Seasonality in pain, sleep and mental distress in patients with chronic musculoskeletal pain at latitude 69° N

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Seasonality is evident in several aspects of human health and behaviour, whereas seasonality in chronic pain is less well studied. We examined seasonal variation in pain severity and pain dissemination, as well as in pain-associated conditions, such as sleep impairment, sleep timing, mental distress, fatigue and physical activity. We also examined if any of these associated conditions moderated the seasonality in pain. This prospective study was conducted in the sub-arctic municipality of Tromsø, Norway (69º North) on a sample of patients with chronic musculoskeletal pain ($N = 56$). Data were collected with self-report questionnaires and objective actigraphy measures (7 days) twice: winter and summer. Mixed linear regression models were fitted. A modest seasonality effect was observed in pain severity (highest in summer), but not in pain dissemination. Seasonality with increased physical activity and delayed sleep timing in the summer was also present. The remaining pain-associated self-report or objective measures indicated no seasonality. The season-pain association was not significantly moderated by any of the pain-associated conditions. Previous studies on healthy individuals residing in polar areas have suggested an opposite seasonal effect with delay of the sleep-wake rhythm in winter. Our results based on a clinical sample thus represent a novel finding that needs to be examined further with regard to seasonal circadian entrainment and alignment in pain populations. These results may have clinical value for the treatment of patients with musculoskeletal pain as seasonality may require seasonal adjustments of pain treatment strategies.

Keywords: Seasonality, Musculoskeletal Pain, Sleep Quality, Chronotype, Mental Distress, Fatigue, Actigraphy

Introduction

Seasonality is a ubiquitous source of circannual fluctuations in environmental conditions. It gathers momentum at more extreme latitudes and drives evolutionary adaptation, and influences various aspects of existence, including human behavior, wellbeing and health. For example, mortality in general, morbidity and mortality from cardiovascular and lung diseases, as well as prevalence of metabolic syndrome seem most prevalent during winter (Johnston and Sears 2006; Kamezaki et al. 2010; Marti-Soler et al. 2014). Sleep behavior also varies with season as sleep problems and delayed sleep timing increase during the dark winter period at high latitudes (Johnsen et al. 2012; Johnsen et al. 2013; Friborg et al. 2014). Although there is limited support for a seasonal ebb and flow in depressed mood in the general population (Johnsen et al. 2012; Friborg et al. 2014; Overland et al. 2019), patients with major depression or bipolar disorder seem to be more susceptible to depression episodes during winter (Geoffroy et al. 2014).

Chronic musculoskeletal pain is a substantial health problem afflicting about one in three of the general population (Bergman et al. 2001). A diagnosis of chronic primary musculoskeletal pain subsumes local, regional or widespread musculoskeletal pain persisting beyond 3 months, which is not better accounted for by any other disease (Nicholas et al. 2019). Clinical experience by ourselves and colleagues at the local university hospital, as well as accounts from Canada (Owen 1995) suggest an increased negative impact of chronic pain during the winter months, among patients dwelling at a high latitude. If present, such variation may motivate seasonal adjustments of pain regimen in these areas. However, research on seasonality in chronic pain is hitherto limited.

In the studies by Moldofsky (1994) and Hawley et al. (2001), patients with fibromyalgia and rheumatic disease respectively reported worse pain, sleep, energy and mood during winter on a self-report seasonal pattern questionnaire. However, studies applying repeated pain assessments across seasons show incongruent results with one study in myofascial facial pain reporting increased pain ratings in the dark months (Gallagher et al. 1995), whereas others report slightly increased pain in summer in rheumatic disease (Hawley and Wolfe 1994; Hawley et al. 2001; Iikuni et al. 2007). These studies were performed at moderate latitudes (New York 40°N, Kansas 39°N and Tokyo 35°N), which may contribute to attenuate seasonal fluctuations.

Pain conditions co-occur with depression, fatigue and sleep disturbances (Bair et al. 2003; Fishbain et al. 2004; Alfoldi et al. 2014). Seasonal variations in these conditions may therefore prompt corresponding variations in pain experience. Several studies in miscellaneous pain conditions, indicate winter-exacerbation in fatigue but not mood (Hawley and Wolfe 1994; Hardt and Gerbershagen 1999; Feldthusen et al. 2016), whereas one study reports more non-specific psychological distress in winter (Gallagher et al. 1995). Prospectively designed studies examining seasonal variations in subjective and objective sleep measures, in patients with primary musculoskeletal pain, which was the impetus for this study, are however lacking.

The current study was conducted in the city of Tromsø, situated above the Polar circle (Norway, 69º North). Here, the sun does not rise above the horizon between November 27th- January 15th, and does not set between May 21st- July 22nd. These extreme light conditions are likely to affect circadian regulation, and possibly sleep behavior and psychological factors, as light is the most important external cue (or Zeitgeber) for circadian entrainment (Arendt 2012). Studies of the general population in Tromsø report delay of sleep phase, increased sleep problems and fatigue in winter

(Husby and Lingjaerde 1990; Johnsen et al. 2012; Johnsen et al. 2013; Friborg et al. 2014). Depressed mood and fatigue may additionally act as moderators by strengthening these seasonal variations (Friborg et al. 2014). Sleep delay in the winter may thus also be expected among pain patients, but it is unknown whether such delay will affect the pain experience.

Reduced physical activity during the winter season is common in general and likely due to cold temperature and lack of sunlight (Cepeda et al. 2018; Schepps et al. 2018). Leading an active lifestyle has been related to more efficient experimental pain inhibition and to reduced pain reports in the general population (Landmark et al. 2013; Naugle et al. 2017). Less pain in the more active summer period could therefore be expected.

