P300 Event-Related Potential Latency Shortening in PTSD Patients Treated with EMDR: A Short Report

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Abstract: Event-related potentials (ERPs) provide a non invasive and cost-effective tool to investigate the neurobiological correlates of psychiatric diseases. Eye movements desensitization and reprocessing (EMDR) effectiveness for post traumatic stress disorder (PTSD) is well-known from clinicians, but contrasts with a limited knowledge of its underlying mechanism of action. In this short report, we assessed five patients suffering from post-traumatic stress disorder with event-related potentials in a modified oddball paradigm containing auditory standard, target, and novel tones. ERPs were assessed before and after five EMDR sessions. Compared to a control group that underwent sham treatment, ERPs of the EMDR-treated patients showed a significant shortening in the post treatment recording of P300 latency. We acknowledge that the small size of our sample is a real limitation but these results suggests a reduced arousal level after the treatment and a better brain functioning that is consistent with literature findings and clinical practice.

Keywords: PTSD, Eye movements desensitization and reprocessing, event-related potentials, P300, biomarker.

INTRODUCTION

The aim of our short report is to compare the electrophysiological profile of patients suffering post traumatic stress disorder before and after EMDR treatment, in search of a specific event-related brain potentials profile for post-traumatic stress disorder and a better knowledge of EMDR mechanisms of action. The small size of our sample incite us to acknowledge that our results shall be considered with caution.

Eye movement desensitization and reprocessing (EMDR) is a quite recent innovative, evidence-based and effective psychotherapy to improve post-traumatic stress disorder (PTSD) symptoms [1] and other diseases like tinnitus [2], obsessive-compulsive disorder, phantom-limb syndrome all linked with previous traumatic experiences. Post-traumatic stress disorder (PTSD) is a highly disabling condition that is associated with hyper-arousal, intrusive recollections of a traumatic event, avoidance of clues associated with the trauma, and psychological numbing. PTSD is yet commonly under-diagnosed and mistreated. Most studies have shown that unrelated to the traumatic event, additional risk factors for developing PTSD include younger age at the time of the trauma, female gender, lower social economic statuts, lack of social support, premorbid personality characteristics and preexisting anxiety or depressive disorders. Although PTSD remains the most widely known disorder, chronic post-traumatic psychiatric disorders have varied clinical expressions. Activation of dysfunctional traumatic memories generates states of re-experiencing. Hyper arousal increases anxious reactivity, and avoidance strategies increase anticipatory anxiety, indicating post-traumatic anxiety disorders as agoraphobia, specific phobia, obsessive compulsive disorder, separation anxiety and social phobia. Post-traumatic depressions and bereavement lead to high risk of suicide, repeated suicidal attempts and self-harm behaviour. A stressful or traumatic event may cause a co-morbid psychiatric disease to relapse and a traumatic experience can also provoke delusions. An impairment of the perception of physical health may also occur with development of somatoform and psychosomatic disorders, comorbidities are frequent and severe (addictive disorders, post-concussion syndrome). The trauma may cause a rupture in the biography of a person, leading to social isolation and personality changes [3].

Event-related potentials (ERPs) are very small voltages recorded from the scalp which originate in the brain structures in response to specific events or stimuli. ERPs are voltage fluctuations that are associated in time with some mental or physical occurrence.They appear as a series of peaks and troughs interspersed in the Electroencephalogram (EEG) waves [4]. Recording these voltage fluctuations provides a safe and non-invasive approach to study psychophysiological correlates of mental processes. These potentials can be extracted from the ongoing electro-encephalogram by means of filtering and signal averaging. ERPs allow the study of the physiological

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E-ISSN: 2310-8231/20

source of psychological processes during their dynamics [5]. In current clinical settings, the monitoring of post-trauma mental health relies on clinical interviews and self-reported symptom checklists.

Although these standard instruments are generally reliable, they are subjective and can be greatly influenced by the accuracy of patient reports [6]. The development of physiological measures that can objectively identify changes in mental health would be a valuable asset in achieving better knowledge of psychotherapy mechanisms of action.

METHODS

Subjects

Five patients (mean age 37.6, range 32-48, five women, all right-handed by self report) who experienced severe traumatic events in their clinical history, all fulfilling the ICD-10 and DSM V criteria for PTSD, were clinically assessed by performing the self-report post traumatic stress disorder check-list scale (PCL-s) (Yao S.N., Cottraux J., 2003). These patients were compared to a control group (sham-treated-group group) with three women patients , (mean age 58,3 range 48-72, all right-handed by self report) also fulfilling the ICD-10 and DSM V criteria for PTSD, and also self-assessed with PCLs, that underwent sham treatment. None of the patients received any pharmacological treatment during the study (self reported).

