Automated Sleep Stage Detection and Classification of Sleep Disorders

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy

by

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DECLARATION

I certify that except where due acknowledgement has been made, the work is that of the author alone; the work has not been submitted previously in whole or in part to qualify for any other academic award; the content of the thesis is the result of work that has been carried out since the official commencement date of the approved research program; any editorial work, paid or unpaid, carried out by a third party is acknowledged; and ethics procedures and guidelines have been followed.

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DEDICATION

I dedicate this dissertation to my parents, brothers and sisters who taught me inquisitiveness and persistence, and to my wife and children who have stood with me during this long and challenging endeavour.

ABSTRACT

Studies have demonstrated that more than 1 million Australians experience some sort of sleep-related disorder in their lifetime [12]. In order to improve the diagnostic and clinical treatment of sleep disorders, the first important step is to identify or automatically detect the sleep stages. The most common method, known as the visual sleep stage scoring, can be a tedious and time-consuming process. Because of that, there is a need to create or develop an improved automatic sleep stage detection method to assist the sleep physician to efficiently and accurately evaluate the sleep stages of patients or non-patients.

This research project consisted of two parts. The first part focused on the automatic sleep stages detection based on two individual bio-signals, which made up an overnight polysomnography (PSG), such as the electroencephalogram (EEG), and electrooculogram (EOG). Several features were extracted from these two bio-signals in the time and frequency domains. The decision tree and classification methods were utilised for the classification of the sleep stages.

The second part of this project focused on the automatic classification of different sleep and psychiatric disorders, such as patients with periodic limb movements of sleep (PLMs), sleep apnea-hypopnea syndrome (SAHS), primary insomnia, schizophrenia and healthy sleep. Different PSG parameters were computed for the classification of sleep disorders, such as descriptive statistics of sleep architecture. In conclusion, the advantage of an automatic sleep stage detection method based on a single-channel EEG or EOG signal can be undertaken with portable sleep stage recording instead of full the PSG system, which includes multichannel bio-signals. An automatic classification method of sleep and psychiatric disorders based on the descriptive statistics of sleep architecture statistics was found to be an effective technique for screening sleep and

psychiatric disorders. This classification method can assist physicians to quickly undertake a diagnostic procedure.

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Journal papers

1. E. Malaekah, S. Shahrbabaki and D. Cvetkovic, “Automatic sleep stage detection and classification Periodic Limb Movements of Sleep, Sleep Apnea Hypopnea Syndrome and healthy control based on of electrooculography (EOG) signals”, Journal of Bioprocessing and Biotechniques, 2015, 5:216.
2. E. Malaekah, and D. Cvetkovic, “Automatic sleep stage detection with high sensitivity on primary insomnia and schizophrenia disorders” Journal of Artificial Intelligence in Medicine (under review).

Conference papers

3. E. Malaekah and D. Cvetkovic, "Automatic detection of the wake and stage 1 sleep stages using the EEG sub-epoch approach", in Engineering in Medicine and Biology Society (EMBC), 35th Annual International Conference of the IEEE, 2013, japaj,pp. 6401-6404.

4. E. Malaekah and D. Cvetkovic, "Automatic sleep stage detection using consecutive and non-consecutive approach for elderly and young healthy subject", in Biosignals and Biorobotics Conference: Biosignals and Robotics for Better and Safer Living (BRC), 5th ISSNIP-IEEE, 2014, pp. 1-6.

5. E. Malaekah, C. Patti and D. Cvetkovic," Automatic Sleep-Wake Detection using Electrooculogram Signals", in Biomedical Engineering and Sciences (IECBES), 2014 IEEE EMBS Conference, 2014.

6. E. Malaekah, H. Abdullh and D. Cvetkovic,” Automatic Sleep stage Detection based on Electrooculogram” in Medical and Biological Engineering & Computing

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8. R. Chaparro-Vargas, E. Malaekah, C. Schilling, M. Schredl, and D. Cvetkovic, "Interdependence of electroencephalographic and electrocardiographic power bands in human sleep", in Biosignals and Biorobotics Conference (2014): Biosignals and Robotics for Better and Safer Living (BRC), 5th ISSNIP-IEEE, 2014, pp. 1-6.

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LIST OF ABBREVIATIONS

AASM	American Academic Sleep Medicine
AR	Autoregressive
ASDA	American Sleep Disorders Association
BP	Back propagation
C.K.	Cohen’s Kappa
CF	Central frequency
CIC	Cascaded integrator-Comb
DDTW	Derivative dynamic time warping
DREM	Density of rapid eye movement
DSMMD	Diagnostic and Statistical Manual of Mental Disorders
EDF	European data format
EDS	Excessive daytime sleepiness
EMD	Empirical mode decomposition
FFT	Fast fourier transform
FRP	First REM period
HHT	Hilbert-Huang transform
HMM	Hidden Markov models

ICD	International Classification of Diseases
ICSD	International Classification of Sleep Disorders
IRA	Inter-rate agreement
KC	K complexes
KNN	K-nearest neighbour
LMS	Least mean square
LOC	Left outer canthus
MAR	Multichannel autoregressive
MPAV	Minimum peak amplitude value
MSLT	Multiple sleep latency test
MT	Movement time
MTM	Multi-taper method
NREM	Non-rapid eye movement
OSA	Obstructive sleep apnoea
OSAHS	Obstructive sleep apnea-hypopnea syndrome
PLM	Periodic limb movements
PLMS	Periodic leg movement syndrome
PMT	Power multi-taper

PR	Power rations
PSD	Power spectral density
PSDR	Power spectral density ratios
PSQI	Pittsburgh Sleep Quality Index
R&K	Rechtschaffen and Kales
RBD	REM sleep behavior disorder
RBSE	Relative band spectral energy
REM	Rapid eye movement
RMSF	Root mean square frequency
ROC	Right outer canthus
RSE	Relative spectral energy
RSEB	Relative spectral energy band
SAHS	Sleep apnea-hypopnea syndrome
SE	Spectral entropy
SEF	Spectral edge frequency
SEM	Slow eye movement
SFS	Sequential feature selection
SHAS	Sleep hypopnea -apnea syndrome

SL	Sleep latency
SREM	Sleep rapid eye movement
SS	Sleep spindles
SWA	Slow wave activity
SWS	Slow wave sleep
SWSD	Slow wave sleep duration
TST	Total sleep time
WASO	Wake time after sleep onset

1 : Introduction

1.1 Introduction

Scientists have indicated that sleep covers approximately one third of a human being`s life. Sleep refers to a period of consolidation of memory and brain recovery. In almost 1000 years ago, scientists wrote about sleepiness and sleep, indicating that the regulation of sleep is associated with heat resulted by human body [1]. Since this period, many scholars have offered different opinions in relation to sleep [2]. It has been pointed out in several studies that sleep is critical for energy preservation, for the restoration of biosynthesis (a simple structure converted to a complex structure in living organisms), facilitating learning and memory. When an individual is sleeping, the mind is strengthened, and motor functioning and performance are improved [3, 4]. It has been suggested that sleep is linked to metabolic function and obesity [5]. Furthermore, short and fragmented sleep has been associated with an increase in susceptibility to the common cold [6]. Sleep can impacts negatively on aspects of cognition, like vigilant attention, and public health [7, 8]. Sleep restriction or disorders can lead to sleepiness and may result in the involuntary onset of sleep, (falling asleep) causing car/truck accidents [9, 10, 11]. Changed wake/sleep patterns can impact negatively on the performance on neuropsychological tests and also in shift work [9].

Over a third of a century ago, Rechtschaffen and Kales (R&K) introduced a sleep manual with rules to detect different stages of sleep, using overnight polysomnography (PSG) [12]. Around a decade ago the American Academy of Sleep Medicine (AASM) revised and expanded the rules to encompass not only the sleep stages but also other abnormalities, including respiratory and cardiac events [13]. Sleep has been monitored through PSG with electrooculogram (EOG), electromyography (EMG) and

electroencephalogram (EEG) electrodes and different sensors. Sleep stages are scored or classified using central EEG, left and right EOG, and chin EMG [12]. The manual scoring of sleep is a subjective and time-consuming process; hence, there is a demand for comprehensive and better automatic techniques that can be applied more easily, and can be used in experimental and clinical, ambulatory research.

Feature extraction is an important tool in the development of scoring algorithms for the detection of sleep stages. Most previous scoring algorithms depended on computationally undemanding, time-domain analyses, such as period amplitude [14] or the interval histogram method [15]. Most of these algorithms use 20- or 30-second epochs for EEG signal sleep stage classification either according to the R&K or AASM rules [16, 17]. However, there is some debate within the sleep research community in connection with the R&K or AASM sleep stage rules [18]. These rules might be accurate only for healthy young subjects and use a tentative resolution based on 20- or 30-second epochs to identify the different sleep stages. Therefore, in this thesis the candidate has attempted to develop an algorithm for automatic sleep stage detection based on consecutive and non-consecutive, 6-second sub-epoch EEG. On the other hand, the scalp EEG electrodes placement may cause sleep disturbance due to using many electrodes during the recording. Therefore, in this thesis the candidate has attempted to utilise a single EEG electrode for automatic sleep stage detection.

This thesis attempts to address the following sets of research questions. The first set focuses on sleep stage detection as follows:

1. Which of the PSG signals are the most efficient in the detection of the different sleep stages?

2. Can the EOG signal be used to automatically detect the sleep stages as an alternative to the EEG signal?

3. What feature extraction parameters from the PSG signals are most suitable to distinguish and characterise various sleep stages?

The second set of research questions focus on the sleep disorder classification as follows:

1. Are there significant differences in the PSG signals characterising healthy subjects and patients with various sleep disorders?

2. Can these differences be utilised to develop a screening method that can effectively classify various sleep disorders?

1.2 Motivation

In Australia, the prevalence of sleep disorders has been studied over different age groups in the general population [19]. In 2010, approximately 1.5 million people (8.9% of the population in Australia) were diagnosed with a sleeping disorder that included 199,000 people with restless limb syndrome (RLS) (1.2%), 492,000 with primary insomnia (3%) and 775,000 in the obstructive sleep apnoea (OSA) (4.7%) [12]. The direct annual cost, including health care and medication is estimated to be $10 billion. The indirect costs (i.e. increased traffic accidents and work, reduced productivity and other medical illness vulnerability) can reach $100 billion [19].

Various theories have been proposed to explain the physiological function of sleep [3]. However, no universally accepted theory exists. Therefore, for individuals to comprehend their sleep function, disorders and physiology, extensive sleep-monitoring studies should be undertaken on different subjects for an extended duration. This

necessitates objective evaluation methods for the sleep process. The recording of sleep stages is vital to the clinical treatment and analysis of sleep disorders. The information obtained from the sleep stages is significant because it can be utilised in estimating respiratory disturbances in various stages of sleep.

1.3 Research aims

The research aims can best be presented in the following manner:

1. Develop an automatic sleep stages detection method:
    a. By utilising only EEG signal for the detection of all sleep stages based on the:
        i. consecutive or non-consecutive EEG sub-epoch approach;
        ii. evaluation of the most suitable spectral estimation methods (nonparametric or parametric);
        iii. evaluation of the most effective consecutive or/and non-consecutive EEG sub-epoch approach with different sleep disorders and ages;
    b. By utilising only the EOG signal for the detection of all sleep stages based on the:
        i. most suitable EEG and/or EOG feature extractions related to the sleep stages.
2. Develop an automatic classification of sleep disorders:
    a. By utilising sleep architecture parameters and rules based on PSG sleep stage parameters;

b. Investigating the significant difference in architecture parameters between healthy and non-healthy sleep.

1.4 Objectives

The general objective of this research is two-fold: firstly, to develop an automatic sleep stage detection method based on the EEG and/or EOG signals; secondly, to utilise the PSG features of sleep stages to develop an automatic sleep disorders classification system. The advantage of an automatic sleep stage detection method based on EEG or EOG signals can be utilised with portable sleep stage recording instead of using multichannel PSG signal. Classification of sleep disorders based on an automatic system can be improved with screening or diagnostic procedures which can be a faster and easier method.

1.5 Thesis composition

This thesis is organised in the following manner:

Chapter 1 presented an introduction to the research. This preamble included the motivation, research approach, and objectives.

Chapter 2 gives an introduction to sleep and its basic concepts. Polysomnography and sleep variables are defined as the tools for the detection of the sleep stages. This chapter describes the difference between the R&K and AASM rules. An overview of automatic sleep stage detection and a description of its components is also presented.

Chapter 3 describes the data and methodology used for the development and validation of the algorithm.

Chapter 4 describes the methods of automatic sleep stage detection.

Chapter 5 describes the classification method for the sleep disorders.

Chapter 6 presents in detail the results of the validation of the algorithms.

Chapter 7 discusses the significance and limitations of the algorithms.

Chapter 8 presents a summary of the research contributions and also provides future works.

2 : Literature Review

2.1 Basis of Sleep

The sleep phenomenon has gained reasonable scientific interest for an extended time. Sleep refers to a behavioral state that varies from wakefulness by a loss of reactivity readily and reversible in relation to events within one`s environment [20]. The reversibility of sleep differentiates it from other types of states of consciousness, such as altered states of consciousness like the state of anesthesia or coma characterised by unresponsiveness and others. Different theories offer insight about the reasons that people sleep. According to the passive theory, sleep occurs because of a lack of sensory stimulation or to prevent tiredness [3, 21]. For many years sleep was considered as a passive state of the brain and the opposite of wakefulness [22]. It was assumed that the excitatory regions of the brainstem and other areas of the brain get exhausted and turn inactive. Hence, sleep was brought about by this inactiveness. The active theories also indicate that the brain aggressively deters consciousness [22].

Prior to the neurophysiologic analysis of sleep, the depth of sleep was assessed behaviourally [23]. Applying data from 211 nights, Michelson attested earlier documentation that sleep depth (estimated as arousal threshold) reached its maximum within approximately one hour after an individual fell asleep. In the course of the night, several sleep depths were indicated as many as four maxima and minima before the lowest depth of sleep during the morning [23]. Deep sleep was later interrelated to 0.5-3Hz low brain waves [24]. The effects of sleep deprivation were measured on several consequences, counting heart rate, memory, and urine examination [25]. Loomis et al. [26] undertook the first organized and systematic neurophysiologic recordings of sleep.

2.1.1 Non-Rapid Eye Moment Sleep

NREM is the classifications of deep sleep N3 (S3, S4) and light sleep N1, N2 (S1, S2). Deep sleep is also known as slow wave sleep (SWS). Sleep stage N2 (S2) is featured by K complexes (KC) and sleep spindles (SS). The abbreviations, MT (movement time), W, S1, S2, S3, S4 and SREM (sleep rapid eye movement), are obtained from the old standard of R&K (1968) [12] and R, W, N1, N2, N3 are derived from the standard of the AASM [13] (the difference between these two standards will explained in section 2.3).

An intensification of NREM sleep, especially during SWS, has been linked to recovery from a deficiency of sleep [27]. In NREM sleep, depolarization of cortical neurons occurs and fire tonically (the same as quiet wakefulness). However, the depolarization upstates are interrupted by short, hyperpolarized downs-states while the neurons stay silent [28].

The SWS part of NREM sleep is fundamental of the markers of the regulation of sleep [27]. Studies demonstrated that extended wakefulness led to an increase in the quantity of SWS in the subsequent recovery of sleep [29]. An EEG delta (0.5-4 Hz) power is applied instead of the visually scored SWS. This can be known as slow wave activity (SWA). Alteration in SWA and SWS have been found in various experimental paradigms [30]. After a total sleep deficiency, recovery sleep indicates an increase in the quantity of SWS [31].

2.1.2 Rapid Eye Movement Sleep

Approximately 140 years ago, Griesinger`s studies suggested a link between somatic muscle and twitching of the eyelids during sleep [32]. In 1877, Dewar recorded eye movements using an electrical method and it was found that the electrical potential

occurred due to involuntary activities of the eyeball [33]. The early assessments presumed that the recorded potential included action-potential (the electrical membrane potential of a muscle rapidly increases and decreases) emerging from the ocular muscle [34]. Later, it was established that the recorded activity was due to the corneo-retinal potential (which is the remaining potential among the cornea and retina) [35]. However, it took long studies (until 1953) when Aserinsky and Kleitman discovered the rapid eye movement (REM) in the course of sleep [36].

A growing interest emerged in regards to assessing eye movement during sleep after Kleitman and Aserinsky`s work. The density of REM (DREM) and REM sleep was linked to sleep, essentially after 1969 [36]. According to Aserinsky, DREM occurs almost after seven to ten hours of sleep [36]. The density of eye movement reduces during recovery sleep after the occurrence of sleep deprivation [37]. Lucidi and colleagues found that a reduction in the density of REM parallels an upsurge in SWS [38]. De Gannaro and colleagues also reported on the similar results [39].

The density of eye movement is increasing in REM sleep periods followed by periods of awakening then followed by NREM sleep [40]. The density of eye movement has been recorded to be highest in 5-10 minutes after the beginning of the REM sleep period followed by a significant reduction after 10 minutes [41]. The density of eye movement has approximately a 10-minute periodicity [42].

2.2 Sleep disorders and psychiatric disorder

Sleep disorder refers to a medical condition, also known as somnipathy [43]. Contemporary studies have argued that severe sleep disorders can interfere with the normal mental, social, emotional and physical functioning of an individual [44]. Actigraphy (a non-invasive technique for monitoring human activity period) and

polysomnography (PSG) (more information in section 2.4) are some of the common tests that have been used in the diagnosis of sleep disorders.

Lack of quality sleep has been associated with adverse impacts on emotional balance, energy, and health. People with good health usually tend to have quality sleep while those suffering from repeated disorders of sleeping might have an underlying severe or minor mental or medical problem. Evidence indicates that even minimal sleep loss puts a toll on people`s moods, wellbeing and their ability to cope with stress [44].

2.2.1 Primary insomnia

Subcategory insomnia complaints commonly include difficulty in initiating (sleep onset insomnia) or/and maintaining sleep. They include extended periods of sleep onset insomnia or/and maintaining insomnia amounts of nighttime sleep [45]. The diagnostic and symptom category of insomnia are best denoted by their subcategory. These subcategories are described by different combinations of repeated sleep problems with sleep duration, initiation, quality and impairment during the daytime [43]. Insomnia complaints can be associated with the perception of non-restorative or poor quality sleep even if the quantity and quality of sleep episodes are perceived as adequate or regular. The meaning of insomnia being a complaint of sleep maintenance, sleep initiation, non-restorative sleep or associated with daytime impairment [46].

Primary insomnia can comprise both extrinsic (the body effected by outside factors) and intrinsic (the body effected by inside factors) factors involved in their etiology. They are not regarded as being secondary to another disorder [43]. The National Institutes of Health Consensus Development Conference for Insomnia in 2004 led to a promotion of comorbid insomnia term to differentiate primary insomnia from forms due to other sleep disorders, psychiatric and medical disorders and insomnia due to drug or medication use [43, 47]. The term, primary insomnia, is applied in the Diagnostic

and Statistical Manual of Mental Disorder (DSMMD) and is listed in the International Classification of Disease (ICD) [48, 49, 50]. Hence, it has a significant advantages for use as a global categorization of insomnia.

The ICSD defines primary insomnia as a syndrome consisting of paradoxical insomnia, psychophysiological insomnia, and idiopathic insomnia [51]. Primary insomnia is regarded as a difficulty in maintaining sleep (early morning awakening or mid-sleep awakening), a difficulty in initiating sleep (sleep onset insomnia) or even non-restorative sleep which is chronic and persists for more than three weeks, notwithstanding that one has adequate opportunity for rest/sleep and it impairs daytime performance [52,53].

Many abnormalities (see Table 1) have been reported with primary insomnia patients [54]. These can be measured using PSG, with a particular focus on the REM stage and N1 stage. It has been reported that patients with primary insomnia most often suffer from difficulty falling asleep as well as intermittent wakefulness during sleep [53]. Moreover, the PSG characteristics in primary insomnia patients show an increase in N1 and a decrease in sleep efficiency (SE) [53]. Table 1 describes the PSG features of primary insomnia disorders.

Table 1: Polysomnographic features for primary insomnia disorders

PSG features of primary insomnia	Increase in N1 sleep stage
	Increase in Sleep latency (SL)
	Increase in REM sleep
	Decrease in total sleep time (TST)
	Increase in N1 sleep stage
	Decrease in sleep efficiency (SE)

2.2.2 Periodic limb movement syndrome

The periodic limb movement syndrome (PLMs) is when a person is unaware of the limb movements caused by muscle contractions during sleep [1, 55]. The episodic limb movement condition occurs during sleep as an independent disorder of highly stereotyped and repetitive limb movements [56]. It is often associated with the syndrome of restless legs [56, 57]. Abnormal considerations include more than five involuntarily movements per hour in sleep whereby each limb movement lasts between 0.5 to 5 seconds [55, 58].

Periodic leg movement disorder is associated with a dopamine (in the brain it is a function as neurotransmitter) responsive disorder, and can be improved through dopaminergic agonistic management [50]. It has been reported that PLMs occur at night during the interval before a person enters REM sleep [50]. According to ICSD that PLMS occur in N1 of the sleep period before reaching REM sleep [50]. Moreover, during the REM period of sleep, an individual`s voluntary muscles are paralysed, keeping them from acting out their dreams. The characteristics of PSG of PLMs are summaried in Table 2.

