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Senior Talk
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Introduction.

The verb 'to yawn' is derived from the Old English *ganien* or *ginian*, meaning to gape or open wide. Yawning is a very common behavior in humans, other mammals, birds and yet the exact mechanism and function of yawning is not well described in the literature. Smith writes that the study of yawning is important because it is a behavior pattern we share with all vertebrates, it occurs in several different contexts and it is contagious.[1]

The mystery of yawning has baffled the greatest minds of our species. Hippocrates described yawning as an exhaustion of the fumes preceding fever.[2] Charles Darwin, in 1838 makes an observation "… seeing a dog and horse and man yawn, makes me feel how much all animals are built on one structure."[3] Over the ages, various superstitions have developed to describe this behavior. The Ancient Greeks believed that yawning was not a sign of boredom, but that a person's soul was trying to escape from its body. Some consider a yawn as a sign that danger is near, while in some Latin American, East Asian and Central African countries yawning is said to be caused by someone else talking about you. Vergil in his *De Rerum Inventoribus*, wrote that "it was customary to make the sign of the cross over one's mouth, since alike deadly plague was sometime in yawning, wherefore men used to fence themselves with the sign of the cross...which custom we retain at this day."[4]

Fig1. Sign of the cross.

Since yawning is so common, at first glance, it can be labeled as a behavior without any significant function. As we learn more about the physiology, neurobiology, pharmacology and psychology of yawning and its association with various diseases, we realize the importance of investigating the function of yawning.

Description of yawning.

Deputte in 1994 describes the physical attributes of a yawn in three phases. During the first phase, prior to a yawn the head is lifted backward and rotated sideways and the mouth is slightly open. During the second phase of the yawn there is continued upward motion of the head, the mouth is fully open and a deep inhalation is undertaken In the final phase, head is lowered, mouth closed rapidly and lips covered with the teeth.[5] The pharynx can quadruple its diameter, while the larynx opens up with maximal abduction of the vocal cords.[2]

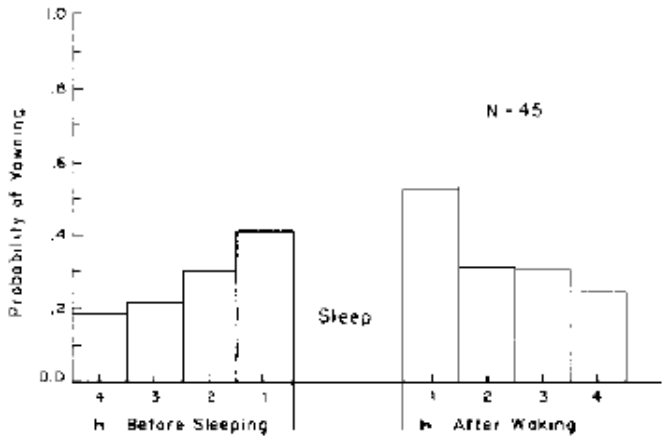

Fig 2. Graphs show the probability of yawning Before and after sleeping.

Using college age subjects, Provine in 1986 characterized the yawn with a mean duration of 5.9 +/- 1.9 seconds, with a highly variable inter-yawn interval of around 68.3 seconds and no relation between yawn frequency and duration. Provine also described yawning as an all or none response, ie no 'half yawns.'[6] In 1987, the same author using 64 subjects and a self reported method, realized that yawning occurred the most during the 1st hour after waking when Compared to the last hour before falling asleep ($p < .005$).[7]

Types of yawns

Although they have similar physical manifestations, two different contexts of yawning have been described. The 'rest yawn' is observed in transitions from rest to waking states and is synonymous with 'true yawns' and the second type is the 'emotion yawn' or 'tension yawn.'[5] Some previous theories by Altmann in 1967 support this hypothesis and state that one can distinguish true yawns from those with socially implied functions only by context. True yawns are presumably stimulated by a lowered oxygen tension in the blood, while social yawns express conflict, anxiety or threat.[8]

