What is the primary function of sleep?

There has been some debate about the definition of sleep. Common elements of definitions include i) a state of greatly reduced sensory awareness and responsiveness to surroundings ii) rapidly reversible iii) governed by circadian regulation and also iv) homeostatically regulated whereby sleep deprivation leads to an increased drive for sleep and subsequent rebound sleep (Mansfield etal2017).

There can be no doubt that sleep must have an evolutionary advantage given that all animals sleep. Humans spend 33% of their life asleep. Historically Aristotle in 350BC stated that sleep arises of necessity for the sake of conservation. Galen in 162A. D. proposed that sleep and wake were governed by brain activity.

Shakespeare described nightmares and the pleasure of sleep in various plays (1598, 1606).

In the mid-17 th century Thomas Willis confirmed Galen’s theory that wake and sleep are controlled by the brain (via experiments lesioning various parts of the brain).

Throughout the 20 th century biological knowledge of sleep has grown at a steady rate.

In the 21 st century there has been consolidation of sleep medicine as a distinct discipline and subsequent growth in knowledge about sleep slowly increasing academic, clinical and societal focus on the importance of sleep, for example the recent report Asleep on the Job (Australian Sleep

Association, 2017), although concern remains that increased numbers are sleeping less (Knutson, 2010).

There have been a number of theories advanced through the last hundred and more years as to the function of sleep. I will now review some of the more common ones remembering that they are not mutually exclusive.

Given that a species does not need to be continually active to survive it was formally presented by Allison (1970) that a major function of sleep was to conserve energy. This theory was advanced by many including Berger (1993) who described the various situations whereby animals drop their core temperature(and presumably metabolic rate) advantageously by sleeping. It has been shown that NREM sleep is relatively hypometabolic (Brown etal, 2013) although the energy-saving is relatively small and another study following ATP consumption highlights that sleep is an energy active process (Dworak, 2010). Debate on the area is not yet complete with a recent mathematical model suggesting the energy conservation may be significantly greater than previously thought (Schmidt etal, 2017). Smaller animals with greater surface area ratios and hence higher metabolic needs don’t necessarily sleep longer and some other animals such as dolphins remain active through sleep and hence their energy conservation during sleep is minimal and yet their sleep processes are similar to other species suggesting this is not the primary purpose the of sleep although may be a secondary function of sleep.

Adaptive inactivity is another suggested function for sleep. When the species is at a relative disadvantage (for example at night if the species has limited

nocturnal vision) they enter sleep and hence are less likely to attract preditors (Meddis, 1975). Conversely if there was not the need to sleep then one would suggest survival would be even better protected and thus it seems unlikely this is the major reason for sleep.

Probably the current strongest theory suggests that sleep has a primary neurophysiological maintenance and restorative role. Sleep has been shown to have beneficial effects on protein synthesis, the immune system, cell maintenance and regeneration. Memory consolidation has been shown to be another important function. Examples of research in these areas will now be presented.

It has been hypothesised that the function of sleep is to regulate and preserve the neural circuits of the brain. Heavily used circuitry during wakefulness are rested in sleep to prevent excessive and continuing up regulation and infrequently used circuits are activated during sleep to essentially preserve them (Krueger et al, 2008).

In a well constructed mice model it was shown that the interstitial space in the brain increased by 60% during sleep and it was shown that during the draining of this fluid during the wake period much of the B amyloid (and by implication other toxins) were flushed out (Xie et al, 2013) suggesting that removal of toxins is a vital role of sleep.

Other animal models have supported the association of sleep deprivation and impaired immune function. A reduction in natural killer cells (thought to inhibit neoplastic cells) and peripheral CD4+ and CD8+ cells (concerned with general immunity) was seen in sleep deprived mice (18 hours wakefulness

for 2, 7, 14 or 21 days) (De Lorenzo etal, 2018). This would suggest greater risk of cancer and possibly infections and neuroinflammatory conditions (including mental health, cardiovascular, endocrine and autoimmune conditions).

There is also data to support the consolidation of memory and learning as a key element of sleep. The ability to learn and memorise and process experiences is of great adaptive disadvantage to a species. A recent study of 57 insomniacs compared to 29 normal sleepers showed clearly inferior neuropsychological performance in spatial span, visuospatial memory tests, fluency, emotional management and continuous performance tasks. It was also noted that BDNF levels were significantly reduced in the poor(<6hours) sleepers (Fan etal, 2018). Sleep deprivation has been seen to impair psychomotor vigilance tasks (Lamond and Dawson, 1999) by implication increasing risks of accidents/harm.

If this was the primary purpose of sleep those species with a complex brain and more complex cognition would require more sleep. However all species sleep and the amount of sleep does not seem to be related to the complexity of cognition. Also, albeit attenuated, memory and learning can still occur in the absence of sleep and hence memory is likely an important, but not primary, function of sleep.

Given sleep is highly complex and interconnected neurologically and functionally it is hard to isolate one particular function as predominant. Hence it could be suggested that the primary function of sleep is summative with all functions combining to provide health to the organism. There is a

large body of human evidence that links sleep dysfunction to various illness states and by implication maintenance of sleep is protective. I will now review a selected literature illustrating this in humans.

