Archives of Psychiatry and Psychotherapy
Volume 6, Issue 4, December 2004
pages 23–29

Distribution of latencies of Visual Evoked Potentials in a sample of schizophrenic patients

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Summary

The aim of the study is an analysis of the distribution of visual evoked potentials (VEP) latencies in the group of schizophrenic and healthy subjects. A study was carried out on a group of 30 patients (8 males and 22 females) with a DSM-III-R diagnosis of schizophrenia (disorganised schizophrenia – 5, paranoid schizophrenia - 12, residual schizophrenia – 6, and undifferentiated schizophrenia – 6). During the study 20 patients were given neuroleptics, 10 patients did not receive treatment. A control consisted of 50 healthy persons (25 males and 25 females).

A stimulation of a chessboard pattern reversal (0.5 Hz, 30', 50 cd/m2) was applied. Evoked potentials were measured between the top of the cranium (Cz) and occipital leads O1 and O2.

Schizophrenic patients frequently have a prolonged N2 latency, and shortened P300 latency. Based on a pattern of latencies three groups of patients have been distinguished: (1) patients with prolonged latencies of all the waves (half of the patients), (2) patients with prolonged N2 latency, and shortened P300 latency (one fourth of the patients), and (3) patients with latencies similar to control (one fourth of the patients).

Key words: visual evoked potentials, schizophrenia

Introduction

The waves of visual evoked potentials (VEP) reflect a course of stimulation in the visual tract and in between the subsequent brain structures during the cognitive process provoked by a visual stimulation of the brain.

Latency of the average visual evoked potentials indicates the speed of transmission of the stimuli in the central nervous system [1]. In the case of persons with a diagnosis of schizophrenia, the curve of evoked potentials often differs from that of the healthy persons. A great number of studies referring to both existence and specificity of those alterations have been conducted [2]. Irrespectively of the type of visual stimulation, major reaction delay, which means a delay of latency of evoked reactions in groups of

schizophrenia sufferers have been usually found [3, 4]. The delay of latency of negative waves N1, N2 and more rarely positive P300 were the most often found. Hypotheses were presented that those alterations are specific for schizophrenia [3, 4, 5] or that they are completely unspecific [6]. There were attempts to associate latency changes with the clinical condition of the ill. Schwarzkopf SB et al. [7] ascertained a statistically significant negative correlation between intensity of positive symptoms and latency of P2 wave and a positive but not statistically significant correlation between intensity of negative symptoms and P2 latency.

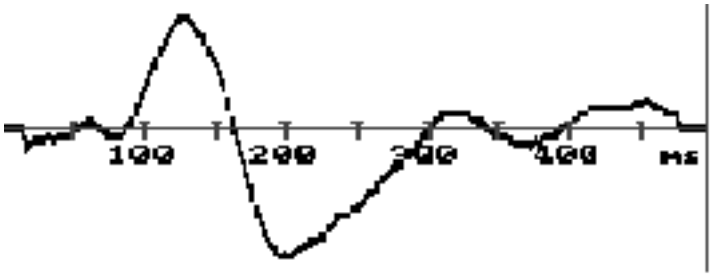
A higher variance of latency wave distribution than in control group was also found, something that indicates to a higher variability of individual results, placed both above and below the average. Heterogeneity of latency in the ill persons determines the starting point for a search of both psychopathological and biological factors related to it [7].

Aim of study

The aim of the study is the analysis of latency of visual evoked potentials profiles in patients with a diagnosis of schizophrenia and healthy persons, in order to find independent groups characterized by similar latency values.

