Role Of Sleep Disorders In Modifying Neuropsychiatric Clinical Entities

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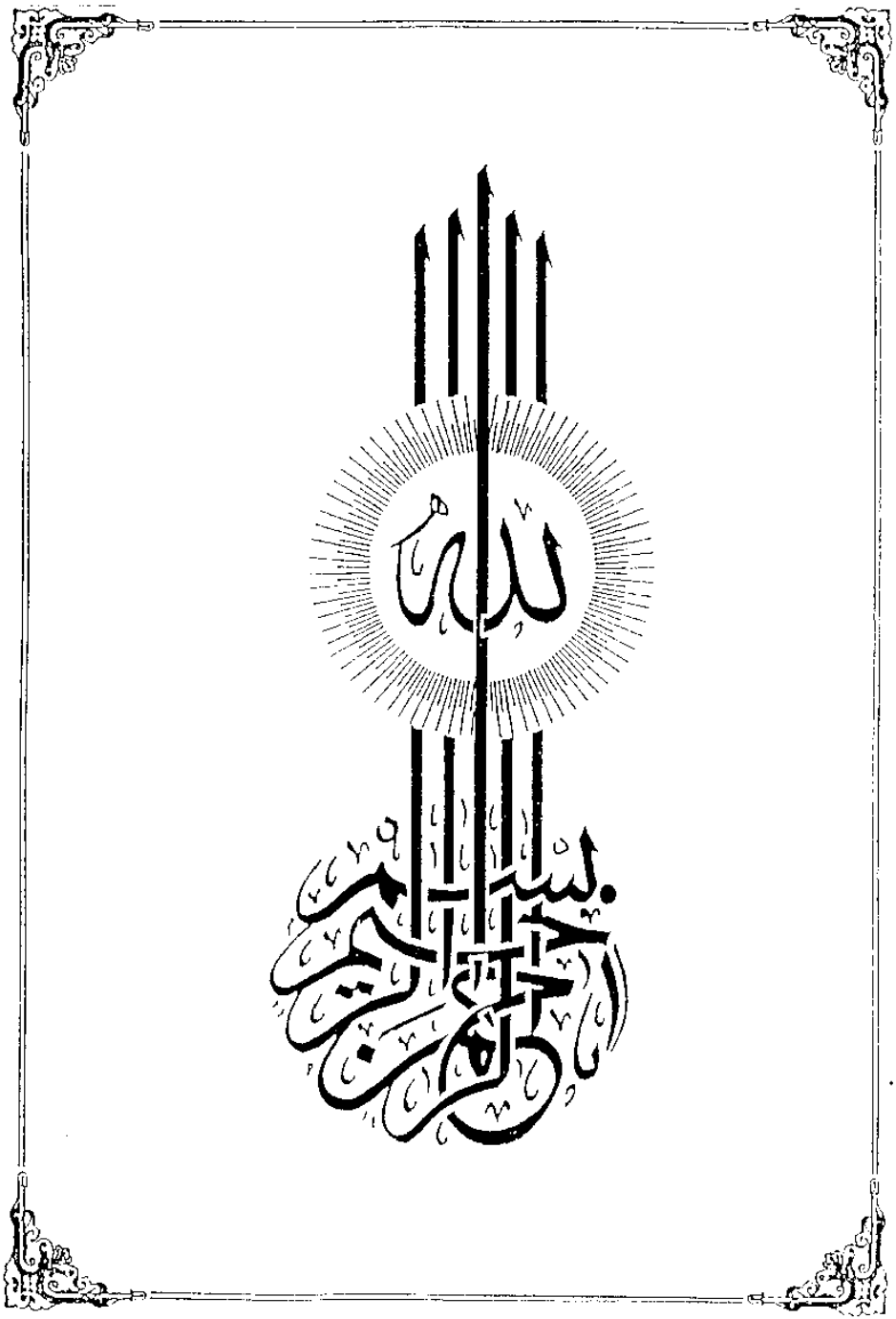

TO THE
MEMORY OF MY FATHER
AND TO MY MOTHER

CONTENTS

Acknowlegdgements II
List of Figures and Tables III
Abbreviations used in the thesis IV
INTRODUCTION 1
CHAPTER 1, BASIC MECHANISMS OF SLEEP 3
Normal Sleep And Sleep Lab. 4
Physiologic Variations In Sleep 17
Physiological Aspects In Sleep 22
Neuronal Systems Implicated In Sleep-Wake State Generation 26
Chemicals Implicated In Sleep-Wake State 37
Chemicals implicated in waking 37
Chemicals implicated In slow-wave sleep 44
Chemicals implicated in REM sleep 50
Circadian Rhythms 52
Circadian rhythms 52
Influence of the human circadian time-keeping system on sleep 63
Circadian rhythms in subjective activation, mood, and performance efficiency 66
Functions Of Sleep 69
Classification Of Sleep And Arousal Disorders . . . 77

