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Rayleigh Ping-Ying Chiang
Shih-Chung (Jessy) Kang *Editors*

Introduction to Modern Sleep Technology

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Introduction to Modern Sleep Technology

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Introduction to Modern Sleep Technology

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Foreword from Ronald R. Grunstein

Ronald R. Grunstein

It is with great pleasure that I am writing this foreword to *Introduction to Sleep Technology* edited by Drs. Kang and Chiang. Both editors are currently involved in a major national effort in sleep technology research in Taiwan and have gathered together an impressive team of authors to define this new growing area of interest.

The growth of sleep research and sleep medicine has been accelerated by advances in technology. The development of electroencephalography allowed the recognition of the nature of sleep, its various stages and wakefulness. Major advances occurred in the 1960s by the integration of these sleep recordings with the measurement of respiratory function and further with the availability of such non-invasive approaches such as oximetry. Diseases such as sleep apnea and other forms of sleep disordered breathing could be measured with a high degree of accuracy. Now the challenge continues in the use of novel markers of cerebral function with magnetic resonance imaging techniques. Furthermore the massive disease burden of sleep apnea is being met by newer technologies that bring diagnosis in the patients home. Challenges for technology remain with the need to accurately phenotype or characterize diseases such as insomnia and restless legs syndrome. More work remains and *Introduction to Sleep Technology* serves to provide a foundation of where the field sits presently.

As a young medical resident training in sleep medicine at the University of Sydney, it was my privilege to be involved in the treatment of some of the earliest patients receiving the then experimental treatment, nasal continuous positive airway pressure (CPAP). Despite its relative simplicity, it was revolutionary paradigm shift in technology. In those days my job was to make moulds of patient's noses for custom made masks and to convince often reluctant recipients of this therapy to glue

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their masks onto their faces on a nightly basis. It may have been primitive but it was a technology grounded in understanding of clinical pathophysiology. I often shake my head incredulously at the huge growth in CPAP-related technology. However it is important to recognize, that the most successful technological advances in the sleep field are those based on building links between clinicians, engineers and other scientists working on developing new medical technologies. It is crucial to assemble people from a range of disciplines together in a interdisciplinary approach to solving some of the technical problems related to sleep measurement and treatment of sleep disorders. This approach is highlighted by the authorship list of this book.

The chapters of this book are organized logically in covering the key clinical interactions with technology. There is a historical emphasis too which is important in understanding how we got to the present state of device development in order to understand future directions. The huge investment in developing an innovative medical technology sector in Asia underpins the planning and contribution of many authors from this region.

Another pleasing aspect of this publication is the international collaboration evidenced by the globally spread author group, in this case led by Asia and Taiwan in particular. As current President of the World Sleep Federation, I am aware of the importance of developing a global approach to scholarship and research. The editors are to be commended for bringing this team, and together and we already look forward to a second revised edition in the not too distant future.

Foreword from Clete A. Kushida

Clete A. Kushida

There has been a dramatic expansion in our knowledge about sleep and its disorders despite the relatively short interval since the discovery of rapid eye movement (REM) sleep, which provided the stimulus for the organized, scientific study of sleep. This accumulated basic and clinical sleep-related knowledge has translated to other disciplines of medicine to the point that our field is truly interdisciplinary, including pulmonary medicine, neurology, psychiatry, internal and family medicine, pediatrics, psychology, otolaryngology, and others. Practitioners and researchers in other specialties of medicine, such as cardiology, endocrinology, and immunology, have also provided insight into the comorbidities and consequences of sleep disorders. The field of ***sleep technology*** provides the technical basis for sleep science and is thus critical to all of these collaborations and the continued growth and success of sleep medicine and research.

Despite the steady development of sleep medicine and research, there are many fundamental basic and clinic questions that need exploration. Without breakthroughs in our field of sleep technology, there will not be new diagnostic tools, medications, or treatments to help us manage the nearly 90 different sleep disorders that we have identified thus far. We need to continue to attract the brightest and talented individuals from all nations to our field. For as citizens, we have learned time and time again that we must pull together to overcome the many crises that impact our world. As the world's economy struggles, we need to pool our talents and resources in order for our field to continue to flourish.

Introduction to Sleep Technology, edited by Drs. Rayleigh Ping-Ying Chiang and Shih-Chung (Jessy) Kang, is a testament to the spirit of international collaboration,

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since top experts from a variety of disciplines, background, and nations have devoted their time and efforts toward developing a book that is extraordinary in its scope and comprehensiveness. This book will enable physicians, technologists, trainees, students, and others to obtain a fundamental understanding of sleep technology and the importance of it. The growth of our field and the exploration of critical questions cannot exist without adequate education and training of sleep center personnel, and we must collectively strive to provide all members of the sleep community with the resources needed to increase their knowledge.

Our field is deeply indebted to the dedication and hard work on the part of the editors Drs. Chiang and Kang and the authors of this invaluable resource.

Foreword from Pei-Ling Liu

Pei-Ling Liu

Disorders and disturbances of sleep are widespread. A large sleep debt may weaken individuals' mental and motor functions and make people unresponsive and forgetful. It has led to several big disasters, for example, the Exxon Valdez oil spill and the nuclear incidents at Chernobyl and Three Mile Island. However, people often underestimate the consequences of sleep deprivation.

The diagnosis and management of sleep disorders have been addressed by sleep medicine and traditional sleep technology. Many creative instruments and treatments have been invented over the past decades. These inventions have helped many people with sleep disorders, but they are of limited use to the people who have minor sleep complaint or pursue higher "sleep efficiency".

The Sleep Technology Special Interest Group in INSIGHT Center, National Taiwan University, has been devoted to developing new sleep technology. The Group does not only concentrate on sleep disorders but also targets at the improvement of sleep quality for the general public. The goals are to better the quality of life and to enhance working efficiency and reduce accidents in work places. In the new setting, multi-disciplinary collaboration and user-centered design constitute the key components in the technology research and development. The Group comprises of experts from diverse fields, including sleep medicine, engineering, psychology, industrial design, management, and so on. They work closely together in the research and development of new devices. A good example is the development of the Sleep Coach introduced in this book. With the contribution from cross-domain experts, the practicability, handiness and competitiveness of the device are ensured. The essence of user-centricity is also realized.

Although Prof. Shih-Chung (Jessy) Kang and Dr. Rayleigh Ping-Ying Chiang had set up a good model for the R&D of sleep technology, they did not stop

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there. They decided to promote this field further. Two successful international sleep technology symposiums were held. Another action was the publication of this book. Top experts from all over the world were invited to contribute a chapter to the book. As the director of the INSIGHT Center, I am really grateful to the editors and all the authors for making this book come true. I believe this book will not only provide basic knowledge but also shed light on the new direction for sleep technology.

Preface

"**A** good night's sleep" has been pursued for thousands of years. And it is well known that the inability to sleep well can have an immediate and potentially chronic impact on the health and mood of most individuals. Furthermore, it has been proven that sleep disorders, such as obstructive sleep apnea syndrome (OSAS) can affect human health by inducing cardiovascular diseases, including high blood pressure and heart disease. In addition, the mortality rate of people who snore and of those with severe OSAS is three to four times higher than healthy adults after stroke. Recent evidence has also shown that people with diabetes are more frequently co-morbid with OSAS than those without diabetes, and have a tendency of difficulty controlling their blood sugar levels when with OSAS. In response to such findings, Backer IDI Collaborating Center of WHO in Australia is now actively setting up a new health policy and launching new research projects on the relationship between diabetes and OSAS. Another group that also has sleep problems is shift workers which comprise around 20% of the entire workforce in USA and over 30% in Taiwan and other countries. Due to disturbances with regards to the circadian system, shift workers have an abnormal body metabolism which could result in high cholesterol and other blood lipids, some types of malignant tumors, including breast cancer, endometrial cancer in females, and non-Hodgkin lymphoma and prostate gland cancer in males. Sleep disorders or sleep deprivation not only endanger the health and well-being of most individuals, but also have a negative impact on public safety. Driving while being sleepy is a common problem among those who are sleep deprived or have sleep disorders. The consequences of sleepy driving, in some circumstances, might be even much more serious than drunk driving. According to records from the US National Highway Traffic Safety Administration, every year more than10,000 registered traffic accidents were related to driving when sleepy or due to drivers nodding off. These accidents led to 76,000 injuries and 15,000 deaths, resulting in medical expenses and lost work costs in excess of one billion USD. Therefore, the importance of sleep science cannot be overemphasized, especially when examining how to help those who suffer from sleep disturbances.

With the rapid advancement of technology during recent decades, we can further improve the quality of sleep of many individuals by developing technology for sleep

medicine. However, current sleep technology focuses mainly on the polysomnography and sleep-technician related issues which are important but cannot represent the term "sleep technology" per se.

Over the past few years, a brand new trend of sleep technology has emerged focusing on cross-domain collaboration. The sleep technology SIG (special interest group) of INSIGHT (innovation and synergy for intelligent home and living technology) center at the National Taiwan University has extended the concept of sleep technology to "Modern Sleep Technology" as being the field of developing new and improved ways to monitor, analyze and assess sleep and circadian rhythms in individuals, in addition to any intervention that may be used to promote sleep, to prevent, diagnose or treat sleep disorders, or for rehabilitation or long-term care of sleep conditions in specific groups. This includes the use of pharmaceuticals, devices, techniques, procedures and organizational systems (adapted from the Proposal for the "Engineering and Information Science in Sleep (E-ISiS) Special Interest Group of World Sleep Federation). Under this definition, "Modern Sleep Technology" is:

1. Sleep technology used in the evaluation and management of sleep disorders, as in traditional sleep technology, including: diagnostic tools (such as polysomnography, actigraphy, and so on.) and therapeutic interventions (such as positive airway pressure, surgical and pharmacologic treatments, and so on.) and patient education
2. Sleep technology for ***prevention*** of sleep disorders and ***reduction*** of morbidity caused by sleep disorders
3. Sleep technology that improves the quality of sleep, ***sleep environment***, daytime performance, workplace safety and ***quality of life***

This book includes the contributions of well-known professional scholars from six different countries. The aim of this textbook is to integrate the various disciplines that are involved in modern sleep technology – sleep science (including the field of sleep medicine, psychology, lucid dreaming and consciousness research), engineering and information science, industrial design, technology management, instrumentation and sleep industry, and to provide this integrated information to people who are interested in or wish to involve themselves in the broad field of modern sleep technology.

This textbook is divided into four parts. Part I introduces the history of sleep technology, the scope of modern sleep technology and the importance of it. Part II covers the evaluation instruments for sleep disorders, including the history and application of polysomnography (PSG), and actigraphy. Part III presents the methodology of management for sleep disorders from the point of view of technology, including cPAP (continuous positive airway pressure), surgical concepts and instruments (including some methods in evaluation of the upper airway), positional therapy, cognitive behavioral therapy, light therapy and the biofeedback. Part IV of this book extends modern sleep technology to daily life. In this part, the application of sleep technology is introduced, including sleep environment control, the application

of biosensors, sleep technology in drowsy driving, sleep technology related to the elderly, education on sleep technology, and the sleep technology industry.

All of the authors in this book are the most prestigious experts in their fields related to sleep science. In each chapter, the most up-to-date works and opinions are presented after critical review by at least two internationally well-known scholars in their respective fields. The goal of publishing this book is to further enhance the knowledge of clinicians and researchers with regards to modern sleep technology and to provide this data in a compact and concise format. Recent research has proven that the advancement of sleep medicine might be able to be facilitated by applying the technology. Furthermore, the interdisciplinary collaboration will also be the future trend of sleep research. With the proceeding of modern sleep technology, the E-ISiS SIG (Engineering and Information Science in Sleep Special Interest Group) was proposed in World Sleep Federation during the Kyoto's "World Sleep 2011 Conference" in October, 2011. Another new global society – ISSTA (International Sleep Science and Technology Association) – will be registered in Berlin, Germany in 2012. All of these are to recruit more experts with and without a medical background to shape and energize the field of sleep technology. With such advances and ongoing studies, modern sleep technology will clearly continue to be enhanced.

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I have to express my highest appreciation to my mentors in Stanford University, the father of obstructive sleep apnea syndrome, Prof. Christian Guilleminault, and the founder of contemporary sleep surgery, Prof. Nelson Powell. Both of them led me into the field of sleep medicine and sleep surgery, and the recondite but attractive sleep research to which I'll devote my whole life.

I also want to thank the chapter authors who were invited as the most prestigious experts in their fields to accomplish the challenging goal of this book by cross domain linkage.

We invited 26 international reviewers (please see the "International Reviewers List") for each chapter. With their contribution, we could keep the highest quality of this book.

I am also very grateful to my wife Shirlin, my daughter Victoria, my son Albert, and my dearest colleagues, the Co-Editor-in-Chief of this book, Prof. Shih-Chung (Jessy) Kang in National Taiwan University, and Prof. Xiangyu Wang in Curtin University, Perth, Australia; Prof. Peiling Liu and Prof. Chuin-Shan David Chen in INSIGHT Center, National Taiwan University; Dr. Gwo-Jiumn Huang in Institute of Information Industry, Taiwan; Prof. Sheng-Po Hao in Shin Kong Memorial Hospital; Prof. Yao-Jen Liang in Fu Jen Catholic University, Taipei; Prof. Michael V. Vitiello in University of Washington, Seattle; Prof. Jean Krieger in Strasbourg, France; Prof. Ron Grunstein in Sydney; Prof. Clete Kushida in Stanford; Prof. Thomas Penzel in Charité – Universitätsmedizin Berlin. Without their encouragement and help, we could not have given birth to this book.

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Introduction of Sleep Technology

Chapter 1
The Scope of Modern Sleep Technology

Rayleigh Ping-Ying Chiang, Chih-Feng Lin, Tzu-Chen Lung, Sung-Lin Kuo, Shih-Yu Chen, Shih-Chung (Jessy) Kang, Fei-Peng Lee, and Nelson Powell

Abstract This chapter provides a brief introduction with regards to sleep technology and strives to raise awareness about its importance. With respect to the history of sleep technology, it is found that the sleep medicine has continued to develop over a period and has gradually evolved over the years. Based on recent advances and related research, a new definition of sleep technology will

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be proposed. This definition emphasizes a broader scope of study when compared with conventional sleep technology. Based on this definition a number of developed categories which are the core contents of this book are summarized. Finally, we provide examples for sleep environments and sleep models to demonstrate the impact of sleep technology. Recent research has proven that the limitations of conventional sleep medicine might be improved upon by applying the appropriate technology and interdisciplinary cooperation which is indeed the future of sleep research.

Keywords Modern sleep technology • Sleep environment • Sleep modeling • Interdisciplinary cooperation • Sleep medicine

1.1 History of Sleep Technology Development

Sleep medicine, though no specific date,person or event can be identified as its beginning, can be traced back to ancient Egyptian times (∼1300 B.C.) when opium was widely used as therapy for insomnia. However, sleep technology cannot be said to truly exist until the development of electroencephalogram, or EEG, which was first applied to human in 1924 by German physiologist and psychiatrist Johannes Berger [16]. He demonstrated the difference in brain activity between wakefulness and sleep utilizing EEG, and made EEG a clinical and diagnostic tool for brain dysfunction. The currently and widely accepted five different stages of sleep, stage 1–4 and REM, were established by Alfred Loomis, E. Newton Harvey and Garret Hobart in 1937, also by utilizing EEG [23].

Contemporary to EEG was the concept of circadian rhythm. Starting in the early 1900s, in which Karl von Frisch and Ingeborg Beling were inspired by observing bees visiting flowers with a degree of regularity, chronobiology was widely studied and its existence in all organisms were generally accepted by the 1960s. The decisive experiment of human circadian rhythm was carried out by Jules Aschoff and Kurt Wever in March 1962 [13]. Done by isolating human subjects in an underground WWII banker without any environmental cues, Aschoff and Wever established that a cycle of human circadian rhythm was slightly longer than 24 h. The importance of light-dark cycle on the guidance of human circadian rhythm was later demonstrated by Czeisler and colleagues [14].

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In addition to the study of chronobiology and changes of electric potentials generated by cortex during sleep, other parameters influencing sleep were noted and investigated. One such parameter is the movement of the eyes during sleep, something that was firstly reported by William Griesinger in 1868 [25]. This finding along with another sleep parameters, such as muscle twitching, led to the discovery of "rapid eye movement (REM) sleep" by Nathaniel Kleitman and his student Eugene Aserinsky in 1953 when documenting dreaming sleep [20]. The combination of the physiologic signals from the brain (EEG), eye movement (EOG) and muscle activity (EMG) gave rise to the idea of modern polysomnography (PSG), a multi-parametric test widely used in the study of sleep medicine and in the diagnosis of sleep disorders. Indicators of breathing functions were further added after the indication of obstructive sleep apnea in the 1965 [18].

In 1986, Allan Rechtschaffen and Anthony Kales developed a standardized method for sleep stage scoring in their text entitled *A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Subjects of Human Subjects* [34]. Many sleep stage scorings carried out in sleep study today are still mainly based on the Rechtschaffen and Kales criteria.

In 1977, multiple sleep latency tests, MLST, were created by Mary Carskadon and William C. Dement. They were developed by repeating a project called the "90-minute day" conducted by Dr. Dement in 1970. Sleep latency was measured in MLST and it was based on the idea that the sleepier the patient, the faster they fall asleep [7, 8].

Besides the diagnostic value described above, traditional sleep technology also has a role in the treatment of sleep disorders. Among them are continuous airway pressure (CPAP) applied to obstructive sleep apnea in 1981 [37]; radiofrequency technique for sleep disordered breathing starting from 1997 [12, 24, 30–32]. Even with the advancements in technology, treatment using primarily traditional sleep technology is still widely utilized in a variety of clinical settings.

1.2 The Scope of Modern Sleep Technology

By definition, the sleep technology is the application of technology on sleep medicine. Our definition, "Sleep Technology" is the field of new and improved ways to monitor and assess sleep and circadian rhythms, in addition to any intervention that may be used to promote sleep, to prevent, diagnose or treat sleep disorders or for rehabilitation or the long-term care of sleep condition in some specific groups. This includes the use of pharmaceuticals, devices, procedures and organizational systems. Based on this definition, sleep technology is for:

1. the *evaluation* and *management* of sleep disorders
2. the *prevention* of sleep disorders and *reduction* of morbidity of sleep disorders
3. *improving* the quality of sleep, sleep environment, daytime performance and quality of life

According to our definition of sleep technology, the categories of development so far are listed as follows:

- Clinical services: methodology and instrumentation of screening, diagnosis and management of sleep disorders
- Basic/clinical sleep research
- Sleep environment
- Sleep modeling
- Sleep-related transportation & work place safety and solutions
- Sleep technology innovation
- Educational courses and training program on sleep science and technology

With the exception of the sleep environment and sleep model, the others will be illustrated in detail in later chapters. Here we provide a brief review of related applications in sleep environment and sleep model and demonstrate the importance of technology.

1.3 The Application of Technology in Sleep Environment

The sleep environment is of crucial importance as a factor that influences the quality of sleep in human. By applying technology to the area of sleep environment, we can free some limitations which are associated with traditional methods. Sleep is a rest state that the human beings need to recuperate normally, and being more sensitive to certain ambient factors, such as environmental noise [26].

Recently, quite a large number studies have demonstrated that ambient factors such as noise, temperature and even bedding environment are strongly correlated with sleep rhythm or sleep disturbances [4, 9]. As a result, establishing an appropriate individualized model for a sleep environment is of paramount importance. Unfortunately, it is difficult to clearly define the most suitable model for each individual given that the physical and psychological states differ from person to person. It has been observed that a large number of studies on sleep medicine use different methodology to analyze problems encountered nightly and daily, presenting the importance of utilizing interdisciplinary combinations in the application of technology in sleep environment.

Polysomnography (PSG) is commonly used to monitor the physiological system of a person and directly reflects the state in real time. However, the electrophysiological signals from PSG are complicated on the surface and require further processing procedures to interpret the characteristics of the results and to make sense of them in clinical practice. For example, Scholz and colleagues [36] have demonstrated that HRV (heart rate variability) could represent the activity of autonomic nerves via Fast Fouier Transform (FFT). Moreover, using the advanced tools of signal processing such as time-frequency analysis, we are able to detect the EEG markers of cognitive decline [2]. For its application in the sleep environment, PSG can serve as an ancillary role to establish the bridge between ambient factors and people,

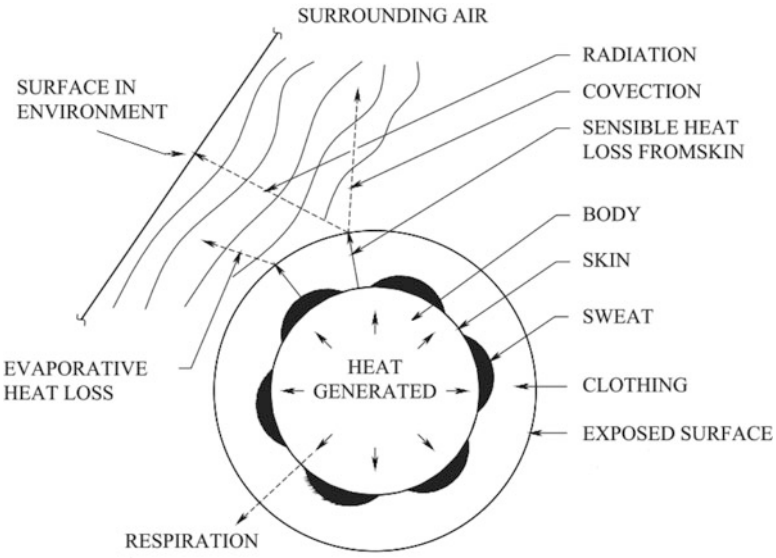

Fig. 1.1 The thermal interaction between a human body and its environment (Adapted from *Fundamentals: 2001 Ashrae Handbook* [3])

By adjusting the ambient factors in different conditions meanwhile simultaneously monitoring PSG signals modified by signal processing method, researchers can build an optimal model regarding an ideal sleep environment for each person.

Basically, the four architecture physics, including noise, light, temperature and ventilation are primary factors for indoor sleep environment and these factors have been demonstrated to be closely related to sleep quality [42]. Among the factors, temperature is a directly perceivable from the environment and is associated with body thermoregulation. Muzet et al. [27] concluded that the most appropriate temperature for sleeping adults is approximately 16°C due to the limited number of wakefulness episodes during a sleeping period. On the other hand, Haskell et al. [19] demonstrated that a cold air temperature (21°C) was more disruptive to sleep as compared with a high temperature (34 and 37°C). Thus, there are some discrepancies which are difficult to explain in this field of study. As a result, Lin and Deng [21] developed a thermal comfort model for a sleep environment based on Fanger's thermal comfort model (shown in Fig. 1.1). The equation of comfort model can be adjusted by five variables, including air temperature, mean radiant temperature, water vapor pressure, air velocity and the total insulation from bedding system, to set up criteria in a variety of conditions.

As indoor moisture also affects the state of health of people, which means that keeping relative humidity (RH) at suitable level is also important for human. The primary risk related to lower RH may be associated with the dryness of the skin, mucous membranes, sensory irritation of the eyes and upper airways [15, 40, 41, 43]. Based on these facts, the optima moisture model according to different moisture

factors, such as air change rate, airflow in bedroom, moisture source and so on, can be derived from the theoretical principle of fluid mechanics as well help to achieve the ideal sleep environment.

In conclusion, based on the facts indicated above, the relationship between ambient factors and people during a sleep state is a significant issue and of interest to study. Applying technology to sleep environment helps ameliorate the traditional limitations when dealing with a more complex model. However, there are still many other ambient factors, such as noise and light which have not been mentioned in this section. These factors can also be detected and modified by utilizing technology to establish a more suitable sleep environment. Overall, technology provides us with the tools to understand problems which influence our sleep environments and gives us the opportunity to improve sleep environment conditions to achieve "healthy sleep."

1.4 Social Factors and Feng-Shui (Geomantic Omen)

In addition to these primary environmental factors described in the above section, social factors might play significant roles in sleep environment. For example, the sleep of students who lived in a dormitory would be affected by their roommates. If one of the roommates snore loudly at night, this could have a negative impact on their quality of sleep. Similar situation can occur in couples. In addition, different schedules of getting-up and bedtime between spouses will definitely affect their sleep mutually. For instance, many husbands have to get up early every day for work while the wives usually get up later. This difference in sleep schedules of couples will definitely influence the quality of sleep.

The ancient Chinese theory of Feng-Shui, the geomantic omen**,** also plays an important role in sleep environment in Eastern society. In traditional Chinese culture, Feng-Shui indicates the probable place or location for buildings or furniture, and so on, which would bring the best luck for people who live in that house or environment, or may even change the fortunes of these people. Therefore, Chinese usually have a philosophy influenced by Feng-Shui in setting up or decorating a sleep environment. For example, one of the rules in Feng-Shui theory is that people should separate the room for sleeping and for reading, which means people should not read or work in bed. The scientific explanation for this rule is that people more easily get insomnia when they are used to read or work in bed. Another example, the mirror is not supposed to face the bed in the bedroom. The psychological background is that the image of the individual shown in the mirror could be a source of scare during sleep or at the moment when getting up. Despite the fact that most people think Feng-Shui to be old fashioned and quite superstitious, many rules behind Feng-Shui theory are actually beneficial for people, and have their scientific explanations.

It is quite crucial to apply sleep technology to deal with these factors in the sleep environment. In the near future, the development of sleep technology will include social factors and Feng-Shui.

1.5 Sleep Modeling

Sleep modeling is a more commonly used name and several studies now have focused on this promising field. However, the specific definition of sleep modeling is still rather ambiguous. In a broader sense, it can include modeling the whole circadian rhythm or chronobiology of human or sleep macro-architecture [11]. On the other hand, it can focus on more specific areas of interest. For example, alpha wave oscillations or sleep spindle modeling of sleep EEG in a short time scale is a prospective issue. Looking at both sides, relative studies have even established a model to monitor sleep state such as sleep quality assessment model [33] or assess sleep related disorders [39]. All of the above can be included in the definition of sleep model here. The following introduction will focus on the fundamental concept of sleep modeling and the related applications of recent modeling, in addition to touching on the remaining challenges in this field.

By exploring the fundamental concept of sleep modeling, a well-known model in the history of sleep medicine, the two-process model [5] was introduced for the first time. That has been proposed and developed for a period and even for the further elaborated three-process model [17]. By means of considerable number of experiments, the two-process model, including homeostatic (Process S) and circadian (Process C), has been successfully demonstrated (Fig. 1.2). That indicates that slow-wave activity (SWA) seems to be serve as a marker of non-REM sleep intensity, as well as an indicator of sleep homeostasis [1]. Process S is mathematically modeled by a saturating exponential function during waking and sleep. In the meantime, Process C is simulated as a clocklike mechanism and independent of prior sleep and waking [6]. The aims of these models are trying to interpret the real sleep characteristics and attempting to use mathematical equation to model the sleep performance. Further definition of sleep model, it can be interpreted as guiding principle to establish a connection between process at different scope of sleep analysis [1].

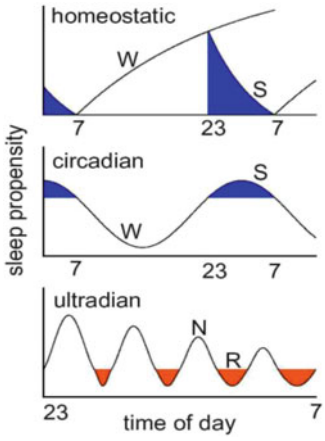

Fig. 1.2 Schematic representation of the three major processes underlying sleep regulation. *W* waking, *S* sleep, *N* non-REM sleep, *R* REM sleep. The progressive decline of non-REM sleep intensity is represented both in the top and bottom diagrams (decline of ultradian amplitude). The increase in the duration of successive REM sleep episodes is indicated [1]

Table 1.1 Different time scales of sleep dynamics [29]

≈24 h	Circadian rhythms and sleep homeostasis
≈90–100 min	Ultradian process, cyclic alternational between NREM and REM sleep
s to min	Transitions between sleep stages
s	Temporal organization of sleep oscillations, e.g. periodic occurrence of sleep spindles (4 s), cyclic alternating patterns (CAPs)
≥1 s	Slow oscillations, cyclic alternation between 'up' (high firing rate) and 'down' (no firing) states
0.05–1 s (1–20 Hz)	Typical sleep oscillations: delta oscillations, sleep spindles, alpha and theta oscillations

Compared with sleep model with long time scales indicating above, it is also important to fathom the characteristics of sleep model with short time scales (e.g. spindles and alpha oscillations). This kind of research aims at how to detect isolated short oscillatory events in sleep EEG. For example, Olbrich et al. [28] proposed a novel detection algorithm based on autoregressive (AR) models. Contrary to traditional method, this algorithm doesn't need predefined frequency band of the specific oscillatory patterns. That can overcome the calculation errors in frequency domain. Through this algorithm, the distribution of oscillatory events is clearly manifested in all frequency range and this result might be further applied to explore the interaction between the occurrence of oscillatory pattern and different time scale characteristics of sleep EEG. The problem of relationship between different time scales is complicated and exactly needs more time series analysis techniques to improve the physiological model. Olbrich et al. [29] also pointed out the multiple time scales of sleep dynamics is exactly a next challenge. Table 1.1 integrates the different time scale of sleep dynamics so far.

In addition, a different defined sleep model can be found in the past literatures and this is also an interesting topic to engage in. Apart from above indicated model, the illustrated models here focus on the assessment for sleep related disease. The standard of procedure aims at establishing a diagnosis model by considerable experiments combined with advanced times series techniques. For example, Lin et al. [22] proposed an assessment model for Alzheimer's disease based on sleep EEG. Lots of past studies [10, 35] have demonstrated the sleep EEG might be correlated with the cognitive performance. Based on this foundation, it is found that the time course of band power between theta and alpha bands performs quite different among non-dementia control and the patient of Alzheimer's disease. Figs. 1.3 and 1.4 show the example for a control and a patient respectively. Therefore, Lin et al. developed quantitative procedure of similarity between two series, establishing the sleep EEG model in Alzheimer's disease. The other example could be taken from the research of Ubeyli et al. [38]. This study focuses on extraction of characteristics from sleep EEG and substituting in the pre-setup neural network model to detect hypopneic episodes during all night.

To sum up, this section has introduced different types of sleep models. Clearly, sleep models play an important role in sleep research and are a paradigm of the application of technology. The most recognized advantage of sleep modeling is

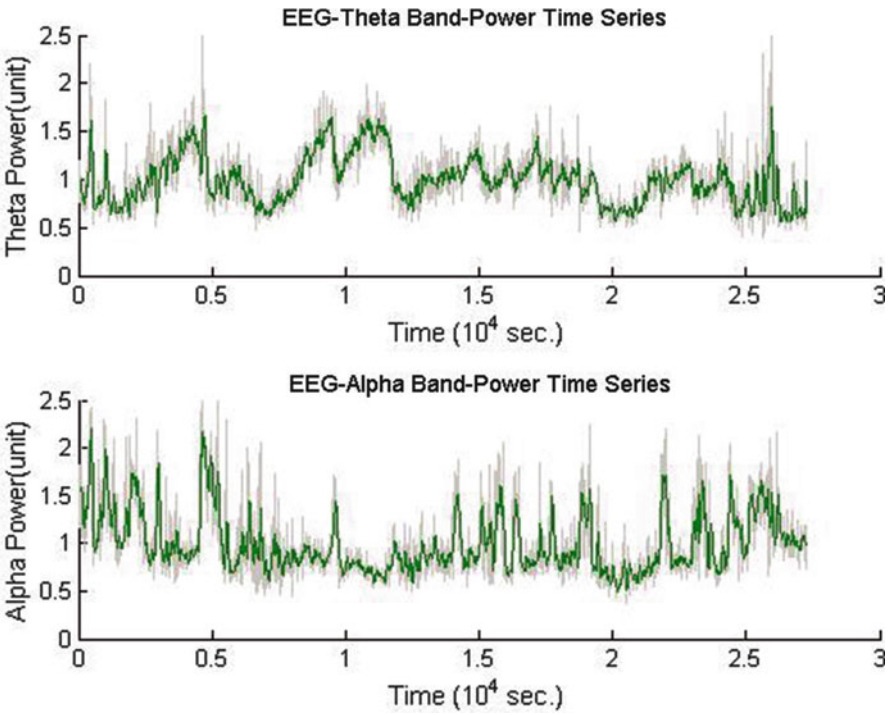

Fig. 1.3 A numerical example for the theta and alpha band-power time series of C3A2 channel from the patients of Alzheimer's disease

that researchers are able to make assumptions or estimations based on a model by evaluating possible consequences and then make proper decisions. Moreover, sleep modeling can be applied to other promising research such as sleep scheduling where we adjust diurnal activities according to an individualized model. However, this poses the question whether or not these kinds of models need more detailed biological evidence and experimental trials to strengthen their validity. Thus, this raises a paramount issue regarding the importance of combining sleep technology with conventional sleep medicine research.

1.6 Future Direction of Modern Sleep Technology

In previous sections, it has been shown that innovations with regards to technology applied to sleep medicine can offer additional benefits for mankind. Except for modern technology, the application of sleep medicine in our daily lives such as sleep modeling also makes sleep technology a much more important subject.

According to a questionnaire survey (effective sample size: 102) from the *First International Sleep Technology Symposium* (1st ISTS, report website: http://insight.

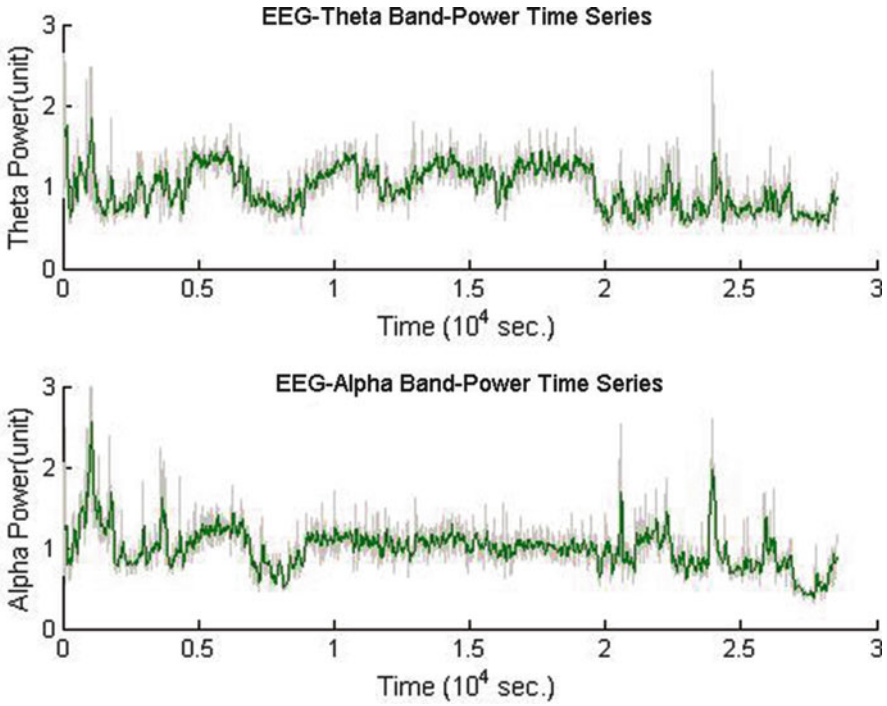

Fig. 1.4 A numerical example for the theta and alpha band-power time series of C3A2 channel from the controls

ntu.edu.tw/ewpg/news/278) which was organized by INSIGHT (innovation and synergy for intelligent home and living technology) Center of the National Taiwan University with the audience from U.S., Japan, Philippines, China and Taiwan, over 50% of the participants believed the important topics of the sleep technology will be issues related to (A) sleep environment arrangement (including environment modifying devices facilitating sleep, bedding and pillow design), (B) sleep related issues in homecare and institutional long-term care, (C) detection, monitoring and application of telemedicine, and (D) development of new modality in diagnosis and treatment of sleep disorders, especially by (E) cross domain collaboration (Fig. 1.5).

In this survey, sleep environment was thought to be the one of the most important areas deserved further study. As mentioned before, there are many environmental factors that can affect quality of sleep, but much more evidence on sleep environment related psychology, physiology and pathophysiology should be elaborated still. In addition, the results of this survey also show that application of new technologies on sleep and circadian rhythm has become one of the most important potential domains in the research of modern sleep technology. In the near future, an international platform will be necessary to open a gate for the experts

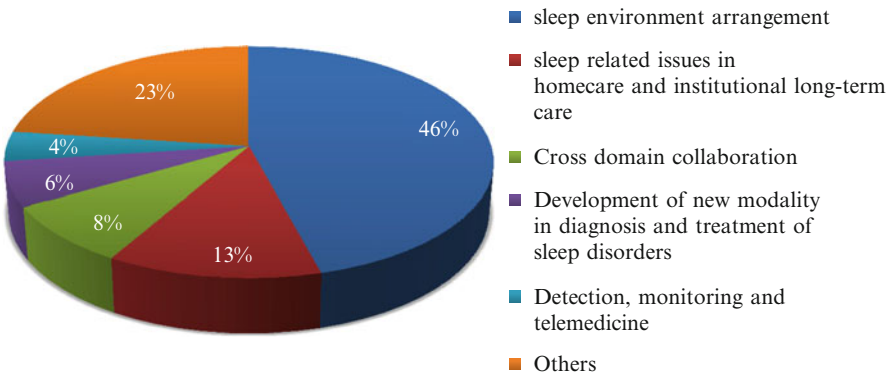

Fig. 1.5 Result of questionnaire survey from the *First International Sleep Technology Symposium*

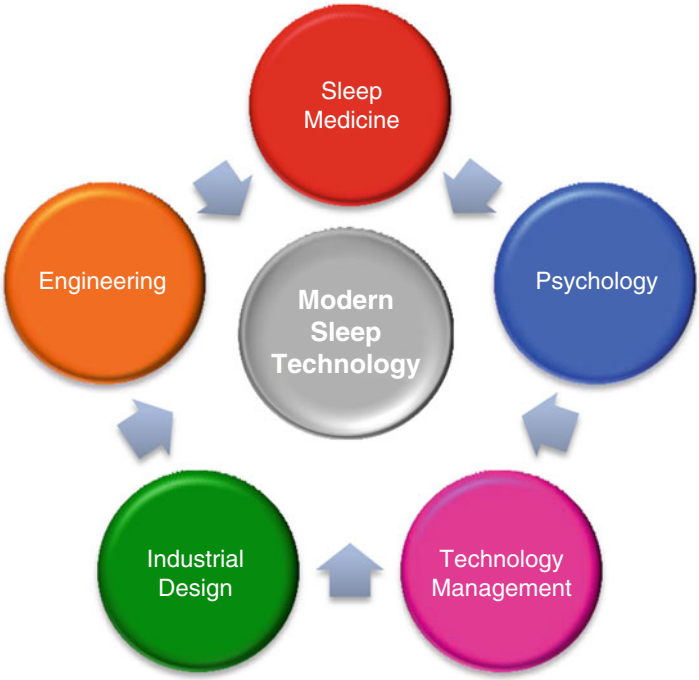

Fig. 1.6 Cross domain chemical reaction between sleep medicine, psychology, engineering, industrial design and technology management to form the field of "modern sleep technology"

with the background of medicine, psychology, engineering, industrial design and technology management (Fig. 1.6) to support this new cross-domain field of modern sleep technology.

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Part II
Sleep Technology in Diagnosis and Screening

Chapter 2
Evaluation Instruments for Sleep Disorders: A Brief History of Polysomnography and Sleep Medicine

José Haba-Rubio and Jean Krieger

Abstract Sleep is a vital biological function and we currently know that sleep disorders are highly prevalent in the population. The history of the development of sleep science and sleep medicine is inextricably tied to the development of polysomnography, used as a means to assess, objectively and in a reproducible way, sleep and wakefulness. Over the past 50 years, technologic advances and scientific progress have permitted huge improvements in the systems used to record sleep. Furthermore, major advances in sleep science and pathology are linked with improvements in the methods of recording and analyzing sleep. It can be asserted that the development of polysomnography transformed sleep research from a speculative area to an experimental science. This chapter has been organized to briefly relate the major developments in sleep medicine and to summarize the evolution of polysomnography.

Keywords Sleep medicine • History • Polysomnography

Sleep and dreams have played a central role in the culture of humankind and has fascinated people for a very long time. Sleep occupies a third of our lives; every night the mystery of sleep unfolds before each of us. However, it was not until recently that we had the opportunity to study sleep from a scientific point of view, in other words, beyond the observations of philosophers, poets and prophets.

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French scientist Henri Piéron (1881–1964) with his work entitled "Le problème physiologique du sommeil" published in 1913, is usually regarded as the pioneer of the modern approach to sleep research. Advances in technology, and in particular the development of polysomnography which allowed the recording of physiologic changes during sleep, was the turning point that enabled a better understanding of sleep and sleep disorders.

2.1 The First Steps: Recording the Electrical Activity of the Brain

Once upon a time, sleep was thought to be a passive state; in fact, sleep was defined as the absence of waking consciousness. Indeed, sleep was often associated to death. In ancient Greek mythology Nyx, the Goddess of Night, had twin sons called Hypnos (Sleep) and Thanatos (Death). Sometimes small figurines depict them as young babies, each suckling on a breast of mother night. Morpheus, the source of dreams, was the son of Hypnos and hence the nephew of Death. This idea that sleep is not an active state runs through most of the history, and it wasn't until the middle of the twentieth century that scientists examined sleep from a physiological perspective.

Previous to this, at the end of the nineteenth century, the Spanish anatomist and neurohistologist Santiago Ramon y Cajal (1852–1934) revolutionized the understanding of the form and nature of cell populations of the nervous system. He demonstrated that the nervous system was composed by independent cells that do not anastomose, but make contact with others at specific points in a highly intricate network. He showed that nervous impulses were transmitted from the cell body out to the axon, and that the axon conducts away from the cell body. Some of the credit for these discoveries belongs to Camillo Golgi (1844–1926), an Italian anatomist and histologist, whose silver stain Cajal modified, and with whom he shared the Nobel Prize in 1906. This work was the basis of our understanding of the functioning of the brain.

A capital contribution to this understanding, and to the development of sleep medicine, was the discovery of the electrical activity of the brain. Luigi (or Aloysio) Galvani (1737–1798) had discovered (working on frogs), at the end of the eighteenth century, that nerve cells of animals produce electricity. Emil DuBois-Reymond (1818–1896), who is considered to be the father of modern electrophysiology, demonstrated the polarized state of nerves and muscle fibers, and showed that the peripheral passage of a nerve impulse was accomplished by an electrical discharge. Hermann Ludwig Ferdinand von Helmholtz (1821–1894) also made significant contributions to the idea that nerve cells use their electrical capabilities for signaling information to one another.

It was finally the Scottish physiologist Richard Caton (1842–1926) who first reported in 1874 the description of the electrical potential changes in the brain

of rabbits and monkeys [9, 13]. He demonstrated that "feeble currents of varying direction" could be recorded from the exposed brain surface of every animal he studied. He conjectured that the activity he observed was related to brain activity, but his work was not recognized until Berger referred to it in his seminal paper in 1929 [4]. Johannes (Hans) Berger (1873–1941) was a psychiatrist from Jena, Germany, and he was the first to record, from the scalp, cortical electrical activity in humans in 1924. He clearly identified the waking alpha rhythm, and observed that if a subject fell asleep, the rhythm disappeared and electrical activity was of very low amplitude or sparse during sleep. Thus, the electroencephalogram (EEG) was born. This discovery constitutes the most critical turning point in sleep research: for the first time, the presence of sleep could be conclusively established without disturbing the sleeper, granted scientists a window into the brain's activity, and the possibility to measure it quantitatively. Lord Edgar Douglas Adrian (1889–1977) was the first scientist to acknowledge and understand the significance of Berger's EEG work, which had been ridiculed as artifact by some.

2.2 Sleep Wave Patterns and All-Night Continuous Recordings

All the major elements of sleep wave patterns were shortly thereafter described in a series of experiences conducted by Alfred Lee Loomis (1887–1975) together with Princeton biology professor, E. Newton Harvey, and a local resident, Garret Hobart III, first in a private laboratory in his mansion in Tuxedo Park, NY, and thereafter at Harvard University, where they were joined by Hallowell and Pauline Davis, a husband and wife team of EEG pioneers from Harvard Medical School [10]. In a series of papers published between 1935 and 1939 [11, 12, 30–32] they were the first to describe the characteristic features that now comprise non-REM sleep. They recorded overnight and day sleep, and characterized sleep into five stages (A, B, C, D and E), listed in order of appearance and in order of resistance to change by external disturbances. These studies were completed by others conducted by Blake, Gerard and Kleitman, at the University of Chicago [5, 6]. They further studied sleep depth, attempting to disturb sleep at each stage and measuring the amount of a stimulus that was required to elicit a response.

These experiments began to improve the methods through which sleep was studied. EEG recording evolved, using amplifiers and high and low pass filters. Experimenters found that certain EEG waveforms were best recorded from specific regions of the brain. As a result, certain channels of the EEG gained importance in the recording of sleep. In addition to EEG, sleep researchers experimented with channels that recorded other physiological parameters, such as heart rate and respiration [13].

Nathaniel Kleitman (1895–1999) was the author of the seminal 1939 book Sleep and Wakefulness, and is recognized as the father of American sleep research.

Kleitman was born in Russia and immigrated to the US in 1915. He earned his doctoral degree in physiology and became professor at the University of Chicago, where he set up a laboratory to study sleep in the early 1920s. He was the first to devote the bulk of his entire professional life to the study of sleep, and his laboratory was the first to be permanently devoted to the study of sleep. Next to his office in the physiology building was an old two-room chemistry lab with a door between the rooms. He set up a cot in the room where volunteers would sleep, and left the other room for the observer [14]. He designed a means of measuring movements during sleep and used this technique during experimental sleep recordings [6].

However, the technology was still too primitive and difficult to use. The very first electrodes were small pins that were stuck into the scalps of stoical volunteers. Only a limited number of channels were available for electrode sites, the amplifiers filled an entire room and the recording system used ink pens and required careful calibration before each study. Furthermore, the studies generated large amounts of paper which were difficult to manage. World War II interrupted most research, but was followed by a rapid improvement in technology because of wartime advances in electronics.

The discovery of rapid eye movement (REM) sleep is one of the major advances in the field of sleep research. In the earlier 1950s, Eugene Aserinsky was a graduate student in physiology in the Chicago University sleep laboratory. Kleitman had given him the assignment of watching people's eye movement as they slept. He started observing infants in their cribs in their homes during daytime, and thereafter adults during the night. Nighttime observations were hard work, and watching for eye movements through the eyelids was a tedious task, so they came up with an easier method of recording eye movements, using electrodes placed on the skin next to the eyeballs (the electrooculogram, EOG). The EOG was a means to conveniently and quantitatively measuring eye movements. When used in conjunction to EEG and body movement channels, EOG extended the ability to evaluate the physiology of sleep. Using this system, they were the first to describe the "rapid eye movement" (REM) periods, different from the slow eye movements at the onset of sleep. Additionally, they noted that respiration and heart rate increased during periods of REM. In addition, awakenings when rapid eye movements were present were often associated with rich dream recall. A correlation between REM sleep and dreaming was hypothesized. In fact then, REM sleep, one of the landmark findings in the sleep field, was discovered essentially by accident in 1952. The seminal Aserinski and Kleitman paper was published in 1953[2].

It is important to note, that at the time, to make the job easier and to save paper, the recordings were made for short periods of time, turning on and off regularly, and somewhat randomly, the recording system during the night. In fact, there was no clear reason at the time to record continuously, and in addition it allowed the observer to take a nap between sampling episodes.

In 1952, William Charles Dement (born 1928), at that moment a young medical student, joined Professor Kleitman's group. One of his first assignments was to awaken people during the night and ask them if they remembered dreaming. Motivated by the desire to expand and quantify the description of rapid eye

movements and its relationship with dream activity, Dement made all-night, continuous recordings (EEG, EOG and movement channels) during sleep. It became possible to describe and to quantify the overall patterns of sleep through the night. The cyclical variations of EEG and EOG patterns during sleep were described, and so the different stages of sleep. They proposed a classification of sleep stages: four stages of non-REM (1, 2, 3, and 4) and REM sleep. This can be regarded as the point at which the study of sleep became a true scientific field, as it was the beginning of studying sleep as a whole. This understanding of the electrophysiological substrate of human sleep has been the basis of the development of sleep science. In the 1950s, studies of sleep were always conducted on male volunteers. William C Dement reports, in his book *The Promise of Sleep* [14] that when he proposed to Professor Kleitman to test a woman for REM sleep, he was absolutely opposed. It was only after Dement married that he was allowed to record the sleep of a woman: his own wife. William C. Dement is a pioneering sleep researcher and founder of the Sleep Research Center, the world's first sleep disorders clinical unit, at Stanford University, in 1964. The first patients seen at the newly opened sleep clinic were insomniacs and narcoleptics. Narcolepsy was by that time fully characterized as an interesting and disabling clinical syndrome, requiring sleep recordings for diagnosis. In 1975 he launched the American Sleep Disorders Association, now known as the American Academy of Sleep Medicine (AASM).

The work of Michel Valentin Marcel Jouvet (born 1925) was also pivotal to the detailed early description of the physiological characteristics of REM sleep. In 1959, Michel Jouvet conducted several experiments on cats regarding muscle atonia during REM sleep. Jouvet demonstrated that the generation of REM sleep depends on an intact pontine tegmentum and that REM atonia is due to an inhibition of motor centers in the medulla oblongata. Cats with lesions around the locus coeruleus have less restricted muscle movement during REM sleep, and show a variety of complex behaviors including motor patterns suggesting that they are dreaming of attack, defense and exploration. He pointed out the absence of muscle potentials during the REM periods in cats [24, 25]. This work led to Michel Jouvet's identification of REM sleep as an independent state of alertness, which he called "paradoxical sleep." Jouvet's work put the emphasis on the importance of recording EMG activity to be able to identify REM sleep. With this addition, the basics of polysomnography (PSG), namely EEG + EOG + EMG of postural muscles were defined.

By 1960 it was accepted that there are two fundamentally different kinds of sleep: REM sleep and non-REM sleep, and by that time it was possible to discriminate them by recording the EEG, the EOG and the EMG.

After Dement and Kleitman's article was published, sleep researchers began to use their description of clinical sleep stages. In 1967 a committee of investigators with experience in scoring sleep, led by Allan Rechtschaffen and Anthony Kales, developed a terminology and scoring system to be universally used by sleep specialists [37]. They developed the first consensus-based guidelines for staging and scoring sleep in normal human subjects, commonly called R&K or Rechtschaffen and Kales. The committee recommended using a minimum of one channel of central EEG (either C3 or C4 to the opposite ear or mastoid), chin EMG, and two channels

of EOG (electrodes placed below and lateral to one eye and above and lateral to the other eye, both referenced to the same ear or mastoid). They recommended an epoch-by-epoch approach to scoring, using epochs of 20 or 30 s. Sleep was scored in five different stages: stages 1, 2, 3, 4 and REM. Recording 1 EEG, 2 EOG and 1 EMG (four channels in total) allowed for recording two subjects simultaneously, since the paper then in use was designed to record 8 channels.

However, the limitations of the R & K system became evident with time, in particular with the emergence of sleep disorders medicine [22]. The rules of R&K were clearly designed for normal, usual sleep patterns, not for abnormal or deviant normal electrophysiological patterns. In addition, the R&K system was designed for paper recordings including specifications for filters, gains, paper speed, pen deflection, number of channels, etc., and most of the requirements and guidelines became obsolete with the use of modern digital equipment. From the EEG information, only one derivation was taken into account. The amplitude criteria for the scoring of slow wave were also criticized, as during normal aging the amplitude of the EEG decreases. The NREM stages 2, 3 and 4 were separated by the percentages of time (<20, 20–50 and >50%, respectively) occupied by delta waves, with no clear scientific basis for appointing these values. Nevertheless, the R&K was used from 1968 to 2007, when the *The AASM Manual for the Scoring of Sleep and Associated Events* was published by the American Academy of Sleep Medicine (AASM) [23]. It revised R & K sleep staging and addressed digital methodology, as well as the scoring of arousals, respiratory events, sleeps related movement disorders, and cardiac abnormalities, with consideration of pediatric and geriatric age groups. Thus, for example, according to the AASM Manual, a minimum of three EEG derivations are recommended in order to sample activity from the frontal, central and occipital regions. Slow wave sleep is represented by stage N3 and replaces the R&K nomenclature of stage 3 and stage 4 sleep.

2.3 Recording Pathological Sleep

The classic all-night sleep recording could yield a great deal of information concerning sleep duration and characteristics of sleep, in particular in insomniacs and narcoleptic patients. But the extension of polysomnography, with the inclusion of additional sources of information and its imposition as the gold standard tool for the study of sleep and its disorders was not an easy road. Most likely, the first reason was the completely unprecedented nature of an all-night diagnostic test. In addition, it was an expensive, time-consuming and labor-intensive process, which required the conjunction of specialized clinicians and skilled technicians. Another factor to be considered was the reluctance of clinical professionals to work at night, and the fact that most clinical practitioners were completely unaware of the existence of sleep disorders. Sleep medicine as a field was not recognized in the medical community, and the investigations were not reimbursed by health care insurance.

However, in the 1960–1970s a new sleep disorder reared his head, and inspired the evolution of polysomnography. In 1956 Burwell and coworkers published their description of the obesity-hypoventilation syndrome, also known as Pickwickian syndrome, based on the similarity to a character in Charles Dickens' The Posthumous Papers of the Pickwick Club [7]. At the time, sleepiness was thought to be the result of hypercapnia, due to alveolar hypoventilation. However in Europe, a group of researchers became conscious of respiratory abnormalities during sleep in these patients. In fact, the first recordings in sleeping Pickwickian patients, as reported by Peretz Lavie [29], were conducted in 1959 by Werner Gerardy and colleagues at the Ludolf Krehl Klinik of Heidelberg University Hospital, who recorded breathing and pulse rate simultaneously to the EEG [19]. It was the first report in the medical literature on apnoeic events in Pickwickian patients. Two years later, Drachman and Gumnit of the National Institutes of Health, at Bethesda, published an article entitled "Periodic Alteration of Consciousness in the "Pickwickian" Syndrome" in Archives of Neurology [16]. Like Gerardy and his colleagues, Drachman and Gumnit made the recordings during the day. They observed that the moment the patient's EEG showed signs of sleep, his breathing ceased and arterial oxygen saturation level dropped to a minimum of almost 50%. Despite this, none of them connected the sleep disorder with daytime sleepiness.

By that time, Kuhlo, Director of the EEG laboratory at Freiburg University, had a great interest in EEG changes that accompany the process of falling asleep and his predecessor, Richard Jung, had a great interest in the Pickwickian syndrome. They recorded EEG, chest movements with an inflatable belt, carbon dioxide content of expired air, and heart rate of these patients, and correctly concluded that excessive daytime sleepiness in Pickwickian patients was related to their sleep fragmentation, and not due to carbon dioxide poisoning [26].

Gastaut, who headed the Neurobiological Research Unit in Marseille, and his former student, Elio Lugaresi from Bologna, attended the conference where Kuhlo presented their findings. After the meeting, Gastaut assigned two of his younger colleagues, Duron and Tassinari, to monitor Pickwickian patients' sleep [29]. Rather than testing the carbon dioxide content of expired air, they used measurements of mouth and nostril airflow in addition to chest movements, and demonstrated that the reason for the apnoeic events during sleep was the blockage of the upper airways during sleep, in spite of continuous respiratory effort [17, 18]. Repetitive episodes of upper-airway obstruction were terminated by briefs arousals, which in turn fragmented sleep. They confirmed that sleep fragmentation was responsible for the excessive daytime somnolence presented by these patients.

Elio Lugaresi and Giorgio Coccagna from Bologna, also recognized the importance of Kuhlo's observations [29]. The Bologna group's findings in Pickwickian patients supported those of Gastaut et al. and documented three types of apnoea: obstructive, central, and mixed [34]. Lugaresi was the head of the Neurology Department in Bologna, where he also made the first sleep recordings in patients with "restless leg syndrome" [33]. When patients with RLS underwent sleep recordings, they demonstrated periodic involuntary leg movements. EEG showed that they were not a form of epilepsy.

These findings stimulated considerable research in the area of sleep and breathing. Thereafter, neurologists Daniel Kurtz and Jean Krieger of Strasbourg introduced the notion of hypopnoea, or partial apnoea, which like apneas, end with a brief awakening and a slight drop in oxygen saturation level [27]. French neurologist and psychiatrist Christian Guilleminault also played a central role in the early discovery of obstructive sleep apnea. In January 1972 he joined the Standford Sleep Center, and working in collaboration with Dr. William C. Dement, Guilleminault established the Apnea/Hypopnea Index (AHI) which is still in use today to diagnose sleep apnea and measure its degree of severity [20]. It was in this paper that the term "Sleep Apnea Syndrome" was first used, and a definition for the syndrome based on polysomnographic findings was provided. Guilleminault later also described Upper Airway Resistance Syndrome (UARS) as a sleep disorder characterized by increased airway resistance to breathing during sleep. The seminal article on UARS is "A cause of excessive daytime sleepiness: The upper airway resistance syndrome", which Guilleminault co-published in the journal *Chest* [21]. To confirm the diagnosis, it was necessary to use a probe to measure esophageal pressure (Pes), to demonstrate a progressive elevation of esophageal pressure swings which terminated with an arousal, in the absence of apnoeas or hypopneas.

The discovery of sleep breathing disorders imposed the use of respiratory and cardiac sensors in sleep studies. Electromyogram (EMG) of the muscle tibialis was added to monitor periodic legs movements.

Thus the need to identify abnormal events during sleep necessitated the inclusion of more sensors in addition to the basic EEG, EOG and EMG recordings required to identify sleep stages. The number and type of additional sensors of course depends on the nature of the suspected disorder for which a given patient is investigated. However, because of the high prevalence of respiratory disorders and periodic movements during sleep, respiratory and leg movement sensors became a routine part of the all-night diagnostic test which was named polysomnography in 1974 by Dr Jerome Holland, a member of the Standford group [3]. The name is derived from Greek and Latin roots: the Greek 'poly' for multi-channel (many), the Latin 'somnus' (sleep), and the Greek 'graphein' (to write). At the initial stage, "poly" was only two, but as we just have described, with the rapid improvement of technology, the number of sources of information soon increased.

In 1975 Mary Carskadon, now Professor in the Department of Psychiatry and Human Behavior at the Warren Alpert Medical School of Brown University, joined the Standford Sleep Center. Along with Dement, she developed the Multiple Sleep Latency Test (MSLT) used to clinically determine sleepiness in sleep disordered patients, particularly by measuring daytime sleep onset latency [8]. Conceiving and developing an objective measure of sleepiness is considered one of the most important advances in sleep medicine [14]. The test consists of four or five 20 min nap opportunities that are scheduled about 2-h apart. The test is often done following an overnight sleep study. During the test, EEG, muscle activity and eye movements are monitored and recorded. These measure the time it takes from the start of a daytime nap period to the first signs of sleep; the sleep latency. With time, other methods have been developed to measure sleepiness "objectively" such as the Maintenance Wakefulness Test (MWT) [15].

Many physiological variables can be recorded during a polysomnography, such as end-tidal or transcutaneous carbon dioxide, temperature (via a rectal probe), additional EMG channels, additional EEG channels (when epilepsy is suspected), CPAP pressure and so on; the choice of the appropriate variables to be monitored depends on the nature of the disorder for which the patient is being investigated.

Each one of the techniques used to record these parameters has undergone its own evolution. This is the example of oximetry [35]. The first oximeters were developed in the early 1940s by a British researcher, Millikan, who developed an ear oxygen meter for aviation, for which he coined the word "oximeter". The system went through many modifications during the 1940s and 1950s, and was eventually manufactured by the Waters Company. In 1964, a San Francisco surgeon developed a self-calibrating, 8-wavelength oximeter that was marketed by Hewlett Packard in the 1970s. However, it was large, cumbersome, expensive, and required the heating of the ear lobe to which it was applied, which added to the discomfort. In the early 1970s, Takuo Aoyagi, a Japanese bioengineer, found that it was possible to use the pulsating changes in the light transmission through the ear to measure arterial oxygen saturation. He then went on to develop a pulse oximeter and applied for a Japanese patent. At the same time, another Japanese researcher from Minolta was working on the same concept and applied for a patent a month later. This patent was denied in Japan but approved in the U.S. In the late 1970s, the Biox Corporation in U.S. made significant advances in pulse oximetry, 2-wavelength measurements. They first introduced the use of Light Emitting Diodes (LEDs) for the red and infrared light sources. It allowed continuous, real time, noninvasive oxygen saturation readings. Ohmeda Corporation purchased Biox, and in the 1980s, along with Nellcor and Novametrix, continued to make significant advances in size and cost reductions. Oximeters became smaller in size, easier to apply, and less expensive. In 1995, fingertip oximeters, which are small enough to put a finger in, first appeared on the market. All these improvements in oximeter techniques were progressively introduced to polysomnographic recordings.

Major improvements have been also made in the methods of recording airflow. The reference standard measurement of airflow is the pneumotachometer. It allows continuous monitoring of total oronasal airflow, which in most circumstances requires a snug-fitting face mask. It is a relatively bulky and uncomfortable system, so historically other methods for recording airflow have been employed [1]. An easier to use method is the detection of airflow by thermal sensors (thermocouples and thermistors) which have been traditionally used to determine airflow during polysomnographic studies. A thermistor is a type of resistor whose resistance varies with temperature, but it provides only qualitative information that is not well correlated with breathing amplitude. Therefore, a relative reduction in amplitude (e.g. >50%) of this signal cannot be used to reliably indicate the presence or absence of a hypopnea. The signals from the thermal sensors have been shown to be non-linearly related to actual airflow, while generally resulting in an overestimation of ventilation. Nasal prong pressure measurements are becoming increasingly popular for quantifying respiratory events during sleep. Detection of fluctuation in nasal pressure during inspiration and expiration reflects changes in inspiratory and

expiratory airflow. Studies have shown that nasal pressure is much more sensitive than thermal sensors for detecting hypopneas and much more comfortable for the patient than pneumotachometers. Other methods to record airflow during sleep include: Dual channel respiratory inductance plethysmography (RIP, the sum of chest and abdominal signals), single channel RIP, piezo sensors, strain gauges, thoracic impedance and expired carbon dioxide.

With regards to the measurement of respiratory effort, esophageal pressure remains the reference standard. It discriminates between obstructive and central hypopneas, and is the gold standard for the diagnosis of upper airway resistance syndrome. Nonetheless, it is a relatively invasive technique which is not always well tolerated during a full-night polysomnography. Detection of flow limitation by nasal pressure monitoring is possible, since the shape of a continuous recording of inspiratory and expiratory pressure can detect flow limitations with either a full face mask or a nasal pressure cannula. However, if only nasal pressure cannulae are used, the technique may lack sensitivity if the patient employs predominantly mouth breathing. Other techniques have been developed to record respiratory effort, such as supraglottic pressure and diaphragmatic surface EMG, but there are no data on accuracy, reliability, or correlation with long term outcome in relation to these techniques.

In many of these technique improvements, in particular in recent years, the effort of commercial companies to improve the performances of polysomnographers, and to develop user-friendly and less expensive systems is obvious. In many cases, market forces dictate which techniques survive and which do not.

2.4 Polysomnography Today

With the advent of the laboratory computer capable of signal processing, it is possible to acquire, manipulate and store multiple physiologic data during sleep. Today, computerized recording and storage systems have all but replaced the paper-based analog polysomnograph recordings. This has solved the storage problems related to the production of massive quantities of paper, and has allowed the possibility of recording multiple channels. From a data processing standpoint, five basic and distinct processes can be defined [36]:

1. data acquisition (recording)
2. data display (viewing)
3. data manipulation (scoring and editing)
4. data reduction (parameterization for reporting)
5. data filing (storage)

Computerized data acquisition and storage permits monitoring numerous functions during a polysomnography, typically including: EEG, EOG, mental-submental EMG, muscle activity (typically, tibialis anterior EMG, to detect leg movements),

electrocardiogram (ECG), airflow, respiratory effort, sound (to record snoring), peripheral pulse oximetry, body position and continuous video recording.

Typically, the sleep laboratory is located in the hospital, and for the standard test, the patient comes in the early evening, and over the next 1–2 h is introduced to the setting, whilst electrodes and other monitoring devices are applied so that the multiple channels of data can be recorded when he/she falls asleep. A sleep technician should always be in attendance and is responsible for attaching the electrodes to the patient and monitoring the patient during the study. During the study, the technician observes sleep activity by watching the video monitor and the computer screen that displays all the data. In most labs, the test is completed and the patient is discharged home by 7 a.m. unless a MSLT or a MWT is to be done during the day to test for excessive daytime sleepiness. After the test is completed, a 'scorer' analyzes the data by reviewing the study in 30 s 'epochs'. Ways to automate sleep scoring have been described, but they cannot replace the visual scoring [36]. Once scored, the test recording and the scoring data are sent to the sleep medicine physician for interpretation. The American Academy of Sleep Medicine has published practice parameters for polysomnography, regarding the indications in the diagnosis of sleep disorders [28].

In addition to full-night polysomnography, daytime nap studies and split-night studies have been developed to reduce costs, and can provide substantial information. Typically, during a split-night recording the first part of the night is devoted to determine the presence and evaluate the severity of a sleep breathing disorder. During the second part of the night, a CPAP titration study is performed to determine the correct amount of pressure, the right mask size, and also to make sure the patient is tolerant to this therapy.

Portable systems have also been developed to record at home a wide range of parameters, similar to those used in laboratories. The diagnostic value of portable devices is reduced by the inability to make behavioral observations, standardize recording conditions, address technical problems, or make interventions during the night.

2.5 Summary

This brief historical review chronicles the parallel evolution of sleep research and polysomnography. The rate of progress has been incredible from the first EEG recordings to computerized multichannel polysomnographs. From the 1930s through the 1950s, scientists worked to reveal the properties of normal sleep. Concomitantly, the technology of recording sleep evolved. By the end of the 1950s, experimenters were performing full-night recordings of sleep. Beginning in the 1960s and going forward, sleep researchers began to apply new technology to study sleep pathology. The field of clinical sleep medicine began to develop beside a growing discipline of sleep research. The 1980s and 1990s saw the expansion of

sleep medicine and the acceptance of polysomnography as an important diagnostic tool. The rapid advancement of sleep research and the growing clinical knowledge of sleep disorders led to an increasing demand for polysomnographies, and centers devoted to the diagnosis and treatment of disorders of sleep have multiplied in recent years. The swift development of polysomnographs was possible thanks to the development of computer polysomnographs. Computerized polysomnography involves recording, analyzing, displaying, scoring, tabulating, distilling, and storing sleep studies. The greatest challenge for the future will likely be the cost-effective expansion of sleep medicine, so that its benefits could be profitable to the entire population. The technology must provide us with better and comprehensive systems to respond to this demand, and provide solutions to the sleep problems faced by individuals and society.

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Chapter 3
Screening Instruments of Sleep Disorders: Actigraphy

Peng-Chih Wang

Abstract Wrist actigraphy is based on the premise that little movement occurs during sleep, but that activity increases when awake. Wrist actigraphy has the advantages of being cost efficient and allowing the recording of sleep in the natural environment. In addition, it can record continuous behavior for 24 h a day, 7 days a week. Although actigraphy is not a replacement for electroencephalography or polysomnography, there are times when it provides clear advantages for data collection.

Actigraphy is particularly useful for studying individuals who cannot tolerate sleeping in a laboratory, for example small children and older adults. It may provide a more accurate estimate of typical sleep duration by providing an opportunity for patients to adhere more closely to their habitual sleep environments. Actigraphy is also becoming an important tool in follow-up studies, and for examining efficacy in clinical outcomes. It has some value in the assessment of sleep disorders, although it may not help in distinguishing between different sleep disorders.

Newer scoring algorithms have great accuracy in determining the variables that are most important in insomnia – that is, they have improved ability to detect wake versus sleep, sleep latency, awakenings during the night, and total sleep time. Actigraphy is superior to a subject's self-reported sleep logs, particularly in detecting brief arousals during the night. It can also be used for the evaluation and clinical diagnosis of circadian rhythm disorders. The ability to detect movement holds promise for the identification of sleep disorders characterized by frequent movements, such as periodic limb movements during sleep, sleep apnea, or rapid eye movement sleep behavior disorders.

Traditionally, the actigraphs are placed on the non-dominant hand, and the data collected is displayed on a computer and examined for activity/inactivity and analyzed for wake/sleep cycles. This chapter will review the development of

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actigraphy, the major areas where it can be used, tips for its successful use, and its limitations.

Keywords Actigraphy • Actiwatch • Ambulatory activity monitors

3.1 Introduction

Actigraphy, a method for estimating sleep-wake schedules by measuring activity, has been used by researchers to study sleep disturbances in a variety of populations, most frequently for the evaluation of insomnia, circadian sleep/wake disturbance and periodic limb movement disorders [7, 47]. The actigraph can collect data continuously for a prolonged period before it is downloaded onto a computer where an algorithm calculates specified sleep parameters.

The device is electrode-free and can be worn continuously 24 h a day, and for longer than 1 week. It is more sensitive than sleep diaries for documenting sleep fragmentation, and can also be used for people who cannot fill out sleep logs, such as infants and adults who cannot read or write. The actigraph is less expensive, noninvasive, and more conducive to repeated measurements in comparison to polysomnography (PSG). Moreover, studies using actigraphy avoid the "first-night effect" on the quality of sleep [40].

There are variables used in actigraphy data analysis included the following: (1) total sleep time (TST); (2) sleep efficiency (the percentage of time in bed spent sleeping, SE); (3) wake time after sleep onset (minutes awake after in-bed sleep onset where sleep onset is defined as completion of 10 continuous minutes of sleep after getting into bed, WASO); and (4) and number of nocturnal awakenings.

