Comparison of sleep structure and psychometric profiles in patients with fibromyalgia, osteoarthritis, and healthy controls.

Running head: Comparison of sleep and psychometrics in fibromyalgia

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SUMMARY

While research indicates that both the macro- and microstructure of sleep may be altered in fibromyalgia syndrome (FMS), few studies have controlled for symptom duration or included pain-control participants (i.e. patients with chronic pain and sleep disturbance not associated with FMS). A frequently reported alteration found in the sleep microstructure of FMS patients is the alpha-delta sleep anomaly. Although alpha waves have been observed during N3 sleep in healthy individuals, it has been proposed that there is an increase in alpha wave activity during slow wave sleep in FMS. Originally considered a possible neurological contribution to FMS, whether the alpha-delta sleep anomaly is fundamental to the development of FMS, or results mainly from the pain experience remains unknown. The present study was designed to compare sleep macro- and microstructure, and psychometric profiles, in three broadly age-matched groups of female participants: FMS patients (n=19); osteoarthritis (OA) patients with sleep disturbance (n=17); and healthy adults (n=10). FMS patients met American College of Rheumatology diagnostic criteria and were recruited within 6 months of diagnosis. Subjective sleep quality was significantly lowest, and levels of anxiety and depressive symptoms were significantly highest for FMS patients. However, the groups showed no significant differences in PSG measures of total sleep time, sleep latency and total wake after sleep onset. Levels of alpha-delta sleep were statistically similar in both clinical (FMS and OA) groups indicating that it is not a specific abnormality of FMS. Overall, subjective measurements of anxiety, depression, fatigue and sleep quality better discriminated between the three groups than did objective measurements of sleep variables.

KEY WORDS: Fibromyalgia syndrome; osteoarthritis; polysomnography; pain; sleep quality; sleep microstructure; spectral analysis

INTRODUCTION

Fibromyalgia syndrome (FMS) is a chronic condition characterised by widespread musculoskeletal pain, fatigue, non-restorative sleep, morning stiffness and cognitive debilitation (Smythe & Moldofsky, 1977). Diagnostic criteria, set by the American College of Rheumatology (1990), include widespread pain in the four quadrants of the body in combination with tenderness at 11 of 18 defined tender point sites (Wolfe et al., 1990). More recently proposed criteria, which produce a widespread pain index and symptom severity score, eliminates the need for tender point examination (Wolfe et al., 2010). FMS affects between 0.5 to 5% of the general population (Branco et al., 2010; White & Harth, 2001), with the majority of sufferers being female (Yunus, 2001) and older (Wolfe et al., 1995). The diagnosis and treatment options for FMS are associated with significant societal and health care costs (Hughes et al., 2006). While the aetiology of FMS remains largely unknown (Hayes et al., 2010), the syndrome has been associated with a distinctive psychological profile characterised by elevated levels of anxiety, depressive symptoms, poor subjective sleep quality, and fatigue (Kurtze et al., 1998; Shuster et al., 2009). However, few studies have simultaneously examined sleep and psychometric status in the same participants.

Sleep Dysfunction in FMS

More than 90% of FMS patients describe some form of impaired sleep quality (Moldofsky, 2008). These sleep symptoms may also impact on pain experience, (Bigatti et al., 2008) since degraded sleep quality increases pain sensitivity (Smith & Haythornthwaite, 2004). A common sleep complaint in FMS is non-restorative sleep (NRS) which is associated with more debilitating daytime symptoms, such as an increase in the number of tender points, increased pain intensity, fatigue, sleepiness and negative mood (Wilkinson & Shapiro, 2012).

Recent studies have shown strong associations between sleeping problems and risk of developing FMS (Mork & Nilsen, 2011). It is unknown, however, whether non-restorative sleep in FMS is a primary or secondary phenomenon.

Studies have shown that FMS patients typically exhibit less total sleep time, lower sleep efficiency, an increase in stage 1 sleep, a reduction in slow wave sleep and an increase in the number of arousals (Harding, 1998; Roizenblatt et al., 2001). A distinctive, but equivocal feature of FMS sleep structure that has evoked controversy is the alpha EEG sleep anomaly. Although alpha waves may be observed in different stages of NREM sleep is a normal occurrence (Finelli, Ackermann, & Borbely, 2001), the alpha anomaly during NREM sleep in FMS has been described as frequent large amplitude alpha waves superimposed onto delta waves. These alpha 'intrusions', and the resulting 'alpha-delta sleep' (Hauri & Hawkins, 1973), remain an inconsistent finding. While some have found alpha-delta sleep in all the FMS patients they examined (Branco et al., 1994), others have found no difference between FMS and control subjects (Besteiro González et al., 2011). The specificity of alpha-delta sleep to FMS is also unclear, since alpha intrusions have also been reported for non-FMS patients with chronic pain conditions (e.g. Wittig et al., 1982). Differences in FMS findings may reflect the different recording methodologies, equipment, patient selection criteria or statistical analyses used. These methodological variations also make comparisons across studies difficult. In addition, many studies use only healthy controls as comparators, and omit 'pain controls' (i.e. patients with chronic pain and sleep disturbance NOT associated with FMS). However, as alpha-delta sleep has been reported for non-FMS patients experiencing chronic pain, the inclusion of pain-control participants would improve the precision of inferences drawn from comparisons.

