

# Desynchronization/synchronization of parasagittal EEG rhythms during habituation to photostimulation in adults

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## ABSTRACT

**Introduction.** Learning by habituation implies a gradual diminution of the organism's responses to non-relevant stimuli. These responses, resulting from electrical oscillations of the brain, can be analyzed through quantitative electroencephalography (qEEG). **Objective.** To characterize the absolute power (AP) in the range of delta ( $\delta$ ), theta ( $\theta$ ), alpha ( $\alpha$ ), beta ( $\beta$ ) in cortical parasagittal regions during habituation to photostimulation (RPh). **Material and methods.** We studied 81 undergraduate students. The EEG was recorded in a Nicolet; awake subjects with closed eyes were photostimulated (5 Hz for 2 s, 20 times, RPh). The UAMI/Yáñez program identifies the RPh signal, chooses and collects 2-sec samples before (Pre) and during RPh, and instruments the Welch periodogram, which integrates the absolute power (AP) of  $\delta$ ,  $\theta$ ,  $\alpha$ , and  $\beta$ . We calculated the average AP (AAP) in Pre and RPh per frequency and lead. AAP differences were assessed with non-parametric tests. Linear regression was used to plot the AAPs of each Pre and each RPh sample, representing the resulting slope with its statistical significance. **Results.** RPh increased the AAP of  $\delta$  in frontal and fronto-central leads of both hemispheres, and its slopes were ascendant. AAP of  $\theta$  increased in fronto-frontal and diminished in the other three leads, its slopes were ascendant in right central parietal and parieto-occipital leads. AAP of  $\alpha$  increased in fronto-frontal leads, did not change in fronto-central, and diminished in the other leads; its slopes were descendent in Pre and ascendant in RPh in both hemispheres. AAP of  $\beta$  increased in the four leads; in Pre,  $\beta$  slopes were descendent in parieto-occipital leads of both hemispheres. During RPh,  $\delta$  slopes were ascendant in right parieto-central and in both parieto-occipital leads. **Conclusion.** The progressive diminution of alpha's desynchronization, which ends in synchronization, is probably due to

## Desincronización/sincronización de ritmos EEG parasagitales en la habituación a la fotoestimulación en adultos

## RESUMEN

**Introducción.** La habituación implica disminución de respuestas ante estímulos no relevantes. Dichas respuestas resultan de oscilaciones eléctricas cerebrales y son analizables mediante el electroencefalograma cuantitativo (EEGc). **Objetivo.** Caracterizar la potencia absoluta (PA) en el rango de delta ( $\delta$ ), theta ( $\theta$ ), alfa ( $\alpha$ ) y beta ( $\beta$ ) en regiones corticales parasagitales durante la habituación a la fotoestimulación. **Material y métodos.** Estudio en 81 estudiantes de licenciatura. El EEG se registró en un Nicolet; los sujetos en vigilia, con párpados cerrados, se fotoestimularon (5 Hz 2 s, 20 veces, FR). El programa UAMI/Yáñez identifica señales FR, toma muestras de 2 s previos (Pre) y durante FR e instrumenta el periodograma Welch (256 Hz), que integra la PA de  $\delta$ ,  $\theta$ ,  $\alpha$  y  $\beta$ . Se calculó el promedio de la PA (PPA) en Pre y en FR por frecuencia y derivación. Las diferencias de PPA se evaluaron con pruebas no paramétricas y con el modelo de regresión lineal se graficó la distribución de los PPA de cada Pre y cada FR, representando la pendiente resultante con su significado estadístico. **Resultados.** La FR aumentó el PPA de  $\delta$  en las derivaciones fronto-frontal y fronto-central de ambos hemisferios y sus pendientes fueron ascendentes; el de  $\theta$  aumentó en fronto-frontal y disminuyó en las otras tres, sus pendientes fueron ascendentes en centro-parietal y parieto-occipital derechas; el de  $\alpha$  aumentó en fronto-frontal, no se modificó en fronto-central y disminuyó en las otras derivaciones y sus pendientes fueron descendentes en Pre y ascendentes en FR en ambos hemisferios; el de  $\beta$  aumentó en las cuatro derivaciones. En Pre sus pendientes fueron descendentes en ambas parieto-occipales; fue ascendente durante FR en parieto-central

*hyperpolarization of neuronal membranes and represents habituation. This is complemented with synchronization of the delta rhythm in anterior cortical areas and of theta and beta in areas of the right hemisphere.*

