Clinical Significance of Yawning in Disorders of Consciousness and Vigilance

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Summary

Yawning is a stereotyped normal behaviour with unknown physiological role. It can occur in excess due to a large variety of medical conditions. Acute bouts of yawning are an early but unspecific warning sign for upcoming disorders of consciousness or clinical worsening, which should prompt the clinician to be prepared for supportive measures. Chronic excessive yawning may lead to medical consultations. In this case, medication side effects and excessive daytime sleepiness are the most frequent aetiologies. Epileptic seizures are occasionally followed by post-ictal yawning which lateralizes the seizure origin to the right hemisphere.

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Gähnen als klinisches Zeichen bei Bewusstseins- und Vigilanzstörungen


Schlüsselwörter: Gähnen, Schlaffrigkeit, Bewusstsein, epileptischer Anfall

Introduction

Yawning is a frequent behaviour occurring in most vertebrate species [1, 2] from foetal stages [3] to old age [4]. In mammals, it consists of an involuntary sequence of about 5 to 10 seconds duration with wide mouth opening, deep inspiration, brief apnoea, and slow expiration. Similar jaw movement sequences have also been observed in reptiles, birds, amphibians, and fish species, but it is controversial to which degree such yawn-like behaviour is homologous to human yawning [5, 6].

The role of normal yawning remains currently unknown, although numerous hypotheses have been put forward throughout the centuries [7]. It is also not known whether the early morning yawns associated with stretching of limb and neck muscles (stretch yawns) are a separate entity or rather a stronger variant of isolated yawns. From an evolutionary perspective, one would expect that such a ubiquitous and frequent behaviour provides an advantage for survival. Yet, no...
consistent physiological effects of yawning could be demonstrated so far. In particular, the wide-spread notion that yawning might oxygenate the blood or increase vigilance could not be confirmed experimentally [8, 9]. The only specific effect of yawning that could be demonstrated so far was its contagiousness in humans and some – but not all – animal species [10 - 13]. Yawning by contagion is associated with activations in neural networks responsible for empathy and social skills [14 - 17]. Hence, there seems to be a link between yawning and social functions [18].

Although yawns are usually accompanied by a pleasant feeling of satisfaction, they can occur excessively in which case they can lead to discomfort and medical consultations [19]. Furthermore, acute bursts of excessive yawning, also labelled “chasm”, should be recognized as early but unspecific warning sign for imminent disorders of consciousness and clinical worsening.

Anatomy

A good understanding of the anatomical basis of yawning would be necessary to fully appreciate the pathomechanisms of excessive yawning. Unfortunately, research has been essentially limited to investigations of pharmacological triggers of yawns, and lesion studies are scarce. Figure 1 gives an overview of the main currently known pathways.

It is unclear whether there exists a centre for yawn execution. However, given the implication of oropharyngeal muscles, it is assumed to be located in ponto-bulbar parts of the brain stem. This centre seems to receive afferents from several deep brain structures, in particular from the paraventricular nucleus of the hypothalamus. Numerous neurotransmitters, neuropeptides, and hormones have been found to modulate yawning. Neuroendocrine substances as diverse as, among others, dopamine, acetylcholine, glutamate, serotonin, nitric oxide, adrenocorticotropic hormone (ACTH) related peptides, oxytocin, and steroid hormones facilitate yawning whereas opioid peptides exert an inhibitory effect. Some of these mediators (e.g., dopamine, glutamate, oxytocin) interact in the paraventricular nucleus of the hypothalamus and induce yawning via oxytoninergic projections to the hippocampus, the pons, and the medulla oblongata. Other pathways seem to be effective for serotonin, acetylcholine, and ACTH related peptides [20].

Figure 1: Pathways of yawn control. The location of the centre for yawn execution is not known, but based on the implicated muscles, it is assumed to lie in ponto-bulbar parts of the brain stem. Additional cortical centres are probable, but insufficiently understood. Abbreviations: Ach, acetylcholine; ACTH, adrenocorticotropic hormone; NO, nitric oxide; OXT, oxytocin.
Chronic excessive yawning and sleepiness

There is convergent evidence from different areas of research that sleepiness triggers yawning. Behavioural studies consistently reported that yawns occur most frequently before and after sleep, i.e., during periods with lower levels of alertness [22, 23]. The circadian distribution of yawns follows the individual sleep-wake rhythm [24, 25, 4], and the individual subjective feeling of drowsiness correlates with increased yawning rates [4]. Furthermore, yawns are accompanied by electroencephalographic (EEG) signs of drowsiness. In particular, power density of delta waves over the vertex, which is considered to be a marker of sleep pressure [26], is greater before yawns than before control movements without yawning [9].

Accordingly, excessive daytime sleepiness is the most frequent cause of excessive yawning [19]. In this case, excessive yawning is usually present chronically over weeks to months. It can be due to lack of sleep or secondary to other sleep pathologies such as sleep apnoea syndrome. Frequent yawning can therefore be one of the symptoms of excessive daytime sleepiness but is often overlooked. Similarly, patients can be instructed to recognize yawns as sign of sleepiness, in particular when driving.

