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REM SLEEP RELATED INCREASE IN BRAIN TEMPERATURE: A PHYSIOLOGIC PROBLEM

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INTRODUCTION

Many Authors have reported changes in brain temperature during the ultradian sleep cycle in several mammalian species. The temperature decrease in NREM sleep is not discussed here since it is a normal effect of thermoregulation operating at a lower set point temperature than in wakefulness. In contrast, the increase in brain temperature related to REM sleep appears paradoxical from the viewpoint of normal thermoregulation. The problem of the physiologic mechanisms underlying this temperature change remains unresolved (cf. 26).

Changes in brain temperature are in general relevant to both the energy metabolism of the brain and the function of the preoptic-hypothalamic thermostat. However, the increase in temperature related to REM sleep, amounting to a few tenths of a degree Celsius at most, may appear of little physiologic importance from a physicochemical viewpoint (Q10 effect). Whereas this assertion applies to neurons lacking high specific thermosensitivity, a different problem is whether such temperature change is a feedback signal for specific thermoresponsive neurons. However, the issue may be resolved considering the depression in the responsiveness of the preoptic-hypothalamic thermostat during REM sleep (cf. 26, 39). Notwithstanding this conclusion, a review of experimental results will show that it is physiologically relevant to appreciate the mechanisms underlying the brain temperature rise related to REM sleep.

PHYSIOLOGIC MECHANISMS FOR BRAIN COOLING

Brain temperature changes are quantitatively expressed as the ratio between the changes in heat content and mass of the nervous tissue multiplied by its specific heat ($\Delta T = \Delta Q/mc$). Heat is produced by cellular energy metabolism and is transferred to the arterial blood in inverse relation to its temperature, which is lower than that of the brain in normal conditions (25). It is obvious that brain homeothermy is altered essentially by quantitative imbalances between metabolic heat production and heat loss.

There are different mechanisms for cooling the brain in mammals and more than a single mechanism may be operative. In general, the cool venous blood flowing

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from the systemic heat exchangers of the body (upper airway mucosa, ear pinna, horn, tail, skin, according to species) to the heart mixes with the warm venous blood returning to the heart from heat-producing body tissues. This systemic mechanism cools the arterial blood including that flowing to the brain (systemic brain cooling). In addition to systemic brain cooling, there is also a mechanism for selective brain cooling. In species like the cat, dog, sheep and goat (23, 25), the carotid blood supply to the brain is again thermally conditioned prior to entering into the circle of Willis by countercurrent heat exchange between carotid rete and venous sinuses (e.g., *sinus cavernosus*). The carotid rete is a network of fine vessels (rudimental in the dog), derived from the external branch of the common carotid artery. The arterial blood flowing to the brain in the carotid rete is surrounded by sinus venous blood cooled in the upper airway mucosa and flowing in an opposite direction to the heart (5, 6, 18, 25). The carotid rete is connected to the circle of Willis through a short artery (homologous to the distal part of the internal carotid artery of species lacking the carotid rete). As a result of the countercurrent heat exchange, the temperature of the carotid blood reaching the circle of Willis is further decreased with respect to that of the aortic arch blood (5, 6, 25). Vertebral artery blood is not thermally conditioned by a countercurrent heat exchange mechanism and enters into the circle of Willis at the temperature of the blood in the aortic arch (25). In conclusion, the difference between the temperatures of vertebral artery blood (systemic cooling only) and carotid artery blood (both systemic and selective cooling) flowing into the circle of Willis depends on the heat loss from the carotid rete. Eventually, the average brain temperature is determined by the relative amounts of carotid and vertebral artery blood contributing to the total blood flow of the brain.

Another mechanism for selective brain cooling is typical of species lacking the carotid rete (e.g., rabbit and rat). It is provided by conductive heat exchange between the basal portion of the brain, including the circle of Willis, and the basal venous sinuses that drain cool venous blood from the upper airway mucosa (13).

The effects of systemic and selective brain cooling appear in the temperatures of the hindbrain and forebrain, respectively. This is shown by the positive difference between pontine and preoptic-hypothalamic temperatures in cats (4, 41), rabbits (41, 42) and rats (11, 41).

