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Alterations of P300 wave in occipital lobe in depressive patients

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Introduction. The objective of this work is to assess neurofunctional alterations in patients with depression, analyzing the neurophysiological activity of P300 wave in bilateral occipital areas during visual attention and visual memory cognitive tasks.

Method. The study was made up of a group of 40 individuals, 21 in the control group and 19 in the group with depression. Visual stimulation was made by means of Cognistin system (ATI). The person is placed at one meter from the screen and remains seated, with no external visual stimulus if possible. All individuals were subjected to two different tasks: visual «oddball» paradigm and visual memory.

Results. A delay exists in latency of the P300 wave, in a global manner, both in visual task discrimination and memory task in patients with depression in the occipital areas. There is negative correlation between the P300 amplitude and severity of the depression, so that greater amplitude in the P300 component implies reduced severity of depression and vice versa. The reaction time in visual discrimination task correlates significantly with severity of depression; greater reaction time reveals greater severity in the depression.

Conclusions. The conclusions of this study reveal neurofunctional alterations in the occipital lobe during visual discrimination and memory task in patients with depression.

Key words:
Depression. P300. Occipital lobe.

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Alteraciones de la onda P300 en el lóbulo occipital en pacientes depresivos

Introducción. El objetivo de este trabajo es valorar las alteraciones neurofuncionales en pacientes depresivos, analizando la actividad neurofisiológica de la onda P300 en áreas occipitales bilaterales durante tareas cognitivas de atención visual y memoria visual.

Método. El estudio se realizó con un grupo de 40 sujetos, de los cuales 21 sujetos formaban el grupo control y 19 el grupo depresivo. La estimulación visual se realizó mediante el sistema Cognistin (ATI). El sujeto se sitúa a un metro de la pantalla y permanece sentado, a ser posible, sin estímulos visuales externos. A todos los sujetos se les aplicaron dos tareas diferentes: paradigma *oddball* visual y tarea de memoria visual.

Resultados. Existe un retraso en la latencia de la onda P300 de forma global, tanto en la tarea de discriminación visual como en la tarea de memoria, en los pacientes depresivos en las áreas occipitales. Hemos encontrado una correlación negativa entre la amplitud P300 y gravedad de la depresión, de tal manera que a mayor amplitud del componente P300, menor gravedad de la depresión y viceversa. El tiempo de reacción en la tarea de discriminación visual es el que se correlaciona de manera estadísticamente significativa con la gravedad de la depresión, a mayor tiempo de reacción mayor gravedad de la misma.

Conclusiones. Las conclusiones de este estudio ponen de manifiesto la existencia de alteraciones neurofuncionales en el lóbulo occipital durante una prueba de discriminación y memoria visual en pacientes depresivos.

Palabras clave:
Depresión. P300. Lóbulo occipital.

INTRODUCTION

Depression has been associated to important changes in cognitive invoked potentials, and with memory and attention problems[1]. Working memory, which is known to be a subsystem of short-term memory (STM) that intervenes in processes such as storing, activation and active maintenance of information, are among the different types of memory damaged[2]. P300 is considered as an element to categorize and evaluate cognitive processes in regards to immediate memory capacity that we need to perform any task[3]. Even

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when memory deficits are recognized in the depressive subjects, the neurophysiological mechanisms are still unknown. For some, the deficits would be in the «central executive system»[4], for others the latency delay in P300 would be an index of cognitive capacity of these patients[5]. As depression becomes more serious, there is greater delay in cortical activity and slow-down in perceptive decision processes[6]. Studies with encephalography (EEG)[7] seem to show an increase of alpha and theta waves in depressive patients, above all in the left anterior part of the brain. This has already classically been called alpha-frontal asymmetry. This type of electroencephalographic abnormalities has been related with hypofunctionality of the frontal and prefrontal lobe[8]. However, there are works[9-11] that justify the importance of the occipital lobe in depressive patients. The occipital lobe, as is well known, is involved in the world of perception and more specifically in that of vision. Recent works using the magnetoencephalography (MEG)[9] have found delta activity in the right occipital lobe, there being a directly proportional correlation between the increase of this delta activity in the right occipital lobe and the score on the Hamilton scale. Thus, this increase in activity is a predictor of risk to suffer depression.