Table 2: Polysomnographic features of PLMs syndrome

PSG features of PLMS	Increase in N1 sleep stage
	Decrease in N2 and N3 sleep stage
	Absent during REM sleep

2.2.3 Obstructive sleep apnea-hypopnea syndrome

Obstructive sleep apnea-hypopnea syndrome (OSAHS) has increased in the last 50 years, causing significant mortality and morbidity in both the developing and developed countries [59]. It causes daytime sleepiness [60]. Hypopnea and apnea are reasoned by

the airway being blacked during inspiration at sleeping periods. This condition occurs when the upper airway dilating muscles (striated muscles) normally relax when sleeping [59]. Patients with OSAHS have no ability for their dilating muscles to oppose the negative pressure in the airway in the course of inspiration [59].

Moreover, most patients have narrow upper airways. The upper airway patency is kept by dilating muscles and it has a higher activity during awake patients. However, in the course of sleep, the muscle tone decreases, narrowing the airway [61, 62, 63]. This may cause snoring with a subsequent airway obstruction and the apnea is episodes. The features of this case are hypercapnia, hypoxemia, changes in the large intra-thoracic pressure (120 mm Hg) and increases in systemic pressure of blood up to 250/150 mm Hg, which is linked to sleep fragmentation and sleep arousal of up to 100 times per hour [59, 61, 62, 63, 64].

The consequences OSAHS include social and neurobehavioral differences, such as: impaired vigilance, excessive daytime sleepiness, cognitive dysfunction, and mood disturbances. Sleepiness can lead to the inability to work efficiently, prevents socialising and can ruin interpersonal relationships [61]. Current studies have demonstrate that sleep-related disorders such as obstructive sleep apnoea may increase the risk of stroke or death [65]. The clinical examination is limited and not sufficiently sensitive; therefore, the PSG features are very important and required for screening the Obstructive sleep apnea (OSA) patients. For example, it has been reported that the characteristic of PSG with OSA patients during sleep is shown increase in sleep N1 and N2 stage, as shown in Table 3 [1].

Table 3: Polysomnographic features of Obstructive sleep apnea

PSG features of OSA	Increase in N1 and N2 sleep stage
	Decrease in N3 sleep stage
	Decrease in REM sleep stage
	Increase of frequency of arousals

2.2.4 Schizophrenia

Schizophrenia is a sleep mental disorder, with this ratio of one in one hundred people that are diagnosed [66]. This disorder affects human on psychiatric perceptions, emotions behavior and thoughts [66]. Sleep problems in individuals with schizophrenia are a familiar occurrence [66]. Although there is no evidence that sleep disorders lead to psychiatric disorders, there is a link between sleep and psychiatric disorders, like depression and schizophrenia, with studies indicating that psychiatric disorders are the leading cause of sleep disorders [67]. Disturbed sleeping patterns are often found in 30-80% of patients with schizophrenia, and it mainly depends on the extent of the psychotic symptomatology [68, 69]. According PSG analyses, total sleep time and sleep efficiency typically decrease, while increased latency of sleep are found for patients with schizophrenia, as shown in Table 4. Studies have reported alterations in N2 sleep stage, REM and SWS, with decreasing REM and REM latency [68, 70]. Some evidence has indicated that patients with schizophrenia have a higher risk of experiencing sleep-linked breathing disorders, more especially the groups who are overweight and have a long-term use of antipsychotics [68]. It is unclear whether restless legs syndrome or periodic leg movement during sleep are found in lower or higher occurrence in schizophrenic individuals [68]. There is no consistent impact of the first-generation antipsychotic medication on sleep continuity, as well as a measure of sleep structure, including REM latency and sleep stages [71, 72].

Table 4: Polysomnographic features of schizophrenia disorders

PSG features of schizophrenia	Increase in SL
	Decrease in SE
	Increase in wake time after sleep onset (WASO)
	Decrease in N3 sleep stage
	Decrease in REM sleep

2.2.5 Classification of sleep disorders

The classification of sleep disorders is essential to differentiate between disorders and enhance the understanding of etiology (that is used to study the cause of sleep disorder phenomena), pathophysiology and symptoms that can enable appropriate treatment [42, 73]. The earliest systems of classification primarily distinguished between sleep disorders depending on the main symptoms and abnormal events occurring in sleep, excessive sleep and insomnia. Hence, the earliest systems of classification were not based on the pathophysiology of sleep since the causes of most disorders were unknown [42, 74]. The first noteworthy classification of sleep disorders was published as the 'Diagnostic Classification of Sleep and Arousal Disorders' [75]. In 1993, a significant effort was made to publish the International Classification of Sleep Disorders (ICSD) as a collaboration between different international sleep societies, such as the American Sleep Disorders Association (ASDA), the European Sleep Research Society, the Japanese Society of Sleep Research and the Latin American Sleep Society [76]. The ICSD has been extensively utilised by clinicians and is essential for diagnostic, epidemiologic (which deals with the study of the patterns, causes and the effective control of disease in the population) and research purposes.

The ICSD version 2 (ICSD-2) was disseminated in 2005, and is currently undergoing further amendments [50]. It integrates symptomatic presentation, such as insomnia with one structured in part of the pathophysiology (i.e circadian rhythms [changes in mental, physical and behaviour during a 24-hour period]) and body systems (i.e breathing disorders). This systematic structuring of sleep disorders is crucial since the pathophysiology of various disorders is still not well-known. The ICSD-2 offers relevant epidemiological and diagnostic knowledge on sleep disorders for easier differentiation from the other emerging disorders [50]. According to the ICSD, there are more than 80 types of sleep-related disorders; among the most common are sleep apnoea, snoring, insomnia, circadian rhythm and parasomnias [77].

2.3 Visual sleep stage scoring

The quantitative visual sleep stage scoring includes sleep stage or event epoch marking, analysis and counting [13, 78]. Events include eye movements, K complexes and sleep spindles. A standard approach to visual analysis includes the segmentation of sleep into 20 or 30 second epochs of movement time (MT), wakefulness (W), sleep stages S1, S2, S3 and S4 from EOG, EMG and EEG .With visual scoring, this data is required to offer consistent, practical and quantitative sleep structure or architecture information [79]. Determining the sleep stages is crucial in the clinical treatment and the diagnosis of sleep disorders [80].

Alongside sleep staging, polysomnography comprises simultaneous reports of various other sleep signals, such as cardiac activity (ECG), blood oxygenation (oxygen saturation - SpO2), and respiration (thermistor, thermocouple). These signals serve as vital measures in the clinical assessment for sleep disorders, as depicted in the ICSD manual [76]. As indicated by Schulz [81], visual sleep staging has undergone an

evolution that led to a standardisation of the rules by Loomis in the 1930s [26], Aserinsky and Kleitman in 1950s [35] and by Rechtschaffen and Kales in 1960s [12].

2.3.1 The Rechtscaffen and Kales scoring rules

Recognising the importance of the ever-increasing need for standardising sleep scoring, a committee was formed comprising the members of the sleep research society in order to create a standardised scoring manual [82]. Rechtschaffen and Kales (R&K) formed standard criteria that segmented sleep into the sleep stages of REM S1, S2, S3, and S4, wakefulness and movement time (MT) based on characteristics of the EMG, EOG and EEG [12, 83]. The SWS is visually defined as waves of lower frequency (below 2Hz), having an amplitude greater than 75 μV (peak to peak). An epoch is described as stage S3 when at least 20% of the epoch (20 seconds) includes SWS and is scored as S4 when more than 50% of the epoch (20 seconds) includes SWS. Stages S4 and S3 are known as SWS and the amplitude is measured from the C3-M2 or C4-M1 channels. M2 and M1 are mastoids, and are used as reference points to measure EEG potentials. Any epoch that does not satisfy S4 or S3 criteria belongs to another sleep stage [84].

The S1 stage of sleep is described as relatively low voltage and mixed-frequency EEG with an activity prominence within the range of 2 to 7Hz. The vertex sharp waves from EEG are rarely as high as 200 μV appear in S1. Also, the S1 stage can be described by slow eye movements. When alpha activity is less than 50% of the epoch and with relatively mixed-frequency, and low-voltage is at least 50% of the epoch, the epoch is classified as stage S1. Sleep spindles or K complexes denote stage S2. Also, S2 is classified when a time interval is less than 3 minutes between sleep spindles and/or K complexes without a sign of pronounced increase or movement arousal of the muscle tone. The REM is relatively low-voltage, mixed-frequency EEG in connection with low

amplitude EMG and episodic REM [12, 84]. Moreover, detailed rules exist for the offset and onset of REM. Fundamentally, REM duration is continuously scored as an REM stage until muscle tones are amplified or spindles appear.

2.3.2 The American Academy of Sleep Medicine scoring rules

The American Academy of Sleep Medicine (AASM) scoring rules represent the development and evolution of the 2007 manual with an objective of consolidating, standardising and restructuring the original (R&K) sleep staging standard rules [13,85]. A major revision to the earlier scoring included changes to EEG electrodes placement of the frontal position to the typically used occipital and central position [13, 81]. Another change included the reclassification of sleep stages to stages N1 to N3 (non-REM),W and R for REM stages [80]. The alteration of abbreviations was to prevent confusion between the two standards of classification whereby the stage S3 and S4 (in R&K rules) were joined to form stage N3, since no clinical or physiologic basis had been discovered for a difference between stages S4 and S3 [51, 86].

Other notable changes included an alteration to the PSG data analysis, which has potential clinical effects [13]. For instance, large variance in the indexes of adult apnea-hypopnea when using the recommended AASM rules versus the earlier rules ("if there was > 50% airflow reduction alone or a lesser airflow reduction associated with ≥ 3% desaturation or ≥ 3-sec EEG arousal"), a decrease in sleep N2 with an increase in sleep N1, and transitions of sleep due to a rule prevailing transition from sleep N2 to N1, increased sleep N3 in adults with the addition of the EEG frontal electrode, enhanced slow wave detection and enhanced reliability of inter-scorer [87].

2.4 Polysomnography and Hypnogram

Polysomnography (PSG) assesses comprehensive sleep using numerous electro-physiological signals. It is the gold standard for measuring sleep stages [88]. Also it identifies stage-dependent pathologies and determines severity and cause [89]. The PSG studies are utilised by clinicians to analyse sleep quality in individuals who have sleep disorders or in research studies for both patients and normal subjects [90]. The PSG can be recorded in a laboratory or at home. It can also investigate the effectiveness of therapeutic regimens. In 1997, the AASM issued practice parameters or signals for PSG and related processes, including cardiorespiratory and oximetry studies that were later updated in 2005 [91].

In the course of PSG studies, numerous electrodes were placed on the individual to measure activities of the eye, brain, heart, and muscles movement [92]. These signals were interpreted by sleep technologists to create an extensive sleep report of the individual`s night sleep. Table 5 shows some of the recommended parameters or signals to be reported for PSG, such as sleep scoring data, and arousal, respiration, cardiac and movement events according to the AASM standards [13].

Table 5: The recommend parameters to be reported for PSG during sleep [13].

Parameter	**Sleep scoring data**	**Arousal events**	**Respiratory events**	**Cardiac events**	**Movement events**
EEG and EOG derivation	Light out clock time (hr: min)	Number of arousal	Number of obstructive apneas	Average heart rate during sleep	Number of PLMS
Chin EMG	Total Sleep Time (TST; in min)	Arousal index	Number of mixed apneas	Highest heart rate during sleep	Number of with arousals
Leg EMG derivation	Total recording time (light out to light in min)		Number of central apneas	Highest heart rate during recording	PLMS index
Oxygen Saturation	Percentage of SE		Number of hypopneas		PLMS arousal index
Airflow parameters	Time in each stage (min)		Hypopnea index		
Body Position	Percentage of TST in each stage		Respiratory effort linked to arousal		

The AASM has developed different recommendations for PSG for various sleep disorders [91]. The PSG with extended video and EEG are recommended for violent sleep behaviors, sleep walking, REM sleep behavior disorders (RBD: patients physically act out their dreams), and forensic cases [91]. For cases of parasomnia (undesirable behavioural or experiential events associated with sleep), PSG is unusual. In cases of narcolepsy (condition characterised by extreme tendency to daytime drowsiness), PSG is combined with the multiple sleep latency test (MSLT, a diagnostic tool for sleep disorder) that should be performed the following day. In nocturnal seizures, PSG with extended tibialis EMG, video and EEG are recommended [91].

PSG requires considerable capital investment in health-care, dedicated, well-trained technical staff and accurate bed space. The interpretation of the generated PSG data is a time-consuming process overall, with the cost of undertaking signals overnight PSG assessment or recording estimated to range between $1,000 and $2,000 [93].

A hypnogram is sleep architecture that represents a form of polysomnography or a graph that depicts the stages of sleep in relation to time. A hypnogram allows for the identification of different stages of sleep, including NREM and REM. Typically, a hypnogram derived from night-long sleep recordings can graphically summarise the stages of sleep a person experiences. The hypnogram usually indicates the descent from W to stage N1 (lasting between 1 and 7 min), N2 (the duration between 10 and 25 min), N3 (can lasting up to 40 min) and REM (can lasting up to 90 min) [12, 94]. The duration of the cycle of sleep stage NREM-REM is expected to be between 90 and 120 minutes, and might be repeated between 4 to 6 times per night. Figure 1 shows a hypnogram sample with the sleep stage and its time duration.

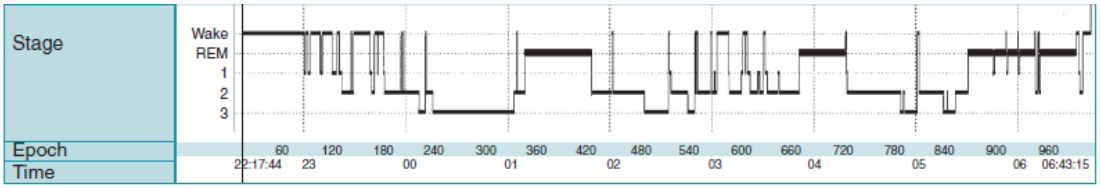

Figure 1: Hypnogram sample, where the y-axis indicates the sleep stages and the x-axis indicates time (epoch) [95].

2.4.1 Electroencephalography (EEG)

EEG measures and spontaneously records the electrical activity of the brain from the scalp [96]. It evaluates voltage potentials resulting from the ionic flows of current within the brain neurons. EEG includes multiple electrodes placed on the scalp [96].

The brain waves generated by the EEG system comprise various frequency bands, such as delta, alpha, theta and beta wave bands [97, 98], as shown in Figure 2. Delta waves range from 0.5 to 4 Hz frequency with 20 to 400 μV amplitude, and occur during low brain activity, such as medium anaesthetic state and deep sleep [99]. Alpha waves range from 8 to 13 Hz frequency with a 2 to 10 μV amplitude range. They are usually recorded when a person is awake with closed eyes and in a mental and physical state of rest. Beta waves are recorded at higher frequencies, ranging from 13 to 30Hz. Their amplitudes range from 1-5 μV [100]. Beta waves are observed at concentrated attentions during the mental working state and also during the REM stage of sleep.

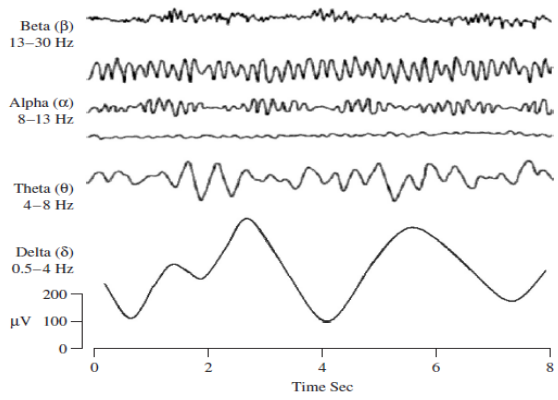

Figure 2: EEG frequency bands, where the y-axis indicates EEG frequency bands and the x-axis indicates time per second (sec) of the brain [101].

EEG signals can differentiate the stages of sleep. There are five phases observed in one's NREM sleep. The Phase 0 wakefulness stage is characterised by low amplitude EEG levels and has two frequency bands – an alpha band of 8–13 Hz and a beta band of 13–30 Hz. Alpha waves are hallmarks of this stage. The Phase 1 stage, associated with drowsiness, is distinguished by higher EEG amplitude levels than the wakefulness stage, and theta bands of 4–7 Hz are more dominant. Two important events, known as the sleep spindle and the k-complex, occur during the Phase 2. The sleep spindle event has a frequency range of 12–16 Hz and can also be present in the Phase 3. Slow wave sleep (SWS), one of the hallmarks of Phases 3 and 4, has a lower frequency range of 0.5–2 Hz but also exhibits higher amplitude EEG levels than the other stages [98]. Table 6 shows the NREM sleep phases and their features.

Table 6: NREM sleep phases and their characteristics [95].

NREM Sleep Phases	Characteristics
Phase 0 (wakefulness)	Low-amplitude EEG, alpha rhythm (8–13 Hz) prominent over occipital regions.
Phase 1	Low-amplitude mixed-frequency and low-amplitude EEG pattern, with theta (4- 7 Hz) rhythm.
Phase 2	EEG with one or more non-arousal KCs or one or more trains of SSs.
Phase 3 and 4	Low-frequency deep sleep EEG activity.

REM sleep refers to the dream state and dreams experienced in this stage can be remembered while in the wakefulness state [101, 102]. This REM stage is usually interspersed between the other stages of sleep, and is linked with low-amplitude EEG, deprived of KCs or SSs, REMs and low chin EMG tone activity [96]

2.4.1.1 10-20 EEG electrode placement system

10-20 system of EEG electrode placement refers to the technique used to depict the location of the scalp electrodes [103, 104,105]. Scalp electrodes are applied in recording EEG through a machine known as an electroencephalograph. The EEG brain activities are generated from activities of thousands of neurons within the brain. The variation of patterns demonstrates the changes of an individual's state. For instance, a relaxed state shows slow EEG waves (8 to 13 Hz) and a state of arousal shows faster waves (13 to 30 Hz) [105].

The 10-20 system is usually applied to describe the scalp electrode positioning of EEG recording [105, 106]. The objective of a 10-20 system is to standardise electrode positions or locations, with the numbers, 10 and 20 describing the distances between adjacent electrodes which are set at 10% or 20% of the right-left or front-back of the skull distance [105].

The 10-20 system is based on the connection between the location of a given conductor and the fundamental area of the cerebral cortex [107]. Each brain area has a letter for the lobe and hemisphere location. The letter O, P, C, T and F stand for the occipital, parietal, central, temporal and frontal respectively [108]. For example, the letter, C, represents the central lobe, z (zero), which is the electrode placed on the midline, and the even numbers (2, 4, 6 and 8) denote electrode positions within the right hemisphere

whilst the odd numbers (1, 3, 5 and 7) denote the left hemisphere [105, 107]. Figure 3 shows the electrode positions of the 10-20 system.

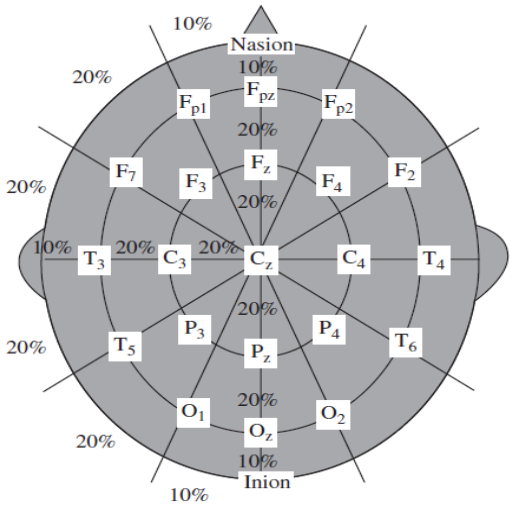

Figure 3: The EEG electrode positions of the 10-20 system [101].

2.4.2 Electrooculogram

Electrooculography (EOG) is a method that records the cornea-retinal standing potential existing between the front and back of the human eye [108]. The resultant signal is known as the electrooculogram. In measuring the eye movement, electrode pairs are located either below and above or to the right and left of the eye [108]. An EOG signal response of positive or negative defection can be recorded if the movement of the eye is made from the central position towards one of the electrodes. Therefore, a potential difference would occur when the eye moves between the placed electrodes. The eye has a standing electrical potential known as the corneo-fundal [109]. This potential is decreased during darkness.

The earlier studies had a different EOG positioning of the electrodes. Loomis and colleagues [110] used only the referential electrode placed above the left eye whilst

Aserinsky and Kleitman recorded two bipolar channels on a single eye [35]. Later, Hord incorporated four electrodes into one bipolar channel in order to increase the common mode rejection ratio of an EEG system (amplifier) [111] but this positioning had shortcomings in the analysis of automatic sleep [112,113].

In the standard manual of the AASM, the EOG electrode positioning is recommended as approximately 1 cm above and faintly lateral to the outer canthus of one eye (E1 and E2, as shows in Figure 4) and a reference electrode on either the mastoid or homo-lateral ear lobe. Figure 4 shows three different electrode positions.

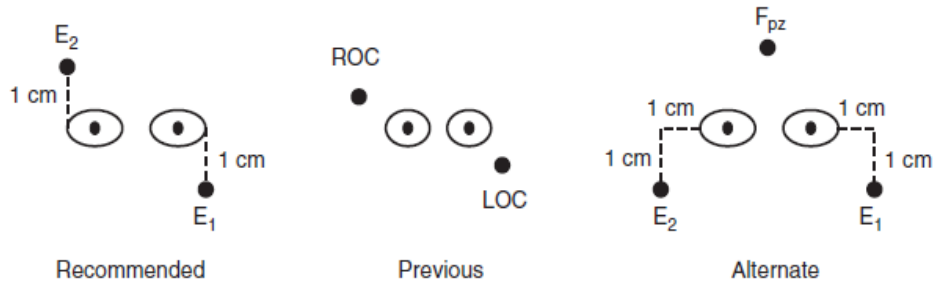

Figure 4: Recommended, previous and alternate electrode locations of the EOG signal. LOC = left outer canthus; ROC = right outer canthus [95].