**Key words.** *qEEG habituation. Alpha desynchronization/synchronization. Delta, theta, beta synchronization. Linear regression. Habituation.*

## INTRODUCTION

Functional characteristics of cerebral electrical oscillations can be analyzed by means of the quantitative EEG (qEEG). Development of this technique gave rise to new possibilities for the study of the spontaneous and induced electrical activity as well as for the diagnosis in cases of central nervous system pathologies. In the last case, it is necessary to establish comparison parameters obtained from healthy populations.<sup>1-3</sup>

The qEEG is a risk-free procedure that can be used in persons of diverse characteristics (gender, age, physical condition, etc.), it is easy to perform, reproducible, and of low cost. It consists of registering the oscillations of the neuronal membrane potential, which depends on its cytoarchitecture and on the effects produced by excitatory and inhibitory postsynaptic potentials (EPSP/IPSP). Therefore, the qEEG allows for the analysis of the magnitude and distribution of the field potentials of multiple cortical neuronal assemblies,<sup>4</sup> from which their morpho-functional dynamic integrity can be inferred (neuroplasticity). This turns the qEEG into an excellent tool to study cortical functions and their interactions with subcortical structures, with a temporal resolution in the range of milliseconds.<sup>5-7</sup> It has been described that oscillations, electrotonically transmitted, modify the excitability of neuronal membranes, constituting a communications system among circuits, or a process that regulates the excitability of neuronal ensembles (circuits),<sup>8-11</sup> which, in turn, adds to the effects of action potentials arising from interneurons and/or distant neurons. According to the type of post-synaptic potential elicited by a stimulus (event), neuronal ensembles can increase their membrane potential (hyperpolarization), which is manifested in the EEG as synchronization, or they can decrease it (depolarization), which can be recorded as desynchronization. Both phenomena are characterized by a clear topo-

derecha y en ambas parieto-occipitales. **Conclusión.** La disminución progresiva de la desincronización alfa, que termina en sincronización, probablemente resulta de hiperpolarización de membranas neuronales y representa la habituación, y se complementa con sincronización del ritmo delta en áreas corticales anteriores y de theta y beta en áreas del HD.

**Palabras claves.** EEGc habituación. Desincronización/sincronización alfa. Sincronización delta, theta, beta. Regresión lineal. Habitación.

graphical location, phasic behavior, and frequency specificity.<sup>12,13</sup>

Some neuronal ensembles of the occipital lobe produce 8 to 13 Hz oscillations known as alpha ( $\alpha$ ), whose cortical-subcortical modulation turns them into a determined “clue” (encoding)<sup>14</sup> that, when repeated in diverse circuits, participates in the sensation-perception of stimuli.<sup>15,16</sup> Besides  $\alpha$ , neuronal ensembles have been described that produce oscillations at different frequencies ( $\delta$ , 1.5-3.5 Hz;  $\theta$ , 4-7.5 Hz;  $\beta$ , 13.5-30 Hz) that, when syntonized to cortical and subcortical neuronal circuits, participate in determined behavioral aspects.<sup>17-20</sup>

In humans, under waking conditions with closed eyes, cerebral oscillations, represented by four frequencies, are in a basal state (“initial electromorphogram established by at least four frequencies”). In the presence of a stimulus, some neuronal circuits of the specific sensory pathway and of the polysensory one become activated and generate an event-related desynchronization (ERD)<sup>21</sup> that includes the process of information identification, establishing new “electromorphograms” (clues; code) that represent both the environment (scenario) and the specific stimulus. This desynchronization, in turn, activates other neuronal circuits giving rise to the corresponding responses, as for example the orienting reflex and sympathetic activation,<sup>22</sup> generating new signals related to the changes in homeostasis of the organism and, probably, activating other hypothalamic circuits, in the temporal (hippocampus) and frontal lobes, including the limbic system. Repeated stimulation, in the same scenario without important changes in an organism’s homeostasis, loses gradually its capacity to activate neuronal circuits, that is, alpha desynchronization diminishes, a phenomenon described by Jasper and Sharpless<sup>23</sup> and Morrell,<sup>24</sup> among others. With diminishing desynchronization, responses also diminish such as the orienting reflex, a phenomenon called “habituation” by Sokolov.<sup>25</sup> If stimulation continues, information is rated as “non

significant”, and the organism learns not to respond. This process has been described in cats by a diminution in visual evoked potentials<sup>26</sup> and, in children, by the diminution in the power of the alpha frequency.<sup>27</sup> All of this has been integrated within the learning process by habituation.

