

Post-ictal forceful yawning in a patient with nondominant hemisphere epilepsy

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ABSTRACT – Yawning has been rarely described in association with seizures and not previously documented by video-EEG. We present a 48-year-old woman with a long history of non-dominant *for speech* hemisphere seizures and post-ictal yawning. Yawning was irresistible, forceful and often repetitive. We reviewed the few similar epileptic cases described in the literature and discussed the possible mechanisms.

[Published with video sequences]

Key words: yawning, epilepsy, autonomic seizures, post-ictal phenomenon

Yawning is a common physiological event in mammals. It may increase vigilance when drowsiness occurs and is probably important for social communication. It has been reported in different pathological conditions (Daquin *et al.* 2001). The occurrence of yawning in relation to epileptic seizures has been rarely described (Penfield and Jasper 1954, Goldie and Green 1961, Donat and Wright 1991, Muchnik *et al.* 2003). We report a patient with non-dominant *for speech* hemisphere seizures and irresistible, repetitive and forceful post-ictal yawning.

– **Seizure type 3**, type 2 progressing to dystonic posturing of the left arm with non-forceful head deviation to the left, and brief unresponsiveness, occasionally followed by a transitory left arm weakness,

– **Seizure type 4**, sudden falls without warning,

– **Seizure type 5**, rare secondarily generalized tonic-clonic seizures (GTCS).

Surface EEG recordings showed ictal epileptic activity over the right centro-parieto-temporal regions. Her neurological examination was normal. Medical history was remarkable for asymptomatic hepatitis C. At 30, she underwent invasive EEG studies, which disclosed epileptiform abnormalities over the right parietal operculum. Brain CT and MR imaging were normal. Neuropsychological evaluation revealed right hemisphere dysfunction (sodium amobarbital test confirmed a left hemispheric dominance for speech). A right inferior parietal and posterior temporal resection did not lead to improvement. Pathological studies showed no specific



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Case report

A 48-year-old, left-handed woman with no neurological antecedents began having intractable epileptic attacks at age 18. She described five types of seizures:

– **Seizure type 1**, isolated myoclonic jerks of the left arm,

– **Seizure type 2**, left arm numbness,

changes. At 31, she had a second resection at the temporal edge of the previous operation, again with no improvement.

In 2004, she underwent further telemetry recordings. Thirty-eight seizures were recorded: 9 were myoclonic jerks; 6, left arm sensory seizures (duration, < 10 s); 22, sensory attacks followed by left hand dystonia, head deviation and loss of awareness (mean duration, 15 s). No falls were recorded but she had one GTCS. Ictal scalp EEG showed no changes with types 1 and 2, and disclosed low voltage fast activity over the right centro-parieto-temporal areas without depression of background activity with all type 3 seizures (*figure 1*). Attacks occurred at random during the day when she was alert and active, and alpha activity was seen before and after each of the 37 seizures that did not generalize. Complete blood count, electrolytes, renal and thyroid function tests were normal, but hepatic enzymes were mildly elevated. Oxygen blood saturation and CO₂ were not measured during yawning, but routine venous blood parameters were normal.

Yawning. In 19 type 3, and in two type 2 seizures, she had repetitive, irresistible and forceful yawning starting from one to 30 seconds (mean, 8.5 s) after the seizure offset. No yawning was detected with myoclonic jerks, and the single GTCS was not included in the analysis. Yawning lasted from five to 60 seconds. There was no change of cardiac rhythm. There was no obvious change in blood pressure, respiration and no skin changes occurred during these episodes. Yawning started with a deep inspiration through her wide-open mouth (*figure 2*). She was alert during all yawning episodes. She received oxcarbazepine 1,800 mg/d during telemetry and her valproate was gradually withdrawn. Her husband had witnessed similar paroxysmal yawning for approximately six years occurring typically at the end or just after type 3 seizures when she received different medications singly or in combinations. Physiological yawning was observed when the patient was tired or bored, with a quality similar to her peri-ictal yawning except for lack of clustering and irresistibility. We found no episodes of peri-ictal yawning when reviewing the earlier (1986 and 1987) prolonged surface and intracranial video-EEG studies. Her seizures remained the same over the years, including those followed by yawning. Repeated high quality MR failed to show a structural lesion, except for postsurgical changes.

