Ictal dysprosody and the role of the non-dominant frontal operculum

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ABSTRACT – Prosody is an important feature of language and refers to variations in the acoustic properties of timing, intensity and fundamental frequency that are used to convey affective or linguistic information. The prosodic component of ictal speech has not yet been specifically studied in epileptic patients. We report the case of a patient with right mesial temporal lobe epilepsy who developed ictal, recurrent speech utterances associated with an altered prosody during both spontaneous seizures and a very localized stimulation-induced discharge of the non-dominant precentral operculum, a finding consistent with results of functional magnetic resonance imaging studies in healthy subjects. This should prompt future studies, with the aim of better evaluating the localizing value of ictal dysprosody in patients with drug resistant, partial epilepsy.
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Ictal speech automatisms or verbalisations are observed in 12% to 39% of patients with drug resistant temporal lobe epilepsy (TLE) (Bingley 1958, Hécaen and Angelergues 1960, Serafetinides and Falconer 1963, McKeever *et al.* 1983, Gabr *et al.* 1989, Yen *et al.* 1996). They are significantly more frequent in seizures originating from the non-dominant than the dominant temporal lobe (Bingley 1958, Hécaen and Angelergues 1960, Serafetinides and Falconer 1963, Mckeever *et al.* 1983, Gabr *et al.* 1989, Yen *et al.* 1996). These automatisms include different types of manifestations, described by Serafetinides (1963) as either warning, irrelevant, emotional, perplexity, or recurrent utterances also defined as speech perseveration (Mckeever *et al.* 1983). This latter type of utterance which lacks a fast rhythmic component in the word repetition must be distinguished from the ictal palilalia related to supplementary motor area (SMA) discharges (Alajouanine and Sabouraud 1960). In contrast with the richness of these clinical descriptions, the prosodic component of ictal speech has not yet been specifically studied in epileptic patients. To our knowledge, only a single case report has mentioned the interictal disruption of prosody in a patient suffering from right frontal lobe epilepsy (Dykstra *et al.* 1995).

We report the case of a patient with spontaneous and electrically-induced ictal dysprosodic speech utterances related to the involvement of the non-dominant frontal operculum.

Case report

This 35-year-old, right-handed man with no history of febrile seizure, brain trauma, central nervous system infection, or neonatal complication, presented a first episode of non-febrile, generalised convulsive status epilepticus at the age of 5. Post-ictal electroencephalography (EEG) recordings showed diffuse abnormalities, and barbiturate treatment was started.

Partial seizures began at the age of 6. According to the patient and his relatives, seizures started with an aura of nausea, followed by a staring gaze, partial loss of consciousness, oro-alimentary automatisms, right-sided version and post-ictal confusion with no noticeable speech difficulties. Ictal speech utterances were clearly described by family members from the age of 18, where they consisted in repetition of stereotyped French or English sentences "maman, je t'aime" or "mummy, I love you, because".

Seizures remained drug-resistant, with an average frequency of 1 to 3 per month, until the age of 35 when a presurgical evaluation was performed. Long-term video-EEG monitoring captured 6 electroclinical seizures and showed interictal bifrontotemporal slow waves. Ictal semiology, which is detailed further, as well as EEG discharges, suggested a right temporal seizure onset. Consistent with these findings, 18-fluorodeoxyglucose-positron emission tomography (FDG-PET) revealed a right-sided, amygdala hypometabolism extending to the right temporal pole and anterior hippocampus, whereas ictal single photon emission computed tomography (SPECT) (neurolite 99^{m}Tc) showed an increased blood flow centered on the right amygdala *(figure 1)*. An intra-carotid amobarbital test demonstrated that the patient had a strictly left-sided language lateralisation and a right-sided memory impairment.

However, an optimal brain magnetic resonance imaging (MRI) failed to detect any abnormality, including signs of hippocampal sclerosis. This prompted us to perform an intra-cerebral, stereo-electroencephalography (SEEG) in order to confirm the right temporal lobe origin of the seizures and to exclude the possibility of an early or prominent involvement of others brain structures.

