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Sleep and Chronic Low Back Pain

by

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**in partial fulfillment of the requirements
for the degree of Doctor of Philosophy**

**Carleton University
Ottawa, Ontario**

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in partial fulfillment of the requirements
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ABSTRACT

Chronic low back pain (CLBP) is a leading cause of disability and results in huge capital costs associated with lost productivity and treatment expenses. Among disorders commonly associated with CLBP, two most frequently cited are depression and sleep disturbance. The synergistic interaction among pain, depression and sleep disturbance is well documented, and this is the first study designed to characterize the sleep disturbance in CLBP taking into account the contribution of depression. It was hypothesized that sleep in CLBP subjects would be characterized by indications of higher arousal and more disturbance relative to that in controls (C), and that this disturbance would be enhanced in the depressed (D) as compared to the non-depressed (ND) pain subjects. Twenty-one subjects (10 CLBP -- 4 D and 6 ND; 11 age-matched C) slept for four consecutive nights in a sleep laboratory while EEG (C_3 , O_2 , F_2), horizontal and vertical EOG, face and leg (bilateral anterior tibialis) EMG, and ECG signals were recorded. Subjects completed questionnaires reporting pain, depression and sleep quality levels.

Remarkably, there were no significant group differences for general measures of sleep -- including heart rate -- across recording nights. Power spectral analyses of EEG activity for the two baseline nights provided quantification (absolute μV^2 values) of five frequency bands -- delta (.5-4 Hz.), alpha (8-12 Hz.), sigma (12-14 Hz.), low beta (14-20 Hz.), high beta (20-25 Hz.). Across-site and -stage analyses of these data resulted in few significant control-pain group differences. Most notable was higher sigma power in C relative to D and ND subjects, suggesting more effective thalamocortical sensory blocking during sleep in controls. Power values in the high beta band were greater for D relative to C and ND subjects, replicating an

association between high beta and depression. Also of note was the absence of control-pain group differences on EEG measures associated with arousal (i.e., alpha and beta). However, one arousal-related measure which was more prominent in pain subjects was a concentration of brief motor events during the first part of the night. The implications for sleep quality of this observation, as well as neurologic and muscular changes occurring in CLBP subjects combined with lower sigma power in these subjects are discussed.

ACKNOWLEDGEMENTS

Conducting a sleep study such as this is a very difficult task. The data collection aspect of this research was extremely challenging, and interpretation of the results brings one to a closer appreciation of how complex and different sleeping is from waking in humans and the difficulty in interrelating measures from either state.

The sheer magnitude of the project along with its complexity required the participation and collaboration of many people whom I would like to acknowledge. My family, Kevin and Mhari Lamarque, put up with the overnight absences and the long, unsure period of completing this dissertation. The subjects, in particular those with chronic low back pain, were cooperative, generous with their time and remarkably tolerant of the strange laboratory surroundings.

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INTRODUCTION

Although symptomatic pain serves an important biologic function by indicating injury or physical distress, some types of acute pain and all forms of chronic pain (CP) are detrimental to the organism.¹⁶ Chronic pain is defined as pain of greater than six months' duration not associated with metabolic disease and not responsive to traditional medical intervention.^{78,88} It has been estimated that CP affects 9-12% of Canadians⁴¹ -- twice as many as those suffering from all cancers combined¹⁶⁶ -- and 33-35% of Americans.¹⁹⁸ Among subtypes of CP, arthritis and back problems are most prevalent in Canada,⁴¹ with chronic low back pain (CLBP) accounting for the largest proportion of compensation payments for a single disability.^{6,117} In the U.S. CLBP is reportedly the third leading cause of physical limitation and disability,²¹¹ with age of onset at 20-30 years, and peak prevalence at 40-60 years.^{79,82,114} In 1992 it was estimated 50 billion dollars were spent on treatment for low back pain alone in the United States.¹⁴⁵ The Nuprin Report¹⁹⁸ indicated that in 1985 in the U.S., 550 million work days--translating into a 55 billion dollar loss in productivity--were lost due to this disorder. The economic cost of this condition is defined not only by lost work days, but also by required investigations, hospitalizations, treatments, therapies, and insurance claims, all of which carry significant costs to society. The individual, social and economic consequences of CLBP rank it among today's great health challenges and despite continuing efforts, treatment is only moderately successful.⁶³

The complexity of interacting physical and psychological factors in CLBP and its management has led to the development of multidisciplinary pain clinics using medical,

psychological and physical therapy interventions. These programs have effectively improved function through decreased medication, improved coping skills, increased level of activity and decreased time in bed.⁶³ However, treatment and management are complicated by the diversity of associated symptoms, including depression, sexual dysfunction, sleep disturbance, loss of self-esteem, guilt, increased suicide risk, irritability, withdrawal of interests, weakening of personal relationships and increased somatic preoccupation.^{78,199} Among disorders commonly associated with CLBP, two of the most frequently cited are depression and sleep disturbance. Either condition can not only interfere with effective pain management, but may exacerbate pain-related symptomatology.

The present study focuses on the nature of sleep disturbance and the extent to which depression contributes to sleep complaints associated with CLBP. This population was selected for study because of the prevalence of CLBP among CP disorders, to increase the homogeneity of the sample and furthermore, discomfort in bed being a potential arousal stimulus, it was considered that people with back pain would have similar strategies regarding positioning while sleeping as compared to subjects with other forms of CP, e.g., chronic headaches. A greater understanding of the correlates of sleep complaints in this population may lead to improved management of CP patients.

The literature review that follows highlights research findings relevant to the present investigation, including studies examining sleep disturbance in clinical and normal populations as well as variations in sleep parameters associated with depression.

Chronic pain and sleep

It might be expected that people with CP would gain relief from their pain during sleep because of the general decrease in sensory and motor responsiveness during this state.^{139,154,197} However, sleep disturbance is virtually universal among those with pain-related conditions,^{42,65,76,77,127,155,177,228,231,232} and such disturbance can further complicate the clinical condition by exacerbating existing physical and psychological impairments.^{72,155} In the complex presentation of CLBP, it is instructive to note the large number of publications that cite sleep improvement as an outcome measure of treatment.^{46,60,169,171,172} This emphasis indicates the importance attributed to sleep disturbance by people with this problem, and the implicit assumption that a decrease in pain will have a positive impact on sleep complaints.^{90,235} However, self-report of sleep quality does not provide an objective and comprehensive understanding of the nature of the presenting sleep disturbance,¹⁴⁶ and there are few studies attempting to describe the underlying pathophysiology of this problem that appears to be a significant contributor to the overall disability of CLBP.

Morning complaints of waking unrefreshed, and 'poor quality' sleep affecting daytime performance have been the focus of many clinical and experimental sleep studies in which investigators have attempted to identify aspects of sleep physiology which can be linked to these self-reports.^{15,17,35,80,116,119,170,192,193} Findings of these studies can be grouped into two general categories of measures which may reflect different features of the sleep process. The first indexes group macroscopic features of sleep, i.e., amounts of sleep stages, level of autonomic activation, level of arousal, and power spectra measures

of EEG activity. The other category includes measures of intermittent sleep influences, i.e., interruptions by phasic events such as leg movements, apnoeic events and arousals. These events effect disturbances in the continuity of sleep. The review that follows will discuss studies that examine these macroscopic and intermittent sleep influences with regard to overall sleep integrity.

Polysomnographic studies in CP (and more infrequently, CLBP) subjects are few and are generally characterized by methodologic shortcomings.^{141,142,148,190,224} For example, Wittig²²⁴ studied a large number of subjects with CP (n=26), but for only a single night and without a control comparison group -- a paradigm which allows for the confounding of adaptation and clinical condition effects.²²⁴ Also in that study, descriptive sleep-related measures, e.g., total sleep time, sleep efficiency, wake after sleep onset and latency to sleep onset were presented, but stage variations were not reported. Morin^{141,142} reported a positive effect of sleep restriction on insomnia associated with CLBP (n=3), but with few subjects in the study and an emphasis on sleep efficiency, the results do not clarify the nature of the underlying sleep disturbance. In a sleep study of 23 out-patients with CLBP, Staedt¹⁴⁸ looked at improvement of sleep quality after a rehabilitation treatment program, and developed two measures of arousal (with and without associated movement) and grouped these measures into clusters across the night. After the treatment program the patients in that study showed a decrease in number of arousal clusters, but not variations in other measures of sleep quality, e.g., sleep efficiency, number of stage shifts or frequency of arousals. There was a positive correlation between the number of arousal clusters and depression, a variable not controlled for in the study. Although

rheumatoid arthritis (RA) is not a subgroup of CP, subjects with this disorder have sleep complaints that have been attributed to their pain, and polygraphic studies have demonstrated evidence of sleep fragmentation in these subjects similar to that reported in other pain conditions.^{119,128} Despite the lack of thorough polysomnographic studies of people with CLBP, the findings cited above agree with questionnaire-based reports from these populations indicating the presence of sleep fragmentation by movement, arousals and awakenings.^{43,76,155,224}

EEG and autonomic measures of sleep and arousal

Variations in cortical activation, respiration and EMG are used to define and describe sleep stages and associated events. Central to this study and of interest when discussing sleep disturbance is the concept of arousal. This phenomenon may be considered from two perspectives, namely in reference to awakening from sleep¹⁹⁷, or as physiologic variations indicating increase excitability when sleep is maintained.¹⁴⁴ The recording of EEG activity provides a readily accessible measure of cortical activation for which there is general agreement regarding arousal correlates. For example, reduced excitability has been associated with high-amplitude low-frequency EEG oscillations and increased excitation with high-frequency low-amplitude activity.¹⁶¹ Other measures frequently used to index variations in arousal include cardiovascular (i.e., heart rate, blood pressure and ventilation^{18,87}) and EMG activities.^{35,112,176,190}

Alpha activity

Among the general CP population, only subjects with fibromyalgia (FM), have been extensively studied in the sleep laboratory. FM is characterized by diffuse,

widespread pain with associated fatigue, unrefreshing sleep and depressive affect.¹⁵⁵ In these patients an EEG alpha intrusion pattern in NREM sleep, termed the alpha-EEG sleep anomaly, has been reported.¹³⁷ This pattern was initially described in psychiatric patients with chronic somatic malaise and fatigue and was characterized as “a mixture of 5-20% delta waves ($>75 \mu\text{V}$, 0.5-2 Hz) combined with relatively large amplitude alpha-like rhythm (7-10 Hz) ... usually 1-2 Hz slower than waking alpha.” (pg. 233).⁷⁴ This EEG sleep anomaly has been assessed by visual evaluation using standardized scoring criteria¹³⁵ as well as by electronic processing of EEG activity using Fast Fourier Transform and power spectral analysis.⁵¹ The latter computerized analyses provide a method for the reliable quantification of EEG activity based primarily on waveform frequency and amplitude characteristics.^{156,233} The alpha-EEG sleep anomaly can occur in all sleep stages,⁵¹ and has been proposed as an indicator of a sleep-arousal disorder and a biologic correlate of nonrestorative sleep.¹²⁸ This anomaly has been noted in other painful conditions, psychiatric illness, medical conditions and sleep disorders^{51,69,74,150,181,182} (reviewed in^{112,128,130,158}). However, not all FM subjects exhibit this sleep anomaly,^{178,216} and it has also been reported in normal subjects with no sleep complaints.^{51,86} There is a need, therefore, to define more clearly the potential of this EEG activity as a biologic correlate of nonrestorative sleep, pain, and fatigue^{112,130} in other populations, such as CLBP.

In keeping with the generally accepted view of alpha activity as indicating arousal, it would be anticipated that compromised sleep continuity would characterize sleep in subjects with the alpha anomaly. However, there is conflicting evidence regarding the

presence of extensive sleep disturbance in subjects with the alpha anomaly, with indications of the absence of major sleep disturbance or other sleep disorders,^{86,181,182,218} as well as reports of both the presence^{138,190} and absence^{137,138,183} of significant motor and EEG disturbance. Although the basis for this alpha activity remains empirically undetermined, its presence in pain-free normal subjects suggests that processes other than, or in addition to, pain may underlie the anomaly.

Another inconsistency in the alpha-EEG anomaly literature is the relationship between this activity and the level of arousal in sleep. Moldofsky *et al.* have recorded the alpha-EEG sleep anomaly in over 100 FM patients¹²⁸ and have documented associated sleep stage characteristics and suggested that these subjects have a higher level of arousal during sleep. They have also reported that after selective stage 4 sleep deprivation healthy normals develop the alpha anomaly during sleep and awaken with somatic complaints similar to those reported in FM subjects.^{136,137} The presence and integrity of stage 4 has been related to a restorative function attributed to sleep,^{72,83} and nonrestorative sleep has been emphasized as a core feature of FM.¹³¹ However, the association of stage 4 deprivation with the EEG anomaly and pain in normal subjects is not paralleled by a stage 4 reduction in FM subjects.^{5,136,137,178} Reports of greater recall of sleep mentation or behavioral performance upon awakening from sleep in both FM^{5,217} and depressed subjects suggest a state of heightened mental awareness, but these studies do not report greater ease in effecting arousal in these subjects. However, heightened recall of sleep mentation does not necessarily lead to the interpretation of a higher level of arousal, as dream recall has been demonstrated from REM and SWS sleep, when arousal threshold is relatively

high.^{27,162,234} In the initial study describing the alpha anomaly⁷⁴ AAT determinations in one patient found that the awakening threshold “...during alpha-delta sleep is deeper than during stage 2 sleep...another similarity between alpha-delta sleep and classical delta sleep.” (pg. 236). Furthermore, alpha EEG activity is reported to decrease across the night in normal¹⁸² and FM¹²⁹ subjects, and AATs during sleep show a similar across-night decreasing pattern.^{26,27,162,218,224} Contrary to the notion of alpha activity reflecting higher levels of arousal, the preceding results suggest that the presence of the alpha-EEG anomaly is associated with a lower level of arousal during sleep.