Acute bouts of yawnings and disorders of consciousness

Excessive yawning can also appear acutely, often in form of bouts or salvoes. In particular, it can be frequently observed in patients presenting current or imminent disorders of consciousness and then opens a large differential diagnosis.

Syncope and malaises with a sudden overstimulation of the parasympathetic system can be preceded by bouts of yawning [27], sometimes even before the appearance of nausea and pallor. The occurrence of yawning during medical interventions may therefore not be due to sleepiness or boredom of the patient, but should prompt the medical attendant to put the patient in a supine position.

Similarly, excessive yawning can be one of the first manifestations of hypoglycaemia in diabetic patients [19]. Yawning is associated with hunger in healthy animals [6], and may therefore be a physiological manifestation of hypoglycaemia.

The frequency of yawning tends to increase in patients with brain lesions, in particular stroke. Lesions in the internal capsule [28], the brain stem [29], as well as in the insula and the caudate nucleus [21] seem to be particularly associated with increased yawning. The mechanisms of this increase are unknown. One reason may be that patients with severe hemiparesis after stroke can experience automatic, involuntary movements of their paralysed arm during yawns. Since this is usually the only occasion when they see their affected arm moving, they are particularly keen to yawn. The movement consists of involuntary rising of the arm and has been named “parakinesia brachialis oscitans” [28]. It is associated with severe motor deficits and disappears in case of clinical improvement. The mechanisms are incompletely understood. Walusinski et al. [28] suggested that it may be mediated by spino-cerebellar pathways which become autonomous due to damage of corticospinal, cortico-nuclear and cortico-cerebellar tracts.

Although the overall yawning frequency can be increased in patients with brain lesions, the appearance of acute, repetitive bouts of yawning is suspicious of additional intracranial hypertension. Although rare, its occurrence in patients with recent trauma or stroke should lead to the consideration of brain imaging. In patients with reduced levels of consciousness, the sudden appearance of yawning may be a sign of herniation.

Of particular interest to epileptologists is yawning associated with seizures. Post-ictal yawns are relatively common and were described in 4% of patients with temporal lobe epilepsy in a systematic retrospective analysis. Interestingly, it occurred only in patients with right temporal seizure origin [30]. Post-ictal yawning therefore seems to have a lateralizing value to the non-dominant hemisphere. In contrast, yawning during actual seizures is very rare and only a few cases have been described [31]. These patients had partial seizures of temporal origin, but yawning during 3/sec spike-wave episodes was also described in young patients with probable idiopathic generalized epilepsy [32]. An epileptic trigger of yawning is particularly probable if it occurs in a stereotyped way during seizures.

Yawning is one of the most common and consistent prodromal symptoms before migraine attacks and seems to occur more frequently before attacks with aura [33 - 35]. It can also occur after the headache period together with tiredness, depressed mood, and concentration difficulties [36]. Rarely, yawning can be painful by itself in patients who do not suffer from headaches. In this case, pain seems to be due to affections of craniopharyngeal muscles or nerves [37].

The mechanisms by which these diverse conditions increase yawning have not been investigated. However, pathological yawns seem to be triggered either by local compression or irritation of the putative yawning centers (in particular the hypothalamus), or by one of the many neuroendocrine substances which have been shown to facilitate yawns in animal models.
Other causes for excessive yawning

Excessive yawning is not always accompanied by disorders of consciousness or excessive sleepiness. For instance, compression of the hypothalamus or the pituitary gland are rare causes of yawn salvoes. They can lead to particularly frequent and disabling yawns [38, 19].

Another important cause for excessive yawning is the intake of neurological and psychiatric medication. Serotoninergic and tricyclic antidepressants are most frequently involved [39 - 42, 19]. In this case, it is important to recognize it as iatrogenic side effect and not to misinterpret it as signs of sleepiness or asthenia of the patients.

Other rare conditions which have been associated with excessive yawning include progressive supranuclear palsy [43] and amyotrophic lateral sclerosis [44]. The mechanisms of this association are unknown.

Conclusions

Frequent yawning can be a normal manifestation of, among others, sleepiness, boredom, hunger, and social interactions [7], as well as associated with a large variety of medical conditions. It is therefore unspecific. Yet, in acute pathological conditions, it usually appears early before the appearance of disorders of consciousness or clinical worsening. Its recognition can give the clinician a head start for preparing therapeutic and supportive measures.

The management of excessive yawning consists in finding and treating the underlying cause. Table 1 gives an overview of the large differential diagnosis. Medication associated with yawning and excessive caffeine consumption should be adapted first. Hereby, it is important to avoid abrupt stopping of opiates or caffeine, as this can lead to excessive yawning. Insufficient sleep or sleep pathologies should be actively searched. Finally, a careful history taking and clinical examination may reveal further abnormalities which guide the treatment, e.g., if they reveal functional disorders, headaches, or neurological deficits. Finally, specialized exams may be considered in selective cases to look for epileptic activity, pituitary pathologies, or brain lesions. Treatment consists in the elimination of the cause.

There is no established pharmacological therapy to reduce yawning frequency, but based on a case report, propranolol can be tried [45]. Finally, it is noteworthy that yawning can also be reduced or suppressed by medical conditions, in particular Parkinson’s disease [46] and neuroleptic drugs [47].

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