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Role of visual evoked potential (VEP) and Somatosensory evoked potential (SSEP) in prediction Parkinson's diseases with dementia

Mohammad Yazdchi¹, Mahnaz Talebi¹, Afshin Mardani Aghbiglo¹, and Omid Mashrabi²

¹Neuroscience research center (NSRC), Department of Neurology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

²Resident of Internal Medicine, Internal Medicine Department, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

*Corresponding author

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A B S T R A C T

Parkinsonism occurs in all races. Its prevalence in the United States and Western Europe is 2.1 persons per 1,000 populations. Approximately one third of patients have cognitive problems that often doubles after 4 years in 80% of patients with dementia and Parkinson's disease occurs in the final stages. The aim of this study was to determine the relationship between visual evoked potential (VEP) and Somatosensory evoked potential (SSEP) findings in patients with Parkinson's disease with dementia. In a case-control study that performed in neurology department of Tabriz University of medical sciences on patients with Parkinson's disease (PD), relationship between VEP and SSEP findings in 60 patients with Parkinson's disease with dementia evaluated. Right VEP amplitude (AMP) in 12 was abnormal and left VEP AMP was abnormal in 13 patients. Mean right VEP P100 was 104 ± 24.18 and mean left VEP P100 was 104.94 ± 24 and also, left and right VEP P100 were abnormal in 24(40%). Significant liner correlation was not found between MMSE score with left and right VEP 100, Left and right VEP AMP, right SSEP P40 and SSEP AMP but, Significant liner correlation was found between MMSE score with left SSEP and SSEP P40. Significant difference was not found in mean of P100 Latency in patients with and without disorder. Significant difference was not found between SSEP AMP of patients with Parkinson's disease with and without functional disorder.

Introduction

Parkinsonism occurs in all races, and its prevalence is 1-2 in every 1000 persons, and is almost viewed in both sexes to a level. With increasing age the probability of the occurrence of this disease ameliorate and is

distinguished by tumor, rigidity and abnormal gait update. The most common type of Parkinsonism occurs without specific cause which is regarded as idiopathic form of Parkinson's disease. After Alzheimer,

Parkinson's disease is the most common fatal disease of the central nervous system resulting in death of dopamine secreting cells in the black body in the brain and erratic body movements occur in the absence of dopamine (1-4). In General, there are four types of Parkinsonism: idiopathic Parkinsonism, secondary Parkinson's disease, Parkinson's syndrome and other neurodegenerative diseases that its primary manifestation is as Parkinsonism (5). Primary Parkinson's disease is the most common initial manifestation of a variety of Parkinsonism and is evident in about 80% of patients with motor disorders. The basic Patho-anatomical findings in patients with idiopathic Parkinson's disease also reveal the loss of neurons containing myelin. These neurons exist in particular areas of the brain including the substantia nigra and *Nucleus locus coeruleus*. Dopamine levels in these patients are approximately 80 percent lower than normal levels (6).

The positron emission tomography (PET) and single-photon emission computed tomography (SPECT) studies have proved that besides the nigrostriatal system changes observed in Parkinson's disease (PD) patients, the additional changes were found in the cerebral cortex and the limbic system in the patients with Parkinson's disease with dementia (PDD) by use of PET which is not observed in the Parkinsonism. In contrast to the Alzheimer's disease (AD) patients with the most magnetic resonance imaging(MRI) changes in the temporal lobes and hippocampus, the occipital lobe atrophy is observed in the MRI of PDD patients. In the SPECT of PD patients, the decreased perfusion is found in the frontal, occipital areas and temporoparietal junction.

The evoked responses techniques are used in the multiple sclerosis (MS) diagnosis to discover the subclinical lesions in the optic nerve, spinal cord and brainstem (7-8). This technique is mostly used to check the

function of the nervous system rather than the diagnosis of function abnormality. In the Celestia and Daly studies, it was demonstrated that the latency of the first major negative-positive waves is increased in the visual evoked potential (VEP) by aging (9).

