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Exercise and sleep – Review and future directions

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Abstract This review focuses on the effects of exercise on sleep. In its early days, sleep research largely focused on central nervous system (CNS) physiology using standardized tabulations of several sleep-specific landmark electroencephalogram (EEG) waveforms. This method has enabled the observation and inspection of numerous uninterrupted sleep phenomena. Research on the effects of exercise on sleep began, in the 1960's, with a focus primarily on sleep related EEG changes (CNS sleep). Those early studies only found small effects of exercise on sleep. However, more recent sleep research has explored not only CNS functioning, but somatic physiology as well. Sleep should be affected by daytime exercise, as physical activity alters circadian pacemaker, endocrine, autonomic nervous system (ANS) and other somatic functions. Since endocrinological, metabolic and autonomic changes can be measured during sleep, it should be possible to assess exercise effects on somatic physiology in addition to CNS sleep quality, evaluated by standard polysomnographic (PSG) techniques. Additional measures of somatic physiology have provided enough evidence to conclude that the auto-regulatory, global regulation of sleep is not the exclusive domain of the CNS, but is heavily influenced by inputs from the rest of the body.

Keywords : exercise, sleep, EEG, body temperature, GH, cortisol, BDNF, fitness

Introduction

The relationship between exercise and sleep has long been of strong interest to both exercise and sleep researchers since the 1960's. However, their relationship is still largely not understood. There are a lot of complexities in the relationship, as physical exercise is mostly related to somatic physiology, while sleep has mainly been evaluated by electroencephalogram (EEG), which is related to central nervous system (CNS) neurophysiology.

This article first reviews the historical background of sleep research and its application to the effects of exercise on sleep. Then, it presents the current knowledge of exercise effects on somatic physiology; and, finally, it proposes a future direction for studying the important topic of the relationship between exercise and sleep.

Sleep research and CNS sleep

Shortly after the discovery of electroencephalography (EEG)[1)], it was applied to sleep research since it was an outstanding noninvasive tool for observing sleep behavior without disturbance. Since then, sleep research has largely focused on CNS physiology by tabulating several sleep-specific landmark EEG waveforms[2)] (Fig. 1). As you can see in fig. 1, early researchers were interested to see dramatic changes in the patterns of EEG waveform distributions through the night; and such findings drove sleep researchers to pursue meaningful physiological correlations underlying these EEG 'events'. The subsequent discovery of rapid eye movement (REM) sleep[3)] stimulated research that has led to the understanding that sleep is not simply a resting state of the brain, but an active, dynamic cycling through multiple sleep-specific states. Computer analyses of sleep EEG[4,5)] and modern neuroimaging techniques[6)] have enabled increasingly detailed analyses of CNS functions during sleep.

In consequence, there have been a huge number of studies on 'daytime load' and its effects on night time sleep stage changes. Examples of daytime load include wake length, psycho-behavioral tasks, light exposure, and exercise. The daytime load with the most pronounced effect is wake length. It is well known that, after a night of total sleep deprivation, slow wave sleep (SWS or non-REM [NREM] sleep stages 3 and 4)[7)] significantly increases. It is also known that there is independent selectivity in NREM and REM sleep deprivation, and selective REM sleep deprivation increases REM sleep length during the

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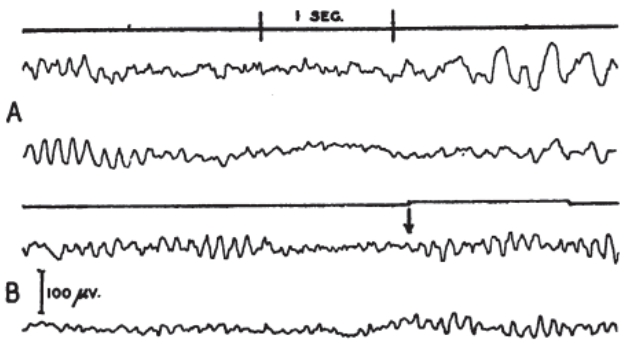

A—Subject falling asleep. Upper line, vertex to ear; lower line, occiput to ear. B—A brief "float," signalled at arrow.