An important distinction regarding this anomaly -- often noted, but not integrated into a differential interpretation of the phenomenon--is that it differs in several respects from occipital alpha activity. The existence of a frontal alpha activity differing from occipital alpha in peak frequency (generally 1-2 Hz slower), spatial distribution (fronto-central focus), and response characteristics (increases, rather than blocks, during increased mental alertness), has been known for nearly 60 years.^{33,86,109} Several reports have noted that alpha sleep anomaly activity is slower than occipital alpha and more frontally concentrated.^{74,86,181,182,185,217} Most sleep investigations documenting the anomaly have recorded from central EEG derivations despite the implicit assumption that the alpha activity recorded was occipitally derived. The fronto-central distribution of alpha activity makes it likely that alpha activity observed in central recordings reflects frontal alpha activity as well -- perhaps to an even greater extent given the more proximal location of central sites to an indicated equivalent source dipole of frontal alpha activity.²³ Based on these considerations, it has been proposed that frontal alpha reflects activity consistent

with a sleep maintaining process which may be invoked in response to sleep disturbing processes, but which otherwise remains at a low level, while the concept of occipital alpha activity as an arousing, sleep disruptive process, remains unchanged.¹⁵⁷ This interpretation is consistent with the presence of this activity in normal subjects without sleep disturbance.

The focus of studies on FM subjects resulted in an emphasis on alpha activity during sleep, but other EEG frequency bands have also been associated with aspects of sleep depth and quality. These correlates are reviewed for the most prominent among these bands, namely, delta (.3-4 Hz), sigma (12-14 Hz) and beta (14-40+ Hz) activities.

Delta activity

By definition, slow wave sleep i.e., NREM stages 3 and 4, is dominated by slowly oscillating delta waves (.3-4Hz).¹⁶³ Slow wave sleep occurs predominantly during the first third of the night,^{19,26} and appears to be an essential element of sleep.⁸⁴ The amount and intensity of slow wave sleep has been positively associated with sleep depth.^{49,68,84,106} During slow wave sleep, there is decreased responsiveness, perhaps 'reflecting whatever recuperative processes the brain undergoes during sleep',⁸⁴ and this process decreases across the night. The two-process model of sleep proposes that two interactive processes (circadian and sleep) result in sleep onset and maintenance, and that the rapid decrease in slow wave sleep propensity after the first part of the night is associated with less of a 'need' to sleep.¹⁹ Slow wave sleep deprivation results in fatigue and decreased performance.³ Also, following sleep deprivation, a slow wave sleep rebound ensues-- an effect interpreted as important for recovery.²¹

Electronic processing techniques have confirmed that the highest delta power is found in slow wave sleep, that it decreases across the night along with a decreasing arousal threshold, and that with aging there is a decrease in delta power.^{26,84,107,159} The importance of preserving slow wave sleep is suggested by the finding that after sleep deprivation, slow wave activity intensifies.^{47,68,84,103} Feinberg has written extensively on variations in delta power across the human life span and has pointed out that decreases in delta power occur in parallel with decreases in cortical synaptic density.^{36,61,205,209} He views slow wave sleep as related to the functioning of the most plastic neurons and suggests a positive correlation with the ontogenetic development of cerebral metabolic rate. He also notes that many chronic insomniacs have decreased slow wave sleep. Generally, more delta power is interpreted as reflecting a sleep process that is deeper.¹³⁴

Sigma activity

Sleep spindles are waveforms (12-14 Hz) that occur in bursts and are considered a hallmark of NREM sleep.²⁰⁹ Spindle activity is used in scoring sleep onset as well as stage 2 sleep,^{163,186,209} is considered a constant component of stages 3 and 4¹⁸⁶ and has been found to be quite stable across age ranges.⁷⁰ Spindles are thought to reflect a sleep protective function,¹⁰¹ with a greater intensity of sleep spindles associated with a greater sleep depth.²² Investigations of computerized EEG focussing on sigma (12-14 Hz) activity have considered activity in this band to reflect primarily spindle activity.^{48,186,209} Using animal preparations, Steriade^{194,195} has recorded spindle activity in sleep from reticular thalamic neurons. The spindle burst activity has been related to thalamic 'gating' of sensorimotor information, thereby decreasing these influences on cortical

activation and promoting, and perhaps ‘deepening’, sleep. In hypersomniacs, there is higher spindle density, suggesting higher thalamic blockade consistent with greater difficulty in arousing these subjects from sleep.²² Power in the sigma band has been demonstrated to vary positively with incidence of sleep spindles.⁴⁸ During sleep, sigma power is reported to be highest in stage 2, lower in stage 4, and lowest in REM,^{8,209} is decreased following sleep deprivation (when delta is high),²⁰⁹ and is believed to have a complex oscillating relationship with delta activity.^{106,209}

Beta activity

EEG activity in the beta range (commonly between 14 and 38 Hz), is a low amplitude, high frequency activity that has been primarily studied in vigilant states. When these activities are recorded in sleep, they have been interpreted as a reflection of arousal, and in depression, increased beta power has been proposed as a correlate of microarousals or lightening of sleep.¹⁰⁴ Uchida²⁰⁷ demonstrated that beta power increased from SWS to stage 2 to REM and that beta and delta frequencies oscillate reciprocally. In contrast, Armitage¹⁰ reported that delta (.5-4 Hz) and beta (16-32Hz) oscillate in phase. These different study findings may be due to the different procedures for data processing and statistical analyses used.

Heart rate

Measurement of autonomic activation during sleep has added to the understanding of dynamic relationships among sleep states and arousal.^{120,152,153} Among autonomic measures, heart rate and heart rate variability have been well studied during sleep.^{30,179,226,227} Heart rate has been demonstrated to decrease across the night, and

increase in variability during REM sleep.^{4,30,187} These measures have been found useful in providing normative data, as well as identifying variations associated with pathological conditions,^{25,71,81,120,180} and have been shown to be sensitive to changes in arousal during sleep.^{4,140,210} Given the potential relevance of level of autonomic activity to issues of sleep continuity and quality, it is noteworthy that there are no published studies of these variables and their relation with sleep complaints in CLBP or any other pain population.

Intermittent disruptive events during sleep

Although sleep quality may be obviously compromised by variations in the physiologic and stage variables discussed above, it has become increasingly clear that discrete, intermittent events can also have a negative impact on sleep quality. This realization has resulted in the emergence of sleep continuity as a potential critical factor to be considered in relation to daytime performance.³⁵ For example, disorders characterized by sleep fragmentation, e.g., periodic limb movements (PLMs) during sleep and sleep apnea, are associated with complaints of poor sleep quality believed due to repeated brief arousals secondary to pathological events.^{35,87,201} People experiencing PLMs often complain of difficulty sleeping and daytime fatigue.¹¹² The covariance of sleep apnea and PLM appears to potentiate the negative effect of resulting arousals.¹²¹ Staedt¹⁹⁰ showed significant EMG-associated arousals in CLBP subjects, and a subgroup of FM subjects have excessive leg movements that are associated with decreased sleep quality.¹³⁸ Models of experimental sleep fragmentation have demonstrated that disturbance of 8-9 arousals/hr throughout the night has the same effect as repeated disturbances only during the first four hours (neither resulting of sleep deprivation) i.e., a

decrement in daytime performance equivalent to approximately 40 hours of sleep deprivation.¹⁹³ This emphasis on the first part of the night is consistent with the notion that slow wave sleep disruption significantly impairs the following day's performance.¹⁹³ Subjects with RA also report significant sleep fragmentation and daytime fatigue. Mahowald *et al.*¹¹⁹ reported a mean of 43.2 (± 34.9) arousals per hour of sleep in these subjects, and this fragmentation occurred in the absence of sleep deprivation. This study was repeated⁸⁰ with similar findings of fragmentation in the RA population, i.e., more awakenings, greater wake time after sleep onset, and a decrease in sleep efficiency, as compared to controls. However, 89.5% of RA subjects also had PLM or restless legs syndrome, contributors to sleep fragmentation not distinguished in that study.

The studies reviewed regarding complaints of unrefreshing sleep report findings related to both macrosleep structure and intermittent influences on sleep. The importance of uninterrupted sleep, particularly during the first part of the night, appears uncontested. Reports from the CLBP population indicating significant sleep disruption and complaints of unrefreshing sleep would suggest that similar tonic and phasic activity correlates would be present in their sleep recordings.

Chronic pain and depression

Chronic pain has a significant impact on virtually every aspect of a person's life. Among the more profound consequences of CP is the effect of the pain experience on the person's psychological status, such as the common occurrence of the development of depression. The relation between CP and depression is supported by a large body of research indicating that many CP patients suffer from a concurrent major depressive

episode.^{55,173} Among the wide range of topics addressed in the CP and depression literature, of greatest relevance to the present study are those dealing with issues of prevalence,^{24,34,50,55,146} interactions between depression and pain,^{24,50,56,95,97,100,115,118,126,151,212,214} and diagnostic difficulties.^{50,66,77,113,173,174,200}

The prevalence estimates of depression in CP range from 0 to 100%, with general consensus being that 50% of people with CP are depressed^{24,34,50,55,146} -- a statistic consistent with estimates in the CLBP population.¹¹³ A substantial portion of this literature describes a synergistic effect between the pain experience and depressed mood. Brown²⁴ studied RA patients and noted that "...pain episodes result in subsequent increases in the severity of depression in CP patients." (pg. 132). CP patients with depression experience an increase in experimental pain threshold, but a decrease in clinical pain tolerance,¹¹⁰ an augmentation of the intensity of incoming signals,^{1,50,126,213} use a greater number of sensory pain descriptors, and also report decreases in pain in association with improvements in depression.^{212,214} General support for these relationships was provided by a multi-site study evaluating the functioning and well-being of 11,242 medically-ill patients. This study reported that the effects of depressive symptoms and medical conditions (including back pain) were additive, often resulting in twice the reduction in social functioning associated with either condition alone.²²⁰ Attempts to predict the development of depression in CP have found that the diffuseness of pain and the extent to which pain interferes with function tend to be the strongest predictors of depression. Clearly, depression is an important factor affecting the management and treatment outcome of CP patients.^{96,151,200}

The issue of diagnosis of depression in CP is complex and requires special consideration. Although all CP patients do not develop depression, the significant interaction between CP and depression has presented difficulties in distinguishing common features and assuring a clear diagnosis of depression, prompting the recommendation that a concerted effort be made to differentiate depressed and non-depressed subgroups.^{50,77,173,174} These diagnostic problems centre around the fact that criterion-based diagnoses commonly used for depression (e.g., DSM-III-R) rely on the identification of a cluster of individual symptoms which includes a range of affective, cognitive and neurovegetative signs. However, in patients with co-occurring medical complaints, including pain, several key diagnostic symptoms may be caused directly by the medical problem itself.⁵⁷ In this situation, the prevalence of depression is likely to be exaggerated by the inappropriate attribution of medical symptoms as indicators of emotional difficulties.²²³ To circumvent this problem, Endicott⁵⁸ proposed a revision to the standard diagnostic criteria for depression that involves replacing somatic items from the symptom list with additional psychological symptoms. These substitutions are reported to be empirically valid¹⁶⁰ and provide “perhaps the best criteria for diagnosing depression in the medically ill”.⁹³

EEG and power spectral correlates of sleep in depression have been studied extensively, but these studies generally involve inpatients who are severely depressed. The measures that consistently discriminate depressed subjects and controls are: longer sleep onset latency, less slow wave sleep, short REM onset latency, and a decrease in delta and alpha power.^{9,10,20,31,62,99,105,167,175} In view of the evidence of variations in sleep

associated with depression and the degree of comorbidity between CP and depression, it is surprising there are no published polysomnographic studies in CP groups in which the compounding influences of pain and depression are evaluated.^{119,146,149,199,224}

Summary

The preceding discussion indicates dynamic interactions among CP, sleep and depression. The few studies specifically examining these relationships confirm the synergism of their interaction. A questionnaire-based longitudinal study found that prior pain exacerbated sleep disturbance, and that together these conditions contributed to subsequent depression ratings.¹⁴⁶ That study noted the “...potentially deleterious impact of the combination of high pain and high sleep problems on current depressive symptoms” and that the “...level of pain substantially altered the manner in which sleep problems affect depression over time” (p. 518). A survey of sleep disturbance, pain and depression in another condition, Parkinson’s disease, found that the severity of reported pain was significantly related to the severity of depression, with depression accounting for most of the variance in the correlation with sleep disturbance and pain.¹⁹¹ In a polygraphic sleep study comparing FM and primary depression patients, alpha EEG activity in NREM sleep was found to be common in both groups--suggesting that such activity might be considered as one of several sleep-related markers for depression.²¹⁶ Recent findings^{76,112,190,223} have confirmed an association among pain, affect and poor sleep.

Despite the growing interest in the relationship among CP, sleep and depression, the relevant literature is restricted to the few studies cited above. Several papers have

called for a polysomnographic assessment of sleep disturbance in CP.^{12,42,43,112,158} This paucity of multicondition investigations prompted the present study.

HYPOTHESES AND PREDICTIONS

Based upon the preceding review of the sleep literature, and consistent with expectations of both general and intermittent sleep disturbance in CLBP subjects, it is hypothesized that these subjects will show signs of increased arousal during sleep and more sleep disturbing events. Also, given the general exacerbation of pain-related effects in depression, depressed subjects are expected to demonstrate more arousal and sleep disruption than either non-depressed or control subjects. Based on these hypotheses, it is predicted that CLBP subjects will evidence:

1. Longer sleep onset latencies, more stage 1, less slow wave sleep, and increased heart rate relative to controls. Power spectral data in these subjects will show increased alpha and beta power and decreased delta and sigma power.
2. Increased intermittent sleep disturbances, including more awakenings, more movement activity, and more stage changes following motor events. These intermittent events are expected to predominate in the first part of the night, particularly in stage 4 sleep.

METHODOLOGY

Subject recruitment and screening

Selection and acceptance of subjects into the study followed a process that required the participation of several clinicians using a pre-determined sequence. Therefore, a flow chart (Figure 1) and the Selection Criteria Checklist (Appendix A) were developed to facilitate the flow of subjects through the process and to assure that all inclusion and exclusion criteria were considered and respected.

To recruit pain subjects, all pain clinics in Ottawa, as well as physiotherapy, chiropractic and psychology clinics with CLBP clientele were contacted and provided with information to identify potential study subjects. Referrals were made only with the patient's consent. Control subjects were recruited from the general population. As indicated in the flow chart, a preliminary interview by the investigator determined subjects' general suitability for the study (e.g., presence of low back pain, use of medication, age of subject). Once such suitability was confirmed, subjects read the information sheet (Appendix B) and had the opportunity to ask further questions before signing the consent form (Appendix C) for participation in the study. All subjects were assigned a code to ensure confidentiality and group membership anonymity during data analyses and publication of results. This step was followed by a series of appointments to make the necessary clinical diagnoses to assure inclusion and exclusion criteria were respected, and to assign group membership.