All participants agreed to participate and provided written informed consent. The research protocol was approved by the local ethics committee.

EMDR Group

The eight phases of EMDR standard protocol [1] were carefully followed to comply with fidelity to treatment procedure and the sessions followed the standard procedures. In brief, the eight phases of the therapeutic protocol were as follows: (1). Client History: history-taking, client evaluation, identification of traumatic memories, treatment planning; (2). Preparation: stabilization and access to positive affects; (3). Assessment: guidance to accessing the perceptual, cognitive, affective, and somatic components of the disturbing memory, as well as to identifying a preferred self–referential positive cognition. Rating of feelings using the Validity of Cognition (VOC) scale, and of level of emotional disturbance by the Subjective Units of Disturbance (SUD); (4). Desensitization: focusing on the traumatic memory for about 30 s while the therapist engages in bilateral stimulation. After each set, the client reports any elicited material, which is then processed until the SUD score decreases to zero; (5). Installation: focusing on the positive cognition while recalling the memory and engaging in new sets of bilateral stimulation, until the VOC score is 7; (6). Body Scan: processing of any residual physical disturbance associated with the memories until the body is clear and free of any disturbance; (7). Closure: Completion of an EMDR session and between sessions is ensured; (8). Reevaluation: at the beginning of subsequent sessions checking whether results were kept unchanged or needed further reprocessing.

The mean duration of EMDR treatment were 2,7 months. Each patient was treated by five EMDR sessions.

Sham-Treated Group

The sham treatment consisted to proceed to slow alternative bilateral stimulation during five seconds, without any focus on traumatic memory.The mean duration of sham treatment were 1,5 months. Each patient was treated by five sham sessions. For ethical reasons, the patients of the sham-treated group were proposed real EMDR treatment when completed the study.

Event-Related Potentials (ERPs)

ERPs were assessed before (T1) and after (T2) a treatment session using the eye movement desensitization and reprocessing method for the treated group and a sham treatment for the untreated group.

Both groups were assessed with event-related brain potentials (ERPs) in a modified oddball paradigm containing auditory standard, target, and novel tones.

The mean duration between ERPs sessions were 5,8 months (treated group) and 1,7 months (sham-treated group).

Unipolar recordings of auditory evoked potentials, with reference to the linked mastoids, were obtained from electrodes at 5 sites (Fz, Cz, Pz, F3, F4), according with the 10–20 electrode system of the International Federation of Clinical Neurophysiology [5]. A ground electrode was positioned at FPz. Electrode impedances were less than 5 kΩ. Each subject was presented with four sequences of stimuli with an

intensity of 90 dB. Each sequence consisted of 600 tone stimuli; two were with an ISI of 800 ms and two with an ISI of 2,400 ms. Three types of stimuli were presented through head- phones: (1) standard stimuli were 1,000 Hz sinusoidal tones of 100 ms duration and represented 75% of stimuli in each sequence; (2) deviant stimuli were 1,300 Hz sinusoidal tones of 100 ms duration and represented 15% of stimuli in each sequence, randomly presented among the standard stimuli; and (3) novel stimuli were complex and non monotonal, as compared to standard and deviant stimuli, with the same duration but with a new different spectral content in each novel presentation. Also novel stimuli were presented randomly in the sequence of standard tones and represented 10% of stimuli.The acquisition epoch length was 1,000 ms and included 200 ms before the stimulus for the baseline automatic correction. Signals were band-pass filtered at 0.5–30 Hz and sampled at 2,000 Hz. Responses were averaged separately for each stimulus type in each subject and the 0 μV baseline was determined as the mean amplitude of the pre-stimulus period. To quantify the MMN, the evoked response to the standard tone was subtracted from the corresponding deviant stimulus response and its amplitude (value relative to baseline) and latency at peak were measured over the midline electrodes, F3 and F4. Similarly, the P3a component of the ERP was obtained by subtracting the response to the standard tone from that to the novel stimuli and its amplitude (value relative to the baseline) and latency at peak were measured over the same five electrodes.

Four ERPs components were studied and there changes in term of latency and amplitude were recorded. These components were mismatch negativity, (MMN) P200, N200 , and P300 (P3a component)

Statistical Analysis

The statistical analysis was calculated by one-way analysis of variance (ANOVA).

