Original Article

Association between Visual Evoked Potential and Disease Severity, Disease Duration and Visual Hallucination in Patients with Idiopathic Parkinsonism

Mahnaz Talebi[1,a], Arash Meshkinghalam[2], Sasan Andalib[1,b]

[1] Neurosciences Research Center, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran
[2] School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Abstract

Background: Parkinson's disease (PD) is a neurodegenerative disorder impairing motor, verbal and other abilities. Visual evoked potential (VEP) assessment is a useful method for analysis of visual system and its function. The present study was designed in order to evaluate whether VEP changes are associated with PD.

Materials and Methods: In the present study, 100 subjects encompassing 40 patients with Idiopathic Parkinson's Disease (Idiopathic PD) and 60 aged-matched controls were selected and assigned into case and control groups, respectively. VEP analysis was conducted in either group and the results were compared.

Results: In the present study, 16 patients (40%) showed prolonged P100 latency. P100 latency in the case group was significantly longer than in controls. P100 Amplitude was significantly higher in case group than control. There were no significant association between prolonged VEP and sex and diseases duration, in the participants. Also from our participants who suffer from visual hallucination, P100 latency was significantly longer than in the controls. There was a significant association between prolonged P100 latency and severity of disease in the case group.

Conclusion: We suggest that prolonged VEP latencies and amplitude are associated with PD and might be associated with a predisposition for visual hallucinations.

Keywords: Idiopathic Parkinson disease, visual evoked potential, visual hallucination

Corresponding Author: [a] Mahnaz Talebi, Neurosciences Research Center, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran. Email: talebi511@yahoo.com
[b] Sasan Andalib, Neurosciences Research Center, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran. Email: andalibsa@tbzmed.ac.ir

Please cite this article as: Talebi M, Meshkinghalam A, Andalib S. Association between Visual Evoked Potential and Disease Severity, Disease Duration and Visual Hallucination in Patients with Idiopathic Parkinsonism. Novel Biomed. 2014;2(4):120-5.

Introduction

Parkinson's disease (PD) is one of the paramount neurodegenerative disorders giving rise to motor and non-motor impairment[1,2]. Over 4 million people with age above 50 years present with PD and this rate is assumed to double during the next 2 decades[3]. Although PD pathogenesis is complex nevertheless, genetics has been shown to be a crucial contributing factor[4]. Tremor is the most apparent symptom in PD; even so, bradykinesia, rigidity, postural instability are present[5]. In spite of the movement difficulties bringing about motor symptoms, PD patients may experience non-motor symptoms encompassing autonomic dysfunction, neuropsychiatric problems and sensory, sleep and visual problems[5]. It is said that 60 to 80 percent of dopaminergic neurons are destroyed in the motor impairment. PD is almost incurable; but Levodopa, which is administered to compensate this imbalance, is a common treatment for PD[6]. MAO-B

inhibitors, dopamine antagonists and surgery have been used to treat PD. Modafinil has also been demonstrated to exert antiparkinsionian effect[7]. One of the manifestations of PD is impaired vision system. Visual hallucination (seeing things)[8] and impaired determination of lines positions and directions[9] are also seen in PD. Patients' visual contrast is also impaired, especially in low-light environments. Not only are PD patients' eyes unable to be kept in top position, but also they cannot focus on objects and follow them[10,11]. This impairment may be due to a reduction in dopamine level in retina, or dopamine's effect upon Geniculatus lateralis nucleus synapsis and visual cortex[12,13]. Visual evoked potential (VEP) refers to a potential resulting from visual cortex response to visual stimuli. It is a useful criterion in order to evaluate visual system function and optic tract. VEP provides valuable information in patients with hemodialysis and peritoneal dialysis . In several studies, VEP analysis has been applied to assess visual system in PD[14,15] multiple sclerosis[16], chronic renal failure[17,18] and diabetes[19]. VEP is classified into PR-VEP (pattern reversal) using checkerboard stimuli and F-VEP using flash stimuli, but the former is more sensitive. VEP results incorporates N75 latency, P100 latency, N140 latency, P100 amplitude; even so, P100 latency is the best wave for assessment of VEP results[9,20]. Several studies devoted attention to impaired visual system in PD patients, howbeit, little is known about the usefulness of VEP findings in diagnosis of PD. Calzetti et al. reported that prolonged VEP latencies were affected by PD, they can be helpful in clinical diagnosis of early PD[21]. Tartaglione et al. also showed that PD gave rise to prolonged Lat P100[22]. The importance of the present study lies in the fact that little is known about the usefulness of VEP findings in diagnosis of PD severity.

