EEG and other physiological signals. Electronic measurement devices connected to small laboratory computers have been set into operation for routine sleep scoring[10,11]. These systems are linked to a data base and greatly facilitate the statistical evaluation of a large number of records. In addition, new procedures have been proposed for the calculation of sleep stages as functions of time, in order to describe more accurately their temporal organization[12]. These and other developments allow much more precise measurements to be obtained, particularly of EEG waveforms, including evoked potentials, and open wide the possibility of new observations.

1 H. Berger, J. Psychol. Neurol. *40*, 160 (1929).
2 A.L. Loomis, E.N. Harvey and G. Hobart, J. exp. Psychol. *108*, 127 (1937).
3 E. Aserinsky and N. Kleitmann, Science *118*, 273 (1953).
4 W.C. Dement and N. Kleitmann, Electroenceph. clin. Neurophysiol. *9*, 673 (1957).
5 A. Rechtschaffen and A. Kales, Public Health Serv., U.S. Government Printing Office, Washington DC 1968.
6 P. Salzarulo, G.C. Lairy, J. Bancaud and C. Munari, Electroenceph. clin. Neurophysiol. *38*, 199 (1975).
7 J. Bert and E. Balzamo, Rev. EEG Paris 4, 501 (1974).
8 M. Anch, Waking Sleeping *1*, 189 (1977).
9 E. Callaway, Brain electrical potentials and individual psychological differences. Grune and Stratton, Inc., New York 1975.
10 J.-M. Gaillard and R. Tissot, Comp. biomed. Res. *6*, 1 (1973).
11 S.Y.W. Su and J.R. Smith, Comp. biomed. Res. *7*, 432 (1974).
12 J.-M. Gaillard, Encéphale *V*, 71 (1979).

3. Behavioral phenomenology of sleep (somatic and vegetative)

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The study of behavioral phenomenology represents the most classical approach to the problem of sleep[1,2]. Such an approach has never lost heuristic incisiveness, as behavior is an expressive modality of the organism whose functional significance can often directly be envisaged by the observer. Moreover, the somatic and vegetative (autonomic) events of sleep are still instrumental in the process of decoding into operational propositions the related patterns of electrochemical activity of neural structures.

The phenomenal evolution shows that the onset of sleep (phase I) is followed by 2 contrasting sets of sleep events (phases II and III) occurring in cycles of ultradian rhythmics and characterized by a functional dichotomy in terms of control theory. In fact, phase III is the result of a functional change which has mainly open loop vs closed loop operations. A reversible release of brain stem structures due to the temporary inactivation, during phase III, of hypothalamic homeostatic mechanisms underlies such a dichotomy in the intact organism[3–5]. This inactivation may be considered the result both of the change in hypothalamic integrative activity occurring in late phase II and of ascending influences related to the brain stem activity of phase III. The pacemaker role of the hypothalamus with regard to the phenomenal evolution of sleep is indirectly shown by the modifications of the sleep cycle elicited in homeothermic organisms by deviations in ambient temperature from thermal neutrality[3–5].

The functional condition of phase III of sleep implies not only that the instability of effector functions is the more marked the less they are endowed with autoregulation and/or controlled by reflex mechanisms, but also, which is more remarkable, that homeostatic regulation is temporarily suspended and replaced by a poikilostatic mode of operation. The alternation of such functional conditions can be considered as a homeostatis-poikiostasis ultradian rhythm. On this basis, phenomenal differences of phase III between species are accounted for by inborn patterns of morphofunctional organization of brain stem and spinal operative levels. Moreover, reflex responses during phase III are the more affected the greater their normal subordination to hypothalamic levels of integration. So, the functional condition of phase III reveals phylogenetically determined degrees of autonomy. In conclusion, during this phase of sleep the encephalon is coping only with its own functional needs (consummatory act of sleep[6]) through a neurochemical process which is incompatible with its specific integrative action.

I. Somatic phenomenology

The somatic phenomenology of sleep concerns primarily motor and postural activities. During phase I the behavioral repertory consists of the search for a safe ecological niche and preparing the body for the natural sleep posture. The latter differs between species, but it is nevertheless clearly related to thermoregulatory and/or safety needs. Therefore, specific behavioral and physiological thermoregulatory capabilities, innate and learned[7] motor and postural behavior and predator-prey relationships[8] are all basic factors underlying the shaping of this phase of sleep. The complexity of such performances implies the integrated activity of several encephalic structures[9,10].

Phase II (synchronized sleep) is characterized by a low level of motor and postural activity resulting in the suspension of the active contact of the organism with the environment. The sleep posture is influenced determinantly by thermoregulation[11]. So, the decrease in muscle postural activity is the result of a change in the regulation of muscle innervation rather than the

expression of a generalized tendency to hypotonia. This protective resting posture, varying among species, reduces energy expenditure to a minimum. The quiescence of phase II in cats is related to a decrease in the driving power of the pyramidal tract on spinal motorneurons[12,13]. Likewise, the Babinsky sign is observed in man[1,14,15].

