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Quantitative and qualitative analysis of ictal vocalization in focal epilepsy syndromes

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ABSTRACT

Purpose: To investigate the frequency, localizing significance, and intensity characteristics of ictal vocalization in different focal epilepsy syndromes.

Methods: Up to four consecutive focal seizures were evaluated in 277 patients with lesional focal epilepsy, excluding isolated auras and subclinical EEG seizure patterns. Vocalization was considered to be present if observed in at least one of the analyzed seizures and not being of speech quality. Intensity features of ictal vocalization were analyzed in a subsample of 17 patients with temporal and 19 with extratemporal epilepsy syndrome.

Results: Ictal vocalization was observed in 37% of the patients (102/277) with similar frequency amongst different focal epilepsy syndromes. Localizing significance was found for its co-occurrence with ictal automatisms, which identified patients with temporal seizure onset with a sensitivity of 92% and specificity of 70%. Quantitative analysis of vocalization intensity allowed to distinguish seizures of frontal from temporal lobe origin based on the intensity range ($p = 0.0003$), intensity variation ($p < 0.0001$), as well as the intensity increase rate at the beginning of the vocalization ($p = 0.003$), which were significantly higher in frontal lobe seizures. No significant difference was found for mean intensity and mean vocalization duration.

Conclusions: Although ictal vocalization is similarly common in different focal epilepsies, it shows localizing significance when taken into account the co-occurring seizure semiology. It especially increases the localizing value of automatisms, predicting a temporal seizure onset with a sensitivity of 92% and specificity of 70%. Quantitative parameters of the intensity dynamic objectively distinguished frontal lobe seizures, establishing an observer independent tool for semiological seizure evaluation.

1. Introduction

Semiological seizure evaluation is mainly based on manual video analysis, inhering a high rate of diagnostic inaccuracy [1]. Ictal sound and speech manifestations are also frequent symptoms of focal seizures, but audio analyses have rarely been performed and observer independent audio analysis tools are as yet missing.

Ictal sound or speech manifestations encompass a broad spectrum from intelligible speech to aphasia, dysphasia, dysprosody, or vocalization [2,3]. Thereby, pure ictal vocalization is defined as an ictal sound not being of speech quality and not accompanying apnea or generalized convulsive seizures [3]. Former studies showed that ictal vocalization occurs in up to 40% of patients with frontal lobe seizures [4–6] and in up to 48% of patients with temporal lobe epilepsy [7–9]. Controversial reports exist about its lateralizing value towards the non-dominant [5] or dominant hemisphere, though more studies support the latter [3,6–8,10,11]. Of note, previous vocalization studies were based on small cohorts of single epilepsy syndromes only and its association with concurrent semiology was not analyzed yet.

Our study thus aimed to (1) investigate the frequency and (2) localizing significance of ictal vocalization in different focal epilepsy syndromes. Further, (3) an observer independent approach was used to perform a quantitative audio analysis and to identify syndrome specific vocalization features.

2. Methods

This study complies with the institutional review board-approved

Abbreviations: ACG, anterior cingulate gyrus; EEG, electroencephalography; ECoG, electrocorticography; SMA, supplementary motor area

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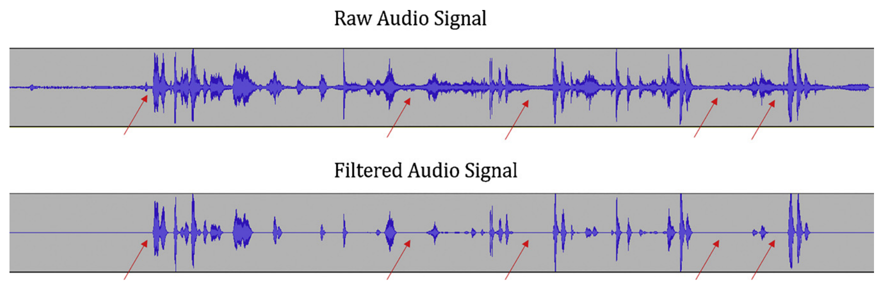

Fig. 1. Raw and filtered audio signal. The arrows indicate different segments of noise in the raw audio signal.

ethical guidelines of the University of Munich and all patients gave written informed consent to the scientific use of their clinically acquired, anonymized data.