Provine mentions that one other type of yawn can be a subset of both of these yawns which is the closed mouth yawn. Study by provine in 1986 showed that while having clenched jaw the number of yawns were not decreased. The study showed that immobilization of the jaw does not stop the yawn from occurring but the satisfaction of the person yawning is not adequate. Subjects were not thoroughly happy with the yawn and felt as if they were hindered from the full benefit of the yawn.[6]

Yawning and stretching

It is almost impossible to describe yawning without mentioning and describing its association with stretching. These two bodily functions do not always occur concurrently. It is a common observation that people usually yawn when they stretch but do not always stretch when they yawn. In a study by Provine, it was shown that significantly more yawn-stretches were performed during the post wake hour then compared to the prebedtime hour. It is mentioned that stretching can be considered as a signal for the preparation for action.[7]

In 1923, British neurologist Sir Francis Walshe noted that 'when hemiplegics yawn, they are startled and mystified to observe that their otherwise paralyzed arm rises

and flexes automatically'. Yawning apparently activates undamaged, unconsciously controlled connections between brain and the cord motor system innervating the paralyzed limb.[9] This observation has been noted in the literature on a number of occasions and yet there is no concrete explanation as to the mechanism of action.

Physiological changes during yawning

During the respiratory phase of yawning, contraction of the diaphragm induces an increase of splanchnic venous return, by compression and by inducing thoracic depression. Contraction of the limbs during stretching induces an increase of venous return to the heart. Deep inhalation stretches the bronchial musculature that stimulates the vagal terminals and the cholinergic pathway that dilates arterioles, thus enhances cerebral blood flow. Dilation of the superior airways and stretching of the terminal bronchioles and alveoli induce an exhalation of carbon dioxide and a hyperoxia.[10] In addition, yawning causes an increase in blood pressure.[11]

Neuropharmacology of Yawning

The foremost question in the study of neuropharmacology of yawning is regarding the prevalence of sympathetic vs. parasympathetic nervous system. This could be useful in determining the role of yawning. In 1996, Askenasy used a microelectrode into the right peroneal nerve in the lateral knee and measured muscle sympathetic nerve activity aka MSNA. It was shown that yawning induced suppression of MSNA while expiration provoked an MSNA discharge. During this time, BP and heart rate decreased as well. Therefore, showing that during the deep inhalation associated with yawning, the efferent sympathetic nerve traffic is blocked and the autonomic nervous system moved to parasympathetic activity.[11]

Another area of study is the localization and the neuropeptides involved in the yawning process. According to the available data, it is suggested that oxytocinergic neurons originating in the paraventricular nucleus of the hypothalamus project to extra-hypothlamic areas (e.g the hippocampus, the pons and/or medulla oblongata) and thereby mediate the expression of yawning in several circumstances. The activation of these neurons by dopamine, excitatory amino acids and oxytocin causes yawning. Inhibition by opioid peptides prevents the behavioral response.[12]

The hypothalamus was also identified as one of the brain areas where ACTH-MSH peptides act to induce the stretching-yawning syndrome.

Neuropeptides	Effect on yawning	Receptor involved	Brain area involved
ACTH/MSH peptides	facilitatory	n.a.	HY
Opioid peptides	inhibitory	μ	PVN, others
Oxytocin	facilitatory	uterine-type	PVN, HI, MO, pons
Neurotensin	inhibitory	n.a.	n.a.
LH-RH	inhibitory	n.a.	n.a.
Prolactin	facilitatory	n.a.	CN

Appropriate references are quoted in the text. ACTH–MSH–adrenocorticotropin–melanocy stimulating hormone; LH-RH=luteinizing hormone-releasing hormone. PVN–paraventricular nucleus of the hypothalamus, HI–hippocampus, HY–hypothalamus, CN–caudate nucleus, MO–medulla oblongata.

Fig3. Role of various neuropeptides during yawning.

