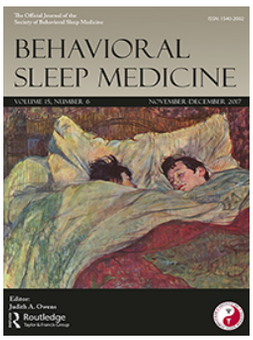

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Fibromyalgia and chronic insomnia are frequently comorbid conditions with heightened sensitivity to painful stimuli, potentially subserved by the hippocampus. Recent evidence suggests moderate alcohol consumption is associated with reduced fibromyalgia symptom severity. We examined the relationship among alcohol use, hippocampal morphology, fibromyalgia, and insomnia symptom severity in 41 fibromyalgia patients (19 with insomnia). A 14-day diary of sleep, pain, and alcohol consumption was followed by structural MRI. Analyses indicated greater bilateral hippocampal volume, lower clinical pain intensity, and better sleep quality in moderate drinkers versus abstainers. Underlying mechanisms may include gamma-amino butyric acid (GABA) receptor agonism, n-methyl d-aspartate (NMDA) receptor antagonism, and psychosocial factors. Further study of the relationship between alcohol use and fibromyalgia and insomnia symptom severity is warranted.

Fibromyalgia syndrome is a chronic condition characterized by widespread musculoskeletal pain as well as somatic and cognitive complaints (Wolfe et al., 2010). Patients with fibromyalgia frequently report fatigue and sleep disruption. For instance, Peres and colleagues (2001) found that 75% of fibromyalgia patients in their study sample had symptoms consistent with chronic insomnia.

Both fibromyalgia and chronic insomnia are characterized by sensitization and exaggerated reactivity to noxious stimuli. For instance, fibromyalgia patients report greater emotional reactivity to pain. This sensitization is reflected in functional measures of brain activity; increased responses to pressure stimulation have been observed in fibromyalgia patients in areas related to both the anticipation of, and emotional response to, pain (Gracely et al., 2004; Ursin, 2014). Likewise, pain perceptions are altered by changes in sleep; poor sleep can result in hyperalgesia, while increased sleep quality is associated with decreased pain in individuals with fibromyalgia (Affleck, Urrows, Tennen, Higgins, & Abeles, 1996; Moldofsky, 1989; Roth, Lankford, Bhadra, Whalen, & Resnick, 2012). However, previous research seems to indicate a reciprocal relationship exists where pain symptoms also alter sleep (Roth et al., 2012).

The Cognitive Activation Theory of Stress (CATS; Ursin & Eriksen, 2007) suggests that sustained hypervigilance to normal bodily processes and sensations is a shared psychological mechanism for both fibromyalgia and chronic insomnia. Maladaptive memory processes subserved by the hippocampus, an important component of the brain's limbic circuitry, may underlie the cognitive bias that forms the basis of the CATS model (Simons, Elman, & Borsook, 2014). Thus, it is a structure of significant interest when considering the neurobiological correlates of both fibromyalgia and chronic insomnia. Previous work has shown hippocampal volume reductions in fibromyalgia patients (Lutz et al., 2008) and chronic insomnia patients (Riemann et al., 2007) separately. In addition, we recently reported results of a structural analysis indicating lower hippocampal volume bilaterally in a mixed cohort of patients with fibromyalgia and fibromyalgia with comorbid insomnia (McCrae et al., 2015). However, not all authors have

replicated these results in insomnia (Winkelman et al., 2010) or other pain-related conditions such as frequent migraines (Maleki et al., 2013) and osteoarthritis (Mutso et al., 2012). Furthermore, to our knowledge, no studies have addressed the potential impact of comorbid insomnia on hippocampal structure in patients with chronic musculoskeletal pain. This question is of particular interest because a comorbid diagnosis of insomnia may represent an additional source of stress under the CATS model that produces an additive or synergistic deprecating effect on hippocampal structure. Therefore, negative effects on hippocampal structure associated with chronic pain conditions and insomnia remains an area in need of further exploration.

