The Rhythms of AMBEs (Arousal-Related Motor Behavioral Episodes) In Agrypnia Excitata: A Video Motor Analysis

Arturo Garay, Daniela L. Giardino, Cristián Huck-Iriart, Susana Blanco, Anthony T. Reder

PII: S1389-9457(20)30322-1

DOI: https://doi.org/10.1016/j.sleep.2020.06.037

Reference: SLEEP 4508

To appear in: *Sleep Medicine*

Received Date: 17 April 2020

Revised Date: 17 June 2020

Accepted Date: 30 June 2020

Please cite this article as: Garay A, Giardino DL, Huck-Iriart C, Blanco S, Reder AT, The Rhythms of AMBEs (Arousal-Related Motor Behavioral Episodes) In Agrypnia Excitata: A Video Motor Analysis, *Sleep Medicine*, https://doi.org/10.1016/j.sleep.2020.06.037.

THE RHYTHMS OF AMBEs (AROUSAL-RELATED MOTOR BEHAVIORAL EPISODES) IN AGRYPNIA EXCITATA: A VIDEO MOTOR ANALYSIS.

Arturo Garay[1], Daniela L. Giardino[1], Cristián Huck-Iriart[2], Susana Blanco[3] and Anthony T. Reder[4]

Medicina del Sueño-Neurología-Centro de Educación Médica e Investigaciones Clínicas “Norberto Quirno” (CEMIC), Ciudad de Buenos Aires , Argentina (1), Escuela de Ciencia y Tecnología, Universidad Nacional de San Martín (UNSAM), Buenos Aires, Argentina (2),Instituto Nacional del Cáncer - CONICET, Ciudad de Buenos Aires, Argentina (3), Department of Neurology, University of Chicago, Chicago, IL, USA (4).

INTRODUCTION

“Agrypnia excitata” (AE) is a term that describes a syndrome caused by a dysfunction in thalamo-limbic circuits, producing severe insomnia, mental confusion, dream enactment, and motor and autonomic activation (1,2).

In patients with Agrypnia Excitata occurring in fatal familial insomnia (AE-FFI), oscillatory EEG rhythms appear during "pseudosleep” (3, 4). In these patients, arousal-related motor behavioral episodes (AMBEs) with and without clearly elaborated behaviors, such as dream-enacting episodes-REM Behavior Disorder, constitute an intriguing finding without a known mechanism (5). We reevaluated a proven FFI case (3,6) using a new motor video technique to analyze the AMBEs behavior.

CASE DESCRIPTION

A 41 years-old male, with a previous history of intermittent neurological symptoms and previously diagnosed as having multiple sclerosis was hospitalized in October 1992 presenting dizziness, diplopia, and worsening of sensory and motor complaints (3,6). Over the following months the patient developed a syndrome characterized by severe insomnia, motor agitation, uncontrollable sleepiness, increased daytime somnolence, oneiric behaviors, some of them mimicking daily life activities and some other more elaborated, like RBD plus autonomic alterations (unstable BP, diaphoresis, tachypnea, unexplained hyperpyrexia) that we conceptualized as Agrypnia Excitata. Moreover, the patients presented psychiatric symptoms (depressive mode and abnormal behavior), memory and attentional deficits, ataxia, dysartria, myoclonus and frontal lobe signs. These clinical features worsened rapidly and myoclonus, dementia, autonomic instability and general inanition resulted in death within 5 months of the first visit reported here. Histopathology showed a virtually complete neuronal loss with gliosis of the ADM nuclei of thalamus. Neuroendocrine studied demonstrated twice normal level of plasmatic cortisol with preserved rhythmicity and normal profile of melatonin secretion. The genetic profile was consistent with FFI showing a mutation of the PrP gene *(*D178N/129M*).*

VIDEO ANALYSIS

We reanalyzed raw data of polysomnograms of our case of FFI (PSGs, n=5) and a nocturnal video polysomnogram of our case of FFI (3, 5). The video motor analysis (VMA) of an 8-hour S-VHS tape recording was done by computer programs using Python 3.7 scripting OpenCV 4.2.0, Numpy 1.17.2, Scipy 1.3.1 and Matplotlib 3.1.1 libraries. These programs were employed to register and analyze movements of the head and legs as a function of time during the four hours considered to analyze correlates of head and leg movements (Figure B and C). The fundamental frequencies were obtained by fast Fourier transform (FFT). Statistical analysis used non parametric t tests, Pearson and Spearman's Covariance Matrix of data.

