King's Research Portal

DOI:

[10.1016/j.sleep.2017.06.031](https://doi.org/10.1016/j.sleep.2017.06.031)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Drakatos, P., Kent, B. D., Birdseye, A., Dastagir, S., Higgins, S., Williams, A. J., & Leschziner, G. (2017). Phasic activity and the importance of irregular breathing. *SLEEP MEDICINE*.
<https://doi.org/10.1016/j.sleep.2017.06.031>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Accepted Manuscript

Phasic activity and the importance of irregular breathing

Panagis Drakatos, Brian D. Kent, Adam Birdseye, Sakina Dastagir, Sean Higgins,
Adrian J. Williams, Guy Leschziner

PII: S1389-9457(17)30300-3

DOI: [10.1016/j.sleep.2017.06.031](https://doi.org/10.1016/j.sleep.2017.06.031)

Reference: SLEEP 3455

To appear in: *Sleep Medicine*

Received Date: 26 March 2017

Revised Date: 4 June 2017

Accepted Date: 21 June 2017

Please cite this article as: Drakatos P, Kent BD, Birdseye A, Dastagir S, Higgins S, Williams AJ, Leschziner G, Phasic activity and the importance of irregular breathing, *Sleep Medicine* (2017), doi: 10.1016/j.sleep.2017.06.031.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Title**Phasic activity and the importance of irregular breathing.**

Authors: Panagis Drakatos¹, Brian D Kent¹, Adam Birdseye¹, Sakina Dastagir¹, Sean Higgins¹, Adrian J Williams^{1,2}, Guy Leschziner^{1,3}

¹ Sleep Disorders Centre, Guy's Hospital, Great Maze Pond, London, SE1 9RT, United Kingdom

² King's College London, United Kingdom

³ Department of Clinical Neurosciences, King's College London, United Kingdom

Panagis Drakatos, Brian D Kent, Adam Birdseye, Sakina Dastagir, Sean Higgins, Adrian J Williams, Guy Leschziner, address: Sleep Disorders Centre, Guy's Hospital, Great Maze Pond, London SE1 9RT, United Kingdom

Corresponding author: Panagis Drakatos, pandrakatos@gmail.com, FAX: +442071886114, Tel.: +442071853390. Mail address: Guy's Hospital Sleep disorders centre 3rd floor, Nuffield House Great Maze Pond London SE1 9RT. United Kingdom.

Word count: The main body of the manuscript is consisted of 521 words. References: 6

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Dr Drakatos reports no disclosures.

Dr Kent reports no disclosures.

Mr Birdseye reports no disclosures.

Mrs Dastagir reports no disclosures.

Mr Higgins reports no disclosures.

Prof. Williams reports previous fee from UCB Pharma as a speaker. Prof. Williams reports no conflicts of interest.

Dr Leschziner reports a received honorarium from UCB Pharma and Somnomed for an advisory board. Dr Leschziner reports no conflicts of interest.

Authors' contributorship statement

PD: Concept, analysis, writing, design, interpretation and discussion; AB, SD, SH: Data acquisition, analysis, interpretation and discussion; BDK, AJW, GL: Concept, interpretation and discussion

Keywords: REM-related irregular breathing; RBD; RWA; Prozac eyes, neurodegenerative RBD

Introduction

In an illustrative case, a 45-year-old patient receiving escitalopram (10mg) daily for generalized anxiety disorder and without co-morbidities, "Prozac" eyes were observed in the polysomnographic recording (Fig.1). Retrospective analysis of relevant cases from our department did not reveal "Prozac" eyes during non-REM (NREM) 3, and when present these were not associated with REM-related irregular breathing (RespREM) (1-4).

When sleep stage-determining markers gradually become indiscernible (as can be seen in patients with idiopathic Parkinson's disease (IPD)), scoring can be difficult. Such a case is presented in figure 2 with electroencephalographic (EEG) signals of a 55-year-old male patient with IPD and without sleep disordered breathing (SDB). From our experience, the only clearly observable sleep stage characteristics in these difficult to score sleep studies are the combination of phasic activity with RespREM as an indicator of REM sleep, highlighting the strong interconnection between them (Fig. 2).