There has been much debate about the contagious nature of yawning. In the past, imitation was considered a mechanism for yawning. If this were true, the 'mirror-neuron system' should be activated while subjects view another person's object-related motor acts. The area in the posteroinferior frontal cortex ie Broca's area in the left hemisphere is considered to specifically support action perception and understanding as a prerequisite for 'true imitation'[13].

In 2005, Platek et al used functional MRI imaging to study activity in people exposed to yawns. They found activity in the posterior cingulate and precuneus brain regions, which are not associated with mirror activity but are involved in self processing such as self reference, theory of mind and autobiographical memory. This could be seen as a primal form of empathy.[14]

In a similar study, volunteers watched videos of actors yawning or control volunteers with stereotypical movement of the mouth and face that are depicted during a yawn. Functional MRI was used to measure the blood oxygen level dependent signals and compare the two groups' tendency to yawn. The posterior part of the superior temporal sulcus (STS) was the most highlighted area while watching yawning when compared to stereotypical facial movement. This activation agreed with the established selectivity of the STS for processing socially relevant cues in the perception of the biological motion in general and of faces in particular.[15]

Absence of activation in Broca's region in the Yawn-Control comparison speaks for the non-imitative nature of the contagiousness of yawning.

Evolutionary perspective

Various theories exist to explain the function of yawning and its presence in almost all vertebrates. Such a widespread function has to have some evolutionary advantage that allows it to be perpetuated. Smith write in 1999, that 'it is reasonable to expect that a behavior that elicits a similar behavior in conspecifics so frequently and with no intention by the yawner has been the object of strong selective pressure.'[1] One of the best avenues of observation for the evolutionary perspective is the yawning reported in utero in human fetuses. Yawning is reported in utero as early as 16- 20 weeks gestation.[16] These are usually recorded as characterized movements of the jaw, eyes with an associated stretching movement.

Fig4. Images in utero of a fetus making the characterized movements of yawning.

Different Theories of yawning

Over the centuries, a number of different functions have been proposed for yawning. Some theories have been negated and some have resurfaced but none have been validated as the actual function of yawning.

1. We yawn when we are bored – Provine in 2005 provides evidence for this theory by showing that when subjects watch music videos versus rotating color bars, they yawned 70% more when watching the color bars. This still does not answer the question of whether subjects are getting ready to fall asleep or trying to stay awake by performing the yawn maneuver.[9]

2. We yawn when sleepy - Various studies have shown that people yawn most when sleepy, especially during the hour after waking, and second most during the pre-bedtime hour.[9]

3. Thermoregulatory hypothesis -- The thermoregulatory mechanism of yawning proposes that yawning evolved to promote/maintain mental efficiency by keeping brain temperature in homeostasis. Using forehead temperature manipulation and using various breathing techniques, it has been shown that cooling the brain leads to less yawns.

