A Comparative Study of Visual Evoked Potentials in Optic Neuritis and Optic Neuritis with Multiple Sclerosis

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Objective: *To compare the visual evoked potentials (VEP) in patients with acute optic neuritis, recurrent optic neuritis, and optic neuritis with multiple sclerosis.*
Material and Method: *The authors retrospectively reviewed VEP latency records of the patients with optic neuritis in Siriraj Hospital from 1995 to 2005 and divided them into three groups, acute optic neuritis, recurrent optic neuritis, and optic neuritis with multiple sclerosis (ON/MS). The patients with non-recordable VEP in the analysis were excluded. Comparison of the mean latency of the VEP in affected eyes among the three groups was statistically analyzed by a nonparametric independent sample test.*
Results: *Twenty-two patients with acute optic neuritis, 8 patients with recurrent optic neuritis, and 22 patients with ON/MS participated in this study. The mean age among the three groups was not statistically significant. The median value of the latency of flash VEP (fVEP) and pattern reversal VEP (PRVEP) in the acute optic neuritis group was shorter than that of the recurrent optic neuritis group, and statistically significant (fVEP, p = 0.012; PRVEP, p = 0.004). The median value of the latency of PRVEP in the acute optic neuritis group was shorter than that of the ON/MS group, and statistically significant (PRVEP, p = 0.002). The median value of the latency of both fVEP and PRVEP in the recurrent optic neuritis group and ON/MS group were delayed with no statistical significance (fVEP, p = 0.458; PRVEP, p = 0.403).*
Conclusion: *The VEP can be used to demonstrate the demyelinating mechanism of optic neuritis and optic neuritis with multiple sclerosis, but cannot determine the susceptibility of the patients with acute ON to become MS. The significantly delayed latency of VEP in recurrent optic neuritis is possibly caused by severe damage of the optic nerve conduction from recurrent attacks.*

Keywords: *Acute optic neuritis, Recurrent optic neuritis, Multiple sclerosis, VEP latency*

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Visual evoked potential (VEP) is an objective test that can detect lesions of the optic nerve. The characteristic finding of the VEP in optic neuritis (ON) is the delayed latency of VEP, which may persist for many years[1-3].

ON may be the initial manifestation of multiple sclerosis (MS) or can occur at some time during the course of MS and a history of recurrent ON is common in patients with MS[4,5].

The objective of the present study was to compare the VEP latency in patients with acute ON, recurrent ON and ON with MS (ON/MS) to see whether there is a high probability of the results being used to predict the chance of ON to turn to be MS.

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Material and Method

Fifty-two patients in the neuro-ophthalmology unit, Siriraj Hospital diagnosed as ON from June 1995 to November 2005 were retrospectively reviewed.

ON was clinically diagnosed in the patients who had decreased visual acuity, impaired color vision, relative afferent pupillary defect, and abnormal visual field along nerve fiber bundle of the retina. The patients with acute ON caused by other diseases except MS were excluded. The fVEP or PRVEP was performed within two months of the onset in all of the patients. The normal value of fVEP and PRVEP latency was not longer than 120 and 100 msec respectively. All patients were classified into three groups that were the acute ON group, the recurrent ON group, and the ON/MS group based on Poser or McDonald criteria[6,7]. The collected data included age, sex, laterality of optic neuritis, and the latency of fVEP or PRVEP in the affected eyes. The median value of the VEP latency in the affected eyes in each group was analyzed and compared among the three groups by a non-parametric independent sample test Kruskal Wallis test and or (Mann-Whitney U test) were appropriated and the non-recordable VEP records were excluded from the statistical analysis. A p-value of less than 0.05 was considered significant difference.

Results

Twenty-two patients with acute ON, 8 patients with recurrent ON and 22 patients with ON/MS (Table 1) were studied.

In the acute ON group, the female to male ratio was 2.7:1. The mean age was 37.4 years (17-57 years of age). Twenty-one patients had unilateral ON and one patient had bilateral ON. The fVEP latency in affected eyes was recorded in 19 patients while one patient had a non-recordable result. The PRVEP in affected eyes was recorded in 12 patients while two patients had a non-recordable result. The median value of the latency of fVEP and PRVEP in the affected eyes was 128 msec (interquatile range, 120.75-139) and 117 msec (interquatile range, 109-135.5) respectively.

