Physical Activity Levels and Diurnal Patterns in COMISA Versus Age- and Sex-Matched Insomniacs and Good Sleepers

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Abstract

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Farin Forouzesh

Background: Over 30% of people with obstructive sleep apnea have co-morbid chronic insomnia. This combination (COMISA) worsens daytime functioning and health outcomes more than either condition alone. Its effects on physical activity (PA) are unknown. This study's aims were to i) compare objectively-measured PA levels and diurnal patterns between people with COMISA and age- and sex-matched Insomniacs (INS) and Good Sleepers (GS); and ii) assess the impact of an 8-week exercise (Ex) or relaxation (Rel) intervention on PA in COMISA.

Methods: This secondary analysis used activity data collected from 15 COMISA participants, 15 INS, and 15 GS matched on age (±5 years) and sex. Participants wore an accelerometer (Actiwatch-2) on their non-dominant wrist and recorded sleep/wake activities in a diary for 14 days. Mean daily PA levels and morning/afternoon/evening PA levels were compared between groups with a repeated-measures ANOVA, as were pre- to post-intervention changes in PA levels in COMISA participants randomly assigned to Ex (N=4) or Rel (N=4).

Results: Mean daily PA was 278±40, 316±108, and 335±121 counts/minute (cpm) in COMISA, INS, and GS respectively. The group difference was not significant, but the effect size was moderate (η_p^2=0.063). Evening PA level was significantly lower than morning or afternoon level across groups ($p<0.001$). Mean PA level did not change after Ex or Rel.

Conclusion: These findings confirm the presence of an evening drop in PA level across populations, signal a moderate negative effect of COMISA on PA levels, and call for interventions specifically targeting PA behavior in this population.

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Contributions of Authors for the Manuscript

Farin Forouzesh is the primary author of the manuscript of this thesis. She was responsible for extracting and handling COMISA physical activity data at the post-intervention time point and for gathering, analyzing, and comparing COMISA, Insomnia and Good Sleepers' physical activity data, developing the literature review and writing the manuscript.

Véronique Pepin is the supervisor of the primary author and oversaw all stages of both the larger research project and this specific study and its related manuscripts. As the primary editor of the manuscript included in the present thesis, she also ensured the accuracy and completeness of its content.

Adam Brown is responsible for COMISA physical activity data extraction and handling at baseline**,** while **Emily Mancinone** is responsible for the Good Sleepers data and **Olivier Roy** is responsible for the Insomnia data at baseline**.**

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1. Theoretical context

1.1. Insomnia

1.1.1 Definition

Sleep plays an important role on elements of mental and physical health, such as learning ability, memory, emotions, and the function of several body systems (e.g, immune, cardiovascular, and metabolic systems).[1] Insomnia symptoms include having difficulty initiating or staying sleep or waking up too early or having poor sleep quality.[2] Insomnia disorder is a common sleep disorder which is associated with one or more of these symptoms (having difficulty to fall or stay asleep or waking up too early in the morning) for minimum three nights per week for minimum three months which leads to daytime sleepiness and distress.[3]

1.1.2 Epidemiological information

The prevalence of chronic insomnia disorder in the general population ranges between 6% and 10%.[4] Two Canadian studies in 2001 and 2005 documented prevalence rates of insomnia symptoms of 13.4% and 24% respectively; the differences in rates may be explained by differences in methodology (for example, different definitions of insomnia, different sampling and assessment methods).[5–7] The prevalence of insomnia symptoms has increased in recent years: in Canadians aged 18 years and more, it increased from 16.8% in 2007-2009 to 23.8% in 2014-2015 period.[8] In the province of Quebec, the prevalence of insomnia symptoms was 35.9% in 2011, while insomnia disorder was present in 10.3% of the population.[5]

Insomnia is more common among the elderly than younger populations. Indeed, the total prevalence of insomnia disorder in older populations ranges from 12% to 20%; furthermore, 30% to 48% of elderly people report having insomnia symptoms.[3] Other factors that lead to an increase

in insomnia prevalence include female gender, psychosocial problems, overwork, and low levels of physical activity.[9]

1.1.3 Burden

Studies have demonstrated that chronic insomnia is associated with psychiatric and physical morbidity. Insomnia is a risk factor for depression and anxiety[2], as well as decreased immune functioning, cardiovascular disease, and mortality.[10] Another consequence of insomnia which presents the greatest health risk is increasing the probability of car accidents. This probability could be 2.5 to 4.5 times more in people with insomnia compared to control group.[2] Absenteeism from work is increased in insomniacs and productivity is decreased because of difficulty to concentrate and perform duties.[2]

Insomnia's direct and indirect costs pose a heavy economic burden to society.[11] Insomnia's costs on US healthcare system is more than $100 billion annually.[12] The total expenditure incurred due to insomnia in the province of Quebec was estimated at $6.6 billion (CAD$). Direct costs of insomnia include medical consultations, prescriptions and drugs, while indirect costs contain absenteeism and loss of productivity.[11,13] In Quebec, the 2007 average annual direct and indirect combined costs for individuals with insomnia disorder was $5,010 compared to $1,431 for those with insomnia symptoms and $421 for good sleeper.[11] Kaufmann and colleagues[14] found that, in adults aged more than 55 years, insomnia symptoms were associated with higher level of hospitalizations, use of home health care services, nursing home placement or combination of health care services.[15]

1.1.4 Insomnia diagnosis and treatment

There are different insomnia assessment tools, including objective measurements (e.g., polysomnography (PSG), actigraphy) and subjective measurements (e.g., the Pittsburgh Sleep

Quality Index (PSQI), Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS)).[14] Although polysomnography is the gold standard tool to identify sleep from wake, it is not essential for the insomnia diagnosis, which could be applied by patient's self-report.[16]

Insomnia Severity Index (ISI) is a brief self-report questionnaire measuring the patients' perception of their insomnia for the preceding month. The evaluation criteria are difficulty of falling or staying asleep or waking up too early, sleep dissatisfaction, interference of sleep problems with daytime functioning, noticeability of sleep problems by others, and being worried because of the sleep problems. For rating items, a 5-point Likert scale is applied (e.g., 0 = no problem; 4 = very severe problem). Range of total score is between 0 and 28. The explanation of the total score is: total score of 0–7 means absence of insomnia; 8–14 is sub-threshold insomnia; 15–21 indicates moderate insomnia; and 22–28 is severe insomnia.[17] ISI is a reliable and valid questionnaire to measure perceived insomnia severity. In addition, ISI could be considered as a useful tool to detect changes in perceived sleep difficulties in insomnia treatment research.[18]

The gold standard treatment for insomnia is Cognitive Behavioral Therapy for Insomnia (CBTi) which involves different components of relaxation training, cognitive-behavioral therapy, and sleep hygiene education. CBTi includes 4–8 sessions with a psychologist or a trained person.[19] Compared to sleep medication, CBTi has a similar efficacy and a more long lasting preservation of benefits after treatment discontinuation.[20] In CBTi, different skills are learned which can be applied by patients even after discontinuation of treatment, whereas sleep medications need to be taken continuously for their effects to be maintained.[20] However, CBTi can be time and resource intensive, as an acute decrease in sleep duration can happen during the first few weeks of CBTi; this can lead to increasing daytime sleepiness and some insomniacs may drop out of treatment. Also, the effects of CBTi on sleep improvements can be seen after only 3-4 weeks of beginning of

the treatment.[21] Adjunct interventions that are more accessible and that have the potential to improve sleep, such as exercise training, have therefore been considered.[22]

1.2 OSA

1.2.1 Definition

Obstructive sleep apnea (OSA) is a common disorder which causes partial or complete blockage of the upper airway during the sleep.[23] The severity of OSA is typically established based on the apnea-hypopnea index (AHI), that is the number of apnea (breathing cessation for ≥ 10 seconds) and hypopnea (partial loss of breath for ≥ 10 seconds) episodes per hour of sleep.[24] The probability of OSA increases with the male gender, older age, and obesity. It leads to snoring, feeling sleepy during the day, cardiovascular problems, and increasing risk of all-cause mortality.[4,24]

1.2.2 Epidemiological information

The prevalence of OSA is currently estimated at about 10% of the general population.[4] However, applying different measurement techniques and definitions can affect the prevalence rate of OSA.[23] The prevalence of OSA in middle-aged men is between 13 and 33% and this estimation for middle-aged women is between 6 and 19%. The prevalence of OSA has increased in recent years because of the increasing rate of obesity in middle- and high-income countries.[24] Indeed, one of the most important risk factors of OSA is obesity, which has increased a lot over the past 25 years; about 70 % of people with OSA syndrome are estimated as overweight or obese.[23,25]

1.2.3 Burden

The American Academy of Sleep Medicine reported that the estimated total cost of OSA is more than $150 billion each year in the United States. Direct costs of OSA include costs of OSA diagnosis and management, such as consultation, testing, CPAP or oral appliance therapy, and

prescription medications costs. Indirect costs are related to increased healthcare utilization for other conditions ($30 billion) that are attributable to OSA (such as cardiovascular, metabolic, and psychiatric disorders such as hypertension, stroke, diabetes, and depression)[23,26], decreased workplace productivity ($86.9 billion), and increased risk of accidents ($26.2 billion) and workplace injuries ($6.5 billion). Therefore, finding strategies to prevent and treat OSA has broad healthcare implications.[27,28]

1.2.4 OSA diagnosis and treatment

The gold-standard method to diagnose OSA is polysomnography (PSG).[29] By applying several physiological electrodes, PSG is able to monitor a person's brain, muscle, and respiratory signals during the night in a sleep laboratory. The number of breathing events (e.g., obstructive apneas, central apneas, hypopneas, or mixed apneas) per hour of sleep can then be counted by a trained sleep technician. The AHI is then used to range the severity of OSA from mild ($5 \leq AHI < 15$) to moderate ($15 \leq AHI < 30$) to severe ($AHI \geq 30$).[30]

OSA is considered as a chronic condition which needs long-term treatment.[24] The gold standard treatment for OSA is continuous positive airway pressure (CPAP) therapy.[31] This positive airway pressure is delivered to the airways during both inspiration and expiration by a special device.[31] The goal is to keep the airways open during sleep.[32] CPAP improves OSA symptoms and reduces healthcare utilization.[24] However, the effectiveness of CPAP is affected by patient adherence.[24] Many patients stop using the CPAP during first year of treatment and can therefore not be effectively treated.[33]

Other treatment options have therefore been considered. These include surgery (e.g., multilevel temperature-controlled radiofrequency tissue ablation, laser-assisted uvulopalatoplasty, and maxillomandibular osteotomy), oral appliances, and lifestyle changes, including diet and exercise

interventions.[24] A regular aerobic exercise program significantly decreases the severity of OSA, even if the body weight does not decrease significantly.[34]