Heat loss from systemic heat exchangers, affecting carotid blood temperature through the systemic venous return to the heart (systemic brain cooling), is the most important determinant of brain temperature in primates (24, 25). Concerning humans, in particular, there is no consensus as to whether a mechanism for selective brain cooling plays a significant role (8, 9, 10, 28, 29, 35).

REM SLEEP RELATED CHANGES IN BRAIN TEMPERATURE

REM sleep in several mammalian species is characterized by a rise in brain temperature (1, 3, 5, 6, 15, 17, 19, 23, 25, 27, 31-33, 40, 44, 51, 56-60). It is remarkable that such rise occurs at ambient temperatures not only above or within the ambient

thermoneutral zone of the species but also below this zone (2, 21, 40, 44-46). In contrast, studies in primates showed a decrease in hypothalamic temperature (24, 25) and cortical temperature (47, 54) in relation to REM sleep at ambient temperatures close to or within the ambient thermoneutral zone of the species.

Concerning REM sleep in the two species (cat and rabbit) considered in detail here, the increase in brain temperature is related to systemic heat exchanger vasomotion that is opposite to that normally observed during NREM sleep under the influence of the same high or low ambient temperature. The proximate causes of such vasomotion are imbalances between transmural pressure and smooth muscle tonus during REM sleep, that appear paradoxical from the thermoregulatory viewpoint (12, 14, 21, 37, 40, 44). The REM sleep related increase in brain temperature at high ambient temperature appears, nevertheless, as a consistent result of the paradoxical replacement of thermoregulatory vasodilatation in NREM sleep by vasoconstriction reducing systemic heat loss in REM sleep. In contrast, the REM sleep related increase in brain temperature at low ambient temperature appears clearly inconsistent with the paradoxical replacement of thermoregulatory vasoconstriction in NREM sleep by vasodilatation increasing systemic heat loss in REM sleep.

MECHANISMS UNDERLYING THE REM SLEEP RELATED INCREASE IN BRAIN TEMPERATURE

From different viewpoints, many studies contributed to the early detection of factors directly underlying the REM sleep related increase in brain temperature (cf. 36). In particular, an increase in the metabolic heat production of the nervous tissue was proposed by several authors (15, 31, 32, 51, 56). Other authors proposed the arterial blood flow as a main factor (17, 30, 48, 49, 54-56), whereas others considered the arterial blood temperature the main factor (5, 6, 25).

The metabolic heat production of the nervous tissue appears an unlikely candidate as the primary cause of the observed change in brain temperature. In fact, several studies suggest that both brain metabolic rate and arterial blood flow increase in REM sleep with respect to NREM sleep (cf. 20, 34). On this basis, the increase in brain metabolic heat production is indirectly related to the rise in heat clearance by the increase in arterial blood flow. Therefore, temperature alone is not a reliable indicator of changes in metabolic heat production (cf. 25, 52, 53). In any case, metabolic heat production is unlikely to play a major role in the increase of brain temperature related to REM sleep particularly on the basis of subsequent experimental evidence.

The other factors at issue are the flow and temperature of the arterial blood supplied to the circle of Willis by different sources.

The effects of the transient fall in common carotid blood flow were studied in cats and rabbits (4, 38, 42). The fall was provoked by short ($\leq$ 100 s) bilateral common carotid artery occlusion during wakefulness and NREM sleep at ambient temperature (25 $\pm$ 2 °C) close to thermal neutrality. A decrease in ear pinna temperature and