The technique used was the one described by Bancaud and Talairach (1973). Eleven electrodes were placed in the right hemisphere *(figure 2)*, targeting the amygdala (A), anterior hippocampus (B), posterior hippocampus (C), parahippocampal gyrus (D), temporal pole (J), posterior part of the first temporal gyrus (H), precentral operculum (P) *(figure 3)*, post-central operculum (E), orbito-frontal cortex (O), subcallosum anterior cingulate gyrus (K) and lower portion of the SMA (S). The trajectories of these electrodes also allowed exploration of the second temporal gyrus (A, B, C, D), the insula (H, P, E) and the second frontal gyrus (K, S). In addition, one electrode was implanted within the left amygdala (A').
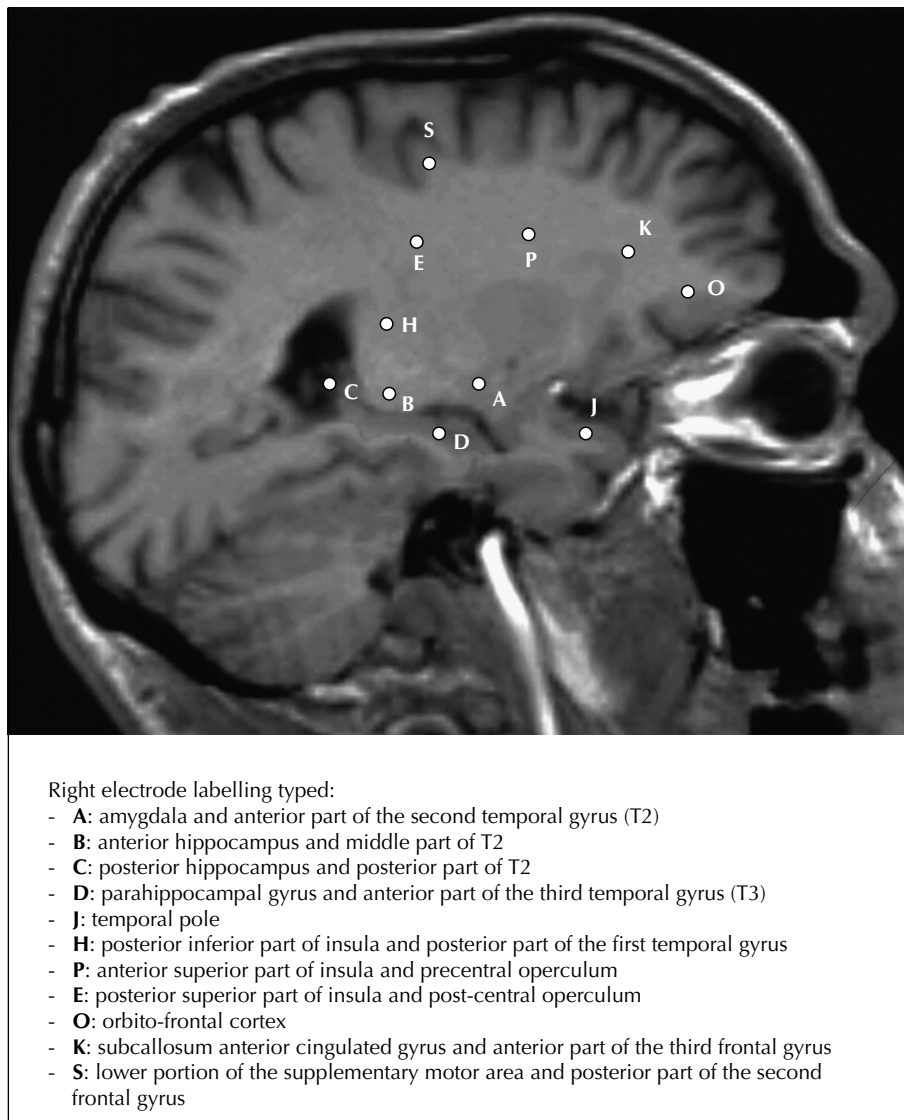
The most prominent interictal abnormalities consisted of spikes and slow waves, recorded within the right amygdala, sometimes extending towards the entire right temporolimbic structures. Intermittent pseudo-rhythmic sharp waves were also recorded in the right temporal pole, as well as slow waves in the left amygdala.

Five stereotyped and spontaneous electroclinical seizures were recorded. Clinical onset was marked by the patient's usual aura of nausea, well described by the patient, then followed by a partial loss of awareness, speech utterances, oro-alimentary automatisms, oculocephalic version to the right side, and postictal confusion without speech disturbance.