The present study covers the gap created by the little available information regarding the association of VEP results with disease severity and visual hallucination. Therefore, our aim was to explore the association of VEP results with severity and visual problems of PD, which was not covered by the previous published studies. To be more precise, we specifically investigated VEP results in PD patients and controls, and assessed the association of VEP results with disease duration, disease severity and visual hallucination.

Methods

In the present study, a case-control design was utilized. Forty PD patients were recruited from November 2008 to April 2010. These subjects were selected from PD statistical population of the East Azarbaijan province (recruited from two different centers include neurology ward of Imam Reza hospital and Sheikhorraeis clinic, Tabriz University of Medical Sciences, Tabriz, Iran). Sixty controls were selected from various hospital wards excepting neurology and ophthalmologic wards to preclude selection bias. The controls were also controlled by a clinician for not presenting with neurologic or ophthalmologic problems. Study size was calculated using data published in a preceding thesis. The case group were clinically selected according to diagnostic criteria for PD[23]. The PD subjects were being treated by Madopar, Amantadine, and Trihexyphenidyl; however, these medications would not affect the VEP finding in PD subjects. It is worth mentioning that PD subjects and controls presenting with diseases, affecting VEP findings such as ophthalmologic diseases, multiple sclerosis, history of stroke, migraine, renal failure, diabetic retinopathy, hypertensive retinopathy, glaucoma, and cataract, were excluded from the study. The cases were then subdivided to 7 subgroups predicated upon Hoehn and Yahr criteria[24] in order to assess the association of VEP findings with increase in disease severity. The subjects were also subdivided into 3 subgroups (< 1 year, 1 year < < 5 years, 5 years <) in order to assess the association of VEP findings with disease duration. Although no previous study utilized such subdivision, this provided a novel and more precise assessment of the duration of PD. The patients with visual hallucination (seeing things) were clinically diagnosed by a neurologist in order to assess the association of VEP findings with visual hallucination. Sixty subjects were selected for the control group (1.5 controls per case). To limit confounding effect, a frequency matching was carried out for cases and controls predicated upon age (>50years & <50years). The outcome included Idiopathic Parkinson Disease which was rated by means of MDS-UPDRS rating scale[25], and the

Table 1: Demographic information of the case and control groups.

	Case group	Control group
Number of participants	40	60
Gender	26 males	36 males
	14 females	24 females
Average age	62.10±10.98 years	62.10±9.8 years
	38-72 years	38- 76 years

exposure was VEP results. A questionnaire was prepared and a complete history of each patient was recorded. All the subjects were assessed for VEP by using four channeled Neuroscan plus Tonnis. By means of Oz-Fz electrode location, an apparatus sensitivity of 20, checker board pattern of apparatus and standard color, visual stimuli were given to visual field. It is worth noting that assessment of VEP is a non-invasive study. All participants gave an informed consent prior to commencement of the study. All the protocols of the research were approved by the ethical research committee of Tabriz University of Medical Science. Statistical analyses were performed using the SPSS statistical software package (Version 15.0). More precisely, Chi square was used for categorical variables and t-test analysis was applied for quantitative variables. The results were significant at the p-value<0.05 level.

Table 2: VEP findings in the case and control groups.

VEP latency and amplitude	**Mean ± Standard deviation**		**P value**
	Case group	Control group	
Lat N75	81.77±9.68	78.33±5.15	0.04*
Lat P100	114.80±16.61	110.44±4.53	0.0001*
Lat N140	159.82±14.99	144.71±9.32	0.0001*
Amp P100	13.51±11.56	8.93±5.20	0.002*

Note: Lat N75: N75 latency, Lat P100: P100 latency, Lat N140: N140 latency, Amp P100: P100 amplitude; *P-value<0.05

Results

Table 1 shows demographic information of the case and control group. No significant difference was observed in gender between cases and controls.

