Research Article

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EEG Findings in Diffuse Lewy Body Disease and Parkinson´S Disease with Dementia

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Abstract

Objectives: Electroencephalography can still reveal a variety of focal abnormalities in different neurological diseases. EEG could represent an easy and economical tool to differentiate parkinsonisms when compare to neuroradiological studies. We want to report the EEG findings in a serie of diffuse lewy body disease and demented Parkinson´s disease patients of our unit of movement disorders, in a prospective and open label study.

Methods: 30 consecutive subjects were enrolled, 10 patients with criteria for diffuse lewy body disease, 10 patients with criteria for Parkinson's disease (demented) and 10 normal subjects. The MMSE, the GDS/FAST staging scale, the UPDRS and the Schwab and England scales and NPI-Q scale were administered. A 36-channel video-QEEG recording and Spectral EEG analysis were determined in patients and subjects.

Results: Diffuse lewy body disease patients showed a mean of occipital frequency of 7.7 ± 0.3 Hz (P: 0.04), 70% of them showed temporal lobe amplitude's asymmetries (P: 0.04) and 90% showed a Frontal Intermittent Delta Activity (P: 0.02). Parkinson's disease patients showed a mean of occipital frequency of 8.8 ± 0.8 Hz, 20% of them showed temporal lobe asymmetries and 10% showed Frontal Intermittent Delta Activity. Frontal Intermittent Delta Activity and temporal lobe amplitude's asymmetries in Diffuse lewy body disease patients were statistically significant compared to the normal subjects, while the Parkinson's disease patients showed no statistical differences from normal subjects.

Conclusions: Electroencephalographic findings in Diffuse Lewy Body Disease patients could represent an electrophysiological marker that might aid in distinguishing Diffuse Lewy body disease patients from Parkinson's disease patients, further studies are needed to validate our results

Keywords: Parkinsonism; EEG; Lewy body disease

Introduction

In the past, identification of focal EEG abnormalities played an important role in the diagnosis of cortical encephalic injuries of different etiologies. With the current availability of neuroimaging techniques such as CT and MRI, EEG has become less widely used, though it is still important in the diagnosis of patients with seizure disorders, epilepsy, and altered mental status. In cognitive disorders, EEG is sometimes used along with the available medical information in the diagnosis and management of patients with neurodegenerative diseases as diffuse Lewy body disease (DLBD) [1-3], Alzheimer's disease [4-6] and Parkinson's disease (PD). Global EEG measures have potential use as biomarkers in the study of both early and late cognitive deterioration in PD [7].

While EEG is no longer a preferred modality for neurophysiological diagnoses in neurodegenerative diseases, it can still reveal a variety of characteristic focal abnormalities in different neurological diseases. A framework for analysing and interpreting focal abnormalities on EEG recordings is necessary for the evaluation of the clinical implications in patients with neurological disorders. For the above reasons, we report in this article the EEG findings of a serie of DLBD and PD (demented) patients of our unit of movement disorders in a prospective open label study.

Materials and Methods

We enrolled 30 consecutive subjects, including 10 patients fulfilling the probable and possible clinical criteria for DLBD [8], 10 patients meeting the Queen Square Brain Bank criteria for PD (Demented) and 10 normal control subjects with similar demographic characteristics. DLBD patients should show the following criteria in the first two years of symptom's onset: 1. Fluctuating cognition with pronounced variations in attention and alertness 2. Recurrent visual hallucinations typically well formed and detailed 3. Spontaneous features of Parkinsonism. As a central feature, a progressive cognitive decline of sufficient magnitude to interfere with normal social and occupational functional. Also, DLBD patients should show deficits on tests of attention and of frontal-subcortical skills and visuospatial ability.

Demented-PD patients should show a clear cognitive decline with a neuropsychological profile of dementia associated to PD (alteration in fronto-subcortical skills and visuospatial ability) sufficient magnitude

to interfere with normal social and occupational functional and such symptoms starting at least 5 years after the onset of motor sings

Patients and normal subjects were evaluated by two neurologists to determine their clinical state. The Mini Mental State Scale (MMSE), the GDS/FAST staging scale, the Unified Parkinson's Disease Rating Scale (UPDRS I, II and III) and the Schwab and England activities of Daily Living scales were administered. Neuropsychiatric inventory scale questionary (NPI-Q) was administered systematically to DLBD and PD patients and a complete neuropsycological battery was performed in all the patients. Patients and control subjects were submitted to a 36-channel video-EEG recording for 30 minutes, and different EEG montages (conventional 10/20 system) were analyzed to determine the electrophysiological parameters in all regions of both brain hemispheres.