There is no consistency in scoring and a wide variability in the information published in studies involving actigraphy. Procedures used for sampling, data processing and analysis are not consistently reported in the literature. The most recent study of this issue is in sleep and circadian rhythms [28]. However, the scope of these parameters is limited, leaving researchers to independently make many decisions regarding procedures. Advancing the quality of information in published results will enable comparison across studies that use actigraphy, and will enhance the testing of interventions to improve activity and sleep rhythms. Therefore, one purpose of this paper is to review the literature on actigraphy in studies using adult patients, to illustrate methodological challenges related to procedures and reporting, and to make recommendations regarding instrumentation, selection of pertinent variables, sampling, and data processing and analysis.

In terms of validity issues, it is important to note that actigraphy is not a unitary methodology. Multiple vendors offer a range of actigraphs with different operating characteristics. The present variability in actigraph hardware probably exceeds the variability of contemporary polygraphs. Actigraphy vendors provide a variety of sleep-scoring software; some score sleep in a single pass, whereas others use rescoring rules. It is important to note that current data constitutes

lower-bound estimates to the degree that these differences augment error variance. This variability may be reduced through standardization, thereby reducing the discrepancies between actigraphy and PSG below current levels. Some sleep-scoring software is better validated against PSG than others.

This chapter reviews three major areas in which actigraphy is used for the measurement of sleep or sleep rhythms. The first area covers the more recent papers on the technology and validity of actigraphy in insomnia. Sadeh et al. concluded that validation studies for normal subjects showed greater than 90% agreement and were very promising [38]. Actigraphy combined with analysis software using different algorithms to process data has been commercially available since the 1990s. Actigraphs differ in how they detect and record movements (e.g. two dimensions vs. three dimensions), and use different methodologies to calculate activity levels.

The second area of review looks at methodological suggestions for using actigraphy in research. From reviewing the current literature, we have found some inconsistencies in the use of the actiwatch in research. Berger and colleagues have tried to address this issue by providing standard formations for future research [5].

The third area of review is examining actigraphy studies in populations with sleep disorders. Actigraphy is being used more often in sleep disorder studies, either as an alternative to PSG, in addition to monitoring, or as a follow-up device.

3.2 History and Background

Actigraphy uses an accelerometer to quantify body movement. Over the last three decades, ambulatory activity monitors (actigraphs) have been improved so that they are precisely calibrated and can store thousands of activity measurements acquired at predetermined times, by use of software-selected amplifier and filter settings (one such monitor is the Motionlogger actigraph, made by Ambulatory Monitoring, Ardsley, New York). The size of these actigraphs has been reduced so that the smallest unit (Mini-Motionlogger) is only slightly larger than a man's wristwatch. A device called the Actillume (also distributed by Ambulatory Monitoring) has also been developed, that uses a linear accelerometer to measure the vigor of movement and provides a second channel for assessing light exposure or temperature.

Advances in computer and video-processing technology have also led to the development of motion-analysis systems that can precisely track and record the two- or three-dimensional position of an object several times per second. For example, the Research Tri-axial accelerometer (R3T; Stayhealthy Inc., Monrovia, CA) is a three dimensional accelerometer. This device was built using the original TriTrac-R3D technology. It is small ($71 \times 56 \times 28$ mm), lightweight (62.5 g), and can store data for up to 21 days [34]. It uses piezoelectric accelerometers that measures motion in three orthogonal dimensions and provides triaxial vector data in activity units [8]. One study compared the equivalence (equivalence test) and agreement (Bland and Altman method) of physical activity output data during walking and running on a

treadmill and on land [50]. The equivalence test showed that output data from the treadmill versus on land were equivalent.

3.3 Advantages and Disadvantages

Although the technology for actigraphy has certainly advanced for many applications, there remains a number of advantages and disadvantages which can be listed as follows:

Advantages	Disadvantages
Recordings done in patient's natural environment.	Behavior during recordings not documented.
Easy to record for long durations.	Home recording conditions difficult to control.
Little or no adaptation effect.	Fewer channels of information available.
Less technician time required per study.	Motion artifacts mistakenly identified as wakefulness.
Fewer recording rooms needed.	Lack of standard procedure.
Lower cost.	

The procedure measures sleep in the normal home environment, which overcomes a significant clinical issue. Parasomnias that decrease in frequency when studied in the laboratory will require fewer studies to record an episode for diagnosis. From a technical perspective, the advantages can also be considerable, since this method requires fewer sleep technicians and recording room facilities.

The disadvantages are mainly technical. The number of channels is very restricted, so that a smaller number of variables can be recorded at one time. Another issue that has been repeatedly raised is the lack of standard equipment, procedures and analytic methods in the application of actigraphy which preclude comparisons and conclusions across studies [37].

3.4 Methodological Issues When Using Actigraphy in Research

Actigraphy has become a valuable research and clinical instrument to evaluate sleep, daytime activity and circadian activity rhythms in healthy individuals as well as persons with primary and comorbid insomnia. However, the procedures used for sampling, data processing and analysis are not consistently reported in the literature. The wide variability in how actigraphy is reported makes it difficult to compare findings across studies. Berger and colleagues reviewed 21 studies that used actigraphs to assess sleep and wakefulness in adult patients with cancer to highlight the differences in reporting strategies [5]. They suggested the following to overcome challenges when using actigraphy:

3.4.1 Instrumentation

A. Resources for purchasing actigraphs and interface units: all actigraphs used in a study, particularly in repeated measure designs, should be the same type, and ideally the same model.
B. Model of actigraphy (to increase validity for estimating total sleep time, consider use of event markers and /or light sensor): reports should provide the registered trademark name of the device and model and the name and location of the manufacturer.
C. Placement of the actigraph: actigraph was placed on the dominant or non-dominant arm or leg.
D. Standardized instructions should be given to participants for wearing the actigraph and completing the daily diary.

3.4.2 Selection of Pertinent Variables

A. Include the following five key sleep variables: time in bed (in minutes), total sleep time after sleep onset (in minutes), number of awakenings, minutes awake (WASO-M), and percent awake after sleep onset (WASO-P)
B. Provide clear definitions of selected variables.

3.4.3 Sampling

A. Data collection environment: Record the location, number of days, with/without sleep partner etc.
B. Duration of data collection period: at least 72 h of data collection and one-minute sampling epochs in adults are recommended [28].
C. Selection of days of the week for monitoring needs to be considered. Since weekdays and weekend activities are different, keeping the days of the week consistent or randomized at each time interval is recommended whenever feasible [5, 6].
D. Keep sleep diary for identifying analysis periods or times when the actigraph has been taken off. Habitual sleep-wake scheduling, substance exposure, daytime napping and other demographic data are collected along with sleep diary since these factors might influence the validity of actigraphic sleep measures.
E. The epoch length is important when studying sleep patterns over time: epoch lengths of up to 1 min provide sufficient data for analysis of sleep with activity counts over three to five nights [28].
F. The mode of data collection for each type of monitoring device should be considered. Examples include zero-crossing mode (ZCM; a way of counting

movements, and the primary mode of data collection for sleep estimation), time above threshold (TAT; an estimate of movement duration that is more indicative of the vigor of activity and used primarily in daytime monitoring of activity), proportional integrating measure (PIM; an estimate of movement intensity most useful for daytime activity levels and patterns), or TRI mode (ZCM/TAT/PIM).

3.4.4 Data Processing and Analysis

A. Plan for and report the name and version of the software used to analyze the data, and the algorithm used for scoring.
B. Automated scoring should not be used.
C. Make data editing rules and decisions.
D. Plan for staff training.
E. Set a minimum level of inter-rater reliability and confirm it periodically.

Many challenging issues related to procedures and reports using actigraphy have been described. Reporting salient sleep, activity, and circadian rhythm variables, whenever appropriate, will allow for comparisons among reports. Details about software programs used to generate results can lead to guidelines that will assist in comparing results from different devices.

The body of knowledge regarding objective measurement of sleep, activity, and circadian rhythms will grow when researchers plan studies that address the methodological challenges related to procedures and reporting results. Understanding relationships between subjective sleep measures and objective actigraphy measures of sleep, activity, and circadian rhythms is essential to enhance our understanding of the physical and mental health outcomes in various populations of children and adults with sleep disturbances.

3.5 Validation and Assessment of Insomnia

In the last three decades, actigraphy and PSG measures of sleep have been strongly correlated in regular sleepers and in sleepers with apnea, with the correlation coefficients ranging from .89 to .98 [9, 11, 19, 26, 30, 36]. Actigraphy can identify sleep patterns characteristic of sleep apnea and periodic leg movements, and has been used in many intervention studies in the past. However, recent publications have raised new concerns about the validity of sleep-wake scoring algorithms in certain populations or specific devices [43]. One of the most important arguments is that most of the studies listed above relied on inappropriate statistical methods, specifically correlations and comparison of means [18]. Insana and colleagues suggest using the Bland-Altman Concordance technique to measure these outcomes.

Insomnia, on the other hand, has been predominantly neglected in validation studies of actigraphy. Individual differences in movement patterns, especially among patients with insomnia, blocks the use of actigraphy. The biggest critique has been that actigraphy scores subjects who are simply still as asleep. Until 2006, only five studies had tested the ability of actigraphy to accurately score the sleep of adult populations with insomnia. The first two studies compared actigraphy and PSG on total sleep time (TST). Hauri and Wisbey stated that the mean error when comparing wrist actigraphy with PSG in insomnia was 49 min; in addition, in two of their participants (6% of cases), the error was larger than 2 h [16]. This margin of error is clearly not acceptable for most clinical research studies. Jean-Louis et al. re-analyzed these finding using the same data, but using different software. The result reduced the average difference to 25 min [21].

There have been two other studies conducted on the accuracy of actigraphy in terms of TST. Kushida et al. [25] found that TST and sleep efficiency (SE) were overestimated by actigraphy in the order of 1.0–1.8 h for TST, and 12.1–29.1%, for SE. This discrepancy was larger than the discordance of subjective estimation (TST: 0.3 h; SE: 2.5%). Vallieres and Morin [51] stated that actigraphy was more accurate than sleep diaries, and recommended its use as a complement to the latter. However, there are some limitations to the above four validation studies of actigraphy with insomnia: all had small a sample size of insomnia patients, only one of them evaluated actigraphic measures of WASO, and only one evaluated actigraphy measures of sleep-onset latency (SOL). Furthermore, none of these studies evaluated sex or age as possible confounding factors. One important study in this area was conducted by Lichstein [27]. Results of this study demonstrated successful validation of actigraphy on four measures of sleep pattern: number of awakenings, WASO, TST, and SE percentage. Validation was based on non-significant mean differences and significant correlation between actigraphy and PSG. SOL with actigraphy was not significantly different from PSG, but was weakly correlated with PSG.

Another recent study reassessed the validity of actigraphy in assessing insomnia by comparing 31 insomnia patients to 31 controls using actigraphy and PSG monitoring in their homes [39]. The authors concluded that actigraphy is a valid tool for assessing sleep in insomnia patients and normal controls studied in their home environment. They also reported that actigraphy was sensitive to variations in subjective perception of sleep quality.

Natale and colleagues stated that the lack of quantitative criteria for identifying insomnia using actigraphy represents an unresolved limit for the use of actigraphy in a clinical setting. Therefore, they conducted a study to evaluate the most efficient actigraphic parameter in the assessment of insomnia and to suggest preliminary quantitative actigraphic criteria (QAC; [31]). The results showed that all sleep parameters recorded by actigraphy significantly differentiated between the insomnia group and the normal sleeper group, except time in bed. Natale et al. also developed criteria called linear discriminate function (LDF), whose function was to identify and combine the most useful actigraphy sleep parameters to separate insomnia patients from normal sleepers. From this research, an LDF analysis showed that

the most useful combination of actigraphic sleep parameters to assess insomnia was TST, SOL, and number of awakenings longer than 5 min (NA > 5), which obtained the best receiver operator characteristic (ROC) and the best balance between positive and negative predictive values compared to any single actigraphy parameter [31]. Further work on this topic is needed to examine results from different types of insomnia using larger clinical samples, such as those per formed in multicenter studies. We also suggest using a larger cohort to evaluate age effect on QAC, and identify which QAC are stable over a lifetime [32]. Additional studies should also compare QAC among different actigraphy models.

From the studies described above, it can be concluded that actigraphy provides sleep assessment with acceptable sensitivity to detect differences between sleep-disturbed and control groups. These findings suggest that actigraphy can provide useful data in the assessment of insomnia. However, we should note that the large discrepancies between the subjective data of insomnia patients and the objective data from researchers or clinicians should not automatically be attributed to inaccurate self-reporting in patients.

3.6 Clinical Research in Different Populations

3.6.1 Actigraphy Studies of Healthy Adults

Several studies involving normal individuals have used actigraphy as a measure of sleep/wake or circadian rhythms. For example, Tworoger et al. studied factors associated with actigraphic and subjective sleep quality in young women [49]. Their results showed that going to bed late, medication use, employment, increased daylight hours, longer menstrual cycle length, and higher body mass index (BMI) were associated with poorer actigraphic sleep measures. Employment, age, and perceived stress were associated with subjective sleep quality. In a study of the effects on sleep from caffeinated beverages in healthy subjects, Hindmarch [17] stated a dose-dependent negative effect (of tea/or caffeine) on TST as estimated by actigraphy [17]. In another study, researchers examined the effects of coffee consumption on the rate of melatonin secretion, as reflected by urinary excretion of 6-sulphoxymelatonin (6-SMT), and sleep quality as assessed by actigraphy [41]. The results showed that drinking regular caffeinated coffee, compared to decaffeinated coffee, caused a decrease in the total amount of sleep time and the quality of sleep, and an increase in the length of time of sleep induction. Caffeinated coffee caused a decrease in 6-SMT excretion throughout the following night. Apparently, actigraphic sleep measures offer objective sleep parameters which also reflect effects from sleep-preventing factors.

In terms of gender difference in healthy adults, Jean-Louis et al. [20] stated that women in their study slept more than men, as reported in other studies. In addition, they had better sleep quality than men as demonstrated by higher sleep

efficiency, shorter sleep latency, and lower frequency of sleep/wake transitions. Another study by Jean-Louis et al. [22], analyzed actigraphy data in a large sample (n = 273) of community-dwelling residents, and the results showed significant gender differences in sleep variables estimated by wrist actigraphy.

The influence of a bed partner was reviewed in two related studies by Pankhurst and Horne [33]. Both involved the use of wrist actimetry and morning sleep logs in subjects aged 23–67 years. In the first study, 46 pairs of bed partners were monitored for 8 nights to assess the extent and concordance of their body movements, and whether the latter exhibited age and gender differences [33]. The researchers stated that participants sleeping with bed partners had a greater number of movements than subjects who slept alone, and movements decreased during the temporary absence of the usual bed partner. Reyner et al. [35] reported that sleep period time was markedly longer for women, and that most reported awakenings were < 5 min. Women reported more awakenings, more total time spent awake during the night and poorer sleep quality; all these findings were most evident in older women, who also took longer to fall asleep than any other group [35].

3.6.2 Actigraphy Studies of Children

Actigraphy has been increasingly used in children, particularly in studies involving children with behavioral or psychiatric conditions. Cortese [10] performed a meta-analysis of subjective (i.e., based on questionnaires) and objective (i.e., using PSG or actigraphy) studies comparing sleep in children with attention-deficit/hyperactivity disorder (ADHD) versus controls [10]. The authors reviewed 16 studies, providing 9 subjective and 15 objective parameters, and including a total pooled sample of 722 children with ADHD versus 638 controls. The results showed that the objective parameters – sleep onset latency (on actigraphy), the number of stage shifts/hour sleep, and the apnea-hypopnea index – were significantly higher in children with ADHD compared to controls. Children with ADHD also had significantly lower true sleep time on actigraphy [10]. These results lay the groundwork for future evidence-based guidelines on the management of sleep disturbances in children with ADHD.

Actigraphy has been used in several studies to provide a more quantitative measure of sleep disruption among traumatized children. Sadeh [36] reported that those who were physically abused had decreased sleep efficiency compared with non-abused inpatients or sexually abused children. They hypothesized that for sexually abused children, the structured and supervised sleep environment of the inpatient setting was actually perceived as safer, given that many had experienced sexual abuse in sleep-related contexts in their communities (e.g., in their bedrooms, or during the night), and they were able to sleep more soundly in this setting [36]. Glod [14] also used actigraphy to compare 15 volunteers, 19 abused children and 10 non-abused children with depression. Abused children were more active than either the non-abused children or children with depression, and were twice as active

as the non-abused children. Abused children took three times longer to fall asleep and had poorer sleep efficiency compared with non-abused children, and also had longer sleep latencies than depressed children. There were no differences in total sleep time or number of nocturnal awakenings. They also found that physically abused children had more impaired sleep efficiency than those who were sexually abused. The physically abused children also trended toward having greater sleep onset latency and increased levels of nocturnal activity [13].

Finally, some studies assessed the validity of actigraphic sleep wake scoring in infants and very young children [15, 42, 43]. For example, So and colleges found that actigraphy was a valid method for monitoring sleep in infants who are younger than 6 months [43]. However, some of these studies reported problems of low sensitivity for actigraphic sleep measures in children's sleep study. In general, validity data which are derived from devices or scoring algorithms developed for adults should not be generalized to children. As for applying actigraphy in children's sleep studies, additional age-specific validation studies are mandatory [18, 29].

3.6.3 Actigraphy in Studies of Older Adults

Actigraphy is particularly useful in studies of older adult populations, both in the community and in the nursing homes. Spira [45] investigated the association between elevated symptoms of anxiety and indices of objectively measured sleep quality in a large sample of older community-dwelling women, before and after adjustment for potential confounding factors. The results showed that elevated anxiety symptoms were associated with poor sleep efficiency and greater time spent awake after sleep onset, after accounting for numerous potential confounding factors and significant depressive symptoms [45]. This result is consistent with observations from studies of younger populations. Elevated levels of anxiety have been linked to worse actigraphic sleep in children and younger adults undergoing surgery, and in premenopausal women [4, 23, 24, 45].

Fetiveit and Bjorvatn investigated the possible effect of bright-light treatment on daytime sleep and waking among nursing home dementia residents [12]. The results showed that actigraphic measurements of average nap duration and total nap duration during the day period were both significantly reduced with bright-light treatment. No significant changes were found in sleep/wake measurements (actigraphy and nursing staff) between pretreatment and baseline recordings taken 8 months before the main experiment. Alessi et al. used wrist actigraphy estimations of sleep as an outcome variable in a controlled clinical trial of physical activity in nursing home residents [2]. The results showed no significant improvement in sleep associated with improved physical function. Alessi also conducted another study which found no significant differences in nighttime sleep variables between subjects taking psychotropic medications and subjects not on these medications in a nursing home setting [1].

Generally speaking, actigraphy is increasingly being used in clinical research involving individuals of various ages, who are of normal health or with a variety of health conditions, and in a number of different settings. In the majority of these studies, actigraphy is used to measure sleep and activity rhythms that might not otherwise be available using traditional (e.g. PSG) techniques.

There is growing literature regarding the use of actigraphy with children. For example, actigraphy has been used to demonstrate differences in the sleep of abused children and those with depression or non-abused children. Actigraphy has also been used to test treatment effects of melatonin therapy in children with severe neurological disorders [14].

Finally, actigraphy has been used extensively in studies involving the elderly, particularly in the nursing home setting. These studies have demonstrated significant sleep disruption among nursing home residents, and sleep and circadian rhythm disturbances have been shown to be more severe among residents with severe dementia.

Taken as a whole, these clinical studies demonstrate increasing use of actigraphy in a variety of populations, conditions and settings. However, the majority of these studies do not report adequate details of the technical aspects of the specific actigraphic devices used. However, it seems clear from these trials that the use of actigraphy enables studies involving multiple days and nights of testing, and allows populations that might otherwise not be studied, such as patients with dementia or young children, to participate in research studies and clinical trials of sleep/wake activity and circadian rhythms.

3.6.4 Current Trends in Actigraphy Research Studies

Recently, new products have been introduced into the market. For example, SOMNOmedics of Germany released a new product called the SOMNOwatch The SOMNOwatch is available with several add-on sensors, allowing it to be used along with the actigraphy apparatus, as a PLM/RLS recorder, respiratory screener, sleep recorder, movement analyzer, long term ECG and EEG recorder. Additional fields of application include monitoring training, sport and rehabilitation, and even the detection of sleep walking. In addition, the same company also provides another multiple channel system (add-on) called SOMNOwatch PLUS. The SOMNOwatch plus respiratory option, for example, includes built-in sensors to monitor variables such as activity, body position, ambient light, as well as a patient marker with additional parameters, such as CPAP/BiPAP pressure, pulse rate and abdominal effort [44].

Recently, researchers have begun to measure three-dimensional activities (e.g. fall risk). In 2008, Stone and colleagues studied actigraphy measured sleep characteristics and risk of falls in older women [46]. This study was the first to examine the relationship between objective estimates of sleep duration and fragmentation

and subsequent risk of recurrent falls. Results shows short nighttime sleep duration and increased sleep fragmentation are associated with increased risk of falls in older women, independent of benzodiazepine use and other risk factors for falls [46]. The limitation of this study is the cross-sectional study design, and that ultimately falls remain unpredictable and there is no way to anticipate or alert caregivers or health professionals in advance. Hopefully newer technology can utilize three-direction acceleration and could transmit signals to cell phones or servers, which may help reduce the burden on caregivers and improve patient well-being.

3.7 Limitations

Comparisons of actigraphy and PSG have found the former technique to be valid and reliable in normal, healthy adult populations [3]. Actigraphy is best for estimating total sleep time. However, as sleep became more fragmented, the actigraph becomes less accurate in the detection of sleep and wakefulness. Newer studies agree with previous research (e.g. [52]) in suggesting that actigraphy may overestimate sleep and thus underestimate wakefulness, particularly during the day when an individual is more likely to sit quietly while awake. In an effort to reduce this error, early investigators developed secondary algorithms that rescore sleep epochs as wake if adjacent to many wake epochs. Besides, although actigraphy has been utilized to evaluate sleep measures of primary sleep disorders, e.g. disordered-breathing sleep, periodic limb movement disorders, we should realize that actigraphy is only used to provide sleep parameters in patients with established diagnoses not to make diagnoses.

Some research suggests that actigraphy consistently overestimates total sleep time and number of awakenings during the night when compared to subjective report measures (e.g. sleep logs); however interpreting this phenomenon is very difficult. First of all, PSG and self-reported sleep logs are not highly correlated, therefore it is possible that the actigraphy data is in fact more accurate than the sleep log estimation. It is difficult to determine which measure is more reliable, but according to Ancoli-Israel et al.'s 2003 review, many studies (especially in insomnia) use subjective measures as the final outcome variables, since researchers believe that the patient's subjective reports are more important than objective data. This statement seems to suggest that neither PSG nor actigraphy is needed for sleep examination – but it is important to remember that actigraphy has the ability to collect data over a period of several days and nights. It is seems reasonable to suggest that both methods (subjective and objective) can be used to collect participant's sleep information. When there is agreement between the two methods, confidence is increased in the results of both. When there is disagreement, it may reveal problems with one or the other. Clinicians can use this information and conduct cognitive behavioral therapy to try to improve the patient's sleep behavior and therefore improve their sleep

quality. For example, one study conducted by Tu and colleagues [48], found in their research that some Chinese dementia caregivers returned their actiwatch and said:

> I bet I had poor sleep over these days, and the watch can speak for me!

However, when the participant's actigraphy data were analyzed, Tu et al. were surprised to find that their sleep effiency was almost 92%. By comparing their score to their Pittsburgh Sleep Quality Index score and sleep log, it was ascertained that these participants spent lots of time falling asleep and therefore felt their sleep was poor. Clinicians can use this objective information to open a discussion with the patient to teach them coping skills and change their sleep behavior to improve their quality of life.

3.8 Summary

In summary, although actigraphy is not as accurate as PSG for determining some sleep measurements, there is general agreement that actigraphy, with its ability to record continuously for long time periods, is more reliable than self-reported sleep logs which rely on the patients' recall of how many times they woke up or how long they slept during the night. In addition, actigraphy is more reliable than observations which only capture short time periods, and can provide information obtainable in no other practical way. It can also have a role in the medical care of patients with sleep disorders.

In conclusion, the latest research suggests that in the clinical setting, actigraphy is reliable for evaluating sleep patterns in patients with insomnia, for studying the effect of treatments designed to improve sleep, in the diagnosis of circadian rhythm disorders (including shift work), and in evaluating sleep in individuals who are less likely to tolerate PSG, such as children and the demented elderly. In addition, when using actigraphy in clinical research, it is recommended that investigators refer to suggestions in the article of Berger et al. [5], which systematically reviews the pros and cons of using actigraphy, and makes concrete suggestions for implementing actigraphy in research reports including, the choice of instrument, selection of pertinent variables, sampling, and data processing and analysis. The body of knowledge regarding objective measurements of sleep, activity, and circadian rhythms will grow when researchers plan studies that address the methodological challenges related to procedures and reporting results. This applies to research with healthy individuals and persons with primary and comorbid insomnia, such as those with cancer. Understanding relationships between subjective sleep measures and objective actigraphy measures of sleep, activity, and circadian rhythms is essential to enhance our understanding of the physical and mental health outcomes in various populations of children and adults with sleep disturbances. Those issues are now being addressed, and actigraphy may now be reaching the maturity needed for application in the clinical arena.

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Part III
Management of Sleep Disorders: Point of Views from Sleep Technology

Chapter 4
Management of Sleep Disorders: CPAP (Continuous Positive Airway Pressure)

Kannan Ramar

Abstract Continuous positive airway pressure (CPAP) is a positive airway pressure (PAP) device that is commonly used to treat sleep disordered breathing (SDB) such as obstructive sleep apnea (OSA). CPAP helps to correct SDB by acting as a passive pneumatic splint for the upper airway and increasing lung volume to exert pharyngeal caudal traction, thereby stiffening the upper airway and reducing collapsibility. Despite its well-known benefits in treating SDB, overall adherence with CPAP is low, predominantly due to its side effects. Side effects are related to the pressure from CPAP (such as rhinitis and mouth dryness), the use of mask interfaces (such as claustrophobia and skin breakdown), and the machine (such as the noise and condensation). Recent advances in technology have led to the development of pressure relief mechanisms (such as C-flex® and EPR®) and auto-adjusting (APAP) machines. Pressure relief mechanisms help by reducing pressure during early exhalation, while APAP might help by reducing the mean optimal pressure required to treat SDB, thereby reducing pressure related side effects. Despite technological advances and efficacy of these devices to control SDB compared to the fixed pressure with CPAP, studies have not conclusively shown improvement in adherence.

Keywords Obstructive sleep apnea (OSA) • Continuous positive airway pressure (CPAP) • Pressure relief mechanisms • Auto-adjusting positive airway pressure (APAP)

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4.1 Introduction

Continuous positive airway pressure (CPAP) is a positive airway pressure (PAP) device that is used to treat sleep disordered breathing (SDB). Obstructive sleep apnea (OSA) is the most common SDB for which CPAP is used. OSA is a common disorder with increasing prevalence that is characterized by sleep fragmentation due to repeated arousals and disruption of normal sleep related to partial or complete airway closure during sleep. The resultant consequences of oxyhemoglobin desaturation and surges of catecholamine release are associated with excessive daytime sleepiness, an increased risk for motor vehicle accidents, impaired daytime functioning, neurocognitive decline and cardiovascular consequences such as hypertension, cerebrovascular accidents, and coronary artery disease.

Understanding upper airway physiology and how it relates to SDB, particularly in OSA, will help us to appreciate the workings of CPAP, its clinical use and benefits, side effects and other alternatives that might help to improve CPAP adherence.

4.2 Upper Airway Physiology

4.2.1 Upper Airway Anatomy

The upper airway extends from the nares to the larynx and serves several functions including respiration, phonation and swallowing. The upper airway is usually divided into four anatomical subsegments; the nasopharynx – extending between the nares and hard palate, the velopharynx or retropalatal oropharynx – extending between the hard palate and soft palate, the oropharynx- extending between the soft palate and epiglottis, and the hypopharynx – extending between the base of the tongue and the larynx. The upper airway is highly adapted for vocalization and deglutition in humans by serving not as a simple rigid tube, but as a semi-rigid conduit, that may be prone to collapse. This collapsible portion of the upper airway extends between the hard palate and larynx (between the retropalatal oropharynx and the hypopharynx). There are at least 26 paired muscles and 5 different cranial nerves that serve to maintain upper airway patency. Intactness of these neuromuscular circuits is of paramount importance to maintain upper airway patency, even in healthy subjects, as there is a decrease in overall upper airway muscle tone during sleep.

4.2.2 Negative Pressure Upper Airway Reflex

There are different neuromuscular circuits to maintain upper airway patency, with one such being the negative pressure upper airway reflex [1]. During inhalation,

the upper airway is subjected to negative pressure generated by respiratory muscle activity. This pressure change is sensed by the mechanoreceptors and other sensory receptors located in the upper airway that send afferents to the nucleus tractus solitarius (NTS). Efferents from the NTS arrive through the hypoglossal nerve to supply the upper airway pharyngeal dilator muscles, including the genioglossus, and therefore maintain patency of the upper airway [2]. Injury or lesion to any part of this reflex may predispose to upper airway collapse.

4.2.3 Anatomical Factors

There are various factors that contribute to upper airway patency and which may promote upper airway collapse. Abnormalities in upper airway mechanics involving both anatomical and neural factors may contribute to pharyngeal collapse during sleep [3].

Anatomical factors to consider include skeletal and soft tissue structures of the upper airway that may narrow the lumen. A narrow upper airway is more likely to collapse than a wider one. Imaging studies have confirmed that the cross-sectional area of the upper airway is reduced in OSA patients compared to those without OSA [4–6]. Important skeletal structures include the mandible, hard palate of the maxilla, and the position of the hyoid bone. Confined within these skeletal structures are soft tissues of the pharynx that include the lateral pharyngeal wall, adenotonsillar tissue, tongue, uvula, and para-pharyngeal fat pads. Either excess soft tissue in the pharynx and/or a small bony cage due to the skeletal structures can narrow the upper airway lumen. Imaging studies suggest that the lateral pharyngeal wall is the most significant risk factor of these for OSA [6].

4.2.4 Neural Factors

Neural factors that play an important role in maintaining upper airway patency include the pharyngeal muscle dilator activity, respiratory control of breathing, and the neurotransmitters.

4.2.4.1 Pharyngeal Dilator Muscles Activity

Among the pharyngeal dilator muscles of the upper airway, the genioglossus muscle is the largest and the most studied pharyngeal dilator muscle. There is an increase in pharyngeal dilator muscle activity during wakefulness in OSA patients to compensate for the narrow upper airway [7]. However, during sleep, OSA patients experience a greater reduction in activity of these muscles in an already compromised upper airway, allowing for upper airway collapse [8]. Though, there

is a reduction in activity of pharyngeal dilator muscle activity in normal subjects without OSA, the lack of anatomic vulnerability may prevent the development of OSA. As the reduction in muscle tone occurs during the transition from wakefulness to sleep [9], SDB events occur during this stage.

Pharyngeal dilator muscles are influenced by inputs from the central respiratory center located in the medulla, vagal input from changes in lung volume, mechanoreceptors located in the pharyngeal mucosa [10], and sleep/wake state of the brain. There is evidence that lesions involving any of these pathways may contribute to upper airway collapse.

4.2.4.2 Neurological Lesions of the Upper Airway

Neurological lesions involving the sensory and motor components of the upper airway have been described in OSA patients [11]. Contractile dysfunction of the pharyngeal dilator muscles (due to inflammation), presence of histological evidence of motor neuron lesions, and actual damage to the palatopharyngeal muscles, all confirm the presence of neurological lesions affecting the motor pathway [12, 13]. Marked reduction in vascular reactivity, loss of sensitivity, significant impairment in the two-point discrimination test, and impaired vibratory sensation of the pharyngeal mucosa are some of the neurological lesions documented in OSA patients that affect the afferent pathway [14–16]. Whether these neurological lesions are a consequence of OSA or a pathogenic mechanism for the development of OSA is unknown. In addition, it is unknown whether CPAP use may ameliorate these neurological lesions, or prevent the development of these lesions if CPAP is instituted at an early stage, such as in snorers or upper airway resistance syndrome (UARS), before the development of OSA.

4.2.4.3 Ventilatory Control Stability

The degree of respiratory control instability can be described and quantified by using an engineering concept called loop gain (LG) [17]. It is a term used to describe the stability of a system controlled by feedback loops; in our case, the stability of the respiratory system in response to perturbations such as apneas and arousals.

The concept of LG in OSA patients has been studied using the proportional assist ventilation (PAV) technique [18]. LG is measured as a ratio of corrective response to a disturbance, in our case an apnea, with the response being the arousal. If the response is over exuberant, the LG is >1, and it results in an unstable respiratory system with periodic breathing. This is certainly true in central sleep apnea (an apnea that is not associated with respiratory effort), but its role in the pathogenesis of OSA is currently being studied. LG appears to be abnormally elevated in patients with OSA [19, 20], but whether this is a consequence of OSA or a pathogenic mechanism for OSA is still debated. Arousals can increase LG, and

though traditionally thought to rescue the OSA patient by opening the upper airway, it may also cause OSA through increasing LG, destabilizing respiratory control, and promoting upper airway collapse, especially during the terminal phase of the hyperpnea, when the ventilatory output to the upper airway muscles is the lowest. The high loop gain also decreases the partial pressure of carbon dioxide (PaCO2) below the apneic threshold during subsequent sleep. This can predispose to apnea, either central or obstructive, depending on the upper airway mechanics.

4.2.4.4 Neurotransmitters

Norepinephrine and serotonin are excitatory to the hypoglossal nerve, which innervates the pharyngeal dilator muscles. Hypothetically, one might increase the activity of the pharyngeal dilator muscles by increasing the levels of neurotransmitters (such as serotonin) at the neuromuscular junction. Drugs that enhance the levels of serotonin such as fluoxetine, protriptyline, and paroxetine, increase the activity of pharyngeal dilator muscles, but unfortunately do not substantially improve OSA. Further work and research is needed in this area.

4.2.5 Lung Volume

Lung volume may be a significant contributor to the pathogenesis of OSA. Upper airway mechanics are altered by changes in lung volume in healthy subjects during wakefulness and during sleep [21, 22]. During wakefulness, there appears to be lung volume dependence on the upper airway cross sectional area, with the effect being more pronounced in OSA than in healthy subjects. During sleep, there is a decrease in functional residual capacity (FRC) and an increase in upper airway resistance [23, 24]. Increasing lung volume during sleep decreases upper airway collapsibility in healthy subjects and improves SDB events in OSA patients. Though the exact mechanism is not known in adults, in animal models, lung inflation increases upper airway caliber and stiffness by caudal traction on the trachea independent of upper airway muscle activity (tracheal tug mechanism) [25, 26].

4.2.6 Critical Closing Pressure (Pcrit)

The pressure at which upper airway closure just begins is called the critical closing pressure (Pcrit), and is a measure of upper airway collapsibility. In healthy subjects without SDB, negative pressure must be exerted to cause airway closure (a negative Pcrit). On the contrary, a positive or elevated Pcrit is seen in OSA [27]. Elevated Pcrit in patients with OSA occurs from a synergistic combination of obesity,

craniofacial anomalies and pharyngeal collapsibility. Although patients with OSA may have an elevated Pcrit, their airways remain open during wakefulness, probably due to increased activity of the pharyngeal dilator muscle, as discussed above. Thus, it is clear that both anatomic and neural factors are necessary for the development of OSA. The precise contributions of the two factors on pharyngeal collapsibility are still debated [3].

4.3 Continuous Positive Airway Pressure (CPAP)

CPAP delivers constant pressure during both inhalation and exhalation. The next few sections will discuss the mechanisms behind how CPAP works, indications for use, titration by overnight polysomnogram (PSG) to determine the optimal fixed pressure, and side effects related to CPAP. A general overview for this chapter, unfortunately, cannot provide in-depth coverage of the large amount of literature that has been published, especially on the efficacy of CPAP in treating OSA. The focus of this chapter will be predominantly on the adult population and OSA, and not central sleep apnea or restrictive lung diseases. The goal is to highlight some important concepts and recent developments in technology that may be relevant for a sleep clinician.

4.3.1 Mechanism

CPAP, by delivering a predetermined constant pressure to the upper airway, serves as a passive pneumatic splint to keep the upper airway from narrowing or collapsing during sleep [28, 29]. CPAP compensates for the abnormally positive Pcrit in OSA subjects, regardless of the cause for the elevated Pcrit, i.e. obesity, neuromuscular problems, or craniofacial abnormalities. During CPAP application, upper airway muscle tone either decreases or remains the same [30], thereby providing proof that CPAP serves as a passive splint to the upper airway. CPAP also increases upper airway size, with imaging studies showing increases in upper airway cross sectional area and volume [31]. The largest changes in OSA patients were noticed in lateral dimensions rather than in the antero-posterior (AP) dimensions with CPAP use [31]. This is in agreement with the pathophysiology of OSA, where cross-sectional imaging studies in OSA patients have shown narrowing of the lateral dimensions of the upper airway, rather than AP dimensions [6, 32].

CPAP also increases lung volume and thereby exerts caudal traction on the pharynx (tracheal tug mechanism). This increases pharyngeal stiffness and prevents pharyngeal collapsibility. CPAP is the most successful way of compensating for an elevated Pcrit in OSA patients.

4.3.2 Benefits of CPAP in OSA

It is beyond the scope of this chapter to discuss all available literature with regards to the benefits of CPAP in the treatment of OSA and other sleep disorders. Some of the benefits of treating OSA with CPAP are summarized in the next few paragraphs.

4.3.2.1 Daytime Sleepiness

Randomized controlled trials (RCT) comparing CPAP to placebo or to sham CPAP have shown improvement in subjective daytime sleepiness as assessed by the Epworth sleepiness scale score (ESS), health related quality measures, and objective daytime sleepiness as measured by the multiple sleep latency test (MSLT) and the maintenance of wakefulness test (MWT) [33–35]. Patient's use of CPAP has also been shown to result in improvements in quality of life and sleeptime of the bed partner [36, 37].

4.3.2.2 Cardiovascular Disorders

(a) Hypertension
CPAP has been shown to acutely attenuate sympathetic drive and nocturnal blood pressure in patients with OSA [38–40]. However, data regarding effects on daytime blood pressure have been more difficult to interpret. A recent meta-analysis of 12 RCTs of blood pressure reduction with CPAP treatment in OSA (both normotensive and hypertensive) showed a net significant reduction in mean blood pressure of 1.5–2 mmHg [41]. The results also suggest a greater antihypertensive effect in those with hypertension and daytime sleepiness at baseline. Another recent well designed and adequately powered trial confirmed the findings of the meta-analyses by demonstrating a reduction in mean blood pressure by about 2 mmHg when moderate to severe OSA patients were treated with CPAP in otherwise untreated hypertensive patients [42]. It is also imperative to emphasize the importance of dose-related benefits of CPAP therapy, with increasing nightly use resulting in a significant mean net change in systolic blood pressure [43].

(b) Congestive heart failure
Two controlled, short-term interventional trials of CPAP for OSA in the setting of heart failure have been performed, both yielding positive results [44, 45]. Kaneko and colleagues [44] reported an approximately 9% increase in left ventricular ejection fraction (LVEF) and significant reductions in blood pressure after just 1 month of CPAP therapy. Mansfield et al. [45], studying a group of subjects with somewhat less severe degrees of both heart failure and OSA than the subjects of Kaneko et al. [44], applied CPAP therapy for 3 months and showed significant improvements in LVEF and reductions in urinary catecholamines, but no changes in blood pressure.

(c) Pulmonary artery pressure
Studies have shown that CPAP reduces both nocturnal and daytime pulmonary arterial pressures [46, 47].

(d) Arrhythmias
Retrospective analysis shows that within 12 months of successful therapeutic electrical cardioversion for atrial fibrillation, untreated sleep apneics were found to have an arrhythmia recurrence rate double that of patients treated with CPAP [48]. CPAP treatment also reduced the frequency of ventricular premature beats in patients with OSA [49]. Some studies also suggest that CPAP may improve bradyarrhythmias such as sinus pauses and A-V block [50, 51].

4.3.2.3 Motor Vehicle Accidents

OSA patients who were untreated had an accident rate 3 times higher than the control group without OSA [52]. Once OSA patients were treated with CPAP, the rate approached close to that of the controls [52]. Another study by Findley and colleagues also showed a reduction in accident rate with the use of CPAP in OSA patients [53].

4.3.3 CPAP Titration

4.3.3.1 Indications for CPAP

The most common indication for the use of CPAP is in the treatment of OSA. Most patients with OSA can be effectively treated with CPAP. The center for Medicare and Medicaid services (CMS) in USA covers the cost of a CPAP device for an apnea-hypopnea index (AHI) $\geq$ 15/h, or for an AHI $\geq$ 5/h with symptoms of either daytime sleepiness, insomnia, impaired cognition, mood disorders, or comorbid conditions such as hypertension, cerebrovascular accidents, or ischemic heart disease. The American Academy of Sleep Medicine (AASM) has also published practice parameters on the indications for CPAP in the treatment of SDB [54].

Central sleep apnea (CSA) patients may also be effectively treated with CPAP. According to the ICSD-2nd edition (2005), CSA syndromes encompass primary CSA, CSA due to Cheyne Stokes breathing pattern, CSA due to high-altitude periodic breathing, and CSA due to drug or substance use such as opioids. Several case-control, randomized crossover, and randomized controlled trials have shown the effectiveness of CPAP in treating CSA (particularly CSA due to Cheyne Stokes breathing and primary CSA) as measured by the AHI, and improvement in the left ventricular ejection fraction and daytime alertness as measured by the ESS [55–58]. CPAP may not be effective in treating CSA due to opioid use [59]. The titration protocol explained below is for CPAP in the treatment of OSA and CSA.

Some patients with sleep related hypoventilation may benefit from CPAP, though most require bilevel positive airway pressure (BPAP). The common causes for sleep related hypoventilation include chronic obstructive pulmonary disease (COPD) and obesity (obesity hypoventilation syndrome). CPAP may work in certain situations probably by increasing lung volume sufficiently enough to maintain minute ventilation during sleep to tide over the hypoventilation. Lack of sufficient data prevents us from determining the type of positive airway pressure device i.e. CPAP vs. BPAP, to use in such situations. There is some data to suggest that a subset of OSA patients, who have comorbid obesity and daytime hypercapnia, prefer BPAP over CPAP in the treatment of OSA [60, 61]. In spite of a lack of sufficient evidence, most clinicians consider BPAP for OSA treatment even in patients without comorbid respiratory disorders, particularly when they are uncomfortable or unable to tolerate CPAP due to the high pressure requirement, or have persistent OSA on CPAP even at a pressure of 20 cm H_2O [62].

4.3.3.2 Titration

The goal with CPAP titration is to identify the optimal pressure. Optimal pressure is the effective pressure that eliminates SDB events (apneas, hypopneas, respiratory effort related arousals, oxygen desaturation, and snoring) without creating any untoward pressure related side effects for the patient. This optimal pressure should be adequate during all stages of sleep and sleep positions (particularly the supine position).

Manual titration of CPAP in a laboratory-based overnight PSG to obtain optimal pressure to treat OSA is well described in recent guidelines published by the AASM [62]. At the initiation of CPAP titration, pressure is normally started at 5 cm H_2O. Occassionally, in some patients who are intolerant even at 5 cm H_2O, CPAP is started at 4 cm H_2O, which is the minimum recommended starting pressure [62]. Some patients may experience insufficient pressure at the start of titration, even when starting at 5 cm H_2O. In such cases, pressure can be increased until the patient is comfortable, and once the patient falls asleep, pressure is then reduced in decrements of 1 cm H_2O at intervals of 5 min until SDB returns or the patient awakens. Pressure should then be increased again to the optimal level to eliminate SDB events. If the patient tolerates the initial pressure before sleep onset, further titration is not performed until the patient falls asleep.

CPAP is then increased incremently by 1 cm H_2O at intervals of no less than 5 min until all SDB events are eliminated [62]. Increments in CPAP are done in the presence of at least two obstructive apneas, or at least three hypopneas, or at least five Respiratory Effort-Related Arousals (RERAs), or at least 3 min of loud or unambiguous snoring [62]. The recommended maximum pressure to titrate CPAP is 20 cm H_2O [62], at which time if there are still SDB events, BPAP titration will need to be considered. Adding supplemental oxygen (O2) for sleep related hypoxemia and/or hypoventilation may also need to be considered.

If the SDB events are not controlled with CPAP due to patient complaints of increased pressure side effects (even at CPAP of less than 20 cm H_2O), then adding a humidifier for nasal congestion, or instituting a pressure relief mechanism at end expiration such as with C-flex or Expiratory Pressure Relief (EPR) should be considered [63–65] (discussed below). If there are persistent SDB events, one may need to proceed with BPAP. Ideally, the optimal pressure is attained in both the supine position and during REM sleep for at least 15 min if possible [62]. If this is not attainable, ideally a repeat titration study should be considered. Some prescribers might advocate an autoadjusting or autotitrating PAP (APAP) in such situations (explained below). Usually, a follow-up is required on APAP to ascertain that the sleep disordered breathing is well controlled.

The titration is usually started with a nasal interface. If the patient exhibits open mouth breathing, either a chin strap or a full face mask should be considered. Some may advocate use of oxymetazoline nasal spray to help with nasal congestion to prevent open mouth breathing. If the spray works, long term use can be accomplished with the use of nasal steroid spray. The same CPAP titration protocol as explained above may be used for CSA.

4.3.3.3 Treatment Emergent Central Sleep Apnea

Some patients may have central apneas that become apparent after CPAP alleviates OSA during CPAP titration. The underlying mechanism for treatment emergent CSA- complex sleep apnea is not yet clear. However, treatment with adaptive servo-ventilation (ASV) that serves to stabilize the upper airway obstruction and addresses the respiratory center dysfunction by providing calculated ventilatory assistance to minimize hypo and hyperventilation, may provide some clues to the underlying pathophysiology. The exact prevalence of this phenomenon is unknown. The term, complex sleep apnea, and its treatment are debatable [66, 67] and is beyond the scope of this review to discuss it in further detail. Suffice to say that these central apneas that appear after OSA treatment with CPAP may contribute to repeated oxyhemoglobin desaturation along with sleep fragmentation. There is no established protocol to address treatment emergent CSA and the treatment options and protocols discussed below are the authors own proposed guidelines until future research can guide us.

As mentioned earlier, one option is to proceed directly to ASV to address treatment emergent CSA after CPAP treatment to treat OSA. This approach may lead to the use of an expensive device without proven long term benefits. The other approach is downward titration by decreasing CPAP by 1–2 cm H_2O and monitoring for 5–10 min. If centrals persist, or OSA recurs at a lower pressure, then it would be advisable to proceed with one of the other approaches discussed. The third approach is to do an upward titration with CPAP, not beyond 5 cm H_2O above the pressure that eliminated the OSA. This upward titration may help in certain cases, especially those where the central apneas may have been misclassified as OSA. If centrals worsen with such upward titration, the pressure should be

brought down to the previous level that alleviated OSA. There is data to suggest that central apneas may dissipate over time with CPAP use [68]. Therefore, some providers may treat these patients with CPAP for a 2–3 month period, before repeating another titration study. If central apneas persist on CPAP on the repeat titration study, then it is recommended to proceed with other treatment modalities such as ASV. The approach that is decided upon may vary based on the sleep center provider's preference based on his/her experience and understanding of this syndrome, patient's preference, attitude, underlying comorbidities, and cost issues. Further research in this area may guide us in the near future.

4.3.4 Problems with CPAP

CPAP is by far the most commonly recommended therapy for OSA. In spite of the overall clinical benefits, CPAP has significant side effects that may affect overall adherence. Early studies suggested that more than 50% of OSA patients developed side effects that persisted even with continued CPAP use [69, 70]. Though the estimated acceptance of CPAP (defined as the patient's willingness to undergo a CPAP titration study and take the device home to use it for at least a week [71]) is reasonable (around 72–91%) [72], CPAP adherence (compliance), defined as >4 h of use on at least 70% of the nights, is only around 40% or less [73]. CPAP adherence is important as it correlates with patient related outcome measures [74, 75]. Most problems related to CPAP use occur during the first few weeks of treatment, which may be the reason for discontinued use [69, 76]. Frequent visits to the healthcare provider and nurses along with intensive educational programs to address side effects improved adherence to more than 70% at a 6 month follow-up visit, despite persistence of side effects [77, 78]. Therefore, the role of the provider does not end with the prescription of the device; rather it is the beginning of a long term relationship and follow-up with patients, as with any chronic medical disorder. If patients perceives the side effects of CPAP use as less bothersome, it is less likely to affect adherence even if side effects persist [69, 79].

The most commonly reported side effects of CPAP are listed in Table 4.1. Nasal congestion and rhinorrhea are the most common nasopharyngeal symptoms related to CPAP use. Epistaxis can be a secondary symptom of nasopharyngeal symptoms. Presence of nasal congestion can also lead to mouth breathing and therefore mouth dryness. Airway dryness used to be the most common complaint prior to the advent of humidification systems [79, 80]. Heated humidification use with CPAP may help with these symptoms and improve adherence [81, 82]. Heated humidification delivers a greater level of moisture than cool humidification. The level of humidity can be adjusted by the patient. Some patients might also benefit from a steroid nasal spray and/or saline nasal spray to address nasal congestion/rhinorrhea and nasal dryness respectively. Use of a chin strap or an oronasal mask interface may help patients who continue to have mouth breathing in spite of the above interventions.

Nasal interface problems such as mask leaks and skin breakdown have been noted in a significant number of patients using CPAP [70, 83, 84]. However, the

Table 4.1 CPAP side effects

Machine related symptoms
Noise
Smell
Mask and tubing condensation from humidifier
Maintenance and cleaning
Bed partner intolerance
Interface related symptoms
Skin reaction to mask
Skin breakdown
Air leaks
Eye dryness and conjunctivitis
Sleep disruption
Claustrophobia
Pressure related symptoms
Nasal congestion
Rhinorrhea
Epistaxis
Sneezing
Mouth dryness and mouth breathing
Ear pain and pressure
Aerophagia with abdominal discomfort and bloating
Belching
Sinusitis
Headache
Difficulty exhaling against pressure
Rare side effects such as
Increased intra ocular pressure
Barotrauma
Pneumocephalus
Pneumothorax
General
Anxiety
Insomnia
Discomfort
Chest, face

advent of humidification systems and different types of nasal, oronasal, and oral mask interfaces have helped to improve adherence [81, 82, 85, 86], though further studies serially following patients before and after specific interventions in the same study population are needed.

4.3.5 Auto-Titrating or Auto-Adjusting Positive Airway Pressure (APAP)

As discussed above, the optimal CPAP is in effect a compromise between the minimal effective pressure required to treat SDB events and avoiding excessive

pressure that may result in pressure-related side effects. This optimal pressure may not be a static value and may change from night to night due to changes in upper airway muscle tone and airway resistance. Similarly, sleep stages and sleep position may also affect the optimal pressure requirement during a particular night. The pressure may also vary across nights and over time due to weight changes, development of nasal allergies, nasal congestion, alcohol use, or use of drugs that may decrease upper airway muscle tone. For all these reasons, continuous automated determination and adjustment of the optimal pressure, dictated by the needs of the upper airway mechanics within preset upper and lower pressure limits, may provide efficacy to treat SDB events and decrease pressure related side effects. Such a device, i.e. APAP, was first described by Teschler and colleagues in 1996 [87]. Treatment with APAP would eliminate the need for an overnight CPAP titration PSG to determine optimal pressure. Description and review of APAP is beyond the scope of this chapter, however, it is important to highlight a few points.

The requirements for any APAP are a method to continuously determine resistance characteristics and flow patterns through the upper airway (detector), an algorithm to determine the correct response to the detected condition (response), and a machine with a response time capable of producing the desired response needed to prevent and treat the SDB events (the machine-APAP). There are several such APAP machines that are currently commercially available in the market. Unfortunately, detection methods to determine the upper airway mechanics for each of these APAP devices vary anywhere from measuring apneas, hypopneas and snoring to flow limitation and forced oscillating technique (FOT) to determine upper airway impedance. Similarly, the response algorithms for these different machines vary significantly, the most notable being the rate and extent to which they respond to SDB events [88–90]. In addition, the detector methods and algorithms that determine the response to the detected event are proprietary information and are not readily available.

While APAP machines are advancement in technology to treat SDB, there are a few important caveats. There may be less than optimal control of apnea-related oxyhemoglobin desaturation with APAP compared to CPAP. Furthermore, improved adherence with APAP compared to CPAP has not been clearly established [91], though a larger benefit in compliance was expected in the APAP users. This is in spite of the mean pressure with APAP being lower than the optimal CPAP to treat SDB, by at least 1–2 cm of water. Similarly, Noseda and colleagues found no improvement in treatment efficacy or compliance with APAP compared to CPAP in OSA patients with significant within-night pressure variability (as in supine or REM dependent OSA patients), though the ESS was lower and there was higher preference for the APAP [92].

In addition, presence of air leaks around the mask or mouth breathing simulates SDB events, which may result in APAP titration errors [87]. Most studies on APAP to date have excluded patients with significant comorbidities such as chronic obstructive pulmonary disease (COPD) and congestive heart failure, along with

patients presenting predominantly with central apneas [93]. Most of the available APAP machines respond so idiosyncratically, the prescriber should be familiar with published evidence about a particular device and the patient population that it was tested on before deciding to prescribe it, and before estimating the likelihood of success.

There is evidence that the APAP is as effective as CPAP in lowering the AHI in most OSA patients [94, 95]. Similarly, other recent trials have shown that APAP is equivalent to CPAP in terms of its impact on sleep quality, reduction in subjective and objective daytime measures of sleepiness, and quality of life measures [96–98].

Bench models that are capable of reproducing respiratory sleep disturbances were developed to assess the performance of several types of APAP devices. These models were developed to counteract the contradictory and confusing results on APAP devices that were obtained in clinical trials. However, all these bench model studies confirmed that different APAP devices respond quite differently with different pressure profiles to the same type of abnormal respiratory events [88–90, 99, 100]. In spite of some of the above limitations, it was expected that APAP may provide a cheaper alternative to the current model of in-lab diagnostic PSG followed by CPAP titration. Surprisingly, only a few studies have addressed cost-effectiveness as a primary outcome measure when comparing CPAP with APAP, with no data on long term therapy. Further long term data is needed [101, 102].

4.3.6 Expiratory Pressure Relief Mechanisms

Patients often complain about discomfort exhaling against CPAP [103], which may decrease adherence. While adequate pressure is required at end exhalation to prevent SDB events [104], the same amount of pressure may not be required during early exhalation as the impedance is low during this portion of the respiratory cycle [105]. This creates opportunity for reduction of pressure during early exhalation to improve comfort without compromising the efficacy of CPAP to treat SDB. Such technology is called ‘pressure relief’ and so far 3 different devices have become available; C-flex® (Respironics, Murrysville, PA, USA), Expiratory Pressure Relief (EPR®, ResMed Inc, Poway, CA, USA) and SoftPAP® (Weinmann, Hamburg, Germany). C-flex® has three comfort settings, with the magnitude of reduction in pressure during early exhalation depending on a proprietary algorithm based on expiratory flow rate [66]. This generally ranges between 1 and 3 mbar. The efficacy is equivalent in treating SDB between fixed CPAP and C-flex [106]. EPR® also has three comfort settings that correspond to a drop in pressure by 1, 2, and 3 cm H_2O during early exhalation. The working of SoftPAP® is not known. Some patients do however report increased machine noise with pressure relief mechanisms. Whether the use of pressure relief devices improve adherence and comfort over longer time periods is not well established.

4.4 Summary

CPAP is well established as the treatment of choice for OSA, with its mechanism of action addressing the pathogenesis of OSA. The efficacy of CPAP in treating OSA is well recognized, with studies demonstrating improvements in excessive daytime sleepiness, cardiovascular and neurocognitive outcomes. In spite of its well-known benefits in treating SDB, the use of CPAP is plagued by side effects that lead to an overall decrease in adherence. There are also important limitations with CPAP use; one such being the need to perform PSG titration studies to determine the optimal pressure that eliminates SDB with minimal pressure-related side effects. Advances in technology and development of novel devices such as APAP and flow contour devices such as pressure relief mechanisms are steps in the right direction in trying to improve adherence and comfort without compromising the effectiveness to eliminate SDB. Importantly, research studies are urgently needed to address this ever widening gap between technological advances with development of newer devices and peer reviewed published literature to assess the effectiveness and improvement in adherence with such treatment modalities [107].

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Chapter 5
Management of Sleep Disorders – Sleep Technology on Surgical Concepts and Instruments

Sung Wan Kim and Michal Alexius Sarte

Abstract We can always rely on sleep technology for continual update and improvement in the way we evaluate and manage sleep disorders, most especially in the realm of the sleep related breathing disorder that is obstructive sleep apnea. In this day and age of evidence-based medicine however, sleep technology should guide us in our quest of continuously providing the best care that we can give to our patients. Evaluation of the upper airway, although initially elusive, is now better understood as a result of sleep technology. This in turn will coach the sleep surgeon in designing a type of upper airway surgery, the precise location/s of which may predict a better treatment success.

Keywords Airway evaluation • Sleep surgery • Surgical instrument

5.1 Upper Airway Evaluation of Obstructive Sleep Apnea Patients

5.1.1 Introduction

Various methods have been used to identify sites of obstruction in obstructive sleep apnea (OSA) patients. All these techniques are subject to methodological limitations, such as invasiveness of the procedure with concomitant sleep disruption in

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optical and manometric evaluation during polysomnographic study, and limitations of recording time and alterations to sleep as a consequence of being induced by drugs during dynamic sleep endoscopic and radiologic procedures.

Early investigations confined the site of obstruction in OSA patients to one particular location, whereas more recent studies have demonstrated multiple sites of obstruction, seesawing patterns of obstructions, and even propagation of obstruction sites in the same individual. Technologic advances in the methods used to detect the sites of obstruction in OSA patients have demonstrated that the upper airway is more dynamic than originally thought. The variability of these obstruction sites involves a complex underlying pathogenesis of upper airway obstruction which is affected by many factors, including neck anatomy, adipose tissue distribution, anesthetics, sleep stage, and a variety of other components which are still unknown. As a result, varying types of obstructions within the same individual consequently leads to difficulty in evaluating obstruction sites. However, trials for evaluating obstruction sites are still very important for determining the most appropriate type of surgery and the indications of each surgery.

Therefore, future work to identify obstruction sites is needed to consider the complex interaction of the numerous factors determining airway obstruction, in a search to find better indications resulting in better success rates of surgery.

5.1.2 Physical Examination

Physical staging is one of the most important methods to identify the obstruction site. However, it is difficult to make a staging system for physical examination which is able to represent the obstruction site.

The nasal cavity and external nose should be evaluated since the nasal airway is an integral part of breathing. All abnormal findings which can cause nasal obstruction, such as nasal valvular problems, hypertrophy of turbinates, septal problems, sinusitis and polyps and tumorous conditions, should be investigated and described.

Fujita reported the types of upper airway according to obstruction sites [13]. However, this method is very subjective and resulted in a huge bias in the evaluation of the airway. Recently, Friedman et al. reported a simple and logical staging of sleep apnea according to anatomical factors such as tonsil size and palate position, and body mass index (BMI). According to the results of uvulopalatopharyngoplasty (UPPP), stage I may represent retropalatal obstruction and stages II and III may represent multilevel or retroglossal obstruction [7]. An interexaminer agreement study supported this use of tongue positioning and found that most OSA patients fall into the intermediate stage where UPPP outcomes are less predictable [11].

Friedman Tongue Position (FTP) is based on visualization of structures in the mouth when the mouth is opened widely without protrusion of the tongue. FTP I allows the observer to visualize the entire uvula and tonsils or pillars. FTP IIa allows

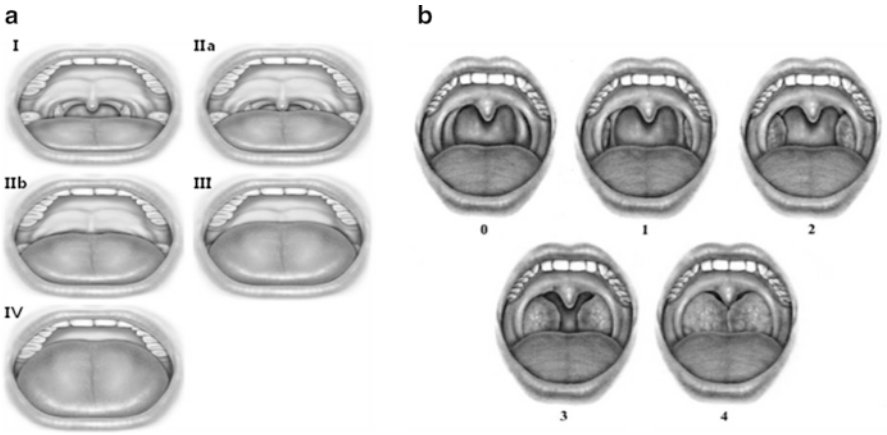

Fig. 5.1 Physical parameters of Friedman staging. (**a**) Friedman tongue position. (**b**) Friedman tonsil grade (Adapted from *Laryngoscope* [7], and *Otolaryngol Head Neck Surg* [11], with permission)

visualization of the uvula, but only parts of the tonsils are seen. FTP IIb allows visualization of the complete soft palate down to the base of the uvula, but the uvula and the tonsils are not seen. FTP III allows visualization of some of the soft palate, but the distal soft palate is eclipsed. FTP IV allows visualization of the hard palate only. Tonsil size is graded from 0 to 4: tonsil size 0 denotes surgically removed tonsils, tonsil size 1 implies tonsils hidden within the pillars, tonsil size 2 implies the tonsils extending to the pillars, tonsil size 3 tonsils are beyond the pillars but not to the midline and tonsil size 4 implies tonsils extend to the midline (Fig. 5.1). Body mass index is another parameter in which the cut-off value is BMI > 40. According to Friedman staging, stage 1 is a combination of FTP I and II, and tonsil size 3 and 4. Stage II is a combination of FTP I and II, and tonsil size 1 and 2, or FTP III and IV, and tonsil size 3 and 4. Stage 3 is a combination of FTP III or IV and tonsil size 0, 1, and 2. Any FTP and tonsil size with BMI > 40 and/or significant craniofacial or other anatomic deformities are included in stage 4.

5.1.3 Endoscopic Examination

Endoscopy represents one of the earliest techniques used to detect the sites of obstruction in OSA patients and involves using a nasopharyngoscope. It allows for the direct visualization of the interior of the upper airway (UA) and can be performed during wake and sleep states. It has been shown that the parameters/indices obtained in the supine position have better predictive values for OSA than those obtained in

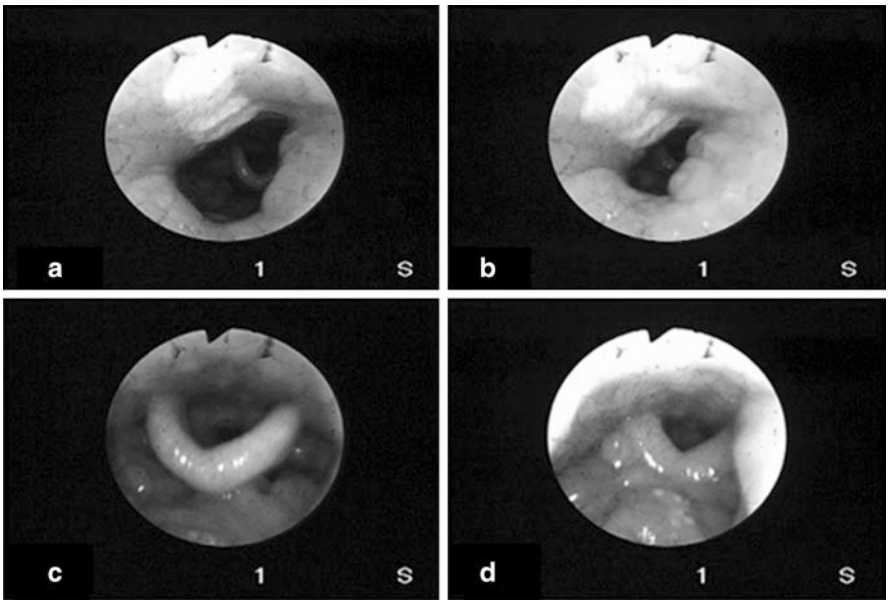

Fig. 5.2 Endoscopic findings in an awake OSA patient. (**a**. **c**) Are findings of a narrow airway in the retropalatal and retroglossal areas during the end-expiratory state. (**b**, **d**) Are findings during Mueller's maneuver at the same level of (**a**) and (**c**)

the erect position. Nowadays, outcome measures have been updated from subjective scales to the digitalized measurement of the airway by using video monitoring combined with CT imaging [18].

When performed whilst the patient is awake, it is useful to investigate the airway shape and to find possible obstruction sites during Mueller's maneuver, which describes a maximal inspiratory effort against a closed mouth and occluded nose. Inevitably, this examination during wakefulness may not reflect the true obstruction site during sleep.

Nasopharyngoscopy is usually performed with the patients in the supine position after topical nasal anesthesia has been administered. A flexible nasopharyngoscope is inserted through the nasal cavity to the hypopharynx. First, measurements are taken at end-expiration. The severity of the obstruction may be described using a scale of 1–4. Second, measurements can be taken during a maximal inspiratory effort against a closed mouth and occluded nose, so-called Mueller's maneuver (MM). During the examination, airway size can be assessed separately in both the retropalatal (upper pharynx) and retroglossal (tongue base) segment. Collapse during MM is rated using the following classification: 1+, 0–25%; 2+, 26–50%; 3+, 51–75%; and 4+, >76% (Fig. 5.2). This technique may be useful for postoperative evaluation after sleep surgery (Fig. 5.3).

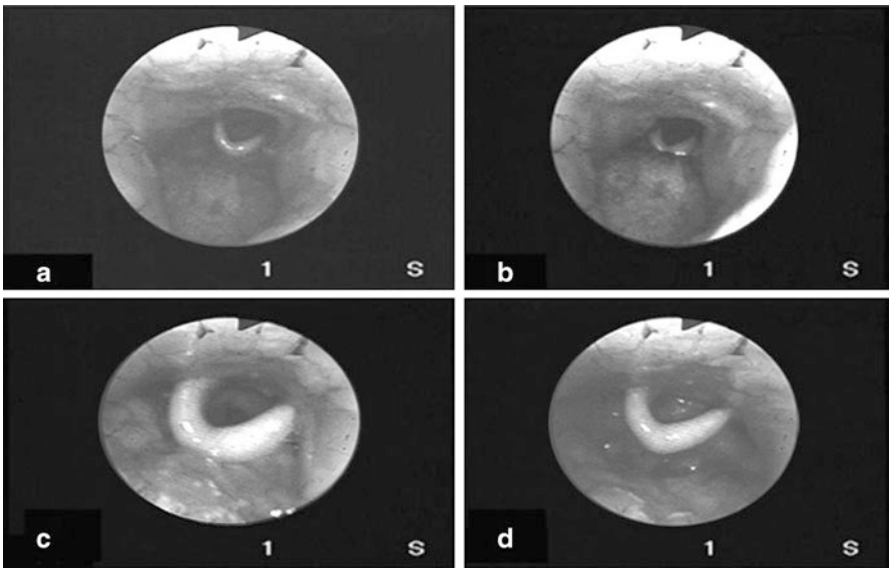

Fig. 5.3 Endoscopic findings during wakefulness for the same patient in Fig. 5.2, but post-operatively. All figures are at the same level. The airway was widened by multilevel surgery using uvulopalatopharyngoplasty and mandibular osteotomy with genioglossus advancement (Discussion of these surgeries can be found in Sect. 5.2)

It is well documented that endoscopic examination during sleep is a more precise technique for identifying the true obstruction site than those performed whilst the patient is awake. This technique can be performed during drug-induced sleep and can be combined with polysomnography as demonstrated by Rojewski et al. [36]. In this study, patients were placed in a supine position on the operating table with dimmed lights. Oximetry and cardiac rhythms were monitored throughout the procedure, and supplemental oxygen was administered by blow-by facemask or nasal cannula as necessary. The intravenous infusion of propofol (1.5 mg/kg) or midazolam (0.05 mg/kg) was used as the sole agent to achieve drug- induced sleep. With the onset of drug-induced sleep, the flexible fiberoptic laryngoscope was passed through the anesthetized nasal cavity to perform the examination.

Even when performing endoscopic examinations during sleep, there are a number of possible limitations, such as the stenting open of the airway by the endoscope, as well as an increase in upper airway resistance and a decrease in airflow caused by the endoscope. The need to move the endoscope for better upper airway visualization during sleep may also induce an arousal. In addition, the duration of testing is variable due to the subjects' ability to tolerate the equipment. The use of anesthesia prior to endoscopy has also been implicated in altering the characteristics of the upper airway. Finally, drug-induced sleep is not the same as natural sleep with regard to sleep architecture, and possibly with regard to airway reflexes, but it appears to be a reasonable approximation of natural sleep.

5.1.4 Radiologic Examination

5.1.4.1 Cephalometry

Lateral cephalometric radiographs provide an inexpensive method to evaluate skeletal and soft tissue abnormalities contributing to obstruction, and have been the most widely used imaging modality to study patients who have OSA [37].

Patients are seated with their heads oriented in the Frankfort horizontal plane and stabilized with a head holder. Patients are instructed to place their teeth in habitual occlusion, keeping the mouth closed and the tongue relaxed on the floor of the mouth. Exposures must be taken at the end of expiration.