Disease duration was from 3 months to 20 years with an average of 8.2±6.45. Nine out of 40 patients presented with visual hallucination (22.5%). Of these patients, 4 cases were male (15.4%) and 5 cases were female (35.7%).

Table 2 provides a breakdown pertaining to VEP results in the case and control groups. P100 latency in the cases was significantly longer than in the controls (p<0.0001). N140 latency in the cases was significantly longer than in

Table 3: Association between duration of disease and VEP findings.

VEP latency and amplitude	**Duration of disease (Mean ± Standard deviation)**			**p-value**
	< 1year	1year< <5years	Less than 5years	
Lat N75	80.95±10.41	81.34±10.72	82.79±8.74	0.852
Lat P100	108.60±26.15	114.38±17.15	118.65±8.66	0.522
Lat N140	159.04±7.41	158.94±16.45	161.82±17.02	0.69
Amp P100	15.99±16.11	15.29±13.45	9.72±2.96	0.505

Note: Lat N75: N75 latency, Lat P100: P100 latency, Lat N140: N140 latency, Amp P100: P100 amplitude; *p-value<0.05

Table 4: VEP findings in patients with hallucination.

VEP latency and amplitude	Mean±Standard deviation		p-value
	Patients with hallucination	Control group	
Lat N75	83.77±12.30	78.33±5.15	0.49
Lat P100	124.22±15.01	110.44±4.53	0.05*
Lat N140	169.56±19.85	144.71±9.32	0.02*
Amp P100	11.17±4.72	8.93±5.20	0.5

Note: Lat N75: N75 latency, Lat P100: P100 latency, Lat N140: N140 latency, Amp P100: P100 amplitude; *p-value<0.05

controls (p<0.0001). N75 latency in cases was significantly prolonged, in comparison with that of control group (p<0.04). P100 amplitude was significantly higher in the case group than in the control group (p<0.02).

There was no significant association between P100 latency between two eyes in cases (p=0.90). Moreover, 24 patients (60%) experienced a normal P100 latency (118 ms), notwithstanding 16 patients (40%) with a P100 latency of longer than normal.

There was no significant association between prolonged VEP findings and gender in the patients with PD. It is worth noting that there was a no significance association between prolonged P100 latency and gender (p=0.343).

Table 3 indicates the association between disease duration and VEP findings. No significant association was found between prolonged VEP findings and disease duration in the patients with PD.

Table 4 depicts VEP findings with hallucination. N140 latency was significantly longer in the patients with hallucination than in the control group (p=0.02). Patients with visual hallucination showed P100 latency longer compared controls (p=0.05). Table 5 illustrates the association of VEP findings with an increase in disease severity. There was a significant association between P100 latency and the increase in disease severity (p=0.04). N140 latency was significantly associated with the increase in disease severity (p=0.006).

Table 5: Association of VEP findings with increase in disease severity.

VEP latency and amplitude	p-value
Lat N75	0.978
Lat P100	0.04*
Lat N140	0.006*
Amp P100	0.34

Note: Lat N75: N75 latency, Lat P100: P100 latency, Lat N140: N140 latency, Amp P100: P100 amplitude; *p-value<0.05

Discussion

Visual problem is one of the characteristics of PD and VEP analysis as a useful assessment of visual system can give assistance to neurologists to diagnose PD visual problems. Recently, there has been an increasing interest in investigating visual problems in PD patients; nonetheless, little is known about the usefulness of VEP findings in diagnosis of PD. This investigation, thus, sought to address the question whether VEP findings are associated with PD. The findings of the present study indicated that all VEP findings including Lat N75, Lat P100, Lat N140, Amp P100 were associated with PD. Our findings produced results, which corroborated the findings of Tartaglione et al. investigating VEP findings in 13 PD subjects and 13 controls[22]. The authors observed that 69 percent of the PD subjects experienced prolonged P100 latencies. Another study was carried out by Calzetti et al. on 9 patients (4 men, 5 women) and 12 controls and significant prolonged latencies were found in VEP results in the patients, compared to the controls[21]. Kurita et al. demonstrated visual hallucination in PD patients[26]. We found that hallucination influenced Lat P100 and Lat N140 in patients with PD. In this regard, our findings were consistent with those of Matsui et al. who studied VEP results in PD patients with hallucination and observed an association between visual hallucination and prolonged P100 latency[27]. Be that as it may, Onofrj et al. reported that abnormal

