Alzheimer Disease and Sleep Disorders: Insights into the Possible Disease Connections and the Potential Therapeutic Targets (Part II)

If we look around ourselves, there are numerous granted bounties by the Creator which are often overlooked, for example, air, water, eyesight, hearing, cognitive power of thinking, power of taste buds, touch and imagination. From a memorable memory to a sincere smile from a friend, we feel the positive energy within. How it changes one’s mood and behaviour? When looking at flowers, feeling the morning breeze or hearing the falling water we can recognize the bounties of the Creator and use them in a way to please our Creator through taking care of His creations, and mankind. Inside our body, within the cells and the organelles, we can see numerous systems working to maintain the health of the body. Many incentives of nature are outside our bodies such as the sun, stars and galaxies. One bounty is physical health whilst the other is our spiritual health. How precious is the value of health, we can ask from the sick especially those in the last stage with a poor glimpse of recovery. Albeit, when the body is healthy it can function and work systematically requiring a good sleep at night with sufficient oxygen. Our parasympathetic system is over dominated by the sympathetic system in such a way that our heart rate reduces and our mind slows down. Our soul is partially divided, one with our physiological body whilst the other part is returned to a temporary phase of its origin. When morning comes they unite as we become a fresh walking, talking, living body ready for the productivity of a new day. So good sleep of 7/8 hours is also a good gift of the Creator, while in some cases, if someone has a sleep disorder such as sleep apnea, the level of oxygen drops causing sleep disturbance. In this special issue, expert researchers in the field of sleep disorders highlight the scientific approach in sleep disorders particularly in neurodegenerative disorders such as Parkinson and Alzheimer's Disease (AD).

Usually, most people, who have sleep disorders, do not come forward to get treatment; therefore, around 15 % of the population are registered for a diagnosis. It has been shown to increase with age. Different types of comorbid sleep disturbances frequently complicate a wide variety of neurologic disorders, and this is mainly related to the damage of neural structure in sleep-wakefulness regulation, pain caused by disease or lesion, reduction of movement and treatment. Sleep disorders can also be an early or even main symptom of various neurological diseases, for example, Rapid eye movement sleep Behavior Disorder (RBD) and Obstructive Sleep Apnea (OSA) in AD. It can occur before the occurrence of neurological diseases, affect the disease process, daytime function, quality of life, morbidity and mortality of the patients. The occurrence of some types of sleep disorders could be useful in the early diagnosis of many neurological diseases. A deeper contribution of OSA to AD pathogenesis is now gaining support from several lines of research. OSA is intrinsically associated with disruptions of sleep architecture, intermittent hypoxia and oxidative stress, intrathoracic and hemodynamic changes as well as cardiovascular comorbidities. All of these could increase the risk for AD, rendering OSA as a potentially modifiable target for AD prevention. Treatment of comorbid sleep disturbances may improve the symptoms of many neurologic diseases. Significant progress has been made in the diagnosis, clinical types and neuropathophysiological mechanisms of sleep disorders in neurological diseases. Despite these primary observations, it is still insufficiently considered in clinical practice, and treatment options are limited. Therefore, the purpose of this special issue is to present high-quality reviews and research articles on the possible disease connections and the potential therapeutic targets between sleep disorders and AD.

Hopefully, this special issue will help researchers to develop therapeutic drugs for sleep disorders. We are thankful to all authors who submitted their articles in this Special Issue, and reviewers, who secured their time in providing valued feedback to improve the submitted manuscripts.

A huge number of individuals today use herbs as drugs alongside medicine and non-physician recommended medications, huge numbers of these herbs can potentially interact with other drugs, causing hazardous adverse effects and/or diminished advantages of prescription. It ought to be comprehended that herbal drugs contain multiple active compounds in different percentages which can change the enzymatic frameworks, transporters and additionally the physiologic processes. Assessment of herbal drug interaction is difficult because of inconstancy in herbal drug composition and meagre information of active constituent pharmacokinetic. These restrictions are further bewildered by the differing points of view concerning herbal product regulation. A basic assessment of certain pharmacokinetic HDI is needed to settle on educated choices in regards to patient safety. The expanding comprehension of HDPKI will make give attention to potential interactions according to Ahmed et al report [1].

Conventionally cardiac biomarkers are recognized as a significant tool to investigate the presence or progression of various cardiovascular diseases. However, in recent years’ data from several clinical trials have successfully sorted out the utility of cardiac biomarkers in diseases that are not primarily regarded as “cardiac diseases”. Results of freshly published trials have endorsed the use of cardiac biomarkers in a variety of diseases that vary from Chronic Kidney Diseases (CKD) to Community-Acquired Pneumonia (CAP), central nervous system disorders and several others. Alzheimer’s disease is also one of the CNS conditions where measuring cardiac biomarkers are useful. Cardiac biomarkers can be helpful in two ways. Firstly, to assess the secondary involvement of the heart during the progression of the primary disease. Secondly, they can be useful in the diagnosis and prognosis of the primary condition itself. Khan and Kamal had collected encouraging results from recent studies and have shown the importance of the most widely recognized cardiac biomarkers. These markers include from the classic ones such as natriuretic peptides including B-type Natriuretic Peptide (BNP) or N-terminal pro-B- type Natriuretic Peptide (NT-proBNP).
and cardiac Troponin (cTn) to newer biomarkers such as the soluble Source of Tumorigenicity 2 (sST2) and Galectin-3 (Gal-3). The results showed that cardiac biomarkers carry significant importance in making diagnosis and prognosis of AD, stroke, pneumonia, and many other conditions and wider recognition and use of these biomarkers is expected in the future [2].