Seasonal variations in light exposure and climate may influence pain conditions directly, as well as indirectly through variations in mood, fatigue, physical activity or sleep disturbance. As seasonal adjustment of multidisciplinary rehabilitation may benefit chronic pain patients, the current study examined seasonal variation in pain and in factors that might influence pain. Confinement to primary musculoskeletal pain was preferred to avoid confounding by any seasonality in comorbid underlying diseases. The first objective was to estimate seasonal variation in pain severity and dissemination with the hypothesis that patients with chronic musculoskeletal pain experience increased pain in winter as compared to summer. The second objective was to estimate seasonal variation in the pain-associated conditions sleep, mental distress, fatigue and physical activity and whether such variations affect seasonal variation in pain. We hypothesized that such seasonality exists and modifies the season-pain relation.

Materials and Method

Study sample

Patients residing in the municipality of Tromsø and attending the Rehabilitation or the Pain outpatient clinic at the University Hospital of North Norway (UNN) were invited by mail. Inclusion criteria were age 18-65 years and diagnosed with musculoskeletal pain (ICD-10 diagnoses in Table 1) within the last 18 months. Exclusion criteria: a) major comorbid medical conditions (cancer, inflammatory-, symptomatic heart or lung-, metabolic- or endocrine disease), neurologic conditions, psychiatric illness or drug abuse, b) a sleep disorder diagnosis other than insomnia, c) pregnancy, or d) participation in ongoing intervention studies.

Design and procedures

The prospective design included two repeated study periods per participant, during mid-summer and during mid-winter. Potential sequence effects were controlled for by counterbalancing the enrollment sequence with approximately half of the participants starting during summer, and the other half starting during winter. The counter-balancing was non-randomized as the participants were enrolled consecutively for practical reasons. The dates; duration of daylight; and median temperature during data collection periods were: June 6th to July 28th 2016; 22-24 hours; 8°C, November 3rd 2016 to February 13th 2017; 0-7 hours; -1°C and May 2nd to July 20th 2017; 19-24 hours; 10°C. (Lilje et al. 2019, 4-27; MET Norway 2020). Each study period comprised self-report data and one week of continuous actigraphy recording with a concurrent sleep log. The first visit was scheduled at UNN, where subjects received detailed written and oral information, completed questionnaires, and had the actigraphy device attached. Participants returned after 7 days for delivery of the actigraphy device and sleep logs.

They were encouraged to conduct their daily life as usual during the study period with regard to sleep schedule, habitual medication and daily activities. A few participants (nurses) working shift schedules, i.e., 2-4 consecutive night shifts followed by a longer period of day and evening shifts, participated during their day-evening shift schedule.

Measurements

Demographics: In addition to age and sex, the dichotomized variables educational level (high school vs higher education), marital status (single vs married/partner), employment (non-employed vs part or full-time employed), and perceived financial situation (good vs medium/bad) were registered. Type of social benefit was registered when applicable.

Brief Pain Inventory (BPI): The pain severity subscale of the validated Norwegian version of the Brief Pain Inventory short form was applied (Cleeland 1991). Participants estimated their worst, least and average pain during the last week, as well as their current pain. Each of the four items were rated on an 11-point numeric rating scale (from 0, no pain, to 10, worst imaginable pain). We calculated a mean score of these four items as a measure of pain severity. The questionnaire also entailed a modified version of the BPI body-map identifying 25 specified body regions. The number of indicated body-regions was used as a measure of pain dissemination.

Hopkins Symptom Checklist 25 (HSCL 25): The HSCL 25 is a self-report inventory designed to screen for symptoms of depression and anxiety, indicating mental distress the last 14 days (Derogatis et al. 1974). The 25 items are rated on a 4-point Likert scale (from 1-not at all to 4-very much), from which a global average score is calculated (range: 1-4).

Chalder Fatigue Scale: The Chalder Fatigue scale covers physical (eight items) and mental (three items) fatigue. The presence of each symptom during the last month is graded on a 4-point Likert scale (1-less than usual, 2-not more than usual, 3-more than usual, 4-much more than usual) (Chalder et al. 1993). The present study used the combined score of mental and physical fatigue.

Insomnia Severity Index (ISI): The insomnia severity index (ISI) includes seven items assessing problems with sleep onset, maintenance and early morning awakening, as well as daytime functioning, sleep satisfaction and worrying about sleep during the previous 14 days (Morin 1993). Items are rated on a five-point Likert scale (0–4), with higher scores indicating worse insomnia (total range 0- 28). ISI is a recommended research measure of insomnia symptoms (Buysse et al. 2006).

Pittsburg Sleep Quality Index (PSQI): The PSQI comprises 19 items probing sleep quality and disturbance during the previous month across seven components: 1) subjective sleep quality, 2) sleep latency 3) sleep duration 4) habitual sleep efficiency 5) sleep disturbance, 6) sleep medication and 7) daytime dysfunction. Each component receives a score of 0-3 based on a scoring algorithm, yielding a global score with a range of 0-21 (higher scores indicate more disturbed sleep), (Buysse et al. 1989). The PSQI is a recommended research measure of global sleep symptoms (Buysse et al. 2006).

Actigraphy: The validated Actiwatch Spectrum Plus device was used to register sleep pattern and mean daytime activity levels (Kahawage et al. 2020). Post-processing of the raw actigraphy data was conducted in the Actiware version 6.0.9 software (both Phillips Respironics, Inc., Murrysville, PA). The Actiwatch was worn on the non-dominant wrist, only to be removed shortly during shower or if required at work (e.g. due to hygiene or safety considerations). Off-wrist periods were excluded from

analyses. The participants were instructed to register time of first sleep attempt and final morning awakening by pushing an event button. Rest intervals were scored manually by a trained research assistant (psychology student) supervised by a specialist in clinical neurophysiology (first author). Both were blinded to participant identity. A significant sustained reduction or increase in activity defined the start and end of a rest period, respectively. If activity- transitions were inconclusive, the event marker, and sleep log information were additionally consulted. The sleep interval was scored within the rest interval by the automated Actiware algorithm, with specification of 30 sec epochs and medium sensitivity (40 activity counts/ epoch) for wake detection. The algorithm requires 10 minutes of inactivity at the start and end of the sleep interval to define sleep onset and offset, respectively. The variables total sleep time (TST, duration of sleep within the sleep interval), sleep onset latency (SOL, time between onset of rest interval and onset of sleep interval), wake after sleep onset (WASO, time awake after initial sleep onset) and sleep efficiency (SE, proportion of the rest interval scored as sleep), were averaged for the recorded week. The midpoint of sleep $\left(\frac{sleep\ onset - sleep\ offset}{2}\right)$ was calculated separately for weekdays and weekends as a measure of sleep timing. To adjust for any sleep deficit accumulation during weekdays, a sleep corrected midpoint of sleep on weekends (MSFsc) was also calculated (Roenneberg et al. 2004). The tendency to delayed sleep timing during weekends, the social jet lag (SJL), was calculated as the absolute difference between midsleep on weekends and workdays, which was additionally corrected for sleep debt accrual (SJLsc) as outlined by Jankowski (2017).