Figure 1. Subject Selection and Group Assignment

Selection criteria

Subjects had to be between 25 and 50 years old, and were matched for age across groups (± 2 yrs.). Both men and women were included in the study (gender representation is approximately equal in CLBP⁶⁴). The upper age limit was chosen because of significant changes in study-related variables reported to occur beyond that age (e.g., decreased amounts of slow wave sleep).^{84,107}

The diagnosis of CLBP was made by a physiatrist using the International Association for the Study of Pain⁸⁸ definition for CP. Pain duration was limited to seven years to provide a time frame (6 mos.- 7 yrs.) satisfying the minimum criterion of chronicity and avoiding an upper limit of 8 years after which it is thought that CP patients demonstrate improved coping skills.⁷⁸ Subjects with neck pain in association with back pain were not excluded from the study. Subjects with CLBP onset during adolescence were excluded to avoid potential developmental differences in pain / depression symptomatology which could differentially influence sleep measures.

Medications are frequently taken by people with CLBP, e.g., analgesics and antidepressants, to help with pain symptoms and sleep complaints, but these medications affect sleep^{85,98,108,165,215} and subjects were not accepted into the study unless they were free of any medication affecting sleep. However, provisions were made to consider medication withdrawal for a two-week washout period prior to the sleep recordings for potential subjects wishing to consider this option.¹⁰⁸ All subjects were assessed for FM by a physiatrist using the American College of Rheumatology Criteria²²⁵ and those meeting these criteria were excluded. The diagnosis of RA or other medical problems

(e.g., cardiovascular pathology, epilepsy) that might contribute to sleep disturbance also resulted in exclusion. In addition on the first recording night subjects were screened for the presence of sleep apnea and restless legs syndrome -- two disorders known to result in significant sleep disturbance.^{35,71,87,176} A clinical interview was conducted by a psychiatrist to exclude subjects with major psychopathology that would affect sleep (e.g., panic disorder, alcoholism), a history of psychiatric illness, and specifically the presence of depression prior to the diagnosis of CLBP. The psychiatrist also provided the clinical judgement that subjects were appropriate for the study, and assured prompt attention and follow-up to those in need of psychiatric attention.

Subjects who met the above inclusion criteria were formally accepted into the study, and the final clinical diagnosis of the presence or absence of depression was made by one of two clinical psychologists using the Modified Structured Clinical Interview for Diagnosis (SCID; reliability: >.9).¹⁸⁸ This interview consists of the depression component of the Mood Disorder module for the SCID, Nonpatient Edition,¹⁸⁹ with additional individual items that pertain to the Endicott criteria⁵⁷ drawn from the SADS.⁵⁸ On the basis of this diagnostic procedure, subjects were assigned to depressed and non-depressed subgroups.

Procedures

To minimize the influence of change in psychological status of pain subjects over time, sleep recordings began within two weeks of the psychiatric interview. Within this two week time frame, all subjects visited the laboratory (Department of Psychiatry, Ottawa General Hospital) where the sleep recordings would be conducted to orient them

to the sleeping room, personnel and equipment, and to complete several questionnaires. This procedure initiated the Post-Selection Testing Schedule (Figure 2). The questionnaires used in this study are described below.

1. The Demographic Screening Questionnaire (DSQ; Appendix D) provided demographic data for each subject, and included questions about sleep and activity levels.
2. The McGill Pain Questionnaire (MPQ)¹²³ is a commonly used, reliable self-report measure which produces a pain rating index (PRI) considered to be an appropriate assessment of pain.²⁰⁶ Documented fluctuations of pain intensity in CP subjects^{91,92,225} influenced the decision to have subjects rate their pain several times. The MPQ was administered at the first visit and prior to sleep and after awakening on each of the recording nights, providing an ongoing index of subjective pain intensity.
3. The Beck Depression Inventory (BDI)¹⁴ is a self-report depression instrument and has been used to determine subtypes of depression in CP patients.^{113,223} The questionnaire was completed on the first visit, on the first recording night, and again on the evening preceding the last recording night.
4. The Pittsburgh Sleep Quality Index (PSQI)²⁹ was completed during the first laboratory visit to provide self-report information on sleep quality and disturbance over the previous month.
5. The Daily Sleep Diary (DSD),⁷⁶ designed for CLBP subjects, provided a morning report of the previous nights' sleep quality and amount. This questionnaire was completed each morning following sleep recordings.

Two week pre-recording		4 night polygraphic sleep recordings							
Questionnaire		pm	am	pm	am	pm	am	pm	am
McGill Pain Questionnaire	✓	✓	✓	✓	✓	✓	✓	✓	✓
Beck Depression Inventory	✓	✓						✓	
Pittsburgh Sleep Quality Index	✓								
Daily Sleep Diary			✓		✓		✓		✓
Debriefing									✓

Figure 2: Post-Selection Testing Schedule

Subjects were given specific instructions regarding study restrictions which were to be followed beginning the morning of the first sleep recording night until the end of the study. They were instructed to avoid caffeine, alcohol and medication intake and not to nap during the day, but otherwise to carry on their regular activities. To aid in monitoring daytime activity and to document the potential occurrence of napping, subjects wore wrist actigraphs continuously beginning the morning prior to the first night's recording until the morning after the final recording night. The actigraph, which measures activity by displacement of an accelerometer inside a wristwatch-like monitor, has been demonstrated to be a reliable measure of daytime napping,⁷⁵ general activity, and global sleep parameters in normal and clinical populations.^{42,111,143,164} Each evening, the actigraph data were downloaded and reviewed by the investigator with the subject to verify activity of the day.

Each evening of the consecutive four night polygraphic study, subjects reported to the laboratory one hour prior to normal bedtime for attachment of electrodes for sleep recordings. To control for the potential effects of hormonal influences on sleep (menstrual cycle), recordings for female subjects were scheduled the week following menstruation. Subjects slept in a sound-attenuated, radio frequency shielded, temperature and humidity controlled room. The investigator and equipment were situated in an adjacent control room. A video camera provided constant visual monitoring of subjects throughout the night.

Since sleep disturbance is common when individuals are initially placed in a new sleeping environment,^{2,5,203} night 1 served as an adaptation night, and nights 2 and 3 as

baseline. Night 4 was used to collect information not reported on in this thesis.

On all nights, standard central EEG (C3/linked mastoids), vertical and horizontal electrooculograms [DC-coupled EOG; from placements above and below the right eye and the outer canthi of the right and left eyes, respectively], and electromyographic (EMG; from bipolar orbicularis oris muscle and bilateral bipolar anterior tibialis placements) activities were recorded on a Grass Model 7 polygraph. In addition, midline occipital (Oz/linked mastoids) and frontal (Fz/linked mastoids) EEG derivations, and two autonomic variables [heart rate (modified lead I placement) and respiration (recorded from a chest strain gauge on night 1 for screening purposes)] were measured. EEG and EMG interelectrode impedance was $< 5k$ ohms. All polygraphic data were recorded on paper write-out for stage scoring and artefact identification and simultaneously collected on a PC hard-drive for electronic processing.

At the conclusion of the study, subjects were given a debriefing sheet (Appendix E) to read with the opportunity to ask questions regarding the experiment.

DATA ANALYSIS

Using standardized criteria,¹⁶³ coded sleep recordings were independently scored blind with respect to subjects' group membership by two individuals with reliability (>.90) established on an epoch by epoch basis. From these analyses, standard sleep parameters were determined (see Table 3. for listing of variables). Additional measures included the quantification during baseline nights of the following intermittent events: awakenings, motor events and stage changes after movements. Awakenings were counted as the number times a subject awakened from sleep after sleep onset (not including the final morning awakening). Three categories of motor events, determined from face and leg EMG recordings, were scored visually (with established reliability >.90) according to the following criteria: brief motor events (M; lasting 0.5-15 sec.) consisting of an increase of $\geq 50\%$ in EMG amplitude relative to the preceding 5 sec. (Figure 3); movement activity (MA; lasting 15-30 sec.) scored when there was an increase of $\geq 50\%$ in EMG amplitude relative to the preceding 5 sec. (Figure 4); and movement time (MT; lasting 15- 30 sec.), scored when there was an increase of $\geq 50\%$ of EMG amplitude relative to the preceding 5 sec. and during which the EEG tracing was obscured for more than half the epoch. Where M and MA events co-occurred, these epochs were scored for MA only.

Eight channels of polygraph signals (3 - EEG, 2- EOG, 2-EMG and 1-ECG) were digitized on-line at 512 Hz and collected directly onto a PC computer, generating a continuous, eight channel file saved every 15 min. These files were later demultiplexed into eight files (one per channel) per 15 min. sample, and then reintegrated into one file

Figure 3: An example of a brief motor event (M) during slow wave sleep. Abbreviations (C₃, O₂, F₂): bipolar (linked mastoids reference) left central, midline occipital and frontal EEG; HEOG, VEOG: bipolar DC horizontal and vertical electrooculograms; ECG: electrocardiogram, EMG_F, EMG_R, EMG_L: bipolar electrographic recordings from facial, and right and left anterior tibialis muscles.

Figure 4: An example of movement activity (MA) during stage 2 sleep.

per channel of continuous all night digitized recordings and stored on CD-ROM for off-line processing. To quantify EEG activity from frontal, central, and occipital placements, the digitized recordings were processed further. The data were divided into 3 sec. segments and following windowing (Hanning) to eliminate the effects of signal aliasing, were submitted to Fast Fourier Transform (FFT) and power spectral analysis. The 3 sec. bin data were then collapsed into 30 sec. intervals. From these data, absolute power values were determined for the following frequency bands: delta (0.5-4 Hz), alpha (8-12 Hz), sigma (12.1-14 Hz), low beta (14.1-20 Hz), and high beta (20.1-35 Hz), then corrected for amplitude using the calibration signal for the recording night. Segments associated with biologic and electronic artifact were excluded and the remaining data matched with 30 sec. visually scored sleep stage epochs. These epochs were then averaged to obtain whole night totals of absolute power for each bandwidth by sleep stage. EEG power data tend to have a skewed distribution which can be corrected using logarithmic transformation.^{94,233} Accordingly, the absolute power values (μV^2) in the present study were subjected to logarithmic transformation prior to statistical analyses.

Whole night baseline (2 nights/subject) electrocardiogram (ECG) recordings were digitized and visually screened for artifact. These artifact-free data were computer processed to determine interbeat interval (RR) to an accuracy of ± 1.95 ms. (Figure 5). This process was also visually monitored to assure correct detections. Heart rate based on these interbeat intervals was calculated and merged with the same stage score file used in the EEG analyses.

Figure 5: An illustration of electrocardiogram recordings showing interbeat intervals (RR). Both heart rate and heart rate variability measures were derived from computer determined RR interval durations.

Statistical comparisons

Within- and between-group comparisons of questionnaire results, sleep parameters, spectral EEG measures, and heart rate variables across nights were assessed using multivariate analyses of variance with repeated measures and analyses of variance. Post-hoc analyses used the Tukey test. Relationships among variables were determined using Pearson product moment correlation coefficients.

RESULTS

Despite the large number of people with CLBP, a sustained active recruitment effort yielded only 11 qualifying CLBP subjects (12 normal controls were matched) who volunteered over a four year period. From the recruited sample, two subjects were excluded from all analyses: one pain subject who had severely limited sleep time in the laboratory and one control subject who experienced a migraine two of the four recording nights. Analyses presented are therefore based upon a dataset of twenty-one subjects [four depressed CLBP (D), six non-depressed CLBP (ND) and eleven normal controls (C)]. The results will be presented in four sections dealing with: ① general characteristics of the subjects as derived from questionnaires; ② measures reflective of sleep induction and maintenance; ③ variables associated with intermittent sleep influences; and ④ relationships among measures of sleep quality, pain and EEG power.

Descriptive and questionnaire data

Subjects' demographic characteristics are presented in Table 1. Age-matching across groups assured comparability on this variable, and the CLBP subgroups did not differ significantly in their pain duration.

The questionnaire data (Table 2) were analyzed for time of administration and group effects. McGill Pain Questionnaire scores averaged over test times showed an overall group difference [$F(2,18)=25.69$, $p<.0005$], with post-hoc comparisons revealing that pain scores for all groups were significantly different ($D>ND>C$; $p<.03$). Since control subjects' scores indicated a virtual absence of pain, further analyses were conducted on the pain subgroups only. To determine the extent to which pain intensity

Table 1. Descriptive characteristics of study subjects including: group size, gender, age (mean, SD) and pain duration (mean, SD).

Group	n	# males	Age – yrs.	Pain duration – yrs.
Control	11	7	33.2 (6.2)	0
Depressed	4	4	36.5 (7.4)	3.75 (1.5)
Non-depressed	6	5	34.6 (8.3)	5.8 (3.6)

Table 2. Average (SEM) group scores on pain, depression and sleep quality measures. Results of statistical comparisons are presented in the text.

Measure	Time*	C	D	ND
MPQ‡	N1 / M1	0 / 0	24.5 (3.47) / 18.5 (4.24)	12.33 (2.83) / 12.83(3.5)
	N2 / M2	0 / .18	31.75 (3.16) / 15.25 (3.53)	8.67 (2.58) / 9 (2.88)
	N3 / M3	0 / 0	21.5 (2.96) / 19 (2.47)	13.5 (2.42) / 13.83(2.02)
	N / M mean	0 / .09	25.92 (2.73) / 17.58 (2.86)	11.50 (2.23) / 11.89 (2.23)
	Total	0.03 (.84)	21.75 (2.02)	11.69 (1.65)
BDI	1 st	1.55(1.1)	24.00 (2.15)	6.5 (1.75)
	2 nd	1.18(1.24)	20.75 (2.91)	6.33 (2.37)
	3 rd	1.73(1.69)	19.5 (3.88)	5.33 (3.17)
	Mean	1.49 (.76)	21.42 (1.26)	6.06 (1.03)
PSQI	Mean	2.11 (1.17)	13.75 (1.73)	10.83 (1.41)
DSD	M2	4 (.27)	2.25 (.41)	3.33 (.33)
	M3	3.91 (.26)	3.25 (.43)	2.67 (.35)
	Total	3.96 (.18)	2.75 (.30)	3.00 (.25)

*Time of questionnaire administration e.g., N(ight)1 - pre-sleep first baseline night / M(orning)1 - first baseline morning

‡Abbreviations: MPQ - McGill Pain Questionnaire, BDI - Beck Depression Inventory, PSQI - Pittsburgh Sleep Quality Index, DSD - Daily Sleep Diary

varied during the study period, analyses were conducted on pre-sleep (night pain) and post-sleep (morning pain) PRI scores. No within-group differences were found for night pain scores across the three recording nights nor for the three morning scores (Figure 6). However, a significant main effect was found for 'time' i.e., night vs. morning pain intensity [$F(1,8)=13.83$, $p=.006$], with D, but not ND subjects, having significantly higher pain scores at night than in the morning [$F(1,8) = 8.142$, $p=.021$], with no significant group by time interaction.