Both fibromyalgia and chronic insomnia are associated with chronic stress and chronic dysregulation of glucocorticoid function, which previous work indicates results in an imbalance of excitatory and inhibitory neurotransmission and atrophy in the hippocampus, further perpetuating an individual's maladaptive hyperarousal (Wood, 2004). Ethanol (alcohol) use is a particularly interesting behavior to consider in this context because of its wide-ranging interactions with a variety of neurotransmitter systems, including agonism of inhibitory gamma amino butyric acid (GABA) receptors and antagonism of excitatory n-methyl d-aspartate (NMDA) receptors (Spanagel, 2009). Critically, fibromyalgia is characterized by elevated levels of excitatory amino acids (i.e., glutamate), which have been associated with hyperalgesia and allodynia (Clauw, Arnold, McCarberg, & FibroCollaborative, 2011). Thus, it is possible that alcohol intake could modulate symptoms associated with fibromyalgia and chronic insomnia by reducing hyperalgesia and allodynia through NMDA antagonism, as well as promoting sleep and anxiolytic effects through GABA agonism. The reduction of both hyperalgesia and temporal summation in fibromyalgia has been demonstrated with the NMDA antagonist ketamine (Graven-Nielsen et al., 2000). Similarly, gabapentin, a drug that has been shown to modulate brain GABA concentrations (Cai et al., 2012), reduces pain and improves sleep in fibromyalgia patients (Arnold et al., 2007). Therefore, it is plausible that alcohol, a drug that increases GABA activity and decreases NMDA activity, may be effective in reducing symptoms of fibromyalgia and chronic insomnia.

A recent epidemiological examination of a large cohort ($N = 946$) of fibromyalgia patients by Kim et al. (2013) suggests that regular consumption of low-to-moderate amounts of alcohol is associated with lower pain symptomatology and disability. Although the Kim et al. study is, to our knowledge, the first to examine the relationship between alcohol consumption and fibromyalgia, other studies have identified reduced risk of rheumatoid arthritis (Kallberg et al., 2009; Maxwell, Gowers, Moore, & Wilson, 2010) and lower levels of inflammatory factors in patients with rheumatoid arthritis (Lu et al., 2010) in drinkers compared to abstainers. Although the mechanism underlying these associations is unclear, it stands to reason that structures comprising limbic and cognitive circuitry, and particularly the hippocampus, may play an important role. The possibility that common comorbidities of fibromyalgia (e.g., chronic insomnia) may modulate the relationship between alcohol consumption and fibromyalgia symptomatology has not been investigated.

This study was designed to address these gaps in the literature. We investigate whether self-endorsement of alcohol consumption in a group of fibromyalgia patients with chronic insomnia (FMI) and without chronic insomnia (FM) is associated with hippocampal structure as assessed using structural magnetic resonance imaging (MRI). We also compared low-to-moderate drinkers and abstainers on an array of sleep and pain-related measures. Based on the CATS model, we hypothesized that pain symptomatology would

be lower and hippocampal volume would be greater in drinkers than in abstainers. Systematic study of the acute and long-term effects of moderate alcohol use on sleep quality is largely lacking; however, the existing literature suggests some short-term benefit from low-to-moderate alcohol consumption in insomnia patients (Roehrs et al., 1999) and provides some evidence for improvement of sleep quality following initiation of a pattern of moderate drinking (Gepner et al., 2015; Shai et al., 2007). On the basis of these findings, we predicted that sleep quality measures would be better in drinkers than abstainers and treated the possibility of an alcohol use X comorbid insomnia interaction as an empirical question. Finally, we asked as an empirical question whether alcohol consumption would have differential effects on hippocampal volume and sleep and pain-related measures between FM and FMI.

METHODS

Participants

Twenty-two women with fibromyalgia (FM) and 19 women with fibromyalgia and chronic insomnia (FMI) were recruited from the north central Florida area through radio, newspaper, and television advertisements. As noted above, an additional analysis including these participants was recently published by our group (McCrae et al., 2015). None of the analyses included here overlap with those in the previous report. Inclusion criteria for FM were: (a) age 18 or older, (b) individual reports currently suffering from fibromyalgia, (c) fibromyalgia confirmed by tender point test, using guidelines established by the American College of Rheumatology (with application of 4kg force, participant reported pain in at least 11 of 18 points, including points in all four body quadrants; Wolfe et al., 2010), (d) no prescribed or over-the-counter sleep medication for at least 1 month, or stabilized on medication for at least 6 months, (e) willing to undergo randomization, and (f) able to read and understand English. FMI participants were required to meet the following additional criteria: (g) individual reports chronic insomnia (sleep onset or awake time during night > 30 min) at least 3 nights per week for more than 6 months, (h) sleep diary confirms chronic insomnia (sleep onset or awake time during night > 30 min) at least 6 nights during a 2-week baseline period (Edinger et al., 2004; Lichstein et al., 2003), and (i) daytime dysfunction due to chronic insomnia (mood, cognitive, social, or occupational impairment).