Discussion

We describe a woman with repetitive yawning as an unusual, isolated, autonomic, post-ictal phenomenon. Yawning appeared immediately or seconds after cessation of seizures, was irresistible and was observed after most (86%) of the focal sensory-motor and some (33%) sensory attacks. We cannot explain why yawning appeared late (approximately 24 years after onset of her seizures and 11

years after her second surgery) during the course of her disorder.

Physiology of yawning. Yawning is a complex spatio-temporal reflex, and neural structures involved are presumably located in the brainstem near respiratory and vasomotor centers, and those that control facial mimicry, mastication, throat movements and stretching. The purpose and mechanism of yawning are not well understood. Three theories have been proposed: a relation to respiration, alertness or communication (Daquin *et al.* 2001). The hypothalamic paraventricular nucleus contains nerve endings that belong to the incerto-hypothalamic dopaminergic system and project to oxytocinergic neurons located in this nucleus. These in turn project to the hippocampus, pons and medulla oblongata and mediate the expression of yawning. Oxytocinergic neurons can be modulated by several neurotransmitters and neuropeptides, such as dopamine, oxytocin, prolactin, excitatory amino acids, acetylcholine and nitric oxide to name the most important ones (Argiolas and Melis 1998). Oxytocin injected in the CA1 field of the hippocampus induced yawning (Melis *et al.* 1986). Acetylcholine and cholinomimetic drugs can induce yawning in rats and muscarinic antagonists can prevent it. Finally, prolactin facilitates and opioids inhibit yawning.

Yawning and epilepsy. We found only six, well documented cases in the literature where yawning was reported in association with epilepsy (*table 1*). Penfield and Jasper (1954) described two adult patients with autonomic seizures and yawning. The first had a tumor infiltrating the left temporal lobe and ipsilateral basal ganglia. She had seizures beginning with a headache associated with yawning, hiccup, urge to void and focal sensory phenomena. In the second patient, attacks were ushered in by sweating of her hands and scalp and a prickling sensation in the scalp and back, and with repetitive yawning, palpitations, visual distortions and weakness. No EEG was reported. Golgie and Green (1961) described an adolescent with “*petit mal*” and found an association between yawning and 3 per second spike and wave discharges. Donat and Wright (1991) reviewed unusual variants of infantile spasms in 11 children (13% of their patients with infantile spasms), and described one, with an unspecified brain malformation, who had a variant consisting of yawning with generalized decremental activity on EEG. This yawning variant and the child’s more typical infantile spasms responded to ACTH. Finally, Muchnik and colleagues (2003) described two patients who had temporal lobe epilepsy and yawning. In the first, yawning occurred during drowsiness and preceded focal seizures. The patient had independent, bilateral, temporal interictal epileptiform discharges, but imaging was not reported. The other, a 17-year-old woman with an insulin-dependent diabetes, had a normal MRI, complex partial seizures and secondary generalization with yawning during the post-ictal period. EEG also showed bilateral temporal spikes.