1.3 Comorbid Insomnia and Obstructive Sleep Apnea (COMISA)

1.3.1 Definition

Co-morbid insomnia and sleep apnea (COMISA) is a common condition which affects daily functioning and quality of life. People with COMISA experience more sleep fragmentation and less amount of deep sleep in comparison with insomnia patients. They experience more respiratory disturbances, more pain and absenteeism from work in comparison with people with OSA. Furthermore, they are faced with higher daytime impairments (e.g., decreasing daytime functioning and quality of life and increasing daytime sleepiness[4]), depression, and psychiatric problems compared to OSA or insomnia patients.[35]

1.3.2 Epidemiological information

Insomnia and OSA co-occur frequently. Different population groups and diagnostic methods may lead to different COMISA prevalence in that specific population.[36] Approximately 30-50% of OSA patients experience insomnia symptoms, and 30-40% of individuals with chronic insomnia report OSA symptoms.[37]

1.3.3 Issue with this specific combination

COMISA presents many challenges to clinicians because it complicates diagnosis and treatment.[4] As insomnia and OSA have some similar symptoms, the diagnosis and measurement of each disorder when they co-exist presents a complexity for clinicians.[4] These similar symptoms (e.g., sleep problems during night, daytime sleepiness, decreased quality of life) lead to difficulties in the assessment of insomnia in presence of OSA before and after treatments.[4]

The recommended clinical management approach for COMISA is the combination of CPAP (for the OSA component) and CBTi (for the insomnia component).[4] COMISA patients have more difficulties adhering to CPAP therapy than those with OSA alone.[4] Insomnia symptoms in COMISA patients cause more waking time during night than OSA alone, which decrease the acceptance and use of CPAP because tolerating CPAP mask during awakening time at night is difficult.[4,35,38] CPAP related side effects are more probable in COMISA people which causes them to remove the CPAP mask, or even reject the therapy.[4] As a result, a combination of CBTi and CPAP is recommended for people with COMISA.[4] CBTi, the gold standard treatment for insomnia, benefits COMISA patients by increasing acceptance of CPAP for long term use.[4]

However, CBTi is costly, time consuming, and difficult to access because most of the time it is delivered by trained therapists during several weeks or months.[39] CPAP long-term effectiveness is affected by nasal discomfort, mask leak, congestion and claustrophobia.[40,41] Thus, other practical solutions for COMISA patients are needed. Exercise training which has shown some positive results on people with OSA[41,42] and insomnia[43] could be considered as an adjunctive intervention for people with COMISA.

1.4 Physical activity levels and diurnal patterns

1.4.1 What is physical activity and why is it important?

Physical activity (PA) can be defined as “any bodily movement produced by the skeletal muscles that results in increased energy expenditure”.[44,45] The term "exercise" has been used interchangeably with "physical activity" but it is not synonymous with physical activity. Exercise is a subcategory of physical activity. Exercise is “physical activity that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective”.[46] PA improves health by preventing cardiovascular disease,

diabetes, some cancers and osteoporosis.[47] PA is a behavior that can be influenced by several personal (e.g., genetic, biological, psychological), social (e.g., family, social groups, work), and environmental factors (e.g., natural environment for doing PA, accessibility of different facilities, etc.).[48] PA level decreases with age, is lower in women, and is higher in high-income countries.[49] PA level also affected by body mass index (BMI). Some cross-sectional studies showed a negative correlation between mean PA level and BMI.[50–52] One study showed that there was a weak (negative and significant) association between PA and BMI in non-obese participants while this correlation was moderate (negative and significant) in obese individuals.[52]

The World Health Organization recommends adults aged 18–64 years to get involved in at least 600 metabolic equivalent minutes (MET-min) per week of combination of moderate- and vigorous-intensity physical activity. This amount is equivalent to 150 minutes of moderate-intensity physical activity (such as brisk walking) or 75 minutes of vigorous-intensity physical activity (such as running) every week.[53] Physical inactivity is one of the most important problem in public health which has been increased in recent years.[54] In one study, involving in less than 600 MET-min per week considered as physically inactive group.[53] The prevalence of physical inactivity is 51% in Canadian adults.[47]

1.4.2 Measurements of physical activity

PA measurements can be divided into three broad categories: criterion methods, objective methods, and subjective methods. Criterion methods refer to gold standard measurements against which other assessment approaches are often validated; for PA, they consist of direct and indirect calorimetry. Objective methods refer to measurement tools that can capture a person's movement (e.g., motion sensors or activity monitors) and/or physiological activation levels (e.g., heart rate monitor, body temperature) to estimate energy expenditure or express PA level with a unit of its

own (e.g., activity counts). Subjective methods rely on the person's assessment and/or recollection of her own behavior and include PA questionnaires and activity diaries.[55,56]

1.4.2.1 Criterion methods

The gold standard method for PA assessment is direct calorimetry, which quantifies energy expenditure by measuring heat production or heat loss. With this method, caloric expenditure is measured by the amount of heat produced.[55,57] However, this method is not practical in many cases because it requires expensive equipment, highly trained personnel, and is time-consuming as only one person can be measured at a time.[55,57] In addition, sweat can lead to measurement errors.[57] Therefore, a more common criterion measurement for validation of PA measurement is indirect calorimetry, which measures heat production, or energy expenditure by measuring oxygen consumption and/or carbon dioxide production.[55] Indirect calorimetry is an accurate and valid way of measuring short term energy expenditure while it is still costly and limited to laboratory setting.[55]

1.4.2.2 Objective methods

Body movement can be detected by motion sensors. These sensors detect acceleration forces produced by skeletal muscles in one, two or three dimensions.[55]

Pedometers are small devices which are worn on the waistband and detect vertical movements and measure step counts during wear time. Only physical activities related to walking or running can be detected by pedometers and upper-body movements, non-vertical activities like cycling, and water activities like swimming cannot be measured. Moreover, the intensity of the movement cannot be measured by this technique.[55,58] Nevertheless, pedometers are considered valuable

devices for measuring the total amount of daily movement as most of our PA consist of walking or running.[55]

Accelerometers, on the other hand, detect motion in more than one direction.[55] They have piezoelectric transducers and microprocessors for quantifying magnitude and direction of the acceleration calling dimensionless activity counts.[55] These devices can therefore detect non step movements as activity counts. The best accelerometers are tri-axial accelerometers, which have the ability to measure all movements in theory (they still cannot detect some complex movements such as cycling and water activities).[55,59] Accelerometer data can be applied to calculate physical activity volume, rate, and the amount of time spent at different intensities of PA.[60] Accelerometry is a popular PA monitoring technique in research, as it gives a valid estimation of PA (more precise than pedometers) while remaining accessible and relatively user-friendly compared to calorimetry.[55]

Accelerometers can be fixed on the hip, the wrist, the arm, or the ankle. It was assumed that the hip worn accelerometers assessed PA more accurately as compared to other types. However, it has shown that the differences in accuracy between hip and wrist accelerometers was small.[61,62] For some reasons, such as increasing wear time and accurately monitoring sleep, wrist accelerometer are often preferred. Accelerometers measure and record some PA parameters such as frequency, duration, pattern, and intensity during weeks or even longer.[62,63] Accelerometers have some limitations: they are more expensive than pedometers and require technical experience and specialized software for data extraction and analysis.[64] In addition, they do not have enough sensitivity to detect sedentary and light-intensity PA.[62,63]

1.4.2.3 Subjective methods

Subjective reporting involves PA logs, PA diaries, and PA questionnaires (global questionnaires, short-term recall questionnaires, quantitative history recall questionnaires).[62] In questionnaires, data from the previous day or week is considered. There are different kinds of questionnaires which collect data on PA frequency or duration, intensity or type then, report PA data based on time or activity scores.[56,62]

Questionnaires are the most common approach used in epidemiological studies. They offer an inexpensive and easy-to-use method, especially for very large samples. However, they rely on participant's age, memory, and interpretation of question, are prone to under and over estimation of PA, and are affected by the different seasons.[55]

1.4.3 Physical activity levels in people with insomnia

Several cross-sectional studies in healthy individuals have found an association between PA/exercise and subjective measures of sleep, most commonly with questionnaires. Subjective insufficient sleep, morning tiredness and daytime sleepiness have shown to be associated with lack of regular exercise or leisure time PA program or even decreased exercise frequency.[65–67] In a cross sectional and retrospective study of 1365 adolescents (aged between 12 to 18) on the association between lifestyle and sleep, no habitual exercise showed the strongest association with insomnia (odds ratio: 3.29).[68] Epidemiological studies have demonstrated a significant association between higher levels of PA and better sleep quality , and lower levels of PA with higher risk of insomnia.[69–73] Another epidemiological study on adults from 5 countries (South Africa, Australia, China, South Korea and the UK) has shown a significant bivariate association between insomnia prevalence and daily or weekly minutes of moderate intensity activity. In addition, it is important to note that at the highest and lowest activity levels, insomnia prevalence was increased.[74] A meta-

analysis has shown that, with regular exercise training, some sleep parameters improves (e.g., total sleep time increased, REM sleep onset delayed by 10 minutes, slow-wave sleep (SWS) increased, and REM sleep decreased by 2–5 minutes).[75]

Studies evaluated the association between intensity, frequency, and level of PA on sleep. As mentioned previously, the minimum PA level recommended by public health guidelines is 150 min of moderate-intensity activity per week.[76] This amount of PA can improve sleep quality in people with insomnia.[76] In one of these prospective cohort study examining the effects of intensity of PA on preventing incident short sleep, the investigators found that moderate high- or vigorous intensity PA for middle aged adults and moderate low-intensity PA for older adults could effectively maintain sleep sufficiency.[43] A prospective study on randomly selected population of adults found both men and women showed significantly reduced risk of sleep disorders if they participated in regular activity at least once a week such as participating in regular exercise program and walking at normal pace for more than 6 blocks per day.[77] Another cohort study on women (aged 20 years or more) found that a low level of PA increased risk of future insomnia and keeping a higher levels of PA or increasing the PA levels over 10 years could partly protect them from self-reported insomnia.[78]

Adults with insomnia symptoms tend to have lower level of PA compared to adults without insomnia, which may happen as a result of excessive daytime sleepiness and fatigue.[67,79] People with heart failure and insomnia who did greater PA (greater activity count per min) during the day experienced a greater total sleep time during the same night, and greater total sleep time was associated with greater PA (greater activity count per min) during the next day.[80]

Several RCTs evaluated the effects of exercise interventions in people with insomnia. Pattern emerging from these RCTs includes a decrease in the ISI score in the exercise intervention group.