Subject and methods

The control group consisted of 50 healthy persons in the age from 18 to 77 years old, the mean being 37 y.o. and included 25 males and 25 females. The group of schizophrenia sufferers consisted of 30 persons in the age from 21 to 72 y.o., the average 31.5 y.o. and consisted in 22 females and 8 males. All the patients had schizophrenia, diagnosed according to DSM-III-R criteria, including 6 persons having disorganized schizophrenia, 12 with paranoid schizophrenia, 6 persons had the residual form, and 4 persons were with undifferentiated schizophrenia. During the course of the study, 20 patients, were treated with neuroleptics, 10 patients did not take psychotropic drugs during the study. Visual stimulation using a black and white alternating chequered pattern board ("pattern reversal" type), with an inversion every 2 sec., angle size 30' and illuminated at 50 cd/m2 were used. Patients were seated in a darkened room. Silver, Plate electrodes covered with silver chloride, filled with conductive paste and attached to the skin with collodium, were used. Electrode-skin impedance did not exceed 10 kΩ. The sampling frequency amounted to 1000 Hz and the analysis time was set to 500 ms. The stimulation was repeated every 2 seconds. A mean result of 64 repetitions of evoked responses was used to obtain the final curve. Artefacts were detected simultaneously using a threshold discriminator which rejected responses with amplitude exceeding ±50 μV. Rejection of 10 subsequent responses caused the discontinuation of measurement. Patients were observed by a video camera. In case of closing one's eyes or head movements demonstrating lack of co-operation, the measurement was also stopped. Potentials were recorded from two leads: between the top of head (Cz) and left occipital area (O1), and between Cz and right occipital area (O2) [8]. An exemplary course of the potential is shown in picture



Pic. 1. **An example of the evoked potential course**

Latencies were counted by measuring the length of time from stimulation to maximal positive or negative deflection (top of the wave). Wave P2 was identified as positive deflection in which the top had been located in a delay range from 83 to 156 ms, wave N2 as negative deflection in a section from 156 to 230 ms. Wave P300 succeeded (followed, came after) N2 (from 230 to 460 ms), whereas wave N1 was identified as negative deflection directly before P2.

Groups including persons with similar latency values were distinguished using variance analysis by the k-variables method with replacement of missing results by the average ones. Differences between the groups were analyzed using non-parametric Mann-Whitney, Wald-Wolfowitz, and Kruskal-Wallis U tests, because latency distributions were not normal.

Results

Table 1 shows the latencies of visual evoked potentials in a group of ill persons and the control group. Average latency values in a group of ill persons were longer or the

Table 1

Latencies of visual evoked potentials in the schizophrenic and control group

Wave	Schizophrenics, n=30		Control, n=50		p1	p2
	Mean latency [ms]	Standard deviation [ms]	Mean latency [ms]	Standard deviation [ms]		
Right-sided waves						
N1	93.2	20.5	84.0	3.8	0.029	0.000
P2	130.7	20.7	114.2	8.3	0.204	0.000
N2	190.4	27.9	177.5	8.1	0.000	0.001
P300	338.2	70.2	304.5	8.3	0.304	0.000
Left-sided waves						
N1	95.2	24.2	83.7	4.1	0.002	0.000
P2	124.0	28.9	113.2	7.5	0.241	0.000
N2	190.7	32.3	170.3	8.3	0.000	0.023
P300	354.3	70.9	304.1	8.3	0.034	0.000

[1] Mann-Whitney U Test
[2] Wald-Wolfowitz runs test

same in comparison with control group considering all waves, both left and right-sided; some differences were statistically variable (bilateral N1 and N2, and left-sided P300). Standard deviations for latency of waves in the group of patients were several times higher than in the control group. Statistically significant differences of the shapes of latency profiles, stated by the Wald-Wolfowitz run test, appeared in all the waves.

Variance analysis in the area of latency of the wave tops was conducted for 2, 3, and 4 clusters. In case of 2 clusters, one included 16 ill persons, the second 14 ill and 50 healthy persons. In case of 3 clusters, two included ill persons (8 and 15 patients). The third one consisted of the whole control group and 7 ill persons. In case of 4 clusters, 2 mixed clusters consisted of ill and healthy persons (21 and 39 persons), and 2 clusters including ill persons (7 and 13), were obtained. Most clearly, the distribution was seen in 3 clusters; in this case variance analysis distinguished the biggest number of schizophrenia patients in separate clusters. Picture 2 shows the mean latencies for every cluster and table 2 shows mean latencies and the results of their comparison between the groups.

Considering the most numerous (57 persons) cluster nr 2 as reference, it is pos-

Pic. 2. **Mean latencies of the fra waves for each cluster**

sible to describe the two other clusters. The first one (nr 1) is characterized by higher average values of latency for all waves, the second one (nr 3) being characterized by similar latency of N1/P2 waves, longer N2 latency, and shorter P300 latency.

