVEPs and

Table 2 To compare the parameters between the two hemispheres

Pair	No.	Mean	Std. deviation	Std. error mean
N75				
L	50	77.50	4.90	0.69
R	50	77.58	5.22	0.74
P100				
L	50	111.22	5.55	0.79
R	50	112.14	5.16	0.73
N145				
L	50	161.56	13.67	1.93
R	50	159.82	13.28	1.88
P100 AMP				
L	50	20.16[a]	9.48	1.34
R	50	17.81	7.35	1.04
N75-N145				
L	50	84.06	14.02	1.98
R	50	83.64	17.92	2.53
N2				
L	50	71.89	5.07	0.72
R	50	72.48	4.73	0.67
P2				
L	50	114.40	13.55	1.92
R	50	115.26	13.45	1.90
N3				
L	50	167.94	27.82	3.94
R	50	168.35	28.40	4.02
P2 AMP				
L	50	19.53	8.67	1.22
R	50	20.97	9.26	1.31

AMP: Amplitude; [a]$P<0.001$.

PVEPs, in order to find the inner connection of the two methods (Table 4). There is not significant event between the two methods.

DISCUSSION

Base on the data distributed character, the means and standard deviations were calculated. We found that the waves of PVEP occurred constantly. Each patient could be recorded to a distinct curve. However not all the waves of FVEP could be recorded distinctly, only waves N2, P2 and N3 could occur 100%. The other waves of FVEP were absent or were difficult to be recognized sometimes. Since all the recruits could exclude the possibility of ophthalmological or nerve system's diseases, so the absence of those waves just meant instability. On the other hand, we searched on the Pubmed, and few article expounded the resource of each waves of FVEP. Therefore we would put more attention on the N2, P2, N3 and P2 AMP in the follow-up study.

From Table 2 we found that in the contrast research of PVEPs females showed shorter latencies and larger amplitudes than males. The latency of P100 have significant difference between males and females ($P<0.05$). And we also found the latencies of N75, N145 showed the trend of shorter, and the amplitudes of P100 were larger in females. While in our research of FVEP, we could not find sex-related difference between the males and females. Dion *et al*[5] reported the same results of VEPs in children, and they analyzed the reasons were associated with the head size. However a few researcher presented other viewpoints, for example in a study performed in children, Malcolm *et al*[6] found that head size differences could not account totally for all sex effects in their sample. Bruno and Stefano reported that females have a shorter latency than males in adults. And head size has a weak though significant influence on the latency [7]. While there is no consensus as to why sex differences are seen, a wide range of factors has been proposed, such as skull thickness, body temperature, pupil size, sex steroids and head size[8-10].

The results for individual children were analyzedby a paired-samples t-test for differences in amplitudes and latencies between hemispheres. Table 3 shows the mean difference of the two hemispheres, and there was no significant difference in latencies between the two hemispheres. But the amplitudes of P100 of left eyes were higher than the right eyes ($P<0.001$). To investigate the reason, we proposed the assumption of dominant eyes[11]. Right eyes as dominant eyes are higher in distribution probability in China. And when the recruits were tested the non-dominant eyes, they would put more attention on the check board. As the amplitudes of P100 are depended on the visual acuity, so the amplitudes of non-dominant eyes (left eyes) were higher than the dominant eyes (right eyes). While, flashes of light stimulate all photoreceptors of the retina, regardless of the patient's cooperation, fixation, or refractive problems, so the FVEPs show no difference between the two hemispheres.

Table 3 To compare the parameters of VEPs between males and females

Sex	No.	Mean	Std. deviation	Std. error mean
N75				
F	43	76.71	3.26	0.50
M	58	78.22	5.96	0.78
P100				
F	43	110.47[a]	4.56	0.70
M	58	112.64	5.70	0.75
N145				
F	43	159.37	15.46	2.36
M	58	161.79	11.66	1.53
P100 AMP				
F	43	19.46	9.06	1.38
M	58	18.42	8.23	1.08
N75-145				
F	43	82.66	15.26	2.33
M	58	84.78	16.48	2.16
N2				
F	43	71.58	5.59	0.85
M	58	72.84	4.50	0.59
P2				
F	43	115.56	12.77	1.95
M	58	114.74	14.32	1.88
P2 AMP				
F	43	18.76	8.45	1.29
M	58	21.28	9.18	1.20

AMP: Amplitude; a: $P<0.05$.