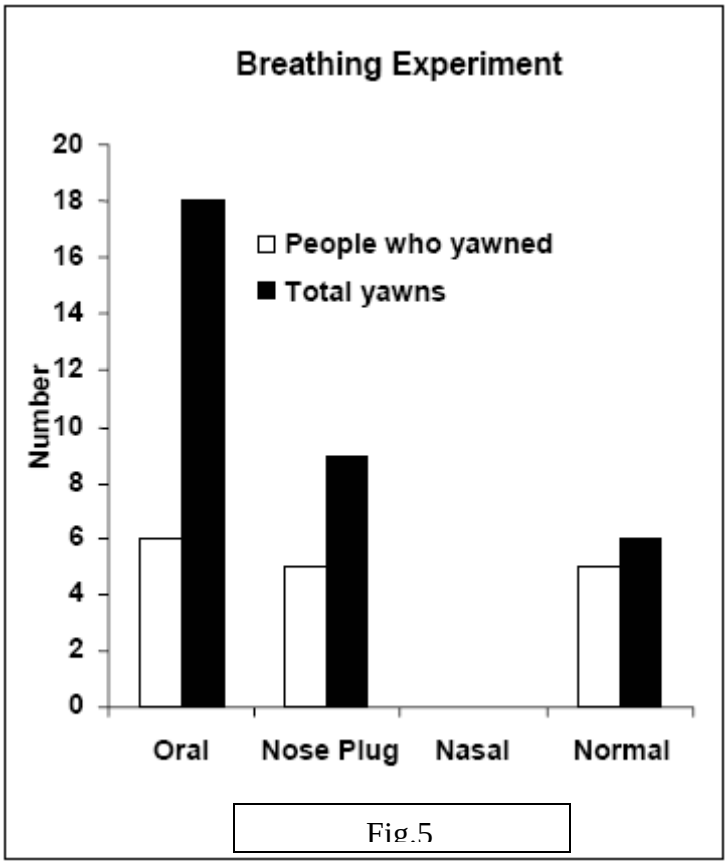

Fig.5

In a study in 2007, participants were asked to sit in front of a computer screen and instructed to either inhale and exhale orally, strictly nasally, strictly orally while wearing a nose plug or allowed to breathe normally. They were instructed to breathe for 2 minutes prior to and while watching a brief video containing 7 second digital videos of people depicting laughing, yawning or neutral facial exppressions. The study showed that the oral breathing group had more people yawning and also a higher total number of yawns. The nasal breathing group had no yawns.[17] Nasal breathing has been identified as one of the mechanisms for brain cooling. The vertebral venous plexus located in the brainstem is cooled by the vertebral artery via nasal breathing.[18] The frontal cortex is also cooled. [19] This experiment suggests that contagious yawning can be eliminated if breathing is done via the nose, which in turn cools the brain.

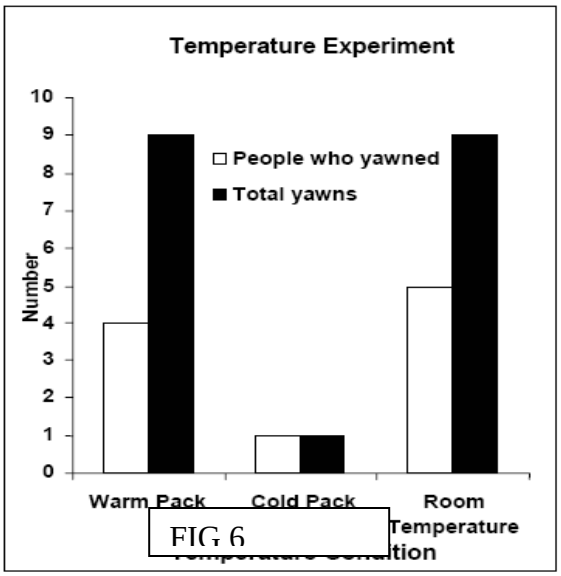

FIG 6

Another study was used to provide evidence for the same mechanism. In this study, the forehead temperature was manipulated by asking people to hold a cold pack (4 degrees), warm pack (46 degrees) and a pack at normal temperature while sitting in front of a computer screen watching short digital videos. The subjects with the cold pack on their forehead were noted to have a decreased incidence of yawning.[17]

In summary, the tow methods that promote brain cooling were found to decrease or eliminate contagious yawning.

Increases in cerebral blood flow have also been noted via the emissary veins of the human head during hyperthermia.[20] In addition, dopamine agonists have been shown to produce yawning[21] but also have been shown to increase heat production.[22] Brain and core temperatures in rats increase with acute dopamine/NE reuptake inhibition.[23] Yawning seems to function like a radiator to produce alteration of temperature in the brain. The gaping of the mouth and deep inhalation of cool air taken into the lungs can alter the temperature of the blood in the brain through convection. Yawning not only provides cooler blood to the brain but also allows for an increased blood flow. This is shown during physiological experiments where constriction and relaxation of facial muscles during yawning increases facial blood flow and these changes alter cerebral blood flow.[24]