In the recurrent ON group, the female to male ratio was 7:1.The mean age was 36.9 years (27-50 years of age). Six patients had unilateral ON and two patients had bilateral ON. The fVEP latency in affected eyes was recorded in six patients. The PRVEP in affected eyes was recorded in seven patients while two patients had a non-recordable result. The median value of the latency of fVEP and PRVEP in the affected eyes was 143.5 msec (interquatile range, 137.25-154.75) and 151 msec (interquatile range, 140.5-154) respectively (Fig. 1, 2).

For nine patients who had bilateral ON, the authors selected the VEP latency of the right eye as the affected VEP latency to prevent bias for statistical analysis.

In the ON/MS group, the female to male ratio was 21: 1. The mean age was 35.0 years (16-51 years of age). Sixteen patients had acute unilateral ON and six patients had bilateral ON. Eighteen of 22 (81.8%) patients suffered recurrent ON, of which 12 (66.7%) patients suffered this before the diagnosis of MS. The fVEP latency in affected eyes was recorded in 17 patients while two patients had a non-recordable result. The PRVEP in affected eyes was recorded in 15 patients while one patient had a non-recordable result. The median value of the latency of fVEP and PRVEP in the affected eyes was 141 msec (interquatile range, 129-148) and 142.5 msec (interquatile range, 134-154.5) respectively.

Comparison of the median value of the latency of VEP in the affected eyes of the recurrent ON group and the acute ON group with a Mann-Whitney U test showed the median value of the latency of fVEP and PRVEP of the recurrent ON group was longer than that of the acute ON group, which was statistically significant (fVEP, $p = 0.012$; PRVEP, $p = 0.004$).

Comparison of the median value latency of VEP in the affected eyes of the ON/MS group and the acute ON group with a Mann-Whitney U test showed

Table 1. The clinical features of the acute optic neuritis group, the recurrent optic neuritis group and ON/MS group

Clinical features	Optic neuritis Group	Recurrent optic neuritis Group	ON/MS Group
Numbers of patients	22	8	22
Sex (female:male)	2.7:1	7:1	21:1
Age (year) mean (range)	37.4 (17-57)	36.9 (27-50)	35 (16-51)
Bilateral Optic Neuritis	1	2	6
Recurrent optic neuritis	-	8 (100%)	18 (81.8%)

ON/MS group = optic neuritis with multiple sclerosis group

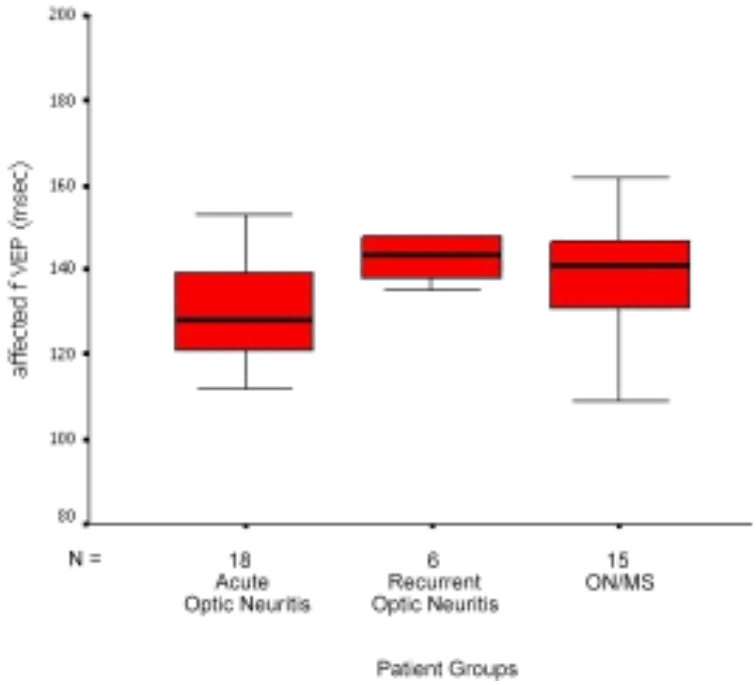

Fig. 1 The median value of the latency of flashed VEP in the affected eyes of the acute optic neuritis group, the recurrent optic neuritis group and ON/MS group (fVEP = flashed visual evoked potential; ON/MS group = optic neuritis with multiple sclerosis group)