In all five seizures, a 2- to 3-Hz spike and wave rhythmic discharge began in the right amygdala (A), about 20 seconds before the first ictal symptom, and then, propagated to the right anterior hippocampus (B) and parahippocampal gyrus (D), while nausea was reported. Then, the concomitant involvement of the left amygdala (A'), the right insula (H,P,E), the right lower portion of the SMA (S) and
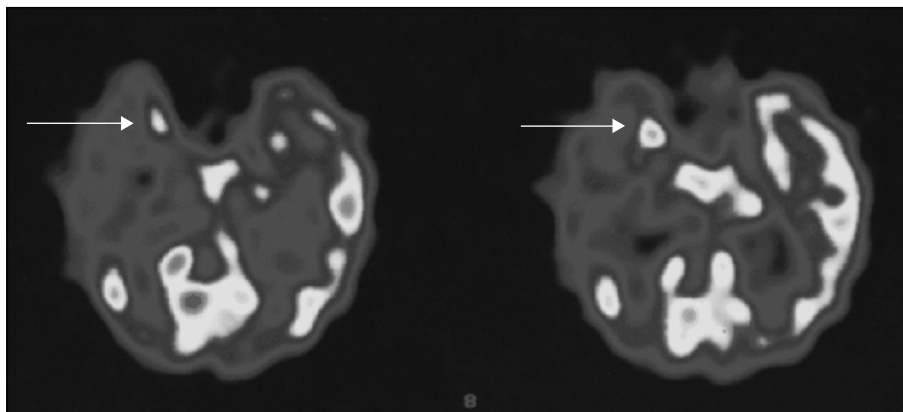
Figure 1. Ictal SPECT (Neurolithe 99^{m}Tc) showed an increased blood flow in the right mesial temporal lobe.

Right electrode labelling typed:
- **A**: amygdala and anterior part of the second temporal gyrus (T2)
- **B**: anterior hippocampus and middle part of T2
- **C**: posterior hippocampus and posterior part of T2
- **D**: parahippocampal gyrus and anterior part of the third temporal gyrus (T3)
- **J**: temporal pole
- **H**: posterior inferior part of insula and posterior part of the first temporal gyrus
- **P**: anterior superior part of insula and precentral operculum
- **E**: posterior superior part of insula and post-central operculum
- **O**: orbito-frontal cortex
- **K**: subcallosum anterior cingulated gyrus and anterior part of the third frontal gyrus
- **S**: lower portion of the supplementary motor area and posterior part of the second frontal gyrus

Figure 2. Eleven electrodes were placed in the right hemisphere and one electrode was placed in the left amygdala.

the right anterior cingulate gyrus (K), was associated with the occurrence of staring gaze, loss of awareness, oro-alimentary automatisms, and oculocephalic version to the right side.

Speech utterances started thereafter while the ictal discharge invaded the posterior aspect of the first temporal gyrus (H), as well as the precentral (P) and postcentral operculum (E) of the non-dominant hemisphere. These utterances were characterized by a disruption of prosody with a monotonous, hypophonic and emotionally neutral repetition of stereotyped sentences, which clearly contrasted with their semantic content ("mummy, I love you"). These utterances persisted until the end of the EEG discharge.

Five second trains of 50 Hz, 1mA stimulation of the right amygdala consistently induced a post-discharge that was associated with nausea similar to that occurring during spontaneous seizures. Similar high frequency stimulation of the right precentral operculum induced a 20 second duration post-discharge restricted to the stimulated electrode, and associated with a disruption of prosody while the patient was counting aloud from 1 to 20. He started counting faster, with a higher pitch, and hypophonia, reproducing some of the characteristic features of his ictal, spontaneous, dysprosodic speech utterances. Right mesial TLE was diagnosed, and the patient underwent a right mesial temporal and temporo-polar resection. He has remained seizure-free over three years of follow-up.
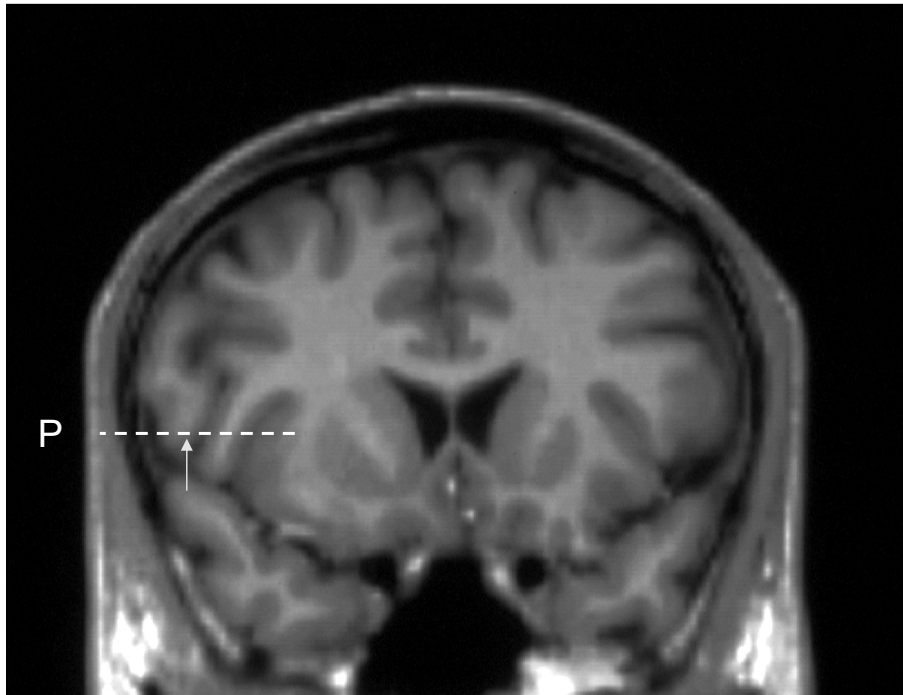
Figure 3. Precentral operculum electrode: ictal recurrent speech utterances associated with an altered prosody occurred during both spontaneous seizures and a very localized stimulation-induced discharge of the non-dominant precentral operculum.