Most research on habituation, due to the prevailing technology at the time, refer mainly to average modifications in  $\alpha$  and  $\theta$  frequencies of the qEEG, without taking into account their localization and/or evaluation during the procedure,<sup>28,29</sup> leaving out the average modifications in  $\delta$  and  $\beta$ , as well as the topographical distribution of the four frequencies during the habituation process.

The objective of this work was to characterize the modifications in the four frequencies ( $\delta$ ,  $\theta$ ,  $\alpha$ ,  $\beta$ ) of the qEEG in four parasagittal cortical regions during habituation to photostimulation in adult volunteer subjects.

## MATERIAL AND METHODS

### Design of the study

A descriptive, transversal study of a sample of undergraduate students majoring in Physical Therapy or Human Communication, with similar socioeconomic and cultural background, informed and openly invited to participate in a research on the characteristics of the EEG.

### Procedure

All participants were briefed on the objective of the research, aimed at knowing the EEG characteristics in relation to the performance in diverse cognitive tasks and that the study did not cause any pain, discomfort, or pose any risk. Those that accepted signed an informed consent format from the Instituto Nacional de Rehabilitación (INR) (National Institute of Rehabilitation) of México. The protocol was approved by the institutional Research and Ethics Committee, considering the guidelines of the Helsinki Declaration. Recordings were made in a digital-analogic electroencephalograph (Nicolet One; 31 channels), placing the electrodes at the 10/20 distribution, paying special attention to the inter-electrodes distance, and confirming that impedance was kept between 5 and 10 k $\Omega$ , along the whole study. For the recording, a bandwidth of 0.3 to 70 Hz with a bandpass filter of 60 Hz was used.

For the analysis, bipolar leads of parasagittal anteroposterior montages was used in the left

(F1F3, F3C3, C3P3, and P3O1) and right (F2F4, F4C4, C4P4, and P4O2) hemispheres. All studies were performed in a dimly illuminated and sound-attenuated chamber; subjects were placed in dorsal decubitus, resting, and asked to remain as motionless as possible. The EEG recording paradigm was as follows: closed eyes (2-3 min); open-closed eyes stage (periods of 10-15 s in each condition, 6-10 repetitions); repeated photostimulation (while in the closed eyes conditions, 20 series of flashes at 5 Hz, 2 s duration per series, at variable intervals of 20-25 s, without previous knowledge of the subjects) applied by means of a stroboscopic Nicolet lamp placed at 70 cm from the subject's face; association (identical procedure to that of repeated photostimulation but adding the indication to press a button placed at the end of a cylinder placed in the dominant hand and to keep it pressed until the end of the series when perceiving the photostimulation); and, finally, hyperventilation (3 min). In this report we present the results of the repeated photostimulation (RPh) stage obtained in the parasagittal regions.

### Data analysis

Data on absolute power (AP) of the qEEG, filtered at a bandpass of 16- to 40 Hz, were analyzed using a specially designed software (UAMI/Yañez), which identifies the signal of the flashes and takes 20 pre-stimulation (Pre) samples, as well as samples of each of the series of 20 RPh. By applying the Welch periodogram (256 Hz), the program integrates and transfers the AP data per frequency,  $\delta$  (1.6-4 Hz),  $\theta$  (4.5-8 Hz),  $\alpha$  (8.5-13 Hz), and  $\beta$  (13.5 Hz), to Excel® spreadsheet. Afterwards, averages of the absolute power (AAP) were calculated for the 20 Pre periods and the 20 RPh periods of each frequency per lead. First, we analyzed the AAP of each frequency in each lead in the basal condition of closed eyes. Differences among leads were evaluated with ANOVA for independent samples (using Dunnett T3 for correction). The next analysis consisted of comparing the differences in AAP of each frequency in the Pre condition *vs.* the RPh condition per lead, using the Wilcoxon test for related samples. Finally, we calculated the AAP distributions in the Pre and RPh conditions, per lead and per frequency, using the linear regression model. The software used for these analyses was the Analyse-it®. The level of significance was set at  $p = 0.05$  (in the sake of brevity we only mention statistically significant differences).