Exclusion criteria were: (a) sleep disorder other than chronic insomnia (e.g., sleep apnea, periodic limb movement disorder), assessed through structured interview and single-night ambulatory monitoring (disqualified if apnea-hypopnea index or myoclonus arousals greater than 15/hr or between 10–15/hr with oxygen saturation below 88%); (b) bipolar disorder or seizure disorder; (c) significant medical (e.g., cancer) or neurological disorder (e.g., dementia); (d) severe untreated psychopathology (e.g., schizophrenia, substance abuse); (e) cognitive impairment based on Mini-Mental State Examination score lower than 24 (9th grade education or higher) or lower than 18 (less than 9th grade education; Murden, McRae, Kaner, & Bucknam, 1991). A physician (RBB) board certified in sleep medicine reviewed all ambulatory monitoring records. Undergraduate research assistants conducted initial screening interviews. Doctoral students in UF's American Psychological Association (APA) accredited clinical psychology program conducted clinical interviews using structured and semistructured instruments. A

licensed clinical psychologist (CSM) certified in behavioral sleep medicine supervised all screening interviews and confirmed final chronic insomnia diagnoses. The University of Florida Institutional Review Board approved all study procedures.

Demographic and Affective Measures

Participants completed a brief demographic questionnaire, provided information regarding the number of years since onset of pain and sleep symptoms (as appropriate), and the Beck Depression Inventory (2nd ed., BDI-II; Beck, Steer, & Brown, 1996).

Pain and Alcohol Daily Diaries

Participants recorded information regarding daily clinical pain and alcohol consumption (number of drinks consumed) for 14 consecutive days prior to structural brain imaging using a paper-and-pencil diary provided by the investigators. Completed diaries were collected prior to imaging. Participants were grouped according to their self-endorsement as drinkers or abstainers in response to the question, "Do you drink alcohol?" Individual averages of pain and alcohol consumption (for drinkers only) were generated from these diaries.

Sleep Diaries

Participants were instructed to complete a paper-and-pencil sleep diary for 14 days at each assessment point. The sleep diary provided the following variables: (a) sleep onset latency (SOL)—time from initial lights-out until sleep onset, (b) wake time after sleep onset (WASO)—time spent awake after initial sleep onset until last awakening, (c) total wake time (TWT)—computed by adding SOL, WASO, and time from last awakening until getting out of bed for the final time, (d) total sleep time (TST)—computed by subtracting TWT from time spent in bed, and (e) sleep efficiency percentage (SE)—ratio of TST to total time spent in bed X 100. A mean was computed for each variable for the 14 days preceding structural MRI. This approach was consistent with both research and clinical standards, as the sleep diary is regarded as the gold standard for subjective sleep assessment (Carney et al., 2012).

Neuroimaging Acquisition

T1-weighted structural MRI scans were acquired using a Philips Achieva 3.0T 2-Series scanner with a Philips eight-channel head coil. The parameters for each T1-weighted structural scan were set as follows: A Fast Field Echo imaging sequence [Slices = 180, acquisition plane = sagittal, flip angle = 8°, field of view = 240 mm x 240 mm x 180 mm, matrix = 240 mm x 240 mm, voxel size = 1 mm x 1 mm x 1 mm, slice gap = 0 mm, Actual TR/TE = 8.1 /3.7] was used. Scans lasted ~6 min (377 s).

Neuroimaging Processing

The automated subcortical segmentation stream in FreeSurfer V.5.1.0 was used to measure hippocampal volume. The software uses Bayesian inference methods relying on prior anatomical probabilities in a labeled data set, along with a priori known T1 intensity characteristics of subcortical regions, as well as T1 intensity information from the scan being processed in order to

label discrete regions (Fischl et al., 2002). Previous research has shown this automated procedure produces accurate and reliable results while taking a fraction of the time of the gold standard of manual segmentation (Fischl et al., 2002; Jovicich et al., 2009).