The aim of the present study, therefore, was to compare sleep macro- and microstructure, and psychometric profiles, in three groups of participants: newly diagnosed FMS patients; a pain-

control group of osteoarthritis (OA) patients with sleep disturbance; and a healthy control (HC) group. The study was designed to address three research questions:

1. When scored according to AASM criteria, does the polysomnographic sleep of FMS, OA, and HC participants show significant differences on measures of: total sleep time (TST); sleep onset latency (SOL); sleep efficiency (SE); wake after sleep onset (WASO); and the percentage of time spent in each stage of sleep?
2. Through spectral analysis, do FMS patients exhibit a significantly greater frequency and power of alpha-delta sleep than OA patients or healthy controls?
3. In comparisons of mean values, do FMS, OA and HC participants show differences on psychometric assessments of: sleep quality; fatigue; daytime sleepiness; pain experience; depression; and anxiety?

METHODOLOGY:

Participants

FMS is more common in females. In order to minimise confounding factors three groups of female only participants (overall age range of 19 to 63) were recruited for the study. The FMS group comprised 19 (mean age=40.7±13.8; range=19-58) newly diagnosed FMS patients, with at least six-month symptom prevalence and fulfilling the American College of Rheumatology (ARS) criteria for FMS (Wolfe et al., 1990). The FMS patients had on average 3.7 Years between onset of symptoms and diagnosis. Average FMS diagnosis length since the study was 31.58±78.72 weeks. The osteoarthritis (OA) group comprised 17 (mean age=46.47±11.61; range=19-63) patients diagnosed with OA and reporting localized joint pain and sleep disturbance. The OA patients were on a waiting list for orthopaedic surgery and were only included if they had a PSQI score $\geq$ 5 and did not have widespread pain. The

OA patients' average diagnosis length since the study was 43.54±36.49 weeks. The healthy control (HC) group included 10 adults (mean age=38.40±13.79; range=23-61) screened for (and free from) chronic conditions and significant symptoms relating to fibromyalgia or chronic pain. All patients and subjects were excluded if there was any subjective evidence of sleep disorders. Clinical patients were recruited from a single rheumatology clinic in the UK; healthy controls were recruited from the local population. The groups were broadly matched for age.

For all groups, exclusion criteria were: currently menopausal; have any sleep disorder diagnosis; receiving HRT; prescribed antidepressant or any psychotropic medications; currently or recently (previous 12 months) pregnant; or a history of any medical condition that could mimic FMS. For the FMS and OA groups any weak opioid drugs were withdrawn three days prior to recording.

Procedure:

All participants were recruited between August 2011 and June 2014. They underwent identical study procedures. FMS patients were invited to participate in the study following their initial diagnosis at the rheumatology outpatient clinic at Trafford General Hospital, Trafford, UK. OA patients were recruited from orthopaedic waiting lists of patients eligible for joint surgery who were also attending the rheumatology outpatient clinic at Trafford General Hospital. HC participants responded to newspaper and local amenity advertisements. Following an expression of interest all participants were visited at home where the study was explained, consent was obtained, and a psychometric profile was obtained. The Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989; the Epworth Sleepiness Scale (ESS; Johns, 1991); the Fatigue Severity Scale (FSS; Krupp et al., 1989); the Brief Pain Inventory (BPI; Cleeland & Ryan, 1994); the Centre for Epidemiological Studies Depression Scale (CES-D;

Radloff, 1977); and the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983) were used in the psychometric battery. Domiciliary polysomnography was conducted over two consecutive nights using an ambulatory sleep-recording system. Logistical constraints meant that the menstrual phase of the patients was not taken into account. Participants were asked to refrain drinking alcohol or coffee on each night of the PSG recordings. After attachment of electrodes in the evening, participants were allowed to move around freely until their usual bedtime, when the portable PSG system (Embla A10) began an automatic recording. Signals were digitized onto a PCMCIA card and were later downloaded onto a computer system. Participants maintained sleep diaries, recording their bedtimes, 'lights-out' times, and rise-times.