CHAPTER 2, SLEEP IN PSYCHIATRIC DISORDERS 80
Introduction 81
Sleep In Affective Disorders 82
Anxiety Disorders 94
Schizophrenia 101
Drug Abuse 106

CHAPTER 3, SLEEP IN NEUROLOGICAL DISORDERS 113
Relationship Between Sleep And Epilepsy 114
Sleep In Degenerative Diseases 125
Parkinsonism 125
Olivopontocerebellar degeneration 131
Progressive supranuclear palsy 133
Huntington's chorea 134
Alzheimer's disease 137
Head Injury 142
Encephalitis 146
Cerebrovascular Disease 150
Brain Tumors 154
Multiple Sclerosis 156
Encephalopathy 158
Hepatic encephalopathy 158
Chronic renal failure 161
COMMENT 164
DISCUSSION 167
SUMMARY 174
REFERENCES 178
INDEX. 201

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Tables and Figures

Table 1: Nomenclature of sleep stages 8

Table 2: Examples of Circadian rhythms in medicine and physiology 53

Figure 1: Human sleep stages 16

Figure 2: Changes with age of the total amount of daily sleep and daily REM sleep 19

Figure 3: Factors that maintain the dynamic equilibrium of the upper reticular formation and the consequent level of sleepiness/wakefulness 35

Figure 4: Diagram of hypothesis of sleep reduction as final common pathway of diverse factors thought to precipitate mania 89

Abbreviations Used In The Thesis

5-HT : 5-Hydroxy Tryptamine
ACTH : AdrenoCorticoTropic Hormone
~~BP : Blood Pressure~~
BSC : Brain Stem-Cerebellar Complex
CBF : Cerebral Blood Flow
ChAT : Choline Acetyl Transferase
CNS : Central Nervous System
CRF : Chronic Renal Failure; Corticotropin-Releasing Factor
CSF : CerebroSpinal Fluid
CVA : CerebroVascular Accident
CVD : CerebroVascular Disease
DA : Dopamine
DSIP : Delta Sleep-Inducing Peptide
ECT : ElectroConvulsive Therapy
EEG : ElectroEncephaloGram
EMG : ElectroMyoGram
EOG : Electro-OculoGram
GABA : Gamma-AminoButyric Acid
HE : Hepatic Encephalopathy
HLA : Human Leucocytic Antigen
HPA : Hypothalamic-Pituitary-Adrenal
HR : Heart Rate
IGL : IntraGeniculate Leaflet
L-D : Light-Dark
LGN : Lateral Geniculate Nucleus
MAOI : MonoAmine Oxidase Inhibitor
MSH : Melanocyte-Stimulating Hormone
NA : Noradrenaline
NE : Norepinephrine = Noradrenaline
NPT : Nocturnal Penile Tumescence
NREM : Non-Rapid Eye Movement
OPCD : Olivo-Ponto-Cerebellar Degeneration
PCS : Post-Concussional Syndrome
PGD_2 : ProstaGlandin D_2
PGE_2 : ProstaGlandin E_2
PGO : Ponto-Geniculo-Occipital
PMS : Periodic Movements in Sleep
PS : Paradoxical Sleep
PSG : PolySomnoGraphy
PSNP : Progressive SupraNuclear Palsy
PTSD : Post-Traumatic Stress Disorder
REM : Rapid Eye Movement
RHT : RetinoHypothalamic Tract
RPO : Reticularis Pontis Oralis

SAD : Seasonal Affective Disorder
SCN : SupraChiasmatic Nucleus
SEM : Slow Eye Movement
SWS : Slow-Wave Sleep
TCA : TriCyclic Antidepressant
TRF : ThyroTropin Releasing Factor
TSD : Total Sleep Deprivation
TSH : Thyrotropin Stimulating Hormone
VIP : Vasoactive Intestinal Peptide

INTRODUCTION

Sleep occupies a significant percentage of our life and turns out to involve not only one, but two basic biological states of the brain and body, so the increasing possibility of sleep disorders is present. Disturbances of sleep, whether in the rhythm (the sleep -wakefulness cycle) or the quality, present an important symptom in various neuro-psychiatric disorders as affective disorders, anxiety, schizophrenias, epilepsies, cerebrovascular disorders, brain tumors, demyelinating diseases, inflammatory and degenerative disorders of the C.N.S.

The pathophysiologic mechanism underlying sleep disturbance in these clinical entities is not specific, as it reflects the patho-physiologic change in the original disease entity.

In recent years, particular chemical transmitters have been identified and localized within groups of cells in the reticular formation, and were found to play important roles in cortical activation and behavior arousal of the organism. These transmitters include NA, acetylcholine, histamine, glutamate, aspartate, GABA, peptides, adenosine and prostaglandins (Jones, 1989).

