A History Of Sleep Medicine

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Abstract

The discipline of sleep medicine has grown dramatically over the past 30 years with diagnostic sleep laboratories now established in most countries. An understanding of sleep physiology and sleep disorders developed through the twentieth century. This review highlights some of the key developments and milestones in the establishment of this relatively new field of sleep medicine.

EARLY CONCEPTS REGARDING SLEEP

There has been an interest in the nature of sleep and dreams throughout recorded history. Insomnia was reported in ancient Egyptian texts and opium was used as possibly the first hypnotic medication. Our knowledge of ancient Egyptian medicine comes from the Edwin Smith papyrus, the Ebers papyrus and Kahun papyrus [1]. These medical papyri make reference to many Egyptian treatments including poppy seeds (opium) to relieve insomnia as well as an anaesthetic. Hippocrates in his texts refers to disordered sleep and dreams. Although the Hippocratic corpus is multi-authored, there are numerous references to sleep in its volumes. The text, De Victo IV, also known as, On Dreams, elaborates on sleep and dreams as a diagnostic tool for somatic complaints [2]. Dreams also played an important role in the writings of Galen. His treatise, On Diagnosis from Dreams (De Dignotione ex Insomnis Libellis) describes dreams, which may mirror the conditions of the body [3]. Dreams and interpretation of dreams are also prominent in sacred texts including the Old and New Testaments of the Bible. Despite these early references, the scientific interest in sleep has emerged over the past 100 years and the field of sleep medicine itself has only existed since the 1970's.

The monograph, The Philosophy of Sleep was written by the Scottish physician, Robert MacNish in 1830 with the first American edition in 1834 [4]. MacNish regarded sleep as a passive process during which the brain had a recuperative function associated with reduced sensory input. Wakefulness on the other hand, represented the activated state of the brain. This dichotomy in which sleep was seen as a passive process and wakefulness as an active state was the prevailing view until scientific discoveries of the mid twentieth century.

MacNish's text approached sleep from a philosophical rather than experimental position. The first text to analysis sleep from a physiological perspective was Henri Pieron's text entitled, Le Probleme Physiologique Du Sommeil [5]. Peiron was a French scientist who published his text in 1913 and the volume is regarded as the beginning of the modern approach to sleep research.

A variety of theories were advanced in the late nineteenth and early twentieth century with regard to the nature of sleep. A vascular theory was popular and proposed that during sleep the blood flow to the brain was reduced and accumulated in the digestive tract. Around the end of the nineteenth century, a chemical process gained popularity with the theory that toxins developed during wakefulness and were gradually eliminated during sleep. The French physiologists Legendre and Pieron did experiments on sleep deprived dogs [6]. When they injected serum from these dogs into awake dogs they became fatigued. They coined the term ‘hynotoxin' to explain this endogenous sleep factor, which promoted sleep.

The development of the EEG in 1929 by the German Psychiatrist, Hans Berger allowed the examination of brain activity during sleep [7]. A series of investigations in the 1930's established the characteristics of an EEG during sleep with the features of high amplitude slow waves and spindles and during wakefulness alpha rhythm and lower amplitude background rhythms. Berger himself documented the changing patterns of EEG associated with wakefulness and sleep. This information led investigators to question the view that sleep was a passive process. Through the EEG research,

it became evident that the brain was in a synchronised pattern of neuronal activity and was not completely idle.

The theory of the reticular activity system developed by pioneering work of Moruzzi and Magown in 1949 led to a greater understanding of the physiological processes of sleeping [8]. Their seminal paper established that the transition from sleep to wakefulness or falling asleep was associated with alterations in the synchronisation of discharges from the brain stem reticular formation to the cerebral cortex. The work of Loomis, Harvey and Hobart in 1937 classified sleep into five stages, A – E [9].

In 1929 Constantin Von Economo proposed that there was a site within the brain that regulated sleep [10]. His interest in sleep emerged from his care of patients suffering from encephalitis. He correctly observed that damage to the hypothalamus resulted in excessive sleepiness while insomnia could occur with lesions in the pre-optic area. The classic conditioning studies on dogs undertaken by Pavlov led him to the theory that sleep was caused by brain inhibition [11]. He proposed that continuous activation of the central nervous system led to sleepiness.

Knowledge regarding the chronobiology or biological rhythms in plant and animal systems gave new insights regarding the nature of sleep. In 1729, Jean Jacques d'Ortous de Mairan described a plant that opened its leaves during the day even after de Mairan blocked the sunlight exposure to the plant [12]. This was the first observation of a biological clock or rhythm, which existed even in the absence of external environmental triggers. In the early part of the twentieth century Von Frisch and Beling noted the behaviour of bees, which visited flowers only at certain times during the day [13]. The same activity was evident when bees visited a man-made feeding station. In 1910 Foral performed further experiments, which showed that bees possessed a biological clock and in 1906 Simpson and Galbraith using a light/dark cycle demonstrated circadian rhythms in animals. Bunning in 1935 coined the term ‘biological clock' which he proposed existed in humans and could in part explain the nature of sleep/wake cycles [14].