2.4.2.1 Slow and Rapid Eye Movements

By 1929, Miles had recorded the importance of the movements of the eye in the changeover from wakefulness to sleep [114, 115]. The difference between drowsiness and alertness was evident in analysing the behavior of the eyes. It is documented that the horizontal eye movements observed at sleep onset were similar to the pursuit movements when an eye is closely watching an object such as a slow swaying swing [115]. According to the manual sleep scoring rules of R&K, the slow eye movements (SEM) do not determine the onset of sleep but are linked to sleep onset, especially S1

which follows wakefulness, is featured by the SEM each taking several seconds, prominent at the early portions of the S1. Within the new scoring (AASM), the SEMs are used to define sleep onset for individuals who do not produce alpha rhythm [13]. They are described as "conjugate with a reasonably regular and sinusoidal eye movements with the initial deflection usually lasting >500 ms" [13]. Other scholars have defined SEM to be 0.25 Hz horizontal, pendular eye movement [116,117]. With the EOG channel, SEM is described as horizontal and lasting for 1 sec or longer at 100 μV amplitude. SEM can be recorded by utilising an electrode on the eyelid [116,118]. This nightcap system employs a 25 mm x 7 mm piezoelectric film that is adhesive-backed and placed on the upper eyelid [118, 119]. The SEM has also been defined as [120]:

- slow sinusoidal excursion of 0.2 to 0.6 and lasts more than 1 sec;
- absence of artefacts like EEG/EMG and blinks;
- movements beginning and ending at approximately zero velocity;
- onset of left and right movement occurs in 300ms of another;
- binocular synchrony with opposed-phase detections in the two EOG channels;
- amplitude of 20-200 μV.

For REM (i.e saccades), many automatic systems for detection have been applied [121, 122]. Many cognitive elements are probed with the movements of the eye, such as responsiveness [121]. With digital progression, Haddad and Gopal created a system based on an amplitude and slope of the detection of eye movement in REM sleep [122]. Tsuji et al [123] utilised a wavelet transformation whilst Tan el al [124] used period–amplitude and fast fourier transform (FFT) analysis to count the number of eye movements during REM sleep. Two-channel EOG was used, referenced to ipsilateral

mastoids. Signals were filtered using a 4th order Butterworth bandpass filter at 1 to 5 Hz using the following steps [125]:

a) **Candidate REM detection**: produces instantaneous signal of at least threshold 10 $(\mu V)^2$ with a local maximum if no higher peak within a time window of 1 sec.
b) **Detection REM features**: Maximum absolute amplitude of right or left EOG, correlation coefficient of two EOG, Calculation of the negative instantaneous product, deflation angle (angles utilising 0.2 sec of data on the right and left side of the peak)
c) **The deflection angles rule for detection REM**: If angle for both the right and left more than 45 degree or if the angle of left side more than 30 degree and the right side more than of 60 degree or if the angle of left side more than 60 degree and the right side more than of 30 degree.

2.5 Automatic sleep stage detection

The development of the first automated EEG analysis system applied to sleep recording [126]. Drohocki`s system was employed in plotting EEG integrated amplitude during the night [127]. The highest values were recorded during S4 and S3. Another researcher employed bandpass filtering, detecting rhythmical EEG wave band [16]. Frost developed portable analog sleep detecting machine that uses 1 channel EOG and 1 channel EEG [128]. This system utilised 0.7-13 Hz amplitude EEG filter and period to produce a continuous sleep depth curve that has the threshold to detect the sleep stages. Three multiple level amplitudes of 20%, 1% and 100% were used, whereby 100% corresponded to wakefulness (highest amplitudes) and only the peaks were integrated with periods. The periods were detected when 20% and 1% thresholds were crossed in a given sequence. The lowest curve values had low periods and high counts of high

peaks. The indicator was 2 to 3 Hz EOG amplitude of REM if EEG showed S1 sleep. Several systems used period–amplitude analysis [129], and analog, hybrid, and early digital automatic sleep analysis systems were reviewed by Hasan [112].

The main purpose of the automated sleep detection and monitoring systems is to accurately detect the sleep stages and the microstructure (i.e. sleep arousal) [130, 131, and 132]. As mentioned, earlier sleep staging is based on the impression that the pattern (characteristic EEG patterns) will exist for a given interval of time before a new pattern emerges, which indicates a change of stage. There is a continuum from sleep stage N2 to sleep stag N3. The artificial differentiation of sleep stages is a facilitation implemented to standardise the examination of automated detection across the sleep laboratories and reviewers [130]. The exact period of change of sleep stages is extremely subjective and leaves room for different interpretations of what the sleep stage indicate to the epochs by scorers. Studies have indicated inter-scorer agreement (epoch by epoch agreement) between 67% and 90% depending on the different number of readers and scoring epoch lengths [133]. Most data from the inter-scorer agreement is based on the study of normal or healthy subjects.

Automatic sleep analysis comprises few consecutive steps, as shown in Figure 5.

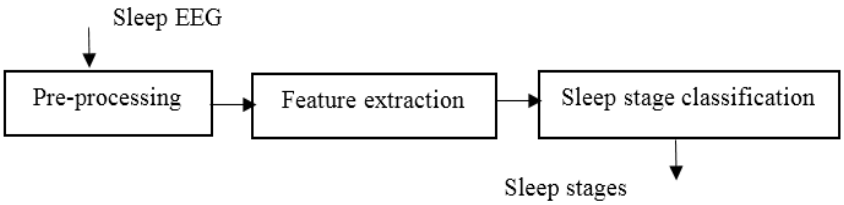

Figure 5: The automatic analysis process [130].

The pre-processing step involves the reduction by statistical tools of the vast amount of the generated raw data to be easily managed. It includes removal of the artefacts in the EEG signal [130, 135]. The next step, feature extraction, can be the power or amplitude

of regular EEG waves (i.e. delta, theta, alpha and beta bands) and transients, such as SS and KC [130]. The analysis can be undertaken in short epochs, ranging from 1 to 20 or 30 seconds to avoid the loss of time resolution [134]. The final step includes the combination of EEG signals and extracted features to reduce the number of sleep stages.

Rule-based logistics are utilised in classifying the stages based on features that are extracted from the EEG that imitate visual inspection according to standards, such as the AASM rules and R&K [130,135]. For clinical systems, the final outcomes of the automatic sleep scoring are required to closely imitate the visual AASM or R&K scoring. Most published studies on automatic sleep stage detection have produced outcomes from healthy persons with dependability between 70 and 90% [130,135].

Feature extraction is an important part in the development of sleep stage scoring algorithms. The majority of the previous sleep stage scoring algorithms depended on computationally undemanding time domain analyses, such as period amplitude [14] as well as interval histogram method [15]. Subsequently, most of the algorithms have been developed before/after 1990 by feature extraction methods, utilising the power spectrum of the EEG, EOG or EMG signals. There are several methods that can execute spectral decomposition by means of discrete Fourier transform (DFT) /FFT [136, 137], autoregressive modelling [138], adaptive filter banks or wavelets [17]. Today, innovative spectral analysis methods are being used for the EEG sleep staging, such as normalisation amplitude of frequency bands [139, 140] and features derived from harmonic, predictor coefficients and Hjorth sub-band energy parameters [141].

Most algorithms have utilised 30- or 20-second epochs for EEG sleep stage classification according to the R&K or AASM rules [17,142]. Because the EEGs are non-stationary signals, the tradition of sleep stage scoring based on a 30-second epoch

might provide less information about the brain activities because it uses a fixed epoch duration. It has been suggested that EEG epoch duration be reduced to 1, 2 or 5 seconds [143].

Due to the non-stationary nature of the EEG signal, time-frequency analysis is used in the decomposition process for classification. The matching pursuit, discrete wavelet transform, wavelet transform modulus maxima, and Gabor transform have been applied to detect the sleep stages [143, 144, 145, 146, 147].

Also significant work has been done in creating systems for sleep staging based on nonlinear and linear classifiers, including fuzzy logic, artificial neural network (ANN) and pattern recognition [81, 148,149]. These classifiers do not need complicated domain knowledge or classification rules. The ANN characterise by learning ability which lets them create their own structures, depending on training sets [130].

One of the primary approaches of computer-assisted sleep stage detection or scoring is the 'special purpose sleep analysing hybrid computer' which utilised three EEG and two EOG signals [142]. This study was able to analyse data in online mode, based on a linear analog filter for detection of sleep spindles as well as the alpha EEG signal. The assessment was made based on a study of 15 healthy subjects aged between 15 and 21 years. The inter-rater agreement between their system and the manual scoring was 83.5%. However, several studies indicated that it was easier to detect sleep stages in young, healthy subjects than in older subjects who suffered from sleep disorders [150]. Agarwal and Gotman [151] presented a computer-assisted sleep staging method that utilised the principles of segmentation and self-organisation (clustering) based on primitive, sleep-related features to find the pseudo-natural (cluster pattern) stages. Their method was developed and tested using 12 subjects of many types (healthy, abnormal

[such as PLMS and sleep apnea], male, female, and different age groups), demonstrating an overall agreement of 80.6% with a manual scoring of 20-second epochs. However, this study reported that the maximum amount of errors occurred in the identification of the highly transitional S1, 54% of which were misclassified into neighbouring S2 or W. Tim Schluter et al. [152] developed automatic sleep stage scoring apnoea-hypopnoea detection based on EEG, EOG, and EMG signals. They utilised several combined techniques, such as FFT, wavelets, derivative dynamic time warping (DDTW), and waveform (pattern) recognition. Their approach was to extract features (frequencies and special patterns) from these signals and use the decision tree classifier to classify the sleep stages. The outcome of this study showed that the accuracy of sleep stage detection was 95.2%. However, this study used several databases without specification of the age or gender of all of its subjects.

Anderer et al. [150] presented automatic sleep stage detection and a classification based on 1 EEG signal, 2 EOG signals and a chin EMG channel. They utilised several methods for automatic identification of sleep/wake-related patterns based on the previous signals, such as to identify alpha and delta signals using period-amplitude analysis, model-based detection, band-pass filtering and spectral analysis. They also used the discrete wavelet transform and period-amplitude analysis methods to identify eye movement and maximal peak-to-peak amplitude as features extracted from the EMG signal. The classification system was based on the decision rules. The outcome of this study showed that the accuracy of a large database compared to manual scoring was 80%. Figure 6 compares the scoring of hypnograms by human experts with automated scoring by the commercial Somnolyzer 24 × 7 system (which developed by Siesta Group in Austria).

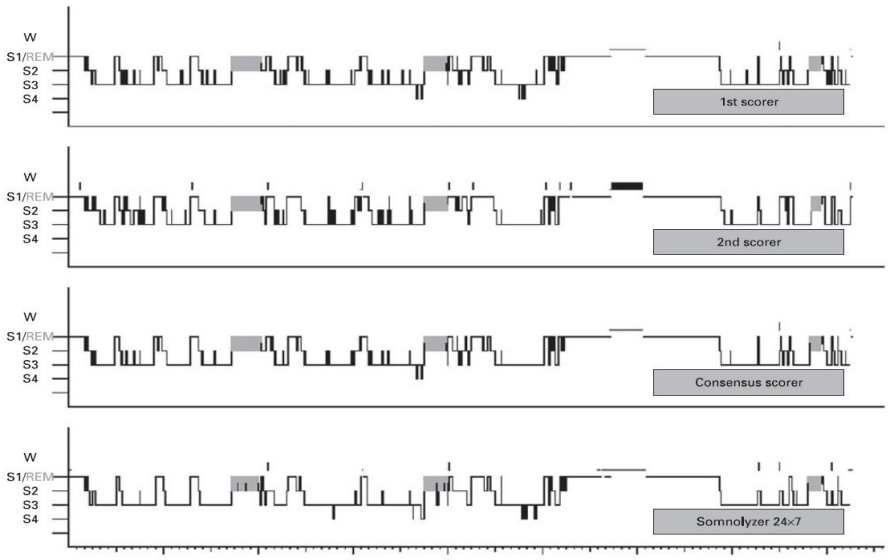

Figure 6: The hypnogram scoring of different human experts vs the Somnolyzer 24×7 system. The first hypnogram is indicate to the first expert scorer of sleep stage, the second hypnogarm is the second expert scorer of sleep stage, the third hypnogram is indicate to the consensus scorer and the final hypnogram is indicate to the Somnolyzer 24×7 system scoring [150].

However, this study faced obstacles in terms of the misclassification for some sleep and wake stages. In particular, subjects with sleep disorders, such as sleep apnea and insomnia had an accuracy of 75.6% and 85.5%, respectively. Susmakova et al. [153] utilised a spectral analysis and the fractal dimensions of the EEG, EOG, and EMG signals and obtained an accuracy of 77% in 20 healthy subjects. The authors faced obstacles in terms of distinguishing between stage N1 and REM sleep that eventually affected the overall accuracy. Recently, several studies have attempted to develop an automated sleep stage detection based on the EEG signals only [14,154]. Zhovna et al. [154] presented a novel method for automatic detection and classification of sleep stages using a multichannel autoregressive (MAR) model. The classification was performed using Kullback–Leibler (KL) divergence. The outcome of the study showed a classification accuracy of 93.2%. However, there was a weakness in their system in that it laced the W stage classification. Liu et al. [14] demonstrated a novel method based on the Hilbert-Huang transform (HHT) and back-propagation (BP) neural

network for automatic sleep stage detection and classification. The HHT was used as a feature extraction from the 30-second epoch of the EEG signal. The results revealed that the method was effective and promising in automatic sleep stage classification. However, this study was not able to differentiate between the N1 and REM stages; thus, they combined these two stages.

Another study employed 2-channel EOG for automatic sleep stage classification, EOG signal were referenced to the left mastoid (M1) [137]. The synchronous EEG activity SWS and S2 were identified by measuring peak-to-peak and the cross-correlation amplitude difference in the 0.5 to 6 Hz and between the 2-channel EOG. Automatic SEM approximation was utilised to designate W, S1, and REM. The EEG alpha power 8-12 Hz and beta power 18-30 Hz were used for detecting wakefulness [137]. Synchronous 1.5 to 6 Hz EEG activity and absence of great movements of the eye were used for the separation of S1 from REM. Also, simple smoothing rules were applied. The EEG, EMG and EOG of sleep were recorded for 256 subjects. To tune the system 132 training subjects' data were used and applied to 131 validation subjects that had different SWS, and S2 epochs were epoch-by-epoch agreement of 72% with Cohen's Kappa (CK) at 0.62. The results indicated an improvement of the specific EEG alpha thresholds for offline applications to 0.63 and 73% [137]. This method can further be developed in order to be applied in ambulatory sleep recording by employing only four disposable, self-applicable and self-adhesive electrodes. Figure 7 shows the study results.

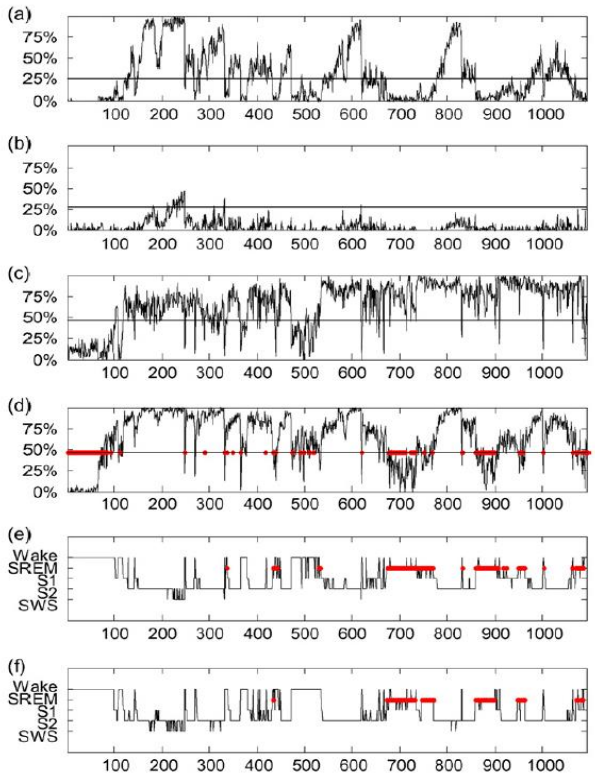

Figure 7: Recording from group (a) percentages of slow wave (SW2 where 2 refers to rule number 2) segments; (b) SW3 (using rule 3) percentages; (c) percentages of rule S; (d) percentages of rule S; (e) automatic sleep stage scoring developed; (f) visual sleep scoring.

One of the first automated pattern recognition systems was developed by Martin in 1972. It employed a low-pass filtered for EEG at 28 Hz and EOG at 14 Hz [136]. The FFT analysis was performed on 30-second epochs to separate S2, S1 and W. Conjugate REMs were identified on 2-channel EOG. Pattern recognition was employed for the EEG delta band detection. Peaks ("the delta measurement program examined successive 30-second increments of EEG data to locate peaks no closer" [136]) were sensed as local maxima with no higher local maxima at 0.5 second. Valleys were detected as the lowest points between two adjacent peaks and peak-to-valley variation had to surpass 75 μV, and the coefficient of correlation of the raw data in the fitted line (straight) from peak-to-valley was at least 0.75 [136]. An agreement of 82% was obtained in separating REM, S1, W, S2, S3 and S4, which was only 7% less than the inter-scorer agreement.

Other recent automated methods including a semi-automated system as Morpheus [155] and automated Somnolyzer 24 X 7 [149] used in the clinical settings. The automated and semi-automated systems of sleep scoring provided an option for time-consuming, costly and variable manual scoring. According to scholars, the automatic analysis of SWS can be more reproducible than the visual analysis [156].

Van et al. [157] employed EEG automatic detection for sleep staging. The method comprised four steps, including segmentation, extraction of parameters, analysis of cluster (aimed to classify (cluster) a number of points into K groups), and classification. The parameters compared included the harmonic, Hjorth and relative band energy parameters. For cluster analysis, the study used a modified version of K-means algorithm. The study concluded that it was capable of extracting information from EEG pertinent for sleep stage scoring, and it was also possible to uncover similar segments and, therefore, automate the sleep detection stages through K-means algorithm. However, it was reported that extra information, such as EOG and ECG was critical for vibrant fine-tuning of various sleep stages [157]. Zhang et al. [158] undertook a study on automatic sleep onset detection utilising EEG electrodes. They proposed a simple and accurate method for sleep onset prediction that was dependent on the EEG signal, obtained from a single frontal electrode within a wireless headband. This method first extracted an energy power ratio of EEG alpha (8-12 Hz) and theta (4-8 Hz) bands along the time domain. The resultant slow waves were used for sleep onset detection by feeding them into a rule-based engine. The polysomnographic method was used to evaluate the effectiveness of the approach and also headband EEG signals were acquired from 20 healthy adult subjects who each underwent two sessions of sleep events; hence, 40 sleep events were collected. The resultant recordings were assessed by an offline PSG technologist through visual observation of the waveforms of PSGs

who annotated sleep stages N2 and N1 by using the AASM scoring rules. This approach achieved 87.5% accuracy when the gold standard was used in sleep onset detection. These results were better and comparable to other techniques employing single or multi-channel data [158].

Several other approaches have been reported based on single EEG channel data. Huang and colleagues [159] developed a system that detected the arousal states of individuals utilising mean frequencies of a single EEG for autoregressive hidden Markov models (HMM). This model accomplished wake-drowsiness detection at a rate of 70%. Novak et al. [160] used more features than the earlier system of Huang et al. [159], including autoregressive parameters, spectral entropy and the complexity stochastic measure in developing an HMM model used for sleep staging. This approach predicted sleep N4 and N3, but it was not able to detect well for stage REM. Rossow, et al. [161] also depicted an approach applying a single-channel EEG modelling using the HMM and Kalman filters. Its agreement rate when tested was 60.14%. Other researchers have adapted different approaches in the automatic determination of patients' sleep stages. Sukhorukova et al. [162] undertook a study to determine the difficulties and solutions of automatic sleep stage identification. They documented various problems, such as the data mining algorithms being challenging since the data set was noisy and colossal, and the signals were complex, thus needing specialists to analyse them. Therefore, the study adapted approaches from four fields involving mathematical optimisation, neural networks, frequency domain and financial forecasting to solve the problem identified in relation to the automatic determination of the patients' stage of sleep. The outcomes of this study, though preliminary, were promising and indicated that a combination of approaches can be more fruitful than relying on a single approach.

Research undertaken using 9-stage sleep onset automatic classifications showed that most hypnagogic imageries were remembered during the stage 5 EEG (theta stage) [163]. These imageries were least recurrent in stage 2 and 1 with EEG alpha activities. When the nine stages were classified depending on the subjective analysis of reaction time, recall rate and behavioral state of hypnagogic, the subgroups were not entirely coincidental. This denotes that sleep onset is influenced by the technique of determination. As the quantity of the subjective responses for having been asleep was 43.7 only in conventional S2, the sleep onset period can be considered as an extension beyond S1. "If the criterion for wakefulness is cognitive response to external stimulation, only in EEG Stages 3, 4, and REM can accurate distinctions between sleep and wakefulness be made. If EEG is the criterion, then the data suggest that cognitive response is possible during Stages 1 and 2 sleep" [163]. Therefore, it seems that the absence or presence of the response is an uncertain measure for sleep onset. Hence, the slowing of reaction time should be applied as an additional parameter [164]. Table 7 shows different automatic sleep stages algorithms, and some of these studies were described in detail [130].