Additionally, the actigraphy-measured mean activity level (mean activity count per minute) during wake time was applied as a measure of general activity levels. This approach has previously been applied in studies of group differences and seasonal

variation in physical activity (Korszun et al. 2002; Brychta et al. 2016). White light exposure during wake periods (mean lux per minute) was also registered by the actigraph.

Statistical procedure

The IBM SPSS 25 was used for all analyses. Independent Student`s t-test and chi-square tests were applied to assess the adequacy of the counter-balancing design. Linear mixed regression models with a random intercept parameter were fit to take care of the dependency in the repeated data. Type III F-tests were applied. The effect of season on pain severity, pain dissemination, mental distress, fatigue, sleep quality and insomnia, as well as actigraphy measures of sleep continuity, sleep timing, physical activity and light exposure, were assessed as crude (Model 1) and adjusted (Model 2) effects. Covariates in Model 2 were sequence of enrolment, age, sex, education, employment, perceived financial status and marital status. In a third model, we examined if the primary association between season and pain was further adjusted and moderated by the self-report (ISI, HSCL, CFS, PSQI), and the actigraphy measures (SOL, SE, TST, midsleep weekdays and activity). To reduce number of covariates and moderator tests and due to substantial correlations between these variables, a principal component analysis was conducted. Optimal linear combinations of scores were saved as three component scores (using the regression method), which were subsequently added to Model 2 as additional covariates (Model 3). Subsequently each component score was tested separately as moderator variables of the season - pain relationship (season*C1/C2/C3). Cohens *d* for repeated measurements were calculated based on the difference in the estimated marginal means (EMM) divided by their observed pooled standard deviation. Residual scores were saved and inspected for non-normality and

heteroscedasticity.

Ethical approval

The study was approved by the Regional Committee for Medical and Health Research Ethics, Office North (reference number 2015/2473). Written informed consent was obtained from all participants, and the study conforms to ethical standards of this journal (Portaluppi et al. 2010).

Results

Sample characteristics

A total of 401 patients were invited to participate, of whom 91 responded. Based on exclusion criteria, 28 patients were excluded and seven patients either moved or withdrew. The final sample consisted of 56 patients, of whom 31 were enrolled during summer 2016 (follow-up during winter 2016/2017) and 25 during winter 2016/2017 (follow-up during summer 2017). Three participants from the summer-enrollment did not attend the follow up. The distribution of ICD-10 diagnoses at their most recent visit at the respective departments at UNN are shown in Table 1. Relatively more females enrolled during summer than winter whereas other demographic variables did not differ between the enrollment groups (Table 2). Among the 42 employed participants, three additionally reported receiving full social security benefit, four received part benefit and seven received benefit of uncertain coverage. Among the 14 unemployed participants, eight received sickness leave compensation and six received disability pension.

Seasonal variations

Seasonal differences for pain severity and pain dissemination are presented in Table 4.

Seasonality was evident for pain severity with less pain in winter compared to summer, whereas there was no season effect for pain dissemination. Adjusting for sociodemographic variables (age, sex, education, employment, perceived financial status and marital status) or sequence of enrollment (Model 2) did not alter the estimated marginal means **(**EMM).

Seasonal differences in questionnaire and actigraphy data are presented in Table 3. As expected, light exposure, as a marker of season itself, was relatively lower during winter. No seasonal variations were observed in any of the self-report measures of insomnia, sleep quality, mental distress or fatigue, or the objective measures of sleep continuity (SOL, SE, WASO) or sleep duration. Significant seasonal effect with lower levels of physical activity during winter compared to summer were noticed. Additionally, there was a significant delay in sleep timing on weekdays and a non-significant tendency towards weekend delay in summer compared to winter. Social jet lag (SJL, later sleep timing at weekends compared to weekdays) of more than 1 hour, which was somewhat smaller for the adjusted SJLsc, was noticed both during summer and winter. The adjustment for sociodemographics, or sequence of enrollment did not notably change the EMM of any of the self-report or objective variables.

In the final regression analysis (Model 3, Table 4), we examined if the questionnaire- and actigraphy-based component scores modified the season-pain association. From PCA we extracted three components C1-3 with an eigenvalue > 1. Self-report instruments (ISI, PSQI, HSCL, CFS) loaded on C1, actigraphy sleep continuity measures (SOL, SE) loaded on C2, and midsleep weekdays loaded on component C3. TST loaded on both C2 and C3, whereas activity loaded on C2 and weakly on C1. There was a significant main effect solely of C1 on pain severity ($p<.001$) and pain dissemination ($p<.05$). None of the interaction terms was significant.

Hence, the additional variables adjusted for in Model 3 did not significantly modify the seasonal variation in the pain measures, and the interaction terms were not kept in the final model.

Discussion

In this study of seasonal variation in musculoskeletal pain in Tromsø, pain intensity was modestly lower during winter than summer, whereas pain dissemination did not display any seasonal variations. Concurrently there was a delay of sleep timing by about half an hour on weekdays in summer compared to winter. No seasonal variation was observed in any other objective or subjective sleep measures, mental distress or fatigue.

Pain

We found that pain intensity was modestly lower during winter than summer; however, the clinical importance of less than half a point change on the BPI is questionable. This effect of season on pain intensity was not related to subjective or objective measures of sleep, mental distress, fatigue or physical activity.