Our case of AE-FFI showed an intra atypical REM sleep fragmentation cycling behavior, characterized according to standard polysomnograms, during AMBEs (3) (Figure A). Segmental analysis using VMA obtained with fast Fourier transform during AMBEs, showed significant peaks for head (H) and right or left leg (L_r /L_l) movements. These peaks cycled in a range of 1.5 to 39 minutes (Figure B and C), with a low correlation between H (Figure D1) and L_r /L_l (r covariance H/ L_l : 0.04; H/ L_r /L_l : 0.08) (Figure

D2). A selected fragment of 10 minutes of VHS video, in which the video was intentionally blur to avoid facial detection, displays the low correlation between head and legs movements frame by frame and exemplifies the body parts movement recordings for posterior signal analysis (see Video).

DISCUSSION

We found a multiplicity of peaks of movements with a striking lack of correlation between head and leg motor movements and between motor movements of the two legs themselves, by using video motor analysis of these segmental motor oscillations with or without purposeful-dream enacting episodes. This poor correlation suggests a disconnection between cortical and sleep postural behavior/movements. The observed disconnection may be related to disruption of the central motor pattern generator (CMPG), that mediates final motor expressions (7). As it is well known the CPMG is largely controlled by neuronal networks of the spinal cord that mediates activities such as walking, flying, swimming, and, in some situations, is capable of self production of locomotor like movements. Since abnormal prion protein has been detected in spinal cord in FFI, the observed lack of correlation between head and leg movements during AMBEs could be due to disconnection between afferents and descending motor inputs of locomotion to the spinal cord or due to dysfunction of the spinal cord itself (8,9).

Our study suggests that spinal cord involvement should be added to the manifestations of thalamo-limbic-brainstem disconnection that were presented in our original case of Agrypnia excitata/FFI, and furthermore, that AMBEs might be incorporated into the context of motor abnormalities observed in prionopathies in addition to FFI (10).

Finally, we underline the use of these techniques of video analysis that are extremely useful and unexpensive for the evaluation (or reevaluation) of patients in whom abnormal sleep patterns are linked with motor (AMBEs), behavioral (RBD), and/or autonomic abnormalities without the use of sensor movements devices, which are not always available.

REFERENCES

[1]. Lugaresi E, Provini F. Agrypnia excitata: clinical features and pathophysiological implications. Sleep Med Rev. 2001 Aug;5(4):313-322.

[2] Ferri R., Lanuzza B., Cosentino I.I., Iero I., Russo N., Tripodi M. and Bosco P. Agrypnia Excitata in a patient with progeroid short stature and pigmented neve (Mulvihil-Smith syndrome). J. Sleep Res. 2005, 14:463-470.

[3] Garay A., Spire J.P., van Cauter E., and Reder A. REM and NoREM Sleep in Fatal Familial Insomnia. Neurology 1994 (Suppl.2):218-219.

[4] Provini F., Cortelli P., Montagna P., Gambetti P and Lugaresi E. Fatal familial insomnia and agrypnia excitata: Sleep and the limbic system. Revue Neurologique 2008, 164: 692-700.

[5] Antelmi E, Ferri R, Iranzo A, Arnulf I, Dauvilliers Y, Bhatia KP, Liguori R, Schenck CH, Plazzi G. From state dissociation to status dissociatus. Sleep Med Rev. 2016 Aug;28:5-17.

[6] Reder AT, Mednick AS, Brown P, Spire JP, Van Cauter E, Wollmann RL, Cervenàkovà L, Goldfarb LG, Garay A, Ovsiew F, et al. Clinical and genetic studies of fatal familial insomnia. Neurology. 1995 Jun;45(6):1068-75.

[7] Guertin P.A. Central pattern generator for locomotion: anatomical, physiological, and patohophysiological considerations. Frontier in Neurology 2013, (3)183: 1-15.

[8] Rudge P., Jaunmauktane Z., Hyare H., Ellis, M. Koltzenburg M., Collinge J.andMeadS. Early neurophysiological biomarkers and spinal cord pathology in inherited prion disease. Brain. 2019 Mar 1;142(3):760-770.

[9] Brown K. and Mastriani J.A. The prion diseases. Journal of Geriatric Psychiatry and Neurology 2010, 23(4):277-298.

[10] Rodriguez-Porcel F, Ciarlariello VB, Dwivedi AK, Lovera L, Da Prat G, Lopez-Castellanos R, et al. Movement disorders in prionopathies: A systematic review. Tremor Other Hyperkinet Mov. 2019; 9. doi: 10.7916/tohm.v0.712.