The main objective of this work is to evaluate neurofunctional alterations in depressive patients, analyzing neurophysiological activity of the P300 wave in bilateral occipital areas during cognitive tasks of visual attention and visual memory.

METHOD

Subjects

The control group is made up of 21 subjects who are comparable in gender, age and cultural level from the Institute of R. Coullaut of Psychiatry, with an age range of 44.08 ± 10.70 years and with no neurological or psychiatric background. The depression group is formed by 19 patients with an age range of 47.40 ± 13.32 with no neurological diseases, mental deficiency or associated medical diseases. All were diagnosed of depression according to the DSM-IV criteria and Hamilton Scale (35 or more points). In order to evaluate cognitive status, all the patients were administered the Mini-Mental State Examination (MMSE).

Procedure

In the first place, a psychiatric examination was performed. This not only included the clinical history but also the DSM-IV criteria, Hamilton scale and MMSE. After, a neurological examination was performed. This included eye fundus, intraocular pressure and examination of cranial pairs. The neuropsychological examination included the Wechsler logical memory (1987): logical memory I (WMS-R) and logical memory II (WMS-R) scale.

Stimulation was done using the Cognistin (ATI) system, a computer program to that makes it possible to construct flexible stimulation protocols in the visual modality, through which the presentation time on the screen in each one of the stimuli and the interval between them can be controlled.

The subject is placed at 1 meter from the screen and remains seated, in a noise free site. Two different tasks are applied to all the subjects: visual oddball paradigm and visual memory task.

The visual oddball paradigm consisted in the presentation of the two types of different visual stimuli (square and circle), that randomly appear in the center of the screen, with different likelihood of appearance (80% for circles vs 20% for squares). The subject had been previously instructed to raise the index finger of the right-hand (dominant) when they square appeared. The stimulus was presented for 200 msec. and the inter-stimulus time was 2,000 msec. The appearance of them also occurred randomly. Duration of each task was approximately 10 minutes.

In the visual memory task, the patient was exposed to the learning of 5 letters seen on the screen for 1 minute. After, these letters were randomly placed with different ones (three distractors per letter learned) and the subject had to raise the index finger of the right hand every time the learned letter appeared. The instructions were presented to the subject visually through the monitor. Duration of the visual task was about 10 minutes.

Recording of the brain activity was carried out by placing a standard headset, following the international system 10/20. For the objective of this study, only electrodes 01, 02, 0z were analyzed and all the channels were amplified with a band process of 0.25-70 Hz and the impedance was <5 K for all the electrodes. To record the motor activity, an active electrode was placed on the common extensor muscle of the right hand and a reference electrode on the back of the right hand.

In the statistical analyses, behavioral variables were analyzed using the Student's *t* test. Neurophysiological variables, latency and amplitude of the P300 component for visual discrimination tasks and memory tasks were analyzed using the ANOVA (analysis of variance) 2×2×2 for repeated measurements with the intergroup diagnostic factor (depression and control) and the hemispheric intergroup factors (right-left) and task (visual area of versus memory task) as independent variables. Given the accumulative effect of error associated to making multiple comparisons, correction was done of the significance levels with the Bonferoni method.

RESULTS

The results indicate that there are significant differences on the Hamilton scale between the depression and control

group. The value t=21.58 p<0.0001 indicates that the Hamilton scores are greater in depressive subjects. We have not found any significant differences in the MMSE, thus the cognitive condition was the same in both groups. In regards to the results related to memory, we verified the principal effect of the diagnostic variables, memory type (F1.38 = 9.87; p<0.003) and modality (F1.38 = 7.72; p<0.008). This indicates that the control group obtained higher scores in memory task (type 1 and type 2 logical memory) then in the depression group. These data indicate that the control group conserves memory better and has a lower rate of forgetfulness than the depression group.