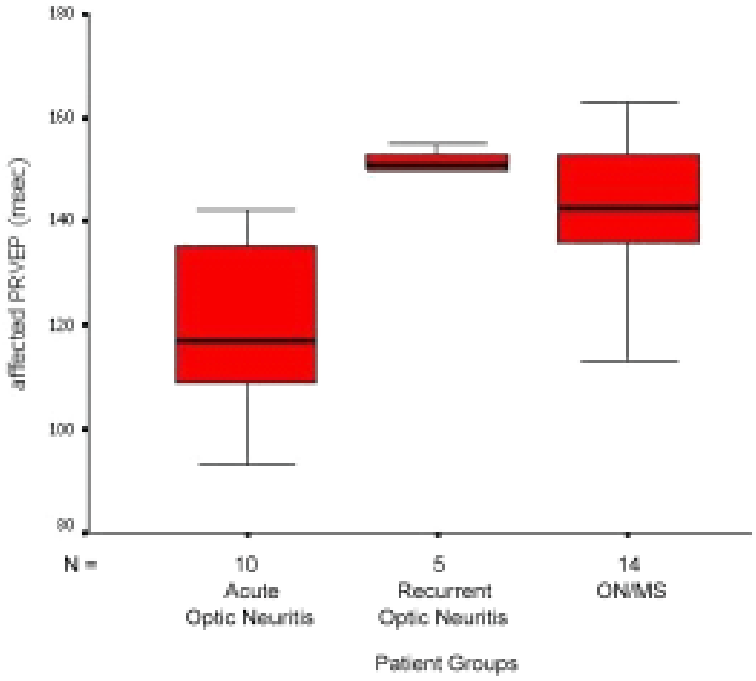

Fig. 2 The median value of the latency of pattern reversal VEP in the affected eyes of the acute optic neuritis group, the recurrent optic neuritis group and ON/MS group (PRVEP = patterned reversal visual evoked potential; ON/MS group = optic neuritis with multiple sclerosis group)

Table 2. Comparisons of the median value of flashed VEP latency in the affected eyes of the acute optic neuritis group, the recurrent optic neuritis group and ON/MS group. The statistical analysis is Mann-Whitney U test and the β-value

Patient Group median fVEP Latency (msec)	Recurrent Optic Neuritis 143.5	ON/MS 141
Acute Optic Neuritis 128	p-value = 0.012	p-value = 0.081
Recurrent Optic Neuritis 143.5	-	p-value = 0.458

fVEP = flashed visual evoked potential; ON/MS = optic neuritis with multiple sclerosis group

Table 3. Comparisons of the median value of pattern reversal VEP latency in the affected eyes of the acute optic neuritis group, the recurrent optic neuritis group and ON/MS group. The statistical analysis is Mann-Whitney U test and the β-value

Patient Group median PRVEP Latency (msec)	Recurrent Optic Neuritis 151	ON/MS 142.5
Acute Optic Neuritis 117	p-value = 0.004	p-value = 0.002
Recurrent Optic Neuritis 151	-	p-value = 0.403

PRVEP = patterned reversal visual evoked potential; ON/MS group = optic neuritis with multiple sclerosis group

the median value of the latency of fVEP of the ON/MS group was longer but was not statistically significant (fVEP, p = 0.081). However, the median value of the latency of PRVEP of the ON/MS group was longer than that of the acute ON group, which was statistically significant (PRVEP, p = 0.002).

Comparison of the median value latency of VEP in the affected eyes of the recurrent ON group and the ON/MS group with a Mann-Whitney test showed the median value of the latency of both fVEP and PRVEP of the recurrent ON group was longer than that of the ON/MS group. However, this was not statistically significant (fVEP, p = 0.458; PRVEP, p = 0.403) (Table 2, 3).

Discussion

The present study showed the same demographic data between the ON/MS group and the ON groups. In the present study, the latency of VEP in the affected eyes of patients with ON/MS and ON both showed delay of the latency as in previous studies[1-3,8,9].

Some patients in the present study had a normal latency of fVEP, but had a prolonged latency of PRVEP. According to a previous study, which explained the delayed PRVEP with a relatively undelayed fVEP that the lesion in ON is likely to be confined to the fibers of the optic nerve, therefore the dissociation between the two responses suggests that they may be mediated by different groups of fibers in the optic nerve[2]. The PRVEP response is known to depend on fibers subserving central vision, which is the portion of the field most affected in ON and the undelayed fVEP response may possibly be mediated by the more peripheral retina, the fibers of which may be relatively preserved[2]. As documented in previous studies, the result of VEP test in the present study is the reliable diagnostic test for demonstrating ON and PRVEP is a sensitive method of detecting the damage to the optic nerve rather than fVEP[1,2].