Since BDI scores did not differ significantly within any group across the three administrations (Figure 7), combined scores were used to examine group differences. Expected main and group effects were present [$F(2,18) = 36.887$, $p<.0005$; $D>ND$, C , $p<.0005$], indicating minor depressive affect in the ND pain group ($\bar{x}=6.05$) and moderate depression in the D group ($\bar{x}=21.42$). These findings validate the group assignment and demonstrate the stability of depressive affect during the study.

Sleep quality measures confirmed the presence of sleep disturbance in pain subjects for the one month prior to the study (PSQI) and during the sleep recording period (DSD; Figure 8), as well as the lack of such disturbance in controls. Group main effects on PSQI scores [$F(2,16)=20.31$, $p<.0005$] reflected poorer sleep quality in pain subjects relative to controls ($C<D$, ND , $p<.0005$), with no pain subgroup differences. The DSD, administered each morning after sleep recordings, did not reveal significant within-group differences between adaptation and baseline morning administrations. However, significant group differences were found [(Control / Pain); $F(2,18)=7.277$ $p=.005$; D and ND reported poorer sleep than C, $p<.008$], with no between-subgroup differences. These

Figure 6. Mean MPQ Pain Rating Index (PRI) scores for [Depressed (D) and Non-Depressed (ND)] CLBP subjects across the study period. Initial entries are averaged across the three nights (N) and mornings (M). For these and following figures, statistical analyses are found in the text.

Figure 7. Illustration of mean Beck Depression Inventory scores for CLBP subgroups across study administrations.

Figure 8. Group mean scores on self-report questionnaires indicating poor sleep quality both preceding (PSQI) and during (DSD) the study period. High PSQI and low DSD scores reflect poorer sleep quality.

results do not reflect an adaptation effect during the study, but confirm the complaints of poor sleep quality in pain subjects and indicate similar levels of such complaints in the pain subgroups.

Sleep induction and maintenance

Sleep measures across recording nights

Sleep parameters were evaluated to determine the extent to which adaptation effects were evident, to confirm the stability of baseline sleep measures, and to assess potential group differences on these variables. For most of the fifteen sleep variables, there were no within-group differences across nights (Table 3). Significant differences which were noted indicated differences on night 1 relative to nights 2 and 3, and involved variables commonly considered to be sensitive to adaptation effects (Table 4). These differences demonstrate general stabilization of sleep after night 1, consistent with previously reported adaptation effects noted in both normal² and clinical^{102,125} populations.

During the eight hours of sleep opportunity in the laboratory, all groups had similar amounts of time in bed, sleep time and equivalent amounts of each stage of sleep on each recording night. The only between-group difference observed was for TWT on night 3 [$F(2,18)=4.09$, $p=.034$; ND > C, $p=.005$].

Heart rate

In analyses of ECG data, technical difficulties necessitated eliminating three subjects from the data set, and because of this decrease in sample size pain subjects were collapsed into a single group for these analyses (C, $n = 9$, $\bar{x} = 34.5$ yrs.; P, $n = 9$ (3 D, 6 ND), $\bar{x} = 34.3$ yrs.). Heart rate and heart rate variability were determined across the entire

Table 3. Mean (SEM) of sleep measures across recording nights. Unless otherwise indicated, tabled values are expressed in minutes.

	Group	Night 1	Night 2	Night 3
TBT*	C	440.73 (19.82)	444 (10.91)	441.73 (11.13)
	D	441.00(32.86)	441.75 (18.09)	436.25 (18.45)
	ND	432.83(26.83)	462.17(14.77)	467.5(15.06)
TST	C	402.27 (20.81)	418.91 (11.37)	423.86 (11.41)
	D	371.87 (34.51)	387.88(18.86)	390.25(18.93)
	ND	358.75(28.18)	426.17(15.39)	416.58(15.45)
SEI (TST/TBT)	C	91.8% (.1.3)	94.9%(1.3)	96.4%(1.06)
	D	85.3%(3.6)	87.0%(3.4)	90.0%(2.3)
	ND	82.0%(5.5)	92.8%(1.2)	89.3%(1.6)
LSO	C	10.5 (6.76)	8.05 (2.15)	3.96 (2.66)
	D	20.75(11.21)	5.5(3.57)	11.13(4.41)
	ND	30.75(9.15)	7.5(2.91)	15.75(3.6)
LREM	C	92.41(16.09)	63.55(9.27)	64.68(8.21)
	D	84.25(26.68)	70.25(15.38)	74.25(13.62)
	ND	99.67(21.79)	72.25(12.56)	74.58(11.12)
S1	C	34.64 (4.48)	28.55 (4.91)	26.45 (3.21)
	D	32.38(7.43)	42.75(8.15)	22.38(5.32)
	ND	28.58(6.07)	30.42(6.65)	31.5(4.34)
S2	C	217.14 (14.55)	225.09 (12.91)	233.86 (11.26)
	D	203.5(24.12)	196.13(21.41)	226.5(18.67)
	ND	195.67(19.69)	224.08(17.48)	220.67(15.24)
S3	C	36.27 (5.69)	38.09 (4.89)	32.36 (5.23)
	D	30.75(9.45)	32.88(8.10)	23.25(8.67)
	ND	33.25(7.71)	37.17(6.62)	38.83(7.08)
S4	C	25.73 (8.45)	21.046 (6.48)	22.82 (6.95)
	D	12.5(14.02)	17.38(10.74)	15.88(11.52)
	ND	20.42(11.45)	22.58(8.77)	16.92(9.41)
SW	C	62.09 (11.77)	59.14 (9.84)	53.41 (10.03)
	D	43.25(19.52)	50.25(16.32)	39.13(16.63)
	ND	53.67(15.94)	59.25(13.32)	55.75(13.58)
REM	C	88.59 (8.84)	106.14 (7.62)	108.55 (8.82)
	D	92.88(14.66)	118(12.64)	102.13(14.63)
	ND	80.83(11.97)	112.42(10.32)	108.67(11.95)
NREM	C	313.73 (15.18)	312.77 (11.86)	313.73 (8.74)
	D	279.13(25.18)	269.25(19.67)	288.13(14.49)
	ND	277.92(20.56)	313.75(16.06)	307.92(11.83)
WASO	C	22.86 (7.65)	12.27 (4.28)	8.73 (4.14)
	D	36.75(12.69)	21(7.09)	21.75(6.86)
	ND	39.25(10.37)	23.5(5.79)	25.08(5.60)
AWAK (# events)	C	12.09 (2.51)	8.82 (2.00)	6.91 (2.31)
	D	12.25(4.16)	11.25(3.32)	11(3.83)
	ND	16(3.4)	12.67(2.71)	14.5(3.13)
TWT	C	32.86 (10.09)	19.59 (5.56)	12.36 (4.46)
	D	55.88(16.75)	24.5(9.22)	32.5(7.4)
	ND	69.33(13.67)	30.83(7.53)	39.75(6.04)

*Abbreviations: TBT= Total bed time, TST= Total sleep time, SEI= sleep efficiency index, LSO= latency to sleep onset, LREM= latency to 1st REM period, S1, S2, S3, S4 = NREM Stages 1-4, WASO= wake after sleep onset, AWAK= number of awakenings, TWT= total wake time.

Table 4. Post-hoc night comparisons for variables showing a main effect for night (N1<N2 & N3) and main effect for group.

Variable	Main effect (night) F(2,36) / <i>p</i>	post-hoc <i>p</i>	Main effect (group) F(2,18) / <i>p</i>	post-hoc <i>p</i>
TST	4.3 / .021	.06	n.s.	n.s.
LSO	4.7 / .015	.05	n.s.	n.s.
REM	6.05 / .005	.04	n.s.	n.s.
WASO	8.62 / .001	.008	n.s.	n.s.
TWT	11.19 / .000	.003	4.09 / .034	.005 ND>C (N3)

Table 5. Whole night and sleep stage-related heart rate and heart rate variability means (SD) for Control (C) and Pain subjects (P).

Condition	Group	BPM mean (SD)	SD of RR mean (SD)
All night	C	56.94 (8.84)	.210 (.067)
	P	58.33 (9.25)	.192 (.065)
Stage 2	C	56.10 (9.07)	.178 (.046)
	P	57.67 (9.18)	.173 (.044)
Stage 3	C	56.45 (9.08)	.213 (.054)
	P	57.63 (9.96)	.204 (.062)
Stage 4	C	58.93 (8.37)	.204 (.058)
	P	57.74 (9.95)	.174 (.053)
REM	C	56.68 (9.03)	.182 (.052)
	P	59.05 (7.9)	.160 (.038)

Abbreviations: BPM (beats per minute), SD of RR (standard deviation of interbeat RR interval).

night on both baseline nights. Within group, between-night comparisons did not indicate significant differences, and therefore the two nights' data were combined for subsequent analyses. Results are reported in beats/min (heart rate) and standard deviation of RR interval (heart rate variability, Table 5, Figure 9). Although pain subjects consistently had higher heart rates than controls, there were no significant between-group differences for either variable.

EEG power spectral analyses

Power spectral results were organized according to the five EEG frequency bands of interest (delta, alpha, sigma, low and high beta) to determine frequency-specific, site and stage group differences. These results are presented in two summary tables (Tables 6 and 7). In each table, results are initially presented for EEG activity across all sites for undifferentiated sleep (shaded row). The remainder of Table 6 is organized by site and shows F- and p-values for significant stage- and group-main effects. Table 7 is also organized by site, but each table cell is divided into two parts. In the first section mean power is ranked (above the dotted lines) by site (all sites, shaded) or stage (for each site O_2 , C_3 , F_2), and significant findings are presented in italics below the dotted lines. In the second part of each table cell, group power is ranked above, and significant post-hoc comparisons are given in italics below, the dotted lines. For example, in the sigma frequency range for C_3 , the mean absolute power for stage 4 was greater than that for stage 3 ... etc., and post-hoc analyses revealed 3 and 4>1, 4>2 and REM < all stages ($p<.003$ for all comparisons). For between-group comparisons, the total power ranking across groups was C>D>ND, with C significantly greater than ND ($p=.002$).

Figure 9. Results of ECG analyses for heart rate (upper panel) and heart rate variability (lower panel). For each variable, all night and stage-specific data are presented.

Table 6. All sites (shaded area) and site-specific stage and group main effects for power spectral analyses.

Effect	Delta (0.5-4Hz)	Alpha (8-12 Hz)	Sigma (12-14 Hz)	Low Beta (14-20 Hz)	High Beta (20-25 Hz)
All sites					
Site F(2,594) <i>p</i>	21.47 .000	4.46 .012	49.31 .000	62.54 .000	33.82 .000
Group F(2,594) <i>p</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	33.82 .000
O_z					
Stage F(4,186) <i>p</i>	3.99 .004	3.41 .011	5.16 .001	4.87 .001	4.17 .003
Group F(2, 186) <i>p</i>	3.39 .036	3.68 .027	8.72 .000	5.54 .005	6.24 .002
C₃					
Stage F(4,186) <i>p</i>	20.85 .000	14.51 .000	27.86 .000	19.8 .000	4.79 .001
Group F(2,186) <i>p</i>	<i>n.s.</i>	4.11 .046	5.78 .004	<i>n.s.</i>	5.75 .004
F_z					
Stage F(4,186) <i>p</i>	25.88 .000	25.52 .000	29.45 .000	21.68 .000	8.3 .000
Group F(2,186) <i>p</i>	<i>n.s.</i>	<i>n.s.</i>	5.31 .006	3.28 .040	4.73 .010

Table 7. Power spectral analysis results, with site/stage absolute power ranking presented above the dotted lines and significant site (shaded area), stage and group post-hoc comparisons presented in *italics*

	Delta (0.5-4 Hz)	Alpha (8-12 Hz)	Sigma (12-14 Hz)	Low Beta (14-20 Hz)	High Beta (20-25 Hz)
Site rank	$F_z > C_3 > O_z$	$F_z > C_3 > O_z$	$F_z > C_3 > O_z$	$F_z > C_3 > O_z$	$F_z > C_3 > O_z$
<i>p</i>	$F_z > C_3, F_z > O_z$.000	$F_z > O_z, C_3 > O_z$.000	$F_z > O_z, C_3 > O_z$.000	$F_z > O_z, C_3 > O_z$.000	$F_z > O_z, C_3 > O_z$.000
Group rank	$C > D > ND$	$D > C > ND$	$C > D > ND$	$C > D > ND$	$D > C > ND$
<i>p</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	$D > C, D > ND$ <.02
O_z Stage rank	4>1>3>REM>2	1>4>3>2>REM	4>1>3>2>REM	1>4>3>2>REM	1>4>3>REM>2
<i>p</i>	2<1, 4 <.02	REM<1, 4 <.05	REM<1, 3, 4 <.02	REM<1, 4 <.02	1>2, REM <.008
Group rank	$D > C > ND$	$D > C > ND$	$C > D > ND$	$D > C > ND$	$D > C > ND$
<i>p</i>	$D > ND$.028	$D > ND$.018	$C > D, C > ND$ <.03	$C > ND$.03	$D > C, D > ND$ <.006
C_3 Stage rank	4>3>1>2>REM	4>3>2>1>REM	4>3>2>1>REM	4>3>2>1>REM	4>3>1>2>REM (C & ND) 4>1>3>REM>2 (D)
<i>p</i>	3, 4>1; 3>2; REM<1, 3, 4 <.02	3, 4>1; 4>2; REM<all <.04	3, 4>1; 4>2; REM<all <.003	4>1, 2; REM<all <.05	2<1; REM<1, 4 <.05
Group rank	$C > ND > D$	$D > C > ND$	$C > D > ND$	$C > D > ND$	$D > C > ND$
<i>p</i>	<i>n.s.</i>	$D > ND$.046	$C > ND$.002	<i>n.s.</i>	$D > C, D > ND$ <.006
F_z Stage rank	4>3>1>2>REM	4>3>2>1>REM	4>3>2>1>REM	4>3>1>2>REM	4>3>1>2>REM (C & ND) 1>4>3>REM>2 (D)
<i>p</i>	3, 4>1; 3>2; REM<1, 3, 4 <.002	3, 4>1; 4>2; REM<all <.02	3, 4>1; 3>2; REM<all <.05	3, 4>1; 4>2; REM<all <.02	1, 4>2; REM<1, 3, 4 <.04
Group rank	$C > D > ND$	$D > C > ND$	$C > D > ND$	$C > D > ND$	$D > C > ND$
<i>p</i>	<i>n.s.</i>	<i>n.s.</i>	$C > ND$.004	$C > ND$.032	$D > C, D > ND$ <.04

Amounts of SWS and total delta power have been shown to decrease across the life span.⁸⁴ Although groups in the present study were age-matched within two years, the relationship between total delta power and subjects' ages was examined to assess the extent of covariation of these variables. The observed correlation ($r=.064$) confirmed the absence of a significant delta power-age relationship in this study sample.