In one of these studies, the effects of 150 min of moderate- to vigorous-intensity PA per week for 6 months on insomnia severity between inactive adults was evaluated by using accelerometer and ISI. Insomnia symptom severity significantly decreased ($F_{8,26} = 5.16$, $P = 0.03$) after the PA intervention, and the average ISI score decreased four points.[76] In that study, the exercise group was instructed to engage in moderate to vigorous PA (brisk walking) for 6 months and after assessing PA by GT3X+ (triaxial Actigraph GT3X accelerometer) and sleep by Actiwatch and ISI, an improvement of ISI score occurred in the exercise group.[76] Another RCTs study randomized participants into two groups of CBTi+PA (guided increased in PA) and CBTi alone, assessed the daily steps and sleep quality by Fitbit and ISI respectively and found that days with greater PA (count per min) were associated with nights with longer sleep duration; however, no association between PA and sleep efficiency and sleep quality was found.[22] Of note, the association between daily steps and sleep duration was significant and positive in mild insomnia, significant and negative in severe insomnia and not significant in moderate insomnia.[22]

Overall, previous research suggests that PA is therefore a promising intervention for people with insomnia. PA increases physical fatigue, decreases stress, and regulates circadian rhythm, which can improve sleep.[43] Also, exercise has antidepressant and anti-anxiety effects which can effectively treat chronic insomnia.[81] It has demonstrated that for less severe insomnia, participating in PA and applying self- guided CBTi app is a convenient and cost- effective way to improve sleep.[22]

1.4.4 PA levels in OSA

PA level and OSA severity have been negatively associated. Indeed, several studies have shown that increased OSA severity is associated with decreased PA assessed by subjective and objective activity measurements.[82–84] In a cross-sectional study on OSA patients looking at the association between objectively-measured PA (with 2 axial accelerometer SenseWear) and OSA severity (with PSG), increased OSA severity was associated with decreased PA (steps per min) while controlling for age, gender and daytime sleepiness.[82] In a prospective study, it was found that a low level of PA (steps per day) was associated with OSA severity while controlling for age and body mass index (BMI) ($p= 0.05$).[85] In another cross-sectional study of adults, a negative correlation between PA level and OSA severity was shown.[24] In a cross-sectional study of 155,448 subjects from the general population, walking and vigorous PA (assessed with the International Physical Activity Questionnaire (IPAQ) and self-reported questionnaire) was shown to be associated with a decreased risk of OSA independent of other risk factors.[86] It was also shown that adults with low levels of PA had higher odds of OSA.[24,87]

A systematic review and meta-analysis demonstrated that several RCTs applied PSG to assess the effects of exercise interventions on the AHI during sleep in people with OSA.[44] A pattern emerging from these studies include significant reductions in AHI in the exercise group compared to the control group.[44,88–91] Other interesting results from the review study is the comparison between PA levels (steps per day) in studies that applied CPAP or an exercise intervention.[44] These results indicated that the differences between PA levels (steps per day) before and after CPAP or exercise interventions were not significant except for one study. In that study, OSA patients with coronary artery disease completed a short-term walking-based exercise training trial (4 weeks) before starting cardiac rehabilitation. After completing this 4-week trial, a significant improvement in PA

levels was observed (i.e. from 3913.3±1100.5 to 8228.5±1125.9 steps per day, $p<0.0001$). Then, a structured maintenance exercise program was necessary to maintain the improvement in PA level.[42,44] The two other trials show no significant changes in PA levels, which is more common after exercise intervention and by objectively measured PA levels.[25,44] This result could be interesting as it highlights the importance of long-term program aimed maintaining increased PA levels.[42,44] Therefore, increasing PA could be happened by applying structured exercise training programs or even walking in OSA patients.[44,86]

Lower levels of PA have been associated with obesity, cardiovascular problem and increased OSA severity.[24,44] It is possible that people with OSA have difficulty in doing exercise because of daytime sleepiness and fatigue, which leads to decreasing motivation and time for PA.[24] Some other potential factors that may prevent OSA patients to be physically active are dyspnea, cardiovascular problem, respiratory muscle dysfunction, peripheral vascular disease, and impairment of skeletal muscle energy metabolism.[24,92] It has been shown there is a 38% lower probability of moderate-to-severe OSA in case of 1–2 hours of weekly exercise.[24] Exercise is considered as an efficient intervention to improve cardiovascular fitness and quality of life in people with OSA.[41] Exercise reduces AHI, hypertension, diabetes, and obesity and finally improves subjective well-being.[24]

Overall, we can see as a result of a systematic review on randomized (ex-group and control group) and non-randomized control trials, exercise is an efficient intervention in decreasing the OSA severity.[41]

1.4.5 PA levels in COMISA

In comparison with OSA and insomnia, the number of COMISA patients who do PA and exercise is lower because of the higher fatigue and lack of motivation.[93,94] In a cross sectional study by Kechribari et al.[95] PA habits were assessed with the IPAQ, and then compared between OSA patients with and without insomnia. Patients with OSA + insomnia spent lower time in PA compared to patients with OSA but no insomnia (10.7 ± 4.6 min/day vs. 21.8 ± 4.8 min/day, $P < 0.001$). The IPAQ provides information on time spent in walking, vigorous, moderate, and sedentary activity for each week, as well as total duration of PA expressed in min/day. Based on global recommendations for PA, participants could be categorized as inactive (PA < 30 min/day) or physically active (PA ≥ 30 min/day).[95,96] Based on this recommendation, participants in Kechribari et al's study were inactive, but those with combined OSA and insomnia were so at a greater degree than those with OSA alone.

Exercise training may improve upper airways muscle tone, which leads to positive effects on the drive to breathe. Also, exercise could activate the musculo-venous pump, preventing accumulation of fluid in the legs during the day and decreasing the amount of fluid shift from legs to the neck during the night. As a result, upper-airway luminal size would increase and upper airway collapse would not happen. These mechanisms have been proposed to explain the beneficial role of exercise in reducing OSA severity.[41,42] In addition, exercise training is an effective intervention for decreasing sleep complaints and insomnia because it manages depression and anxiety and also improves quality of life.[81] Thus, it could be a good idea to consider and evaluate exercise intervention as a treatment method for COMISA patients. However, to date, no study has investigated PA levels in COMISA before and/or after a PA/exercise intervention. In this regard, we focus on the effects of exercise training on PA level in COMISA patients.

1.4.6 PA diurnal pattern

There are not many studies comparing PA patterns in healthy people or people with chronic diseases. Based on the scarce literature available, factors that seem to affect diurnal PA patterns include age, the presence of a chronic disease, employment status and aerobic fitness.

Increasing age has been associated with decreasing mean daily PA level after the age of 50.[97] In terms of diurnal patterns, older and younger people have shown similar PA levels in the morning, while older people have shown lower PA levels as the day continues. Older people prefer to do their daily tasks, such as bathing and exercising, in the morning. Since older people have lower threshold of fatigue, and since they are more active in the morning, they feel fatigue for the rest of the day, which may contribute to lower activity levels as the day advances.[98]

Studies have also suggested that the presence of chronic disease may affect diurnal PA patterns. For example, "A-shaped" diurnal PA patterns (where the highest PA level was seen in the afternoon) seem more common in healthy people, while descending PA patterns (where PA level decreased from morning to evening) appear more likely in people with chronic diseases, such as COPD [99,100] However, this finding remains to be confirmed because it is based on very few studies and may be confounded by age, as mentioned previously, and by employment status. Indeed, in a study by Tabak and colleagues[100], a significant drop in PA level was observed from the morning and afternoon to the evening in 32 unemployed COPD patients; the same pattern (although not significant) was seen in seven employed COPD patients and 10 unemployed healthy controls. In contrast, an "A-shaped" pattern was observed in 11 employed healthy controls. Of note, the healthy control group in Tabak et al.'s study was significantly younger than the COPD group.[100] Whether

COPD per se, employment status, or age was the predominant factor affecting diurnal PA patterns remains unclear.

Aerobic fitness may also impact PA patterns. Fitter participants have shown a lower decrease in PA level between the first and second half of the day, compared to less fit participants.[97] Increasing age and decreasing PA are associated with decreasing aerobic fitness.[97] People with lower aerobic fitness have been shown to feel more fatigue throughout the day and, as fatigue is associated with reduction in PA level, these people may be less active especially in the last hours of the day.[97,101] Thus, aerobic fitness is a covariate in PA studies.[97]

2. Rationale

There is a bidirectional relationship between sleep and PA, where poor sleep leads to less PA, and lower levels of PA are associated with poorer sleep.[102] Previous studies have shown that OSA[44] and insomnia[79] are associated with decreased PA levels during the day and that people with OSA or insomnia have less motivation to exercise because of fatigue and sleepiness.[24] Insufficient PA can lead to obesity, metabolic problems and lower cardiorespiratory fitness, which can worsen the OSA condition.[44]

Studies have shown that for people with COMISA, treating both OSA (with CPAP) and insomnia (with CBTi) is recommended.[4] However, each method has its limitations and has no documented effects on increasing PA level.[44,103] Thus, adjunct therapies that have the potential to positively impact both OSA and insomnia would be useful in COMISA.

Exercise training has been suggested as a non-pharmacological treatment for insomnia and sleep-disordered breathing. Exercise can lead to weight loss, pain prevention, and mood and sleep quality improvement in insomniacs.[104] In addition, exercise can decrease OSA severity by inducing weight loss and reducing instability of the respiratory system and nasal resistance.[24] Exercise has also shown promising effects on increasing OSA patients' PA level.[44]

Studies examining PA levels and diurnal PA patterns in people with COMISA and their response to an exercise intervention are lacking. In this project we aimed to assess PA levels and diurnal PA patterns in people with COMISA vs age and sex matched insomniacs (INS) and good sleepers (GS). Furthermore, as a pilot study, we evaluated PA levels in the COMISA group before and after an exercise-training intervention.

3. Objectives and Hypotheses

3.1 Objectives

Primary Objective

The primary objective was to objectively assess PA levels and diurnal PA patterns in people with COMISA and compare them to those of age- and sex-matched INS and GS.

Secondary Objective

The secondary objective was to examine the correlations between: *i*) insomnia symptom severity (measured with insomnia severity index, ISI) and PA levels in all three groups (COMISA, INS, and GS); and *ii*) daytime sleepiness (measured with the Epworth Sleepiness Scale, ESS) and PA levels in the COMISA and INS groups.

Tertiary Objective

The tertiary objective was to compare objectively measured PA levels and diurnal PA patterns in people with COMISA before and after 8 weeks of exercise (Ex) training or 8 weeks of relaxation (Rel) intervention (active control).

Quaternary objective

The quaternary objective was to examine the correlation between the changes in insomnia symptoms (ISI) and changes in PA levels after 8 weeks of Ex training or Rel intervention in people with COMISA. In a previous study from our team, one of the objectives was to see whether there was a relationship between changes in ISI scores and changes in cardiorespiratory fitness. No significant correlation between these two parameters was found.[105] In the present project, we

wanted to see if the decrease seen in insomnia symptoms (ISI) after the 8-week intervention phase was linked with an increase in PA levels.

