

## Fou Rire Prodromique

### Case Report and Systematic Review of the Literature

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*Fou rire prodromique* is a rare behavioral abnormality characterized by prolonged burst of uncontrolled laughter preceding the onset of an acute neurological deficit [1–3].

#### Case Report

A 51-year-old hypertensive woman, with a history of previous left dorsal midbrain hematoma and multiple cavernomas identified by MRI, was admitted because of a speech disorder and right-sided weakness, preceded by an uncontrolled fit of laughter. The laughter was of abrupt onset and inappropriate to the situation, and the patient could not stop it voluntarily. Throughout the episode the patient was always able to establish contact with her husband. The laughter lasted 30 min and ended abruptly, and was followed in seconds by the onset of a speech disorder and right-sided weakness. The husband described the patient as a strict and emotionally stable person prior to this event.

On admission, the patient was drowsy, dysarthric, with a non-fluent aphasia and a right-sided hemiparesis. There was a residual left Horner syndrome and left limb ataxia from the previous brainstem hematoma. The patient was continuously whimpering. Cranial CT scan (fig. 1) revealed a left hematoma involving the anterior part of the thalamus and the internal capsule.

On following days, drowsiness, dysarthria, aphasia and motor deficit improved. The patient kept whimpering continuously and was abulic. Two months later, she was improved but had a residual right motor deficit. Pathological laughter did not recur. MRI de-

icted a resolving hematoma in the left thalamus, an old left dorsal midbrain hemorrhage, periventricular white matter changes, and two cavernous angiomas localized to the head of right caudate nucleus and right temporal lobe (fig. 2). We plotted the thalamic hematoma on a horizontal section of thalamic nuclei [4]. For this purpose, a bidimensional atlas of the thalamus [4] and co-planar coordinates were used. The lesion was localized to the internal ventro-oral, ventrointermedial, intralamellary, external ventro-oral and median nuclei of the left thalamus (fig. 3).

#### Systematic Review of Previously Reported Cases

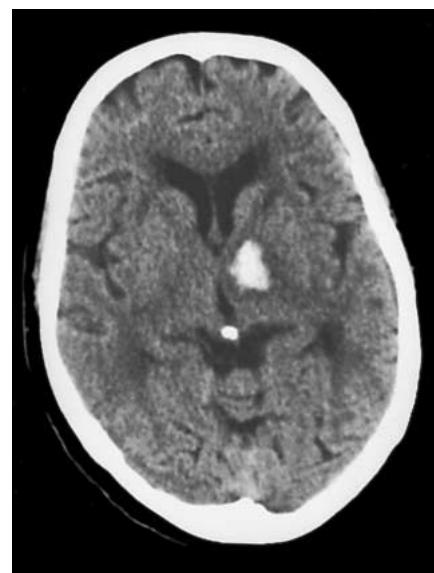
##### Review Method and Conduction

A literature search was based on: (i) a Medline search using the key words ‘fou rire prodromique’, ‘pathological laughter’, ‘pathological mirth’ and ‘gelastic seizure’; (ii) a hand search of references of published cases/case series; (iii) a hand search on textbooks of neurology, epilepsy and cerebrovascular diseases. Excluded from this review were non-prodromal cases of pathological laughter and cases of gelastic seizures. Also excluded were papers written in languages other than English, Portuguese, French, Spanish or Italian.

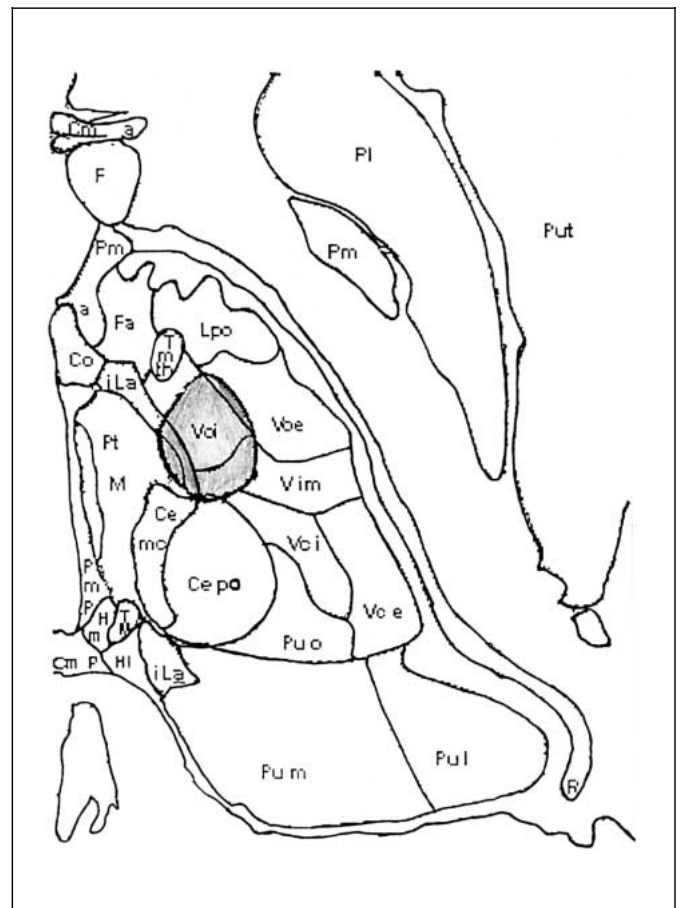
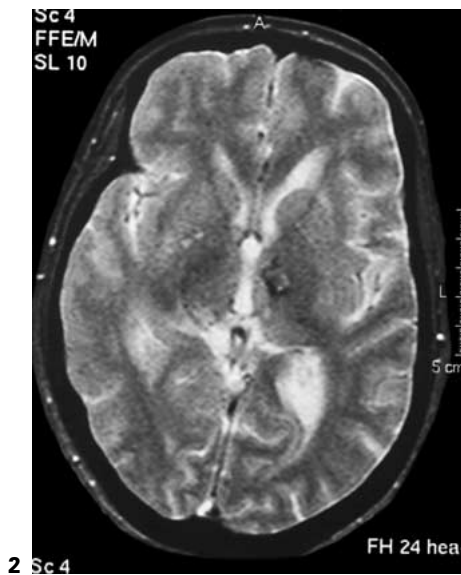
For each case report, the following data was extracted: gender, age and history of previous stroke; duration of laughter and latency to neurological deficit; other behavioral disturbances; results of neuroimaging and/or autopsy; recurrence of laughter.