So the VEP could be valuable in the study of diseases such as Parkinson's which is intensified by the aging. Also Bodie and Yah indicated the abnormal latency in the major positive wave of the PD patients in their research. The increased latency in patients who were treated with Levodopa was lower. They also proved that there is a correlation between disease severity and prolongation of latency (10). The Somatosensory evoked potential (SSEP) test shows the sensory electrical signals, coming from the different organs to the brain or spinal cord.

The signals indicate whether a nerve connected to the spinal cord is able to send and receive the sensory information such as pain, temperature and touch or not. SSEP combined with electromyography (EMG) and nerve conduction velocities (NCV) is used to detect the spinal cord injuries. The main clinical benefit of the SSEP is to evaluate the patients with the generalized disorders in the nervous system such as Parkinson's, MS, etc.

Nowadays, few studies have been conducted to examine the relationship between VEP, SSEP and the dementia in the PD patients. So in this research, it has been decided to examine the relationship between VEP, SSEP findings and the dementia in patients suffered from Parkinson's. The only techniques to determine the PDD are PET scan and SPECT which may not be accessible for all patients, but the VEP and SSEP are available in any rehabilitation specialist and neurologist's offices which are

less expensive as compared to PET and SPECT.

The aim of this study is to analyze the relationship between VEP, SSEP findings and the dementia in the PD patients.

Materials and methods

In a case-control study conducted in neurology Department at Medical Sciences of Tabriz University on the PD patients, we were evaluated the relationship between VEP, SSEP findings and the dementia in Parkinsonism.

In the present research, 60 PD patients hospitalized in the neurology Department of Imam Reza hospital were selected and enrolled.

In this study, 30 PD patients with partial cognitive impairment and 30 PD patients without any partial impairment were selected and enrolled.

Selected patients were evaluated in terms of dementia by mini-mental state examination (MMSE) test and SSEP and VEP tests were performed for all patients by a person who was unaware of the test results. The SSEP and VEP results of all patients were recorded and were assessed.

Inclusion criteria

Being diagnosed with Parkinson's disease the patients in treatment process

Exclusion criteria

1. Diabetic patients
2. The patients with ocular diseases such as cataract and glaucoma
3. History of eye laser therapy
4. Retinopathy

5. Having a cervical radiculopathy and neck pain
6. An MMSE score below 15
7. Onset of disease without visual hallucination
8. After 5 years the patient not be wheelchair bounded

The MMSE test was conducted to evaluate the presence of dementia in all the 60 patients. Accordingly, patients were divided into two 30 patients groups: the patients with Parkinson's and Dementia, the patients with Parkinson's disease without dementia.

The SSEP and VEP were performed for all patients by a person who was unaware of the MMSE results then the SSEP and VEP results of all patients were recorded and were statically assessed.

The VEP was performed for the no-demented, Parkinson patients by a person who was unaware of the MMSE test results and the VEP results of these cases were recorded and were assessed.

The SSEP was performed for the no-demented, Parkinson patients by a person who was unaware of the MMSE test results and the SSEP results of these cases were recorded and were assessed.

Ethical considerations

Since all the measures taken in this study were conducted to diagnosis the disease and assess the patient's condition and also no additional costs impose on the patients, so the written consent is not necessary. However it should be noted that all the secrets or personal information of the patients and also their names and addresses were not mentioned anywhere during our research.

Limitations and potential problems and solutions:

1. Lack of Patients cooperation to participate in this research
2. Preventing the physical injuries and securing the personal information of the participants in the research.
3. Providing the impossible budget to conduct the VEP and SSEP examinations.

Statistic analysis

Descriptive methods (frequency, percentage, mean \pm SD) were used for statistical analysis and the chi-square test (X^2) and mean difference test were used to compare. All statistical analyzes were performed with SPSS 17 statistical software. The $p < 0.05$ was considered significant in all cases.

Result and Discussion

In the present study we were researched on the 60 PD patients, 30 of whom with partial impairment and other cases without any partial impairment. Their symptoms were evaluated by use of VEP and SSEP and the following results were obtained:

The VEP and SSEP findings have been shown in Table I which represents that there was no significant difference between the mean of amplitude (AMP) and VEP P100 and also the average of AMP and bilateral SSEP P40 in cases.