an increase in both preoptic-hypothalamic and pontine temperatures were elicited by this procedure. Different mechanisms underlie these temperature changes. The short latency and the steepness of the initial rise in preoptic-hypothalamic temperature appear as an obvious effect of brain autoregulation of flow for the following reason. In response to the metabolic demand of the cerebral bed, suddenly raised by the fall in the carotid artery share of cerebral blood flow, autoregulation (cf. 7) buffers the fall in carotid blood supply by increasing the supply of vertebral artery blood. The flow increase in vertebral artery blood, warmer (systemic cooling only) than carotid artery blood (both systemic and selective cooling), initially contributes more to the increase in preoptic-hypothalamic temperature than the depression of selective brain cooling. This temperature approaches but does not reach the also rising value of the pontine temperature during the short duration of bilateral common carotid artery occlusion. The pontine temperature rises with a lesser slope than preoptic-hypothalamic temperature as it is driven by the increasing temperature of vertebral artery blood. The latter rise is a result of the decrease in common carotid artery blood flow depressing systemic heat loss from upper airway mucosa and ear pinna. Moreover, the degree of this effect depends also on the surface area of the ear pinna, since the pontine temperature increases more slowly and less in cats than in rabbits (4, 42). In support of the importance of autoregulation of blood flow, it is worth mentioning that electroencephalographic signs of ischemia are absent during bilateral common carotid artery occlusion of long (up to 300s) but evidently harmless duration in cats (4). In this case, the preoptic-hypothalamic and pontine temperatures tend to a plateau following the initial rise. This is a sign of the new thermal equilibrium existing between metabolic heat production and decreased systemic and selective heat loss. In conclusion, changes in metabolic heat production are not necessarily involved in these experimentally induced temperature changes during wakefulness and NREM sleep.

Additional experimental evidence shows that the previous argument also applies to the spontaneous increase in preoptic-hypothalamic and pontine temperatures related to REM sleep (4, 38, 42). This increase is characterized initially by a rather steep slope from the level attained at the end of NREM sleep and subsequently by a plateau. The temperature plateau lasts for the duration of the REM sleep episode and shows opposite variations to those of ear pinna temperature, that is systemic heat loss.

Bilateral short ($\leq$ 100 s) occlusion of the common carotid artery at REM sleep onset in cats and rabbits does not affect or only scarcely enhances the spontaneous decrease in ear pinna temperature and the spontaneous increase in both preoptic-hypothalamic and pontine temperatures. This is a crucial result showing that common carotid blood flow is spontaneously decreased on REM sleep occurrence. Such decrease may be considered the trigger of an autoregulatory response increasing brain blood flow in REM sleep. There is experimental evidence in the cat that the increase in hypothalamic blood flow during REM sleep is preceded by an initial transient decrease (16, 50). On this basis, the conclusion is warranted that bilateral occlusion of common carotid artery in wakefulness and NREM sleep mimics a

hemodynamic condition occurring spontaneously in REM sleep. In contrast, short bilateral common carotid artery occlusion after the end of REM sleep stops both the spontaneous increase in ear pinna temperature and the spontaneous decrease in pontine and preoptic-hypothalamic temperatures. This shows that common carotid artery blood flow spontaneously increases after the end of REM sleep: the increase enhances both systemic and selective brain cooling in turn whereas vertebral artery blood flow decreases. The indirect experimental evidence of a spontaneous fall and rise in common carotid artery blood flow during and after REM sleep, respectively, has recently been confirmed by direct measurement of this flow in rabbits (43).

As mentioned before, preoptic-hypothalamic temperature rises during REM sleep also at low ambient temperature (2, 21, 40, 44-46). The event is fairly inconsistent with the actual increased heat loss due to paradoxical vasodilatation of the systemic heat exchangers of the head (ear pinna, upper airway mucosa). This fact adds further indirect evidence that autoregulation of brain blood flow in REM sleep counterbalances the decrease in carotid blood supply by the increase in vertebral blood supply that is warmer than the former.

The described hemodynamic mechanisms apply not only to cats and rabbits but probably also to rats that show comparable REM sleep related changes of upper airway mucosa, preoptic-hypothalamic and pontine temperatures (11, 12). On the other hand, the remarkable morphofunctional prevalence of the internal carotid arteries over the vertebral arteries in primates (18) underlies unfavorable hemodynamic conditions, particularly in humans (22), for a significant enhancement of the blood supply of the vertebral arteries to the brain during REM sleep. Although the lack of adequate experimental evidence precludes any definitive conclusion, it is probable that brain temperature changes in primates depend only on changes in systemic brain cooling during REM sleep.