RESULTS

Clinical Treatment Effects

As expected by therapist, significant improvement were found for all three psychometric variables: post-traumatic check-list scale, SUD and VOC. Psychometric assessment revealed a marked improvement of the PTSD symptoms after five EMDR sessions with a high degree of significance for each variable, whereas, in sham-treated group, we found no significant clinical effect after five sessions (Table **2**). Mean PCLs score is 68,2 (T1) and 66,4 (T2).

Table 1: Clinical Treatment Effect

Variable	Pre	Post	Significance (p-value)
PCL-s	65.4	23.8	<0.01
SUD	8.7	0.6	<0.01
VOC	2.4	6.6	<0.01

Electrophysiological Effects

Our primary goal was to focus on functional changes in information processing intuitively expected after EMDR therapy.

In EMDR-treated group we found no significant changes from pre to post-treatment sessions for any parameters. However, we noticed a shortening of P300 latency between T1 and T2. These results were obtained by subtracting T2 from T1 value. Mean shortening is 47,4 ms.

We also noticed a small but non significant enhancement of P300 amplitude. Mean enhancement is 0,8 microvolts. We found no significant changes from T1 to T2 for MMN latency (p=0,306), MMN amplitude (p=0,640), P200 latency (p=0,533), P200 amplitude (p=0,908), N200 latency (p=0, 363), N200 amplitude (p=0,831), P300 latency (p=0,008), P300 amplitude (p=0,524)

In sham treated-group we found no significant changes from pre to post-treatment sessions for any parameters between T1 and T2. We also noticed a shortening of P300 latency between T1 and T2 but about four times smaller than in EMDR treated-group. (Mean shortening: 12,4 ms). In other words, according to this result, the ability for EMDR-treated group to shorten P300 latency in T2 is about four times higher than what is yielded by sham-treated group. In conclusion, compared to the sham treated control group, ERPs of the patients showed a significant shortening in the post-treatment recording of P300 latency (p=0,001). We also noticed a reduction of P300 amplitude between T1 and T2 (-1microvolt).

DISCUSSION

Several questions must be discussed about P300 processing in PTSD. Recent numerous studies reports

Table 2: Neurophysiological Features and Research Agenda

EMDR T1

Name	Age (years)	laterality	Sex	T1		MMN latency T1	MMN amplitude T1	P200 latency T1	P200 amplitude T1	N200 latency T1	N200 amplitude T1	P300 latency T1	P300 amplitude T1
EMDR 1	34	right-handed	F	April 2011		149.6	4.6	114.4	5.2	175.0	3.1	323.4	5.4
EMDR 2	36	right-handed	F	August 2011		126.2	1.8	118.4	4.7	206.2	1.6	319.5	10.5
EMDR 3	32	right-handed	F	July 2011		106.2	6.2	124.2	4.8	202.1	3.6	276.6	7.3
EMDR 4	38	right-handed	F	October 2011		122.3	4.2	149.6	2.6	175.0	6.3	335.2	4.2
EMDR 5	48	right-handed	F	August 2011		130.1	5.3	147.7	1.8	192.6	3.3	374.2	7
					Mean T1	126.9	4.4	130.9	3.8	190.2	3.6	325.8	6.9
					SD T1	15.6	1.6	16.6	1.5	14.7	1.7	35.0	2.4

EMDR T2

Name	Age (years)	laterality	Sex	T2		MMN latency T2	MMN amplitudeT2	P200 latency T2	P200 amplitudeT2	N200 latency T2	N200 amplitude T2	P300 latency T2	P300 amplitude T2
EMDR 1	34	right-handed	F	January 2012		148.0	3.7	110.5	9.3	192.6	3.2	237.6	8.8
EMDR 2	36	right-handed	F	January 2012		130.1	3.2	116.4	1.8	180.3	2.6	243.4	9.11
EMDR 3	32	right-handed	F	January 2012		132.3	7.1	167.2	3.2	206.2	3.5	276.6	7.2
EMDR 4	38	right-handed	F	January 2012		141.8	8.9	161.3	1.7	206.2	5.6	339.1	6.2
EMDR 5	48	right-handed	F	February 2012		126.2	2.5	143.7	3.9	206.2	4.2	296.1	7.3
					Mean T2	135.7	5.1	139.5	4.0	198.3	3.8	278.6	7.7
					SD T2	9.0	2.8	25.6	3.1	11.7	1.1	41.5	1.2