Fig. 1 EEG waveforms in early publication. EEG changes in sleep onset were quoted from reference (2).

following recovery night. These changes are visible only by polysomnographic (PSG) recording. This valuable information encouraged sleep researchers to investigate additional components affecting sleep. Thus, since an early era, investigations of exercise effects on sleep have mainly focused on EEG changes in sleep, which reflect CNS functions during sleep.

Effect of exercise on CNS sleep

The first scientific paper studying the effect of exercise on subsequent night sleep was written by Baekeland and Lasky[8]. In their study, ten physically fit college students, accustomed to participating in strenuous athletics of various kinds, underwent three conditions that provided afternoon exercise, evening exercise and no exercise. Afternoon exercise resulted in significantly more SWS during the following night's sleep, as compared with sleep after the no-exercise condition. After evening exercise, however, the amount of SWS fell between the "no-exercise" and "afternoon exercise" conditions, but with no significant differences from either. Despite several drawbacks, including limited control for the type (aerobic or anaerobic) and intensity of exercise, and the limited descriptions of exercise timing, the authors highlighted three essential observations that have repeatedly been confirmed in studies since then. First, among these observations, a single bout of exercise can increase the amount of subsequent SWS. Second, exercise shortly before going to bed can also produce a stress effect that can reduce the amount of subsequent SWS. Third, relative to other studies, the amount of SWS following the no-exercise condition still exceeded prior normal values, which might be attributable to the subjects' overall fitness and exercise habits, i.e. habitual exercise may increase SWS.

Much subsequent research on exercise and sleep has tested whether there are significant increases in SWS after a single bout of daytime exercise. Walker et al.[9] also tested this "SWS-exercise hypothesis" and failed to find a significant increase. They also reviewed past papers and reported only three out of nine papers confirming this effect. Other scientific papers, on the topic, were listed in a relatively recent review article[10], and the concluding effects were "modest", as sample sizes were small in most cases.

Meta-analysis is useful in examining the weak effects of small sample size studies. Fig. 2 was compiled from meta-analytic studies by Kubitz et al.[11] and Youngstedt et al.[12], who examined acute (single bout) and chronic (habitual) exercise effects on sleep (these two studies also provide very comprehensive bibliographies). Although fig. 2 requires careful consideration due to the varying size of each effect, it provides a good overview of how daytime exercise affects nightly sleep.

Overall, studies of both acute and chronic exercise have found that the effects of exercise on subsequent sleep include longer periods of NREM sleep stages and shorter periods of REM sleep. One of the hypotheses of the acute effect of exercise was body temperature elevation. The relationship between body temperature regulation and sleep has been studied in depth[13]. In research on humans, there have been several studies which measured core body temperature during sleep after bouts of exercise, with a variety of inconsistent results ranging from no change[14], to body temperature elevation[15,16]. A theoretical basis for sleep enhancement by body temperature elevation has been proffered by the hypothesis that SWS, which is associated with effects that reduce body temperature, might be promoted by a higher body temperature before bedtime[17]. Further research is needed to determine whether the exercise effect of enhanced SWS is due to such a mechanism.

In contrast to the modest effect of acute exercise, the review of chronic exercise studies reveals robust and consistent data. Meta-analyses summarizing chronic exercise effects reveals significantly shorter sleep onset latency, time awake after sleep onset, and significantly longer total sleep time.