2.1. Participants and clinical procedures

Adult patients with drug resistant focal epilepsy syndrome (n = 316) were identified from the database of the Epilepsy Center of the University Hospital Munich. All patients underwent continuous long-term EEG-video-monitoring between 1995 and 2015 with closely spaced surface electrodes using the international 10-10 system of electrode placement. A subsample of 66 patients had additional electrocorticography (ECoG) or stereoencephalography (stereo-EEG) with electrical stimulation mapping in order to precisely distinguish eloquent brain regions. EEG was recorded using XLTEK Neuroworks software (Natus Medical Incorporated, San Carlos, CA, USA) with a sampling rate of 256 Hz or 1000 Hz and 12–16 bit A–D conversion. For intracranial EEG, the amplifier XLTEK EMU128FS was used. Beneath EEG and video recording, all patients had simultaneous electrocardiographic and pulsoxymetric recording. Syndrome classification and localization of the epileptogenic zone were specified in an interdisciplinary patient management conference based on the available EEG data, seizure semiology, neuropsychological test results, as well as functional and structural imaging data. Seizure freedom after focus resection would be the gold standard for seizure focus localization, but not all of the patients have undergone resection of the epileptogenic zone up to the time of our study analysis. As we aimed to investigate the localizing value of ictal vocalization, we thus included only patients with the most clear-cut epilepsy syndromes, i.e. patients with unifocal seizure onset and concordant MRI lesion (n = 294). Only patients who experienced at least one habitual seizure during EEG-video-monitoring were included in the study, those with only auras or subclinical seizures were excluded (n = 17). Relevant clinical data was extracted from the standardized data base of the EEG Video Monitoring Unit.

2.2. Qualitative analysis of ictal vocalization

Up to four consecutive focal seizures were evaluated in the final sample of 277 patients, excluding isolated auras and subclinical seizure patterns. According to previous studies [3,5,7], vocalization was considered to be present if observed in at least one of the analyzed seizures, not being of speech quality and not accompanying apnea, generalized convulsive or clonic seizures. Thus, only verbal vocalizations were included in the study. Stereotypic repetitions of intelligible words for example were not classified as ictal vocalizations. Using this definition of a pure ictal vocalization allowed not only a comparison of our results with previous reports, but was also shown to have a high interobserver agreement [5]. The video recordings were reviewed with respect to ictal vocalization and co-occurring seizure semiology by one of the authors blinded to patients' clinical data. This particular author did not participate in the presurgical evaluation of any of the patients in the study. Unclear files were additionally reviewed by another experienced epileptologist. In the case of disagreement on the presence or abundance of vocalization, the seizure was excluded.

2.3. Audio signal analysis of ictal vocalization

Audio signals were recorded with Shure MX202 microphones (Shure, Niles, IL, USA), using the uncompressed PCM format and a bitrate of 64 kbit/s, and saved as waveform files. For vocalization analysis, the video files were converted to "m4v" and imported to the Macintosh application program Garage Band® (version 10.1.4, Apple Inc©, Cupertino, CA, USA) to extract the audio tracks from the video files. Audio signals were then loaded into Audacity® software (Version 2.1.2, freeware, ©1999-2014 Audacity Team. http://audacity.sourceforge.net/. The name Audacity® is a registered trademark of Dominic Mazzoni) for background noise reduction. The noise reduction algorithm implemented in Audacity is the spectral noise gate algorithm [12,13]. The algorithm detects the noise profile of the recording and then uses this profile to filter and smooth the audio signal. Audio files were filtered using the following settings: -30 dB noise reduction, 6.0 sensitivity parameter. The volume of noise reduction can be depicted in Fig. 1. To verify the output quality of the resulting audio signals, three people without previous knowledge of the audio contents were asked to validate the results.

Vocalization intensity is a quantified measure for the energy or loudness of a sound. Of note, its level is thus not only influenced by the patients` gender (male versus female voice), but also by the distance between the microphone and the sound source. Quantifications of vocalization intensity were obtained by using the intensity listing tool of the audio-analysis software Praat (Version 6.0.05, freeware, www.fon.hum.uva.nl/praat/; ©1992–2015 by Paul Boersma and David Weenink, University of Amsterdam, Netherlands) [14]. Analysis of vocalization intensity was performed for up to five vocalizations within the patient´s first seizure included in the study. Ictal audio signals were determined as separate vocalizations if they were at least 200 ms apart. Intensity analysis was not possible in seizures with bad audio quality or too much background noise caused by e.g. ictal testing or ictal movement. Audio analysis was focused on six different features: intensity minimum, maximum, mean and delta (i.e. the intensity range between minimum and maximum), as well as intensity variation (i.e. the standard deviation of the intensity values) and the velocity of the intensity increase rate at the beginning of the vocalization (see Fig. 2). To calculate the latter, the time needed to pass the baseline intensity + 15 dB was determined (intensity increase rate = 15 dB/time [dB/s]). The pitch could not be used for vocalization characterization, as the automatic pitch identification did not work well for many of the vocalizations.

2.4. Statistical analysis

Mean and standard deviation were calculated for quantitative parameters. Two-tailed *t*-test was performed for group comparison of continuous data and two-tailed Fisher´s exact test was applied on categorical data. Statistical significance was considered at $p < 0.05$. Multiple testing was accounted for by a Bonferroni-Holm review of the resulting p-values. Statistical testing was performed using Microsoft®