FUNCTIONAL IMPLICATIONS

The inference of cerebral autoregulation of vertebral blood flow drawn from the previous experimental results is fundamental to explain in detail the mechanism underlying the REM sleep related rise in preoptic-hypothalamic temperature in cats and rabbits. However, it should not be overlooked that the decrease in common carotid artery blood flow, characterizing REM sleep (43), reveals a systemic hemodynamic depression that appears so conspicuous as to negatively affect also vertebral artery blood flow and consequently cerebral autoregulation. In contrast to this inference, an increase in cerebral blood flow during REM sleep with respect to NREM sleep was observed in several species including the cat and rabbit (cf. 20, 34). Therefore, a basic question is how to reconcile the systemic hemodynamic depression in REM sleep with the autoregulatory increase in cerebral blood flow. This is conceptually possible considering the factors that may contribute to an adequate autoregulation of cerebral blood flow in spite of systemic unfavorable hemodynamic circumstances. The anatomical data (cf. 18) point to important morpho-

functional differences between the carotid and vertebral tributaries of the circle of Willis in the species considered (e.g., complex network of fine vessels of the carotid rete in the cat; vertebral arteries larger than internal carotid arteries in the rabbit). On this basis, higher inflow impedance for the carotid blood supply than for the vertebral blood supply to the circle of Willis is likely in both cats and rabbits. In this respect, the disappearance of the negative hydrostatic load as result of the lowered head posture, and a decrease in cerebral vascular impedance in relation with cortical activation in REM sleep also deserve consideration. The existence of conditions enhancing the vertebral blood supply to the brain in the rabbit during REM sleep is also shown by the fact that arterial blood flow increases more in the hindbrain than in the forebrain (cf. 20).

The autoregulatory response to the decreased common carotid artery blood supply to the forebrain is a result of the alteration of homeostatic cardiovascular regulation during REM sleep (cf. 37). However, an additional autoregulatory increase in vertebral blood supply is likely to occur as a response to brain activation in REM sleep with respect to NREM sleep. The former autoregulatory response is the most variable, since the "steal" of common carotid artery blood is due to autonomic events that are intrinsically irregular. The latter autoregulatory response is the most stable as the expression of actual flow-metabolism coupling due to the stereotyped pattern of brain activation in REM sleep. Eventually, the overall temporal coupling of flow and metabolism in the brain is less consistent in REM sleep than in both wakefulness and NREM sleep, according to the different time courses of randomly interacting peripheral and central physiological processes during REM sleep.

CONCLUSION

Summing up, three main factors have been considered as possibly underlying the brain temperature rise related to REM sleep: namely, changes in i) the metabolic heat production of the nervous tissue, ii) the arterial blood flow, iii) the arterial blood temperature. The present discussion points out that the first factor is practically not relevant to the problem. The experimental evidence supports the view that the proximate causes of the rise in brain temperature related to REM sleep are the quantitative shift from carotid blood supply to vertebral blood supply to the circle of Willis and the depression of systemic and selective brain cooling. A remote cause of the rise in brain temperature is the systemic hemodynamic alteration in REM sleep. The instability of autonomic cardiovascular regulation brings about a "steal" of common carotid artery blood supplying the brain and the systemic heat exchangers of the head. A "steal", depressing both systemic and selective brain cooling, to be counterbalanced in the species considered by blood flowing to the brain primarily from the vertebral arteries.

SUMMARY

The roles of metabolic heat production, arterial blood flow and temperature in the genesis of the brain temperature increase related to REM sleep occurrence in several mammalian species are discussed on the basis of available experimental evidence. The experimental data show that only changes in arterial blood flow and temperature consistently underlie the rise in brain temperature in presence (cat) or absence (rabbit) of the carotid rete. The alteration of cardiovascular regulation in REM sleep is the remote cause of such rise. The proximate causes are decrease in carotid blood supply and increase in vertebral blood supply to the brain and related depression of systemic and selective brain cooling.