As Youngstedt et al.[12] discussed in detail, many factors contribute to the inconsistent effects of acute exercise on sleep. In their meta-analysis, they identified several moderator variables including fitness of subjects, exercise heat load, duration and time of day, subject light exposure, and sleep schedule, as well as small sample sizes and overall study quality issues. Thus, studies that do not control for these factors will not give consistent results. Even so, another important difference between acute and chronic exercise is that chronic exercise substantially changes somatic functions in ways one bout of exercise does not. These somatic changes include changes in the circadian pacemaker, basic metabolic rate, cardiac function, glycemic control, immune function, and long-term improvements in body composition, as have been studied in chronic somatic diseases[18,19]. In addition to such somatic changes, it is known that exercise also improves

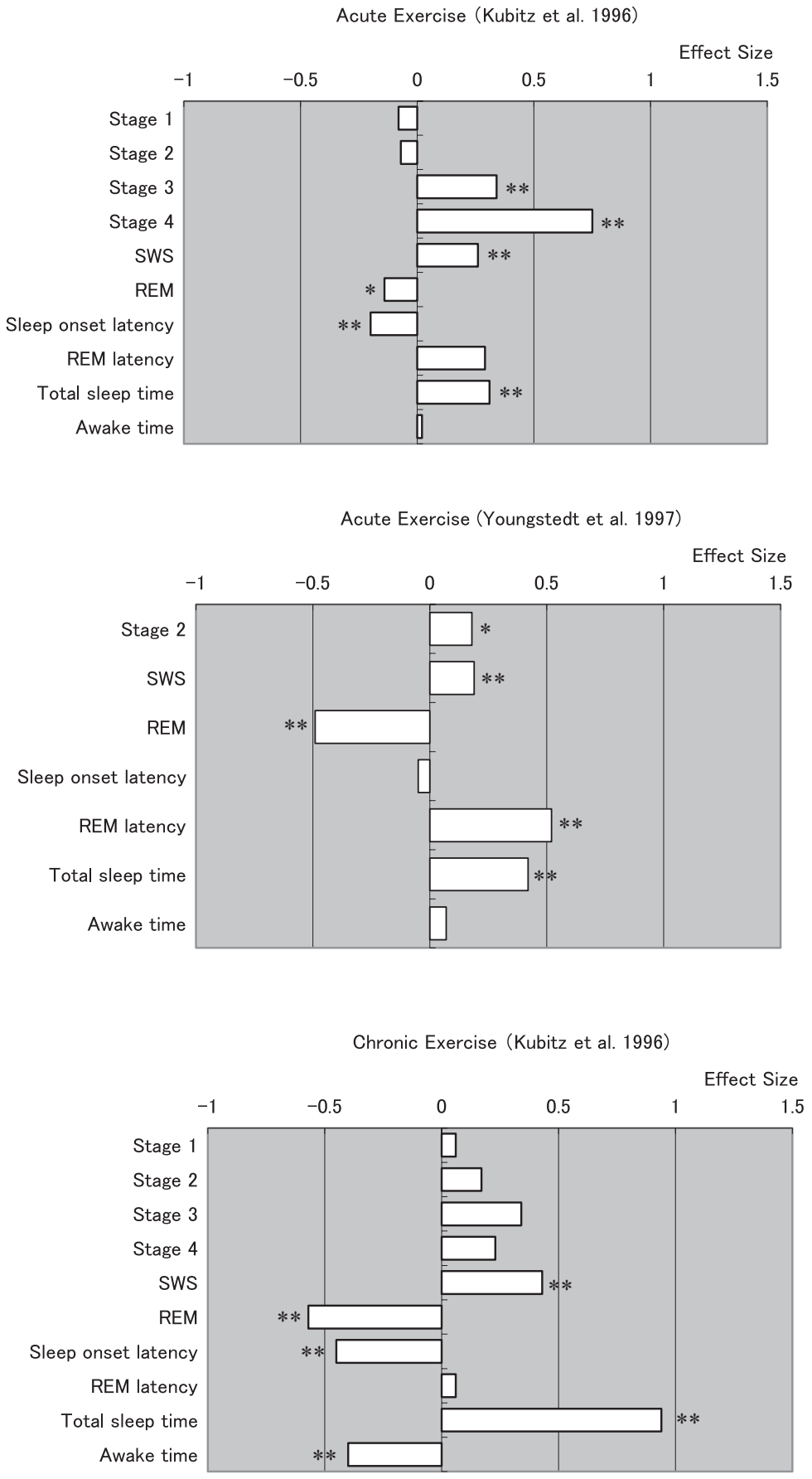

Fig. 2 Meta analyses of acute and chronic exercise effects on sleep parameters. Note that chronic exercise resulted in larger effects on improving sleep quality, which appeared in total sleep time extension and awake time reduction.
*p<0.05 and **p<0.01.

mood state[20,21], which can also be an additional factor in improving (or disrupting) sleep. Such long-term changes in overall health status should be considered when changes in sleep quality are evaluated in chronic exercise conditions.

Effect of exercise on the circadian pacemaker

It is an established fact that exercise has effects on the circadian pacemaker. In animal studies, the free-running rhythm was shortened when a blind rat had access to a running wheel[22].

The phase response curve of exercise on the human circadian pacemaker was reported by Buxton et al.[23]. Their data indicated that evening exercise induced a phase advance and night exercise induced phase delay; morning and afternoon exercise had no effect on the circadian phase. However, Honma's group questioned the data, as their group showed that an afternoon, as well as midnight, single bout of exercise significantly phase delayed the melatonin rhythm[24]. They also showed that a 12-day period (cycle) of exercise twice per waking period (per day) of a 23 h 40 min sleep-wake schedule, significantly phase advanced the melatonin rhythm. Thus, they showed the chronic exercise effect on the human circadian pacemaker. It is interesting to conclude that morning to afternoon daily exercise could have a phase advance effect. Incorporating these results, the current knowledge is that morning exercise is likely to phase advance; but more data is needed to determine how afternoon to evening exercise effect the human circadian rhythm.

