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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

from relaxed wakefulness to sleep is very small[19], so there is little energy saving here, which could be diverted to increase protein synthesis without a net change in metabolism during sleep. It has been claimed[12] that cellular ATP levels are particularly high during sleep, enhancing protein synthesis. But such conditions would produce large amounts of ADP. As ADP stimulates O_2 consumption, then a heightened metabolism would still be expected.

Although the fact that circadian peaks in mitosis occur in certain tissues during sleep could be used in support of a body restitutional hypothesis for sleep, such peaks still occur without sleep[20]. Also, there are in man individual differences in these peak times, resulting in peaks well before the sleep period[21]. These findings suggest that such peaks are a result of inactivity rather than of sleep per se. This proposal is supported by the findings that exercise reduces mitosis and that cortisol has a major inhibitory influence over mitotic rates[21]. As cortisol has a pronounced and sleep-independent circadian rhythm[22], again it would seem that a mitotic peak during sleep is only a concomitant phenomenon. Rodents have mitotic peaks clearly associated with sleep[23,24] but as these animals are very active during wakefulness[25,26], sleep may just be an enforced immobiliser; if other immobile states were possible then mitotic rates would presumably be the same as for sleep.

Exercise and physiological stress

The findings of increases in SWS following exercise[27] have favoured a body restitutional role for SWS. But more recent studies[28–31] refute this exercise effect. Whereas one study[28] reported an increase in sleep hGH, another found no such change[29]. A parsimonious explanation[30] for all these findings is that although the exercise recovery process begins with the end of exercise, it may intrude into sleep, rather than require general or specific forms of sleep.

Increases in SWS following unusual metabolic demands have been reported after the following: very heavy exercise[32], starvation[33], sauna[34] and in hyperthyroidism[35]. Although none of these studies assessed hGH, the SWS effects may be associated with stress or re-distribution of energy substrates and not necessarily with increases in body tissue restitution. But, of course, changes in sleep following extreme stress or illness may not indicate the normal functions of sleep.

If SWS or non-REM sleep facilitates body restitution, then prolonged rest might be expected to reduce one or both of these types of sleep. However, 6 weeks of bed-rest in healthy young adults produces no change in any form of sleep[36]. The only long term immobility study[37] of quadriplegics and paraplegics, showed that patients under 35 years of age averaged 11% SWS (normal value: approx. 16%). As most of the patients were totally immobile, much less SWS would be expected if this type of sleep were for body restitution. Interestingly, whilst non-REM sleep had higher than normal values, REM sleep was substantially reduced.

To summarise the discussion so far, the evidence surveyed suggests that human sleep, particularly non-REM sleep or SWS, is not causally related to body restitution and that for man, sleep may only be a convenient vehicle for these processes, being little better than other relaxed states. However, for mammals which show little relaxed wakefulness, sleep may well be an enforced immobiliser which results in levels of restitution higher than those to be found during (active) wakefulness.

There are indications that SWS is a resilient and necessary form of sleep, superseding REM sleep in both these respects. For example: SWS is more prominent in the early sleep period than is REM sleep; a SWS rebound appears to take priority over a REM sleep rebound following total sleep deprivation[38,39]: SWS appears to take precedence over REM sleep in enforced, limited sleep regimes[40,41], and in natural short sleepers[42,43]; SWS is much harder to deprive selectively than REM sleep[44]; SWS unlike REM sleep, is positively correlated with the length of prior wakefulness[45,46] suggesting that SWS may be more associated with restitution than is REM sleep. As human sleep may be oriented towards brain restitution, then SWS may be associated with this restitution.

SWS and the cerebral cortex

It could be assumed that the EEG delta activity of SWS represents an immature or vegetative state of the cortex. But SWS, especially stage 4, appears to be one of the last sleep stages to develop during primate ontogeny[47]. During SWS, the cortex has adequate energy substrates and cortical unit firing rates are not low[48,49]. SWS may represent a unique cortical state, as this EEG activity may be due to a reduced thalamocortical drive, resulting in a form of cortical isolation[48,50]. Such peculiar isolation may be reflected in the numerous reports of high arousal thresholds for SWS, and in sleepwalking: a phenomenon almost exclusive to SWS[51].

Sleep neurophysiology usually concerns itself with neurons rather than with neuroglia. However, with mammalian evolution neuroglia become increasingly prominent in the cerebrum, and it has been proposed in an interesting and detailed review[52] that non-REM sleep (including SWS) represents increased anabolism in neuroglia, whereas REM sleep reflects heightened neural metabolic activity.

Whether or not non-REM sleep has a restitutional role for the brain is a matter of contention, as REM sleep is usually solely identified with this role. However, there is recent evidence that if realistic forms of high cognitive load are given during wakefulness in

humans, then it is SWS rather than REM sleep which is increased[53]. It was argued[53] that the many studies on the effects of learning upon sleep generally do not 'exert' the cerebrum and probably produce little cerebral fatigue.

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5. The biology of natural sleep in animals

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'Sleep is a natural, repeated
unconsciousness that we do
not even know the reason for.'
(K.R. Popper and J.C. Eccles[1], p.496.)

The present-day experiments on sleep are a typical example of the way in which experimental research stretches far beyond the mere description of natural processes. To fill the gap between the two approaches, some elements of comparative zoology will be considered here. Like many other vital functions, sleep is common to both humans and animals, so that a comparison can be made. This is especially the case when the comparison takes evolution into account; then conclusions can be expected from the comparative aspects of anatomy and behavioral psychology.

Sleep, as we know it in man, cannot be proved for all animals; it appears to be a 'monopoly' of vertebrates, which means that it is phylogenetically of late appearance. So long as we are dealing with homoiothermic animals, i.e. birds and mammals, we are on relatively safe ground; it becomes less certain the further we descend through the grades of vertebrates to the poikilothermic animals, through reptiles to amphibians and fish.

The drawing of this somewhat uncertain deep boundary agrees more or less with the definition quoted from Popper and Eccles[1]. If 'sleep is a natural state of unconsciousness', this presupposes a state of consciousness also. In fact, we find pre-forms of 'consciousness' – in the sense of a simple awareness of the animal's own body (including the shadow) – even in some fish[2].