3.2 Hypotheses

Primary Hypothesis

We hypothesized that PA levels would be lowest in people with COMISA, followed by those of INS and by GS, respectively (COMISA<INS<GS). Also, we anticipated seeing more descending diurnal PA patterns in people with COMISA than in INS and GS and more "A-shaped" diurnal PA patterns in GS.

It has been shown that people with insomnia or OSA are less active compared to people without sleep problems.[102] In COMISA, we have OSA in addition to insomnia, therefore we anticipated this comorbid condition would further reduce PA levels compared to insomnia alone. In addition, previous studies suggested that descending PA pattern was more common in chronic diseases while "A-shape" pattern was more common in healthy controls, which is why we expected more descending patterns in COMISA and more "A-shape" patterns in GS.[99]

Secondary Hypothesis

We hypothesized that there would be a significant negative correlation between PA levels and ISI score (since a high ISI score reflects more severe insomnia symptoms) in our full sample (COMISA, INS, and GS). A negative correlation has previously been observed between ISI scores and number of steps taken.[106] Likewise, we hypothesized that there would be a significant negative correlation between PA levels and daytime sleepiness (ESS score), since daytime sleepiness and fatigue are commonly cited reasons affecting PA levels in INS and OSA patients.[102] However, this relationship may be moderated by age since PA levels were shown to be significantly lower in

younger (20–39 years) and older (≥ 60 years) adults with more frequent daytime sleepiness, but not in middle-aged (40–59 years).[107]

Tertiary Hypothesis

It has been shown that PA levels increase after a short-term (4 weeks) walking-based exercise intervention in patients with OSA and coronary artery disease.[42] In another study, no significant differences between baseline and post-intervention weekly steps was shown after either a CBTi only or CBTi +PA intervention in veterans who had chronic insomnia and might have mild or moderate OSA.[103] Of note, these veterans were highly active at baseline (> 9,500 steps per day), which may have led to a ceiling effect. In the present study, people with COMISA who regularly engaged in moderate-to-vigorous structured exercise training were excluded. We therefore hypothesized that PA level would increase in the COMISA group assigned to the Ex-intervention. As for the Rel group, our team previously showed a small improvement in insomnia symptoms (ISI) with the Rel training.[105] Therefore, if these participants' sleep improved, their PA level may also show slight improvements given the bidirectional relationship between sleep and PA. However, we expected a larger improvement in PA in the Ex-group than in the group undergoing the Rel intervention.

Quaternary Hypothesis

It has been shown that increasing PA to the levels recommended in public health guidelines leads to decreasing insomnia symptom severity and ISI score.[76] It has also been shown that increasing the number of steps taken leads to decreasing ISI values, and that the decrease in ISI is moderately and negatively associated with the change in PA.[108] Therefore, we hypothesized that a significant negative correlation would be observed between changes in PA level and changes in ISI score within the group receiving the Ex intervention.

4. Article: Physical Activity Levels and Diurnal Patterns in COMISA Versus Age- and Sex-Matched Insomniacs and Good Sleepers

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4.1 Abstract

Background: Over a third of people with obstructive sleep apnea have co-morbid chronic insomnia. This combination (COMISA) is associated with worse daytime functioning, quality of life, and health outcomes than either condition alone. Studies examining physical activity (PA) level and patterns and their response to exercise training in people with COMISA are currently lacking.

Research objectives: The primary objective of this study was to objectively measure PA levels and diurnal PA patterns in people with COMISA versus age- and sex-matched Insomniacs (INS) and Good Sleepers (GS). The secondary objective was to examine the association between *i*) PA levels and insomnia symptoms (Insomnia Severity Index, ISI) in participants from the three groups; and *ii*) PA levels and daytime sleepiness (Epworth Sleepiness Scale, ESS) in the COMISA and INS groups. The third objective was to compare objectively measured PA levels and patterns before and after 8 weeks of exercise (Ex) versus 8 weeks of relaxation (Rel) intervention (active control) in people with COMISA. The fourth objective was to examine the correlation between changes in PA levels and changes in ISI after 8 weeks of Ex or Rel intervention in COMISA.

Methods: This secondary analysis used activity data collected from four studies, all conducted in the same sleep lab using the same equipment and procedures. PA data were available for 15 COMISA participants and 15 INS and 15 GS matched on age (±5 years) and sex. Participants wore an accelerometer (Actiwatch-2) on their non-dominant wrist and recorded sleep/wake activities in a diary for 14 days. Mean daily PA levels, in counts per minute (cpm), and morning, afternoon, and evening PA levels were compared between groups with a repeated-measures ANOVA, as were pre- to post-intervention changes in PA levels in COMISA participants randomly assigned to Ex (N=4) or Rel (N=4). Spearman's correlations were used to assess associations between ISI and PA, ESS and PA, and changes in ISI and changes in PA.

Results: The sample mainly included middle-aged adults (54±13 years). Mean daily PA was 278±40, 316±108, and 335±121 cpm in COMISA, INS, and GS respectively. The group difference was not significant, but the group effect size was moderate (η_p^2=0.063). Evening PA level was significantly lower than morning or afternoon level across groups ($p<0.001$). The correlation between ISI and mean daily PA in participants from the three groups combined was very weak

and not significant (Spearman's rho= -0.03, p=0.84), as was the correlation between ESS and mean daily PA (Spearman's rho= -0.06, p=0.77). Mean daily PA went from 313±17 to 309±44 cpm in Ex and from 265±27 to 270±56 cpm in Rel (p=NS). There was a weak negative and not significant correlation between changes in ISI and changes in PA level after intervention (n=8, Spearman's rho=-0.04, p=0.93).

Conclusion: These findings confirm the presence of an evening drop in PA level across populations, signal a moderate negative effect of COMISA on PA levels, and call for interventions specifically targeting PA behavior in this population.

Keywords: physical activity level and diurnal pattern, comorbid insomnia and sleep apnea (COMISA), Actiwatch 2, insomnia severity index (ISI)

4.2 Introduction

Insomnia is a common sleep disorder which is associated with having difficulty falling or staying asleep or waking up too early in the morning, for a minimum of three nights per week for a minimum of three months, and leading to daytime sleepiness and distress.[3] Obstructive sleep apnea (OSA) is another common sleep disorder which is caused by partial or complete blockage of the upper airway during the sleep[23] and associated with snoring, daytime sleepiness, cardiovascular problems, and increased risk of all-cause mortality.[4,24] Over a third of people with OSA have co-morbid chronic insomnia, a combination commonly referred to as COMISA.[37] COMISA is associated with more sleep fragmentation and less amount of deep sleep in comparison with insomnia alone.[35] People with COMISA experience more respiratory disturbances, pain, and absenteeism from work in comparison with OSA patients.[35] Furthermore, they are faced with higher daytime impairments (e.g., decreasing daytime functioning and quality of life and increasing daytime sleepiness[4]), depression, and psychiatric problems compared to OSA or insomnia patients.[35]

Sleep disorders can also affect physical activity (PA) habits. Previous studies have shown that OSA[44] and insomnia[79] are associated with decreased PA levels due to daytime sleepiness and/or fatigue.[102] Other potential factors that decrease PA levels in OSA patients are increased OSA severity, dyspnea, cardiovascular problem, respiratory muscle dysfunction, and impairment of skeletal muscle energy metabolism.[24,82–84,92] Insufficient PA can, in turn, worsen the insomnia and OSA condition. In insomnia, as a result of the bidirectional relationship between sleep and PA, lower levels of PA are associated with poorer sleep.[102] In OSA group, insufficient PA have been associated with obesity, cardiovascular problem and increased OSA severity.[24,44]

Due to the significant impact of PA on insomnia and OSA patients' physical condition, PA could play an important role in COMISA patients' condition as well.

The recommended clinical management approach for COMISA is the combination of continuous positive airway pressure (CPAP) therapy (for the OSA component) and Cognitive Behavioral Therapy for Insomnia (CBTi) (for the insomnia component).[4] COMISA patients have more difficulties adhering to CPAP therapy than those with OSA alone.[4] Insomnia symptoms in COMISA patients cause more waking time during night than OSA alone, which decrease the acceptance and use of CPAP because tolerating a CPAP mask during nighttime awakenings is difficult.[4,35,38] CPAP related side effects are more probable in people with COMISA, which causes them to remove the CPAP mask or even reject the therapy.[4] CPAP long-term effectiveness is also affected by nasal discomfort, mask leak, congestion and claustrophobia.[40,41]As a result, a combination of CBTi and CPAP is recommended for people with COMISA.[4] CBTi, the gold standard treatment for insomnia, benefits COMISA patients by increasing acceptance of CPAP for long term use.[4] However, CBTi is costly, time consuming, and difficult to access because it is typically delivered by trained therapists during several weeks or months.[39] Thus, other practical solutions for COMISA patients are needed. Exercise training has been suggested as a non-pharmacological treatment for insomnia and sleep-disordered breathing. Exercise can lead to weight loss, pain prevention, and mood and sleep quality improvement in insomniacs.[104] In addition, exercise can improve OSA severity by inducing weight loss, and reducing instability of the respiratory system and nasal resistance.[24] Exercise training, which has shown some positive results in people with OSA[41,42] and insomnia[43], could be considered as an adjunct intervention for people with COMISA.

Studies examining PA levels and diurnal PA patterns in people with COMISA and their response to an exercise intervention are lacking. In this study, we aimed to compare PA levels and diurnal PA patterns in people with COMISA versus age- and sex-matched insomniacs (INS) and good sleepers (GS). In addition, as a pilot study, we aimed to assess PA levels in people with COMISA after 8 weeks of exercise (Ex) or relaxation (Rel) intervention.

4.3 Methods

4.3.1 Study Design

1) COMISA, INS, GS at baseline

For the first part of the project, secondary analyses of data obtained via four larger studies were conducted to compare PA levels and diurnal PA patterns in people with COMISA versus age- and sex-matched INS and GS. Data for INS and GS were obtained from three distinct studies: i) Impact of insomnia treatment on mood, brain function and cardiovascular health[109] (trial registration: ISRCTN13983243); ii) Impact of Insomnia Treatment on Brain Responses During Resting-state and Cognitive Tasks (trial number: ClinicalTrials.gov ID: NCT04024787); and iii) Coupling of Neural Oscillations in Sleep, in Relation to Cognition and Aging. Data for the COMISA participants were obtained from one pilot randomized trial (called APNex) investigating the effects of exercise training alone or in combination with cognitive behavioral therapy on insomnia symptoms and sleep quality in people with COMISA (https://www.isrctn.com/ISRCTN63989489). Table 1 represents age and sex matched participants in the three groups.

