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Is sleep in animals affected by prior waking experiences?

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Abstract

Methods to assess changes in the mental state of animals in response to their environment can be used to provide information to enhance animal welfare. One of the most profound changes of mental state observable in mammals is the change between wakefulness and sleep. Sleeping mammals have characteristics that are similar to one another and are measurable, such as specific behaviours, changes in responsiveness to external stimuli and changes in electrophysiology and neurochemistry. Although sleep is a ubiquitous behaviour in the life of mammals, there has been relatively little research on this topic in domesticated animals. All animals are motivated to sleep and this motivation increases after a prolonged period of wakefulness. In humans, sleep can be affected by what has occurred in the prior period of wakefulness and this has also been demonstrated in some non-human mammals. An important aspect of human sleep medicine is the association between stress and subsequent sleep disturbances. Studying changes in amount, bout length, distribution or type of sleep after exposure to potentially stressful events, could help us understand how animals respond to changes in their environment. It is possible that different types of stressors could affect sleep characteristics in different ways and that monitoring and identifying these changes could be useful in providing an additional way of identifying management procedures that have the potential to affect welfare. Sleep measurement is a potentially valuable tool in studies to assess animal welfare.

Keywords: *animal welfare, non-REM, REM, sleep, stress, wakefulness*

Sleep and animal welfare

Some animal welfare studies try to ascertain what an animal feels about its experiences (Duncan 1993). However, the various methods used to obtain objective data from animals are indirect measures that in some circumstances may be related to the subjective mental experience of animals. One of the most profound changes of mental state observable in mammals is the change between wakefulness and sleep. Stenberg (2007) described sleep as "a reversible, physiological state with reduced mobility and reduced responsiveness to sensory stimuli". Sleeping mammals have characteristics that are similar to one another and are measurable, such as specific behaviours, changes in responsiveness to external stimuli and changes in electrophysiology and neurochemistry. Although sleep is a ubiquitous behaviour in the life of mammals, there has been relatively little research on this topic in domesticated animals (Abou-Ismail *et al* 2007). Sleep is often not considered a 'behaviour' but merely a form of inactivity. This attitude is misplaced, as sleep is a very important behaviour in the life of all mammals and birds. All vertebrates undergo a period, or several periods of reduced vigilance during the 24-h period (Meddis 1975; Campbell & Tobler 1984). The number of hours a day spent sleeping varies between different species of mammals. For mammals such as cats, sleep is the major behaviour/mental state in which they live, spending 65% of their lives sleeping (Allison & Cicchetti 1976). Humans sleep on average 7.5–8 h per day, but the percentage of time spent sleeping can range from 16 to 46% of the time (Mahowald & Schenck 2005). Although other mammals, such as sheep, spend less time asleep, it still occupies about 15% of their time (Ruckebusch 1972). Siegel (2005) considered that diet was an important factor affecting sleep in that carnivores sleep for longer per day than omnivores and herbivores sleep for the least time. This might be due to the vulnerability of herbivores to predators or the need to spend a large proportion of the day grazing. In small animals, the duration of a sleep cycle (the time taken to cycle from non-Rapid-Eye-Movement [non-REM] sleep, through Rapid-Eye-Movement [REM] sleep to waking) is shorter than in larger animals.

In humans, waking experiences can affect subsequent sleep and sleep disturbances can affect subsequent waking performance (eg Åkerstedt *et al* 2000). There is potential to examine whether waking experience and sleep are interconnected in animals and whether this information can be useful when assessing the welfare of animals. This review will show that the potential applications of studies of sleep in domesticated animals are large and diverse. For example, sleep could be useful in assessing how comfortable animals are with their environment. In experimental studies, changes in sleep in response to earlier stressors, eg a change in the social environment, might indicate that a psychological change had resulted in a measurable physiological change. In studies of chronic environmental effects, eg of barren housing, measurement of sleep could be combined with other types of measurement to study whether there is evidence of 'depression' in the animals. The consequences of potentially painful conditions, eg arthritis or surgical mutilation, could be assessed by measurements of disturbance to sleep. There are also potential welfare consequences of management procedures, such as long distance transportation or manipulation of lighting patterns on sleep deprivation, the development of fatigue and the disruption of established circadian rhythms of sleep.