Image analysis

Slow eye movements are observed in the electro-oculography of the polysomnographic recording of this patient during NREM1 and NREM2. These eye movements are not associated with changes in breathing pattern as derived from inductance plethysmography (Fig. 1).

Rapid eye movements coincide with the presence of RespREM as derived from inductance plethysmography, in a patient with IPD and difficult to score EEG (Fig. 2).

Figure 1. "Prozac" eyes during non REM.

Example of "Prozac" eyes during four-minute epoch of non REM 1 and non REM 2 sleep stages. From the top down, the two first channels are the right and left electro-oculograms with slow eye movements, followed by F3-M2, F4-M1, C4-M1, C3-M2, O1-M2, and O2-M1, chin electromyography (EMG), left and right-leg tibialis EMG, oronasal flow and chest wall and abdomen signal from inductance plethysmography, pulse rate and pulse oximetry. Electrocardiographic artifacts can be seen in the electrooculograms.

Figure 2. Presence of rapid eye movements and REM-related irregular breathing in a difficult-to-score electroencephalography in a patient with idiopathic Parkinson's disease.

An example of a four-minute epoch with a transition between a presumed Wake to REM sleep stage. From the top down, the two first channels are the right and left electro-oculograms followed by F3-M2, F4-M1, C4-M1, C3-M2, O1-M2, and O2-M1, chin electromyography (EMG), left and right-leg tibialis EMG, oronasal flow and chest wall and abdomen signal from inductance plethysmography, pulse rate and pulse oximetry. The red bar indicates the presence of rapid eye movements with mild drop in chin EMG and prominent drop in chest wall signal and irregular breathing thereafter.

Discussion

Irregular breathing is a known characteristic of REM sleep but it is not included in the current scoring rules, primarily due to concerns of possible presence of concomitant SDB (2, 5). RespREM may be a particularly useful scoring tool in cases where SDB is not

present and characteristics of REM sleep are missing (eg, REM without atonia or REM sleep behavior disorder (RBD)) (3). Phasic activity and RBD-like movements during NREM can be observed in patients with neurodegenerative RBD (6). The combination of phasic activity with irregular breathing could serve as an additional proof of REM intrusion in NREM, therefore supporting that the abnormal nocturnal behaviors observed are likely REM-related rather than NREM-generated or drug-related. It should, however, be kept in mind that irregular breathing may be transiently seen on NREM sleep during stage transition and arousal.

"Prozac" eyes are slow-rolling eye movements thought to be due to disinhibition of "omnipause neurons" in the brainstem, which normally inhibit saccadic eye movements (1). Our findings support the hypothesis that SSRI-induced eye movements during NREM do not represent REM dissociation (1).

Acknowledgments: None

References

1. Armitage R, Trivedi M, Rush AJ. Fluoxetine and oculomotor activity during sleep in depressed patients. *Neuropsychopharmacology* 1995;12:159-65.
2. Aserinsky E. Periodic respiratory pattern occurring in conjunction with eye movements during sleep. *Science* 1965;150:763-6.
3. Drakatos P, Higgins S, Duncan I, et al. The utility of respiratory inductance plethysmography in REM sleep scoring during multiple sleep latency testing. *Respir Physiol Neurobiol* 2016;230:1-4.
4. Geyer JD, Carney PR, Dillard SC, Davis L, Ward LC. Antidepressant medications, neuroleptics, and prominent eye movements during NREM sleep. *J Clin Neurophysiol* 2009;26:39-44.
5. Silber MH, Ancoli-Israel S, Bonnet MH, et al. The visual scoring of sleep in adults. *J Clin Sleep Med* 2007;3:121-31.
6. Miguel R, Arnulf I. Phasic activity during non REM sleep. *Sleep Med* 2017;29:37-40.

Highlights

- REM-related irregular breathing is a cardinal feature of REM sleep.
- It can be a useful tool in identifying REM sleep and REM intrusion in NREM sleep.
- "Prozac eyes" are not associated with REM-related irregular breathing.