Data Analysis

All analyses were conducted using IBM SPSS v20 Statistics (IBM Corp., Armonk, NY). Two participants whose reported alcohol use patterns exceeded National Institute on Alcohol Abuse and Alcoholism guidelines for moderate drinking by a substantial margin were excluded, resulting in a final sample size of 39. Potential differences in demographic, affective, and pain- or sleep-related variables were assessed using 2 (alcohol use: drinker vs. nondrinker) X 2 (group: FM vs. FMI) analysis of variance (ANOVA). Left and right hippocampal volume measures were subjected to analysis of covariance (ANCOVA) controlling for potentially confounding factors (total gray matter volume, MRI signal-to-noise ratio, BDI, and age). In addition, semipartial correlations controlling for the factors previously noted were constructed to examine the relationships between hippocampal volume and FM/FMI symptomatology, and between quantity of reported alcohol use and hippocampal volume among drinkers. The threshold for statistical significance in this study was set to $\alpha = .05$ without experiment-wise correction for multiple comparisons. Effect sizes are reported for all analyses so that the relative importance of a given result can be better interpreted and to provide a basis for the planning of future studies.

RESULTS

Participant characteristics are presented by group in Table 1.

Demographics, Affect, and Medication Use

No main effects of alcohol use status or insomnia comorbidity were detected for age (Cohen's $d = 0.32$ and Cohen's $d = 0.22$; $p > .39$), BDI-II scores (Cohen's $d = 0.62$ and Cohen's $d = 0.59$; $p > .10$), or pain symptom duration (Cohen's $d = 0.23$ and Cohen's $d = 0.10$; $p > 0.47$). Duration of sleep-related symptoms for FMI participants did not differ between drinkers and abstainers (Cohen's $d = 0.22$; $p > 0.66$). Alcohol use status X participant group interactions for age ($\eta_p^2 = 0.04$), BDI-II ($\eta_p^2 = 0.04$), and pain symptom duration ($\eta_p^2 = 0.03$) were also not significant (p's > 0.23). Taken together, results suggest these variables did not differ reliably between participant groups. Notably, a significant proportion of study participants reported having current prescriptions for hypnotic medications, including 33.3% of abstainers and 22.2% of drinkers. Similarly, 42.9% of abstainers and 38.9% of drinkers reported current prescriptions for analgesic medications. The percentage of patients reporting medication use did not differ by group for either hypnotic ($X^2 = 0.591$, $p = 0.44$) or analgesic medications ($X^2 = 0.063$, $p = 0.80$).

Pain Intensity

Drinkers reported significantly lower pain intensity ($F_{1,35} = 6.39$, $p = 0.02$; Cohen's $d = 0.70$; Figure 1) than abstainers. FM participants reported lower pain than FMI, although this difference

TABLE 1
Participant Characteristics

	FM		*FMI*	
	Drinkers (n = 9)	*Abstainers (n = 12)*	*Drinkers (n = 9)*	*Abstainers (n = 9)*
	Mean (SD)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Age (years)	54.22 (11.58)	45.08 (12.83)	51.00 (10.56)	52.78 (19.58)
BDI-II	11.89 (10.81)	20.23 (11.20)	10.56 (7.30)	12.00 (8.33)
Drinks/day	0.33 (0.50)	—	0.55 (0.37)	—
Pain intensity (0–100 VAS)[1]	39.38 (13.01)	43.95 (18.98)	39.77 (19.99)	64.23 (17.88)
Pain symptomatology duration (years)	13.80 (8.83)	12.47 (12.24)	13.72 (11.26)	10.30 (5.86)
Sleep symptomatology duration (years)	—	—	8.43 (12.98)	11.44 (14.77)
SOL (min)	24.70 (5.28)	45.81 (36.08)	46.62 (30.74)	39.97 (22.75)
WASO (min)[2]	19.45 (18.38)	28.02 (27.22)	59.79 (53.36)	51.87 (18.40)
TWT (min)[3]	66.01 (34.76)	97.17 (49.87)	114.24 (58.60)	124.02 (46.59)
TST (min)[4,5]	452.87 (61.78)	437.61 (82.87)	396.76 (38.80)	329.18 (57.39)
SE (TST/time in bed)[6,7]	0.88 (0.065)	0.81 (0.11)	0.78 (0.08)	0.72 (0.099)
Right hippocampal volume* (mm^3)[8]	3970.47 (389.11)	3867.59 (427.40)	4033.68 (461.90)	3584.71 (331.63)
Left hippocampal volume* (mm^3)[9]	3804.44 (423.88)	3675.72 (394.68)	3907.54 (441.88)	3553.56 (513.29)

