Epilepsy & Behavior 70 (2017) 80–86

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

The relationship between mood disorder and insomnia depends on race in US veterans with epilepsy

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ARTICLE INFO

Article history:
Received 10 January 2017
Accepted 2 February 2017
Available online 12 April 2017

Keywords:
Insomnia
Sleep
Race
Depression
Mood
Epilepsy

ABSTRACT

Purpose: Few data exist on race, medical/psychiatric comorbidities, and insomnia symptoms in US veterans with epilepsy. Our aims were to examine 1) whether insomnia symptom prevalence was different between Black and White veterans and 2) whether predictors of insomnia symptoms varied by race.
Methods: This retrospective, cross-sectional study included veterans evaluated in an epilepsy clinic over the course of 1.5 years. Individuals completed standardized assessments for epilepsy and sleep complaints. Insomnia criteria were met by 1) report of difficulty with sleep initiation, maintenance, or premature awakenings accompanied by daytime impairment or 2) sedative-hypnotic use on most days of the month. Demographics, medical/psychiatric comorbidities, and medications were determined per electronic medical record review. Hierarchical multivariable logistic regression analyses were performed to determine if race, medical/mental health comorbidities, and the potential interaction of race with each comorbid condition were associated with insomnia.
Results: Our sample consisted of 165 veterans (32% Black). The unadjusted prevalence of insomnia was not different between Black and White veterans (42% vs 39%, $p = 0.68$). In adjusted analyses, the association between mood disorder and insomnia varied by race. Depressed White veterans had over 11-times higher predicted odds of insomnia (OR 11.4, $p < 0.001$) than non-depressed White veterans, while depressed Black veterans had 4-times higher predicted odds of insomnia (OR 4.1, $p = 0.06$) than non-depressed Black veterans. Although mood disorder diagnosis was associated with insomnia for both racial groups, White veterans had a stronger association between mood disorder diagnosis and insomnia than Black veterans.
Conclusions: The relationship between mood disorder diagnosis and insomnia was stronger for White than Black veterans with epilepsy. Future studies are needed to explore mental health symptoms and psychosocial determinants of insomnia with larger samples of minority individuals with epilepsy.

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1. Introduction

Insomnia disorder is characterized by difficulty with falling asleep, maintaining sleep, or with premature early morning awakenings, and accompanying daytime impairments stemming from such disturbances [1]. In the general population, older age, female gender, a greater burden of medical/psychiatric comorbidities, and chronic pain have all been associated with increased prevalence of chronic insomnia disorder [1–4]. Over the last decade, insomnia disorders have increasingly been recognized in adults with epilepsy with estimates ranging from 25% to 76% in clinical samples [4–12]. However, less attention has been given to the role that comorbid conditions may play in relation to insomnia complaints in individuals with epilepsy. In a prior study of 165 military veterans with epilepsy, we showed that insomnia was significantly associated with post-traumatic seizure etiology (OR 2.9, 95% CI 1.1–7.6), mood disorders (OR 6.5, 95% CI 2.6–16.4), and psychotic spectrum disorders (OR 7.8, 95% CI 2.6–21.7) [6]. In another epilepsy clinic study ($n = 90$), Yang et al. reported that insomnia severity was associated with a history of head trauma, comorbid asthma/chronic obstructive pulmonary disease, depressive symptoms, and sedative-hypnotic use [11]. With the exception of antiepileptic drug (AED) polypharmacy, no other epilepsy variable was linked to insomnia. Similarly, Vendrame et al. ($n = 152$) found that a greater degree of insomnia was associated with a higher burden of depressive symptoms among patients with epilepsy [8]. In a study comparing 200 individuals exhibiting well-controlled epilepsy and devoid of medical and psychiatric comorbidities (e.g. anxiety/mood disorders) with 100 age- and gender-matched controls, Unterberger et al. reported that the prevalence of sleep disturbances did not vary significantly between persons with epilepsy and controls (1.5% vs 3.0%, $p = 0.41$) [13]. Thus, insomnia may be a consequence of medical or mental health comorbidities, and not a consequence of epilepsy itself. As insomnia in individuals with epilepsy can

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http://dx.doi.org/10.1016/j.yebeh.2017.02.004
1525-5050/Published by Elsevier Inc.

be associated with increased seizure frequency and decreased quality of life [8,12,14], further characterizations of the relationship between medical and psychiatric comorbidities and insomnia are warranted.

An important omission of recent US studies examining the relationship between comorbid illnesses and insomnia has been that of the racial and/or ethnic composition of clinical epilepsy samples [8,11]. This is salient as non-Hispanic Blacks have been shown to bear a disproportionate burden of epilepsy, comorbid illnesses, and insomnia as compared to non-Hispanic Whites (herein referred to as Blacks and Whites, respectively) [15–20]. For example, among Medicare beneficiaries, Blacks have been found to have significantly higher prevalence and incidence rates of epilepsy relative to Whites (18.7 vs 10.2/1000; 4.1 vs 2.3/1000, respectively) [20]. In regard to sleep, Blacks have been shown to have longer sleep onset latency, greater sleep fragmentation, and shorter habitual sleep duration than Whites [17]. As Blacks with epilepsy have been reported to have poorer adherence to AEDs and seizure control [21,22], it is possible that increased psychological distress (e.g. seizure worry during the night or upon awakening) or other chronic stressors place them at greater risk for insomnia symptoms compared to Whites [11,23]. Furthermore, Blacks and Whites may differentially 1) report medical and mental health symptoms, 2) receive diagnoses of comorbid conditions, 3) adhere to treatment recommendations, or 4) cope with the stress of these chronic illnesses [15,24–27]. Thus, the relationship between diagnosed medical/mental health comorbidities and insomnia may depend on race in persons with epilepsy. As there are existing racial health disparities in epilepsy outcomes, there is a need for better understanding of treatable conditions like insomnia, which may contribute to these differential outcomes [23]. To our knowledge, the potential for racial differences in insomnia or its determinants in individuals with epilepsy have not been previously examined.

