

SLEEP and SLEEP DISORDERS

Role of the Preoptic Area in the Inter-relationship Between Thermoregulatory and Sleep Regulatory Mechanisms

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The sleep related changes in body temperature and the effects of environmental temperature on sleep, had given rise to the thought that the regulation of sleep and body temperature are intimately related. Another strong reason for this belief is the fact that the preoptic area which participates in the regulation of sleep is also considered as the main center for regulation of body temperature. Manipulations of the preoptic area temperature also alter sleep. The thermosensitive neurons of the preoptic area have been implicated not only in the regulation of body temperature but also of sleep. It was suggested that the thermoreceptors in the preoptic area may provide the input to the sleep-regulating mechanisms situated in this area. But the preoptic lesion and stimulation studies have shown that these regulations are controlled by independent, but overlapping neuronal mechanisms. The preoptic area could be playing an important role in fine-tuning the energy reserves, in which sleep and temperature regulations may be involved. The role of the preoptic area, in the inter-relationship between thermoregulatory and sleep regulatory mechanisms, which has given rise to the formulation of several hypotheses on sleep function, is addressed in this review. (Sleep and Hypnosis 1999;1:1-9)

Key words: preoptic area, sleep, thermoregulation, interrelationship, lesion, stimulation, energy, neuronal activity, temperature

INTRODUCTION

Several brain regions are implicated in the regulation of sleep. Similarly a number of brain regions are also involved in the regulation of body temperature. In the hierarchy of neural structures regulating the body temperature, the preoptic area (POA) plays an important role (1-4). But we cannot talk about such a hierarchy for sleep regulation. At the same time, there is growing evidence in favor of the theory that the hypothalamus is the major center regulating slow wave sleep (SWS), sleep-wake cycle, and even wakefulness, though the role of the brain stem in the genesis of rapid eye movement (REM) sleep, and the thalamus in the genesis of the EEG spindles, cannot be underestimated. Chemical stimulation and neurotoxic lesion studies showed that the medial preoptic area (mPOA) of the hypothalamus, play an important role in the regulation of sleep (5-7).

There is drastic reduction, but no abolition of sleep, after the destruction of the neurons in the mPOA. The

major deficit which is observed in the rats is the inability to maintain sleep, rather than sleep initiation (7,8).

Sleep, sleep-wake cycle and even circadian cycle of sleep were still present in those lesioned rats. Earlier lesion studies had shown a major thermoregulatory deficit in the POA lesioned animals (9,10). This had given rise to the feeling that the POA plays a major role in thermoregulation, and a less important, rather subservient, role in sleep regulation. But recent neurotoxic lesion studies, in which the neurons are destroyed, sparing the fibers of passage, had shown that the mPOA lesion does not abolish the thermoregulatory ability of the animal. But it only resets the body temperature at a higher level (11).

The range of body temperature variation is also increased, resulting in exaggerated ultradian and circadian fluctuations of body temperature in the lesioned rats.

Several terms were used for describing the area in the anterior hypothalamus which regulates the body temperature and sleep. Though the term POA is most commonly used, other terms like anterior hypothalamus, preoptic-anterior hypothalamic area (POAH), the basal forebrain are very frequently used (12-20).

In addition to these, the terms like mPOA, and lateral preoptic area, which would restrict anatomically the area

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under study, is also extensively used (7,11,21).

The usage of different terminologies not only makes the comparison of one study with the other difficult, but also renders it almost impossible to correlate the anatomical structures regulating sleep with those regulating temperature. In addition to the different terminologies used in different studies, most of the sleep studies have not paid attention to the thermal alterations taking place simultaneously with the changes in vigilance states. Similarly, studies on thermoregulation have not taken into consideration the alterations in sleep. Those few studies which have looked at both these changes have shown that these two parameters are usually altered by manipulation of the same area, and the most effective region is the mPOA (7,8,21).

In addition, there is difficulty in comparing the human thermoregulation studies with animal experiments. Though it is possible to define the thermoneutral zone as the comfortable atmospheric temperature for human beings, it is not easy to use the same definition for experimental animals. If the thermoneutral zone is defined as the range of ambient temperature in which metabolic heat production is minimal, for the inactive rat this range is approximately 26-33°C (22,23).