The PSG recording montage consisted of seven electrophysiological derivations. This included two electrooculographic channels referenced to the single mastoid (LOC/A1 & ROC/A1), two electroencephalographic channels referenced to each mastoid (C3/A2 & C4/A1), a bipolar-mentalis electromyogram, a bipolar prefrontal EEG channel (Pf1/F3) and a bipolar occipital EEG channel (O1/P3). EEG and EMG channels were sampled at 200 Hz, and EOG at 100 Hz. Electrodes were attached in accordance with the 10:20 system of electrode placement. In order to maintain amplifier inputs within a small voltage range relative to the amplifier's zero voltage level, a ground was placed on the Fpz electrode site, 10% above the Nasion.

Analysis

Sleep Macrostructure

Only data from the second night were used for analysis to allow for some habituation with the equipment. Recordings were imported into Somnologica 5.1., and scored according to AASM criteria (Silber et al., 2007) by a trained sleep scorer. It was not possible to have the primary

scorer blinded to the diagnosis but concordance in sleep staging was ascertained using a blinded secondary scorer with an 83% concordance guideline (Rosenberg & Van Hout, 2013). Each night was scored in 30-s epochs, arousals were computed automatically by the system, and the sensitivity of detection was calibrated in accordance with AASM criteria: an abrupt shift in frequency lasting for at least 3 seconds with 10 seconds of stable sleep preceding. Arousals from 20% of participants were scored visually to ensure reliability. Sleep onset was defined as the period from 'lights out' to the first two epochs of uninterrupted stage N2 sleep.

Sleep Microstructure

Spectral analysis on the C3-A2 channel was employed after demeaning, detrending and applying a Welch taper to each single FFT window. The C3-A2 channel was selected to give the strongest signal across all frequencies. Each analysis window equates to 512 points (2.56 seconds) long, giving a frequency resolution of 0.39Hz, with 23 overlapping windows covering each 30s epoch. An artefact rejection algorithm was also used to discard outlier epochs from the computation of average spectral power. Each frequency band was decomposed and power averaged over the whole night of sleep. Frequency bands were also separated into sleep stages N2, N3 and REM. The natural logarithmic transformations for all power bands were computed and used for statistical analysis. Alpha intrusion was quantified by measuring the mean alpha power during stage N3. Alpha power was also evaluated cycle by cycle for the first three sleep cycles.

Inter-group differences for normally distributed variables were assessed using one-way ANOVA. Homogeneity of variance was ascertained using the Levene's F-test, and post-hoc comparisons (appropriate for smaller sample sizes) were conducted using Games-Howell test for multiple comparisons. The Kruskall-Wallis ranks test was used for inter-group

comparisons of spectral data, with Mann-Whitney comparisons (used with Bonferroni corrections) to investigate group differences. All statistical analyses adopted the 0.05 level of significance and were conducted using IBM SPSS 22.

RESULTS:

Participant Characteristics:

Participant characteristics are shown in Table 1. One way ANOVAs found a significant main effect of pain severity and pain interference. The clinical groups showed significantly greater pain severity and pain interference (p<.001) than the healthy control group, with no differences between the clinical groups. Sleep quality as a component score of the PSQI showed an overall significant main effect, with our clinical groups having a greater perception of disturbed sleep than the healthy controls (p<.001); FMS patients also had a worse perceived PSQI rated sleep quality than OA patients (p=.023). FMS patients had greater perceived sleepiness than both OA (p=.033) and HC (p=.034), who had similar levels of sleepiness. They were also more fatigued than OA and HC (p<.001); OA patients were also significantly more fatigued than the HC group (p<.001).

The clinical groups (FMS and OA) showed greater amounts of depression symptomatology than the healthy controls (p<.001); FMS and OA both showed similar levels of depression.

Main effects were found for both state and trait anxiety. Post-hoc analysis showed FMS patients had greater state anxiety than healthy controls (p<.001). However, no differences were found in comparisons between the other groups. For trait related anxiety, FMS patients had significantly greater trait anxiety scores than both OA (p<0.05) and HC (p=.001). OA and HC participants had statistically similar levels of trait anxiety.

Sleep Macrostructure

Descriptive sleep variables were analysed between the three groups using a one way ANCOVA whilst controlling for age. Table 2 displays the mean descriptive scores and statistics of sleep as measured using PSG. As indicated, no main effects were observed for the majority of sleep variables, except for sleep efficiency and sleep stage transitions. For sleep efficiency, post-hoc analysis showed FMS patients having significantly lower sleep efficiency compared to healthy controls (p=.033). No statistically significant differences were found for other comparisons.

Sleep stage transitions (SST) were used as a measure of sleep stage maintenance and sleep fragmentation. An SST ratio was calculated as a function of total sleep time. Results indicated a significant main effect for SST, and post-hoc analysis found the clinical groups had significantly greater SSTs than healthy controls in both FMS (p=.021) and OA (p=.003); FMS and OA both had statistically similar amount of SSTs. In order to explore the influence of pain severity, inter-group values of sleep efficiency and sleep stage transitions were compared in one way ANCOVAs controlling for age and BPI-S scores. No significant main effects were found for sleep efficiency (F (2, 41) = .899, p=n.s.) or for sleep stage transitions, (F (2, 41) = 1.622, p=n.s.).

