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Yawning, fatigue, and cortisol: Expanding the Thompson Cortisol Hypothesis

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ABSTRACT

Yawning and its involvement in neurological disorders has become the new scientific conundrum. Cortisol levels are known to rise during stress and fatigue; yawning may occur when we are under stress or tired. However, the link between yawning, fatigue, and cortisol has not been fully understood. Expansion of the Thompson Cortisol Hypothesis proposes that the stress hormone, cortisol, is responsible for yawning and fatigue especially in people with incomplete innervation such as multiple sclerosis. This informs our understanding of the functional importance of the brain stem region of the brain in regulating stress and fatigue.

Introduction

Scientists, neurologists, and philosophers have proposed many explanations for why people yawn. The most common theory of yawning is to replace an oxygen deficiency in the blood, or that stretching the lungs leads to a feeling of being more awake [1]. This is a credible explanation because stretching these muscles involves control systems in the brain such as the locus coeruleus, paraventricular nucleus of the hypothalamus, and the reticular activating system. However, evidence from ischaemic stroke patients may point to other brain structures, such as the insular and caudate, being implicated in yawning [2].

Hippocrates in 400 BC, observed that yawning often precedes a high body temperature, and commented that the large quantity of air collected within the lungs ascends all at once with a lifting action, similar to a lever that opens the mouth to let air escape (like escaping quantities of steam from hot cauldrons when water boils) to lower the body temperature [3].

Although this was a rather simplistic and interesting early observation of the yawning mechanism, elaboration of this hypothesis was not advanced for many centuries; and more recently, animal models have led researchers to provide evidence of the thermoregulatory theory of yawning [4]. Evidence is also cited from people with incomplete innervation, such as multiple sclerosis, who tend to excessively yawn [5,6]. Although this provides an explanation for the lowering of brain temperature during excessive yawning [7], it is apparent that brain structures, apart from the hypothalamus (considered important for body temperature regulation), may also be involved such as the pons, medulla and midbrain [1,8–10]. The thermoregulatory theory fails to adequately explain social "contagious" yawning, and it is possible that yawning shares the neural networks involved in empathy [9].

It has been proposed that yawning may serve as a warning for untoward disorders [1]. Since yawning occurs in every human even at pre-term [11,12] and also in a variety of non-humans such as vertebrates [13], yawning may be linked more intrinsically and biologically in the blood cortisol levels [14,15]. Depressed mothers are more likely to give up breastfeeding early which can damage the stress response within the infant and they may become flooded with cortisol [16]. Since yawning is frequently observed together with fatigue, which is often evidenced in people with multiple sclerosis, it is proposed that fatigue may occur in association with elevated cortisol levels.

Although several neurotransmitters and possibly hormones, for example, oxytocin [17], may also be associated with yawning [18], the hormone, cortisol, may be the most important in the yawning episode. It is the body's natural defence against the effects of stress [19], and is released also to protect the body against the effects of cold [20]. Released by the pituitary gland, cortisol participates in the hypothalamus–pituitary–adrenal (HPA) axis that is important for the maintenance of the circadian rhythm [21] which controls our sleeping pattern. Sleep deprivation and fatigue may be found together with lowered cortisol levels [22]. Therefore, cortisol plays a crucial role in the body's overall welfare and maintenance programme, promoting rest and rejuvenation.

In a study investigating biomarkers of energy metabolism, Kokavec and Crebbin [23] found migraineurs to have altered

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glucidic methabolis thought to be due to carbohydrate-induced hyperinsulism. After sucrose ingestion, significant differences were observed between migraine and non-migraine participants, in the level of serum insulin, serum dehydroepiandrosterone sulphate (DHEAS), and the cortisol:DHEAS ratio. Migraine participants on average recorded a higher sucrose-induced serum insulin level and lower DHEAS level and cortisol:DHEAS ratio. While sucrose consumption may potentiate serum insulin in migraineurs, the authors concluded that this does not result in the development of sucrose-induced hypoglycaemia in migraine or non-migraine participants.

It is proposed that cortisol plays an important role in circadian rhythm as well as in metabolic changes. The role of cortisol in the human body may have been underestimated in the past, and its connection and significance with one of the most primitive activities, yawning, may have been overlooked.