##### Review Results

We found 18 published cases of *fou rire prodromique* (table 1), including thirteen strokes [1, 3, 5–15] (one haemorrhagic [5]). Pontine infarcts were found in five patients [3, 6, 8, 9, 15], but cortical [10, 11, 16] and sub-cortical [1, 7, 13] lesions are also reported. In four patients [6, 9, 12, 15] the *fou rire* relapsed. Behavioral distur-



**Fig. 1.** CT scan. Hematoma in the anterior part of the left thalamus and the left internal capsule.



**Fig. 2.** MRI. Hematoma in the left thalamus and two cavernous angiomas in the right caudate nucleus and right temporal lobe.

**Fig. 3.** Hematoma plotted on a horizontal section of thalamic nuclei, 2.7 mm superior to anterior commissure–posterior commissure line. M = Median nucleus; iLa = intralamellary nucleus; Voi = internal ventro-oral nucleus; Voe = external ventro-oral nucleus; Vim = ventrointermedial nucleus; CePc = centralis parvocellularis nucleus; Cm a = anterior commissure; Cm P = posterior commissure; Pu m = medial pulvinar nucleus; Pu l = lateral pulvinar nucleus.

**Table 1.** Case reports of fou rire prodromique

Case reports (n = 18)	Gender	Age	History of past stroke	Duration of laughter	Latency to neurological deficit	Autopsy	Neuroimaging	Other brain lesions	Pathological crying/laughter or other behavioral disturbance	Recurrence
Féré [17] 1903	M	64	no	n.a.	4 months	no	n.a.	n.a.	memory deficit; decrease intelligence; somnolence	no
Andersen [5] 1936	F	58	previous pseudo-bulbar palsy	1½ h	immediate	bilateral thalamic, capsular and lenticular hemorrhage with intraventricular blood, originating from posterior communicating artery	n.a.	n.a.	no	n.a.
Martin [12] 1950	M	25	no	n.a.	n.a.	large basilar aneurism	n.a.	n.a.	no	two episodes previous to neurological deficit
	F	25	no	n.a. (<24 h)	2 months	no	n.a.	n.a.	no	no