If the absence of behavioral thermoregulation of the rat is taken as a criterion, the range is 18-28 °C (22). The maximum REM sleep time is also used to define the thermoneutral temperature. The comparison of sleep stages in human subjects and animals is difficult, as the five-stage classification of sleep, is not possible for animals. Classification of sleep into three stages and wakefulness into two stages was the best that we could achieve for cats and rats (5,7,24). In addition, there is confusion in the literature caused by the use of the term SWS. In the human, SWS denotes a substage of non-REM (NREM) sleep, i.e. stages 3 and 4, during which slow wave activity is at a high level. In animals, NREM sleep is not divided in that manner, and SWS is used synonymously with NREM sleep. In this review also these two terms are used in an interchangeable manner, but an attempt is made to use the term preferred by the author. In addition, it is necessary to keep in mind the differences between the REM sleep in man and animals. Though the REM sleep is the deepest stage of sleep in animals, it is just the opposite in human subjects.

REGULATION OF BODY TEMPERATURE AT VARIOUS VIGILANCE STATES

The normal body temperature varies with the time of day and is apparently under a circadian control (25-27). The body temperature is altered during the various vigilance states also. In the rat, the major part of the variation of brain (cortical) temperature is accounted for by vigilance states, whereas only a minor part can be attributed to a direct effect of the circadian pacemaker (28). NREM sleep is associated with a decrease in brain temperature, and REM sleep with an increase, in many mammalian species like rabbit, rat, cat and sheep (29-33).

The close correlation between thermoregulation and sleep is formed in mammals even at an early stage of postnatal life (34). The increase in the brain temperature

together with the decrease in muscle temperature during REM sleep, as well as the decrease of both temperatures during NREM sleep were observed even in 4-day old rat puppies. It is now well accepted that all the behavioral thermoregulatory responses are possible only during wakefulness (35).

SLOW WAVE SLEEP

Changes in brain, core and tail skin temperatures, associated with transitions in the arousal states, occur in rats throughout the 24 h diurnal cycle at different atmospheric temperatures (10 °C, 21 °C and 29 °C). Falling asleep was accompanied by decreases in both brain and core temperatures at all the above mentioned temperatures. But increase in skin temperature and vasodilation were possible only at lower temperatures (10 °C and 21 °C). At 29 °C, tail vessels were permanently dilated, and further dilation was not found on sleep onset. Brain and core temperature, however, continued to decrease during NREM sleep. These changes are likely to result from reductions in heat production and increased conductive heat loss. During awakening, the changes in brain, core and skin temperature were opposite to those on falling asleep (36). It was suggested that the suppression of sleep in the cold, and the enhancement of NREM sleep in the heat, promote thermoregulation.

It has been suggested that there is an alteration in the hypothalamic thermostat during sleep, rather than a failure in thermoregulation. According to this concept, the brain temperature is actively down-regulated during SWS. The hypothalamic set points for heat production and heat loss are at a lower level in SWS in the kangaroo rat and the pigeon (26,37).

It was hypothesized that the SWS-induced brain and body cooling would lower the energy utilization and reduce cerebral metabolism. In other words, SWS acts as a protection of the brain against the sustained high temperatures of wakefulness. So, it was suggested that the POA integrates thermoregulatory and hypnogenic controls. It was proposed that the quantum of SWS or the NREM sleep is influenced by the heat load accumulated during prior wakefulness (38,39). On the basis of these observations, it was proposed that the function of SWS is to cool the brain (40).

The behavioral state-dependent changes in the hypothalamic temperature of homeotherms reflect extracerebral adjustments in circulatory variables to influence the temperature and flow of the arterial blood which could cool the brain. There are different mechanisms for brain cooling, i.e. systemic and selective brain cooling, which are affected by the changes in body posture and vasoconstrictor sympathetic outflow related to wake-sleep behavioral states (41).

