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# Monitoring peri-ictal changes in heart rate variability, oxygen saturation and blood pressure in epilepsy monitoring unit

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ABSTRACT

*Purpose:* The peri-ictal autonomic disturbances have been studied as predictors of seizure outcome and as markers of seizure onset. We studied the changes in heart rate (HR), HRV, oxygen saturation and blood pressure (BP) in the peri-ictal period in patients with drug-resistant localization-related epilepsy.
*Methodology:* Ninety one subjects undergoing video-EEG monitoring, underwent continuous HR, $SpO_2$, BP and Lead II ECG monitoring. The changes during the preictal, ictal and postictal periods were analyzed for 57 seizures in 42 patients with artifact-free recordings and correlated with VEEG ictal onset and MRI characteristics.
*Results:* Ictal tachycardia was noted in 15 (26.3%) seizures, of which, 60% had temporal lobe onset. HR increased by an average of 20.1% from pre-ictal to ictal phases ($p = 0.04$). Ictal bradycardia was noted in one event with right temporal seizure onset. Heart rate variability (HRV) analysis of the preictal, ictal and postictal phases showed an increase in the sympathetic and decrease in parasympathetic activity during the ictus with relatively preserved total power. Ictal oxygen desaturation ($84.1\% \pm 3.5\%$) was noticed in 10 (17.5%) seizures. Ictal hypertension was observed in 15 (26.3%); ictal hypotension was noted in 5 (8.7%) seizures. Both the systolic BP and diastolic BPs increased from the pre-ictal to ictal phase ($p = 0.01$).
*Conclusions:* Peri-ictal dysautonomia can present in variable patterns and can be measured and compared over different modalities such as BP, HR and HRV. Though degree of tachycardia and increase in BP were higher during extratemporal onset of seizures, a fall in variability was noted in seizures of temporal lobe origin. Oxygen desaturation is not an uncommon event during the peri-ictal period in localization related epilepsy.



## 1. Introduction

Seizure is a clinical manifestation consisting of sudden and transient abnormal phenomena due to abnormal excessive or synchronous neuronal activity in the brain, which may include alterations of consciousness, and/or motor, sensory, autonomic or psychic events perceived either by the patient or an observer (Fisher et al., 2005). More often than not, the history of autonomic dysfunction is either missed or neglected during history taking and examination or during evaluation of patients with drug resistant epilepsy and all attention is paid to the localization of seizure focus and surgical planning. Heart rate changes occurring at the onset of the seizures are often overlooked as a clinical sign. There have been persistent efforts to quantify and evaluate the patterns of autonomic changes in patients with epilepsy (Ansakorpi et al., 2011; Leutmezer et al., 2003a; Opherk et al., 2002; Zijlmans et al., 2002). The ictal autonomic signs/symptoms not only give us an idea about seizure onset and spread (e.g., seizures from insular cortex present with sensation of epigastric rising, orbitofrontal seizures presenting with ictal sweating, amygdalar seizures presenting with bradycardia and apnea) but also tell us about the risks that these patients carry for untowardly cardiorespiratory events such as asystole, hypertension, laryngeal spasm, pulmonary edema, Sudden Unexpected Death in Epilepsy Patients (SUDEP) (Kriegel et al., 2012). Studies have shown that the patterns of autonomic

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changes tend to vary depending upon the type of epilepsy, with the changes being present both during the inter-ictal and the peri-ictal phases (Garcia et al., 2001a; Meghana et al., 2012; Surges et al., 2009; Zaatreh et al., 2003). The autonomic changes accompanying a seizure have been recorded by several methods, from polysomnographic recording (Nashef et al., 1996) to the use of digital signal processing and spectral mapping of ECG changes and more complex analysis of abnormal ECG patterns such as ST elevation/depression, T wave inversion and AV blocks (Dericioglu et al., 2013; Zijlmans et al., 2002). The list of measures used are, heart rate (Garcia et al., 2001a), heart rate variability (HRV) (Tomson et al., 1998), blood pressure (BP) (Bozorgi et al., 2013; Geersing et al., 2011; Poh et al., 2012), oxygen saturation ($SpO_2$) (Bateman et al., 2008b; Blum et al., 2000) and plethysmography (Nashef et al., 1996). The parameters that are used most commonly are heart rate variability and blood pressure changes (Ansakorpi et al., 2011). Changes in respiratory patterns and consequent oxygen desaturation are well documented in both generalized tonic clonic seizures as well as in partial seizures. Changes such as apnoea, oxygen desaturation, bradycardia/tachycardia, asystole have been noted in association with seizures and with a higher incidence in patient with near-SUDEP/SUDEP (Nei et al., 2004; Shorvon and Tomson, 2011). Most of the studies available in the literature have focused largely on the changes in autonomic function in the inter-ictal phase (Ansakorpi et al., 2011; Magnaes and Nornes, 1974; Zaatreh et al., 2003). There are fewer studies that have looked at the changes occurring in the peri-ictal phase (Bozorgi et al., 2013).