To evaluate the intra and interobserver agreement of the EEG reading, the EEGs were interpreted by two EEG trained neurologists. Observer number one performed three readings on three different moments to assess intraobserver agreement, while the third reading was blind for the diagnosis. Interobserver agreement was assessed with a single blind reading for the diagnosis of the two observers. Agreement was measured with the kappa index.

Intraobserver agreement to differentiate if the EEG was normal or abnormal was substantial when the three readings were compared (kappa index: 0.66-0.78). The interobserver agreement assessing between abnormal or normal EEG was slight (k=0.12).

Activation methods were photo-stimulation and hyperventilation. There was considered to be an asymmetry of amplitude in a subject if there was an amplitude difference between two homologous brain regions greater than 50%.

Spectral EEG analysis and QEEG was determined in patients and subjects. For each subject, 20 mini-epochs of artefact-free 4 s sections were selected for a total sample size of 80 s. Amplitude and frequency spectral analyses were performed using a commercial software package which calculates the fast Fourier transform on 4 s mini-epochs with a resolution of 0.25 Hz. Four frequency bands were defined as δ (0.75-3.75 Hz), θ (4.00-7.75 Hz), α (8.00-12.75 Hz) and β (13.00-20.25Hz).

A mean value of the spectral analysis of the subjects of each group was also determined at the end of the study.

Patients and subjects were asked not taking any other drug (opioids, benzodiazepines or other EEG drug-modifying), which could modify the EEG recording at least one week before the test (EEG).

Cranial angio-MRI and Datscan was perfomed in all DLBD and PD patients.

Descriptive statistics were carried out and a Fischer`s exact test was used to compare categorical variables between the three groups. Statistical significance was considered to be $p<0.05$. All data were analyzed with the SPSS statistical software package.

The one-way multivariate analysis of variance (one-way MANOVA) was used to determine whether there were any differences between independent groups.

All procedures were carried out with the adequate understanding and written consent of the subjects involved in this study and with the approval of the ethical board of our hospital.

Results

Clinical findings

The 10 DLBD patients consisted of 6 men and 4 women with a mean age of 72 ± 2 years. Stages II or III, in the Hoehn and Yahr scale. Ten patients showed well-structured visual hallucinations from the very beginning of the disease and such hallucinations were not depending on the l-dopa dose. The Mean l-dopa dose was 330 ± 10 Mg and they were not taking other dopamine agonists. Patients scored a mean of 23 ± 1 points on the total UPDRS scale, and the mean scores on the Schwab and England scale was 80%. All the DLBD patients showed a GDS fast scale stage 6 (Moderately-Severe Cognitive Decline) and scored a mean of 19 ± 2 points on the MMSE scale, a mean of 16 ± 1 in the NPI-Q. Ten PD patients (7 men and 3 women, mean age 70 ± 3 years), stages III, in the Hoehn and Yahr scale, scored a mean of 28 ± 2 points on the UPDRS total scale, 20 ± 2 points on the MMSE scale, 3 of them stage 6-B on the GDS fast scale and the other 7 PD patients showed stage 6-C of the GDS fast scale. A mean of 80% on the Schwab and England scale. PD patients showed a mean of 14 ± 2 in the NPI-Q and 4 PD patients reported well-structured visual hallucinations which were likely related to L-dopa doses. PD patients showed a mean l-dopa dose was 625 ± 15 mg. Normal subjects with similar demographic features showed no hallucinations, Parkinsonism, or cognitive decline (Table 1).

	Age	Sex (M/F)	Onset years	GDS fast	MMSE	Visual Hallucinations	H-Y	UPDRS	S-E	NPI-Q l-Dopa
			(Mean)	(Mean)	(Mean)		II and III	(Mean)		
DLBD	72 ± 2	6/4	4	6-A	21 ± 2	8 (80%)	6/4	23 ± 1	80%	16 ± 1 330 ± 10
PD	70	7/3	7	6-B	20 ± 2	2 (20%)	7/3	28 ± 2	80%	14 ± 2 610 ± 15
Subjects		8/2	-	-	30	0	-	-	-	- -

Table 1: Demographic features of DLBD and PD patients and normal subjects.

Radiological findings

At the cranial angio-MRI, DLBD patients showed a global brain hypotrophy (10/10, 100 %, p: 0.02), and in 9/10 of the patients (90%, p: 0.02) hyper-intensity signals in T2 sequence in brainstem, particularly in the pons. 10 of the DLBD patients (90%, p: 0.02) showed a reduction in SNPc with statistical significance when compared to PD patients and normal subjects.

EEG findings	Occipital frequency Mean ± SD (Hz)	Temporal amplitude Mean ± SD (Mv)	Temporal lobe amplitude asymmetry (Mv)	FIRDA
DLBD	7.7 ± 0.3 P: 0.04	46 ± 2.8	7 (70%) P: 0.04	9 (90%) P: 0.02
PD	8.8 ± 0.8	38 ± 1.9	2 (20%)	1 (10%)
Subjects	10.2 ± 1.1	58 ± 2.2	1 (10%)	0

Table 2: EEG findings in DLBD and PD patients compare to normal subjects.