Sleep Microstructure

Sleep microstructure was analysed via spectral analysis. Absolute average power was calculated over the frequency range 0.1-48Hz and log transformed. Kruskall-Wallis rank test was conducted for each power band between the three groups in total NREM (Stages N1-N3), N2, N3 and REM sleep. Table 3 displays the means and the results from the analysis for night two. Figure 1 (A-D) displays these values graphically.

Total (0.1-48Hz)

For total averaged power, a significant main effect was found during stage N3. Post-hoc analysis showed no significant differences between FMS and OA (U=108.00, p=n.s.) or FMS and HC (U=80.00, p=n.s.). The OA group had a significantly lower total absolute power than the HC group (U=37.00, p=.045).

Sigma-2 (14-16Hz)

Differences were observed in the Sigma-2 range (14-16Hz) for total NREM, N2 and N3. Gradient trends show the FMS group having the greatest sigma-2 power, stepping down for OA and the lowest power in the healthy group. Post-hoc analysis for total NREM found no significant differences between FMS and OA (U=150, p=n.s.) or between FMS and HC (U=53.00, p=n.s.). OA patients however, had significantly greater sigma-2 power than the HC group (U=33.00, p=.003). For stage N2, no significant differences were found between FMS and OA (U=146.00, p=n.s.) or FMS and HC (U=50.00, p=n.s.); OA patients showed greater sigma-2 power than the HC group (U=35.00, p=.033). Stage N3 showed similar findings, with no significant differences between FMS and OA (U=158.00, p=n.s.) or FMS and HC (U=49.00, p=n.s.). OA patients had greater sigma-2 power in stage N3 than the HC group (U=37.00, p=.045).

Delta-1 (0.1-1Hz)

For low frequency activity, a significant effect was found during stage N3. Post-hoc comparisons showed no significant differences between FMS and OA (U=95.00, p=n.s.) or FMS and HC (U=69.00, p=n.s.). However, OA had a significantly lower average power of Delta-1 during stage N3 compared to HC (U=25.00, p=.006).

Alpha (8-12Hz)

Sleep scorers have identified that all patients and subjects were found to have alpha waves in N3 sleep. We did not find any significant difference between the groups with neither total alpha power nor cycle-by-cycle analysis. In relation to alpha intrusion in N3, we found numerically greater alpha power in FMS but this was not statistically significant (Table 3 and Table 4).

DISCUSSION

This is the first systematic study comparing sleep macro- and microstructure in FMS patients, non-FMS chronic pain patients, and healthy controls. In recruiting the groups for this study, considerable care was taken to ensure unambiguous and recent diagnoses of FMS, broadly similar ages across the three groups, and the presence of significant pain-related sleep disturbance within the FMS and OA groups. While both clinical groups showed PSQI scores exceeding (>10) the 'poor sleeper' range (PSQI scores $\geq$ 5) and FSS scores indicative of elevated daytime fatigue at screening, the healthy control group showed a sleep profile consistent with their age and health status with no significant sleep symptoms. Given also the exclusion criteria adopted, we are confident that the present groups are representative of the intended clinical and non-clinical groupings, and provide a valid basis for tests of between-group differences.

In relation to the first research question, sleep macrostructure was remarkably similar in the 3 groups, with no significant differences present in TST, SOL, WASO, or the percentage of time spent in each sleep stage. However, relative to healthy controls FMS patients did show significantly lower sleep efficiency. Given the absence of statistical differences for the variables, which comprise sleep efficiency, this difference possibly arises from the additive magnitude of SOL, WASO and time spent awake in bed after the final

awakening in the FMS group. It is also relevant to note that the FMS group overall, had a numerically greater 'time in bed' (Table 2) over the course of the night. Without evidence of shortened objective total sleep time, the contribution of reduced SE to the elevated levels of sleepiness and fatigue seen in the FMS group (Table 1) is unclear. Both clinical groups (FMS and OA) also showed significantly higher SST ratios, indicative of greater sleep fragmentation. That these between-group differences (in SST outcomes) did not achieve significance in ANCOVA models controlling for age and BPI-S scores strongly suggests that pain severity is an influential factor mediating the structural quality of sleep in FMS.

Regarding sleep microstructure, no significant differences were found for the power of the alpha frequency signal during N3 sleep. These findings do not support the view that alpha wave intrusion is a primary abnormality found in FMS. The two patient groups (FMS and OA) did not exhibit significant differences in pain measures, but did show a numerically greater alpha power than the healthy controls that was consistent throughout the night. Our data does not explain this observation but both pain and sleep disturbance may be contributory. However, our data does not support alpha intrusion being a specific finding in fibromyalgia.