## RESULTS

### AAP profile of each frequency per lead and hemisphere in resting condition with closed eyes

Previous (basal) electrical activity presented characteristic topographical distribution profiles for each frequency. The AAP in leads of the left (LH) and right (RH) hemispheres were similar, as seen in figure 1; the AAP of  $\delta$  diminished from fronto-frontal to fronto-central leads, whereas it increased from centro-parietal to parieto-occipital. The AAP of  $\theta$  was similar in the first three leads but increased from centro-parietal to parieto-occipital ones. The AAP of  $\alpha$  showed a significant increase from one to another lead, from fronto-frontal to parieto-occipital in both hemispheres (voltage gradient). The AAP of  $\beta$  diminished from fronto-frontal to fronto-central, but the difference was only significant in the right hemisphere, whereas it increased from centro-parietal to parieto-occipital in both hemispheres.

### AAP modifications of each frequency per lead and hemisphere during the 20 RPh

When comparing the AAP of the 20 photostimulations with the 20 previous conditions, significant changes were found ( $p = 0.05$ ) in the four frequencies. As can be seen in figure 2, during RPh, the AAP of  $\delta$  in fronto-frontal and fronto-central leads of both hemispheres increased significantly; the AAP

of  $\theta$  increased significantly in both fronto-frontal leads and diminished in the other three leads, but without reaching statistical significance. The AAP of  $\alpha$  increased significantly in both fronto-frontal leads, did not change in fronto-central of both hemispheres, and diminished in centro-parietal and parieto-occipital leads in both hemispheres. The AAP of  $\beta$  increased significantly in all studied leads.

The analysis of averages conceals the AP changes that occur at each time before stimulation and those evoked by each photostimulation. To be able to discern these changes, we analyzed the AAP distribution in each Pre and each RPh sample applying the simple linear regression model of each frequency per lead. The latter indicated relevant differences in the evolution of the intra- and inter-hemispheric AAP.

Figure 3 depicts the ascending slopes of the AAP before (Pre, black line) and during photostimulation (RPh, grey line) for delta in fronto-central and centro-parietal leads of both hemispheres, which were significant ( $p = 0.05$ ).

Figure 4 depicts the ascending slopes of the AAP before (Pre, black line) and during photostimulation (RPh, grey line) for  $\theta$  in the right centro-parietal and parieto-occipital leads, which were significant.

Figure 5 depicts the descending slopes of AAP before (Pre, black line) and ascending slopes during RPh (grey line) for  $\alpha$  in fronto-central, centro-parietal, and parieto-occipital leads of both hemispheres, which were significant. In all cases, the first photostimulations produced diminution of the AAP; how-

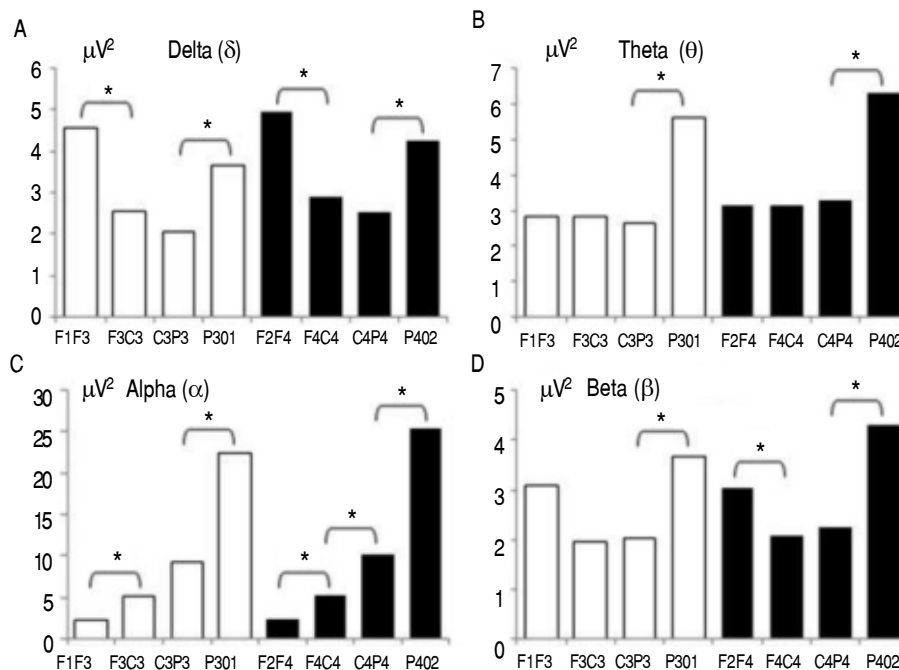


Figure 1. Average of the absolute power (AAP) of each frequency per lead. White bars indicate LH leads and those in black correspond to the RH. Asterisks indicate significant differences ( $p = 0.05$ ).

ever, this effect diminished with advancing photostimulation and even reverted with the final RPh (synchronization). Because the slope is descending during Pre and ascending during RPh, these lines intercept; this occurs first in frontal leads and, at last, in occipital leads.