The central autonomic network includes the hypothalamus, the insular and anterior cingulate cortex, the amygdala, the peri-aqueductal gray matter, the parabrachial complex of the pons, the nucleus of the tractus solitarius, the ventrolateral reticular formation of the medulla, and the raphe nuclei. In medial temporal lobe epilepsy, the underlying pathology is most often Ammon's horn sclerosis or end folium sclerosis. It is possible that coexisting amygdalar sclerosis or insular gliosis plays an important role. Electrical stimulation of the brain has helped elucidate the connections between various cortical areas and the autonomic nervous system (Sperling, 2010). Affection of specific areas of the brain may lead to specific autonomic responses (Baumgartner et al., 2001; Devinsky et al., 1994).

We hypothesized that there exists a difference in the autonomic responses in patients with lesional temporal and extratemporal lobe epilepsy, due to the differences in the anatomical (defined by MRI) and electrophysiological (defined by ictal EEG onset) involvement. In this study, we tried to evaluate the simultaneous changes noted in BP, oxygen saturation ($SpO_2$) and HRV during the peri-ictal phases in patients with localization related epilepsy based on 1) MRI localization and lateralization and 2) VEEG localization and lateralization.

## 2. Materials and methods

This prospective observational study was performed in the video telemetry unit of a tertiary care neurological hospital from March 2012 to January 2014. The study was approved by the Institutional Ethics Committee.

### 2.1. Patients

A total of 91 consecutive patients who were diagnosed by a comprehensive analysis of clinical semiology, routine scalp EEG and neuroimaging studies (MRI/CT showing a definite lesion) as 'symptomatic localization related epilepsy', were monitored as a part of either presurgical evaluation for epilepsy (n = 74) or for characterization of seizures (n = 21). All patients were of drug resistant epilepsy (Kwan et al., 2010) and were on either on monotherapy or 2–3 AEDs prior to the recording. Symptoms or signs of illness other than epilepsy such as non epileptic attack disorder (NEAD), diabetes mellitus, cardiovascular diseases, renal failure, smoking and alcoholism or medications known to affect the autonomic nervous system were used as exclusion criteria (Bakvis et al., 2009). The patients underwent continuous video—EEG, non invasive blood pressure (NIBP), oxygen saturation ($SpO_2$) and ECG recording and AEDs were withdrawn to induce seizures. It has been established that the withdrawal of the AEDs does not alter ECG and has no effect on HRV in the short term in patients undergoing VEEG monitoring. This makes it possible for us to measure only the effects of the seizures and not any other influences on the ECG (Stefani et al., 2013). Further, to ensure more robust results, we included individuals only between 15–55 years. A written informed consent was taken from all the patients. Each patient's history was recorded in a proforma including demographic details such as the duration of epilepsy, the semiology of seizures, seizure frequency, and the current medications. Neuro-imaging was carried out using 3 T MRI scanners- Skyra, Siemens and Achieva, Philips. 2 subjects had undergone a CT scan which was positive for a lesion. The images were analyzed and the lateralization, localization and natures of the lesion were determined.

### 2.2. Data acquisition

Video-EEG was recorded using EBNeuro Galileo NT Line™ system with the standard international 10–20 electrode placement of Ag/Agcl electrodes. The additional channels included ECG, $SpO_2$, and beat-to-beat non-invasive blood pressure (NIBP). ECG was recorded using two electrodes placed on the chest in the right and left infraclavicular regions. Three parameters, $SpO_2$, instantaneous HR and NIBP were recorded using the CNAP 500® [sampling rate (SR):256 Hz]. $SpO_2$ was recorded using a pulse oximeter probe. Blood pressure was recorded using an in-built finger sensor with a proximal inflatable cuff applied to the forearm. Evaluating the signals of the seizures with secondary generalization were associated with artifacts and signal discontinuation because of which they were excluded from the further analysis. A total of 57 seizures were limited to partial seizures (Table 1). BP was recorded from the relative unaffected limb. The medications were tapered to half the dose in all the patients starting one day prior to the recording and stopped completely during the period of recording.

## 3. Data analysis

### 3.1. VEEG analysis for seizure records

Data were initially independently analyzed by JC and GC and consensus was obtained by an unbiased review by PSC and SS. Ictal onset was defined both clinically and electrographically. Recordings were reviewed by the authors to determine the following: seizure onset determined using ictal EEG changes i.e., point of stable ictal electrographic onset and/or when the first behavioral change is noted (whichever comes first) (Ebersole and Pacia, 1996; Garcia et al., 2001b; Zijlmans et al., 2002), onset localization (temporal vs. extratemporal), and lateralization (right vs. left).

### 3.2. Analysis of HR, $SpO_2$ and BP data

The pre-ictal phase was taken as one minute prior to seizure onset and the post-ictal phase was taken as one minute after seizure offset (Bateman et al., 2008b; Zijlmans et al., 2002). The data of the heart rate, oxygen saturation and blood pressure were extracted in ASCII format (SR:128 Hz). While the values of the HR