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EDITORIAL

Sleep Deprivation and Depression

A bi-directional association

Mohammed A. Al-Abri

الحرمان من النوم والاكتئاب

ارتباط ثنائي الاتجاه

محمد عبد الله العبري

In this issue of SQUMJ, Al-Maddah *et al.* reported a significant association between sleep deprivation among medical trainees and depressive indices using the Beck Depression Inventory-2.[1] Using a cross-sectional study design, the authors found that depressive symptoms were more profound with acute rather than chronic sleep deprivation. They attributed the emerging depressive symptoms among medical residents to the acute lack of sleep because of long working hours, but not to the number of on-call nights per week.[1] However, there was no follow-up to ascertain the cause-and-effect relationship between chronic sleep deprivation and depressive indices.

Sleep occupies about a third of our lives and is vital to fulfil physiological needs, particularly in terms of cognitive function and mood. Disrupted sleep is very distressing for most individuals and may have a negative impact on their quality of life. Sleep deprivation has been shown to alter performance among medical professionals and shift workers, with several studies addressing its association with depressive symptoms.[2–4] Residents and medical interns often suffer from reduced sleep which may lead to neurobehavioural impairment. Rosen *et al.* reported that medical interns with chronic sleep deprivation displayed high levels of depression and burnout over a period of one working year.[5] In another study, Papp *et al.* found that chronic sleep loss had a negative impact on residents' personal lives and their ability to perform their work.[6] This supports the idea that chronic rather than acute sleep deprivation may result in depression, contrary to the findings of Al-Maddah *et al.*[1]

Night shift work is a well-known cause of daytime sleepiness and mood disorders among workers. These results might also be attributable to chronic sleep loss and changes in circadian rhythm.[7] However, one night of fragmented sleep was shown to cause normal subjects to feel sleepier during the day, impair subjective assessments of their mood and decrease mental flexibility and sustained attention.[8] Therefore, clinical depression might result from the accumulative effect of chronic sleep fragmentation, deprivation and disturbance.[8]

There is a strong bi-directional relationship between sleep deprivation/disturbance and depression. Although disturbed sleep is associated with psychiatric disorders and is traditionally considered to be a symptom of depression,[9] research suggests that the relationship between sleep changes and mood disorders may work in the other direction as well.[10] In addition to being a symptom, disrupted or a lack of sleep may also be a causal factor that contributes to the development of mood disorders.[10,11] Chronic insomnia was found to increase the odds ratio of developing depression in several longitudinal studies.[9,12] Alterations in sleep patterns are associated with depression, a fact which has been reported in the literature for over three decades.[11,12] Additionally, certain sleep breathing disorders have a strong association with depression. Obstructive sleep apnoea syndrome is significantly associated with an impairment in cognitive function due to sleep disturbance and subsequent daytime sleepiness.[13] Peppard *et al.* found a dose-response association between sleep-related breathing disorders and depression.[14] This finding might be attributed to frequent awakening due to the sleep apnoea, in addition to repeated hypoxic stress to the brain as a result of desaturation.[14]

Contrarily, acute sleep deprivation has been long reported to be beneficial in treating depression. An early study revealed that a single night of sleep deprivation had an antidepressive effect.[15] Therapeutic sleep deprivation was performed either as total sleep

Department of Clinical Physiology, Sultan Qaboos University Hospital, Muscat, Oman
E-mail: malabri@squ.edu.om

deprivation or with selective non-rapid eye movement (REM) sleep deprivation.[16,17] The efficacy of either method has not yet been well investigated, although the impression received suggests that total sleep deprivation is superior to the selective technique.[15] Nonetheless, therapeutic sleep deprivation is not free of side-effects. Depressed individuals may experience increases in impulsiveness and drive.[17] In addition, they would also suffer from excessive daytime sleepiness, which might be difficult to distinguish, especially in non-responders, with a worsening of the depressive symptoms.[17]

Two processes mainly regulate sleep. Firstly, the circadian process regulates the daily rhythms of the body and brain.[18] The circadian pacemaker is found in a group of cells in the suprachiasmatic nucleus of the hypothalamus.[18,19] These cells provide an oscillatory pattern of activity that drives rhythms such as sleep-wake activity and endocrine secretions. They are markedly affected by light and darkness and, to some extent, by temperature.[19] Bright light in the evening will delay the 'clock' and bright light in the morning is necessary to synchronise individuals to a 24-hour rhythm. All animals have a form of this process and the specific period and timing appear to be dependent on particular genes, which are similar in fruit flies and mammals.[20]

There is strong evidence to support the role of the sleep-wake cycle and circadian rhythm in the pathogenesis of major psychiatric disorders, particularly depression.[18] Melatonin, a peptide synthesised by the pineal gland, has been shown to play a role in the modulation of the circadian rhythm.[21] Disrupted melatonin secretion and abnormal circadian rhythms have been reported among depressed subjects and the elderly; this could be the cause of sleep-phase shifts and consequent daytime sleepiness among these groups.[22,23] As part of the circadian clock, the drive to sleep in normal sleepers slowly begins to increase a few hours after sunset and gradually reaches a peak in the early morning. The timing of REM sleep is linked to the circadian rhythm, closely mirroring the core temperature of the body. Thus, the maximum propensity for REM sleep is usually in the second half of the night with the onset of slow-wave sleep at the beginning of the night.[24,25] The occurrence of REM sleep during daytime naps indicates a pathological daytime sleepiness, as can be observed in cases of narcolepsy.[24]

Secondly, the homeostatic process is the other important regulatory factor for sleep. It increases via sleep deprivation and peaks 16 hours after morning awakening and then decreases again during sleep. When there is a lack of sleep or the duration of sleep is shorter than usual, there is an increase in the homeostatic process. Consequently, this works to ensure that the sleep deprivation is made up for during the next sleep period, by accelerating the time before sleep and by possibly increasing sleep depth and duration.[25]

In animal models, chronic sleep restriction for more than a week was shown to lead to alterations in the neurotransmitter receptor systems (serotonin-1A receptor and corticotropin-releasing hormone receptor systems) and neuroendocrine stress systems (hypothalamic-pituitary-adrenal axis).[26] These changes are similar to those reported for major depression. The link between sleep and depression occurs through the serotoninergic system, which is active during wakefulness and inactive during sleep. Serotonin release is very much inhibited during slow-wave and REM sleep.[22] Endogenous depression is associated with the functional impairment of several neurotransmitter systems, particularly monaminergic neurotransmission. Likewise, evidence of decreased serotoninergic activity was observed in the brains of depressed patients.[27]

In conclusion, chronic sleep deprivation rather than acute sleep loss may lead to depression that is potentially attributable to the neurochemical changes that occur in the brain. On the other hand, depression may lead to disturbed sleep which could manifest as a symptom of a mood disorder. Short sleep duration has been shown to be increasing in prevalence worldwide with a concurrent increase in depressive symptoms, mainly among the younger population.[28] Further epidemiological studies are required to ascertain the prevalence of such an association among the local population in Oman.

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