Limb muscles in cats are hypotonic according to the depression of fusimotor functions observed during this phase of sleep[16–23]. In contrast, the postural activity of the neck and intercostal muscles is consistent with a posture varying with ambient temperature[11,24]. In man too, the depression of the phasic stretch reflex[25,26], and the H-reflex[27,28], e.g., is associated with the tonic contraction of the orbicularis[9] and extrinsic (Bell phenomenon)[2] muscles of the eye. Such differential patterns of postual activity are specific and depend on the influence of structures located above the brain stem. In fact, decerebrate and pontine preparations cannot assume normal sleep postures[29]. In this respect, the influence of hypothalamic thermoceptive structures on gamma motor activity[17] acquires a remarkable significance insofar as sleep posture is an aspect of behavioral thermoregulation.

During phase III (desynchronized sleep) the postural activity of neck[30] and intercostal musles[24,31,32] is also abolished. Such generalized atonia depends on tonic brain stem inhibitory influences on spinal motorneurons effective during this phase of sleep[21–23,33–40]. In fact, periodic atonia is observed also in decerebrate and pontine preparations[29,30]. However, the problem arises of determining the mechanisms underlying the appearance of such a singular phenomenon in animals with intact nervous sistems. As postural activity in phase II is clearly related to behavioral thermoregulation, its abolition during phase III suggests that a change in the hypothalamic control of brain stem structures may release the mechanism producing general atonia in normal animals[3,24]. This hypothesis is consistent with the fact that fusimotor activity is influenced by thermal and electrical stimulation or lesions of the hypothalamus[17,41–45]. Moreover, statistically significant changes in hypothalamic unit activity are temporally bound to the beginning of phase III[46,47]. These patterns of unit activity are surely related to a new mode of operation of hypothalamic structures. The random appearance of myoclonic twitches during phase III is the result of phasic excitatory influences of brain stem structures[48–51] and phasic enhancements of pyramidal discharge[12] on spinal motorneurons. Phasic contractions of extrinsic eye (REMs[52,53]) and middle ear[54] muscles are other aspects of phasic activation typical of this phase of sleep. In conclusion, the somatic phenomenology of phase III is not indicative of a continuous process of sleep deepening beyond phase II, but rather the sign of a functional dichotomy in the sleep cycle. Postural atonia and myoclonic twitches are both expressions of an open-loop mode of operation at spinal and higher levels in connection with the release of the brain stem tonic postsynaptic inhibition of spinal motorneurons, phasic presynaptic inhibition of muscle and cutaneous afferents, and the phasic excitatory influences mentioned before[55]. In this respect, it is worth noting the disappearance of the Babinsky sign[14,15] and of the H-reflex[27,28,56] in man.

II. Vegetative phenomenology

The somatic motor and postural repertories of phase I are obviously related to changes in vegetative functions supporting muscular activity, that, however, are not specific to sleep. In contrast, phase II and III are characterized by specific vegetative changes.

The vegetative phenomenology of phase II depends on closed-loop operations preserving homeostasis at a lower level of energy expenditure than during wakefulness. So, restoration under conditions of maximal anabolic utilization of energy is possible. This functional level was defined as trophotropic endophylactic by Hess[57]. In short, the vegetative phenomenology of phase II is elicited by a regulatory system that has shifted from the control of activity to that of rest without changing its operational logic. The basic vegetative event is a tonic increase in the parasympathetic outflow combined with a slight attenuation of sympathetic activity. In particular, the pupil becomes myotic[9,58], the heart frequency and systemic arterial pressure decrease[53,59–70] according to this new vegetative equilibrium. Although the circulatory control mechanism appears to be tuned to a lower activity level, it maintains all compensatory physiological responses to chemoceptive and baroceptive inputs[65]. Also the decrease in psychogenic sweating in man and cats[71–76] is a consistent phenomenon as sweat glands receive sympathetic secretory fibres. Contrasting results were reported concerning gastrointestinal motility and secretion probably because each variable chan-