The increase of slow wave activity (mean power density in the 0.75-4.0 Hz range) of rats, and the decrease of cortical temperature in NREM sleep episodes, were not correlated. The lack of a relationship between changes in cortical temperature and slow wave activity indicates that separate mechanisms underlie the regulation of brain temperature and sleep intensity (28).

There are reports which have shown that the decrease in body temperature in the initial part of a sleep period was independent of SWS (42). Furthermore, the largest fall in body temperature, often related to SWS, which peaks at the beginning of a sleep episode, is associated with the change in body posture from an upright position to a recumbent position, and not with NREM sleep stages 3 and 4 (43).

REM SLEEP

REM sleep was associated with a sharp rise in brain temperature. The rise in brain temperature was the largest in the cold and was attenuated at 29 °C in rats. Core temperature decreased and skin temperature increased in the cold, whereas core temperature tended to increase, and skin temperature to decrease, in the heat. The paradoxical peripheral vasomotion during REM sleep supports the previous suggestions on severe thermoregulatory impairment in rats during REM sleep as in other species (36).

It was generally believed that during REM sleep, thermoregulatory responses are virtually absent and body temperature becomes temporarily dependent on ambient temperature. Therefore REM sleep has been referred to as a poikilothermic state (35). But it was shown that the posterior hypothalamic lesions were followed by either a suppression of the increase (or even a decrease) of brain temperature during REM sleep while skin temperature variations were not modified. The decrease in cerebral blood flow, which was also always associated with brain temperature increase, was suppressed after the posterior hypothalamic lesion. So, it was hypothesized that the decrease in brain blood flow depends upon an active vasoconstriction process originating in the posterior hypothalamus (44).

In the cold ambient temperature, deep interscapular (just below the brown fat lobes) temperature decreases during desynchronized sleep. This change in temperature probably results from a depression in sympathetic vasoconstrictor influences, producing blood and brown fat cooling during this stage of sleep (45,46). But the increase in hypothalamic temperature during this stage of sleep occurs independently of a transfer of heat from interscapular brown fat (45,46).

Regardless of the fact that temperature regulation is suspended or not, brain temperature invariably increases during REM sleep in most mammalian species that have been investigated, including man. In human subjects, the tympanic temperature (which could be taken to represent the brain temperature), and even the forehead skin temperature, increases during the REM sleep (47). Increasing the ambient temperature from 25 to 41 °C during well-established SWS and REM sleep episodes in male subjects, showed that during REM sleep, sweat gland activity persists at a lower level than during SWS. The lower sensitivity of the thermoregulatory system during the REM sleep episodes could be interpreted as an increase of the hypothalamic set-point temperature, or as an action of extra-hypothalamic thermosensitive neurons. However, a change in the response of the sweat glands cannot also be ruled out (48).

These findings and the observation that REM sleep propensity is highest when core body temperature reaches its lowest physiological level, led to the suggestion that REM sleep represents a regulated mechanism for warming the central nervous system (49). There was an increase in oxygen consumption in human subjects during REM sleep (47). It has been shown that the increases in tympanic temperature, following REM sleep onset at 21 °C were negatively correlated with absolute tympanic temperature. The temperature of the skin of the limb extremities declined at 21 °C during REM sleep. Unsuppressed REM sleep in association with peripheral vasoconstriction and increased tympanic temperature and oxygen consumption, in cold-exposed humans, do not signify an inhibition of thermoregulation during this sleep stage as has been observed in other mammals (47). Skin temperature showed a small, but significant, increase during REM sleep at 29, 34, and 37 °C, but the rectal temperature did not change during REM sleep at any atmospheric temperature. Shivering was present during wakefulness at 21 and 24 °C but occurred only occasionally during stages 1 and 2 sleep at 21 °C. The increases in oxygen consumption and the absence of marked changes in vasomotor tone during REM sleep in the cold were unexpected and possibly indicate that REM sleep is not as thermally disruptive in humans as in other mammals (50). These differences in thermoregulation should be also viewed along with the differences in REM sleep itself, in man and other animals.