Increased pain rating in summer compared to winter, and late spring compared to late autumn has previously been observed in rheumatoid arthritis, osteoarthritis and fibromyalgia (Hawley and Wolfe 1994; Hawley et al. 2001; Iikuni et al. 2007). In these studies, current pain was assessed by VAS scale repeatedly during the year. The season effect was modest and the clinical importance was questioned by the authors (Hawley et al. 2001; Iikuni et al. 2007). On the other hand, one previous study found increased pain in winter in myofascial facial pain patients (Gallagher et al. 1995). Participants in this latter study reported their worst pain during the last month on four different pain instruments combined into a composite score. Such a composite score may reflect

broader aspects of the pain experience than the ratings applied in the current and the previously mentioned studies, which may underlie this apparently opposing finding.

In Hawley's study (2001), in addition to repeated rating of current symptoms, patients, at one occasion, self-reported their annual symptom patterns by month of the year. By this approach, a more pronounced seasonality emerged, where pain displayed a bimodal pattern with a smaller peak in summer months and a larger peak in winter months. This finding suggests that patients have a sense of seasonality, which may give rise the common assumption that pain patients are more troubled by their pain condition in winter. The authors discuss the possibility of attribution and somatization underlying the apparent discrepancy between this approach and the repeated pain ratings (Hawley et al. 2001). Indeed, Meyers and Young (2015) demonstrated the moderating effect of illness attitudes on the association between fatigue (which commonly increases in winter) and psychological symptoms such that persons with higher negative appraisal also experienced increased psychological symptoms as a response to fatigue. They propose this as a possible mechanism for seasonal variation in psychological symptoms. However, the potential involvement of similar implicit illness attitudes in seasonality of other symptoms, including pain, remain to be tested empirically.

Physical activity

The lifestyle in Tromsø includes more outdoors leisure activities during summer and more indoor socializing during winter, as the actigraphy recordings in our study indicate with increased average activity in summer. Although physical activity has been related to pain inhibition and reduced pain reports in the general population (Landmark et al. 2013; Naugle et al. 2017), we did not observe less pain in the more active summer period in the current study. On the contrary, pain increased rather than decreased in the

more active summer period, however the daily activity measure did not modify the seasonality in pain.

One may speculate whether musculoskeletal pain may be perceived as more debilitating during summer when increased activity is anticipated and reports of splendid outdoors adventures and vacations are repeatedly conveyed in media and social media. Vice versa, there may be an acceptance of symptoms during winter, due to lower anticipations of physical activities and higher appreciation of indoors tranquil activities and socializing. This is a hypothesis that future studies may address more specifically.

Psychological factors

Seasonal variations in symptoms of anxiety, depression and fatigue may be hypothesized as a link between season and pain since these factors are associated with pain (Hawley et al. 2001; Bair et al. 2003; Fishbain et al. 2004). However, in the current study there was no seasonal variation in mental distress or fatigue. Although patients with major depression disorder may be more vulnerable to depressive episodes during winter, our observations corroborate previous studies in the general population and among pain patients, which have found minor to nonexistent seasonal variation in mood (Hawley and Wolfe 1994; Hardt and Gerbershagen 1999; Oyane et al. 2005; Friborg et al. 2012; Johnsen et al. 2012; Friborg et al. 2014; Geoffroy et al. 2014; Overland et al. 2019). On the other hand, the literature suggest increased fatigue in winter (Friborg et al. 2012; Friborg et al. 2014; Feldthusen et al. 2016), but this was not observed among pain patients in the present study. Of note, in the current study a potential seasonal variation in fatigue and mental distress with increased symptoms in winter may have been masked by the decreased pain in winter compared to summer.

Seasonality in psychological well-being may be of a more multifaceted character than is usually assessed in specific questionnaires or selected items in research studies, as Gallagher et al. (1995) found increased non-specific psychological distress in winter. Non-specific psychological distress was described as a measure covering diverse emotional and cognitive symptoms collectively termed demoralization. The finding may indicate that seasonal psychological variations are of a diverse, non-specific character. However, the study did not test whether demoralization was associated with the corresponding pain increase which was observed in winter.

Sleep

In the current study, there was no seasonality in objective or subjective measures of sleep quantity, quality or insomnia. Little is known about seasonality of sleep quality and insomnia in pain patients, but previous studies in the general population report somewhat diverging results. Most studies did not find seasonality in sleep duration (Oyane et al. 2008; Sivertsen et al. 2011; Friborg et al. 2012; Johnsen et al. 2012; Friborg et al. 2014; Brychta et al. 2016). While some studies from northern Norway found support for increased subjective sleep problems in winter (Husby and Lingjaerde 1990; Friborg et al. 2012; Johnsen et al. 2012; Friborg et al. 2014), other studies from Norway and Japan did not (Oyane et al. 2008; Sivertsen et al. 2011; Itani et al. 2016). Methodological differences in study design and operationalization of sleep disturbance/ insomnia may underlie some of these differences. Insomnia-symptoms in winter have been related to the concurrently observed delayed sleep phase in northern Norway, as sleep initiation problems under certain conditions may be an overlapping symptom (Hansen et al. 1987). Among the pain patients in our study, we did not find such delay in sleep phase in winter, which may contribute to the lack of seasonality in sleep

problems in our study.

In the current study, sleep timing was delayed during summer rather than winter, which is an opposite seasonal effect than previously observed in the general population in The Tromsø Study (Johnsen et al. 2013). The midpoint of sleep on free days (MSFsc) in our study was thus 5:15 h and 4:56 h compared to 3:55 and 04:08h in summer and winter respectively, in The Tromsø Study. However, in the current study the seasonal effect was significant only on weekdays, with approximately 30 minutes delay in summer, whereas in The Tromsø Study there was no season effect during weekdays.