REFERENCES

1. ADAMS, T. Hypothalamic temperature in the cat during feeding and sleep. *Science*, **139**: 609-610, 1963.
2. ALFÖLDI, P., RUBICSEK, G., CSERNI, G. AND OBÀL, JR. F. Brain and core temperatures and peripheral vasomotion during sleep and wakefulness at various ambient temperatures in the rat. *Pflügers Arch.*, **417**: 336-341, 1990.
3. ALLISON, T. AND VAN TWYVER, H. Sleep in the moles, *Scalopus aquaticus* and *Condylura cristata*. *Exp. Neurol.*, **27**: 564-578, 1970.
4. AZZARONI, A. AND PARMEGGIANI, P.L. Mechanisms underlying hypothalamic temperature changes during sleep in mammals. *Brain Res.*, **632**: 136-142, 1993.
5. BAKER, M.A. AND HAYWARD, J.N. Carotid rete and brain temperature of cats. *Nature*, **216**: 139-141, 1967.
6. BAKER, M.A. AND HAYWARD, J.N. Autonomic basis for the rise in brain temperature during paradoxical sleep. *Science*, **157**: 1586-1588, 1967.
7. BUSIJA, D.W. AND HEISTAD, D.D. Factors involved in the physiological regulation of the cerebral circulation. *Rev. Physiol. Biochem. Pharmacol.*, **101**: 162-211, 1984.
8. CABANAC, M. Keeping a cool head. *News Physiol. Sci.*, **1**: 41-44, 1986.
9. CABANAC, M. *Human Selective Brain Cooling*. Springer-Verlag, Heidelberg, 1995.
10. CABANAC, M. AND CAPUTA, M. Natural selective cooling of the human brain: evidence of its occurrence and magnitude. *J. Physiol., Lond.*, **286**: 255-264, 1979.
11. CALASSO, M. AND PARMEGGIANI, P.L. Thermogenesis of interscapular brown adipose tissue selectively influences pontine and preoptic-hypothalamic temperatures during sleep in the rat. *Brain Res.*, **1015**: 103-106, 2004.
12. CALASSO, M., ZANTEDESCHI, E. AND PARMEGGIANI, P.L. Cold-defense function of brown adipose tissue during sleep. *Am. J. Physiol.*, **265**: R1060-R1064, 1993.
13. CAPUTA, M., KADZIELA, W. AND NAREBSKI, J. Significance of cranial circulation for the brain homeothermia in rabbits. II. The role of the cranial venous lakes in the defence against hyperthermia. *Acta Neurobiol. Exp.*, **36**: 625-638, 1976.
14. CIANCI, T., ZOCCOLI, G., LENZI, P. AND FRANZINI, C. Loss of integrative control of peripheral circulation during desynchronized sleep. *Am. J. Physiol.*, **261**: R373-R377, 1991.
15. DELGADO, J.M.R. AND HANAI, T. Intracerebral temperatures in free-moving cats. *Am. J. Physiol.*, **211**: 755-769, 1966.
16. DENOYER, M., SALLANON, M., BUDA, C., DELHOMME, G., DITTMAR, A. AND JOUVET, M.