Table 1. Age and sex matched participants in COMISA, INS, and GS study

Trio ID	Sexe	Age		
		COMISA	INS	GS
1	F	70	65	72
2	F	68	65	66
3	F	67	65	65
4	F	63	63	59
5	F	61	61	58
6	F	57	57	57
7	F	55	55	56
8	F	29	29	29
9	M	62	64	61
10	M	60	56	60
11	M	56	55	59
12	M	53	48	54
13	M	47	46	47
14	M	36	36	36
15	M	29	29	27

2) COMISA before and after the 8-week interventions

For the second part of this project, which aimed at comparing PA levels and patterns in COMISA participants before and after an Ex or a Rel intervention, data were obtained from the pilot trial APNex. The trial followed a randomized controlled parallel-group design where participants were randomly assigned to one of two intervention arms (Ex or CBTi-Ex) for 16 weeks and were assessed at three time points: pre-, post-8 weeks and post-16 weeks intervention. The Ex-group received two back-to-back 8-week phases of structured exercise training. The CBTi-Ex group received self-guided Rel training for the first 8-week phase, followed by a combination of CBTi and structured exercise training (CBTi-Ex) for the second 8-week phase. This thesis project uses physical activity data collected in the APNex trial and focuses on the first 8-week portion, that is the comparison between Ex training (intervention of interest) and self-guided Rel training (active control intervention) (Figure 1).

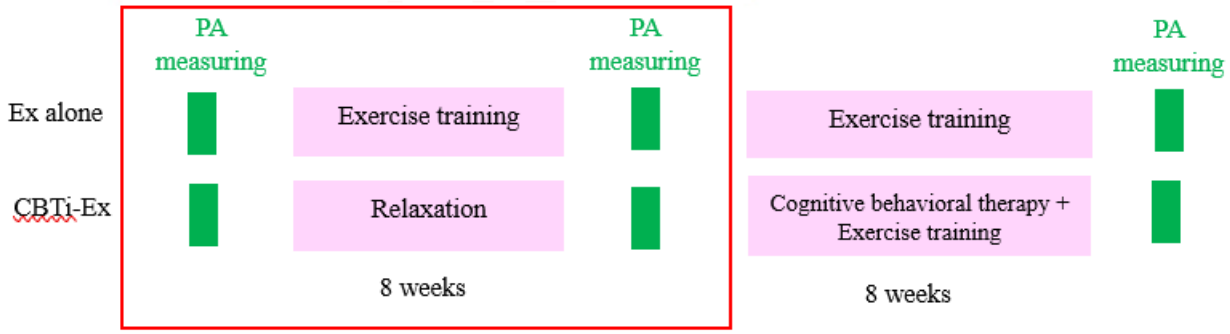

Figure 1. Study design for the larger pilot trial, with the red box representing the focus of this thesis project

4.3.2 Participants

Participants for all four trials were recruited through poster advertisements sent via newspaper or email. To determine the eligibility, participants underwent three levels of screening including phone-based screening, a diagnostic interview, and polysomnography. In the first step, participants' general eligibility was assessed on the phone. Then, a semi-structured diagnostic interview was applied to confirm the diagnosis of chronic insomnia (in INS and COMISA participants) and assess the presence of other physical or mental disorders. Finally, subjects underwent overnight polysomnography to evaluate for OSA (to confirm an OSA diagnosis in COMISA participants and confirm the absence of OSA in INS participants and GS) and exclude any other sleep disorders before entering the study.

Inclusion criteria:

INS and COMISA participants had to have a diagnosis of insomnia disorder, defined as experiencing problems falling or staying asleep for minimum 3 nights per week for minimum 3 months. INS participants needed to have primary insomnia with no other current comorbidities. COMISA participants also had to receive a diagnosis of mild to moderate OSA by a physician, with an apnea-hypopnea index between 5 and 30, confirmed during the baseline polysomnography. COMISA participants under CPAP treatment were also included if they had been using CPAP for at least 3 months before the study. GS were participants who self-identified as good sleepers, with no sleep complaint.

Exclusion criteria:

In all studies, participants younger than 18 years old were excluded. Patients with other sleep disorders, such as narcolepsy, restless leg syndrome, and REM sleep behavior disorder, were

excluded from the study. Other medical problems included stroke, heart problems (myocardial infarct, heart failure, heart surgery, pacemaker, etc.), diabetes, cancer treatment in the last 2 years, schizophrenia or bipolar disorder, epilepsy, neurological disease (e.g., multiple sclerosis, Parkinson's disease, dementia), major surgery in the last 3 months, chronic pain syndrome which interfered with sleep, or having severe infection in the past 3 months were excluded. Working night shifts, alcohol or drug abuse, being pregnant or breastfeeding, or being unable to stop medications such as benzodiazepines for at least two weeks before the first assessment and during the study caused exclusion. An exclusion criterion specifically related to the insomnia studies was the presence of sleep apnea with an AHI of 15 per h. In the APNex study individuals reporting performing more than 150 minute per week of structured moderate-to-vigorous intensity exercise were excluded to avoid a ceiling effect with the exercise-training program.

Ethical approval for the "APNex" (Certification Number: 30007287), "Coupling of Neural Oscillations in Sleep, in Relation to Cognition and Aging" (Certification Number: 30002645) and "Impact of insomnia treatment on mood, brain function and cardiovascular health" (Certification Number: SPF#30005506) was obtained from Concordia University's Human Research Ethics Committee. "Impact of Insomnia Treatment on Brain Responses During Resting-state and Cognitive Tasks" CCER-19-20-04 was approved by Comité central d'éthique de la recherche (CCER). All participants signed the written informed consent form. From the 16 COMISA participants who completed baseline actigraphy data collection, we identified 15 INS and 15 GS participants with adequate age and sex match (maximum accepted age difference: ± 5 years). Analyses were therefore performed on 15 trios of participants matched for age and sex. From the 15 COMISA participants, only 8 participants (4 in Ex and 4 in the Rel group) had valid PA data at the baseline and post-8 weeks intervention points.

4.3.3 Physical activity assessment

Participants were instructed to wear an Actiwatch-2 (Phillips Respironics, USA) on their non dominant wrist for 14 consecutive days and then to return it to the sleep lab. The Actiwatch-2 is a wristwatch which has a small piezoelectric sensor to monitor gross motor activity. This device has been validated to monitor sleep quality and patterns and is also used to measure PA levels in counts per unit time.[110] The device detects acceleration forces and then converts these forces into voltage signals. After that, these signals are integrated as an average or peak acceleration based on the epoch length and then reported as activity counts (AC).[111] The AC recorded for each epoch can then be exported in an Excel working sheet and averaged during daytime.[112] Daily mean activity count per minute (AC/min) and daily total AC is automatically calculated by the Philips Actiware Export File (Version 05.00) software. Activity count data between Actiwatch-2 and GT3X monitoring devices, which is a gold standard tool for measuring PA, acceptably correlate.[111] Although accelerometers worn around the waist are considered the gold standard for assessing waking movement (e.g., PA) (as they detect gross movements at the trunk), it was suggested that the validity and reliability of wrist-worn Actiwatch-2 is comparable to a reference accelerometry device (GT3X).[111,113] In addition, the Actiwatch-2 shows a high level of reproducibility to predict PA during sedentary and active time in a laboratory environment.[111,114]

Once activity data was collected from participants, they were downloaded using the Actiware software in the PERFORM Sleep Lab. For determining onset of bedtimes and waketimes, two of three factors including white light (recorded by the Actiwatch), the event marker (which was pressed by the participant to mark the sleep onset and rise time), and the sleep diaries were considered. After that, data were extracted into Excel files and treated following handling recommendations from "A Catalogue of Rules, Variables, and Definitions Applied to

Accelerometer Data in the National Health and Nutrition Examination Survey".[115] All activity data were visually inspected from wake time to bedtime. Periods with more than 60 min of consecutive zeros were excluded because it was considered as non-wear time. A day with less than 10 hours of PA data or more than three hours of consecutive missing data was considered invalid and was excluded.[115] After the data were treated for valid days, 30-second epochs of activity counts were reintegrated into 60-second epochs of activity counts to allow the comparison of the results with other references available on PA levels. Finally, daily activity count per minute (cpm) was calculated by dividing the total sum of activities per day by total valid minutes per day. Daily average cpm was calculated by taking the average of cpm for valid days.

Diurnal PA patterns were calculated based on a tercile approach. Rise-time and bedtime were averaged for each participant over valid days. Average bedtime was subtracted from average risetime to obtain the average number of daytime hours per participant (e.g. if average bedtime was 22:30 and average rise time was 7:30, then average daytime hours were 15 hours). That amount was then divided by three to get the duration of each tercile (e.g. here, 5 hours) and terciles were determined accordingly (e.g., morning tercile: 7:30–12:30, afternoon tercile: 12:31–17:30, evening tercile: 17:31–22:30). Finally, diurnal PA patterns (average cpm for each tercile) was established by calculating the average cpm for each tercile during valid days.

4.3.4 Insomnia Severity Index (ISI) and Epworth Sleepiness Scale (ESS)

Insomnia Severity Index (ISI) is a self-report questionnaire measuring a person's perception of their insomnia for the preceding month. For rating items, a 5-point Likert scale is applied (e.g., 0 = no problem; 4 = very severe problem). The total score ranges between 0 and 28, with the following interpretation: 0–7: absence of insomnia; 8–14: sub-threshold insomnia; 15–21: moderate insomnia; and 22–28: severe insomnia.[17]

The ESS is a questionnaire which includes eight questions and provides information about a person's level of daytime sleepiness. Each question asks how likely it is to fall asleep in each situation such as while watching television, sitting and reading, etc. Each question can be scored from 0 (no sleepiness) to 3 (significant sleepiness) points. Total score ranges from 0 to 24 points.[116,117] An ESS score for normal daytime sleepiness is between 0 and 10, mild excessive daytime sleepiness between 11 to 12, moderate daytime sleepiness between 13 and 15, and severe excessive daytime sleepiness between 16 and 24. This survey have moderate to strong reliability and validity in general population.[118]

4.3.5 Interventions for COMISA participants

4.3.5.1 Exercise Training Protocol

The exercise-training intervention consisted of three weekly sessions. One session took place at Concordia University's PERFORM Center, under the supervision of a trained exercise physiologist, while the other two weekly sessions were unsupervised, occurring at the participants' home or community gym or center. The 60-minute exercise sessions consisted of 40 minutes of moderate-intensity aerobic exercise training followed by resistance training. Aerobic training included a 5-minute warm-up, 30 minutes of aerobic exercise (walking, cycling and running) performed at the target intensity (i.e., heart rate corresponding to the participant's ventilatory threshold determined from prior cardiorespiratory exercise testing), and a 5-minute cool down. Resistance training consisted of one set of 12-15 repetitions of 6-8 different exercises. For supervised sessions, resistance training exercises included the chest press, bicep curl, triceps extension, low row, leg press, leg extension, leg curl, and plank. For unsupervised session, they

consisted of the chest press, leg press, seated calf press, seated row, single leg hamstring curls, lateral band walk, bicep curl, and triceps press.