The VEP and SSEP findings in patients with and without partial impairment have been shown in Table II, which suggests that there was no significant difference between the findings of VEP P100 and AMP and the findings of AMP and bilateral SSEP P40 in patients with and without partial impairment. Evaluation of MMSE, Montreal and YAHR Score of patient's base on VEP and SSEP abnormality were shown in table III.

Furthermore, there was no significant linear relationship between MMSE score of

patients with AMP and bilateral VEP P100 and AMP and SSEP P40 on the right side ($P=0.576$), but there was a significant inverse linear relationship between the MMSE score of the PD patients and the AMP and SSEP P40 on the left side.

There was no relationship between Montreal score of the PD patients with the AMP and bilateral VEP P100 and the AMP and bilateral SSEP P40.

The YAHR score was not significantly related to the bilateral VEP P100 but there was a significant inverse linear relationship between the YAHR score and the bilateral VEP AMP in cases.

There was a significant direct linear relationship between YAHR score of the PD patients with the AMP and bilateral SSEP P40.

Parkinson's disease is a progressive, degenerative neurological disease, with abnormal gait which is characterized by a decrease in dopaminergic function. The first clinical symptoms occur after the 80% degeneration of dopaminergic cells in substantia nigra (11). Although the disease is characterized by symptoms, abnormal movements, but cognitive and psychiatric disorders are frequently observed in these patients (12). Approximately one third of patients have cognitive problems that often doubled after 4 years and dementia are observed in 80% of PD patients in the last stages of the disease (13). The cognitive changes in Parkinson's disease can affect the patient's daily life and even interfere with their social or occupational performance. The assessment of life quality indicates that there is a direct relationship between the poor cognitive function and the patients' life quality (14). Nowadays, the only paraclinical techniques to determine the PD from PDD are PET scan and SPECT. In this study

we've researched in order to achieve the inexpensive and readily available techniques to evaluate the PD patients. Since the VEP and SSEP are available in any neurologist's office and the technique is less expensive as compared to PET so, this study was performed by use of this technique.

Muslimovic and colleagues expressed that 50% of patients suffered from the cognitive deficits and 9% were diagnosed with dementia by the evaluating the progress of cognitive deficits among the patients with Parkinson's disease in a period of three years (15). Mc Kinlay and colleagues examined the cognitive functions in 40 patients with Parkinson stated that PD patients had worse performance in executive function, problem solving and visual - spatial skills compared to the healthy controls but there is no difference between them in the fields of attention, memory and planning (16).

Aarsland and colleagues compared the cognitive functions in 196 PD patients and demonstrated the patients with Parkinson's would act worse than the control group in all of neuropsychological tests and they believed that the awareness of high level of cognitive deficits in early stages of the disease could be very helpful in the diagnosis and management of Parkinson's disease (17).

Aarsland et al researched on the mild cognitive deficits in 1346 PD patients and suggested that the PD patients have respectively more defects in the fields of memory, visual-spatial skills, attention and executive functions (18). Mamikonian and colleagues examined the cognitive functions in the PD patients by use of the Mini Mental Status Examination so they concluded that the cognitive deficits are common in these patients and their most deficits are in memory, attention and executive functions (19).

According to the disease pathogenesis, these decreased cognitive functions could be explained in the patients with Parkinson's disease. Decreased dopamine in dorsolateral prefrontal and lateral orbitofrontal circuits could be considered as a mechanism of cognitive deficits in PD patients (20-21).

Whereas the degeneration of dopaminergic neurons of the midbrain is the pathological hallmark of Parkinson's so It appears that the cognitive deficits caused by the frontal lobe dysfunction, which is the result of the direct damage of mesocortical dopaminergic transmission or the secondary result of nigrostriatal dopaminergic performance (22). The most problem of the PD patients is in the field of the executive functions (23).

The basal nucleuses are involved in the parallel processing of sensory-motor information. The ability to distinguish two sensory stimuli and also processing the simultaneous stimuli appear to be impaired in PD patients (23).

Since the neuronal death, leading to primary motor symptoms of Parkinson's disease occurs in the central part of substantia nigra which is the sub cortical brain structure associated with the frontal cortexes and the prefrontal cortex so the dementia associated with Parkinson's disease is considered as a sub-cortical dementia. In the sub-cortical dementia, the recognition memory and higher-level language functions are less altered and the aphasia, apraxia and agnosia are rarely observed (24).