THE MODERN ERA

The work of Nathaniel Kleitman at the University of Chicago identified rapid eye movement (REM) sleep and represents a pivotal stage in the development of sleep medicine. Dr Kleitman who is regarded as the father of American sleep research began his work in the 1920's examining sleep and wakefulness and the nature of a circadian rhythm. In 1951, Dr Eugene Aserinsky, a doctoral student, observed rapid eye movements firstly in sleeping infants and then in adults. Their work initially consisted of observational studies carried out throughout the night. It was refined by the application of electro-oculography (EOG), which allowed them to record the bursts of electrical potential changes associated with eye movements. Their observational studies did not allow the differentiation between slow and rapid eye movements, but this clearly became apparent when measurements were taken with EOG. Their seminal paper was published in 1953 describing REM sleep and this represented a break-through in sleep research [15].

Figure 1

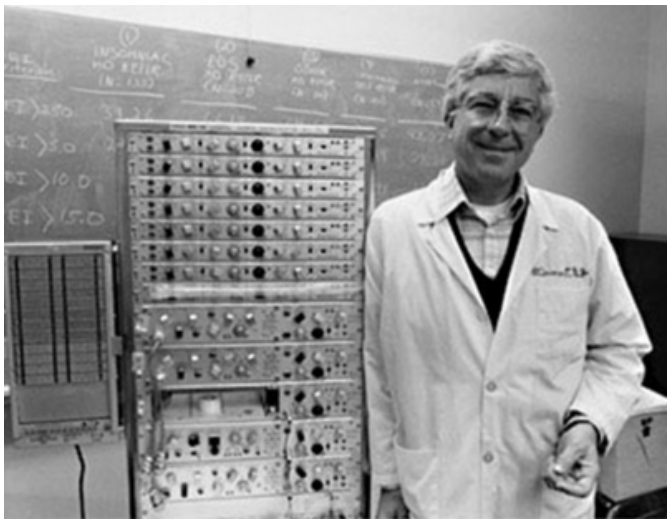
Figure 1: Dr Nathaniel Kleitman, University of Chicago

Dr William Dement was another of Kleitman's graduate students and in a series of papers he described the cyclical nature of sleep and the association between REM sleep and dreaming. The work of Dement and Kleitman established the cyclical nature of EEG recordings during sleep which occurred at intervals between 90 and 100 minutes. They observed the association between REM sleep and dreaming. During REM sleep the brain wave patterns resembled light sleep. This pivotal work further supported the concept that sleep could not be regarded as merely a passive state distinct from wakefulness [16]. Principally through the discoveries of Kleitman and Dement, sleep was classified as either non-REM or REM sleep. Non-REM was further divided into 4 stages, numbered 1,2,3 and 4. The onset of sleep is typically stage 1 with progression into later stages. Sleep becomes

deeper in stages 3 and 4 also known as delta sleep. REM sleep is also known as stage 5.

Figure 2

Figure 2: Dr William Dement, Stanford University



The observation of REM sleep in cats associated with an activated EEG, twitching of whiskers and paws led to a further questioning about the passive nature of sleep. Important studies undertaken by Michel Jouvet in Lyon, France incorporating EMG as well as EEG analysis during sleep led him to propose that REM sleep was an independent state of alertness. He referred to this as 'paradoxical sleep' [17]. Microelectrode studies on cats undertaken by Evarts and investigations of cerebral blood flow by Reivish and Ketty further established that REM sleep was an active process [18].

SLEEP APNOEA

The condition of sleep apnoea was discovered independently by Gastaut, Tassinari and Duron in France and Jung and Kuhlo in Germany [19,20]. Apnoea is derived from the Greek; a-, privative and pnéein, to breath. The reports both appeared in 1965 with the observation of patients with excessive daytime sleepiness, snoring and breathing abnormalities during sleep. This was the first conclusive evidence that disordered sleep could be associated with daytime somnolence.

Knowledge of sleep disorders has a much longer history. William Osler observed the association between obesity and hypersomnolence and described the obesity-hypoventilation syndrome in 1918. He coined the term 'Pickwickian syndrome' based on the literary reference of Charles Dickens to Joe in the Pickwick Club. Joe was a somnolent young man referred to in Charles Dickens, The Pickwick Papers (The Posthumous Papers of the Pickwick Club) [21]. 'Fat Joe' had such profound sleepiness that he fell asleep standing up while in the process of knocking on the door. Subsequently sleep apnoea was frequently referred to as the Pickwickian syndrome. This term is now reserved for patients with obesity and hypoventilation. It is characterised by obesity (body mass above 30 Kg/m2), hypoxia and hypercapnia as a result of hypoventilation during sleep. Obstructive sleep apnoea often co-exists [22].

