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YAWNING

*FLÁVIO ALÓE**

SUMMARY - The ubiquitousness of normal yawning and the existence of abnormal yawning warrant an understanding of this reflex. Its mechanisms and functional role are not entirely known. A review of the literature reveals that yawning is a brain stem arousal reflex with both peripheral and central loops subserving reversal of brain hypoxia or hypoxemia. Behaviorally, yawning is a semi-involuntary act that occurs also because of loss of interest in the surroundings and it is not necessarily associated with fatigue. Socio-environmental factors can influence the emergence of yawning. Dopaminergic, acetylcholinergic, ACTHergic and oxytocinergic systems are involved in the generation and modulation of yawning in animal experimentation.

KEY WORDS: yawning, fatigue, drowsiness, brain hypoxia, dopamine, acetylcholine, ACTH, oxytocin.

Bocejo

RESUMO - A ubiquidade do bocejo normal e a existência de bocejo de caráter anormal justificam o conhecimento deste reflexo. Muito pouco se sabe a respeito dos mecanismos fisiológicos e papel funcional dos bocejos. Uma revisão da literatura mostra que o bocejo é um reflexo de alerta cerebral com alças centrais e periféricas, cujo objetivo é reverter hipoxia ou hipoxemia cerebral. Comportamentalmente, bocejar é ato semi-involuntário que ocorre também por causa de perda cognitiva de interesse pelo meio ambiente e não está necessariamante associado com sensação de fadiga. Fatores sócio-ambientais podem influenciar o aparecimento de bocejos. Os sistemas neuronais dopaminérgico, colinérgico, ACTH e oxitocinérgico estão envolvidos na geração e modulação do bocejo em animais de experimentação.

PALAVRAS-CHAVE: bocejo, fadiga, hipoxia, sonolência, dopamina, acetilcolina, ACTH, oxitocina.

Yawning is a common phenomenon expressing certain physiological and psychological states. It is a reflex act involving the central nervous system (CNS), lungs, blood vessels, salivary and lacrimal glands, respiratory (diaphragm and acessories) and other skeletal muscles[5,9,11]. Historically, Hippocrates described yawning as an exhaustion of the fumes preceding fever[11]. In the early XVII Century, Gallien and Oribase mentioned yawning in their work. In the XIX Century, Charcot also referred to yawning in his lessons on medicine[11]. Yawning is present in all mammals and at least its mandibular form occurs in all vertebrates[9]. The earliest appearance of yawning in man was observed in a 15-week-old embryo[12]. Yawning is a complex behavior not yet fully understood[18] and in man it is thought to relate more to boredom than to feelings of physical fatigue[7].

On the basis of certain relevant clinical and experimental data, a review of yawning appears to be justified.

DESCRIPTION. Once initiated, yawning can not be suppressed but its manifestations can be modified. In humans, yawning can be divided in three distinct phases: a long inspiratory phase; a brief acme; a rapid expiration phase[11]:

* Sleep-Wake Disordes Center, Department of Neurology of the University of São Paulo Medical School.
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Dr. Flávio Aloé - Al. Jaú 1791 - 01420-002 São Paulo SP - Brasil. FAX (55.11) 280-9519.

1) Inspiratory phase. Yawning may be preceded by looking about, moving or arranging one's hair. Then the lower jaw opens involuntarily reaching maximal widening while a 4 to 6 seconds long and deep inspiration drains air through both the mouth and the nose. The nostrils flare, the respiratory thoracic accessory muscles contract in an increased inspiration placing a larger volume of air in contact with the maximally widened nasopharynx [28]. The soft palate moves up sealing rhinopharynx momentarily and the vocal cords abduct maximally. The sub-hyiod muscles contract bringing the tongue forward, descending the hyiod bone to the level of the seventh cervical vertebrae. The mid-inspiration closure of the Eustachian tubes produces a transient hypoacusia whereas the end-inspiratory opening of the Eustachian tubes produces a clicking in the ears[28]. Yawning is usually associated with vigorous stretching of the limbs, torso and a brief shivering. During stretching, the soleus, lateral pterygoids and the diaphragm muscles contract emptying their voluminous venous plexus, thus increasing the venous return to the heart with a slight of increase of the heart rate[18]

2) Acme. This brief phase only lasts 2 to 4s. Extension of the neck, forced closure of the eyes, lacrimation and salivation occur and a vague sensation of pleasure is also described to occur. A larger bolus of air is placed in contact with the maximally exposed nasopharynx[28] at the acme.