Table 7: An overview of automatic sleep staging methods and studies based on feature extraction, classifier, number of subjects, accuracy and signals.

Author(s)	Features	Classifier	Number of Subjects	Accuracy (%)	Signals
Principe (1989) [165]	frequency bands, spindle, K-complex	Fuzzy logic	5 healthy	84.74	1-EEG,2-EOG EMG
Schwaibold (2001) [149]	periodic activity, spindles, K-complexes	ANN	8 OSA patients	31.5 - 87.4	2-EEG 2-EOG 1-EMG
McGrogan (2001) [166]	reflection coefficients	ANN	9 healthy, 3 non-healthy	72.2 - 96	1 EEG
Flexer (2002) [167]	reflection coefficients, stochastic complexity	HMM	40 healthy	68 - 82	1 EEG
Hanaoka (2002) [168]	zero-crossing, wave period, amplitude,	decision tree learning	1 healthy	40 - 91.8	1-EEG 1-EOG 1-EMG

	duration, transient events				
Huang (2003) [169]	Lempel-Ziv complexity measure	ANN	6 healthy	90.83	2-EEG
Huuponen (2003) [170]	amplitude spectrum of subbands	rule-based	15 healthy	76.80	7-EEG
Gudmundsson (2005) [171]	Hjorth parameters, power spectrum, amplitude and frequency distribution	SVM, ANN	4 healthy	81	1 EEG
Song (2007) [172]	wavelet transform modulus maxima	rule- based	4 healthy	55.4 - 97.7	1 EEG
Virkkala et al. (2008) [137]	spectrum of bandwidth, frequency distribution	Decision tree	256 healthy and non-healthy	74	2-EOG
Güneş et al, (2010) [173]	Welch spectral analysis	K-NN & decision tree	5 healthy	82.15	1-EEG
Dong et al. (2010) [175]	empirical mode decomposition (EMD) algorithm, Fourier transform or non-stationary signals, Harmonic components,	FFT	15 non healthy	80	1-EEG
Hedner et al. (2011) [174]	PAT recorder signals, Itamar Medical, Caesarea	Fuzzy logic	227 including healthy & non-healthy	59 - 94	2-EEG, 2-EOG, EMG, ECG
Liang et al. (2012) [176]	multiscale entropy (MSE) and autoregressive (AR) models	LDA	20 healthy	76.91	1-EEG
Tagliazucchi et al. (2012) [177]	periodic-activity, spectrum of bandwidth, fMRI scanner	Binary support vector machine, multiclass	73 healthy	80	1-EEG-fMRI
Diego (2013) [178]	spectral analysis	Fuzzy logic	33 non-healthy	84	2-EEG, 2-EOG, EMG
Correa et al. (2014) [179]	spectral analysis,Time analysis, Wavelet decomposition	ANN	16 non-healthy	83.6 - 87.4	3-EEG
Popovic et al. (2014) [180]	spectral analysis	Decision tree	29 healthy	80	1-EEG

3 : Subjects and data sets

3.1 Subjects

This section describes the three PSG databases used in this research. The following section 3.1.1 describes the PSG napping or daytime PSG data. Sections 3.1.2 and 3.1.3 describe the whole-night PSG data.

3.1.1 Data set No.1

This existing PSG napping data set consisted of 10 healthy adult male subjects ranging in age from 21 to 43 years (M = 29) (see Table 8). None of the subjects had a previously diagnosed sleep disorder. RMIT Ethics approval was granted for the recording of this PSG data and all subjects signed the consent letters. A single continuous PSG recording of 20 minutes in duration was undertaken for each subject. This existing data was provided by Dr. Dean Cvetkovic, which originated from ARC linkage grant (2005-2009). All six channels were utilised for automated sleep scoring undertaken by Hypnolab commercial software (SWS Soft, Italy, 2006-2008), but only 1 EEG channel (C3-A2) data was used in this analysis. All subjects were exposed to audio and photic stimulation under biofeedback operant conditioning, influencing wake and sleep states. Therefore, the influence of these stimuli may have caused the PSG transients to differ considerably as compared to 'normal' wake and sleep conditions. Also, this PSG data can be considered to be recorded from 20 minute napping conditions rather than 20 minute sleep/wake conditions. Sleep stage 1 (N1) and wake (W) were detected during these napping conditions. The PSG recording for each subject contained 6 channels, 2 EEGs (O2-A1 and C3-A2), 2 EOGs (right outer canthus (ROC) and left outer canthus (LOC)) and an ECG (Lead II using torso electrode placement). The sample frequency was 256 Hz for each signal.

Table 8: Summary of the PSG napping data.

Type of subjects	Healthy
Number of subjects	10
Gender (male/female)	(10/0)
Age (mean years and range)	29 (21-43)
TRT (min)	195
W (% of TRT[1])	92.1
N1 (% of TRT)	7.9

[1]TRT = total recording time

3.1.2 Data set No.2

The existing PSG data was downloaded from the online database [181]. This data is under the terms and conditions of the Attribution-NonCommercial-NoDerivs 3.0 Unported (CC BY-NC-ND 3.0) License. Each use of one of these databases and/or its content is attributed to the University of MONS - TCTS Laboratory (Stéphanie Devuyst, Thierry Dutoit) and Université Libre de Bruxelles - CHU de Charleroi Sleep Laboratory (Myriam Kerkhofs). Each PSG data file consists of at least 2 EOG, 3 EEG and 1 EMG submental channel, at the sampling frequency of 200 Hz. All sensitive information was coded by this institute and the data does not show any patient names, except their group, age and gender. All PSG data files are up to 8-9 hours of recording of overnight sleep. The overnight PSG data was recorded from 13 healthy adult subjects, 10 with periodic leg movement syndrome (PLMS), 10 with sleep apnoea-hypopnoea syndrome (SAHS) as shown in Table 9. The sleep stages were manually scored by an expert according to the AASM criteria.

Table 9: Summary of PSG data set 2.

Group of subjects	Group1: Healthy control	Group2: PLMS	Group3: SAHS
Number of subjects	13	10	10
Gender (male/female)	(3/10)	(8/2)	(6/4)
Age (mean years and range)	42.5 (20-65)	49 (22-46)	56 (38-74)
TRT (Min)	6627.8	5262.8	5249
W (% of TRT[1])	16.8	25.2	25.4
N1 (% of TRT)	6.6	8.8	8.8
N2 (% of TRT)	45.7	47.5	51.5
N3 (% of TRT)	16.3	7.8	5
R (% of TRT)	14.6	10.7	9.3

[1]TRT = total recording time

3.1.3 Data set No.3

The PSG dataset was recorded by the Central Institute of Mental Health (Mannheim, Germany). Each donated PSG patient data file consisted of up to 15 channels: 3 EEG, ECG, EMG, 2 EOG, nasal and oral airflow, snoring sound, breathing effort (measured at the chest and abdomen), oximetry and actigraphy recording body positioning and leg movements. The sampling frequency varied from 200, 256 to 500 Hz. In addition to each European data format (EDF) file, the institute's sleep technicians manually/visually scored the sleep stages according to the AASM criteria.

The PSG database included 30 subjects who were divided into three groups, each consisting of 5 males and 5 females (see Table 10). Group 1 consisted of 10 primary insomnia patients, in Group 2 was 10 schizophrenia patients and Group 3 contained 10 healthy subjects. All patients and subjects were diagnosed on the basis of the Diagnostic and Statistical Manual (DSM-IV) and were recruited during in-house treatment at the Central Institute for Mental Health. The criteria for inclusion in the study included being aged between 18 and 60 years, the ability to provide informed consent, a stabilised disease course, stable (for at least two weeks) psychopharmacological treatment in the form of monotherapy with a second generation antipsychotic, and the absence of psychiatric comorbidity.

Table 10: Summary of PSG data set 3.

Type of subjects	Group 1: Primary insomnia	Group 2: Schizophrenia	Group 3: Healthy
Number of subjects	10	10	10
Gender (male/female)	(5/5)	(5/5)	(5/5)
Age (mean age and range)	31.3 (18-45)	31.7 (22-46)	31 (20-47)
TRT (Min)	4647	4899.5	4870
W (% of TRT[1])	22.1	14.05	22.98
N1 (% of TRT)	10.2	7.95	9.34
N2 (% of TRT)	40.6	43.06	42.45
N3 (% of TRT)	18.2	18.28	12.77
R (% of TRT)	8.9	16.63	12.75

[1]TRT = total recording time

4 : Automatic sleep stage detection methods

This chapter describes various methods and materials utilised to develop an automatic detection of sleep stages. Section 4.1 describes the materials and methods utilised to develop an automatic detection of wake and sleep stage N1 based on EEG sub-epoch signal. Section 4.2 describes the materials and methods that were utilised to develop an automatic detection of sleep stage based on the consecutive and non-consecutive EEG sub-epoch approach. Section 4.3 describes the materials and methods utilised to develop an automatic detection of sleep stages based on EOG signals.

4.1 Automatic detection of wake and sleep stage N1 using EEG sub-epoch approach

4.1.1 Subjects

Ten healthy adult male subjects were used, as described in Section 3.1.1

4.1.2 EEG signal processing method

Figure 8 shows the flowchart for the proposed consecutive and non-consecutive, 6-second sub-epoch comparison approach comprised of six parts: EEG segmentation of the 30-second epochs (part 1); filtering (part 2); EEG segmentation of the 30-second epochs into 6-second sub-epochs (part 3); feature extraction (part 4); sleep stage scoring rules (part 5); and checking three consecutive and non-consecutive 6-second sub-epochs (part 6).

Part 1 segmentation of the 30-second epochs: The full length of this data was segmented into 30-second epochs for scoring the sleep EEGs prior to pre-processing.

Part 2 Filtering: The EEG signal was processed utilising a 6-order Butterworth band pass filter for the different band frequencies, as follows: theta (θ, 4–7Hz), alpha (α, 8–12Hz) and beta (β, 13–30Hz).

Part 3 Further segmentation of each of these 30-second epochs into 6-second sub-epochs: Prior to feature extraction, the 30-second epochs were divided into five sub-epochs of six seconds each.

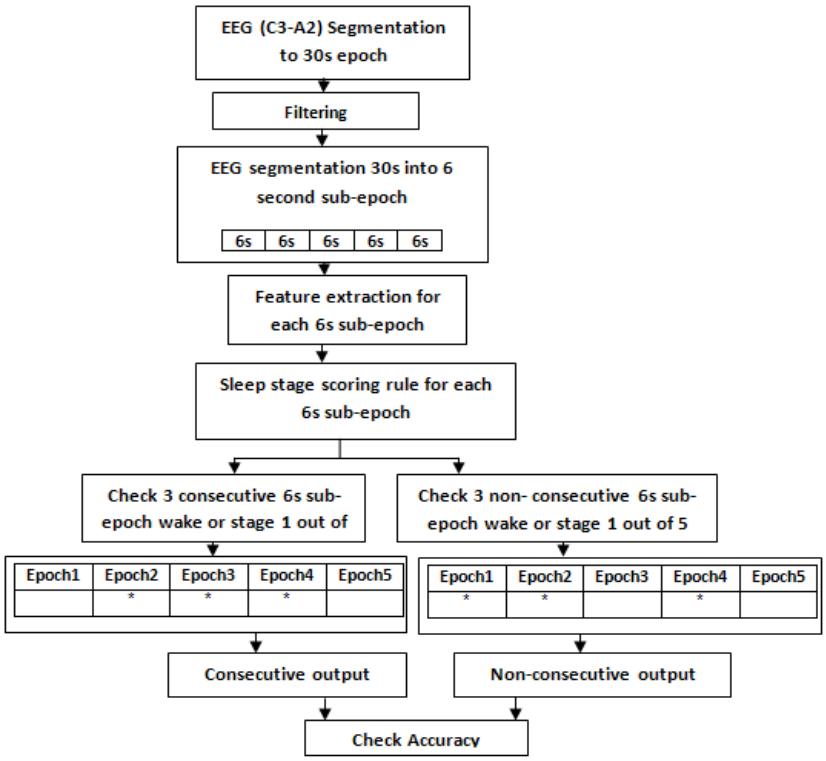

Figure 8: Flow-chart describing the consecutive and non-consecutive, 6-second EEG epoch approach.

Part 4 Feature extraction: Frequency domain feature extraction was applied, calculating the relative spectral energy band (RSEB) for the θ, α and β EEG bands from the were computed of parametric and non-parametric power spectral densities

(PSD_θ, PSD_α PSD_β). The RSEB can be calculated as follows:

$$\text{Total power} = PSD_\theta + PSD_\alpha + PSD_\beta \quad (1)$$

$$RSEB(\theta) = PSD_\theta \,/\, \text{Total power} \quad (2)$$

$$RSEB(\alpha) = PSD_\alpha \,/\, \text{Total power} \quad (3)$$

$$RSEB(\beta) = PSD_{\beta} / \text{Total power} \quad (4)$$

Part 4.1 Non-parametric method: Thomson's multi-taper method (MTM) [182] was used to estimate the PSD of each EEG band. The advantage of using the MTM is that it reduces the variance of the spectral estimate by utilising a few groups of tapers, as proposed by Thomson (1982) and Percival and Walden (1992) [183]. The computation of the power multi-taper method (PMTM) was put forward in [184].

Part 4.2 Parametric method: Non-parametric methods have the drawback of spectral leakage effects because of windowing, which can result in a weakening of the signal components. Using parametric methods to compute PSD is a solution to spectral leakage and provides optimal frequency resolution. In this study, Burg's autoregressive (AR) method was applied in this analysis to calculate the PSD. The main concept of Burg's method is that it attempts to reduce the forward and backward prediction errors by accepting the Levinson-Durbin recursion [185]. The reflection coefficients are estimated directly in Burg's method rather than calculating the autocorrelation function.

Part 5 Sleep stage scoring rules: In this part, rules for scoring the sleep stages in each 6-second epoch were applied. For example, according to the R&K rule, an epoch is scored as a W stage if RSEB(α) represents more than 50% of the 30-second epoch. On the other hand, the epoch is scored as stage 1 when the RSEB(θ) is more than 50% of the epoch. In addition, N1 can be scored when the RSEB(α) is less than 50% of the epoch.

Part 6 Checking the three consecutive and non-consecutive 6-second sub-epoch: This was accomplished by investigating whether three out of five consecutive or non-consecutive 6-second sub-epochs indicated W or N1 sleep. The three out of five consecutive and non-consecutive 6-second sub-epochs characterised 60% of

predominant band power in its total, 30-second epoch, making the detection more difficult based on the rule criterion of 50% predominant power.

4.2 Automatic detection of sleep stages using EEG sub-epoch approach

4.2.1 Subjects

Thirty-nine subjects were used in this study. Ten healthy subjects were utilised for the development of this algorithm (see section 3.1.2) and 29 subjects were utilised for the validation (see section 3.1.3)

4.2.2 Automatic sleep stages detection algorithm

Algorithms for automated sleep stage detection were previously explored with varying degrees of success (the algorithm was succeed with healthy subjects of varying age) [186]. Here, the candidature focused on the approach outlined in [186], using a single EEG (CZ-A1) channel and validated against the AASM criteria. An algorithm, outlined in Figure 9, involves a consecutive or non-consecutive sub-epoch approach, and seven steps that are summarised as: (1) preprocessing; (2) EEG signal segmentation into 30-second epochs; (3) 30-second epoch split into five, 6-second long sub-epochs; (4) filtering; (5) feature extraction within sub-epochs; (6) using three consecutive or non-consecutive 6-second sub-epochs; and (7) a ‘smoothing’ rule. The algorithm introduces several new aspects including the new segmentation strategy and application of an adaptive filter to remove electrocardiogram (ECG) artifacts from the EEG signal. The following subsections detail the explanation of the specific procedures:

1. Preprocessing and EEG Signal Segmentation

   During initial preprocessing, a baseline drift is removed, eliminating any linear trends and removing the mean value. As mentioned in section 3.1, the EEG data was segmented into 30-second epochs. Additionally, since EEG signals can be

affected by ECG, an adaptive filter based on a least mean square (LMS) algorithm was employed to eliminate artifacts from the EEG data. Subsequently, the 30-sec EEG signal epochs were divided further into five sub-epochs of 6-second duration each,

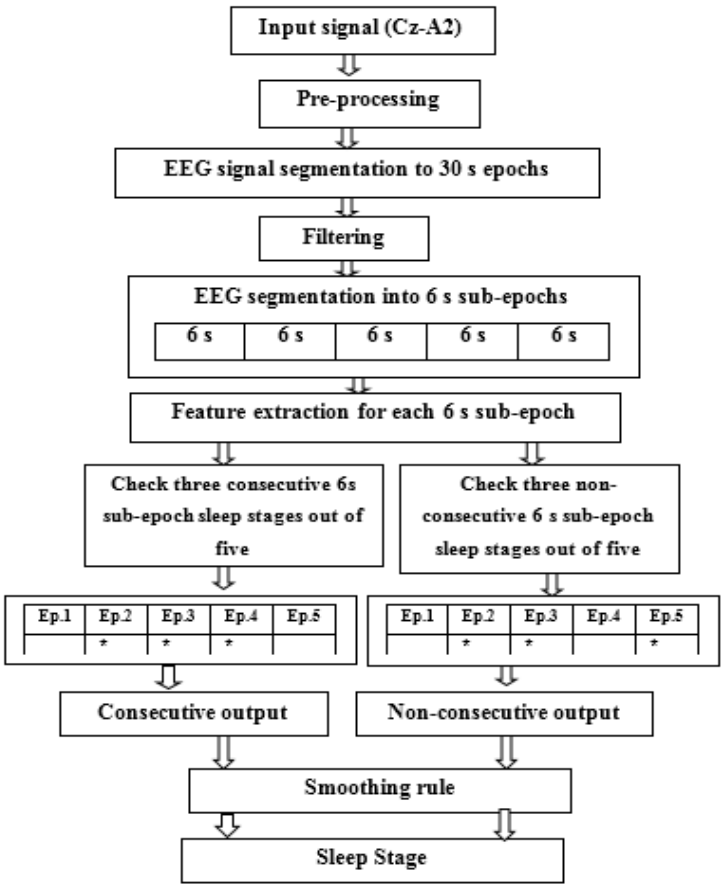

Figure 9: Flow chart describing the automated sleep stage detection algorithm based on the three consecutive and non-consecutive 6-second EEG sub-epochs approach. Where the '*' is indicated to 3 consecutive or non-consecutive out 5 sub-epoch approach.

2. Filtering

A zero-phase bandpass filter was applied to the EEG data. The filter was a sixth-order cascaded integrator-comb (CIC) type that selects the following EEG frequency bands of interest: delta 1 (δ1, 0.5–2 Hz), delta 2 (δ2, 2–4 Hz), saw-tooth

waves (2-6Hz), theta (θ, 4–8 Hz), alpha (α, 8–13 Hz), sigma (σ, 12–15 Hz), beta 1 (β1, 13–20 Hz) and beta 2 (β2, 20–30 Hz).

3. EEG Feature Extraction

In order to extract features from the 6-second long EEG signal sub-epochs, spectral analysis was used. Burg's parametric method was used to calculate the power spectral density (PSD) and estimate the spectral content by an autoregressive linear prediction filter model. Suitability of this approach was confirmed by the Akaike information criterion (a test effective in assessing the relatively quality of models) [187]. The parametric method was chosen because of its ability to resolve spectral leakage caused by 'windowing' and because it provides optimal frequencies.

Relative spectral energy (RSE) of the *i*th frequency band, B_i, is the sum of power within the band's frequency range relative to the overall power in the entire considered spectrum, which can be written as:

$$RSE_i = \frac{\sum_{f \in B_i} P(f)}{\sum_{f_L}^{f_H} P(f)} \tag{5}$$

where f_L represents the lowest (0.5Hz) frequency and f_H represents the highest frequency (30 Hz) contained in the EEG signal. $P(f)$ is the power at a given frequency, f.

The power spectral density ratios (PSDR) is defined, as (an example):

$$\frac{PSDR_{\alpha}}{PSDR_{\delta}} = \frac{\sum_{f=8Hz}^{12Hz} P(f)}{\sum_{f=0.5Hz}^{2Hz} P(f)} \tag{6}$$

Central frequency (CF) is determined by

$$FC = \frac{\sum_{f_L}^{f_H} f * P(f)}{\sum_{f_L}^{f_H} P(f)} \tag{7}$$

The 90% Spectral Edge Frequency (SEF) is

$$SEF = 0.9 \sum_{f_L}^{f_H} P(f) \tag{8}$$

where *L* is the 'length' of the RSE array and is determined by a number of frequency 'windows' used in the calculation.

Root mean square frequency (RMSF) was defined as:

$$RMSF = \sqrt{\frac{\sum_{f_L}^{f_H} f^2 P(f)}{\sum_{f_L}^{f_H} P(f)}} \tag{9}$$

4. The Three Consecutive and Non-Consecutive 6-Second Sub-Epochs Approach

   Varying segmentation strategy can have a drastic effect on the efficacy of algorithms. Segment length is not the only important factor. Here, the purpose of this step is to investigate whether three (out of five) consecutive or non-consecutive 6-second sub-epochs are most effective at detecting the sleep stages. Since three out

of five consecutive (or non-consecutive) 6-second sub-epochs contain only 60% of the predominant band power in the total 30-second epoch, detection could be expected to be more difficult, based on the rule of 50% predominant power [185]. However, the approach can be surprisingly effective, when the appropriate technique is applied.

5. Identification of Sleep Stage Based on the Three Consecutive and Non-Consecutive 6-Second Sub-Epochs Approach

Increasing the number of features used to identify each sleep stage is known to offer better detection performance [153,188,189]. Table 11 shows the sleep stage features and the associated rules used in this study. The algorithm process is outlined in Figure 9.