As in previous reports, the result of the present study also showed that the mean latency of the VEP in affected eyes with acute ON was significantly shorter than that with ON/MS[3,8]. Moreover, the authors found that it was significantly shorter than that of recurrent ON also. Previous studies explained that the progressive shortening of VEP latency was caused by an ongoing process of remyelination, which took from several months to more-than-two-years to be completed[9]. The axonal regeneration of the optic nerve, which temporarily occurs in some patients, could make the prolonged VEP latency in the recovery stage of the disease to a normal value range. However, the latency was delayed again due to the recurrent attack of ON[10]. Therefore, in the present study, the lengthening of mean VEP latency in recurrent ON and ON/MS over that in acute ON was possibly caused by the greater degree of involvement of the optic nerve conduction from the recurrent attacks and MS itself.

In the present study, more than a half (12/22)

of the patients in the ON/MS group had a history of recurrent ON before the diagnosis of CDMS. Previous studies concluded that recurrent ON is one of the factors influencing the risk of multiple sclerosis[4,5,11,12]. Although the present study could not find any influence of recurrent ON to turn to be definite MS, the authors were able to demonstrate the similarity between ON/MS and recurrent ON, especially the lengthening of VEP latency in the affected eyes over that of the acute ON.

The delay of VEP latency, especially from PRVEP, can be used to demonstrate the demyelinating mechanism of ON and ON/MS. The VEP latency in the affected eyes of ON/MS and of recurrent ON is significantly longer than that of acute ON. The present study used a retrospective method, with a short follow up period and a small sample size. Therefore, the authors cannot determine the susceptibility of the patients with ON, especially recurrent ON, to turn to be MS. However, physicians should pay attention to the additional neurological symptoms suggestive of MS in patients with recurrent ON.

References

1. Asselman P, Chadwick DW, Marsden DC. Visual evoked responses in the diagnosis and management of patients suspected of multiple sclerosis. Brain 1975; 98: 261-82.
2. Halliday AM, McDonald WI, Mushin J. Delayed visual evoked response in optic neuritis. Lancet 1972; 1: 982-5.
3. Frederiksen JL, Petrera J. Serial visual evoked potentials in 90 untreated patients with acute optic neuritis. Surv Ophthalmol 1999; 44(Suppl 1): S54-62.
4. Compston DA, Batchelor JR, Earl CJ, McDonald WI. Factors influencing the risk of multiple sclerosis developing in patients with optic neuritis. Brain 1978; 101: 495-511.
5. Isayama Y, Takahashi T, Shimoyoma T, Yamadori A. Acute optic neuritis and multiple sclerosis. Neurology 1982; 32: 73-6.
6. Poser CM, Paty DW, Scheinberg L, McDonald WI, Davis FA, Ebers GC, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol 1983; 13: 227-31.
7. Polman CH, Reingold SC, Edan G, Filippi M, Hartung HP, Kappos L, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria". Ann Neurol 2005; 58: 840-6.
8. Jones SJ. Visual evoked potentials after optic neuritis. Effect of time interval, age and disease dissemination. J Neurol 1993; 240: 489-94.
9. Brusa A, Jones SJ, Plant GT. Long-term remyelination after optic neuritis: a 2-year visual evoked potential and psychophysical serial study. Brain 2001; 124(Pt 3): 468-79.
10. Hidajat RR, Goode DH. Normalisation of visual evoked potentials after optic neuritis. Doc Ophthal mol 2003; 106: 305-9.
11. Cohen MM, Lessell S, Wolf PA. A prospective study of the risk of developing multiple sclerosis in uncomplicated optic neuritis. Neurology 1979; 29: 208-13.
12. Nilsson P, Larsson EM, Maly-Sundgren P, Perfekt R, Sandberg-Wollheim M. Predicting the outcome of optic neuritis: evaluation of risk factors after 30 years of follow-up. J Neurol 2005; 252: 396-402.