The most commonly used soft tissue cephalometric measurements include tongue size, soft palate length (PNS-P), and posterior airway space (PAS). PAS has been defined as the distance from the base of the tongue to the posterior pharyngeal wall on the line between the supramentale and gonion. The mandibular plane-hyoid distance (MPH) is also measured as the distance between the plane parallel to the inferior mandibular border and the hyoid because the inferior displacement of the hyoid leads to an increased degree of tongue base projection into the hypopharynx, as well as lengthening of the airway, contributing to collapse. The relationship of the cranium to the maxilla and the mandible are assessed by measuring angles between the sella, nasion, and anterior nasal spine (SNA) for the maxilla; and the sella, nasion, and supramentale (SNB) for the mandible (Fig. 5.4).

Limitations of this technique included studying a dynamic three-dimensional object with a static two-dimensional picture. Additionally, lateral cephalometric radiographs are performed whilst the patient is awake and in the upright position, which provides limited characterization of obstruction during sleep.

5.1.4.2 Fluoroscopy

Fluoroscopy is a technique used to observe the internal structure of the upper airway (UA) using x-rays. It has previously been performed using barium contrast ingestion to visualize the airway [43]. However, ingestion of barium is no longer necessary due to the development of imaging machines with high resolution. Fluoroscopy has become increasingly valuable since video monitoring systems were introduced. It provides not only a dynamic view of the UA during sleep, but also allows the visualization of events outside the pharyngeal airway, such as movements of the cervical spine, downward motion of the hyoid bone and jaw movements at the end of an apnea.

During this procedure, patients are placed on a C-arm table in a supine position with their head on a pillow. They are instructed to breathe in and out naturally. Oxygen saturation is monitored throughout the examination. During normal respiration before sedation, a wake event is recorded. Thereafter, sleep is induced by

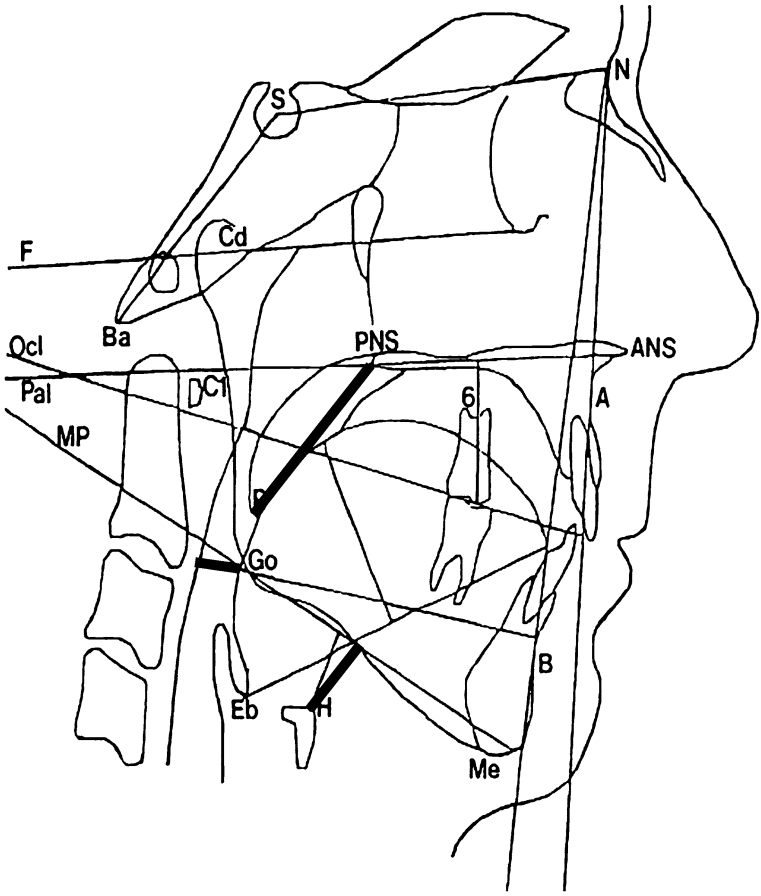

Fig. 5.4 Cephalometric analysis. Soft palate length (*PNS-P*), posterior airway space (*PAS*) and mandibular plane-hyoid distance (*MPH*) are denoted by *thick lines*

intravenous administration with midazolam. After the patient falls asleep, sleep examination commences. Various parameters can be observed during normal sleep, as can sleep events such as snoring and apnea with or without desaturation.

Fluoroscopy has a number of disadvantages. For example, the use of radiation can limit the number of apneas that can be recorded in each patient. Consequently, not all stages of sleep can be examined. UA collapsibility may vary between rapid eye movement (REM) and non-REM (NREM) sleep. Another disadvantage is that lateral fluoroscopy visualizes the UA in only two dimensions, making it difficult to obtain precise measurements of the UA lumen with this technique. Other disadvantages include the use of sedation (e.g., benzodiazepines) to induce sleep which is not natural sleep [16], and the health risks of radiation exposure.

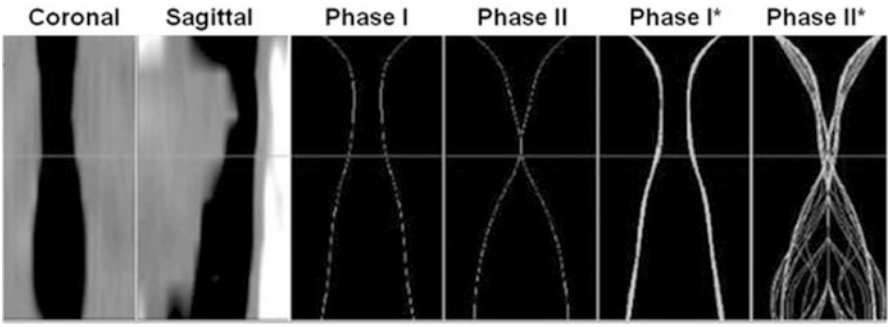

Fig. 5.5 The simulated longitudinal display of the oropharynx showing the results of MDCT in wake and sleep states. *Coronal*: coronal scout view of oropharynx, *Sagittal*: sagittal scout view of oropharynx, *Phase I*: minimal cross-sectional area (*mCSA*) of oropharynx in wake state, *Phase II*: mCSA of oropharynx in sleep state, *Phase I**: dynamic imaging of mCSA according to respiration in wake state, *Phase II**: dynamic imaging of mCSA according to respiration in sleep state. The *horizontal line* represents the uvular level of the oropharynx (Images courtesy of Prof. Jung Soo Kim)

5.1.4.3 Computed Tomography

CT scanning is a noninvasive imaging technique that can provide a quantitative assessment of the upper airway (UA). Initially, many studies evaluating OSA using CT were generally based on static images which compared healthy subjects to patients with OSA. More recently, 3D airway CT was introduced to evaluate dynamic airway obstruction in OSA [4]. Three-dimensional reconstructed CT scans provide an easier way to assess the caliber of the UA than unreconstructed CT scans [1]. Although a CT scan during wakefulness has limited application to finding the obstruction site in OSA patients, it is still useful to visualize and study the airway shape and volume.

The development of dynamic cine-CT, such as multi-detector CT (MDCT) and electron beam tomography (EBT) provide images of changes in the pharyngeal lumen by cross-sectional area during sleep. EBT is a valuable method of dynamic CT but its application is limited by the expense of the accompanying software. On the contrary, MDCT is a widely available dynamic technique. Scanning with MDCT can be carried out in a wake and/or sleep state. First, the neck, designated from the hard palate to epiglottis, is divided into several levels depending on the patient's neck length. Scanning is repeated 25 times at each level with an interval of 0.3 s and a scan time for each image of 0.4 s. Thereafter, midazolam or propofol can be intravenously injected and when the patient begins to snore, scanning begins through the same levels as during the wake state. With the computerized data obtained from MDCT, the maximal (MCSA) and minimal cross sectional area (mCSA) can be measured at each level and the degree of collapsibility of the UA during respiratory events may be calculated using the collapsibility index ($CI = (MCSA - mCSA)/MCSA \times 100$). Changes in the cross sectional area of the UA can be visualized by a digitalized program which draws a simulated diagram of the longitudinal view using the data gathered (Fig. 5.5).

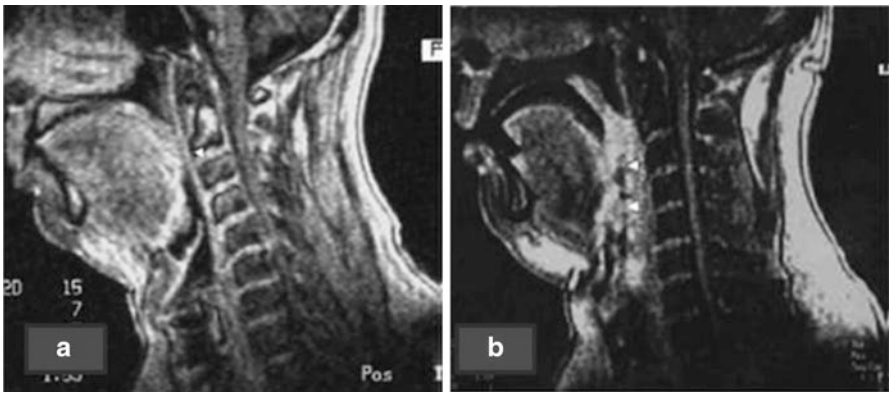

Fig. 5.6 MRI image of airway in OSA patients. (**a**) Single obstruction, (**b**) multiple obstructions (Courtesy of Dr. Hiroto Moriwaki)

The advantages of CT scanning include the ability to scan the entire airway, the ability to combine it with polysomnography and to image adjacent structures, and the noninvasive nature of the technique. The disadvantages of CT scanning may include the use of only axial images, the inability to see the entire pharyngeal airway in a single plane, the short recording time and the risk of radiation exposure.

5.1.4.4 Magnetic Resonance Imaging

MRI provides unparalleled anatomic definition of soft tissue structures and allows for multiplanar imaging at the same time. MRI can now also be used to image the dynamic changes in upper airways of OSA patients. Ultrafast dynamic MRI has further increased the potential for the technique in this field (Fig. 5.6; [31]). MRI has many of the advantages of CT scanning. It is able to provide a better image of the surrounding soft tissue compared to CT without radiation exposure, which is particularly useful for evaluation of the upper airway in children [2]. Difficulties arise concerning patient comfort, concurrent sleep evaluation, scanner noise (requiring possible sedation) and examination expense. These factors have limited the number of studies using MRI to assess sleep. Confounding variables include rate of image acquisition and measurements of wake periods.

5.1.5 Acoustic Reflection

Acoustic reflection is a noninvasive technique for measuring cross sectional area or volume of the airway by reflection of sound waves. A probe generates an audible sound signal that is transmitted through the mouth into the oropharynx and hypopharynx. Areas of impedance alter the amplitude of the signal, allowing for calculation of cross-sectional area.

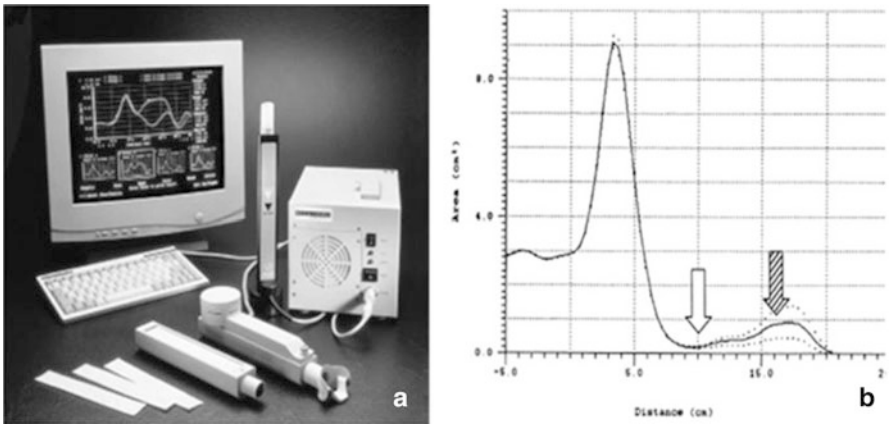

Fig. 5.7 Acoustic reflection. (**a**) Acoustic Pharyngometer. (**b**) Snoring curve showing velopharyngeal junction (*white arrow*) and pharyngeal dome (*shaded arrow*) (Courtesy of Dr. I Kamal)

There are currently major limitations of this acoustic reflection technique; in particular, it can only be performed in awake patients as it measures the cross-sectional area of the oropharynx and hypopharynx [20]. However, it is a very safe and reproducible method to evaluate the airway without radiation and is therefore still a promising method, especially if a probe can be developed to be used during sleep to measure the velo- and nasopharynx (Fig. 5.7).

5.1.6 Manometric Examination

The manometry technique is a valuable method for identifying the obstruction site which uses a catheter with pressure sensors in the UA to measure the pressure at various sites in the airway. The main advantage of pressure manometry is that it can differentiate between retropalatal and retroglossal obstruction during the entire sleep cycle.

Multisensor catheter manometry has been performed concurrently with nocturnal polysomnography over an entire night. The catheter is inserted via a nostril and its position is confirmed by a lateral neck X-ray. The pressure sensors on the catheter must be located at the mid-esophagus (first sensor), the tip of the epiglottis (second sensor), the tip of the uvula (third sensor) and the posterior part of the nasal cavity (fourth sensor; Fig. 5.8). When the subject breathes without airway obstruction, a sinusoidal wave appears at all four sensors (Fig. 5.9a). When retropalatal obstruction develops, a flat wave appears at the fourth sensor and normal sinusoidal waves remain at the other sensors (Fig. 5.9b). On the other hand, when retroglossal obstruction develops, flat waves appear both at the third and fourth sensors and normal sinusoidal waves remain at the other sensors (Fig. 5.9c). Retropalatal and retroglossal obstructive events including both apnea and hypopnea have been

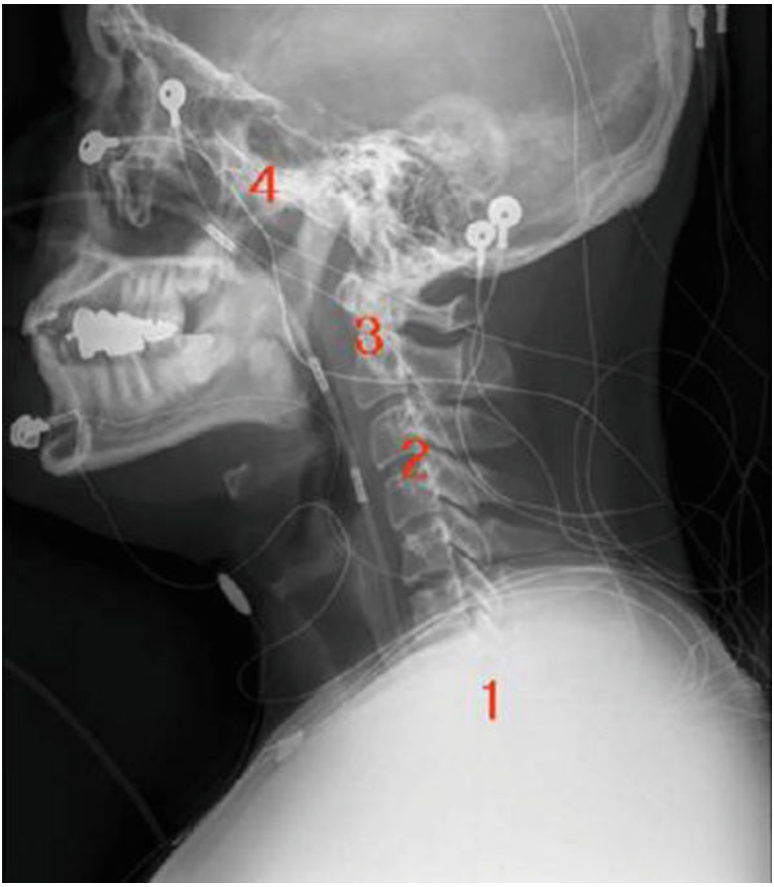

Fig. 5.8 Location of the pressure sensors. *1*: Midesophagus, *2*: the tip of the epiglottis, *3*: the tip of the uvula, *4*: posterior part of the nasal cavity (Courtesy of Prof. Jeong-Whun Kim)

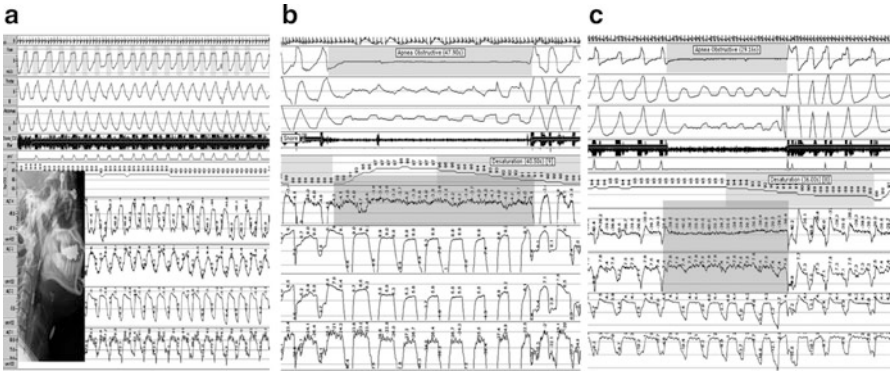

Fig. 5.9 Manometric patterns of upper airway during sleep. (**a**) Normal breathing, (**b**) retropalatal obstruction, (**c**) retroglossal obstruction (Courtesy of Prof. Jeong-Whun Kim)

analyzed using nocturnal polysomnography [23]. The manometry technique seems ideal because it can monitor the entire sleep cycle over the course of a whole night. However, the key limitation of this technique is that retroglossal obstruction measured as tongue base can have concomitant palatal obstruction which cannot be detected using this technique. This examination is also somewhat invasive which may affect the sleep itself. Positioning of the sensors can also be displaced by movements of the patient during sleep.

5.1.7 Anatomic Optical Coherence Tomography

Anatomic optical coherence tomography (aOCT) is a novel, minimally invasive endoscopic technique based on near-infrared light that has been found useful in the quantitative assessment of shape and size of the upper airway (UA).

The technique is adapted from optical coherence tomography (OCT), a medical imaging modality. OCT is an optical sectioning microscopy modality that has been used to image subsurface tissue morphology in fields including ophthalmology, dermatology, vascular medicine, gastroenterology, and urology.

The aOCT technique generates quantitative, real-time images of the UA and allows for imaging of the entire airway in patients in real time during sleep. An optical probe is placed inside a catheter, which is inserted via the nares to the level of the midesophagus. Rotation of the probe within the catheter provides a 360° profile of surrounding tissue. The optical probe can be systematically moved within the catheter, allowing the upper airway to be scanned at multiple sites without stimulating the airway mucosa. As the probe moves along the length of the airway, it creates images based upon changes in phase characteristics of the light reflected back from the tissues (Fig. 5.10; [3]).

The technique avoids exposure to radiation and can be performed without the need for sedation. The major limitation of this technique involves patients with very irregular upper airways, in whom tissue can be hidden from the view of the optical probe. In addition, this imaging technique does not directly examine the surrounding soft tissue structures and can also disturb sleep due to the inconvenience of the probe. Furthermore, the catheter might stent the airway and affect the dynamics of UA collapse. However, development of aOCT is ongoing and it is a promising method for a more complete characterization of the UA during all stages of sleep in OSA patients.

5.2 Concepts of Sleep Surgery

5.2.1 Introduction

Sleep surgery is a very important treatment option for patients with obstructive sleep apnea (OSA), particularly for those who have failed or cannot tolerate positive

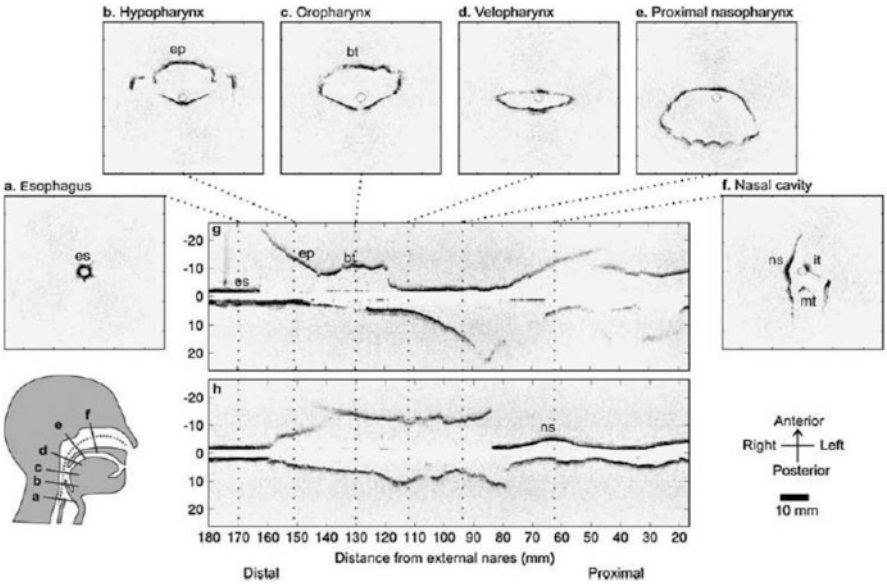

Fig. 5.10 Selected images from a "pullback scan" of a subject without sleep apnea. The scan started in the upper esophagus (180 mm, from the external nares). (**a–f**) Images of 52–52-mm cross-sections selected to show various anatomic features of the pharynx and nasal cavity. (**g**, **h**) Anteroposterior (**g**) and lateral (**h**) sections relative to the catheter. *bt* base of tongue, *ep* epiglottis, *es* esophagus, *it* inferior turbinate, *mt* middle turbinate, *ns* nasal septum (Adapted from *Am J Respir Crit Care Med* [3], with permission)

airway pressure (PAP) therapy. Surgery aims to reduce anatomical obstruction in the whole upper airway (UA). The anatomical concept of surgical treatment may be simply explained by the "Box and Contents" theory. "Box" means the bony and cartilaginous framework of the UA, and "Contents" include all the soft tissue filling the upper airway. When the box is not big enough to contain the contents, the UA can be obstructed, especially during sleep (Fig. 5.11).

Aside from these anatomical factors, there are functional factors, such as critical muscle tone and surface tension of the upper airway mucosa [21]. Surgery cannot consider these factors because they are not usually correctable by surgery. Although surgery may still affect these factors, there is no published evidence describing these outcomes.

Procedures addressing nasal obstruction include septoplasty, various kind of turbinoplasty including radiofrequency ablation (RFA) and microdebriderand removal of the obstructing mass such as polypectomy or tumor excision. Surgical procedures on the retropalatal level include tonsillectomy, uvulopalatopharyngoplasty, uvulopalatal flap, laser-assisted uvulopalatoplasty, and conservatively, RFA of the soft palate and palatal implant. Surgery to the hypopharyngeal or retrolingual level may be related to an enlarged tongue, or more commonly due to maxillomandibular deficiency. Surgeries in these cases are aimed at reducing the bulk of

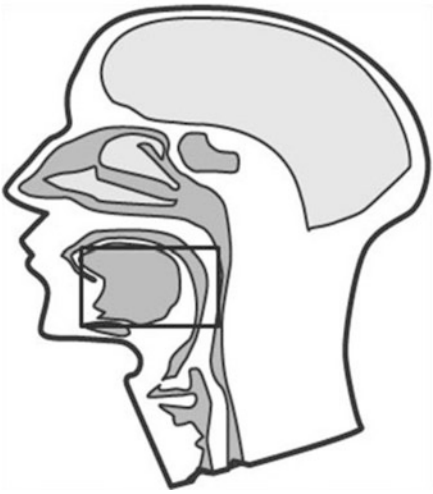

Fig. 5.11 "Box and Contents" concept

the tongue base, creating more tension in the tongue muscles or providing more space for the tongue in the oropharynx so as to limit posterior collapse during sleep. These procedures include RFA of tongue, midline glossectomy or lingualplasty, genioglossus advancement (GA), hyoid myotomy suspension (HMS), and tongue base suspension with sling. These palatal and tongue base procedures may be performed separately (unilevel surgery) or in combination (multilevel surgery; [29]).

Maxillomandibular advancement (MMA) is a method of widening the entire UA with one procedure, however it is not recommended as the first step of surgical treatment of OSA since it is the most aggressive form of sleep surgery which can lead to morbidity, airway compromise and change of facial shape [25]. In addition, there is an option of tracheostomy, which can bypass the crowded upper airway.

Successful surgery depends on proper selection of patients and surgical procedure, and the experience of the surgeon. Proper patient selection is one of the most controversial factors in sleep surgery due to the limited information on the indications for each surgical procedure. Surgery should widen the airway but it is difficult for a surgeon to determine that widening achieved by a certain surgical procedure is enough to prevent airway collapse during sleep, since the upper airway shape may look amply wide when the patient is awake. Selection of the appropriate surgical procedure is also very difficult for a sleep surgeon because there are no standard methods to reveal the obstruction site and all methods to evaluate the UA to find the obstruction site have their own limitations [34]. Most of the published results for surgical treatment are not from randomized trials which are desirable for providing the strongest evidence as to the efficacy of each surgical procedure [42]. Since most surgeries are performed in combination, it is difficult to interpret the efficacy of individual procedures. Whilst surgery does not usually eliminate OSA on polysomnography, it has been shown to provide important improvements in clinical outcomes [35, 49, 52]. Therefore, surgery remains an important therapeutic

consideration and an inevitable treatment option in all patients with OSA, despite the limited data meaning the outcome is not as predictable as PAP therapy which is itself limited by lower compliance and unavoidable lifelong use of a treatment device.

5.2.2 Nasal Surgery

Nasal surgery is very different to other sleep surgeries. The goal of nasal surgery is to improve nasal airway blockage caused by bony, cartilaginous, or hypertrophied tissues to restore normal breathing. Nasal surgery is also very helpful to optimize nasal Continuous PAP use [45]. Furthermore, a patent nasal airway is important for reducing mouth breathing which worsens UA obstruction by forcing the lower jaw to rotate downward and backward and pushes the tongue into the posterior pharyngeal space [22]. A high palatal arch however may be another factor for nasal blockage and cannot be correctable by nasal surgery.

5.2.3 Palatal Surgery

5.2.3.1 Classical Palatal Surgery

The palatal and lateral pharyngeal tissues are usually compliant and collapsible during sleep in certain OSA patients. Uvulopalatopharyngoplasty (UPPP) aims to enlarge the retropalatal airway by trimming and reorienting the posterior and anterior lateral pharyngeal pillars, and by excising the uvula and posterior portion of the palate. This surgery is often performed in conjunction with tonsillectomy to widen the retropalatal and retrolingual airway ([19]; Fig. 5.12). Uvulopalatal flap (UPF), a modification of the UPPP, involves retraction of the uvula superiorly toward the hard–soft palate junction after a limited removal of the uvula, lateral pharyngeal wall and mucosa, thereby widening the oropharyngeal airway. UPF is preferred over UPPP in most cases because it reduces the risk of nasopharyngeal incompetence by using a potentially reversible flap that could be taken down in the early postoperative period. Less postoperative pain compared with traditional UPPP or laser therapy may be expected because there are no sutures along the free edge of the palate. Complications are similar to those of UPPP ([28]; Fig. 5.13). Laser-assisted uvulopalatoplasty (LAUP) is a potential office-based surgical procedure that was introduced in 1990. This technique shortens and tightens the uvula and palate by carbon dioxide laser incisions and vaporizations. However, LAUP has become less popular for the treatment of OSA because of possible early postoperative edema of the UA and thermal injury of the palatal mucosa which can create large scarring on the palate and consequently induce severe nasopharyngeal stenosis and significant postoperative pain [48].

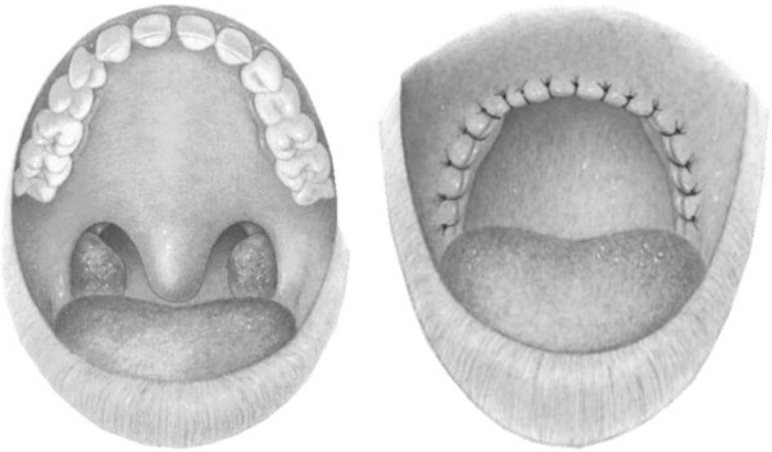

Fig. 5.12 Uvulopalatopharyngoplasty

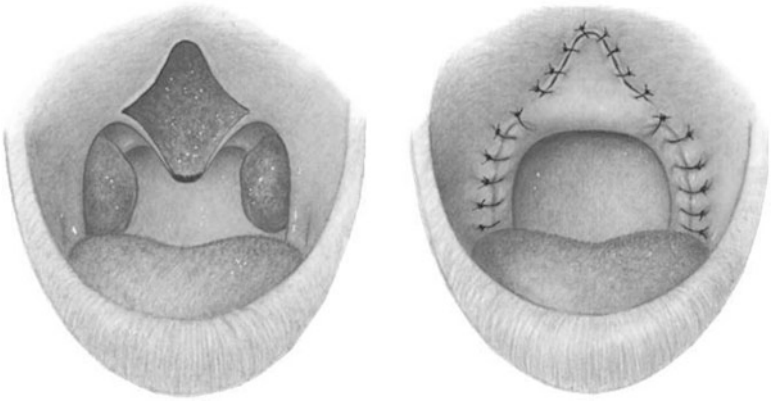

Fig. 5.13 Uvulopalatal flap

In addition, Z-palatoplasty has been performed in patients without tonsils who received UPPP previously [8, 10]. Relocation pharyngoplasty has also been introduced to retain normal pharyngeal function [24]. Alongside these techniques, many surgical procedures have been developed to improve their success rate and avoid complications, but further study is still necessary to determine the efficacy of these procedures.

5.2.3.2 Conservative Palatal Surgery

RFA of the soft palate has been used to treat patients with mild OSA or simple snoring. This procedure results in fibrosis and scarring inside the soft palate

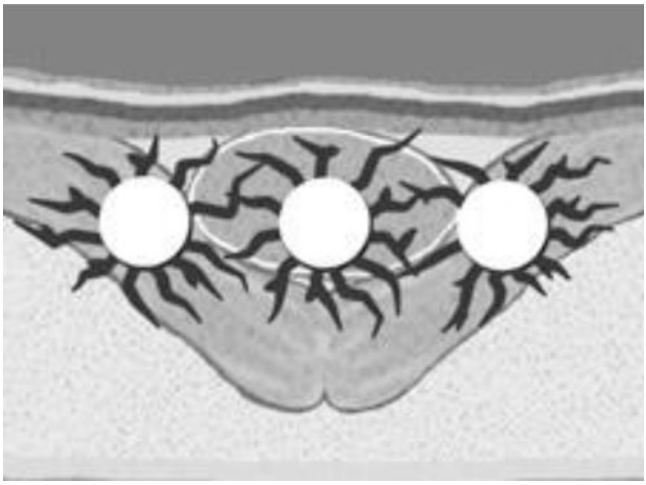

Fig. 5.14 Placement of implanted material and fibrosis around the Pillar implant

muscles which may stiffen and reduce the size of the soft palate. Many options for this technique are available due to the kind of machines used and the choice of site to which it is applied. RFA with bipolar type RF generators needs multiple punctures, while that of monopolar type RF generators use one or two pucture sites. This is still considered to be a minimally invasive and less morbid procedure without compromising treatment efficacy. Disadvantages of this procedure are the need for multiple treatments, unavoidable late evaluation of efficacy, and possible postoperative relapse [39, 41, 46].

Palatal implant (Pillar®) is a newly developed technique for stiffening the palate to treat primary snoring, UA resistance syndrome and mild OSA. The concept of the Pillar system is almost the same as RFA of palate but may be more convenient since it comprises of a single painless procedure [9, 12]. The implant is not migrated by fibrotic surroundings and produces stiffening of the soft palate (Fig. 5.14). Overall effectiveness however remains limited [38].

5.2.4 Tongue Base Surgery

5.2.4.1 Classical Tongue Base Surgery

The genioglossus muscle is attached to the lingual surface of the mandible at the geniotubercle and also to the hyoid complex just above the larynx. Movement forward of either or both of these anatomic structures will stabilize the tongue base along with the associated pharyngeal dilators. Genioglossus advancement (GA) may enlarge the retrolingual airway specifically by advancing forward the site of

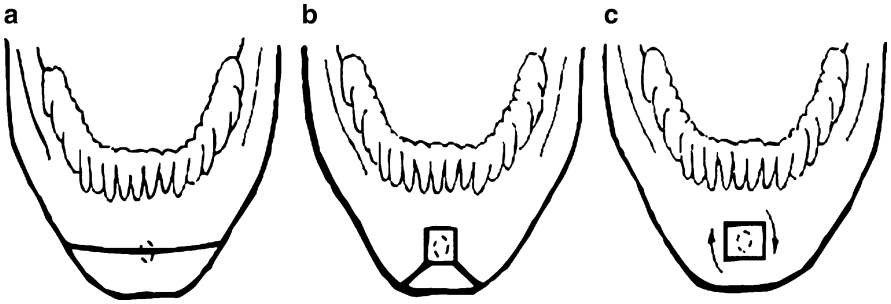

Fig. 5.15 Various methods of genioglossus advancement. (**a**) Sliding genioplasty, (**b**) modified mortise osteotomy, (**c**) geniotubercle advancement

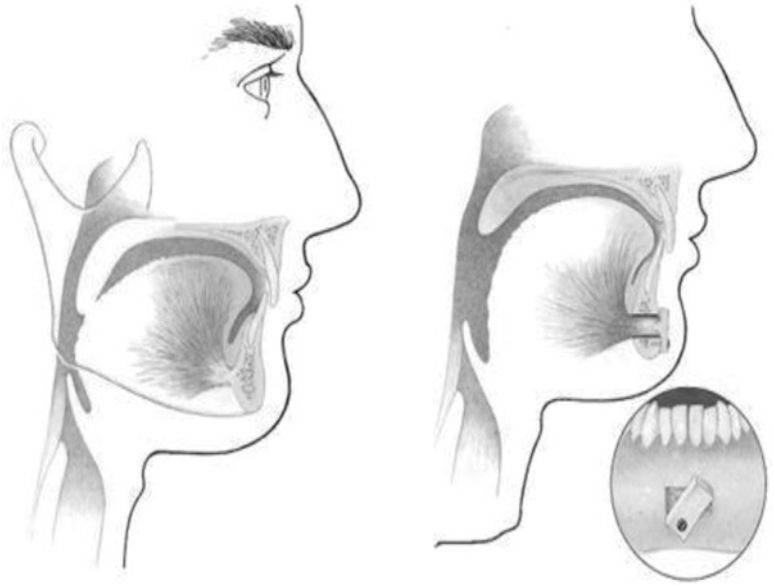

Fig. 5.16 Geniotubercle advancement

geniotubercle of the mandible through a mandibular osteotomy, thereby forcing an anterior advancement of the tongue base [26]. There are several methods to advance the geniotubercle, such as modified mortise technique, genial tubercle advancement, and sliding genioplasty (Fig. 5.15).

However, the main function of the GA is to give the genioglossus augmented tension to prevent collapse of the UA at the tongue base level, even though this technique cannot achieve a widening of the retrolingual space in the airway evaluation. In terms of this concept, modified mortise technique and sliding genioplasty may achieve more tension to the genioglossus but these procedures can weaken the mandible. Therefore, genial tubercle advancement is performed more frequently (Fig. 5.16).

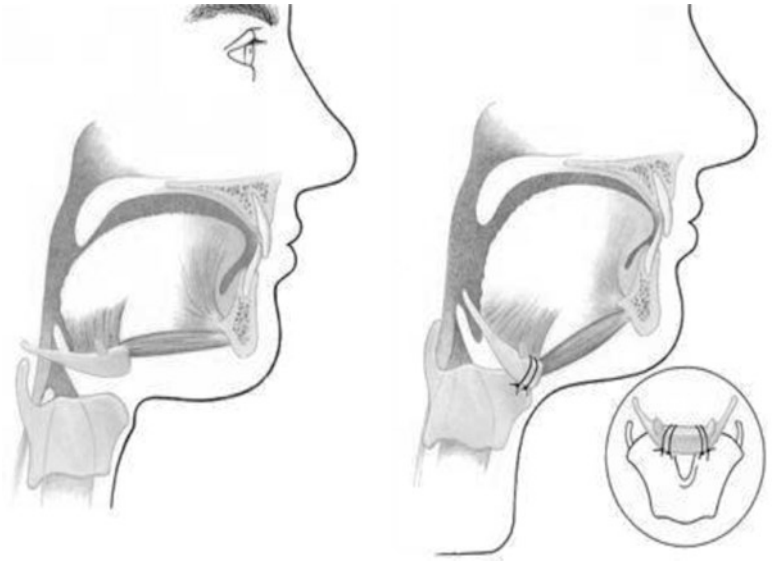

Fig. 5.17 Hyoid myotomy suspension

The hyoid complex also helps to maintain the upper airway space, and forward movement of the complex may improves the UA patency behind the tongue [46, 47]. Hyoid myotomy suspension (HMS) is one option for the OSA patient with tongue base obstruction. The concept of HMS is the same as GA. HMS can give enhanced tension to the pharyngeal dilators which are inserted into the hyoid. HMS may be performed as a primary surgery for tongue base obstruction in OSA patients, especially in contraindication of GA, for example, edentulous patients and dental problems. It is also used as an adjunctive surgical procedure for the failure of GA (Fig. 5.17). Both GA and HMS address the movement of the attachment of pharyngeal dilator muscles, not reduction of "Contents". Therefore, both procedures may be considered as part of "Box Surgery".

Tongue reduction surgery, which is removal of the central portion of the tongue base using laser and Coblation, and lingualplasty, may be used as a "Contents Surgery" for the tongue base [13]. These procedures are currently seldom used due to significant morbidities such as massive bleeding, postoperative edema, and the need for a temporary tracheostomy. However, with the advancement of technology, newer instruments (e.g., Coblation, which is a suctioning, irrigating, bipolar device) have minimized these problems and increased use of this procedure without the collateral tissue damage, bleeding, edema, and need for temporary tracheostomy. These tongue reduction procedures may be particularly useful in selected patients with a large tongue base, for example, Down syndrome or acromegaly.

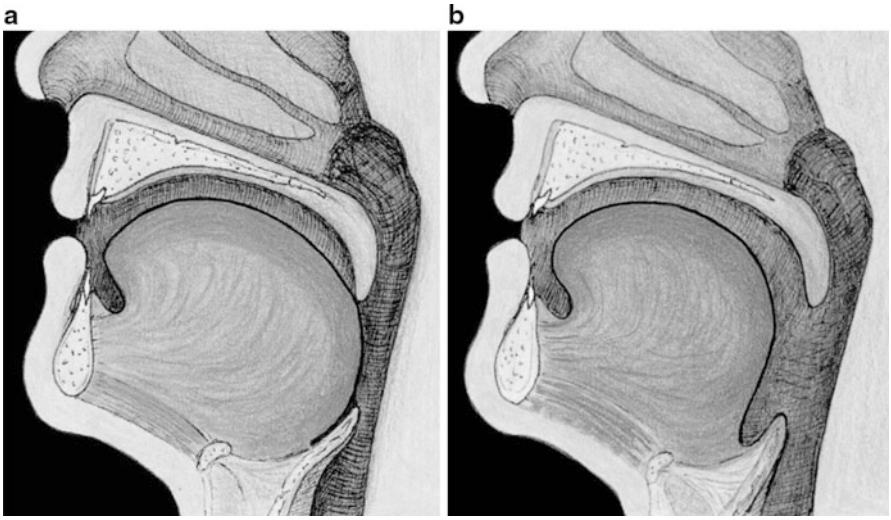

Fig. 5.18 RFA of tongue base. Relative large tongue (**a**) is ablated by RF treatment to reduction of posterior tongue base (**b**)

5.2.4.2 Conservative Tongue Base Surgery

RFA of the tongue base is useful for treating snoring and OSA in selected patients [33]. RF of the tongue base can make a stiff and hard tongue and achieve a partial reduction in tongue volume. This procedure can be performed with all kinds of palatal surgery because it is safe and has mild morbidity [27]. The surgical technique chosen is variable according to the type of machine used. This procedure is also used as an adjunctive procedure in insufficiently improved patients after other classical surgical procedures (Fig. 5.18).

Tongue suspension by sling (Repose®) is also a useful option for the retrolingual level. This procedure is a new, minimally invasive surgery that uses a titanium screw and a permanent suture to anchor and stabilize the tongue base to the inner mandibular cortex [50]. When tightened, the suture supports the anterior hypopharyngeal airway and tongue base, preventing retrolingual collapse (Fig. 5.19). This procedure can be used as a modified method of hyoid suspension and is a relatively simple and less invasive procedure than GA or HMS as it has a similar effect on the upper airway in the retrolingual level. However, tongue suspension by sling does not achieve the enhanced tension of the genioglossus muscle but anteriorly displaces the tongue base itself. Despite this, hyoid suspension by the Repose system has a similar effect on the tongue base to HMS.

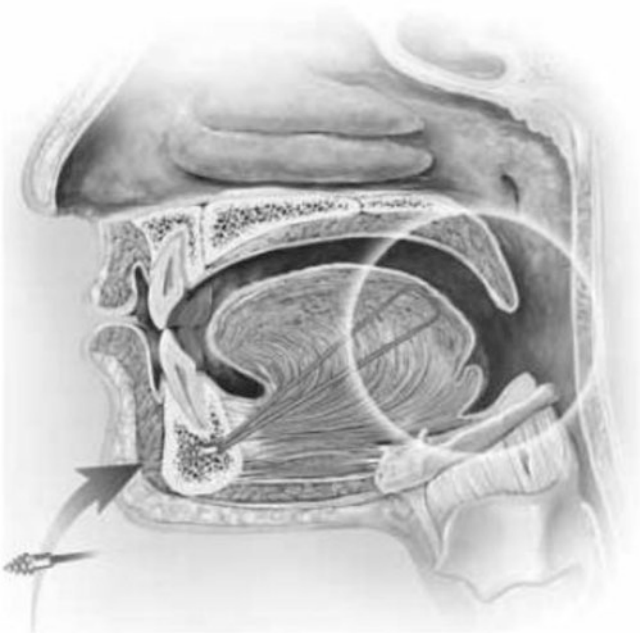

Fig. 5.19 Tongue suspension using Repose system

5.2.5 Maxillomandibular Advancement

Maxillomandibular advancement (MMA) is probably the most effective surgery for improving OSA, short of tracheostomy [25]. The maxilla and mandible are advanced simultaneously by means of LeFort I maxillary and sagittal-split mandibular osteotomies to enlarge the retrolingual and retropalatal airway (Fig. 5.20). Achieving such clearance, especially for long-term improvement, usually necessitates an advancement of 10–15 mm of the maxilla and mandible. This is a concept of whole airway reconstruction which can achieve widening of the retropalatal and retroglossal area. This procedure is also performed using a palatal (maxillary) expansion technique in patients with a high palatal arch and malocclusion. MMA is a real "Box Surgery" which can make a huge space for the "Contents" in the upper airway. In meta-analysis, surgical success and cure (apnea-hypopnea index; AHI < 5) rates were 86.0 and 43.2%, respectively. Younger age, lower preoperative weight and AHI, and greater degree of maxillary advancement were predictive of increased surgical success. The major and minor complication rates were 1.0 and 3.1%, respectively [17]. This procedure can also be modified to prevent changes of the facial shape ([15]; Fig. 5.21).

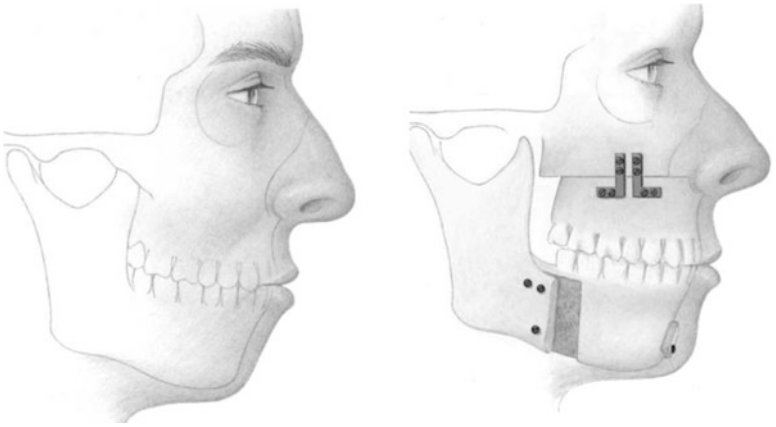

Fig. 5.20 Maxillomandibular advancement.

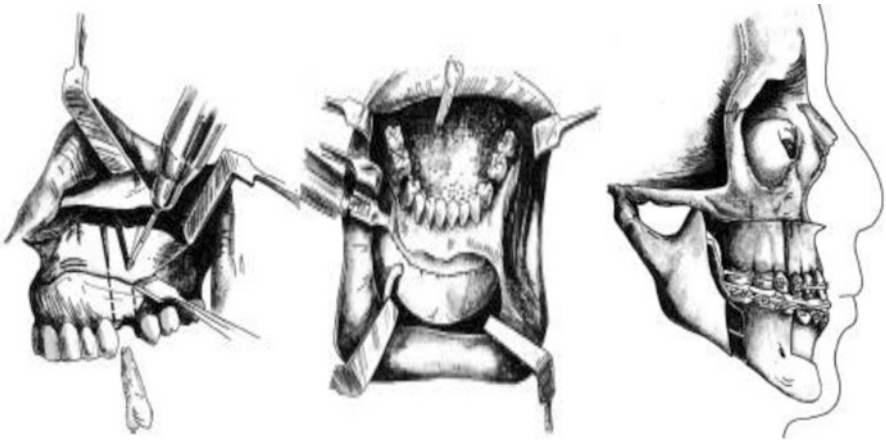

Fig. 5.21 Modified maxillomandibular advancement (MMA) (Courtesy of Dr. Yau Hong Goh)

5.3 Surgical Instruments, Devices, and Machines

Various surgical instruments are available for sleep surgery, from instruments for classical oral surgery and otolaryngology, to newly developed machine and devices. Which machine or device is chosen depends on the surgeon's preference, and the economic situation of both the patient and care provider.

5.3.1 Instruments for Classical Palatal Surgery

Surgical instruments for palatal surgery are typically classical since they are similar to the instruments of tonsillectomy (Fig. 5.22). The tongue should be displaced

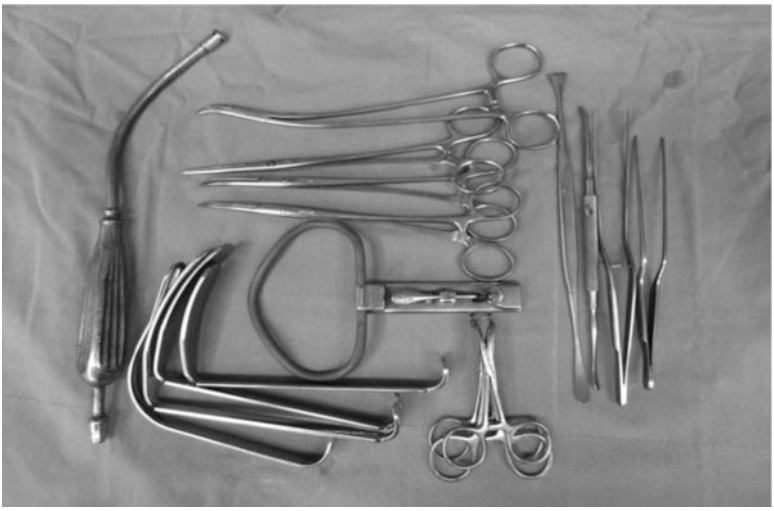

Fig. 5.22 Instruments for classical palatal surgery

anteriorly and laterally in order to approach the palate. Various kinds of mouth gags can be used for tongue displacement and opening the mouth appropriately. We prefer the McIvor mouth gag which is a ring type tongue retractor with groove blade for the endotracheal tube. This mouth gag is very useful to open the mouth and provides good exposure of the whole palate. A mirror is needed to see the retropalatal space before and after the surgery. Other instruments are general surgical tools. A number 15 blade is usually used for remodeling the palate and a curved needle holder is also useful to suture the wound. Thermal surgery such as electrocautery and Coblator® can be used for tonsillectomy but cold knife surgery is preferred for the palatal resection for excellent and early wound healing and to prevent the detachment of the surgical margin.

5.3.2 Instruments for Classical Tongue Base Surgery

Genioglossus advancement (GA) is a kind of bone surgery which is very different from soft tissue surgery and needs various instruments for bone work. Instruments for elevation of the sublabial flap and exposure of the mandible include a periosteal elevator, various retractors such as the Minnesota retractor and right angle and reverse right angle retractors. An oscillating sagittal saw, electrical drill with cutting burr, screws, freer elevator, kocher and curved Kelly are useful to make a bone window in the mandible. The size of the cutting saw depends on the size of the mandible but a 0.9–1 cm wide saw is usually used. The size of the screw for the handling of bony fragment is 2×10 mm, whereas a 1.2×10 mm is used for fixation

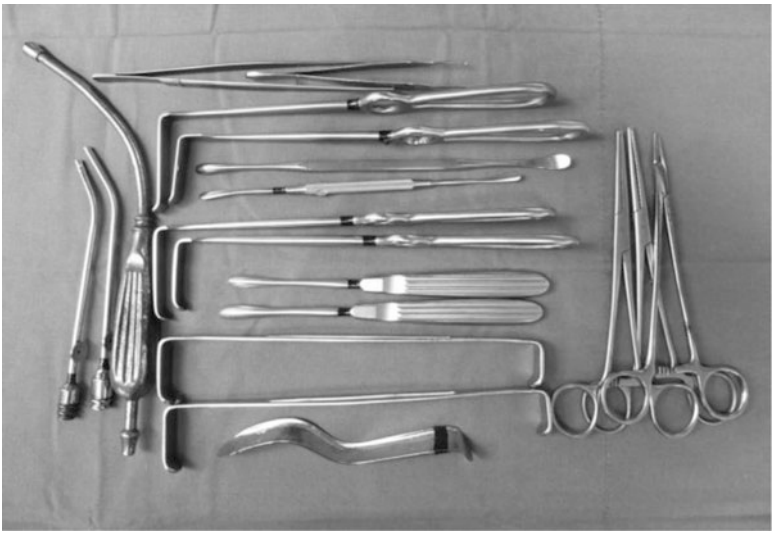

Fig. 5.23 Instruments for genioglossus advancement

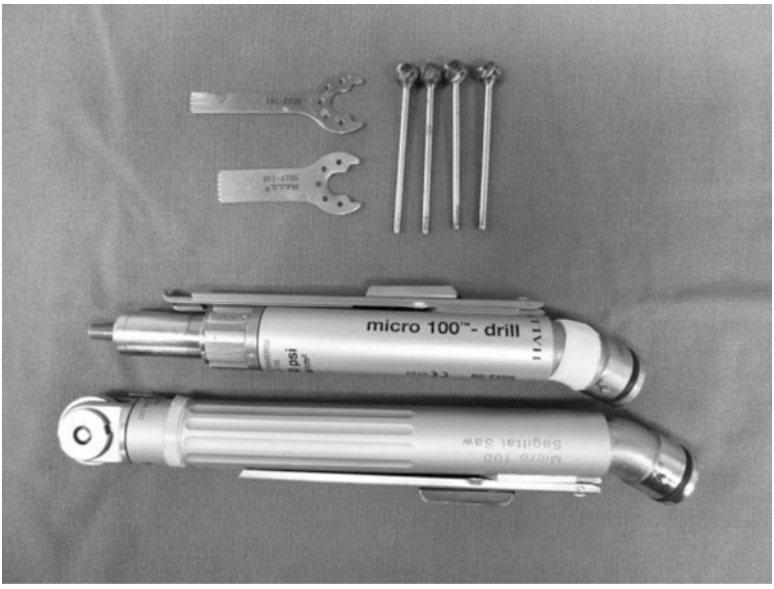

Fig. 5.24 Oscillating sagittal saw and drill

of the bony fragment. Selection of suture material may be important to prevent infection of the mandible. Absorbable monofilament materials such as chromic cat gut or PDS are more desirable than multifilament sutures such as vicryl or dexon (Figs. 5.23 and 5.24).

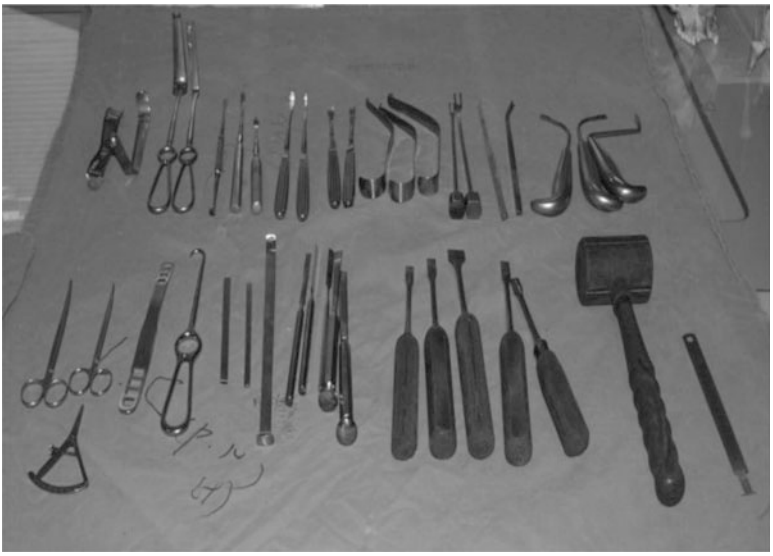

Fig. 5.25 Instruments for maxillomandibular advancement

Hyoid myotomy suspension is surgery for movement of the hyoid bone without cutting of cartilage or bone. Basic neck surgical instruments including a towel clip for handling the hyoid, and non-absorbable suture materials for fixation of the hyoid bone to the thyroid cartilage are usually used.

5.3.3 Instruments for Maxillomandibular Advancement

Instruments for maxillomandibular advancement are similar to that of orthognathic surgery. Several kinds of osteotomes including curved varieties, bone hook, caliper, stripper, septum and bone seperators, and retractors are needed for the handling of the maxilla and mandible (Fig. 5.25). In addition, microplates and miniplates with screws and wires are needed for the fixation of separated bony fragments.

5.3.4 Radiofrequency

Various radiofrequency (RF) generators have been introduced to sleep surgery to achieve rapid wound healing and less painful surgery. Some operations, like Coblation assisted uvulopalatoplasty, include cutting of the uvula and palate but RF is usually used as a channeling surgery for the turbinate, palate and tongue base. In essence, RF is a kind of electrosurgery which uses a lower applied frequency and

working temperature than conventional electrosurgery, resulting in improved wound healing with less morbidity and discomfort [33]. Each RF generator has advantages and disadvantages and different protocols to treat the turbinate, palate, and tongue, but a comparative study of 4 RF generators revealed similar efficacy and safety for these different generators [6].

5.3.4.1 Somnoplasty

The Somnoplasty Generator (Fig. 5.26. Model S2, Gyrus ENT, Bartlett, TN) is used for delivery of radiofrequency energy during somnoplasty surgery. This is the most widely studied RF generator. The SP 1,100 hand piece for turbinate surgery, SP 1,010 for palatal surgery and SP 1,200 single tongue-base needle for tongue reduction can be selected as a needle device (length of active electrode 1 cm, thickness approximately 1 mm). Two thermocouples, one at the tip of the electrode and one at the insulation, continuously monitor temperature and impedance during electrode penetration and treatment. A dispersive electrode is applied to the patient's back to return current to the control unit. The target temperature is set to 80–85°C, and the maximum power is set to 10 W with the amount of energy controllable according to the user's preference. Somnoplasty needle thickness is equivalent to a 23-gauge needle [5].

Investigations on lesion formation in RF surgery using this machine indicates that the application of 600 J at 85°C leads to maximal lesion diameters. Increasing the energy applied does not lead to a significant increase in tissue necrosis and therefore may not have relevant additional clinical effects [40]. A multi-institutional study of radiofrequency volumetric tissue reduction for OSAS has shown that electrolyte solution injection (local anesthetic with or without saline solution) improved the efficacy and reliability of treatment outcomes, significantly decreasing the time required for each treatment [51]. It is hypothesized that saline and local anesthetic injection might increase the concentration of ions surrounding the electrode, which would make energy transfer more efficient.

5.3.4.2 Celon and Sutter

Bipolar type RF generators have been developed which have theoretical advantages over the monopolar RF generator. For example, a skin lesion caused by a neutral electrode can be avoided, as can the possibility of passing an electric current through the body from the probe to the neutral electrode. Bipolar RF generators may be less painful compared to monopolar ones and wound healing may also be faster.

The Celon system (Fig. 5.27. Celon AG Medical Instrument, Berlin) is one of the more widely used RF generators. It consists of the CelonLab ENT RF generator and a disposable bipolar electrode probe. In this system, the probe for the palate and tongue base is the same. Each electrode has an insulating cover that allows exposure of only 1 cm of active electrode to avoid surface damage

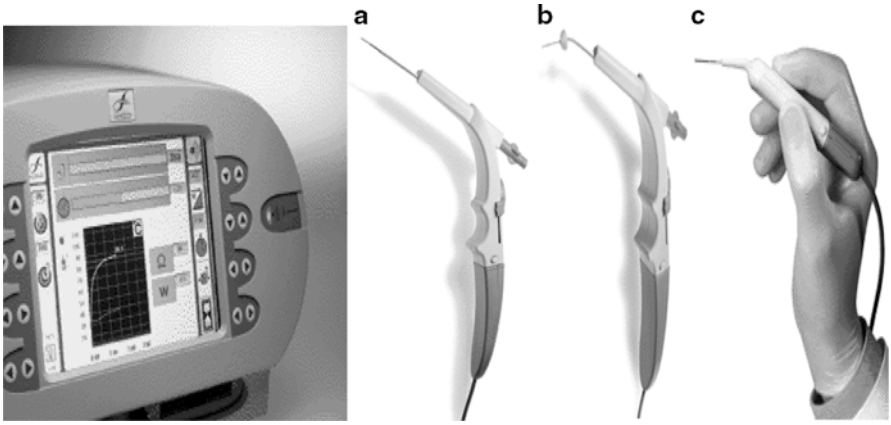

Fig. 5.26 The S2 control unit and various Somnoplasty hand pieces. (**a**) Handpiece for palate surgery, (**b**) handpiece for tongue surgery, (**c**) hand piece for turbinate surgery (Adapted from www.somnus.com)

Fig. 5.27 Celon RF generator and probes. CelonProSpeech for polypectomy, CelonProBreath for turbinoplasty, and CelonProSleep for palate and tongue ablation (Adapted form www.celon.de)

during treatment. Application time varies according to the type of tissue. The power used is 10 W for palate and tongue surgery and 15 W for turbinate surgery. The procedure is terminated by an acoustic end-indication and autostop facilitated by the thermistor and tissue impedance measured at the probe tip. The energy delivered at each puncture site is 60 J [44]. The CelonProBreath for turbinoplasty and the CelonProSleep for palate and tongue ablation can be used for sleep surgery.

Sutter BM-780 II, Fig. 5.28 is also a bipolar RF generator developed by Sutter Medizintechnik, Freiburg, Germany. Although very few studies using the Sutter have been published, it is a widely used RF generator because of its price, convenience, and reusable tips [30].

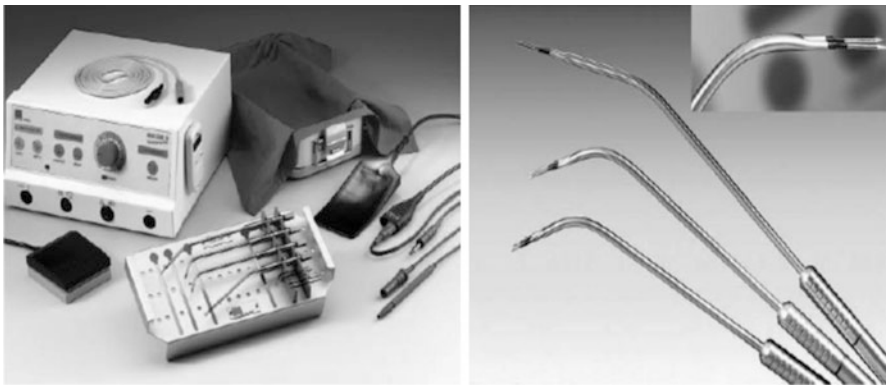

Fig. 5.28 Select-Sutter BM-780 II and various tips (Adapted from www.sutter-med.de)

Fig. 5.29 Coblator II and various types of wand for coblation. Reflex UltraPTR and Reflex Ultra45 can be used for turbinate reduction in pediatric and adult patients. Reflex Ultra55 is used for soft palate reduction. Reflex Ultra65 is for soft tissue reduction in tongue reduction and Reflex UltraSP can be used for uvulopalatopharyngoplasty (Adapted from www.arthrocareent.com)

5.3.4.3 Coblator

An extension of the standard radiofrequency ablation is Coblation, introduced as a procedure for tonsillectomy in 1998, which is a low temperature-controlled, bipolar radiofrequency modality that ablates tissues by generating a field of ionized sodium molecules. The Coblator II surgery system (ArthroCare Inc., Sunnyvale, CA, USA) is the most recent model. Coblation has demonstrable advantages over standard radiofrequency ablation for tonsillectomy and a reduction in hypertrophied inferior turbinates, removing tissues more successfully with shorter treatment times, and therefore may have substantial utility in the tongue base as well. The ReFlex Ultra Plasma Wand is used to perform plasma-mediated electrosurgery tissue reduction for the palate and tongue (Fig. 5.29). The Coblator has an Evac and PROcise

Wand for tissue removal which is used for adenoidectomy, tonsillectomy, lingual tonsillectomy, and midline glossectomy.

Radiofrequency energy excites electrolytes in a conductive medium, such as saline, creating a precisely focused plasma. The energized particles in the plasma have sufficient energy to break molecular bonds, excising or dissolving tissue at relatively low temperatures, thereby preserving the integrity of the surrounding tissue [14]. This is in contrast to other heat-based technologies that burn tissue. The Coblator operates between 40 and 70°C, whereas electrocautery creates temperatures of 400–600°C [32]. Operating at a lower temperature, lower frequency, and higher impedance, the Coblator is expected to cause little collateral tissue damage.

5.3.5 Palatal Implant

The Pillar implant is a disposable device consisting of a cylindrical implant and a delivery tool. The implant is a braided segment of polyester filaments intended for permanent implantation. The implant is 18 mm in length and has an outer diameter of 1.5 mm (Fig. 5.30). The delivery tool consists of a handle and 14-gauge needle, with the implant preloaded. The implant is then deployed by retracting the thumb switch.

5.3.6 Repose System

The Repose system consists of a bone screw inserter, suture passer, bite block, Mayo needle, and tongue retractor. The bone screw inserter is a disposable battery-operated machine which deploys the bone screw into the inner surface of the mandible. The suture passer is a sharp-tipped disposable device which is used to pass the suture through the tongue to the tongue base (Fig. 5.31).

5.4 Conclusion

Evaluation and management of the upper airway in obstructive sleep apnea (OSA) can be better understood with improvements to the diagnostic and surgical armamentarium available to sleep surgeons. It is likely that a multi-modality and even a multi-discipline approach may be needed to firmly establish the obstruction site. Although these approaches increase confusion as to the specific predictive results of individual diagnostic and surgical technologies, a focused understanding as well as a continuous hands on experience with each of the modalities discussed will ultimately benefit the sleep surgeon, providing the best possible outcomes for patients presenting with OSA.

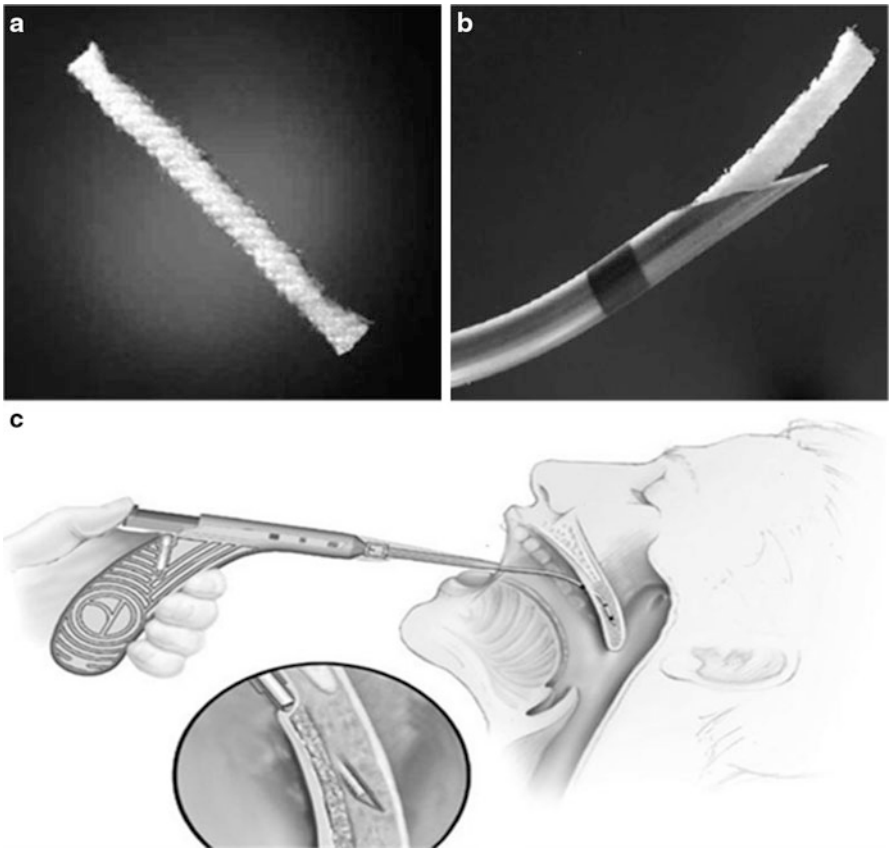

Fig. 5.30 Pillar implant. (**a**) Polyester filament, (**b**) tip of needle with pillar, (**c**) delivery tool

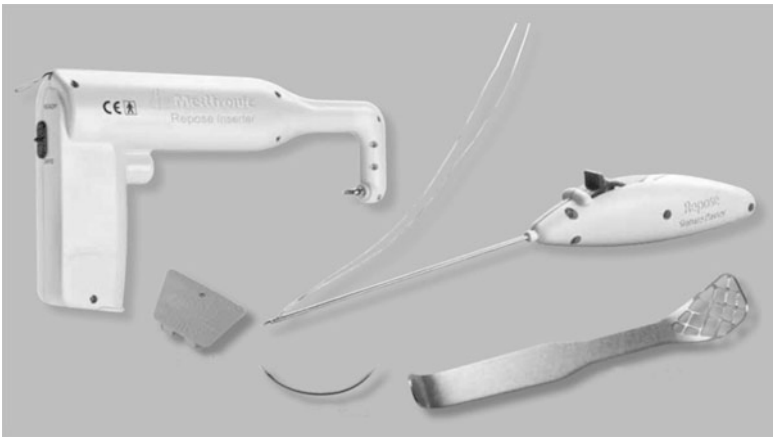

Fig. 5.31 Repose system

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Chapter 6
Management of Sleep Disorders-Sleep Technology on Positional Therapy

Chol Shin and Jung Bok Lee

Abstract Positional patients are defined as obstructive sleep apnea (OSA) patients in whom respiratory disturbance index (RDI) or apnea-hypopnea index (AHI) is at least twice as high in the supine position than in the non-supine position. Positional therapy (the avoidance of the supine posture during sleep) is a simple behavioral therapy for mild and moderate sleep disordered breathing. In this chapter, we 1) provide an overview of position dependent sleep and positional therapy for sleep disordered breathing, 2) update the clinical evidence for positional therapy and position dependent sleep advances in sleep technology, and 3) discuss issues regarding implementing positional therapy.

Keywords Position dependency • Body posture • Collapsibility • Lateral position • Sleep disordered breathing

6.1 Introduction

It has been reported that obstructive sleep apnea syndrome (OSAS) and sleep disordered breathing (SDB) are very prevalent in the general population across regions and populations [1, 2]. SDB has been identified as a severe risk or prognostic factor for many chronic diseases [3–6]. There are different treatment options for OSAS and SDB, which consist of (1) behavioral therapy including

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weight loss, reduction of alcohol intake, stopping sedatives or sleep medication; (2) conservative interventions including mandibular repositioning, continuous positive airway pressure (CPAP) titration; and (3) medication and surgical therapy [7]. Of the many treatment options, CPAP treatment has been recognized as the most efficacious therapy and has been recommended as the primary option for OSA [8, 9]. However, major concerns about CPAP treatment include not only non-adherence with CPAP therapy [10], but also the limited therapeutic benefits of CPAP treatment in mild OSAS patients [11]. This was illustrated by Rosenthal et al. [12] who demonstrated that adherence to CPAP in mild OSAS was suboptimal. The success of CPAP therapy was even more problematic, even though the initial acceptance of CPAP was relatively good [13].

As an alternative, positional therapies for OSAS and SDB have been highlighted. Cartwright [14] made critical contributions to positional therapy, even defining positional patients. Positional therapy has not only had limited acceptance, but has also been regarded as a secondary or supplemental therapy for OSAS and SDB. This difficulty in therapeutic acceptance is due to the lack of reliable evidence, as well as the non-elaborate (or naive) devices used to correct body posture. However, recently many studies have investigated the efficacies and beneficial aspects of positional therapy, including comparative studies with CPAP treatment and combinational effects of other treatments.