Figure 6 depicts the descending slopes of AAP before (Pre, black line) and the ascending ones during RPh (grey line) for  $\beta$  in parieto-occipital leads of both hemispheres, which were significant. In the right fronto-central lead both slopes were ascendant and significant.

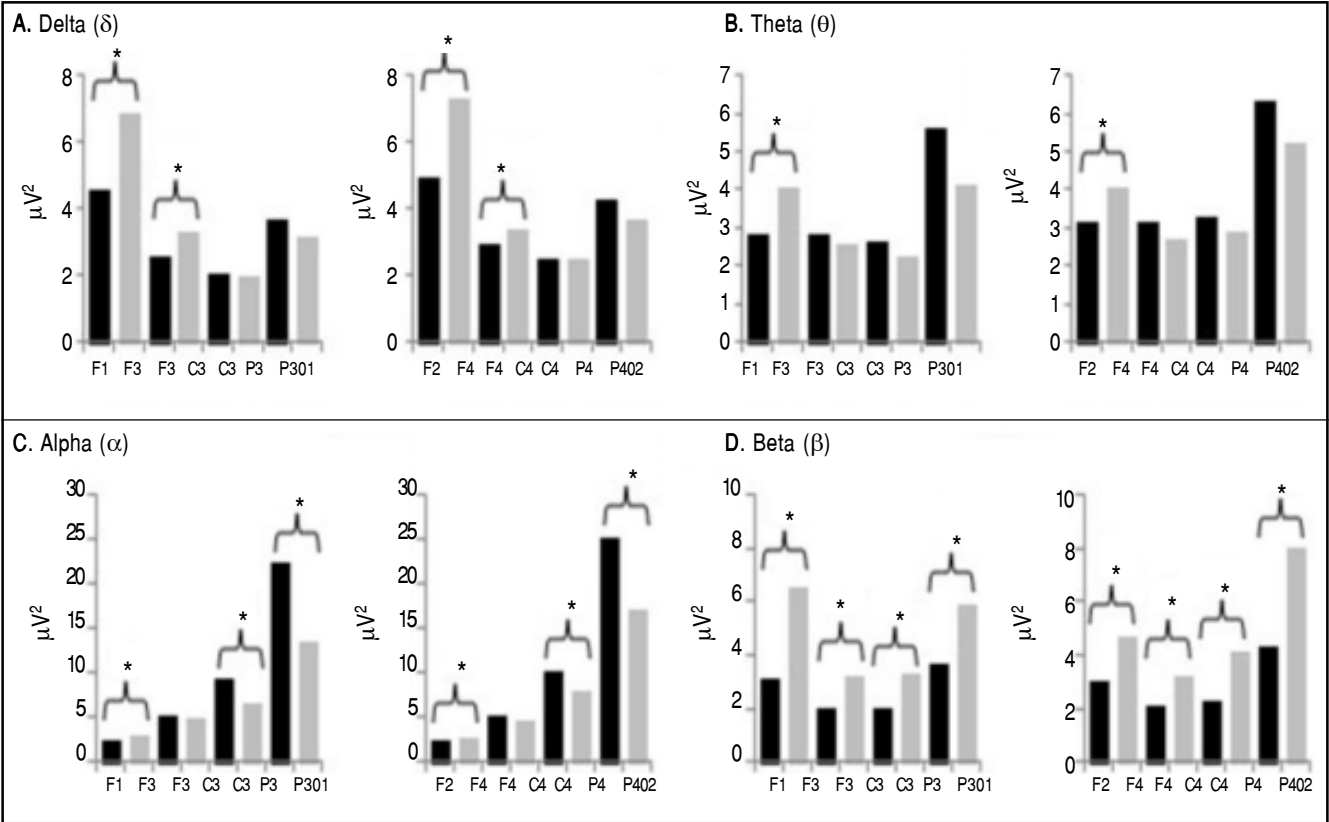


Figure 2. AAP before (black bars) and during RPh (grey bars) of each frequency and lead. Asterisks indicate significant differences ( $p = 0.05$ ).