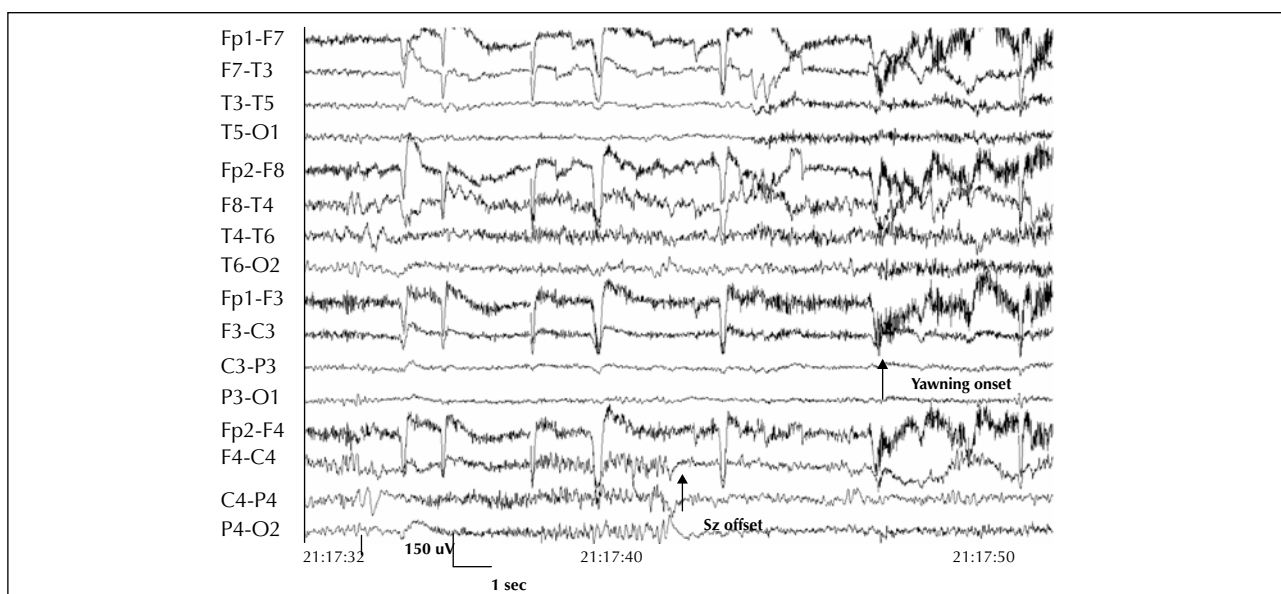


Figure 1. A) Ictal and post-ictal EEG. In this seizure (type 3), the patient demonstrated yawning 6 sec after seizure-offset (first arrow). Ictal discharge started approximately 8 to 10 sec before seizure offset, and was seen in the right centro-parieto-temporal region. There was no post-ictal depression of EEG activity. **B)** Post-ictal yawning.

Table 1. Patients with peri-ictal yawning.

Ref./Sex/Age at sz onset (y)	Age at yawning onset (y)	Yawning duration	Relation to seizure	Associated clinical manifestations	EEG	Risk factors, imaging or pathology
2/F/23	23	"Continuous" (during ictal phase, time not specified)	Ictal	Headache, hiccups, urge to void, numbness L arm and mouth	-	L T astrocytoma (pathology)
2/M/?	-	3 min to 3h	Ictal and post-ictal	Sweating hands and scalp, paresthesias scalp and back, palpitations	-	Head trauma
3/F/7	7	Seconds	"Interictal"	None	Preceding or during bursts of 3Hz SW	None
4/?/infancy	Infancy	Seconds	Ictal	Infantile spasms variant (with yawning), typical spasms (without yawning)	During decremental activity	"Brain malformation"
5/M/95	95	30 s	Pre-ictal	During drowsiness, before CPS	Bil T	Diffuse brain atrophy (CT)
5/F/15	15	-	Post-ictal	After CPS and generalization	Bil T	Normal (MR)
Our patient/ F/18	42	5-60s	Post-ictal	Focal sensory-motor attacks (types 2 and 3)	R CTP	No lesion except surgical (MR)

y = years, sz = seizure, min = minutes, L = left, R = right, h = hours, s = seconds, SW = spike and wave, bil = bilateral, C = central, T = temporal, P = parietal, CPS = complex partial seizure.