Longer term sleep disorder has been suggested to lead to increased mortality. From 1985-88 a population of 10, 000 underwent a clinical examination and general health questionnaire including how long they slept at night. 8000 were followed up in 1991-92 and in this phase 3 of the study further questions were asked about time with family and at work. Results were grouped into low levels of sleep (<5 hours sleep), normal levels (6-8hours) and extended sleep (> 9). Those whose sleep altered across categories during the course of the study were reviewed as separate groups.

Mortality was followed via the NHS central registry until September 2004. Hence the death rate was monitored for a period of 17 years from phase 1 and almost 12 years post phase 3. The study gathered covariates such as sociodemographic factors, existing morbidity, cardiovascular risk factors, and health related behaviours via the general health questionnaire.

It should be noted that 81% of the participants from phase 1 were able to be followed at phase 3. 5% of those who were unable to be followed up were found to have died. The review of this data found a U-shaped association with short sleep (<5hrs) and long sleep (> 9hours) and all causes mortality compared to ‘ normal’ sleepers and this was statistically significant after adjustment for the covariates with hazard ratios of more than 2 (Ferrie et al, 2007).

The large population size and the extended longitudinal nature of the study provide a strong suggestion that poor sleep is associated with mortality. There were some limitations study including the data on the sleep being gained from questionnaires and not supported by sleep diaries, actigraphy or PSG. It also did not specifically differentiate between time of going to bed and when sleep was attempted.

A the more recent meta-analysis reviewing 13 studies covering a population of 1, 383, 000 found very similar results with short sleep inferring a 1. 12 hazard ratio and with long sleep associated with a 1. 3 hazard ratio (Cappuccio et al, 2010).

Those with sleep disorder have been seen to have a higher than expected rate of psychiatric illness. A 1989 community-based sample of 10, 534 were interviewed via a general health questionnaire including sleep-related questions. 10% of respondents reported insomnia and 3% hypersomnia. There was a comorbid psychiatric illness in 40% of those with insomnia and 46% of those with hypersomnia. The rate of psychiatric illness in those with no sleep disturbance was 16% (Ford et al, 1989). 7954 of the respondents were able to be re-questioned after one year. Those with initial insomnia and no psychiatric comorbidity had a 57% rate of developing a new mental health condition and those with hypersomnia and no comorbid mental health issue had a 64% rate of developing a new mental health condition through the year. Those without insomnia at baseline had a 25% rate of developing a mental health condition. Of note substance use disorders were considered as mental health conditions and with anxiety disorders and depression were the highest mental health diagnoses.

It is well established that those with mental health conditions have attenuated lifespans. Although this is most overt in schizophrenia (Ringen et al, 2014) it has been seen to a lesser extent in those with high prevalence mental health disorders (Lawrence et al, 2001). One of the hallmark studies in the area, Duty to Care, followed the health outcomes for up to 20 years of approximately 200, 000 patients who had received mental health care. They noted a 20% percent reduction in lifespan for those with schizophrenia, and 10% reduction in those with depression anxiety and substance use disorders (Lawrence et al, 2001).

A growing amount of research has been considering increased cardiovascular disease and sleep disturbance. This is most prominent with sleep apnoea and there has been some linkage with shift workers. Recently a multinational double-blind randomised controlled trial enrolled 13, 000 patients less than 30 days after an acute coronary event. There was a sleep and shiftwork survey together with the Berlin questionnaire screening for OSA. In summary patients who slept less than six hours a night had a 29% risk of a new cardiac event compared to those with longer sleep. Those who screened positively for OSA had a 12% higher risk of a cardiac event. Overnight shiftwork lead to a 15% higher risk. Individuals with all three sleep-related risk factors had twice the risk of cardiac events. The authors concluded that short sleep duration, OSA and overnight shiftwork were predictors of adverse outcomes after acute coronary syndrome (Barger et al, 2017).

Short sleep duration and higher BMI and weight gain was noted in a cohort of 3055 older men and 3052 women followed in an Osteoporotic Fractures

Study. Sleep was determined with actigraphy and sleep diaries. OSA was identified via home PSG in those at high risk group. Those with less than 5 hours sleep a night had BMIs on average of 2. 5 (males) and 1. 8 (female) higher than those with normal sleep after covariates such as OSA were considered. (Patel, 2008).

In another large study of 18, 121 of which 4318 had impaired glucose metabolism and 4225 type II diabetes sleep of 9+ hours was associated with worse glycaemic control for those with impaired glucose metabolism and diabetes but not for the controls (Zheng et al, 2015). Other studies have shown a strong association between short sleep and poor glycaemic control in those with type II diabetes (Tang et al, 2014) (Knutson et al, 2006).

Both obesity and diabetes have been shown to significantly shorten life.

In summary initially this paper illustrates the importance of sleep to human psyche via a brief historical review and then some of the recent hypotheses on the functions of sleep are considered. Rather than trying to delineate which of the interconnecting functions of sleep is the primary one it is suggested that the combination of the functions form the primary role which is to assist in the survival of the species.

Some illustrative articles have been reviewed to indicate the associations and probable linkage of poor sleep with increased mortality and specifically higher rates of mental illness, substance use disorder, cardiovascular disorders and metabolic disorders. This is not an exhaustive review of links and associations between sleep and health but does give weight to the view that the prime purpose of sleep is to maintain health.

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