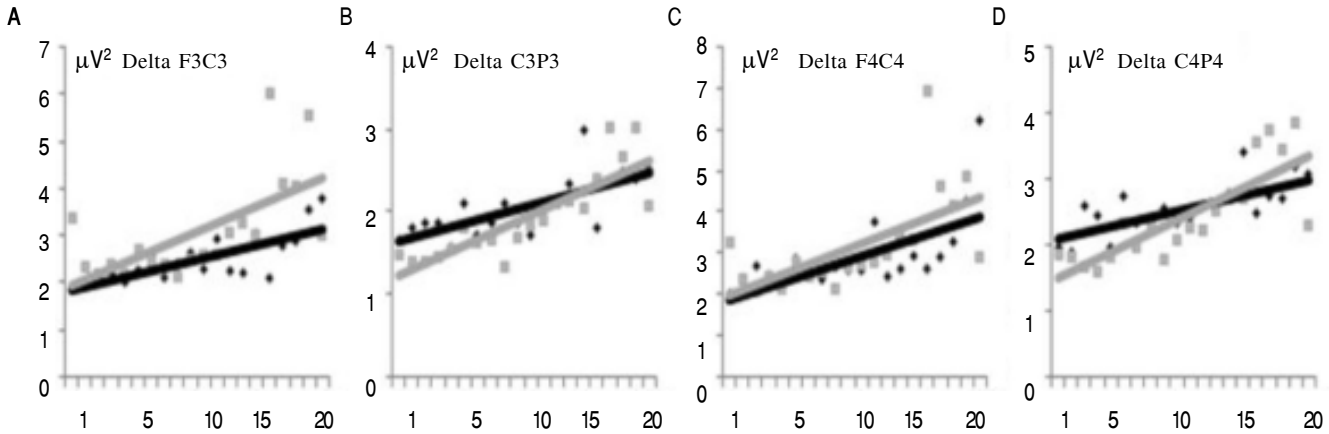


Figure 3. Changes in delta's AAP during RPh. Leads in which delta slopes were significant are depicted. Black line: previous condition. Grey line: photostimulation.

## DISCUSSION

The AP magnitude of oscillations, analyzed in the range of four frequencies, is a measure of the synchronization of the field potentials of cortical circuits with a given cortical topographic distribution. This

allows for their localization (intra-hemisphere and inter-hemisphere), as well as inferring the anatomic-functional condition of its components, represented by relevant electrical and, probably, functional asymmetries. The description of the basal condition confirms that there is a different electromorphogram in diverse cortical regions, establishing also the absolute power profiles of at least four frequencies<sup>30</sup> that are modified by sensory stimulations.

Based on the aforementioned, it is important to recapitulate on the modulation of the delta rhythm with different topographical distributions and intensities before and during the repeated photostimulation. This delta modulation can result from actions of different proportions exerted by the thalamic-cortical connections on the cortical neuronal ensembles, as described by Steriade.<sup>31</sup> There are few publications on the functions of the delta rhythm, however, it has been described that this rhythm can be an important integrator of cortical activity in several areas,<sup>32-34</sup> which is supported by the increase in delta's absolute power. We propose that delta's synchronization generates a diminution in excitability,

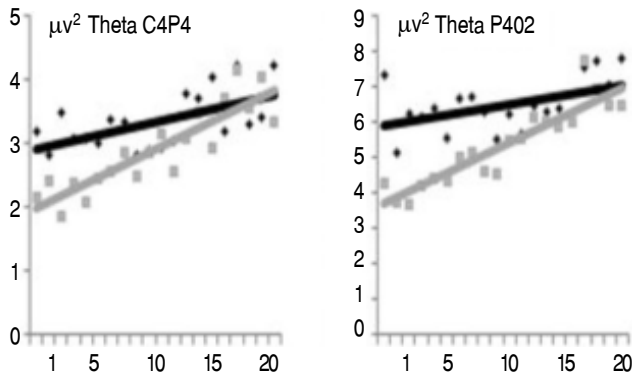


Figure 4. Changes in theta's AAP during RPh. Leads in which theta slopes were significant are presented. Black line: previous condition. Grey line: photostimulation.

