Pathological yawning as a presenting symptom of brainstem ischemia in two patients

Authors:

LUIGI CATTANEO, MD ¹
LAURA CUCURACHI, MD ¹
ELISABETTA CHIERICI, MD ¹
GIOVANNI PAVESI, MD ¹

¹ Sezione di Neurologia, Dipartimento di Neuroscienze, Università degli Studi di Parma, Parma, Italy

Corresponding author:

Luigi Cattaneo
Sezione di Neurologia, Dipartimento di Neuroscienze, Università di Parma.
Via Gramsci 14, 43100 Parma (Italy)
Tel and Fax: +39-0521-703126
Email: luigi.cattaneo@nemo.unipr.it

Key words: yawn, brainstem stroke, brainstem, involuntary movements, focal lesions

Word count: 1379

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in JNNP and any other BMJ PGL products and sublicences such use and exploit all subsidiary rights, as set out in our licence (http://jnnp.bmjjournals.com/misc/ifora/licenceform.shtml).
ABSTRACT

We report two cases of brainstem stroke involving the upper pons and the ponto-mesencephalic junction, presenting with transient excessive pathological yawning, associated with gait ataxia and in one subject by upper limb and facial hemiparesis. In these patients we hypothesise a causal relationship between the brainstem lesion and pathological yawning, possibly related to denervation hypersensitivity of a putative brainstem centre of yawn. Excessive yawning can be a heralding sign of brainstem ischemia.

INTRODUCTION

Yawning is a very common and phylogenetically old behavioural event that occurs in vertebrates under different conditions. A yawn consists of a stereotyped behavioural pattern that begins with an inspiration associated with marked dilatation of the pharynx. At the peak of inspiration there are associated facial movements and the final part of yawning is passive rapid expiration. During yawning a coordinated sequence of events takes place, involving facial, oropharingeal, tongue, and respiratory muscles, associated with activity in the axial extensor and limb extensor muscles and with autonomic changes characterized by an increased parasympathetic outflow.[1] The physiological stimuli that give rise to the yawning response and its functional significance are not clear. It has been shown that yawning frequency is not modified by hypercapnia or by pure oxygen breathing, it does not seem therefore to have a straightforward respiratory function.[2] Yawning occurs preferentially in conditions of low vigilance and causes transient increases in arousal as indicated by EEG desynchronisation though an active role in the maintenance of arousal has not been demonstrated. The social importance of yawning is particularly evident in mammals, where it seems to have a communicative role in conditions of decreased vigilance.[2] The neural structures that control yawning are presumably located in the brainstem near or within other respiratory and vasomotor centres, especially those that control facial mimics, mastication, throat and respiration and possibly stretching.[3] Excessive or pathological yawning, is defined as a compulsive, repetitive action that is not triggered by appropriate stimuli such as fatigue or boredom. We describe here two cases of excessive yawning behaviour associated with ischemic lesions in the brainstem.

CASE REPORTS

Patient 1: A 74 years old male was admitted to our clinic complaining of unsteadiness of stance and gait lasting for 12 hours. The patient referred the acute onset of excessive repetitive,
compulsive yawning that he was unable to control; the yawns were repeated at a frequency of about 3 per minute. Forty minutes later the patient noticed also gait ataxia and inability to stand without assistance. When admitted to the hospital, the neurological examination showed a slight intention tremor of the left arm and slight dysmetria in the finger-to-nose manoeuvre; no limb weakness was present and tendon reflexes were normal. The patient was able to stand and walk but the gait was possible only with enlarged base, irregular steps and leftward veering. Cranial nerves were unaffected and nystagmus was not present. The state of vigilance was constantly normal. The patient reported abnormally frequent yawning for three days following the acute onset with progressively longer intervals between one yawning act and the other. Three days later the neurological examination was normal and all symptoms had disappeared.

An MRI scan, executed 3 days after the onset of the neurological deficit, showed a small hyperintense lesion in the left paramedian region of the middle pons on fluid attenuated inversion recovery (FLAIR) images (Figure 1). The lesion was also evident as an area of hyperintense signal in T2-weighted images. At a three months follow-up the patient was free of all symptoms.

**Patient 2:** A 66 years old woman presented with acute-onset unbalance of stance and gait, followed two hours later by a single episode of vomiting and by weakness of the left upper limb. She reported that the symptoms were preceded 20 to 30 minutes before by unjustified excessive yawning, at a frequency of approximately one event every 2 minutes. On admission to hospital the clinical examination disclosed in the cranial district a slight left lower facial paresis, a horizontal nystagmus beating leftwards and a right-sided internuclear ophtalmoplegia. A pronator drift in antigravitary posture and clumsiness in distal finger movements were observed in the left upper limb. Slight proximal weakness was present also in the left lower limb. Tendon reflexes were normally elicitable in the four limbs. An extensor plantar response was present on the left side. Finger to nose and reaching manoeuvres showed slight dysmetria on the right and could not be evaluated on the left due to the motor deficit. No sensory deficit could be observed both in the trigeminal and somatic territory. The patient showed wide-base gait and a marked left lateropulsion on stance. Vigilance was normal. An MRI scan obtained at 5 days from the onset of symptoms showed a right pontine ischemia (Figure 1) and MRI-angiography disclosed a pseudoocclusive stenosis of the basilar artery. The frequency of yawning gradually decreased and returned to normal within 36 hours. The motor deficit on the left side and the gait ataxia was still present, though moderately improved, at three weeks from onset.
DISCUSSION

We describe here for the first time two patients with brainstem ischemic stroke presenting with excessive yawning. The possible causal relationship between the brainstem lesion and the excessive yawning behaviour could provide useful information on the anatomical location of the neural systems controlling yawning in humans.