An examination of the magnitude and distribution of EEG power derived from the three recording sites revealed that the preponderance of EEG power falls in the delta range of activity, followed by alpha, high beta, low beta and sigma, respectively (Tables 6 and 7, shaded area; Figures 10 and 11). The site distribution ranking within each frequency band shows a consistent frontal to occipital decrease in power across bands, with significantly greater power at F_z and C_3 than O_z for each frequency with the exception of delta, where $F_z > C_3$ and O_z , but $C_3 \approx O_z$. The ND group showed the lowest mean power values across sites, but the only significant group difference was reflected in depressed pain subjects showing significantly greater power than comparison groups in the high beta frequency. When viewed in this global fashion, i.e., irrespective of sleep stage, with the single exception of high beta, the magnitude and distribution of EEG power values does not differentiate among groups. It is of note that in all statistical analyses of power spectral data, i.e., those presented above as well as those to follow, there were no group by site or group by stage interactions.

With respect to the site-specific distribution of EEG power among sleep stages (Figures 12-16), some expected relationships were observed (e.g., concentration of delta power in slow wave sleep, reduced sigma power in REM), and there was a general

Figure 10. Group by site comparisons for mean all night delta and alpha power. Three groups: Controls (C), Depressed CLBP (D) and Non-Depressed CLBP (ND) are presented. In this and subsequent figures, statistical findings are presented in the text.

Figure 11. Group by site comparisons for mean all night sigma, low beta and high beta power.

Figure 12. Group by stage comparisons for mean all night delta power across sleep stages.

Figure 13. Group by stage comparisons for mean all night alpha power across sleep stages.

Figure 14. Group by stage comparisons for mean all night sigma power across sleep stages.

Figure 15. Group by stage comparisons for mean all night low beta power across sleep stages.

Figure 16. Group by stage comparisons for mean all night high beta power across sleep stages.

predominance of power across frequencies in fronto-central derivations in NREM relative to REM sleep. Group differentiations by EEG frequency were often consistent across recording sites. For example, relative to ND subjects, those in the depressed group showed significantly more alpha occipitally and centrally and more high beta activity across all sites. These groups were similarly differentiated for delta activity occipitally. Control subjects had significantly more sigma power than ND subjects across sites and more than D subjects occipitally. Controls also exhibited significantly more low beta activity relative to ND subjects occipitally and frontally. Only D subjects showed significantly more power for any EEG frequency band relative to controls, with more high beta power across sites.

Alpha activity consistent with descriptions of the alpha-EEG anomaly was clearly evident in the sleep records of some subjects but in all groups. Examples of such activity are presented in Figures 17-19 which pair high and low alpha power subjects from each group. These examples also illustrate the general findings of greater power of all EEG bands at frontal and central, relative to occipital, sites. Since the activity occurred across groups, was generally continuous and not episodic when it was present, and was reflected in the alpha power spectral data, sub-analyses based on the anomaly were not conducted.

Intermittent sleep influences

Several intermittent, potentially sleep disturbing variables were examined to determine the relative incidence of such events across groups and to explore the relationship of these events to sleep quality. These variables included: number of awakenings, abrupt EMG variations, and stage changes after motor events.

Figure 17. Illustration of control subjects exhibiting high (upper tracing) and low (lower tracing) amounts of alpha activity during slow wave sleep. Note the concentration of this activity in fronto-central recordings in this and Figures 18 and 19. The high-level examples in these figures reflect the presence of the alpha-EEG anomaly in these subjects.

DEPRESSED**High Alpha** **Low Alpha**

50 μ V |
5 sec.

Figure 18. Illustration of depressed CLBP subjects exhibiting high (upper tracing) and low (lower tracing) amounts of alpha activity during slow wave sleep.

NON-DEPRESSED CLBP**High Alpha** **Low Alpha**

50 μ V |
5 sec.

Figure 19. Illustration of non-depressed CLBP subjects exhibiting high (upper tracing) and low (lower tracing) amounts of alpha activity during slow wave sleep.

As reported in the first section of the results, there were no group or night differences in the number of awakenings. However, on night 3 there was a relative increase in TWT in both pain groups.

Movement-related variations in EMG activity during the night were scrutinized both because of the nature of the study group, i.e., low back pain, and because the literature has documented the disturbing effects on sleep of abrupt increases in motor activity. The frequency of motor events (M, MA, MT) was averaged per group within REM and NREM states and within sleep cycles (since all subjects had at least four sleep cycles, analyses were restricted to this number of cycles to maximize subject representation). Between group comparisons of all night motor events revealed no differences for all categories of movement combined, nor when considered individually [$F(2,18) = .973, p=.397$]. Prior to conducting cycle by cycle analyses, cycle (NREM and REM) durations were compared between baseline nights, to assure between-night similarity, and no differences were found (REM cycles: $p=.256$; NREM cycles: $p=.930$), therefore the two nights' data were combined for analyses. Group comparisons of cycle duration on a cycle by cycle basis did not reveal significant differences for either REM or NREM cycles, thereby assuring similar temporal opportunity across groups for cycle-related events.

With the assurance of comparability, motor events were then analyzed according to REM and NREM cycles. Analyses of brief motor events (M) during the first four NREM cycles revealed no significant group differences (Figure 20), but there was a main effect for cycle [$F(3,114) = 3.96, p=.010$], with M event frequency linearly decreasing

Figure 20. Frequency of brief motor events (M) across the first four NREM and REM sleep cycles

across the night [$F(1,38) = 9.97, p=.003$]. Group by cycle comparisons revealed a significant effect in the first cycle [$F(2, 39) = 3.46, p=.042$], with ND subjects having significantly more events than C ($p=.058$). As with the NREM data, M-activity during the first four REM periods did not differentiate groups, but a significant cycle effect was present [$F(3, 108) = 10.07, p<.0005$]. However, unlike the NREM data for this variable, the trend was for movements to increase linearly across REM cycles [$F(1,36) = 28.42, p<.0005$]. A significant group by cycle interaction was also noted [$F(6, 108) = 3.19, p=.016$], reflecting a decrease in M events in cycle 4 in the depressed group.

There were no significant group differences for movement activity (MA) during the first four NREM cycles (Figure 21), but a significant effect for cycle was found [$F(3, 114) = 2.83, p=.05$; cycle 2 > 4, $p=.002$]. MA event frequency linearly decreased across sleep cycles [$F(1,38) = 5.84, p=.021$]. There were also no significant group differences for MA events in REM sleep cycles, but once again a significant cycle effect was present [$F(3,102) = 10.86, p<.0005$], with linearly increasing MA events across cycles [$F(1, 34) = 13.69, p=.001$]. Further analyses revealed significantly more MA events in cycle 1 relative to cycles 2 ($p=.014$) or 3 ($p=.001$). There was a decrease in M's and MA's in the D group in the fourth cycle, but as reported above, cycle duration, and therefore opportunity for these events during this cycle to occur, was not different among groups.

A significant group effect for movement time (MT) was found [$F(2,38) = 3.89, p=.029$], with D subjects showing more movement than controls during the first two NREM cycles ($p=.011$ and $.038$, respectively; Figure 22). A significant cycle effect was also observed [$F(3, 114) = 2.8, p=.05$], with cycle 3 >4 ($p=.023$). MT event frequency

Figure 21. Incidence (mean values) of movement activity (MA) across the first four NREM and REM sleep cycles

Figure 22. Mean frequency of movement time (MT) across the first four NREM and REM sleep cycles

linearly decreased across NREM sleep cycles [$F(1, 38) = 4.75, p=.035$]. Comparisons across the first four REM periods revealed a significant group effect for this variable [$F(2, 35) = 3.29, p=.049$], with depressed subjects showing significantly more MT events in cycles 1 (D>C and ND, $p=.03$) and 3, (D>C, $p=.03$). A significant cycle effect was present [$F(3, 105) = 5.17, p=.004$] with a significant quadratic trend [$F(1, 35) = 9.21, p=.005$; cycle 3>1, $p=.002$]. There is also a significant group by cycle interaction [$F(6, 105) = 2.59, p=.031$], with D subjects showing a decrease in MT's in cycle 4 relative to cycles 1-3 and ND and C groups' MT incidence remaining relatively linear across REM cycles.

To examine the potentially disturbing effect of these movements on sleep, stage changes following each movement category were counted and averaged per group within the first four NREM sleep cycles. For all categories, between-night comparisons were made to determine night-to-night stability. These analyses did not detect any significant cycle by cycle between-night differences, and therefore data were collapsed across nights for subsequent analyses. No group differences were found for combined movement categories. However, a significant cycle effect [$F(3, 348) = 5.09, p=.003$; cycle 1>4, $p=.003$ and cycle 2>4, $p=.012$] was present. Analyses for each movement category-associated stage change also failed to detect significant group differences (Figure 23). However, a cycle effect for M-associated stage changes was present [$F(3, 114) = 3.63, p=.022$; cycle 1>4, $p=.030$], and there was a linear decrease in M-stage change events across sleep cycles [$F(1, 38) = 11.01, p=.002$]. MA-associated stage change analyses revealed no group differences, but a significant cycle effect [$F(3, 114) = 3.04, p=.04$;

Figure 23. Frequency of movement (M and MA) associated stage changes across the first four NREM sleep cycles.

cycle 1>4, $p=.03$ and cycle 2>4, $p=.002$]. MT- associated stage change analyses revealed neither group nor cycle effects.

Taken together, these analyses indicate that a higher incidence of movement-associated stage changes occur following both M and MA events during the initial sleep cycles -- an effect present in all groups.

Relationships among measures of sleep quality, pain, depression and EEG power

Analyses were conducted to evaluate relationships among group discriminating sleep variables and measures of pain, sleep quality, and depression. Frontal EEG power spectral measures were excluded since results from frontal and central sites were virtually identical, because of proposed functional differences for central and occipital sites, and since multiple across-stage differences were obtained for these sites in this study.

Correlational analyses require similar types of variables and since the log transformed EEG μV^2 values are non-linear, non-transformed EEG data were used for these comparisons. EEG power during slow wave sleep was used in these correlations because of observed group differences in motor events occurring during the first sleep cycle, the concentration of SWS at this time, and the reported importance of SWS integrity for sleep quality.^{61,84,103}

The correlations were generally low and predominantly non-significant (Table 8). The only comparisons that reached significance were positive relationships involving ND and C subjects and EEG measures derived from the central site. ND subjects exhibited greater high beta power and more night pain ($r=.75$), suggesting higher levels of arousal associated with high pre-sleep pain scores, and higher alpha power with higher morning

Table 8. Pearson product moment correlations between sleep quality, pain, depression scores and site-specific SWS EEG power (μV^2) D/ND/C – C₃ above the solid line, O₂ below.

	Delta	Alpha	Sigma	High Beta	Quality	BDI
Npain	<u>.68/.38</u> .70/.15	<u>-.19/.62</u> .03/.34	<u>-.06/.50</u> .42/-.30	<u>-.39/.74*</u> -.60/.19	-.43/-.34	.56/.24
Mpain	<u>-.21/.14</u> .11/.05	<u>-.04/.75*</u> .55/.13	<u>.11/.36</u> .69/-.16	<u>-.26/.55</u> .32/.001	-.51/-.17	.58/.19
Quality	<u>.06/.03/.40</u> .09/.28/.20	<u>.04/.001/.56*</u> -.19/.12/.38	<u>.008/.03/.18</u> -.25/.36/.05	<u>.11/-.12/.58*</u> -.007/.05/.18		-.21/-.41
BDI	<u>.12/-.03</u> .59/-.58	<u>-.53/-.28</u> .06/-.33	<u>-.32/-.51</u> .58/-.60	<u>-.73/.26</u> -.50/.13		

*p<.05

pain scores. Controls had a positive relationship between alpha and high beta power and sleep quality -- the polar opposite to expected associations. Although there were few significant correlations among these variables, certain trends warrant mentioning. For example, the association between pain (whether prior to, or after sleep) and C₃ EEG power in SWS was opposite for the two pain subgroups, i.e., it was generally negative and low for D subjects and positive and relatively high for ND subjects. ND subjects showed essentially no association among pain levels and any occipitally-derived EEG parameter. For D subjects there is an indication that higher morning pain scores are associated with high occipital sigma power ($r=.69$), and higher pre-sleep pain scores are associated with decreased high beta power ($r= -.60$). Also there was a positive correlation among pain scores and depression for D subjects [$r=.56$ (pre-sleep pain); $r=.58$ (morning pain rating)]. There was a notable lack of significant correlations among sleep quality measures, EEG power measures in SWS and depression scores among pain subjects.

DISCUSSION

The present study was conducted to evaluate various sleep parameters in CLBP subjects, relate variations in these measures to sleep complaints, and determine the comparability of these variables across pain subjects with and without depression.