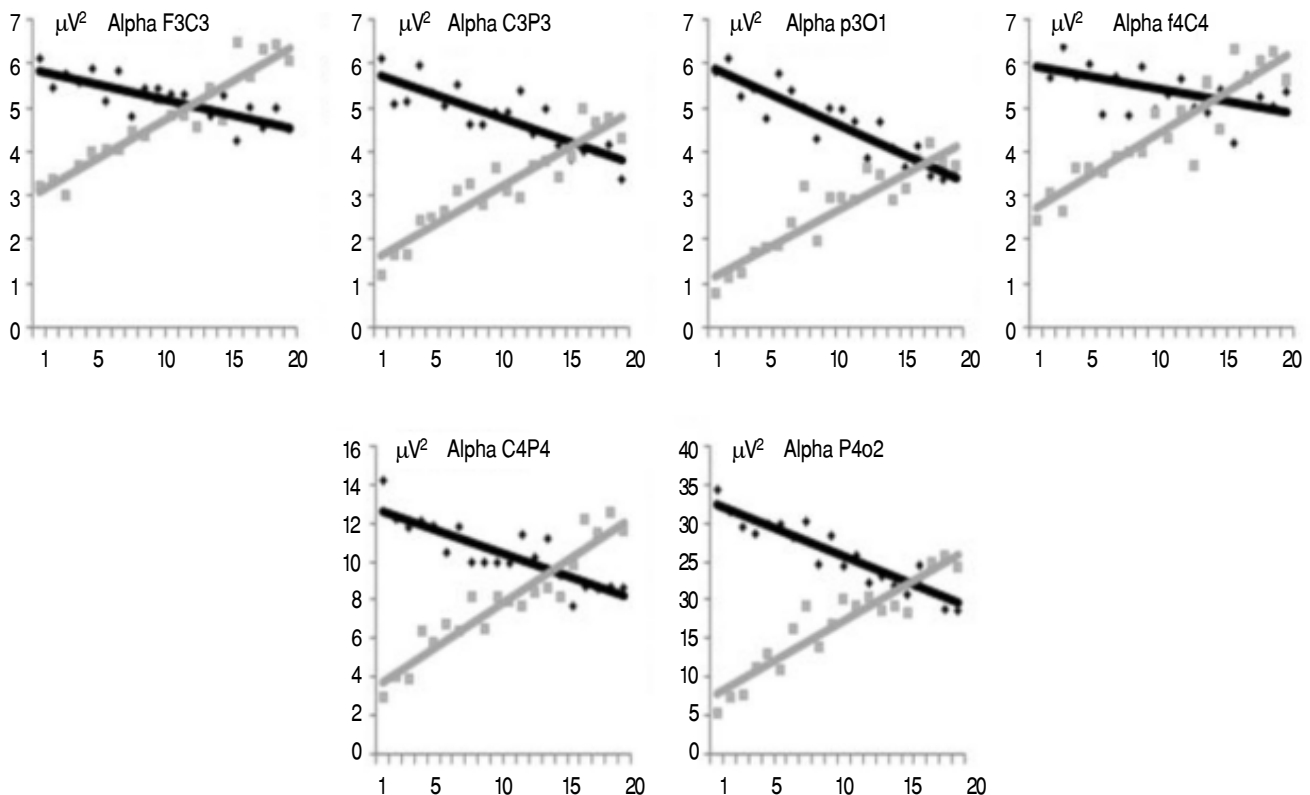


Figure 5. Changes in alpha's AAP during RPh. Leads in which alpha slopes were significant are presented. Black line = previous condition. Grey line = photostimulation.

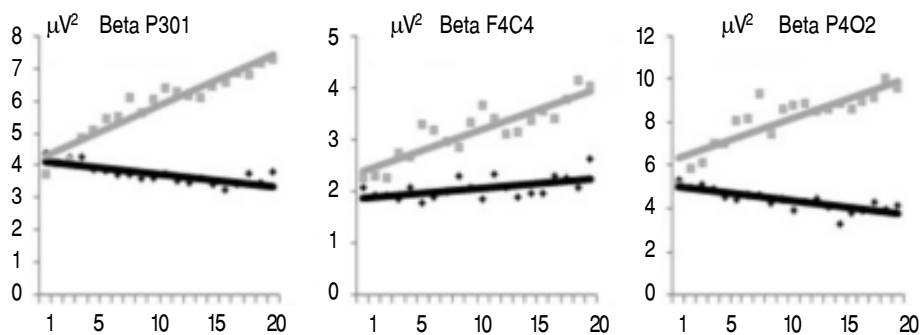


Figure 6. Changes in beta's AAP during RPh. Leads in which beta slopes were significant are presented. Black line: previous condition. Grey line: photostimulation.

a process needed for the occurrence of learning by habituation.