A disturbance in any of these biological mechanisms, may lead to the disruption of sleep rhythm or quality eg. drugs that enhance catecholamines are known to prolong and enhance wakefulness and vice versa .

Hence, there is no universal treatment for certain sleep disorders regardless of the etiology, but proper management is

dependent on the underlying etiology. For example, the treatment of insomnia in depression is not the same as that of insomnia associated with anxiety, schizophrenia or organic brain syndromes.

Without doubt, a much more proper management will be achieved if the exact pathogenesis of sleep disturbance in each of these conditions is understood. Moreover, this will enormously depend on knowing the pathogenesis and pathophysiologic basis of the disorder in question.

Aim of work

Correlating the pathogenesis of sleep disturbance in the various neuro-psychiatric disorders, with the pathogenic mechanisms involved in such disorders, in order to have a better understanding and hence a more suitable management of sleep disorders.

Chapter 1,
Basic Mechanisms Of Sleep

NORMAL SLEEP AND SLEEP LAB.

Sleep is an active physiological process with clearly defined electrocorticographic and behavioral changes, dependent on specific neurochemical activity of the brain stem nuclei and areas extending from the medulla to the posterior diencephalon (Moruzzi, 1963).

According to a simple behavioral definition, sleep is a reversible behavioral state of perceptual disengagement, and unresponsiveness to the environment. It is also true that sleep is a very complex amalgam of physiological and behavioral processes (Carskadon and Dement, 1989).

Within sleep, two separate states have been defined based on a constellation of physiological parameters which will be described in detail in the section of sleep laboratory. These two states are non-rapid eye movement (NREM) and rapid eye movement (REM), and they are as distinct from one another as is each from wakefulness.

NREM sleep is conventionally subdivided into four stages, that are relatively differentiated from one another, though somewhat arbitrarily. The four NREM stages (stage 1,2,3 and 4) roughly parallel a continuum of the sleep depth, with arousal thresholds generally lowest in stage 1 and highest in stage 4 (Carskadon and Dement, 1989).

REM sleep, by contrast, is defined mainly by a specific EEG pattern, muscle atonia, and episodic bursts of rapid eye movements. The most striking behavioral change in REM sleep is body paralysis

with exception of the eyes, the body being effectively isolated from the brain. Physiologically, there are two ways to prevent body movement: the brain can either withhold excitatory impulses form motor neurons, or actively inhibit them. Recently, it was found that motor neurons are actively inhibited, the caudal locus ceruleus inhibiting actions of skeletal muscles and the medial stimulating oculomotor nuclei (Bridgeman, 1988).

REM sleep is generally not divided into stages, though tonic and phasic types are often distinguished for certain research purposes. Tonic versus phasic distinction is based upon short-lived events that tend to occur in clusters separated by episodes of relative quiescence. The most commonly used marker of REM sleep phasic activity in humans is, of course, the bursts of rapid eye movements (Carskadon and Dement, 1989).

The mental activity of human REM sleep is associated with dreaming, based on vivid dream recall from approximately 80 % of arousals from this state of sleep (Hauri, 1982).

Progression Of Sleep Across The Night And The Sleep Laboratory

The Sleep Laboratory

Most Knowledge concerning sleep in humans has been gathered in sleep laboratories, Which usually function as follows: the subject, either a normal volunteer or a patient suffering a sleep disorder, comes to the lab one or two hours before his usual bed time. After the subject fills out a questionnaire concerning his day time

activity and his current mood, electrodes and sensors are applied. At least eight electrodes are needed to determine sleep stages: two central scalp electrodes (C_3 and C_4) to record an electroencephalogram (EEG), two at outer canthi of the eyes to record eye movements (the electro-oculogram (EOG)), two chin electrodes to record mentalis electromyogram (EMG), and two reference electrodes in the ear lobes (A_1 and A_2). However, for clinical assessment of sleep disorders, many more electrodes are usually required. For evaluation of insomnia, for example, one usually needs sensors that measure respiratory rate and breath-by-breath airflow, an oxymeter, EEG leads, and surface EMG leads over the right and left tibialis anterior muscles. On the other hand, a full clinical EEG is rarely obtained in sleep studies. After electrode application, the subject retires in a relatively quiet and comfortable bedroom, separate from the equipment room but connected to it electronically and by an intercom system. A technician monitors the polysomnogram: the continuous recording of EEG, muscle tension, eye movements, and other activities being observed (Hauri, 1982). EEG is the mere measurement of polysomnography. The four stages of NREM sleep are distinguished from one another principally along this dimension (Carskadon & Rechtschaffen, 1989).

Concerning EOG, there are two primary reasons to record eye movement activity during sleep. The most obvious is to record the