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Cognitive Disorders: Diagnosis and Treatment

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Abstract: During the last half century, medical developments have expedited an increase of life expectancy all over the world. Owing to this extension of life, some pathological processes that formerly were considered to exhibit low prevalence now have become top priorities for public health programs. Among these pathological processes, cognitive diseases stand out, the two most frequent being Alzheimer's disease and cognitive disorders of vascular etiology, for which humans are at increased risk beyond age 65. We studied 120 adults with cognitive disorders representing a variety of etiologies. We performed a comparative statistical study between members of this group of patients and a group of general patients by means of different neurophysiological examinations: acoustically evoked potentials, P300, brain electrical activity mapping both in the resting state and under complex stimulation, and Doppler ultrasonographic extracranial and transcranial assessment. The comparative study between both populations revealed significant differences in results of the various tests. Neurotransmitter equilibrium (dopamine, acetylcholine, gamma-aminobutyric acid [GABA], etc.) in the areas of the cerebral cortex related to cognitive disorders is essential in the diagnosis and treatment of these diseases.

Key Words: acoustically evoked potentials; brain electrical activity mapping; cognitive disorders; diagnosis; Doppler ultrasonography; P300; treatment

During the last half century, medical developments have expedited an increase in life expectancy all over the world [1]. Owing to this extension of life, some pathological processes that formerly were considered to exhibit low prevalence now have become top priorities for public health programs. Among these pathological processes, cognitive diseases stand out, the two most frequent being Alzheimer's disease and cognitive disorders of vascular etiology, for which humans are at increased risk beyond age 65.

According to a United Nations estimate, the general population will grow 15% between 1980 and 2025, whereas the population in 60 years is expected to grow approximately 80%. Based on these same projections, the average increase in cognitive disorders would reach 87.2% by 2060.

The objective of our research was to study a group of adult patients presenting with cognitive disorders. We used neurophysiological measurements: acoustically evoked potentials, P300, brain electrical activity mapping both in the resting state and under complex stimulation, and extracranial and transcranial Doppler ultrasonography (USD).

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MATERIALS AND METHODS

We selected 120 adults from the Neurofisiología Otooftalmológica data bank for our study. Their average age was 60.82 ± 14.61 years. The reasons for their consultation were difficulty in concentration and loss of memory. Audiological and ophthalmological examinations did not show any noteworthy pathology. It should be pointed out that 20% of the patients exhibited dizziness with a sensation of unsteadiness, and 44% reported a background of cardiovascular alterations, such as hypertension and hypotension. Cerebral magnetic resonance imaging revealed signs of early cortical cerebral atrophy in 24% of the cases and cerebral vascular lesions in 25%. Various studies were carried out.

Mapping Acoustically Evoked Potentials

We employed P300 wave studies corresponding to the responses of primary auditory areas P2–N2 and to

Table 1. Mapping Acoustically Evoked Potentials

	No.	P300 Wave on Right Stimulation	P300 Wave on Left Stimulation
General	287	327.41 ± 32.04	330.52 ± 38.16
Adults	120	339.64 ± 37.06	349.07 ± 42.63

cognitive areas and to associated temporoparietooccipital areas. Wave P300 was selected for statistical purposes, and its time of latency, amplitude variations, and temporospatial distribution all were analyzed. P300 potential is the neuronal correlation for attention, auditory differentiation capacity, short-term memory, and decision-making capacity [2].

For this study, we used Akonic equipment, model Bio-PC with 21 unipolar derivation channels (Akonic S.A., Buenos Aires, Argentina). An auditory burst tone at 80 dB of intensity was used as the stimulus, at a repetition frequency of 0.5 Hz with contralateral white sound hidden at 50 dB of intensity.

A 1-kHz auditory tone was classified as *frequent* and alternated at random with another auditory stimulus of 4 kHz of frequency (classified as *infrequent*). Patients were expected to calculate mentally the number of infrequent stimuli that appeared during the presentation of all stimuli.

Measuring Cortical Brain Responses

We tested cortical brain responses in the resting state and under complex stimulation (hyperventilation and auditory and visual stimulation). We used the same Akonic Bio-PC equipment to accomplish this measurement, evaluating frequency, amplitude, temporal distribution of the waves, and *Z*-score. Brain electrical activity mapping was carried out in 21 monopolar derivation channels, referred to bilateral mastoids linked through resistances [2,3].

Evaluating Vascular Pathology

We carried out USD extracranial and transcranial evaluation [4] that consisted of supporting in the skull area a probe capable of producing a sound in a frequency. To simplify compilation of statistics, values corresponding to the supratrochlear artery are shown later in the section Results and Comments. The breakeven point of the intracranial inner carotid circuit with the extracranial circuit is the supratrochlear artery. This artery is easily found at the level of the upper and inner angle of the eye. The sound is reflected by the blood cell column that circulates through the artery, thereby allowing for the evaluation of different arterial parameters by means of computer methods: speed, flow, direction of the bloodstream, peripheral resistance, and degree of stenosis.