Classification of sleep phenomenology

Criteria	Sleep phases I	II	III
Behavioral	Somatic	Vegetative	Vegetative
Bioelectrical	Desynchronized	Synchronized	Desynchronized
Ethological	External appetitive	Internal appetitive	Internal consummatory
Hierarchical	Prosencephalic	Diencephalic	Rhomboencephalic
Operational	Closed-loop	Closed-loop	Open-loop
Teological	Homeostatic	Homeostatic	Poikilostatic

ges in relation to an autochthonous ultradian rhythm almost independently of sleep evolution[77–79]. In fact, decrease in gastric motility and increase in gastric acid secretion[80], decrease in both[81,82], increase in gastric motility[83], decrease in duodenal motility[78] were observed. Breathing is in general slower and more regular than in wakefulness[9,10,53,62,66,84–86]; in man, particularly, irregular and periodic patterns were also observed[87–89] during early phase II (EEG stages 1 and 2). Such transitory events appear to be the necessary result of the resetting of feedback mechanisms (set point, gain, threshold) according to the functional state of late phase II (EEG stages 3 and 4). In late phase II chemoceptive and mechanoceptive respiratory reflexes are unchanged with only exception of a moderate decrease in CO_2-sensitivity[90]. Physiological and behavioral thermoregulatory mechanisms are still operative[11,24,91–96], although core temperature is regulated at a lower level than in wakefulness[73,97–99]. Most interesting with respect to the evolution of the sleep cycle is the decrease in preoptic temperature which is necessary for the occurrence of phase III in cats[98].

During phase III vegetative changes with respect to phase II appear to be the result of an open-loop mode of operation which contradicts the logic of neural control of homeostasis (from this point of view phase III is really paradoxical!). The suspension of hypothalamic homeostatic action is more evident for those vegetative functions which, like thermoregulation, are based on highly integrated mechanisms, whereas for others it may be more or less masked by the persistence of autoregulation or single reflex regulation. For example, during phase III in cats, a drop in systemic arterial pressure is observed which is so enhanced to produce signs of transient cerebral ischemia after suppression of chemoceptive reflexes[65,100,101]. The basic vegetative event of phase III in animals is the tonic decrease in sympathetic outflow[102–104]. In particular, the pupil narrows further when it has not reached the minimum size in phase II[58]. An almost generalized decrease in sympathetic vasoconstrictor outflow occurs in phase III, regarding the skin[94,105], mesenteric[105–107], and renal[105,107,108] beds, leaving out only limb muscle beds[105–107] as a result of a reflex mechanism[109]. Concomitantly, heart rate and output are reduced[65,68,106,107,110]. On this basis, the drop in systemic arterial pressure observed by many investigators[59,60,63,65] is not surprising. In cats, oxyceptive inputs still influence circulation, whereas baroceptive reflexes are strongly depressed[65,100,101]. In man, heart rate and systemic arterial pressure generally increase with respect to phase II[53,61,62,66,67,70], while tonic sweating is further decreased[72,74,111]. Penile erection occurs in man[112,113] and monkeys[66] during phase III. The variables considered also undergo phasic changes due either to random bursts of sympathetic outflow, or to phasic decreases in parasympathetic outflow, depending on effector innervation[58,68]. Such phasic events are more or less related to those of somatic phenomenology (the relationship with rapid eye movements was particularly analyzed[48,52,53,66,77]) and may underlie the variability of collected data. Concerning gastrointestinal motility and secretion the same consideration advanced for phase II applies to phase III. The particular autonomy of such functions from central control may explain the contrasting results of different investigators: increase in gastric motility and decrease in gastric acid secretion[80], decrease of both gastric acid secretion[82,114,115] and gastric motility[81,83], and increase in duodenal motility[78] were observed with respect to phase II. No clear evidence exists, moreover, of a relationship between gastrointestinal phasic motility and rapid eye movements. In animals the breathing frequency is irregular during phase III and on average increases above the eupneic values[11,24,31,32,84–86] or decreases below the polypneic values[11,24] of phase II. Moreover, the respiratory electrical activity of intercostal muscles is tonically depressed and irregular, while diaphragmatic electrograms are scarcely affected, except for random disturbances related to phasic events (REMs, myoclonic twitches) of phase III in animals[24,31,32,116] and infants[117]. The tidal volume is decreased during this phase of sleep in eupnea[84–86]. Concerning the mechanisms of such respiratory changes, the tonic inhibitory influences of brain stem structures on spinal motoneurons affecting intercostal postural activity (see section I), underlie also the depression of intercostal respiratory activity[24,118]. On the other hand, the changes in frequency are probably the result of a release of respiratory centers from hypothalamic tonic influences exerting a negative and a positive chronotropic effect in eupnea and polypnea, respectively, during phase II[11,24,92,118]. In man, respiratory rate and amplitude are irregular[52,53,62,66,88,119], an increase in frequency and a decrease in amplitude often occurring in relation to rapid eye movements[120]. Alveolar ventilation is variable too as shown by either a decrease[86,119,121] or no change[84,122,123] in PCO_2. In dogs and infants, respiratory responses to hypercapnia are depressed[124,125], those to hypoxia unchanged[123,126,127]. Lung deflation and inflation reflexes persist in the opossum[128], whereas the inflation reflex is abolished in dogs[86] and infants[129]. The changes in chemoceptive and mechanoceptive respiratory reflexes are not only the direct effect of the activity of the brain stem structures underlying the occurrence of phase III of sleep[130–133], but also the result of the suppression of hypothalamic regulatory influences on lower levels of integration[118].