Discussion

We report the case of a patient with right, mesial TLE who developed ictal recurrent speech utterances associated with an altered prosody during both spontaneous seizures and a very localized stimulation-induced discharge of the non-dominant precentral operculum.

This report is of interest in two respects. Firstly, ictal dysprosody has not yet been formally described and could prove to be a clinically useful ictal sign for localizing areas of seizure onset or propagation. Secondly, it provides a unique opportunity to revisit the neural basis of prosodic functions.

Our patient kept repeating stereotyped sentences during his seizures but was then amnesic of his speech disturbance. As a matter of fact, ictal speech automatisms are defined as utterances of identifiable words or sentences that are linguistically correct, and which the patient does not usually recollect (Serafetinides and Falconer 1963). These automatisms are also referred to as speech perseverations when stereotyped as observed in our patient. They differ from paroxysmal ictal dysphasia, which can be recalled by the patient, and from palilalia, which consists of repeating a speech fragment that was meaningfully spelled immediately prior to seizure onset (Serafetinides and Falconer 1963).

Prosody is an important feature of language and refers to variations in the acoustic properties of timing, intensity and fundamental frequency that are used to convey affective or linguistic information. Dysprosody, which was initially described by Monrad-Krohn in 1947, defines the loss of language melody, and usually implies a deficit in all three of the above acoustic properties (Dykstra *et al.* 1995). However, recent findings from heterogeneous clinical populations indicate that these properties may be differentially disturbed, depending on the site of brain dysfunction (Danly and Shapiro 1982, Klouda *et al.* 1988, Gandour *et al.* 1989).

In fact, the neuroanatomic substrates of emotional and linguistic cues are not clearly defined in adults. Whereas some authors have reported a right hemispheric specialization in prosodic functions (Heiman *et al.* 1975, Ross and Mesulam 1979), and proposed a functional-anatomic organization which would mirror that of propositional language in the left hemisphere (Ross 1981, Gorelick and Ross 1987), several series have failed to demonstrate a significant difference in prosody between right and left brain-damaged patients (Weintraub *et al.* 1981, Emmorey 1987, Ryalls *et al.* 1987, Behrens 1988). Moreover, while some investigators believe that the right hemisphere is dominant for all prosodic information, others have suggested that the latter only controls the emotional aspects of prosody, whereas the left hemisphere may be responsible for the processing of nonverbal, linguistic cues. All these hypotheses were based on information derived from brain-lesions studies.

The brain regions involved in recognition of prosody in healthy subjects is also a matter of debate, according to recently performed functional MRI studies. Initially, Buchanau *et al.* (2000) demonstrated a bilateral but asymmetrical involvement of temporal and frontal lobes in the detection of emotion in language with a right-side predominance. Mitchell *et al.* (2003) then demonstrated that passive listening of emotional prosody consistently activated the superior and/or middle temporal gyri, with a right-side predominance regardless of the semantic content of the stimulus. Finally, Kotz *et al.* (2003) found a bilateral, fronto-opercular activation to prosodic speech listening of various emotional intonations. In the same manner, attempts to recognize the emotional content associated with either speech prosody or facial expression activate the right, fronto-parietal operculum (Adolphs *et al.* 2002).

Overall, results from these studies point to the role of the non-dominant hemisphere in the processing of emotional prosody, and particularly to the right, fronto-opercular and temporal cortices.

Accordingly, the electroclinical data recorded in our patient demonstrate that the brain regions involved in his dysprosody primarily include the right frontal operculum. To our knowledge, this is the first time that a very localized and transient brain dysfunction is associated with an alteration of prosodic function. However, due to the intrinsic limitation of SEEG anatomical sampling, we can not exclude the role of other regions adjacent to the stimulated frontal operculum. This should prompt future studies, with the aim of better evaluating the localizing value of ictal dysprosody in patients with drug-resistant partial epilepsy. □

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