Although no differences were found in alpha power, the results of the spectral analysis demonstrated significant differences in the average power of the sigma-2 frequency in NREM sleep as a whole and when separated into N2 and N3. The greatest numerically observed power was found in the FMS group, followed by OA with the HC group having the lowest averaged power. However, only the OA group exhibited a significant finding of increased sigma-2 power compared with the HC group for all three sleep stage groupings. Again, this may point towards higher frequency intrusions as a function of pain. In this context, it is interesting that the groups did show significant differences in extreme slow wave activity in the 0.1-1Hz range, with the OA group having much lower delta-1 power than

both FMS and HC participants during stage N3. This reinforces the notion that a modified sleep structure may be a function of chronic pain rather than specific to FMS. However previous research has described FMS patients as having less slow wave sleep than healthy controls (Dauvilliers & Touchon, 2001). In the present study, relative to HC participants, FMS patients exhibited similar amounts of slow wave sleep in addition to similar levels of delta power.

Clearly, the greatest differences among the experimental groups arose in the psychometric measures assessing subjective sleep quality (PSQI), fatigue (FSS), daytime sleep tendency (ESS) anxiety (STAI) and depressive (CES-D) symptoms. In each case, values showed a severity gradient, being lowest for the HC groups, and highest for the FMS group. That FMS patients reported significantly worse sleep quality, and higher levels of fatigue and daytime sleepiness despite recording ostensibly similar proportions of time in N1, N2, N3 and REM. It is possible, however, that the negative affective status of FMS patients (characterised by higher levels of anxiety and depressive symptoms) might act as a 'filter' through which subtle differences in sleep continuity (as indexed by SSTs) are experienced and, perhaps, amplified. Such an influence would allow the conclusion that sleep symptoms in FMS patients (but not, or less so, in OA patients) may have a basis in sleep-stage continuity. An important caveat here is that the directionality of mood-sleep influences was not assessed. As a result, the alternative possibility that the experience of poor sleep quality impacts and degrades mood should also be acknowledged. While the present study provides important new insights into the psychological profiles of chronic pain patients, the results also emphasise the need for longitudinal studies of the sleep natural history in FMS.

We recognise that this study has limitations. Although sleep stage transitions were visually scored and may be relevant to the subjective sleep quality found in these patients, arousals may also be related to sleep quality but were scored automatically. A further

potential limitation of the present study is the possibility that sleep quality and sleep structure in FMS degrade progressively over time. It is also noted that menstrual phase was not taken into account when taking these recordings, the phases of the menstrual cycle may have some effect on the participants' sleep, although it is not deemed significant enough to impact the results. In the present study, the selection of newly diagnosed female FMS patients aimed to reduce heterogeneity in symptom profiles. It remains a possibility that, as the syndrome progresses, the severity of sleep disturbance and symptoms may increase in severity, allowing the further possibility that inter-group differences might be more prominent in more 'advanced' FMS cases. Again, this possibility emphasises a need for longitudinal data to understand symptom evolution in fibromyalgia syndrome.

Conclusion

Despite a normal sleep time, both FMS and OA patients have disturbed sleep from sleep stage transitions. Patients with FMS have more psychological symptoms and worse subjective symptoms of sleep, fatigue and sleepiness compared with patients with OA who complain of pain disturbing their sleep. While the alpha-delta sleep anomaly does not appear to be specific to FMS, an increase in sigma activity within these patient groups may reflect subtle differences in sleep pathology, which may not be explained by pain experience alone.

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Table 1 Psychometric profiles of fibromyalgia (FMS), osteoarthritis (OA) and healthy control (HC) participants

	FMS *(19)*	**OA** *(17)*	**HC** *(10)*	***F***	***df***	***p***	η_p^2
Age	40.74 ± 11.45	46.47 ± 11.61	38.40 ± 13.79	1.706	2, 43	.194	.074
BPI-S[1]	6.17 ± 1.75	4.93 ± 2.01	0.10 ± 0.32	144.098†	2, 24.62	.000***	.674
BPI-I[2]	6.30 ± 2.04	4.55 ± 2.43	0.01 ± 0.04	116.103†	2, 22.62	.000***	.606
PSQI[3]	13.89 ± 3.40	10.88 ± 3.08	3.70 ± 1.16	89.225†	2, 28.15	.000***	.648
ESS[4]	9.89 ± 4.54	6.47 ± 3.20	5.90 ± 3.45	4.998	2, 43	.011*	.189
FSS[5]	52.47 ± 6.74	38.06 ± 10.57	22.60 ± 10.91	35.238	2, 43	.000***	.621
CES-D[6]	23.11 ± 10.13	16.06 ± 7.44	4.80 ± 2.62	37.58†	2, 27.50	.000***	.441
STAI-Y1[7]	42.74 ± 11.17	36.53 ± 8.12	27.10 ± 8.29	8.819	2, 43	.001**	.291
STAI-Y2[8]	49.63 ± 12.59	39.82 ± 11.80	31.90 ± 7.52	8.485	2, 43	.001**	.283