EFFECT OF AMBIENT AND BODY TEMPERATURES ON SLEEP

Further evidence for a close relationship between sleep regulation and temperature regulation has been derived from experiments in which changes in sleep were observed after experimental manipulations of ambient, body and brain temperatures.

AMBIENT TEMPERATURE

Acute exposure to ambient temperatures outside the thermoneutral range has a prominent effect not only on the temperature regulatory measures, but also on sleep. Decrease in atmospheric temperature decreases both REM and NREM sleep. REM sleep seems to be more sensitive to atmospheric temperature than NREM sleep. In the rat, a general linear decrease in the percentage of REM sleep from 23 °C to 10 °C has been reported (30,36,51). Thus, the REM sleep is reduced during that period of sleep in which the regulation of body temperature is affected. The amount of NREM sleep is also decreased by low brain and atmospheric temperatures (30,36). According to one report, cold (21 °C) produced increase in wakefulness, and decrease in stage 2 sleep, without significantly affecting other stages (47).

The ability to sleep was tested in male subjects sleeping nude, except for shorts, at 5 different ambient temperatures, ie. 21, 24, 29, 34, and 37 °C. Temperatures above or below thermoneutrality (29 °C), produced a decrease in REM sleep. This probably resulted from a general disruption of sleep processes rather than a specific

failure of the thermoregulatory system during REM sleep (50).

Even within the thermoneutral zone, low ambient temperature suppressed sleep (SWS and REM sleep) and mild environmental warming enhanced sleep in normal rats (52,53). At approximately 30 °C, maximum values of REM sleep are obtained (23,30,36,52). This effect may represent a heat-defense response. The involvement of warm-receptors was suggested in this response, as sleep induction was attenuated in rats treated with capsaicin, which cause impairment of warm-receptors (54).

BODY AND BRAIN TEMPERATURES

Despite thermoregulatory responses, there is always some small alteration in body temperature, even in homeotherms, with changes in atmospheric temperature. The body and brain temperatures in the rat increased by more than 1 °C over a 24 h period, when the ambient temperature was increased from 21 °C to 29 °C (36). Increase in the body and brain temperatures can evoke an increase in NREM sleep or SWS during recovery from heat exposure in animals and human subjects (38,39,40,55-57). SWS is facilitated when brain temperature is increased (40). It was suggested that the POA thermoreceptors may provide input to the POA sleep-regulating mechanisms to increase sleep (18). Stimulation of central receptors by changing blood temperature is likely to be an important source of the impulses driving the sleep-inducing structures of the basal forebrain (58). It was hypothesized that the SWS in mammals and birds is controlled by thermoregulatory mechanisms (49). Sleep, induced by warming of hypnogenic areas, further substantiates this hypothesis. Local warming of the POA/POAH produces sleep and increases EEG delta frequency activity during SWS (13,17,18,59). Sleep could be induced by radio frequency diathermic warming of the POA in cats and opossum (13). So, it was suggested that the POAH thermoregulatory mechanisms participate in the regulation of the depth of SWS (60). According to the hypothesis of McGinty and Szymusiak, sleep intensity, as quantified by the level of NREM sleep, is a function of the level of brain and body temperatures (40).

PREOPTIC NEURONAL ACTIVITY AS THE BASIS FOR SLEEP TEMPERATURE

INTER-LINK

The modulation of the thermoregulatory responses by the vigilance state could be also observed even at the level of neuronal activity of the POA, which has been described as the integrator. There are a number of neurons in the POAH that are thermo-sensitive. It has been demonstrated that there are neurons in the mPOA involved in the regulation of sleep and body temperature (14,15,20,61). Thermo-sensitive neurons of the POAH have been implicated in the regulation of both body temperature and SWS (62,63). Thermo-sensitivity of some POA neurons were reduced in NREM sleep as compared to the wakeful state (16,61).