Note. *Estimated marginal means controlling for age, BDI-II, MRI signal-to-noise ratio, and total grey matter volume. [1]Significant main effect of alcohol ($p = 0.02$). [2]Significant main effect of FMI status ($p = 0.004$). [3]Significant effect of FMI status ($p = 0.02$). [4]Significant effect of insomnia status ($p < 0.001$). [5]Significant effect of alcohol use ($p = 0.05$). [6]Significant effect of insomnia status ($p = 0.005$). [7]Significant effect of alcohol use ($p = 0.05$). [8]Significant effect of alcohol use ($p = 0.02$). [9]Significant effect of alcohol use ($p = 0.05$).

did not reach significance ($F_{1,35} = 3.24$, $p = 0.08$, Cohen's $d = 0.64$). A trend toward an alcohol use status X group interaction was also observed ($F_{1,35} = 3.00$, $p = 0.09$; $\eta_p^2 = 0.08$). No significant relationships between left ($r = 0.15$) and right hippocampal volume ($r = 0.09$) and reported pain intensity were noted (p's > 0.39).

Sleep Quality/Quantity

Main effects of drinking status were revealed for TST ($F_{1,35} = 3.99$, $p = 0.05$, Cohen's $d = 0.45$) and SE ($F_{1,35} = 4.01$, $p = 0.05$, Cohen's $d = 0.63$), with drinkers having greater TST and SE than abstainers. Drinking status did not have significant effects on WASO (Cohen's $d = 0.04$) or TWT (Cohen's $d = 0.36$; p's > 0.19). As anticipated, FMI participants' comorbidity was reflected in sleep-related variables, including greater WASO ($F_{1,35} = 9.58$, $p = 0.004$, Cohen's $d = 0.98$), less TST ($F_{1,35} = 15.74$, $p = < 0.001$), more TWT ($F_{1,35} = 5.78$, $p = 0.02$, Cohen's $d = 0.72$), and lower SE ($F_{1,35} = 9.11$, $p = 0.005$, Cohen's $d = 0.91$). SOL did not differ between participant groups (Cohen's $d = 0.23$, $p > 0.37$). No alcohol use status X group interactions were noted for WASO ($\eta_p^2 = 0.02$), TST ($\eta_p^2 = 0.04$), TWT ($\eta_p^2 = 0.01$), or SE ($\eta_p^2 = 0.00$; p's > 0.12). Across participants, neither left nor right hippocampal volume correlated with WASO ($r = 0.20$ and $r = 0.14$; $p > .11$), TST ($r = 0.07$ and $r = 0.19$; $p > .14$), TWT ($r = 0.07$ and $r = 0.009$; $p > .59$), or SE ($r = 0.00$ and $r = 0.09$; $p > 0.40$).

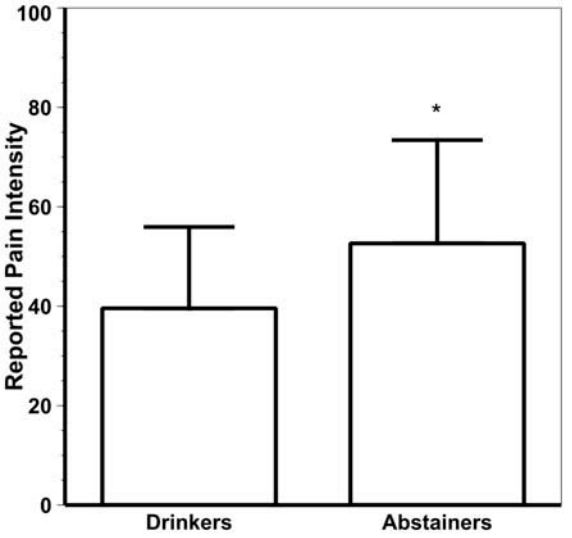

FIGURE 1 A main effect of alcohol use status was detected, such that drinkers had significantly lower pain than abstainers ($F_{1,35} = 6.39$, $p = 0.02$; Cohen's $d = 0.70$). Error bars represent standard deviation.