4.3.5.2 Relaxation protocol

Relaxation training consisted of self-guided sessions with digital audio recordings for at least three sessions weekly. Participants were followed up by calling to see whether they spent enough time on Rel training. The audio recordings consisted of information on stress and relaxation, diaphragmatic breathing exercises, progressive muscle relaxation, and guided imagery.

4.3.6 Statistical analysis

Descriptive statistics were obtained to characterize the sample and assess the data distribution of our main outcomes for normality (e.g., age, body mass index [BMI], ISI, PA level and diurnal PA pattern). Key baseline characteristics (e.g., BMI, ISI, ESS, etc.) were compared between COMISA, INS and GS with repeated-measures ANOVA (since groups were matched) to see if significant differences were present.

A 3 x 3 repeated-measures ANOVA was conducted to assess the effect of group (3 levels: COMISA, INS, GS), the effect of tercile (3 levels: terciles 1, 2, and 3) and the interaction effect of group by tercile on PA level. Both group and tercile were considered within-subjects measures since participants from the three groups were matched on age and sex. The repeated-measure ANOVA is known to be robust against violations of the normality assumption. Partial eta squared (η_p^2) obtained with the repeated-measures ANOVA were used to describe the effect size of group, tercile, and group by tercile, with values ≥ 0.01 indicating a small effect, ≥ 0.06 a medium effect, and ≥ 0.14 indicating a large effect.[119]

A 2 x 2 ANOVA was conducted to evaluate the effects of time (within-subjects variable with 2 levels: pre and post-8 weeks intervention, i.e. PRE vs POST) and group (between-subjects variable with 2 levels: Ex versus Rel) on PA levels in COMISA participants. Partial eta squared obtained with the repeated-measures ANOVA were used to describe the effect size of group, time, and group by time.

Spearman's bivariate correlations were used to evaluate the association between ISI and PA levels in the full sample (COMISA, INS, GS together) and ESS and PA levels in COMISA and INS participants. Spearman's bivariate correlations were also used to determine whether a pre-to-post-intervention change in PA level was associated with a change in ISI in COMISA participants who underwent Ex or Rel. A p value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 29.0.

4.4 Results

Baseline characteristics for the 45 participants (15 COMISA, 15 INS, 15 GS) are shown in Table 2. The sample mainly included middle-aged adults (54±13 years) with a large age gap (45 years) between the youngest and oldest participant. The number of females was one more than male (F/M: 8/7) in each group.

One-way repeated measure ANOVA results revealed a significant difference in mean BMI between the three groups ($p=0.02$, $\eta_p^2=0.54$, observed power=0.75), but this result must be taken with caution because it only applies to 40% of the sample (18/45 participants). Indeed, due to missing data, especially in the GS group, BMI was only available for 6 trios of participants. Pairwise comparisons further showed a borderline significant difference in BMI between the COMISA and INS groups ($p=0.053$), but no significant difference between COMISA and GS ($p=0.061$) or between INS and GS ($p=0.41$).

One-way repeated measure ANOVA results revealed a significant difference in mean ISI between the three groups ($p<0.001$, $\eta_p^2=0.75$, observed power=1). Pairwise comparisons further showed that the difference was significant between COMISA and GS ($p<0.001$) and between INS and GS ($p<0.001$), but not between COMISA and INS ($p=0.61$). One-way repeated measure ANOVA results also revealed no significant difference in mean ESS between COMISA and INS ($p=0.22$, $\eta_p^2=0.146$, observed power=0.22).

Table 2. Demographics for all participants (N total = 45, N for each group = 15)

Variable	COMISA	INS	GS
Age (years), Range	29-70	29-65	27-72
Mean ± SD	54 ± 13	53 ± 13	54 ± 13
Median ± IQR	57 ± 16	56 ± 18	58 ± 14
Sex (F/M)	8/7	8/7	8/7
CPAP Use (Y/N)	8/7	n/a	n/a
Baseline Height (cm), Range	157-182	151-191	unavailable
Mean ± SD	168 ± 8	170 ± 13	unavailable
Median ± IQR	169 ± 16	166 ± 24	unavailable
Baseline Weight (kg), Range	45.1-142.3	52.2-111.1	unavailable
Mean ± SD	88.0 ± 28.1	72.2 ± 14.8	unavailable
Median ± IQR	77.5 ± 28.8	70.3 ± 19.0	unavailable
Baseline BMI (kg/m²), Range	17.9-54.2	20.5-43.3*	21.5-28.3**
Mean ± SD	31.1 ± 9.6	25.4 ± 5.9*	24.6 ± 2.6**
Median ± IQR	29.1 ± 11.8	23.7 ± 5.6*	24.6 ± 4.9**
ISI, Range	8-25***	11-27	0-12
Mean ± SD	18 ± 5***	18 ± 5	4 ± 4
Median ± IQR	18 ± 8***	17 ± 7	3 ± 5
ESS, Range	2-20***	0-16***	unavailable
Mean ± SD	10 ± 5***	7 ± 5***	unavailable
Median ± IQR	7 ± 9***	6 ± 10***	unavailable

SD = standard deviation; IQR = interquartile range; CPAP = Continuous Positive Airway Pressure; n/a: not applicable; BMI = body mass index; ISI = Insomnia Severity Index. ESS = Epworth Sleepiness Scale. *N=14, **N=6, ***N=13

PA Levels and Patterns in COMISA Versus INS and GS

Table 3 represents the mean daily activity count per minute (cpm), rise time, and bedtime averaged over the 14-day monitoring period for COMISA, INS and GS. Mean daily PA data was normally distributed for COMISA but not for INS and GS. All COMISA participants except for one had a rise time before 9:08 and all but four had a bedtime before midnight. In the INS and GS groups, all participants had a risetime before 9:13 and 8:58, respectively. In INS, all participants had a bedtime before midnight. In GS, all except four participants had bedtime before midnight. Mean number of valid days in COMISA, INS and GS was 12.5±1.9, 11.7±2.8 and 9.2±3.2 respectively. One-way repeated measure ANOVA results revealed a significant difference in mean number of valid days between the three groups ($p=0.008$). Pairwise comparisons further showed that the difference was significant between COMISA and GS ($p=0.003$) and between INS and GS ($p=0.04$), but not between COMISA and INS ($p=0.38$).

Table 3. Objectively Measured Daily PA (cpm), Rise Time, Bedtime, Split Times, Number of Valid and Missing Days

Variable	COMISA (N=15)	INS (N=15)	GS (N=15)
Daily PA (cpm)			
Range (min-max)	227-364	201-610	203-577
Mean ± SD	278 ± 40	316 ± 108	335 ± 121
Median	269	286	292
Rise Time, hr:min			
Range (min-max)	6:13-13:14	5:22-9:13	5:54-8:57
Mean ± SD	7:57 ± 1:42	7:14 ± 0:59	7:25 ± 0:50
Median	7:35	7:04	7:25
End T1/start T2, hr:min			
Range (min-max)	11:28-17:49	11:09 – 12:59	11:30 – 13:59
Mean ± SD	13:03 ± 3:35	12:11 ± 00:42	12:35 ± 00:45
Median	12:40	12:14	12:21
End T2/Start T3, hr:min			
Range (min-max)	16:38-22:24	16:54 – 18:31	16:42 – 19:07
Mean ± SD	18:22 ± 4:48	17:36 ± 00:28	16:58 ± 03:26
Median	17:59	17:40	17:28
Bedtime, hr:min			
Range (min-max)	21:17-2:58	22:12-23:26	21:03-0:52
Mean ± SD	23:23 ± 1:32	22:49 ± 0:24	23:08 ± 1:01
Median	22:53	22:45	23:00
Number of valid days			
Range (min-max)	7-14	5-14	4-13
Mean ± SD	12.5 ± 1.9	11.7 ± 2.8	9.2 ± 3.2
Median	13	13	11
Number of missing days			
Range (min-max)	1-8	1-10	2-11
Mean ± SD	2.5 ± 1.9	3.3 ± 2.8	5.8 ± 3.2
Median	2	2	4

PA= physical activity, cpm = counts per minute, hr = hours, min = minutes, SD = standard deviation

Figure 2 illustrates the mean daily PA (cpm) for each terciles for COMISA, INS, and GS participants. The repeated-measures ANOVA revealed no significant main effect of group (F=0.94, p=0.4); however, the effect size for group was moderate (η_p^2=0.063). The interaction of group by tercile was also not statistically significant (F=0.67, p=0.61,) with a small effect size (η_p^2=0.046). Of note, the observed power of 0.2 for the group and interaction effects suggests that we were underpowered for these analyses. A statistically significant main effect of tercile was detected (F=29.7, p<0.001) with a large effect size (η_p^2=0.68) and observed power of 1. Follow-up pairwise comparisons revealed that PA level was statistically significantly lower in the third tercile compared to the first and second terciles regardless of group (p<0.001), suggesting an evening drop as illustrated in Figure 2.

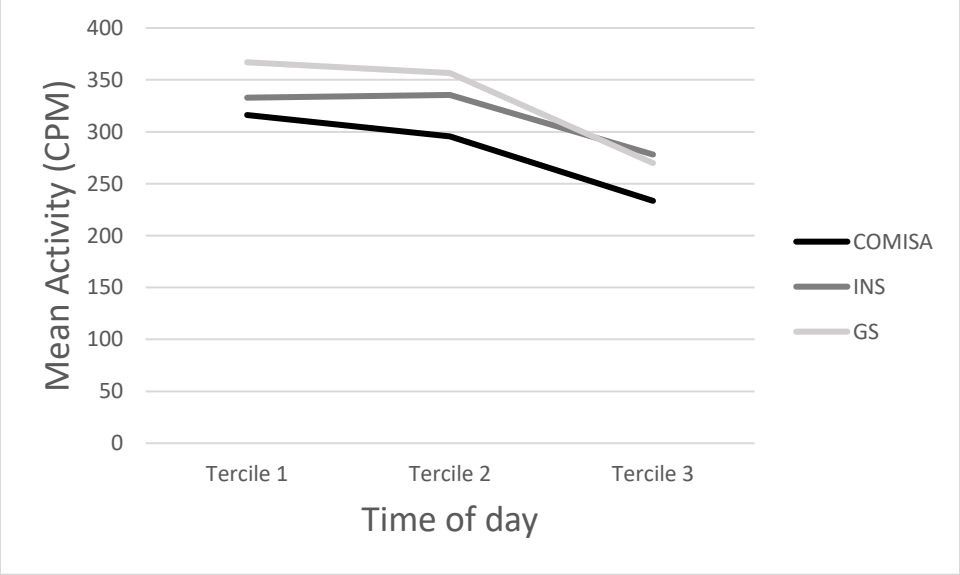

Figure 2. Mean activity (cpm) for each tercile for COMISA, INS and GS participants

Figure 3 illustrates individual diurnal PA patterns for COMISA (Panel A), INS (Panel B) and GS (Panel C). Four different activity patterns were detected across the groups: an "A-shaped" activity pattern where the highest PA level was seen in the afternoon; a "V-shaped" pattern where lowest PA level occurred in the afternoon; a "descending" pattern where PA level decreased from morning to evening; and an "evening drop" activity pattern where PA level remained stable from morning to afternoon and dropped in the evening. In the COMISA group, four participants showed an "A-shaped" pattern, two a "V-shaped" pattern, seven a "descending" pattern, and two an "evening drop" pattern. In the INS group, six participants showed an "A-shaped", two a "V-shaped", six a "descending" pattern, and one an "evening drop" pattern. In the GS group, four participants showed an "A-shaped" pattern, two a "V-shaped" pattern, six a "descending" pattern, and three an "evening drop" pattern.