**Table 1** (continued)

Case reports (n = 18)	Gen-der	Age	History of past stroke	Duration of laughter	Latency to neurological deficit	Autopsy	Neuroimaging	Other brain lesions	Pathological crying/laughter or other behavioral disturbance	Recurrence
Swash [14] 1972	F	45	no	3 h	n.a.	no	Scan Tc 99m: increased uptake in lateral, anterior and inferior aspects of left temporal lobe	no	pathological laughter; no aphasia; mumbling voice, neologisms; neglect; perseveration of speech and gestures	no
Walli [3] 1993	F	35	no	15 min	15 min	no (patient died)	MRI: bilateral symmetrical infarct of basis pontis, mainly left half	no	no	no
Ceccaldi [1] 1994	F	47	no	15 min	few min	no	MRI: posterior part of left parahippocampal gyrus, left posterolateral thalamus and adjacent part of internal capsule	no	no	no
Ceccaldi [16] 1995	F	57	no	10–15 min	3 episodes before deficit; 24 h between last episode and deficit	no	MRI: right prerolandic tumor	no	no	no
Ertekin [9] 1997	M	57	no	60 min	n.a.	no	MRI: left pontine infarct	no	pathological crying and laughing	few times in first 3 days after stroke; one year later with infarct at head of caudate nuclei
	M	67	no	60 min	n.a.	no	MRI: normal	no	pathological crying and laughing	no
	F	85	no	15 min	n.a.	no	CT: normal; MRI not possible to perform	no	no	no
Tei [15] 1997	F	69	n.a.	15–30 s	n.a.	no	MRI: ventromedial pontine infarct	no	no	several spells during 3 weeks
Lago [11] 1997	M	78	no	15 min	n.a.	no	CT: infarct in posterior territory of left MCA	sub-acute infarct of posterior branches of right MCA	agitation	no
Carel [7] 1997	M	61	n.a.	2 min	immediate	no	MRI: left infarct in lenticular nuclei, caudate nuclei and anterior insula	no	no	no
Assal [6] 2000	F	61	no	approximately 12 h	n.a.	no	MRI: infarction in right ventral pons	no	mild attentional deficit and decreased phonological fluency	several spells during a week
Garg [10] 2000	F	50	no	15 min	immediate	no	CT: cortical infarct in the territory of superior division of left MCA	no	no	no
Couderq [8] 2000	M	49	yes (right MCA stroke; no sequelae)	15 min	immediate	no	CT: infarct in left pons; spontaneous hyperdensity in basilar artery	old infarct in superficial territory of right ACM	time and place disorientation; visual and auditory hallucinations without insight	no
Osseby [13] 1999	M	12	no	1 min	immediate	no	MRI: infarction of left lenticular nucleus, left insula and mild involvement of left internal capsule	no	simultaneous pathological crying; aphasia; occasional pathological laughter	no

n.a. = Not available; MCA = middle cerebral artery.

bances were present in nine patients [6, 8, 9, 11, 13–15, 17]. In one patient [13], there was simultaneously a pathological fit of laughter and crying preceding the neurological deficit. In another two [9] patients, typical spasmodic laughter and crying developed a few days after the onset of stroke. In the reported cases, *fou rire* usually lasts between a few seconds to several hours (table 1). The latency between its ending and the start of neurological deficit varies widely, between milliseconds to months (table 1).

#### Discussion

When preceding the onset of an acute neurological deficit, pathological laughter is named *fou rire prodromique* [2, 3, 11, 15], as first reported by Féré in 1903 [7]. In some reported cases [12, 17], the neurological deficit started more than 24 h after the *fou rire*. In these cases, it is not appropriate to describe the *fou rire* as prodromique. The reports of one patient [13] with *prodromique* laughter and crying, and of another two patients [9] with pathological crying and laughter following the *fou rire*, suggest that *fou rire* and spasmodic laughter may share common physiopathology [9]. In the case we report, *fou rire* was followed by prolonged continuous whimpering. Although an EEG could not be performed during the episode of laughter, the duration of the laughter (much longer than the usual 30 s of gelastic seizure), the persistence of consciousness and the lack of automatisms are not in favor of a gelastic seizure [2, 11, 16].

Wilson [18] proposed the existence of a supranuclear pontobulbar facio-respiratory center for the control of laughter, connecting the facial nucleus in the pons with that of the tenth nerve in the medulla and the phrenic nerve in the upper cervical cord. An integrative center has been proposed, located in the medial thalamus, hypothalamus and subthalamus. This center would be under the voluntary control of bilateral corticobulbar tract and involuntary control of bilateral orbitofrontobulbar respiratory tract. The orbitofrontobulbar would inhibit the corticobulbar one. A lesion in any of these tracts or centers would deregulate the system and provoke pathological laughter. This is in accordance with the various locations of lesions causing pathological laughter. A recent alternative hypothesis [19], claiming a role of a lesion of the cerebro-ponto-cerebellar pathways for pathological laugh and crying is also compatible with the various distributions of lesions that we found in the systematic review. Gelastic seizures elicited by electric stimulation [20] suggest the involvement of the anterior cingulate gyrus in the motor act of laughter. Subthalamic nucleus stimulation for Parkinson's disease induced mirthful laughter in two patients [21]. The authors ascribed this effect to damage to the limbic portion of the subthalamic nucleus and its interconnections to the basal ganglia and thalamus, or, alternatively, to electric current diffusion to neighboring structures such as the hypothalamus.

In our case, the origin of *fou rire prodromique* may be due to the interruption of efferent pathways from the medial, intralaminar and ventrolateral formations of the thalamus [20] to the anterior cingulate gyrus [22]. The medial thalamic lesion may cause prolonged and inappropriate laughing by disrupting integration of the cognitive and emotional clues that trigger laugh in adequate social context. The lesion responsible for the *fou rire* must be smaller than the hematoma depicted on CT, because the *fou rire* ended before the start of motor deficit, being substituted by continuous whimpering. However, the presence of a previous hematoma, multiple cavernomas and subcortical white matter lesions make inferences on the anatomical interpretation of *fou rire* difficult in this case. The presence of the other vascular lesions localized to the left dorsal midbrain, head of right caudate nucleus and right temporal lobe, in combination with the

thalamic hemorrhage could be the trigger of the *fou rire*. Finally, other hypothesis should be considered, such as the thalamic hematoma causing ephaptic excitation of the internal capsule or disinhibition of neighboring structures.

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