Sleep behaviour

The clearest physiological evidence of sleep is brain electrical activity — the electroencephalogram (EEG) — which is difficult to measure outside the laboratory or clinic. It is therefore useful to identify behaviours and other more easily recognised features associated with sleep. Many animals choose specific locations in which to sleep. They may use these areas only for sleeping and not just for other resting behaviour at other periods. The sleeping sites often act as protection from predators for prey animals and usually afford the animal some shelter or comfort (Anderson 1998). A sleeping animal can be recognised by lack of movement. There can be minor changes in posture and twitches (Tobler 1995). Furthermore, the postures adopted by mammals when sleeping are often characteristic, repeated and a reliable indicator that a sleep bout is occurring, is just about to occur, or has just finished. In rats, three main sleeping postures have been related to specific changes in the spectral properties of the EEG. The posture adopted varies according to species, but generally, the posture chosen is a relaxed one, allowing for a reduction in muscle tone with deepening sleep (Tromp *et al* 1990). Some mammals, such as horses, can undergo light sleep when standing up, but most mammals must adopt a relaxed posture, eg lying down, during deeper sleep.

Responsiveness to external stimuli during sleep

The change from 'consciousness' to 'unconsciousness' in the transition from wakefulness to sleep is the most obvious change in mental state in both humans and other animals (Vanderwolf 1992). There is a change in both awareness and the responsiveness of humans to their environment during the transition from wakefulness to sleep and within the levels of deepening sleep (Williams *et al* 1964). Humans and non-human mammals need a greater stimulus to induce a behavioural response when in deep sleep than in light sleep (Dillon & Webb 1965; Vanderwolf 1992). To provoke a response from a sleeping human the stimulus needs to be intense or relevant to the human (eg saying their name; Bastuji *et al* 2002). In rats, auditory arousal stimuli have to be louder when they are asleep than when awake and there are differences in the arousal threshold in different stages of sleep (Neckelmann & Ursin 1993).

Electrophysiological characterisation of sleep

Sleep is often thought of as a period of inactivity however the brain remains active throughout sleep. The changes in electrical activity in the brain result in differences in voltage potentials that can be recorded on the surface of the brain as an electrocorticogram (ECoG) or on the surface of the scalp as an EEG.

The different electrophysiological characteristics of the stages of sleep during the sleep cycle of a normal, healthy, adult human, and a standardised method of scoring them, have been described in detail by Rechtschaffen and Kales (1968). In humans, there are four stages of non-REM sleep. A 'fifth' stage is that of REM sleep, identified when the posture becomes relaxed and only eye movements and occasional twitches are seen. REM sleep is sometimes referred to as 'paradoxical sleep' as the EEG contains beta activity, primarily seen during wakefulness, yet humans are asleep during this sleep stage. Humans in REM sleep are difficult to awaken, but when woken they report feeling alert, quite different from being woken from non-REM sleep. In addition, when woken from REM sleep, humans will usually report that they have been dreaming, which is only reported in about 20% of the times when humans are woken from other sleep stages (Jouvet 1967).

Sleep in non-human animals is also split into two main stages, REM and non-REM sleep. In the rat, the non-REM period is either treated as one sleep stage, or split into two main stages (often referred to as 'light sleep' and 'slow-wave sleep'). However, Timo-Iaria *et al* (1970) suggested that rat non-REM sleep was as complex as human sleep (albeit shorter) and at least three distinct stages could be differentiated. In primates, non-REM sleep can be split into four stages, similar to those of humans (Kripke *et al* 1968). However, if non-invasive EEG techniques or behavioural recordings are used, it is not possible to reliably identify the different characteristics of the various stages in non-REM sleep and only wakefulness, non-REM and REM sleep can be differentiated (Balzamo *et al* 1998).