Table 4 The correlation of latency and amplitude of P100 and P2

Model	No.	Beta(r)	T	Sig.
P100/P2	101	0.130	2.745/1.302	0.007/0.196
P100 AMP/P2 AMP	101	0.346	6.597/3.672	0.000/0.000

AMP: Amplitude; $r<0.3$ no correlation, $0.3<r<0.5$ weak correlation, $0.5<r<0.8$ middle correlation, $0.8<r<1$ high correlation.

Table 5 Pearson correlation analysis at age level

Parameters	No.	Pearson correlation	Sig.
N75	101	-0.005	0.512
P100	101	0.324	0.002
N145	101	0.217	0.931
P100 AMP	101	-0.178	0.043
N75-N145	101	0.143	0.038
N1	76	-0.369	0.001
P1	76	0.267	0.015
N2	101	-0.120	0.232
P2	101	0.217	0.032
N3	101	-0.003	0.984
P3	86	0.034	0.763
N4	87	-0.134	0.202
P1 AMP	76	-0.163	0.162
P2 AMP	101	0.203	0.045
P3 AMP	86	-0.027	0.837

AMP: Amplitude; $r<0.3$ no correlation, $0.3<r<0.5$ weak correlation, $0.5<r<0.8$ middle correlation, $0.8<r<1$ high correlation.

From Table 4 we made a regression analysis of the FVEPs and PVEPs, in order to find the inner connection of the two methods. However we did not find any significant event regrettably, except for the amplitudes of P100 and P2 show a weak correlation ($r=0.346$).

And we also studied the changes of age-related in the VEPs. From Table 5 we found all regression fits were not statistically significant except for an small increase in latency of P100 ($r=0.32$; $P<0.0001$), the same as some research reported[12]. The degree of correlation is so weak, we even could not draw a logical regression curve. As known, the latency is connected with the maturation of the myelination. So the general developmental pattern was a rapid decrease in the first 6mo of life, especially in the first 3mo, a gradual decline from 6 to 12mo of age, and then a steady reduction from 12 to 18mo of age[13-14].

The VEP represents the response of the visual cortex to stimuli presented in the visual field. In our study, the waves of PVEPs are stable and distinct, but the waves of FVEP show large differences among the different healthy children. The differences between the PVEP and FVEP results might be connected to the origin of these two responses. The wide distribution of the potentials of FVEP may be due to activation of alternative visual pathways including the visual projection to the superior colliculus which in turn project to large areas of the visual cortex via the pulvinar[15-16]. Responses to pattern stimuli originate in the macular (small checks) and paramacular (large checks) regions. The major positive component of PVEP, P100, is generated in the cortical area V1. The origin of the FVEP components is currently under investigation. The P2 wave is likely generated in the cortical areas V1-V3, and P3 is generated in the area V4. PVEP is sensitive to changes in the central visual field and FVEP is sensitive to changes in the peripheral field. Meanwhile FVEP is helpful in the estimation of visual acuity for non-cooperative patients. An intact FVEP proves that some visual input has reached the occipital cortex, but cannot determine if that input arose from macular or peripheral retina. Additionally an intact FVEP does not demonstrate the presence of conscious visual perception[17].

In our study, neither PVEPs nor FVEPs has significant changed with age growth in children. And the difference between sexes only be presented in the waves of PVEP. It shows the shorter latencies of N75, P100, N145, and larger amplitudes of P100 in female children. We also found that the amplitudes of P100 of left eyes were higher than the right eyes in children. That was not reported before, we proposed the assumption of dominant eyes.

In conclusion, these two stimuli should be used in a complementary manner not as alternative examinations[18-19]. Currently, the ISCEV standard generally recommends flash stimuli for patients who are unable or unwilling to cooperate for PVEP, and in cases where optical factors, such as media opacities, prevent the valid use of pattern stimuli.

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