During phase III hypothalamic thermoregulatory mechanisms are inactivated, as shown by the disappearance of shivering[11,24,91,134,135], polypnea[11,24,91–93], vasomotion[94], thermal sweating[74,76,111], and thermoge-

nesis[95,96]. Such events are temporally related to changes in hypothalamic unit activity which appear to underlie the suspension of the hypothalamic drive on spinal somatic and sympathetic neurons effecting thermoregulatory responses[47,136].

Conclusions

The foregoing analysis of behavioral sleep phenomenology shows that the most significant factual and theoretical aspects of sleep can be logically organized only according to several criteria, it being impossible to choose a singli one as truly paradigmatic. For this reason an ordinal classification of sleep phases was preferred. This fact does not detract from the usefulness of classifications based consistently on 1 criterion at a time (e.g.: synchronized - desynchronized; quiet - active; orthodoxical - paradoxical; NREM-REM; homeostatic - poikilostatic; spindle wave - slow wave - fast wave; external appetitive - internal appetitive - internal consummatory; and so on). In this respect, the bioelectrical classification is surely the best as it allows an analytical subdivision of the evolution of sleep with high resolving power[137-139]. In particular, the electroencephalographic activity of late phase II (stage 4 in man[139] and slow wave[11] or deep slow wave[140] sleep in the cat) appears to be related to the triggering mechanisms and to the quantitative regulation of the circadian amount of phase III[3,5,11,140]. However, in extending the field of functional implications of sleep phenomenology other criteria may be more significant. In fact, the somatic and vegetative events of sleep also lend themselves to an analysis according to the behavioral model of ethology[6,141-144] and the theory of homeostasis[3-5,145], respectively. As an example, a number of classifying criteria are indicated in the table, where others, particularly neurochemical ones[146,147], could be added. At any rate, the difficulty of organizing sleep events into a satisfactory operational scheme is due to the fact that sleep is still an open problem as far as its mechanisms and functional significance are concerned.