Examination of the descriptive characteristics and questionnaire data confirmed both the effectiveness of efforts to reduce known sources of between-group variability (e.g., age and correlated EEG changes) and to ensure the presence of intended between-group differences (e.g., pain, depression and sleep quality). The control group proved to be free from complaints of pain and depression, and exhibited stable, good sleep quality. In one respect, categorizing the limited number of pain subjects into depressed and non-depressed groups diminished the statistical power of the study by further dividing an already relatively small sample. However, finding significant differences between these pain subgroups on behaviours (e.g., higher pre-sleep pain levels in D subjects) and sleep-associated measures (e.g., higher power in delta, alpha and high beta activities in D subjects) reinforces the previously recognized need to assess the contribution of depression in studies of pain populations where this condition has been shown to be a prominent factor.^{12,42,43,112,158}

General sleep characteristics

The analyses of global sleep measures demonstrated that all groups evidenced significant degrees of sleep disturbance on night 1 relative to nights 2 and 3, with little variability on the latter baseline nights -- findings consistent with adaptation to the laboratory environment. The absence of group differences on night 1 indicates that the

CP condition, even when compounded by depression, does not exacerbate sleep disturbance associated with the adaptation effect. This adaptation night sleep disturbance might be expected to result in a significant decrease in sleep quality relative to baseline nights. However, although all groups reported some improvement in sleep quality on mornings following baseline nights relative to that following the adaptation night, these variations were not statistically significant. These findings may highlight an unexpected result that suggests the DSD questionnaire is not sensitive to objective changes that occur with adaptation or that the nature of adaptation night disturbances does not impact significantly on this sleep quality measure. Nevertheless, the questionnaire consistently indicated significantly poorer sleep quality in pain subjects relative to controls throughout the study, and the mean scores observed in the present study were comparable to those reported in the validation study for that measure using CLBP subjects.⁷⁶ It is apparent that the objective measures of sleep and sleep disturbance measures used in this study do not accurately reflect subjective complaints of reduced sleep quality

In view of the persistent complaints of sleep disturbance and reduced sleep quality described by CLBP subjects in this study and in the literature,^{119,155,224} it was surprising that none of the sleep measures expected to reflect these complaints, i.e., latency to sleep onset, total sleep time or sleep stage amounts significantly differentiated study groups. The one significant group difference which was observed, i.e., TWT on night 3 (ND>C), does suggest increased sleep disturbance in pain subjects relative to controls, but this difference could be explained by the decreasing amounts of TWT in controls across study nights. The failure to detect previously reported depression-related sleep variations in

this study, e.g., shortened REM onset latency or longer early REM periods,⁹ or to observe the hypothesized enhanced differences for depressed pain subjects on other sleep measures, is likely due in part to the reduced severity of depressive symptomatology in the pain subjects relative to depressed subjects without complaints of pain in other studies.^{8,28} Still, the literature strongly indicates a synergistic effect between pain and depression -- an effect which was expected to be reflected in modified sleep architecture in depressed pain subjects. Such variations were not observed despite the subjects' self-reports reflecting significantly impaired sleep quality and continuous high pain intensity.

Taken together, the evaluation of general sleep characteristics provided little evidence of group differentiation. This may indicate that CLBP subjects, who report poor sleep quality on a regular basis, are adapted to sleep disturbance and are less sensitive to changes that might be appreciated by normals (such as night 1 disturbance), or that the standard sleep parameters do not reflect the source(s) of their sleep complaints.

Physiologic measures and arousal during sleep

Heart rate

This study was the first to analyse heart rate variables during sleep in any pain population, and consistent with suggestions of 'lighter' sleep or an increased level of arousal in pain subjects, it was hypothesized that CLBP subjects would show increased heart rate and/or heart rate variability. Results of these analyses, based on a large, carefully screened, precisely measured dataset (i.e., two whole nights), were unequivocal in not demonstrating any significant differences among groups on these cardiovascular measures. CLBP subjects did have a higher mean heart rate (but n.s.) suggesting a

possible physiologic difference consistent with a higher level of arousal in these subjects. However, other behavioural factors known to result in elevated heart rate characterize CLBP, e.g., a low level of fitness.¹²²

EEG power spectral analyses

Power spectral analysis of EEG activity during sleep provides information which supplements that obtained by visual stage scoring. With this approach quantification of specific EEG frequency bands -- not considered because of the amplitude criteria-based stage scoring,¹⁶³ or simply impossible to evaluate by visual inspection -- can be determined and compared. Accordingly, these analyses were expected to provide additional evidence of increased arousal in pain subjects relative to controls.

In the present study, the observed EEG power values across frequency bands and the distribution of these activities across sites are generally consistent with published reports using power spectral analysis in normal adult populations, i.e., delta EEG power was highest, with power across bands focussed fronto-centrally.^{8,11,53,54,105} Across frequencies REM sleep exhibited the lowest power values in all but one of fifteen site- and stage- specific comparisons. The few significant group- and frequency-specific stage differences which were observed will be discussed and related to measures of arousal and sleep quality.

Delta activity

Delta activity, the principal component of slow wave sleep, has been associated with sleep maintenance and sleep depth.^{47,48,61,83,101,106,205,207} Since slow wave sleep is compromised by sleep fragmentation,¹⁷ it was hypothesized that there would be less delta

power in the pain subjects. In the present study, delta power values were the highest of all frequency bands, showed a fronto-central concentration, was most prominent in slow wave sleep, but had substantial representation across sleep stages. However, although the fronto-central concentrations of delta power were lower in D and ND than in C subjects, these differences were not significant. Consequently, to the extent that delta activity can be taken to reflect sleep depth and level of arousal, these results suggest no significant differences between pain and control subjects along this dimension. Since functional correlations of delta power relate to this activity at frontal and central sites,¹⁶¹ the finding that occipital delta power was greater in D subjects relative to ND is of uncertain significance.

Alpha activity

Alpha EEG activity during sleep has been associated with arousal (but see¹⁵⁷) and the presence of alpha activity in slow wave sleep (alpha-EEG anomaly) has been interpreted as a basis for non-restorative sleep complaints.^{128,132,133,222} It was therefore expected that there would be more alpha activity in the pain groups than controls across recording sites.

All groups exhibited this activity during all sleep stages, with the least amounts in REM across sites, and highest amounts in SWS frontally and centrally (Figure 13). The D subjects showed the highest power across recording sites -- amounts not different than controls -- but significantly greater occipital and frontal power than ND subjects. The alpha-EEG anomaly as described,^{74,136,137} was clearly evident in the polygraphic sleep recordings (Figures 17-19) of several subjects and was reflected in higher power spectral

values for alpha in these subjects. However, such subjects were present in all groups. These observations, together with the absence of pain-control group differentiation based on amounts of alpha activity, do not indicate the selective occurrence of this anomaly in pain subjects. Furthermore, in the absence of evidence in pain subjects of lighter sleep (e.g., no increase in number of awakenings), these analyses do not support the interpretation of the alpha-EEG anomaly as an indication of a higher level of arousal during sleep. One finding consistent with expectations was that of higher alpha power across groups recorded at the fronto-central, relative to occipital sites. Although an alternative functional interpretation of fronto-central vs. occipital alpha activity has been proposed,¹⁵⁷ i.e., that fronto-central alpha activity is associated with a sleep maintenance function, the lack of group differentiation at these sites does not provide additional insight into these considerations.

Sigma activity

Although sleep spindles are considered defining characteristics of stage two sleep, they are present in all sleep stages except stage 1 and REM.¹⁶³ Spindles have been reported to reflect thalamocortical activation associated with a decrease in sensorimotor transmission,¹⁹⁶ and are considered to be 'sleep protective'.¹⁰¹ In the whole night analyses of sleep EEG activity, power spectral analysis does not selectively quantify periodic waveforms or rhythms such as spindles, but combines periodic and aperiodic activity within frequency bands. Consequently, the sigma frequency band, although including spindle activity, does not represent only spindles, but all activity falling within the 12-14 Hz. frequency range. Dijk⁴⁸ studied the spindle/sigma relationship using power spectral

analysis and an automated spindle detector, and concluded that changes in sigma power across the night closely correlated with the pattern of spindle activity. This association has been adopted by others as an accepted approach to power spectral analysis of spindle activity.¹⁰⁷ For the reasons cited above, accepting sigma power as a discriminating measure of spindle activity is questionable. An indication of the extent to which sigma activity occurs independent of spindles is evident in the presence of appreciable amounts of sigma activity in stage 1 and REM sleep, both states during which, by definition, spindles do not occur. These observations raise questions regarding whether sigma activity during sleep, when it is not reflecting rhythmic spindling, still represents the thalamic blockade of sensory information as has been shown for spindles.¹⁶³ Although this relationship has not been evaluated, the following discussion assumes that sigma activity is associated with a sleep protective function.

Since a greater intensity of sleep spindles is associated with more sleep protection, or a greater sleep depth,²² it was expected that control subjects would have more sigma activity than pain subjects, reflecting a “deeper”, undisturbed sleep. This expectation was confirmed across sites, with controls having significantly greater sigma power than non-depressed subjects fronto-centrally. Analyses of sigma activity at the occipital site produced the only power spectral finding distinguishing controls from both pain subgroups -- i.e., higher sigma power in C relative to either D and ND subjects. With the view that higher levels of sigma activity indicate more effective thalamocortical gating of sensory information, reduced sigma activity in pain subjects may be interpreted as increased sensory processing during sleep which could interfere with the processes

contributing to perceived “good sleep”.

The stage power ranking for sigma activity found in this study (4>3>2>1>REM) differs from findings in the literature that indicate the highest sigma power in stage 2.^{8,48,54,209} However, since these cited publications differ from the present study in terms of data collection (electrode montage⁵⁴), processing techniques (period amplitude analysis⁸), and statistical procedures (the use of Z-scores^{48,209}), it is impossible to determine whether this difference is real or procedural in nature.

Delta and sigma activity have been described as reciprocally related during NREM sleep (i.e., when delta power is high at the beginning of the night, sigma is low, and as the night progresses, delta power decreases and sigma increases), but not during REM sleep, when both delta and sigma power are low.²⁰⁹ In the present study, the fronto-central concentrations of these activities show virtually identical between-group across-stage patterns (Table 7). Although analyses were not conducted to evaluate cycle by cycle delta-sigma reciprocal relationships, if this relationship were present it would be expected that power in stage 4 would be high for delta and low for sigma. The finding that both frequencies demonstrated their highest power values at this time does not provide support for such a relationship.

Beta activity

Beta activity, considered to be an index of arousal during wakefulness and sleep, is reported to be fronto-centrally focussed, with maximal power found in higher frequency bands.²³⁰ In keeping with the postulated increased arousal in pain subjects, it was hypothesized that beta power would be higher in these subjects than controls. Low

(14-20 Hz) and high (20-25 Hz) frequency beta were examined in this study, and high beta values were greater across sites consistent with other findings.²³⁰ Similar to the present results, Traschel²⁰⁴ reported greater low beta power in SWS and stage 1 relative to REM. Others have reported a progressive increase in high beta power from slow wave to stage 2 to REM sleep.^{207,208} These results were obtained using different statistical procedures, perhaps explaining the different findings from the present study where REM sleep ranked among the lowest power values. Neither high nor low beta activity differentiated control from both pain groups. Differences which were present discriminated C from ND (occipital and frontal low beta) or D subjects from ND and C (high beta, all sites).

Increased beta power (18-28 and 28-50 Hz bands) has also been observed in depression and interpreted as indicating a 'higher level of arousal' during sleep.^{104,208} The high beta band in the present study falls within these frequency ranges and, in agreement with Uchida's findings,²⁰⁷ D subjects consistently had significantly greater high beta power than either comparison groups across sites. Although this group differentiation supports the high beta-depression association, the extent to which it is related to the pain experience and arousal remains to be demonstrated.

Power spectral beta activity has also been evaluated in terms of patterns of activation across the night. Uchida²⁰⁷ reported differences in these patterns between low (15-23 Hz) and high (20-28 Hz) beta, with high beta displaying clear oscillations positively related to delta power oscillations in NREM and REM, and low beta not exhibiting clear cyclic patterns. Although high-low beta differences were evident in the

present study, i.e., when ranked by stage, low beta rankings were more similar to those of slower frequency bands and unlike high beta ranking, the presence of in-phase, delta-high beta variations could not be evaluated since the cycle-based analyses of Uchida cannot be compared to whole-night, stage-specific EEG power as this study.

Sleep fragmentation

Although it appears obvious that major interruptions of sleep would result in daytime reports of poor sleep quality, it is less apparent that brief disturbances, which are often unnoticed by the sleeper, should have a significant impact on sleep quality. However, interruption of sleep continuity by brief arousals, particularly during the first part of the night and which do not effect a significant decrease in total sleep time, has been shown to result in reports of poor quality sleep and decrements in daytime performance.^{17,170,193} Several studies have reported the presence of high numbers of fragmentary events, such as leg movements and awakenings, in the sleep of CLBP subjects.^{138,190} It was therefore expected that such disruptions would characterize sleep in pain subjects in this study. Surprisingly, the whole-night averages of sleep fragmenting events (number of awakenings and motor events) did not differentiate pain from control subjects. However, analyses of the distribution of motor events across the night revealed a reduced incidence in C during the first NREM cycle, compared to a concentration of these events at this time for D and ND subjects. All categories of movement events showed similar patterns of incidence across the night, i.e., most frequent in the first NREM cycle and subsequently decreasing during NREM sleep, but increasing across REM periods. Of the various categories of motor events, MT presents the most

significant sleep disruption, and D subjects had significantly more MT events during the first two NREM and the first and third REM cycles relative to the comparison groups. However, since compared to M's and MA's these events occur infrequently (Figures 20-22), it is unlikely that they contribute significantly to sleep disturbance having an impact on sleep quality measures.

The brief motor events reported here resemble PLMs, but do not meet PLM criteria,²⁰¹ since PLMs are noted primarily during lighter sleep (stages 1 and 2) and are virtually absent in REM, whereas in the present study M events were focussed in SWS, dominating the first NREM cycle, and were also present in REM sleep. Since several studies have shown the importance of sleep continuity to sleep quality during the first part of the night,^{17,116,170,193} it may be that the increased motor events, particularly the higher incidence of M events at this time, are sufficiently disturbing to contribute to the sleep complaints in this population.

Interactions between sleep/chronic pain

The effect of sleep on pain

It would be logical to expect that the decreases in sensory transmission and awareness during sleep would provide some relief from pain for CLBP subjects. However, behaviours during wakefulness can also influence sleep, e.g., exercise or acute psychological distress^{13,73,84} The complex pathophysiology of CLBP and its impact on measures in both waking and sleep make interpretation of interacting factors difficult. The results of this study, while not offering resolutions of these condition (pain) - state (sleep-wake) interactions, nonetheless provide suggestive insights into these

relationships. For example, regarding the effects of sleep on pain perception, CLBP subjects did not report awakenings resulting from an awareness of pain during sleep. However, analyses of pain scores revealed that ND subjects' pre- and post-sleep pain generally remained the same, but D subjects reported lower pain in the morning relative to pre-sleep ratings. Furthermore, consistent with the finding that self-reports of symptoms are often amplified in depression,^{1,50,126,213} D subjects in this study generally reported greater pain than ND subjects. These findings differ from reports of FM subjects who rate their pain higher in the morning compared to the night before.¹³¹ Since ND subjects did not report a decrease in pain after sleeping, apparently the ameliorating effect of sleep on pain -- as limited as it might be -- occurs only with depressed CLBP subjects. One speculative explanation for this observation could be that the fragmentation of sleep in D subjects has a beneficial effect on depressive symptoms²²⁹ in a way which, because of the interaction among depression, sleep and pain, results in lower pain perception in the morning.