Most neurons became thermo-insensitive in REM sleep. The activation of sleep-related warm-sensitive neurons and the deactivation of wake-related cold-sensitive neurons may play a key role in the onset and regulation of SWS (62,63). During SWS, a majority of POAH warm-sensitive neurons exhibit increased discharge as compared to wakefulness. Cold-sensitive neurons exhibit reduced discharge in SWS, as compared to wakefulness. Warm-sensitive neurons with increased discharge in SWS exhibited increased thermo-sensitivity during SWS as compared to wakefulness. Cold sensitive neurons with decreased discharge during SWS exhibited decreased thermo-sensitivity in SWS. In addition, some neurons that were thermo-insensitive during wakefulness became warm-sensitive during SWS. Changes in POAH neuronal thermo-sensitivity could be a component of the mechanism for stabilization of state after state transition (12).

Warm-sensitive neurons did not exhibit a significant change in thermo-sensitivity during REM sleep as compared with wakefulness and SWS (62,63). In contrast, cold-sensitive neurons exhibited decreased mean thermo-sensitivity during REM sleep compared with wakefulness. Cold-sensitive neurons as a group did not retain significant thermo-sensitivity in REM sleep. These findings are consistent with the evidence that thermo-effector responses to cooling are lost in REM sleep, whereas some responses to warming are preserved (62,63). On the other hand, when the thermo-sensitivity and spontaneous activity of thalamic midline neurons were compared with those of the neurons in areas widely regarded to be involved in thermoregulation (POAH and posterior hypothalamus), there were no significant differences in the degree of the thermo-sensitivity or the proportion of thermo-sensitive neurons in the three areas (64). Midline thalamic neurons also show changes in their discharge with changes in cortical EEG (65,66). So, the relationship with vigilance state and thermo-sensitivity is not restricted to the POAH.

CHANGES IN SLEEP AND TEMPERATURE AFTER PREOPTIC LESION

The mPOA lesions do increase the rectal temperature (11,67-69). There is also a reduction in sleep after lesion of the mPOA (8,11). It could be argued that warm-sensitive neurons which induce sleep, and may even be essential for normal sleep, have been destroyed after the lesion of the mPOA. So, the increased brain and body temperatures are not able to produce an increase in sleep. Though this is a strong argument in favor of the hypothesis that sleep is controlled by the thermoregulatory mechanism, a careful observation of the changes in temperature and sleep after lesion of the POA, casts doubts on this theory. Hyperthermia, observed during the first week after the mPOA lesion, was severe. This was followed by a constant mild hyperthermia during the subsequent weeks (7,11). On the other hand, there was no variation in the magnitude of reduction in sleep throughout the post-lesion period. Thus, there was no temporal correlation between the sleep and temperature changes after the mPOA lesion. Though hyperthermia is the commonly reported observation,

hypothermia was also reported after the lesion of the POA depending on the extent of the area involved and the technique employed for lesion (21,70,71). But, reduction in sleep is almost a consistent observation after the POA lesion. Recent transplant studies in the POA lesioned rats, also show that the recovery of these two functions are not simultaneous. The sleep came back to prelesion level by 20 days after the transplantation. On the other hand, the temperature was restored back to normal only 60 days after the transplantation. The early recovery of sleep could be attributed to the humoral substances which might be released by the graft (70,72) as sleep is said to be controlled by the dynamic interplay of the neural and humoral systems (73). On the other hand, neural connectivity of the POA graft with the host may be essential for the regulation of the temperature. It could also be possible that the respective time courses of recovery of sleep-wakefulness and rectal temperature are different. Recovery of sleep after a short period, and of body temperature after a long period, would also suggest that the sleep inducing function of the POA is not dependent on the thermoregulatory function of this area. Though it could be inferred from the results of lesion studies that both these functions are modulated by the POA, the transplantation studies suggest the possibility that sleep and body temperature are controlled through independent neuronal circuits. As mentioned earlier, moderate increase in the ambient temperature, significantly enhanced sleep, and the decrease in environmental temperature reduced it (54,74). When cats were exposed to 13 °C, 23 °C and 33 °C, they slept the maximum at 23 °C. But, after the lesion of POAH, sleep was maximum at 33 °C (69). They also showed that though sleep was reduced in the lesioned animals, it was restored to the prelesion level, when they were exposed to a high atmospheric temperature of 33 °C. High brain temperatures were required to elicit not only the normal amounts of SWS, but also the panting response, after the POAH damage. So, it was suggested that impaired hypothalamic sensitivity to heat was responsible for both deficits. These results supported the hypothesis that thermosensitive neurons participate in the tonic regulation of sleep and arousal (69). But, some other findings do not support this contention. It was shown that higher ambient temperature can increase sleep period in rats whose warm receptors (central and peripheral) have been destroyed by the administration of capsaicin (74). In our laboratory it was shown that the rats exposed to 18, 24 and 30 °C, had linear increase in sleep at higher ambient temperatures. Both SWS and REM sleep were maximum at 30 °C. There was a reduction in SWS and REM sleep after the lesion of the mPOA, but the linear increase in sleep with increase in atmospheric temperature was still present in the lesioned rats. So, it would be wrong to assume that sleep was restored when the appropriate temperatures were provided. On the other hand, these findings show that environmental temperature can influence sleep even in the absence of the mPOA neurons. It also shows that the interaction between temperature and sleep could be taking place at some level, other than the mPOA. Moreover, the ability of the warm atmospheric temperature to restore sleep, is observed not only in the POA lesioned animals,