VEP results did not correlate with the incidence of hallucination in patients with PD[28]. According to our results, no relationship was observed between VEP findings and duration of disease. We also found that prolonged P100 and N140 latencies were associated with increase in severity of disease. This result support the findings of Kupersmith et al., reporting a positive association of P100 latency with the severity of the movement disability[29]. The evidence from the present study suggests that prolonged latency and high amplitude of VEP may be associated with PD.

In conclusion, our results met the aims of this study indicating that VEP results may be associated with severity of PD. Taking into the account of the results of the present study and those corroborating our results, VEP analysis can be suggested as a useful assessment in the diagnosis of visual problems in early PD. However, further work should be undertaken to establish whether VEP analysis can be effectively used in this regard. It is, thus, suggested that the effectiveness of VEP assessment in diagnosis of early PD is investigated in future studies.

Acknowledgment

None declared.

References

1. Braak H, Ghebremedhin E, Rub U, Bratzke H, Del Tredici K. Stages in the development of Parkinson's disease-related pathology. Cell Tissue Res. 2004;318(1):121-34.

2. Perfetti B, Moisello C, Lanzafame S, Varanese S, Landsness E, Onofrj M, Di Rocco A, Tononi G, Ghilardi MF. Attention modulation regulates both motor and non-motor performance: a high-density EEG study in Parkinson's disease. Archives italiennes de biologie. 2010;148(3):279-88.

3. Dorsey ER, Constantinescu R, Thompson JP, Biglan KM, Holloway RG, Kieburtz K, Marshall FJ, Ravina BM, Schifitto G, Siderowf A, Tanner CM. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology. 2007;68(5):384-6.

4. Andalib S, Vafaee MS, Gjedde A. Parkinson's disease and mitochondrial gene variations: A review. J Neurol Sci. 2014. DOI: 10.1016/j.jns.2014.07.067 (In Press)

5. Jankovic J. Parkinson's disease: clinical features and diagnosis. J Neurol Neurosurg Psychiatry. 2008;79(4):368-76.

6. Savitt JM, Dawson VL, Dawson TM. Diagnosis and treatment of Parkinson disease: molecules to medicine. J Clin Invest. 2006;116(7):1744-54.

7. Farhoudi M, Sadigh-Eteghad S, Andalib S, Vafaee MS, Ziaee M, Mahmoudi J. An analytical review on probable anti-parkinsonian effect of modafinil. J Analyt Res Clin Med. 2013;1(2):58-62.

8. Armstrong RA. Visual symptoms in Parkinson's disease. Parkinsons Dis. 2011;2011:908306.

9. Bandini F, Pierantozzi M, Bodis-Wollner I. Parkinson's disease changes the balance of onset and offset visual responses: an evoked potential study. Clin Neurophysiol. 2001;112(6):976-983.

10. Antal A, Terney D, Bodis-Wollner I. Parkinson's disease, aging, and visual cognition. Topics in Geriatric Rehabilitation. 2008;24(2):166-81.

11. Onofrj M, Bonanni L, Albani G, Mauro A, Bulla D, Thomas A. Visual hallucinations in Parkinson's disease: clues to separate origins. Journal of the neurological sciences. 2006;248(1):143-150.

12. Okuda B, Tachibana H, Kawabata K, Takeda M, Sugita M. Visual evoked potentials (VEPs) in Parkinson's disease: correlation of pattern VEPs abnormality with dementia. Alzheimer Dis Assoc Disord. 1995;9(2):68-72.

13. Gottlob I, Schneider E, Heider W, Skrandies W. Alteration of visual evoked potentials and electroretinograms in Parkinson's disease. Electroencephalogr Clin Neurophysiol. 1987;66(4):349-357.