In this chapter, we briefly describe reviews of position dependency and positional therapy in Sect. 6.2 and present updated clinical evidences in Sect. 6.3. Oksenberg and colleagues comprehensively explain most issues on positional therapy in their excellent review [15].

6.2 Overview of Positional Therapy

6.2.1 Definition of Positional Sleep Apnea

Cartwright [14] first defined positional patients as OSA patients who had an overall apnea-hypopnea index (AHI) that was greater than 5. Additionally, these patients had a supine AHI that was at least two times greater than in the non supine position [15] (Table 6.1).

Some researchers have even more strict requirements including (1) AHI < 15 in the non-supine position, or (2) at least one rapid eye movement (REM) period [16], or (3) more than 1 h of sleep in a non-supine position [17]. For diagnosis of positional dependency, body position monitoring during a full polysomnography is recommended. There is no accepted guideline for the minimum time in which to assess positional differences. Mador et al. [18] demonstrated that there were no differences between a minimum of 15 and 30 min in each position.

As shown in Table 6.1, the definition of positional sleep apnea is very simple, but there are some points to consider. Oksenberg and Silverberg [15] summarized practical points to diagnose positional sleep apnea:

Table 6.1 Summary of positional sleep apnea

	Definition	Remark
Requirements	Overall AHI > 5	
	AHI in supine > 2 × AHI in non-supine position	
Optional criteria	More than two supine positions	Selection of options may apply
	>1 h of non-supine position	
	AHI < 15 in the non-supine position	
	At least one REM period in the non-supine position	
	More than 15 min per supine or non-supine posture	

- The monitoring and recording of body position should be included.
- Sufficient sleep time in supine and non-supine positions is necessary for diagnostic evaluation.
- The severity of the disease is related mainly to the sleep time spent or not spent in the supine position.

These practical points are why some researchers include some of the optional criteria listed in Table 6.1.

An example hypnogram of a typical positional sleep apnea patient is shown in Fig. 6.1. The patient's overall AHI was 14.3, whilst their AHI in supine and non-supine positions were 26.3 and 2.9 respectively. During supine position sleep, apnea, hypopnea events, and snoring increased, even when other events were dramatically decreased. Oksenberg [19] also compared hypnograms of non-positional and positional patients. He emphasized that the OSA severity of position dependency was entirely dependent on the sleep time spent or not spent in the supine position.

Mador et al. [18] emphasized the importance of accurate recording and scoring. Digital position monitoring, when compared to direct review of videotape recordings of the patient, has not been disappointing. Mador et al. [18] recommended that real-time position scoring by on-site technicians appeared to be highly accurate. Direct comparison of real-time position scoring with video recording has shown that direct patient observation provides an accurate record. Real-time observation of the patient by the on-site technician can be an acceptable method for posture scoring.

6.2.2 Prevalence of Positional Sleep Apnea

During the 1980s–1990s, the prevalence of positional patients in OSA covered a broad range, from 9 to 60% [14, 20–25]. Oksenberg and Silverberg [15] explained that this wide variation was due not only to small sample sizes, but also the different types of OSA patients studied. Cartwright [14] reported that the prevalence of positional patients was 58.3% of 24 OSA patients in one study, and 55.9% of 574 OSA patients in another study by the same group [24].

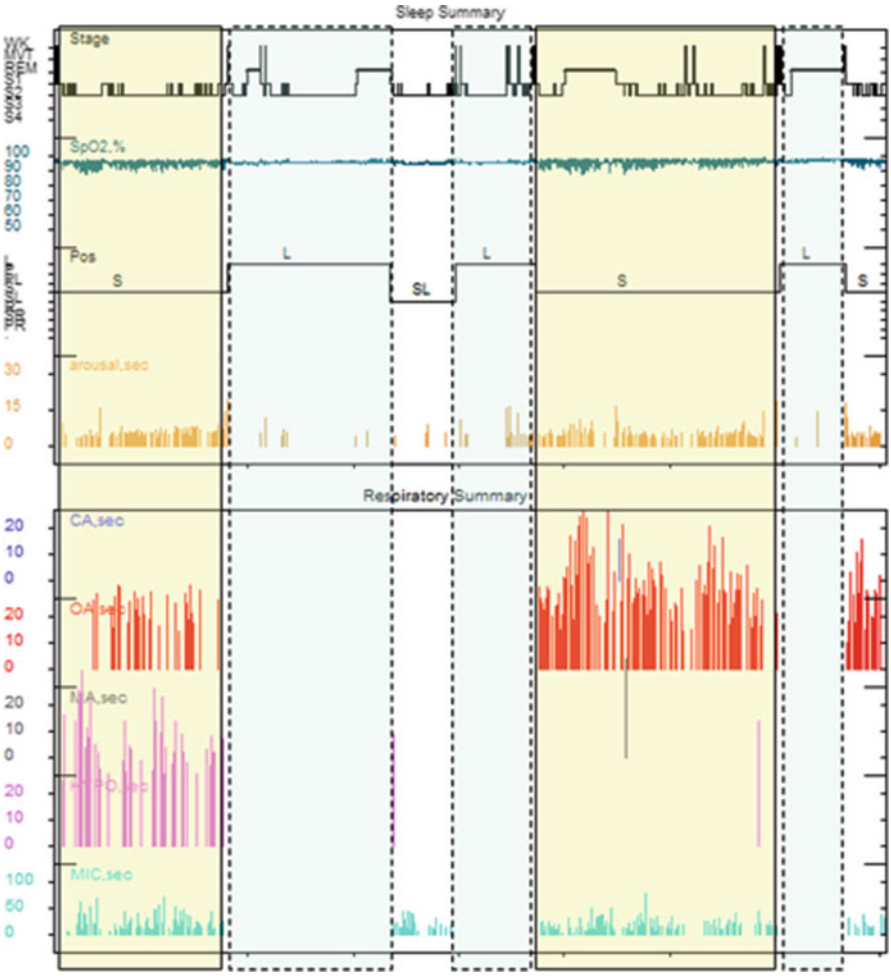

Fig. 6.1 Hypnogram example of positional sleep apnea: *Box* with *solid line* indicates supine position and with *dashed line* indicates non-supine position

In the 2000s, three prevalence studies of relatively moderate OSA patient sample sizes were reported in the US, Europe, and Korea [18, 26, 27]. In the study by Richard et al., 55.8% of the 120 patients had dependent OSAS. Mador et al. [18] and Kim et al. [26] reported the prevalence of positional OSA according to the OSA severity in US and Korean patients (Fig. 6.2). In Mador et al.'s study, 49.5% of mild OSA patients were positional, whilst the percentages in moderate and severe decreased to 19.4 and 6.5% respectively. Kim et al. [26] also reported similar prevalence rates to Mador et al.'s study.

From the studies cited above, it becomes evident that (1) positional OSA is more prevalent in mild OSA; that is to say position dependency is highly related to OSA severity, and (2) that the prevalence of positional OSA is approximately 50% or

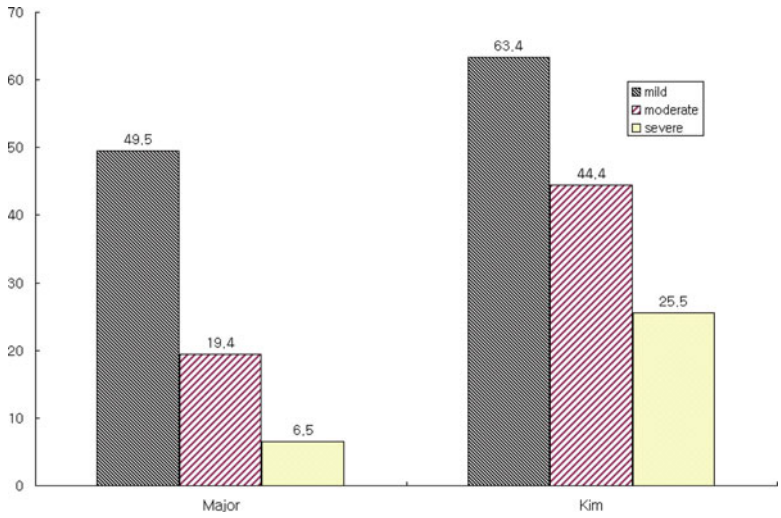

Fig. 6.2 Prevalence of positional sleep apnea according to OSA severity

Table 6.2 Summary of position dependency predictors

Factors	Conditions	Statistical significance
Age	Younger age	Borderline
Gender	No significance	Non significant
Obesity	Less obese	Significant
Severity (or AHI)	Highly correlated: mild or moderate	Significant
Snoring	Change apnea events to snoring Reduce intensity	Significant
Sleep stage	Less AHI in positional patients during REM	Significant

more in mild OSA patients. Since position dependency may be a characteristic of the natural development of OSA, positional OSA may develop to a non-positional condition as the severity increases [24].

6.2.3 Factors Influencing Position Dependency

- Age
  As a predictor of positional dependency, there are discrepancies between prevalence studies. In Oksenberg et al. [24], two younger groups showed equal prevalence of positional patients, while in the elderly group, the prevalence of positional patients decreased. This finding was of borderline statistical significance. In Richard et al.'s study, positional patients were significantly younger than non positional patients, while Kim et al. [26] and Mador et al. [18] did not observe any significant age effects.

Consequently, age is a weak contributing factor, but elderly OSA patients are less likely to be positional [15].

- Gender
  No gender differences have been reported in positional OSA patients.
- Obesity
  Lloyd and Cartwright [22] found that the degree of obesity correlates better with the AHI in the supine position than in the non-supine position. This finding suggests that weight loss is an effective behavioral therapy [15]. Various studies have demonstrated that obesity is highly correlated with positional OSA. In Oksenberg et al. [24], body mass index (BMI), and weight were significantly lower in positional than in non-positional patients, while weight, waist circumference, and waist-hip ratio (WHR) were significant in Kim et al.'s study [26].
- Severity
  The severity of OSA is highly associated with positional dependency.
- Snoring
  There is no objective evidence for positional effects on snoring. Braver and Block [28] reported that positional therapy was not effective for snoring. Nakano et al. [29] demonstrated not only that snorers showed decreased snoring both in duration and intensity in the non-supine position, but also that in the apneic group, the positional dependency of snoring was correlated with supine AHI. In fact, OSA patients with a higher supine AHI tended to show decreased apnea and increased snoring in the non-supine position. This phenomenon could be viewed as a predictor of disease progression. Oksenberg and Silverberg [15] reported that the supine position in habitual snorers had a general detrimental effect on snoring and on the arousals from it. Choi et al. [30] provided clinical evidence that the snoring rate was significantly lower during positional therapy than at baseline.
- Sleep Stage
  In epidemiologic studies [18, 27], the AHI during REM was found to be significant higher in non positional patients. However, the AHI during REM sleep was significantly less in the non-supine position compared to the supine position in positional patients. There has been controversy regarding the association of sleep stage and OSA. In early studies, George et al. [20] suggested that the apnea index (AI) was higher in the supine position only in the non-REM sleep stage, while the duration of apnea was longer during REM sleep regardless of the body position. However, several studies [25, 31] have demonstrated the positional effect in non REM sleep, but that some patients lose their positional susceptibility while in REM sleep [15].

6.2.4 Mechanism

The prominent pathomechanism of OSA is partial or complete obstruction of the upper airway accompanied by oxygen desaturation [32, 33]. The effect of gravity to decrease the lumen of the upper airway during supine sleep is probably the

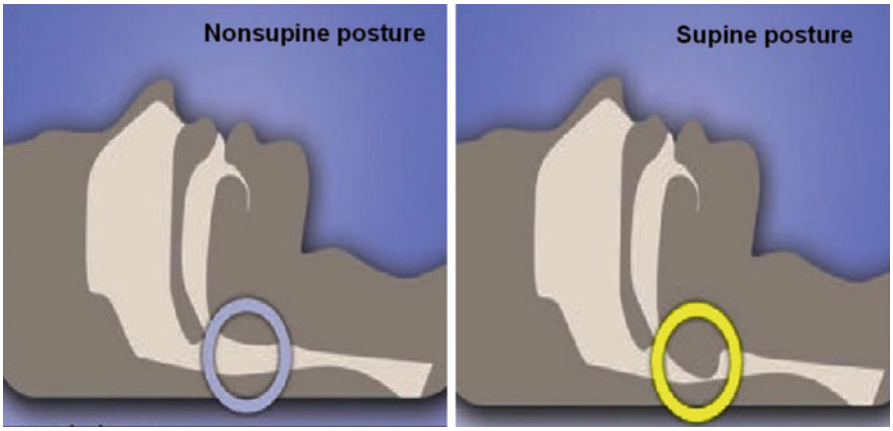

Fig. 6.3 An illustration of pharyngeal collapsibility in the nonsupine (lateral position) and supine posture

most dominant factor responsible for any physiological changes observed in this posture [15].

Sleeping in the lateral position reduces the pharyngeal collapsibility that can be caused by several mechanisms [34]. Since the tongue plays a role in upper airway obstruction, the lateral position provides a protective function by preventing the tongue from occluding the airway when the genioglossus muscle is hypertonic [32] (Fig. 6.3).

6.2.5 General Guidelines for Positional Therapy

The most recent guidelines for positional therapies was published by the Standard of Practice Committee of the American Academy of Sleep Medicine (AASM) in 2006 [9]. Although positional therapy is a simple, effective approach for position dependent patients, it is not considered a primary therapy, but is limited to secondary and supplementary treatment.

Positional Therapies

Positional therapy, consisting of a method that keeps the patient in a non-supine position, is an effective **"secondary therapy"** or can be a **"supplement to primary therapies"** for OSA in patients who have a low AHI in the non-supine versus that in the supine position.

– Standard of Practice Committee of the American Academy of Sleep Medicine

Table 6.3 PubMed search result from AASM

				AASM
First author	Year	Subject	Evidence level	Review criteria
Cartwright	1985	Positional therapy	III	
Cartwright	1991	Positional vs nasal therapy	II	Satisfied
Jokic	1999	Positional vs CPAP	II	Satisfied
Kushida	1999	Positional therapy	III	Satisfied
McEvoy	1986	Positional therapy	III	
Miki	1988	Positional therapy	III	
Neill	1999	Positional therapy	III	
Series	2001	Positional vs CPAP	II	

Another AASM publication provided evidence levels of clinical trials for positional therapies as in table 6.3 [52]. Unfortunately, there is no evidence level I study for positional therapies (Level I Study: Randomized well-designed trials with low-alpha & low-beta errors). In addition to PubMed searching of AASM, Skinner et al. [35] and Zuberi et al. [36] satisfied the AASM review criteria, therefore a total of five publications were considered by the Standard of Practice Committee of AASM.

6.3 Update of Clinical Evidence for Positional Therapy

6.3.1 Optimal Sleep Position

Many researchers have investigated SDB such as OSA and snoring, in which the collapse of the upper airway is the primary event [37, 38]. Numerous medical devices have been developed to eliminate SDB symptoms [14, 21, 36, 39]. Different sleeping positions have been proposed for the improvement of OSA symptoms [40, 41].

Few studies have investigated the optimal sleeping position to reduce upper airway sleep apnea andor snoring symptoms. There are several reasons why sleep position is difficult to study. In the natural sleeping position, patients unconsciously rotate approximately 90° in the lateral position without awareness of their degree of rotation during sleep. Several studies have investigated the relationship between sleep posture and the collapsibility of the upper airway. They have reported that a 20° head extension cervical support [39], a 45° incline on both sides [36], or an elevation of body position [35] are effective in reducing sleep apnea andor snoring.

However, few studies have theoretically evaluated several characteristics of body position that play key roles in determining the parameters of positional therapy. In Lee et al. [42], effective sleep positions and a combination of sleep

position determinants were evaluated to examine their effect on reducing snoring and/or apnea. These parameters include cervical vertebrae support with head tilting, scapula support (SS), and being in the lateral position for sleep. The study focused on determining the potential optimal position in patients with snoring and sleep apnea. Thus, response surface analysis, a complex statistical method, was used for the following purposes: (i) to determine the factor levels that will simultaneously satisfy a set of desired specifications, (ii) to determine the optimum combination of factors that yield a desired response and describes the response near the optimum, and (iii) to achieve a quantitative understanding of snoring and sleep apnea behavior over the region evaluated.

After response surface model fitting, the data from this study demonstrated that the optimal sleeping position for eliminating snoring was not only highly associated with the lateral position, but also its interaction with cervical vertebrae support with head tilting. The results also showed that the interaction of the lateral position with cervical vertebrae support with head tilting and SS was effective in reducing sleep apnea. The principal conclusion of this study was that more than a 30° rotation and a 20 mm elevation of the upper trunk with moderate support (60–70 mm) of the cervical vertebrae were effective in reducing snoring. For sleep apnea, a >40° rotation with higher levels of cervical vertebrae support with head tilting (>70 mm) and SS (30 mm) were recommended for an AHI reduction >80%.

Based on the estimated regression equation, the optimal sleeping position ideally reduces the snoring rate to 0% during the entire sleeping period, when a 40° lateral rotation and a 60 mm cervical vertebrae elevation in mild snoring patients (i.e. a snoring rate: 20%) is employed. In addition, AHI could be decreased to <80% in the case of a 40° lateral rotation and a 30 mm SS with the appropriate cervical vertebrae support with head tilting in mild or moderate sleep apnea.

6.3.2 Intervention Studies

Until now, many studies have reported the usefulness and efficacy of positional therapy and it is summarized in Table 6.4. Various positional devices have been used including position alarms [43], tennis or soft balls [14, 16, 24], and pillows and a head support device [35, 36, 39].

There are several studies on positional therapy using specially designed pillows. One study was conducted to determine the ability of a specially designed, triangular double-inclined pillow with an arm position recess on both sides in the base under the incline to treat snoring and OSA [36]. In patients (n = 19) with mild (respiratory disturbance index [RDI] < 20) and moderate (20 < RDI < 40) OSA, the RDI decreased significantly from 17.4 to 5.1, and snoring decreased in 15 (78.9%) of the 19 patients. The effects of cervical position with neck extension on snoring and OSA were investigated using a custom-designed cervical pillow [39]. In patients

Table 6.4 Summary of intervention studies using medical devices

First author	Year	Device type	Study design
Cartwright	1985	Tennis ball technique	Pre-post
Cartwright	1991	Tennis ball with alarm	Semi-crossover
Braver	1994	Tennis ball with nasal spray	Pre-post
Jokic	1999	Tennis ball vs CPAP	Comparative: crossover
Choi	2000	Jaw and head position	Comparative
Kushida	2001	Pillow	Pre-post
Bliwise	2004	Knees-up position	Comparative: crossover
Skinner	2004	Head elevation device	Pre-post
Zuberi	2004	Pillow	Pre-post
Loord	2007	Soft vest attached to pillow	Pre-post
Choi	2009	Vest type	Pre-post
Permut	2010	Tennis ball type vs CPAP	Comparative

with mild OSA (n = 3), the RDI decreased significantly from 14.7 to 10.5 and the mean percentages of snoring and snoring duration were slightly reduced, though this was not statistically significant. In patients with moderate (n = 4) to severe OSA (n = 5), RDI, the mean percentages of snoring and snoring duration were not significantly decreased. However, in another study [44], the mean AHI decreased significantly during treatment from 21.8 to 14.3 in 18 patients with OSA. Thirteen (72.2%) of the 18 patients experienced decreases in AHI, but their mean percentages of snoring increased during treatment from 30 to 38%. In addition, 11 (61.1%) of the 18 patients snored without change (2/18) or more frequently (9/18) during treatment. It is thought that these different results for snoring may be due to differences in the design of the pillow, different study groups, or different indications for treatment and assessment of snoring.

Choi et al. [30] proposed a vest-type design and a connected controller with two 5-mm air tubes. Two air chambers are installed in parallel on the left and right side of the back of the vest. During sleep, one of the chambers is inflated to prevent the supine position, and then deflated after a pre-specified time and the other chamber is inflated. Using the controller, the user can select from a number of options: (1) sleep time (20, 30, or 60 min); (2) position preference (left, right, or both sides); and (3) time for maintaining inflation (60, 90, or 120 min). Based on a pre- and post- treatment comparative parallel study, both the mean total snoring rate (from $36.7 \pm 20.6\%$ to $15.7 \pm 16.2\%$) and snoring rate in the supine position (from $45.8 \pm 22.8\%$ to $25.4 \pm 20.6\%$) decreased significantly with use of the vest. The mean percent change of the total snoring rate between baseline and with the positional device was significant ($63.5 \pm 22.5\%$). Of the 17 subjects, 15 (88.2%) decreased their snoring rate more than 50% without subjective or objective adverse effects.

In a previous study of Oksenberg et al. [24] on positional therapy using a tennis ball, the usefulness the tennis ball technique (TBT) during a 6-month period in 78

consecutive positional OSA patients was examined [13]. A questionnaire was used to obtain information and 50 (64.1%) of the 78 patients returned the questionnaire. Of these patients, 19 (38%) still used the TBT, 12 (24%) used it initially and stopped within a few months, but still avoided the supine position. Nineteen (38%) stopped using the TBT within a few months without learning how to avoid the supine position during sleep. The most common reasons for stopping use of TBT were that it was uncomfortable; it kept moving; patients still slept supine with it; there was no improvement in sleep, snoring, or alertness; and it caused backache. Compared to positional therapy using a pillow or vest-type device, positional therapy using a ball or alarm may cause not only frequent arousal or disrupted sleep, but also is not effective in patients who may not feel the pressure of the ball due to obesity, or who may not hear the alarm due to loud snoring or hearing problems.

6.3.3 Comparison of CPAP Treatments

CPAP therapy has long been the primary treatment for most patients with OSA. It provides not only efficacy in sleep apnea and beneficial effects on sleep quality and daytime alertness [45], but it also improves cognitive performance [46]. There are disadvantages to CPAP treatment such as patient non-compliance and higher treatment costs. Also, many researchers have focused on improvements in the AHI with positional treatments, rather than functional outcomes such as sleep quality, daytime alertness, and cognitive performance [16].

There are only two clinical studies that compare CPAP treatment and positional therapy. Jokic et al. [16] postulated that positional treatment improved sleep quality and daytime performance, as compared to CPAP in the management of positional OSA. Based on a crossover design, 14 positional OSA patients were recruited. In this study, it was concluded that positional treatment has no clinical advantage over CPAP in the treatment of positional OSA. Positional therapy is not equivalent to CPAP treatment in reducing AHI and in improving subjective or objective sleep quality and arousal index. However, as the efficacy advantages of CPAP over positional therapy did not translate into a functional improvement with CPAP treatment, Jokic et al. (1999) emphasized that positional treatment appears to be an effective alternative treatment to CPAP, at least in the short term, in positional OSA.

Contrary to Jokic et al. [16], another comparative study demonstrated that positional therapy is equivalent to CPAP for normalizing the AHI in patients with positional OSA, with similar effects on sleep quality and nocturnal oxygenation [17]. In the study, four major findings were reported. First, in patients with positional OSA, positional therapy is equivalent to CPAP therapy in normalizing the AHI to fewer than five events per hour. In addition, the AHI was decreased by more than 50%. Second, positional therapy is similar to CPAP therapy in regard to effects on sleep quality and nocturnal oxygenation. Thirdly, there is minimal night-to-night

variability in the nonsupine AHI in patients with positional OSA. The fourth finding was that positional therapy is effective at maintaining patients in the nonsupine position throughout the night [17].

Compared to Jokic et al.'s study, Permut et al.'s results emphasize that positional therapy can be a primary treatment "for positional OSA patients who have treatment effect." However, to be a primary treatment, it is necessary to confirm the equivalence or superiority of sleep quality, cognitive function, and the quality of life between CPAP and positional therapy. Superior patient compliance of positional therapy over CPAP must also be demonstrated.

6.3.4 Long-Term Follow Up Study

Positional therapy is a less frequent form of therapy than CPAP treatment, but it appears to be an adequate form of therapy for positional OSA patients [13]. In order for positioning therapy to be a primary treatment for positional OSA, it is important to evaluate long-term efficacy, safety and compliance as well as comparative studies with active controls. Since there is no accepted evidence of the efficacy of positional therapy from a long-term follow-up study, clinicians hesitate to try the positional therapy for positional OSA patients. Unfortunately, there has been no long-term study of positional therapy for 20 years since Cartwright's contribution on this topic. Oksenberg and Silverberg as far back as 1998 emphasized that well-designed, long-term evaluations of the efficacy of positional therapy in large populations were urgently needed. However, only two studies with small sample sizes have been published.

In Oksenberg et al.'s follow-up study [13], in 50 positional OSA patients after a 6 month period, 19 (38%) reported they were still using TBT. Another 12 (24%) of these patients said they stopped TBT, since they had learned to avoid the supine position during sleep. Based on these reports, the overall compliance rate of TBT was estimated to 38–62%. Patients still using the TBT showed a significant improvement in their self-reported sleep quality, daytime alertness, and a decrease in snoring loudness. Most of the patients that had stopped using the TBT after a short period of time, complained that it was "uncomfortable." Interestingly, age was the only predictor that significantly differentiated between patients who complied and who did not comply. Age was higher in two groups either "still using the TBT" group or "learned to sleep on their side without the belt" group than in any other groups.

Recently Bignoid et al. [47] reported another long-term study with a longer (mean 2.5 years) follow-up time. However, the sample size was small. Among the 62 respondents of the study, only 4 (6.0%) reported they were still using the TBT. Nine (13.4%) subjects were no longer using TBT, because they had learned to avoid the supine position during sleep. These results are similar to Oksenberg et al. [13], in that the major reason for patients stopping TBT treatment was the high degree of discomfort (63.0% of respondents).

The long-term compliance of TBT appears to be poor; as low as 19.4%, with the level of discomfort cited as a major problem. It is essential to develop alternative high-tech devices to guarantee patient comfort for positional treatment in addition to improving patient compliance with the device.

6.3.5 Combinational or Supplemental Therapy

According to the guidelines of AASM, positional therapy is a secondary and supplemental therapy for positional OSA. Recently there have been a few clinical studies to evaluate auxiliary, supplemental and combinational effects of positional therapy. Of the early studies, Cartwright et al. [43] found that adding a tongue-retaining device (TRD) to positional therapy was better than each treatment alone. Braver and Block [28] demonstrated that the combination of nasal spray and positional therapy produced a small, but significant improvement in the AHI of 20 snorers. However, Braver et al. [48] emphasized the importance and usefulness of combinational or adjunct therapy.

When patients with severe non positional OSA had a large number of apneic events in both the supine and the non-supine posture, the apneic events during the supine posture were more severe than the apneic events occurring in the non-supine posture. Penzel et al. [32] emphasized that the collapsibility of the upper airway was strongly influenced by body position and proposed that as a consequence, lower CPAP pressure was needed during lateral positions compared to supine positions. This result implies that positional therapy may contribute to a lower titration of CPAP in severe (non-) positional OSA patients to improve the acceptance and compliance of CPAP treatment.

More evidence for the importance of combination therapy was provided by Chung et al. [49], who investigated the treatment outcomes of mandibular advancement devices (MADs) for positional and non-positional obstructive sleep apnea. The percent change of AHI in non-positional patients was 46.03%, while that in non-positional patients was 74.69%.

This clinical evidence will motivate more detailed clinical evaluations to demonstrate niche effects of positional therapy, as well as its use as primary treatment for positional OSA.

6.3.6 Central Sleep Apnea

Central sleep apnea is common in patients with heart failure in which central apneas alternate with hyperpneas that have a waxing-waning pattern of tidal volume [50, 51]. A few research papers have reported that positional therapy is highly effective in attenuating the severity of central sleep apnea with Cheyne Stokes Respiration. The reader is referred to Szollosi et al. [52] and Joho et al. [53].

6.4 Concluding Remarks: Challenging Issues in Positional Therapy

Positional therapy is an effective intervention for positional OSA and SDB patients of mild or moderate severity, and is very simple, non-invasive, and inexpensive [15]. Positional therapy can be used as an auxiliary, supplemental and combinational therapy to any other form of therapy for SDB patients.

However, lack of clinical evidence means clinicians hesitate to utilize positional therapy. Patient noncompliance due to discomfort is another major obstacle. Consequently, the following are essential for positional therapy to be elevated in the SBD armamentarium.

- Long-term follow-up studies with larger sample sizes are necessary for the evaluation of efficacy, safety and compliance.
- Innovative high-tech devices should be developed to guarantee patient comfort during use.
- Comparative studies to evaluate (1) a primary therapy such as CPAP, (2) devices for position change or avoiding supine position, and (3) another therapy such as an oral device, should be performed.
- As a niche effect, combinational or auxiliary effects with any other forms of therapy should be explored.

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Chapter 7
Management of Sleep Disorders – Cognitive Behavioral Therapy for Insomnia

Chien-Ming Yang and Fan-Chi Hsiao

Abstract Insomnia is a common complaint in the general population. Hypnotics are the most common treatment for insomnia, despite some unwanted effects such as tolerance and dependence. Cognitive Behavioral Therapy for Insomnia (CBT-I) was shown to be effective in the treatment of chronic insomnia. Recent studies comparing CBT-I treatment with hypnotics further demonstrated that the CBT-I treatment was at least as effective as hypnotics during acute treatment, and may be more effective than medication during long-term follow-ups. This chapter describes the role of neurophysiological and psychological factors in the regulation and dysregulation of sleep. Further, the rationales and procedures of CBT-I are introduced. Lastly, the application of CBT-I with modern information technologies is discussed.

Keywords Insomnia • Cognitive behavioral therapy for insomnia • Internet

Insomnia is a common complaint in the general population. The prevalence of insomnia varies depending on its definition. In a survey study conducted in seven European countries (France, the United Kingdom, Germany, Italy, Portugal, Spain, and Finland) with a representative sample consisting of 25,579 subjects, approximately 37% of the subjects had sleep complaints, 9.8% had sleep symptoms and daytime consequences, and 6.6% satisfied the DSM-IV diagnostic criterion for insomnia [49]. The disorder is more common among women, older adults, and those with medical and psychological disorders [8, 26].

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Hypnotics are the most common treatment for insomnia, despite some unwanted effects such as tolerance and dependence [45]. Many psychological interventions have been shown to be effective in the treatment of chronic insomnia. In several meta-analyses and reviews, it was shown that psychological treatments for insomnia could benefit around 70–80% of patients with insomnia [30, 39–41, 43, 44]. The 2005 State-of-the-Science Conference of the National Institutes of Health of United States also recognized the effectiveness of psychological and behavioral therapies to treat chronic insomnia in adults [45]. These treatment techniques are usually combined into Cognitive Behavioral Therapy for Insomnia (CBT-I). Many studies have supported the efficacy of CBT-I. Recent meta-analyses reported moderate to large effects of CBT-I in improving sleep latency, duration of wakening, and sleep quality in patients with primary insomnia [39, 44]. Recent studies comparing CBT-I treatment with hypnotics further demonstrated that the CBT-I treatment was at least as effective as hypnotics during acute treatment and may be more effective than medication during long-term follow-ups [27, 40, 41]. In addition, the subjects were more satisfied with CBT-I than with medication [40, 41]. Therefore, there is a great need to introduce insomnia patients to this evidence-based treatment option.

In this chapter, we will begin with an introduction of the neurophysiological mechanisms of normal sleep regulation, and then provide a framework to conceptualize the contribution of behavioral factors for the development of insomnia. Further, we will describe the rationales and procedures of CBT-I. Lastly, we will discuss the application of CBT-I with modern information technologies.

7.1 The Pathological Model of Insomnia

7.1.1 Neurophysiological Regulation of Sleep

Insomnia can be construed as a disruption of the neural systems that normally regulate the sleep and waking cycle. The neural systems that regulate sleep and waking may include a homeostatic system that accumulates sleep propensity with each passing hour of wakefulness, a circadian process that generates a biological rhythm of sleep and wake tendency over the course of a day, and an arousal system that promotes wakefulness and counteracts sleep drive [6, 33, 55].

The function of the homeostatic system is to maintain an adequate amount of total sleep over successive nights. The level of sleep drive present on the basis of this homeostatic mechanism is, at any given time, determined by prior durations of sleep and wakefulness. Sleep deprivation leads to an augmented sleep drive and an increased likelihood of accumulating extra recovery sleep during subsequent night(s), thereby restoring the balance. Oversleeping, by contrast, reduces the homeostatic sleep drive, leading to shorter or lighter stints of sleep.

The circadian system is regulated primarily by an internal clock in the hypothalamus that generates a rhythm of sleepiness and alertness independent of prior sleep history. Studies with both animals and humans have identified the genetic basis of

this cycle [29, 63]. The typical endogenous circadian cycle in human beings has a period of slightly over 24 h [11, 12]. Therefore, there is an innate tendency for our bedtimes and rising times to slowly drift later in time. This propensity is often revealed during vacation periods, when we are not as constrained by externally imposed schedules. Exposure to environmental time cues, especially daylight in the morning, can stabilize an endogenous circadian rhythm that would otherwise "free run." The circadian and the homeostatic systems interact reciprocally with each other to initiate and maintain sleep. Under normal conditions, homeostatic drive is built up during the day when circadian propensity for wake is high. Circadian wake propensity then falls off in the evening that allows sleep to occur. Circadian sleep tendency reach its peak and maintain the sleep in the middle of night when homeostatic sleep drive has been partially satiated. Sleep disturbances thus may occur when the homeostatic system mis-phased with the timing of the circadian system.

The arousal system counteracts the sleep drive by promoting arousal. The system could be activated by internal thoughts and emotions as well as by external stimulation. It can be viewed as a mobilizing system intended to arouse an individual when he or she is at risk. In contrast to the homeostatic mechanism that gradually strengthens the sleep drive as our waking hours pass, alertness can soar in a moment, as required in an emergency. While this arrangement may be adaptive from an evolutionary standpoint, it does work against the prospects for sleep in insomnia patients. Their careful preparations for sleep can be overturned in an instant by an errant thought.

Several models highlighting the role of arousal as a cause of insomnia conceptualize the disorder as a manifestation of hyperarousal [4, 50]. Individuals with insomnia have been shown to have elevated activities of autonomic nervous system, indicated by higher metabolic rate, body temperature, heart rate, urinary cortisol and adrenaline excretion, skin conduction, and muscle tension [3, 62], as well as increased cortical arousal, as indicated by faster EEG frequencies [17, 32, 51], enhanced activating components, and decreased inhibitory components in event-related potentials [66] and PET [48] during sleep initiation. These results further suggest that insomnia may result from an inability to lower general attention or the arousal process and an impairment in the sleep-specific inhibitory process associated with sleep initiation.

7.1.2 Psychological and Behavioral Factors Affecting Sleep

Although the systems that regulate sleep are physiologically based, they are susceptible to interruption by psychological and behavioral factors. Sleep is readily deferred, at least in the short run, in the efforts to complete tasks deemed sufficiently important or to maintain vigilance in the face of real or perceived threats. In patients with chronic insomnia, the efforts to fall asleep and the threat of an upcoming sleepless night may lead to increased arousal that further exacerbates the already fragile sleep.

Transient insomnia resulting from acute stress is a nearly universal experience. It may be associated with autonomic nervous system (ANS) activation and hormone release subserving the normal stress reaction [62]. Arousal in chronic insomnia patients is however often associated with excessive cognitive activities around bedtime. Previous studies have provided evidence suggesting that anxious or dysphoric thoughts are not conducive to sleep [15, 16, 19, 38, 46, 64]. Insomnia is clearly associated with worrying that has a "real world" basis, or with exposure to traumatic events. Furthermore, in chronic insomnia patients, arousal is often associated with concern that centers on sleep itself. After experiencing frequent sleepless nights, recalling long hours of nocturnal wakefulness and consequent daytime listlessness as well as anticipating more of the same may elicit further arousal and disrupt sleep. Arousal can also be a learned response through classical conditioning. After repeated pairings of bedroom environment with the experience of sleeplessness, bedtime, with its attendant rituals, begins to offer contextual cues for arousal rather than sleep [5].

Some misconceptions about sleep may also be adverse to poor sleepers. Patients who have unreasonable expectations about sleep may be frustrated by not being able to fulfill these expectations. Poor sleepers who feel that their insomnia is "inevitable" and will necessarily lead to dire health consequences may also become frenzied by bedtime. Directly challenging dysfunctional thinking about sleep through education and cognitive therapy has been shown to improve sleep [21, 42]. Furthermore, the extent to which the anxiety-provoking cognition decreased following CBT-I was associated with the level of improvement after treatment [42]. Misconceptions about sleep may disrupt normal sleep regulation through maladaptive sleep practices. Over-concern about the consequences of poor sleep often leads to pernicious behavior practices that originate in the desire to compensate for poor sleep or its daytime effects [20]. It is common to hear patients sleeping into the morning following a disrupted night when their schedules allow or of taking an afternoon nap. These responses may bring short-term relief from the effects of sleep loss, but at the cost of reducing the amount of sleep drive available to induce sleep at bedtime or disrupting the circadian processes that regulate sleep and wakefulness. Figure 7.1 provides a simplified framework that shows how cognitive and behavioral factors may affect sleep through the mediation of the neurophysiological systems that regulate sleep and wakefulness. The techniques of CBT-I are aimed at adjusting these factors to help patients regain the balance of the neurophysiological regulation of sleep and wakefulness.

7.1.3 The 3P Model of Insomnia

Over time, the physiological, psychological, and behavioral factors may all contribute, in varying degrees, to the development of insomnia in an individual patient. The waxing and waning of these factors along with their interaction can complicate

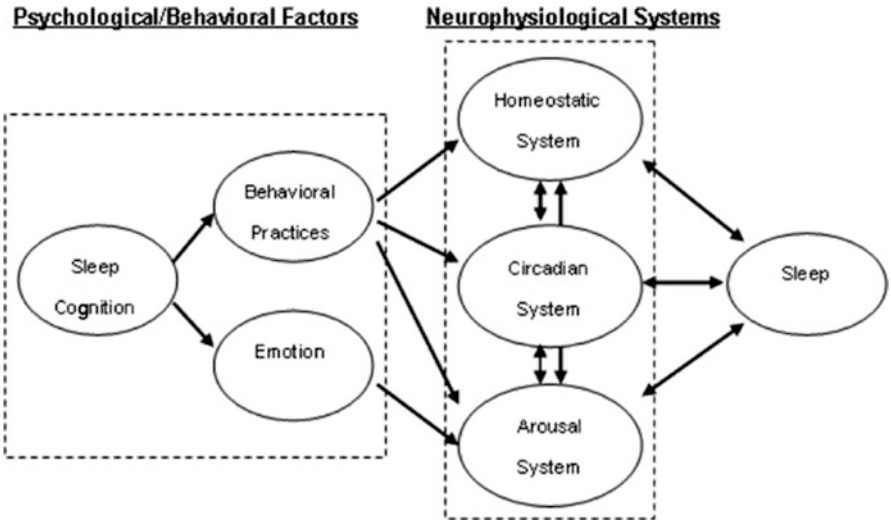

Fig. 7.1 A conceptual model shows that psychological/behavioral factors influence sleep mediated by the neurophysiological systems for sleep regulation (Adapted from Yang et al. [67])

the clinical assessment of the disorder. Spielman introduced a model that is very useful for understanding the genesis of insomnia in a patient. The 3P Model of insomnia groups the etiological factors of the disorder temporally into the Predisposing factor that sets the stage for its development, the Precipitating factor that triggers its onset, and the Perpetuating factor that maintains the sleep difficulty in the long term [56] (see Fig. 7.2).

Difficulty sleeping can arise from inherited predispositions pertaining to each of the three neurophysiological systems subserving sleep and wakefulness described above. These predisposing characteristics are often present for years before chronic insomnia takes hold. Some individuals possess an inherently weak homeostatic sleep drive. Others are under the sway of an atypical circadian system. For example, the endogenous circadian clock of those with a "night owl" sleep pattern under typical circumstances may have a greater tendency to be shifted later in time; thus, they may experience sleep initiation difficulties following occasions that require staying up late. Finally, the sleep of those who have hyperaroused constitutions may be especially vulnerable to disruption when encountering stressful events [13]. Previous studies have also shown that those who tend to internalize conflicts through self-inhibition, denial, or suppression seem to be more susceptible to the impact of acute stress [28].

The events or stressors that trigger the onset of insomnia in these examples are the precipitating factors. Patients tend to label these precipitating events as the "cause" of their insomnia since they usually appear just prior to or concurrently with the sleep disturbance. These factors may be as dire as divorce or serious illness, or as

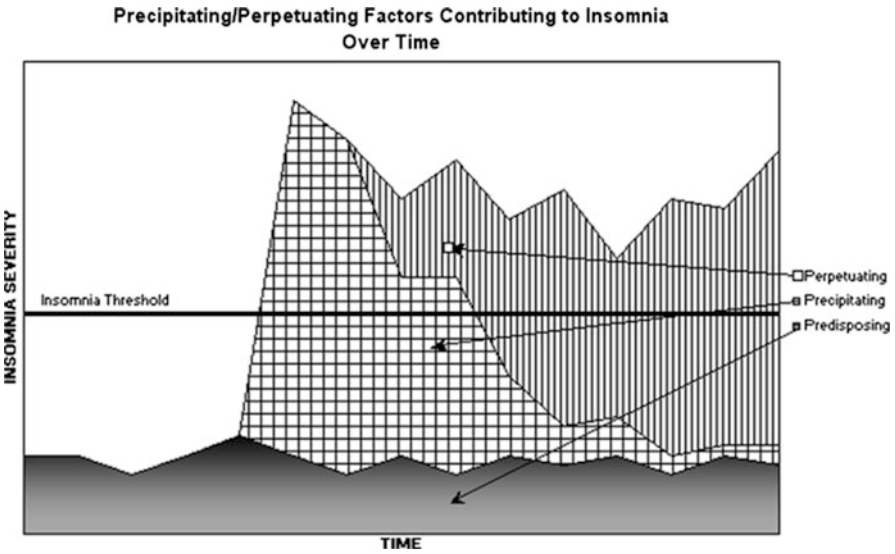

Fig. 7.2 The 3P model of insomnia, in this case illustrating the major contributions of Precipitating and Perpetuating factors and the minor contribution of Predisposing factors (Adapted from Spielman et al. [58])

elating as a newborn or a job promotion. However, in chronic insomnia, the sleep disturbance lasts even after the impact of the precipitating event has subsided or resolved. The cognitive and behavioral factors described above often become the major contributing factors and maintain the sleep disturbance.

These perpetuating factors are the major targets of CBT-I in patients with chronic insomnia. However, other factors in the 3P Model should not be overlooked. As predisposing characteristics increase the risk of developing insomnia, any mitigation of their contribution would be helpful. Similarly, addressing the precipitating factors of sleep loss directly, such as marital conflicts or performance anxiety, can prevent the recurrence of sleep disturbance after the perpetuating factors are controlled.

7.2 The Structure of CBT-I

CBT-I is usually conducted in groups with a structured program or is administered individually with selected techniques tailored for an individual. In order to facilitate the treatment process, it is suggested that patients be prepared before instituting the treatment techniques. First, just like all types of psychotherapies, a good conceptualization of the patients' problem may add to the effectiveness of the treatment. Prior to initiating CBT-I, it is important to conduct a thorough evaluation to identify possible contributing factors. Patients with sleep disturbances often

have some misconceptions regarding the causes of their sleep problem or may be puzzled by their condition. The feeling of being out of control and the mystery of what is causing the problem could generate anxiety that may further disrupt their sleep. Therefore, sharing the conceptualization with the patient is therapeutic in that such an approach restores some modicum of control and reduces unnecessary anxiety. This understanding, furthermore, may motivate the patients to practice the behavioral techniques.

In addition to the evaluation and etiological formulation, providing a description of the treatment procedure as well as the rationale of the treatment may comprise a comprehensive first treatment session. It is useful for patients to know what to expect from the treatment. A series of office visits or group sessions are scheduled on a weekly or biweekly base while maintaining a sleep log in between sessions. For both individual and group CBT-I, the entire program usually takes 4–8 weeks, although an abbreviated, 2-session CBT-I was also reported to be effective in primary care settings [14]. In addition, the patients should expect the effects of the behavioral techniques to be manifest in a few weeks. Unrealistic expectations of immediate improvement may lead to premature demoralization. The patient should also understand that reliably carrying out behavioral practices is crucial for the treatment to be effective.

Different treatment techniques will be introduced during the course of the treatment sessions. As mentioned earlier, the procedure of CBT-I could be a standardized structured program or could be tailored according to the etiological formulation of an individual session. The patients may be required to change their sleep habits and daily life routines and to practice some behavioral techniques in between sessions. In subsequent sessions, the "prescribed" sleep and behavioral practices may be adjusted depending on the outcomes following the treatment and the difficulties encountered in carrying out the techniques. Table 7.1 provides an example of a structured CBT-I program that is conducted in our treatment outcome studies.

7.3 CBT-I Techniques

CBT-I comprises three components: an educational, a cognitive, and a behavioral component. The educational component aims to enhance the understanding of basic mechanisms of sleep regulation, etiological factors of insomnia, and sleep and daily life practices that are compatible with good quality sleep. The behavioral component includes specific techniques that enhance the quality of sleep by adjusting the sleep schedule and employing relaxation training that can reduce tension and anxiety. Finally, the cognitive component aims to correct beliefs and attitudes about sleep that may be anxiety-provoking and may lead to maladaptive sleep practices. In the following section, we will describe the rationale and principles of the techniques.

Table 7.1 A sample of a structured CBT-I program

Week 1	Education:
	Mechanism of sleep regulation
	Neurophysiological model of insomnia
	The 3P model of insomnia
Week 2	Education:
	Sleep hygiene education and pre-sleep behaviors
	CBT-I techniques:
	Stimulus control
	Sleep restriction: introduction
	Relaxation training: diaphragmatic breathing
Week 3	Education:
	Circadian rhythm and sleep
	CBT-I techniques:
	Sleep restriction: sleep schedule titration
	Relaxation training: progressive muscle relaxation
Week 4	Education:
	Hypnotic introduction and tapering
	Sleep disturbance
	CBT-I techniques:
	Sleep restriction: sleep schedule titration
Week 5	CBT-I techniques:
	Cognitive restructuring
	Sleep restriction: sleep schedule titration
	Relaxation training: direct relaxation
Week 6	Education:
	Relapse prevention
	CBT-I techniques:
	Review of CBT-I techniques

7.3.1 Sleep Hygiene Education

Sleep hygiene refers to the practices of everyday living and sleep-related activities that promote good quality sleep and those that make sleep more resistant to disruption. The objectives of sleep hygiene education are to improve basic knowledge about sleep and modify counterproductive sleep practices [24]. Understanding the mechanisms of sleep regulation and the etiology of their sleep problem empowers the patient and eliminates unnecessary worry about their insomnia. It also provides the rationale for sleep promoting behavioral practices. In terms of sleep hygiene practices, the clinician reviews daily life practices and sleep-wake habits with the patient and identifies a set of practices that are not consistent with good sleep hygiene. The patient is asked to refrain from maladaptive activities and, in some cases, engage in sleep promoting behaviors.

Sleep hygiene education is usually a standard part of a more comprehensive treatment program. Sleep hygiene education alone has been shown to be less effective than the other behavioral treatments [30]. Many patients are aware of

sleep hygiene practices, but they do not believe that the practices will produce significant changes in their sleep. It is important to convey to such individuals that insomnia is the result of the interaction of multiple factors. Eliminating maladaptive sleep hygiene practices may not solve the problem. A successful treatment result, however, may not be achieved without changing poor sleep hygiene practices.

7.3.2 Cognitive Therapy

As described above, misconceptions about sleep may lead to increased arousal and/or sleep-disruptive behavioral practices. Changes of dysfunctional thoughts can reduce worries, and therefore, break the vicious cycle that leads to arousal. Part of the disruptive cognitions about sleep may be corrected with sleep hygiene education. Cognitive restructuring, on the other hand, addresses sleep-disturbing cognitions directly, and replaces these thoughts with more realistic thoughts and positive ideas [22, 37]. In conducting this part of CBT-I, dysfunctional sleep cognition should be identified by discussing the worries of patients prior to sleep or with the assistance of self-report questionnaires [37]. After the belief has been identified, the validity of the belief can be challenged with evidence from scientific knowledge as well as the observation of the experiences of the patient—for example, if a patient believes that "if I don't get enough sleep, I will perform poorly on my job." The clinician may educate patients about the scientific facts of the effect of a few nights of poor sleep on performance and ask the patients to rate the level of job performance along with maintaining a sleep log. The association between job performance and sleep quality may not be as consistent as expected by the patient. If the belief is proved to be valid, the utility of the thoughts can be examined. This can be done by querying the consequences of maintaining this belief. For example, although poor sleep usually leads to poor performance on the job, constantly thinking about it does not help matters. The clinician can question the patient about how he/she feels and what he/she will do if the patient continues ruminating about this belief. It is very likely that the belief may increase anxiety and negative mood that may further disrupt his/her sleep.

7.3.3 Stimulus Control Therapy

The objective of stimulus control therapy is to disrupt the association of bedtime cues with wakefulness and arousal. The patients are instructed to get out of bed if unable to fall asleep and return to bed when ready to sleep. The following are specific instructions followed in stimulus control therapy: (1) go to sleep only when feeling sleepy; (2) do not use the bed or bedroom for other activities except for sleep (sexual activity is the only exception); (3) if you do not fall asleep within approximately 20 min, go into another room and do something relaxing; (4) go

back to bed only when feeling sleepy again; (5) repeat the procedure of getting out of bed if you still cannot fall asleep rapidly; (6) get up at the same time each morning regardless of how much you have slept; and (7) avoid napping in the daytime. Over time, the repeated association of bedroom cues with rapid sleep onset brings sleep under the stimulus control of the bedroom environment [5].

These seemingly simple instructions are difficult to carry out regularly among many patients. Initially, patients will spend considerable time out of bed, and thus, suffer some sleep loss. It is important to motivate the patients by letting them fully understand the rationale of this treatment procedure. Although daytime functioning and mood may be impaired temporarily, the partial sleep deprivation will foster both rapid sleep onset and increased sleep. Further, the clinician may need to prescribe activities to perform during the night that are not too taxing or activating for the patients who do not know what to do when they are unable to sleep during the night.

7.3.4 Sleep Restriction Therapy

The basic assumption underlying sleep restriction therapy is that the homeostatic sleep process can self-correct sleep loss. Sleep restriction therapy promotes sleep by inducing mild sleep loss initially and gradually increasing sleep time after sleep is stabilized. On the other hand, this procedure, which is the same as the stimulus control therapy, can also break the maladaptive association between anxiety and bedtime cues by decreasing the chance of lying awake in bed [18, 57]. The specific procedures of this therapy are as follows:

- Patients complete a sleep log that records the daily sleep pattern over a 2-week period.
- The average total sleep time per night during this 2-week period is then prescribed as the time in bed for the following week. To avoid the effects of severe sleep deprivation, the minimum time in bed is never set below 4.5 h. Lying down or napping outside the scheduled bedtimes is not permitted.
- Patients fill out a sleep daily log to record bedtimes and estimated total sleep time. Sleep efficiency (SE) (estimated total sleep time/time in bed $\times$ 100%) is evaluated every week.
- Prescribed time in bed is adjusted by three criteria: (1) when the mean SE is equal to or more than 90% (85% in older individuals), then the subject's time in bed is increased by 15 min by setting the retiring time earlier; (2) if the mean SE is less than 85% (80% in seniors), the time in bed is decreased by 15 min; and (3) when the SE is between 85 and 90% (80–85% in seniors), then the time in bed remains the same.

Some modified procedures to adjust time in bed have been proposed and utilized. One way is to increase the time in bed progressively by 15 or 30 min each week until the patient is spending 7 h in bed. Further changes of time in bed may be made based on daytime functioning, fatigue, and sleepiness [54]. Further, a sleep compression

procedure has been utilized to gradually reduce time in bed in 5 weeks instead of curtailing it abruptly. This procedure was found to be helpful for elderly patients with insomnia [31].

Similar to the instructions for stimulus control therapy, patients should be told to expect mild sleep loss and daytime deficits at the initiation of the treatment. It should be stressed that short-term sacrifice will produce long-term gains. Patient may have difficulty resisting the temptation to go to bed earlier than the preset schedule. Clinicians should provide the rationale and encourage the patient to continue following the instructions. For some patients, it may be necessary to plan specific activities to increase their time in the evening before going to bed.

7.3.5 Relaxation Training

As described earlier, thoughts and behavior resulting in arousal may interfere with sleep. For the same reasons, relaxation training, aiming to reduce arousal, may facilitate sleep. Various relaxation techniques have been developed to assist in the reduction of tension and anxiety. Many of them have been utilized in the treatment of insomnia, such as progressive muscle relaxation that reduces muscle tension by sequential tensing and relaxing of the main muscle groups [7, 47], autogenic training that produces somatic relaxation by inducing sensations of warmth and heaviness of the body [47], and guided imagery that aims to channel mental processes into a vivid story line [65]. Biofeedback has also been utilized to assist the mastering of relaxation techniques and has generated positive results [23, 25]. Relaxation training usually starts with a demonstration of how the procedure is carried out. The patients are then instructed to practice the technique once or twice a day at home in between sessions. The instructions of the relaxation procedures can be recorded during the session for the patients to practice at home. Commercial relaxation training CDs are also available to facilitate practice at home. It is suggested that a patient's level of relaxation should be assessed before and after each practice session in order to monitor the progress of the training. It may take weeks for some individuals to be able to relax on cue. Only after mastering the procedure is the patient told to use it to facilitate falling asleep at the beginning of sleep or following a nocturnal awakening. It is crucial to help motivate the patients to continue practicing the technique and to help them deal with obstacles they encounter.

7.3.6 Light Therapy

Light therapy is often included as part of a comprehensive CBT-I program especially for those patients whose contributing factors include the misalignment of endogenous circadian rhythms with environmental time. Exposure to bright light has been shown to shift the phase of circadian rhythms. The magnitude and direction of the

phase shift depend on the intensity and timing of the exposure [10, 35]. In general, morning light exposure in individuals following a nocturnal sleep schedule will tend to advance the circadian sleep phase. Evening light exposure, by contrast, tends to delay the circadian sleep phase.

7.4 Information Technology and CBT-I

Although the treatment efficacy of CBT-I has been well established by empirical studies, the application of CBT-I in the clinical field is limited by an insufficient number of well-trained professionals to administer this treatment. In addition, the arrangement to see a therapist once or twice a week for several consecutive weeks is not feasible for individuals with busy schedules. Self-help approaches or telephone consultations to reduce costs and improve accessibility have been evaluated in research. One study demonstrated that group therapy and telephone consultations were as effective as individual therapy [2]. Many forms of self-help approaches, such as bibliotherapy with or without minimal professional guidance, have also shown to be effective [1, 34, 36]. The effect of self-help treatments was found to be nearly equal to individual and group treatments, and was improved by adding telephone consultations [30, 39].

With the rapid development of information technologies and the accessibility of the Internet, several studies have evaluated self-help treatment for various conditions through the Internet (e.g. [9, 52, 61]). In one study of insomnia, 109 insomnia patients were randomly assigned to an Internet-based self-help CBT-I treatment or a waiting-list control condition. The CBT-I treatment includes sleep restriction, stimulus control, and cognitive restructuring. Sleep log data were completed for 2 weeks before and after the 5 weeks treatment. It showed that total sleep time, total wake time in bed, and SE were significantly improved in the CBT-I self-help treatment [59]. Another study evaluated the effect of a self-help sleep-improving program that adopted part of the concept and technique of CBT-I. Forty-three subjects recruited through a website were randomly assigned to two groups—an intervention group and a waiting list group. The intervention group participated in a 2 weeks Internet-based program that provided advice for sleep-related daily practices and monitored those behaviors along with sleep quality. The results showed that the Internet-based self-help programs improved subjective sleep quality and sleep-onset latency [60]. A recent study further confirmed the efficacy of intervention through the Internet for patients with insomnia. Forty-five insomnia patients were randomly assigned to an Internet intervention or a wait-list control group. The Internet intervention program incorporated the primary components of CBI-I, including sleep restriction, stimulus control, sleep hygiene, cognitive restructuring, and relapse prevention. The results showed that scores on the Insomnia Severity Index, wake after sleep onset, and SE were significantly improved in the Internet group but not in the control group [53].

7.5 Summary

Insomnia is a condition with a high prevalence. Although nonpharmacological treatment is available, most insomnia sufferers may not have access to the treatment. This limitation may be resolved by the rapid development of information technology. Although preliminary studies have shown promising results with Internet-based CBT-I programs, those studies lacked good controls. Future studies with better controls and more rigorous protocols are needed to clarify those questions and substantiate its effectiveness. Further, these programs primarily used the Internet to provide information and contact patients. Future research should utilize advanced technology not only to deliver the CBT-I material but also to evaluate the patients and facilitate the practice of CBT-I techniques at home.

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Chapter 8
Management of Sleep Disorders: Light Therapy

Wei-Chung Mao, Hsin-Chien Lee, and Hsi-Chung Chen

Abstract The circadian system in humans encompasses all organs, tissues and cells. Coordination of central and peripheral clocks and synchronization of cellular clocks within the brain regulate daily phases, neurophysiology and behavior. The mechanism of action of the circadian system is complex, but is centered on the paired structure of the suprachiasmatic nuclei (SCN) that serves as a pacemaker in humans. Light adjusts the phase of the SCN oscillator to the environmental light-dark cycle. Light therapy has been developed for clinical use and many apparatus and parameters have been extensively studied. Bright light therapy is the treatment of choice for seasonal affective disorder and circadian rhythm sleep disorders. Cumulative studies support the efficacy of light therapy for some clinical conditions which are characterized by seasonality or disrupted circadian rhythms. The benefit of light therapy is significant and warrants further clinical studies to optimize the treatment effect.

Keywords Bright light therapy • Suprachiasmatic nucleus • Circadian rhythm • Seasonal affective disorder • Depression • Antidepressant effect

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8.1 Introduction

Light therapy, or phototherapy, is used as monotherpay in some sleep disorders, especially in those related to disturbance of circadian rhythm, but has become increasingly popular as adjunctive treatment to pharmacotherapy. Light therapy includes the use of ultraviolet light to treat psoriasis and other skin disorders, and full-spectrum bright light to treat seasonal affective disorder (SAD). The latter, first introduced in the 1980s, is now a widely approved form of treatment for SAD [1, 2].

The effects of light therapy are comparable to those found in many antidepressant pharmacotherapy trials [3]. In the last two decades, many research groups have launched clinical trials which have resulted in light therapy being extended to other conditions, including non-seasonal mood disorders, Alzheimer's disease, circadian-related sleep disorders, jet lag, eating disorders, shift-workers, and other behavioral syndromes [3–9]. Although a meta-analysis on the efficacy of light therapy in treating mood disorders [3] highlighted methodological limitations in some clinical trials which included brief treatment periods, small study groups, lack of replication, and study design issues (e.g., lux parameters for the active treatment, characteristics of placebo control, and random assignment to treatment conditions), it nonetheless concluded that bright light treatment and dawn stimulation for SAD, and bright light for non-seasonal depression are efficacious [10].

This chapter focuses on the application of bright light therapy in order to improve the understanding of its mechanisms as exploratory treatment for specific disorders. Light plays a major role in influencing the retino-hypothalamic tract to the suprachiasmatic nuclei (SCN), and in adjusting melatonin secretion. The SCN is intrinsically photosensitive, communicating with the dorsomedial hypothalamic nucleus (DMH) to regulate the circadian pattern of sleep-wakefulness, feeding, locomotor activity, and serum corticosteroid levels [11]. The DMH receives both direct and indirect SCN inputs and sends a predominantly GABAergic projection to the sleep-promoting ventrolateral preoptic nucleus, and a primarily glutamate-thyrotropin-releasing projection to the wake-promoting lateral hypothalamic area, including orexin (hypocretin) neurons [11]. In human, the 24-h circadian rhythm shifts through its daily phase mostly as a result of light exposure. The accumulated amount of light exposure alters the sleep-wake cycle and regulates the autonomic nervous system, the endocrine system, and internal homeostasis. Longer period is found for totally blind individuals, whose circadian pacemaker cannot be entrained by the environmental light-dark cycle. Pagani et al., hypothesized that circadian properties between blind and sighted groups differed for physiological reasons rather than genetic ones. Under certain circumstances these blind individuals can become entrained to the 24-h day via nonphotic cues such as exercise, food, and activity [12].

Light itself has a therapeutic effect on depression. The underlying mechanism has been associated with the phase shift [13–15] and more specifically, its effect on monoamine activity in the brain [16, 17]. Some studies manipulating these factors directly or indirectly suggest that light therapy attenuates depression [18–20].

Minimal adverse responses and promising treatment outcomes are encouraging for its clinical application. Light therapy has been applied to seasonal affective disorder, non-seasonal depression, bipolar depression, circadian rhythm sleep disorders, shift work, and specific conditions such as bulimia nervosa, late luteal phase dysphoric disorder (LLPDD), attention deficit hyperactivity disorder (ADHD), and dementia. However, its use for some of these conditions warrants further studies to demonstrate its validity and efficacy.

8.2 Mechanism of Action

Circadian rhythms include sleep-wake cycles that are endogenously driven by the SCN in the anterior hypothalamus. Light is the most potent external influence that can adjust the phasing of the SCN, and light therapy is mainly used to reset the circadian system. The SCN is functionally subdivided to generate a coordinated rhythm of neuronal and hormonal activities. Such activities incorporate photic and nonphotic time cues that reset the circadian phase of the SCN itself, and transmit circadian output signals to effector systems such as other brain regions and peripheral organs [21]. Outputs include neuronal connections, endocrine signals, body temperature rhythms, and indirect cues, provoked by oscillating behavior (e.g., feeding-fasting rhythms generated by rest-activity cycles). The SCN acts as a circadian pacemaker, and serves as a central station for processing top-down coordination. It is therefore associated with synchronizing circadian rhythms within other biological systems with daily changes in the environment (e.g., fluctuations in light intensity and temperature) [21]. This ever-regulating process entrains the nearly 24-h rhythm of internal activity in the SCN to the 24-h light-dark cycle given by the Earth's rotation ("circa diem" means "approximately a day").

8.2.1 Ocular Mechanism

The photoperiod is the most dominant environmental Zeitgeber (time giver) for the phase entrainment of circadian oscillators. Light enters the visual system and further alters the phase of 'clock' gene expression in a subset of SCN neurons (Fig. 8.1). The visual system consists of the eye (in particular the retina), optic nerve, optic

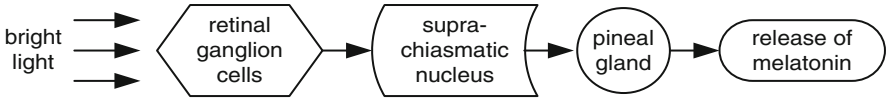

Fig. 8.1 Circadian system includes neuronal and hormonal activities

chiasma, optic tract, lateral geniculate body, optic radiation, visual cortex, and visual association cortex, all of which enable people to see. By this system, information from visible light is interpreted to an assembled representation of the outside world.

Mammals perceive light information mainly via the retina of the eye, where non-image- forming photoreceptors termed photosensitive retinal ganglion cells (pRGC), which express the photopigment melanopsin [22, 23]. Photic information reaches the SCN directly from the retino-hypothalamic tract (RHT) and indirectly through other retinorecipient structures, including the intergeniculate leaflet (IGL) in the thalamic lateral geniculate nucleus (LGN) [24].

8.2.2 Suprachiasmatic Nucleus (SCN)

The SCN is located at the base of the hypothalamus. SCN neurons display intrinsic circadian oscillations, orchestrated at the molecular level by translational and transcriptional loops in specific 'clock' genes [25, 26]. The rhythm in the SCN is conveyed to various endogenous neural systems governing physiologic and behavioral functions [27]. It remains unclear how SCN neurons actually communicate with their CNS target neurons. Understanding how these neurons are functionally connected will illuminate the mechanism of circadian rhythm and its regulation.

Based on differences in chemoarchitecture, peptide phenotype and afferent-efferent projection pattern, the mammalian SCN consists of ventrolateral (SCNvl) and dorsomedial (SCNdm) components [24]. There are three major afferent pathways to the SCN in rats: one from the outside photic input via the RHT, and two from nonphotic inputs of the IGL (via geniculo-hypothalamic tract, GHT), and serotonergic (5-HT) inputs from the dorsal and median raphe nucleus (DRN and MRN, Fig. 8.2). The monosynaptic RHT fibers terminate directly on neurons in the SCNvl that express vasoactive intestinal polypeptide (VIP). This photic signaling pathway of the RHT mainly expresses the excitatory neurotransmitter glutamate and the neuropeptide pituitary adenylate cyclase-activating protein (PACAP) [28]. The RHT projects to both the SCN and IGL, while the IGL projects to the SCN via the GHT. Thus, the GHT can indirectly involve processed light information by releasing neuropeptide Y (NPY) and gamma-aminobutyric acid (GABA) [29]. As such, the SCN receive two different triggers upon light stimulation of retina: one directly via the RHT and the other indirectly via the GHT. This suggests that the pathway via the IGL enables integration of photic and non-photic signals to entrain the SCN. In terms of the day-night switch, it is posited that the RHT relays photic information from the eyes to the SCN to adjust circadian timing via a glutamatergic pathway at night, and then adjusts the biological clock by a PACAP/cAMP- dependent mechanism during the daytime [28].

To function as a circadian pacemaker and master synchronizer, intrinsic time-keeping signals from the SCN must be transmitted to other brain and peripheral clocks. Efferent connections from the SCN have been identified by injecting antero-

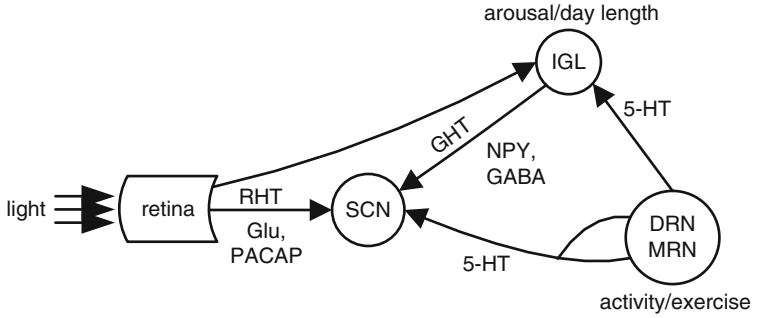

Fig. 8.2 Main afferent pathways to the SCN in rats. *5-HT* 5-hydroxytryptamine, *DRN* dorsal raphe nucleus, *GABA* gamma-aminobutyric acid, *GHT* geniculohypothalamic tract, *Glu* glutamate, *IGL* intergeniculate leaflet, *MRN* median raphe nucleus, *NPY* neuropeptide Y, *PACAP* pituitary adenylate cyclase-activating peptide, *RHT* retino-hypothalamic tract, *SCN* suprachiasmatic nuclei (Modified from Dibner et al. [21])

and retro-grade tracers. In the hypothalamus, efferent fibers from the SCN terminate most densely to the subparaventricular zone (SPZ or sPVZ), which is located immediately dorsal to the SCN and extends dorsocaudally to the paraventricular hypothalamic nucleus (PVH) [24, 30, 31]. Tracing studies suggest that the SCNvl projects predominantly to the lateral SPZ, whereas the SCNdm projects more densely to the medial SPZ [32]. Other SCN projections have been identified rostrally in the preoptic area (POA), bed nucleus of the stria terminalis (BNST), and the lateral septum (LS); and dorsally in the dorsomedial hypothalamic nucleus (DMH), and the arcuate nucleus (ARC).

It is postulated that the SPZ functions as an amplifier of circadian output from the SCN. In studies of fetal SCN grafts, transplanted SCN tissue can be implanted into many brain areas to restore rhythms [33, 34]. However, cell-specific lesion experiments show that ventral SPZ injury causes a profound reduction in the circadian rhythms of sleep and locomotor activity, while dorsal SPZ lesions caused greater reductions in the circadian index of body temperature [35]. Lesions of the PVH had no significant effect on any measured circadian rhythms. These findings suggest that the SPZ is part of the primary neuronal pathway mediating the output of SCN-generated circadian rhythms.

The SCN also controls the autonomic nervous system (ANS); SCN neurons that project to PVH are important target areas of biological clock output. They also harbor the pre-autonomic neurons that control peripheral sympathetic and parasympathetic activities [36]. A direct projection from the SCN to the PVH mediates rhythmic control of melatonin secretion from the pineal gland, while an indirect projection via the DMH is critical for the circadian release of corticosteroids [37]. Metabolic activity and glucose uptake in the SCN are dependent on time [36] as well as on expression of clock genes [38]. Kalsbeek et al. have proposed that the SCN generates a daily rhythm in plasma melatonin concentration via the combination of a continuous (glutamatergic) stimulation of neurons in the PVH

that are at the root of sympathetic innervation of the pineal gland, as well as a nocturnal withdrawal of the inhibitory (GABAergic) SCN inputs to these neurons. In Kalsbeek's study, activation of PVH neuronal activity induced hyperglycemia. However, such physiological changes are time-dependent and can be caused by GABA-antagonists only when administered during the light period. Likewise, feeding-induced plasma glucose and insulin responses are suppressed by inhibiting PVH neuronal activity only during the dark period. These results suggest that the pre-autonomic neurons in the PVH are controlled by the interplay of inhibitory (GABAergic) and excitatory (glutamatergic) inputs. At the same time, the timing information of both sympathetic and parasympathetic pre-autonomic PVH neurons is provided mainly by the SCN GABAergic outputs [36].