3) Expiration. The acme comes suddenly to an end, the muscles involved in the two previous phases relax and a quick passive expiration occurs and subsequently a brief apnea ensues[18].

MECHANISMS. Fatigue and boredom are the two most potent stimuli causing yawning whereas drowsiness is the most common cause of it in humans[29]. When the environment is boring and no longer able to sustain the subject's attention, the bored mind has to make an effort to maintain contact with the surroundings. These feelings of boredom through the prefrontal cortex modify the pattern of activity of the brain stem reticular formation and of the brain stem midline raphe serotoninergic system. This generates a subjective sensation of drowsiness[29] which induces yawning.

Various physiological changes occur during yawning. Vigorous stretching of limbs with contraction of the lateral pterygoids, soleus, diaphragm and other muscles (the so-called peripheral hearts), increase the venous return to the right chambers of the heart, thus increasing the cardiac output and consequently increasing cerebral blood flow[18]. The deep and prolonged inspiration phase of yawning reverses hypoxia, hypercapnia and alveolar collapse[31]. The deep inhalation also stretches the terminal bronchioles and alveoli. This will also dilate bronchial musculature stimulating the vagal terminals, thus releasing acetylcholine which in turn dilates the systemic arterioles even further. The result is a decreased peripheral resistance, increased arterial cerebral blood flow, increased oxygen saturation and decreased CO_2[14,18,31]. Hyperoxygenation and increased cerebral blood flow activate the brain stem reticular formation leading to increased alertness[24].

Yawning seems indeed to be an alerting reflex. In that line, Karasawa et al showed that in patients with occlusive cerebrovascular disease yawning emerged when the EEG showed slowing of the posterior background activity occurring simultaneously with a mild hypoxemia[17]. Apparently, boredom, fatigue and drowsiness all lead to hypoventilation and mild hypoxia. Yawning would be a response of the brain stem reticular formation to reverse drowsiness and to maintain attention and alertness[18].

Yawning is at the neuronal level the result of concertedly functioning complex neuronal networks whose anatomical center is most likely located in the lower brain stem nearby the brainstem reticular formation[11]. The yawning neuronal complex is interconnected with the neuronal aggregates of: (a) respiratory neurons; (b) motor nuclei of the 5th, 7th, 10th, and 12th cranial nerves; (c) the phrenic nerve and accessory respiratory muscles; (d) the parasympathetic terminals of the lacrimal glands; (e) the frontal cortex[9,11,18]. In favor of this anatomic location there is the report by Geschwend who described a tetraplegic patient with a pontine glioma who could not open his mouth spontaneously but was able to yawn[16]. Opening of the mouth through the motor cortex was impossible but reflexogen yawning was still possible because of the short interconnections between the reticular neurons and the motor axons of the fifth and seventh cranial nerves. Another tetraplegic and locked-in syndrome patient suffering from a glioma of the anterior pons could yawn but could not open his mouth voluntarily[6]. The preservation of the reticular formation network made yawning possible whereas the interruption of the cortical motor fiber in the ventral pons prevented voluntary mouth opening[6,16].

ABNORMAL YAWNING. Abnormal repetitive yawning may be the consequence of opiate withdrawal; intoxication with CNS depressants; drug side effects (tricyclic antidepressants, reserpine)[28]; lesions to the CNS such as postencephalitic conditions, CNS tumors, apallic syndrome, cerebral malformations, transtentorial herniations[11]. Yawning is associated with diminished brain oxidative metabolism. Such is the case of anemia or cerebral anemia (occlusion of the carotid arteries), hypoglycemic states[18]. In these situations, yawning through its action on the cerebral blood flow, is a protective homeostatic reflex to increase brain oxygen levels[18] in situations of decreased brain oxidative metabolism.