1 N. Kleitman, Sleep and Wakefulness. University of Chicago Press, Chicago 1963.
2 W.P. Koella, Sleep: its Nature and Physiological Organization. Thomas, Springfield, Ill. 1967.
3 P.L. Parmeggiani, Brain Research *7*, 350 (1968).
4 P.L. Parmeggiani, in: The Sleeping Brain, vol. 1, p. 108. Ed. M.H. Chase. Brain Information Services, UCLA, Los Angeles 1972.
5 P.L. Parmeggiani, Waking Sleeping *1*, 123 (1977).
6 P.L. Parmeggiani, in: Sleep: Physiology, Biochemistry, Psychology, Pharmacology, Clinical Implications p.210. Ed. W.P. Koella and P. Levin. Karger, Basel 1973.
7 J. Bert, in: Sleep: Physiology, Biochemistry, Psychology, Pharmacology, Clinical Implications p. 446. Ed. W.P. Koella and P. Levin. Karger, Basel 1973.
8 T. Allison and D.V. Cicchetti, Science *194*, 732 (1976).
9 W.R. Hess, Helv. physiol. pharmac. Acta *2*, 305 (1944).
10 P.L. Parmeggiani, Helv. physiol. pharmac. Acta *20*, 347 (1962).
11 P.L. Parmeggiani and C. Rabini, Archs ital. Biol. *108*, 369 (1970).
12 P.L. Marchiafava and O. Pompeiano, Archs ital. Biol. *102*, 500 (1964).
13 R. Hodes and J.-I. Suzuki, Electroenceph. clin. Neurophysiol. *18*, 239 (1965).
14 C. Batini, J. Fressy and H. Gastaut, Electroenceph. clin. Neurophysiol. *16*, 412 (1964).
15 A. Fujiki, A. Shimizu, Y. Yamada, J. Yamamoto and Z. Kaneko, Electroenceph. clin. Neurophysiol. *31*, 610 (1971).
16 C. von Euler and U. Söderberg, Experientia *12*, 278 (1956).
17 C. von Euler and U. Söderberg, Electroenceph. clin. Neurophysiol. *9*, 391 (1957).
18 C. von Euler and U. Söderberg, Acta physiol. scand. *42*, 112 (1958).
19 J.S. Buchwald and E. Eldred, Electroenceph. clin. Neurophysiol. *13*, 243 (1961).
20 T. Hongo, K. Kubota and H. Shimazu, J. Neurophysiol. *26*, 568 (1963).
21 M.M. Gassel and O. Pompeiano, Archs ital. Biol. *103*, 347 (1965).
22 K. Kubota and R. Tanaka, Brain Res. *3*, 198 (1966).
23 K. Kubota, R. Tanaka and T. Tsuzuki, Jap. J. Physiol. *17*, 613 (1967).
24 P.L. Parmeggiani and L. Sabattini, Electroenceph. clin. Neurophysiol. *33*, 1 (1972).
25 M.A.M. Lee and N. Kleitman, Am. J. Physiol. *67*, 141 (1923).
26 W.W. Tuttle, Am. J. Physiol. 68. 345 (1924).
27 R. Hodes and W.C. Dement, Electroenceph. clin. Neurophysiol. *17*, 617 (1964).
28 Y. Hishikawa, N. Sumitsuji, K. Matsumoto and Z. Kaneko, Electroenceph. clin. Neurophysiol. *18*, 487 (1965).
29 P. Bard and M.B. Macht, in: Neurological Basis of Behaviour, p.55. Ed. G.E.W. Wolstenholme and C.M. O'Connor. Ciba Found. Symp., Churchill, London 1958.
30 M. Jouvet, Archs ital. Biol. *100*, 125 (1962).
31 J. Islas-Marroquin, Archs Sci. physiol. *20*, 219 (1966).
32 B. Duron, J. Physiol. (Paris) *61*, Suppl. 2, 282 (1969).
33 M.M. Gassel, P.L. Marchiafava and O. Pompeiano, Archs ital. Biol. *102*, 471 (1964).
34 M.M. Gassel, P.L. Marchiafava and O. Pompeiano, Archs ital. Biol. *103*, 25 (1965).
35 S. Giaquinto, O. Pompeiano and I. Somogyi, Archs ital. Biol. *102*, 245 (1964).
36 S. Giaquinto, O. Pompeiano and I. Somogyi, Archs ital. Biol. *102*, 282 (1964).
37 A.R. Morrison and O. Pompeiano, Archs ital. Biol. *103*, 497 (1965).
38 F. Baldissera, G. Broggi and M. Mancia, Archs ital. Biol. *104*, 112 (1966).
39 K. Kubota, Y. Iwamura and Y. Niimi, J. Neurophysiol. *28*, 125 (1965).
40 K. Kubota and Y. Kidokoro, Jap. J. Physiol. *16*, 217 (1966).
41 R. Granit and B.R. Kaada, Acta physiol. scand. *27*, 130 (1952).
42 W.J. Freeman and D.D. Davis, Am. J. Physiol. *197*, 145 (1959).
43 J.A. Hobson, Electroenceph. clin. Neurophysiol. *19*, 41 (1965).
44 W.W. Roberts and T.C.L. Robinson, Exp. Neurol. *25*, 282 (1969).
45 W.W. Roberts, E.H. Bergquist and T.C.L. Robinson, J. comp. physiol. Psychol. *67*, 182 (1969).
46 A.L.R. Findlay and J.N. Hayward, J. Physiol. (London) *201*, 237 (1969).
47 P.L. Parmeggiani and C. Franzini, Electroenceph. clin. Neurophysiol. *34*, 495 (1973).
48 M.M. Gassel, P.L. Marchiafava and O. Pompeiano, Archs ital. Biol. *102*, 449 (1964).
49 O. Pompeiano and A.R. Morrison, Archs ital. Biol. *103*, 569 (1965).
50 O. Pompeiano and A.R. Morrison, Archs ital. Biol. *104*, 231 (1966).
51 A.R. Morrison and O. Pompeiano, Archs ital. Biol. *104*, 214 (1966).
52 E. Aserinsky and N. Kleitman, Science *118*, 273 (1953).
53 E. Aserinsky and N. Kleitman, J. appl. Physiol. *8*, 1 (1955).
54 W. Baust, G. Berlucchi and G. Moruzzi, Archs ital. Biol. *102*, 657 (1964).