At first, each rule was utilised for each sleep stage and both the three consecutive and non-consecutive 6-second sub-epoch method. Initially, RSE was applied because these features are well known from the AASM and R&K rules for the detection of sleep stages. For example, when RSE (α) represents more than 50% of the epoch's total spectral energy, then rule 1 (R1) is positive and the epoch is scored as the W (waking) stage. For example, in the first step (R1) RSE (α) feature was used to split the W from the other sleep stages (see Figure 2). In the second step the slow-wave sleep (N3) was split from sleep stages, N1, N2 and R, using rule 4 (R4) and RSE (δ1), as this sleep stage is characterised by lower EEG delta activity. In the third step, sleep stage N2 is split off from sleep stage N1 and R by rule 3 (R3) as this sleep stage is characterised by sleep spindles. Sleep stage R is characterised by saw-tooth wave and was split from N1 in the fourth step by rule 5 (R5). A similar procedure was done for the power ratio features in the event of negative rule outcomes in the previous steps. The remaining

rules (R11, R14-R17) and associated features represent contrasts between neighbouring stages and may be needed prior the sub-epoch being identified as a particular sleep stage.

Table 11: Sleep stage algorithm rules.

		W	N1	N2	N3	R
	AASM rule [13]	EEG Alpha >50 % of epoch. If alpha rhythm is present for part of the epoch (even <15 sec) score as wake stage	EEG Theta >50% of epoch or EEG Alpha <50 % of epoch	Present sleep spindle & k-complex	EEG Delta >20 % of epoch	Low amplitude mixed frequency EEG Theta, Low chin EMG Rapid eye movement EOG
Algorithm Rule	RSE feature [190]	**R1**:RSE(α) >50% of epoch	**R2**:RSE (δ2) <15% and RSE (β2)>10 % of epoch or RSE(θ)> 50%	**R3**: RSE (δ2) <20% & RSE (β2)<10 % of epoch, or RSE (σ) >10%. respectively	**R4**: RSE (δ1) >20% or >50 of epoch	**R5**: RSE (saw-tooth wave) >.5% Or RSE (β) and (σ) <10 % of epoch, RSE (β2) approximately 10% and RSE (δ2) <15 %
	Power ratio	R6: α /β1> 7.8	R7: α /β1<2.5	R8: σ/ β2 >3.5	**R9**: δ1/θ>5.5	R10: δ1/θ < 1.6
	Central frequency	R11: CF (α) > 40% of epoch	-	-	-	-
	Root mean square spectrum	R12: RMSF (α) > 40 % of epoch	R13: RMSF (α) >19 % & < 40 %	-	-	-
	Spectral edge frequency (90 %)	R14: SEF >=8 and <=13 Or SEF 20> and <=30	R15: SEF >=4 and <=8	R16: SEF >=12 and <=15	R17: SEF>=.5 and <=2	-

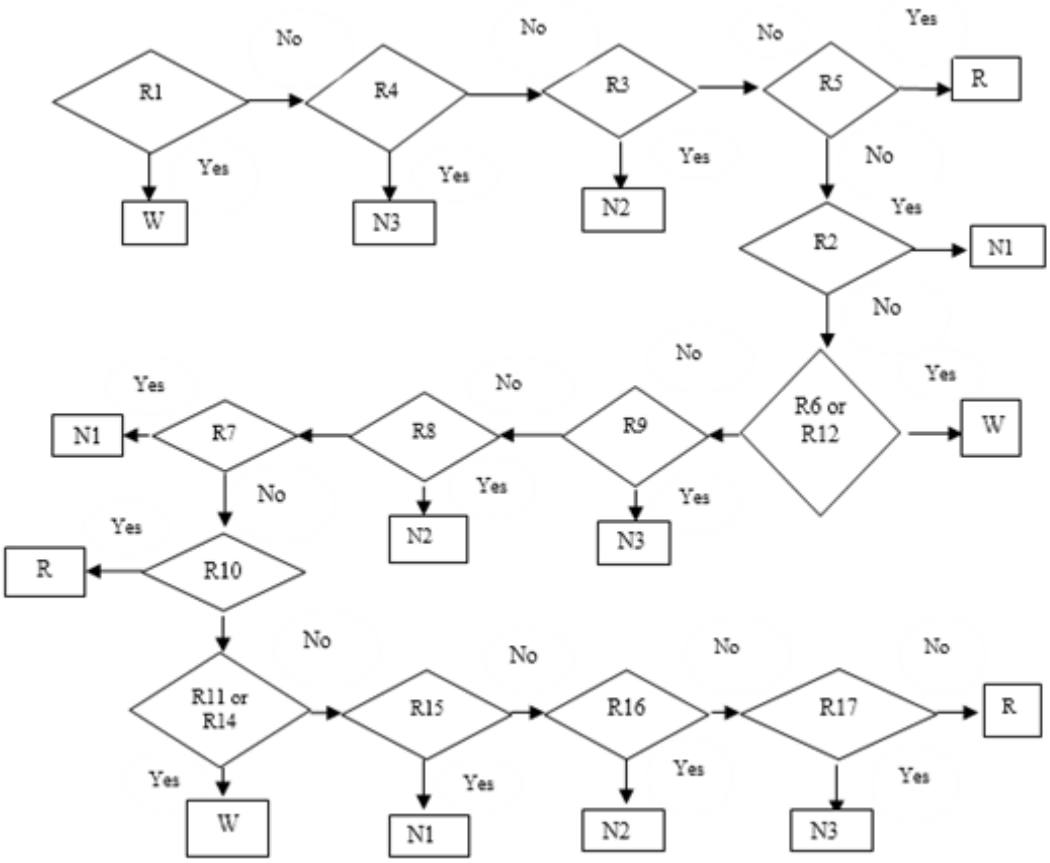

Figure 10: Flow chart depicting process for sleep stage identification applied for both the three consective and non-consecutive epoch approaches.

6. The Smoothing Rule

Due to fluctuations in the recorded signals, it is desirable to 'smooth' the outputted sleep stage values to reduce output 'jitter' (misclassification of sleep stage, see Table 12 for the list of smoothing rules). For example, if the case detection of the sleep stage was a consecutive sequence such as W- (any stage)-W then, the consecutive sleep stage value should be replaced as W-W-W (e.g. see rule number 1, Table 12).

Table 12: The smoothing rules

Rule number	Case detection	Replace to consecutive sleep stage
1	W-(any stage)-W	W-W-W
2	N1-(any stage)-N1	N1-N1-N1
3	N2-(any stage)-N2	N2-N2-N2
4	N3-(any stage)-N3	N3-N3-N3
5	R-(any stage)-R	R-R-R

4.3 Automatic detection of sleep stages using EOG

4.3.1 Subjects

Thirty subjects and patients were used in this study, as described in section 3.1.

4.3.2 EOG signal Method

Figure 11 describes the algorithm for detecting the sleep stages based on EOG signals. It includes five steps, as shown in Figure 11.

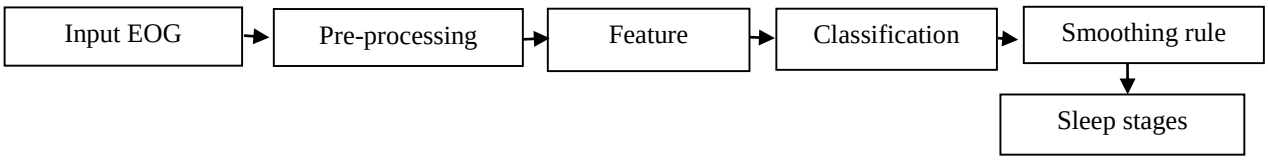

Figure 11: Block diagram of the automatic sleep stage detection method using EOG signals.

4.3.2.1 Pre-processing

The EOG data was segmented into 5-second epochs. The entire EOG signal was processed utilising a zero-phase bandpass filter with a cascaded integrator-comb (CIC) filter of order 6, for the following different frequency bands: delta (0.5-2 Hz), delta1 (2-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), sigma (12-16 Hz), beta1 (16-20 Hz), and beta2 (20-30 Hz). Since an EOG signal might be affected by EMG, and ECG artifacts, launching a suitable algorithm in order to remove the artifacts and noise was necessary.

A cascade of three adaptive filters based on a least mean square (LMS) algorithm was employed, to eliminate ECG, and EMG artifacts [191].

4.3.2.2 Feature extractions

Several features were extracted from the EOG signal in the time and frequency domain, such as variance, the maximal peak amplitude value (MAX-PAV), the minimum peak amplitude value (MIM-PAV), energy entropy, Shannon entropy, and cross-correlation. In order to select the best feature that classified the variations in sleep stages and wakefulness, the sequential feature selection method (SFS) was used.

The definitions of the features are as follows :

- **Energy entropy (EE)**

The energy entropy was performed, utilising wavelet packets as

$$EE(s) = \sum_i \log(s_i^2) \tag{10}$$

Where (s) is the EOG signals and s_i is the coefficient of (s).

- **Shannon entropy (SE)**

The Shannon entropy was performed by utilising wavelet packets as

$$SE(s) = -\sum_i s_i^2 \log(s_i^2) \tag{11}$$

Where (s) is the EOG signals and s_i is the coefficient of (s).

- **Cross correlation**

For each 5-second epoch, the cross-correlation between each frequency band of EOG left, EOG right channels, and peak-to- peak amplitude differences from EOG left – right were calculated [137].

- **Maximum peak amplitude value**

The maximum peak amplitude value (MAX-PAV) is a measure of the EOG signal amplitude value at the highest point (i.e. the maximum positive value) in both EOG right and EOG left signals.

- **Minimum peak amplitude value**

The minimum peak amplitude value (MIM-PAV) is a measure of the EOG signal amplitude value at the lowest point, (i.e the minimum negative value), EOG right and EOG left.

- **Variance**

The variance of the EOG signal is a measure of the signal power calculated as

$$VAR = \frac{1}{N}\sum_{i=1}^{N}(x_i - \bar{x})^2$$

Where x_i is ith sample of EOG signal, $\bar{x}$ is the mean and 'N' is the epoch size for computing features.

4.3.2.3 Classification using K-nearest neighbour classifier

In this study, the K-nearest neighbour (KNN) classifier was used for classification of the sleep and wake stages. The KNN is based on a nonparametric method and can be employed for a different pattern classification approach, which represents as one robust classifier [192]. The KNN classifier is based on a comparison between a new sample (testing data) and baseline (training data). It attempts to find out the K-nearest neighbour within the baseline, and indicates a class which seems more normally in the nearest neighbour of K. The value of K might need to be diverse in order to detect the corresponding class between the training and testing data. In this study, the value of K

varies from 1 to 5. The Euclidean distance metric is utilised for calculating the distance between the two points. The training and testing data was evaluated based on 10-fold cross-validation.

4.3.2.4 Smoothing rule

The smoothing rule is used to increase the detection accuracy of the sleep stages (for more information see Table 12).

4.4 Sleep architecture statistical method

In order to evaluate the performance of the algorithms for automatic sleep stage detection, the sensitivity and specificity were calculated for each sleep stage. The inter-rater agreement (IRA) and Cohen's Kappa were calculated in order to evaluate the overall performance of the algorithms. In this dissertation the criteria of calculation sensitivity and specificity methods that were utilised for the sleep stages was done according to Devuys et al. criteria [193].

- $Sensitivity = \frac{TP}{TP + FN}$ (12)

- $Specificity = \frac{TN}{TN + FP}$ (13)

where TP is true positive; FN is false negative; FP is false positive; TN is true negative.

- The IRA was calculated as the following:

$$IRA = \frac{The\ total\ correct\ \ stage\ detection}{Total\ stages} \quad (14)$$

- The Cohen's Kappa was utilised to evaluate the IRA matrix, 'k', which can be calculated as [194]:

- $K = \frac{p_o - p_c}{N - p_c}$ (15)

where p_o is the total correct stage detection (sum of the diagonal), 'N' total stages and p_c is the expected frequency for the number of agreements that would be expected by chance for each stage.

The interpretation of Cohen's Kappa coefficient was as the follow: < 0.00 (poor agreement); 0.00 - 0.20 (slight agreement); 0.21- 0.40 (fair agreement); 0.41- 0.60 (moderate agreement); 0.61- 0.80 (substantial agreement); > 0.80 (excellent agreement) [194].

5 : Automatic classification of sleep disorders

5.1 Classification of primary insomnia, schizophrenia and healthy sleep

5.1.1 Subjects

Thirty subjects participated in this study (see date set No. 3).

5.1.2 Method

5.1.2.1 Calculating PSG sleep stage parameters

In this study, we used the visual sleep stage scoring according to the AASM rules to measure different PSG sleep stage parameters, such as sleep latency (SL), sleep efficiency (SE), number of awakenings (NW), total sleep time (TST), waking after sleep onset (WASO), slow wave sleep (SWS), REM sleep, the first REM period, and the characteristics of the sleep stages (N1, N2, N3 and R).

5.1.2.2 Decision tree analysis

A decision tree analysis was used to classify the three groups based on the following rules:

- R1 was used for the first REM period parameter to separate primary insomnia from schizophrenia patients. If R1 (first REM period) was less than two minutes then it would be classified as primary insomnia; if R1 (first REM period) was more than two minutes and less than 10 minutes it was classified as schizophrenia.
- R2 was used for the N1 sleep stage parameter to identify the primary insomnia patients that R1 was unable to identify. If R1 (first REM period) was more than five minutes and R2 (sleep stage 1) was more than 12.5 % of the total time of sleep then it was classified as primary insomnia.
- R3 was utilised for SL to distinguish between the schizophrenia and healthy (control) subjects. If R3 (SL) was less than 19 minutes, then it was classified as a

healthy control. All of these rules were based on some percentage of sleep stage and time duration of sleep parameters, such as SL and the first REM period. The automatic classification algorithm is described in Figure 12.

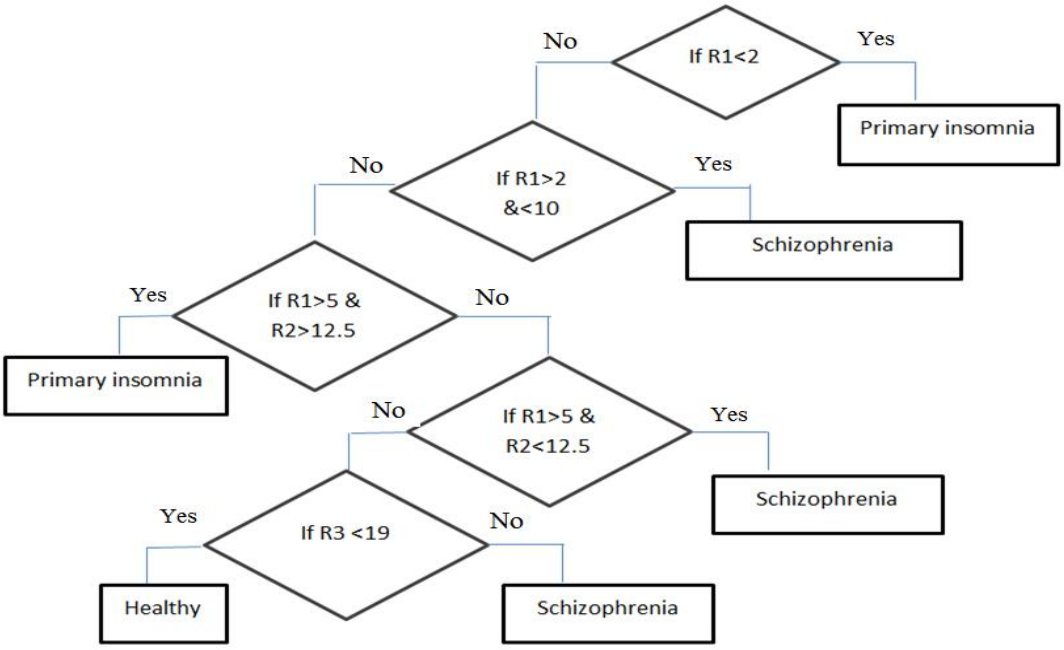

Figure 12: Flow chart describing the automatic classification algorithm for primary insomnia, schizophrenia and healthy (control) patients based on the decision tree analysis. R1 is characterised by the first REM period in minutes, R2 by the % of sleep stage 1, and R3 by the SL in minutes.

5.1.2.3 Statistical analysis

A statistical analysis was conducted using post-hoc tests to ascertain whether there were significant differences between the three groups. Sensitivity and specificity tests as well as Cohen's Kappa were conducted to evaluate the automatic classification algorithm for the three groups.

5.2 Classification of PLMS, SAHS and healthy sleep

5.2.1 Subjects

Thirty subjects were utilised in this study (see data set No. 2 in section 3.1.2).

5.2.2 Method

5.2.2.1 Computing PSG sleep stage parameters

In order to classify the PLSM, SAHS, and healthy (control) subjects, different PSG sleep stage parameters were first computed, such as SL, SE, the number of times the subject woke up (NW), TST, WASO, SWS, and REM. During the first REM period, characteristics of the sleep stages (N1, N2, N3 and R) were based on the automatic detection system detailed in the previous section (4.3).

5.2.2.2 Decision tree analysis

A decision tree analysis was preformed to classify the three groups of subjects based on the following rules:

- Rule (1) used the percentage of the sleep stage N1 parameter to separate the SAHS patients from the PLMS patients and healthy (control) subjects. If N1 (%) was more than 7% and less than 9% of the total sleep time, then a subject was classified as an SHAS patient; if N1 (%) was less than 4% of the total sleep time, then a subject was classified as a healthy (control) subject; if N1 (%) was more than 10% of the total sleep time, then a subject was classified as a PLMS patient.
- Rule (2) used the percentage of the N2 sleep stage parameter to separate the SHAS from PLMS patients. If N2 (%) was more than 80% of the total sleep, a patient was classified as an SAHS patient; If N2 (%) was less than 80% and more than 60%, of the total sleep, a patient was classified as a PLMS patient.
- Rule (3) utilised slow wave sleep duration (SWSD) in minutes and the percentage of the N3 sleep stage to discriminate between PLMS and healthy (control) subjects. If SWSD was more than 70 minutes and N3 (%) was more than 20% of the total sleep, a subject was classified as a healthy (control) subject. All of these rules were based on a percentage of the sleep stage and the time duration of the sleep

parameters, such as N1%, N2%, and SWSD. The automatic classification algorithm is described in Figure 13.

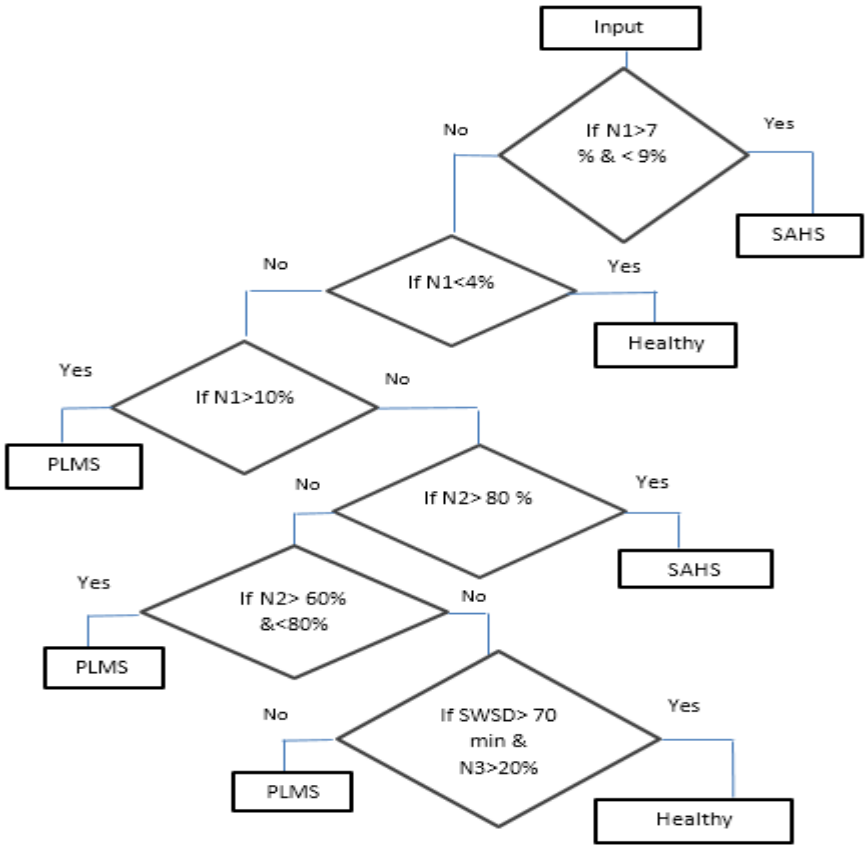

Figure 13: Flow chart based on decision tree analysis describing the automatic classification algorithm for PLMS and SAHS patients, and healthy subjects. N1 and N2 are the sleep stage percentages and SWSD is the duration in minutes.

5.2.2.3 Statistical analysis

The statistical method was mentioned in section 5.1.2.3.

6 : Results

6.1 Automatic detection of wake and sleep stage N1 using EEG sub-epoch approach

The aim of this study was to detect the W and sleep S1 based on consecutive and non-consecutive sub-epoch of EEG, and then compare the performance of the conventional 30-second epochs with the three consecutive and non-consecutive 6-second epochs for detection W and sleep S1. As an example Figure 14 shows the hypnograms for subject 22, using the parametric methods. The figure also shows the difference between using 30-second epochs and three consecutive and non-consecutive 6-second epochs for identification of the W and sleep S1. From Figure 14, it is clear that the three consecutive and non-consecutive 6-second sub-epochs provide slightly better results than the 30-second epoch method. In addition, the non-parametric method showed lower detection accuracy for the W stage but higher detection accuracy for sleep S1. It is clear from Table 13 that the non-consecutive 6-second epoch method was able to detect both sleep stages better than the 30-second epoch method.