Three mechanisms might explain peri-ictal yawning. First, activation of the brainstem structures related to a change in the level of alertness. In our patient, yawning was never caused by a change in her level of alertness. This mechanism however, could be a factor in the two patients of Muchnik and colleagues (2003). Second, a direct activation of brainstem structures by the epileptic discharge. The

fact that yawning appeared immediately or just a few seconds after a right centro-parieto-temporal epileptic discharge and seizure offset, suggests a fast operating process that activated the brainstem structures. We can not explain why yawning did not occur during the attack. Third, a seizure-mediated secretion of endogenous neurohumoral substances such as prolactin or oxytocin may cause yawning. The latter is less likely since a prolactin surge should only occur after a few minutes (Pritchard *et al.* 1983), and activation of oxytocin in the hypothalamic paraventricular nucleus was found to occur only 1.5 hours after kainic-induced seizures in rats (Sun *et al.* 1996). We did not however, measure plasma concentration of prolactin or oxytocin in our patient. There is no evidence that her medications were responsible for yawning since the patient's husband and she herself did not notice any change in the yawning pattern over the previous six years when taking various drugs.

In keeping with previous reports implying preferential non-dominant hemisphere for the induction of autonomic peri-ictal symptoms such as spitting, water drinking, vomiting, urinary urge or coughing (Baumgartner *et al.* 2001), yawning in our patient occurred after seizures arising in her non-dominant hemisphere. However, such non-dominant lateralization may not be absolute, since a patient with yawning and seizures related to a left temporal tumor was reported (Penfield and Jasper 1954). It is remarkable that forceful yawning has been so rarely described in association with seizures. □

Legends for video sequences

Video 1

Type 3 seizure followed by a single brief episode of yawning (EEG, *figure 1A*). Before seizure onset patient is alert and watches TV. EEG onset is at 21:17:34 and offset at 21:17:43. Yawning starts 6 sec after the end of the attack, and patient remains alert throughout the event.

Video 2

Type 3 seizure followed by repetitive yawns and a transitory left arm weakness. EEG seizure starts at 12:22:54 and ends at 12:23:05. Ictal discharge is followed by a continuous polymorphic slow wave activity seen in the right centro-parieto-temporal area for approximately 60 sec. Forceful, repetitive yawns (and few coughs) start at 12:23:22 and persist until 12:24:30 when patient declares that she just had a seizure.

References

- Argiolas A, Melis MR. The neuropharmacology of yawning. *Eur J Pharmacol* 1998; 343: 1-16.
- Baumgartner C, Lurger S, Leutmezer F. Autonomic symptoms during epileptic seizures. *Epileptic Disord* 2001; 3: 103-16.
- Daquin G, Micallef J, Blin O. Yawning. *Sleep Med Rev* 2001; 5: 299-312.
- Donat JF, Wright FS. Unusual variants of infantile spasms. *J Child Neurol* 1991; 6: 313.
- Goldie L, Green JM. Yawning and epilepsy. *J Psychosom Res* 1961; 5: 263-8.
- Melis MR, Argiolas A, Gessa GL. Oxytocin-induced penile erection and yawning: site of action in the brain. *Brain Res* 1986; 398: 259-65.
- Muchnik S, Finkielman S, Semeniuk G, et al. Yawning and temporal lobe epilepsy. *Medicina (B Aires)* 2003; 63: 137-9; [Spanish].
- Penfield W, Jasper H. In: *Epilepsy and the functional anatomy of the Human Brain*. Boston, Mass: Little, Brown & Co, 1954: 416-8.
- Pritchard 3rd PB, Wannamaker BB, Sagel J, Nair R, DeVillier C. Endocrine function following complex partial seizures. *Ann Neurol* 1983; 14: 27-32.
- Sun Q, Pretel S, Applegate CD, et al. Oxytocin and vasopressin mRNA expression in rat hypothalamus following kainic acid-induced seizures. *Neuroscience* 1996; 71: 543-54.