REM sleep and non-REM sleep are positively correlated, ie animals which show a large amount of non-REM sleep will show a large amount of REM sleep (Siegel 1995). The REM period is approximately 25% of total sleep (Hendricks & Morrison 1981; Horne 2000). Differences between mammals occur in the density of eye movements during REM bouts and in the total and bout durations of REM sleep (Adams & Barratt 1974). Brief arousals occur in animals after the majority of REM sleep bouts (eg in rats: Timo-Iaria *et al* 1970; in cats: Jouvet 1967). There is a transition process from wake to sleep, where changes in the EEG are seen. In humans, during relaxed wakefulness prior to sleeping and specifically with the eyes closed, alpha rhythms dominate the EEG (Gottesmann 1996). This may be similar to drowsiness in ruminants, which occurs when the animal is lying down during rumination prior to sleeping (Ruckebusch 1972).

Possible functions of sleep

Sleep function across taxa has been reviewed by Allison and Cicchetti (1976) and Lima *et al* (2005). The suggested functions of non-REM sleep include: physiological restoration (Inoue *et al* 1995); rest for the pre-frontal cortex (Muzur *et al* 2002); memory processing (Cai 1995); and reducing energetic output to increase efficiency (Meddis 1975; Berger & Phillips 1995). There are perhaps even more suggested functions for REM sleep. These include: the 'sentinel hypothesis' — being able to respond quickly to relevant stimuli (eg Cote *et al* 2001; Lima & Rattenborg 2007); recuperative functions (Brunner *et al* 1990); and complex memory consolidation and learning (Sejnowski 1995; Smith 1996; Maquet 2001). In addition, the majority of REM episodes in humans involve dreams and there is evidence that other mammals experience dream-like occurrences during REM sleep (Jouvet 1972).

Sleep and stress

Studies within human sleep medicine have shown that waking experiences and subjective feelings can affect subsequent sleep latency, quality and quantity and that disturbance to sleep can affect subsequent waking performance (Van Reeth *et al* 2000; Komada *et al* 2001). Åkerstedt *et al* (2002) found associations between 'psychological stress', eg worrying about work, and disturbed sleep. Major stressful events leading to post-traumatic stress disorder in humans have also been shown to affect sleep, years after the original stressor (Germain & Nielsen 2003; Otte *et al* 2005). Likewise, Feng *et al* (2007) showed that in rats stressors early in life could have long-term effects on sleep.

There does not appear to be a clear and direct relationship between sleep and the release of hormones involved in the hypothalamo-pituitary-adrenal axis during stress (Buckley & Schatzberg 2005). In humans, non-REM sleep is reduced by infusions of corticotropin-releasing hormone and ACTH, but is increased by cortisol, and REM sleep is reduced by infusions of ACTH and cortisol (Steiger 2007). There is however, a circadian pattern to the secretion of hypothalamic-pituitary-adrenal hormones, which may have a sleep regulatory function (Friess *et al* 1995). In the absence of stressors, corticotrophin-releasing hormone appears to contribute to the regulation of spontaneous waking without activating the hypothalamo-pituitary-adrenal axis (Sanford *et al* 2008). Meerlo *et al* (2001) suggested that some stressors may be associated with an increase in arousal and alertness and that this could 'inhibit the occurrence of sleep'. Other, perhaps more 'emotionally extreme', stressors could build up a sleep debt, increasing both the motivation for sleep and the 'intensity' of the sleep experienced.

Pawlyk *et al* (2008) reviewed the literature on relationships between stress and sleep in rodents. Short periods (1–2 h) of immobilisation stress can increase the time spent asleep. This effect did not appear to be related to the associated increased corticosterone release, but they considered that it might be associated with opioid and noradrenergic activation. Longer periods (22 h per day) of immobilisation reduce the time spent asleep and electric shock treatments can result in reduced REM sleep. These treatments activate corticotrophin-releasing hormone and serotonin neurotransmission and these are inhibitory to sleep, and to REM sleep in particular. Sanford *et al* (2003) showed decreased REM sleep in mice that were trained to associate an auditory signal with a foot-shock. The mice showed reduction in REM sleep after presentation of the auditory signal alone, and this response was seen for two days after the presentation of the signal. This suggested that sleep was affected by the stressor/painful stimulus itself and the psychological association, eg anticipation and fear, of the stimulus.

