

## Background

Heart rate variability (HRV) is influenced by autonomic function and a decrease in HRV may predict a poor prognosis in cardiovascular disease. Although periictal alterations in HRV, including a reduction in RMSSD (root mean square of successive differences) after generalized convulsive seizures (GCS), have been reported in people with epilepsy (PWE), substantial interindividual variability exists, and the mechanisms responsible for these alterations are not clear.

The relationship between HRV and postictal respiratory depression has also not been clearly defined despite the latter's relevance to sudden unexpected death in epilepsy (SUDEP). We recently showed that low interictal central CO<sub>2</sub> chemosensitivity as measured by the hypercapnic ventilatory response (HCVR) was associated with worse respiratory depression after GCS.

Because autonomic function is modulated by the respiratory network, we speculated that central CO<sub>2</sub> chemosensitivity would be associated with HRV, and that this relationship would be strongest when cortically mediated influences on breathing are minimal: during sleep and after a GCS.

## Objectives

- 1) To analyze the relationship between **interictal HCVR** and **HRV** during the postictal period.
- 2) To analyze the relationship between **postictal respiratory depression** and **HRV** during the postictal period.

## Methods

Retrospective analysis of PWE admitted to the epilepsy monitoring unit (EMU) for video EEG study, and who experienced GCS.

EEG was recorded using scalp electrodes with a standard 10-20 placement system in addition to T1/T2 electrodes.

Interictal hypercapnic ventilatory response (HCVR) test was performed using a modified hyperoxic rebreathing technique and an Ultima PFX Respiratory Gas Analyzer.

Time-domain, frequency-domain, and nonlinear HRV measures were calculated during 5-minute of the postictal using artifact free recordings.

Spearman's correlation test, univariate and multivariate generalized linear models were used.

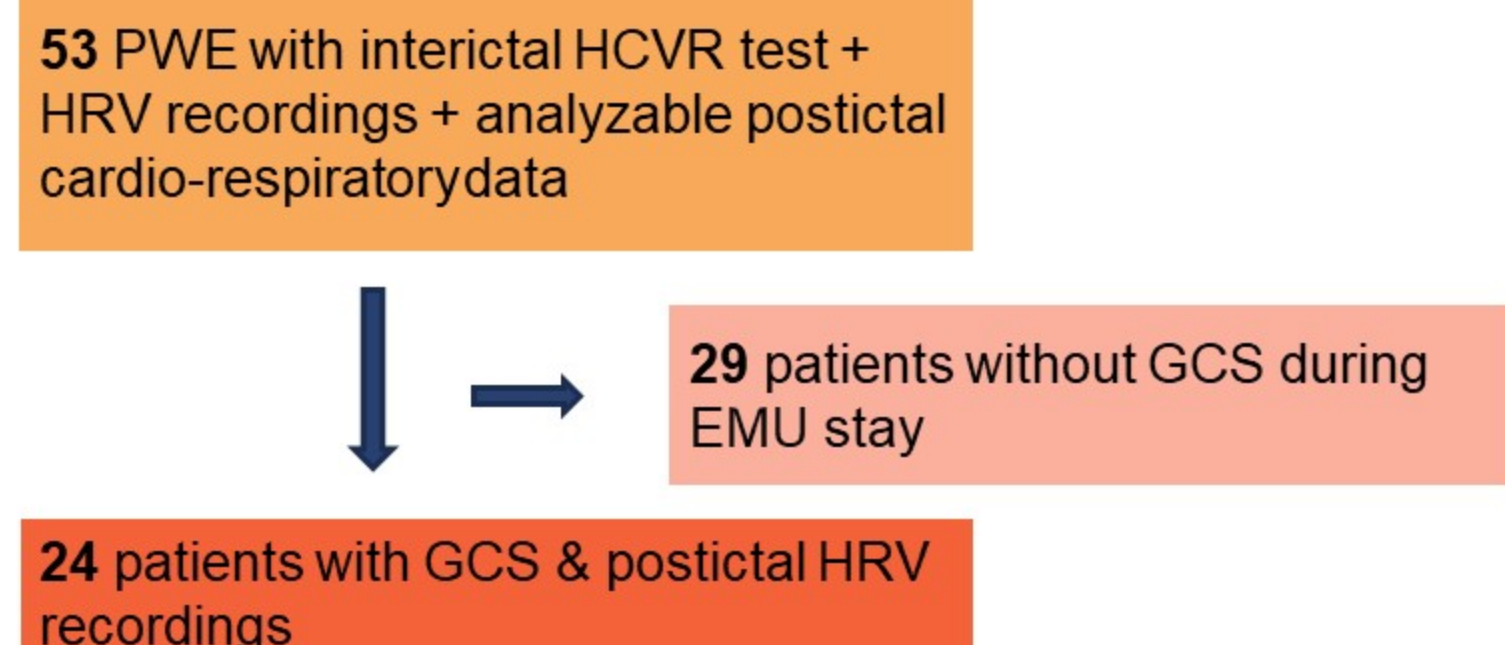
## Results

- Population characteristics:
- Age 34.5 [26-45] years,
  - Duration of epilepsy 12 [5-25] years,
  - Number of current AEDs 2 [2-3],
  - Interictal HCVR slope varied from 0.17 to 5.10 (median 1.89) L/min/mm Hg.