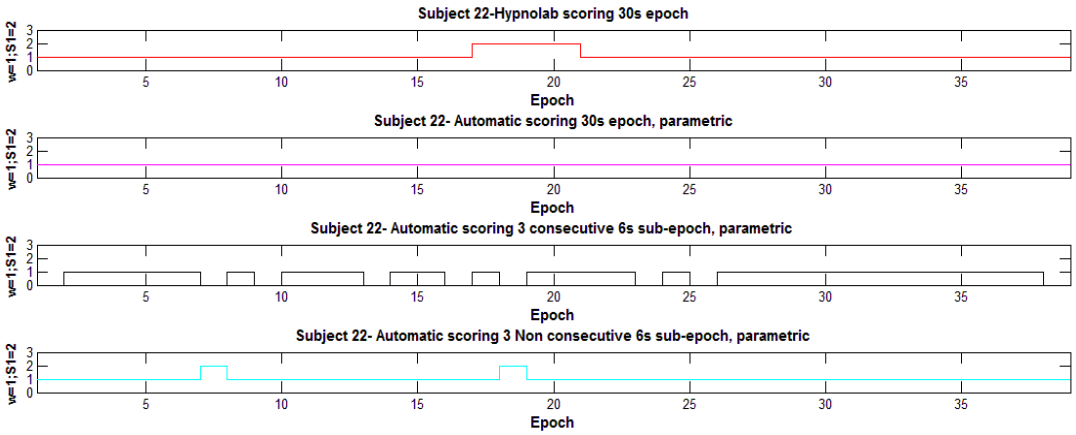

Figure 14: The hypnograms for subject S22 using the parametric approach, comparing the 30-second and the three consecutive and non-consecutive 6-second epochs methods. 'W' = the wake stage; 'S1' =stage 1; 0 = misclassification.

Table 13 describes the count of W and stage S1 epochs automatically detected by the parametric and non-parametric methods, and compared to the commercial 'Hypnolab' tool. The 20-minute PSG recording translated into 39 epochs, each epoch consisting of 30-second epochs (the last 30 seconds were not scored). While the sum of the W and S1 epochs was expected in all subjects (there were no other stages present), the W stages were all accounted for both parametric and non parametric and its three methods (30-second epoch, consecutive and non-consecutive sub-epochs). However, for S1, not all epochs were detected with the three epoch/sub-epoch methods. Some subjects did not have any stages detected by Hypnolab, such as S18, S23, S29 and S30. Therefore, the validation for S1 for those subjects was not available (noted by N/A in Table 13). Also, for some subjects the consecutive and non-consecutive sub-epoch methods showed instances of not classified or misclassified, noted by M/C in Table 13.

Table 13: The count of W and S1 stages scored epochs from the three automated detection methods using parametric and non-parametric spectral density functions, and compared with the commercial 'hypnolab' sleep scoring.

Method	Non-Parametric						Parametric						'Hypnolab'	
	Wake stage scored epochs			Stage 1 scored epochs			Wake stage scored epochs			Stage 1 scored epochs			Wake & Stage 1 scored epoch	
Subject	30-s epoch	3 consecutive 6-s sub-epoch	3 non-consecutive 6-s sub-epoch	30-s epoch	3 consecutive 6-s sub-epoch	3 non-consecutive 6-s sub-epoch	30-s epoch	3 consecutive 6-s sub-epoch	3 non-consecutive 6-s sub-epoch	30-s epoch	3 consecutive 6-s sub-epoch	3 non-consecutive 6-s sub-epoch	Wake 30-s scored epochs	Stage 1 30-s scored epochs
S18	39	38	39	N/A	N/A	N/A	39	36	39	N/A	N/A	N/A	39	N/A
S19	13	12	21	26	9	18	35	26	35	4	M/C	4	34	5
S20	27	14	20	12	11	19	39	23	35	M/C	M/C	4	33	6
S21	25	30	36	14	1	3	39	30	37	M/C	M/C	2	35	4
S22	35	25	36	4	2	3	39	30	37	M/C	M/C	2	35	4
S23	8	2	6	31	2	33	39	31	37	M/C	1	2	39	N/A
S25	33	16	26	6	M/C	13	39	30	38	M/C	M/C	1	38	1
S27	34	34	38	5	1	1	39	28	36	M/C	1	3	28	11
S29	33	25	34	6	M/C	5	39	33	39	M/C	M/C	-	39	N/A

S30	33	36	39	6	M/C	M/C	39	31	38	M/C	M/C	1	39	N/A
Mean	**28**	**23**	**29**	**12**	**4.3**	**11.8**	**38.6**	**29.8**	**37.1**	**4**	**1**	**2.37**	**35.9**	**5.1**
S.D.	**10**	**11**	**10**	**9**	**4.4**	**11**	**1.26**	**3.58**	**1.44**	**0**	**0**	**1.18**	**3.6**	**3.3**

Note: N/A = not available; M/C = not classified or misclassified.

Table 14 revealed achieved an accuracy with the non-parametric spectral density 30-second epoch method of 71.4% in the wake stage and 47.5% in stage 1, while the accuracy of the three consecutive 6-second sub-epoch method was slightly lower than the 30-second method, as 59.3% in the wake stage and 35% in stage 1. The three non-consecutive 6-second method revealed a slight improvement in accuracy as compared to the 30-second epoch method (non-parametric), at 77% (increase by 5.6%) for the wake stage and 55.8% (increase by 8.3%) for S1. Moreover, for some subjects the three consecutive and non-detection method for S1 proved to be more effective over the conventional 30 sec epoch method. For example, from Table 14, the accuracy of the detection of S1 for subjects S20 and S22 was higher by 80% with the three consecutive and non-consecutive 6-seconds methods. While, the accuracy of the 30-second method was 60% for subject S20 and 25% for subject S22, the average accuracy for all 10 subjects was higher with the 30-second method as compared to the consecutive and non-consecutive methods. This standard deviation was also large in these subjects with the SD at 25-30% for the 30-second epoch and 40-46% for the consecutive and non-consecutive 6-second sub-epoch methods.

On the other hand, the parametric method revealed a significant accuracy in the detection of the W stage, wherein the accuracy of the 30-second method was 98.5%, the three consecutive 6-second method was 75.6% and the accuracy of the three non-consecutive 6-second method was 95.1%. The S1 detection was 0% for both the 30-second epoch and 6-second consecutive sub-epoch methods, and 10.8% for the 6-second non-consecutive sub-epoch.

Table 14: The comparison of the accuracy between the three automated detection methods using non-parametric and parametric spectral density functions.

Method	Non-Parametric						Parametric					
	30-s epoch		3 consecutive 6-s sub-epochs		3 non-consecutive 6-s sub-epochs		30-s epoch		3 consecutive 6-s sub-epochs		3 non-consecutive 6-s sub-epochs	
Subject /W&S1 %(	W (%)	S1 (%)	W (%)	S1 (%)	W (%)	S1 (%)	W (%)	S1 (%)	W (%)	S1 (%)	W (%)	S1 (%)
S18	100	N/A	97.4	N/A	100	N/A	100	N/A	92.3	N/A	100	N/A
S19	38.2	100	32.3	80	58.8	80	88.2	0	67.6	0	88.2	0
S20	70.5	60	35.2	80	53.9	80	97	0	61.7	0	91.1	40
S21	60.0	0	74.2	0	91.4	0	100	0	74.2	0	94.2	0
S22	91.4	25	68.8	50	100	75	100	0	77.1	0	97.1	25
S23	20.5	N/A	5.1	N/A	15.3	N/A	100	N/A	79.4	-	97.4	-
S25	86.8	100	42.1	0	68.4	100	100	0	76.3	0	97.3	0
S27	82.1	0	82.1	0	96.4	0	100	0	64.2	0	89.2	0
S29	84.6	N/A	64.1	N/A	87.1	N/A	100	N/A	84.6	N/A	100	N/A
S30	84.6	N/A	92.3	N/A	100	N/A	100	N/A	79.4	N/A	97.4	N/A
Mean	**71.4**	**47.5**	**59.3**	**35**	**77**	**55.8**	**98.5**	**0**	**75.6**	**0**	**95.1**	**10.8**
S.D.	**25.2**	**46.2**	**28.1**	**39.8**	**27.9**	**44.9**	**3.74**	**0**	**9.3**	**0**	**4.3**	**17.4**

Note: N/A = not available in subject file.

6.2 Automatic detection of sleep stages using EEG sub-epoch approach

6.2.1 Overall Performance

To help gauge the overall effectiveness of this study's automatic detection approach, it was compared with the visual scoring method done by an expert (see Table 15 for the results of the performance and comparison). The rows and columns of the confusion matrix show the results of visual detection and automatic detection, respectively. Whilst the three consecutive sub-epoch approach yielded only 64.2% (0.50 Cohen's Kappa) epoch-by-epoch agreement detection of the 5-stages for group 1, the three non-consecutive sub-epoch method gave 82.4% (0.75 Cohen's Kappa). The situation was similar for Group 2, where the three consecutive and non-consecutive sub-epoch method agreement was 71% (Cohen's Kappa = 0.62) and 86.6% (Cohen's Kappa = 0.82), respectively. Likewise, in Group 3, the overall agreement of the three consecutive and non- consecutive sub-epoch method with visual detection was 68.35% (0.60 Cohen's Kappa) and 80.85% (0.74 Cohen's Kappa), respectively.

When comparing the visual detection hypnogram to the automatic sleep stages determined by the 30-second epochs (for patient no. 8 from Group 2), a relatively poor comparison can be seen as in Figure 15. On the other hand, the automated three consecutive and non-consecutive 6-second sub-epoch methods were closer to the hypnogram that was visually scored. Upon closer inspection, when considering the finer details between the 300 and 400 epoch numbers, it can be clearly seen that the three non-consecutive approaches were more closely matched with the visual detection approach than the other methods.

6.2.2 Comparison of sleep stage detection method

As shown in Table 15, the sensitivity and specificity of the five stages for each group of patients or subjects was better for the three non-consecutive 6-second sub-epoch method than the three consecutive 6-second sub-epoch method. For example, for Group 1 the performance of the three non-consecutive method for all stages (stage (sensitivity, specificity)) was W (84.8, 89.9), N1 (68.83, 89.8), N2 (87.7, 96.7), N3 (73.4, 97.4) and R (83, 98.8), and similar to the performance for the three consecutive approach, which was W (70.9, 77.3), N1 (48.8, 64.3), N2(66.7, 92.2), N3(58.4, 94.4), R (69.1, 91.3).

Table 15: The overall performance and comparison between visual and automatic detection (by both 3 consecutive and non-consecutive sub-epoch approaches) for the three groups.

3 Consecutive 6 sec-sub epoch Method

Group1: Primary insomnia

Visual detection \ Automatic detection	W	N1	N2	N3	REM	Sensitivity (%)
W	**1460**	267	308	16	7	70.9
N1	200	**450**	116	150	43	48.8
N2	558	310	**2518**	320	75	66.7
N3	191	354	123	**982**	31	58.4
REM	82	145	10	20	**576**	69.1
Specificity (%)	77.3	64.3	92.2	94.4	91.3	
kappa	0.50					
Agree (%)	64.2					

Group2: Schizophrenia

Visual detection \ Automatic detection	W	N1	N2	N3	REM	Sensitivity (%)
W	**840**	374	57	71	35	61.2
N1	134	**534**	47	43	22	65.2
N2	1167	264	**2477**	255	57	59.4
N3	136	24	68	**1558**	6	78.4
REM	149	56	6	5	**1414**	91.8
Specificity (%)	88.9	93.6	68.9	82.8	84.3	
kappa	0.62					
Agree (%)	71					

Group3: Healthy

Visual detection \ Automatic detection	W	N1	N2	N3	REM	Sensitivity (%)
W	**1219**	703	57	194	66	52.8
N1	151	**543**	72	71	43	59.2
N2	598	415	**2638**	406	78	64.2
N3	35	9	63	**1134**	3	91.1
REM	58	46	5	3	**1130**	91.2
Specificity (%)	84.1	93.2	67.83	86.9	87.9	
kappa	0.6					
Agree (%)	68.35					

3 Non-Consecutive 6 sec-sub epoch Method

Group1: Primary insomnia

Visual detection \ Automatic detection	W	N1	N2	N3	REM	Sensitivity (%)
W	**1746**	135	161	15	1	84.8
N1	81	**661**	160	53	4	68.83
N2	238	125	**3316**	99	3	87.7
N3	64	167	211	**1234**	5	73.4
REM	80	30	1	0	**722**	86.6
Specificity (%)	89.9	89.8	96.7	97.4	98.8	
kappa	0.75					
Agree (%)	82.4					

Group2 : Schizophrenia

Visual detection \ Automatic detection	W	N1	N2	N3	REM	Sensitivity (%)
W	**1086**	189	37	45	20	82.2
N1	133	**584**	30	26	7	75.8
N2	551	63	**3522**	81	3	85.2
N3	31	2	48	**1711**	0	85.2
REM	45	2	1	0	**1582**	97.1
Specificity (%)	89.8	97.2	97.8	98.4	99.7	
kappa	0.82					
Agree (%)	86.6					

Group3: Healthy

Visual detection \ Automatic detection	W	N1	N2	N3	REM	Sensitivity (%)
W	**1664**	358	46	154	17	74
N1	183	**625**	36	28	8	68.7
N2	498	161	**3316**	154	6	80.8
N3	5	1	41	**1197**	0	96.2
REM	22	5	0	1	**1214**	97.7
Specificity (%)	89.4	93	97.3	95.7	99.4	
kappa	0.74					
Agree (%)	80.85					

6.3 Individual subject performance

To obtain a view of the performance per subject, Cohen's Kappa coefficients were computed for the automatic sleep stage detection based on the 30-second epoch, three consecutive 6-second sub-epoch and three non-consecutive 6-second sub-epoch methods for each group of patients: Primary insomnia (Figure 16), schizophrenia (Figure 17) and healthy (Figure 18).

For all three groups it can be seen from the Cohen's Kappa coefficients that automatic detection (by the three non-consecutive 6 second sub-epoch method) agrees substantially better with the visual detection (expert) than with the automatic detection by the three non-consecutive 6-second sub-epoch and 30-second approaches).

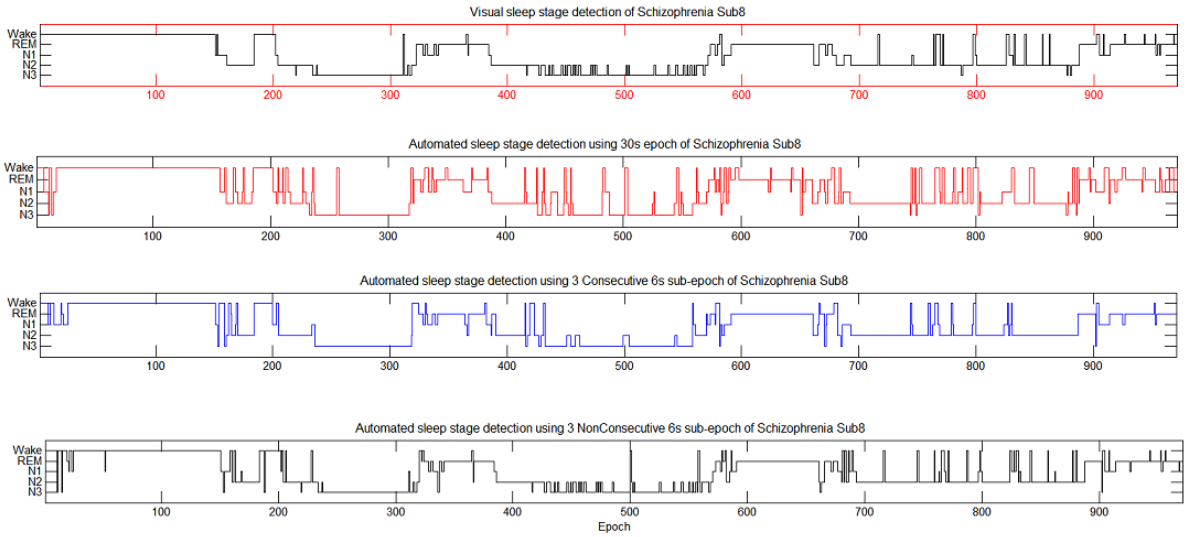

Figure 15: Hypnogram of visual sleep stage scoring versus automatic sleep stage scoring using 30-second epoch, three consecutive 6-second sub-epoch and three non-consecutive approaches, respectively.

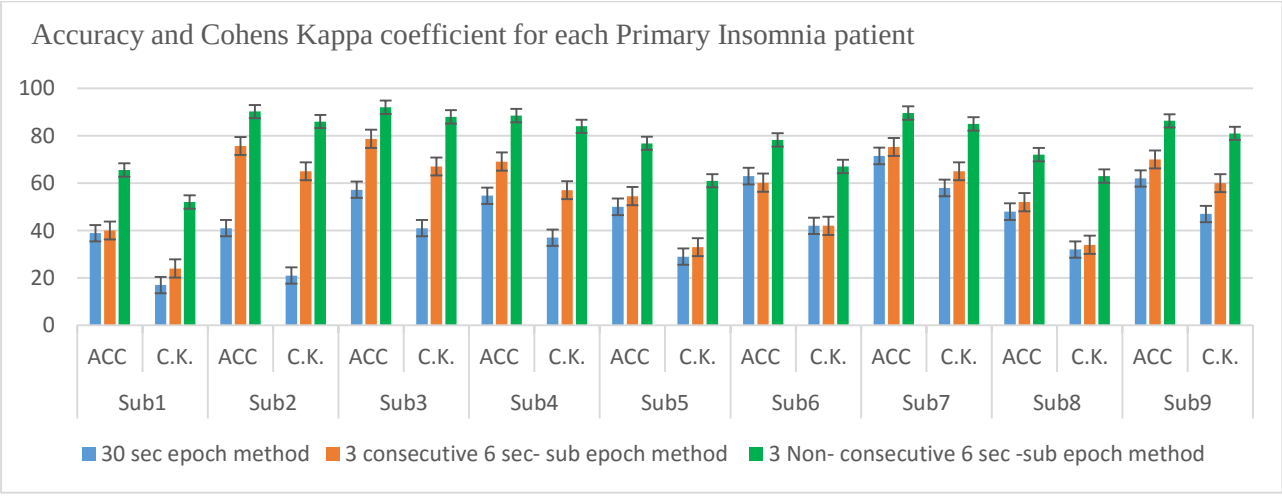

Figure 16: Cohen's Kappa (C.K.) and accuracy (ACC) agreement of automatic detection approaches using 30-secend epoch, three consecutive 6-second and three non-consecutive 6-second methods with visual detection by expert for each primary insomnia patient (n=9 subjects, Sub 1-9).

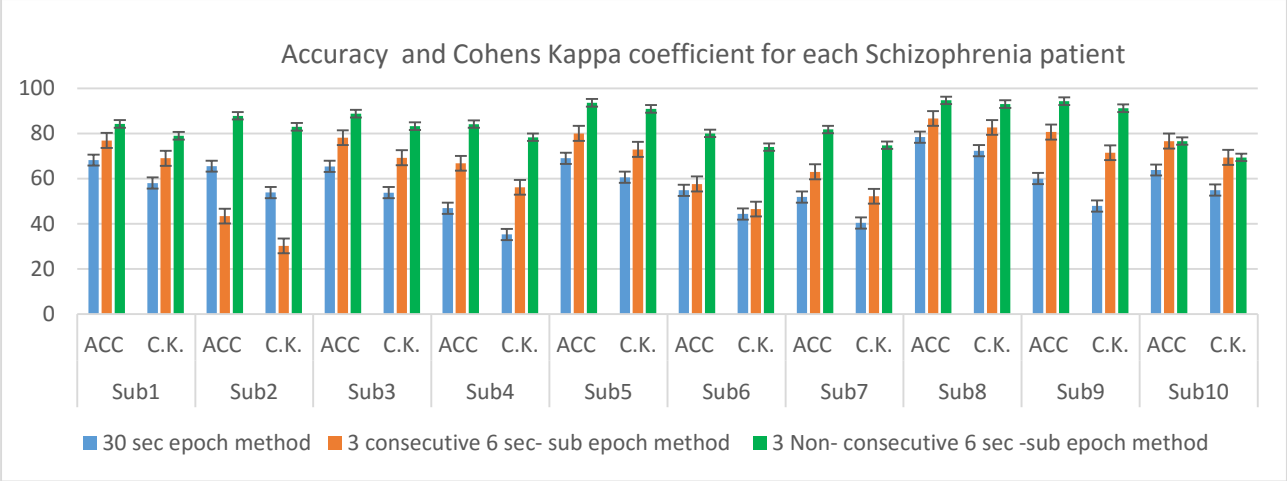

Figure 17: Cohen's Kappa (C.K.) and Accuracy (ACC) agreement of automatic detection approaches using 30-second epoch, three consecutive 6-second and three non-consecutive 6-second methods with visual detection by expert for each schizophrenia patient (n = 10 subjects, Sub 1-10).