There has been very little research on the effects of stressors on sleep in livestock. Ruckebusch (1975a,b) showed that cattle experienced increased fragmentation of sleep after changes in housing and had reduced total sleep time after parturition and again when the calf was removed.

An important aspect of human sleep medicine is the association between stress and subsequent sleep disturbances. There is potential to examine whether these relationships exist in domesticated animals and to study their significance for animal welfare. Studying any changes in amount, bout length, distribution or type of sleep after exposure to potentially stressful events, could help us understand how animals respond to changes in their environment. It is possible that different types of stressors could affect sleep characteristics in different ways and that monitoring and identifying these changes could be useful in providing an additional way of identifying management procedures that have the potential to affect welfare.

Sleep and subjective mood

Humans with clinically depressive moods can have differences in sleep pattern compared with healthy people (Thomsen *et al* 2003). Moreover, people with sleep disorders, such as sleep apnoea, are more likely than healthy people to suffer from depression (Vandeputte & de Weerd 2003). The effects of chronic mild stress regimes in non-human animals are often used as models for human depression and the behavioural alterations in rats after a regime of chronic mild stress are similar to those seen in humans (Grønli *et al* 2004).

Depression in humans is associated with a reduction of serotonin in the brain. Serotoninergic systems are active during wakefulness and inactive during sleep, and inactive during the transition to and in REM sleep (Adrien 2002). Adrien (2002) suggested that if there is a reduction of serotonin associated with depression, then the transition and continuation of REM sleep would be facilitated.

The changes in the sleep/wake pattern in humans with depression are a shortening in the latency to exhibit REM sleep and an increase in the frequency of REM sleep (Rotenberg *et al* 2002). The quality of REM sleep is also affected by depression; patients with clinical depression have a greater density of eye movements during the eye-movement bursts that are present during REM sleep (Douglass *et al* 1992; Buysse *et al* 2001). In addition, Röschke and Mann (2002) showed changes in the spectral qualities of the EEG during non-REM sleep in depressed humans.

Sleep is not just related to negative moods and depression in humans, but it is also related to positive moods. People who were rated as happy also self-reported that they slept well. In addition, the majority of such people viewed sleep as a positive experience saying 'they look forward' or 'enjoy' going to sleep (Dement 2000). If evidence of this, including measurably distinct sleep characteristics, were to be demonstrated convincingly in animals, it might lead to ways of indicating positive welfare states, or their absence.

Sleep and pain

It is well documented in human medicine that sleep can be affected by aversive experiences such as a painful condition (reviewed by Moldofsky 2001). Drewes *et al* (1998) showed that humans with rheumatoid arthritis were more likely to experience shorter, more fragmented, sleep bouts than healthy controls. There are also relationships between sleep and pain in non-human animals. Rats with adjuvant arthritis showed a significant reduction in REM sleep, a reduction in the highest amplitude slow-wave sleep, a lowering of the amplitude of slow waves throughout the sleep periods and could not sustain long periods of sleep (Landis *et al* 1989). Cats given formalin injections showed 'pain-related behaviours' and decreased sleep, particularly non-REM sleep as compared with handled controls (Moldofsky 2001). Onen *et al* (2001) showed a two-way relationship between pain and sleep. By depriving rats of REM sleep and then testing for pain sensitivity, they found that rats that had been deprived of REM sleep had lower thresholds in response to minor pain and increased their behavioural responses to electrical stimulation compared to handled controls (Onen *et al* 2001). After sleep recovery, the thresholds for pain had returned to pre-sleep deprivation levels. This suggests that the efficacy of the pharmacological manipulation of pain, to aid sleep, or of sleep, to alleviate pain, or both, may be worthwhile welfare-enhancing strategies to explore in animals (Mellor *et al* 2009).