Nature has bestowed mankind through additional resources Natural Products (NPs) on earth with water. However, NPs have a significant function in the avoidance of disease by boosting health in humans as well as animals. These NPs have been scientifically acknowledged to have a range of biological characteristics like antioxidant, anti-inflammatory actions. Both in vitro and in vivo studies have recognized the convenience of NPs in different preclinical models of neurodegenerative disorders. Moreover, most NPs comprise phytoconstituents, including polyphenolic antioxidants; originate in herbs, fruits, nuts, vegetables as well as in marine with freshwater flora. These phytoconstituents might actively repress neuro-degeneration and recover memory as like cognitive actions of the brain. Moreover, they are well recognized to participate in an essential position in the prevention like healing of dissimilar neurodegenerative diseases, like AD, Parkinson’s disease, epilepsy, and additional neuronal disorders. In general, the large-scale neuro-pharmacological actions of NPs have been familiar owing to the consequence of also the inhibition of inflammatory processes, or the up-regulation of various cell endurance proteins or a mixture of them together. Owing to the shortage of human studies on neuroprotective belongings of NPs, Rahman et al., highlighted a variety of documented actions of NPs in vitro and in vivo preclinical models and their possible neuro-protection applications by the accessible awareness in their writing [3].

Dementia is a diverse category of a chronic and progressive disorder, which is commonly associated with loss of memory, difficulty in judgment, impaired language, cognitive impairment, and various other symptoms that affects a person’s daily routine life and social life [4]. Autophagy is a necessary process of cellular protein clearance mechanism, which is dependent on lysosomes. It is a basic physiologic process that performs the crucial function of maintaining cellular protein homeostasis. The autophagic dysfunction in dementia further complicates the disease by hampering the degradation and removal of abnormal pathogenic proteins. To understand autophagic dysfunction, it is essential to know the genetics of autophagy as well as the mutations which cause autophagic dysfunction. Kumar et al. shared their understanding at the genetic level to define the relationship between dementia and autophagic dysfunction for developing potential remedies for the treatment of dementia [4].

Alzheimer’s disease, characterized by abnormally phosphorylated tau, PHFs, NFTs, deregulated mTOR, Aβ deposits, is a multifactorial disease with sleep disorders being one of its major causative agents [5]. Mueed et al. reviewed the literature and have tried to decode the existence of positive feedback, reciprocal and a bidirectional relationship allaying between sleep disturbances and AD. Much light has been thrown on the role of tau pathology and amyloid pathology in sleep pathology, its association with AD pathology and the role of melatonin in regulating sleep disorders and AD. The neuroprotective action of melatonin via inhibiting tau hyperphosphorylation and Aβ deposition has also been pondered upon. Moreover, astrocytes involvement in aggravating AD has also been highlighted. Several therapeutic approaches aimed at improving both sleep disorders and AD had been duly discussed such as administration of antidepressants and antihistamines, immunotherapy, metal chelators, melatonin supplementation, light therapy, and physical activity [5].

Lack of sleep generated many disorders bruxism is one of them. It has affected almost 31% of the world’s population. Heyat et al. determined the volume of the research conducted on bruxism and created a database [6]. They highlighted open research questions and critical issues for further research commitments and communications by designing a comprehensive and very perception-based picture of bruxism disorder. That work used three methods such as systematic mapping process, network visualization, and literature review by using some software such as VOSviewer, MATLAB, and MEGA-X to analyze the data related to the understanding of bruxism disorder from dental to psychological concepts, from engineering detection to clinical treatment, and from temporomandibular disorder to biological genes. They concluded that Bruxism is a sleep, neurological, and dental disorder [6].

Alzheimer’s disease is a progressive neurodegenerative disorder characterized by sleep, behavioural, memory, and cognitive deteriorations [7]. Sleep Disturbance (SD) is a major disease burden in AD which has a reciprocal relationship with AD pathophysiology. It aggravates memory, behavioural, and cognitive complications in AD. Different studies found that melatonin hormone levels reduce even in the pre-clinical stages of AD. Melatonin is the major sleep-regulating hormone and a potent antioxidant with neuroprotective roles. The decrease in melatonin levels can thus promote SD and AD neuropathology. Exogenous melatonin has the potential to alleviate neuropathology and SD in AD by different mechanisms. Various studies have been conducted so far that assessed the efficacy of exogenous melatonin to treat SD in AD. Though most of the studies suggest that melatonin is useful to ameliorate SD in AD, the remaining studies show opposite results. The timing, dosage, and duration of melatonin administration along with disease condition, genetic, environmental, and some other factors can be responsible for the discrepancies between the studies. Larger trials with longer durations and higher dosage forms and studies including bright light therapy and melatonin agonists (ramelteon, agomelatine, and tasimelteon) should be performed to determine the efficacy of melatonin to treat SD in AD [7].

While in the previous volume (I) there were seven articles, which covered various aspects, such as the following: 1. A bibliometric analysis in sleep disorders research from 1945 to 2020 [8]; 2. Modifiable risk factors associated with AD with special reference to sleep disturbance [9]; 3. Cellular and molecular mechanisms of dementia [10]; 4. Functional neuroproteomics [11]; 5. Neuroblastoma and stem cell therapy [12]; 6. Hematopoietic stem cell treatment for epilepsy [13] and 7. Experimental rodent models of vascular dementia [14].
Last but not the least, GEs are also thankful to the editor-in-chief (Prof. Edoardo Spina) and the management of CNS & Neurological Disorders - Drug Targets for their cooperation throughout the processing of the manuscripts.

REFERENCES

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