# sleep - its physiology & pathology

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Sleep as Oswald put it "is a recurrent, healthy condition of inertia and unresponsiveness associated with various physiological changes"; so much so that the knee-jerk disappears (though some superficial reflexes remain), urine secretion decreases, stomach secretion is reduced (inspite of increased hunger contractions), heart rate slows down (due to general body inactivity) and the blood pressure falls. The B.M.R., oxygen saturation and rate of respiration all tend to decline, so that there is a general reduction of activity. Yet recent findings about sleep indicate that it is not merely an inactivation but a different sort of vigilance and activity. The *REM* state of sleep alone, is considered on the basis of certain biochemical evidence as an active state controlled at the level of the brain stem and marked by increased cerebral metabolism. Despite a seemingly sophisticated arrangement to ensure motor paralysis through the reduction of tonic and spinal reflexes in sleep there is during the *REM* phase an outbreak of diffuse motor-impulses within the central nervous system.

**THE SLEEP — AROUSAL CYCLE**

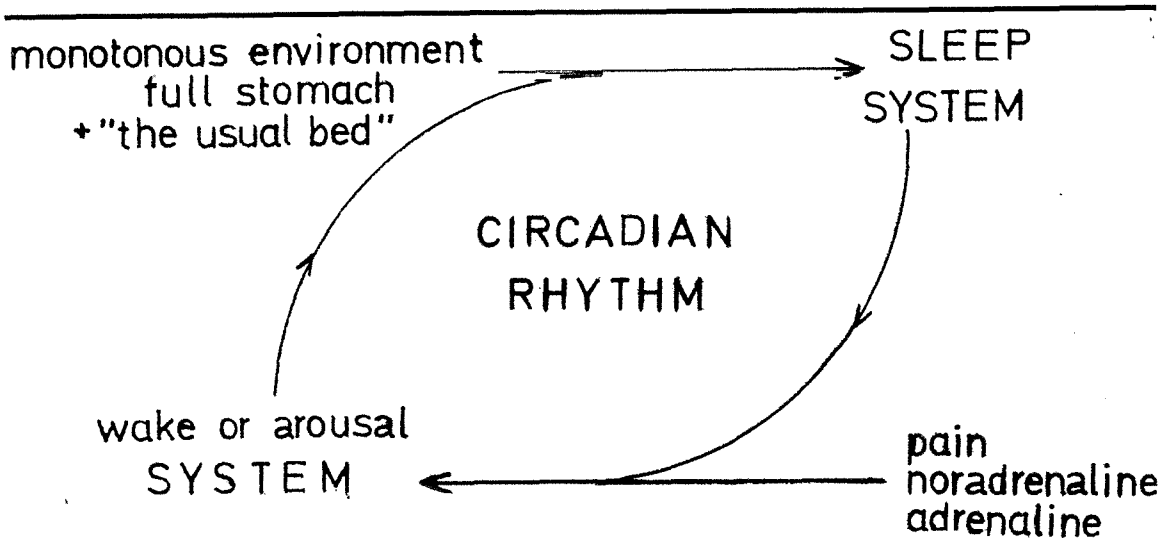
The mechanism of sleep-arousal cycles is not as yet established with certainty though we know that the sympathetic system is predominant in states of excitability and wakefulness while the parasympathetic largely takes over when sleep ensues. Hess postulated a sleep-centre in the thalamus, activation of which leads to sleep; Lindsley on the other hand later on thought that sleep is due to a "tonically acting arousal system"; the waking system of the brain is in fact today known to be the *ascending reticular activating system of Moruzzi and Maggoun* at the level of the mesencephalon; Fairly recent experiments have now demonstrated that stimulation of different mid-brain areas can produce arousal or sleep and it is now thought that the balance between the two states is determined by two antagonistic systems, reciprocally inhibitory. Furthermore the ascending reticular system probably mediates both, depending on the frequency stimulation through a polysynaptic pathway (and therefore requiring considerable temporal summation of successive stimuli) causes arousal which low frequency stimulation though a di-or trisynaptic one leads to drowsiness or sleep. Even more recently a "hypnogenic circuit" was postulated. This pathway involves the limbic system, preoptic region of the hypothalamus, interpeduncular nucleus and tegmentum. Acetylcholine crystal implantation in these regions induces sleep in cats.