The posterior hypothalamus is responsible for the increase of brain temperature during paradoxical sleep. *Exp. Brain Res.*, **84**: 326-334, 1992.
17. DUFOUR, R. AND COURT, L. Le débit cérébral sanguin au cours du sommeil paradoxal du lapin. *Arch. Ital. Biol.*, **115**: 57-76, 1977.
18. EDVINSSON, L., MACKENZIE, E.T. AND MCCULLOCH, J. *Cerebral Blood Flow and Metabolism.* Raven Press, New York, 1993.
19. FINDLAY, A.L.R. AND HAYWARD, J.N. Spontaneous activity of single neurones in hypothalamus of rabbits during sleep and waking. *J. Physiol., Lond.*, **201**: 237-258, 1969.
20. FRANZINI, C. Brain metabolism and blood flow during sleep. *J. Sleep Res.*, **1**: 3-16, 1992.
21. FRANZINI, C., CIANCI, T., LENZI, P. AND GUIDALOTTI, P.L. Neural control of vasomotion in rabbit ear is impaired during desynchronized sleep. *Am. J. Physiol.*, **243**: R142-R146, 1982.
22. HALE, A.R. Circle of Willis: functional concepts, old and new. *Am. Heart J.*, **60**: 491-494, 1960.
23. HAYWARD, J.N. Brain temperature regulation during sleep and arousal in the dog. *Exp. Neurol.*, **21**: 201-212, 1968.
24. HAYWARD, J.N. AND BAKER, M.A. Role of the cerebral arterial blood in the regulation of brain temperature in the monkey. *Am. J. Physiol.*, **215**: 389-403, 1968.
25. HAYWARD, J.N. AND BAKER, M.A. A comparative study of the role of the cerebral arterial blood in the regulation of brain temperature in five mammals. *Brain Res.*, **16**: 417-440, 1969.
26. HELLER, H.C. *Temperature, Thermoregulation and Sleep.* Pp. 292-304. In: KRYGER, M.H., ROTH, T. AND DEMENT, W.C. (Eds.), *Principles and Practice of Sleep Medicine.* Philadelphia, Saunders, 2005.
27. HULL, C.D., BUCHWALD, N.A., DUBROWSKY, B. AND GARCIA, J. Brain temperature and arousal. *Exp. Neurol.*, **12**: 238-246, 1965.
28. JESSEN, C. *Temperature Regulation in Humans and Other Mammals.* Springer-Verlag, Berlin, 2001.
29. JESSEN, C. AND KUHNEN, G. No evidence for brain stem cooling during face fanning in humans. *J. Appl. Physiol.*, **72**: 664-669, 1992.
30. KANZOW, E., KRAUSE, D. AND KÜHNEL, H. Die Vasomotorik der Hirnrinde in den Phasen desynchronisierter EEG Aktivität im natürlichen Schlaf der Katze. *Pflügers Arch. Gesamte Physiol.*, **274**: 593-607, 1962.
31. KAWAMURA, H. AND SAWYER, C.H. Elevation in brain temperature during paradoxical sleep. *Science*, **150**: 912-913, 1965.
32. KAWAMURA, H., WITHMOYER, D.I. AND SAWYER, C.H. Temperature changes in the rabbit brain during paradoxical sleep. *EEG. Clin. Neurophysiol.*, **21**: 469-477, 1966.
33. KOVALZON, V.M. Brain temperature variations during natural sleep and arousal in white rats. *Physiol. Behav.*, **10**: 667-670, 1973.
34. MAQUET, P. Functional neuroimaging of normal human sleep by positron emission tomography. *J. Sleep Res.*, **9**: 207-231, 2000.
35. NIELSEN, B. AND JESSEN, C. Evidence against brain stem cooling by face fanning in severely hyperthermic humans. *Pflügers Arch.*, **422**: 168-172, 1992.
36. PARMEGGIANI, P.L. *Temperature regulation during sleep: a study in homeostasis.* Pp. 97-143. In: OREM, J. AND BARNES, C.D. (Eds.), *Physiology in Sleep. Research Topics in Physiology.* New York, Academic Press, 1980.
37. PARMEGGIANI, P.L. *The Autonomic Nervous System in Sleep.* Pp. 194-203. In: KRYGER, M.H., ROTH, T. AND DEMENT, W.C. (Eds.), *Principles and Practice of Sleep Medicine.* Philadelphia, Saunders, 1994.
38. PARMEGGIANI, P.L. Brain cooling across wake-sleep behavioral states in homeothermic species: an analysis of the underlying physiological mechanisms. *Rev. Neurosci.*, **6**: 353-363, 1995.