Lack of the entraining effect of morning light presumably drives the phase-delay during winter in healthy and general population samples residing in regions with moderate and extreme seasonal light variation (Arendt 2012; Johnsen et al. 2013; Friborg et al. 2014; Hashizaki et al. 2018). The delay may be further amplified by mental distress (Friborg et al. 2014). We are not aware of previous studies probing this seasonal phenomenon in patients with chronic pain, and the observed delay of sleep schedule in summer rather than winter is somewhat puzzling.

In Tromsø, there is sunlight around the clock during the summer months. One may speculate that persons with chronic pain may be exposed to bright light in advance of their diurnal lowest core body temperature, nadir, due to late bedtime, nightly awakenings or early morning awakening. Such sleep patterns may be a consequence of the pain condition itself, concurrent insomnia, or an intrinsic late chronotype. Given that light exposure prior to nadir has a delaying effect on the sleep wake rhythm, this may potentially have contributed to the summer phase delay observed in our study.

In the current study sleep timing was later than in The Tromsø Study, at both seasons. Our sample is slightly younger with more females than the population study, which may contribute to the observed delay, since sleep phase tends to advance with

higher age, more among males than females (Fischer et al. 2017). Accordingly, a study among young students in Tromsø reported MSFsc between 05:05 (autumn) and 05:37 (winter) (Friborg et al. 2014). Yet differences in demography do not seem likely to completely account for the delay in sleep schedule in our sample.

Mode of measurement differentiates the studies from Tromsø, since the population study applied the self-report Munich chronotype questionnaire (MCQ) that may introduce memory biases regarding habitual sleep times for work- and free days. Validation of MCQ with actigraphy have shown similar estimated MSFsc when recorded during the same week (Santisteban et al. 2018). The student study applied sleep diaries. In the current study, the objective actigraphy-data are used, and weekends were assumed as free days. This approach does not take into account that some participants may have had free days during the week, and oppositely may have had work scheduled during weekends. Anyhow, using objective recordings is an advantage since sleep misperception is common among poor sleepers (Harvey and Tang 2012).

Chronotype has been linked to overall mortality and adverse health outcomes including musculoskeletal disorders (Knutson and von Schantz 2018). Evening types seem to report more general and work-related musculoskeletal complaints (Merikanto et al. 2014; Zhang et al. 2018) and fibromyalgia patients with evening chronotype have higher pain scores and general symptom load (Kantermann et al. 2012). In corroboration an experimental study of 31 healthy male students indicates evening types to be more sensitive to heat pain (Jankowski 2013). Thus, there seem to be emerging evidence for an association between chronotype and musculoskeletal pain. In the current study, we did not inquire about morning/ evening preferences, and the general delay among patients compared to the general population could be explained either by chronotype differences or by their pain condition. Further studies on chronotype and

seasonal fluctuations of circadian rhythm by additional indicators, such as cortisol, melatonin, core body temperature and genetic polymorphisms in pain patients could provide important information about the role of chronotype, circadian entrainment and misalignment in pain conditions. Yet, the main objective of this study was to investigate seasonal variations in pain, and since this is a paired study, chronotype as a presumed stable trait is unlikely to explain the observed seasonality in pain severity.

Limitations

There are several limitations to the current study**.** The final sample consisted of 56 of the invited 401 patients. Patient privacy regulations prohibited access to any information concerning the non-consenting patients. However, information from comparable patient groups suggest that our sample has similar age, levels of mental distress and cohabitation, but somewhat lower pain severity, higher education, larger female ratio, and higher employment rate (Anke and Granan 2017). We did not include other somatic patient groups, and we can accordingly not assess if the observed seasonal patterns are specific for the CMP population. We did not include a healthy control group because our main objective was to study seasonality in pain and pain-related conditions such as sleep and psychological factors. However, future studies would benefit from including a control group in order to compare the effects of seasonality on pain- related conditions directly between healthy subjects and pain patients. The relatively low sample size may have limited the study power, however most of the non-significant findings display low effect sizes, thus the risk of Type 2 error is less likely. Limited assessment of pain interference was included, thus missing information on how pain is perceived to affect physical, psychological and social aspects of life at different seasons. Such information could potentially have contributed to understanding the

finding of increased pain in summer. Physical activity was solely included as a daily average measure. By this approach, we did observe a seasonal variation in activity levels, yet it may be less sensitive than for example peak activity levels or differentiating time spent in sedentary, moderate and vigorous activity in detecting associations with pain (Kop et al. 2005). Lastly, current vacation during data collection is a possible confounder for the observed summer delay, which we did not control for. However, the preserved social jet lag (later sleep timing at weekends compared to workdays) in summer indicates continued work routines.

Conclusion

There is a paucity of studies on seasonal variations of symptoms in patients with chronic pain. In this longitudinal study, we observed an unexpected modest increase in pain severity in summer compared to winter. This seasonal variation in pain was not related to mental distress, fatigue, sleep complaints or objective sleep measures. As the current findings correspond less well with clinical experience, this issue needs to be examined further, possibly also by adding a qualitative study arm connected with a quantitatively designed study presumably replicating the present findings. Contrary to findings in the general population, we also observed a sleep delay in the summer, with the largest effect on weekdays (~half an hour). This observation suggests that attention should be paid to seasonal changes in sleep-wake patterns in patients with musculoskeletal pain. Hence, this study may spark future research that may provide new knowledge on seasonal variations in sleep wake cycles among these patients. The potential benefit of managing sleep delay in summer should also be further explored.

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References

Alfoldi P, Wiklund T, Gerdle B. 2014. Comorbid insomnia in patients with chronic pain: a study based on the Swedish quality registry for pain rehabilitation (SQRP). Disability and rehabilitation. 36(20):1661-1669.

Anke A, Granan LP 2017. Norsk nakke- og ryggregister Årsrapport for 2016 [Norwegian neck and back registry Annual report 2016]. [Accessed March 17 2020]. https://www.kvalitetsregistre.no/registers/norsk-nakke-og-ryggregister.

Arendt J. 2012. Biological rhythms during residence in polar regions. Chronobiol Int. 29(4):379-394.

Bair MJ, Robinson RL, Katon W, Kroenke K. 2003. Depression and pain comorbidity: a literature review. Archives of internal medicine. 163(20):2433-2445. eng.