but also in the brain stem lesioned animals. At a room temperature of 23 °C, the duration of the paradoxical sleep and their episodes were significantly reduced in cats with lesion in the pontine tegmentum. At a slightly warmer ambient temperature of 30 °C, the total REM sleep and the episode durations were increased toward normal values in the lesioned animals (75).

CHANGES IN SLEEP AND TEMPERATURE AFTER THE PREOPTIC STIMULATION

Though the possible inter-relationship between the regulations of body temperature and sleep-wakefulness was suggested on the basis of single unit and local warming studies, neurotransmitters and their antagonists, injected at the mPOA, could not always produce simultaneous alterations in sleep and body temperature (76-78). Carbachol and noradrenaline (NA) administration at the mPOA in rats produced hypothermia and arousal. But the changes in these physiological parameters did not have a temporal correlation. The arousal response outlasted the changes in body temperature (77,78). Administration of serotonin at the mPOA produced hyperthermia without any change in S-W (79). Bilateral microinjection of ethanol at the POA of rats caused a dose-dependent hypnotic effect at doses that did not affect brain temperature (80). Administration of small doses of adenosine and A1 receptor agonist cyclopentyladenosine increased sleep without affecting the brain temperature, while a non-selective adenosine A1/A2 receptor agonist N-ethyl-carboxamido-adenosine, and high doses of cyclopentyladenosine increased total sleep along with hypothermia (81). So, it is possible that the changes in S-W resulting from the mPOA stimulation are not dependent on the body temperature changes. Thus, it may be suggested that the mPOA controls sleep and temperature through independent, but overlapping, neuronal circuits (82).

Earlier studies showed that the local application of NA at the mPOA produced arousal and hypothermia (77). This was also taken as an argument against the hypothesis of an inter-link between thermoregulation and sleep, and it was suggested that sleep and temperature were regulated by two different sets of neurons in the mPOA (77). The noradrenergic (NE) fibers projecting to the mPOA may be acting on thermoregulatory neurons to bring about heat loss and hypothermia. On the other hand, it may be acting on sleep-wake regulating neurons to bring about arousal. Further studies showed that the influence of the adrenergic system on the mPOA is not as simple as envisaged.

Destruction of the NE fibers projecting to the mPOA produces an increase in wakefulness. Application of NA at the mPOA in the rats with NE fiber lesion, brought about sleep and hypothermia (5). This could be taken as an argument in favor of the hypothesis that sleep and thermoregulation are inter-linked at this area of the brain. Local application of alpha-2 adrenergic agonists (clonidine) and antagonist (yohimbine), which could preferentially act on the alpha-2 receptors, which were believed to be primarily present at the presynaptic nerve terminals, further clarified our concept (6,83,84). Though arousal was produced in normal rats by the injection of clonidine, at the mPOA, it