HIGHLIGHTS

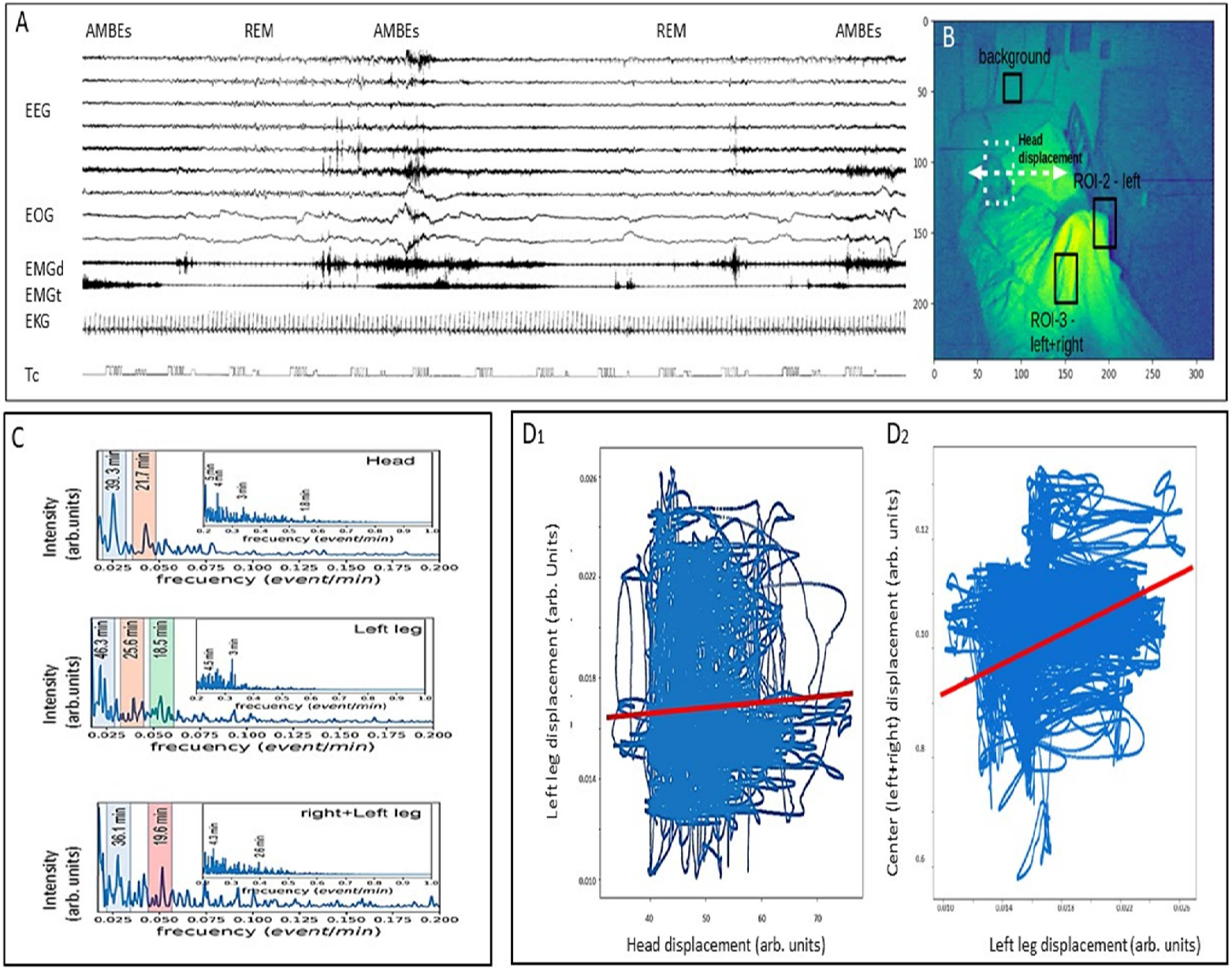
- In patients with Agrypnia Excitata with fatal familial insomnia (AE-FFI), oscillatory EEG rhythms appear during "pseudosleep" and during atypical REM sleep
- Arousal-related motor behavioral episodes (AMBEs) with and without clearly elaborated behaviors, such as REM Behavior Disorder, constitute an intriguing finding without a known mechanism.
- Spinal cord involvement should be added to the manifestations of thalamo-limbic-brainstem disconnection.
- AMBEs can be incorporated into the context of motor abnormalities observed in FFI and other prionopathies.