The DMH projects to brain areas involved in the regulation of the sleep-wakefulness switch that includes a primary GABAergic projection to the ventrolateral preoptic nucleus (VLPO). The VLPO, located in the anterior hypothalamus, is thought to promote sleep via its inhibitory projections to the ascending monoaminergic arousal system [39]. The DMH sends a predominantly glutamatergic projection to the lateral hypothalamus (LHA) which harbors the wake-promoting population of orexin-expressing neurons [11]. Briefly, the DMH receives circadian input directly from the SCN and indirectly via the SPZ, and extends to the VLPO and LHA to regulate sleep-wakefulness cycles (Fig. 8.3). The transmission of SCN circadian signals in the SPZ and then the DMH may allow for alteration of circadian rhythms by other inputs, such as food availability, external temperature, or social cues.

8.2.3 Light and Circadian Rhythms

Light synchronizes or entrains the internal clock to the 24-h period, with precision accomplished though daily phase shifts (a move to either an earlier or a later time of the day) resulting from light exposure [40, 41]. The effect of light on circadian rhythms follows a so-called phase-response curve (PRC) [42] that quantifies the phase dependence of light-induced phase shifts obtained by a PRC. The effect of light on the direction of a phase shift depends on the time of the day, and intensity and duration of exposure. Using this mechanism of a PRC, light can have two conflicting effects on circadian rhythm [43]. When light exposure occurs in the evening, it tends to phase delay with rising effects through the night. However, after core body temperature reaches nadir, light exposure tends to have the opposite effect of phase advance. Thus, applying bright light in the morning has an advancing effect on patients with delayed sleep phase syndrome.

The intensity and duration of light exposure follows a dose effect on the impact of phase shift. Bright light of 2,500 lux has been previously regarded as an intensity threshold to suppress nighttime melatonin production in humans. As such, brighter light and longer light exposure means greater suppression [44]. However, it is now

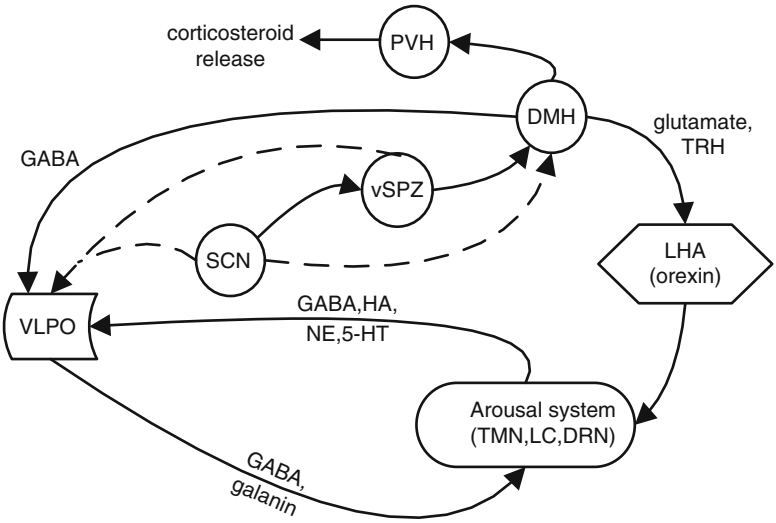

Fig. 8.3 Circadian regulation of sleep-wakefulness: *Solid arrows* indicate prominent neuronal projections and *dashed arrows* indicate relatively minor projections. *5-HT* 5-hydroxytryptamine, *DMH* dorsomedial hypothalamic nucleus, *DRN* dorsal raphe nucleus, *GABA* gamma-aminobutyric acid, *HA* histamine, *LC* locus coeruleus, *LHA* lateral hypothalamic area, *NE* norepinephrine, *PVH* paraventricular hypothalamic nucleus, *SCN* suprachiasmatic nuclei, *TMN* tuberomammillary nucleus, *TRH* thyrotropin-releasing hormone, *VLPO* ventrolateral preoptic nucleus, *vSPZ* ventral subparaventricular zone (Modified from Gooley and Saper [24])

suggested that low intensity (e.g. 180 lux as from an ordinary room light or even the light from a television set) has the potential to cause phase shifts [43, 45, 46]. This is clinically important for patients with delayed sleep phase syndrome, since even the dim light from a computer or a TV set may be a factor that impedes sleep onset. Given its phase-shifting properties, light is used for the management of different conditions, such as delayed sleep phase syndrome, advanced sleep phase syndrome, shift work, sleep maintenance insomnia, and seasonal affective disorder [47–50]. Light can be delivered using natural sources or light boxes with standard intensity of 10,000 lux for 30 min [51]. Their efficacy also depends on the distance from the light source to retina and duration of light exposure.

Melatonin is synthesized by the pineal gland, as well as in the retina and gastrointestinal tract. Control of melatonin secretion relies on neural input to pinealocytes in the pineal gland, which mainly contain adrenergic receptors, hence beta-blockers such as propranolol and atenolol can reduce the effects of melatonin. Melatonin secretion is similar in men and women, but gradually decreases in magnitude with aging after adolescence [52]. Melatonin has two main effects: a direct hypnotic effect on sleep and an effect on the circadian oscillator [53]. Light has a dose-dependent inhibitory influence on melatonin, and the SCN has a high density of melatonin receptors that modulates phase shifting via melatonin.

8.2.4 Antidepressant Effect of Light Therapy

Lewy proposed the phase-shift hypothesis (PSH), which posits that the depression seen in seasonal affective disorder (SAD) patients is as a result of a phase delay of the endogenous circadian oscillator relative the sleep-wake cycle [15]. Corroborating this hypothesis, the circadian rhythm of body temperature, melatonin, and cortisol secretion are known to be phase-delayed in SAD patients compared to controls [13, 14]. Administration of bright light in the morning, but not in the evening, is considered therapeutic because it corrects the abnormal delay in seasonal depression. In studies on morning versus evening light exposure for the antidepressant response of light therapy, 1-week phototherapy in early morning was superior than either in the evening (responding rate: 53% vs. 38%), dim light (11%), or brief light control [54]. In a another study, there was a positive association between lowered mood in winter and winter phase delay among a random community sample [55]. However, the degree of clinical improvement does not appear to correlate with baseline circadian phase or the degree of phase change associated with treatment [56–59]. These studies are therefore inconclusive as to whether circadian phase advance mediates the therapeutic mechanism in SAD patients. Lewy has since clarified the PSH and proposed that light treatment operates not by advancing circadian phase per se, but by normalizing the phase angle between sleep and circadian rhythms [60]. This revised hypothesis is supported by some studies [18, 61], but more sophisticated approaches that focus not only on phase shift in circadian rhythm, but also neurotransmitter activity are warranted.

The monoamine hypothesis of SAD has been another focus of interest in the past decade. Monoamine systems includes dopaminergic (DA), noradrenergic (NE) and serotonergic (5-HT) neurons. The treatment response to bright light was comparable to heterocyclic antidepressants and monoamine oxidase inhibitors (MAOI) [16]. Light deprivation for 6 weeks damaged monoamine neurons, in particular those located in the locus coeruleus (LC), and produced a depressive behavioral phenotype in rats. It was also found that the antidepressant desipramine decreased these neural and behavioral impacts of light deprivation [19]. These studies suggest an important link between the antidepressant effect of light therapy for SAD, and an underlying pathogenesis involving monoamine neurotransmitters.

Other studies suggest that the therapeutic effects of bright light in SAD may involve a serotonergic mechanism. As early as the 1980s, atypical symptoms in SAD patients, such as hyperphagia, carbohydrate craving or hypersomnia, were found to be associated with a dysfunctional serotonergic system [17]. Using the paradigm of tryptophan depletion (to deplete serotonin in humans), deficits in the brain serotonin system were found to play a key role in the pathogenesis of SAD, and it was hypothesized that light therapy may compensate for these underlying disturbances [62]. Serotonergic stimulation induces phase-shifting effects, and studies have demonstrated that tryptophan depletion did not worsen depression in untreated SAD patients, but by contrast, induced transient depressive relapses in stable patients who had received successful light therapy [20, 63, 64]. Sleep deprivation is a condition of reducing sleep time and not having enough sleep. Total sleep deprivation (TSD)

and light therapy could enhance these 5-HT effects. In another study on bipolar depression, repeated TSD and morning light therapy were used as intervention therapy. In this 1-week treatment study with a before/after comparison of biological correlates, the responders (about two-thirds of the patients) showed an increase in daytime activity, reduced nighttime sleep and phase-advance of the activity-rest rhythm for 57 min compared to the pre-treatment baseline [18]. These results support the hypothesis that the antidepressant effects of light are partly mediated via serotonergic systems.

8.2.5 Side Effects of Light Therapy

The side effects of light therapy are small and usually temporary, and can be generally remedied by reducing exposure time. The appearance of side effects relates in part to the parameters of light exposure, including intensity, duration, spectral content, and methods of exposure (diffuse vs. focused, direct vs. indirect, as well as angle of incidence relative to the eyes). The most common side effects are headache and eye/vision problems (strain, excess glare, seeing spots, blurring and irritation) [65]. Other side effects include nausea, sedation, dizziness, irritability or tightness in the chest. Unless the patients are in severe discomfort, these side effects are generally well tolerated. Eye discomfort can be alleviated by sitting farther from the lights, taking a shorter period schedule, or by installing a humidifier. Bright light may worsen pre-existing eye problems or cause a skin rash in patients with a skin condition, and requires caution if glaucoma, cataracts, retinal detachment or retinopathy is reported by patients. The most profound side effect is a mood switch to hypomania with difficulty sleeping, becoming restless or irritable, and feeling speedy or “too high”. Nevertheless, such a change occurs quite infrequently [66]. Another rare complication of light therapy for SAD is suicidal tendencies; some cases have been reported [67].

8.3 Practical Aspects of Bright Light Therapy

Since the introduction of artificial bright light for the treatment of winter depression in 1984 [2], several protocols and apparatus for bright light therapy have been developed and adopted across a variety of studies and clinical settings. Conventionally, bright light therapy means the administration of visible light producing at least 2,500 lux at eye level [68]. However, dosing and timing regimens still need to be established for each clinical condition. Even for SAD, which has been the most extensively studied in clinical trials, the basic protocol requires revision to accommodate the introduction of many new devices [69]. Staring from the apparatus, important parameters for bright light therapy such as light intensity, length of session, treatment duration, timing, and wavelength are reviewed and discussed in the following section.

8.3.1 Apparatus

The standard 60 by 120-cm fluorescent ceiling unit was used in many early studies [51]. This light box has a plastic prismatic diffusion screen and is placed vertically on the table about one meter from the user. It could provide approximately 2,500 lux illuminance to the eyes. Increasingly, more and more commercial products have been launched on the market, but not all of them have been tested through well-designed clinical trials. Some of these apparatus have not even been calibrated to demonstrate an equivalent output level to the standard light box. In fact, lamp type, filter, ballast frequency, radiating surface and heat emission differ among devices and could result in various outcomes.

Besides the light box, the light visor has been introduced for its convenience of use. With head-mounted ambulatory lighting units, the light visor provides bright light therapy without interfering with normal activities. An earlier multicenter clinical trial showed an antidepressant response to bright light therapy by using light visors [70]. In this 2-week randomized clinical trial, 105 patients with SAD received three intensities of light (60, 600, and 3,500 lux) delivered by the light visor. All three intensities produced a similar frequency of antidepressant response. Furthermore, Boulus and colleagues used a head-mounted light visor to demonstrate circadian phase shifting by bright light therapy [71]. They chose 20 individuals travelling from Zurich to New York (a westward flight across six time zones) and provided 3,000 lux bright white light or 10 lux dim red light for 3 h on the first two evenings after the flight. Results indicated a larger phase delay in the bright light group. However, the information regarding the clinical efficacy of the light visor remains scant. Thus, the use of light visors is not currently recommended [51, 68].

The light therapy room is another alternate configuration of bright light therapy and is usually applied in hospital settings. The light room setting provides full-spectrum light by fluorescent tubes in the ceiling and on the walls. There are white walls and light-colored furniture in the light room. Rastad and colleague studied the clinical efficacy in 50 patients with SAD randomized into light room therapy and waiting-list groups [72]. After 10 days of bright light treatment in a light therapy room, self-reported depression in subjects was reduced and the therapeutic effect was maintained after a 1-month follow-up. Still, more experimentally controlled studies are warranted to verify the clinical efficacy and safety of the light therapy room in other health conditions before recommendation. Currently, light boxes remain the mainstream device to deliver bright light therapy.

8.3.2 Intensity

In the early history of bright light therapy, 2,500 lux fluorescent illumination measured at eye level was the standard parameter for clinical protocols [2]. An earlier review by Terman and colleague indicated the clinical efficacy of 2,500 lux intensity light exposure for at least 2 h daily in the treatment of SAD by analyzing

332 patients in 25 studies [54]. Bright light therapy, with 2,500 lux illuminance, whether administrated in the early morning, evening, or midday, was shown to reduce depressive symptoms significantly compared to dim light controls.

Since a reciprocity between light intensity and duration has been found, a high-intensity fluorescent lighting system with 10,000 lux illuminance, having an irradiant dose estimated at 0.016 J/cm^2, was developed and clinically tested. Studies have shown that the clinical efficacy of 30 min of bright light treatment with the 10,000 lux illuminance is comparable to that of 2 h treatment with 2,500 lux illuminance recommended in earlier studies [73]. Because the 10,000 lux intensity of light requires less time than the former 2,500 lux apparatus to achieve the same therapeutic effect, high-intensity light therapy has been recommended as the standard treatment dose for SAD. As regards to some other health conditions, devices yielding a maximum illuminance of 10,000 lux have been adopted and demonstrate clinical benefit [74–76]. In addition, bright light therapy with intensities between 2,500 and 10,000 lux are still applied in some clinical settings [77, 78]. Although 30 min of bright light treatment with the 10,000 lux illuminance is widely adopted nowadays, recommendations for light therapy dose levels should be cautious since the data is changing rapidly [79].

Safety concerns for high-intensity light therapy, in particular the potential impact on the eyes, have been raised. Indeed, side effects including headaches and eye or vision problems have been reported, but were mild and transient and did not interfere with treatment [65]. Gallin and colleagues performed ophthalmologic examinations in 50 patients with SAD before and after bright light therapy for 30 min at an illuminance level of 10,000 lux [80]. They did not detect any ocular changes after either short-term or long-term treatment. Still, patients with pre-existing ocular abnormalities or using photosensitizing drugs were suggested to undergo light therapy only with ophthalmologic monitoring.

8.3.3 Length of Session and Treatment Duration

As stated above, daily light exposure for 30 min at an illuminance level of 10,000 lux gives an equal effect to 2-h light exposure at 2,500 lux for the treatment of seasonal affective disorder. Thus, the length of treatment session varies across studies mainly based on the intensity of the lighting system, but also dependent on the targeted symptoms or diseases [79].

Early studies suggested that treatment response might occur within 2–4 days, and achieve remarkable improvement within 1–2 weeks [2]. Comparing treatment response in bright light therapy at the first and second week, Labbate and colleagues suggested the necessity of longer trials of bright light therapy [81]. In a recent study, treatment durations as long as 5 weeks of 60 min 10,000 lux lighting was applied to patients with non-seasonal depression [82]. Furthermore, long-term bright light therapy of up to 2 years with daily light exposure is suggested for patients with mild cognitive impairment and early dementia [83].

8.3.4 Timing

Researchers have found that the greatest therapeutic effects are achieved when light therapy is administered in the morning. An early meta-analysis by Terman and colleagues showed a greater remission rate when bright light therapy was administered for patients with SAD in the early morning [54]. Although some researchers claimed that bright light therapy in SAD is independent of time of day or circadian phase [59], morning light was found to produce phase advances in melatonin rhythm [84]. Based on their findings, the administration of light therapy is suggested to be optimal about 8.5 h after melatonin onset or 2.5 h after the sleep midpoint to potentiate therapeutic effects. Thus, patients with SAD might be given bright light sessions shortly after awakening. Although some of them would oversleep and need to wake up earlier to take their light treatment [85].

A similar strategy is applied to other health conditions, except for advanced sleep phase syndrome. However, to ensure the timing of light exposure is appropriate for an individual's circadian rhythm, a simple solution is to apply the Horne-Östberg Morningness–Eveningness Questionnaire [86]. The score of this questionnaire correlates strongly with melatonin onset and can be used to estimate the optimal timing for bright light therapy [51, 69].

8.3.5 Wavelength

Initially, full-spectrum lights were used in bright light therapy. However, in addition to the intensity of light, ultraviolet and visible light could lead to ocular damage. Unfortunately, the potential hazard of ocular damage may still occur for unclear spectral emission of lamps. Reme and colleagues have reported irradiant doses for several bright light therapy regimens and analyzed the potential hazards [87]. They proposed screening out ultraviolet light and some low-wavelength visible light in a range up to 500 nm, which may potentially damage the eyes. Recently, a prismatic diffusion screen with ultraviolet filtering has become a standard component of bright light treatment devices. It has been demonstrated that ultraviolet light is not necessary for the clinical efficacy of bright light therapy in SAD [88].

Identifying optimal wavelengths for bright light therapy is important in optimizing clinical efficacy. Which spectral colors of light are the most efficient for treatment remains controversial, although shorter wavelength light has been shown to be more effective than longer wavelengths in suppressing nocturnal melatonin [89]. To balance the risk and benefit, filtering of wavelengths less than 450 nm might achieve clinical efficacy and lower the blue-light hazard, which is magnified in the range of 435–445 nm.

An earlier study by Oren and colleagues found that green light induced greater antidepressant effects than red light [90]. However, a later study on green light for elderly patients with depression did not show a significant antidepressant effect [91].

Recently, technological advancements in light emitting diodes (LEDs) allow for much narrower bandwidths of light, which enable more accurate and precise efficacy studies of different light wavelengths. Using blue LED units producing 468 nm light versus dimmer red light in a 3-week randomized controlled study, Glickman and colleagues demonstrated a significant therapeutic effect in a sample of 24 patients with seasonal depression [92]. A more recent study by Strong and colleagues verified the effectiveness of narrow-band blue light treatment in a 3-week, parallel, double-blind trial compared with red light [93]. They proposed that blue-light therapy could produce results similar to those of earlier 10,000 lux full-spectrum light studies and many medication studies.

However, although multiple blue-light devices have been developed under this concept, they require individual testing in clinical trials. In fact, there are still scant comparative dose-response studies to support the application of such blue-enriched device [94].

8.3.6 Other Considerations

Although more and more bright light therapy devices are available on the market, only some of them have been carefully evaluated in clinical trials. Besides the treatment protocols, comparing devices is difficult due to the problematic specification of lux, the dosing variable [51]. The power received from the light source could vary if the spectral composition of the light is different. Therefore, caution is required when choosing bright light therapy devices, and is preferable to make choices based on clinical evidence.

Another concern stems from patient's compliance. A study by Michalak and colleagues identified a high drop-out rate of 31.6% among patients with SAD [95]. Among those completing treatment, compliance to the prescribed duration of exposure averaged 83.3% in the 4-week protocol. How to improve patient's compliance in clinical practice by improving the convenience of the device and reducing adverse reactions, though not studied extensively, is indeed an important issue.

In summary, a prescription for bright light therapy of 30–120 min of daily exposure to a broad spectrum, ultraviolet-filtered 2,500–10,000 lux illuminance remains the typical for bright light therapy. New devices such as light visors, light therapy rooms and narrow-band blue light from LEDs require more evidence to support their clinical efficacy. At this moment, the dosing regimen and protocol are suggested to be tailored according to the needs of individual patient with various health conditions. In the next section, the application of bright light therapy in each clinical condition will be discussed individually.

8.4 Clinical Application of Bright Light Therapy

8.4.1 Seasonal Affective Disorder

Seasonal affective disorder (SAD) is a recurrent subtype of depression characterized by a predictable onset in the fall/winter months and spontaneous remission in the spring/summer period. Seasonal variations in affect, cognition, and drive occur in many individuals. Once these changes meet clinical severity and fulfill the diagnostic criteria for a major depressive episode, it can be determined whether the seasonal pattern is specified. Specified seasonal patterns can be regarded as patterns of Major Depressive Episode in Bipolar I Disorder, Bipolar II Disorder, or Major Depressive Disorder, Recurrent. Major depressive episodes that occur in a seasonal pattern are often characterized by prominent anergy, hypersomnia, overeating, weight gain, and craving for carbohydrates [96]. The prevalence of SAD in the general population is 2–4% in temperate climates and increases with higher latitudes [97]. Around 15–20% of patients with mood disorders have a seasonal pattern [68].

The pathogenesis of SAD remains unclear. Light insensitivity [98, 99], reduced ambient light during fall/winter [100] and disturbed monoaminergic pathways [17, 63, 101] are proposed in the pathophysiology of SAD. One leading hypothesis for SAD is the phase shift hypothesis. Lewy et al. [102] have provided evidence that the prototypical SAD patient is phase delayed [102]. Phase delays in the 24-h rhythm in cortisol [13], core body temperature [13, 103] and melatonin secretion pattern [13, 104] are also detected in SAD patients. Abnormal circadian patterns of melatonin secretion are also considered to play a central role in the pathophysiology and rationale for phototherapy of SAD [105]. A phase delay of melatonin secretion takes place in SAD, as well as changes in the onset [14], duration [106, 107] and offset [107] of melatonin secretion. These observations might partially explain the effectiveness of bright light therapy, which suppresses extended melatonin level production and provides a corrective phase advance in SAD patients. However, it could be a summation of different mechanisms that underlie how light works.

Bright light therapy is the treatment of choice for SAD [104]. A work group organized by the American Psychiatric Association (APA) Council on Research has assessed evidence for the efficacy of light therapy in treating SAD. Their meta-analysis reveals that a significant reduction in depression severity is associated with bright light treatment in SAD (eight studies, with an effect size of 0.84 and 95% confidence interval [CI] of 0.60–1.08) [3]. The effect size is comparable to those of most antidepressant pharmacotherapy trials. In addition, a randomized controlled study has shown that light room therapy is also effective in reducing depressive symptoms in subjects with sub-clinical SAD [72].

There are treatment guidelines for bright light therapy in SAD patients. Some guidelines suggest scheduling 1–2 h of 2,500–10,000 lux exposure immediately upon awakening [102]. In contrast, others recommend conservatively in treatment duration, i.e. not more than 30 min or a maximum of 1 h [51]. The treatment

response begins 2–4 days after the start of light therapy and it is usually completed within 2 weeks. If there is still no response, a trial of evening bright light (7–9 p.m.) may be necessary since a smaller subgroup of SAD patients may be phase advanced [108].

A further refinement of the timing of light relative to endogenous melatonin onset has also been proposed. Terman et al. have shown that within the favored morning interval, light administered 7.5–9.5 h after evening melatonin onset produces twice the remission rate (80% vs. 40%) of light presented 9.5–11 h after melatonin onset [84].

In a randomized controlled trial, cognitive-behavioral therapy (CBT), light therapy and both in combination significantly improved depression severity of SAD patients relative to the control group, but only the combination treatment had a significantly higher remission rate than the control [109]. However, light therapy alone had a higher 1-year recurrence rate than CBT and the combination treatment. One substantial problem may be non-adherence. Long-term compliance of daily light therapy during the symptomatic months each year is questionable, and self-reported adherence is unreliable [110]. A pilot study suggests that adherence to light treatment in SAD patients has a similar order of magnitude to antidepressant medication. Therefore, evaluating adherence to light therapy and evidence-based techniques for maximizing treatment adherence are suggested in clinical practice [95].

The treatment efficacy of SAD using novel LED devices with 1,350 lux white light has been demonstrated in a randomized, double-blind, placebo-controlled trial [111]. An early meta-analysis suggests that light of short-to-medium wavelengths (blue/green/yellow) may be essential for the therapeutic effect of light on SAD [112]. Furthermore, recent evidence supports claims that wavelengths of 470 nm account for the documented effectiveness of light therapy. Glickman et al. [92] report a placebo-controlled parallel trial of SAD comparing blue-light (blue LED units producing 468 nm light at 398 lux) with dim red-light (red LED units producing 654 nm light at 23 lux). This 3-week study showed that narrow bandwidth blue light outperforms dimmer red light in reversing the symptom severity of SAD [92].

In addition to better alleviation of depression symptoms, another recent randomized, double-blind, placebo-controlled trial also showed that treatment with narrow-band blue LED panels has a better response rate (60%) (Clinical Global Impression-Improvement ≤ 2) compared to treatment with red LED panels (13%) in SAD patients [93]. In the future, determining the potency of narrow-band short wavelength light relative to current standard treatment and other comparable conditions (e.g. narrow-band short wavelength light with equal photon density compared to broad-spectrum white light) is needed.

8.4.2 Non-seasonal Depression

The early hypothesis that light therapy specifically enables SAD patients to overcome long winter nights tends to overlook its use in non-seasonal depression

[69]. Interestingly, in recent years, cumulative evidence tends to support the use of light treatment alone for non-seasonal depression [113–118] or combined with antidepressants [119–124]. Nonetheless, applications for other forms of non-seasonal depression, such as antepartum depression [125, 126], postpartum depression [127–130], and chronic depression [114], also show promise.

In fact, seasonality lies on a continuous spectrum rather than on distinct all-or-none categories [131]. In clinical observations, recurrent or chronic depression can occur at any time of the year but are usually exacerbated in winter. Therefore, non-seasonal depressions also manifests some seasonality, which may be the key to the treatment response from light therapy. In addition, depressive symptoms usually hinder normal social activities. Long-term absence of zeitgebers that entrain the internal clock to local time can further delay the circadian rhythm phase. Such delays may be causes of depression by themselves regardless of the season [69] and may explain the efficacy of light therapy for non-seasonal depression.

The APA work group has also examined the efficacy of light treatment for non-seasonal depression, both alone and as an adjuvant to antidepressants [3]. This meta-analysis of efficacy studies for light therapy alone in non-seasonal depression in the period 1975–2003 shows reduced significant reduction in depressive symptoms (effect size 0.53; 95% CI = 0.37–1.08; only three studies fulfilled the strict criteria for inclusion in the meta-analysis). In contrast, adjuvant light therapy in non-seasonal depression does not show significant efficacy (five studies; effect size = −0.01, 95% CI = −0.36 to 0.34). The heterogeneity of the methodology used in these studies, i.e. light intensity, duration of daily light, color of light and trial duration, is the major limitation in the general applicability of this negative finding [68]. After refining the inclusion criteria and recruiting up-to-date large studies [122, 123], a later systematic review has reversed this conclusion and offers evidence for the efficacy of light therapy as an adjuvant treatment to antidepressants [10]. However, most of the extracted studies poorly controlled the issue of blindness and are still limited by small sample sizes. Overall, light therapy alone or as adjuvant strategy for non-seasonal depression has vast potential. Future clinical trials should evaluate the differential efficacy for heterogeneous subgroups of patients with non-seasonal depressions.

8.4.3 Bipolar Depression

Bipolar depression is one of the most difficult psychiatric conditions to treat. A series of studies have been conducted to investigate the mechanisms and efficacy of chronotherapeutic interventions on bipolar depression [18, 132–135]. Neumeister et al. suggest bright light therapy may stabilize the antidepressant effect of partial sleep deprivation [136]. Subsequently, it was found that the combination of total sleep deprivation and light therapy in bipolar depression causes rapid antidepressant effects and its mechanism of action reportedly involves the phase advance of biological rhythm [18] and the enhancement of all monoaminergic systems targeted

by antidepressant drugs [132, 135]. Benedetti et al. [133] combined 1-week administration of bright light therapy, three nights of total sleep deprivation, and concurrent antidepressants and lithium salts in the treatment of drug-resistant and non -resistant bipolar depression. Overall, 70% (23/33) of non-resistant versus 44% (12/27) of drug-resistant patients achieved response, with 57% (13/23) of non-resistant and 17% (2/12) of drug-resistant responders becoming euthymic after 9 months. These results suggest chronotherapeutic intervention with existing pharmacotherapy has remarkable success in managing bipolar depression even though drug-resistant responders are significantly more likely to relapse over the follow-up period [133]. Whether or not the maintenance regimen of light therapy helps prevent a relapse of depression in the long-term remains unknown.

Meanwhile, treatment parameters associated with light therapy for bipolar depression should be more carefully adjusted than those of SAD. The reported efficacy and does-range safety in nine women with long-standing non-seasonal bipolar I or II disorder in which mood stabilizers controlled the manic phase, but antidepressants did not relieve the depression phase, showed that three of four subjects treated with morning light developed mixed states [137]. To decrease the risk of inducing mixed episodes, the time of light exposure was changed to midday. Of the five women who received midday light therapy, two achieved full response and two exhibited early improvement but required a dose increase to sustain response. Obviously, this case series is a reminder of the substantial risk of inducing mixed states by light therapy in women with bipolar depression. Initiating treatment for a brief duration (15 min) of midday light for bipolar depression is advised [137].

8.4.4 Circadian Rhythm Sleep Disorders

Disorders of the circadian timing system are known as circadian rhythm sleep disorders (CRSD). According to the International Classification of Sleep Disorders, version II (ICSD-2), the essential feature of CRSD is a persistent or recurrent pattern of sleep disturbance due primarily to alternations in the circadian time-keeping system or a misalignment between the endogenous circadian rhythm and exogenous factors that affect the timing or duration of sleep. The etiology of this syndrome is multi-factorial such that biologic, psychosocial, and environmental factors all contribute to this syndrome [138]. In ICSD-2, CRSD is composed of six distinct disorders, namely: (1) delayed sleep phase type (DSPT), (2) advanced sleep phase type (ASPT), (3) irregular sleep-wake phase type, (4) free-running type, (5) jet lag type, and (6) shift work type.

The prevalence of CRSD is unknown, especially since there are few community-based epidemiologic studies. In Japan, a two-stage nationwide epidemiology survey estimated the prevalence of DSPT to be 0.13% (age, 15–59 years) [139]. Another study that combined formal diagnostic criteria with an epidemiologic sample suggests that the prevalence of shift work type CRSD is approximately 10% in the

night and rotating shift work population [140]. More consistently, DSPT is the most common syndrome (71–85%) in patients with CRSD [141–143].

The light-dark cycle is the principle time cue for resetting human circadian rhythms. In healthy subjects, the most sensitive phase of PRC to light coincides with sleep, while the timing of the monophasic sleep-wake cycle is itself a major determinant of light input on the pacemaker [138]. Theoretically, precisely timed white light of suitable intensity and duration will both phase advance and phase delay circadian rhythms according to a PRC [144, 145]. The rationale of light therapy for CRSD is based on these patterns of human PRC to light, even though clinical application remains empirical. In general, bright light exposure before the core body temperature minimum causes phase delay, and bright light exposure after core body temperature minimum causes phase advance of the circadian rhythm. However, the minimum or optimal intensity or duration of light therapy for each CRSD remain unknown [79].

DSPT that occurs when the circadian timing system is altered relative to the external environment, is a representative syndrome of CRSD. Initiating insomnia accompanied by difficulty awakening in the morning is the typical manifestation. Although evidence is limited, a review by the American Academy of Sleep Medicine (AASM) suggests that light therapy may be a rational and effective intervention for DPST [146]. Practice parameters have been recommended by an earlier clinical guideline, which was reviewed and approved by the AASM in 1999. Bright light therapy with 2,000–2,500 lux from 6 to 9 a.m. is advised. Based on patient tolerance and preference, either a fixed regimen (i.e. based on targeted awakening timing) or a "nudging" technique (i.e. step-by-step phase advance of awakening timing) can be administered. Wearing dark goggles from 4 p.m. to dusk is an optional combination strategy [68, 79].

However, the sleep-wake cycle does not necessarily correlate with the circadian phase in severely afflicted individuals. Early morning light may be unintentionally given on the delayed part of the PRC and worsen the problem [147]. In addition, non-adherence also compromises the practicality of bright light therapy for DSPT because many individuals find it difficult to wake in time for the treatment [148]. Similarly, ASPT is a disorder wherein the patient's sleep episode is advanced relative to the desired clock time. This syndrome is characterized by falling asleep in the evening and awakening earlier than desired. Effective approaches include 2,500 lux from 8 p.m. to midnight, or 4,000 lux from 8 or 9 p.m. to 11 p.m., which have been validated in the elderly [48, 149].

Another group of CRSD where the physical environment is altered relative to internal circadian timing is shift work and jet lag. Although rationale and simulation studies [150–155] for this group indicate bright light therapy as a potential treatment modality, practical application studies are limited. For shift workers, there are insufficient field studies that evaluate the long-term effectiveness of timed bright light therapy. Moreover, incorporating bright light treatment into the workplace seems difficult. As for jet lag, there is even less evidence [4, 79, 156] and fewer randomized controlled trials.

8.4.5 Bright Light Therapy in Specific Populations

Since bright light therapy is tuned into clinical conditions with symptom seasonality or desynchronized circadian rhythms, some specific populations may theoretically benefit. For example, bulimia nervosa and LLPDD patients are observed to have winter exacerbation of mood symptoms. Previous studies successfully demonstrated the effectiveness of bright light therapy for these two disorders [74, 157, 158].

In addition to a higher rate of winter depression, individuals with adult ADHD manifest later circadian preference [159, 160]. In the fall/winter period, a mood-independent delay in circadian phase is noted to contribute to the core pathology in many adults with ADHD [161]. Hence, effectiveness of light therapy for adult ADHD is hypothesized. Empirically, a 3-week open trial has shown that light therapy is a useful adjunct, with clinical improvement in core ADHD symptoms regardless of depression [162].

Bright light therapy is also a viable treatment for elderly patients with nonseasonal depression and dementia. As for nonseasonal major depressive episode, exposing to 1-h early-morning bright light (pale blue, approximately 7,500 lux) for 3 weeks, light therapy improved mood, enhanced sleep efficiency, and increased the upslope melatonin level gradient. Besides, continuing improvement in mood and an attenuation of cortisol hyperexcretion after discontinuation of treatment was observed [163]. With regard to dementia, changes in the SCN and environmental factors in nursing homes (i.e. noise and irregular light exposure) concomitantly contribute to a disrupted rest-activity pattern that accompanies dementia [164, 165]. In earlier studies, evidence of morning bright light therapy show inconsistent but promising effects for behavioral and psychological symptoms of dementia [166–169]. After prolonged duration of bright light exposure (whole day bright light with $\pm$1,000 lux), a recent 5-year, randomized, controlled study presents a modest benefit from light therapy in attenuating cognitive deterioration, depressive symptoms, and function impairment [170]. The need for non-pharmacological management of many clinical conditions, e.g. elderly dementia, augurs well for bright light therapy.

8.5 Conclusions and Future Directions

Light theraphy has been developed for clinical use and many apparatus and parameters have been extensively studied. Bright light theraphy is the treatment of choice for SAD and CRSD. However, as for other clinical conditions, the benefit and dosing regimen of light theraphy warrants further studies to optimize the treatment effect. In addition, new devices such as light visors, light theraphy rooms and narrow-band blue light from LEDs require more investigations to examine their efficacy and saftey.

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Chapter 9
The Management of Insomnia – Biofeedback

Pei-Shan Tsai

Abstract This chapter introduces the management of insomnia using biofeedback. A brief overview of the principle, definitions and organizations of biofeedback is provided followed by an overview of insomnia and its physiological underpinnings, and an introduction to the terminology and recorded signals of various instrumentations relevant to the management of insomnia. Finally, the rationales, treatment protocols, and treatment efficacy of selected biofeedback modalities for the management of insomnia are described.

Keywords Biofeedback • Insomnia • Electroencephalography biofeedback • Neurofeedback • Self-regulation • Sleep

9.1 Introduction to Biofeedback

This section gives a brief introduction to biofeedback. The principle, definitions of biofeedback and history of different professional organizations are provided.

9.1.1 The Principle

Biofeedback is a learning therapy based on the operant conditioning paradigm. It is an offspring of instrumental conditioning. It was research on the instrumental conditioning of visceral responses mediated by the autonomic nervous system that prompted the development of applied psychophysiology and clinical

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biofeedback [1]. Until now, biofeedback therapists have relied heavily on such principles of operant conditioning including schedules of reinforcement, shaping, extinction, and fading. Stress research, relaxation therapies and other techniques of stress management are also used in combination with biofeedback [1].

9.1.2 Definitions

Biofeedback is a group of therapeutic procedures that measure, process, and provide information with educational and reinforcing properties to a subject for the purpose of teaching him/her to learn voluntarily control over his/her physiological processes [2]. In these procedures, electronic or electromechanical instruments are used for the precise measurement of autonomic and/or neuromuscular activity underlying the symptoms or conditions and for the display of these measurements to both the participant (i.e., trainee) and the therapist. The feedback display is delivered in the form of analog or binary; auditory and/or visual signals. Applied biofeedback modalities include electromyography (EMG), skin temperature, electrodermal activity (i.e., perspiration), heart rate, blood volume, blood pressure, and electroencephalography (EEG) [2].

Optimally, the two major goals of biofeedback are (1) to teach the trainee how to obtain self-regulatory skills and (2) to institute physiological and behavioral changes.

9.1.3 Professional Organizations

Originally established as the Biofeedback Research Society in 1969, the Association for Applied Psychophysiology and Biofeedback (AAPB) is now a non-profit organization with goals to promote the public's understanding of biofeedback and to advance methods used in the practice of biofeedback.[1] The AAPB offers training courses for those who wish to become a provider of biofeedback and also provides continuing education opportunities for practitioners of biofeedback. Two important AAPB's publications are *Applied Psychophysiology and Biofeedback* and *Journal of Behavioral Medicine*, both of which are Social Science Citation Indexed peer-reviewed journals.

The European counterpart, the Biofeedback Foundation of Europe sponsors education, training and research activities in biofeedback.[2]

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[1]Readers who are interested in learning more about the organization may visit the website: http://www.aapb.org/about_aapb.html. Address: AAPB 10200, West 44th Avenue, Suite 304, Wheat Ridge, CO 80033.

[2]For more information, visit: http://www.bfe.org/contact.html. Address: P.O. Box 555, 3800 AN Amersfoort, the Netherlands.

The International Society for Neurofeedback & Research (ISNR) was founded in 1995 as the Society for the Study of Neuronal Regulations. It was shortened to Society for Neuronal Regulation for simplicity. The name was changed again in 2002 to International Society for Neuronal Regulation and again in 2006 to International Society for Neurofeedback & Research to better reflect the fact that research is a critical function of the society.[3] It is now an international membership organization of professional disciplines conducting neurotherapy and neurofeedback training and research. The ISNR publishes the *Journal of Neurofeedback*. The ISNR became the first professional organization dedicated specifically to neurotherapy.

The Biofeedback Certification International Alliance (BCIA), formerly the Biofeedback Institute of America, was created in 1981. The BCIA is an organization that certifies individuals who meet education and training standards in biofeedback and progressively re-certifies those who advance their knowledge through continuing education. BCIA certification establishes that the individual has met entry-level requirements for the clinical practice of biofeedback. BCIA has three certification programs: General Biofeedback, EEG Biofeedback, and Pelvic Muscle Dysfunction Biofeedback.[4]

9.2 Overview of Insomnia

This section gives an overview of the diagnosis and physiological underpinnings of the etiology of insomnia.

9.2.1 Diagnosis of Insomnia

Insomnia is the most common sleep disorder. It is a heterogeneous complaint reflecting reduced quality, duration, or efficiency of sleep. The most frequently reported insomnia symptoms are difficulty in initiating sleep (sleep-onset insomnia), difficulty in maintaining sleep (sleep fragmentation), early morning awakening, and non-restorative sleep. Insomnia may arise from psychiatric disorders, medical conditions, and drug/alcohol use or abuse, and in these instances is termed comorbid insomnia. Primary insomnia probably accounts for around 15% of chronic insomnia cases. It is more common in women than in men, and the usual age of onset is 20–40 years old [3]. *The Diagnostic and Statistical Manual of Mental Disorders* defines primary insomnia as a disorder in which the predominant complaint is dissatisfaction with quantity or quality of sleep accompanied by at least one

[3] For more information, visit: http://www.isnr.org/mission.cfm.

[4] For requirements on these programs, contact: BCIA 10200 W., 44th Ave, Ste 310, Wheat Ridge, CO 80033-2840. E-mail: info@bcia.org; or visit the website: http://www.bcia.org/index.cfm.

symptom manifesting significantly impaired daytime functioning [4]. To make the diagnosis, one or more of the following sleep complaints must be present: difficulty initiating sleep, difficulty maintaining sleep, early morning awakening with inability to return to sleep, non-restorative sleep, and prolonged resistance to going to bed and/or bedtime struggles (children only). In addition, the sleep difficulty must occur at least three nights per week, last for at least 3 months, and occur despite adequate age-appropriate circumstances and opportunity for sleep. It might be argued that insomnia is a symptom rather than a primary diagnosis, but untreated insomnia will lead not only to increased psychological distress, but also to such clinical conditions as anxiety and depression.

9.2.2 Physiological Arousal in Primary Insomnia

The "behavioral" model of insomnia suggests that insomnia occurs acutely in association with predisposing and precipitating factors and is chronically maintained by perpetuating factors [5]. Primary insomnia is usually diagnosed when somatized tension and learned sleep-incompatible behaviors play a predominant role in the maintenance of poor sleep [6]. In other words, people with insomnia exhibit an apprehensive over-concern about sleep, while the maladaptive sleep-preventing behaviors perpetuate sleep disturbances. According the "psychophysiological" model of insomnia, conditioned arousal may act as a perpetuating factor [6]. Other perpetuating mechanisms include dysfunctional sleep-related behaviors, learned sleep-preventing associations and other cognitive factors [7].

The delay in sleep onset in individuals with insomnia compared with normal sleepers suggests that insomnia may be associated with inappropriate physiological arousal. Previous findings across a broad range of physiological systems consistently support the concept of physiological arousal in individuals with primary insomnia [7, 8]. Compared with normal/good sleepers, individuals with primary insomnia have increased high-frequency EEG activation, abnormal hormone secretion, increased whole body and brain metabolic activation, and elevated heart rate and sympathetic nervous system activation during sleep [8]. Evidence of a link between physiological arousal and primary insomnia has implications for clinical management.

9.3 Biofeedback Instrumentation

This section introduces the terminology and biofeedback signals relevant to the treatment of insomnia.

9.3.1 Terminology

1. Voltage, also known as electric potential difference, is a measure of the energy of electricity. Electric potential is the energy required to move a unit of electric charge to a particular place in a static electric field. The unit of measurement is the volt.
2. Electric current is a flow of electric charge carried by moving electrons in a conductor such as wire through a medium. The unit for measuring the rate of flow of electric charge is the ampere (amp.), which is charge flowing through some surface at the rate of 1 C/s.
3. Polarity refers to the direction in which electrons flow. Direct current means electricity flowing in a constant direction (constant polarity). Alternating current means that the polarity changes, reversing positive and negative over time.
4. Frequency refers to cycles per second and is measured in hertz (Hz). Muscles generate frequencies in the range of 0–1,000 Hz.
5. A filter is a device designed to attenuate specific ranges of frequencies, while allowing others to pass, and in so doing limit the frequency spectrum of a signal. A passband is the range of frequencies that can pass through a filter without being attenuated.
6. The combination of two active leads and one ground is referred to as bipolar.
7. Signal is defined as the information that the therapist intends to measure. A signal is a discrete part of a communication.
8. Noise is defined as the unwanted information. Any electrical device generates unwanted noise.
9. A differential amplifier rejects electrical artifact.
10. An integrated signal is a signal calculated by the integrator.
11. An electronic signal is a signal generated by electronic means.
12. Smoothing is an example of data enhancement methods that are used to process raw signals in order to improve the quality of the data.
13. Integration is a method of quantifying the EMG signals and refers to measuring the area under a curve over a time period.

9.3.2 Biofeedback Signals

9.3.2.1 Electromyography (EMG)

Surface electromyography (EMG) is a noninvasive method of measuring muscle contraction. Muscle is a force-generating/force-transmitting tissue. Each striated muscle is innervated by a single motor nerve. Muscle fibers do not contract individually; instead, an entire set of muscle fibers, innervated by a single motor neuron, contract simultaneously. This functional physiological unit is called the

motor unit. The EMG monitors the electrical signals emanating from muscles and thus EMG is an electrical correlate of muscle contraction. Electrical signals are generated by *single motor units* and indexed in *microvolts*. In EMG, ionic signals originating from the muscles are converted into electronic signals which are measured by the instrument.

The detection of EMG signals from a localized muscle region requires meticulous attention to noise reduction and grounding, electrode site preparation and placement, as well as appropriate differential pre-amplification and preliminary signal conditioning [9, 10]. Most EMG pre-amplifiers include filters to eliminate noise. However, these filters may not be selective and effective. It is therefore important to minimize noise through appropriate placement and shielding of equipment as well as careful grounding of the participant.

EMG utilizes surface electrodes (sensors) which are directly attached to the skin using adhesives. The sensor consists of an insulated shell in which there is an imbedded metal plate. A conductive gel should be used to bridge the gap between the plate and the skin. Most of the disposable sensors are pre-gelled and have built-in adhesives. Prior to the attachment of the conductive gel and electrodes, the skin surface is usually cleaned to remove dirt and oil and gently abraded to reduce inter-electrode impedance. Each set of EMG sensors constitutes one channel of feedback. An EMG biofeedback electrode channel generally consists of two active electrodes and one inactive (ground or reference) electrode. This is referred to as a bipolar sensor arrangement, now the most commonly used method of recording EMG signals. The amount of EMG recorded is the sum of all action potentials of the contracting muscle fibers between the electrodes.

If the active sensors are placed perpendicular to the muscle fibers, more muscle activity within the general area will be sampled. For a general relaxation placement, the ground sensor can be placed halfway between the two active sensors. If the active sensors are placed parallel to the underlying muscle fibers, then the underlying muscle activity will be picked up and the signals primarily reflect specific muscle activity. The ground sensor should be attached to a bone prominence near the two active leads for a specific muscle site placement.

EMG signals are amplified using differential amplifiers in which the difference signal between two electrodes is amplified and carried through the signal processing chain. As a result, any bioelectrical or extraneous electrical signal that is common to both electrodes is attenuated. An EMG detection passband from 10 to 500 Hz or 1,000 Hz is usually chosen. Selection of an EMG detection passband is based on the consideration of (1) susceptibility to artifact, (2) presence of extraneous electrical noise, (3) need to minimize cross-talk, (4) high-frequency noise internal to the amplifier and (5) the amplitude of the EMG signals to be detected. EMG signals are then conditioned. The raw, filtered EMG signal is a stochastic train of motor unit action potentials. Without conditioning, raw EMG signals are unsuitable for quantification. Usually the signal is rectified and passed to an integrator or smoother for signal conditioning [9].

9.3.2.2 Respiration Monitoring

Respiration sensors include a sensitive and repeatable girth sensor (also known as a strain gauge sensor) using a latex rubber band fixed with a self-adhering belt for monitoring respiration rate, waveform and amplitude. The respiration belt can be worn over the thorax or over the abdomen. When connected to a computer-based system, the strain gauge sensor allows observation of the expansion of the chest or the abdomen during each breath.

9.3.2.3 Photoplethysmography for Pulse Rate Monitoring

Pulse rate is usually recorded using a blood volume pulse (BVP) sensor. The BVP sensor is a blood volume pulse detection sensor (also known as a photoplethysmography sensor) housed in a small finger-worn package to measure heart rate and provide BVP amplitude, BVP waveform, heart rate and heart rate variability (HRV) feedback.

By attaching the BVP sensor to the skin, it is relatively easy to detect the pulsatile component of the cardiac cycle. Each cardiac cycle appears as a peak. With each cardiac cycle the heart pumps blood to the periphery. Even though this pressure pulse is somewhat damped by the time it reaches the skin, it is enough to distend the arteries and arterioles in the subcutaneous tissue. The change in volume caused by the pressure pulse is detected by illuminating the skin with the light from a light emitting diode and then measuring the amount of light either transmitted or reflected to a photodiode. A common sensor placement is the second digit of the right hand. When connected to a computer interface, the BPV sensor allows for measurements of beat-to-beat pulse variations.

9.3.2.4 Electroencephalography (EEG)

Electroencephalography (EEG) provides a noninvasive measurement of brain electrical activity. The electrical activity in the brain recorded from surface electrodes is an alternating current in which the polarity changes (i.e., a current switching between positive and negative directions over time). If the polarity reverses three times per second or less, the range of frequencies is referred to as delta (1–3 Hz). Similarly, if the polarity reverses between four and seven times per second, it is referred to as theta (3.5–8 Hz). Alpha range is between 8 and 13 Hz. Beta range is 14 Hz or higher. Sensorimotor rhythm (SMR) is the activity between 12 and 15 cycles/s which is close to sigma band (12.5–14.5 Hz).

Commercially available surface EEG electrodes consist of hollow metallic discs or cups which are filled with conductive gel before application. Electrodes may be attached to the scalp of the patient singly using adhesive material or as a group using a cap or net. The scalp is usually abraded before placing the electrodes.

9.3.3 Computerized Biofeedback Systems for Professional Use

Computerized biofeedback systems are commercially available for professional use. A list of the systems and manufactures for biofeedback is provided in Appendix 1. Computerized systems specifically designed for neurofeedback are listed in Appendix 2.

9.4 Application of Biofeedback Modalities for Insomnia

According to the Practice Parameters Paper from the American Academy of Sleep Medicine, biofeedback that provides visual or auditory feedback to patients to help them control some physiologic parameters (e.g., muscle tension) in order to seek reduction in physiologic arousal is effective and recommended therapy in the treatment of chronic insomnia [11]. This section introduces the application of biofeedback modalities for the treatment of insomnia. The rationale and treatment protocol are provided. The treatment efficacy is also discussed.

9.4.1 Frontalis Electromyography Biofeedback

9.4.1.1 Rationale and Protocol

Frontalis EMG biofeedback has been widely used in the clinical setting to treat sleep-onset insomnia. The rationale for employing frontalis EMG biofeedback to treat insomnia is that it may induce the relaxation response and reduce physiological arousal. The EMG instrument records electrical signals generated during muscle action. Surface EMG measures electrical signals carried by motor units and thus serves as an electrical correlate of muscle contraction. EMG recorded on the frontalis muscle on the forehead correlates well with generalized muscle tension [12] and can be a good indicator of general arousal. When employing frontalis EMG biofeedback, participants are provided with feedback signals concerning the level of muscle tension in their forehead. In practice, two active electrodes are placed on the frontalis muscle of the forehead, one inch above the eyebrows and directly over the eyes. The reference electrode is placed on the center of the forehead equidistant from the other two active electrodes. The feedback signals provided to the patient can be visual, auditory, or a combination of both. During the EMG biofeedback session, the patient usually lies on a reclining chair and is instructed to concentrate on bringing the feedback signals down to a desired level that is below a predetermined level (threshold). Alternatively, the muscle activity is transformed into a tone where the

frequency of the sound varies with the amount of the muscle tension. The participant is instructed to decrease the frequency of the sound and thereby learn to decrease tension of his/her muscle.

9.4.1.2 Treatment Efficacy

EMG biofeedback is a popular relaxation therapy. However, the efficacy of EMG biofeedback as a treatment modality for sleep-onset insomnia remains somewhat equivocal. In previous studies, a typical treatment protocol was composed of 10–12 sessions, each 15 or 35–45 min in length [13, 14]. One study employed 6 weeks of twice weekly EMG biofeedback sessions plus daily home practice [13]. The EMG activity was transformed into a tone (click) with frequency varying with the amount of muscle tension, in other words, the frequency of the tone increased as muscle tension increased. The subject was then provided with the auditory feedback and was instructed to decrease the frequency of the sound and therefore decrease muscle tension.

It has been shown that frontalis EMG biofeedback is as effective as progressive muscle relaxation (PMR) [15, 16] or pseudofeedback [14] but has not demonstrated superiority in reducing sleep onset latency (SOL) for individuals with sleep-onset insomnia. A summary of the findings from previous studies on the efficacy of EMG biofeedback for sleep improvement is shown in Table 9.1. These studies did not provide conclusive evidence to support the efficacy of EMG biofeedback for sleep improvement due to the small sample size used and questionable rigor of the study design (e.g., no random group assignment).

A review commissioned by the Standards of Practice Committee of the American Academy of Sleep Medicine rated EMG biofeedback as a 'probably efficacious' treatment of insomnia based on the Empirically Supported Treatment (EST) grading system from the American Psychological Association (APA) [17]. Accordingly, criteria for 'probably efficacious' treatments include: (1) two experiments showing the treatment is (statistically significantly) superior to a waiting-list control group, (2) one between-group design experiment with clear specification of group, use of manuals, and demonstrating efficacy, or (3) a small series of single case design experiments ($n > 3$) with clear specification of groups, use of manuals, good experimental designs, and compared the intervention to pill or psychological placebo or to another treatment [18].

9.4.2 Respiratory Sinus Arrhythmia Biofeedback

9.4.2.1 Rationale and Protocol

Respiratory sinus arrhythmia (RSA) is a naturally occurring variation in heart rate that occurs during a breathing cycle and is characterized by a shortening of heart

Table 9.1 Summary of findings on the efficacy of electromyography biofeedback for sleep improvement

Author/year	Design	Number of participants	EMG treatment dosage	Control conditions	Sleep outcome
Coursey/1980	Non-randomized controlled study	22	35–45 min/session, twice/week, 12 sessions	1. Autogenic training 2. Non-relaxation treatment	50% of the EMG and 33.3% of the autogenic participants achieved meaningful improvement in sleep (a global subjective assessment of marked improvement in SOL, a 33% reduction in SOL from baseline and less than 35 min in daily sleep log, and a 25% reduction in SOL from baseline and less than 30 min in EEG.) None of the non-relaxation participants produced meaningful improvement.
Freedman/1976	Non-randomized controlled study	18	30 min/session, 6 sessions	1. PMR 2. Placebo	Both the EMG and PMR groups improved significantly more than the control group in SOL. The EMG and PMR groups were not significantly different in the improvement of SOL.
Nicassio/1982	Non-randomized controlled study	40	30 min/session, twice/week, 10 sessions	1. PMR 2. Placebo 3. No-treatment	Both the EMG and PMR groups improved significantly in SOL compared with the placebo and no-treatment groups. The EMG and PMR groups were not significantly different in the improvement of SOL.
VanderPlate/1983	Non-randomized controlled study	24	15 min/session, 10 sessions	1. Pseudo-Biofeedback 2. Self-monitoring 3. Waiting-list	Both the EMG and pseudo-biofeedback groups showed significantly greater improvement in SOL than the waiting-list group. No significant difference in the improvement in SOL was found between the EMG and the pseudo-biofeedback groups.

EEG electroencephalography, *EMG* electromyography, *PMR* progressive muscle relaxation, *SOL* sleep onset latency

periods (increasing heart rate) with inspiration and a lengthening of heart periods (decreasing heart rate) with expiration in a phase relationship [19]. RSA has been utilized as an index of vagal control of the heart in psychophysiolological research. It is sensitive to behavioral or cognitive states. In humans, the magnitude of the RSA increases with self-induced, relaxed breathing. RSA biofeedback training involves pacing breath rhythm at approximately 6 breaths/min. Lehrer and colleagues [20] proposed that the participant should breathe at his/her resonance frequency so that a resonance between respiratory and baroreflex rhythm can occur to increase the overall HRV amplitude. The resonant HRV frequency is in the vicinity of 0.1 Hz (i.e. 6 cycles/min). At this frequency, HR and respiration oscillate in phase with each other, with inhalation coinciding with HR accelerations and exhalation with decelerations. When participants breathe at their resonant frequency, respiratory effects on HRV stimulate baroreflex effects and produce large increases in both HRV and baroreflex gain [21].

When applying RSA biofeedback, feedback is usually given in the form of a visual display of variations in heart rate in a phase relationship with inspiration and expiration. In practice, a respiration strain gauge sensor is applied over the abdomen and a BPV photoplethysmography sensor is attached to the second finger of the right hand. The participant is instructed to breathe approximately in phase with heart rate changes. A beat-to-beat cardiotachometer, superimposed in phase with heart rate changes is a typical form of feedback display.

The participant can also directly received HRV biofeedback. HRV represents beat to beat changes in the inter-beat interval and is generally considered to be a measure of autonomic tone. Decreased HRV is generally an outcome of autonomic nervous system imbalance, specifically excessive sympathetic activation and deficient parasympathetic activity [22]. Biofeedback training can teach patients to increase the percentage of total HRV in specific frequency ranges. HRV biofeedback training is aimed at teaching people to decrease physiological arousal by increasing HRV amplitude [20]. The monitoring of HRV activity is detected through ECG or through photoplethysmography as previously described. Respiration measures are usually incorporated into HRV biofeedback to facilitate the learning of diaphragmatic breathing.

RSA treatment is usually delivered in multiple sessions. A suggested RSA treatment protocol has been outlined by Lehrer et al. [20]. According Lehrer's manual, the participants receive 5–6 sessions, each 30–50 min, with one session per week. During the initial session, the objective is to determine the participant's resonant frequency. This is accomplished by having the participant breathe at different frequencies ranging between 4 and 7 breaths/min and finding the frequency (resonant frequency) that yields the highest amplitude of heart rate oscillations. A pacing stimulus is presented on a computer display screen, instructing the participant when to inhale and exhale. Then, in the subsequent sessions, the participant is instructed to breathe abdominally at his/her resonant frequency to produce the maximal increases in the amplitude of HRV.

9.4.2.2 Treatment Efficacy

RSA or HRV biofeedback is usually applied to clinical situations where a reduction in physiological arousal is desired. Empirical data on the effect of RSA biofeedback for improving insomnia is lacking. In a study testing the effect of RSA biofeedback for anxiety disorders, RSA biofeedback, using a home training device (StressEraser), significantly improved total sleep time but not overall sleep quality [23]. In another study, RSA biofeedback using the StressEraser reduced the score of the Insomnia Severity Index in individuals with posttraumatic stress disorder, however the effect was not superior to PMR [24]. In both studies, the participants were instructed to practice breathing with the StressEraser device 20 min daily for 3–4 weeks. Home training of RSA has the advantages of being cost-efficient and convenient. Future studies will continue to monitor the effectiveness of home-based RSA training programs on sleep improvement.

9.4.3 Neurofeedback

Neurofeedback, also known as EEG biofeedback, refers to learned self-regulation of specific EEG frequency components.

9.4.3.1 Rationale and Protocol

Sensory motor rhythm (SMR) is an oscillatory idle rhythm of synchronized electromagnetic brain activity. For most individuals, frequency of the SMR is in the range of 12–15 Hz. Barry Sterman's groundbreaking research showed the connection between SMR EEG activity and epilepsy. When cats sit quietly, they show an episodic 12–14 cycles/s rhythm over the sensorimotor cortex. Sterman et al. [25] trained cats to produce increased levels of this rhythm by operant conditioning during wakefulness. These cats subsequently showed more 12–14 Hz waves during sleep and produced longer epochs of undisturbed sleep than control cats. The first evidence of clinical EEG and sleep EEG changes with SMR training in humans was reported by Sterman and Shouse in [26].

In a typical SMR training protocol, the EEG is recorded from C3 or C4 with a reference electrode placed on one ear. Audiovisual reward is given for production of brief bursts of 12–14 Hz activity [27, 28]. The goal is to increase the production of 12–14 Hz activity, while suppressing 4–7 Hz activity [29]. The recorded EEG signals are displayed on a computer screen in the form of analog/digital signals or transformed into a tone. In order to achieve the training goal, participants are given instructions on how to produce the desired or targeted signals on the computer screen and/or to produce a reward tone while suppressing an unwanted tone through trial and error.

Theta waves define stage I sleep, the transition phase between full wakefulness and sleep. Theta feedback has been employed to facilitate sleep for those who suffer from sleep-onset insomnia. When an individual learns to voluntarily generate enhanced levels of theta activity, sleep onset is more rapid. In practice, EEG is recorded from Oz or C4 with a reference electrode placed on the ear or forehead. For individuals with anxiety disorders, theta enhancement protocols train the participant to produce 3.5–7.5 Hz activity while suppressing 8–12 Hz activity [29, 30]. The feedback modality is given primarily in the form of auditory feedback with eyes closed. Participants strengthen their self-regulation of EEG waves by means of producing a desirable tone and/or suppressing an undesirable (e.g. annoying) tone.

9.4.3.2 Treatment Efficacy

A summary of the findings on the efficacy of neurofeedback for sleep improvement is shown in Table 9.2. Both SMR and theta feedback significantly improved self-reported sleep parameters in individuals with insomnia [31], however the effect of neurofeedback was not superior to the control condition [32]. Interestingly, individuals with insomnia responded well to SMR feedback if they were relaxed at baseline whereas those who were initially tense and anxious benefited from theta training [31]. SMR feedback also showed a dose-dependent treatment effect, as the number of feedback sessions positively correlated with sleep improvement [32]. A recent study showed that instrumental conditioning of SMR (12–15 Hz) shortens sleep latency and increases the number of sleep spindles as well as declarative learning in healthy participants [27]. In summary, the effect of SMR conditioning on sleep spindle bursts has been demonstrated in healthy individuals, however its sleep improvement effect on individuals with insomnia warrant further investigations. Theta feedback-assisted relaxation training may help reduce tension and improve sleep, but its efficacy as a treatment for sleep improvement in individuals with insomnia remains to be examined.

9.5 Conclusions and Future Directions

Insomnia is now been described as a “disorder of hyperarousal”. Stressful life events, appraisal of stressors, and associated coping skills are possible precipitating and/or perpetuating factors that chronically maintain poor sleep. Managing chronic insomnia must involve a change in an individual’s lifestyle. As the goal of biofeedback is to teach the participant to learn voluntarily control over his/her physiological processes and to institute a behavior change, it has great potential to be used as a stand-alone treatment for insomnia or as an adjuvant to pharmacological and cognitive psychotherapy. Unfortunately, there has been a lack of well-conducted randomized-controlled trials examining the efficacy of various biofeedback modalities on sleep improvement in individuals with insomnia. Definitive conclusions

Table 9.2 Summary of findings on the efficacy of neurofeedback for sleep improvement

Author/year	Design	Number of participants	Neurofeedback; protocol	Control conditions	Sleep outcome
Hauri/1981	Randomized controlled trial	48	1. SMR 2. Theta plus EMG 1–2 h/session, 2–4 times/week, 15–62 sessions	3. EMG biofeedback 4. No-treatment	Changes in sleep parameters in the three biofeedback groups were not significantly different from those of the control group.
Hauri/1982	Randomized controlled trial	16	1. SMR 2. Theta 2–3 times/week, 26 sessions		Both the SMR and theta feedback groups showed significant pre-test to post-test improvements in TST, SOL and number of awakenings per night as assessed by daily sleep logs. There were no significant pre-test to post-test changes in any sleep variable when assessed by PSG.
Hoedlmoser/2008	Randomized controlled trial	27	SMR 1 h/session, daily, 10 sessions	Randomized frequency conditioning	The SMR group showed a significant improvement in SOL and sleep spindle number from pre-test to post-test as determined by PSG, compared with the control group.

EMG electromyography, *PSG* polysomnography, *SMR* sensorimotor rhythm, *SOL* sleep onset latency, *TST* total sleep time

regarding the effectiveness of biofeedback modalities for the treatment of insomnia has yet to be determined. Future research should employ larger sample sizes with adequate statistical power and use a randomized controlled design to examine the effectiveness of each biofeedback modality for improving sleep in individuals with insomnia. The mechanisms underlying the sleep improvement effect of biofeedback, if any, should also be explored.

Appendix 1: Computerized Biofeedback Systems

System	Manufacturer	Contact information
ProComp (Infiniti) BioGraph EEG, EMG, GSR, Temp, HR, Resp System	Thought Technology, Ltd.	20 Gateway Drive, Plattsburgh, New York 12901 Tel: 1-800-361-3651 or (514) 489-8251 Fax: (514) 489-8255
ProComp2 (Infiniti) 2 Simultaneous Channel EEG, EMG, GSR, Temp, HR, Resp System	Thought Technology, Ltd.	Web: http://www.thoughttechnology.com/index.html
ProComp5 (Infiniti) 5 Simultaneous Channel EEG, EMG, SC, Temp, HR, Resp System	Thought Technology, Ltd.	Web: http://www.thoughttechnology.com/index.html
Cardiopro Biofeedback Module (RSA) for the ProComp + Infiniti EEG, EMG, SC, Temp, HR, Resp System	Thought Technology, Ltd.	Web: http://www.thoughttechnology.com/index.html
Myotrac Dual EMG Clinical System System	Thought Technology, Ltd.	Web: http://www.thoughttechnology.com/index.html
Computerized EEG, EMG, SC, Temp, HR, Resp Systems	BrainMaster Technologies, Inc.	195 Willis Street, Bedford, OH 44146 Phone: (440) 232-7300 Web: http://www.brainmaster.com
Windows based systems EEG, EMG, SC, Temp, HR, Pneumograph Systems	J&J Engineering	22797 Holgar Ct. NE, Poulsbo, WA 98370 Web: http://www.jjengineering.com/index.htm
Bio Integrator Biofeedback & Neurofeedback System (2 EEG Channels, 2 EMG Channels, 1 Temp Channel, 1 SC Channel, 1 HR Channel,1 Resp Channel)	Bio-Medical Instruments Inc.	2387 East 8 Mile Rd., Warren, MI 48091-2486, USA

EEG electroencephalography, *EMG* electromyography, *HR* heart rate, *Resp* respiration, *RSA* respiratory sinus arrhythmia, *SC* skin conductance, *Temp* temperature

Appendix 2: Computerized Biofeedback Systems (Neurofeedback Only)

System	Manufacturer	Contact information
ProComp (Infiniti) BioGraph Multichannel EEG (up to 8 channels)	Thought Technology, Ltd.	20 Gateway Drive, Plattsburgh, New York 12901 Tel: 1-800-361-3651 or (514) 489-8251 Fax: (514) 489-8255
ProComp2 (Infiniti) 2 Simultaneous Channel EEG, (or 2nd channel -EMG, SC, Temp, HR, Resp) System	Thought Technology, Ltd.	Web: http://www.thoughttechnology.com/index.html
Bio Integrator Dual EEG (Synchrony)	Bio-Medical Instruments Inc	2387 East 8 Mile Rd., Warren, MI 48091-2486, USA
2E channel EEG Biofeedback System	BrainMaster Technologies, Inc.	195 Willis Street, Bedford, OH 44146 Phone: (440) 232-7300 Web: http://www.brainmaster.com
Windows based systems EEG Systems	J&J Engineering	22797 Holgar Ct. NE, Poulsbo, WA 98370 Web: http://www.jjengineering.com/index.htm

EEG electroencephalography, *EMG* electromyography, *HR* heart rate, *Resp* respiration, *SC* skin conductance, *Temp* temperature

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Part IV
Sleep Technology in Work and Life

Chapter 10
Sleep Environmental Control: From Sleep Coach to Sleeper-Centered Bedroom

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Abstract Sleep environment is important for sleepers. Many investigators have revealed the influence from the environment including lighting, noise and temperature. This chapter summarizes the scientific evidences from the related fields. It also reveals an innovative environmental control system, *Sleep Coach* to promote high-quality sleeping. A control system, *Sleep Coach*, was proposed. Sleep Coach is composed of three type of controllers: proactive controller, knowledge-enhanced controller, and sensor-enhanced controller. This control system not only ensures the optimal setup for the sleepers but also links the sleeping environment with the physician using the log in the control system. The smart control system can increase sleeping quality for the users and eventually can realize the goal of sleeper-centre bedroom.

Keywords Sleep coach • Sleeper-centered bedroom

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10.1 The Importance of Sleep Environment

Sleep environment is usually the place in which people sleep but at this time there is no clear definition. According to the book "Cognitive Behavioral Therapy for Insomnia" , there is a sleep environment checklist to show that a sleep environment would contains six physical elements such as light, noise from external environment, interior temperature, humidity and air circulation, and settings (including bedding and pillows) and 1 psychological element, safety [1]. Moreover, Kim et al. [2] mentioned that people's sleep would be affected by changes in air temperature, relative humidity, indoor air quality (IAQ), illumination, and noise [2]. They investigated the sleep environment and sleep quality in certain individual's own bedroom in Korea and found out that air temperature, humidity, and CO2 concentrations were connected to people's sleep problems. Therefore, we will introduce several elements, such as light, noise, and air temperature, in the bedroom to better illustrate the importance of these factors as they relate to our sleep.

Light might be the most influential environmental element over our sleep, because it has been seen as a zeitgeber, an external time cue which could regulate the individual's sleep-wake circadian rhythm. Meijer et al. [3] had found that the suprachiasmatic nuclei (SCN) is the primary pacemaker of the mammalian circadian system which contain cells to sense environmental light intensity to alter their level of activities [3]. The timing and physical characteristics of the light stimulus will indeed influence the individual's sleep-wake circadian rhythm. Previous studies have shown that bright light exposure later in the day delays the sleep-wake circadian and earlier in the day may advance the circadian rhythm [4, 5]. The shorter wavelength (e.g. blue and green) is more effective in phase advance than longer wavelength (eg. red light) [6, 7]. However, the function of individual sensitivity to light could also affect the circadian effect of light exposure.

Noise is defined as unwanted sounds and this affects everyone every day and every night [8]. It has two main sources, one is from outside bedrooms such as transportation(/traffic) noise, and the other one is from inside buildings including mechanical devices (e.g. elevators, ventilation, pumps, and water pipes) or domestic noises (e.g. neighbour's voices, TV set, pets, and musical instruments). Noise has been proven to have adverse effects on individuals' sleep, such as, shortening the sleep length due to prolonging sleep latency, increasing the number of awakenings and modifying sleep-stage. Carter [9] reported that slow-wave sleep (SWS) could be reduced due to intermittent traffic noises. REM sleep rhythmicity could also be affected by environmental noise exposure. As previous studies have already shown, SWS is related to an energy restoration state of the sleeping body and REM sleep is related to mental and memory processes. Therefore, noise can also cause daytime dysfunction, such as excessive daytime sleepiness. However, the noise sensitivity of the sleepers depends on their personal characteristics such as age, sex, personality characteristics and self-estimated sensitivity to noise. Muzet [8] had mentioned that elderly people complain much more than younger adults about environmental noise.