55 O. Pompeiano, in: Handbook of Sensory Physiology, vol. 6-I, p. 583. Ed. H.H. Kornhuber. Springer, Berlin 1974.
56 A. Shimizu, Y. Yamada, J. Yamamoto, A. Fujiki and Z. Kaneko, Electroenceph. clin. Neurophysiol. *20, 337* (1966).
57 W.R. Hess, Helv. physiol. pharmac. Acta *5*, Suppl. 4 (1947).
58 G. Berlucchi, G. Moruzzi, G. Salvi and P. Strata, Archs ital. Biol. *102*, 230 (1964).
59 O. Candia, E. Favale, A. Giussani and G.F. Rossi, Archs ital. Biol. *100*, 216 (1962).
60 E. Kanzow, D. Krause and H. Kühnel, Pflügers Arch. ges. Physiol. *274*, 593 (1962).
61 F. Snyder, A.J. Hobson and F. Goldfrank, Science *142*, 1313 (1963).
62 F. Snyder, A.J. Hobson, D.F. Morrison and F. Goldfrank, J. appl. Physiol. *19*, 417 (1964).
63 M.M. Gassel, B. Ghelarducci, P.L. Marchiafava and O. Pompeiano, Archs ital. Biol. *102*, 530 (1964).
64 D.W. Richardson, A.J. Honour, G.W. Fenton, F.H. Stott and G.W. Pickering, Clin. Sci. *26*, 445 (1964).
65 M. Guazzi and A. Zanchetti, Archs ital. Biol. *103*, 789 (1965).
66 F. Snyder, Res. Publ. Ass. nerv. ment. Dis. *45*, 469 (1967).
67 I.M. Khatri and E.D. Freis, J. appl. Physiol. *22*, 867 (1967).
68 W. Baust and B. Bohnert, Exp. Brain Res. *7*, 169 (1969).
69 J.D. Bristow, A.J. Honour, T.G. Pickering and P. Sleight, Cardiovasc. Res. *4*, 476 (1969).
70 G. Coccagna, M. Mantovani, F. Brignani, A. Manzini and E. Lugaresi, Electroenceph. clin. Neurophysiol. *31*, 277 (1971).
71 D. Hawkins, H. Puryear, C. Wallace, W. Deal and E. Thomas, Science *136*, 321 (1962).
72 T. Satoh, T. Ogawa and K. Takagi, Jap. J. Physiol. *15*, 523 (1965).
73 E.H. Geschickter, P.A. Andrews and R.W. Bullard, J. appl. Physiol. *21*, 623 (1966).
74 T. Ogawa, T. Satoh and K. Takagi, Jap. J. Physiol. *17*, 135 (1967).
75 Y. Niimi, K. Kubota and Y. Iwamura, Jap. J. Physiol. *18*, 190 (1968).
76 C.M. Shapiro, A.T. Moore, D. Mitchell and M.L. Yodaiken, Experientia *30*, 1279 (1974).
77 W. Baust, in: Ermüdung, Schlaf und Traum, p. 99. Ed. W. Baust. Wissenschaftliche Verlagsgesellschaft MBH, Stuttgart 1970.
78 C.A. Tassinari, G. Coccagna, M. Mantovani, B. Dalla Bernardina, J.P. Spire, D. Mancia, A. Velta and P. Vallicioni, in: The Nature of Sleep, p. 55. Ed. U.J. Jovanović. Fischer, Stuttgart 1973.
79 J.F. Hiatt and D.F. Kripke, Psychosom. Med. *37*, 320 (1975).
80 W. Baust and W. Rohrwasser, Pflügers Arch. ges. Physiol. *305*, 229 (1969).
81 G. Stacher and G. Fink, in: The Nature of Sleep, p. 59. Ed. U.J. Jovanović. Fischer, Stuttgart 1973.
82 G. Stacher, B. Presslich and H. Stärker, Gastroenterology *68*, 1449 (1975).
83 J.A. Yaryura-Tobias, J.S. Hutcheson and L. White, Behav. Neuropsych. *2*, 22 (1970).
84 J.E. Remmers, D. Bartlett, Jr, and M.D. Putnam, Respir. Physiol. *28*, 227 (1976).
85 J. Orem, A. Netick and W. Dement, Respir. Physiol. *30*, 265 (1977).
86 E.A. Phillipson, E. Murphy and L.F. Kozar, J. appl. Physiol. *40*, 688 (1976).
87 K. Bülow and D.H. Ingvar, Acta physiol. scand. *51*, 230 (1961).
88 B. Duron, Bull. Physiopathol. Respir. (Nancy) *8*, 1031 (1972).
89 E. Lugaresi, G. Coccagna, M. Mantovani and R. Lebrun, Electroenceph. clin. Neurophysiol. *32*, 701 (1972).
90 E.A. Phillipson, A. Rev. Physiol. *40*, 133 (1978).
91 P.L. Parmeggiani and C. Rabini, Brain Res. *6*, 789 (1967).
92 P.L. Parmeggiani, C. Franzini, P. Lenzi and G. Zamboni, Brain Res. *52*, 189 (1973).
93 P.L. Parmeggiani, C. Franzini and P. Lenzi, Brain Res. *111*, 253 (1976).
94 P.L. Parmeggiani, G. Zamboni, T. Cianci and M. Calasso, Electroenceph. clin. Neurophysiol. *42*, 372 (1977).
95 S.F. Glotzbach and H.C. Heller, Am. J. Physiol. *228*, 1880 (1975).
96 S.F. Glotzbach and H.C. Heller, Science *194*, 537, (1976).