In the study conducted by Okuda and colleagues (1995) the relationship between VEP patterns and dementia has been examined in patients suffered from Parkinson's. The results of this study showed that the latency 100 in the patients with dementia is significantly longer than the non-demented cases and the latency 100 is

associated with the illness period in the patients with Parkinson's. The findings of various researches indicate that VEPs dysfunction is independent of disease progression in the demented patients. The non dopaminergic neurotransmitter systems might involve in the development of latency VEPs (24).

In our study, there was no significant linear relationship between MMSE score of patients with VEP P100 on the right side ($P=0.369$) and VEP P100 on the left side ($P=0.253$) and also there was no significant linear relationship between YAHR score of patients with VEP P100 on the right side ($P=0.160$) and VEP P100 on the left side ($P=0.614$). In our study, VEP P100 on the right side was found In the 24 abnormal patients (13 patients without partial impairment and 11 patients with partial impairment) and VEP P100 on the left side was observed In the 24 abnormal patients (14 patients without partial impairment and 10 patients with partial impairment). In our study, VEP AMP on the right side was found In the 12 abnormal patients (9 patients without partial impairment and 3 patients with partial impairment) and VEP AMP on the left side was observed In the 13 abnormal patients (8 patients without partial impairment and 5 patients with partial impairment).

In a study conducted by Dr. Taliban and al, (2010), the p100 latency in Parkinson patients was significantly longer than the control group. This difference was more intense, especially in patients with severe Parkinson associated with the hallucinations. (25) The role of lewy body and the degeneration in the cerebral cortex and limbic structures is confirmed in the recent studies on dementia due to Parkinson's.

Considering the appropriate response to cholinesterase inhibitor therapy in these patients, it seems that the dominant neurochemical problem is in the impaired cholinergic pathway and not in dopaminergic pathway (26).

In the study conducted by Zimmer and colleagues at the University of Munich at Germany, they believed that that there was no significant correlation between disease duration and VEP findings in patients with Parkinson's and there was also a significant difference between P2 Latency in the PD patients and normal cases (27). In the a study conducted by Takeda and colleagues at the University of Hyogo, Japan, the VEP results were evaluated in patients with Alzheimer's and they believed that the patients with Alzheimer's disease have a significant increase In the P100 Latency and in the patients with Alzheimer's, there was a significant correlation between MMSE score and P100 Latency. In addition, the P100 Latency is increased in PD patients with dementia compared to the control group (28).

In our study, the MMSE scores of the patients had no significant linear relationship with the bilateral VEP P100, bilateral VEP AMP, and SSEP P40 on the right side and SSEP AMP on the left side but the SSEP P40 on the right side and SSEP AMP on the left side were significantly related to the MMSE score in the patients.

In a study conducted by Peppe and his colleagues at the University of Lueia at Rome, the VEP findings were examined in the patients suffered from Parkinson and the increased P100 Latency in the cases (29) was reported.

Table.1 VEP and SSEP results of patients in both sides

	Mean ± Std Deviation	P
VEP P100 Right	104.00 ± 24.18	0.778
VEP P100 left	104.94 ± 24.60	
VEP AMP Right	2.84 ± 1.24	0.206
VEP AMP Left	3.08 ± 1.48	
SSEP P40 Right	39.77 ± 4.08	0.339
SSEP P40 Left	39.20 ± 3.98	
SSEP AMP Right	1.18 ± .67	0.141
SSEP AMP Left	1.02 ± .49	

Table.II Evaluation of VEP and SSEP abnormality with MMSE abnormality

		MMSE		P
		Normal	Abnormal	
VEP P100 Right	Normal	17	19	0.598
	Abnormal	13	11	
VEP P100 left	Normal	16	20	0.292
	Abnormal	14	10	
VEP AMP Right	Normal	21	27	0.053
	Abnormal	9	3	
VEP AMP Left	Normal	22	25	0.347
	Abnormal	8	5	
SSEP P40 Right	Normal	21	22	0.774
	Abnormal	9	8	
SSEP P40 Left	Normal	26	25	1
	Abnormal	4	5	
SSEP AMP Right	Normal	5	2	0.277
	Abnormal	7	8	
SSEP AMP Left	Normal	2	1	1
	Abnormal	11	9	