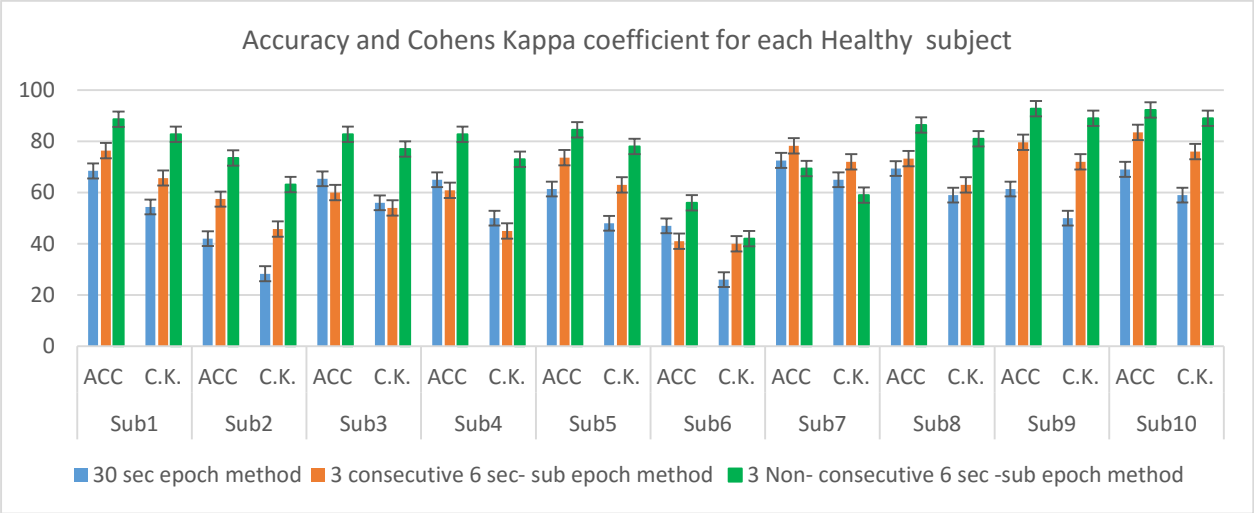

Figure 18: Cohen's Kappa (C.K.) and Accuracy (ACC) agreement of automatic detection approaches using 30-second epoch, three consecutive 6-second and three non-consecutive 6-second methods with visual detection by expert for each healthy subject (n = 10 subjects, Sub 1-10).

6.4 Automatic detection of sleep stages using EOG

In this study, the EOG signal was utilised for the detection of the sleep stages of 30 patients, comprising 10 healthy (controls), 10 PLMS, and 10 SAHS. Several features were extracted from the EOG signal based on different frequency bands, as mentioned in the previous section (refer to section 4.3.2.2). The overall agreement, sensitivity and specificity of the sleep stage detection for healthy (control) subjects were 83.5%, 85%, and 88% respectively. The Cohen's Kappa was 0.79. Table 16 shows the confusion matrix with the sensitivity and specificity after applying the smoothing rule 1, for a single healthy subject. The results showed that the best detection was in W, and N3 (the sensitivity was 91%). The detection of sleep stage N1, after utilising the smoothing rule, was significantly improved. The overall agreement, sensitivity, and specificity for the detection of the sleep stages of the PLMS patients was 80%, 82%, and 86%, respectively. The Cohen's Kappa was 0.71, which was lower than the Cohen's Kappa for the healthy (controls) subjects. The reason for this is that the normal distribution of sleep stages with healthy subjects was much more consistent than with the PLMS patients. Table 17 shows the confusion matrix, sensitivity and specificity of the sleep stages for a single PLMS patient. It is clear that the total number of sleep stage N2s was higher than the other sleep stages; therefore, the detection of stages N1 and R was slightly lower than other stages. On the other hand, the overall agreement, sensitivity, and specificity for the detection of the sleep stages with the SAHS patients were 78%, 77%, and 80%, respectively, whilst the Cohen's Kappa was lower than in the other two groups (healthy and PLMS) by 0.67. Table 18 shows the confusion matrix, sensitivity and specificity of the sleep stages for a single SAHS patient. It is clear that the lower sensitivity was in the wakefulness stages, with an improvement in the detection of sleep stage N1.

Table 16: The confusion matrix of a single healthy (control) subject.

		Automatic detection					
		W	N1	N2	N3	R	Sensitivity (%)
Visual detection	W	**575**	18	120	5	16	91
	N1	22	**238**	108	5	29	78
	N2	15	10	**2280**	39	62	80.6
	N3	3	1	168	**1018**	46	91
	R	11	3	150	43	**1065**	87.4
	Specificity (%)	90	85	70	87.4	81.2	

Table 17: The confusion matrix of a single PLMS patient.

		Automatic detection					
		W	N1	N2	N3	R	Sensitivity (%)
Visual detection	W	**524**	6	163	5	28	87
	N1	50	**150**	163	9	36	70
	N2	25	5	**3091**	13	44	80
	N3	10	0	191	**224**	19	85
	R	186	11	277	16	**836**	78
	Specificity (%)	88	88	60	87.6	82.2	

Table 18: The confusion matrix of a single SAHS patient.

		Automatic detection					
		W	N1	N2	N3	R	Sensitivity (%)
Visual detection	W	**547**	10	153	17	43	66
	N1	29	**134**	181	11	59	72
	N2	38	13	**2893**	68	138	79.5
	N3	3	2	104	**731**	24	84
	R	11	12	255	32	**968**	85.7
	Specificity (%)	85	75	66	96	85	

Figures 19, 20 and 21 show the hypnograms of visual sleep stage scoring vs. automatic scoring for a healthy (control), a PLMS and an SAHS patient, respectively. It can be observed that some sleep stages were scored as sleep stage N2 or N3 which made the hypnogram included some incorrect classifications. Figures 22, 23 and 24 show the accuracy of the selected features for the detection of the sleep stages for each group.

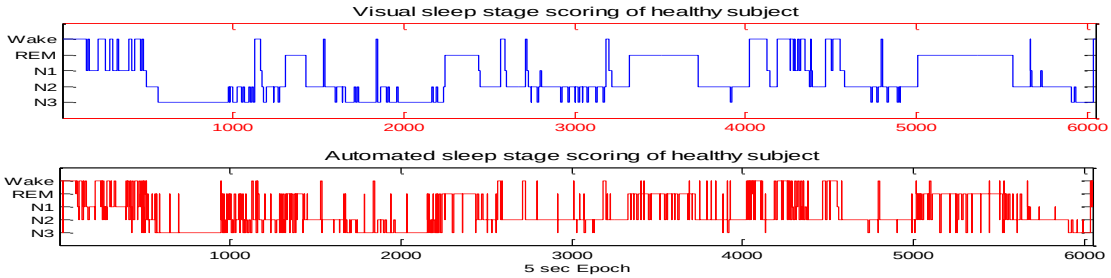

Figure 19: The hypnogram of visual sleep stage scoring vs. automatic scoring for a single healthy (control) subject.

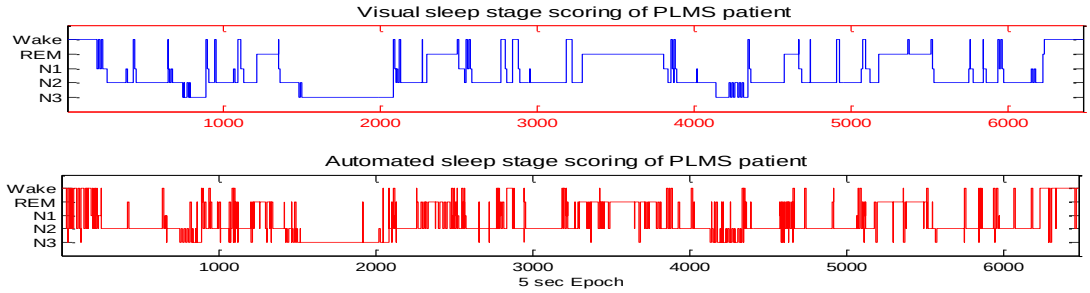

Figure 20: The hypnogram of visual sleep stage scoring vs. automatic scoring for a single PLMS patient.

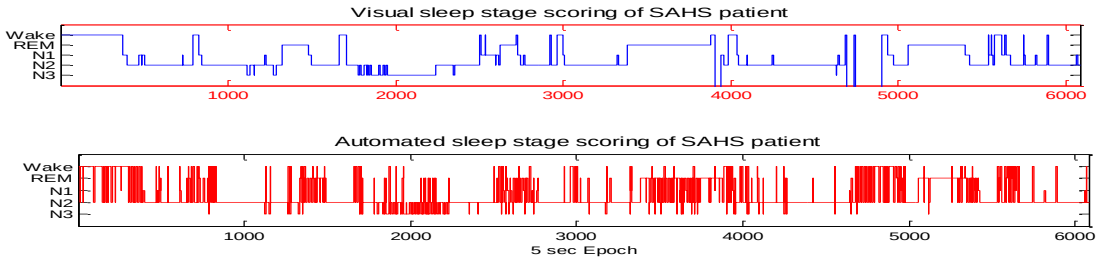

Figure 21: The hypnogram of visual sleep stage scoring vs. automatic scoring for an SAHS patient.

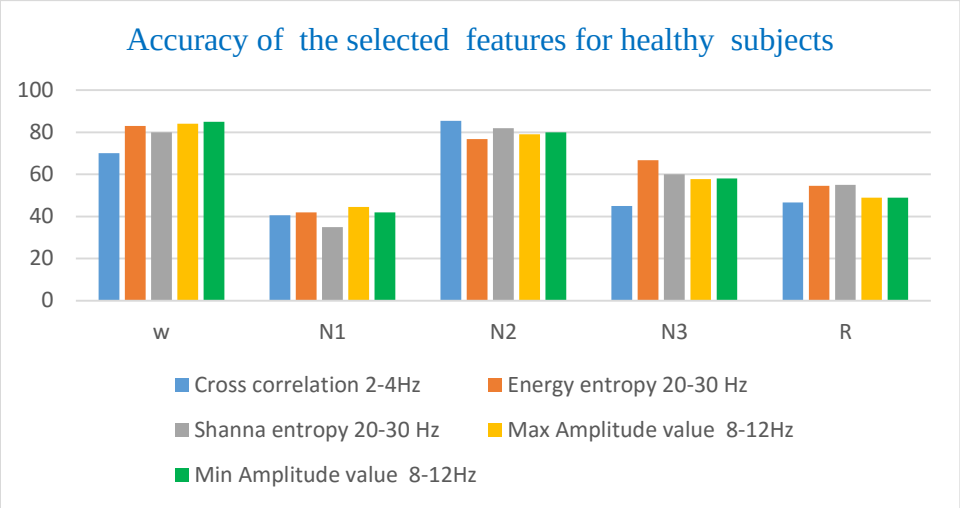

Figure 22: The accuracy of the selected features for the detection of sleep stages for healthy subjects.

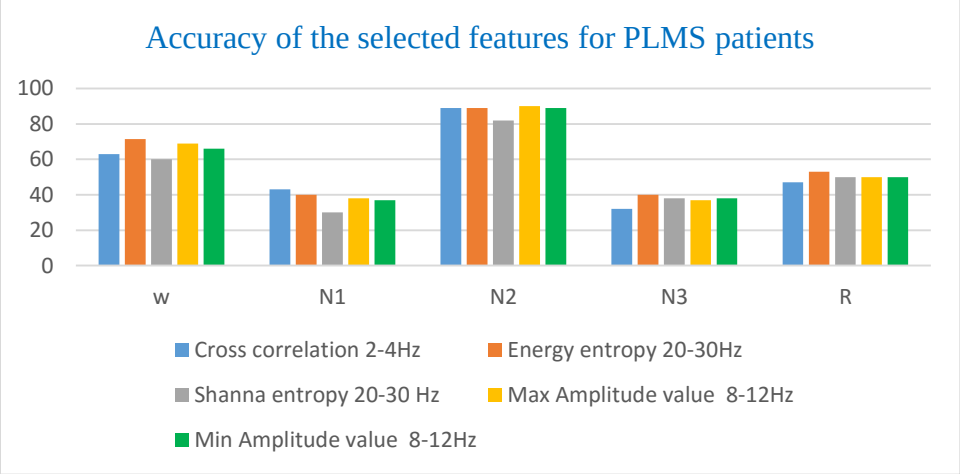

Figure 23: The accuracy of the selected features for detection sleep stages for PLMS patients.

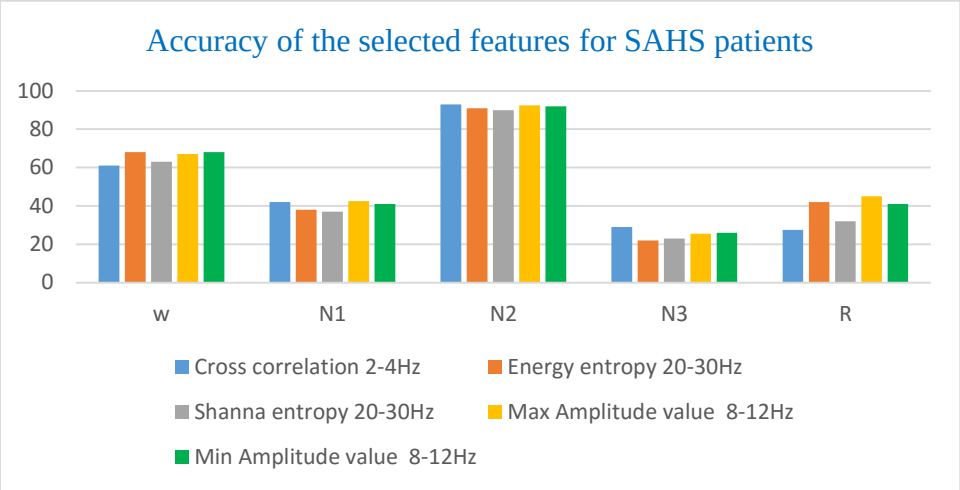

Figure 24: The accuracy of the selected features for the detection of sleep stages for SAHS patients.

6.5 Classification of insomnia, schizophrenia and healthy sleep

Figure 12 shows the automatic classification algorithm used to identify the patients with primary insomnia, schizophrenia and the healthy (control) patients. The sleep parameters of SL, the first REM period and sleep stage N1 were used to classify these three groups on the basis of the thresholds as described in the previous section (refer to section 5.1.2.2). Table 19 shows the post-hoc *t*-test analysis for the three groups of patients. There were significant differences (p = 0.01 and 0.00 respectively) between the primary insomnia patients and the healthy (control) subjects, particularly in sleep stages N1(%) and R(%). Moreover, there were significant differences between the schizophrenia patients and the healthy (control) subjects in the sleep parameters of WASO (p = 0.05), NW (p = 0.05) SWS duration (p = 0.04). The primary insomnia significantly differed from the schizophrenia patients in some sleep parameters, such as SL (p = 0.04), WASO (p = 0.00), NW (p = 0.00) and the REM duration (p = 0.00). Figure 25 shows the bar plots of the sleep parameters of the three patient groups. The

SL, NW, first REM period (FRP) and R sleep stages were all significant sleep stage parameters for the schizophrenia patients. Sleep stage N1(%) was a significant sleep parameter for the primary insomnia patients. The sensitivity and specificity of the identification the primary insomnia patients were 90% and 95%, respectively. For the schizophrenia patients, it was 90% and 81%, respectively. For the healthy (control) subjects it was 70% and 99 %, respectively (see Table 20). The level of accuracy and Cohen's Kappa was 83.4 % and 0.75, respectively.

Table 19: The post-hoc *t*-tests of the differences in the sleep parameters between the three groups.

Sleep parameters	Primary insomnia vs. healthy			Primary insomnia vs. schizophrenia			Schizophrenia vs. healthy		
	t	*SD*	*p*	*t*	*SD*	*p*	*t*	*SD*	*P*
Sleep Latency	-0.1	26	0.85	2.2	18.6	*0.04	1.3	27.8	0.21
Sleep efficiency	0.7	16.5	0.47	1.6	6.6	0.13	1.4	16.1	0.18
WASO	-0.6	73.9	0.55	-4.2	21.2	*0.00	-2.1	64.4	*0.05
Number of awakenings	-0.6	148.4	0.50	-3.4	48.8	*0.00	-2.1	128.8	*0.05
REM latency	0.4	56.2	0.67	-0.1	81.4	0.87	0.1	77.7	0.88
First REM period	-1.	5.8	0.08	1.6	8.9	0.13	0.3	10.3	0.76
Total sleep time	1.1	80.2	0.28	1.3	38	0.21	1.9	74.2	0.08
SWS duration	1.8	59.5	0.10	-0.1	38	0.88	2.3	43.3	*0.04
REM duration	-1.9	28.3	0.07	4.7	24	*0.00	1.7	34.5	0.10
N1 (%)	-7.7	20.2	*0.01	-0.8	10	0.43	-0.6	11.8	0.50
N2 (%)	-0.5	13.2	0.57	-0.9	8.6	0.34	-2	7.7	0.06
N3 (%)	1.7	13.9	0.11	-0.5	16	0.61	8.9	8.1	0.28
R (%)	-3.1	5.6	*0.00	4.3	6.3	*0.00	1.3	6.8	0.20
N1/N2	-0.8	24.5	0.41	-0.6	19.2	0.53	-1.1	28.5	0.26
N1/N3	-0.12	48.1	0.9	0.2	38.1	0.78	0.1	34.2	0.88

* $p < 0.05$.

Table 20: Confusion matrix of detection of the three participant groups based on the decision three analysis.

		Automatic classification			
		Primary insomnia	Schizophrenia	Healthy	Sensitivity (%)
True classification	Primary insomnia	9	1	0	90%
	Schizophrenia	1	9	0	90%
	Healthy	0	3	7	70%
	Specificity (%)	95%	81%	99%	
	Cohen's Kappa		0.75		

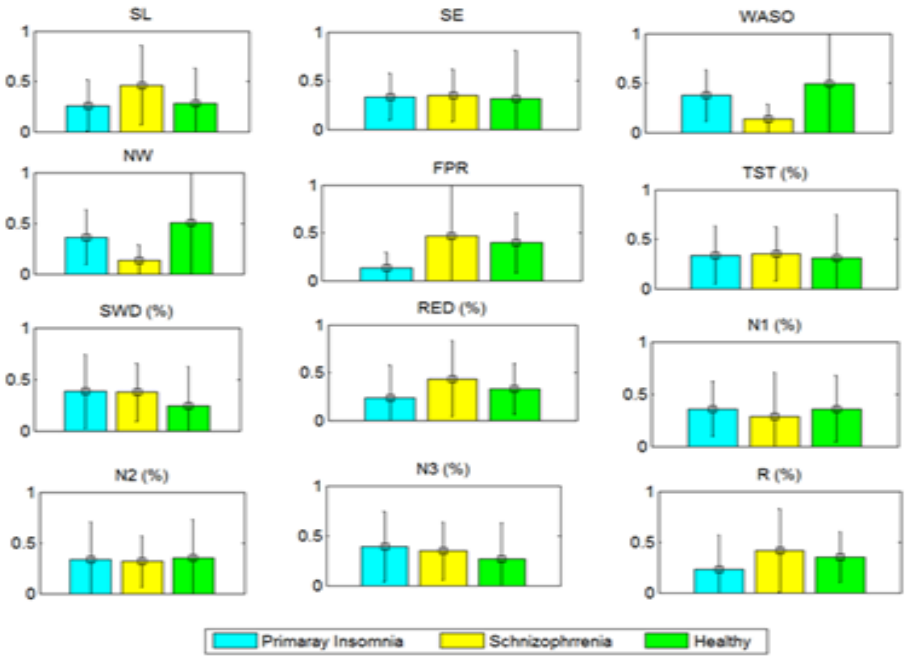

Figure 25: Bar plots of the different sleep parameters for the primary insomnia patients, schizophrenia patients and the healthy subject. SWD = slow-wave sleep duration; FPR = the first period REM; RED = the REM duration.

6.6 Classification of PLMS, SAHS and healthy sleep

Figure 13 shows the automatic classification algorithm used to classify the PLMS and SAHS patients, and the healthy (control) subjects. The significant sleep parameters of N1(%), N2(%), and SWSD were used to identify the three groups on the basis of the thresholds, as described in the previous section (see section 5.2.2.2).

Table 21 shows the post-hoc *t*-test analysis for the three groups of patients. There were significant differences between the PLMS patients and the healthy control participants, particularly in sleep stages N2(%) (p = 0.01), N3(%) (p = 0.01) and SWS(%) (p = 0.03) duration. Furthermore, there were significant differences between the SAHS patients and the healthy (control) subjects in the sleep parameters of SWS duration (p = 0.01),

REM duration (p = 0.01), and sleep stages N2 (%) (p = 0.01), N3 (%) (p = 0.01), and R (%) (p = 0.01).

Table 21: The post-hoc *t*-tests of the differences in the sleep parameters between the three patient groups.

	PLMS vs Healthy			PLMS vs SAHS			SAHS vs Healthy		
Sleep parameters	*t*	*SD*	*p*	*t*	*SD*	*p*	*t*	*SD*	*p*
Sleep latency	0.37	43.2	0.71	0.2	40.2	0.81	0.28	21.5	0.77
Sleep efficiency	-0.62	22.4	0.54	-0.57	18.3	0.57	-0.24	14.5	0.81
WASO	0.61	94.9	0.55	0.50	81.04	0.62	0.29	59.6	0.77
Number of wakings	0.58	1.13	0.57	0.48	193	0.64	0.28	143	0.78
REM latency	1.9	48.36	0.07	-0.43	101.7	0.67	1.4	95.2	0.17
First REM period	-2.07	0.08	0.06	-1.0	0.60	0.34	0.69	0.60	0.5
Total sleep time	-0.41	118.9	0.68	-0.51	90.6	0.61	-0.03	77.3	0.97
SWS duration	-2.56	70.5	*0.03	50.2	0.51	0.62	-6.01	34.38	*0.01
REM duration	-1.8	41.7	0.10	1.0	32.9	0.33	-3.25	33.4	*0.01
W (%)	0.30	23.2	0.76	0.30	18.8	0.76	0.08	15.38	0.93
N1 (%)	2.07	6.1	0.06	1.2	5.7	0.25	1.34	4.23	0.21
N2 (%)	2.95	16.6	*0.01	-2.93	10.2	*0.01	5.25	15.06	*0.01
N3 (%)	-3.04	15.2	*0.01	0.80	11.7	0.44	-7.61	7.30	*0.01
R (%)	-1.38	10.3	0.2	1.75	6.1	0.11	-2.78	9.03	*0.02

* $p < 0.05$.