In regards to the recording of evoked potentials, we found the existence of the first positive peak at about 200 msec followed by a negative peak at approximately 250 msec (N200) and another positive peak around 300 msec (P300) that is slowed in the depressive group as well as the motor reaction time in both the visual and memory task (fig. 1).

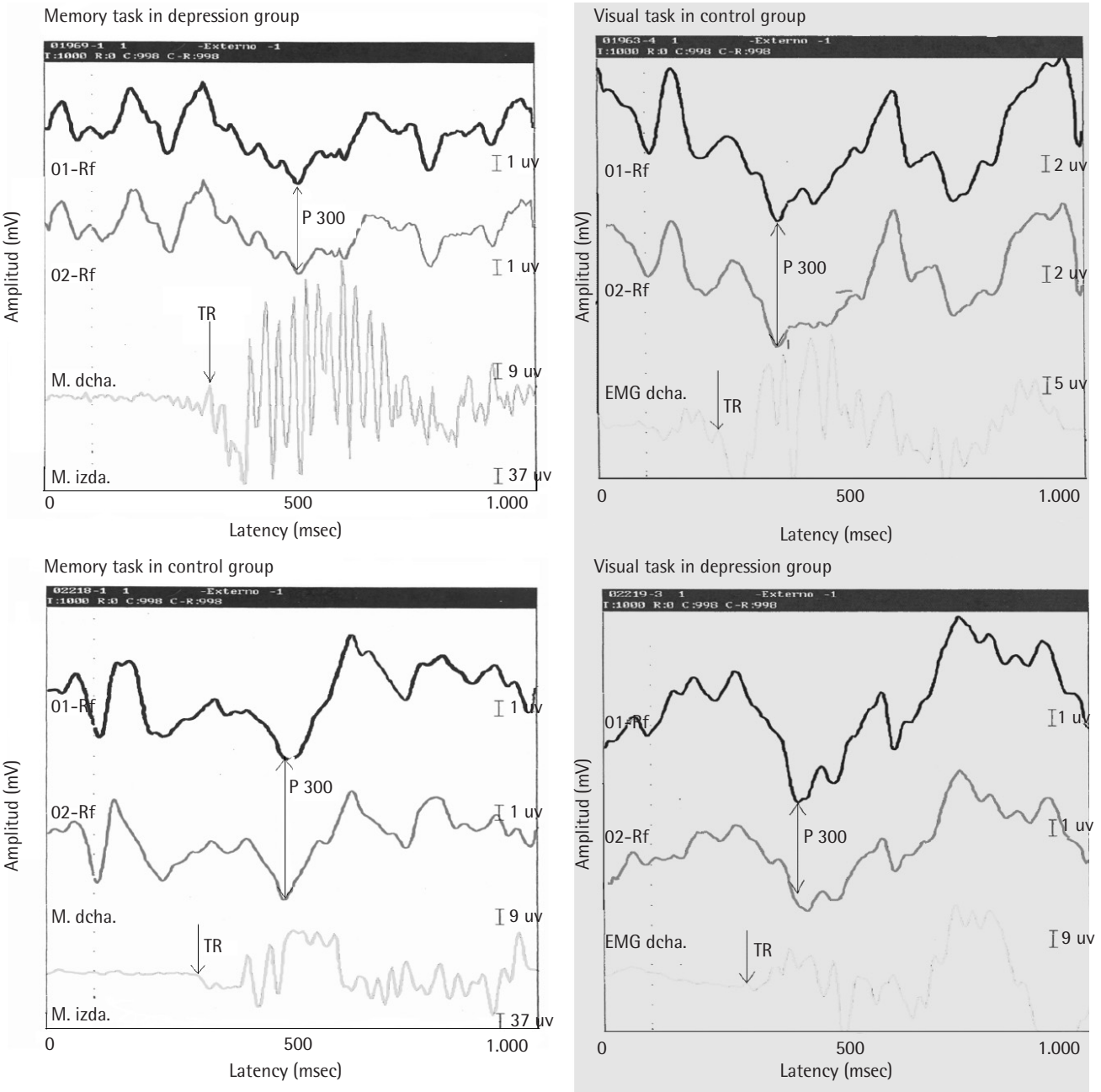

Figure 1 *Chart that shows the electroencephalographic P300 and electromyographic responses (motor response of index finger) in both groups and tasks.*