39. PARMEGGIANI, P.L. Thermoregulation and sleep. *Frontiers in Bioscience*, **8**: s557-567, 2003.
40. PARMEGGIANI, P.L., AGNATI, L.F., ZAMBONI, G. AND CIANCI, T. Hypothalamic temperature during the sleep cycle at different ambient temperatures. *EEG. Clin. Neurophysiol.*, **38**: 589-596, 1975.
41. PARMEGGIANI, P.L., AZZARONI, A. AND CALASSO, M. A pontine-hypothalamic temperature difference correlated with cutaneous and respiratory heat loss. *Respir. Physiol.*, **114**: 49-56, 1998.
42. PARMEGGIANI, P.L., AZZARONI, A. AND CALASSO, M. Systemic hemodynamic changes raising brain temperature in REM sleep. *Brain Res.*, **940**: 55-60, 2002.
43. PARMEGGIANI, P.L., CALASSO, M. AND ZOCCOLI G. Decrease in the carotid share of cerebral blood flow during REM sleep. *J. Sleep Res.*, **11**, (Suppl. 1): 169, 2002.
44. PARMEGGIANI, P.L., FRANZINI, C., LENZI, P. AND CIANCI, T. Inguinal subcutaneous temperature changes in cats sleeping at different environmental temperatures. *Brain Res.*, **33**: 397-404, 1971.
45. PARMEGGIANI, P.L., ZAMBONI, G., CIANCI, T. AND CALASSO, M. Absence of thermoregulatory vasomotor responses during fast wave sleep in cats. *EEG. Clin. Neurophysiol.*, **42**: 372-380, 1977.
46. PARMEGGIANI, P.L., ZAMBONI, G., PEREZ, E. AND LENZI, P. Hypothalamic temperature during desynchronized sleep. *Exp. Brain Res.*, **54**: 315-320, 1984.
47. REITE, M.L. AND PEGRAM, G.V. Cortical temperature during paradoxical sleep in the monkey. *EEG. Clin. Neurophysiol.*, **25**: 36-41, 1968.
48. REIVICH, M. *Regional cerebral blood flow in physiologic and pathophysiologic states.* Pp. 191-228. In: MEYER, J.S. AND SCHADÉ, J.P. (Eds.), *Cerebral Blood Flow*. Progr. Brain Res. Amsterdam, Elsevier, **35**: 1972.
49. RISBERG, J. AND INGVAR, D.H. *Increase of regional cerebral blood volume during REM-sleep in man*. Pp. 384-388. In: KOELLA, W.P. AND LEVIN, P. (Eds.), *Sleep: proceedings of the first european congress on sleep research.* Basel, Karger, 1973.
50. ROUSSEL, B., DITTMAR, A. AND CHOUVET, G. Internal temperature variations during the sleep wake cycle in the rat. *Waking Sleeping*, **4**: 63-75, 1980.
51. SATOH, T. Brain temperature of the cat during sleep. *Arch. Ital. Biol.*, **106**: 73-82, 1968.
52. SEROTA, H.M. Temperature changes in the cortex and hypothalamus during sleep. *J. Neurophysiol.*, **2**: 42-47, 1939.
53. SEROTA, H.M. AND GERARD, R.W. Localized thermal changes in the cat's brain. *J. Neurophysiol.*, **1**: 115-124, 1938.
54. SEYLAZ, J., MAMO, H., GOAS, J.Y., MACLEOD, P., CARON, J.P. AND HOUDART, R. Local cortical blood flow during paradoxical sleep in man. *Arch. Ital Biol.*, **109**: 1-14, 1971.
55. SHAPIRO, C.M. AND ROSENDORFF, C. Local hypothalamic blood flow during sleep. *EEG. Clin. Neurophysiol.*, **39**: 365-369, 1975.
56. TACHIBANA, S. Relation between hypothalamic heat production and intra- and extracranial circulatory factors. *Brain Res.*, **16**: 405-416, 1969.
57. VAN TWYVER, H. AND ALLISON, T. Sleep in the opossum *Didelphis marsupialis*. *EEG. Clin. Neurophysiol.*, **29**: 181-189, 1970.
58. VAN TWYVER, H. AND ALLISON, T. Sleep in the armadillo *Dasypus novemcinctus* at moderate and low ambient temperatures. *Brain Behav. Evol.*, **9**: 107-120, 1974.
59. WALKER, J.M., WALKER, L.E., HARRIS, D.V. AND BERGER, R.J. Cessation of thermoregulation during REM sleep in the pocket mouse. *Am. J. Physiol.*, **244**: R114-R118, 1983.
60. WURTZ, R.H. Physiological correlates of steady potential shifts during sleep and wakefulness. II. Brain temperature, blood pressure, and potential changes across ependyma. *EEG. Clin. Neurophysiol.*, **22**: 43-53, 1967.