Table 22: Confusion matrix of detection of the PLM and SAHS patients and healthy subjects based on the decision three analysis.

		Automatic classification		
		PLMS	SAHS	Healthy
True classification	PLMS	**9**	1	0
	SAHS	0	**9**	1
	Healthy	1	0	**9**
	Sensitivity (%)	90	90	90
	Specificity (%)	95	95	95
	Cohen's Kappa		0.85	

The PLMS differed from the SAHS patients within the sleep parameters of sleep stage N2 (%) (p = 0.01). Figure 26 shows the bar plots of the three groups. The SL, WASO, and NW were all significant sleep stage parameters for the PLMS patients. Sleep stage N2 was a significant sleep parameter for the SAHS patients. The sensitivity and specificity of identification in the PLMS patients was 90% and 95%, respectively, the SAHS patients was 90% and 95%, respectively, and the healthy (controls) was 90%

and 95%, respectively (see Table 22). The level of accuracy and Cohen's Kappa were 90% and 0.85, respectively.

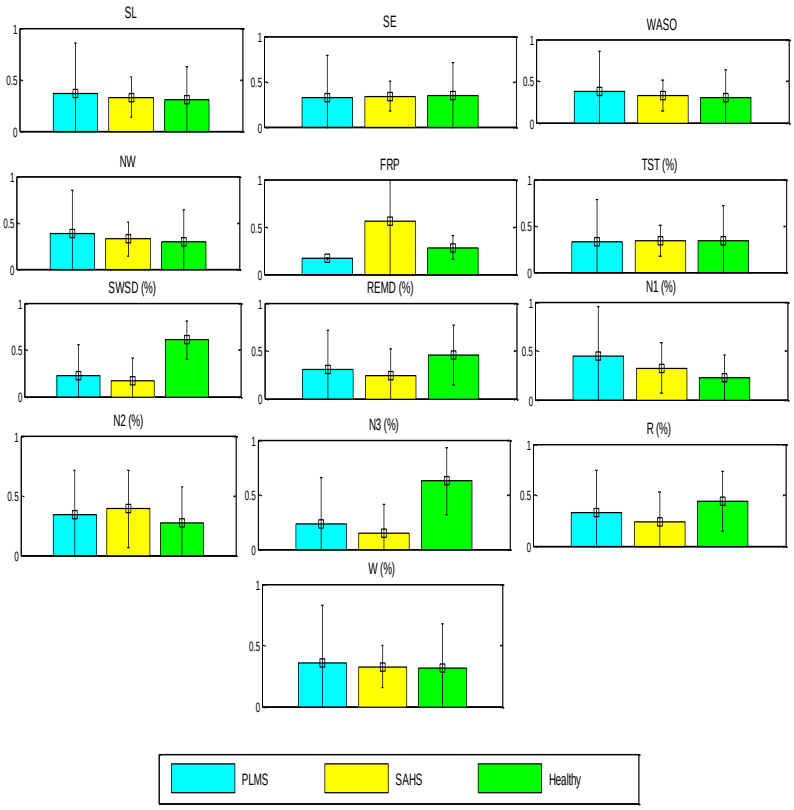

Figure 26: Bar plots of the different sleep parameters for the PLMS and SAHS patients and healthy subjects.

7 : Discussion

7.1 Automatic detection of wake and sleep stage N1 using the EEG sub-epoch approach

The results of this study confirmed the possibility of using the 30-second epoch and the three consecutive or non-consecutive 6-second epoch methods for the scoring of W and stage S1 sleep. Whilst the accuracy varied between subjects, the non-parametric method proved to be more effective with stage S1 sleep detection, whereas the parametric method was more effective for the W stage detection. The non-consecutive sub-epoch method was more effective and the three consecutive method was least effective in the non-parametric stage S1 detection. The 30-second epoch method was most effective for the parametric W stage detection.

Parametric and non-parametric methods with approach of consecutive and non-consecutive sub-epochs, using EEG signals to evaluate PSG (napping) database can contribute to improving the discrimination between W and sleep S1. These methods can also be used in evaluating the excessive daytime sleepiness (EDS) conditions.

However, there were limitations in this pilot study. There is a need to design an adaptive detector that is intelligent enough to know when to apply the non-parametric and parametric 30-second and the consultative/non-consecutive sub-epoch methods. Accuracy was calculated independently for W and S1, rather than combined. The PSG data, recorded without biofeedback conditions, would process different results, which subjects would exhibit non-induced W and S1 EEG activity. Other improvements to these results may be found in including relative EEG delta power. Also, the frequency bands that were used in this study were based on the study of Diego [178]. Therefore, further improvement may occur in the detection of S1 if the frequency band of theta to

be between 4 to 8 Hz. Moreover, using the smoothing rule that was described in the previous section (see section 4.2.2) may also improve the accuracy of detection W and S1, which was not applied in this study. Also, the pre-processed step of filtering may also need to be excluded to improve the EEG bands power computations.

7.2 Automatic detection of sleep stages using EEG sub-epoch approach

In this study, the main aim was to detect the sleep stages based on three consecutive and non–consecutive sub-epochs by using a single channel EEG (Cz location). The algorithm performance was reliable and satisfactory across all subjects. The overall agreement between the manual and automatic scoring was 67.85% for the three consecutive 6- second sub-epoch method, and 83.3% for the three non-consecutive 6-second sub-epoch method. The reason that an overall accuracy was low (see Table 15) for the three consecutive 6-second sub-epoch method, is that some 30-second epoch were not included in three consecutive sub-epoch of any sleep stages.

It is challenging to discriminate the sleep stage R from N1 or W stage with an automatic sleep detection approach [195,196] because of the criteria that scoring R sleep is based on, the EOG signal (present REM), and EMG (muscle atonic) according to the AASM standard. The spectral analysis of the EEG signal showed the frequency mixture throughout the R stage with delta and sigma band power [197, 198]. The combination between these frequencies has been reported as a distinctive EEG marker of R sleep [197]. In order to distinguish between R sleep and other sleep stages, the three consecutive and non-consecutive sub-epoch was utilised with the band power of saw-tooth (2-6 Hz) or a combination between the delta2 (2–4 Hz), sigma (12–15 Hz), beta1 (13–20 Hz) and beta2 (20–30 Hz).

Table 23 compares the three consecutive and non-consecutive 6-second sub-epoch approach with four commercial sleep stage detection algorithms of FP-STAGER [180], ASEEGA [197], ZEO [198] and ARES [199]. These algorithms all use a single EEG signal and were compared by epoch-by-epoch manual scoring. The candidature's own 3 consecutive and non-consecutive 6-second sub-epoch approach with a single EEG (Cz channel location) was also compared with the expert epoch-by-epoch scoring, as shown in Table 23.

Table 23: A comparison of candidature own approach with existing commercial algorithms based on the single EEG channel.

References	Number of subjects	Signal EEG	Sensitivity (%)	Specificity (%)	Agreement (%)	Cohen's Kappa
[180]	29	EEG (Fp1-Fp2)	-	-	80.0	0.75
[197]	15	EEG (Cz-Pz)	82.5	-	82.9	0.72
[198]	26	EEG (Fp1-Fp2)	-	-	84.0	0.57
[199]	20	EEG (Fp1-Fp2)	-	-	83.2	0.74
Candidature result	29	EEG (Cz)	82.9	95.2	83.3	0.77

Note. - = not measured.

Candidature results indicated that the detection of W stage with some subjects (in Group 3) had low accuracy (74 %), due to a very low alpha activity over Cz location, which did not satisfy the criteria of scoring the W stage. Other algorithms performed similarly [199]. Additionally, most algorithms [182, 200] showed a very low detection accuracy for sleep stage N1. However, the three consecutive and non-consecutive 6-second sub-epoch (EEG 'Cz') approach yielded improved detection of sleep stage N1.

The candidature attempted to compare the performance of the automatic detection of sleep stages based on 30-second epoch (prior to dividing the 30-second epoch into sub-epoch approach). There was a significant improvement when utilising the three consecutive and non-consecutive sub-epoch in comparison to the 30-second epoch.

This study had some limitations. Firstly, this approach was validated on a small population of young healthy and non-healthy subjects. Therefore, additional studies on elderly healthy and non-healthy subjects is necessary to fully evaluate this algorithm. Secondly, the features used in this algorithm were selected based on the optimal features for each sleep stage that were described in previous studies [153,188,189]. An algorithm can be optimised by selecting the best features for detecting each sleep stage. Finally, the sleep stage rules where optimized for this PSG data and thus the algorithm presented here may be suboptimal if utilised with different sleep stages rules or data.

7.3 Automatic detection of sleep stages using EOG and classification of PLMS, SAHS and healthy sleep

This pilot study used EOG signals for automatic sleep stage detection, and then used the data (sleep stages that detected automated to measure sleep parameters) to classify PLMS and SAHS patients and healthy (control) subjects. The overall inter-rater agreement between the visual and automatic sleep stage scoring for the three groups was 80.5%, with a Cohen's Kappa of 0.73. On the other hand, the agreement level of the automatic classification of sleep disorders was 90%, and Cohen's Kappa was 0.85.

Different features were employed extracted from the EOG signals and then fed into the KNN classifier for detection of the wake and the sleep stages. Some studies have used the decision rule-based approach with various thresholds to predict the sleep stages [137]. However the results indicated a slight improvement of the specific EEG alpha thresholds for offline applications, with an accuracy of 73%. Therefore, the present study used the KNN classifier due to its simplicity and strength in detecting the sleep stages. Several studies have employed signals in addition to EOG signals for automatic

sleep stage detection, such as EEG and EMG signals [150,151,178]. These require more electrodes and more complicated algorithms to increase the accuracy level. On the other hand, some studies used only one EEG signal for automatic sleep detection [176,201].

Since the predominance of sleep stage N2 in PLMS and SAHS patients was more than in the healthy (control) subjects, this was a distinct difference between these three groups. This led to the overall accuracy of the sleep stages of the PLMS and SAHS patients to be very low (80% and 78% respectively), which meant that the KNN classifier detected the other sleep stages as sleep stage N2. In Table 17, for example, it was obvious that the total number of occurrences of sleep stage N2 was higher than in the other sleep stages, which caused an increased overall detection of the other sleep stages or the wakefulness stage.

Similar studies have utilised the EOG signal for the detection of the sleep stages, or of one particular sleep stage such as SWS (N3) [136,201]. An automatic method was previously developed for detection of SWS based on two EOG channels [136]. This study employed the amplitude criterion for detecting SWS, and beta power [18-30] was utilised to reduce the artefact. The result showed inter-rater agreement between the visual and the developed automatic method was 93%, with a Cohen's Kappa value of 0.70. The sensitivity and specificity was 75% and 96%, respectively. Another study employed two-channel EOG with the reference to the left mastoid (M1) for the automatic sleep stage detection [136]. The synchronous EEG activity during S2 and S3 was detected by calculating peak-to-peak and cross-correlation amplitude differences in the 0.5-6 Hz range (between the two EOG channels). The result indicated that the epoch-by-epoch agreement between the visual scoring and the automatic method was 72%, with a Cohen's Kappa value of 0.63.

The second aim of this study was to utilise the automated detection of sleep stages for the purpose of classifying PLMS and SAHS patients, and healthy (control) subjects. The results provided evidence to support the use of the PSG sleep stage parameters, such as sleep stage N1(%), N2(%), and SWSD in order to automatically classify PLMS and SAHS patients, and healthy (control) subjects. The stage N1 (%) was the most significant parameter distinguishing the SAHS patients from the healthy (control) subjects. The study found that sleep stage N1 (%) was 9% for seven SAHS patients. Conversely, eight healthy subjects had a sleep stage N1 (%) for less than 5% of the total sleep duration. However, some patients with PLMS showed higher sleep stage N1 (%), which led the mean average of sleep stage N1 (%) to be higher than in the other two groups. Figure 26 presents evidence that the mean average of sleep stage N1 (%) for the healthy (control) group was lower compared with the other groups (PLMS and SAHS).

The sleep stage N2 (%) was used to distinguish between the SAHS and PLMS patients and healthy (control) subjects. This study found that most of the SAHS patients had a higher sleep stage N2 (%) (above 80%) than the PLMS patients. Figure 13 shows the threshold that was used to successfully distinguish between the SAHS patients and the other two groups (PLMS and healthy). The SWSD and sleep stage N3 (%) was used to discriminate the PLMS patients from the healthy (control) subjects. It was found that most of the PLMS patients had shorter SWSDs compared to the healthy subjects. The longest SWSD of the healthy (control) group was above 70 minutes. The reason for using sleep stage N3 (%) was because some PLMS patients had similar SWSDs to the healthy (control) group. The overall accuracy was 90%, and the Cohen's Kappa was 0.85.

7.4 Classification of insomnia, schizophrenia and healthy sleep

This pilot study provided evidence to support the use of the PSG sleep stage parameters, such as SL, FRP, WASO and sleep stage N1(%) for an automatic classification of primary insomnia and schizophrenia. The first REM period was the most significant parameter to distinguish between the primary insomnia and schizophrenia patients. The study found that this period was less than two minutes for eight primary insomnia patients. Conversely, eight schizophrenia patients showed a first REM period of 2 to 10 minutes. Figure 25 presents evidence that the mean average duration of the first REM period for the primary insomnia group was lower compared with the other groups (schizophrenia and healthy). Therefore, this parameter was used to discriminate the primary insomnia from the schizophrenia patients. To avoid misclassifications between the primary insomnia and schizophrenia patients, the sleep stage N1 (%) parameter was applied, as patients with primary insomnia showed an increase in sleep stage N1 (%) [54]. Figure 12 shows that the threshold used for addressing this problem was above 12.5% N1 (%). Therefore, the sensitivity in identifying primary insomnia from schizophrenia was 90%, which meant that nine patients from each group were accurately identified. The SL parameter was used to distinguish between the schizophrenia patients and healthy subjects since most studies have shown that patients with schizophrenia have a long SL [202]. Here, seven out of ten healthy (controls) subjects were perfectly classified and three patients were identified as schizophrenia patients, as shown in Table 20. The reason for this might be that, in relation to the schizophrenia patients, these three participants had the first degree of the schizophrenia condition. In order to investigate the sleep quality parameters, a post-hoc *t*-test analysis was used. There was a significant difference between the primary insomnia patients and healthy subjects in sleep stages N1 (%) and R(%). The

schizophrenia patients varied from the healthy subjects in some sleep parameters, such as WASO, NW and the SWSD. However, this study found that there was no significant difference between the schizophrenia patients and healthy subjects in the R(%) sleep over the total sleep stages, which could be due to the effects of the monotherapy (second generation antipsychotic). Also, while some studies have confirmed that patients with schizophrenia seemed to exhibit regular R(%) sleep stage [203, 204], the schizophrenia patients in this study showed a significant discriminate with the primary insomnia patients in the sleep parameters of SL, WASO, NW and the RED.

8 : Conclusion and future work

8.1 Conclusion

To address the abnormal phenomena that occurs during the process of sleep, a proper diagnosis by a sleep physician is required. Firstly, the aim of this thesis was to focus primarily on the evaluation of the macrostructure of sleep and the detection of the sleep stages. Secondly, the information from the sleep stage feature extracts were applied in the process of classifying various sleep disorders and healthy (control) . In this thesis, two types of PSG data were used involving the short-time PSG recording (napping) and long-time PSG recording (overnight). For these PSG recordings, multiples electrodes were utilised which often cause to sleep disturbance. Therefore, this thesis used a single electrode for the recording of the EOG or EEG signal for the detection of the sleep stages. The first type of data included only the W and N1 sleep stages. These two stages are very important for the assessment/evaluation of the EDS condition. Two techniques were employed the parametric and non-parametric methods in order to evaluate the short-time data PSG recording and analysis of the napping data. The results of this study provided evidence of the effectiveness of these methods to successfully detect the W and N1 sleep stages.

Most studies have had difficulty implementing automated detection methods to distinguish between sleep stages, in particular the sleep stages, N1 and R [14,153]. This thesis aimed to effectively overcome this problem, by applying the consecutive and non-consecutive EEG sub-epoch approach. The results confirmed the benefit of automatic sleep stage scoring based on 6-second sub-epochs. In particular, the non-consecutive sub-epoch method was a favourable method for the detection of all sleep stages and for all groups. The application of this method could be used to improve the detection of sleep stages in ambulatory sleep monitoring conditions.

In this thesis, visual sleep stage scoring information (measured sleep quality parameters) was used for the automatic classification of primary insomnia, schizophrenia and healthy (control) subjects. The results have provided evidence to support the hypothesis that the PSG sleep stage parameters, (i.e. SL, FRP, WASO and sleep stage N1) can successfully be applied to automatically classify primary insomnia and schizophrenia. The results indicated that the first REM period was the most significant sleep stage parameter used to distinguish between primary insomnia and schizophrenia patients. The results have shown that the sensitivity of identifying primary insomnia, schizophrenia and healthy (control) subjects was high.

Furthermore, this thesis aimed also, to develop an automatic method for the detection of the sleep stages based on EOG signals, and then utilised these sleep stage parameters for the classification of the PLMS and SAHS patients, and healthy (control) subjects. There is a significant advantage that supports the use of automatic sleep stage detection based on only EOG signals for future ambulatory sleep monitoring. The sensitivity of identifying PLMS and SAHS patients and healthy (control) was very high. This suggests that using an automatic classification system in screening processes is more effective and efficient compared to some standards, such as the Pittsburgh Sleep Quality Index (PSQI) [205].

In terms of publications, it can be summarised that each of the publications has addressed each of the aforementioned research aims (section 1.3) and have made a contribution to the body of knowledge.

Here, citations refer to the previous section (see List of Publications). The author's following papers (2) (3) (4) present a new approach for automatic sleep stage detection based on the sub-epoch of the EEG signal. Instead of utilising multiple electro-

physiological signals, such as EEG, EOG and EMG for the detection of the sleep stages, a single EEG signal alone can provide a significant advantage to reduce the sleep disturbance caused by multiple electrode connections and to simplify the training and eliminate the reliance on sleep experts. In addition, the classification of the sleep stages based on the consecutive or non-consecutive sub-epoch approach led to an increase in the degree of successfully distinguishing between the sleep stages. Through these publication research aims 1(a), 1(b), 1(c) and 1(d) (refer to section 1.3) are achieved and the results are validated. Thus, these provide a contribution to the body of knowledge.

The author's following papers (1) (5) (6) (see List of Publications) address the challenge in the detection of the sleep stages based on the EOG signals only. This work can be applied in the future development of ambulatory sleep monitoring by using two or four electrodes for an automatic sleep stages detection. Several features were extracted from the EOG signals to improve the detection of the wakefulness and sleep stages. The results showed a strong possibility of detecting the sleep stages using only EOG signals. Through these publications, the research aims 1(e) and 1(f) (refer to section 1.3) are achieved and the results are validated.

All these publications individually show the positive optimal outcome meeting the second research aim (develop an automatic classification of sleep disorder (refer to section 1.3))

The author's following paper (1) (7) (see List of Publications) presents a new approach for the automatic classification of sleep disorders. The existing methods rely on the Pittsburgh Sleep Quality Index (PSQI), as a standardised subjective measure to evaluate sleep quality. PSQI is based on several questions relating to the evaluation of sleep

quality for a duration of one month. This is a tedious and time-consuming task for sleep physicians. The best solution for this problem is to develop an automatic system based on PSG sleep stage parameters in order to classify different sleep disorders. Consequently, the results provide significant evidence to support the use of the PSG sleep stage parameters in the classification of different sleep disorders, thus assisting the sleep physician during the screening processes. Hence, through this publication, research aims 2(g) and 2(h) (refer to section 1.3) and results have been validated.

8.2 Future Work

In order to know when to use the parametric and/or non-parametric method, there is a need to develop an intelligent adaptive filter. Also, the development of new sleep stage rules for different patient age groups and sleep disorders is recommended for future work. Moreover, to extract more features from the EEG and EOG signals is recommended for future work to improve the detection of the sleep stages.

It is recommended to develop rules for detection of sleep stage based on the R&K manual scoring. Furthermore, it is recommended to utilise the algorithm of consecutive and non-consecutive sub-epoch EEG for detection of sleep microstructure events such as various arousals. Moreover, it is recommended to evaluate for the effectiveness of the consecutive and non-consecutive sub-epoch approaches with other PSG signals such as EOG and EMG in order to detect the sleep stages. In order to compare the accuracy and speed of detection sleep stage with respect to the consecutive and non-consecutive sub-epoch EEG algorithm, other classification systems such as artificial neural network (AAN) and support vector machines (SVM) can be tested.

Also, there is a need to extend the range of parameters and rules for the classification of sleep disorders based on sleep quality. This thesis limitation was based on the validation of an algorithm on a small population of young healthy and non-healthy subjects; there is a need for future studies on elderly healthy and patients, with a large sample size.

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