WHY WE YAWN. It is not entirely clear why people yawn[18]. It could not purposelessly have survived the evolutionary process without a reason.

Whereas actual yawning is not elicited voluntarily, it is an ideomotor action easily elicited by suggestion, by thoughtful preoccupation with yawning, and by unconscious imitation[18]. It is layman's knowledge that yawning is a contagious behavior. Bell et al were able to induce yawning in undergraduate students by instructing them to think about it, showing yawning is perhaps a stereotyped imitative behavior[7,26,27]. It is also common knowledge that yawning can emerge before psychologically or physically strenuous situations. No explanation for this is found in current medical literature. On the other hand, psychotic patients have a tendency to yawn less[18]. This has perhaps some bearing on the finding of increased yawning after apomorphine in animals[20].

Yawning may have acquired a paralinguistic meaning with evolution[11]. As a nonverbal passive behavior, it may have a role in human communication expressing a refusal to participate in a dialogue[5]. Alternatively, the purpose of yawning has to do with the sense of smell as a larger bolus of air is placed in contact with the maximally exposed nasopharynx[28]. Yawning possibly is a protective response with a more logical reason for its existence than to reverse hypoxia and alveolar collapse during periods of hypoventilation[31].

BIOCHEMISTRY OF YAWNING. Various agents can induce yawning in animals. Dopaminergic and cholinergic agonists, ACTH-MSH, oxytocin produce yawning in rats[1,19,20,30].

The stretching-yawning syndrome in animals (SYS) which includes penile erection is believed to involve dopaminergic inhibitory circuits and cholinergic activation[19,25,30]. The intraventricular administration of ACTH and alpha-MSH stimulating hormones induce SYS in different animal species[2]. This is a specific and centrally mediated effect of the ACTH-MSH peptides and it is not obtained after peripheral administration[2,3,19]. It has been suggested that septal-hippocampal cholinergic neurons are involved in the production of SYS following administration of these peptides[19]. This same effect of ACTH is also found interspecies. Hypothalamic extract from rats will induce this behavior in recipient rabbits[13].

Another hypothalamic peptide, oxytocin, was found to be the single most potent stimulus producing yawning, stretching and penile erections in animals when injected directly into the CNS (intraventricularly)[1,2]. Systemic injection of apomorphine and other dopaminergic or cholinergic agonists also produce SYS[2,21,22,30]. Apomorphine may induce yawning by increasing the release of oxytocin directly from the Paraventricularis Nucleus (PVN) of the hypothalamus[3,21,22]. Among pharmacological agents able to prevent oxytocin, ACTH-MSH and apomorphine-induced yawning and penile erection, morphine is certainly one of the most effective[13,1,8,23]. Dopaminergic, oxytocinergic, cholinergic antagonists prevent SYS[13,32]. Lesions to the PVN prevent apomorphine but not ACTH-induced yawning suggesting ACTH induces yawning through different pathways from those of dopamine agonists[4].

Hypothalamic oxytocin probably functions as the final common pathway neuropeptide released in response to different chemical stimuli[2,4]. Centrally injected ACTH-MSH seems to induce yawning through the release of a second and yet undetermined messenger[23]. ACTH-MSH does not act on the PVN of the hypothalamus[15] nor is it mediated by the release of oxytocin like apomorphine[3,23].

CONCLUSIONS

1. No single, peptide, neurotransmitter, neuronal system alone can be assigned to yawning. Yawning involves dopaminergic, cholinergic neuronal systems, ACTH-MSH, oxytocinergic peptides and its anatomical center is most likely located in the lower brain stem. 2. Yawning is a multifarious reflex possibly subserving the purposes of: a) protectively enhancing arousal and attention; b) reversing mild brain hypoxia or hypoxemia; c) enhancing the sense of smell; d) non-verbal communication.

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