Table III: evaluation of MMSE, Montral and YAHR Score of patient's base on VEP and SSEP abnormality

		MMSE	P	Montral	P	YAHR	P
VEP P100 Right	Normal	1.53 ± 0.51	0.289	23.39 ± 5.33	0.341	1.50 ± 0.88	0.011
	Abnormal	1.46 ± 0.51		22.21 ± 3.41		2.33 ± 1.34	
VEP P100 left	Normal	1.56 ± 0.50	0.025	23.86 ± 4.50	0.054	1.56 ± 0.94	0.032
	Abnormal	1.42 ± 0.50		21.50 ± 4.63		2.25 ± 1.33	
VEP AMP Right	Normal	1.56 ± 0.50	0.462	23.08 ± 4.81	0.584	1.65 ± 1.00	0.052
	Abnormal	1.25 ± 0.45		22.25 ± 4.14		2.58 ± 1.44	
VEP AMP Left	Normal	1.53 ± 0.50	0.183	23.36 ± 4.59	0.162	1.55 ± 0.93	0.005
	Abnormal	1.38 ± 0.51		21.31 ± 4.73		2.85 ± 1.34	
SSEP P40 Right	Normal	1.51 ± 0.51	0.721	22.74 ± 5.21	0.652	1.42 ± 0.73	<0.00
	Abnormal	1.47 ± 0.51		23.35 ± 2.91		2.88 ± 1.36	
SSEP P40 Left	Normal	1.49 ± 0.50	0.148	23.49 ± 4.21	0.022	1.67 ± 1.01	0.058
	Abnormal	1.56 ± 0.53		19.67 ± 5.98		2.78 ± 1.48	
SSEP AMP Right	Normal	1.29 ± 0.49	0.649	23.00 ± 3.37	0.583	3.00 ± 1.63	0.057
	Abnormal	1.53 ± 0.52		21.60 ± 6.16		1.53 ± 0.83	
SSEP AMP Left	Normal	1.33 ± 0.58	0.028	14.33 ± 7.51	0.018	3.00 ± 1.73	0.215
	Abnormal	1.45 ± 0.51		22.60 ± 4.90		1.95 ± 1.28	

In this study, the average of VEP P100 on the right side and VEP P100 on the left side were respectively 104 ± 24.18 and 104.94 ± 24.60 . Furthermore, the abnormal VEP P100 on the left and right sides were observed in the 24 patients (40%).

In a study was conducted by Okuda et al, in Hyogo College at the Nishinomiya, Japan, the VEP findings were evaluated in the demented and non-demented Parkinson patients and it was found that the P100 Latency in the PD patients with demania is longer than the non-demented cases (30).

In our study there was no a significant difference between the P100 Latency average of the patients with and without disorders.

In the a study conducted by Langheinirich and colleagues (2000) in the Freiburg at Germany, the VEP findings were examined in the PD patients and it was observed that the SSEP amplitude was not significantly differed in the patients with and without dysfunction (31).

In the present study, the SSEP amplitude has not significantly differed in the patients with and without dysfunction.

Conclusion

The VEP AMP on the right side and the VEP AMP on the left side were respectively abnormal in 12 and 13 cases. There was no significant linear relationship between MMSE score of PD patients and the VEP P100 on the right and left sides, the VEP AMP on the right and left sides, the SSEP AMP on the right side but there was a significant inverse linear relationship between the MMSE score of the PD patients and the SSEP P40 on the left side, the SSEP P40 on the right side.

The average of VEP P100 on the right side and VEP P100 on the left side were respectively 104 ± 24.18 and 104.94 ± 24.60 . Furthermore, the abnormal VEP P100 on the left and right sides were observed in the 24 patients (40%).

It was observed that there was no significant difference between the average of P100 Latency of the PD patients with and without disorder and the SSEP amplitude has not significantly differed in the patients with and without dysfunction.

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