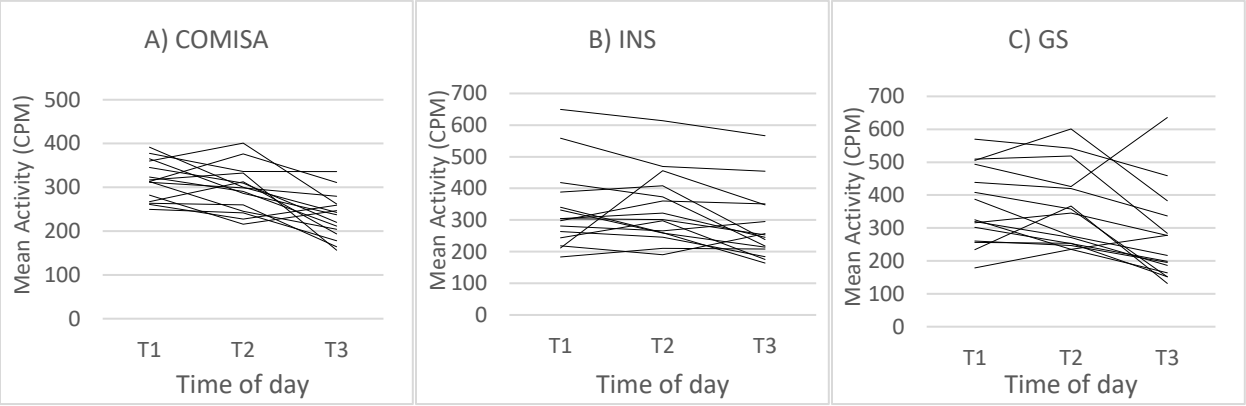

Figure 3. PA pattern for of COMISA (A), INS (B) and GS (C)

Correlations between ISI, ESS and PA

The correlation between ISI and mean daily PA in participants from the three groups combined was very weak and not significant (Spearman's rho= -0.03, p=0.84), as was the correlation between ESS and mean daily PA in COMISA and INS participants (Spearman's rho= -0.06, p=0.77). Since a borderline significant difference in BMI was seen between the COMISA and INS groups and

since BMI has been associated with PA levels in the literature[50–52], we conducted a posteriori correlation analyses between BMI and mean daily PA. A moderate negative and borderline significant correlation was found (Spearman's rho= -0.33, p=0.052).

Demographics of COMISA participants before and after EX (N=4) or Rel intervention (N=4) are shown in Table 4. One-way repeated measure ANOVA results showed a significant difference in mean ISI between PRE to POST intervention in Ex-group (p=0.01) but not between PRE to POST intervention in Rel-group (p=0.46). One-way repeated measure ANOVA results also revealed no significant difference in mean BMI before and after Ex (p=0.17) or before and after Rel (p=0.16) as well as in ESS before and after Ex (p=0.07) or before and after Rel intervention (p=0.38).

Table 4. Demographics for COMISA participants before and after Ex (N = 4) or Rel intervention (N= 4)

Variable	**COMISA PRE Ex**	**COMISA POST Ex**	**COMISA PRE Rel**	**COMISA POST Rel**
Age (years), Range	36-70	-	29-67	-
Mean ± SD	57.5±14.8		52.8±16.9	
Median	62		57.5	
Sex (F/M)	3/1	-	1/3	-
BMI (kg/m²), Range	17.9-35.9	17.4-35.9	24.1-42.6	27.9-40.2*
Mean ± SD	25.9±7.6	25.5±7.8	31.6±7.8	32.8±6.5*
Median	24.9	24.3	29.9	30.2
ISI, Range	15-25	12-20	10-18	9-23
Mean ± SD	20.8±4.3	15.3±3.6	15±3.6	16.5±6.6
Median	21.5	14.5	16	17
EES, Range	4-17	2-14	2-10	4-15*
Mean ± SD	10.3± 6.7	8.3± 5.7	6.3±3.3	8.3±5.9*
Median	10	8.5	6.5	6

SD = standard deviation; BMI = body mass index; ISI = Insomnia Severity Index. ESS = Epworth Sleepiness Scale. *N=3

PA Levels and Patterns Before and After 8 weeks of Ex or Rel intervention in COMISA

Figure 4 represents the mean daily activity count per minute (cpm) averaged over the 14-day monitoring period for COMISA participants before and after their intervention. The average level of PA went from 313±17 to 309±44 in the Ex subgroup and from 265±27 to 270±56 in the Rel subgroup. Mean number of valid days before and after intervention was 11.9±2.2 and 12.1±3.4 respectively.

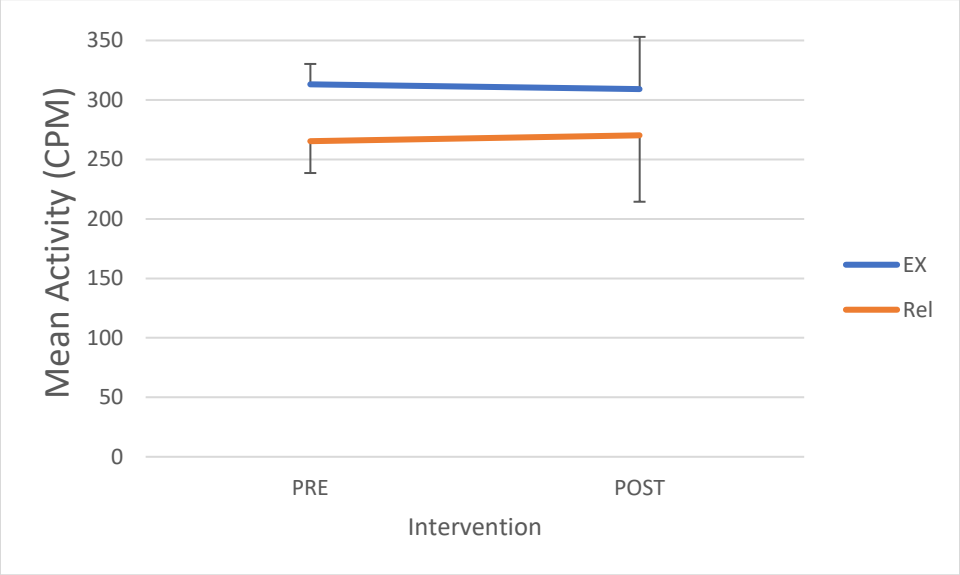

Figure 4. Mean daily activity count per minute (cpm) for COMISA participants before and after Ex or Rel intervention

A repeated-measures ANOVA revealed no significant main effect of group (Ex vs Rel, F=5.6, p=0.099), main effect of time (PRE vs POST, F=0.003, p=0.96), or group by time interaction (F=0.06, p=0.82). A large effect size was observed for group (η_p^2=0.65), whereas small effect sizes were seen for time (η_p^2=0.001) and for the interaction of time by group (η_p^2 =0.02).

Figures 5 and 6 illustrate the individual PA patterns for COMISA participants before and after Ex (N=4) or Rel intervention (N=4). In the Ex-group, there were two "A-shaped" and two "descending" patterns PRE Ex (fig 5A), while there were one "A-shaped", two "descending", and

one “evening drop” pattern POST Ex (fig 5B). In the Rel group, there were three “descending” and one “evening drop” patterns PRE Rel (fig 6A), while there were one “descending”, one “V-shaped”, one “evening drop”, and one “A-shaped” pattern POST Rel (fig 6B).