Simply explained, when the arousal system is predominant it inhibits the sleep system. After some time however this inhibition diminished and the sleep system takes over gradually. There are further excitatory influences to both systems, these being direct and conditioned neural pathways and possibly chemical factors as well. While sleep is therefore facilitated by such visceral stimuli as a monotonous environment, a full stomach or a satisfied mating urge and conditioned reflexes as "the usual bed", arousal can be induced by the sensation of pain or perhaps by adrenaline. The awake-sleep balance thus depends not only on the inherent rythmicity of the mutually antagonistic systems but also on the impulses reaching these systems. A new excitation can even produce a partial or complete arousal.

It is worth mentioning here that the cortex can influence the neural excitations affecting arousal by acting on the afferent impulses. Besides the sensory stimuli these systems are affected by the "limbic system" (fibres connecting cortex and mid-brain and concrned with anxiety and emotions). Thus the hippocampal part of the limbic system gives sleep when the "emotion centre" is quiet while insomnia results in upset conditions. Experiments by Koller and Graber in 1963 pointed towards the existence of a sleep factor which was later isolated from the blood by dialysis by Honnier and Hosli. When it was injected into recipient rabbits these fell asleep soon afterwards and gave normal EEG records.

**PARADOXICAL AND SLOW SLEEP**

We can go deeper into recent findings on the subject by treating the so-called paradoxical and slow sleep separately. The former also known as Rapid Eye Movement[7], deep, fast wave, desynchronised or dreaming sleep refers to periods of sleep when muscular activity disappears completely, these are rapid eye movements and spikes of high voltage appear at the level of the pontine reticular formation, just




behind the mid-brain. Slow sleep is the orthodox sleep which often precedes it. Here cortical activity of the waking state slows down to slow waves of high voltage.

By making sections at various parts of the central nervous system it has been found that structures responsible for paradoxical sleep are situated at the level of the pons. Furthermore these lesions which suppress the tonic phenomena (paradoxical sleep is marked by tonic cortical and subcortical activity as well as phasic high voltage spikes corresponding respectively to muscular atonia and rapid eye movements) have been found to coincide with the region of locus coeruleus nuclei. These nuclei are rich in monoamino-oxidese, an enzyme playing a role in monoamine catabolism. They are in fact almost exclusively composed of neurones containing noradrenaline. MAO inhibitors have been found to permit the elective suppression of paradoxical sleep for a very long period, without affecting either waking or slow sleep (Normally increased paradoxical sleep period during recuperation of such lost sleep is approximately equal to half the duration of the experimental deprivation).

**CEREBRAL SEROTONIN**

Now histological techniques have led to the discovery of the existence of nervous structures inhibiting the reticular activating system. These have revealed the existence at the level of the raphe nuclei, situated exactly along the midline of the brain stem, of a system of neurones showing yellow fluorescence under u-v light. This fluorescence is due to neurones containing serotonin. Besides neuropharmacological indications of the role of seroronin in sleep, it has now been established (Michel Jouvet 1967) that a close correlation exists between the quantity of cerebral serotonin and the amount of time spent sleeping. In fact the greater a lesion of the raphe system, the greater the decrease in cerebral seroronin and the greater the time of wakefulness. It thus appears that cerebral monoamines are of great importance to the sleep mechanism.

**SEX HORMONES**

The many sex hormones of the human body also appear to exert a powerful influence over states of consciousness. Progesterone, for example, the sex hormone responsible for mammary gland and placenta development and others of the twelve sex hormons have been used as sedatives in experiments. Could not hormones be responsible for the exhausted sleep which follows giving birth? All normal women experience some transit between exhileration and depression at the onset of menstuation. Could not this parallel a rise and fall of some particular hormone? If there is a strong connection between sex hormones, sleep and mood, this is not an academic matter for women who take contraceptive or fertility pills every day. These are concentrations of female sex hormones whose action takes place in the brain. The required contraceptive action occurs when the synthetic harmone influences a neural region that affects the pituitary and prevents it from releasing its usual train of hormones that liberate and nourish an egg in the ovary. Instead the brain acts as if pregnancy had already begun. Just as few women react extremely to menstruation or pregnancy a few react to some of these hormones with irritation or depression and in high doses even with transitory psychosis. The compounds make their

impact on brain regions promoting fertility and on those concerned with emotions; thus they affect sleep. Experimental evidence shows that conversely some drugs such as morphine affect fertility.