SHAM T1

Name	Age (years)	laterality	Sex	T1		MMN latency T1	MMN amplitudeT1	P200 latency T1	P200 amplitudeT1	N200 latency T1	N200 amplitude T1	P300 latency T1	P300 amplitude T1
SHAM 1	55	right-handed	F	October 2011		143.7	2.8	126.2	3.0	196.3	2.1	301.9	7.9
SHAM 2	48	right-handed	F	December 2011		175.0	1.5	162.0	1.8	198.4	2.3	346.9	3.6
SHAM 3	72	right-handed	F	December 2011		130.1	1.6	153.7	3.7	192.1	1.2	335.2	4.2
					Mean T1	149.6	2.0	147.3	2.8	195.5	1.9	328.0	5.2
					SD T1	23.0	0.8	18.7	1.1	3.0	0.6	23.3	2.3

SHAM T2

Name	Age (years)	laterality	Sex	T2		MMN latency T2	MMN amplitudeT2	P200 latency T2	P200 amplitudeT2	N200 latency T2	N200 amplitude T2	P300 latency T2	P300 amplitude T2
SHAM 1	55	right-handed	F			126,1	2,8	110,5	6,2	197,1	1,8	294,1	4,5
SHAM 2	48	right-handed	F			138,9	3,7	159,4	5,3	204,1	1,4	352,7	4,8
SHAM 3	72	right-handed	F			137,9	2,8	128,1	3,0	206,4	1,7	306,0	3,5
				Mean T2		135,3	3,1	132,7	4,8	197,4	1,0	315,6	4,2
				SD T2		6,3	0,5	24,6	1,7	8,7	2,1	32,3	0,6

Shortening of latency parameters (T1-T2) in ms

	MNN	P200	N200	P300
EMDR treated group	8,8	8,6	8,1	47,2
Sham treated group	14,3	14,6	1,6	12,4

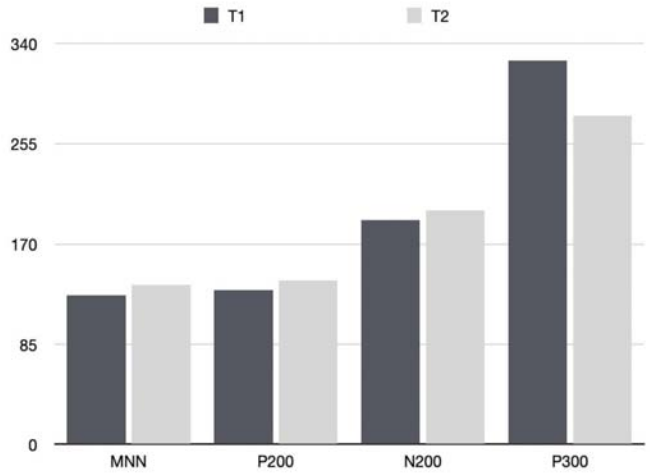

Figure 1: T1/T2 latency parameters (in ms).

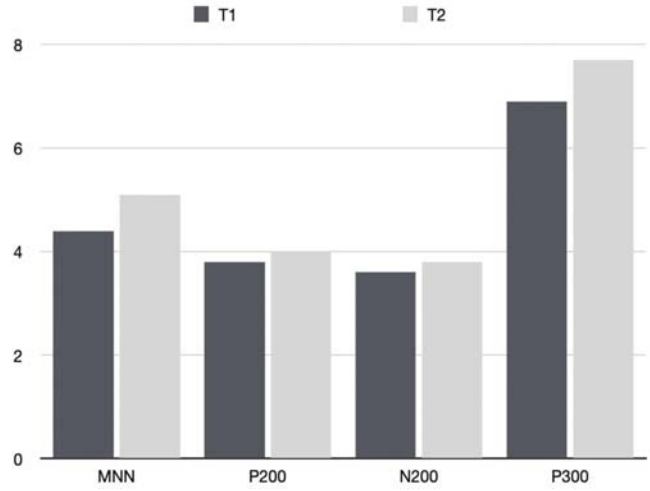

Figure 2: T1/T2 amplitude parameters (in µV).