1. Brief Pain Inventory – Pain Severity, 2. Brief Pain Inventory – Pain Interference, 3. Pittsburgh Sleep Quality Index Global Score, 4. Epworth Sleepiness Scale, 5. Fatigue Severity Scale, 6. Centre for Epidemiological Studies for Depression Scale, 7. State Anxiety, 8. Trait Anxiety; ***p<.001, **p<.01, *p<.05; † - Welch's F Statistic; values are mean ± *SD. P values were calculated using analyses of variance followed by post-hoc analysis with corrections for multiple comparisons;*

Table 2 Polysomnographic sleep characteristics of fibromyalgia (FMS), osteoarthritis (OA) and healthy control (HC) participants

	FMS *(19)*	**OA** *(17)*	**HC** *(10)*	***F***	***df***	***p***	η^2
TIB(Mins.)[1]	505.76±83.51	475.65±74.12	475.50±75.21	.826	2, 43	.445	.037
TST(Mins.)[2]	428.14±14.89	415.17±16.04	421.75±20.70	.173	2, 43	.842	.008
SOL(Mins.)[3]	29.73±4.90	32.55±5.28	24.48±6.82	.426	2, 43	.656	.020
ROL (Mins.) [4]	73.21±31.58	75.00±23.17	68.90±16.63	.175	2, 43	.840	.008
WASO(Mins.)[5]	48.39±6.28	35.15±6.76	27.12±8.73	2.247	2, 43	.118	.097
S.E. (%)[6]	84.96±1.52	86.72±1.63	91.82±2.11	3.559	2, 43	.037*	.145
N1(%)	2.28±.74	2.25±.80	4.62±1.03	2.020	2, 43	.145	.088
N2(%)	47.79±2.37	46.37±2.55	46.65±3.30	.090	2, 43	.914	.004
N3(%)	26.35±2.25	29.15±2.42	23.38±3.13	1.048	2, 43	.360	.048
REM (%)	23.61±.93	22.23±1.01	25.35±1.30	1.747	2, 43	.187	.077
SST Ratio[7]	.274±.02	.303±.02	.182±.03	6.598	2, 43	.003**	.239
Awakenings	14.37±1.56	15.24±1.68	9.59±2.17	2.260	2, 43	.117	.097
Arousals	146.60±27.83	130.78±29.97	100.04±38.68	.484	2, 43	.620	.023

1. Time in Bed, 2. Total Sleep Time, 3. Sleep Onset Latency, 4. REM Onset Latency 5. Wake After Sleep Onset, 6. Sleep Efficiency, 7. Sleep Stage Transitions Ratio;*p<.05, **p<.01; values are mean ± *SD.* P values were calculated using analyses of variance followed by post-hoc analysis with corrections for multiple comparisons;

Table 3 Profiles of Absolute Spectral Power for fibromyalgia (FMS) osteoarthritis (OA) and healthy control (HC) participants