All DLBD and PD patients showed a lower activity of presynaptic DAT (23-I Ioflupane (Datscan®) presynaptic) suggesting presynaptic degeneration (Tables 2 and 3).

QEEG findings (Spectral analysis)

DLBD patients exhibited a mean occipital frequency of 7.7 ± 0.3 Hz (p=0.04) and a mean amplitude of 46 ± 2.8 mV (p=0.6); no inter-hemispheric asymmetries in amplitude were found in the occipital lobes. In the temporal lobe regions, DLBD patients showed a mean frequency of 5.6 ± 1.1 Hz (p=0.9) and a mean amplitude of 35 ± 0.8 mV (p=0.7). Inter-hemispheric temporal lobe asymmetries in amplitude were found in 7 of 10 patients (70%) (p=0.04). The mean frontal frequency was 16 ± 1.8 Hz (p=0.8) with a mean amplitude of 20 ± 2 mV (p=0.6). Nine of 10 DLBD patients (90%) showed frontal intermittent recurrent delta activity (FIRDA) (p=0.02) for a mean duration of 3 seconds at a mean frequency of 3.5 ± 0.3Hz and an amplitude of 80 ± 3 mV, the spectral analysis showed a predominant delta activity in frontal regions in the nine DLBD patients who had FIRDA (Figure 1); other abnormal EEG activities were not found. Inter-hemispheric asymmetries in amplitude in frontal regions were not found in DLBD patients.

In the occipital region, PD patients displayed a mean frequency of 8.8 ± 0.8 Hz (p=0.08) and a mean amplitude of 55 ± 1.9 mV of amplitude (p=0.8), and no interhemispheric amplitude asymmetries were observed.

Temporal lobe regions showed a mean frequency of 5.2 ± 0.7 Hz and mean amplitude of 38 mV (p=0.6). Two of the 10 (20%) PD patients showed interhemispheric temporal lobe amplitude asymmetry (p=0.07).

FIRDA was found in 1 of the 10 PD patients (p=0.12). Interhemispheric asymmetries in frontal regions were not found in the PD patients (Table 3).

Figure 1: FIRDA and temporal lobe amplitude's asymmetry in a DLBD Patient.

From the eight DLBD patients with visual hallucination only two showed this visual perceptive disorder during the EEG procedure and none PD patient showed hallucination during EEG.

	SNPc reduction	Brainstem hyper intensity	Global hypo trophy
DLBD n=10	10 (100%), p:0.02	9 (90%) %, p=0.02	10 (100%), p: 0.02
PD n= 10	6 (60%,) p: 0.04	2 (20%), p: 0.07	4 (40%), p: 0.05

Table 3: Cranial MRI findings DLBD and PD patients. DLBD patients showed: SNPc reduction, Brainstem hyper intensity and Global hypo trophy statistically significance compared to PD patients.

Discussion

Diffuse Lewy body disease (DLBD) is a neurodegenerative disorder characterized by cognitive decline, Parkinsonism and perceptual disorders such as visual hallucinations. Fluctuations in state of awareness and susceptibility to neuroleptic drugs are also accepted as secondary diagnostic clinical findings in DLBD patients [8,9]. Other radiological, neurophysiological and blood tests provide few information to confirm DLBD diagnosis. Electroencephalographic studies have reported findings in DLBD and AD patients [10-13]; however, EEG is not a widely employed diagnostic measure in the study of neurodegenerative and other cognitive disorders.

We observed FIRDA in 9 of 10 DLBD patients (90%) (p=0.04), whereas only 1 PD patient showed FIRDA. Some authors have pointed out that FIRDA is typically observed after frontal and parietal injuries resulting from tumors or ischemic strokes [14,15]. Frontal visual alteration is a typical finding in the neuropsychological profile of DLBD patients, and we hypothesized that abnormal FIRDA activity observed in DLBD patients may originate from cortical or subcortical frontal injuries, which are difficult to observe with available neuroimaging techniques (PET, SPECT). Eight of our 10 DLBD patients showed well-structured, visual hallucinations, but this does

not provide evidence for a definitive relationship between FIRDA and visual hallucinations. In fact, we did not observe any temporal relationship between the QEEG findings described above and visual hallucination in DLBD patients. Further studies should be conducted to determine whether FIRDA may be an electroencephalographic marker of visual hallucinations.

FIRDA and generalized intermittent rhythmic delta activity (GIRDA) are usually associated with a global cerebral dysfunction due to metabolic disorders. According to some authors, these are rarely caused by subcortical lesions or elevated intracranial pressure [16-18]. FIRDA can also be a normal finding in elderly subjects, especially during states of drowsiness; however, all patients in this study were alert and awake when FIRDA was observed [19].