Hippocampal Volume

Greater hippocampal volume was noted in drinkers than abstainers for both the left and right hemispheres ($F_{1,30} = 4.13$, $p = 0.05$, $\eta_p^2 = 0.12$ and $F_{1,30} = 5.65$, $p = 0.02$, $\eta_p^2 = 0.16$, respectively; Figure 2). No main effect of chronic insomnia comorbidity was apparent for left or right

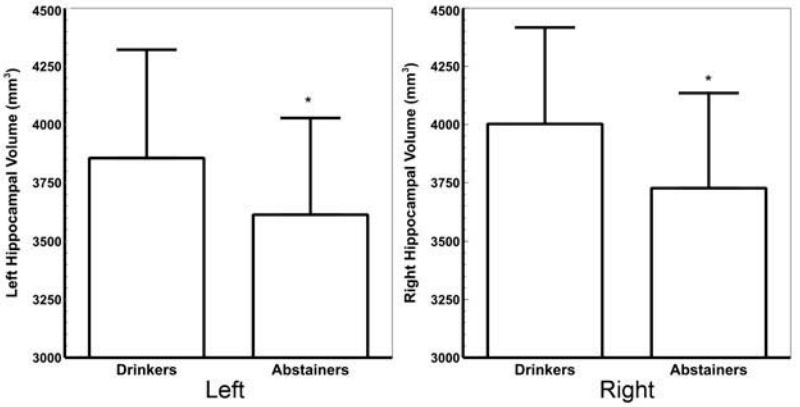

FIGURE 2 A main effect of drinking status was detected across participants, with drinkers having greater hippocampal left and right hippocampal volume than abstainers ($F_{1,30} = 4.13$, $p = 0.05$, $\eta_p^2 = 0.12$ and $F_{1,30} = 5.65$, $p = 0.02$, $\eta_p^2 = 0.16$, respectively). Estimated marginal means adjusted for signal-to-noise ratio, total gray matter volume, BDI-II scores, and age are presented. Error bars represent standard deviation.

hippocampal volume (Cohen's $d = 0.31$ and Cohen's $d = 0.33$, respectively; p's > 0.31). Likewise, no interactions were noted for either the left ($\eta_p^2 = 0.03$) or right hemisphere ($\eta_p^2 = 0.11$, p's > 0.11). Left and right hippocampal volume did not correlate with duration of pain ($r = 0.17$ and $r = 0.16$, respectively; p's > 0.16) or sleep symptomatology (r = -0.11 and r = –0.05; p's > 0.57). Finally, average number of drinks per night reported by drinkers in their daily diary did not correlate with left (r = –0.10) or right (r = –0.05) hippocampal volume (p's > 0.59).

Discussion

Taken together, the results of this study provide general support for our hypotheses and corroborate recent epidemiological work suggesting that low-to-moderate alcohol consumption is associated with less severe FM symptomatology than abstinence (Chung & Wang, 2013; Kim et al., 2013). Greater hippocampal volume was detected bilaterally in drinkers versus abstainers, a finding that has not previously been reported. Interestingly, no correlations between hippocampal volume and sleep or pain measures approached significance, undermining hypotheses regarding the role of the hippocampus in fibromyalgia and insomnia as framed within the CATS model. However, the reason underlying the lack of correlation between these measures is unclear. It is possible that alternative approaches to the characterization of hippocampal morphology may prove informative. In particular, it is possible that the integrity of particular subfields of the hippocampus (e.g., CA1-4, dentate gyrus, entorhinal cortex, etc.) may relate more strongly to sleep and pain symptomatology than gross hippocampal volume, especially given the differential roles each of these regions plays in hippocampal function (van Strien et al., 2009). This possibility should be investigated in future studies. For frame of reference, the hippocampal volumes of FM/FMI patients reported in this study are similar to those reported in previous reports regarding hippocampal structure in FM (Lutz et al., 2008), chronic insomnia (Riemann et al., 2007), and irritable bowel syndrome (Labus et al., 2014), although differences in study populations (e.g., age, comorbidities, etc.) and analysis method (e.g., manual segmentation vs. automated segmentation and software packages used) complicate direct comparison.