The effect of pain on sleep

Relevant to the consideration of how CP might influence sleep are recent efforts to explain CP on the basis of CNS sensitization. It is believed that injury results in an alteration of sensory transmission such that stimuli not normally perceived as painful evoke a painful response (allodynia)³² and an excessive response is elicited by a noxious stimulus (hyperalgesia).³⁸ The persistence of this sensitization leads to behaviours in animals consistent with symptoms of chronic pain in humans. This state of hypersensitivity is referred to as a 'windup' of sensory processing and occurs in the spinal

cord, thalamus and cerebral cortex.^{37,52,124} The role of windup in animal models of CP is currently the focus of intense study, with drug trials involving the use of *N*-methyl-*D*-aspartate (NMDA) and sodium channel blockers in an attempt to attenuate the negative effect of windup on pain perception.^{39,40,45,59,184,202,219} Still unknown is how and within what time frame the CNS can and will “unwind”. If the windup model does mimic CNS processes involved in human CP, then perhaps the decreased motor and sensory transmission that occurs during sleep provides a dampening of neurotransmission and a consequent decrease in sensitization, until awakening re-activates the system and movement re-stimulates nociceptors. With this view, the first NREM sleep cycle -- which is normally associated with high arousal thresholds, reduced motor activation and which occurs contiguously with daytime wakefulness -- presents the first opportunity for the sensitized CNS to wind down. This initial sleep period may be associated with decreased sensory transmission, but, as with twitches in REM sleep,⁶⁷ if activation is sufficient, motor responses will be expressed and possibly disturb sleep. Such motor-release activity during early sleep periods is not unprecedented, e.g., hypnic jerks (brief motor events, comparable to M events) are considered normal, are associated with sleep onset, but tend to decrease in frequency as greater EEG synchronization (slow wave sleep) occurs.⁴⁴

Are there muscle-related changes in CLBP subjects that may relate to increased motor activity during early sleep periods? It is recognized that changes in muscle physiology secondary to low back pain are inevitable, because with a decreased ability to carry out regular activity without pain, people with CLBP avoid excessive movement

which results in a lower level of fitness. This decrease in muscular activation is associated with localized as well as general muscle atrophy in the presence of muscle spasm associated with the injury. Together, these factors lead to muscular imbalance, with excessive activation of weak muscles and increased muscle tone.^{122,147,168,221} During the relaxation process which accompanies sleep onset, muscular tension progressively decreases, a process which can be facilitated by relaxation training.⁸⁹ CLBP is associated with higher levels of paraspinal muscle tension as measured by EMG⁷ requiring a greater potential decrease in muscle tone to achieve relaxation during sleep. Sleep-onset hypnic events are thought to be triggered by phasic reticulospinal activation of alpha motor neurons and result in motor unit firing.⁴⁴ The potentially longer period required to achieve muscle relaxation in CLBP subjects, coupled with sleep onset alpha motor neuron activation of an already sensitized CNS, could explain the higher incidence of motor events during the first NREM cycle, as well as the return to normal levels of motor activity at later times when muscle relaxation has occurred. The impact of these events on sleep quality may be amplified by the postulated reduction in thalamocortical gating associated with lower levels of sigma power in pain subjects.

CONCLUSION

CLBP, like most CP conditions, is characterized by a complex combination of interacting physiologic and psychologic features which contribute to the intensity and chronicity of the clinical condition. The study variables chosen for evaluation, i.e., measures of sleep disturbance and the presence of depression, are among the most commonly presented complaints in CLBP and have been demonstrated to have a synergistic effect on pain intensity. This investigation was designed to identify the nature of sleep disturbance in CLBP subjects and perhaps provide insight into future treatment strategies that could decrease the contribution of disturbed sleep on waking pain and depression complaints. It was also hoped that results of this study might provide objective correlates of reports of poor sleep quality and unrefreshing sleep characteristic of CP subjects.

To achieve these goals, a wide array of physiological measures and analytical procedures were employed and interrelated. Also, waking measures of pain intensity, sleep quality and depression were collected and analysed. Surprisingly few of these measures distinguished control from pain subjects. In fact, although poor quality sleep is a very common complaint in these subjects, when compared with the extent of sleep disruption occurring in major sleep disorders, the nature of the sleep disturbance in CLBP as reported here, might be viewed as 'minor'. The few comparisons that did demonstrate group differences, suggest that increased motor activity early in the night, coupled with indications of reduced sensorimotor gating (i.e., low sigma power), may contribute to reports of poorer sleep quality in these subjects. The fact that D and ND subjects were

significantly different on several measures, and that often C subjects ranked between D and ND subjects on power spectral parameters, demonstrated the different presentation of CLBP with and without depressive symptoms, and underscores the importance of considering the influence of depression in the evaluation of sleep in clinical populations. .

CLBP subjects were selected for study because of the importance and prevalence of this problem, but also to evaluate the generalizability of previous findings -- largely from studies of FM subjects -- to other CP populations. In this regard, the present findings indicate that sleep has different effects on reported pain levels in FM, D and ND pain subjects. Unlike D and ND subjects, those with FM report increases in pain after sleep.¹³⁷ Furthermore, in contrast to both ND and FM subjects, D subjects reported an improvement in their post-sleep pain scores. Since the majority of FM patients are depressed,¹²⁸ and FM and D subjects' post-sleep pain reports change in opposite directions, there appears to be a differential effect of sleep on pain. The findings suggest that when considering the interaction among pain, depression and sleep, the type of CP needs to be differentiated.

In summary, the study successfully provided a relatively comprehensive evaluation of sleep parameters in CLBP and the results offer insight into the complex sleep-wake interactions in these subjects which could have treatment implications. However, the extent to which the findings provide a better understanding of the physiologic basis for the measure of sleep quality will have to await studies of larger, diverse populations with these complaints.

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APPENDICES

APPENDIX A - Inclusion /Exclusion Criteria Checklist

Inclusion/Exclusion Criteria Checklist
"Chronic Pain, Sleep and Depression"

PART A - TRC - Multidisciplinary Pain Clinic _____ **DATE:** _____
TRC - Complex Pain Consult Clinic _____
OGH - Pain Clinic _____
OCH - Pain Clinic _____

Candidate's Name _____ **Phone Number:** _____
 (Only provide name and phone number if individual meets initial selection criteria)

Inclusion Criteria:	IF EXCLUDED, SPECIFY:
(1) Chronic Low Back Pain	Diagnosis:
- 6 months - 7 years duration	
- the presence of neck pain with back pain does not exclude the candidate	
(2) 25 - 50 years old	Age:

Exclusion Criteria:

(1) Adolescent Onset of Pain (before 18)	YES _____	NO _____	
(2) Hard of Hearing	YES _____	NO _____	
(3) Fibromyalgia			
i) History			
Pain left side of body	YES _____	NO _____	
Pain right side of body	YES _____	NO _____	
Pain above waist	YES _____	NO _____	
Pain below waist	YES _____	NO _____	
Axial Skeleton pain	YES _____	NO _____	
- Above pain at least 3 months			
ii) Tender Points - Pressure Threshold Meter Protocol			
- Positive if 4 kg or less elicits a "yes" response to discomfort.			
- Test to be stopped at sign of discomfort or at 5 kg. force.			
- Force applied at the rate of 1 kg/second, 90 degree angle to skin.			
- Repeat testing of same trigger point at least 5 mins. apart.			
Occiput (suboccipital muscle insertion site)	R _____	L _____	
Low Cervical C5 C6 intertransverse space	R _____	L _____	
Trapezius - mid point (upper border)	R _____	L _____	
Supraspinatus - above scapular spine (medial)	R _____	L _____	
Second Rib - costochondral function	R _____	L _____	
Lateral epicondyle - 2 cm distal	R _____	L _____	
Gluteal - upper outer quadrant	R _____	L _____	
Greater trochanter - just post. to troch. prominence	R _____	L _____	
Knee - medial fat pad proximal to jt. line	R _____	L _____	

TOTAL SCORE _____

Fibromyalgia Diagnosis Yes _____ NO _____
 YES - If positive history + 11/18 trigger points

(4) **Patient is on medication that would affect sleep?** NO _____
 YES - Specify _____

 Narcotics - less than 180 mg/day of codeine or other narcotic equivalent
 Antidepressant - subtherapeutic for depression e.g. <75mg amitriptyline

Appropriate for Withdrawal	YES _____	NO _____
Has candidate been counselled on medication withdrawal?	YES _____	NO _____
Has candidate agreed to withdrawal schedule?	YES _____	NO _____

		Present	Absent	Not Assessed
(5)	Medical Disorders Known to Affect Sleep			
	neurological disorders	_____	_____	_____
	parkinsonism	_____	_____	_____
	dementia	_____	_____	_____
	epilepsy	_____	_____	_____
	asthma	_____	_____	_____
	chronic obstructive lung disease	_____	_____	_____
	restrictive lung disease	_____	_____	_____
	cardiovascular disease	_____	_____	_____
	nocturnal angina/arrhythmias/hypertension	_____	_____	_____
	gastrointestinal disorders	_____	_____	_____
	gastroesophageal reflux during sleep	_____	_____	_____
	neuromuscular disease	_____	_____	_____
	affecting respiratory status	_____	_____	_____
(6)	Sleep Disorders			
	sleep apnea	_____	_____	_____
	narcolepsy	_____	_____	_____
	restless legs syndrome	_____	_____	_____
	hypersomnia (e.g. Kleine-Levin Syndrome)	_____	_____	_____
(7)	Other conditions known to affect sleep			
	shift work	_____	_____	_____
	bruxism	_____	_____	_____
(8)	Current Psychiatric Disorders	COMPLETE IN CLINIC (IF KNOWN)	DR. SWENSON	
-	schizophrenia	_____	_____	
-	anxiety	_____	_____	
-	alcoholism	_____	_____	
-	other drug abuse	_____	_____	
-	dysthymia	_____	_____	
-	mania	_____	_____	
	Psychiatric history			
-	depression prior to chronic pain	_____	_____	

CONSULT sent to J.R. Swenson YES ____ NO ____ (screening only)
 If yes, reason for Consult: _____

SCID Assessment (if available):

Psychologist _____
 Classification: Depressed ____ Not Depressed ____

Complete any information available for Part A (8),
 CALL J. D'EON (564) to pick up form

PART B - Katherine Harman (CALL 737-8064)

Date Seen: _____

Checklist:

_____ consent form
 _____ medication withdrawal (date: _____)
 _____ questionnaires
 _____ daytime recording

PART C - Dr. J.R. Swenson - Psychiatric Screening - Part A, (7) above

Date Seen: _____

Subject suitable for participation in project? YES ____ NO ____

Comments: _____

Request follow-up evaluation for depression management: YES ____ NO ____

PART D - Audiology Evaluation

Hearing Normal YES ____ NO ____

PART E - SCID Assessment - If not completed in Clinic

Psychologist _____

Date Seen _____

Classification: Depressed ____ Not Depressed ____

PART F - SLEEP RECORDINGS

Dates 1. _____
 2. _____
 3. _____
 4. _____

Notes: _____

APPENDIX B - Information sheet

FACULTÉ DE MÉDECINE
FACULTY OF MEDICINE

FEUILLE DE RENSEIGNEMENTS

Ce projet est fait en collaboration avec l'Université d'Ottawa, l'Université de Carleton, l'Hôpital Générale d'Ottawa, the Royal Ottawa Health Care Group, sous la direction du Dr. R.T. Pivik.

Titre: *La douleur chronique, le sommeil et la dépression.*

Description générale

Cette étude a pour but d'évaluer la perturbation du sommeil vécue par les personnes ayant de la douleur chronique au niveau du dos. De ces personnes, certaines sont déprimées et d'autres ne le sont pas. Dans cette étude, nous étudierons ces deux groupes. De plus, dans un but de comparaison, nous étudierons aussi les personnes qui n'ont pas de problèmes de sommeil, de douleur chronique ou de dépression. Pour des raisons de méthodologie, nous allons étudier les sujets 25 à 50 ans. Nous vous avons choisi parce que vous appartenez à un des groupes décrit ci-dessus.

Si vous acceptez de participer à ce projet, vous devez remplir des questionnaires qui portent sur le niveau de votre douleur, la qualité de votre sommeil et comment vous vous sentez et vous aurez une entrevue avec un psychiatre, un psychologue, une évaluation d'un médecin et une d'un audiologiste. Vous serez invité à venir au laboratoire de sommeil à l'Hôpital Générale pour cinq visites. La première visite se déroulera durant la journée afin de vous familiariser avec le laboratoire, l'environnement et les procédures d'enregistrement. Au cours de cette rencontre, des électrodes et des moniteurs vous seront installés. La durée de la séance d'enregistrement est environ d'une heure. Pour les quatre rencontres qui suivront, vous allez dormir dans le laboratoire où les mêmes procédures d'enregistrement seront appliquées. Vous devez vous présenter une heure avant votre heure normale du coucher afin de nous laisser le temps d'attacher les électrodes. Celles-ci vous seront installées pour toute la nuit. Au matin, les coûts pour un petit déjeuner à l'hôpital et le stationnement ou l'autobus vous seront défrayés. Durant les quatre jours de l'étude, on vous demande de ne pas faire de siestes ni de consommer de l'alcool, mais de continuer toute autre alimentation habituelle ainsi que vos activités de routine. Afin d'enregistrer vos activités durant la journée, on vous demande de porter un moniteur de l'activité (un "actigraph"), qui ressemble un montre, durant les mêmes quatre journées.