The clusters have not differed in any statistically significant manner in means of the age of those studied (the means were proportionally: 34.4, 38.2, and 33.0 y.o.; Kruskal-Wallis test: $H (2, N=78) = 0.84$ $p=0.66$) and in the fact that there was pharmacotherapy (Kruskal-Wallis test: $H (2, N = 30) = 1.33$ $p =0.52$). Clusters included,

Table 2

Latencies of visual evoked potentials in 3 groups

Wave	Median latency [ms]			p-v*	p-w*	p-c*
	Cluster 1	Cluster 2	Cluster 3			
Right sided waves						
N1	100	84	84	0.014	0.171	0.302
P2	124	112	130	0.071	0.240	0.217
N2	204	172	198	0.000	0.027	0.000
P300	416	304	252	0.000	0.000	0.000
Left sided waves						
N1	100	84	90	0.001	0.354	0.405
P2	132	112	132	0.037	0.820	0.236
N2	204	168	190	0.000	0.242	0.001
P300	416	308	252	0.000	0.000	0.000

* Mann-Whitney U Test

respectively 15, 5 and 4 medicated patients. The mean age of the ill persons (34.1 y.o.) was lower than the age of the control group (38.7 y. o.), however comparison using the Mann-Whitney test showed that the difference is not statistically significant (Z = 1.08, p = 0.28).

Discussion on the results

The results explain how the variance of latency of visual evoked potentials in schizophrenia sufferers is significantly higher than in the control group because of the heterogeneity of the schizophrenia group. Variance analysis enabled us to distinguish 3 subgroups of patients: (1) having prolonged latencies of all waves, (2) having latencies similar to latencies in the control group, and (3) having prolonged N2 latency and shortened P300. The most numerous - group 1 includes half of the number of patients, the other two groups account for about one fourth of the ill persons. The most constant characteristic of the ill persons is a prolonged N2 latency found in two groups of patients (1 and 2). 57% of patients had a longer N2 latency than a longest latency in the control group. The result is consistent with Brecher M. and coll. [3], Matsuoki and coll. [4] announcements, showing an increase of N2 latency in groups of the ill. Prolongation of N2 wave latency is therefore the most characteristic for the persons studied with a schizophrenia diagnosis. However it is impossible to refer this feature to all patients, 43% of them had N2 latency in a variability range of the control group.

Connolly and coll. [9] showed a prolongation of P2 wave latency in a group of schizophrenic patients, whereas Schwarzkopf SB and coll. [7] showed a correlation of P2 latency on the type and intensity of schizophrenic symptoms. Our study confirmed a slight increase of P2 latency in the ill, statistically significant for the group

1, whereas insignificant for group 2. There is possibility that this result is related to the intensification of symptoms, however we were not able to ascertain this according to our results.

From among the distinguished 3 groups of the ill, group 1 had a longer average P300 latency than the control group, group 2 had a shorter latency, whereas group 3 had similar latency results. The ill persons differed in P300 latency from the healthy persons and from each other. Exclusively 4 persons (13.3%) with schizophrenia had the P300 latency localized in a variability range of the control group. The remaining 27 patients (86.7%) had a longer or shorter latency among the ill. It is worth noticing that stimulus in the form of a chequered pattern is proper exclusively to the study of early components of evoked potentials (P1, N1, P2, N2). The experimental system which does not require any reaction from the studied person does not allow analysis of the P300 wave, which in the case may exist only in residual form.

Age differences between the group of the ill and the control group, and between the groups with various wave latency patterns, were not large and were statistically insignificant. It seems that the variable of age had no influence on the obtained results, especially in the area of prolongation of early negative waves [10].

Schizophrenia sufferers were in the greater part treated by neuroleptics, on the contrary the control group was not. The information from a scientific literature point-of-view however is that prolongation of latency of evoked potentials exists also in non-treated schizophrenia sufferers [11, 12]. Cluster 1 included slightly more than a half of the medicated patients. It is possible, that prolongation of all latencies in cluster 1 in comparison with other clusters is due to medication.

Conclusions

Patients with schizophrenia had the most often increased latency of N2 and N1 waves, and a variable P1 and P300 latency. 3 groups of ill persons differing by the pattern of latency changes have been distinguished: (1) with prolonged latencies of all waves, (2) with latencies as in the control group, and (3) with prolonged N2 latency.

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