4. We yawn to increase oxygen and decrease carbon dioxide – A study from 1987 aimed to address this question. Subjects breathed one of 4 gas mixtures through a mask, 100% oxygen; 3% Co_2, 21% O_2, 76% N_2; 5% CO_2, 21% O_2, 74% N_2 and normal compressed air 20.95% O2, 0.03% Co2, 79.02% N2, and inert gases. All yawns were self reported. Respiratory rate increased with all gas mixtures, which was attributed to the use of masks. Carbon dioxide and oxygen content of inspired gases had no significant impact on yawning rate or duration, when compared to either baseline or compressed air controls. The hypothesis that yawning is a response to a high levels of carbon dioxide or low levels of oxygen in the blood was not confirmed.[25]

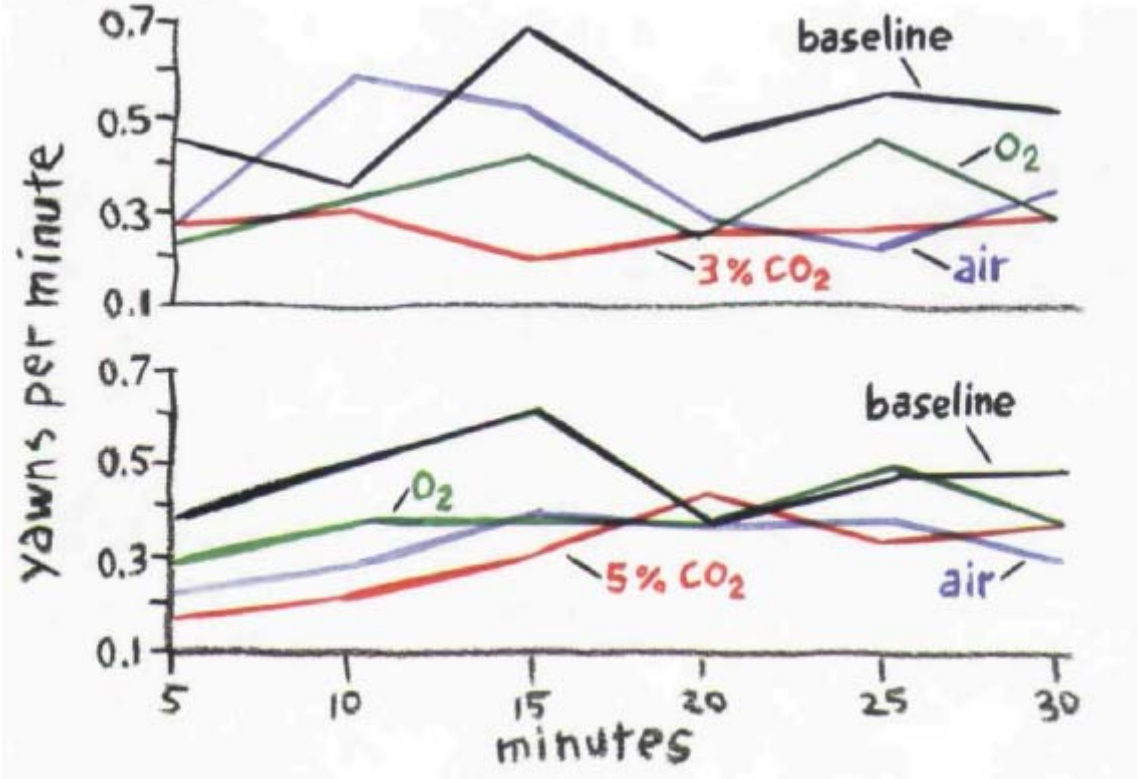

Fig 7. Top and bottom figure shows no changes in the number of yawns with any of the gas mixtures