Our aims were to examine 1) whether insomnia prevalence was different between Black and White veterans with epilepsy and 2) whether predictors of insomnia varied by race. Specifically, we explored whether the relationship between medical comorbidities, chronic pain, mental health conditions, and insomnia varied by race. We hypothesized that Black veterans would have higher prevalence of insomnia and a stronger relationship between medical/mental health comorbidities and insomnia than White veterans with epilepsy.

2. Methods

This was a retrospective, cross-sectional study of consecutive epilepsy patients initially evaluated at the Miami VA Healthcare System (VAHS) epilepsy clinic over an 18-month period. Epilepsy diagnosis was determined with the International League Against Epilepsy criteria by a board-certified epileptologist (MRL). The Miami VAHS institutional review board approved the study protocol.

The following variables were extracted from the medical record at the initial epilepsy clinic visit: self-reported race (White, Black, Other), ethnicity (Hispanic vs Non-Hispanic), age, gender, medical and psychiatric comorbidities, epilepsy subtype (focal or generalized), seizure etiology (idiopathic, post-traumatic, or secondary to other factors), seizure intractability (breakthrough seizures despite using two AEDs) and current AED treatment. The Charlson comorbidity index was calculated to provide a weighted measure of overall medical illness burden [28]. Chronic pain was recorded if a veteran 1) was prescribed pain medication (i.e. opioid, muscle relaxant, or anti-inflammatory) at the time of the epilepsy visit or 2) had been evaluated in the pain clinic within the preceding year. Psychiatric diagnoses (mood disorder, post-traumatic stress disorder [PTSD], psychotic spectrum disorders [schizophrenia, schizoaffective disorder, psychosis NOS], and substance abuse/dependence) were recorded if assigned by a psychiatry attending physician in the year preceding the epilepsy clinic visit. At the time of the study, these diagnoses were based on the Diagnostic and Statistical Manual of Mental Disorders IV-Text Revision criteria [29].

During the epilepsy clinic visit, individuals were queried about insomnia symptoms and repercussions with the following questions: 1) "Do you have difficulty falling, staying, or waking up earlier than desired on most days of the last month?" and 2) "Does your sleeping difficulty cause problems for you during the day?". Diagnostic criteria for insomnia were fulfilled if 1) veterans endorsed both questions or 2) if veterans reported using sedative-hypnotic medication on most days of the month. Medications prescribed for sleep onset, maintenance, or premature morning awakenings were considered sedative-hypnotics. We recorded the type of sedative-hypnotic medication category prescribed, and calculated the proportion of individuals who attended a sleep clinic consultation and polysomnography.

2.1. Data analysis

First, we compared the demographic, clinical, and medication factors between White and Black veterans with epilepsy. We grouped Non-Hispanic and Hispanic White veterans into the same racial group as we have previously shown that Hispanic White veterans are highly acculturated to the US lifestyle and report equivalent degrees of insomnia symptoms compared to non-Hispanic White veterans [24,30]. Second, we compared these same characteristics between veterans with and without insomnia stratified by race to determine if associations with insomnia varied by race.

Continuous variables were reported as mean ± SD. Comparisons of age and the Charlson co-morbidity index (continuous variables) between groups were made with Student's t-test. All other variables were categorical and were reported as frequencies (%). Chi-square or Fisher's exact tests were used to compare the categorical variables. As sedative-hypnotic medication prescription was used to partially define the outcome of insomnia, we did not examine sedative-hypnotics as predictors of insomnia or examine their differential association by race.

Hierarchical multivariable logistic regression analyses were performed to determine if race, medical/mental health comorbidities, and the potential interaction of race with each comorbid condition were associated with insomnia. White race served as the reference group. The interaction of race with each medical/mental health comorbidity was of particular interest to determine if the relationship of each comorbid condition with insomnia varied by race. Based on our prior findings and the existing insomnia literature, we examined the following 5 variables: weighted medical comorbidities (Charlson Index), chronic pain, mood disorder, PTSD, and psychotic spectrum disorder [1,6,8,31]. For each comorbid condition of interest, the model initially contained two variables: race and the comorbidity variable. Each comorbidity model was sequentially adjusted for covariates shown to be associated with insomnia based on existing literature and on our prior findings: demographic factors (Model 1: age and gender), seizure-related factors (Model 2: epilepsy etiology, lamotrigine, and levetiracetam treatment), and the other remaining medical/psychiatric comorbidities (Model 3: Charlson Index, chronic pain, PTSD, mood, and psychotic spectrum disorders) [1,3,6]. Lastly, Model 4 introduced the race by comorbidity interaction term. Given the exploratory nature of our analysis, we retained interaction terms in the models testing at a level of significance of $p < 0.10$. Race-comorbidity interactions were visualized by plotting these dichotomous variables with the estimated insomnia probability.

For all analyses, $p \leq 0.05$ was defined as statistically significant. As our analyses were exploratory, we did not correct the statistical significance level for multiple comparisons. Statistical analyses were performed with SPSS Statistics 20.0 (SPSS, Chicago, IL).

3. Results

3.1. Demographic and clinical characteristics: comparisons by race

The sample consisted of 52 Black and 113 White (28 of these of Hispanic ethnicity), middle aged, predominantly male veterans with

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