Sleep environments that are too hot or cold will also negatively affect individuals' sleep quality, and the amount of sleep stages. Ohayon and Zulley [10] investigated the predictive factors for global sleep dissatisfaction (GSD) in a population of 4,115 Germans and found that bedrooms which are too hot is one of the most predictive factors. Individuals would remain more awake (sleep less), and have more sleep stage 1, stage 2 and Rapid Eye Movement (REM) sleep in a cold environment than in natural or hot environments [11].

Notably, the physical elements of sleep environment were related to individual's sleep disturbances. A previous study has shown that dissatisfication with sleep environment was an important predictor for long-term insomnia in a population of 6,277 Japanese subjects [12]. As we know, insomnia is a highly prevalent complaint among the general population in modern society. About one-third of the adult population exhibit at least one symptom of insomnia [13]. Furthermore, in this population, an estimated 6% of adult's symptoms meet the diagnosis criteria of insomnia. Insomnia can adversely affect different aspects of an individual, such as health, quality of life and occupational or academic performance. Furthermore, the risks of traffic or work-site accidents and psychiatric disorders may increase. Therefore, we should pay more attention to how to design our sleep environment to decrease the opportunity to develop insomnia symptoms. As for those who have been diagnosed with sleep disorders, such as insomnia, sleep disordered breathing, sleep walking, sleep eating, REM behavioral disorder and so on, a sophisticated modification of the sleep environment is indispensable to help improve such diseases and for prevention of further complications. The term "Environmental Sleep Disorders" is also used to emphasized the importance of the sleep environment. Therefore, Perlis et al. [1] suggested that the clinical assessment of insomnia should include information regarding an individual's sleep environment.

A sleep environment is indeed related to how well we sleep. Hence, how to help individuals adjust their sleep environment could be a predisposing factor to having better sleep quantity and quality. Utilizing a new technology might be one of the solutions, so we will introduce three types of sleep technologies which aim to control our sleep environment in the following paragraphs.

10.2 Existing Technologies for Sleep Environment Control

As technology advances, more and more devices or products have been developed to help users to adjust to their sleep environments. Overall, there are basically three kinds of sleep environment control technologies, proactive controller, knowledge-enhanced controller, and sensor-enhanced controller, and we will introduce each controller in following paragraphs and illustrate the last one in more detail with a case study.

Fig. 10.1 Proactive controller

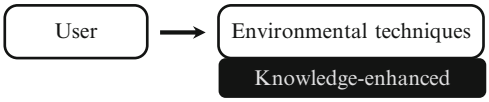

Fig. 10.2 Knowledge-enhanced controller

10.2.1 Proactive Controller

Users adjust their sleep environment by themselves based on how comfortable they feel. Sometimes they will adopt an expert's suggestions if they believe that they will help them to achieve better sleep (shown in Fig. 10.1). Most of the time, the behavior of adjusting their sleep environments are related to how much users can detect their physiological status. Light switches, air conditioners, and dehumidifiers are examples that belong to this kind of controller.

10.2.2 Knowledge-Enhanced Controller

Nowadays some sleep technologies have been developed with sleep medicine knowledge to adjust the users' sleep environment. These new sleep technologies will integrate professional suggestions from the experts or physicians to help the users (shown in Fig. 10.2).

"Sleep Light Wizard" is one example of knowledge-enhanced controller to help user create a better illumination of sleep environment based on the know-how from light therapy and the knowledge related to human sleep-wake circadian rhythm. It has three major components, an interactive control panel, the ceiling which is equipped different wavelength and intensity of Light Emitting Diode (LED) lights, and individual reminding device. Sleep Light Wizard has three main functions, spatial atmosphere simulation, light sleep-helper, and light clock. The user can use the interactive control panel to adjust the characteristics of illumination, such as location, intensity and wavelength, to simulate different spatial atmospheres, such as a party in the living room or sleep time in a bedroom. The aim of individual reminding devices is to awake each person who sleeps in the same space at a different time by using directional light and acoustic sounds [14]. The algorithm of the light clock comes from the concept of light therapy. If there is a couple, husband needs to get up at 7:30 a.m. and the wife needs to get up at 9:00 a.m., they could set the clock time separately. At 7:00 a.m. the next morning, the acoustic source and

Fig. 10.3 The components of sleep light wizard

Fig. 10.4 Sensor-enhanced controller

the light source begin to emit prompts toward the husband. Next, between 7:00 a.m. and 7:30 a.m., the strength of light source would get stronger step by step until the husband is woken up. At 8:45 a.m., the acoustic source and the light source begin to emit prompts toward the wife and then the intensity will become more stronger when the time is close to 9:00 a.m. The components of the Sleep Light Wizard are shown in Fig. 10.3.

10.2.3 Sensor-Enhanced Controller

There are some controllers which change elements automatically via the users' personal data. Most of the time, the data is collected from the sensors which are equipped in the controllers (Shown in Fig. 10.4).

Gajjar [15] had proposed a concept of an "Environmental Control System", which is related to an interior environmental controlling system. This system involves multiple sensors and control systems to modify the internal temperature and humidity. "*iWakeUp*" is another example [16] which is an intelligent alarm clock driven by video-based monitoring. The aim of this new technique is to wake the user up when they are having light sleep which may result in a better mental status. It will determine the sleep status and then find out the optimal wakeup time to wake the user up via analysing the amount of movement from video recordings. They also found that the subjects using *iWakeUp* reported a lower level of sleepiness and higher level of vigour than subjects who did not use it. Figure 10.5 shows that the conceptual model of *iWakeUp* system.

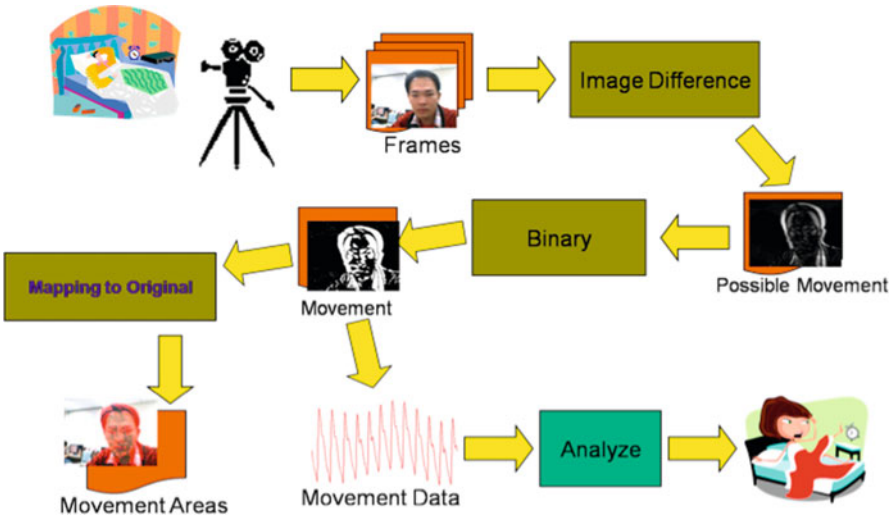

Fig. 10.5 Conceptual model of iWakeUp system

10.3 Case Study – Sleep Coach

The remainder of this chapter presents a new environmental control sleep system, *Sleep Coach*, which integrates the characteristics of three types of environmental controllers. *Sleep Coach* is essentially the result of multidisciplinary research including input from those with industrial design, medicine, psychology and engineering backgrounds. It is not only a bedroom environmental control device or a sleeper to set up their own sleep environment, but also contains a sleep-promotion program in it. This sleep-promotion program was designed based on the concept of "Cognitive Behavioral Therapy for Insomnia CBT-I" and therefore, *Sleep Coach* is especially suitable for people with insomnia symptoms.

Insomnia is a highly prevalent complaint among the general population in modern society. According to one epidemiological study [13], approximately one-third of the adult population exhibit at least one symptom of insomnia. Furthermore, among this population, an estimated 6% of adult's symptoms meet the diagnosis criteria of insomnia. Insomnia is defined as repeated sleep difficulties, such as difficulty with sleep initiation, maintenance or quality that occurs during adequate sleep time and opportunity which typically leads to some forms of daytime impairment, such as daytime sleepiness [17]. Moreover, insomnia also has adverse effects on different aspects of an individual, such as health, quality of life and occupational or academic performance. Furthermore, the incidence of traffic, work-site accidents or psychiatric disorders may increase if someone suffers from insomnia symptoms. It has been shown that pharmacotherapy is efficacious on situational insomnia which is often caused by acute stress. However, it is not suitable for chronic insomnia and may cause several side-effects, such as increasing tolerance and dependence when medications are used over a long period. Therefore, some researchers have

suggested that the CBT could be an alternative therapy for insomnia and its efficacy has been proven in many studies [18–20]. One study showed that CBT treatment can help improve the sleep difficulties of 70–80% of insomnia sufferers [21]. The most frequently used CBT therapies for chronic insomnia are stimulus control, sleep restriction, sleep hygiene, relaxation training, and cognitive therapy. The basic idea of CBT is to take the maladaptive sleep habits, autonomic and cognitive arousal, dysfunctional beliefs and attitudes about sleep as risk factors to suffering from chronic insomnia. Therefore, if we can remove these factors, the severity of the insomnia will decrease. Edinger et al. [22] showed that the CBT is useful to reduce dysfunction beliefs about sleep rather than using progressive muscle relaxation training only or a sham behavioral intervention. However, when attempting to use CBT, it really requires a great deal of cooperation between the patients and physicians. In addition, it takes time to teach the idea or concept of CBT to patients. The average duration of CBT for one section is between 6 and 10 weeks. Moreover, the patient has to apply these techniques thus proving its efficacy, so the patient will lose patience with the process and will not continue to follow the instructions of their physicians. Moreover, CBT combines several instructions together, thus the patients may become easily confused and then might be frustrated when applying these instructions. For example, they might forget how to practice certain relaxation techniques, even though they had learned them in the hospital and may be frustrated when they were trying to practice them again at home. Moreover, it combines several instructions which may change a little bit for each individual, thus these characteristics of CBT may result in a lower compliance of patient. On the other hand, clinical professionals do not have viable instruments to monitor the patient's compliance and practicing performance. All they can do is to trust their patient based on their self-reports and these reports might not represent the real situation. Therefore, the *Sleep Coach* is not simply a environmental controller, but also a therapy-assistance device.

Sleep Coach has two versions for two main users, one part is called *Sleep Coach for user*, which is used by the sleeper, and the other part is called Sleep Coach-Doc which is used by the physicians or professionals. The reason why Sleep Coach has different versions will be illustrated later. There are five modules in *Sleep Coach*, including Environmental Control and other modules for CBT treatment, includes Screening, Diary, Training and Advice. *Sleep Coach-Doc*, which is used by physicians, has four corresponding modules which are Diagnosis, Training, Advice, and Environmental Controller (shown in Fig. 10.6).

The environmental controller module plays the role of environment control, and the other modules serve as a part of a sleep-promotion program. The ***Environmental Controller Module*** (Fig. 10.7) is used to adjust the environmental elements of the bedroom to remove external affective factors on sleep. There are two elements, light and air temperature, which we had mentioned earlier. Moreover, curtains are commonly seen in the bedroom, so the user also can control the curtains through the *Sleep Coach*. Except in cases where the user changes the elements on their own, the *Sleep Coach* is equipped with biosensors which can detect the changes in the user's physiological status and then make adjustments to the environment automatically.

Fig. 10.6 Modules of sleep coach and Sleep Coach-Doc

Fig. 10.7 The conceptual interface of environmental controller module

Now we're going to introduce the remaining modules which serve as the sleep promotion program in the *Sleep Coach*. ***Screening Module*** and ***Diary Module*** are used to portray an individual's personal sleep situation. The main content of the screening module is a Brief Insomnia Screening Scale (BISS-C) which was developed according to International Classification of Sleep Disorder [17], the newest version of diagnosis criteria for sleep disorders. This scale provides the user with a chance to analyze his/her sleep problems in a short time by using only 31 items. The items are related in to four categories, including sleep environment (SE), sleep opportunity (SO), insomnia symptoms (IS), and daytime symptoms (DS).

Fig. 10.8 Training modules of Sleep Coach

Chiang et al. [23] have shown that BISS-C is a reliable and valid instrument to evaluate the insomniac symptoms of individuals. The ***Diary Module*** is used to overview the user's sleep conditions and it is the most basic and useful instrument for assessing insomnia in clinics. However, it has some disadvantages when it is used, for example, it's hard to keep the user to using it on an ongoing basis. Therefore, diary modules in *Sleep Coach* attempted to resolve this issue by using an interactive interface and passive fill-out reminders, where users can record valuable sleep events following instructions and can be reminded to record this with a dim light from the Sleep Coach screen.

Training Module (shown in Fig. 10.8) consists of new relaxation Chinese-version tasks which are designed with the concept of eastern culture and related relaxation techniques, such as breathing relaxation techniques, autogenic training and guided imaging. When users are practicing tasks, they should do so with biosensors to record their physiological status and then they can compare their recent status with the prior status. Users can get real-time feedback and do regular training activities while at home. Screening, Dairy and Training Modules can be used as a database to understand the user's sleep condition.

The last two modules are ***Advice Module*** and ***Diagnosis Module***. The goal of having an advice module was to help users record all of their prescriptions at home. Physicians might conduct several treatments at the same time and each of them has their own related details. For example, when the physician asks the user to practice sleep limitation treatment, the patient has to remember the time he/she has to perform. If he/she forgets the correct time, all he/she has to do is to check the advice module instead of calling the physicians. The aim of diagnosis module is to help physicians make a more accurate diagnosis and give the patients more useful advice through summarizing data from the screening and diary modules in *Sleep Coach*, as well as additional items for screening some physiological and

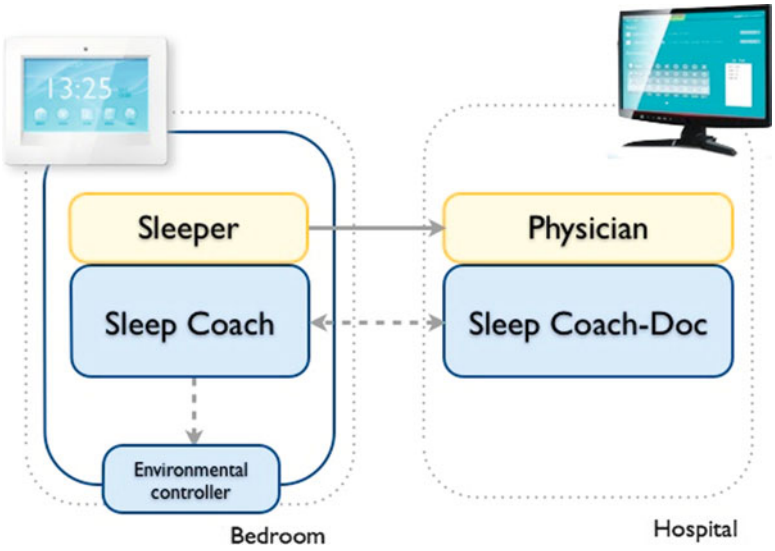

Fig. 10.9 Scenario of Sleep Coach

psychological disorders that might be the main reason behind the insomnia. This module is used through the *Sleep Coach-Doc* interface. The rest of the modules in *Sleep Coach-Doc* correspond to *Sleep Coach* and they are used by the physicians to set up *Sleep Coach*.

We envisage the scenario of *Sleep Coach* as shown in Fig. 10.9. The user always has *Sleep Coach* with them in their bedroom. The sleeper can either adjust the environment based on their own preferences or based on their bio-information to create a unique and ideally suitable sleep environment. Moreover, Sleep Coach could help users identify their sleep quality, remind them to type-up their sleep diary, offer home-based training programs and provide (or repeat) the advice of their physicians. If there is something wrong with the user's sleep, he could go to the hospital with Sleep Coach. The user has already prepared the initial data to highlight his sleep issues for the physician. In the hospital, the physician could use the Sleep Coach-Doc to access the data in Sleep Coach. After reviewing the data in Sleep Coach-Doc, the physicians would have a snapshot of the patient's sleep conditions and quickly grasp the reasons behind the sleep disturbance. With the data in the Sleep Coach-Doc, physicians have the confidence to design tailor-made treatment plans for these patients. They even can input prescription information and the detailed instructions into Sleep Coach via Sleep Coach-Doc interface. Furthermore, this device is portable and usable by patients anywhere and anytime. *Sleep Coach* integrates CBT and thus provides a complete solution for treating insomnia. With a thoughtful design and multiple user tests, the device and its interfaces are user-friendly and easy to use at home. The user can use Sleep Coach to follow the

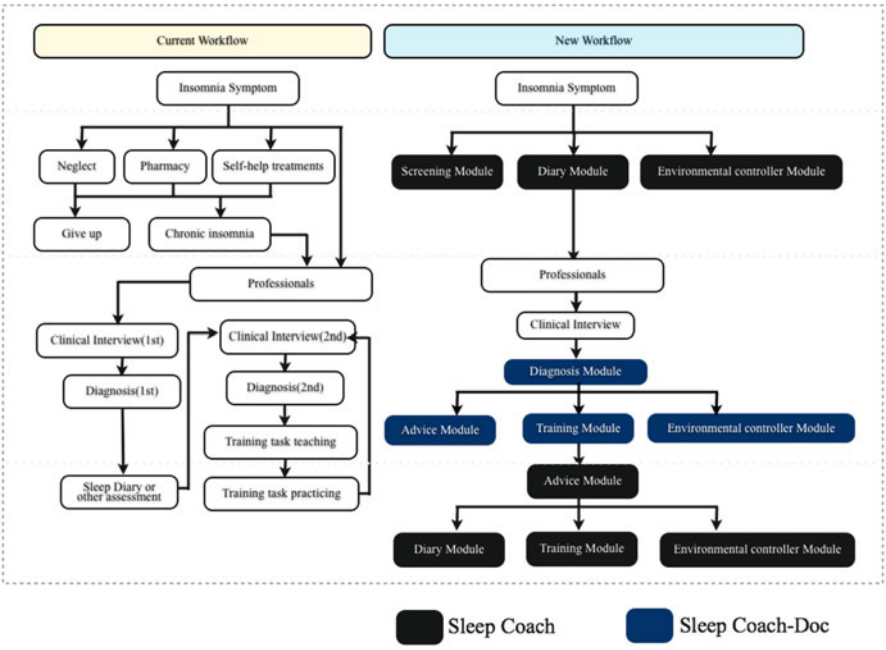

Fig. 10.10 Comparison between the current workflow and the new workflow with Sleep Coach

treatment schedule more regularly. Moreover, physicians can monitor how well the user has complied with the instructions. Sleep Coach shortens the distance between patients and physicians.

This new sleep technology proposes a new workflow for when Sleep Coach is introduced into the medical system. A comparison of the current workflow and the new workflow is shown in Fig. 10.10. There are three major advantages of the new workflow, it is time-saving, provides a precise treatment plan and offers compliance monitoring for professionals. Users can identify their sleep problems immediately and prepare personal data and a sleep diary before going to the hospital. Therefore, they can receive suggestions from their doctor at their first meeting and they do not need to waste their time with trying useless or unsuitable treatments. Once at the hospital, the physician can get the entire profile of the patient just by connecting Sleep Coach to Sleep Coach-Doc. With this useful data, the physician could immediately understand the users' issues related to sleep and then make a more precise diagnosis. After seeing the physicians, the users would then carry out treatment plans with Sleep Coach and their compliance will also be recorded in this little device. This could help professionals to evaluate the efficiency of their various treatment plans.

Up to now, the hardware of Sleep Coach has three shapes, including a handheld device shaped, digital frame shaped, and one with a book-shaped (as shown in Fig. 10.11). The handheld device is equipped with three biosensors on the right

Fig. 10.11 Hardware prototype of Sleep Coach

side, which are used to gather users' biological data, such as heart rate variability (HRV) and skin conductance level (SCL). It also includes a touch panel that allows users to interact with the system using their fingers. But there are three design issues with this format. First, the device is too small, so that it's hard for people who have big hands to use its touch panel. Moreover, although the user could carry around this small device more easily, but it seems that there is no connection between it and sleep or bedroom. It might take time for users to get used to it. The last problem is that when users are trying to practice the training program, it's hard for them to hold this device and try to relax at the same time. Consequently, the second format of Sleep Coach, digital frame, attempted to resolve some of the problems mentioned above. First, it is equipped with a screen that is similar to a 10-in. notebook. Therefore, even a person with big hand can use this device more conveniently. Second, the format is similar to an alarm clock which we would put beside our bed. Hence, this image could more easily fit in the bedroom. Third, the digital frame shaped Sleep Coach has a moving screen saver. The user would not forget to use it because of the eye-catching and interactive screen saver. Moreover, the user could conveniently put this device on the table to practice the training program. On the other hand, the book-shaped one is designed to function like an ordinary book. The design concept is based on an observation of users' behavior and their bedroom environment. Most people would consider reading a book before they sleep, then the image of a book is easier to fit into a bedroom setting. There are two versions of this prototype, a pink version and blue version, for different users. The process of developing this prototype is shown in Fig. 10.12.

A researcher conducted the first usability test of the handheld prototype in July 2008[24]. It recruited seven participants. Physicians had diagnosed all of them as insomniacs. Each testing session was approximately 2 h. They designed multiple tasks to observe whether they could complete the tasks using our prototypes. Some tasks focused on examining hardware design, such as the button locations or size of the device. The other tasks focused on the software design. For example, they designed a task to figure out whether the users could follow the instructions in Sleep Coach and complete the assigned tasks. Many usability problems were identified during the testing. Moreover, they also invited five participants to evaluate the validity of training tasks in Sleep Coach. All participants have to practice two tasks including a visualized signal breathing task (SB) and a hearing guide imaging task

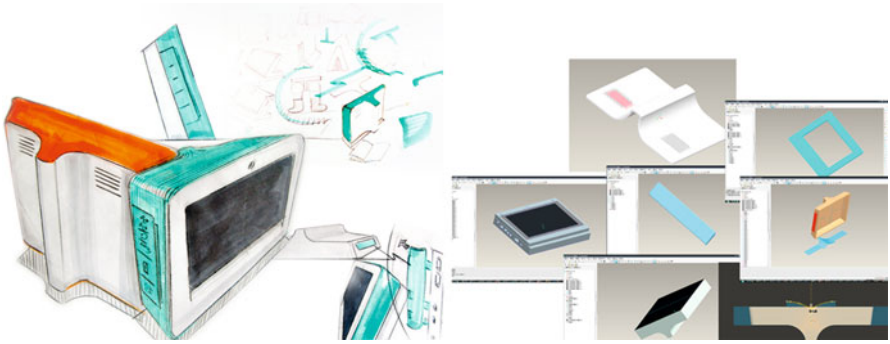

Fig. 10.12 The developing process of book-shaped Sleep Coach

(GI) measuring their pulse rate at the same time. From the tests in the sleep lab, we found that users will naturally work with Sleep Coach, and that use of the training module can result in a significantly reduced pulse rate, which indicates better relaxation [25].

10.4 From Sleep Coach to Sleeper-Centered Bedroom

Since everyone spends around one third of their life at sleep, one's quality of sleep is an absolutely important determinant of quality of life. In addition, the sleep disorders will negatively affect individuals during daytime, including both physiological and cognitive function. The creation of an ideal smart living space cannot exist without a well-designed sleep environment. It needs to integrate at least seven fields of knowledge, such as sensor technologies, architecture environment, sleep medicine, business, persuasive computing, user-centered design, and usability testing (Shown in Fig. 10.13).

Sleep Coach is the first step to realize the concept of a sleeper-centered bedroom (Shown in Fig. 10.14). The starting point of building a sleeper-centered bedroom is to develop cheap and portable **biosensor-monitoring techniques,** which can be used to detect the sleeper's physical condition, such as HRV, blood pressure, skin conductive level (SCL), and respiratory condition. For patients who suffer from sleep disorders, this information could become baseline data, which could help physicians to make a diagnosis or to evaluate the validity of certain treatments. Even more so such biosensor data with the use of other sensors in a smart living space could establish as a complete caring-network to establish the sleeper's own sleep database. The second stage of building a sleeper-centered bedroom is to develop **sleep-promotion program.** This program would be equipped with a smart calculation module to analyzing the database based on physician's diagnostic guidelines and knowledge of Sleep Medicine. At this stage the user could get the appropriate advice and could learn to develop proper sleep-promoting skills or activities. After gathering and analyzing the sleeper's own profile, these suggestions

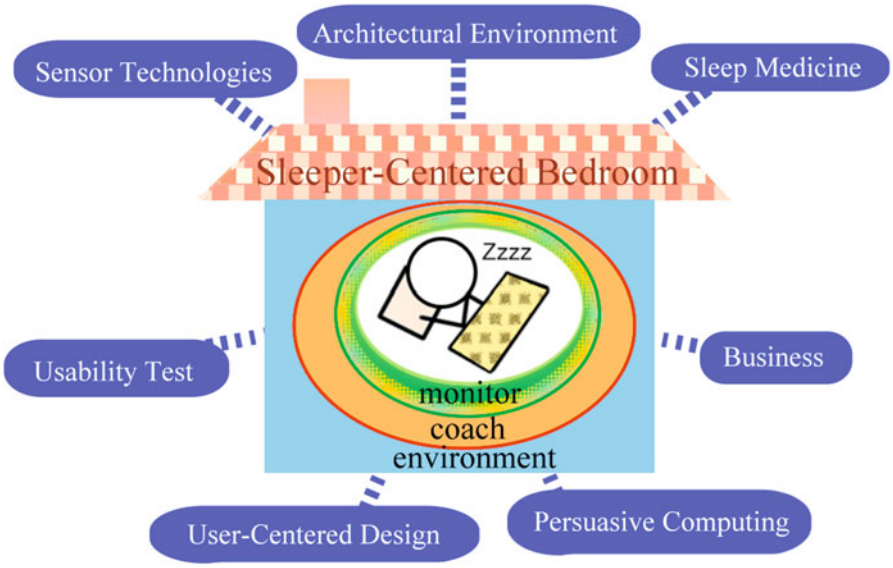

Fig. 10.13 The involved fields of a sleeper-centered bedroom

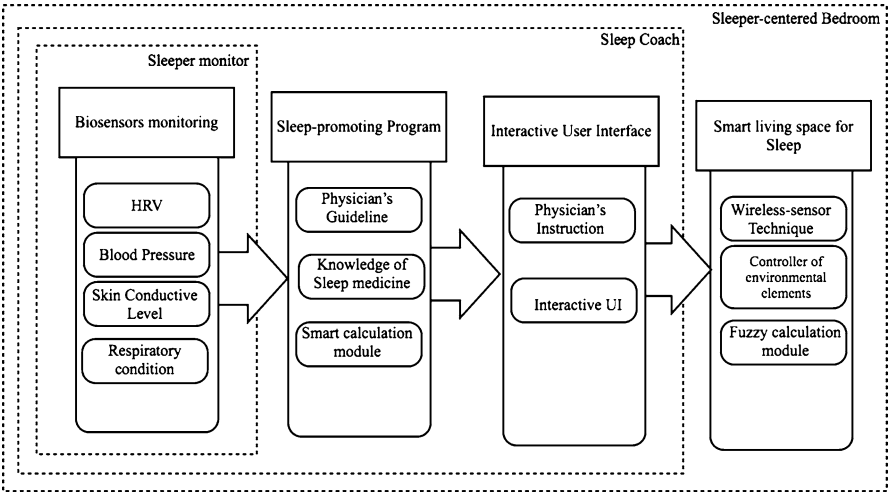

Fig. 10.14 The structure of sleeper-centered bedroom

would be presented through an **interactive user interface** helping the sleeper clearly understand a physician's instructions. A smart living space for sleep can be established by integrating the elements mentioned above utilizing wireless-sensor techniques, environmental controllers and fuzzy calculation.

10.5 Conclusion

Sleep environment is critical for sleepers. From the related literature, we have found that lighting, noise and temperature significantly influence the sleep condition. We therefore focused on the improvement of the sleep environment. A new environmental controller, *Sleep Coach*, was introduced in this chapter. It integrates light sensors, biosensors and a microprocessor in the system. It is composed of three types of controllers: proactive controller, knowledge-enhanced controller, and sensor-enhanced controller to enable the automatic adjustments to the sleep environment according to the users' unique needs. In fact, *Sleep Coach* promotes the concept of a sleeper-centered bedroom. Instead of fighting against an uncomfortable environment, *Sleep Coach* integrates existing technologies and knowledge with regards to sleep medicine to create a friendly environment for users. Sleep Coach can further become a bridge between the patient and the physicians. By collecting a sleepers' physiological data, physicians can use this data and can more easily diagnose the reasons behind a patient's sleep disorder and more effectively provide the treatment. In short, with the help such technologies, we can create an ambient environment which promotes the quality of sleep effectively.

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Chapter 11
Biosensors for Sleep Technology

Jen-Kuang Lee and Chih-Ting Lin

Abstract Biosensing is an essential technique for monitoring and analyzing responses related to sleep status, and is undergoing rapid development. In this chapter, biosensing systems for sleep technology are introduced. First, we describe in detail non-invasive sensing methods such as polysomnography, MRI and contact/non-contact sensors. We then discuss biomolecular analysis. Finally, biochip technology is presented as we explore the potential development of nano/micro biotechnologies.

Keywords Biosensor • Biomolecular analysis • Polysomnography

11.1 Polysomnography

Polysomnography has been used for decades to study sleep and is generally considered to be the standard experimental method for monitoring sleep behavior. It uses an electrical multi-parametric test to extract biophysiological information related to sleeping patterns. A polysomnography monitors several electro-physiological signals, such as electrocardiography (ECG), electroencephalography (EEG), electromyography (EMG) and electrooculography (EOG). These techniques require many electrical devices for measuring and recording signals and the equipment is typically operated by well-trained technicians. Consequently, these methods are characterized as laboratory-based methods. Given the prevalence of these four electrophysiological techniques in sleep technology literature [1–4], we will briefly describe them in the following section.

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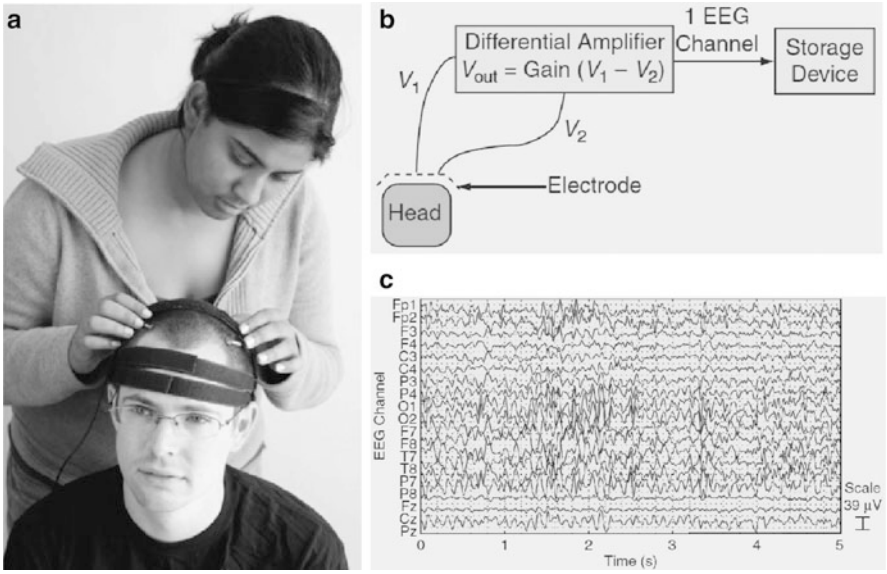

Fig. 11.1 (**a**) Application of EEG electrodes; (**b**) A schematic of the EEG interface circuit; (**c**) Experimental data from an EEG [6]

11.1.1 Electroencephalography (EEG)

EEG is used to measure the electrical response of the brain. The brain is composed of a large number of neurons which communicate with each other to transmit and receive information. Within an individual neuronal cell, information is delivered via action potentials. Action potentials are generated by the opening and closing of ion channels on the cell membrane. An ion channel opening induces a local ion-concentration difference which allows an electrical potential gradient to be generated and propagated along the axon or dendrite. At the end of the axon/dendrite, the action potential stimulates other bio-reactions to release neurotransmitters for further signal conduction between neurons. Since the action potential has inherent electrical characteristics, this activity can be monitored electrically. Therefore, EEG employs electrodes attached to the scalp to detect the electrical activity generated by neurons, although it should be noted that these electrodes record the integrated effect of groups of neighboring neurons and not individual cells. It is critical to recognize the signal pattern difference between different electrodes to reveal physiological reactions [5].

From a systematic point of view, the schematic of an EEG can be shown as illustrated in Fig. 11.1 [6]. To obtain the electrical signal, the electrode makes contact with the scalp through a conductive gel. The signal electrode and a system-common reference electrode are connected to a differential amplifier. The differential amplifier amplifies the voltage difference between the signal electrode

and the reference electrode. This circuit is used to eliminate the common-mode noise from the environment. After the differential amplifier, several filters such as a notch filter and a band pass filter are needed to obtain the signals of interest. Typically, the frequency of the band of interest is in the range of 1–50 Hz. The signal is then stored in a digital or analog device for further analysis. Each electrode represents a single point measurement in a spatial domain and is recorded as data from one channel. To obtain the overall response of the brain, it is necessary to have an array of sensing electrodes, typically between 8 and 256.

Because of the simplicity of EEG, this technique has been widely used to study various phenomenon related to brain function. However, the complicated electrode setup and recording equipment has restricted use of this technique to within laboratories and medical centers. To overcome these obstacles, researchers have developed dried electrodes [7], low power interface circuits [8] and wireless configurations [9] to promote the usage of EEG systems.

11.1.2 Electromyography (EMG)

EMG is used to examine the activity of neurons which control muscles, and is used clinically to test for neuromuscular disease. Because EMG responses can be mapped to human body gesture, EMG can also be applied to human-machine interfaces [10]. In sleep technology, EMG is used to evaluate sleep status. Unlike an EEG, EMG can be both non-invasive (surface EMG) or invasive (intramuscular EMG). The setup of the non-invasive configuration is similar to that of an EEG, as shown in Fig. 11.2. By contrast, the setup of the invasive configuration uses conductive needles to penetrate muscle tissue. This can help to target a specific muscle unit for detailed examination, including sensing and stimulation. However, the reliability of implantable needles and electrodes has been identified as a critical issue to the use of invasive EMG [12]. Consequently, invasive EMG is typically employed by well-trained medical technicians within well-controlled environments. In sleep monitoring therefore, surface EMG is widely used in preference to intramuscular EMG.

For sleep research, EMG is similar to EEG in terms of equipment setup. An array of surface electrodes, multiple wires and parallel recording channels are connected to the subject. The data is obtained and recorded by digital media. The result is then compared to EEG data to extract relevant information. It is clear that pattern recognition and extraction is extremely important for data analysis. Consequently, many researchers are working on developing mathematical algorithms for EMG data analysis. In addition, a major advancement in sensor instruments has been the development of the wireless body network. This technique replaces connecting signal wires with wireless transceivers. Since wires limit limb movement during sleeping, wireless techniques improve the potential to apply EMG to sleep technology. However, since electrodes can shift on skin, this can introduce additional noise to the signal conditioning system, and it should be noted that EMG therefore suffers from more noise than EEG during gesticulations.

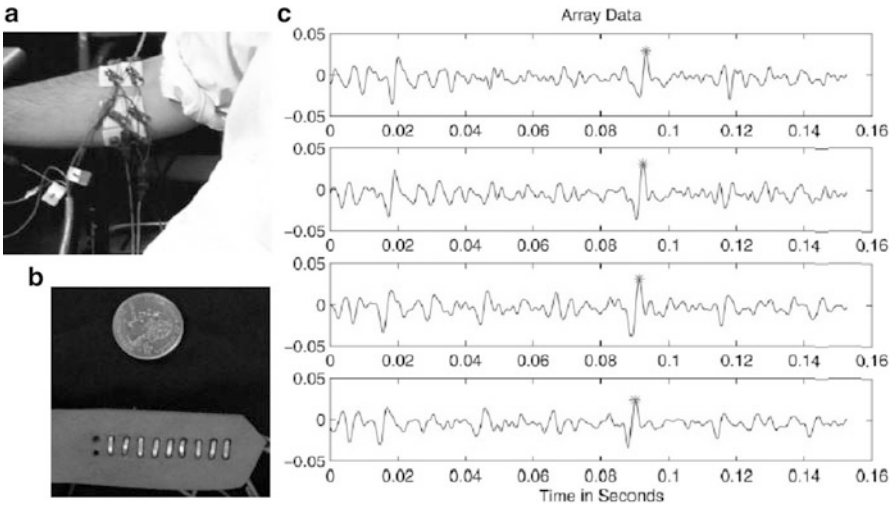

Fig. 11.2 (**a**) Schematic of an EMG experiment; (**b**) The electrode array of an EMG; (**c**) Typical experimental data from an EMG [11]

11.1.3 Electrocardiography (ECG)

Sleep is deeply linked to the autonomic nervous system, reflected by RR intervals (RRIs) on the ECG. Previous reports have shown that "falling asleep" is preceded by changes in autonomic nervous system signaling, notably an increase in vagal tone and reduction of sympathetic drive [13, 14]. A shift in the dynamic balance of the autonomic nervous system is associated with various disease states. This phenomenon is also noted during sleep. Heart rate variability (HRV) may be measured in both the time and frequency domains (spectral analysis) for vagal activity estimation (Fig. 11.3) [15]. HRV is a well-characterized index of the autonomic system and can be used to detect in interpret rapid changes in RRIs. Therefore, HRV and sleep have been investigated in numerous studies [13, 14, 16].

During sleep, HRV shows signs of relative sympathetic dominance in patients with coronary artery disease and after myocardial infarction [17–19]. Obstructive sleep apnea syndrome (OSAS) is a medical condition of research interest due to its prevalence and its cardiovascular consequences. Mendez et al. [20] demonstrated the importance of using time-variant or time-frequency approaches for correctly managing signal non-stationarities, typical of apnea episodes [20]. It is reported that increased sympathetic activity during sleep may provide a link between OSAS and cardiovascular disease [21]. Milos et al. also published similar results [22]. Previous research has also shown that HRV is the best predictor of sleep quality, and a significant reduction in cardiac vagal modulation of heart rate during nocturnal sleep has been identified in chronic fatigue syndrome [16].

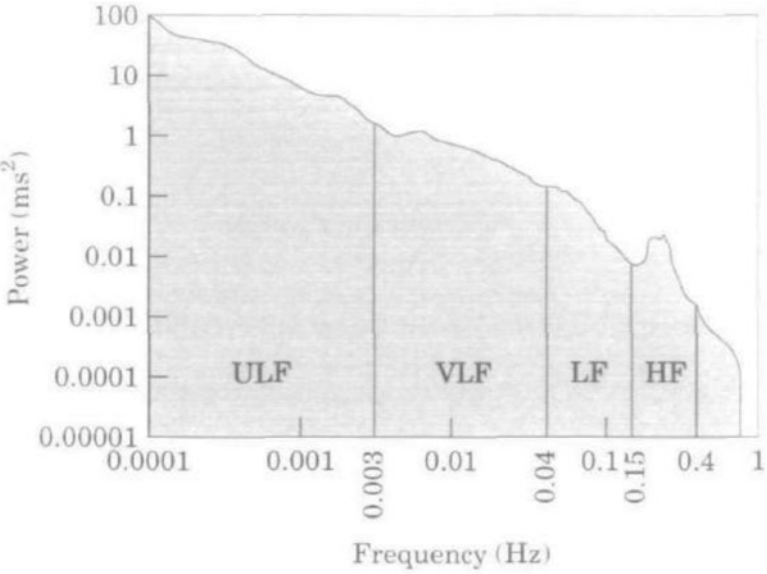

Fig. 11.3 Example of an estimate of power spectral density obtained from the entire 24-h interval of a long-term Holter recording [15]

11.1.4 Electrooculogram (EOG)

Sleep is composed of a rapid eye movement (REM) and non-rapid eye movement (NREM) cycle. These are alternated continuously during the whole course of sleep. As its name suggests, rapid eye movement involves significant eye activity during sleep. An electrooculogram (EOG) is obtained by placing electrodes around the outside of the eyes and recording changes in electrical potential between the back of the eye and the front of the eye (Fig. 11.4). EOG is therefore a helpful instrument in identifying REM cycles. A technician uses two EOG channels to measure vertical and horizontal eye movements. The measurements can detect slow rolling eye movements that are typically present when the patient is initially falling asleep. They can also detect the onset of the REM sleep cycle as well as its duration.

Studies have shown that REM sleep is concomitant with significant alterations in heart rate, respiratory rate and even blood pressure [19, 24]. EOG is well documented as an important indicator for REM sleep [25], and time domain analysis of EOG is a well-established technique used to define the phasic or active state of REM sleep [25]. EOG is also considered to be an index of arousal or attention, which may reflect the level of consciousness during sleep [26]. Previous reports have also shown that EOG, as analyzed in the frequency domain, may also provide information on sympathetic activity during night sleep [27].

These four electrophysiological methods, (EEG, EMG, ECG, and EOG), are similar in their applications for sleep research, but differ in their analysis algorithms

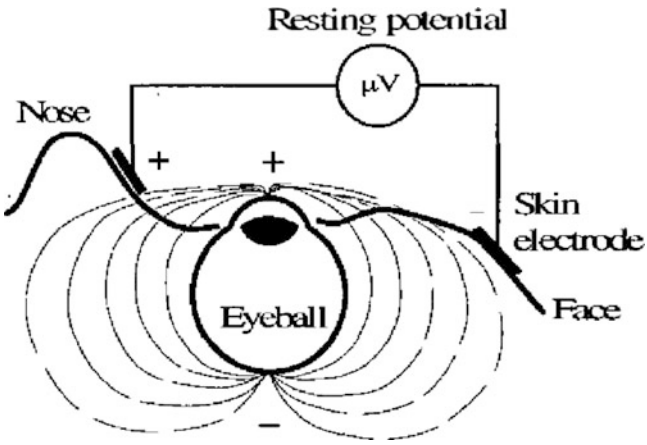

Fig. 11.4 A schematic diagram of an electrooculogram [23]

and electrode positions (see references for further details). Since it is critical to keep electrodes still during signal recording, most electrophysiological measurements are implemented by laboratories and hospitals. To improve the usage of these methods, their capacity for widespread use must be improved, and this constitutes the next challenge for these electrophysiological techniques.

11.2 Functional Neuroimaging: fMRI and PET

Recently, neuroimaging methods have been used to investigate whether sleep disorders are associated with changes in structure or regional activity. Functional imaging is used to detect brain function in discrete areas which are inaccessible by other means. Nuclear imaging has been used to observe changes in function across the sleep and wake cycle. For example, non-rapid-eye movement (NREM) sleep seems to be related to a decline in function in the heteromodal association cortex in the frontal, parietal and temporal lobes, as well as in the thalamus [28–32], whereas REM sleep is characterized by relative increases in limbic and paralimbic function (Fig. 11.5) [34–37].

Positron emission tomography (PET), using [^{15}O]-labeled water ($H_2^{15}O$) or [^{18}F] fluorodeoxyglucose (18FDG), and functional magnetic resonance imaging (fMRI) are used to depict functional neuroanatomy. Global and regional patterns of brain activity during sleep are different to during wakefulness. There are also major functional differences between rapid eye movement (REM) sleep and non-REM sleep. During non-REM sleep, there is a global decrease in cerebral blood flow (rCBF) and in particular in the dorsal pons, mesencephalon, thalamus basal ganglia, basal forebrain and anterior hypothalamus, prefrontal cortex, anterior cingulate

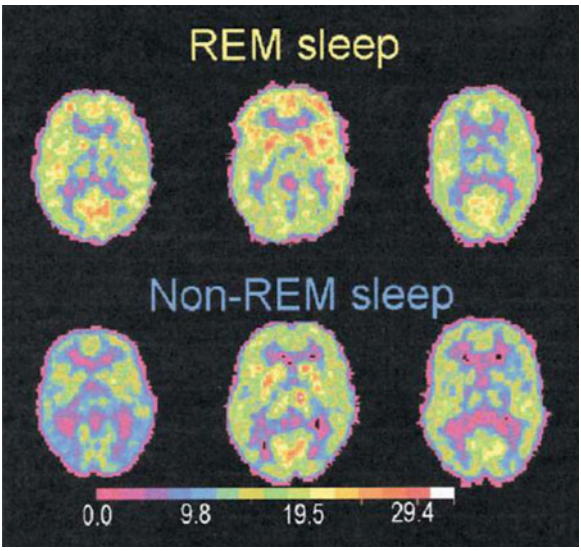

Fig. 11.5 Fluorodeoxyglucose (*FDG*) uptake in three healthy individuals during REM sleep (*top*) and three individuals in non-REM sleep (*bottom*). Higher metabolic rate is observed in REM sleep, especially in the cingulate [33]

cortex and precuneus [31, 38, 39]. In contrast, there is sustained neuronal activity and cerebral blood flow during REM sleep [40–44]. During REM sleep, regional activations are found in the pontine tegmentum, thalamus, amygdala, hippocampus, anterior cingulate cortex, temporo-occipital areas, basal forebrain, cerebellum and caudate nucleus (Fig. 11.6).

Primary insomnia is characterized as inadequate sleep or poor sleep quality, which is unrelated to other concomitant medical conditions. Patients usually have difficulty with falling asleep, maintaining sleep and early awakenings. Consequently, they may have daytime dysfunction. Patients exhibit fatigue, mood symptoms, decreased attention, vigilance and concentration, all of which may cause clinically significant distress or impairment in social, occupational or other important areas of functioning. In one study, rCBF was assessed in patients suffering from primary insomnia, using single-photon emission computed tomography (SPECT) with technetium – 99m – hexamethylene – propyleneamine Oxime (Tc-99m-HMPAO), a gamma-emitting radionuclide imaging agent [46]. Significant rCBF decreases were found during the first non-REM sleep cycle in medial frontal, parietal and occipital cortices, with the largest reduction in the basal ganglia in patients compared to controls. In another study, the same group examined the effects of behavior therapy (BT) on rCBF during non-REM sleep. They showed that BT is an effective treatment of insomnia which they hypothesized constituted a reversal of the previously reported patterns of cerebral deactivation after the therapy. They found a significant rCBF increase in the basal ganglia when comparing post- to pre-treatment imaging [47].

OSAS is characterized by repeated complete or partial collapses of the upper airway during sleep. It is a common disorder affecting up to 28% of the adult population. The pathogenesis of OSAS remains unclear. Abnormal upper airway

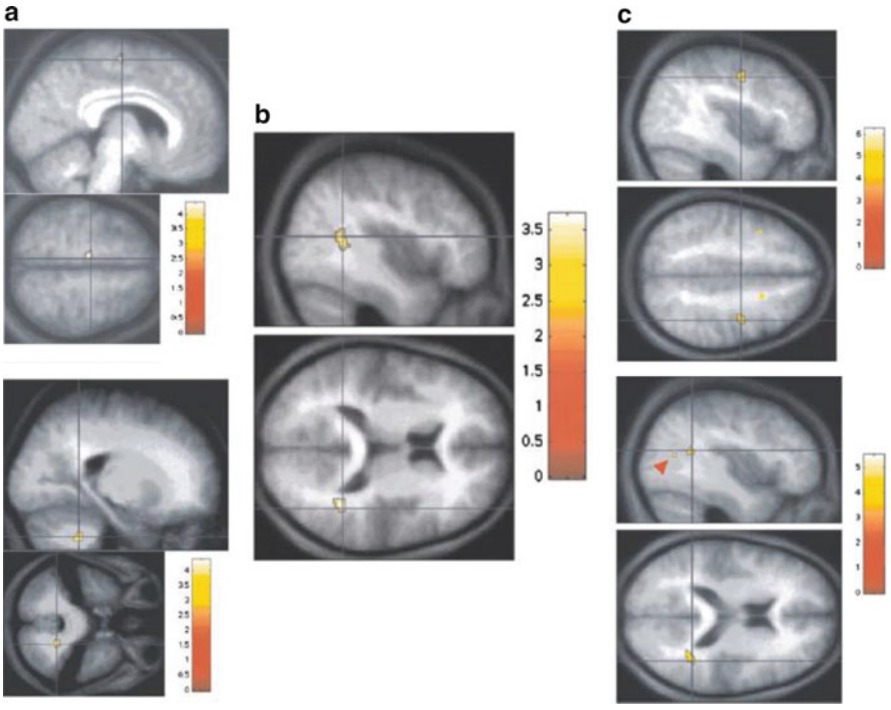

Fig. 11.6 Effects of sleep and sleep deprivation on pursuit task learning, assessed by fMRI. (**a**) Main effect of learning. Activation foci (SEF on the *upper panel*; DN on the *lower panel*). (**b**) Trajectory by group interaction. The STS is significantly more active in the learned condition in sleeping subjects. (**c**) Results of the second-level analysis based on psychophysiological interactions. *SEF* supplementary eye field, *DN* dentate nucleus, *STS* superior temporal sulcus [45]

anatomy may lead to mechanic collapsibility; however, OSAS cannot only be explained by this mechanism. Several studies have used MRI with the voxel-based morphometry (VBM) technique to assess structural changes in the brain associated with OSAS. Macey et al. reported the presence of widespread gray matter loss in patients compared to controls [48]. There were also unilateral gray matter losses in regions including the left ventro-lateral frontal cortex, anterior cingulate cortex and cerebellum, which are brain structures involved in upper airway motor regulation. This may potentially modulate cardiovascular and respiratory function. It is possible therefore that these volume changes may be present before the onset of OSAS, and the authors speculated this may contribute to a progression of neural damage underlying this pathology. They also reported a diffuse and bilateral gray matter loss mainly in the parietal and frontal cortex and a bilateral loss in the parahippocampal gyrus of the temporal lobe, which was suggested to be the result of repetitive and intermittent hypoxemic episodes. These damages to frontal, parietal and temporal regions may contribute to cognitive deficits frequently accompanying OSAS [48]. Other studies used single voxel proton magnetic resonance spectroscopy (1H-MRS)

to investigate brain metabolic impairments induced by hypoxemia in OSA. In a study conducted in 25 patients, Kamba et al. [49] found a significant inverse relationship between the severity of OSAS and N-acetylaspartate (NAA)/choline (Cho) ratio in cerebral white matter. Recently, Alchanatis et al. demonstrated a significant decrease in NAA/Cho and Cho/creatine ratios, as well as in absolute concentrations of NAA and Cho, in the frontal white matter in OSAS patients [50]. These results suggest that OSAS may cause axonal damage and myelin impairment, especially in the frontal white matter.

Using neuroimaging, we can explore sleep physiology in humans by describing the functional changes at different stages of sleep. We can correlate brain images with dreaming features and demonstrate precise cerebral reactivations during sleep. In sleep pathology, neuroimaging findings are classified into several categories. Firstly, we use structural MRI studies and VBM techniques to look for morphological changes. Secondly, PET/SPECT assess dysfunction in neurotransmission. Thirdly, spectroscopy studies are designed to detect signs of neuronal loss or damage and abnormality in energy metabolism. Finally, changes in cerebral blood flow, glucose metabolism or Blood-Oxygen-Level-Dependent (BOLD) fMRI signal is compared between sleep-disordered patients and healthy controls to reflect regional brain activity.

11.3 Contact/Non-contact Sensors

Measuring physiological information such as respiration and heart rate during sleep is of great importance for public health care. In sleep disorders, this is especially important for early diagnosis of cardiorespiratory sleep disorders. However, use of polysomnography encounters several problems including that the sensor(s) may be removed or damaged and thus interrupt measurement during sleep, and that it is a physical and psychological burden to have sensors attached to patient's body, thus making the sleep pattern differ from daily sleep. Many new techniques for unconstrained sensing of physiological information have been developed to overcome these problems. Novel sensor devices have been developed for long term monitoring of the cardiorespiratory signals during sleep and can be used by healthcare professionals for research into sleep disorders.

Over the past few years, numerous attempts have been made to develop unconstrained sensors for in-sleep monitoring of physiological information (see Fig. 11.7). For example, Alihanka et al. [52] and Salmi and Leinonen [53] proposed a static charge sensitive bed for unconstrained monitoring of respiration and heart rate during sleep. Nishida et al. [54] embedded 221 pressure sensors in a bed in order to monitor respiration and body movement during sleep. Similarly, Tanaka [55] and Watanabe and Watanabe [56] developed pressure sensor embedded air mattresses for monitoring in-sleep respiration and heart rate.

Although the contact-pressure sensor method has been applied in many ways to detect sleep disorders, some investigators assert that non-contact evaluation is

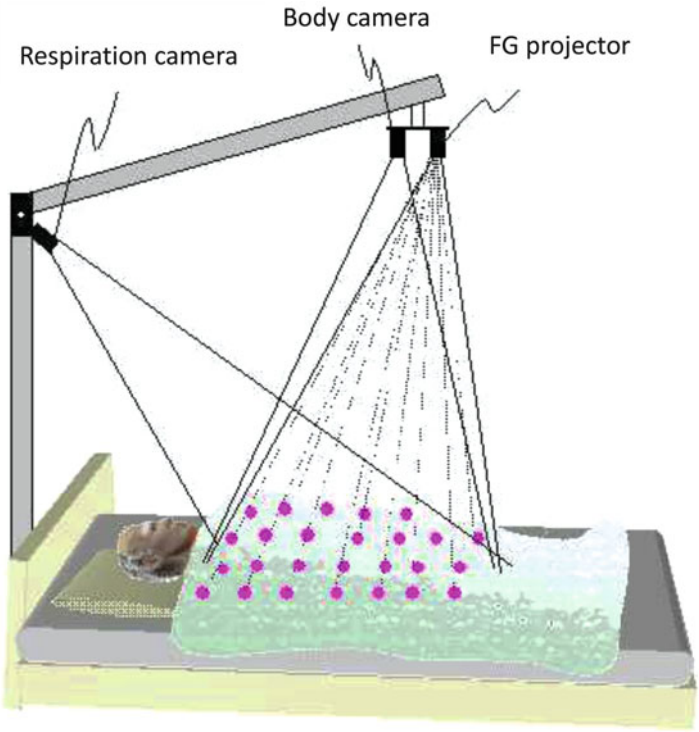

Fig. 11.7 Non-contact, fully automated breath motion monitoring system. *FG* fiber grating [51]

a better approach. The best clinical assessment of sleep in the home environment is a sleep diary. The patient is asked to record every event including "going to bed", "lights out", "sleep onset latency", and so on. The Pittsburgh sleep diary is a well-accepted standard for recording such observations in a written format [57]. However, sleep diaries correlate quite poorly with objective measurements of the same parameters. The results may confuse healthcare professionals and lead to incorrect diagnosis. New methods are needed for monitoring sleep in the home environment; specifically, a non-contact sensor which tracks a person's movement and respiration patterns whilst they are in bed. These signals can be used to estimate sleep and wakefulness [58].

11.4 Biomolecular Analysis

Recently, much research has focused on the molecular basis of sleep in order to better understand its physiological basis. Although not directly detectable, the function of sleep is hypothesized to restore brain energy expended during active

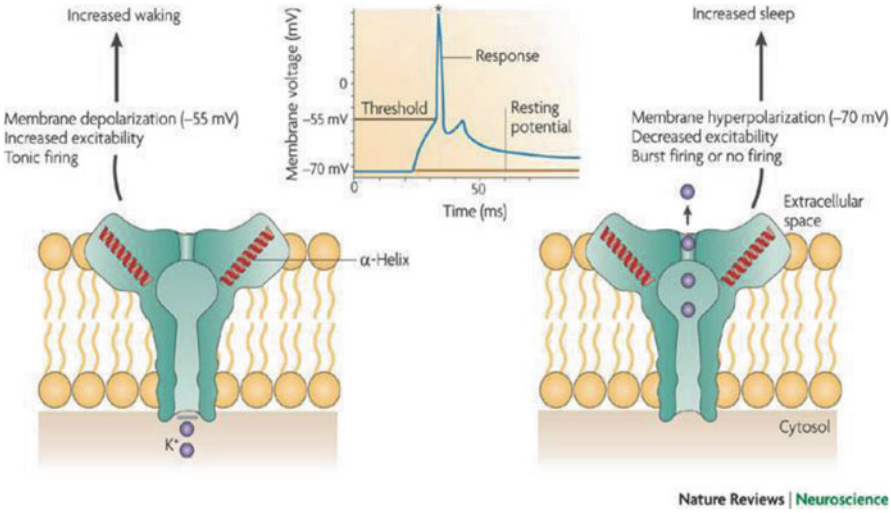

Fig. 11.8 Normally, the opening of Shaker-encoded channels allows potassium ions to exit the neuron, hyperpolarizing (reducing) the membrane potential to close to the resting membrane potential. Mutations that reduce the total number of these channels and/or decrease the time the channels remains open tend to bring the membrane potential to more depolarized (more positive) levels, closer to the threshold for firing an action potential (*blue line in graph*) [61]

waking [59]. Dworak et al. reported that ATP (the energy currency of brain cells) levels show a surge in the initial hours of spontaneous sleep in wake-active but not in sleep-active brain regions of the rat [60]. This surge is dependent on sleep, but not time of day, and permits energy consuming anabolic processes, such as protein and fatty acid synthesis, to occur. This increase in ATP levels during sleep provides molecular evidence in support of the classical view that an important function of sleep is to provide the brain with increased energy stores.

Genetic mechanisms of sleep are not well understood. Most studies are primarily descriptive but nevertheless, genetic data provides a new way to address the regulation and function of sleep. It is clear that circadian genes affect the timing of sleep. Core circadian genes include *CLOCK*, *BMAL*, and *Cry*. If there are mutations in these genes or other circadian regulators, the amount of sleep is changed (see Fig. 11.8). *Dec*2, a basic helix–loop–helix (bHLH) protein, is thought to function as a repressor of *CLOCK/BMAL* and therefore may regulate sleep length [62]. These genetic studies may provide insights into the function of sleep, and the potential of this field is only beginning to be realized. Genetics also allows identification of specific signaling pathways involved in sleep.

OSAS is a common medical condition that occurs in a considerable percentage of the population. Biomolecular analysis has also been applied to OSAS Substantial evidence has shown that patients with OSAS have an increased incidence of hypertension compared to individuals without OSAS, which suggests that OSAS is a risk factor for the development of hypertension. It has also been noted that OSAS

may be associated with stroke and transient ischemic attacks. Although the precise link between OSAS and cardiovascular disease is unknown, there is evidence that proinflammatory and prothrombotic factors are increased in OSAS. These factors may lead to atherosclerosis, resulting in cardiovascular disease and stroke. Hypoxemia and sleep deprivation also leads to increased levels of inflammation and inflammatory markers [63–65]. Patients with sleep apnea have increased interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), and C-reactive protein (CRP) [64]. Inflammation is an important component in the pathogenesis of cardiovascular disease, and inflammation with elevated CRP leads to atherosclerosis and endothelial dysfunction. Furthermore, OSAS has been associated with enhanced platelet activity and aggregation, as well as leukocyte adhesion and accumulation on endothelial cells, which are common to both OSAS and atherosclerosis. By detecting these biomarkers, it is possible to evaluate the impact of OSAS on clinical disease. Healthcare professionals should be aware that OSAS may be a risk factor for the development of cardiovascular disease.

11.5 Novel Biochip Technology Application

Traditionally, biomolecular diagnostic technology has been improved by employing optical detection and signal processing techniques that suppress background noise. At the same time, advances in nano/micromachining over the last decade have brought revolutionary changes to biomolecular diagnosis. These changes have provided miniaturization, simplification and automation for bioanalytical methods. Technological advancements such as these open the door for development of new micro technologies for future molecular detection using non-traditional approaches.

In the non-labeled method, the use of aggregated nanomaterial molecular probes has been proposed to amplify signals, leading to increased sensitivity and selectivity of biomolecular sensing. Mirkin [66] first demonstrated formation of macroscopic gold nanoparticle aggregates using DNA oligonucleotides capped with thiol groups as particle binding agents. Based on this principle, Taton demonstrated signal amplification by forming a sandwich structure on a substrate surface which consists of a silver-coated gold nanoparticle specifically bound to a target DNA molecule as shown in Fig. 11.9 [67]. The amplified signal produced with this method permits DNA detection at a concentration of 50 fM. This demonstrates the ability to use nanostructures to detect genomic DNA without PCR at concentrations relevant to real medical diagnostic applications. A similar nano-detection technology, the bio-bar-code assay, can be used for low-concentration protein detection. Utilizing the bio-bar-code assay, Nam et al. achieved 30 atto-molar sensitivity for protein detection [68]. This was accomplished by using two types of particles for biomolecular purification, detection and amplification; the first is a microparticle with an antibody to a target antigen and the second is a nanoparticle with a recognition agent that can sandwich the targeted antigen with the microparticle. Because of the presence of targeted antigens, these two kinds of particles form a sandwich structure.

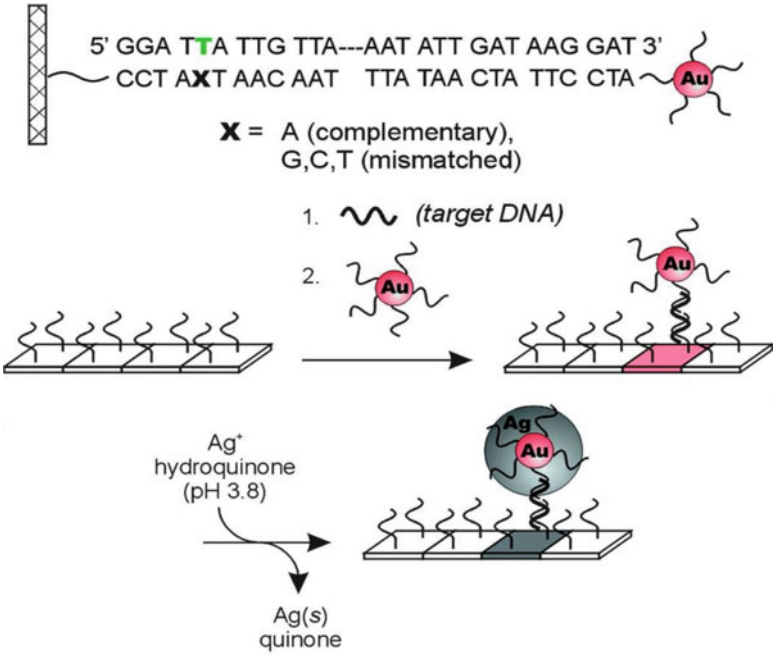

Fig. 11.9 Scanometric DNA array detection using silver-coated gold nanoparticles for recognizing DNA segments on a chip [67]. The nanoparticles are fixed onto a substrate through specific antibody-analyte binding. The presence of the target protein is detected by identifying the oligonucleotide sequence of the encoding DNA strands released from the nanoparticle probes

An external magnetic field can then be used to separate the sandwiched target from the sample solution for further detection. Unfortunately, one of the major drawbacks of this technique is that it requires a very long reaction time between thiol groups attached to the DNA and nanoparticles.

As an alternative approach, micro-mechanics and nano-electronics are also used in developing label-free protein detection technology. Utilizing specific biomolecular interactions on one surface of a microcantilever beam can cause beam bending [69], as illustrated in Fig. 11.10a. The micro-cantilever bending can be sensed by a position-sensitive diode through a laser beam reflected from the beam. The detection of two forms of prostate-specific antigen (PSA) has been achieved over the concentration range of 8 *p*M–2uM in a background of human serum albumin (HSA). In addition, silicon nanowire field-effect devices can be introduced to detect PSA though electrical detection as shown in Fig. 11.10b [70]. Protein detection is achieved by measuring the conductance of the nanowire using lock-in technology. This device has a detection capacity of 4 *f*M with multiplexing capability. However, these methods require additional device surface modification for detection. This increases the complexity of the diagnostic assay and creates time-consuming sample preparation. An important point to note is that the sensitivity demonstrated by

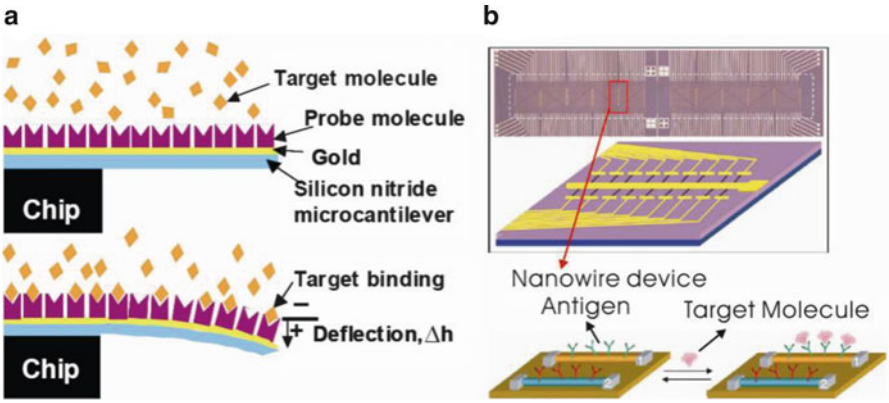

Fig. 11.10 (**a**) Detection of target protein by micro-cantilever beam bending [69]. (**b**) Nanowire protein detection devices with femto-molar sensitivity [70]

nanowires is much lower than the binding affinity of PSA and the anti-PSA antibody – 2×10^{10} L/mol. In other words, the bioconjugated pair (PSA and the anti-PSA antibody) cannot bind to each other effectively in the *f*M range. Since sample buffers also have charged ions, the external applied electrical field from the nanowire might also attract these ions and affect detection. Experimental results should be examined carefully to understand the details of this technology.

11.6 Conclusion

The demands of modern healthcare means sleep status has become one of the most important parameters for monitoring both physical and mental health. To provide this information, it is necessary to have systems with multiple-inputs, such as biophysical and biochemical analysis. In this chapter, we have briefly introduced the most commonly used techniques in sleep technology. As many innovative techniques are currently in development, we encourage readers to explore future developments.

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Chapter 12
Sleep Technology for Driving Safety

Sei-Wang Chen, Kuo-Peng Yao, and Hui-Wen Lin

Abstract In this chapter, a vision system for monitoring driver vigilance is presented. The level of vigilance is determined by integrating a number of facial parametric values including: percentage of eye closure over time, average eye closure duration, eye blinking frequency, average degree of gaze, average duration of mouth openness and head nodding frequency. Initially, facial features including the eyes, mouth and head are first located in the input video sequence. They are then tracked over subsequent images. Facial parameters are estimated during facial feature tracking. A number of video sequences having drivers of both sex and of different ages under various illuminations and road conditions are employed to test the performance of the proposed system. Finally, we suggest future work on how to extend the system in terms of both efficiency and effectiveness.

Keywords Vision system • Driver vigilance monitoring system • Facial feature detection and tracking • Facial parameter estimation • Fuzzy reasoning

12.1 Introduction

Although many drivers abhor drink driving, they may willingly drive with impaired vigilance due to factors such as tiredness, somnolence, diversion and illness. However, driving whilst weary, drowsy, distracted, or unwell can be equally as dangerous as drunk driving [1, 2] since all can reduce visual activity, perceptual sensitivity, situational awareness and decision-making capability. According to the National Highway Traffic Safety Administration (NHTSA), approximately 100,000 fatigue or somnolent-related accidents occur every year resulting in 1,550 fatalities,

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71,000 non-fatal injuries and costing around $12.5 billion annually. This suggests we should campaign to increase awareness of the dangers of driving whilst fatigued to a similar degree as drink driving. In this study, we focus on the detection of driver fatigue and drowsiness so we may alert the driver's attention as soon as possible.

Many techniques have been proposed for monitoring driver vigilance. They can be divided into three categories: (1) physiological response, (2) driving behavior and (3) facial expression approaches. In the physiological response approach [3–6], the readings from apolysomnography which include ECG (heart activity), EMG (muscle activity), EDA (skin conductance), EEG (brain activity), and EOG (eye movement) have been used to assess human alertness. Some of these physiological signals (e.g. EEG and EOG) have revealed a high level of correlation with alertness. However, the electrode-based sensors used to measure these physiological signals are obtrusive in that they have to be in physical contact with subject in order to acquire a reading. To measure these physiological parameters whilst driving, sensors have either been installed on the seat and the steering wheel or been embedded in such devices as elastic straps, wristbands, helmets, and contact lenses. Even so, these devices can make the driver uncomfortable and interfere with normal driving behavior. Furthermore, compared with the other approaches the sensitivity and specificity of the physiological approach need improvement [7].

In the driving behavior approach [8, 9], an assortment of driving data obtained from the vehicle and the road including steering wheel angle/torque, gas/brake pedal positions, gear change, vehicle speed/acceleration, lane position and course shift have been applied to interpret driver vigilance. In order to gather these diverse measurements of driving data, a variety of sensors are introduced to the vehicle. However, the installation of multiple sensing devices not only increases cost but are also restricted by limitations including vehicle type, driver experience and road conditions [10]. Moreover, unlike physiological signals that are directly measured from the driver, driving data collected from the vehicle and the road have to be transformed to relate to the driver. In addition, different kinds of driving data have distinct units and scales. Both data transformation and data unification will inevitably introduce uncertainties.

The facial expression approach [10–23] is primarily inspired by the ability of the human visual system to effortlessly identify the vigilance level of a person based on his or her facial expressions. Facial expressions convey inward feelings including both psychological (e.g. cheer, anger, delight, disgust, fear and surprise) and physiological (e.g. vitality, fatigue, drowsiness, alertness, distraction, attention, drunkenness and illness) reactions [24]. Facial expressions relating to these two classes of reactions are typically distinct. In this study, the physiological reactions of fatigue and drowsiness are the primary focus. The associated facial expressions include eye blinking, gaze fixation, yawning and head nodding.