97 H. T. Hammel, D.C. Jackson, J.A.J. Stolvijk, J.D. Hardy and S.B. Strømme, J. appl. Physiol. *18*, 1146 (1963).
98 P.L. Parmeggiani, L.F. Agnati, G. Zamboni and T. Cianci, Electroenceph. clin. Neurophysiol. *38*, 589 (1975).
99 H.C. Heller and S.F. Glotzbach, in: Environmental Physiology II, vol. 15, p. 147. Ed. D. Robertshaw. University Park Press, Baltimore 1977.
100 M. Guazzi, G. Baccelli and A. Zanchetti, Science *153*, 206 (1966).
101 M. Guazzi, G. Baccelli and A. Zanchetti, Am. J. Physiol. *214*, 969 (1968).
102 Y. Iwamura, Y. Uchino, S. Ozawa and S. Torii, Proc. Jap. Acad. *42*, 837 (1966).
103 Y. Iwamura, Y. Uchino, S. Ozawa and S. Torii, Brain Res. *3*, 381 (1966).
104 W. Baust, H. Weidinger and F. Kirchner, Archs ital. Biol. *106*, 379 (1968).
105 D.J. Reis, D. Moorhead and G.F. Wooten, Neurology *18*, 282 (1968).
106 G. Mancia, D.B. Adams, G. Baccelli and A. Zanchetti, Experientia *25*, 48 (1969).
107 G. Mancia, G. Baccelli, D.B. Adams and A. Zanchetti, Am. J. Physiol. *220*, 1086 (1971).
108 G. Baccelli, M. Mancia and A. Zanchetti, Eur. J. clin. Invest. *1*, 125 (1970).
109 G. Baccelli, R. Albertini, G. Mancia and A. Zanchetti, Circulation Res. *35*, 625 (1974).
110 T. Kumazawa, G. Baccelli, M. Guazzi, G. Mancia and A. Zanchetti, Experientia *23*, 1021 (1967).
111 R. Henane, A. Buguet, B. Roussel and J. Bittel, J. appl. Physiol. *42*, 50 (1977).
112 I. Oswald, Sleeping and Waking: Physiology and Psychology. Elsevier, Amsterdam 1962.
113 G. Fisher, J. Gross and J. Zuch, Arch. gen. Psychiat. *12*, 29 (1965).
114 R.H. Armstrong, D. Burnap, A. Jacobson, A. Kales, S. Ward and J. Golden, New Physician *14*, 241 (1965).
115 W.C. Orr, W.H. Hall, M.L. Stahl, M.G. Durkin and T.L. Whitsett, Arch. intern. Med. *136*, 655 (1976).
116 D.J. Henderson-Smart and D.J.C. Read, in: Sleep Apnea Syndromes, vol. 11, p. 93. Ed. C. Guilleminault and W.C. Dement. Kroc Foundation Series, A.R. Liss, New York 1978.
117 K. Tusiewicz, H. Moldofsky, A.C. Bryan and M.H. Bryan, J. appl. Physiol. *43*, 600 (1977).
118 Parmeggiani P.L., in: The Regulation of Respiration during Sleep and Anesthesia, p. 47. Ed. R.S. Fitzgerald, H. Gautier and S. Lahiri. Plenum Press, New York 1978.
119 K. Bülow, Acta physiol. scand. *59*, Suppl. 209 (1963).
120 E. Aserinsky, Science *150*, 763 (1965).
121 R.H. Wurtz and J.J. O'Flaherty, Electroenceph. clin. Neurophysiol. *22*, 30 (1967).
122 M. Guazzi and E.D. Freis, Am. J. Physiol. *217*, 1623 (1969).
123 S.A. Fagenholz, K. O'Connell and D.C. Shannon, Pediatrics *58*, 31 (1976).
124 M.H. Bryan, R. Hagan, G. Gulston and A.C. Bryan, Clin. Res. *24*, A689 (1976).
125 E.A. Phillipson, L.F. Kozar, A.S. Rebuck and E. Murphy, Am. Rev. respir. Dis. *115*, 251 (1977).
126 D.P.G. Bolton and S. Herman, J. Physiol. (London) *240*, 67 (1974).
127 E.A. Phillipson, C.E. Sullivan, D.J.C. Read, E. Murphy and L.F. Kozar, J. appl. Physiol. *44*, 512 (1978).
128 J.P. Farber and T.A. Marlow, Respir. Physiol. *27*, 73 (1976).
129 N.N. Finer, I.F. Abroms and H.W. Taeusch, Jr., J. Pediatr. *89*, 100 (1976).
130 J.A. Hobson, R.W. McCarley, R.T. Pivik and R. Freedman, J. Neurophysiol. *38*, 497 (1974).
131 R.W. McCarley and J.A. Hobson, J. Neurophysiol. *18*, 751 (1975).
132 A. Netick, J. Orem and W. Dement, Brain Res. *120*, 197 (1977).
133 J. Orem, in: Sleep Apnea Syndromes, vol. 11, p. 65. Ed. C. Guilleminault and W.C. Dement. Kroc Foundation Series, A.R. Liss, New York 1978.
134 J.M. Affanni, E. Lisogorsky and A.M. Scaravilli, Experientia *28*, 1046 (1972).
135 H. Twyver van and T. Allison, Brain Behav. Evol. *9*, 107 (1974).
136 P.L. Parmeggiani and C. Franzini, Brain Res. *29*, 347 (1971).
137 R. Hess, Jr., Electroenceph. clin. Neurophysiol. *16*, 44 (1964).

