Psychiatry Research 200 (2012) 742–747

Contents lists available at SciVerse ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Ultra-Slow delta power in chronic fatigue syndrome

Olivier Le Bon [a,b,*], Daniel Neu [a], Yves Berquin [c], Jean-Pol Lanquart [b], Robert Hoffmann [d], Olivier Mairesse [a], Roseanne Armitage [d]

[a] Brugmann University Hospital, Sleep Laboratory and Unit for Chronobiology U78, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium
[b] Hôpital Erasme, Sleep Research Unit, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium
[c] APRECO Technologies, Brussels
[d] Sleep and Chronophysiology Laboratory, University of Michigan, Department of Psychiatry, Ann Arbor, MI, USA

ARTICLE INFO

Article history:
Received 19 November 2011
Received in revised form
3 May 2012
Accepted 20 June 2012

Keywords:
Alpha–delta
Sleep
SWA
Sleepiness

ABSTRACT

The role of sleep in patients diagnosed with chronic fatigue syndrome is not fully understood. Studies of polysomnographic and quantitative sleep electroencephalographic (EEG) measures have provided contradictory results, with few consistent findings in patients with Chronic Fatigue Syndrome (CFS). For the most part, it appears that delta EEG activity may provide the best discrimination between patients and healthy controls. A closer examination of delta activity in the very slow end of the frequency band is still to be considered in assessing sleep in CFS. The present preliminary study compared absolute and relative spectral power in conventional EEG bands and ultra-slow delta (0.5–0.8 Hz) between 10 young female patients with the CFS and healthy controls without psychopathology. In absolute measures, the ultra-slow delta power was lower in CFS, about one-fifth that of the control group. Other frequency bands did not differ between groups. Relative ultra-slow delta power was lower in patients than in controls. CFS is associated with lower ultra-slow (0.5–0.8 Hz) delta power, underscoring the importance of looking beyond conventional EEG frequency bands. From a neurophysiological standpoint, lower ultra-slow wave power may indicate abnormalities in the oscillations in membrane potential or a failure in neural recruitment in those with CFS.

1. Introduction

Although Chronic Fatigue Syndrome (CFS) is recognized by the Center for Disease Control (CDC) criteria, the existence of this condition is still debated. The points of view are so divergent that CFS has been considered the expression of somatic complaints accompanying psychiatric syndromes, or, by contrast, the result of a viral infection, hormonal dysregulation, auto-immune disease or the consequences of poor sleep, whether specific or not.

The 1994 CDC criteria (Fukuda et al., 1994) are the most frequently used for research purposes, as this definition is neutral in term of etiology or pathophysiology. However, as the syndrome is mainly defined by its core symptom of fatigue, it may include different conditions under the same name. Primary sleep disorders, generally associated with sleepiness, for instance, have been estimated somewhere between 0% (Reeves et al., 2006) and 62.5% (Krupp et al., 1993). Major Depression Disorders (MDD), which includes fatigue as one of the nine DSM-IV criteria, is often associated with similar sleep complaints to CFS (cf Benca et al., 1992).

Both population and clinically based studies showed that the most prevalent complaint within the eight CDC criteria is sleep (Sharpe, 1991; Jason et al., 1999; Reyes et al., 2003; Unger et al., 2004). CFS patients usually describe their sleep as non-refreshing or light. When they occasionally have a better than usual night, patients do report improved mental or physical effort the next day, supporting the importance of sleep in the pathophysiological process of fatigue.

Laboratory studies of polysomnography and quantitative sleep electroencephalographic (EEG) have identified a cluster of sleep abnormalities associated with CFS, summarized in Table 1. With regard to quantitative sleep EEG measures, excessive alpha (8–12 Hz) waves during SWS ("alpha–delta-sleep", or "alpha-intrusion") were reported in earlier studies (Hauri and Hawkins, 1973) with mixed support in more recent work (Whelton et al., 1992; Krupp et al., 1993). Alpha–delta sleep has also been described in fibromyalgia (Harding, 1998), and conditions involving pain, such as Lyme's disease (Greenberg et al., 1995), irritable bowel (Shen and Soffer, 2001) or migraine (Dowson and Jagger, 1999) and in healthy controls (Moldofsky et al., 1975; Conneman et al., 2001). Moreover, links were found between alpha–delta and anxiety symptoms, but not fatigue (Van Hoof et al., 2007). A comprehensive review (Mahowald and Mahowald, 2000) identified a number of methodological factors contributing to discrepancies among studies, including: lack of

* Correspondence to: Tivoli University Hospital, Université Libre de Bruxelles (U.L.B.), Department of Psychiatry, 37 Avenue Max Buset, 7100-La Louvière, Belgium. Tel.: +32 64 27 61 11; fax: +32 64 27 63 26.
E-mail addresses: olebon@chu-tivoli.be, lebono@skynet.be (O. Le Bon).