To examine facial expressions of drivers, various visual sensors have been reported. Hayami et al. [14] incorporated a CCD camera, a mirror and an infrared LED into a headgear for detecting and tracking the driver's eyes. The headgear had its own light source and a special configuration between the camera and mirror

which successfully avoided disturbance from ambient lights. Lalonde et al. [17] used a near-infrared (NIR) source to illuminate the driver's face, which can then be captured by an ordinary black/white camera. Low contrast images increases the reliability of detecting facial features. Ito et al. [16] and Park [20] projected a pulsed infrared (IR) light onto the driver's face, which was then captured by a CCD camera synchronized with the IR pulse. Facial images produced this way can remain stable over a large range of illuminations. Ji et al. [10] and Bergasa et al. [11] built an illuminator consisting of two sets of IR LEDs. These two sets of LEDs were synchronized so that the sub-images formed from the even and odd fields of an image acquired using a narrow-angle CCD camera contain bright and dark pupils, respectively. By taking the difference between these two sub-images, pupils are highlighted in the resulting image.

Both IR and NIR illuminators can work well under controlled environments, but they are compromised by strong lights and dynamic backgrounds and only work over a limited distance. A further disadvantage is their restricted spectral bands, which forces their accompanying visual sensors to overlook other spectral information. However, it is well recognized that color information provides important cues for object detection, tracking and recognition [25]. There have been a larger number of face detection studies based on chromatic evidences [26–34]. However, very few studies [18, 22, 33] have considered facial feature detection of drivers using color videos inside vehicles. Potential challenges to such work includes video instability due to moving vehicles, rapid illumination variation resulting from ambient lights, abrupt lighting changes (e.g. entering/exiting tunnels and sunshine/shadow) and partial occlusion. In this study, we have developed an in-vehicle vision system for monitoring driver fatigue and drowsiness in the daytime using a video camera without supplementary light.

The rest of this chapter is organized as follows: Sect. 12.2 outlines the proposed system, including its configuration and workflow, Sect. 12.3 details the implementation of the system components, Sect. 12.4 demonstrates the viability of the proposed system and finally concluding remarks and future work are discussed in Sect. 12.5.

12.2 Drowsiness/Fatigue Monitoring System

In this section, the configuration and workflow of the proposed system is discussed.

12.2.1 System Configuration

The system is composed of three major components: a video camera, a host computer and a warning device. Of these three components, the camera, which provides the input data to the system, plays an important role in determining the

Fig. 12.1 Installation of the video camera

Fig. 12.2 Example images captured by the onboard video camera

technique and workflow of the system. As discussed earlier in this chapter, there are several challenges to the system but proper installation of the camera can address some of these issues. Takai et al. [33] attached their video camera to the rearview mirror in order to monitor the driver's face. Since drivers often adjust the rearview mirror before driving, adequate configuration of the camera and the mirror ensures the camera is appropriately placed once the rearview mirror is adjusted. However, since the rearview mirror is located near the upper center of the front windshield, a camera attached to the mirror will capture side-view images of the driver. Moreover, the facial features of the driver can be obstructed when the driver turns his or her head. For this study, we mounted a video camera on top of the dashboard directly behind the steering wheel with a tilt angle of about 30° to the driver's face (see Fig. 12.1). Figure 12.2 demonstrates the images captured by this video camera with different head orientations of the driver.

12.2.2 System Workflow

Figure 12.3 shows a block diagram of the system process. There are five blocks in the diagram which denote preprocessing, facial feature extraction, face tracking, parameter estimation and reasoning. Each block represents a major step of the system process.

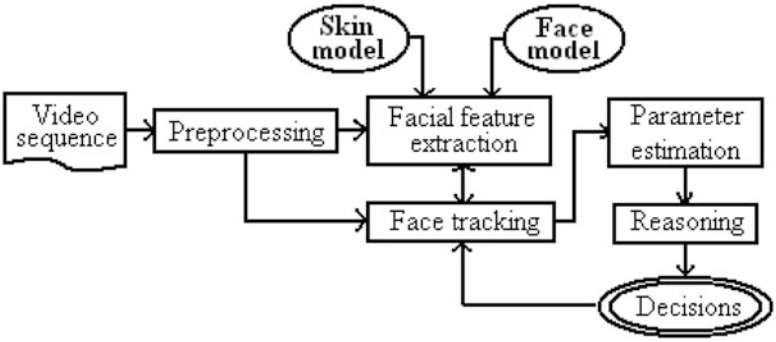

Fig. 12.3 Block diagram for the proposed driver vigilance monitoring system

12.2.2.1 Preprocessing

Considering an input video image, in the preprocessing step a brightness normalization process is first applied to the image (see Sect. 12.3.2) in order to alleviate abrupt lighting changes (e.g. sunlight and shadows) and rapid illumination variations (e.g. entering or exiting a tunnel). Next, for each image pixel we calculate a number of chromatic values which are then used to detect facial features in the image.

12.2.2.2 Facial Feature Extraction and Tracking

In the facial feature extraction step, we locate the face, eyes and mouth of the driver in the input image. Figure 12.4 shows a flowchart for this step. There are three stages to this process: skin location, eye and mouth detection and face determination.

Skin location relies on a skin model (see Sect. 12.3.1.1), which is prescribed in terms of the chromatic characteristics of skin. Based on this model, a pixel is regarded as a skin pixel if its chromatic value fits the skin model. However, frequently false positives (i.e. skin pixels are determined to be non-skin) and false negatives (i.e. non-skin pixels are determined to be skin) can occur. The former results in holes within skin areas, whereas the latter leads to noisy patches. We preserve only the largest connected skin area since it most likely corresponds to the face region.

Instead of detecting the eyes and mouth within the retained skin area, we look for them throughout the entire image due to the potential unreliability of the skin area. However, this can be time consuming and consequently we introduce a tracking process characterized by the well-known Kalman filter [35] to trace the face over the video sequence after it has initially been detected. This tracking process is much faster than the detection process. The detection process (discussed in Sect. 12.3.3.) is only required when the tracking process loses its target. The tracking process not only expedites facial feature location but also improves accuracy.

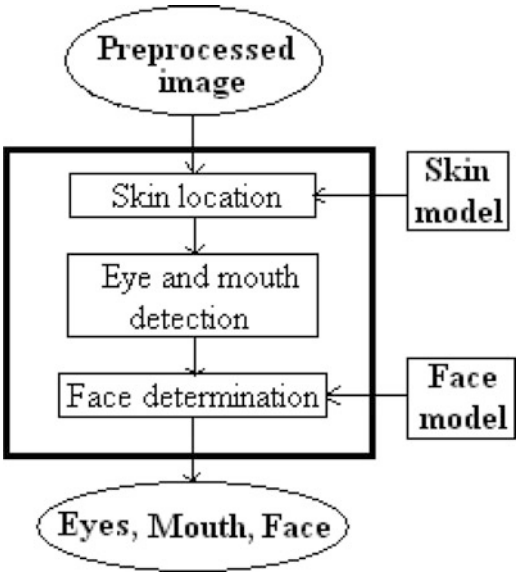

Fig. 12.4 Flowchart of facial feature extraction

Note that it is common for a number of eye and mouth candidates to be obtained during facial feature extraction. In the face determination stage, each time two eye candidates and a mouth candidate are chosen to form a face candidate. A confidence value is evaluated for the face candidate based on a prescribed face model (see Sect. 12.3.1.2) and the distance between the face candidate and the preserved largest skin area. The face determination stage returns the face candidate with the largest confidence value.

12.2.2.3 Parameter Estimation and Reasoning

During face tracking, a number of facial parameters (discussed in Sect. 12.3.4) including percentage of eye closure over time, average eye closure duration, eye blinking frequency, average degree of gaze, average duration of mouth openness and head nodding frequency are estimated at every fixed time interval. An integration process based on fuzzy reasoning (Sect. 12.3.5) then amalgamates the parametric values to determine the vigilance level of the driver. This information can be utilized by adaptive systems to manage noncritical operations including activating a fan, turning on a radio, or providing entertainment options. In a state of severe non-vigilance, the system can warn the driver of his or her current state and may even alert others to the driver's critical condition.

12.3 Implementation

In this section, major techniques including the skin and face models, brightness normalization, facial feature detection, facial parameter estimation, and fuzzy reasoning are described in detail.

12.3.1 Skin and Face Models

12.3.1.1 Skin Model

The skin model is described in terms of the chromatic characteristics of skin. Since the appearance of skin color can vary significantly under different lighting conditions, imaging distances and backgrounds, no single color space can adequately delimit the boundary of the skin-tone cluster. In this study, the *RGB*, YC_rC_b and $L\hat{U}\hat{X}$ color spaces are considered. The *RGB* space is included because the input images are represented in this space. Skin color in the *RGB* space has larger R than G values under various illumination conditions. Therefore, we have the first criterion for the skin model, which states that skin pixels have their R values larger than G values.

However, the skin-tone cluster in the *RGB* space is loosely distributed because each of the R, G and B components possesses both chrominance and luminance constituents. There are many color spaces [15, 31, 32, 36] with separate chrominance and luminance constituents. In this study, the YC_rC_b color space [30] is chosen because of its perceptual uniformity, low degree of luma dependency and compactness of the skin-tone cluster. The YC_rC_b and *RGB* spaces are related by $\begin{bmatrix} Y \\ C_r \\ C_b \end{bmatrix} = \begin{bmatrix} 0.299 & 0.587 & 0.098 \\ 0.500 & -0.4187 & -0.0813 \\ -0.1687 & -0.3313 & 0.500 \end{bmatrix} \begin{bmatrix} R \\ G \\ B \end{bmatrix} + \begin{bmatrix} 1 \\ 128 \\ 128 \end{bmatrix}$, where Y is the luminance component and C_r and C_b are the chrominance components. Skin color in the YC_rC_b space has C_r and C_b ranges of [133, 173] and [77, 127] respectively [26]. However, the C_r range shrinks and shifts as the Y value becomes either large or small. We hence include only the C_b range in the skin model. In particular, skin pixels have their C_b values falling between 133 and 173.

In order to compensate for this limitation of the C_r range, we further include the $L\hat{U}\hat{X}$ color space [32], in which $\hat{U}$ is nonlinearly related to C_r and can be directly computed in the *RGB* space by $\hat{U} = \begin{cases} M - \frac{M}{2}(\frac{G+1}{R+1}) & \text{If } R > G \\ \frac{M}{2}(\frac{R+1}{G+1}) & \text{Otherwise} \end{cases}$, where M is the dynamic range of gray levels. Recall that skin pixels have R values larger than G values. In the above equation, we are interested in $\hat{U} = M - \frac{M}{2}(\frac{G+1}{R+1})$, whose value falls between 120 and 240 for skin color.

We can summarize the skin model by the following: (a) $R > G$, (b) $C_b \in [77, 127]$ and (c) $\hat{U} \in [120, 240]$.

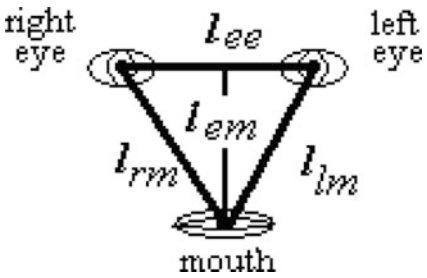

Fig. 12.5 Diagram of the face model

12.3.1.2 Face Model

The face model prescribes the structural relationships among facial features. A face candidate formed from eye and mouth candidates will be overlooked if it cannot fit the face model. As shown in Fig. 12.5, there are five constraints constituting the face model: (1) the mouth is lower than both eyes, (2) the horizontal position of the mouth is between those of the eyes, (3) the tilt of the line connecting the two eyes from the horizontal should be smaller than 15°, (4) the angle between the line joining the two eyes and the line connecting the mouth and any eye should be between 45° and 75°, and (5) $l_{ee} < l_{lm}$, $l_{ee} < l_{rm}$, and $l_{lm}/l_{rm} \approx 1$.

12.3.2 Brightness Normalization

Let $I(R,G,B)$ be an *RGB* color image. To perform brightness normalization on this image, we first estimate its brightness. To do this, we transform the color image I into its gray scale version I' by $I' = (R + G + B)/3$. Next, we calculate the histogram $h(I')$ of I', which gives the statistical distribution of the brightness of image I. Thereafter, we measure the asymmetricity, s, of $h(I')$ with respect to its mid dynamic range L, $m = L/2$, where L is the dynamic range of $h(I')$. Mathematically, $s = M_3/(M_2\sqrt{M_2})$, where $M_2 = \sum_{l=0}^{L-1} h(l)(l-m)^2 / \sum_{l=0}^{L-1} h(l)$ and $M_3 = \sum_{l=0}^{L-1} h(l)(l-m)^3 / \sum_{l=0}^{L-1} h(l)$ are the second and third moments of $h(I')$ about m. The value of s can be positive or negative indicating relative brightness or darkness of image I.

Having obtained the asymmetricity s of $h(I')$, if $s \leq -10$, then for each color component $C(= R, G, B)$ of image I, the C values of p-percentage of the image pixels with large C values are averaged to obtain a_c, where $p = \alpha e^{-\beta(s+128)}$ (empirically, $\alpha = 0.713$ and $\beta = 0.013$). Next, for each pixel of I, its C-value (c) is adjusted by $\min\{255, 255c/a_c\}$. This increases the brightness of the image. In a similar way, if $s \geq 50$, we scale pixel values c by $\max\{0, 255[1-(255-c)/255-a'_c]\}$, where a'_c is the average value of p'-percentage of the pixels with small values and $p' = \alpha' e^{-\beta'(s+128)}$ (empirically, $\alpha' = 0.323$ and $\beta' = 0.011$). This decreases

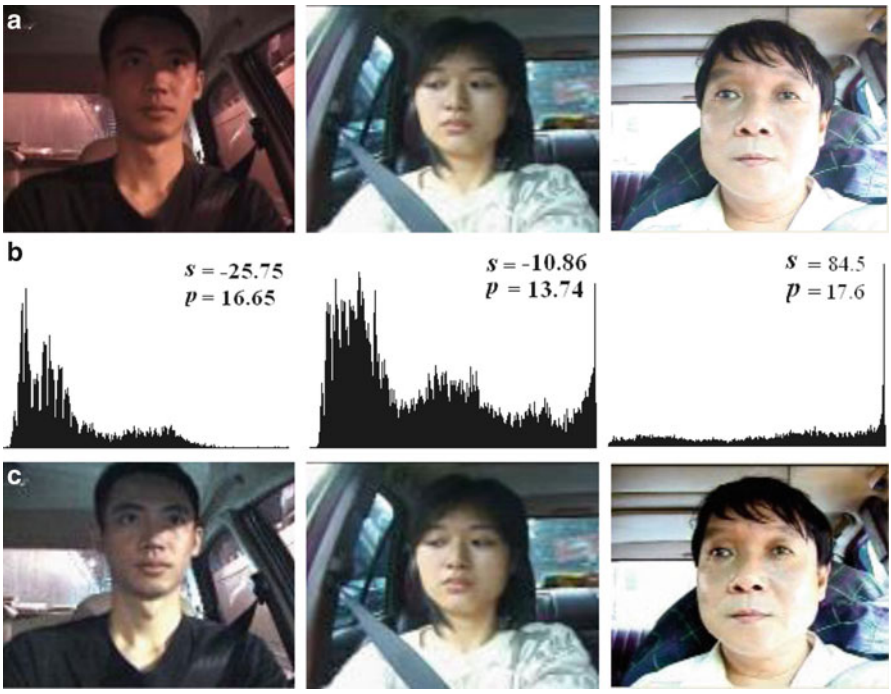

Fig. 12.6 Brightness normalization: (**a**) input images, (**b**) histograms, histogram asymmetricities, and pixel ratios, and (**c**) resultant images

the brightness of the image. No brightness normalization is applied to the image when $-10 < s < 50$. Figure 12.6 shows representative images of the brightness normalization process. The first row illustrates the input images, the second row depicts their histograms, histogram asymmetricities and pixel percentages and the third row shows the brightness normalization results of the original images.

12.3.3 Facial Feature Extraction

The technique previously developed by Hsu et al. [30] is employed to detect the eyes and mouth in an image. Since multiple eye and mouth candidates tend to be identified, we present a technique to determine the actual face. Let $I(R, G, B)$ be the input color image and $I'(Y, C_r, C_b)$ be its YC_rC_b version.

12.3.3.1 Eye Detection

To detect eyes, two maps M_e^C and M_e^L are first calculated from $I'(Y, C_r, C_b)$ which emphasize the chrominance and luminance characteristics of eyes respectively.

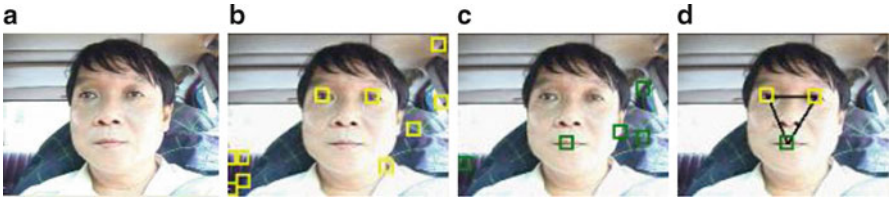

Fig. 12.7 Facial feature extraction: (**a**) input image, (**b**) extracted eye candidates, (**c**) extracted mouth candidates and (**d**) determined face

$M_e^C = (C_b^2 + \tilde{C}_r^2 + C_b/C_r)/3$, where $C_b^2, \tilde{C}_r^2 = (255 - C_r)^2$ and C_b/C_r have been scaled to $[0, 255]$, and $M_e^L = (Y \oplus s)/(Y \ominus s + 1)$, where $\oplus$ and $\ominus$ are morphological dilation and erosion operators and s is a structuring element. Next, M_e^C and M_e^L are integrated into M_e by $M_e = \min\{M_e^C, M_e^L\}$. Eyes are highlighted in the map M_e and can easily be located by sequential operations of thresholding, connected component labeling and size filtering. In general, a number of eye candidates are detected. Figure 12.7 shows an example, where the input image is given in Fig. 12.7a and the located eye candidates are shown in Fig. 12.7b.

12.3.3.2 Mouth Detection

In mouth detection, a map M_m, which emphases the mouth, is first calculated by $M_m = C_r^2 \cdot \left(C_r^2 - \eta \cdot C_r/C_b\right)^2$, where both C_r^2 and C_r/C_b have been scaled to $[0, 255]$, $\eta = 0.95 \sum_{(x,y)\in F_g} C_r(x,y)^2 / \sum_{(x,y)\in F_g} \frac{C_r(x,y)}{C_b(x,y)}$ and F_g is the largest skin region which was detected previously. The mouth is then located in map M_m by sequential operations of thresholding, connected component labeling and size filtering. In the example given in Fig. 12.7, the located mouth candidates are shown in Fig. 12.7c.

12.3.3.3 Face Determination

Let S_e and S_m be the sets of eye and mouth candidates, respectively. Between the eye pair candidates and the mouth candidate, we form a triangle called a face candidate for convenience. Let S_f be the set of all face candidates formed from S_e and S_m. For each face candidate, $f_i \in S_f$, if it is fit for the face model depicted in Fig. 12.5a confidence value c_i is calculated for f_i, which indicates the likelihood of f_i being an actual face. Two factors determine the confidence value: (1) how closely does the face candidate match an equilateral triangle and (2) how close in distance is the face candidate to the largest skin area located earlier. Let α and β denote these respective measurements of closeness.

We define $\alpha = \frac{1}{\pi} \max_{1\le i\le 3} \left\{\left|\theta_i - \frac{\pi}{3}\right|\right\} \cdot \min\{\frac{l_{lm}}{l_{rm}}, \frac{l_{rm}}{l_{lm}}\}$, where θ_i is any internal angle of the face candidate and $l_{lm}(l_{rm})$ is the length between the left (right) eye and the

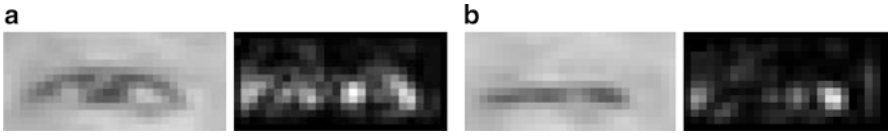

Fig. 12.8 (**a**) Open eye and (**b**) closed eye

mouth of the face candidate. Next, we define $\beta = e^{-\|\boldsymbol{c}_f - \boldsymbol{c}_s\|}$, where $\boldsymbol{c}_f$ and $\boldsymbol{c}_s$ are the centers of gravity of f_i and the largest skin area, respectively. Finally, the confidence value of f_i is defined as $c_i = e^{\alpha\beta}$. We choose as the actual face the face candidate with the largest confidence value, i.e. $f^* = \arg\max_{f_i \in S_f} \{c_i\}$. In Fig. 12.7, the determined actual face is shown in Fig. 12.7d.

12.3.4 Facial Parameter Estimation

Facial parameters under consideration include percentage of eye closure over time, average eye closure duration, eye blinking frequency, average degree of gaze, average duration of mouth openness and head nodding frequency. They are estimated ate very fixed time interval (or every 300 video frames).

12.3.4.1 Eye Parameters

Figure 12.8 shows an open eye and a closed eye with their vertical edge magnitudes. The open eye has a relatively stronger edge magnitude than the closed eye. Let E_{le} and E_{re} be the averages of edge magnitudes of the left and right eyes, respectively. We define the degree $d_e$of eye closure as $d_e = \min\{E_{le}, E_{re}\}/255$. Here, a small d_e indicates a high degree of eye closure.

Figure 12.9a shows the distribution of d_e values calculated for a sequence of 300 eye images. There are a number of significant valleys along the distribution curve (later referred to as the d_e-curve). These valleys correspond to eyes with high degrees of closure. To highlight significant valleys, we transform the d_e-curve into a v_e-curve by $v_e = (d_e - m)^2$, where $m = \frac{1}{300}\sum_{i=1}^{300} d_{e_i}$. Figure 12.9b depicts the v_e-curve, on which the prominent peaks correspond to the significant valleys on the d_e-curve. We then threshold the v_e-curve to obtain the binary b_e-plot displayed in Fig. 12.9c. On the b_e-plot, we note peaks at images 80 and 148. Figure 12.10a, b show the eye images at 80 and 148, respectively; the eyes are either closed or near closed.

Based on the b_e- plot, we are able to calculate the parameters of (a) percentage of eye closure over time: $P_e = \frac{1}{300}\left(\sum_{i=1}^{300} b_i\right)$, where b_i is the binary value of the b_e-

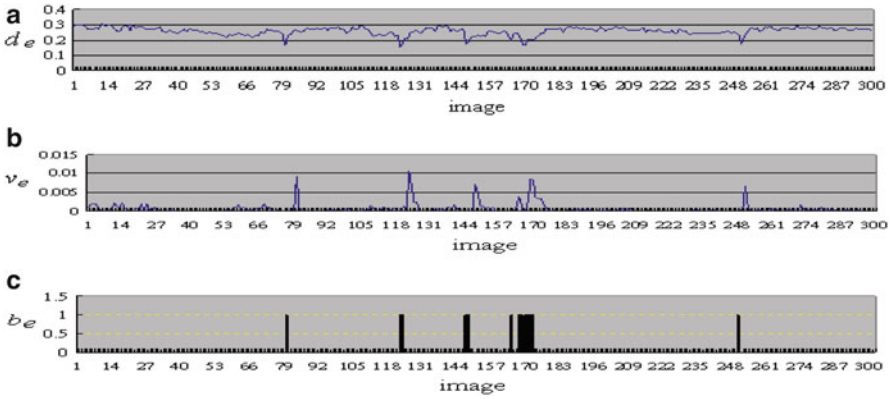

Fig. 12.9 The (**a**) d_e-curve, (**b**) v_e-curve, and (**c**) b_e-plot calculated from a sequence of 300 eye images

a

Image #	78	79	80	81	82
Right eye					
Left eye					

b

Image #	145	147	148	149	150
Right eye					
Left eye					

Fig. 12.10 Sequence of images captured centered around. (**a**) image 80 and (**b**) image 148

plot at image i, (b) eye blinking frequency: $f_e = n_e/300$, where n_e is the number of pulses on the b-plot and (c) average eye closure duration: $D_e = \frac{1}{n_e} \sum_{j=1}^{n_e} D_{ej}$, where D_{ej} is the time interval of pulse j.

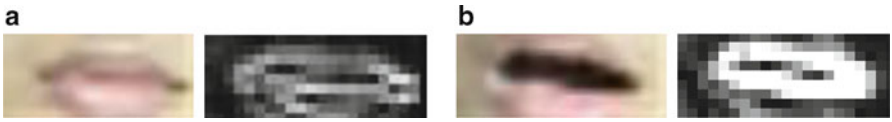

Fig. 12.11 (**a**) Closed mouth and (**b**) open mouth.

12.3.4.2 Mouth Parameter

Figure 12.11 shows a closed mouth and an open mouth with their edge magnitudes. The open mouth has stronger edge magnitudes than the closed mouth. Let E_m be the average edge magnitude of a mouth. We define its degree of openness as $d_m = E_m/255$. Similarly, we can transform d_m into v_m values by $v_m = (d_m - m')^2$, where $m' = \frac{1}{300}\sum_{i=1}^{300} d_{m_i}$, followed by thresholding to obtain a binary b_m value. The average duration of mouth openness is then defined as $D_m = \frac{1}{n_m}\sum_{j=1}^{n_m} D_{mj}$, where n_m is the number of pulses on the b_m-plot and D_{mj} is the time interval of pulse j.

12.3.4.3 Gaze Parameter

A person gazing at something will keep their eyes open and their head stationary. Let d_t denote the degree of gaze at time t. Recall that the larger d_e, the lower the degree of eye closure and the higher degree of eye openness. Therefore, $d_t \propto d_{e_t}$, where d_{e_t} is the d_e at time t. Let m_t specify the head movement at time t, which can be calculated during facial tracking. Since the smaller head movements represent a higher degree of gaze, mathematically, $d_t \propto 1/m_t$. Based on these observations, we can define $d_t = \frac{e^{m_t/d_e}}{1-e^{m_t/d_e}}$, which states that the larger d_{e_t} and the smaller m_t, the larger d_t becomes. The average degree of gaze is defined as $d_g = \frac{1}{300}\sum_{t=1}^{300} d_t$.

12.3.4.4 Head Parameter

As per the face model illustrated in Fig. 12.5, both l_{rm} and l_{lm} will decrease if the face model is lowered or raised. We define the inclination degree of the head as $d_h = \min\{|a_r|, |a_l|\}$, where $a_r = (l^t_{rm} - l^{t-1}_{rm})/l^{t-1}_{rm}$ and $a_l = (l^t_{lm} - l^{t-1}_{lm})/l^{t-1}_{lm}$. The head will be regarded as performing a nod if its inclination degree is larger than a threshold, i.e. $a > \tau$. The head nodding frequency is then calculated by $f_h = n_h/300$, where n_h is the number of head nods observed in the video clip under consideration.

12.3.5 Reasoning

In this study, a process characterized by fuzzy integral is introduced to infer the driver's vigilance level based on his or her facial parametric values.

12.3.5.1 Fuzzy Integral

The fuzzy integral provides an elegant nonlinear numerical approach to integrating multiple sources of information to arrive at a value that indicates the degree of support for a particular hypothesis or decision. There are several variants of the fuzzy integral [37, 38] characterized by either the Lebesque or Riemann integral. In this study, the Sugeno fuzzy integral based on the Lebesque integral is considered.

Let $f : S \to [0, 1]$ be a function defined on a finite set S and $g : P(S) \to [0, 1]$ be a set function defined over the power set of S. Function $g(\cdot)$, referred to as the fuzzy measure function, satisfies (i) $g(\emptyset) = 0$ and $g(S) = 1$, (ii) $\forall A, B \subset S$, if $A \subseteq B$, then $g(A) \leq g(B)$, and (iii) $\forall A, B \subset S$, $A \cap B = \phi$,

$$g(A \cap B) = g(A) + g(B) + \lambda g(A)g(B), \lambda \geq 1. \tag{12.1}$$

The fuzzy integral of $f(\cdot)$ with respect to $g(\cdot)$ is defined as:

$$e = \int_S f(s) \cdot g = \sup_{\alpha \in [0,1]} \{\alpha \wedge g(A_\alpha)\}, \tag{12.2}$$

where $\wedge$ represents the fuzzy intersection and $A_\alpha = \{s \in S | f(s) \geq \alpha\}$.

Suppose we have a collection of information sources, $S = \{s_i, i = 1, \cdots, n\}$, and a set of hypotheses, $H = \{h_i, i = 1, \cdots, m\}$. A decision D is to be made from H based on S using the fuzzy integral approach. To this end, for each hypothesis $h \in H$ we calculate its fuzzy integral value e_h according to Eq. (12.2). The decision is then determined as $D = h^* = \arg\max_{h \in H} e_h$.

To calculate e_h, we first define two functions $f(\cdot)$ and $g(\cdot)$. Function $f(\cdot)$ receives an information source $s \in S$ and returns the value $f(s)$ that indicates the level of support of s for hypothesis h. Function $g(\cdot)$ takes as input a subset A of $S$and gives the value $g(A)$ which specifies the degree of worth of subset A relative to the other sources in S. Unlike $f(\cdot)$, $g(\cdot)$ does not depend on the hypothesis under consideration. We can calculate $g(A)$, $\forall A \subseteq S$, prior to hypothesis testing. To calculate $g(A)$, we first determine the degrees of worth of individual information sources, $W = \{w(s_i), i = 1, \cdots, n\}$, where $w(s_i) = g(\{s_i\}).g(A)$ can then be recursively calculated using Eq. (12.1),

$$g(A) = \left(\prod_{s_i \in A} (1 + \lambda w(s_i)) \right) - 1)/\lambda. \tag{12.3}$$

Table 12.1 Transfer functions for facial parameters

Percentage of eye closure over time ([0, 1])	Eye blink frequency (time/min)
$P_e(x) = \begin{cases} 0 & x \le 0.12 \\ 3.57x - 0.43 & 0.12 < x < 0.4 \\ 1 & x \ge 0.4 \end{cases}$	$f_e(x) = \begin{cases} 0 & x \le 20 \\ 0.05x - 1 & 20 < x < 40 \\ 1 & x \ge 40 \end{cases}$
Average eye closure duration (seconds)	Average degree of gaze ([0,1])
$D_e(x) = \begin{cases} 0 & x \le 0.15 \\ 0.35x - 0.05 & 0.15 < x < 3 \\ 1 & x \ge 3 \end{cases}$	$D_g(x) = \begin{cases} 0 & x \le 0.5 \\ 0.05x - 0.05 & 0.5 < x < 1.0 \\ 1 & x \ge 1.0 \end{cases}$
Average duration of mouth openness (seconds)	Head nodding frequency (time/min)
$D_m(x) = \begin{cases} 0 & x \le 3 \\ 0.33x - 1 & 3 < x < 6 \\ 1 & x \ge 6 \end{cases}$	$f_k(x) = \begin{cases} 0.05x - 1 & x < 5 \\ 1 & x \ge 5 \end{cases}$

Since $g(S) = 1$, $(\prod_{s_i \in S} (1 + \lambda w(s_i)) - 1)/\lambda = 1$. Parameter λ can be determined by solving $\lambda + 1 = \prod_{s_i \in S} (1 + \lambda w(s_i))$.

Let $S' = \{s'_1, s'_2, \cdots, s'_n\}$ be the sorted version of S such that $f(s'_1) \ge f(s'_2) \ge \cdots \ge f(s'_n)$. Equation (12.2) can be rewritten as

$$e = \int_S f(s) \cdot g = \sup_{\alpha \in [0,1]} \{\alpha \wedge g(A_\alpha)\} = \bigvee_{1 \le i \le n} [f(s'_i) \wedge g(S'_i)], \tag{12.4}$$

where $\vee$ represents fuzzy union and $S'_i = \{s'_1, s'_2, \cdots, s'_i\}$. Note that Eq. (12.2) requires 2^n subsets of S to complete the fuzzy integral, whilst the above equation needs only n subsets.

12.3.5.2 Fuzzy Reasoning

Since different facial parameters have values of differing scale and range, in order to unify parametric values to obtain a value of "drowsiness", we introduce a fuzzy set. Different facial parameters are all related to this fuzzy set. Accordingly, their values are transferred in order to be interpreted as levels of drowsiness. Table 12.1 lists the transfer functions of the facial parameters ($P_e, f_e, D_e, f_h, D_m, d_g$) used in this study. Let $S = \{s_1, s_2, \cdots, s_6\}$ be a set containing the transferred values of the facial parameters. Set S then serves as the set of information sources, from which we determine the hypothesis set as $H = \{m, m + 0.1, m + 0.2, \cdots, M\}$, where $m = \left\lfloor 10 \times \min_{s_i \in S} s_i \right\rfloor /10$ and $M = \left\lceil 10 \times \max_{s_i \in S} s_i \right\rceil /10$, in which $\lfloor \cdot \rfloor$ and $\lceil \cdot \rceil$ denote the floor and ceiling operators, respectively. The hypothesis selected will be the drowsiness level of the driver.

Let $w_1, w_2, \cdots, w_6$ be the degrees of worth of the six facial parameters, respectively. In this study, we set $\{w_1, w_2, \cdots, w_6\} = \{0.9, 0.8, 0.7, 0.5, 0.2, 0.3\}$, which

have been empirically determined on the basis of the criteria of importance and accuracy of the parameters. The degree of worth of any subset $A \subseteq P$, $g(A)$, can then be calculated according to Eq. (12.3).

Considering any hypothesis $h \in H$, we calculate the support levels of information sources $s_i{}'s$ to h by $f_h(s_i) = 1 - |s_i - h|$. Clearly, the larger the difference between s_i and h, the lower the support level of s_i to h. We next sort the information sources in S according to their support levels. Let $S' = \{s'_1, s'_2, \cdots, s'_8\}$ be the sorted version of S such that $f(s'_1) \geq f(s'_2) \geq \cdots \geq f(s'_8)$. Substituting $f(s'_i)$ and $g(S'_i)$ into Eq. (12.4), we obtain the fuzzy integral value e_h of h. The above process is repeated for all hypotheses in H. Finally, the drowsiness level of the driver is determined as $h^* = \arg\max_{h \in H} e_h$.

12.4 Experimental Results

The proposed driver drowsiness monitoring system was developed using the Borland C++ Programming Language run on an Intel Solo T1300 1.66 GHz PC running under Windows *XP* Professional. The input video sequence was at a rate of 30 frames per second. The size of video image was 320×240 pixels. We have divided our experiment into two parts. The first part examines the accuracies and efficiencies of the major steps of the system process. The second part demonstrates the performance of the entire system.

12.4.1 Accuracies and Efficiencies of Major Steps

There are five major steps: preprocessing, facial feature extraction, face tracking, parameter estimation and drowsiness reasoning involved in the proposed system. The second and third steps dominate the processing speed of the system and the last two steps determine its accuracy.

12.4.1.1 Facial Feature Extraction and Tracking

Figure 12.12 shows the experimental result of facial feature extraction and face tracking over a video sequence. Initially, the system repeatedly detected the same facial features in two successive video images (2 and 3). The face formed by the facial features was then regarded as the actual face of the driver and was traced over the video sequence. The tracking module continued until it missed the right eye of the driver in image 198 due to a swift turning of the driver's head between images 197–198. The system immediately reinitiated the facial feature extraction module, which repeatedly located the same facial features in images 199 and 200. Thereafter, the tracking module took over and traced the face formed by the facial features all the way to the end of the video sequence.

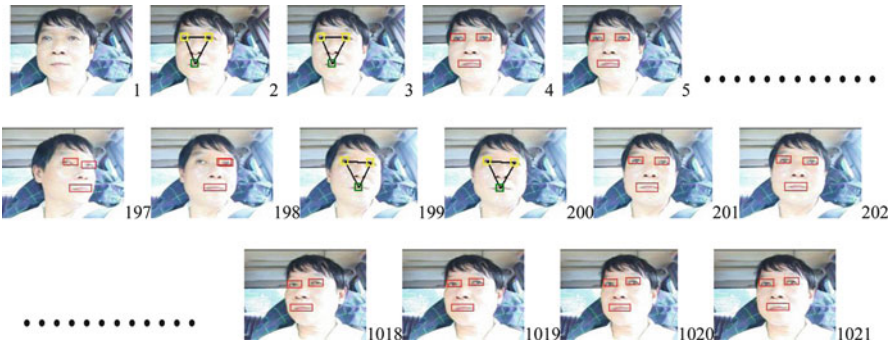

Fig. 12.12 Facial feature extraction and face tracking over a video sequence

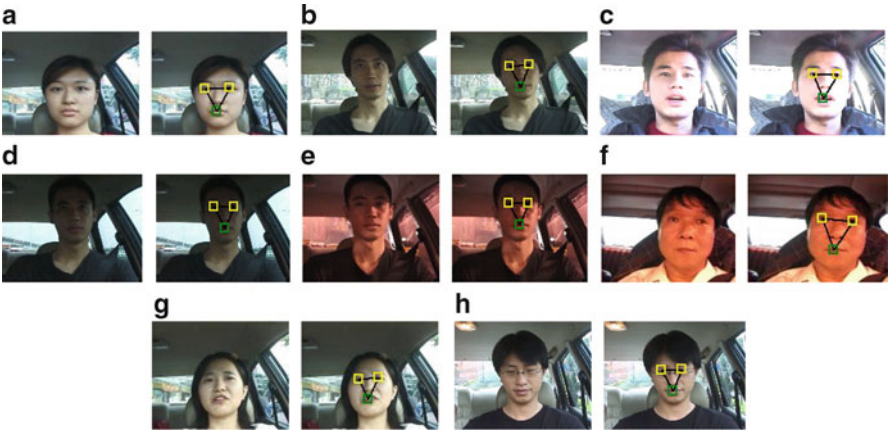

Fig. 12.13 Robustness of facial feature extraction under various conditions. (**a**) Clear day, (**b**) Cloudy day, (**c**) Bright sunshine, (**d**) Twilight, (**e**) Underground passage, (**f**) Tunnel, (**g**) Facial expression, and (**h**) Wearing an accessory

Our facial feature extraction module takes about 1/4 of a second to complete facial feature detection in an image and our face tracking module takes around 1/25 of a second to carry outface location in an image. Since the facial feature extraction module takes the most time, it determines the efficiency of the system. Figure 12.13 shows the robustness of the facial feature extraction module under different conditions of illumination, sex, facial expression, and wearing accessories. However, since the higher the face tracking rate, the fewer number of times the facial feature extractions module is necessary, it is the performance of the face tracking module which determines the efficiency of the system.

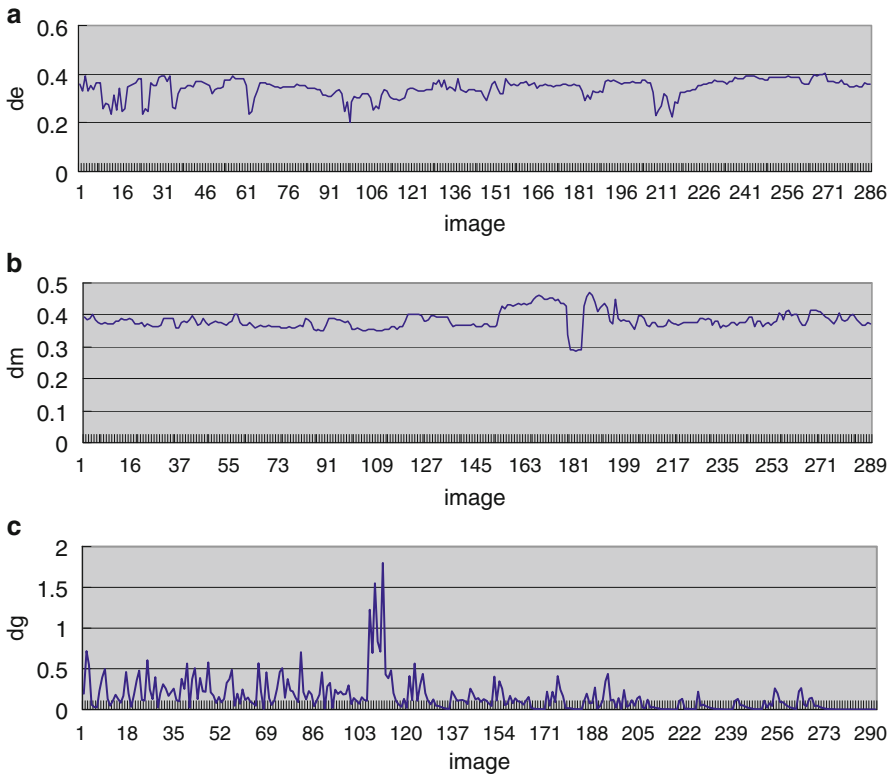

Fig. 12.14 The degrees of (**a**) eye closured_e, (**b**) eye gaze d_g, and (**c**) mouth openness d_m calculated from a video sequence of 300 images

12.4.2 Facial Parameter Estimation

In the drowsiness reasoning step, both the values and degrees of worth of the facial parameters are needed for the fuzzy integral process to infer the drowsiness level of the driver. Two criteria have been considered for determining the degree of worth of facial parameters: importance and accuracy. The former is essentially intuitive, whereas the latter is quantitatively analytic. A series of experiments using 20 different video sequences of 300 images (about 10 s) have been conducted to investigate the accuracy of facial parameter estimation.

For each experimental video sequence, the facial features of the driver were located in every image by either facial feature detection or face tracking. The degrees of eye closure d_e, eye gaze d_g, mouth openness d_m and head inclination d_h were automatically calculated by the system from the located facial features. Figure 12.14 shows the calculated degrees of d_e, d_m and d_g of an experimental video

Table 12.2 Facial parametric values provided by the system for an experimental video sequence

	P_e (pulses/s)	f_e (blinks/s)	D_e (sec)	d_g	D_m (sec)	f_h (nods/s)
System	1.50	0.8	0.071	0.36	1.86	0
Manual	1.40	0.8	0.066	–	1.80	0
Error(%)	7.14	0.0	6.0	–	3.30	0.0
Average error(%)	5.38	2.89	4.52	–	3.17	2.12
Worth deg.	0.7	0.9	0.8	0.4	0.2	0.5

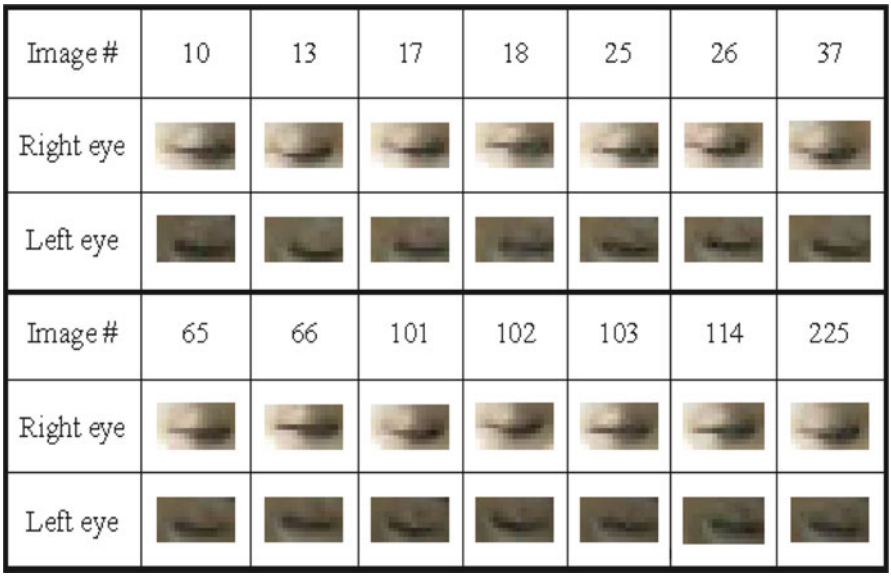

Fig. 12.15 The images containing closed eyes manually extracted from the experimental video sequence

sequence. Based on the calculated degrees, the facial parameters of percentage of eye closure over time (P_e), eye blinking frequency (f_e), average eye closure duration (D_e), average gaze degree (d_g), average duration of mouth openness (D_m) and head nodding frequency (f_h) are estimated by the system, with results given in the second row of Table 12.2.

In order to examine the accuracy of the estimated facial parametric values, we examined the video sequence under consideration. Figure 12.15 shows the images containing closed eyes which were extracted by hand from the video sequence. There are 14 images in the figure. The percentage of eye closure over time (P_e) is $14/10 = 1.4$ pulses per second. Compared with the 1.5 pulses per second estimated by the system, the measurement error is $|1.5 - 1.4|/1.4 = 0.0714$. Examining Fig. 12.15 again, there are eight eye blinks around images 10–13, 17–18, 25–26, 37, 65–66, 101–103, 114, and 225. The eye blinking frequency (f_e) is hence $8/10 = 0.8$

Image #	154	155	156	157	158	159	161
Mouth							
Image #	···	181	182	183	184	185	186
Mouth	···						
Image #	···	202	203	204	205	206	207
Mouth	···						

Fig. 12.16 Images from a video sequence where the mouth is yawning

blinks per second, which matched that estimated by the system. Next, the average eye closure duration (D_e) is $(4+2+2+1+2+3+1+1)/(8 \cdot 30) = 0.0667$ seconds. Since the system returned 0.0708 s for D_e, the measurement error is $|0.071 - 0.067| / 0.067 = 0.06$.

Figure 12.16 shows a clip of the experimental video sequence where the mouth is yawning. This is the only yawn present in the sequence. The average duration of mouth openness (D_m) is $(206 - 154 + 1)/30 = 1.8$ s. Since the system returned 1.95 s for D_m, the measurement error is $|1.86 - 1.8| / 1.8 = 0.033$. Next, in the experimental video sequence under consideration no head nod is observed. The head nodding frequency (f_h) is zero, which agrees with the value given by the system. Finally, we have excluded the average gaze degree (d_g) in Table 12.2 because its calculation requires measurements of head movement, which cannot be manually obtained from the video sequence.

In the fifth row of Table 12.2, we averaged the measurement errors of facial parameter estimation over 20 experimental video sequences. The results revealed that in terms of average estimation error $f_h > f_e > D_m > D_e > P_e$, where $>$ indicates "better than". However, the order of the worth degrees assigned to the facial parameters shown in the last row of Table 12.2 is $f_e > D_e > P_e > f_h > d_g > D_m$, which is different from the sequence arranged only according to estimation error. The latter order is determined based on both the importance and estimation accuracy of facial parameters. Specifically, if we examine the parameters of percentage of eye closure over time (P_e) and average mouth openness duration (D_m) although D_m attained a relatively smaller estimation error (3.17%) than P_e (5.38%), we assign a larger degree of worth (0.7) to P_e than that to D_m (0.2). This is because mouth openness may occur during both talking and yawning.

12.5 System Performance

A number of video sequences of different drivers, sexes, accessories and illumination conditions were used to demonstrate the performance of the system. Figure 12.17 shows some of the video sequences used in our experiment, where one image is displayed for each video sequence. Table 12.3 summarizes the experimental results of the first eight video sequences. In this table, columns 2–5show the lengths (n), facial feature detection ratios (r_d), face tracking ratios (r_t), and processing speeds(s) of video sequences, respectively. The length n of a video sequence is its number of constituent images. Its facial feature detection ratio r_d is defined as $r_d = n_d/n$, where n_d is the number of images to which facial feature extraction is applied. Similarly, its face tracking ratio r_t is defined as $r_t = n_t/n$, where n_t is the number of images on which face tracking is performed. Finally, the process speed is $s = T/n$, where T is the total processing time of the video sequence.

In Table 12.3, the second row shows the experimental result of the first video sequence. This sequence has 19,650 constituting images. The time of acquiring this sequence is10.9 min ($=19{,}650/(30\times 60)$). However, our system spent about 17.4 min ($=19{,}650/(18.8\times 60)$) to process the sequence. The processing time of this sequence is nearly twice as long as its acquisition time. In order to achieve real-time processing, our system has to ignore every other input image during

Fig. 12.17 Representative images from experimental video sequences

Table 12.3 Performance of the system on experimental video sequences

Video	Video length n (#images) t(min)	Facial feature detection ratio r_d (%)	Face tracking ratio r_t (%)	Processing speed s (images/s)
1	19,650	15.4	84.6	18.8
2	15,790	14.0	86.0	19.1
3	13,290	17.3	82.7	18.0
4	15,850	11.4	88.6	21.7
5	11,400	37.6	62.4	12.3
6	12,070	23.7	76.3	16.9
7	16,780	30.8	69.2	14.2
8	14,470	62.2	37.8	7.2

processing. Furthermore, the facial feature detection ratio (15.4%) and face tracking ratio (84.6%) of the video sequence indicate that the corresponding modules take about 0.124 (≈1/8) and 0.042 (≈1/25) s respectively to locate facial features in an image. Clearly, the efficiency of our system heavily relies on the success rate of face tracking. In rows 2–6 of Table 12.3, the face tracking ratios of video sequences 1–4 are all larger than 83%. The processing speeds of these sequences are around19 images per second. However, video sequences 5 and 7 have relatively low face tracking ratios(62.4 and 69.2%) and hence have relatively slow processing speeds (12.3 and 14.2 images per second). This is probably because the driver of video 5 is wearing a pair of glasses and the vehicle of video 7 was passing through an underground passage. Examining the processing times (15.5 and 19.7 min) and acquisition times (6.3 and 9.3 min) of these two video sequences reveals that the processing times are almost 2.5 times as long as the acquisition times. Our system has to ignore one in every three input images in order to achieve real-time processing.

Finally, video sequence 8 was acquired whilst driving through a tunnel. This sequence suffers from both low intensity and brightness variation originating from the lights of the tunnel as well as neighboring vehicles. Although brightness normalization process has been incorporated into our system for coping with adverse illumination conditions, the process did not work well under these conditions because image colors were significantly distorted. Unfortunately, color information plays a critical role in our facial feature extraction.

The estimated drivers' drowsiness levels of videos 1–7 are plotted in Fig. 12.18. We ignore video 8 here because of its random distribution of calculated drowsiness levels. Interpreting the plots of videos 2, 4 and 7 reveals busy distributions of relatively high drowsiness levels. However, most of calculated drowsiness levels are still smaller than 0.5. Furthermore, different drivers have different tolerance levels of drowsiness. We propose that a drowsy face would exhibit a number of continuous intervals of high drowsiness levels (as a suggestion, 0.35). Accordingly, the drivers of videos 2 and 7 are appear to be very drowsy.

12.6 Concluding Remarks and Future Work

While there have been many vision systems developed for detecting and monitoring driver drowsiness or fatigue, few systems utilize chromatic images as their input data. In this study, we present a system for monitoring driver vigilance, which uses color images acquired by a video camera as the input data. Although colors provide rich information, they are compromised by low intensity and brightness variation. In order to compensate for these disadvantages, we introduced a brightness normalization process in our system. However, this process can significantly distort the chromatic characteristics of images under severe illumination conditions. We hope further work to develop color constancy techniques will improve the brightness normalization process.

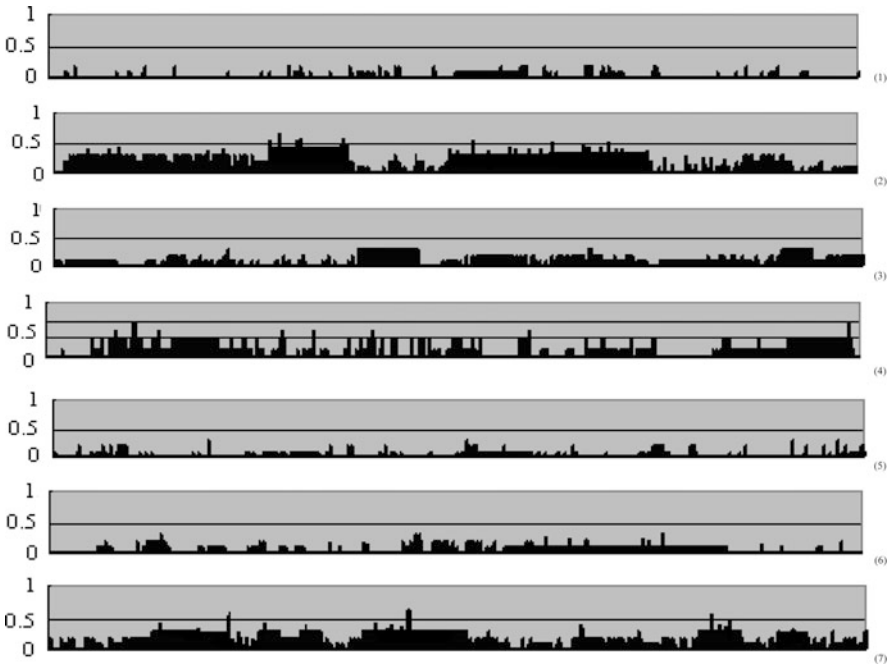

Fig. 12.18 Estimated drivers' drowsiness levels of video sequences 1–7

Several techniques utilized to implement the steps of the proposed system can be modified or replaced. For example, supervised SVM and ADBOOST approaches may be incorporated in the facial feature extraction step. Particle filters and mean shift methods may replace the Kelman filter currently used to trace faces over video sequences. We intend to explore these approaches in the future.

A number of video sequences of different drivers, sexes, accessories, and illumination conditions have been employed in our experiment to examine its efficiency and effectiveness. Whilst our current system performed reasonably well in daytime, these results were not replicable at night. To extend the system to be able to work at nighttime, additional visual sensors such as IR and NIR imaging devices would have to be incorporated. Our ultimate goal is to integrate heterogeneous sensing data, including physiological signals and driving behavior information in addition to visual data, to achieve accurate and reliable vigilance monitoring.

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Chapter 13
The Effective Assessment and Management of Sleep Disturbances in Community-Dwelling and Institutionalized Older Adults

Michael V. Vitiello

Abstract Older adults represent a rapidly growing proportion of the population of industrialized nations, with a corresponding increase in the number of patients with significant sleep disturbances that adversely impact both health and quality of life. There is increasing focus on the importance of sleep's interactions with health in the context of aging and over the last decade there have been significant and rapid advances in our ability to diagnose and treat sleep disorders in older adults. Thorough assessment of sleep problems is often iterative, time consuming, and may require serial evaluations and information from multiple sources. Accurate assessment and effective management of disturbed sleep in older adults, while often complex, is ultimately rewarding. This chapter provides an overview of the effective assessment and management of sleep disorders in older adults, both in community and long-term care settings.

Keywords Older adults • Aging • Long-term care • Nursing home • Insomnia • Primary sleep disorder

13.1 Introduction

The proportion of older adults in the population of industrialized nations is growing rapidly. In the United States for example, persons 65 years of age or older comprised approximately 12% of the population in 2006, a figure which is projected to rise to

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20% by 2030. This demographic is increasing twice as fast as other age groups, so that by 2030 the number of persons aged 65 years or over will effectively double to 72 million. Similar population shifts are occurring in other industrialized nations, which has profound implications for worldwide healthcare.

Sleep disturbances, including a number of specific sleep-related disorders, are common in the general population and grow in prevalence with advancing age. Sadly, there is a major misconception about the reasons for this phenomenon. It is commonly assumed that this increasing prevalence of sleep disturbance is effectively the result of normal aging. However, such sleep disruption is more likely to be the result of medical and psychosocial co-morbidities that typically increase with age [7, 13, 14, 42]. There is a strong bi-directional relationship between medical and psychosocial problems and sleep disorders in older adults. Older adults with sleep disturbances are at increased risk of developing depression, hypertension and other significant illnesses and correspondingly, individuals with these diseases are at increased risk of developing sleep disorders [12, 30, 40]. Many clinicians often fail to appreciate the potential morbidity associated with sleep problems in older adults, which is distinct from that of co-morbid illnesses. Furthermore, the complicated, often multi-factorial interactions that may cause sleep disturbances in older adults and impact effective treatment pose unique and significant challenges to clinicians.

There is increasing focus on the importance of sleep's interactions with health in the context of aging, and over the last decade there have been significant and rapid advances in our ability to diagnose and treat sleep disorders in older adults [43]. Recently it has been suggested that the complex area of sleep difficulties in older adults should be approached as a "multi-factorial geriatric syndrome" [41]. In this context, a group of recognized sleep medicine and geriatrics experts including the author, representing 13 major geriatric interest groups and societies, recently conducted an extensive review of geriatric sleep disorders literature and developed a set of evidence-based recommendations for the assessment and management of sleep disorders in older adults including those in long-term care settings [7].

This chapter provides an overview of the effective assessment and management of sleep disorders in older adults, with a primary focus on insomnia, both in community and long-term care settings. For a more extensive exposition of this important area of healthcare treatment, including an evaluation of the evidence base supporting state-of-the-art management approaches, the reader is referred to the comprehensive review by Bloom and colleagues.

13.2 Assessment and Management of Sleep Disorders in Community Dwelling Older Adults

Healthcare practitioners should never assume that an older adult will necessarily volunteer a complaint of disturbed sleep. Many older adults, in a manner similar to many clinicians, assume that disturbed sleep is simply a part of aging and there is little that can be done to improve the situation. The most effective way of

detecting sleep problems in community dwelling older adults is simply to enquire regularly about their sleep. This is best achieved as a routine part of a patient visit; alternatively, a staff member can administer a brief sleep quality questionnaire during standard vital signs assessment. When available and appropriate, a bed partner can often assist in providing sleep-related information.

An excellent sense of an individual's sleep quality can be obtained with the following questions:

1. What time do you typically go to bed at night and get up in the morning?
2. Do you frequently have difficulty falling asleep at night?
3. How often do you typically awake during the night?
4. When you awake during the night, do you typically have difficulty falling back asleep?
5. Are you aware, or have you been told, that you often snore, stop breathing or gasp for air during your sleep?
6. Are you aware, or have you been told, that you often kick or thrash around in your sleep?
7. Are you aware, or have you been told, that you often walk, eat, punch or scream in your sleep?
8. Are you often sleepy or tired during the day?
9. Do you often doze off unexpectedly during the day?
10. How often do you nap?
11. How much sleep do you believe you need to feel fully alert and functional during the day?
12. Are you currently taking any medications, herbal remedies or other preparations to help you sleep?

If the patient's answers to any of these questions indicate a possible sleep complaint then further, more detailed questions should be asked to better clarify the nature and severity of the problem [7]. Such questions are best presented in the context of a detailed sleep history [47]. The patient's responses to these questions guide how to proceed further with a more detailed history, focused physical examination, specific laboratory tests, or referral. Typically a patient's complaint will center on one or more of the following; (1) difficulties in falling, staying asleep, waking up too early or feeling un-rested (insomnia), (2) feeling excessively sleepy and falling asleep during the day (hypersomnia), or (3) unusual sleep-related behavior (parasomnia) or movement (movement disorder). A diagnostic algorithm which can help guide the assessment process is provided in Fig. 13.1, below.

13.2.1 Insomnia

Insomnia is very common in older adults. Numerous epidemiological studies have reported that as much as 50% of the older adult population complains of significant sleep disturbance, and the prevalence of diagnosable insomnia is 6–10% in the general population, and higher groups seeking healthcare, such as many older adults

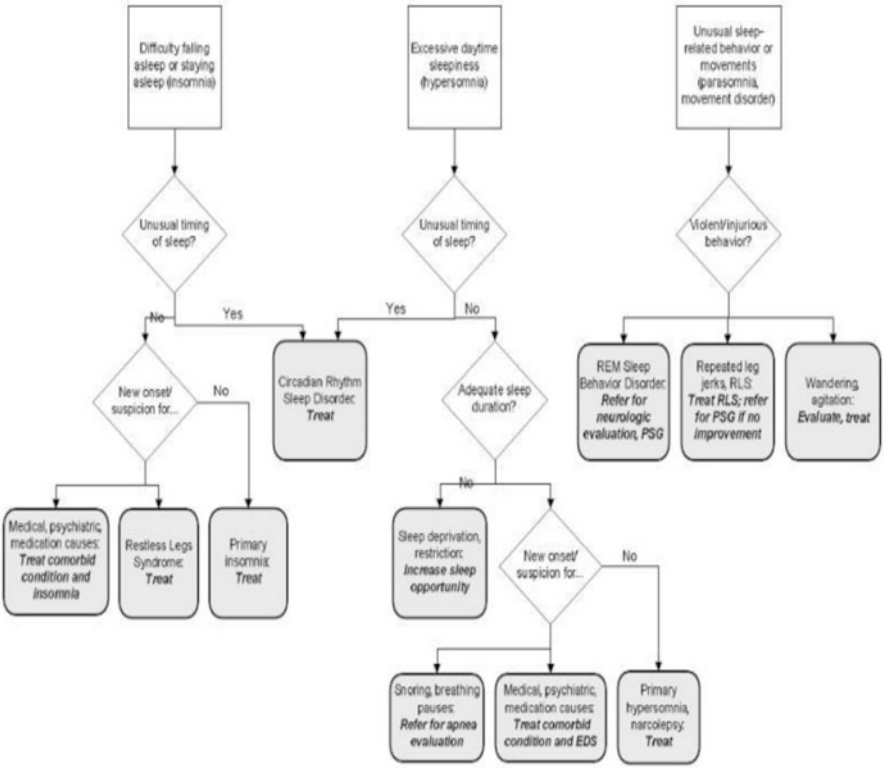

Fig. 13.1 Algorithm for the diagnosis of sleep disorders in older adults [7]

[28]. Insomnia is defined as a complaint of disturbed sleep, despite having adequate opportunity to sleep; in other words, it is not willful sleep restriction.

13.2.1.1 Assessment

A complaint of insomnia involves difficulties in falling or staying asleep, waking up too early, or feelings of non-restorative or poor quality sleep, which must be accompanied by a negative impact on some aspect of daytime functioning, such as difficulty concentrating, moodiness and so on. A diagnosis of insomnia requires that these difficulties and impairments be present for at least 1 month.

Insomnia can be either primary (having no apparent cause) or co-morbid. Co-morbid insomnia, which is much more common (particularly in older adults) is most often associated with medical disorders (e.g. pain syndromes, cardiopulmonary disorders, neurodegenerative disorders), psychiatric disorders (e.g. depression, anxiety) and other primary sleep disorders (e.g. obstructive sleep apnea syndrome, restless legs syndrome). It is important to note that co-morbid insomnia is not "caused" by the other condition(s), but rather that the insomnia and the other

condition(s) co-exist and may interact, requiring careful clinical management of both complaints.

The differential diagnosis of insomnia is broad and complex, particularly in older adults who may have multiple medical and psychosocial co-morbidities and who are likely to be taking multiple medications. A thorough medical history, focused physical examination and careful review of all prescription and non-prescription drugs are essential. While a diagnosis of insomnia does not require polysomnographic confirmation, appropriate laboratory tests based on the results of medical history and physical examination may also be employed.

13.2.1.2 Management

Treatments for insomnia can be classified as behavioral, pharmacological and complementary and alternative. Behavioral approaches to insomnia treatment are highly effective in older adults [24, 26] and should typically be the first treatment modality considered.

There are a number of behavioral approaches that have been used to successfully treat insomnia. The most recent successful treatment trials make use of a combination of behavioral treatments delivered together, commonly referred to as Cognitive Behavioral Treatment for Insomnia (CBT-I). Other behavioral approaches include physical activity/exercise, light therapy and complementary and alternative approaches ranging from massage and movement therapies such as Tai Chi to acupuncture. While any of these approaches might prove beneficial for the treatment of insomnia in individual older adults, only two behavioral approaches meet strict evidence-based criteria for efficacy in this population; sleep restriction therapy and CBT-I [20].

CBT-I for older adults typically includes sleep hygiene instruction, stimulus control and sleep restriction and may include cognitive restructuring and/or relaxation techniques. Sleep hygiene instruction consists of a variety of sleep scheduling, environmental, dietary and activity recommendations which are intended to facilitate sleep onset and sleep maintenance [16, 39]. Stimulus control instructions strengthen the patient's association with the bedroom environment as a cue for falling asleep, weaken it as a cue for sleep-incompatible activities (including worries or concerns about an inability to fall asleep) and help the patient develop a regularized sleep rhythm [8]. Sleep restriction instruction involves limiting a patients time in bed in an effort to consolidate their actual time asleep. Recommended sleep times are based on patient sleep logs and time in bed is slowly increased on a weekly basis as their sleep efficiency increases until an optimum sleep time is achieved [38]. CBT-I may also include cognitive restructuring to correct misconceptions about sleep and normal aging as well as to improve the amount of sleep achieved. It may also involve some form of relaxation, such as diaphragmatic breathing, guided imagery, meditation or autogenic training. Finally CBT-I includes motivational strategies to enhance compliance with treatment and teaches problem solving skills to facilitate the patient's ability to carry out stimulus control and sleep restriction instructions.

A particular strength of CBT-I is its long-term efficacy, which has been consistently demonstrated both for primary (e.g. [23]) and co-morbid (e.g. [45]) insomnia in older adults. This is of particular importance as insomnia tends to be a chronic condition and the behavioral changes brought about through CBT-I appear to be continuously effective over follow-up periods of up to 2 years.

While a review of sleep hygiene and CBT-I are considered the most appropriate initial therapeutic approach to treatment of insomnia [26], not every patient is either willing or able to participate in CBT-I treatment. In such cases, pharmacological treatment for insomnia may be considered. Appropriate pharmacotherapy requires matching the nature of the patient's complaint with the characteristics of a particular drug. Particular care should be taken in older adults who may be particularly susceptible to potential side effects of such pharmacotherapy, including an increased risk of falls, impaired daytime cognition, and so on. As a rule, particularly with older adults, all pharmacotherapy should be started at the lowest available effective dose. The U.S. Food and Drug Administration (FDA) has approved 11 drugs for the treatment of insomnia. These include benzodiazepines, non-benzodiazepines, a melatonin receptor agonist [7] and most recently, a low-dose formulation of the tricyclic antidepressant doxepin.

The benzodiazepines are a class of psychoactive drugs that act agonistically at the benzodiazepine receptor complex and have varying sedative, hypnotic, anxiolytic, muscle relaxant and amnestic actions. The newer agents are non-benzodiazepines which are structurally unrelated to benzodiazepines but act through the same receptor complex. While non-benzodiazepines have a better safety profile than benzodiazepines, adverse effects can still be problematic [26]. The melatonin receptor agonist is thought to facilitate the circadian timing of a normal sleep-wake schedule. Doxepin is believed to exert its sedative effect through the histamine (H1) receptor. These melatonin and histamine based agents received FDA approval after the NIH Conference and so were not evaluated, but appear to have minimum potential for abuse or adverse effects such as cognitive or motor impairment.

Limited information is available supporting a combined therapy approach which utilizes both CBT-I and pharmacotherapy. Only one randomized trial has tested this approach [25] and concluded that, "... the addition of medication to CBT produced added benefits during acute therapy, but long-term outcome was optimized when medication is discontinued during maintenance CBT." Currently there are insufficient studies to draw any firm conclusions regarding the potential advantages or disadvantages of this type of combined therapeutic approach for the treatment of insomnia.

13.2.2 Sleep Apnea

Sleep apnea is condition marked by apneas (complete cessations of respiration) and hypopneas (decreases in respiratory volume) during sleep. Apneas and hypopneas can occur frequently and result in hypoxemia and autonomic activation resulting in increases in systemic blood pressure and changes in cerebral blood flow [5]. These

respiratory disturbances are typically terminated by an arousal, which fragments sleep, and likely contribute to the excessive daytime sleepiness (EDS) and cognitive impairment seen in sleep apnea. There are two general classes of sleep apnea recognized: central and obstructive. Obstructive sleep apnea (OSAS) is more common and is marked by periodic obstruction of the upper airway during efforts to breathe, resulting in diminished or absent airflow. OSAS is common in older adults, and is reported in the majority of older men and women [3]. The prevalence of OSAS increases in both sexes with aging and occurs increasingly in post-menopausal women.

13.2.2.1 Assessment

OSAS is typically characterized by a history of EDS and snoring. Other symptoms of OSAS may include observed apneas and hypopneas, gasping for air or choking upon awakening during the night, morning headache and nocturia. Older OSAS patients are uncommonly obese, in contrast to younger OSAS patients [46]. Because OSAS is common in older adults, all older adults should be screened for this disorder by identifying the presence of its three key features; EDS, snoring and apnea/hypopnea. OSAS is assessed by history, physical examination focusing on the upper airway, differential diagnosis for other potential causes of EDS (such as sleep deprivation, depression and hypothyroidism) and polysomnographic evaluation to objectively document the presence and severity of OSAS and provide a baseline to measure treatment efficacy.

13.2.2.2 Management

Effective management of OSAS typically involves continuous positive airway pressure (CPAP) as the primary treatment for most patients. CPAP works by providing sufficient air pressure into the airway and lungs to stent open the airway in the presence of inspiratory pressure, allowing the patient to breathe normally. Recent studies have demonstrated that older adults, even those with a neurodegenerative dementing disorder, can tolerate sustained CPAP, which may slow cognitive decline in this population [4, 9, 10].

Currently there are no effective pharmacological treatments for OSAS, but there are several other management approaches that can be useful in treating OSAS, although they have not been evaluated as rigorously as the use of CPAP. These include: avoidance of respiratory depressants such as alcohol, opiates and sedative-hypnotics; weight loss, which can be effective as long as it is maintained; and oral appliances, which advance the lower jaw to open the upper airway and can be an efficacious alternative to CPAP, particularly in cases of mild to moderate OSAS.

As OSAS is a chronic disorder, typically associated with major co-morbidities such as hypertension and cardiovascular disease, a major component of its effective management is frequent follow-up, particularly within the first few months of treatment. This is to ensure that CPAP use and additional treatment provisions such

as avoidance of alcohol are adhered to as prescribed, or to problem solve solutions such as comfort and function of headgear and optimal pressure. Re-evaluation may be necessary if EDS returns or if CPAP becomes less efficacious or is not properly employed or discontinued by the patient.