The central anatomical pathways subserving yawning have not been clearly defined. The evidence in literature indicates the presence in mammals of a sub-cortical circuit mediating the yawning phenomenon, involving the hypothalamus, the midbrain and the reticular formation of the pons and medulla. In the rat experimentally induced excessive yawning behaviour can be produced by direct or indirect activation of the oxytocinergic neurones in the paraventricular hypothalamic nucleus, which is thought to play a primary role in initiating the yawning phenomenon. The activity of hypothalamic yawning related neurons undergoes a complex pharmacological control, being enhanced by dopamine D2 and possibly D3 agonists, nitric oxide, acetylcoline and ACTH – MSH peptides, orexins and serotonin and downregulated by opioids. Similar pharmacological mechanisms may act in humans, where D2 agonists, SSRI agents and withdrawal from morphine exert a facilitatory effect on the yawning behaviour. Also Valproate overdose, Imipramine and oestrogen substitution may cause pathological excessive yawning.

The existence also in humans of a putative yawning centre in the lower brainstem is suggested by lesional data. Three reports have described patients with locked-in syndrome, with preserved yawning movements and complete volitional paralysis of the bulbar musculature. Also, it has been observed that yawning movements persist in anencephalic infants. Up to now the existence of a cortical representation of yawning has not been clearly demonstrated, though a recent brain-imaging work demonstrated the presence of an area in the posterior cingulated cortex that is activated by observation of yawning and is supposed to be involved in the well-known phenomenon of contagious yawning.

In both our cases, we observed excessive yawning behaviour associated with a brainstem infarction. The lesion was located in the paramedian region in the ponto-mesencephalic junction in both patients, though the lesion in patient 2 was much more extended caudally, involving also the upper half of the pons (Figure 1). The clinical picture was characterised by gait ataxia in both patients which is known to occur extremely frequently in paramedian mesencephalic and pontine infarction. Only in patient 2, due to the anterior extension of the lesion also a motor deficit was present. Focal brainstem lesions have already been reported to cause pathological yawning. Jurko et al. reported excessive yawning during hyperventilation in patients who had previously...
undergone thalamotomy or with recent head trauma and concluded that excessive yawning can be a sign of brainstem damage. None of our patients did report a facilitatory effect of hyperventilation. Arai et al.[13] reported excessive yawning in a patient with tumour of the floor of the fourth ventricle and Postert reported excessive yawning as a symptom of brainstem localization of multiple sclerosis.[14] Additionally, excessive yawning has been observed in progressive supranuclear palsy, intracranial hypertension and in temporal lobe epilepsy, though it was not given a specific value in the localization of the epileptic focus.[15] [16]

The exact mechanism of excessive yawning following focal brain lesions is not fully understood. Possibly the pathological behaviour is the expression of the liberation from the control of more cranial structures of a putative yawning centre, caudal to the lesion, analogously to the hypothesis postulated for hiccups caused by medullary lesions[17] or for the symptom of excessive yawning behaviour in patients with ALS.[18] Also in our two patients we hypothesise that the pathogenesis of the excessive yawning could be related to a denervation hypersensitivity mechanism. To our knowledge, this is the first report of excessive yawning after brainstem stroke and, more importantly, in both patients yawning appeared as the earliest symptom reported of the ischemic insult. We conclude that excessive yawning can be a presenting symptom of an acute brainstem lesion and should not be overlooked.

Competing interests

The authors declare having no competing interest.

FIGURE LEGEND

Figure 1: Fluid attenuated inversion recovery (FLAIR) brain images of the two patients. A) Patient 1. Axial section showing a small hyperintense left paramedian area at the ponto-mesencephalic border. The scan was acquired at 3 days from onset of the symptoms B) Patient 2. Coronal section, showing the ischemic area in the right paramedian pons and ponto-mesencephalic border. The scan was acquired at 5 days from onset of the symptoms
REFERENCES


Pathological yawning as a presenting symptom of brainstem ischemia in two patients

Luigi Cattaneo, Laura Cucurachi, Elisabetta Chierici and Giovanni Pavesi

*J Neurol Neurosurg Psychiatry* published online September 20, 2005

Updated information and services can be found at:

http://jnnp.bmj.com/content/early/2005/09/20/jnnp.2005.075267.citation

These include:

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**

Articles on similar topics can be found in the following collections

- Brain stem / cerebellum (670)
- Immunology (including allergy) (1943)
- Stroke (1449)

**Notes**

To request permissions go to:

http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:

http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:

http://group.bmj.com/subscribe/