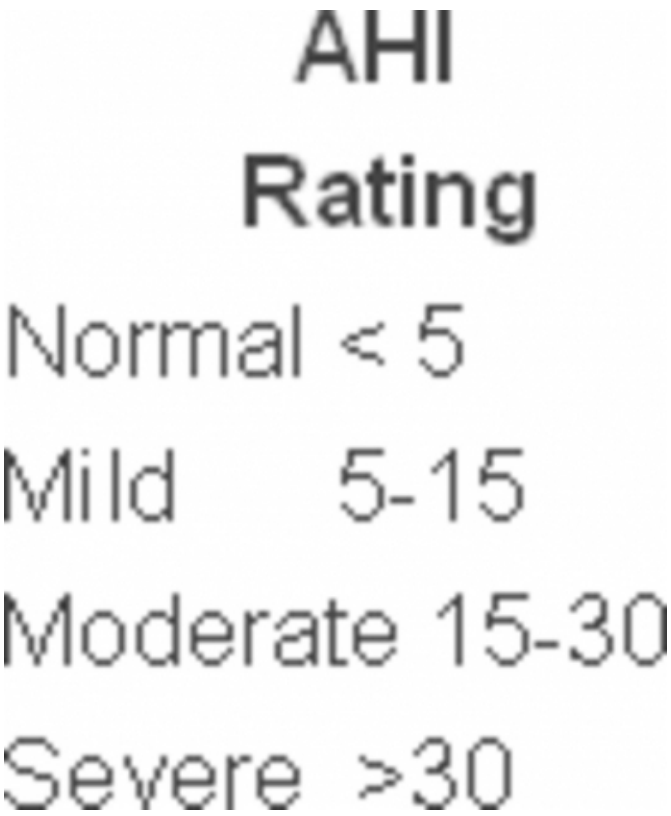
Tassinari and Lugaresi in Bologna in 1970 provided a full description of the sleep apnoea syndrome [23]. For the first time they noted the occurrence of sleep apnoea in non-obese patients and outlined the cardiovascular complications in this condition including hypertension and stroke. Initially sleep apnoea was considered an uncommon condition without known neurological or vascular complications.

The current understanding of sleep apnoea has depended on the recording of EEG and respiratory movements during sleep. Newer techniques made it possible to record the spectrum of waveforms on EEG to describe the stages of sleep. Modern recordings allow the detection of arousal responses in EEG, which may be triggered by respiratory events. These events could be correlated with periodic breathing abnormalities (hyponoea or apnoea) associated with oxygen desaturation.

In 1972,the first sleep centre performing polysomnography was established at Stanford University. Dr Jerome Holland a member of the group coined the term 'polysomnography' [24]. This involved all night sleep studies associated with EEG, EMG and oximetry. Their work led to standardisation of the procedure. An apnoeic event was defined as a 10 second breathing interval and either a neurological arousal (a 3 second or greater shift in EEG frequency) or a blood oxygen desaturation of greater than 4% or both. The apnoea-hyponoea (AHI) index is the number of apnoeas or hyponoeas per hour. (Figure3.) The procedures have refined since then but the development of sleep centres and the performance of polysomnography has been a worldwide feature in the last 30 years.

Figure 3

Figure 3: AHI rating in diagnosis and severity of sleep apnoea



Treatments for sleep apnoea soon developed. Tracheostomy was effective but a drastic step first proposed by Kuhlo and Doll in 1972. This led to an understanding that sleep apnoea was due to obstruction of the upper airway. Uvuloplatopharyngoplasty (UPP) was developed for snoring, but with limited effectiveness for the apnoea syndrome. The first report of continuous positive airways pressure (CPAP) was by an Australian chest physician, Colin Sullivan working in Toronto in 1981 [25]. It soon became apparent that this was an effective treatment but modification of pumps and facial masks was required. Early pumps were simply reverse vacuum cleaners and masks were glued to the face. Currently masks and nasal pillows are used which has established CPAP as the most common treatment for sleep apnoea.

Sleep medicine was recognised as a specialty by the American Medical Association in 1996. This gave formal recognition to the enormous advances made in the study of sleep and sleep disorders not only in North America but also in many countries worldwide [26]. Since the 1970's sleep medicine has been emerged as a valuable discipline in the identification and treatment of sleep apnoea and related conditions. Through the 1990's there has been an acceptance of sleep medicine and improved awareness about the condition of sleep apnoea in the community. National sleep foundations and support organisations for patients have expanded over the past decade. Despite this progress, the availability of sleep services is very uneven and the public heath challenge is to increase access to sleep investigation centres to reduce the public health burden of sleep deprivation and its consequences.

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