	Group	Total	Delta-1	Delta-2	Theta	Alpha	Sigma-1	Sigma-2	Beta-1	Beta-2	Gamma
T-NREM	**FMS**	5.64 ± .59	4.63 ± .69	4.54 ± .54	3.73 ± .60	2.99 ± .63	1.84 ± .67	1.12 ± .80	1.17 ± .80	.35 ± .88	.28 ± 1.02
	OA	5.49 ± .30	4.36 ± .42	4.49 ± .29	3.67 ± .33	2.82 ± .53	1.65 ± .50	.98 ± .39	1.08 ± .38	.10 ± .37	-.21 ± .31
	HC	5.68 ± .30	4.77 ± .35	4.64 ± .31	3.70 ± .27	2.70 ± .38	1.82 ± .50	.61 ± .27	.97 ± .46	.18 ± .60	-.03 ± .62
		1.944(p=n.s.)	5.304(p=n.s.)	1.021(p=n.s.)	.451(p=n.s.)	1.554(p=.460)	.504(p=n.s.)	**6.276(p=.043)***	1.789(p=n.s.)	1.824(p=n.s.)	5.681(p=n.s.)
N2	**FMS**	5.24 ± .35	4.02 ± .41	4.11 ± .31	3.50 ± .44	2.88 ± .49	1.82 ± .54	1.15 ± .62	1.20 ± .54	.34 ± .58	.21 ± .70
	OA	5.17 ± .28	3.84 ± .36	4.14 ± .26	3.50 ± .34	2.76 ± .50	1.67 ± .51	1.09 ± .42	1.18 ± .36	.18 ± .36	-.15 ± .30
	HC	5.28 ± .24	4.14 ± .30	4.21 ± .22	3.51 ± .27	2.70 ± .42	1.97 ± .52	.72 ± .27	1.08 ± .50	.28 ± .64	.07 ± .68
		1.745(p=n.s.)	4.896(p=n.s.)	.874(p=n.s.)	.635(p=n.s.)	1.034(p=n.s.)	2.567(p=n.s.)	**6.467(p=.039)***	2.502(p=n.s.)	2.071(p=n.s.)	4.733(p=n.s.)
N3	**FMS**	6.29 ± .90	5.50 ± .93	5.18 ± .84	4.08 ± .92	3.19 ± 1.03	1.88 ± 1.07	1.04 ± 1.21	1.11 ± 1.31	.33 ± 1.43	.34 ± 1.59
	OA	5.97 ± .27	5.07 ± .38	4.97 ± .28	3.90 ± .31	2.92 ± .60	1.62 ± .53	.82 ± .41	.94 ± .42	-.01 ± .40	-.29 ± .34
	HC	6.27 ± .28	5.58 ± .35	5.19 ± .25	3.93 ± .23	2.66 ± .35	1.64 ± .44	.44 ± .33	.79 ± .49	.04 ± .60	-.16 ± .60
		6.000(p=.05)*	**9.809(p=.007)****	3.999(p=n.s.)	.506(p=n.s.)	3.439(p=n.s.)	.055(p=n.s.)	**6.267(p=.044)***	1.318(p=n.s.)	.963(p=n.s.)	5.031(p=n.s.)
REM	**FMS**	4.56 ± .45	3.03 ± .55	3.45 ± .42	3.13 ± .53	2.20 ± .65	.61 ± .60	.33 ± .60	1.24 ± .59	.42 ± .60	-.01 ± .55
	OA	4.46 ± .42	2.86 ± .51	3.35 ± .43	3.02 ± .47	2.08 ± .57	.59 ± .42	.39 ± .41	1.33 ± .41	.44 ± .46	-.08 ± .32
	HC	4.43 ± .28	2.93 ± .25	3.36 ± .21	2.92 ± .39	1.96 ± .56	.48 ± .45	.17 ± .46	1.12 ± .58	.31 ± .68	.03 ± .77
		1.248(p=n.s.)	1.171(p=n.s.)	.314(p=n.s.)	2.567(p=n.s.)	1.495(p=n.s.)	.682(p=n.s.)	2.305(p=n.s.)	3.584(p=n.s.)	1.447(p=n.s.)	.829(p=n.s.)

Logarithmic absolute mean power in all frequency bands (Total 0.1-48Hz, Delta-1 0.1-1Hz, Delta-2 1-3.5Hz, Theta 3.5-8Hz, Alpha 8-12Hz, Sigma-1 12-14Hz, Sigma-2 14-16Hz, Beta-1 16-24Hz, Beta-2 24-32Hz, Gamma 32-48Hz) in the sleep EEG (C3-A2 derivation) for sleep stages Total NREM (N1-3), N2, N3 and REM.

FMS, patients with fibromyalgia syndrome (n=19); OA, patients with osteoarthritis (n=17); HC, healthy controls (n=10); T-NREM, total NREM; *p<.05; **p<.01; values are mean ± *SD*.