5. Arousal Hypothesis -- A logical explanation for yawning would be that humans yawn to keep themselves awake by providing increased oxygen and blood flow to the brain. Guggisberg et al. in 2007 evaluated the functional relationship between yawning and vigilance by measuring electrophysiologic markers of vigilance in temporal relationship with yawning. A total of 16 subjects were recruited to sit in a quiet, darkened room trying to stay awake. A continuous EEG recording was analyzed for these subjects. Theta and delta waves in the EEG segments before yawns were used as markers of drowsiness and alpha waves after yawning as markers of the arousal level. The study showed that yawning occurs during progressive drowsiness, which is compatible with the notion that yawning is triggered by states of low vigilance. But alpha waves in the EEG did not positively correlate with the yawning showing that yawning does not have an arousal effect.[26]

In this case, we can think that the motor activity observed after yawning is not an indicator of an arousal effect of yawning, but an effective countermeasure against the underlying drowsiness. Perhaps yawning is a futile effort that only allows for partial countermeasure but does not cause full arousal.

5. Yawning as a communication - Evolutionary biologists consider yawning a mechanism for communication. It has been postulated that this was a way for animals to communicate danger in a nonverbal manner and also prepare themselves for action. In humans, for example, it can be considered a non verbal cue for the speaker to work harder to engage his/her audience.

6. Reversal of hypotonia -- REM sleep is characterized by a peripheral muscular hypotonia, upon waking yawning and stretching reverse the muscular hypotonia. The wide inspiration triggered by the yawn improves lung compliance by reinflating collapsed airways and alveoli. REM sleep in human declines from 50% of total sleep time (8h) and a frequency of 30/50 yawns per day in the newborn to 15% of total sleep time (1h) and less than 20 yawns per day in the adult.[27] Perhaps this study can be used as evidence that yawning plays a role in improving alertness after awakening.[27]

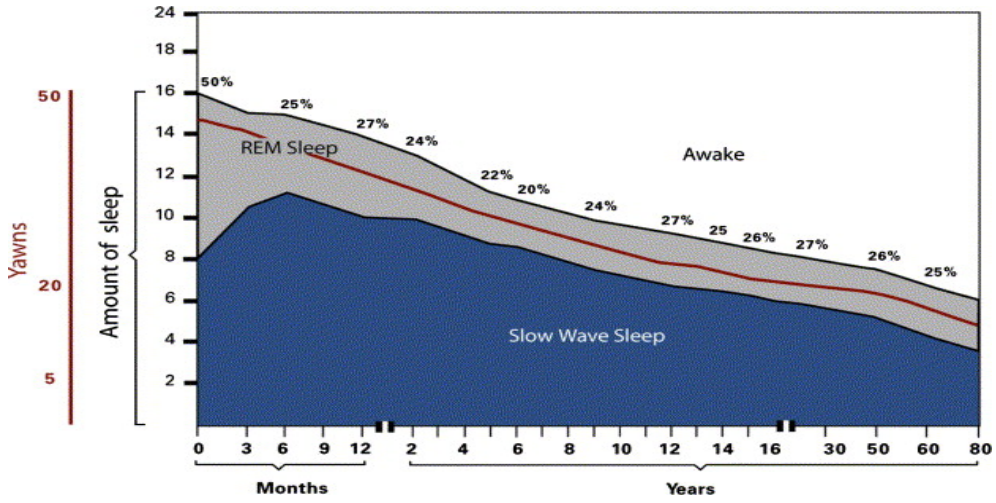

Fig 8. Shows the parallel nature of decline between the REM sleep and the number of yawns.