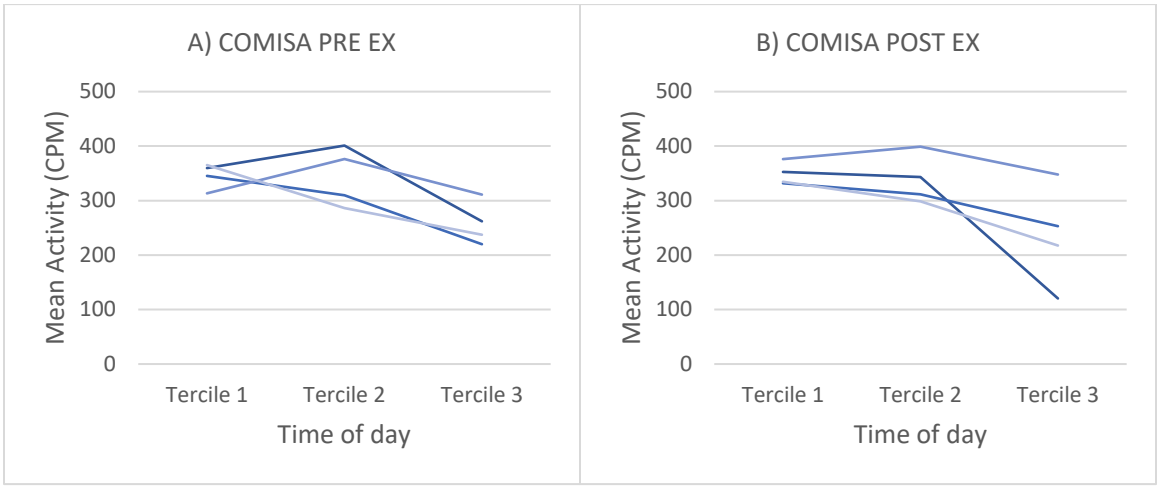

Figure 5. PA pattern for COMISA participants. A: PRE Ex, B: POST Ex

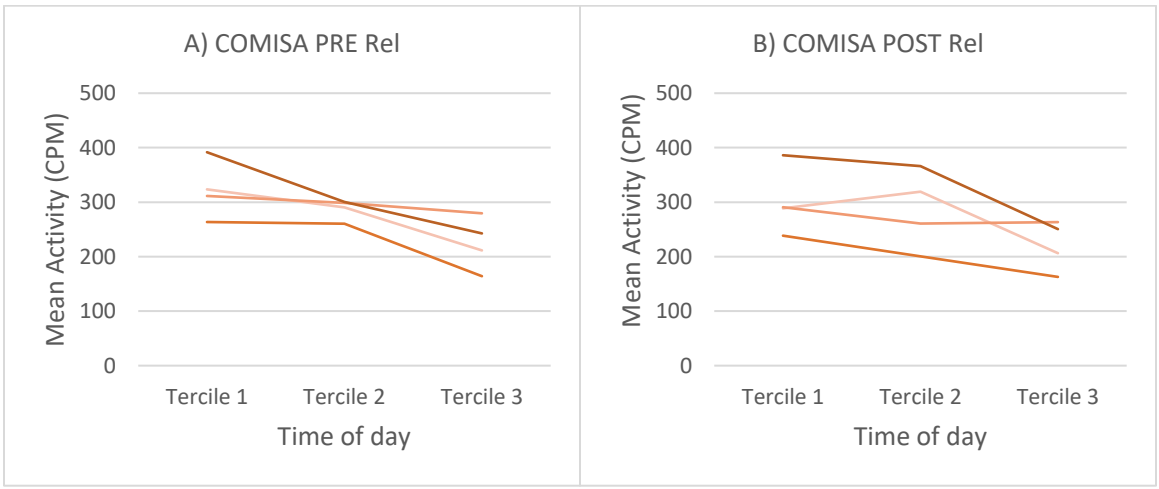

Figure 6. PA pattern for COMISA participants. A: PRE Rel, B: POST Rel

Correlations between changes in ISI and changes in PA

There was a weak negative and not significant correlation between change in ISI and change in PA level after the interventions (Spearman’s rho=-0.04, p=0.93).

4.5 Discussion

The primary aim of this study was to compare objectively measured PA levels and diurnal PA patterns in people with COMISA to those of age- and sex-matched INS and GS. Another aim was to assess the impact of 8 weeks of Ex versus Rel intervention (active control) on PA levels in a pilot sample of people with COMISA. The main findings can be summarized as follows. First, the mean and median values for daily PA level were lowest in COMISA, followed by INS, and then by GS, as expected. Although group differences were not statistically significant, the effect size for group was moderate (η_p^2=0.063). Second, the interaction of group by time-of-day (tercile) on PA level was not significant and the effect size was small, and the distinct PA patterns observed (e.g., "A-shaped", descending, etc.) were spread as heterogeneously within the groups as they were between the groups, suggesting no differentiation in diurnal PA patterns between COMISA, INS, and GS. Evening PA level was significantly lower than morning and afternoon PA level across the three groups, confirming earlier reports of an evening drop in PA level. Lastly, 8 weeks of moderate-intensity Ex training did not elicit any change in PA level nor did Rel training in a pilot subsample of people with COMISA.

To our knowledge, this is the first study to report on objectively measured PA levels and diurnal PA patterns in people with COMISA versus age- and sex-matched INS and GS. Mean and median values for daily PA followed the expected direction (COMISA < INS < GS). Although group differences were not statistically significant, the effect size for group was moderate and the observed statistical power for this analysis was low despite the paired study design, suggesting that this observation should be confirmed in a larger sample.

Studies have shown that there is a bidirectional relationship between sleep and PA.[102] Poor sleep leads to less PA, and lower levels of PA are associated with poorer sleep.[102] It has been shown that

people with insomnia or OSA are less active compared to people without sleep problems.[102] Reasons that may affect PA levels in INS and OSA patients include daytime sleepiness and/or fatigue.[102] Other potential factors in OSA patients include increased OSA severity, dyspnea, cardiovascular problem, respiratory muscle dysfunction, and impairment of skeletal muscle energy metabolism.[24,82–84,92]

We examined the association between mean daily PA and insomnia symptom severity (ISI) as well as daytime sleepiness (ESS) and found very weak and non-significant correlations. This result is in line with two prior studies on the correlation between sleepiness and PA levels – one in OSA participants and the other in multiple sclerosis participants – as they found no statistically significant correlation between PA and ESS.[82,120] However, this result is not aligned with findings from a study on students (20.9 ± 1.4 years) showing a significant negative correlation between ISI and number of steps taken.[106] This inconsistency may happen possibly because both sleep and PA are affected by many factors including age.[3,97]

We also looked at the association between BMI and mean daily PA after noting differences in BMI between the three groups. We found a signal suggesting that a higher BMI was linked with a lower mean daily PA level. Prior cross-sectional studies found a negative correlation between PA and BMI.[50–52] One study showed that there was a weak negative significant association between PA and BMI in non-obese participants while this correlation was moderate negative significant in obese individuals.[52] Since BMI was higher in the COMISA group than in the INS and GS groups, the lower mean value for daily PA level observed in COMISA may be related to the elevated BMI more than to the presence of COMISA per se. The proposed downward crescendo in mean daily PA level from GS to INS to COMISA patients will have to be confirmed in a larger sample. In

order to isolate the impact of the sleep disorders on PA level, future studies should control for BMI in addition to age and sex.

The present study is also the first to report on diurnal PA patterns in people with COMISA, INS, and GS. Our results suggest no clear differentiation in diurnal PA pattern between these groups, but rather variability that point towards interindividual differences. This finding does not support our hypothesis, which was that we would see more descending patterns in people with COMISA and more "A-shaped" patterns in GS. This hypothesis was based on prior studies suggesting that the descending pattern was more common in chronic diseases while "A-shaped" pattern was more common in healthy controls.[99] These studies were scarce and conducted in small samples, therefore our finding adds nuance to this literature.

Our findings are in line with earlier studies that documented an evening drop in PA level in people with chronic obstructive pulmonary disease (COPD).[99] Guidelines regarding healthy sleep recommend avoiding evening exercise because it can delay circadian rhythm and disrupt sleep. However, because of work or study commitments, many people do not have enough time in the morning to accumulate enough PA by the end of the day; by discouraging them to do exercise in the evening, this recommendation may decrease their overall PA level.[121] Studies have shown mixed results of negative, null, and positive effects of evening PA on sleep.[122–124] One study showed that there is not a meaningful relationship between evening PA and sleep quality or duration.[121] A systematic review and meta-analysis also showed that evening exercises does not have negative effects on sleep.[125] However, vigorous exercise ending less than one hour before bedtime could impair sleep onset latency, total sleep time, and sleep efficiency probably because of an incomplete recovery of the cardiovascular system, which causes increasing heart rate.[125] Overall, these studies suggest that people should not avoid evening PA for subsequent sleep

considerations. Behavioral strategies maybe needed to improve evening PA level. One of them is making PA a purposeful activity. In this regard, dog walking could be a good example which brings motivation for the owner. Studies showed dog walking provides a physically active lifestyle which causes the owner to reach the minimum recommended PA level.[126] By better understanding PA behaviours such as evening drops, healthcare practitioners will be able to make a better plan of PA programming for individuals.

This study also provides pilot results on the impact of 8 weeks of Ex training versus Rel training (active control) on PA levels and patterns in a subsample of people with COMISA. Mean daily PA levels remained remarkably similar from pre- to post-intervention in both groups, suggesting no effect of Ex or Rel intervention on habitual physical activity behaviour. This finding must be interpreted with caution since it was obtained in only 4 participants per group. A review study examined the effects of exercise as an intervention on PA level in people with OSA in three randomised control trials.[44] The results suggest that, although exercise training can reduce the OSA severity and improve sleepiness and VO_{2peak} (without any changes in BMI)[88,127], it may not improve PA level significantly [25,44], which supports our results. This review study suggests that improving sleep or sleep apnea may not be enough to change PA level.[44] It also suggests that longer rehabilitation programs of more than 12 weeks may be more effective on changing PA level[44]. Longer rehabilitation programs may have greater impacts on PA level in both pulmonary and cardiac rehabilitation and also on patient's ability to maintain the new health behavior after finishing the treatment.[44,128,129] It is also noted that PA should be considered as a multidimensional and complex health behavior when designing an intervention to increase PA level.[44] PA counselling has shown positive results in increasing PA level in chronic insomnia. The results from a randomized control trial on participants with chronic insomnia who were randomized into PA

counseling + sleep restriction therapy (PASR) or sleep restriction alone showed that PA level significantly increased with PASR ($P<0.05$). Future studies should consider using PA counselling in addition to an exercise intervention to see whether it can improve PA level in COMISA group.[130]

4.5.1 Strength and limitations

One of the most important strengths of this study is that COMISA participants were compared to age- and sex-matched INS and GS. Another strength is that although this study is a secondary analysis of activity data collected from four different studies, all studies used the same instrument and methodology to assess activity data. These studies also used complete evaluation for the diagnosis of insomnia (with interview and screening) and COMISA (with polysomnography). We also objectively measured PA level using Actiwatch-2, which is a valid and reliable tool for activity monitoring.[111] The exercise program in the COMISA group was planned, delivered, and supervised by trained kinesiologists. Overall, these methodological aspects ensured good internal validity.

The main limitation of this study is the sample size, which decreases the power of study. Another limitation was technical issues with the Actiwatch-2, which caused missing data, especially in post intervention participants (in the COMISA group). Excluding COMISA participants performing more than 150 minute per week of moderate-to-vigorous intensity exercise (to ensure participants would benefit from the exercise-training program) was another limitation, as this may have excluded the most active COMISA patients. Another weakness was not having data on participants' employment status, which may have mediated PA levels. In addition, in GS group, BMI was unavailable for many participants, while studies have shown a significant negative correlation between BMI and PA level in healthy adults aged 44.9±15.8 years.[131]

4.5.2 Future Directions

Future studies should include a larger sample size, with BMI-matched (in addition to age- and sex-matched) comparison groups (e.g., INS and GS) to confirm our findings. In addition, having information about employment status could be helpful, as it affects PA levels and patterns. In future studies, it may be of interest to consider the obstructive sleep apnea severity (apnea-hypopnea index or AHI) of COMISA patients to help identify if it would be a key factor influencing mean PA levels. We would also recommend examining PA counseling interventions in addition to excise intervention for improving PA level in COMISA patients.

4.5.3 Conclusion

In conclusion, results from this study confirm the presence of an evening drop in PA level across various populations. They also signal a moderate negative effect of COMISA on PA levels, a finding that will need to be confirmed in a larger sample. Lastly, they call for interventions specifically targeting PA behavior, such as PA counselling, to help populations at risk of decreased PA levels, such as those with sleep disorders.

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6. Appendix: COMISA participants' flowchart