It is interesting that if chronic exercise can phase advance the human circadian pacemaker, it could affect sleep quality as well. And, as people who exercise tend to go to bed earlier, they average more sleep time. This could also be a mechanism in the effect of chronic exercise on night time sleep.

The effect of exercise on the circadian pacemaker was well reviewed by Yamanaka et al.[25].

Effect of exercise on cardiac and autonomic function during sleep

It was noticed, in an early study, that daytime exercise also increased heart rate (HR) during sleep[9], a finding that has since been reported in several other studies[26-29]. Clearly, the increases in HR are partly due to increased physiological demands during exercise. However, during sleep, while the body is basically stationary, changes in HR would be attributable to alterations in autonomic activity. Thus, measures for HR are extremely useful tools for investigating autonomic changes during sleep.

As a continuously varying measure, HR can be assessed over a wide range of time frames. Accordingly, changes in HR variability (HRV) were looked at in some studies, along with HRV relationships with sleep stages[30]. Such relationships have only recently become a focus of interest.

It has been shown that chronic exercise affects HR and HRV[31-33]. Recent meta-analysis of the effect of exercise therapy on HRV[34] indicates that habitual exercise enhances vagal modulation, resulting in bradycardia. A recent intensive review on exercise therapy and HRV[33] also confirmed that chronic exercise increased vagal tone and decreased sympathetic activity. Such enhancement of vagal function could reflect the enhancement of parasympathetic control, which could, thus improve both sleep and mood.

Only one extensive study by Catai et al.[35] has examined exercise and HRV during sleep. For the study, 10 young and 7 middle-aged sedentary subjects were recruited for a three-month aerobic training program, during which HRV was examined during sleep. Unfortunately, sleep EEG was not recorded. No changes in HRV were found after three months of the aerobic training program. Recently, Myllymäki and colleagues published two papers focusing exclusively on cardiac autonomic function during sleep[36,37]. Their studies were designed to observe the acute effects of single bouts of exercise on later sleep. As expected, they confirmed HR elevations, but could not find significant HRV changes, even during sleep, that occurred shortly after vigorous exercise. Since there were no significant elevations of either sympathetic or parasympathetic nervous system activities, the authors concluded that vigorous late-night exercise does not disturb sleep quality.