Bergman S, Herrstrom P, Hogstrom K, Petersson IF, Svensson B, Jacobsson LT. 2001. Chronic musculoskeletal pain, prevalence rates, and sociodemographic associations in a Swedish population study. The Journal of rheumatology. 28(6):1369-1377.

Brychta RJ, Arnardottir NY, Johannsson E, Wright EC, Eiriksdottir G, Gudnason V, Marinac CR, Davis M, Koster A, Caserotti P et al. 2016. Influence of Day Length and Physical Activity on Sleep Patterns in Older Icelandic Men and Women. J Clin Sleep Med. 12(2):203-213.

Buysse DJ, Ancoli-Israel S, Edinger JD, Lichstein KL, Morin CM. 2006. Recommendations for a standard research assessment of insomnia. Sleep. 29(9):1155-1173.

Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. 1989. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry research. 28(2):193-213.

Cepeda M, Koolhaas CM, van Rooij FJA, Tiemeier H, Guxens M, Franco OH, Schoufour JD. 2018. Seasonality of physical activity, sedentary behavior, and sleep in a middle-aged and elderly population: The Rotterdam study. Maturitas. 110:41-50.

Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, Wallace EP. 1993. Development of a fatigue scale. J Psychosom Res. 37(2):147-153.

Cleeland CS. 1991. Pain assessment in cancer. In: Osoba D, editor. Effect of cancer on quality of life. Boca Raton, FL: CRC Press; p. 293-305.

Derogatis LR, Lipman RS, Rickels K, Uhlenhuth EH, Covi L. 1974. The Hopkins Symptom Checklist (HSCL): a self-report symptom inventory. Behav Sci. 19(1):1-15.

Feldthusen C, Grimby-Ekman A, Forsblad-d'Elia H, Jacobsson L, Mannerkorpi K. 2016. Seasonal variations in fatigue in persons with rheumatoid arthritis: a longitudinal study. BMC musculoskeletal disorders. 17(1):59. eng.

Fischer D, Lombardi DA, Marucci-Wellman H, Roenneberg T. 2017. Chronotypes in the US - Influence of age and sex. PloS one. 12(6):e0178782.

Fishbain DA, Cutler RB, Cole B, Lewis J, Smets E, Rosomoff HL, Rosomoff RS. 2004. Are patients with chronic low back pain or chronic neck pain fatigued? Pain medicine (Malden, Mass). 5(2):187-195.

Friborg O, Bjorvatn B, Amponsah B, Pallesen S. 2012. Associations between seasonal variations in day length (photoperiod), sleep timing, sleep quality and mood: a comparison between Ghana (5 degrees) and Norway (69 degrees). Journal of sleep research. 21(2):176-184. eng.

Friborg O, Rosenvinge JH, Wynn R, Gradisar M. 2014. Sleep timing, chronotype, mood, and behavior at an Arctic latitude (69 degrees N). Sleep Med. 15(7):798-807. eng.

Gallagher RM, Marbach JJ, Raphael KG, Handte J, Dohrenwend BP. 1995. Myofascial face pain: seasonal variability in pain intensity and demoralization. Pain. 61(1):113-120. eng.

Geoffroy PA, Bellivier F, Scott J, Etain B. 2014. Seasonality and bipolar disorder: a systematic review, from admission rates to seasonality of symptoms. J Affect Disord. 168:210-223.

Hansen T, Bratlid T, Lingjarde O, Brenn T. 1987. Midwinter insomnia in the subarctic region: evening levels of serum melatonin and cortisol before and after treatment with bright artificial light. Acta psychiatrica Scandinavica. 75(4):428-434. eng.

Hardt J, Gerbershagen HU. 1999. No changes in mood with the seasons: observations in 3000 chronic pain patients. Acta psychiatrica Scandinavica. 100(4):288-294. eng.

Harvey AG, Tang NK. 2012. (Mis)perception of sleep in insomnia: a puzzle and a resolution. Psychol Bull. 138(1):77-101.

Hashizaki M, Nakajima H, Shiga T, Tsutsumi M, Kume K. 2018. A longitudinal large-scale objective sleep data analysis revealed a seasonal sleep variation in the Japanese population. Chronobiol Int. 35(7):933-945.

Hawley DJ, Wolfe F. 1994. Effect of light and season on pain and depression in subjects with rheumatic disorders. Pain. 59(2):227-234.

Hawley DJ, Wolfe F, Lue FA, Moldofsky H. 2001. Seasonal symptom severity in patients with rheumatic diseases: a study of 1,424 patients. The Journal of rheumatology. 28(8):1900-1909. eng.

Husby R, Lingjaerde O. 1990. Prevalence of reported sleeplessness in northern Norway in relation to sex, age and season. Acta psychiatrica Scandinavica. 81(6):542-547.

Iikuni N, Nakajima A, Inoue E, Tanaka E, Okamoto H, Hara M, Tomatsu T, Kamatani N, Yamanaka H. 2007. What's in season for rheumatoid arthritis patients? Seasonal fluctuations in disease activity. Rheumatology (Oxford). 46(5):846-848.

Itani O, Kaneita Y, Munezawa T, Mishima K, Jike M, Nakagome S, Tokiya M, Ohida T. 2016. Nationwide epidemiological study of insomnia in Japan. Sleep Med. 25:130-138.

Jankowski KS. 2013. Morning types are less sensitive to pain than evening types all day long. European journal of pain (London, England). 17(7):1068-1073.

Jankowski KS. 2017. Social jet lag: Sleep-corrected formula. Chronobiol Int. 34(4):531-535. eng.

Johnsen MT, Wynn R, Allebrandt K, Bratlid T. 2013. Lack of major seasonal variations in self reported sleep-wake rhythms and chronotypes among middle aged and older people at 69 degrees North: the Tromso Study. Sleep Med. 14(2):140-148. eng.

Johnsen MT, Wynn R, Bratlid T. 2012. Is there a negative impact of winter on mental distress and sleeping problems in the subarctic: the Tromso Study. BMC psychiatry. 12:225. eng.