Indeed, the occurrence of yawning with elevated cortisol levels has only recently been linked [1] yet yawning has been observed in many disorders over centuries. In 1923, a British neurologist, Sir Francis Walshe, commented on the curious finding that around 80% of stroke patients with hemiplegia could raise their paralysed arm when spontaneously yawning [24]. This was termed an "associated response". This unusual phenomenon was presented in the iconic 1964 film character, Strangelove [25]. Since then, a number of scientific reports have commented on the observation, particularly found in stroke patients with ischaemic brain-stem lesions [26,27] and termed *parakinesia brachialis oscitans* when the paralysed arm rises involuntarily during a yawn. This has even been seen during thrombolytic therapy [28].

Yawning may signal fatigue before the onset of sleep, and there is evidence to suggest that excessive yawning may occur when the brain stem is affected by lesion, and is a signal of brain stem infarction [29,30].

Expanding the Thompson cortisol Hypothesis

The Thompson Cortisol Hypothesis [15] proposes that rises in cortisol levels are associated with yawning. Furthermore, there is an increase in electro-muscular activity around the jaw line as both yawning and cortisol elevation occurs [31]. The author's research team has been the first to comment on the 'yawning envelope' – a profile of electro-muscular activity that "captures" the pattern of a yawning episode [31]. The link between fatigue and yawning is known particularly in the presence of tiredness, anxiety and stress [19]. However, the link between cortisol, electro-muscular activity, and fatigue was not yet established until recently [14].

Fatigue has been found in association with elevated salivary cortisol levels in elite tennis players [32]. 'Fatigue' has often been defined in terms of tiredness due to physical exercise but can also be observed in mental concentration on tasks that demand prolonged attention or alertness. Some researchers believe that our brains are more efficient when they are cooler and therefore a deep breath of fresh air can cool an overheated brain [5].

Alertness and attention may be affected by fatigue. Attention is defined as the mental ability to select behaviourally relevant stimuli, responses, memories or thoughts from amongst the many others that are irrelevant [33]. In an effective connectivity study of healthy subjects performing an alertness task, evaluation was made of the directed interactivity of an attention network during intrinsic and phasic alerting tasks. Functional interactivity was significantly reinforced during the phasic alertness task and appeared to preferentially involve activity in the dorsolateral prefrontal cortex (DLPFC) region, whereas the path coefficients of the model were balance during intrinsic alertness [34]. This study highlights the predominant role of the DLPFC region in maintenance of a state of alertness and in temporal preparation during an alertness task.

The author's team at Bournemouth University, UK, together with the French teams at Amiens University Hospital and the University of Picardy Jules Verne [34] are testing the theory that intrinsic and phasic fatigue may be associated with cortisol levels; and that yawning, known to be associated with elevated cortisol levels [15], may also occur in association with fatigue. This may help to explain why people with multiple sclerosis yawn when they are observed to be frequently fatigued.

Linking together the known phenomena about yawning is important to understand fully the involvement of yawning in stress, brain cooling and the attentional system. The intimate association with neurobiology of the body cannot be ignored, and interestingly, it has also been proposed that yawning may also be influenced by the status of cerebrospinal fluid [35]. During rest, the default-mode network is thought to be active but is switched to the attentional system with the increase in circulation of cerebrospinal fluid. This process increases clearance of somnogenic factors such as prostaglandin D(2), adenosine, and others accumulating in the cerebrospinal fluid [35].

An expansion of the Thompson Cortisol Hypothesis is proposed, stating that a threshold level of hormones such as cortisol, as evidenced by the author's team [15,36], and possibly also cerebrospinal fluid, is necessary for yawning to occur. Contagious yawning seems to be triggered by social conditions and empathy; therefore, it is proposed that these particular setting conditions may also have direct influence on the body's hormones, as they do when experiencing stress, so as to regulate, for example, cortisol, to elicit the yawning response.

Conclusions

It seems certain that the brain stem region of the brain is implicated in the yawning response and that excessive yawning even occurs in the peri-ictal period preceding or following seizures [37]. These seizures have been proposed as an autonomic seizure originating from diencephalic/brain stem structures, manifesting with yawning as an ictal phenomenon [37].

The coexistence of fatigue, yawning, electro-muscular activity, and cortisol level fluctuation, potentially provides us with a better understanding of the importance of yawning and, importantly, the functional importance of the brain stem region of the brain in the regulation of stress and fatigue. It remains to be seen whether or not the coexistence of fatigue and cortisol is the best explanation of the yawning episode; certainly, the evidence is very compelling.

Conflicts of interest

None.

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