Sleep and sleep deprivation

In studies in humans and/or rats, sleep deprivation has been shown to increase extracellular serotonin concentration (Lopez-Rodriguez *et al* 2003), reduce reaction times (Scott *et al* 2006), adversely affect immunity (Everson 1995; Ozturk *et al* 1999), increase food intake (Rechtschaffen *et al* 1983; Rechtschaffen & Bergmann 1995) and reduce REM sleep during the recovery period (Cajochen *et al* 1999). In rats, sleep deprivation, can cause activation of the hypothalamo-pituitary-adrenal axis (Sgoifo *et al* 2006), and alter the reaction to subsequent stressors (Meerlo *et al* 2002) and ACTH (Sgoifo *et al* 2006). There has been little research into sleep deprivation in livestock. In cattle, Ruckebusch (1974) studied the effects of REM sleep deprivation on subsequent sleep periods. REM sleep was prevented by restricting lying for 14 h per day for 4 weeks, 20 h per day for 2 weeks and 22 h per day for 2 weeks. The sleeping pattern of the cattle adapted within 5 days so that a similar total amount of REM sleep to that during the baseline period (no lying restriction) was seen, but it occurred during the day when lying was permitted. In the final 4 weeks, REM sleep was much reduced (and absent in the 22 h per day deprivation weeks). There was an increase in non-REM sleep during this time while the cows lent on the strap that stopped them from lying down. The bouts of non-REM sleep decreased in duration as compared to the baseline period. In the fourth day post-deprivation, rebounds were seen in both non-REM and REM sleep. Fragmentation of non-REM was reduced, ie bouts increased in duration, and REM sleep showed double the number of episodes compared to baseline values. This included sleep during the day, although by the fifth day, post-deprivation sleep only occurred at night.

Sleep and fatigue

There is a confusion of terminology between feeling sleepy and feeling fatigued (Loge *et al* 1998). Fatigue is not a simple phenomenon; there are many emotional, behavioural and cognitive factors which build up to the subjective feeling of fatigue (Dirnberger *et al* 2004). Sleepiness is defined as the increased feeling and propensity to go to sleep. Mental fatigue is difficult to define but is different to sleepiness. Humans report feeling mentally fatigued during mental tasks and this requires rest, not sleep to recover (Johns 2000). When humans are mentally fatigued, they tend to report that they have trouble 'thinking clearly' and may have difficulty completing tasks that require motivation or attention (Lichstein *et al* 1997). Mental and physical fatigue can also both be described as tiredness, where rest is needed, not necessarily sleep and a common term used when people report fatigue is that they feel 'exhausted' (Hartz *et al* 2003), but these descriptions are also synonymous with sleepiness (Pigeon *et al* 2003). However, fatigue does have a relationship with sleep (Dawson & McCulloch 2005). Humans that reported mental fatigue (cognitive impairment) were shown to be more likely than non-fatigued controls to suffer from disturbed sleep (Åkerstedt *et al* 2004).

Apart from physiological measurements of muscle fatigue, fatigue in non-human animals is an under-researched area. However, the study of fatigue has the potential to increase understanding of several issues, such as the welfare implications of long distance transportation and the use of animals for draft, racing and riding. The problems in studying fatigue (definitions, confusions between sleepiness and other forms of tiredness, etc) are increased by the inability for non-humans to self-report their feelings. However, studies, such as those carried out on dairy heifers by Jensen *et al* (2005), using demand functions for rest and lying behaviour, may be useful approaches to assess fatigue and associations with animal welfare.

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Circadian rhythms of sleep and wakefulness

Humans and non-human animals undergo sleep cycles, which may be monophasic (one period of sleep per day) or polyphasic (many periods) depending on the species. All animals follow a 24-h pattern in their sleep and wake cycles. There are two main controls of an animal's daily activity rhythms: light and an internal 'clock' (Lavie 2001). The endogenous rhythm (stabilised by the internal 'clock') runs slightly slower than 24 h. Light acts on the internal 'clock' to maintain the 24-h rhythm and synchronises the endogenous rhythm with the exogenous world. The suprachiasmatic nucleus of the hypothalamus is considered to be the location of the internal 'clock' in rats. (Ibuka & Kawamura 1975). In humans, disruptions to established circadian rhythms can result in mental fatigue and the timing of, but not necessarily the quality of, sleep (Mahowald & Schenck 2005). Disruption of sleep from the dark to the light period for humans and from the light to the dark period for rats can result in shorter and fragmented sleep (Kunz & Herrmann 2000). Recognising such sleep characteristics in nocturnal laboratory animals may be a means of assessing the extent to which, for example, interacting with them during daylight hours might be functionally disruptive (Mellor *et al* 2009).