Johnston NW, Sears MR. 2006. Asthma exacerbations center dot 1: Epidemiology. Thorax. 61(8):722-728. English.

Kahawage P, Jumabhoy R, Hamill K, de Zambotti M, Drummond SPA. 2020. Validity, potential clinical utility, and comparison of consumer and research-grade

activity trackers in Insomnia Disorder I: In-lab validation against polysomnography. Journal of sleep research. 29(1):e12931.

Kamezaki F, Sonoda S, Tomotsune Y, Yunaka H, Otsuji Y. 2010. Seasonal variation in metabolic syndrome prevalence. Hypertens Res. 33(6):568-572. English.

Kantermann T, Theadom A, Roenneberg T, Cropley M. 2012. Fibromyalgia syndrome and chronotype: late chronotypes are more affected. J Biol Rhythms. 27(2):176-179.

Knutson KL, von Schantz M. 2018. Associations between chronotype, morbidity and mortality in the UK Biobank cohort. Chronobiol Int. 35(8):1045-1053.

Kop WJ, Lyden A, Berlin AA, Ambrose K, Olsen C, Gracely RH, Williams DA, Clauw DJ. 2005. Ambulatory monitoring of physical activity and symptoms in fibromyalgia and chronic fatigue syndrome. Arthritis Rheum. 52(1):296-303.

Korszun A, Young EA, Engleberg NC, Brucksch CB, Greden JF, Crofford LA. 2002. Use of actigraphy for monitoring sleep and activity levels in patients with fibromyalgia and depression. J Psychosom Res. 52(6):439-443.

Landmark T, Romundstad PR, Borchgrevink PC, Kaasa S, Dale O. 2013. Longitudinal associations between exercise and pain in the general population--the HUNT pain study. PloS one. 8(6):e65279.

Lilje PB, Helleland B, Johannessen FE, Leifsen T, Ørstavik IB. 2019. Almanakk for Noreg for året etter Kristi fødsel 2020 [Almanac for Norway]. Oslo (Norway): Universitetet i Oslo, Institutt for Teoretisk Astrofysikk, Gyldendal. p. 4-27.

Marti-Soler H, Gonseth S, Gubelmann C, Stringhini S, Bovet P, Chen PC, Wojtyniak B, Paccaud F, Tsai DH, Zdrojewski T et al. 2014. Seasonal Variation of Overall and Cardiovascular Mortality: A Study in 19 Countries from Different Geographic Locations. PloS one. 9(11). English.

Merikanto I, Lahti T, Seitsalo S, Kronholm E, Laatikainen T, Peltonen M, Vartiainen E, Partonen T. 2014. Behavioral trait of morningness-eveningness in association with articular and spinal diseases in a population. PloS one. 9(12):e114635.

MET Norway, The Norwegian Meteorological Institute. Oslo (Norway) [accessed 2020 March 16]. https://www.seklima.met.no

Meyers K, Young MA. 2015. Illness Attitudes Associated with Seasonal Depressive Symptoms: An Examination Using a Newly Developed Implicit Measure. Depress Res Treat. 2015:397076.

Moldofsky H. 1994. Chronobiological influences on fibromyalgia syndrome: theoretical and therapeutic implications. Baillieres Clin Rheumatol. 8(4):801-810.

Morin CM. 1993. Insomnia: Psychological assessment and management. New York: The Guilford Press.

Naugle KM, Ohlman T, Naugle KE, Riley ZA, Keith NR. 2017. Physical activity behavior predicts endogenous pain modulation in older adults. Pain. 158(3):383-390.

Nicholas M, Vlaeyen JWS, Rief W, Barke A, Aziz Q, Benoliel R, Cohen M, Evers S, Giamberardino MA, Goebel A et al. 2019. The IASP classification of chronic pain for ICD-11: chronic primary pain. Pain. 160(1):28-37.

Overland S, Woicik W, Sikora L, Whittaker K, Heli H, Skjelkvale FS, Sivertsen B, Colman I. 2019. Seasonality and symptoms of depression: A systematic review of the literature. Epidemiol Psychiatr Sci.1-15.

Owen JE. 1995. Comment on D.G. Hawley and F. Wolfe. Pain. 62(1):125-126.

Oyane NM, Holsten F, Ursin R, Bjorvatn B. 2005. Seasonal variations in mood and behaviour associated with gender, annual income and education: the Hordaland Health Study. Eur J Epidemiol. 20(11):929-937.

Oyane NM, Ursin R, Pallesen S, Holsten F, Bjorvatn B. 2008. Self-reported seasonality is associated with complaints of sleep problems and deficient sleep duration: the Hordaland Health Study. Journal of sleep research. 17(1):63-72.

Portaluppi F, Smolensky MH, Touitou Y. 2010. Ethics and methods for biological rhythm research on animals and human beings. Chronobiol Int. 27(9-10):1911-1929.

Roenneberg T, Kuehnle T, Pramstaller PP, Ricken J, Havel M, Guth A, Merrow M. 2004. A marker for the end of adolescence. Curr Biol. 14(24):R1038-R1039. English.

Santisteban JA, Brown TG, Gruber R. 2018. Association between the Munich Chronotype Questionnaire and Wrist Actigraphy. Sleep Disord. 2018:5646848.

Schepps MA, Shiroma EJ, Kamada M, Harris TB, Lee IM. 2018. Day length is associated with physical activity and sedentary behavior among older women. Sci Rep. 8(1):6602.

Sivertsen B, Overland S, Krokstad S, Mykletun A. 2011. Seasonal variations in sleep problems at latitude 63 degrees -65 degrees in Norway: The Nord-Trondelag Health Study, 1995-1997. Am J Epidemiol. 174(2):147-153.

Zhang Y, Duffy JF, de Castillero ER, Wang K. 2018. Chronotype, Sleep Characteristics, and Musculoskeletal Disorders Among Hospital Nurses. Workplace Health Saf. 66(1):8-15.