7. Contagiousness of Yawning -- Yawning occurs in almost all vertebrates, but contagious yawning has only been demonstrated in human beings, chimpanzees and some species of monkeys. One person's yawn can cause many people around them to yawn. Spontaneous yawning occurs as early as the 16th week in the womb but contagious yawning hasn't been detected in children until several years after birth which suggests a recent evolutionary origin. Disappearance of yawning in certain neurological and psychiatric disorders also suggests that contagious yawning is a measure of sociality.[9]

Although common knowledge, Provine in 2005 showed that subjects were more than twice as likely to yawn while observing yawns (55%) as to yawn while viewing a comparable series of smiles (21 %). He also showed that a gaping mouth is not the essential signature of a yawn. Yawning faces that have been edited to mask the mouth were just as effective in producing yawns as the intact face. He also showed that a disembodied yawning mouth was no more effective in evoking yawns than a control smile. Provine theorizes "…as if the gaping mouth is an ambiguous stimulus" meaning that the observer can not tell if the gaping mouth is yelling or singing. The viewer seems to be responding to the overall pattern of the yawning face and upper body, not a particular facial feature.[9]

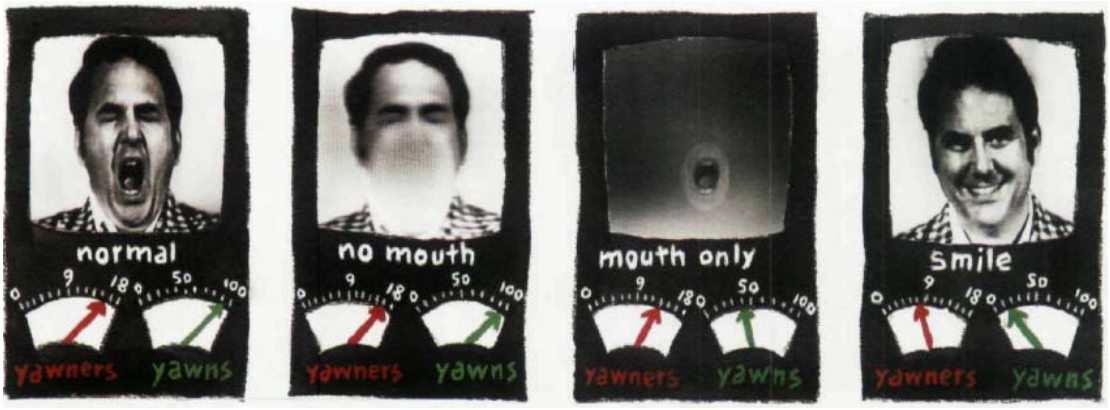

Fig 9. Shows that while watching the mouth, the number of yawns are decreased when compared to the normals..

Platek et al in 2003 tested the hypothesis that "contagious yawning occurs as a consequence of a theory of mind, the ability to infer or empathize with what others want, know, or intend to do. Seeing or hearing about another person yawn may tap a primitive neurological substrate responsible for self-awareness and empathic modeling which produces a corresponding response in oneself."[28]

To determine the significance of empathetic modeling, a study was conducted using a schizotypal personality questionnaire or SPQ and having subjects watch digital videos of people with neutral facial expression, laughing or yawning. The study showed that as SPQ total score increased, the incidence of the evoked yawning decreased ($p<0.01$). It can be inferred from the evidence that in order to engage in mental state attribution, an individual must be able to engage in self-introspection. In this study, the people who yawned the most were people who scored low on the schizotypal personality test and

used their left hands to respond to the facial recognition test which is consistent with the performance of self-processing in the right hemisphere.[14]

Chimpanzees and certain other monkey species have been shown to have the self recognition and self awareness characteristics considered to be required for contagious yawning. Six adult female chimpanzees were shown video scenes of chimpanzees repeatedly yawning, or of chimpanzees showing open-mouth facial expressions that were not yawns. Adult chimpanzees yawned 4.7 times during and after watching the open-mouth videos, and this rose to 10 yawns during and after the yawn videos.[39] In addition, yawn videos of monkeys were shown to stumptail macaques with controls. On average, each monkey yawned 2.4 times during the control video compared to the 4.3 times for the yawn video which was a statistically significant difference.[29]

re 1. Frame sequences from sample videos. (*a*) Yawn sequence, (*b*) control sequence.