FIGURE
Footnote (Legend)

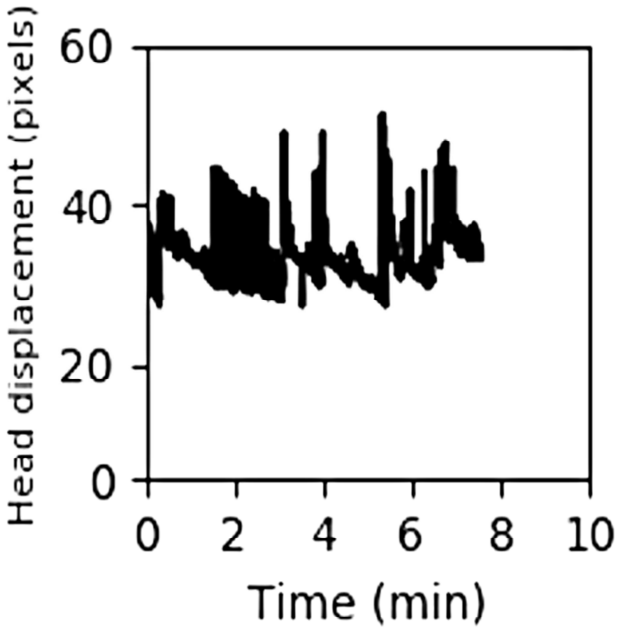
Figure. A) Representative nocturnal polysomnographic record showing “atypical REM sleep” – AMBEs (arousal-related motor behavioral episodes) oscillations (EEG: electroencephalography; EOG: electrooculography; EMG: electromyography, digastric(d), tibial (t); EKG: electrocardiography); B) Selected regions of interest (head ROI and legs ROI) and the quiescent background ROI used in our FFI patient. In the case of legs, frame analysis (30fps) detect changes of integrated monochromatic intensity of a selected region of interest (ROI), normalized with the integrated intensity of a quiescent ROI as background (Movements were expressed as M(t) = intensity_ROI/intensity_background where t is time). In the case of the head, we followed the center of mass of the head averaging 1D profile in the horizontal axis; C) Segmental analysis using FFT of video motor

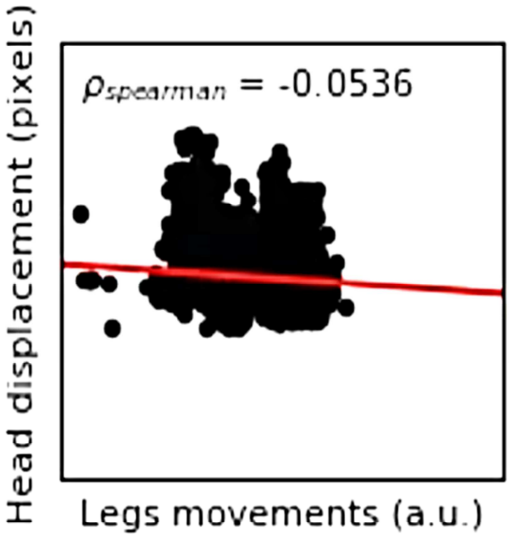
analysis; D1) Spearman's Rho for Head and Legs; D2) Spearman's Rho for Legs.