Seven of the 10 DLBD patients (70%) showed voltage amplitude asymmetries between the temporal lobes (p=0.04), and this is a finding that has been reported previously in DLBD patients. Some neuropathological studies have reported temporal lobe asymmetry in DLBD patients related to Lewy neurites in the hippocampal CA2-3 region [20]. Amplitude asymmetries were uncommon in our PD patients and were not statistically significant when compared to normal subjects. Lewy neurite deposits in subcortical regions of the frontal lobe could provide a possible explanation for FIRDA.

Widespread asymmetries in the amplitude of the background activity should be interpreted with caution because these can occur in healthy patients. However, focal asymmetries are frequently associated with significant pathology; for example, a temporal lobe voltage asymmetry greater than 50% has been commonly associated with structural brain lesions [21,22].

DLBD patients describe in this article ,showed more global brain hypotrophy in the cranial MRI when compare to PD patients however they showed no relevant brain asymmetry in the cranial MRI that can explain the inter-hemispheric asymmetry shown in the EEG.

DLBD patients showed a mean occipital frequency of 7.7 Hz, which is considered slow for posterior activity; this was significantly different from activity observed in normal subjects. PD patients did not exhibit statistically significant differences in the background frequency compared to normal subjects, which is notable if we take into account that DLBD and PD patients showed similar cognitive status in this study. Thus there appears to be a relationship between cognitive decline and the slowing of the background frequency in our DLBD patients, and this observation has been reported in past research.

We decided to compare the QEEG findings in patients with well-defined clinical criteria of DLBD and demented-parkinson´s disease patients due to the clinical and neuropathological similarities of those both alpha-sinocleinopathies. We are aware that the small number of patients included in this study limits the validity and the reliability of the results. Further studies with larger population should focus in diffuse lewy body disease and demented-Parkinson´s disease patients because probably larger population studies could show different electrophysiological findings and therefore different conclusions could be taken in this case.

The two most frequent alpha synucleinopathies, Parkinson disease (PD) or brainstem predominant type of Lewy bodies, and dementia with Lewy bodies (DLB), are neurodegenerative multisystem disorders with widespread occurrence of α-synuclein containing deposits in the central, peripheral, and autonomic systems [23].

Both, DLBD and PDD-dementia are part of a spectrum of the Lewy bodies disease affecting the cortical areas from the very beginning in the case of DLBD or as a late phenomenon resulting from the late spreading from subcortical to cortical areas in PD- dementia [24].

Unlike normal aging, cognitive decline is associated with alterations in the temporo-spatial characteristics of EEG patterns. Diagnosis of the initial stages of dementia is based mainly on neuropsychological testing and on clinical suspicion, with EEG findings generally being nonspecific. Klassen BT et al have proposed that the QEEG measures of background rhythm frequency and relative power in the band are potential predictive biomarkers for dementia incidence in PD [25].

It is interesting to note that in our EEG recordings, FIRDA and temporal lobe amplitude asymmetries in our DLBD patients were significantly different compared to the normal subjects and demented-PD patients, while the PD patients showed no statistical differences from the control group (Figure 2).
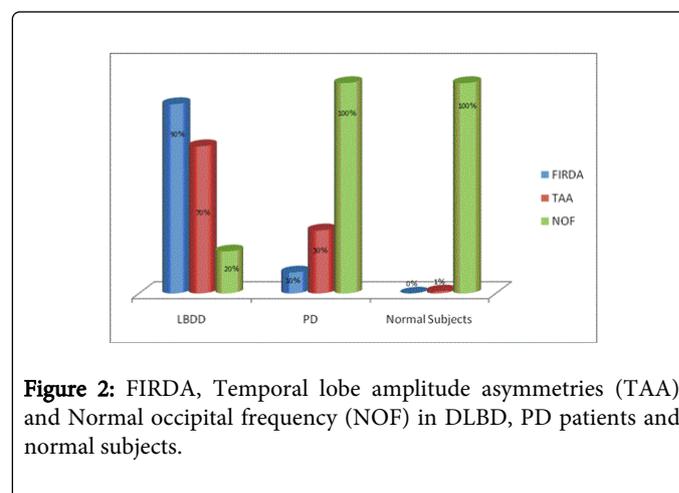

Figure 2: FIRDA, Temporal lobe amplitude asymmetries (TAA) and Normal occipital frequency (NOF) in DLBD, PD patients and normal subjects.

Finally, EEG alterations in DLBD patients could represent an electrophysiological marker that might aid in distinguishing DLBD patients from Demented-PD patients. As the present study has some limitations, we believe that further studies in larger patient populations are necessary to confirm our findings.

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