0165-1781/$ - see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.psychres.2012.06.027

Table 1
Macrostructure and quantified EEG findings of sleep in CFS.

Sleep characteristics	
Lower sleep efficiency	(Morriss et al., 1993; Fischler et al., 1997; Sharpley et al., 1997; Stores et al., 1998)
Longer sleep latency	(Morriss et al., 1993; Fischler et al., 1997)
More intermittent awakenings	(Fischler et al., 1997; Sharpley et al., 1997; Stores et al., 1998)
Longer duration of intermittent awakenings	(Fischler et al., 1997; Stores et al., 1998; Ball et al., 2004)
Less REM sleep	(Whelton et al., 1992; Sharpley et al., 1997)
More REM sleep	(Moldofsky et al., 1975)
Less Stage 1 and/or Stage 2	(Zubieta et al., 1993; Fischler et al., 1997; Ball et al., 2004)
More Stage 3 or Stage 4 or SWS	(Moldofsky et al., 1975; Zubieta et al., 1993; Fischler et al., 1997; Sharpley et al., 1997; Van Hoof et al., 2007; Le Bon et al., 2007; Neu et al., 2009)
Less SWS	(Guilleminault et al., 2006)
Higher microarousal index	(Le Bon et al., 2007; Neu et al., 2009)
Quantified EEG	
Higher Delta in SWS	(Guilleminault et al., 2006)
Lower Delta in SWS Activity	(Decker et al., 2009)
Higher Delta in Stage 1 and REM sleep	
Lower Alpha in Stage 2, REM sleep, SWS	
Lower Theta, Sigma, Beta in Stage 2, REM sleep and SWS	
Lower Delta in response to homeostatic challenge	(Armitage et al., 2007)
Higher Cyclic Alternating Pattern (CAP)	(Armitage et al., 2009)

SWS=N3=Stages 3+4 sleep.

appropriate control subjects, non-standardized EEG recording techniques and the difficulties in visual scoring of EEG frequency events. However, studies that have attempted to these methodological concerns have often reported very subtle differences between CFS patients and healthy controls (Armitage et al., 2007, 2009). One study only identified lower delta power in CFS under sleep challenge conditions but did not find evidence of increased alpha–delta sleep or polysomnographic abnormalities in CFS (Armitage et al., 2007). By contrast, one study reported higher delta in CFS (Guilleminault et al., 2006). Thus, even when methodological issues are addressed, the findings have remained contradictory.

Although the role of delta sleep EEG is not fully understood, it has been the focus of many studies on CFS. Delta sleep EEG is homeostatically regulated (Borbély, 1982) and intensifies as a function of prior wake duration. It has been hypothesized to reflect the restorative aspect of sleep and is often associated with "feeling rested" after sleep. Sleep disturbances in a number of clinical disorders have been associated with reduced delta EEG or impaired homeostasis, including major depressive disorders (Armitage, 2007), insomnia (Dijk, 2010) and CFS (Armitage et al., 2007). Moreover, response to a sleep challenge may be blunted in those with CFS, resulting in a lower delta EEG increase in response to increased prior wakefulness (Armitage et al., 2009). However, conventional delta EEG bands typically include activity from 0.5 to 4 Hz. This is a broad frequency range for slow waves: the highest-frequency ones in the delta spectrum may be eight time faster than the slowest. Hence, we cannot exclude that delta waves harbor oscillations which behave distinctly from each other and might be linked to distinct neurophysiological processes.