The relationship between low-to-moderate alcohol consumption and FM/FMI symptomatology is particularly interesting in the context of the CATS model. Alcohol use may reduce CATS-related hyperarousal via either biological factors (i.e., direct agonism of GABAergic neurotransmission and antagonism of NMDA receptors), or by psychosocial factors (enhanced social engagement, improved mood, and stress reduction) among chronic sufferers (Chung & Wang, 2013). It is also possible that acute moderate alcohol use has an analgesic effect, given its modulation of opioidergic signaling (Spanagel, 2009). Therefore, alcohol may affect FM/FMI symptomatology by acting on multiple levels of the biopsychosocial framework. While it is possible that alcohol use may have short-term effects on clinical symptomatology (i.e., pain reports), we do not believe it is likely that 14 days of low-level alcohol use alone (i.e., the length of the diary period in this study) would have measurable effects on hippocampal structure. Rather, it seems that a lifestyle of moderate drinking may affect brain morphology over an extended period, directly or indirectly.

Although suggestive of a potentially important link between alcohol consumption and brain structure and FM/FMI symptomatology, this study's results should be interpreted with caution. The relatively small sample size may have limited power to detect potentially important effects; thus, although statistically reliable patient group by alcohol use status interactions were not detected for pain intensity, sleep-related measures, or right-left hippocampal volume in the current study, it is possible a larger study with greater power could find a modulatory effect

of fibromyalgia comorbidity. In addition, because the study is cross-sectional and nonexperimental, a causal relationship between low-to-moderate alcohol use and FM/FMI symptomatology or hippocampal morphology cannot be inferred. Indeed, these data did not indicate a significant correlation between drinks consumed per day during the diary period and hippocampal volume for FM or FMI drinkers. It is possible the lack of correlation reflects poor reliability of the effect of drinking status on hippocampal volume measures that we detected. However, we suggest it is more likely it is due to the limited range of drinks consumed per day as reflected by participants' daily diaries. Additional studies including patients with a greater range of typical drinking would address this possibility. Furthermore, it is possible that endorsement of alcohol use acted as a behavioral marker for patients with relatively lower pain intensity and better symptom management. Although we cannot rule out this possibility, we noted no differences in endorsement of sleep or pain medication use between drinkers and abstainers in this sample.

Measures of alcohol use were not collected using instruments that assist participants in reporting their alcohol consumption in terms of standard drinks (i.e., quantity-frequency index; Cahalan, Cissin, & Crossley, 1969). Thus, it is possible that participants over- or underreported their actual alcohol use. Future studies should use standardized measures of alcohol intake to address this limitation. However, it should be noted that the increased error variability associated with this lack of standardization should theoretically result in decreased power to detect effects, increasing confidence in the reported results. An additional benefit of the use of quantity-frequency measures in future studies is that they provide more complete information regarding participants' history of alcohol consumption. For purposes of this study, we assumed that participants' reports of daily alcohol consumption were reflective of their typical drinking pattern. Previous studies of alcohol consumption using daily diaries (e.g., Armeli et al., 2005; Sacco et al., 2014) provide some precedent for this assumption, but explicit measurement in future studies using standardized instruments would improve confidence in results.

Furthermore, previous research indicates even small amounts of alcohol consumed close to an individual's bedtime can disturb sleep. However, participants' timing of alcohol consumption was not collected in this study. This limitation should be addressed in follow-up studies. Finally, although Kim et al. (2013) found that drinkers with fibromyalgia who exceeded moderate drinking guidelines demonstrated few of the purported benefits of low-to-moderate drinking, we were unable to examine such effects because heavier drinkers were not included in our sample.

In summary, individuals with fibromyalgia alone or fibromyalgia and chronic insomnia endorsing low-to-moderate alcohol consumption reported lower pain symptomatology and had significantly larger hippocampi than abstainers. Based on these findings, systematic prospective and longitudinal work examining the relationship between drinking pattern and FM/FMI symptomatology is warranted. Furthermore, laboratory studies examining the acute effects of alcohol administration on quantitative measures of pain sensitivity in patients with fibromyalgia and chronic insomnia may provide important information regarding mechanisms underlying alcohol's effects on symptomatology associated with these conditions.

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