14. Yazdchi M, Talebi M, Aghbiglo AM, Mashrabi O. Role of visual evoked potential (VEP) and Somatosensory evoked potential (SSEP) in prediction Parkinson's diseases with dementia. Int J Curr Res Aca Rev.2(7):177-86.

15. Gawel MJ, Das P, Vincent S, Rose FC. Visual and auditory evoked responses in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry. 1981;44(3):227-32.

16. Klistorner A, Garrick R, Barnett MH, Graham SL, Arvind H, Sriram P, Yiannikas C. Axonal loss in non-optic neuritis eyes of patients with multiple sclerosis linked to delayed visual evoked potential. Neurology. 2012;80(3):242-5.

17. Talebi M, Sayadnasiri M, Azar SA. Effect of renal transplantation on visual evoked potential abnormalities of chronic renal failure. Transplant Proc. 2010;42(10):3994-7.

18. Azar SA, Talebi M, Aghdam AT, Shishavan RH, Andalib S. Comparison of Visual Evoked Potentials in Patients Undergoing Peritoneal Dialysis and Hemodialysis and its Association with Blood Biochemical Profile. J Expand Clin Neuro. 2014;1(1). DOI: http://dx.doi.org/10.13183/jecns.v1i1.4 (In Press)

19. Karlica D, Galetovic D, Ivanisevic M, Skrabic V, Znaor L, Jurisic D. Visual evoked potential can be used to detect a prediabetic form of diabetic retinopathy in patients with diabetes mellitus type I. Coll Antropol. 2010;34(2):525-9.

20. Sener HO, Akbostanci MC, Yucesan C, Dora B, Selcuki D. Visual evoked potentials in Parkinson's disease-correlation with clinical involvement. Clin Neurol Neurosurg. 2001;103(3):147-50.

21. Calzetti S, Franchi A, Taratufolo G, Groppi E. Simultaneous VEP and PERG investigations in early Parkinson's disease. Journal of Neurology, Neurosurgery & Psychiatry. 1990;53(2):114-7.

22. Tartaglione A, Pizio N, Bino G, Spadavecchia L, Favale E. VEP changes in Parkinson's disease are stimulus dependent. Journal of Neurology, Neurosurgery & Psychiatry. 1984;47(3):305-7.

23. Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. Archives of neurology. 1999;56(1):33-9.

24. Hoehn MM, Yahr MD. Parkinsonism: onset, progression, and mortality. 1967. Neurology. 2001;57(10 Suppl 3):S11-26.

25. Goetz CG, Fahn S, Martinez-Martin P, Poewe W, Sampaio C,

Stebbins GT, Stern MB, Tilley BC, Dodel R, Dubois B, Holloway R, Jankovic J, Kulisevsky J, Lang AE, Lees A, Leurgans S, LeWitt PA, Nyenhuis D, Olanow CW, Rascol O, Schrag A, Teresi JA, Van Hilten JJ, LaPelle N. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Process, format, and clinimetric testing plan. Mov Disord. 2007;22(1):41-7.

26. Kurita A, Murakami M, Takagi S, Matsushima M, Suzuki M. Visual hallucinations and altered visual information processing in Parkinson disease and dementia with Lewy bodies. Movement Disorders. 2010;25(2):167-71.

27. Matsui H, Udaka F, Tamura A, Oda M, Kubori T, Nishinaka K, Kameyama M. The relation between visual hallucinations and visual evoked potential in Parkinson disease. Clin Neuropharmacol. 2005;28(2):79-82.

28. Onofrj M, Thomas A, D'Andreamatteo G, Iacono D, Luciano AL, Di Rollo A, Di Mascio R, Ballone E, Di Iorio A. Incidence of RBD and hallucination in patients affected by Parkinson's disease: 8-year follow-up. Neurol Sci. 2002;23 Suppl 2:S91-4.

29. Kupersmith MJ, Shakin E, Siegel IM, Lieberman A. Visual system abnormalities in patients with Parkinson's disease. Arch Neurol. 1982;39(5):284-6.