Recently, the authors studied the effect of vigorous late-night exercise on night sleep. HRV was separately analyzed in NREM and REM sleep for each sleep cycle; and it was found that the sympathetic nervous system activity parameter high frequency / low frequency (HF/LF) ratio was significantly elevated during the second NREM cycle[16].

Thus, it is probably premature to make firm conclusions based on the current lack of consistent HRV data of effects during sleep after exercise. Although the studies to date were specifically aimed at examining exercise effects on the cardiac system, they still reflect early efforts in this field of study. As in the case of the early studies of exercise effects on sleep EEG, examination of sleep-specific exercise effects on the cardiac system may also require careful controls for relevant covariates such as the aerobic/anaerobic qualities, intensity and timing of exercise, and fitness status of subjects.

Effect of exercise on endocrine function during sleep

In early studies, two research groups examined the effect of exercise on endocrinological changes during sleep. The groups' interests were mainly driven by changes in growth hormone (GH) secretion, which was already known to be closely related to sleep[38]. Once again, as

with other sleep-related physiological studies, early findings were contradictory. Adamson et al.[39] found that GH increased during sleep after exercise, while Zir et al.[40] found it didn't. However, Adamson et al. also found decreased cortisol secretion after exercise, while later studies found increases in cortisol[29] and urinary norepinephrine excretion[26].

In a relatively new and extensive study, Kanaley et al.[41] examined GH secretion patterns with repeated bouts of aerobic exercise, and then observed the amount of GH release during the following night's sleep. Compared to its release after a single bout of exercise, GH release was increased by repeated bouts of aerobic exercise; but there were no changes in the pattern of GH release during sleep.

More research needs to be done on the effects of exercise on hormonal levels during sleep. As with the effects of exercise on sleep EEG, sleep specific endocrine responses to exercise have to be studied in greater depth, taking into account various factors such as exercise type, intensity, timing, subjects and differences between acute and chronic exercise.

Effect of exercise on metabolic functions during sleep

There has been increasing interest in the relationship between sleep and metabolic functioning[42], following epidemiological investigations detailing the relationships between sleep loss, obesity and diabetes, etc.[43]. An extensive experimental study[44] indicated that the blood glucose level is high during sleep, mainly because of the less active state of the brain as a whole (although some sleep-specific functions can drive local brain areas to high levels of activity), which is the largest glucose-consuming organ[44] (Fig. 3).

However, almost no data has been obtained to examine exercise effects on subsequent metabolic functions during sleep. As described above, since there have been reports that vigorous late night exercise increases HR during sleep, it is reasonable to expect that there should also be some changes in the metabolic rate during sleep. Such studies are not only important with regard to emerging global health problems, but they would be of special interest for the therapy and prevention of Type II diabetes.

Effect of exercise on mood

It has long been known[45,46] that exercise has beneficial effects on mood. Recent extensive studies on the therapeutic effects of chronic exercise for depressive symptoms indicate that exercise could become an adjunctive, or possibly alternative therapy for depression[20,21]. Since sleep disturbance is one of the core symptoms of depression, and because improved depressive symptoms are also associated with improved sleep quality, it is plausible that the effects of chronic exercise on improving sleep quality could be a relevant mechanism.

Biological models for such a therapeutic mechanism have been studied. Several hypothetical mechanisms have been suggested, including monoamine activation, hypothalamus-pituitary-adrenal activation or brain-derived neurotrophic factor (BDNF) mediated changes[47]. Among these, BDNF has recently drawn particular research attention. It has been well established that exercise increases BDNF concentration in the brain[48]. There have also been reports of a therapeutic effect of BDNF for depressive symptoms[48-52]. Recently, serum BDNF in depressive patients was also found to normalize after exercise[53]. Another recent study also suggested that exercise epigenetically changes BDNF production in the brain[54]. All of these effects could mediate improvement in sleep, even if the subject is not in a pathologically depressed state.