We relate the significant increase in the absolute power of theta in centro-parietal and parieto-occipital regions of the right hemisphere during RPh with processes of identification and memorization of information needed to diminish responses in learning by habituation, although the involvement mainly of the right hemisphere is noteworthy. These modifications can be the result of thalamic nuclei activation and of cortical-thalamic feedback circuits.<sup>35-37</sup> Although the possibility of electrotonic propagation of the theta rhythm by its main producer, the hippocampus, and even through neuronal connections of the paleocortex<sup>36</sup> must be acknowledged. A modification of the oscillations in the alpha range in the condition before photostimulation, which was not expected, but seems “logical” *a posteriori*, is the progressive desynchronization during the waiting time starting at the first series of photostimulation. We interpret this desynchronization as the starting point of analyzing the meaning of the sudden stimulation, and explain it as resulting from the activation of descending circuits that reactivate the reticular-thalamic system on one side and, on the other side, the motor and vegetative systems responsible for the orienting reflex and sympathetic activation. Repeated photostimulation produces an important desynchronization that, however, diminishes with increasing photostimulations and is manifested in an ascending slope that intercepts the descending slope of the previous periods. We assume that if the recordings of the previous condition were continued and more repeated photostimulations were applied both slopes would eventually reach a plateau, during which the corresponding meaning (non significant stimulus) will be assigned, establishing the new condition for the electromorphogram in the multiple neuronal circuits. Hence, habituation is represented by the diminution in desynchronization, becoming synchronization, a

process that occurred in the fronto-central, centro-parietal, and parieto-occipital regions. This type of synchronization correlates with the diminution in action potential discharges, described in monkeys during learning processes,<sup>38</sup> and supports the participation of alpha in sensory-motor and cognitive functions, once a given level of coherence is reached among the different neuronal ensembles or circuits.<sup>18,33</sup> In addition, the alpha/theta interaction has been described as an important part in signals recognition and in their memorization.<sup>9,34-36</sup> Besides, importantly, oscillations in the frequencies within delta and theta ranges became synchronized in the previous conditions, which probably represents the mechanism inducing activity diminution in the frontal and parietal regions that contribute to habituation.

Lastly, regarding beta, little is known about its distribution and functions; for now, we describe the activity of generators in this frequency in cortical regions of both hemispheres, predominating in the posterior region of the right hemisphere, which is the non-dominant for most of the studied subjects; like Barry, *et al.*,<sup>39</sup> we cannot explain yet its significance. However, the descriptions presented herein provide support to the hypothesis that when beta synchronizes in the different cortical regions it coordinates the attention and sensory-perception processes and motor functions, as proposed elsewhere.<sup>10,33,34</sup> In this work, we interpret beta's synchronization as of synchronization, which diminishes the excitability of the neuronal ensembles indispensable for learning by habituation.

Although the present paper relates the modifications of the cerebral oscillations intensity recorded at the cortical level with habituation, it does not allow identifying the origin and sequence of the modifications. To elucidate the latter, we are applying currently computational procedures to analyze the coherence of the frequencies in the different regions at different moments of the process. Another limita-

tion is the lack of recordings of representative variables of the sympathetic system; therefore, in the following studies we have added recordings of cutaneous conductance and cardiac frequency variability. However, the present results have enabled us to analyze, in patients with sequelae of diverse acquired diseases, the described functional changes.

## CONCLUSION

We show the progressive diminution of alpha's desynchronization that, eventually, with continuing stimulation not affecting the homeostasis of the organism, becomes synchronized. The latter, probably, resulting from the hyperpolarization of neuronal membranes responsible for habituation. These changes in alpha are complemented with synchronization of diverse cortical areas, mainly by an increase in the delta frequency and by the changes in theta and beta frequencies in given areas of the right hemisphere.

## ACKNOWLEDGMENTS

We thank Ingrid Mascher for editorial assistance and Dr. Teodoro Flores for administrative support. This study was performed with support from CONA-CyT-México, Protocol-Salud 2011 1 161587.

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*Recibido el 03 de marzo 2014.*

*Aceptado el 24 de junio 2014.*