La préparation dans le laboratoire

Un technicien placera les électrodes sur votre tête, sur votre visage, sur votre thorax, sur un doigt, et sur vos deux jambes, pour enregistrer l'activité électrique quand vous dormez. Pour ne pas briser la peau, les électrodes seront installées en surface. Les fils électriques étant minces, ils sont ramassés derrière la tête et sont connectés à l'ordinateur. Vous dormez sur un lit simple qui est dans une petite pièce insonorisée. Vous êtes toujours en contact verbal

avec le technicien qui est installé dans la pièce adjacente. Lors de la quatrième nuit, une mesure additionnelle enregistrera sera prise, le son le plus bas nécessaire pour vous réveiller. Un petit transmetteur de tonalité sera placé dans votre oreille et un bouton sera placé dans votre main. Pendant la nuit, environ 8 à 10 fois, des tonalités vous seront présentées à travers le transmetteur. Aussi-tôt que vous entendez les tonalités vous devez presser le bouton dans votre main trois fois et dire au technicien quel est le niveau de votre douleur à ce moment précis (échelle de 0 à 5). Puis vous pouvez retourner à votre sommeil. Une fois que les électrodes sont enlevées (au matin), il reste un peu de colle qui peut être facilement enlevée avec de l'eau tiède et du savon.

Les risques et inconvénients

Un lit différent et l'attachement des électrodes pourraient perturber votre sommeil. Pour ces raisons, il faut étudier le sommeil durant quatre nuits consécutives. Normalement, vous devriez être adapté par la troisième nuit. À cause de la présentation des tonalités, c'est possible que durant la quatrième nuit vous allez sentir que votre sommeil est un peu perturbé. À part ce léger dérangement du sommeil, il n'y a pas de risque ou d'inconvénient associée à cette étude.

Bénéfices

Le but de l'étude est de mieux comprendre la perturbation du sommeil vécue par les personnes ayant de la douleur chronique. Les conclusions de cette étude nous aiderons à développer de nouvelles approches de traitement pour ces problèmes. Le seul bénéfice direct que le sujet pourrait gagner est une plus grande compréhension du dérangement de son sommeil.

Participation dans l'étude

Votre participation dans ce projet est complètement volontaire. Vous avez le droit de refuser de participer sans craindre d'un impact sur votre traitement éventuel. De même, vous pouvez vous retirer de l'étude sans porter préjudice à votre traitement. Une copie du formulaire de consentement dûment signée vous sera remise.

Confidentialité

Vous êtes assuré que toute l'information vous appartenant sera traitée seulement en référence d'un numéro assigné et que pour de futures publications ou présentations. Seulement les chercheurs impliqués dans le projet auront accès aux données de l'étude. Comme participant à l'étude, vous pouvez contacter Dr. Pivik pour obtenir de l'information sur l'étude en cours.

Pour de plus amples informations, appelez: Dr. R.T. Pivik, Dept. Psychiatrie, pièce 4431, l'Hôpital Générale, 737-8040; Dr. Goss, le Président du comité de déontologie (l'Hôpital Générale), 737-6792, ou Dr. Latter, le Président du comité de recherche de déontologie (Centre de Réadaptation), 737-7350.

FACULTÉ DE MÉDECINE
FACULTY OF MEDICINE

INFORMATION SHEET

This is a collaborative research project, under the direction of Dr. R.T. Pivik, between the University of Ottawa, Carleton University, the Ottawa General Hospital and the Royal Ottawa Health Care Group.

Project title: *Chronic Pain, Sleep and Depression*

General Description:

This is a study of sleep disturbance experienced by people with chronic low back pain. Some people with chronic pain are clinically depressed and others are not. We will study both groups. We will also study and compare the sleep of people who do not have problems with sleep, pain or depression. The investigation will include subjects 25-50 years old. You are being asked to participate in this study because you fall into one of the above categories.

If you agree to participate in this study, you will complete questionnaires on pain levels, sleep quality and how you are feeling, and you will be interviewed by a psychiatrist, a psychologist, examined by a physician and an audiologist. You will also be required to come to the sleep laboratory at the Ottawa General Hospital five times. The first time will be during the day to introduce you to the laboratory staff, environment and recording procedures. This will take approximately one hour. For four nights, you will sleep in the lab overnight where the same recording procedures will be followed. You will come to the lab approximately one hour before your usual bedtime for electrode application. In the morning, we will provide breakfast at the hospital cafeteria, and will compensate you for parking costs or bus fare. During the four days of the study, we ask you to refrain from daytime napping and alcoholic beverages but to otherwise carry on normal food and drink consumption, and normal daily activities. In order to monitor your daytime activity, you will be asked to wear a wristwatch-like unit on your non-dominant wrist during the daytime of the recording period.

Laboratory Recordings:

A technician will attach small disc electrodes on your head, face, chest, finger and legs to record activity from these sites while you sleep. These electrodes are attached to the skin with adhesive collars, except on the scalp where the presence of hair will not allow the use of these collars; here an adhesive mixture is used which is washed off in the morning. Spontaneous signals detected by the electrodes are led to equipment which records this activity. The single bed is in a sound-insulated room, and you are in voice contact via an intercom system with the technician (in the adjacent room) throughout the night.

During the fourth night of recordings an additional measure -- of the lowest sound required to awaken you -- will be taken. An earphone will be placed in your ear and a button-press taped to your hand. Approximately 8-10 times throughout the night, tones will be presented to you through the earphone. As soon as you are aware of the tones, you are asked to press the button in your hand three times and then tell the technician what the level of your pain is at that time (on a scale of 0 - 5). Then you will be permitted to go right back to sleep.

Risks/Discomforts:

Sleeping in a new environment, combined with the apparatus necessary for monitoring sleep patterns, may initially disturb your sleep. However, these disturbances commonly decrease across recording nights. Also, during the fourth night, you may feel that your sleep is disrupted due to the awakenings. Other than these minor disturbances, there are no risks nor discomforts related to this study.

Benefits:

This study is being conducted to learn about sleep disturbance in people with chronic pain. We hope it will provide new insights into the development of different treatment approaches for these problems. The only direct benefit a subject is expected to gain is a greater understanding of the sleep disturbance she/he is experiencing.

Participation in the study:

Your participation in this project is completely voluntary. You can refuse to participate without any concern that future treatment will be compromised. If you agree to participate, but at a future date decide to withdraw from the study, you may do so, again without any impact on treatment. You will receive a copy of the signed consent form.

Confidentiality:

Confidentiality and anonymity are assured by assigning a code number to your data. These data will only be referred to by that number in publications or presentations. Only investigators in the project will have access to study data. As a study participant, you can contact Dr. Pivik at any time to obtain information regarding the study.

For more information, call: Dr. Pivik -- Department Psychiatry, Room 4431, Ottawa General Hospital, 737-8040; Dr. Goss -- Chair, Ethics Committee (Ottawa General Hospital), 737-6792; or Dr. Latter -- Chair, Research Ethics Committee (The Rehabilitation Centre) 737-7350.

APPENDIX C - Consent Form

**HÔPITAL
GÉNÉRAL
D'OTTAWA**
501 Smyth, Ottawa, Ontario K1H 8L6

**OTTAWA
GENERAL
HOSPITAL**

**CONSENTEMENT DU PATIENT/
PROCURATION À DES RECHERCHES MÉDICALES**
PATIENT/PROXY CONSENT FOR MEDICAL RESEARCH

Nom de l'étude CHRONIC PAIN, SLEEP AND DEPRESSION		Name of research project	
Je confirme que j'ai expliqué la nature ainsi que les complications connues de ce projet de recherche/procuration du patient. Dr. R. T. Pivik (chercheur)		I confirm that I have explained the nature of and known complications of the research project to the patient/proxy. (researcher)	
Je consens à la participation de : Nom du patient	N° de projet	I consent to the participation of : Patient's name	Research no.
à l'étude précitée et j'autorise par la présente le(s) médecin(s) et le(s) chercheurs(s) à procéder aux examens et/ou à dispenser les traitements suivants :		In the above study and I hereby authorize the physician(s) and investigator(s) to proceed with the following questionnaire, examinations and/or to administer these treatments:	
Recording of brain wave activity, muscle activity, eye movement and autonomic activity during sleep and wakefulness, auditory arousal threshold determinations during sleep.			
J'ai lu la feuille d'explication détaillée approuvée par le Conseil d'éthique en recherches et je suis au courant des effets secondaires et des risques connus ayant trait aux examens et aux traitements.		I have read the detailed information sheet approved by the Research Ethics Board and am aware of the known side effects and risks related to the examinations and treatments.	
J'ai également reçu une description de tous les avantages à attendre de ces examens et de ces traitements. On m'a fait connaître d'autres formes d'examen et de traitement.		I have also received a description of any benefits that may be expected from these examinations and treatments. As well, other forms of treatment and exams have been disclosed to me.	
J'ai eu l'occasion de poser des questions au sujet de ces examens et de ces traitements et on y a bien répondu.		I have been given an opportunity to ask questions concerning the examinations and treatments involved and the questions which I have asked have been adequately answered.	
On m'a dit que je pouvais retirer le consentement et suspendre la participation à l'étude à n'importe quel moment et pour quelque motif que ce soit et que cette action n'affectera pas la qualité des soins en cours et futurs.		I have been told that I can withdraw consent and stop participation in the study at any time and for any reason, and that such action will not affect the quality of ongoing and future care.	
Je reconnais qu'en agissant, comme procurateur, ce sera dans le meilleur intérêt du patient.		I acknowledge that if I am acting as a proxy that I am acting in the best interest of the patient.	
En toute connaissance de cause, je consens volontairement à ce que _____ participe à cette étude.		With full knowledge of this, I voluntarily consent to the participation of _____ in the study.	
Ce protocole a été approuvé par le Conseil d'éthique en recherches de l'Hôpital général d'Ottawa. Ce conseil étudie les aspects éthiques de tous les projets de recherche sur les humains. Si je le désire, je peux contacter le président de ce comité.		This protocol has been approved by the Research Ethics Board of the Ottawa General Hospital. This Board considers the ethical aspects of all hospital research projects using human subjects. If I wish, I may contact the Chairperson of the Board with questions.	
Nom (lettres moulées) - Name (print)	Signature	Lien de parenté - Relationship	
PATIENT OU PERSONNE LÉGALEMENT RESPONSABLE (PROCURATION) - PATIENT OR PERSON LEGALLY RESPONSIBLE (PROXY)			
Nom du témoin (lettres moulées) - Name of witness (print)	Signature	Date (j/d-m/m-à/y)	

APPENDIX D - Demographic Screening Questionnaire

DEMOGRAPHIC AND SCREENING QUESTIONNAIRE

Thank you for agreeing to take part in our study entitled "Chronic Pain, Sleep and Depression". The purpose of this questionnaire is help us select the most appropriate subjects for our study. However, for reasons of methodology, some of you may not be selected. We therefore ask that you answer each question as completely as possible. Be assured that all information gathered will be kept in total confidentiality, and will only be referred to through subject numbers assigned.

Subject name: _____

Subject number : _____

Birthdate: / / Age:
 m d yr

1. Have you ever had any consultation or treatment for psychiatric condition (for example, depression)?

Yes No

Please describe _____

If yes, was this prior to the beginning of your pain?

Yes No No pain

2. Have you ever had any consultation or treatment for a problem sleeping (eg. insomnia, narcolepsy, restless leg syndrome, snoring? see last page for explanations).

Yes No

Please describe _____

If yes, was this prior to the beginning of your pain?

Yes No No pain

3. Will you agree to abstain from alcohol for the duration of the study?

Yes No

-2-

4. Will you agree to attempt to maintain a normal sleep and exercise routine, avoiding daytime napping?
Yes ____ No ____
5. Are you right-handed or left-handed?
Right ____ Left ____
6. Do you work odd hours (eg. shift work)?
Yes ____ No ____
7. Do you have any medical condition (other than pain and possibly depression) that you are presently or have recently been treated for?
Yes ____ No ____
Please describe _____
8. Are you presently taking medication?
If yes, please list _____

9. Do you have difficulty finding a comfortable position in bed at night?
Yes ____ No ____
10. For sleeping, how many pillows do you use?
One ____ Two ____ More ____
11. Do you exercise regularly?
Yes ____ No ____
12. If yes, how often?
Once per week ____
Twice per week ____
More than twice per week ____

-3-

13. If you exercise regularly, on average, for what length of time each session?
- 0 - 5 minutes ____
5 - 15 minutes ____
15 - 25 minutes ____
more than 25 minutes ____
14. Whether you exercise regularly or not, does exercise decrease, increase or have no effect on your pain?
- no effect ____ increase ____ decrease ____ no pain ____
15. Do you smoke cigarettes?
- Yes ____ No ____
16. Would you describe your pain as constant, or intermittent?
- Constant ____ Intermittent ____ No pain ____

Definitions:

Narcolepsy: A syndrome of unknown origin that is characterized by abnormal sleep tendencies, including excessive daytime sleepiness with overwhelming pressure to sleep and often disturbed nighttime sleep.

Restless legs syndrome: irresistible leg movements often accompanied by a creeping sensation deep in the limbs. Bedtime is a major problem, since rest, particularly lying down in bed, is associated with increased leg movements, which interfere with sleep onset.

Snoring: this can be an indication of sleep apnea. Apnea is a period of time during which breathing temporarily stops.

APPENDIX E - Debriefing Sheet

DEBRIEFING:

People who experience chronic pain (of greater than six months' duration and resistant to treatment) commonly also have disturbed sleep. About half of these people are also depressed. Each of these three conditions, i.e., chronic pain, sleep disturbance and depression, are disturbing in themselves, but when they co-exist it is possible that they interact, making treatment difficult. This study was conducted to understand the correlates of, and interaction among, these conditions.

Sleep disturbance can be examined by self-report questionnaires, but when this is the sole measure the exact nature of the sleep disturbance remains unclear. However, such information permits comparison of the sleep disturbance with others which have been similarly documented. Polysomnography (surface electrodes recording brain and electrical activity of the nervous system during sleep) is required to quantitatively characterize sleep. Both types of measures aid in the development of treatment interventions for sleep disturbance.

From the sleep recordings and questionnaires that were completed, we expect to find evidence of a higher level of arousal during sleep in people with chronic pain than in the normal controls. We expect there will be a ranking such that people with depression and pain will have more severe sleep disturbance than those without depression.

Our findings may influence the treatment approach used at chronic pain clinics, such as suggesting specific treatment protocols for people with depression or behavioral training to improve sleep habits.

We would like to thank you for participating in this research. Your time and effort has been greatly appreciated.

If you have any questions or comments about this research, then please feel free to contact Dr. R. T. Pivik (Principal Investigator - 737-8040).

If you have any ethical concerns about this research, then please contact Dr. G. D. Goss - 737-6792 (Chair, Ethics Committee, Ottawa General Hospital).

IMAGE EVALUATION TEST TARGET (QA-3)

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