Effect of exercise on sleep: Future directions

Reviewing the past studies of the effects of exercise

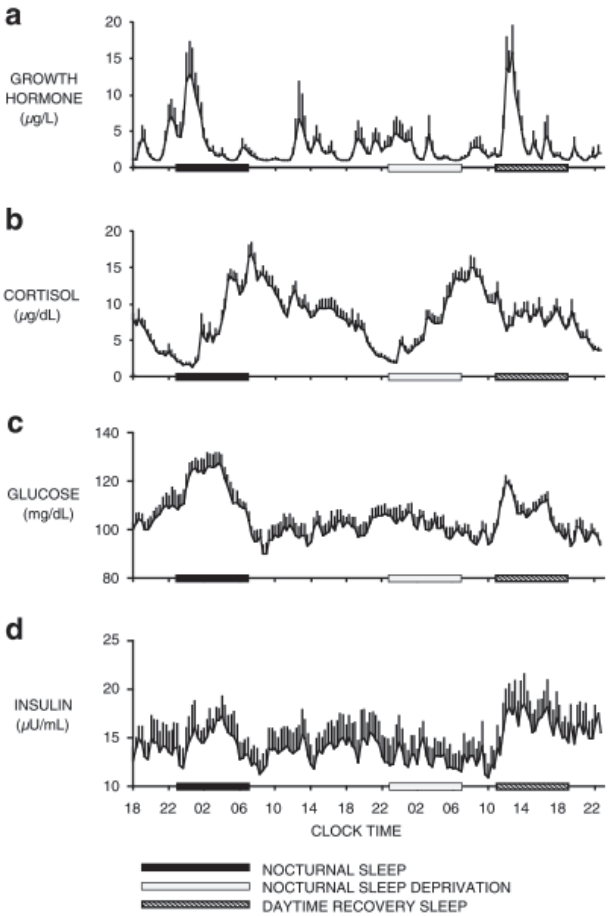

Fig. 3 Fluctuation of GH, cortisol, glucose and insulin during, wake, sleep, sleep deprivation and recovery daytime sleep. GH has sleep dependent, and cortisol has circadian dependent secretion patterns. Glucose is at high levels during sleep. The brain, especially, which is the largest glucose consumption organ, has high levels during sleep, though it is relatively inactive. Figure is adapted from reference (42), which was adapted from (44).

on sleep suggests several pathways through which exercise could have positive effects on sleep quality (Fig. 4). These pathways could be classified into three categories based on acute effects, acute, but with subsequent chronic effects, and effects arising after patterns of chronic exercise.

Conceivable acute effects would include CNS fatigue, body temperature elevation, or HR/HRV changes. Whether fatiguing physical exercise causes directly analogous CNS fatigue is an ongoing question. Even so, the effect should not be significant, given the inconsistent results obtained when the effects of one bout of acute exercise on SWS were examined. The hypothesis that body temperature elevation itself enhances SWS is theoretically interesting, but should be studied in more detail, particularly in humans, and especially to compare the effects of passive body heating with body temperatures after late-night exercise. Most studies have confirmed HR elevation during subsequent sleep, when HR is elevated during exercise. In addition to HR elevation, sympathetic enhancement was also reported. However, whether these changes have disturbing effects on sleep also needs further study.