In the reaction time for the visual task, the results are significant in regards to the comparison between the means of the control and depression groups (t = 4.92; p < 0.0001). This indicates that the reaction time is faster in the control group if we compare it with the disease group. There are no significant differences in the reaction time for the memory task between both groups. However, the memory task (of greater cognitive complexity) generates higher reaction times than the visual discrimination task (t = 8.55; p < 0.0001) (fig. 2).

Analysis of the P300 component latency shows the principal significant effects of the Diagnostic factors (F1.38 = 44.95; p < 0.0001) and task factors (F1.38 = 44.16; p < 0.0001). The first one indicates that the P300 latency is delayed globally, both in visual discrimination as well as in memory tasks, in the depressive patients. Similarly to that seen in the reaction times, we can say that, independently of the group, the memory task produces a significant delay in the P300 component, probably associated to its complexity. Finally, the Hemispheric factor has no type of significant effect on P300 latency (fig. 3).

The measurements of the P300 amplitude show once again the principal significant effects of the diagnostic factors (F1.38 = 9.87; p < 0.003) and task factors (F1.38 = 7.72; p < 0.008). In this case, it is seen how the controls have a greater global amplitude for both tasks and that the visual task produces greater P300 amplitudes than the memory task. However, a significant diagnostic × task interaction is observed (F1.38 = 3.86; p < 0.05). This indicates to us that in spite of the fact that the P300 amplitude is generally greater in the visual discrimination task, this is fundamentally due to the control group (p < 0.002), since it is only in this group where the differences between the tasks are really significant. The hemispheric factor also has no significant influence, in this case, on the dependent variable (fig. 4).

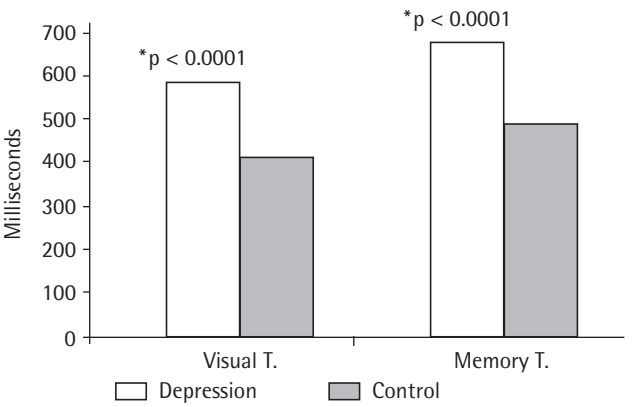

Figure 3 *Chart representative of the P300 latency between the diagnostic and task effect.*

Analysis of the behavior of these coefficients confirms that shown by the analysis of correlations: the positive relationship between the Hamilton depression scale and latency in memory task (t = 4.86; p < 0.0001) and between the Hamilton and reaction time in visual task (t = 3.89; p < 0.0001). These results indicate that there is a positive relationship between the Hamilton, P300 latency and reaction time in the visual task. This indicates that when there is greater latency and reaction time, there is greater severity of the depressive symptoms.