การศึกษาเปรียบเทียบการตรวจประสาทตาด้วยคลื่นไฟฟ้าในผู้ป่วยโรคเส้นประสาทตาอักเสบและผู้ป่วยโรคเส้นประสาทตาอักเสบร่วมกับโรคมัลติเพิลสเคลอโรซิส

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วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบการตรวจประสาทตาด้วยคลื่นไฟฟ้าในผู้ป่วยโรคเส้นประสาทตาอักเสบและผู้ป่วยโรคเส้นประสาทตาอักเสบร่วมกับโรคมัลติเพิลสเคลอโรซิส*

วัสดุและวิธีการ: *ทำการศึกษาย้อนหลังผลการตรวจประสาทตาด้วยคลื่นไฟฟ้าในผู้ป่วยโรคเส้นประสาทตาอักเสบที่ภาควิชาจักษุวิทยา คณะแพทยศาสตร์ศิริราชพยาบาลระยะเวลาตั้งแต่ พ.ศ. 2538 ถึง พ.ศ. 2548 โดยแบ่งผู้ป่วยออกเป็น 3 กลุ่มได้แก่ผู้ป่วยโรคเส้นประสาทตาอักเสบ ผู้ป่วยโรคเส้นประสาทตาอักเสบที่กลับเป็นซ้ำอีก และผู้ป่วยโรคเส้นประสาทตาอักเสบร่วมกับโรคมัลติเพิลสเคลอโรซิส โดยคัดกลุ่มผู้ป่วยที่วัดค่าผลของการตรวจประสาทตาด้วยคลื่นไฟฟ้าไม่ได้ ออกจากการศึกษา และนำค่าเฉลี่ยของ latency ของผลการตรวจประสาทตาด้วยคลื่นไฟฟ้าในผู้ป่วยแต่ละกลุ่มมาเปรียบเทียบทางสถิติ*

ผลการศึกษา: *ผู้ป่วยโรคเส้นประสาทตาอักเสบที่ทำการศึกษามีจำนวน 22 ราย ผู้ป่วยโรคเส้นประสาทตาอักเสบที่กลับเป็นซ้ำอีกมีจำนวน 8 ราย และผู้ป่วยโรคเส้นประสาทตาอักเสบร่วมกับโรคมัลติเพิลสเคลอโรซิสมีจำนวน 22 ราย โดยทั้งสามกลุ่มมีอายุเฉลี่ยไม่แตกต่างกัน ค่าเฉลี่ยของ latency ของผลการตรวจประสาทตาด้วยคลื่นไฟฟ้า (flash VEP และ pattern reversal VEP) ในผู้ป่วยโรคเส้นประสาทตาอักเสบ สั้นกว่าในผู้ป่วยโรคเส้นประสาทตาอักเสบที่กลับเป็นซ้ำอีกอย่างมีนัยสำคัญทางสถิติ สำหรับค่าเฉลี่ยของ latency ของผลการตรวจประสาทตาด้วยคลื่นไฟฟ้า (pattern reversal VEP) ในผู้ป่วยโรคเส้นประสาทตาอักเสบสั้นกว่าในผู้ป่วยโรคเส้นประสาทตาอักเสบร่วมกับโรคมัลติเพิลสเคลอโรซิส อย่างมีนัยสำคัญทางสถิติ แต่ค่าเฉลี่ยของ latency ของผลการตรวจประสาทตาด้วยคลื่นไฟฟ้า (flash VEP และ pattern reversal VEP) ในผู้ป่วยโรคเส้นประสาทตาอักเสบที่กลับเป็นซ้ำอีก และผู้ป่วยโรคเส้นประสาทตาอักเสบร่วมกับโรคมัลติเพิลสเคลอโรซิสไม่แตกต่างกัน*

สรุป: *ค่า latency จากผลการตรวจประสาทตาด้วยคลื่นไฟฟ้าที่ยาวกว่าปรกติในผู้ป่วยโรคเส้นประสาทตาอักเสบอาจจะแสดงถึงการที่มีภาวะเยื่อไมอีลินเสื่อมร่วมด้วย แต่ไม่สามารถนำมาใช้พยากรณ์โรคว่าผู้ป่วยโรคเส้นประสาทตาอักเสบรายใดจะมีโอกาสกลายเป็นโรคมัลติเพิลสเคลอโรซิสในอนาคต ส่วนค่า latency ที่ยาวกว่าปรกติในผู้ป่วยโรคเส้นประสาทตาอักเสบที่กลับเป็นซ้ำอีกน่าจะเกิดจากการที่มีพยาธิสภาพที่เส้นประสาทตาบ่อย ๆ จนทำให้การนำสัญญาณประสาทเสียไปอย่างมาก ไม่ได้แสดงว่าผู้ป่วยจะมีโอกาสเป็นโรคมัลติเพิลสเคลอโรซิสเพิ่มขึ้น*