8. Fetal Yawning--Although not a lot of data is available, fetal yawning has been noted in utero via ultrasound. Its specific role is not understood. Fetal yawning activity in normal and high risk fetuses was studied by Pertrikovsky in 1999. Using ultrasound, fetal movements were recorded. The number of yawning movements over a 60 minute observation period was 5+/-4 in normal fetuses, 8+/-5 in the growth restricted fetuses and 12+/-6 in anemic fetuses. Unusual bursts of fetal yawning activity were recorded in anemic fetuses. It has been theorized that yawning may possibly change the intrathoracic pressure and thereby increase venous return to the heart.[30]

Drugs and Yawning

There are a number of classes of medications that have been implicated as having yawning as a side effect. A systematic review of the French Pharmacovigilance database looked at various reports of yawning as an adverse drug reaction from 1985 to 2004. Majority of reactions were secondary to SSRIs (12), dopaminergic agents (7), opioids (4), benzodiazepines (4) and sodium channel inhibitors (3). Four patients were hospitalized because yawning induced a jaw subluxation.[31]

There are two case reports of patients on SSRIs as treatment for depression and after 2 month of treatment noted increasing yawning for 1-2 hours in a day and this hindered in their quality of life. A decrease in dosage led to a halt in excessive yawning.[32]

Yawning and Cardiac Tamponade –

A case has been reported of cardiac tamponade temporally associated with repetitive yawning. A 59 year old latino man with stage IV non small cell lung cancer presented to the emergency department after 3 days of progressive dyspnea and malaise. Patient reported that pt had been yawning repeatedly for 24 hours. By history, physical exam and echocardiogram patient was noted to have tamponade and a pericardiocentesis was performed with removal of ~2 L of serosanguinous fluid. Immediately after drainge, patients repetitive yawning resolved completely.

Various hypotheis exist as to why this was the case:

1. Inhalation to total lung capacity during a yawn may reverse the microatelectasis associated with breathing at low lung volumes as might occur when the lung is compressed by the expanded pericardial sac.
2. Right phrenic nerve passes along the pericardium over the right atrium and left phrenic nerve runs along the pericardium superficial to the left atrium and the left ventricle. Yawning may be due to irritation of the phrenic nerves from pericardial inflammation.
3. Although less likely, yawning may lead to a compensatory response to the decreased systemic venous return. It may enhance venous return by augmenting diaphragmatic contraction.[33]

Yawning and Neurological disorders

Two patients with pontine ischemia have been reported that had excessive yawning as their presenting symptom. The authors' hypothesize that the pathogenesis of excessive yawning could be related to a denervation hypersensitivity mechanism.[34]

Another case report describes a patient with excessive yawning, hemi-paresis and facial paresis as a symptom of relapsing multiple sclerosis. Yawning occurred four times per minute and there were multiple lesions of the brainstem on the MRI. With steroid therapy the yawning disappeared, as did other acute symptoms.[35]

Migraine and yawning -- Spontaneous yawning is a frequent symptom before, during and after migraine attacks. A growing body of evidence suggests that dopaminergic neurotransmission is a major pathophysiologic component of migraines. This evidence is supported by the observation that when a dopamine agonist is injected into patients with migraines, it tends to produce a greater number of yawns than in normal patients. These patients are labeled as having dopaminergic hypersensitivity.[36]

Basal ganglia disorders -- Yawning seems to be abnormally infrequent in Parkinson's disease and more frequent than the general population in Huntington's disease.[37]

Mandibular dislocation from yawning during induction of anesthesia -- yawning during induction of anesthesia may prompt TMJ dislocation in the patient with pre existing TMJ laxity.[38]

Summary

Yawning is a common behavior that has been observed in almost all species. Many theories have been used to explain the mechanism and function of yawning, yet no one unifying theory has been able to explain this intricate behavior. No matter the final verdict, the study of yawning provides scientists with an interesting question and allows for collaboration between psychologists, neurologists, pharmacologists and sociologists. As we progress in our knowledge, perhaps we will be able to elucidate the function of this behavior that has eluded us for centuries.

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