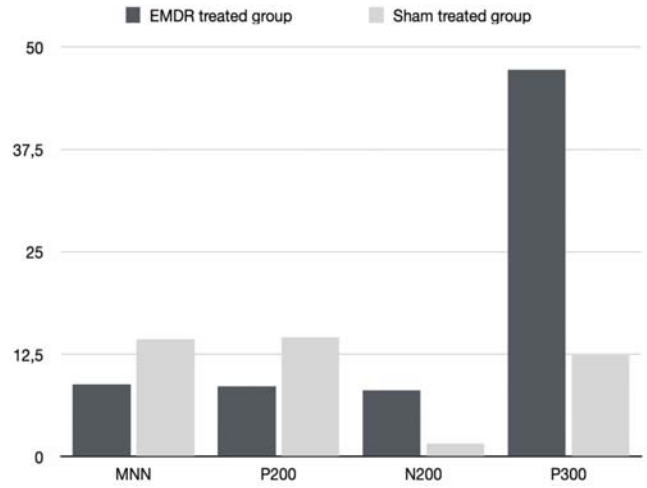

Figure 3: Shortening of latency parameters (T1-T2) in ms.

abnormal P300 activity in PTSD patients in civilian and military populations. What are the main perturbations observed? A meta-analytic review of the literature [7] suggest that in patients with PTSD, the P300 amplitude was attenuated in response to neutral stimuli but was enhanced in the context of emotional or trauma-related stimuli. One interpretation is that attention in PTSD is biased towards threat stimuli at the expense of attentional resources for processing emotionally neutral information.

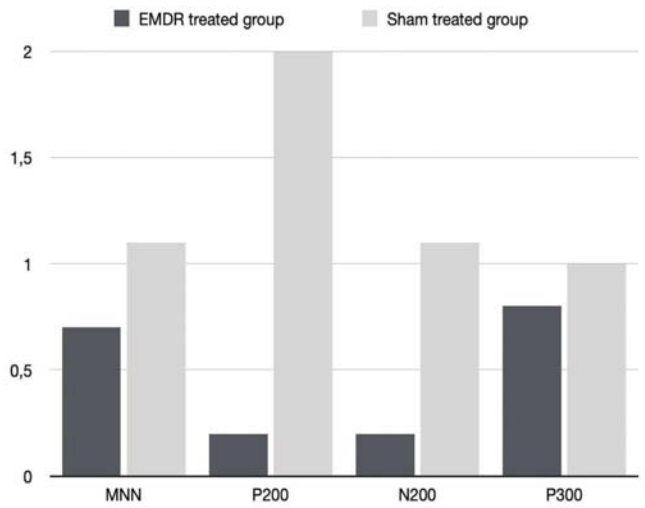

Figure 4: Variations of amplitude parameters (T1-T2) in µV.

In contrast, P300 latency was found to be delayed in PTSD patients regardless of stimulus type [8] suggesting a general slowing of cognitive processing. Is P300 a trait or state marker?

It is unclear whether P300 ERP is a relatively stable trait-like disease marker, or a state-like marker that can vary over time as a function of changes in symptom severities. Longitudinal studies are required to address these questions. The properties of state-like markers are perhaps more important for clinical uses as they may signal the emergence of post-trauma mental problems, guide early intervention, and quantify response to treatment.

Could P300 event-related potential be used as a diagnostic biomarker? P300 by itself is unlikely to confirm a specific diagnosis. Abnormalities in P300 have been characterized not only in PTSD but also in a wide range of other neurological and psychiatric disorders including those comorbid with PTSD such as depression, anxiety, alcoholism, dementia, and schizophrenia [9].

A previous study have shown that in PTSD patients, the current source density of P300 is significantly reduced in the inferior frontal gyrus, pre-central gyrus, insula, and anterior cingulate compared to healthy controls [10].

Could P300 assess psychotherapy effectiveness?

Lamprecht *et al*. (2004) [11] recorded ERPs using a three-stimulus oddball paradigm from 10 patients with PTSD before and after the eye movement desensitization and reprocessing therapy (EMDR).

The study revealed a trend of correlation between the changes of the P3a amplitude and the clinical improvement in symptom scales confounding factors impacting the association between subjective symptom ratings and objective physiological measures. In a recent longitudinal study [8], it was described that changes in P300 amplitude as well as latency were associated with fluctuations in symptom levels of PTSD; changes in P300 amplitude were also associated with fluctuations in symptom levels of depression and psychosocial functioning: increased amplitude and shortened latency of P300 was correlated to improved mental health status.These findings are in line with the notion that the P300 amplitude and latency is often inversely related (Polich, 1992) [12] and high amplitude and short latency typically suggest good brain functioning [13].

For clinical utility the P300 measures may be particularly informative if the inverse amplitude-latency relationship holds. Our results are pointing this way.