138 W. Dement and N. Kleitman, Electroenceph. clin. Neurophysiol. *9*, 673 (1957).
139 A. Rechtschaffen and A. Kales (eds.), A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Public Health Service, Publication No. 204, U.S. Government Printing Office, Washington D.C. 1968.
140 R. Ursin, Brain Res. *20*, 91 (1970).
141 M. Holzapfel, Naturwissenschaften *28*, 273 (1940).
142 H. Hediger, Med. Klin. *20*, 938 (1959).
143 H. Hediger, Proc. Roy. Soc. Med. *62*, 153 (1969).
144 G. Moruzzi, Archs ital. Biol. *107*, 175 (1969).
145 W.B. Cannon, Physiol. Rev. *9*, 399 (1929).
146 M. Jouvet, Physiol. Rev. *47*, 117 (1967).
147 M. Jouvet, Ergebn. Physiol. *64*, 166 (1972).

4. Sleep and body restitution

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Summary. Although human non-REM sleep is usually associated with body restitution, such an hypothesis is debatable. This sleep, like REM sleep, may have a beneficial role for the brain. Because man demonstrates relaxed wakefulness, body restitution may not be confined to human sleep. However, for active mammals, sleep may be an enforced immobiliser facilitating this restitution.

It appears that the substantial findings from human sleep deprivation research are not amongst measures of somatic functioning, but are within performance, behaviour and EEG changes[1,2]. This suggests that, in man, sleep may be more directed towards brain rather than body restitution. However, it is commonly supposed that human non-REM sleep, particularly stages 3 and 4 (collectively called slow wave sleep (SWS); not to be confused with the S.W.S. of non-primate mammals) are associated with body restitution, especially as human growth hormone (hGH) is found in large quantities in the plasma during SWS. But, the possible orientation of human sleep towards the brain suggests that any identification of SWS or of any other form of human sleep with body restitution, needs further consideration. In fact, as will be seen, human sleep may be an unnecessary but convenient vehicle for body restitution. It will be assumed here that SWS may be an intense form of non-REM sleep, both in terms of EEG characteristics and of function.

SWS and hGH

The link between SWS and hGH has also been shown through studies of, for example: *a*) afternoon naps[3] which contain both SWS and an hGH peak, whereas morning naps contain REM and stage 2 sleep, with no hGH peak; *b*) schizophrenia[4] and depression[5] which have disturbances of both SWS and the sleep hGH peak. However, as hGH-deficient children have normal SWS levels, but no sleep-related hGH release[6] and as hGH inhibiting factor can shift the hGH peak to stage 2 sleep[7], the link between hGH and SWS may not be causal. In sleep, unlike in wakefulness, the hGH release is not related to normal plasma levels of free fatty acids, amino acids, glucose etc., present at the time and it has been suggested[8] that, for unknown reasons, the sleep-hGH release may be under neural rather than metabolic control.

It is generally believed that the main function of hGH is the promotion of anabolic processes, especially of protein synthesis. However, recent reviews[9,10] on the actions of hGH in adults show that this may not be so and that the emphasis of hGH action is upon protein sparing and the regulation of energy substrates, especially fats. There is no reason to exclude the brain as a target site for the sleep-hGH release. Finally, it must be noted that this release may not be central to sleep function, as such a phenomenon is not found in the majority of other mammals so studied[11].

Protein synthesis and mitosis during sleep

It has been proposed[12] that sleep, particularly non-REM sleep, provides for high levels of tissue restitution (e.g. increases in protein synthesis and mitosis). However, increases in protein synthesis during human sleep are probably unlikely for 2 main reasons: a) lowered night-time levels of plasma amino acids, b) reduced metabolism of sleep. A major factor governing the rate of protein synthesis is the availability of amino-acids to the cell[13], but plasma amino acid levels are low during sleep[14] because of the normal night-time fast. Thus it might be expected that protein synthesis could not be high during sleep and very recent work[15] on humans supports this viewpoint. It was shown that at night-time, including sleep, both protein synthesis and degradation were reduced, resulting in an overall condition of protein conservation. For any elevation of protein synthesis to take place during sleep it would seem that regular feeding throughout this period is necessary[16].

Protein synthesis and precursory activities require much energy (ATP) and probably account for a significant proportion of resting metabolism[17]. However, metabolism during sleep is lower than in relaxed wakefulness[18] and follows the circadian temperature rhythm. Combining these points, increased levels of protein synthesis would be unlikely during sleep. The overall extent of decreased muscle tonus