DISCUSSION

The present investigation studied the values of latency and P300 component amplitude for visual discrimination and memory tasks. In regards to latency, the results indicate that this component is delayed in visual discrimination task. In this sense, different works[3] justify that the delay in P300 latency could be due to cognitive disorders

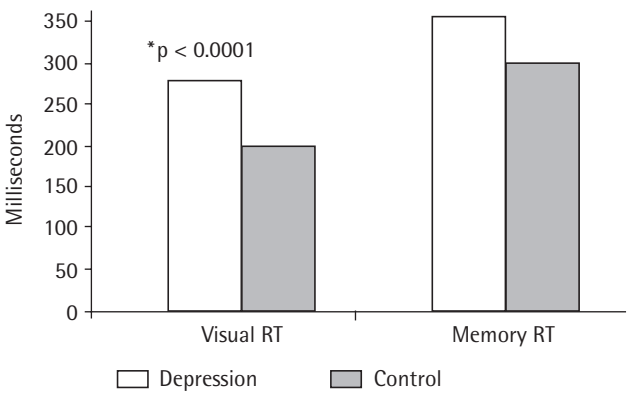

Figure 2 *Comparative chart of both groups and both tasks in the reaction time.*

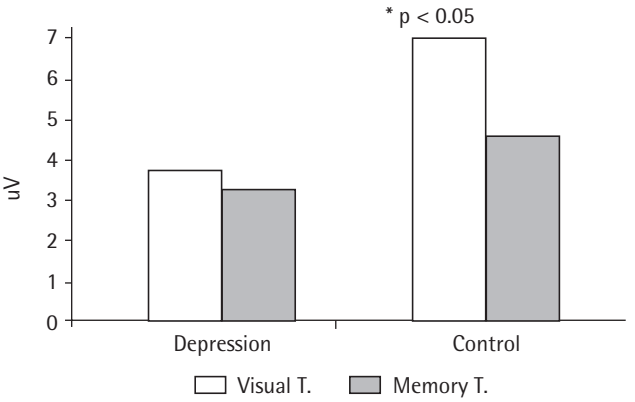

Figure 4 *Chart representative of the P300 amplitude between diagnostic and task effect.*

in processing of visual information in depressive patients. On the other hand, we also find a significant delay of the latency of the P300 component in the memory task. This could be related directly with greater complexity of the task and consequently with greater cognitive resources that the patient with major depression does not have. In fact, previous works[1,10] have verified the existence of cognitive defects, mainly in the working memory in depressive patients. This greatly hinders their capacity to discriminate, adequately perceive and process complex cognitive stimuli.

The results of our study confirm the decrease of the P300 wave amplitude, directly associated with attentional processes in depressive patients in the visual task. Given that this is a very simple and automatic task that does not need great attention, the results could be explained by the lack of attention on the depression in common and normal situations of daily life. This could be associated with a low level of expectation, attention and motivation towards the task. This specific deficit of the attentional processes is associated with an alteration in frontal cortical activity[13,14]. These regions have been identified as specific to neuronal activity of attention and memory[15,16]. Mentioned should be made of the inversely proportional correlation between the wave amplitude and depression severity measured on the scores obtained on the Hamilton test. Thus, the greater amplitude of the P300 component, the less the severity of the depression and vice versa. The reason could be due to a greater decrease in cognitive resources, mainly attention and working memory, as the depression becomes more severe.

Our results show a lower reaction time in the visual task than in the memory one and that the reaction time is less in the control group if we compare it with the disease group only in the visual task. This is not true with the memory task. These data could be explained, on the one hand, by the greater complexity of the memory task and by the greater cognitive views when performing this type of task, which does not explain the differences in the motor response. On the other hand, depressive patients not only slow down in the cognitive process but also with motor processes in simple tasks on almost automatic execution[17-19]. In fact, one of the characteristic signs of depression is motor slow down.

Our own results together with those of other investigators[9-11] give evidence of the currently existing interests to relate the occipital lobe with depression, considering the usual perceptive type variables. In this sense, in our study, our attention is drawn to the fact that in our study, reaction time in the individual task together with the delay of the P300 latency are those that are most closely related with depression severity, thus significantly demonstrating again the effect that the emotional and affective type (depressive status) variables have on the perceptive world (visual task).

In our study, we can conclude that neurofunctional disorders of the occipital lobe are important in visual perceptive memory and discrimination in depressive disease.

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