Sleep in animal welfare studies

Notwithstanding the opportunities noted above, there are three main difficulties in using sleep as a method of animal welfare assessment. These are technical difficulties in recording sleep from animals, understanding the complex inter-relation between experiences during wakefulness and subsequent sleep alterations, and ascertaining how important sleep is to the animal.

The technical difficulties with recording and measuring sleep in non-human animals have been reduced by digital technology. The size of data acquisition devices has reduced and ethical concerns may lead to a preference for non-invasive electrophysiological techniques. Non-human animals bring other difficulties in the recording of a non-invasive EEG, such as the effect of equipment on the behaviour of animals (Storch *et al* 2004).

Understanding how sleep, wakefulness, and mental states interact with one another is a more difficult problem to overcome. It seems that sleep and wakefulness interact in a subtle manner. The problem of understanding sleep and wakefulness is exacerbated within non-human animals, as many responses of sleep to waking experiences may be species specific.

When humans experience disturbed sleep patterns, they report changes in subjective mood and changes in ability to remember things and learn new tasks. When asked how important a 'good night's sleep' is, most people rate it very highly in comparison to other activities (Åkerstedt *et al* 2004). Sleep is important to humans. As yet, we do not know how important sleep is to other animals. All mammals and birds sleep, and some animals spend two-thirds of their lives sleeping. It may seem as if it is obvious that sleep is important to them. However, this may only be the case when food is plentiful or predators are few.

Conclusion

Human studies and non-human animal work have shown that prior waking experiences affect sleep (eg Ruckebusch 1975a; Meerlo *et al* 2001). The minimum that can be said about this relationship is that the physiological control of sleep in humans and some non-human animals has been affected by the physiological consequences of the waking experience. Sleep, therefore, could be a valuable tool in studies to assess animal welfare. The qualities and duration of any post-experience sleep disturbance could be recorded to assess the responses of the animal to the experience. In human studies, sleep disturbance that follows experiences while awake has a strong emotional content and is affected by subjective feelings, not just physiological differences. It may be speculated that sleep disturbances that following experiences while awake in non-human animals could also be due, at least in part, to emotional changes of the animal.

Sleep may be altered by an emotional reaction, even after that reaction has passed. Sleep may not be as important to non-human animals, especially those that spend less time sleeping than humans. On the other hand, sleep, in animals that are only able to sleep for short periods, might be even more important and inelastic than it is to humans.

Research into how aversive experiences affect sleep could expand our understanding of how animals react to such experiences. Reliable electrophysiological techniques to use on animals outside of the laboratory need to be developed to enable sleep to be used as a tool for assessing animal welfare. One of the biggest problems in animal welfare studies is how to assess the long-term effects of environments on animal feelings. It is possible that chronic mild stress could lead to signs similar to that of depression in humans (as noted above, chronic mild stress regimes in rats are used as a model for depression in humans). A measure of sleep disturbance, which seems so intensely connected with depression in humans, may provide animal welfare studies with a method of assessing long-term chronic stress in animals.

Studies have been undertaken to determine the effects of potentially aversive experiences on lying and resting behaviour, but there are few studies that record sleep specifically. However, recording lying behaviour itself (especially in detail) will provide information about the ability of the animal to rest. If animals are unable to lie down then sleep deprivation is a likely outcome, potentially leading to a change in the animals' ability to cope with future stresses (Meerlo *et al* 2002).

There is potential to examine whether relationships exist in domesticated animals between stress and subsequent sleep disturbances. Characterising animal sleep and then studying any changes in amount, bout duration, distribution or type of sleep after exposure to potentially stressful events could help us understand how animals respond to their environment and assist us to manage them more knowledgeably.

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