did not produce arousal in the rats with noradrenergic fiber lesion. Clonidine did not alter the rectal temperature in normal rats but it induced hypothermia in the lesioned rats. Injection of yohimbine, at the mPOA, induced sleep in rats with intact NE fibers. However, the sleep inducing effect of this drug was very much attenuated in the lesioned animals. There was no significant change in body temperature, in both normal and NE fiber lesioned animals, after yohimbine administration. On the basis of these findings, it was suggested that there are two separate groups of afferent noradrenergic inputs, ending on the mPOA neurons. One of them, terminating on sleep inducing neurons, is activated during sleep. Those afferents which synapses on the temperature regulatory neurons are suggested to be normally inactive and may be activated only when the heat loss mechanism is to be stimulated (6). An intact catecholaminergic pathway within the anterior hypothalamus is required for the rat's physiological control of heat loss in a warm environmental temperature (85).

These findings indicate that there are separate sets of noradrenergic terminals for regulation of sleep and body temperature and the thermal changes do not contribute towards the induced alterations in sleep-wakefulness.

ENERGY CONSERVATION AND REGULATION OF SLEEP

Closely related to the heat-load hypothesis is the hypothesis that sleep is an adaptive behavior for energy conservation (3,31,86). Sleep, especially SWS, is accompanied by a decrease in metabolic rate and energy expenditure. Total sleep and SWS are highly correlated with reduction of oxygen consumption. On the other hand, oxygen consumption showed increase during REM sleep as compared to SWS (47). There was greater decrease of oxygen consumption during sleep, as compared with wakefulness, in rats acclimatized to cold at 6 °C (87).

Furthermore, those states showing energy conservation such as hibernation and torpor, are entered via NREM sleep and have been therefore interpreted as evolutionary extensions of this sleep state (3,86). It has been recognized for a long time that hibernation and SWS are homologous processes for energy conservation. Numerous EEG studies have demonstrated that during entrance into hibernation REM sleep disappeared under cerebral temperature below 25°C, and that in deep hibernation, animals were preferentially in NREM sleep. It is also suggested that a bout of hibernation is not NREM sleep, but would be the

equivalent of a sleep debt (88).

In human subjects, sleeping at different ambient temperatures, the oxygen consumption increased during sleep as a whole as the atmospheric temperature departed from thermoneutrality (29 °C) and was significantly greater during REM sleep than during NREM sleep periods at low and high atmospheric temperatures (50). Oxygen consumption was higher in REM sleep, than in quiet sleep, not only in adults, but even in children at all ages (2 days to 3 months).

The changes in metabolic rates were not completely in tune with some of the other thermoregulatory changes, like evaporative heat loss. Total evaporative water loss fell linearly with falling environmental temperature, both within and below the temperature range at which the metabolic rate was minimal.

Sweating was occurring, both at temperatures at which the metabolic rate was minimal and at those at which it showed an increase. Thus, it was not possible to define a temperature range over which both metabolic rate and evaporative water loss were at minimum values (89).

Alteration in food intake can also disrupt sleep (90). Food deprivation in birds and squirrels resulted in a lowering of the thermoregulatory set point during sleep, along with increased SWS (55). There are reports in the literature which indicate that the REM sleep deprivation or total sleep deprivation increases the food intake (91-93). But the decrease in SWS and PS, resulting from the mPOA lesion, did not produce any increase in food intake and water intake (7). Though there was no significant persistent change in food intake, there was a reduction in the body weight of the rats after the lesion of the mPOA (7,53).

Higher locomotor activity and increased body temperature, after the mPOA lesion, would produce increased energy expenditure. This might have resulted in a decrease in the body weight as there was no concomitant compensatory increase in energy intake (food intake). Therefore, after the lesion, the animals did not recognize low energy reserves, and so they did not bother to conserve energy. Thus, it can be hypothesized that the mPOA lesioned animals had lost the mechanism for the fine tuning of food intake regulation in response to the alteration in body homeostasis. The functional integrity of the mPOA may be essential for the regulation of food intake, in response to alterations in the temperature, locomotor activity and Sleep-wakefulness. It can also be argued that the POA would normally facilitate sleep, an energy-conserving state, when energy reserves are at a critical level.

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