RESULTS AND COMMENTS

In the mapping of acoustically evoked potentials (P300) in patients in the general group, we observed delayed latency time of wave P300 which was more predominant on left stimulations (Table 1). In cognitive disorders of adults, a reduction of amplitude is observed, as are spatial variations in forming the potential, in keeping with the pathology. In the case of cortical atrophies and Alzheimer's disease, the temporospatial distribution of the potential prevails in frontal areas. In vascular pathological processes, temporospatial distribution of the potential prevails in temporoparietooccipital areas.

In brain electrical activity mapping in the resting state, no significant rhythm differences were observed between those in the general population and the patients having cognitive diseases (Table 2). During hyperventilation and auditory stimulation, in the group of patients with cognitive pathologies, we observed a reasonable increase of alpha rhythm and a drop in theta rhythm as compared to results in the general population (Tables 3 and 4). Under visual stimulation, in the group of patients with cognitive disorders, we observed a remarkable increase in beta-1 rhythm and a drop in delta rhythm that exceeded the normal statistical range (Table 5).

USD performed in the group of patients with cognitive diseases showed significant variations of the different parameters with respect to the general statistics. Those results indicated a high incidence of the vascular component in cognitive diseases of adults (Table 6).

Table 2. Brain Electrical Activity Mapping: Resting State

	No.	Delta Band	Theta Band	Alpha Band	Beta-1 Band	Beta-2 Band
General	353	25.80 ± 14.11	18.53 ± 9.83	41.15 ± 16.58	10.99 ± 7.79	3.52 ± 3.71
Cognitive pathology	120	26.61 ± 13.99	16.68 ± 9.41	41.18 ± 12.51	11.22 ± 5.65	3.78 ± 2.96

Table 3. Brain Electrical Activity Mapping: Stress Due to Hyperventilation Stimulation

	No.	Delta Band	Theta Band	Alpha Band	Beta-1 Band	Beta-2 Band
General	316	29.47 ± 14.84	20.57 ± 12.85	36.49 ± 15.44	10.51 ± 7.22	3.11 ± 2.81
Cognitive pathology	120	30.05 ± 16.41	16.91 ± 10.92	40.10 ± 15.61	9.98 ± 7.13	3.02 ± 2.85

Table 4. Brain Electrical Activity Mapping: Stress Due to Auditory Stimulation

	No.	Delta Band	Theta Band	Alpha Band	Beta-1 Band	Beta-2 Band
General	293	27.68 ± 13.52	18.23 ± 6.15	37.04 ± 17.23	12.32 ± 7.92	4.79 ± 4.25
Cognitive pathology	120	27.75 ± 14.14	15.55 ± 5.89	40.34 ± 18.63	12.46 ± 7.68	4.71 ± 4.22

Table 5. Brain Electrical Activity Mapping: Stress Due to Visual Stimulation

	No.	Delta Band	Theta Band	Alpha Band	Beta-1 Band	Beta-2 Band
General	293	29.52 ± 12.67	16.51 ± 8.19	27.18 ± 12.25	16.25 ± 9.28	4.57 ± 3.21
Cognitive pathology	120	24.68 ± 11.34	16.36 ± 6.54	29.74 ± 13.92	22.32 ± 9.87	6.91 ± 4.04

Table 6. Doppler Ultrasonography of the Supratrochlear Artery

	MSV	MDV	SI
General	14.30 ± 9.25	6.93 ± 4.30	26.04 ± 21.02
Cognitive pathology	21.24 ± 6.10	9.66 ± 5.24	54.60 ± 19.61

MDV = maximum diastolic velocity; MSV = maximum systolic velocity; SI = stenosis index.

CONCLUSIONS

Recent studies have demonstrated that the proper level of neurotransmitters is essential to obtaining so-called superior cerebral functions, particularly language, the praxis, and spatial organization. However, our experience has shown us that drug monotherapy, involving agents that appeal to only some of the trigger mechanisms over the neurotransmitters, shows no positive results.

This finding was observed in studies performed on a 70-year-old patient with slight cognitive disorders and arterial hypertension background, in whom magnetic resonance imaging revealed signs of cortical atrophy. Disorganization in the electroencephalographic design was evident in the *Z*-score, which revealed an increase in the waves corresponding to the beta-1 band during visual stimulation, whereas responses obtained in the resting state remained within normal range. Acoustically evoked potentials (P300) demonstrated pathological latency and amplitude, but the temporospatial distribution was normal. The USD extracranial assessment of the supratrochlear arteries showed an important increase of the stenosis index and of the maximum systolic velocity.

This patient was medicated with piracetam, 200 mg twice daily; donepecil, 10 mg once daily; and nimodipine, 30 mg twice daily, for 3 months. Results obtained after treatment showed that the electroencephalographic design had returned to normal, with a normal *Z*-score, normal amplitude of potential P300, and shortening of the latency. USD of the supratrochlear arteries also was normal.

In everyday practice, we always employ a multidrug approach:

1. Neuronal metabolic stimulants (piracetam, aniracetan, etc.)
2. Modifiers of the dysfunction of the neurotransmitters (acetylcholinergic [cdp-choline, lecithin]; anticholinesteric [donepecil]; and glutamine regulators [memantine])
3. Cerebral circulation enhancers (calcium antagonist [nimodipine] and rye ergot derivatives [ergotoxin])

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