13.2.3 Restless Legs Syndrome

Restless legs syndrome (RLS) is a sleep disorder which is characterized by unusual and unpleasant sensations in the legs that interfere with sleep onset and maintenance. The prevalence of RLS in the general population is approximately 10%, and includes both primary and secondary forms. Primary, or idiopathic, RLS develops at an early age and likely has a genetic basis. Secondary RLS is associated with a variety of medical conditions such as iron-deficiency anemia and renal failure, which is also associated with iron deficiency. This may explain why the prevalence of RLS increases with age, with higher symptom reporting in women [2].

13.2.3.1 Assessment

Assessment of RLS is made primarily by history, often accompanied by a thorough neurological examination and an assay for serum ferritin [15]. The key questions to include in the history are:

1. Are there unusual, unpleasant or uncomfortable sensations in the legs that cause an urge to move them?
2. Are these sensations initiated or made worse during periods of inactivity or rest, such as sitting or lying down?
3. Does movement, such as walking, pacing or stretching partially or completely relieve these sensations?
4. Do these sensations occur primarily or get worse in the evening or night?

The differential diagnosis of RLS includes vascular disease, peripheral neuropathies, akathesias, venous varicosities and arthritides, which can be determined with a sufficiently careful history [15].

13.2.3.2 Management

Effective management of RLS is pharmacological. While benzodiazepines, opioids and anticonvulsants have been used, preferential treatment is with dopaminergic agents, particularly the newer dopamine receptor agonists (i.e.; ropinirole and pramipexole), which are associated with less rebound and symptom augmentation than dopamine precursors [17].

Non-pharmacological approaches can be useful adjunctives to pharmacotherapy and include mild exercise, alcohol and caffeine avoidance, smoking cessation and discontinuation of medications that may exacerbate RLS such as tricyclic antidepressants, SSRIs, antipsychotics (dopamine antagonists) and lithium [29].

13.2.4 REM Behavior Disorder

Parasomnias are involuntary, frequently problematic events that occur during sleep or arousal from sleep. These events can include abnormal movements and behaviors, dream enactment and strong emotions and perceptions and can be associated with specific sleep states (i.e. NREM, REM). NREM parasomnias are common in children, while the most common REM parasomnia is REM Behavior Disorder (RBD) [35].

13.2.4.1 Assessment

RBD is diagnosed by sleep history and polysomnographic evidence of high electromyographic activity during REM corresponding to a lack of REM-related muscle atonia, due to a dysfunction of the motor neuron inhibition that normally occurs during REM sleep. This polysomnographic finding may be accompanied by complex, potentially violent motor behaviors, typically accompanied by dream enactment [34, 35]. RBD is seen in association with various disorders, including brain-stem abnormalities, Parkinson's disease, progressive supranuclear palsy and medication and alcohol toxicity and withdrawal. The differential diagnosis of RBD includes non-REM parasomnias, OSA and periodic limb movements during sleep.

13.2.4.2 Management

RBD is managed pharmacologically and by making changes to ensure a relatively safe sleep environment. A number of medications may be efficacious in managing RBD, including levodopa, dopamine agonists and melatonin, but clonazepam is the treatment of choice. Supportive environmental changes include removing dangerous objects from the home, padding sharp edges and hard surfaces near the bed, and covering windows with heavy drapery. Bed partners of RMD patients may consider the use of separate beds or bedrooms.

13.2.5 Circadian Rhythm Sleep Disorders

Circadian rhythm sleep disorders (CRSD) are characterized by relatively normal sleep occurring at abnormal times [32, 33]. The two CRSDs that occur most

commonly in older adults are advanced sleep phase disorder (ASPD) and irregular sleep wake disorder (ISWD) [33]. ASPD is characterized by sleep that begins and ends at unusually early times [33]. ISWD is characterized by sleep that is scattered across the day and night in sleep bouts of irregular duration [48].

An individual obtains optimal sleep when their desired sleep time coincides with a high homeostatic drive to sleep, coupled with appropriate timing of the endogenous circadian rhythm of sleep/wake propensity. In older adults there is a decrease in overall homeostatic sleep drive, which when coupled with alterations and poor environmental cuing of the circadian clock, are thought to contribute to the development of CRSDs.

13.2.5.1 Assessment

Accurate assessment of CRSDs requires a careful clinical and sleep history and a weeklong sleep log, optimally accompanied by wrist actigraphy [22]. Markers of circadian phase, such as core-body temperature rhythm and dim-light melatonin onset may also prove useful. Polysomnographic evaluation is not typically required, although given the high prevalence of other sleep disorders such as OSAS, RLS and RBD in older adults, a careful assessment for these as well as psychiatric conditions such as depression and anxiety that frequently accompany CRSDs, should always be part of the differential diagnosis.

13.2.5.2 Management

ASPD is typically treated using a combination of good sleep hygiene practice and various methods to delay the timing of sleep. Two approaches have been used to delay sleep to correct ASPD; chronotherapy and light therapy. Chronotherapy involves advancing sleep time (moving it even earlier against clock time) every few days until a desired sleep/wake timing is achieved. However this approach is of limited clinical practicality in that it requires stringent adherence, close and near continuous monitoring and is a rather lengthy process. Consequently the treatment of choice is the use of light therapy; application of bright light during the early evening (~7:00–9:00 p.m. [6, 22]).

The erratic, fragmented sleep pattern that characterizes ISWD is most commonly seen in patients with dementing neurodegenerative disorders, particularly those who have been institutionalized, although it can also be seen in individuals with traumatic brain injury and mental retardation [33]. ISWD in community dwelling Alzheimer's disease patients can be treated with caregiver-facilitated corrective sleep hygiene combined with regular exercise and increased light exposure [19, 21]. Management of ISWD in institutionalized older adults is discussed at length in the next section of this chapter.

13.3 Assessment and Management of Sleep Disorders in Institutionalized Older Adults

Sleep disturbances are extremely common in older adults living in long-term care and nursing home environments. Although there are few studies that have attempted to quantify the scope of this problem, it has been observed that older adults in these settings typically spend considerable time asleep during the day, corresponding to excessive wakefulness at night [18]. Institutionalized older adults are at particular risk of significant sleep disturbances which can further compromise their already restricted quality of life. In addition to the many potential factors that disturb the sleep of older adults discussed earlier, individuals in these settings also tend to be frail and are more likely to suffer from serious medical and psychiatric illnesses including pain, depression, neurodegenerative disorders, gastro-esophageal reflux and nocturia. They also tend to experience many factors intrinsic to their living conditions that further contribute to sleep disturbance such as lack of contact with the community outside their institution, limited (if any) exposure to bright light, physical and mental inactivity, extended time in bed and nighttime noise and light due to staff and roommate activities. Given all of these contributory factors, sleep disturbance should be considered as a potential problem in all institutionalized older adults.

13.3.1 Assessment

Accurate assessment of sleep disturbance in institutionalized older adults is challenging as a significant proportion of these individuals suffer from neurodegenerative disorders that can severely limit their ability to articulate even serious problems. Careful observation is often key to detecting such problems. In addition to the various assessment techniques detailed above, two additional techniques are extremely helpful in sleep disturbance assessment in this unique population; behavioral observation by staff and wrist actigraphy, both of which can be very useful in determining the nature and severity of the problem. Wrist actigraphy has the distinct advantages of being both easy to implement and objective, and can also be useful in assessing the impact of any management strategies employed, even in patients who cannot easily communicate their situation.

13.3.2 Management

Management of sleep disturbances in institutionalized older adults falls into three major categories: environmental factors, such as lack of light and physical and social activity, excessive time in bed, noise, etc.; medication issues, including both

prescription medications that may be causing or exacerbating a sleep disturbance, and prescription medications given to aid sleep that are either inappropriate (not FDA approved) or ineffectual and finally occult sleep disorders, such as undiagnosed OSAS or RLS.

At the institutional level, much can be done to ensure an environment conducive to quality resident sleep. There is excellent evidence demonstrating that daytime exposure to bright light can improve the sleep-wake patterns of residents [11, 37]. Facilities should be encouraged to introduce procedures to increase the exposure of their residents to either artificial or natural daytime bright light and to increase daytime levels of physical and social activity, as well as decrease daytime sleeping and excessive time in bed for residents [1, 27, 31]. Similarly, facilities should be encouraged to make the nighttime environment maximally conducive to sleep by minimizing nighttime noise, light exposure and procedures to the minimum necessary to ensure appropriate patient care [36].

At the level of the individual resident, it is important to recognize that a careful and regular review of their medical and psychiatric condition as well as their medication use will ensure that they are not causing or contributing to a sleep problem. If this is suspected, adjustment of type, dose and timing of medication(s) with appropriate follow-up is warranted to determine the potential impact on sleep. There is essentially no evidence to support the use of sedative-hypnotic medications in long-term care or nursing home facilities. The potential benefits and risks of such medications, particularly in regard to increased risk of falls and daytime cognitive impairment in a population where these problems are major concerns, needs to be carefully reviewed for any resident receiving such medications. Similarly, medications to promote sleep that are not approved by the FDA for such purposes should not be used in nursing home residents, as there is no evidence to support such use. In particular, use of sedating antidepressants and sedating antipsychotics should only occur if their primary indication is exhibited (e.g. depression or agitation).

A final concern in effective management in this difficult population is the accurate assessment and treatment of occult sleep disorders, particularly in those residents whose cognitive impairment may interfere with their ability to articulate the problem, even when they are actively queried. Of particular concern (because of their high prevalence) are OSAS, RBD and RLS. Fortunately, these disorders can be well managed, assuming they are accurately identified. OSAS can often be identified by reports of snoring and observed apnea/hypopnea by staff, assuming they are asked to make and report such observations. Similarly, the rather frank nighttime behaviors associated with RBD can also be readily observed and reported if staff are appropriately educated and tasked. In the case of RLS, special attention is required for patients who demonstrate signs of leg discomfort, excessive motor activity of the lower limbs, signs that this discomfort and activity is worse during periods of rest, signs that movement seems to relieve the apparent discomfort and signs that this discomfort and excessive leg activity is worse in the evening or night. Staff should be educated as to the likelihood of occult OSAS, RBD and RLS in institutionalized older adults and the importance of reporting such possibilities, as these disorders can all be effectively managed.

13.4 Conclusions

There is a growing appreciation of the importance of sleep's interactions with health and quality of life, particularly in the context of aging, and the last decade has seen significant and rapid advances in our ability to diagnose and treat sleep disorders in older adults [43]. Although there is much to learn (see [7, 44] for discussion of this), a firm evidence-based foundation for the accurate diagnosis and effective management of sleep disturbance in older adults currently exists [7].

Accurately assessing and effectively treating disturbed sleep in an older adult, while often complex, is ultimately rewarding. However, it requires an appreciation of the many ways that sleep can be disturbed in such individuals, an understanding that sleep may be disturbed for multiple reasons, and the willingness to parse what those casual agents might be and then institute the most effective treatment. It is important to recognize that several factors may be contributing to the sleep disturbance of an older adult, who might well be experiencing disturbed sleep as the result of prescription drug side effects, a learned insomnia or a primary sleep disorder, such as OSA or RLS. To further complicate the situation, all of these factors might be present in an institutionalized, cognitively impaired older adult who cannot effectively communicate the nature of their problem.

Effective assessment of sleep disturbances in older adults can only be achieved in the context of associated medical and psychiatric disorders, primary sleep disorders, prescription and non-prescription drug use and behavioral and environmental conditions. Thorough assessment of sleep problems is often iterative, takes time and may require serial evaluations and information from multiple sources. Accurate identification of underlying causes and their effective treatment will address most sleep disturbances in older adults, helping to ensure that growing older does not mean sleeping poorly.

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Chapter 14
A Historical Note on the Development of Sleep Medicine Technology Education

Mia Zaharna and Christian Guilleminault

Abstract Sleep Medicine was created in the early 1970s, and since efforts have been made to have a field based on organized education of professionals. Educational programs were aimed at physicians, researchers and technologists. Greater efforts were made initially in Europe and North America that took the lead in creating professional organizations and specialty teaching leading to specialty diploma recognizing expertise in the field. Such efforts are now replicated in many part of the world.

Keywords Sleep medicine • Education • Professional organizations • Technologist development

Sleep Medicine cannot exist without appropriate standardization and teaching of sleep technology. The concept of "sleep medicine" came to life in late 1969. The demonstration that many neuronal networks were firing very differently based on states of alertness, with demonstration that some neurons stopped completely discharging or started firing based on specific sleep states, led to this idea. It also appeared that the autonomic nervous system (ANS) showed important changes in its regulation based on these states, with the balance between sympathetic and parasympathetic tones very much dependant on sleep/wake states. As the ANS is very much involved in modulating the activities of many vital organs, these findings led to questions regarding the control of vital functions during sleep states compared to wakefulness: Could some disease-entities have their presentation modified and

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possibly worsened by the changes in states? What is the effect of these changes on organ functioning? Could there be some abnormalities that are state-specific and are unmasked only during a specific state of alertness? These were the questions raised, at least in the mind of one individual, when considering the neuro-science reports.

These questions led to the opening of a clinical sleep laboratory in the Hopital de la Salpetriere in Paris, France in 1970 by Christian Guilleminault. The goal was to appreciate the impact of states of alertness on specific vital functions (namely cardiovascular and respiratory function) and potential changes in organ functioning in relation to sleep state. Simultaneously, in 1970 at Stanford University in California, interest in looking at insomnia and understanding better the impact of hypnotics on sleep led to the beginning of an insomnia clinic. This service was developed in parallel to the already established UCLA Sleep Laboratory, hosted in the Department of Psychiatry, which was already performing hypnotics studies in collaboration with the pharmaceutical industry.

In 1970, the concept of "sleep medicine" was really limited to Paris, although sleep research was being done throughout the world with leaders such as G. Mosuzzi who summarized in an important monograph, knowledge on sleep-wake cycle in 1972 [5], or the group of Mancia and Zanchetti which from the late 1960 till the mid-1970s systematically studied the neural and non-neural influences of sleep and sleep states on the cardio-vascular system in cats. All the individuals involved in human investigation during sleep were tributary of their specialty background. Henri Gastaut's team of neurologists in Marseille (France), which recorded many abnormal behaviors during sleep, was looking at dissociating epileptic from non-epileptic syndromes. Meanwhile, Elio Lugaresi's team of neurologists in Bologna (Italy) had provided a description of the sleep problems associated with the Pickwickian syndrome including the associated cardiovascular risk [4]. The tools used were those seen in clinical neurophysiology laboratories of the time, including in Osaka (Japan). In the USA, psychiatrists and psychologists dominated the scene. The discovery of REM sleep and the demonstration that elaborates dreaming occurred during REM sleep had attracted the attention of psychiatrists. The influence of psycho-analysis was important, but efforts were made to create a more "biological based" psychiatry, and investigation of sleep, particularly REM sleep in mental disorders was a new window. Neurology and psychiatry were two well-established fields, and the idea of "sleep medicine" was very foreign to most and even considered a threat to some. For example, in the USA, research funding was allocated to federal institutions based on well established medical fields. The funding for sleep research often came from the National Institutes of Health, and, more particularly, the division covering mental health and neurological diseases. Researchers did not want to be "cut" from their sources of funding by intruding sleep researchers. A similar phenomenon was happening in other countries like France where a field called "experimental medicine" came to include those leading researchers that did not "fit" well in established departments. The well-known sleep researcher Michel Jouvet was one such individual who had as colleague in the same "specialty" a specialist pursuing the possibility of performing liver transplants.

In January 1972, William C. Dement wanted to extend the understanding of REM sleep and the only known syndrome associated with an abnormality of REM sleep occurrence: Narcolepsy. This is when Christian Guilleminault was offered the opportunity to come to Stanford University primarily to conduct clinical narcolepsy research, and, as a secondary aspect, to further develop his concept of Sleep Medicine. The parallel efforts of both individuals led to the recognition of "sleep" as an independent field of research and the creation of an Institute of Sleep Research in the National Institutes of Health in 1993 on one side. On the other side this effort culminated with the creation of a specialty of "Sleep Medicine" with delivery of a diploma obtained after a mandatory 1 year of training in an accredited Sleep Medicine service and passage of a board examination all under the auspices of the "American Council for Graduate Medical Education". In the European Community, different avenues have been followed in each country. For example, in France, there is a "University Diploma" (DU), in Germany, a "general recognition of training", and in Portugal, a Ph.D. As the EU is trying to unify its medical training, further developments can be expected.

The field of "Sleep Medicine" could not have developed without the creation of technologies and efforts to standardize the evaluation of patients. This sector is in continuous evolution with introduction of new technologies, sensors, computerized sleep systems, and respiratory related equipment leading to regular updates of technological recommendations. There is however a base on which one can build and this basic level of knowledge is important. It must also be acknowledged that some of the criteria considered today may not be valid tomorrow; and one has to fight against too much rigidity and make regular revisions of criteria. This last factor is a significant problem: it is sometimes difficult to move forward when a "heavy machine" exists as it becomes static and interests other than those related to improvement of patient care may emerge.

In 1975, when the American Association of Sleep Disorders (ASDA) was created, there were five initial members, and the number stayed low for some time. It was easy to find a simple majority to change statutes; however this is not the case today. This has an impact on several aspects of the field, the most obvious being in pediatric sleep medicine where many recommendations are not consistent with today's level of knowledge. Some of the reasons for such problems in pediatric sleep medicine are obvious. For example, many criteria are based on adult investigations. One instance of this are the EEG arousal scoring recommendations which are based on those written for adults even though several articles have indicated that EEG arousals as defined are infrequent in pre-pubertal children. A more important problem is the definition of "hypopnea" in pre-pubertal children. A pre-pubertal child with normal breathing during wakefulness has a normal lung volume with an oxygen saturation of 99.9% and high oxygen tension. Initially, studies of infants and young children involved measurement of oxygen tension; but the ease of monitoring finger pulse-oximetry has led to monitoring of oxygen saturation (SaO_2) with a finger probe during sleep studies. However, the well-known hemoglobin-oxyhemoglobin dissociation curve shows a clear difference in linearity between oxygen tension and SaO_2: there is a very small decrease in SaO_2 despite a linear

decrease in tension until the values reach the well defined " knee" of the saturation curve. Changes in tension early on are often ignored, and an undue value is placed on SaO_2 readings in defining abnormal breathing during sleep in pre-pubertal children. The definition of "hypopneas" in pre-pubertal children is clearly a major problem, recognized by all pediatric sleep specialists, as these definitions are based on adult definitions in the currently published "official" atlases. These errors will be progressively corrected but, in the interim period, teaching may be erroneous, and this may have an impact on recognition of abnormal events during sleep. It is important to develop an appropriate teaching manual that outlines techniques and technologies.

The "weight" given to some national criteria may also be a handicap. It is clear that in the USA significant effort has been made to have appropriate well documented baseline knowledge. The publications from the American Academy of Sleep Medicine (AASM) have had a lot of reverberation internationally as well, and while this is often justified, one has to recognize when national elements that are not universal across countries may impact the recommendations.

The AASM is the very young offspring of the older "Association for the Psychophysiology Study of Sleep" (APSS), an international group created by William C. Dement in the late 1960s aimed at creating a common scientific language of sleep. The most well-known work of this association was the creation of an atlas for scoring normal sleep in adults edited by Allan Rechtschaffen and Anthony Kales [8], and, a bit later, an atlas to score sleep in infants edited by a team of individuals lead by Dr. Arthur Parmelee [2]. In 1975, the ASDA selected these atlases to score sleep/wake in patients. However, the realization that problems existed led the ASDA to consider changes, and an addition published in the journal Sleep was made to the atlas to include scoring "short EEG arousals" in adults [1].

The introduction of new technologies (mostly the nasal cannula pressure transducer) and the awareness that there were patients with clear breathing problems during sleep that were not recognized by the well established definitions of "sleep apnea" and "sleep hypopneas" at the time led to the creation of an international taskforce that met in the city of Chicago in the late 1990s. It was here that the "Chicago Criteria for Sleep Disordered Breathing" and the definition of a "respiratory-event-related-arousal" (RERA) was created [9]. However, these criteria were mostly ignored by the international community. The USA was already in the midst of an obesity epidemic, and obese individuals with a high body mass index and high waist circumference often had important SaO_2 drops during sleep for which these changes in criteria were important. In countries like Thailand where abdominal obesity was not prevalent, the non-integration of the Chicago criteria has had a very negative impact on recognition of abnormal breathing in pre-menopausal women. The obesity epidemic is now world wide, at least in industrialized countries, but is often less marked than in the USA.

These problems are related to the large development of "Sleep Medicine" in the USA and that fact that the AASM has to respond first to its national membership. There are clear idiosyncratic issues between the sleep-medicine specialist in the USA and those in other countries. For example the sleep physician in the United

States must respond to the requirements of local insurance companies as well as those of federal institutions such as “Medicare”, a health insurance program covering elderly retirees. This means that the AASM may not represent an international consensus but that decisions are taken in relation to national pressures from a national membership. But AASM guidelines can be changed: as often efforts to integrate scientific information are made, but today one has to recognize that some decisions may be related to local conditions. One example of this, is the new AASM atlas to score sleep/wake. Clearly some European countries have decided not to follow some of the recommendations. Italian and Germanic researchers have published that the elimination of NREM sleep stages 3 and 4 in favor of collapsing everything to a singular “N3” scoring system [6,7]. Databases used to look at distribution of the Non-REM sleep stages are not valid anymore. Furthermore stage 2 *new* criteria does not match stage 2 *old* criteria; but the most problematic issue is the disappearance of a “stage 4” independent of stage 3 sleep. It has regularly been shown that growth hormone secretion is associated with delta sleep, i.e. stage 4 NREM sleep. It was demonstrated that important decreases in stage 4 sleep, but presence of stage 3 sleep, could be associated with abnormal growth hormone secretion particularly in children. Also, delta sleep has been shown to be associated with emergence of abnormal behavior out of stage 4 NREM sleep in children. Many European sleep laboratories have decided to keep the old way of scoring sleep due to such factors. Clearly, as sleep medicine becomes more international, there will be a need to have more consensus conferences to integrate changes.

To date, the AASM new proposal for scoring sleep has not been integrated everywhere and two parallel sleep scoring systems exist. Concurrently, ways of looking at sleep pathology vary among regions as well. Sleep laboratories in the south of Europe and in some Latin-American countries such as Brazil, have integrated the usage of the “cycling alternating pattern” (CAP) scoring system in their approach to diagnose sleep disorders. However, some other countries have had little interest in integrating CAPs despite development of a valid computerized automatic scoring system and demonstration that identification of changes in CAP type and distribution may be helpful in explaining symptoms. An atlas for scoring CAPs has been developed and distributed to an international audience [3].

Independent of these issues, the need for education of technologists and the need to have standard guidelines and technical recommendations became evident very early on. The individuals involved in the development of sleep medicine as a field had often received training in clinical or experimental neurophysiology. Sleep and wake are brain controlled states and to ignore the brain when looking at these behaviors is impossible. Basic sleep technology training implied usage of polygraphs and, today, computerized systems. The sensors and monitored variables are mostly the same as in the early years, however even more attention is often needed since computerized systems more easily hide erroneous settings. The need to have appropriate validation of techniques used and to have trained individuals in handling these techniques has been a key in the development of the field. It was so much appreciated that many countries refused to recognize sleep laboratories – the back-bone of sleep medicine – without trained technologists and accreditation.

Such requirements were based on the need to have reproducible findings from one place to another and to have a unified approach for diagnosis of syndromes. The fact that investigations often had to be performed on a sleeping subject meant that nocturnal work was needed to collect data followed by daytime analyses of the collected information.

Sleep medicine very early on led to the creation of teams calling upon individuals trained in specific technologies. These individuals needed specialized training and had to be able to troubleshoot with engineers and computer programmers on a daily basis. EEG technologists were the first individuals involved in monitoring sleep medicine patients, but it became obvious very quickly that more training was needed. In 1972 a track was created for training individuals interested in this new field. Trainees usually had a "Bachelor in Science or Art" and were looking at a possible long term career in health care. The need for teaching venues became obvious. In 1975, Dr Mary Carskadon, who was working on a Ph.D. in sleep research, wrote the first standardized manual for in-house training of technologists. Two other individuals, David Raynal and Robert Philips, contributed to this effort by creating standardized monitoring of respiratory and cardiac variables. Roger Baldwin led the development of a standardized approach to pediatric technology. Two individuals became very involved in the training program: Dr. Carskadon focused more on training those involved in research protocols while Dr. Sharon Keenan, who had a background in EEG technology, focused on the training of sleep medicine technologists. This "intra-muros" program became progressively open to outsiders, with a section of the Stanford Sleep Medicine Clinic dedicated to a Stanford Technology Training Program headed by Dr. Keenan. In 1982, a manual entitled "Sleeping and waking disorders: indication and techniques" was published [9]. This was the first textbook of sleep medicine that addressed technology. The teaching program became a demanding feat, and the University decided to make it a private, independent entity with a contractual agreement with the sleep clinic. The "School of Sleep Medicine" was thus opened in Palo Alto, California, with Dr. Keenan as director. It was the first educational entity dedicated to technology and sleep medicine training open to national and international applicants.

Since the 1990s, other training facilities have followed both nationally and internationally. South Korea developed a School of Sleep Medicine in Seoul, and many other foreign countries have followed suit. University based programs which award degrees to technologists have developed in the United States. Pomona College in southern California was the first college to include sleep medicine technology as a degree program. Over the years, different types of training tracks and degree programs for sleep medicine have been created. In the United States, one can pursue a diploma in "Behavioral Sleep Medicine" which is open to individuals with a clinical psychology degree and is aimed at non-drug treatment of insomnia syndromes. Sleep medicine technologists that work in laboratories have had a well defined training program for over 15 years. Trained sleep technologists have an official exam and are awarded a diploma which grants them the title of "registered sleep medicine technologist". Accreditation of an official sleep medicine laboratory

cannot be obtained without a "sleep-medicine specialized physician" and a "sleep-medicine registered technologist". Several European countries request similar proof of specialized training.

This short review emphasizes the importance of education in the field of sleep medicine. As foreign countries such as Taiwan progressively open up to the field of Sleep Medicine, the development of appropriate training in this field is of great importance.

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Chapter 15
Pervasive Health-Care Device Industry Analysis: Focusing on Sleep-Treatment Applications

Peter Liu, Hung-Hsiang Chu, Dai-Luan Wu, and Seng-Cho Chou

Abstract In this chapter, we want to determine the factors and risks that affect the viable business model for pervasive healthcare systems – with an emphasis on sleep treatment devices. We used a hybrid analysis utilizing, (i) Porter's Five Forces, to determine the competitive advantages of the pervasive healthcare industry and (ii) Delta Model, to determine the three strategic options related to customer bonding and adaptive processes which support these options. We have found that, with the hybrid analysis, pervasive healthcare industry will be highly competitive and strive to meet customer needs which makes it the next big trend in the medical industry overall. In particular, the ability to customize accordingly to the patients individual conditions is a key differentiator in such an industry. In addition, the major players and value chain of the sleep treatment industry are illustrated.

Keywords Pervasive health care • Hybrid analysis • Sleep treatment • Sleep health care industry • Business model

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15.1 Motivation of Research

There is an increasing percentage of the population living in modern urbanized society where several factors drive the increase of the average lifespan of humans. The factors include (i) greater access to medical facilities; (ii) greater knowledge with regards to illness prevention; (iii) new and advanced medical treatment for major illness; (iv) shifts with regards to human behavior towards healthier dietary practices.

From a World Ageing Report [21], the aging society in turn drives the healthcare market since people aged 60+ utilize 3–5 times more healthcare services than younger people. In 2009, 11% (606 million) of the global population was aged 60+. By 2050 this will be more than 22% of the entire population (2 billion). This is shown in Fig. 15.1.

From the study from Centers for Medicare and Medicaid Services [3], in 2004 the costs for healthcare in the United States have increased above 16% of the gross national product (GNP). This correlates with the fact that we are facing an aging population and an increasing number of chronically ill people.

Considering diabetes as an example, the proportion of persons of the age 65 with a chronic diabetes condition is approximately one in five (18.7%) [2]. Even assuming that this ratio remains constant in the future and does not get worse, the expected overall increase in percentage of persons with chronic diabetes conditions due to the aging of society is quite alarming. This development is not restricted to the US but it is a worldwide problem that particularly developed countries are facing. Hence, a major challenge in healthcare is to improve the quality of care for an increasing number of patients using limited financial and human resources.

The major factors contributing to breakdown of current healthcare system are threefold, (i) rising costs; (ii) fast changing demographics; and (iii) degrading quality. Global medical cost spending can be seen from the following Fig. 15.2.

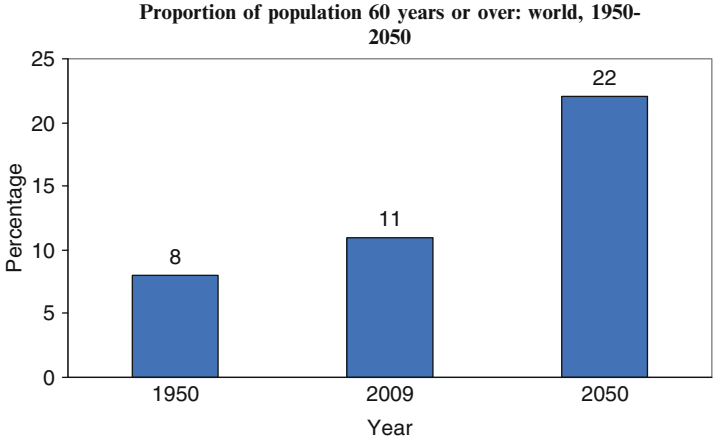

Fig. 15.1 Population and portion of population aged 60 or over. Source: UN World Population Ageing [21]

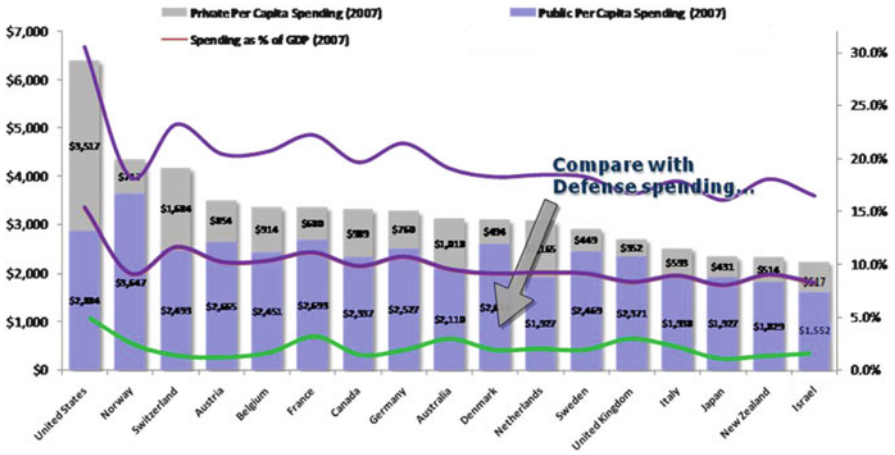

Fig. 15.2 Rising healthcare cost spending. Source: Frost and Sullivan [10]

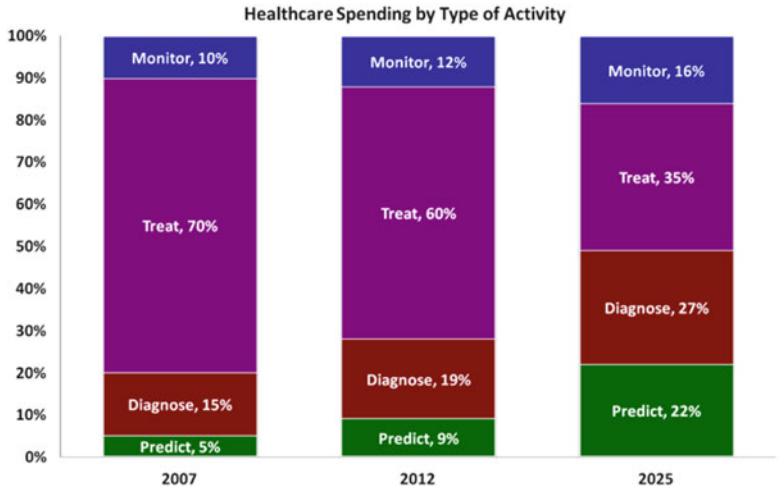

Fig. 15.3 Change in healthcare spending demographics. Source: Frost and Sullivan [10]

If current trends hold, we can see by 2050, healthcare spending will almost double, claiming 20–30% of GDP for some economies in Frost and Sullivan [10]. Also, for almost all economies worldwide, healthcare spending per capita is rising faster than per capita income. As for changing demographics, health economics dictates a shift in spending away from treating and towards predicting, diagnosing and monitoring (as depicted in Fig. 15.3).

As for quality [10], data in the following presents the current quality degradation.

- 15% of patients admitted to hospital suffer an adverse event.
- 8% of adverse events result in death.
- 6% of adverse events result in permanent disability.

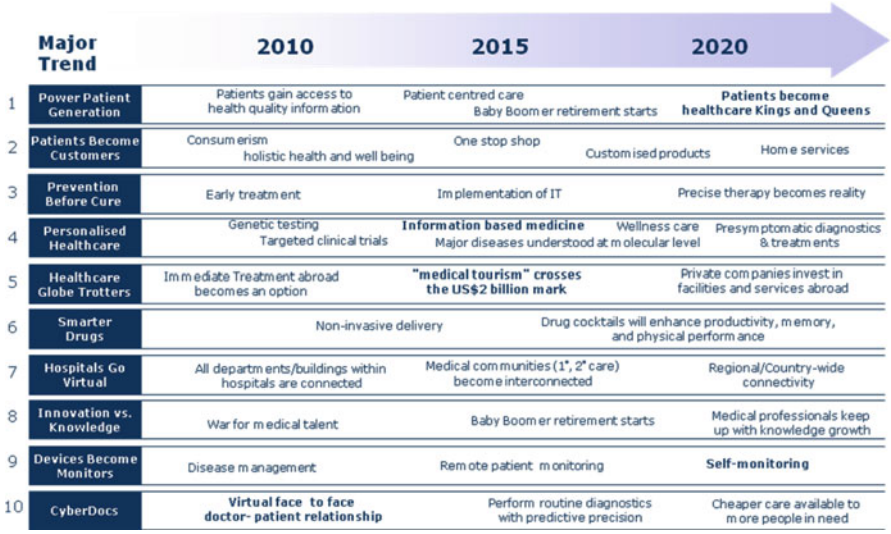

Fig. 15.4 Change in healthcare spending demographics. Source: Frost and Sullivan [10]

- 10–20% of all adverse events are caused by medication errors.
- 10–15% of hospital admissions occur because providers do not have access to prior care records.
- 20% of laboratory tests are requested because the results of previous investigations are not accessible.

In light of the above, there is an urgent need to establish a new type of healthcare system. We will now try to define the building blocks for such a healthcare system. A clear trend is patient centric healthcare, which interconnects medical communities and virtualizes patient doctor relationship. This trend is depicted in Fig. 15.4. Take note here, that throughout this chapter patient-centric healthcare and pervasive healthcare will be used interchangeably.

15.1.1 Problem Statement

In light of the above, we find it interesting to research the business developments and opportunities for this emerging industry of pervasive healthcare systems. In addition, we must understand what drives this new healthcare system to competitiveness, meeting customer needs, and adding value. Therefore, the problem we will focus on addressing in this chapter is defined as follows.

15.1.1.0.1 Problem Statement: Determine the factors and risks affecting the viable business model for pervasive healthcare systems – with a focus on sleep treatment devices. Viability is assumed when both the users of the system and the providers of the system perceive sufficient value of their participation [7]. There

are no theories on how to approach development of business models in healthcare. Business modeling is considered an effective approach to assess value creation and assess market adoption possibilities. Nevertheless, business modeling in traditional healthcare is a relatively new field in science, not to mention business model development for the emerging pervasive healthcare industry.

Many of the sleep enhancement devices readily available in the over the counter markets, are only marketed as non-treatment devices or relaxation related devices. To determine why a limited number of devices exist in the market that can claim actual medical treatment in a pervasive environment is very interesting. These factors may be used as criteria to determine whether the roadmap planned or developed for future devices will be successful.

The remaining of this chapter is organized as follows. In Sect. 15.2, we look into previous works which have looked into related business aspects for healthcare systems. In Sect. 15.3, we introduce our hybrid analysis methodology/approach to the research problem. In Sect. 15.3, we show the results and discussion when applying the hybrid methodology to the research problem. In addition, some risks are addressed. In Sect. 15.4, we give an analysis on the sleep industry and relate value chain. In conclusion, we summarize the contributions of this section and possible future research directions in Sect. 15.6.

15.2 Background and Literature Review

Pervasive healthcare systems, in which a large percentage focus on remote patient monitoring and management, are increasingly recognized as having the potential to help overcome the challenges of traditional healthcare mentioned in Sect. 15.1. Per its definition, in a remote pervasive healthcare system, the caregiver is geographically separated from the consumer with the care plan being individually tailored to the patient needs.

This patient-centered concept, bringing the care from the hospital (or the doctor's office) to the patient at home, results in cost-reduction and improved quality of care. Being able to more frequently observe the patient's state of health by performing remote measurements of the patient's vital signs enables optimizing the patient's medication and treatment accordingly to each individual patient's needs.

This results in longer independent living for older patients and lower mortality rates. Through increased frequency of daily automated, but personalized, patient intervention, the care providers can manage a broader range of chronic disease patients meanwhile improving efficiency. However, the biggest opportunity for reduction in costs is not in lower costs for nurse visits but rather in a reduced need for high-cost chronic care and hospitalization.

In addition to the care being provided in a remote and personalized way, an important factor for enabling the success of future pervasive health systems is to make the last technological hop to the patient, wireless. This is also along the lines of technology development trend shown in Fig. 15.5.

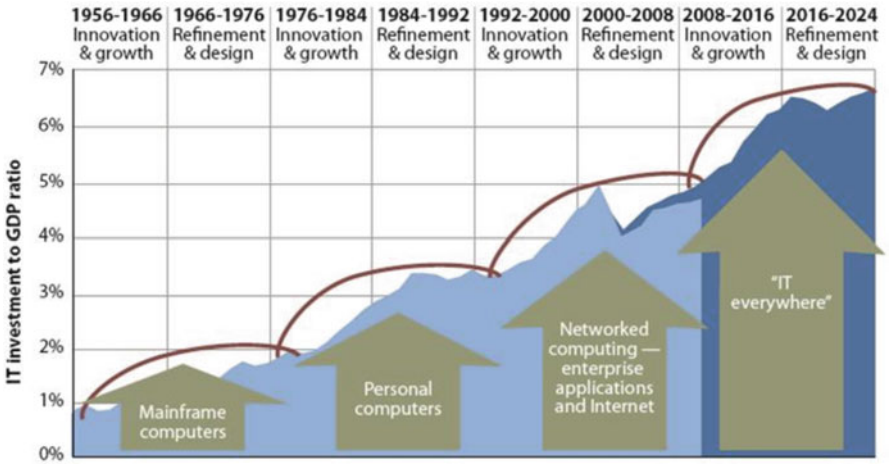

Fig. 15.5 IT investment trend forecast. Source: Forrester Research [9]

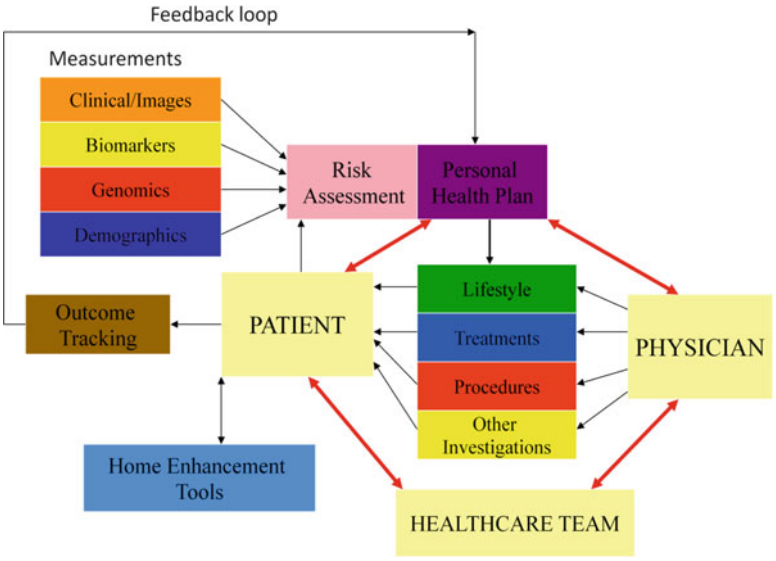

Fig. 15.6 Example of patient centric healthcare workflow. Source: Forrester Research [9]

By introducing wireless technology, cumbersome cables can be eliminated, enabling greater physical mobility and making the system more unobtrusive and ubiquitous for the patient. This is due to the fact that the technologies being considered for the wireless link at the patient side now range from enabling a simple cable-replacement to allowing real networking of vital sign measurement devices, as for example in the context of body sensor networks (BSN) [9]. An example of a patient-centric pervasive health system is shown in Fig. 15.6.

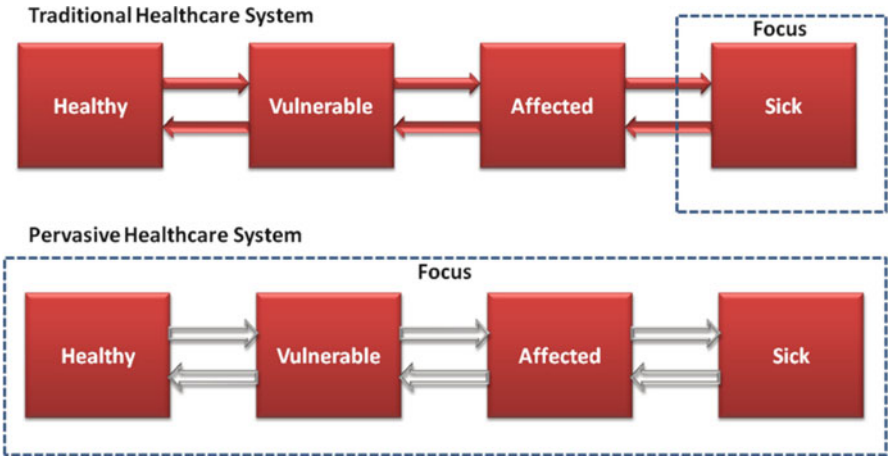

Fig. 15.7 Comparison between traditional healthcare system and pervasive healthcare system

15.2.1 Pervasive Healthcare System Market Characteristics

15.2.1.1 Market Scope

The market perspective for pervasive healthcare systems, compared to traditional healthcare systems, focuses on a larger scope, that blurs the lines between populations and provides more personalized healthcare. This concept is depicted in Fig. 15.7.

As we can see from Fig. 15.7, the pervasive healthcare industry compared to traditional healthcare focuses on all the different stages of heath of a human. In other words, monitoring and prediction is not only for people that are already ill, but also for the healthy, vulnerable, or affected. Therefore, addressing a broader scope of targeted customers in market terms provides us with a larger total addressable market (TAM).

15.2.1.2 Market Dynamics

Here, we shall look at (i) the pros and cons that drive and restrain the market for pervasive healthcare industry; (ii) the factors that individually and together affect the market; and (iii) discuss how healthcare, technology, information trends explicitly or implicitly shapes the trend of the pervasive health market. The general market dynamics are shown in Fig. 15.8.

An abundance of patient-centric research has been set-forward. As we can see from the report [10], the health care paradigm shifts clearly points out that pervasive health systems is the future (depicted in the following Fig. 15.9).

This pervasive healthcare trend arises from being a potential solution to the aforementioned problems existing in traditional healthcare–low quality and high

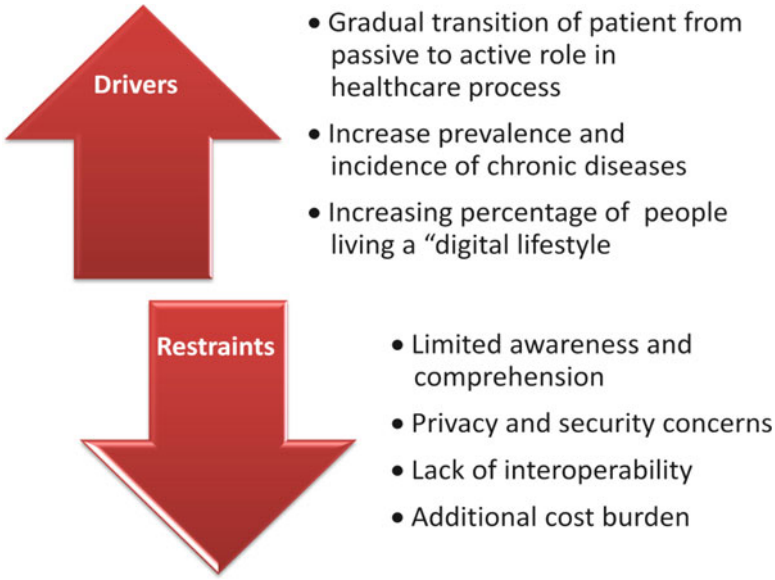

Fig. 15.8 Market dynamics of pervasive health systems. Source: Fass [8]

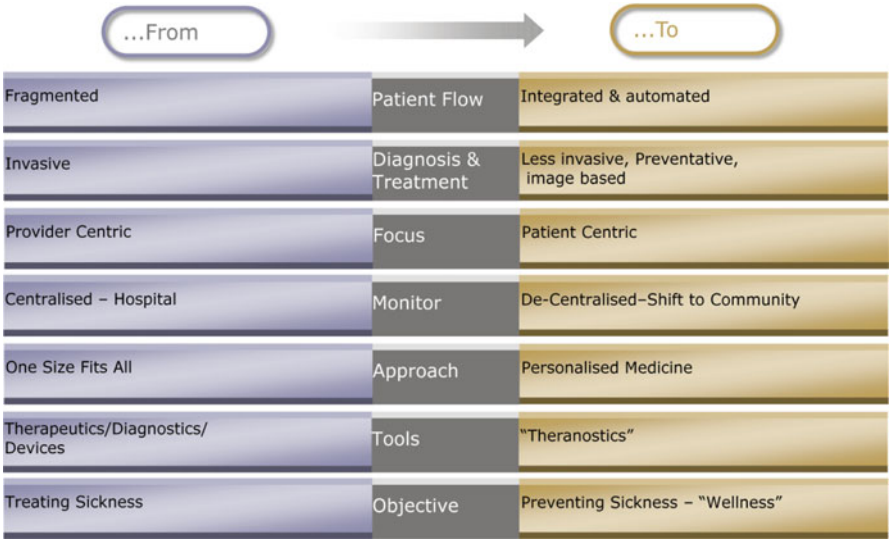

Fig. 15.9 Healthcare paradigm shifts. Source: Frost and Sullivan [10]

rising costs. Interesting to note, from an industry competition point of view, this is just what makes healthcare different from other industries. As the paper from Porter and Teisberg [19] states, competition over the time should drive up quality while lowering costs for customers. However, this is not true for healthcare related

business due to current policies, lacking of information in customers. Pervasive healthcare industry proves to be just the opposite. In addition, in the work from Grimson [11] states that "movement towards shared or integrated care in which the single doctor–patient relationship is giving way to one in which an individual's healthcare is the responsibility of a team of professionals across all sectors of the healthcare system. This is being accompanied by a very significant growth in home care which is increasingly viable even for seriously ill patients through sophisticated telemedicine services facilitated by intelligent sensors, monitoring devices, hand-held technologies, and the Internet." In the paper [17], they used actual case studies of around one hundred patients and found that tele-healthcare along with electronic health records has a positive impact in lowering medical costs and improving quality of treatment over a period of 3 months.

Many researches discuss the feasibility of such a pervasive health system. The interoperability of both physical wireless protocols and data format is the main obstacle to both business and technical feasibility [6, 20]. To be interoperable, certain standards and formats should be followed for product development or service providing. Thus the problem arises of license and royalty issues, which in business aspects, implicitly defines the non-trivial revenue sharing model. However, this remains yet to be defined and optimized.

This brings us to an important aspect that needs to be revisited – the concept of business model. The concept business model is widely used [4], but rarely well defined [1]. Sometimes the term business model is reserved for only one company and describes in the business model the role of that company in its environment. Other visions are that a business model is a model of profits, and the concept of generating these profits is considered to be the business model. These last visions do not describe the cooperation in networks or chains that might be required in order to create customer value [12]. Nevertheless, as mentioned in Sect. 15.1, business models for healthcare system are yet to be defined clearly and remains and open problem yet to be investigated.

15.3 Research Approach and Methodology

Here we use two models to determine the factors and risks that contribute to a viable business model for pervasive health devices. Take note that healthcare devices in general, compared to consumer products, are subject to extremely strict regulatory environments. This is especially non-trivial for devices that claim to have treatment purposes. In addition, the channels for marketing and selling such products are different – through conferences and hospital distribution channels.

From a business standpoint, the pervasive healthcare industry is an emerging market. New firms wanting to establish a foothold in the marketplace in this emerging industry will face several challenges. Therefore, the most important strategies the firm must address are (i) identify competitive advantages and (ii) capture and retain customers.

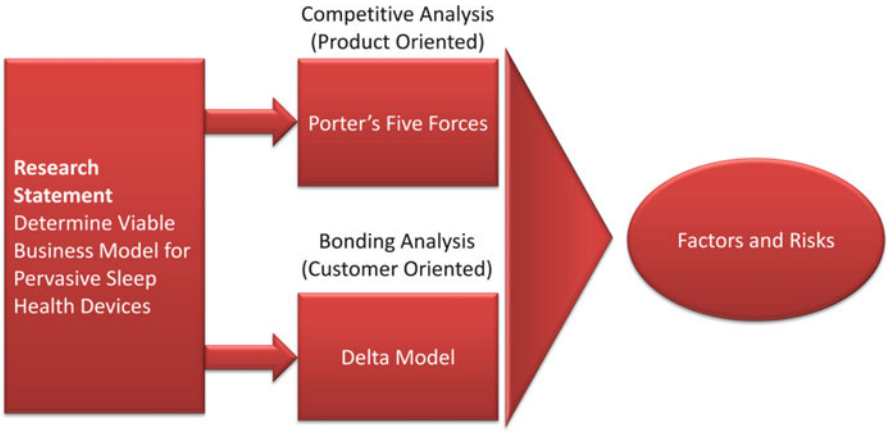

Fig. 15.10 Hybrid analysis to determine factors and risks [16]

15.3.1 Hybrid Analysis

In light of the above, we use a hybrid analysis consisting of three models, (i) Porter's Five Forces [18], to determine the industry/product's competitiveness and (ii) Delta Model [13, 14], to determine the strategic options from a customer bonding point of view and adaptive processes that support the options. This hybrid model is depicted in Fig. 15.10.

We briefly explain the model used in the hybrid analysis in the upcoming subsections.

15.3.2 Porter's Five Forces Model

Pervasive healthcare industry is relatively new compared to the traditional healthcare industry. Many of the companies just entering this industry are small to middle sized enterprises (SMEs) which either do not have the resources or the brand recognition of large firms. In the work of Kleindl [15], the authors used Porter's five forces model to analyze the new competitive forces impacting SMEs. We therefore utilize this model in analysis to the pervasive healthcare industry.

The Five forces analysis looks at five key areas namely the (i) threat of entry, where not only existing firms but also the possibility of new firms may enter the industry affects competition; (ii) the power of buyers, where this considers the impact that customers have on a producing industry; (iii) the power of suppliers, where this considers the producing industry relationship to raw materials used to create products, e.g., labor, component and other supplies; (iv) the threat of substitutes, where this refers to products in other industries; and (v) competitive

rivalry, where competition among rival firms drives profit to zero. The following are main influences of determining the high or low effects of each force.

15.3.2.1 Threat of Entry

- Economies of scale e.g. the benefits associated with bulk purchasing.
- The high or low cost of entry, e.g. how much will it cost for the latest technology?
- Ease of access to distribution channels
- Cost advantages not related to the size of the company
- Will competitors retaliate?
- Government action e.g. will new laws be introduced that will weaken our competitive position?
- How important is differentiation

15.3.2.2 Power of Buyers

- Are the buyers concentrated? If so, buyer power is powerful, e.g., there are a few buyers with significant market share
- Are powerful if the cost of switching between suppliers is low

15.3.2.3 Power of Suppliers

The power of suppliers tends to be a reversal of the power of buyers.

- Where the switching costs are high e.g., switching from one supplier to another
- Power is high where the brand is powerful
- There is a possibility of the supplier integrating forward
- Customers are fragmented (not in clusters) so that they have little bargaining power

15.3.2.4 Threat of Substitutes

- Where there is product-for-product substitution
- Where there is substitution of need
- Where there is generic substitution

15.3.2.5 Competitive Rivalry

This is most likely to be high where entry is likely; there is the threat of substitute products, and suppliers and buyers in the market attempt to control.

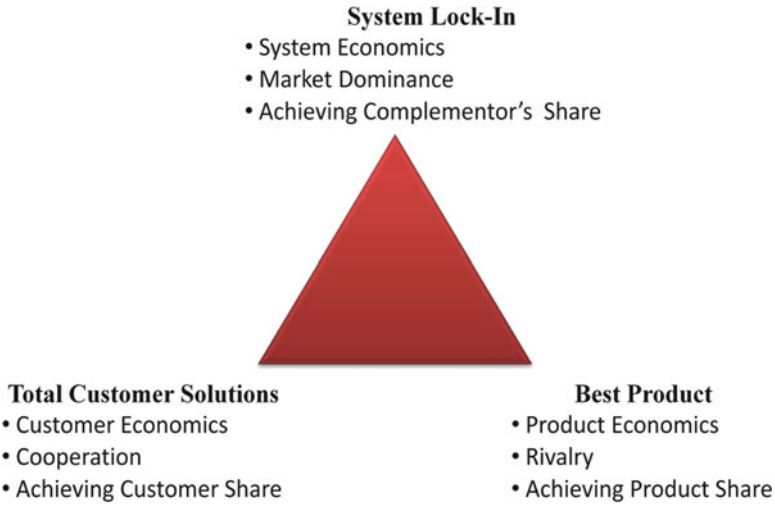

Fig. 15.11 Delta Triangle analysis on customer bonding. Source: Hax and Wilde [13]

15.3.3 Delta Model

For pervasive healthcare systems, one of the main business model characteristics is patient (customer)-centric concept. However, as we can see from the previous Porter's five forces, the primary role of strategy is that the firm achieves a unique competitive advantage. In other words, the goal of the strategy is to beat your competitors by utilizing unique capabilities or resources. Seemingly, we need to put more emphasis on the customers. Therefore, we utilize the Delta Model proposed in Hax and Wilde [13] to analyze whether or not pervasive healthcare has the characteristics to support a customer-centric strategy. In addition, this model defines strategic positions that reflect fundamentally new sources of profitability, provides strategic alignment with the firm's internal activities, and introduces adaptive processes that allow the firm to respond to uncertainties. These are all issues that new entrants in the pervasive healthcare industry have to address.

This customer-centric analysis on the firm focuses on utilizing to Triangle by offering three strategic options, (i) best product, where the company bonds with the customer through intrinsic superiority of the product or service it provides; (ii) total customer solutions, where the company bonds with the customer by keeping within close proximity to the client which allows the company to anticipate needs and work jointly to provide to develop products; and (iii) system lock-in, where the company tries to gain a complementors' share in order to lock-out competitors and lock-in customers (achieving a de facto proprietary standard, Hax & Wilde [14]). This is depicted in Fig. 15.11.

Take note that the above strategic options need not be mutually exclusive. The firm may find its activities taking a hybrid position between two strategic options in the triangle.

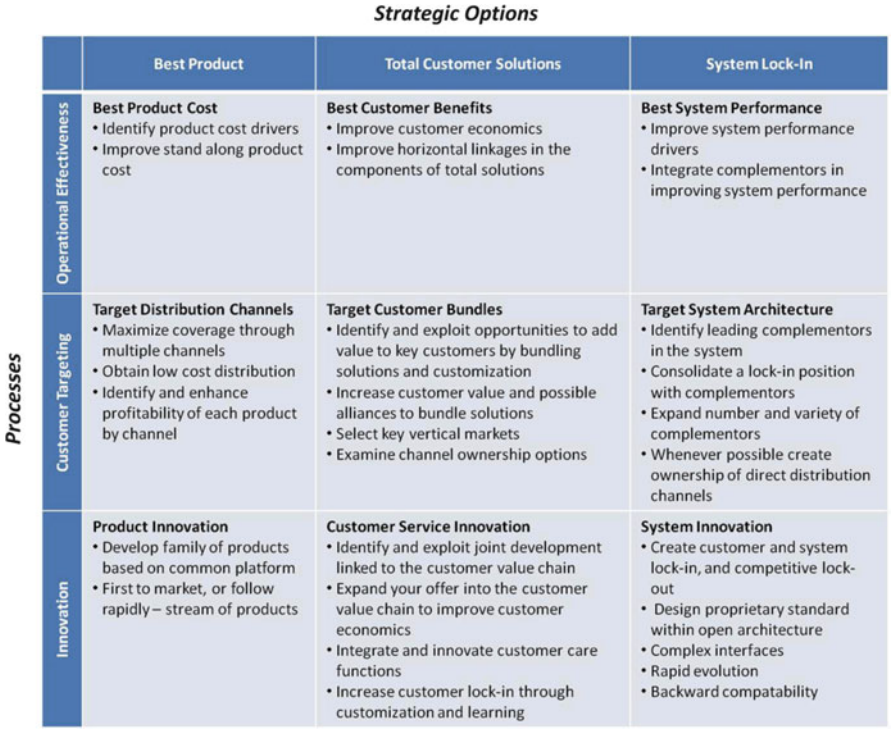

Fig. 15.12 Process support for strategic option execution. Hax and Wile [14]

The above triangle determines the firm's business strategy. However, how to execute these strategies is yet another challenge. Hence, we can utilize a set of adaptive processes to support the three strategic options as follows.

- Operational effectiveness–This process defines the providing the product/services to the customer. This addresses the most effective cost and asset infrastructure of the internal supply chain of the firm and should be extended to suppliers, customers, complementors.
- Customer targeting–This process defines the business to customer interface. This addresses the customer relationship management which includes customer attracting, satisfying and retaining. This is to establish an optimized revenue infrastructure for the firm.
- Innovations–This process ensures that there are upcoming new products/services to make the business sustainable. Take note that we do not restrain ourselves to only product/service innovation but also production and marketing capabilities such that the firm sustains superior financial performance.

These processes are considered to be continuous and suit a changing business environment. We use Fig. 15.12 to show in detail how each process supports the various strategic options.

The results and discussions based on applying the hybrid analysis to the research problem are given in Sect. 15.5.

15.4 Sleep Healthcare Industry

As shown in Fig. 15.13, sleep healthcare industry is encompassed by three major role players – (i) sleep medicine; (ii) sleep technology; and (iii) other sleep supportive devices.

The supply chain of a typical sleep healthcare industry is shown in Fig. 15.14. The value chain is depicted in Fig. 15.14.

15.5 Results and Discussion

We now apply the hybrid analysis in Sect. 15.3.1 to the problem statement taking into consideration the Sleep Coach Device [5, 16] as an example. We will first use Porter's Five Forces for industry analysis [18].

15.5.1 Threat of New Entry

- Newcomers need access to sleep medicine knowhow
- Sleep medicine field is limited to a number of professionals

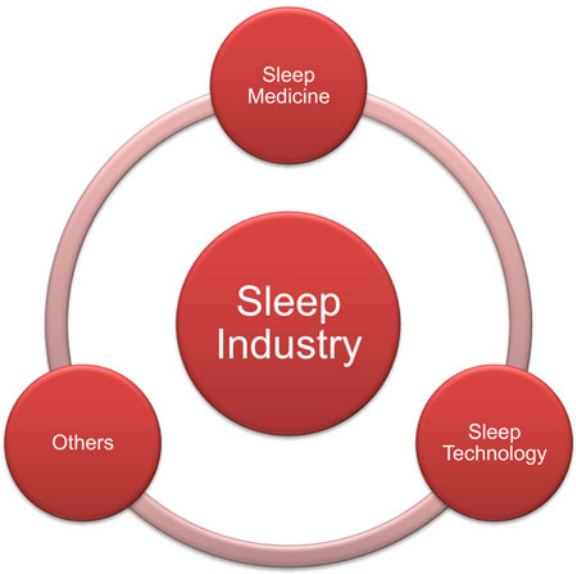

Fig. 15.13 Three major roles in sleep healthcare industry

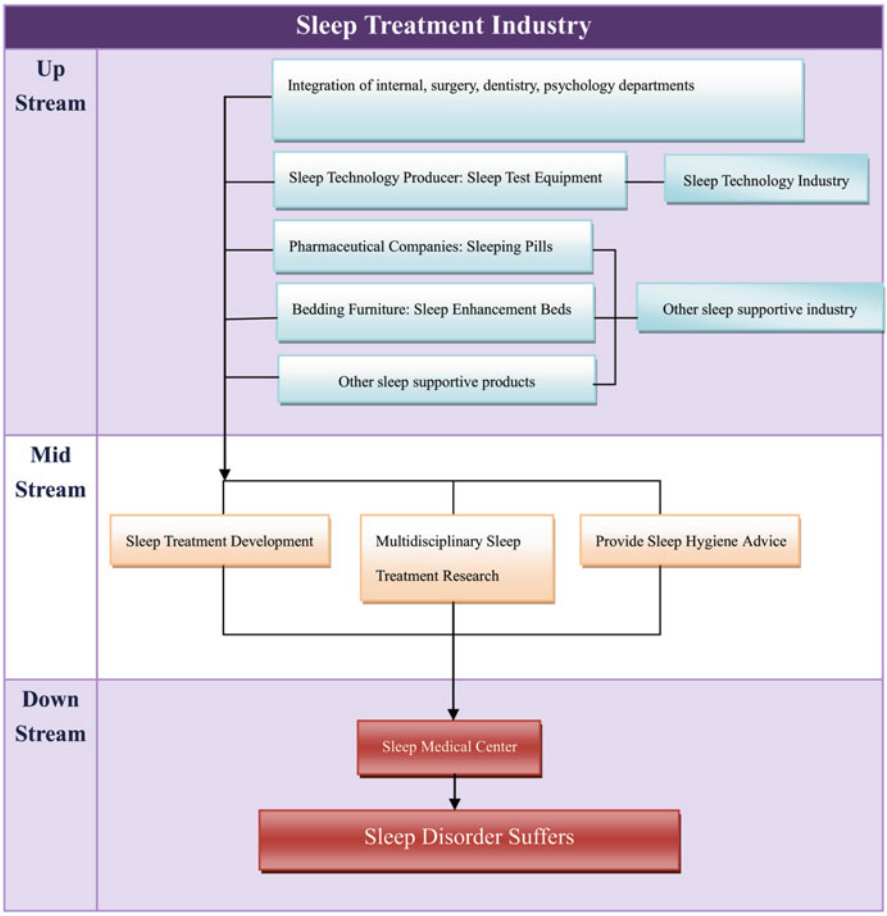

Fig. 15.14 Upstream to downstream sleep treatment industry

- Regulations for treatment activities, even non-obtrusive technologies, are strict
- Key ideas have been patented
- Interoperability verification tests are time consuming

15.5.2 Supplier Power

- Mobile Personal Digital Assistant (PDA) hardware platforms, e.g., Qualcomm, TI, Intel are highly standardized, therefore switching costs are low
- Typical biofeedback sensors, e.g., heart rate, skin conductance (key metrics for human stress levels), are now highly standardized and commoditized

15.5.3 Buyer Power

- Buyers can be subsidized (or reimbursed) by health insurance companies
- No similar sleep treatment products in the market, therefore switching costs are high for the consumer
- Price sensitivity for healthcare products is low especially for sleep treatment aides since sleep can be viewed as a necessity

15.5.4 Threat of Substitution

- Most devices claiming to provide sleep treatment at home are only health supplements and not real treatments

15.5.5 Competitive Rivalry

- Number of similar devices claiming sleep treatment at home are minimal
- Quality will meet FDA requirements and sleep medicine standards
- Low cost to leaving market

The five forces diagram is shown in Fig. 15.15.

In the following, we analyze a firm using the Delta Model. From the standpoint of best product, we have the following differentiations:

- Provide at home diagnosis and treatment
- Provide physician interactions
- Straightforward and friendly user interface
- FDA approved

From the standpoint of customer solutions, we have the following characteristics:

- Customized treatment
- Insurance coverage

From the standpoint of a system lock-in, we have the following characteristics.

- Cooperation with sleep treatment centers in hospitals
- Collaborate with professionals in the field of sleep medicine
- Turnkey solution with both a patient side sleep coach and physician side sleep doc

We then use the matrix analysis to define the adaptive processes that support the above options as shown in following Fig. 15.16.

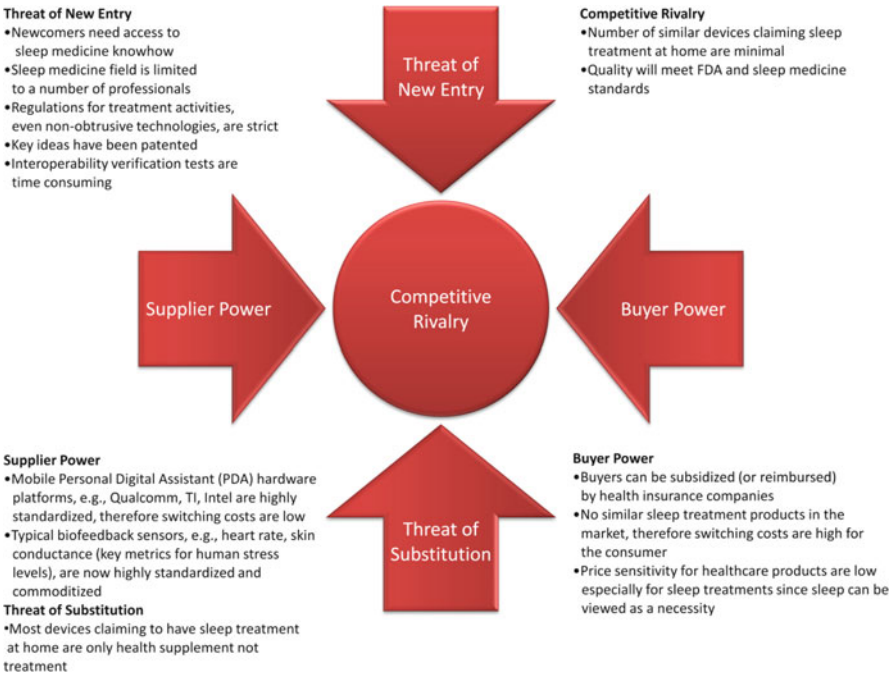

Fig. 15.15 Five forces analysis for sleep treatment device industry

	Best Product	Total Customer Solutions	System Lock-In
Operational Effectiveness	**Best Product Cost** • Minimize software developer overhead	**Best Customer Benefits** • SW components modulized for low cost re-use • Collaborate on PDA platform Intel CPU + MS Windows Mobile OS to improve costs	**Best System Performance** • Integrate complementors in improving system performance
Customer Targeting	**Target Distribution Channels** • Maximize coverage through sleep medicine conferences, medical device shows, etc	**Target Customer Bundles** • Add value to all customers by customization of treatment • Interactivity with physicians	**Target System Architecture** • Identify leading KOLs, professional and physician in sleep medicine field • Possible direct distribution through hospital channels
Innovation	**Product Innovation** • Develop family of products based on common platform – sleep coach and sleep doc	**Customer Service Innovation** • Customer care functions through SW module update and monitoring of customer needs • Increase customer lock-in through customization and learning of sleep medicine hygiene and treatments	**System Innovation** • Rapid evolution to embed newest CBT theory • Backward compatibility due to open platform

Fig. 15.16 Matrix analysis for delta model on example in (Liu 2009) [16]

15.5.5.1 Risk Factors

Here, we discuss the factors from two viewpoints that may threaten the viability of the business model for pervasive healthcare systems. The first one is threats where the firm in the future can itself address. The second are externalities, where the firm cannot address these issues directly by strategies or decision made internally.

15.5.5.2 Threats

- Interoperability of Technology–as briefly stated in Sect. 15.2, many standards exist for communication protocols and data format. Development of services and products in the pervasive healthcare based on a non-mainstream standard will lead to waste of time and money to a large scale
- Security Issues–Personal information, especially medical information have a higher risk of security breaches due to open communication between the hospital/physician to patient link
- Complexity of Revenue Sharing Model–Still uncertain is the revenue between patients, insurers, hospitals, channels, providers. This is especially true as pervasive healthcare is carried out at home and not in a professional facility

15.5.5.3 Externalities

- Ethical Issues–Health regulatory bodies are still uncertain on whether allowing home treatment or tele-treatment
- Overdependence on Automated Processes–The higher the percentage the medical personnel use automated or digitized processes, which pervasive healthcare technology relies on, the easier it will be for these people to be helpless or lost if these processes fail
- Big "cost' impacts–This is a risk for all healthcare related developments in a sense not only in terms of money but also life and death

15.6 Conclusions

We have defined a problem statement for an emerging pervasive healthcare industry and a strong motivation to analyze the problem. Then we introduced a hybrid analysis framework approach to the research statement where we addressed the competitive advantages and customer bonding strategies for a pervasive healthcare industry. We also provided an initial analysis to the major players in sleep industry and the value chain. As for future research, there are several directions that are worthwhile looking into. As mentioned in the previous sections, optimization of the revenue sharing model for pervasive healthcare systems is still yet to be understood.

We also need to define what it takes for a medical procedure (diagnosis/treatment) to be able to be transferred to a pervasive healthcare system. Finally, the current healthcare regulations do not address to complete aspect of a pervasive health system. To be able to overcome the ethical issues, regulations that ensure the safety of the procedure carried out in a remote place must be laid down.

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