Some acute endocrine and metabolic effects of exercise may produce chronic effects when exercise becomes habitual. Habitual repetitions of acute elevations in glucose metabolism, GH and BDNF releases are conceivable mechanisms that could lead to alterations in sleep. Late-night exercise could lower the glucose level during sleep; although we still do not know its effects on sleep. Even without long-term adaptation, exercise-related glucose reductions could have a favorable effect on Type II diabetes, as glucose levels are typically relatively high during sleep[44]. Similarly, exercise increases daytime GH release, which might directly affect sleep quality. However, since GH secretion is closely related to SWS[38], the long term effect of repeatedly increased GH releases over 24 hours could alter sleep quality.

It is also known that exercise acutely enhances BDNF production. It has not yet been established whether BDNF directly alters sleep quality or not. However, the antidepressant effects of exercise have recently been well documented, and improved mood, attributable to BDNF elevation as a result of exercise, could indirectly improve sleep quality. Such pathway relationships between the acute and chronic effects of exercise and alterations in sleep should be examined in future studies.

An interesting chronic effect of exercise is that it advances the human circadian pacemaker[24]. This effect will not directly change the quality of sleep. However, in real life, an early bed time is mostly associated with longer sleep time.

One certain beneficial effect of habitual exercise is improved health. Besides, some psychological benefits (which should not be ignored), as well as their interactions with acute and chronic physiological alterations over time, could themselves improve sleep. The addition of noninvasive long-term physiological measurements that do not disturb sleep, such as measurements of parasympathetic predominance measured by HRV, can reveal such sleep promoting alterations. Studies have shown that exercise definitely changes body composition[55] and cardiovascular fitness levels[56]. Meta-analyses (Fig. 2) indicate that chronic exercise yields more stable and persistent improvements in sleep. These benefits likely reflect the additive and interacting benefits of numerous physiological alterations, by chronic exercise, that directly and indirectly affect sleep quality (Fig. 4).

Lifelong, apparently passive, automatic homeostatic cycling between wakefulness and sleep is influenced by several factors, including physical activity, which also involve prior activity in a large network of neurons of the CNS. These activities influence the global tendency of the CNS for sleep-wake oscillation[57]. Exercise could be a robust stimulus for the auto-regulatory global phenomenon that affects all of a sleeper's physiological mechanisms. Appropriate amounts of exercise could alter those mechanisms in a positive direction toward restoration of the levels humans originally needed and adapted to for living, and offsetting some important health consequences attributable to conveniences in modern society.

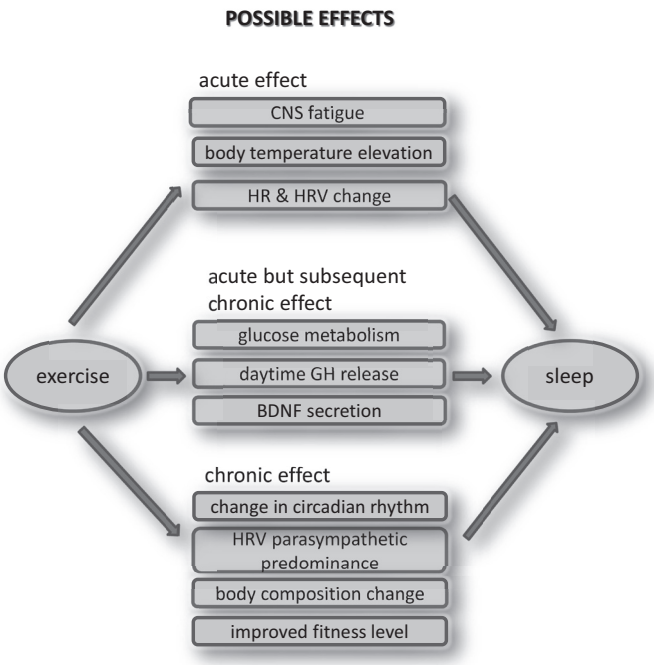

Fig. 4 A hypothetical model of the exercise effects on sleep. Exercise effects on sleep could be classified into three categories, which are "acute", "acute but subsequent chronic effect" and "chronic effect". These hypothetical schemes should be confirmed in future experiments.

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