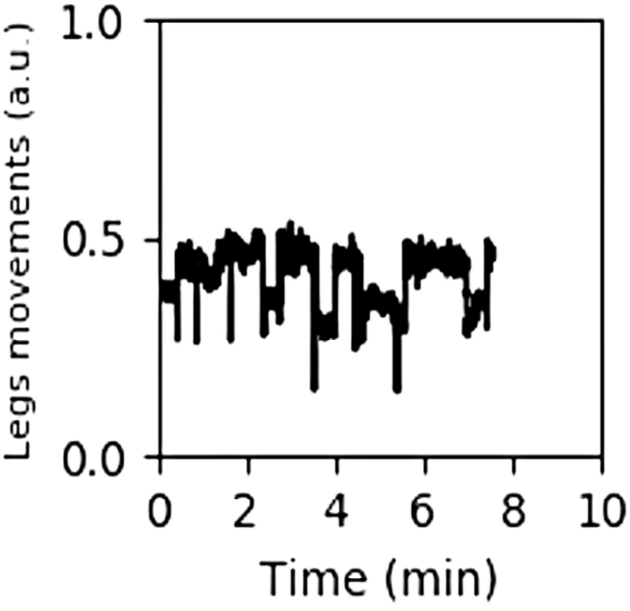
‘

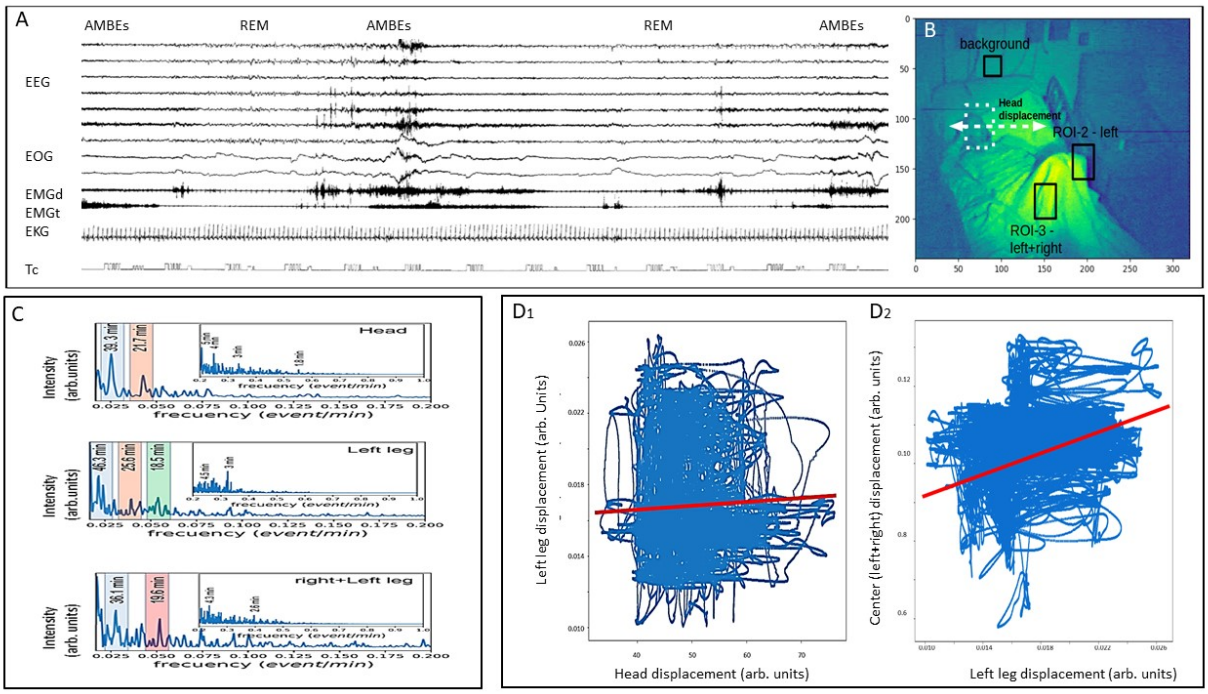


VIDEOSTILL


Head displacement (pixels)
60
40
20
0
0
2
4
6
8
10
Time (min)


$\rho_{spearman}$ = -0.0536
Head displacement (pixels)
Legs movements (a.u.)


Legs movements (a.u.)
1.0
0.5
0.0
0
2
4
6
8
10
Time (min)



THE RHYTHMS OF AMBEs (AROUSAL-RELATED MOTOR BEHAVIORAL EPISODES) IN AGRYPNIA EXCITATA: A VIDEO MOTOR ANALYSIS.

HIGHLIGHTS

- In patients with Agrypnia Excitata with fatal familial insomnia (AE-FFI), oscillatory EEG rhythms appear during "pseudosleep" and during atypical REM sleep
- Episodes of arousal-related motor behavioral episodes (AMBEs) with and without clearly elaborated behaviors, such as REM Behavior Disorder, constitute an intriguing finding without a known mechanism.
- Spinal cord involvement should be added to the manifestations of thalamo-limbic-brainstem disconnection.
- AMBEs can be incorporated into the context of motor abnormalities observed in FFI and other prionopathies.

THE RHYTHMS OF AMBEs (AROUSAL-RELATED MOTOR BEHAVIORAL EPISODES) IN AGRYPNIA EXCITATA: A VIDEO MOTOR ANALYSIS.

CREDIT AUTHORS STATEMENT

Arturo Garay, MD, PhD

Conceptualization, Methodology, Formal Analysis, Writing

Daniel L. Giardino, MD

Conceptualization, Writing, Formal Analysis

Cristián Huck, PhD

Conceptualization, Software, Validation, Visualization

Susana Blanco, PhD

Software, Writing, Formal Analysis

Anthony T. Reder, MD

Conceptualization, Formal Analysis, Writing

Dr. Arturo Garay, MD, PhD
Sleep Medicine
Neurosciences Unit
CEMIC
Av. Galván 4102, 1431 CABA, Buenos Aires, Argentina
Phone: +541152990100 int 2936
www.cemic.edu.ar