For instance, Ultra-Slow (US) oscillations (<1 Hz), also called Slow Oscillations or Low-frequency Oscillations, have been described in anesthezised cats (Steriade et al., 1993), and in humans (Achermann and Borbély, 1997; Amzica and Steriade, 1998). They are supposed to reflect the rhythmic alternation of up- and down-states occurring at the cellular level in the neocortex (Steriade et al., 1993). They might thus better reflect the physiological processes underlying sleep restoration than when studied globally within the traditional definition of delta activity.

Exploring US frequency delta may provide further insight into those disorders associated with impaired sleep homeostasis or complaints of non-restorative sleep. The present study compared US delta and conventional Delta EEG (average of three recording sites) in the Slow Wave Sleep (SWS) of young female CFS patients ($n=10$) to age- and gender-matched healthy controls. Other results are provided descriptively. Based on the findings of Armitage et al. (2007), we hypothesized lower US delta power in those with CFS.

2. Participants and methods

2.1. Patients and subjects

The CFS patients were referred to the sleep unit of the Brugmann University Hospital by the medical department of another institution (tertiary-care setting) after a full medical check-up. Study participants were chosen from an available pool of 87 patients evaluated between 2008 and 2009. Procedures for inclusion in the final study sample are outlined below.

CDC criteria were used for a first selection of CFS patients (Fukuda et al., 1994): (1) clinically evaluated, unexplained or relapsing chronic fatigue – that is of new or definite onset – is not the result of ongoing exertion nor is alleviated by rest, and resulting in the substantial reduction of previous levels of occupational, educational, social or personal activities; (2) concurrent occurrence of four or more of the following symptoms, all of which must have persisted or recurred during six or more consecutive months of illness and must not have predated the fatigue: self-reported impairment in short-term memory or concentration; sore throat; tender cervical or axillary lymph nodes; muscle pain; multi-joint pain without joint swelling or redness; headaches of a new type, pattern or severity; unrefreshing sleep; post-exertion malaise lasting more than 24 h; (3) exclusion of any active medical condition that may explain the presence of chronic fatigue; any previous and still present condition which might explain fatigue; substance abuse within two years prior to onset; severe obesity.

In addition, an Apnea-Hypopnea Index (AHI) or Periodic Limb Movement index (PLMI) $>=5$/h, meeting clinical criteria for narcolepsy or idiopathic hypersomnia or present DSM-IV Axis I diagnoses, and current medication use were also exclusionary. Conventional regular sleep schedules were required and no shift work or time zone travel was permitted within the last two weeks prior to study. Daytime napping was proscribed. Patients with a consumption of more than two units of alcohol per day were excluded. Caffeine-including beverages were not available after 3 p.m. but caffeine and tobacco consumption were not controlled. The final sample included 10 women.

A second sample of 10 locally recruited healthy female controls (HC) were selected as an exact match on gender and within 2 years of age difference as the CFS patients. They received 100 Euros for their participation through private funding. No significant somatic condition and no current or past mental disorder were allowed. Further exclusion criteria were identical to patient groups.

All CFS and HC subjects filled out a sleep diary two weeks prior to sleep recording. The diaries were analyzed to check for unauthorized sleep–wake schedules. No patient or subject was excluded on this basis. All participants also underwent a physical examination and structural clinical interview using the Mini-International Structured Interview (MINI SCID-I) for DSM-IV (Sheehan et al., 1998) conducted by one of the authors (DN).

The study was conducted in accordance with the rules and regulations for clinical trials stated by the World Medical Assembly in Helsinki.

2.2. Clinical rating scales

On the admission before the first night, participants filled in the Pittsburgh Sleep Quality Index (PSQI, Buysse et al., 1989), the Fatigue Severity Scale (FSS, Krupp et al., 1989) and the Epworth Sleepiness Scale (ESS, Johns, 1991). The FSS is a self-report instrument used to assess levels of fatigue and its effect on daily functioning. The ESS is one of the most widely used scales of subjective sleepiness. Scores above 10 are commonly interpreted as increased daytime sleepiness.

2.3. Polysomnographic recording

All participants had two consecutive all-night polysomnograms. Only the second night was used here to avoid first-night effects in CFS (Le Bon et al., 2003) and in US bands in HC (Le Bon et al., 2001).

Recordings were randomly performed for two consecutive nights between Mondays and Wednesdays or between Wednesdays and Fridays. Patients were prepared for