CONCLUSION

EMDR therapy provides clinical improvement and significant P300 event-related potentials latency shortening. A global normalization of the morphological features of the ERPs was observed in the post-treatment recording of the EMDR-treated group, not in the sham-treated group. We found no significant difference in P300 amplitude when treated group was compared to sham treated group. We observed a significant shortening in P300 latency when EMDR treated group was compared to sham treated group. These results are consistent with literature findings and clinical treatment effects, suggesting a global better brain-functioning with reduced intrusive thoughts, avoidance clues and arousal level after the treatment. We hypothesized that the shortening in the latency of P300 could easily be used in clinical practice as an interesting biomarker to assess effectiveness of psychotherapeutic treatment for PTSD patients.

ACKNOWLEDGEMENTS

We thank A. Boxus for data calculation and S. Sanchez for technical assistance.

DISCLOSURE

All the authors declared an absence of conflict of interest for this publication.

REFERENCES

[1] Shapiro F. Eye movement desensitization and reprocessing. Basic principles, Protocols, and Procedures second ed. The Guilford Press, New York, 2001; p. 398.

[2] Luyten T, Van de Heyning P, Jacquemin L, Van Looveren N, Declau F, Fransen E, Gilles A. The value of Eye Movement Desensitization Reprocessing in the treatment of tinnitus: study protocol for a randomized controlled trial. Trials 2019; 20(1): 32. https://doi.org/10.1186/s13063-018-3121-6

[3] Auxéméry Y. Posttraumatic stress disorder (PTSD) as a consequence of the interaction between an individual genetic susceptibility, a traumatogenic event and a social context. Encephale. 2012; 38(5): 373-80. https://doi.org/10.1016/j.encep.2011.12.003

[4] Huang WJ, Chen WW, Zhang X. The neurophysiology of P 300--an integrated review.Eur Rev Med Pharmacol Sci 2015; 19(8): 1480-8.

[5] Raggi A, Tasca D, Rundo F, Ferri R. Stability of auditory discrimination and novelty processing in physiological aging. Behavioural Neurology 2013; 27: 193-200. https://doi.org/10.1155/2013/462462

[6] Trongnetrpunya A, Rapp P, Wang C, Darmon D, Costanzo ME, Nathan DE, Roy MJ, Cellucci CJ Keyser D. Single-Trial Mechanisms Underlying Changes in Averaged P300 ERP Amplitude and Latency in Military Service Members After Combat Deployment. Front Hum Neurosci 2019; 13: 377. https://doi.org/10.3389/fnhum.2019.00377

[7] Karl A, Malta LS, Maercker A. Meta-analytic review of event-related potential studies in post-traumatic stress disorder. Biol Psychol 2006; 71(2): 123-47. https://doi.org/10.1016/j.biopsycho.2005.03.004

[8] Wang C, Rapp P, Darmon D, Trongnetrpunya A, Costanzo M, Nathan DE, Celucci CJ, Roy, MJ, Keyser D. Utility of P300 ERP in monitoring post-trauma mental health: A longitudinal study in military personnel returning from combat deployment. J Psychiatr Res 2018; 101: 5-13. https://doi.org/10.1016/j.jpsychires.2018.02.027

[9] Hansenne M. The p300 cognitive event-related potential. I. Theoretical and psychobiologic perspectives. Neurophysiol Clin 2000; 30(4): 191-210. https://doi.org/10.1016/S0987-7053(00)00223-9

[10] Bae KY, Kim DW. Im CH, Lee SH.Prog Source imaging of P300 auditory evoked potentials and clinical correlations in patients with post-traumatic stress disorder. Neuro-psychopharmacol Biol Psychiatry 2011; 35(8): 1908-17. https://doi.org/10.1016/j.pnpbp.2011.08.002

[11] Lamprecht F, Köhnke C, Lempa W, Sack M, Matzke M, Münte TF. Event-related potentials and EMDR treatment of post-traumatic stress disorder. Neuroscience Research 2004; 49: 267-272. https://doi.org/10.1016/j.neures.2004.02.013

[12] Polich J. On the clinical application of P300. Biol Psychiatry 1992; 31(7): 647-9. https://doi.org/10.1016/0006-3223(92)90273-3

[13] Polich J, Herbst KL. P300 as a clinical assay: rationale, evaluation, and findings.Int J Psychophysiol 2000; 38(1): 3-19. https://doi.org/10.1016/S0167-8760(00)00127-6

Received on 22-04-2020 Accepted on 12-05-2020 Published on 10-06-2020

DOI: https://doi.org/10.12970/2310-8231.2020.08.02