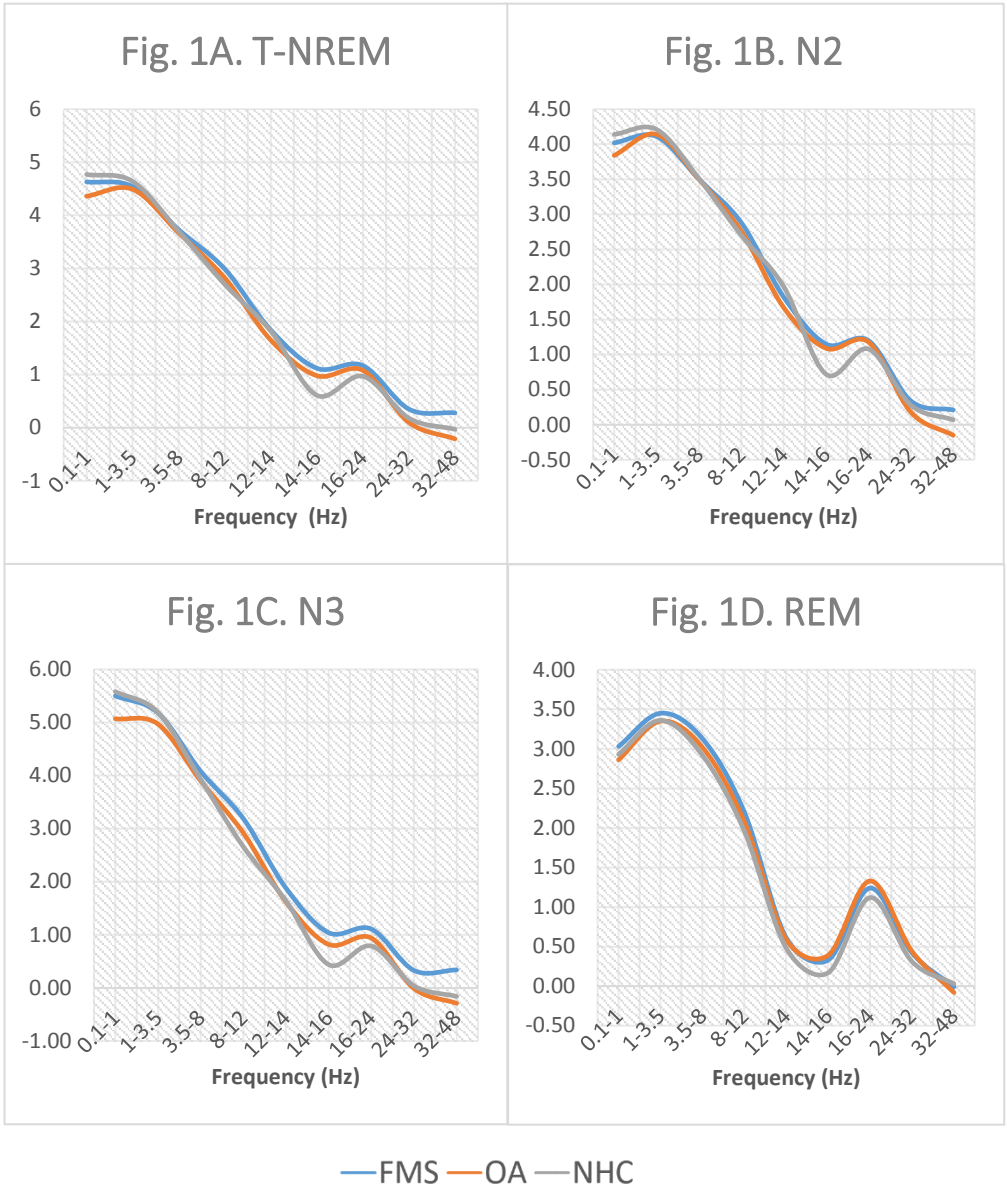

Fig. 1A. T-NREM – Total NREM sleep; Fig. 1B. N2 – Total Stage N2 sleep; Fig. 1C. N3 – Total Stage N3 sleep; Fig. 1D. REM – Total REM sleep.

Table 4 Cycle analysis of absolute spectral power for fibromyalgia (FMS) osteoarthritis (OA) and healthy control (HC) participants in the alpha power band (8-12Hz)

		Cycle 1	Cycle 2	Cycle 3
Sleep Stage	**Group**	**Alpha (*n*)**	**Alpha (*n*)**	**Alpha (*n*)**
T-NREM	**FMS**	3.00 ± .46 (19)	2.90 ± .53 (19)	2.87 ± .52 (19)
	OA	2.99 ± .62 (17)	2.86 ± .54 (17)	2.83 ± .5.3 (17)
	NHC	2.79 ± .35 (10)	2.68 ± .39 (10)	2.72 ± .42 (10)
K(p)		1.846(p=n.s.)	1.287(p=n.s.)	.711(p=n.s.)
N2	**FMS**	2.95 ± .47 (19)	2.86 ± .48 (19)	2.85 ± .51 (19)
	OA	2.90 ± .47 (16)	2.82 ± .51 (17)	2.80 ± .52 (17)
	NHC	2.89 ± .44 (10)	2.77 ± .46 (10)	2.74 ± .45 (10)
K(p)		.283(p=n.s.)	.257(p=n.s.)	.331(p=n.s.)
N3	**FMS**	3.02 ± .45 (18)	3.02 ± .49 (18)	2.95 ± .50 (18)
	OA	3.03 ± .67 (17)	2.89 ± .59 (17)	2.95 ± .57 (17)
	NHC	2.77 ± .33 (10)	2.69 ± .33 (9)	2.77 ± .42 (10)
K(p)		2.616(p=n.s.)	2.733(p=n.s.)	1.576(p=n.s.)
REM	**FMS**		2.22 ± .70 (18)	2.29 ± .66 (19)
	OA		2.13 ± .64 (17)	2.09 ± .55 (17)
	NHC		2.22 ± .61 (10)	2.00 ± .56 (10)
K(p)			.766(p=n.s.)	2.144(p=n.s.)

Logarithmic absolute mean power of Alpha 8-12Hz power band in sleep EEG (C3-A2 derivation) for sleep stages Total NREM, N2, N3 and REM. FMS, patients with fibromyalgia syndrome; OA, patients with osteoarthritis; HC, healthy controls; T-NREM, total NREM; values are mean ± SD; Note, due to the way sleep cycles were calculated, there is no REM data for cycle 1.

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