Table 1. Distribution of ICD-10 diagnoses

	n
M54.2 Cervicalgia	12
M54.5 Low back pain	11
M54.6 Pain in thoracic spine	1
M54.8 Other dorsalgia	2
M54.9 Dorsalgia, unspecified	11
M79.1 Myalgia	10
M79.6 Pain in limb	3
M79.7 Fibromyalgia	6

Table 2. Demographic characteristics according to season of enrollment

	Summer enrollment n= 31	Winter enrollment n=25	*p*
Age, M (SD)	40.3 (10.6)	43.5 (11.1)	ns
Female n (%)	27 (87.1)	15 (60.0)	0.03
Married/ partner, n (%)	18 (58.1)	17 (68.0)	ns
Higher education, n (%)	23 (74.2)	12 (48.0)	ns
Employment, n (%)	23 (74.2)	19 (76.0)	ns
Perceived financial situation (good), n (%)	9 (29.0)	7 (28.0)	ns

Table 3. Seasonal differences (estimated marginal means) in self-report and actigraphy measures

	Model 1			Model 2		
	Summer (M CI)	Winter (M CI)	Cohens *d*	Summer (M CI)	Winter(M CI)	Cohens *d*
ISI	11.45 9.63-13.26	11.66 9.83-13.49	-0.03 ns	11.46 9.66-13.26	11.67 9.85-13.48	-0.03 ns
PSQI	9.98 8.86-11.11	9.12 7.97-10.26	0.20 ns	9.99 8.88-11.10	9.12 7.99-10.24	0.20 ns
HSCL	1.74 1.59-1.88	1.74 1.59-1.88	0.00 ns	1.74 1.60-1.88	1.74 1.60-1.88	0.00 ns
Chalder	15.57 14.02-17.12	16.19 14.62-17.77	-0.10 ns	15.58 14.02-17.13	16.20 14.62-17.77	-0.10 ns
TST, min	395.3 381.6-409.1	395.1 381.0-409.1	0.00 ns	394.8 383.7-406.0	395.2 383.8-406.7	-0.01 ns
SOL, min	17.1 12.4-21.7	14.5 9.7-19.3	0.16 ns	17.0 12.6-21.5	14.5 9.9-19.1	0.14 ns
SE, %	86.3 84.7-87.9	86.2 84.6-87.8	0.01 ns	86.3 84.8-87.8	86.2 84.7-87.7	0.01 ns
WASO, min	37.6 33.2-42.0	37.2 32.7-41.7	0.02 ns	37.6 33.1-42.2	37.2 32.9-41.8	0.02 ns
Midsleep weekdays, h:min	4:15 3:57-4:33	3:42 3:24-4:00	0.48***	4:15 3:57-4:33	3:42 3:24-4:00	0.48***
Midsleep weekend, h:min	5:27 5:05-5:49	5:09 4:47-5:32	0.20ns	5:27 5:04-5:49	5:09 4:46-5:32	0.20ns
MSFsc, h:min	5:15 4:52-5:38	4:55 4:32-5:20	0.21 ns	5:15 4:51-5:38	4:56 4:32-5:20	0.20 ns
Social Jet Lag, min	79.9 65.2-94.7	93.7 78.4-109.1	-0.25 ns	80.1 65.5-94.7	93.7 78.6-108.8	0.24 ns
SJLsc, min	64.2 48.9-79.6	80.8 64.8-96.7	-0.26 ns	64.5 49.0-80.0	80.5 64.4-96.6	0.25 ns
Activity, Activity Count/min	263.6 246.0-281.2	247.1 229.2-264.9	0.26*	263.4 245.6-281.2	247.0 229.0-265.0	0.24*
Light exposure, Lux/min	303.9 258.9-348.9	82.4 36.2-128.6	1.36 ***	303.7 257.3-350.1	83.1 35.4-130.7	1.35***

Note: * p<0.05, *** p<.001, CI: 95% Confidence Interval, ISI: Insomnia Severity Index, PSQI: Pittsburgh Sleep Quality Index, HSCL: Hopkins Symptom Checklist, TST: Total sleep time, SOL: Sleep onset latency, SE: Sleep efficiency, WASO: Wake after sleep onset, MSFsc: Midsleep free days sleep corrected, SJLsc: Social jet lag sleep corrected. Model 1: crude, Model 2: Adjusted for sequence of enrollment, age, sex, education, employment, perceived financial status and marital status

Table 4. Seasonal differences (estimated marginal means) in pain severity and pain dissemination

	Pain Severity			Pain Dissemination		
	Summer (M $_{CI}$)	Winter (M $_{CI}$)	Cohens *d*	Summer (M $_{CI}$)	Winter (M $_{CI}$)	Cohens *d*
Model 1	4.38 $_{3.99\text{-}4.76}$	3.95 $_{3.55\text{-}4.34}$	0.28*	7.05 $_{5.68\text{-}8.42}$	6.91 $_{5.52\text{-}8.30}$	0.03 ns
Model 2	4.38 $_{4.01\text{-}4.76}$	3.95 $_{3.57\text{-}4.33}$	0.28*	7.09 $_{5.78\text{-}8.40}$	6.93 $_{5.61\text{-}8.26}$	0.03 ns
Model 3	4.39 $_{4.05\text{-}4.73}$	3.95 $_{3.60\text{-}4.29}$	0.29*	7.09 $_{5.79\text{-}8.38}$	6.94 $_{5.63\text{-}8.26}$	0.03 ns

Note: Model 1: crude, Model 2: Adjusted for sequence of enrollment, age, sex, education, employment, perceived financial status and marital status, Model 3: Model 2 additionally adjusted for principal component score (PCA)-based component scores C1, C2 and C3. The variables entered into the PCA were Insomnia Severity Index, Pittsburgh Sleep Quality index, Hopkins Symptom Checklist, Chalder Fatigue Scale and the actigrahy measures; sleep onset latency, sleep efficiency, total sleep time, midsleep weekdays and average activity counts, which could be satisfactorily summarized by three component scores with eigenvalues > 1.