**SLEEP IN DISEASE**

Perhaps the most thoroughly understood kind of sleep from the biochemical point of view is the unpleasant sleepiness of people with severe liver disease, resulting on intake of protein foods. Depression, lethargy, disorientation, odd behaviour and sleepiness are symptoms of cirrhosis and eventually lead to coma. The ammonia forming out of the nitrogen from the protein in the intestine cannot be detoxified by the liver. Thus it therefore accumulates and surges through the blood stream to the brain where it affects consciousness.

Research on brain amines may soon allow us to conquer the symptoms of depression, by drugs. The amines, compounds including noradrenaline, seotonin, depamine and tryptamine are chemically related to ammonia. It is now believed as indicated above that certain enzymes may release the potent amines from protein foods of the brain so that a drug that depletes the quantity of brain amines can then make a man depressed and vice versa. As the amine levels change so does the timbre of the personality ,the kind of sleep and its *REM* dreaming. Therefore a M.A.O. inhibitor increases the brain's amine supply giving a cheerful and alert individual after less than eight hours of sleep. Using 5 H.T.P. with M.A.O. inhibitor still increases the amine supply since the former enhances amine production. These drugs are therefore known by the name of "psychic energies."

**SLEEP DEPRIVIATION**

In the past sleep deprivation has been closely followed and found to be a stress condition met by increased ATP, adenylic acid and fructose diphosphate's specific activities; paradoxical sleep deprivation studied in various animals showed few characteristic troubles and therefore gave no clue of any vital function performed, even though recuperation was always observed. However research uncovered the facts that in the course of evolution slow sleep preceded paradoxical sleep so that reptiles do not have the latter sleeping state, hunted animals have a small percentage of it while animals of prey enjoy a relatively high proportion of it; in contrast paradoxical sleep has been found to precede the appearance of slow sleep in the development of the mammalian young. Studies on hibernation — a very much related subject, have revealed that the critical temperature which triggers off the actual falling to sleep is only the culminating point of a long sequence of physiological changes which represent a yearly rhythm, affected by a wide range of variables which tend to confuse the picture. A reduction in blood circulation and in the respiratory rate with a consequent drop in heat production have been observed during hibernation. The weights of the adrenals and pituitary drop to a third of their "summer weight", the thyroid becomes less active and there is an increased secretion of insulin and serum magnesium. The latter has a considerable effect on the nervous system especially on the parasympathetic. However, while the key secretion seems to be insulin, since it is possible to induce artificial hibernation by injections of insulin coupled with fasting, the exact roles of the pituitary and adrenals has not yet been worked out.

*Poor, good,* and *abnormal* sleep have also been compared with a view of discovering more about sleep. Experimental records have revealed that a poor sleeper sleeps closer to the waking state than the good sleeper for the simple reason that his heart beat rate is faster by about four beats a minute and his body temperature higher by some 4°F. during sleep The poor sleeper also shifts a lot more in bed and spends considerably less time in the *R.E.M.* period. Using the Cornell Medical Index it was found that the good sleepers are much more healthier. Another analysis also revealed that the poor sleepers are more anxious, introverted, hypochondriacal and emotionally disturbed than the good sleepers. Worse than a good sleeper is the insomniac who is unable to sleep for a good two-thirds of the night. Classed as abnormal sleep is also sleep resultant from narcoleptic, cataleptic seizures. Narcoleptic sleepiness takes place rapidly at wrong times and in peculiar places. About 60% of narcolptic cases however are marked with peculiar reactions to emotion. The subject in the predicament cannot laugh at a joke, spank his child or exhibit any strong feelings without collapsing into the unconscious. Of course sleep in such cases is also marked with transient hallucinations and a state of apparent paralysis upon waking. Even sleep in epilepsy (which is congenital or resulting from brain damages left by a childhood virus disease) follows emotion, fear and convulsions.

**CONCLUSION**

Therefore the regions of the brain responsible for the three states of the nervous system — wakefulness, sleep and paradoxical sleep have now been mapped out. Chemicals which appear to control those regions have also been identified but the TRUE function of sleep still remains a mystery. A number of observations and recordings are still meaningless and have to be sorted out. It is in fact really strange that a phenomenon can be analysed with such accuracy without this analysis revealing its possible functions. In spite of all this, current research on the topic is expected to lead in the near future, to a good evaluation of many medical problems, not excluding several pathological conditions.

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