Note: RMSSD represents parasympathetic activity

## Results continued

**Fig 1. Flow chart of the study**

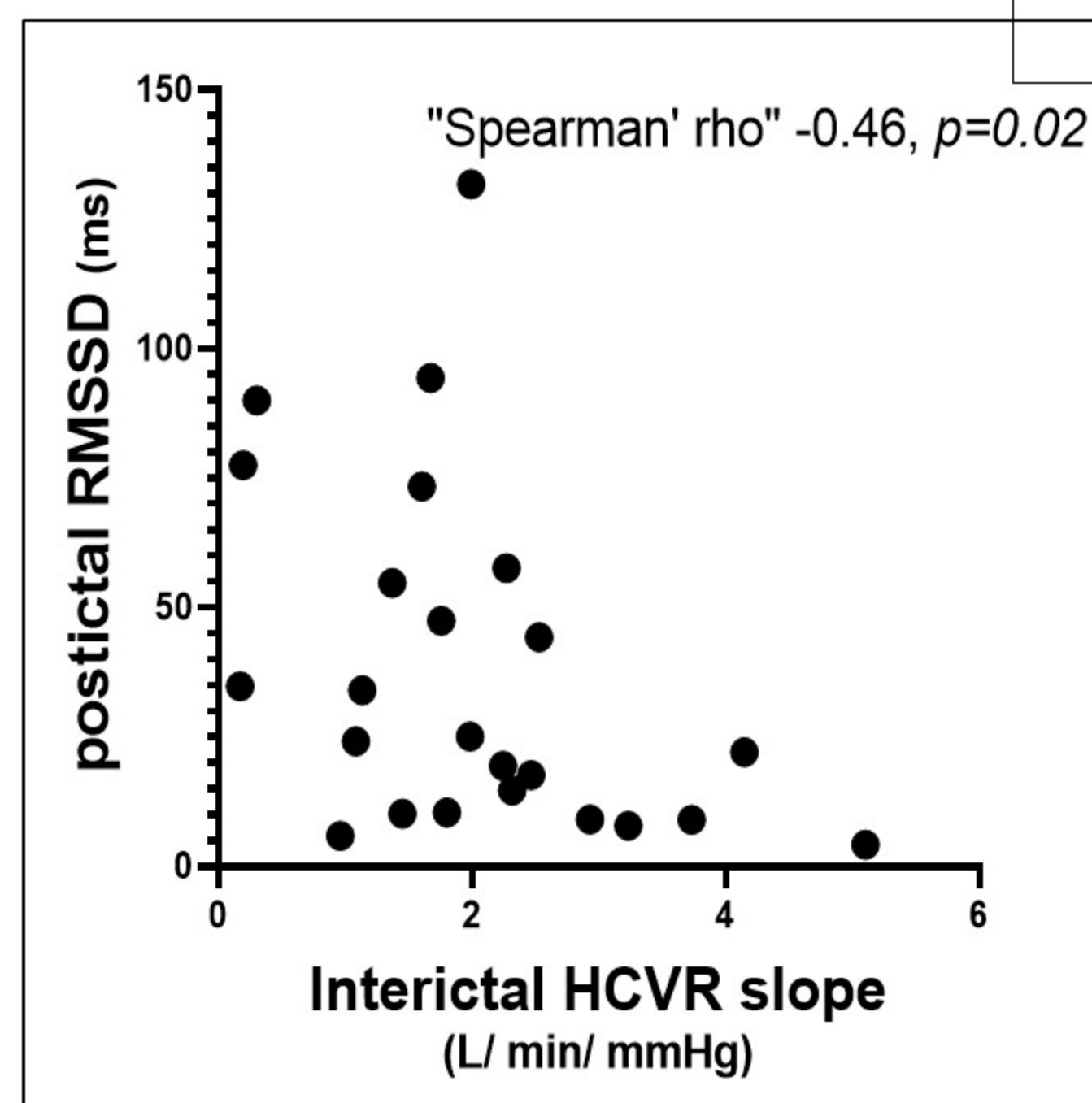
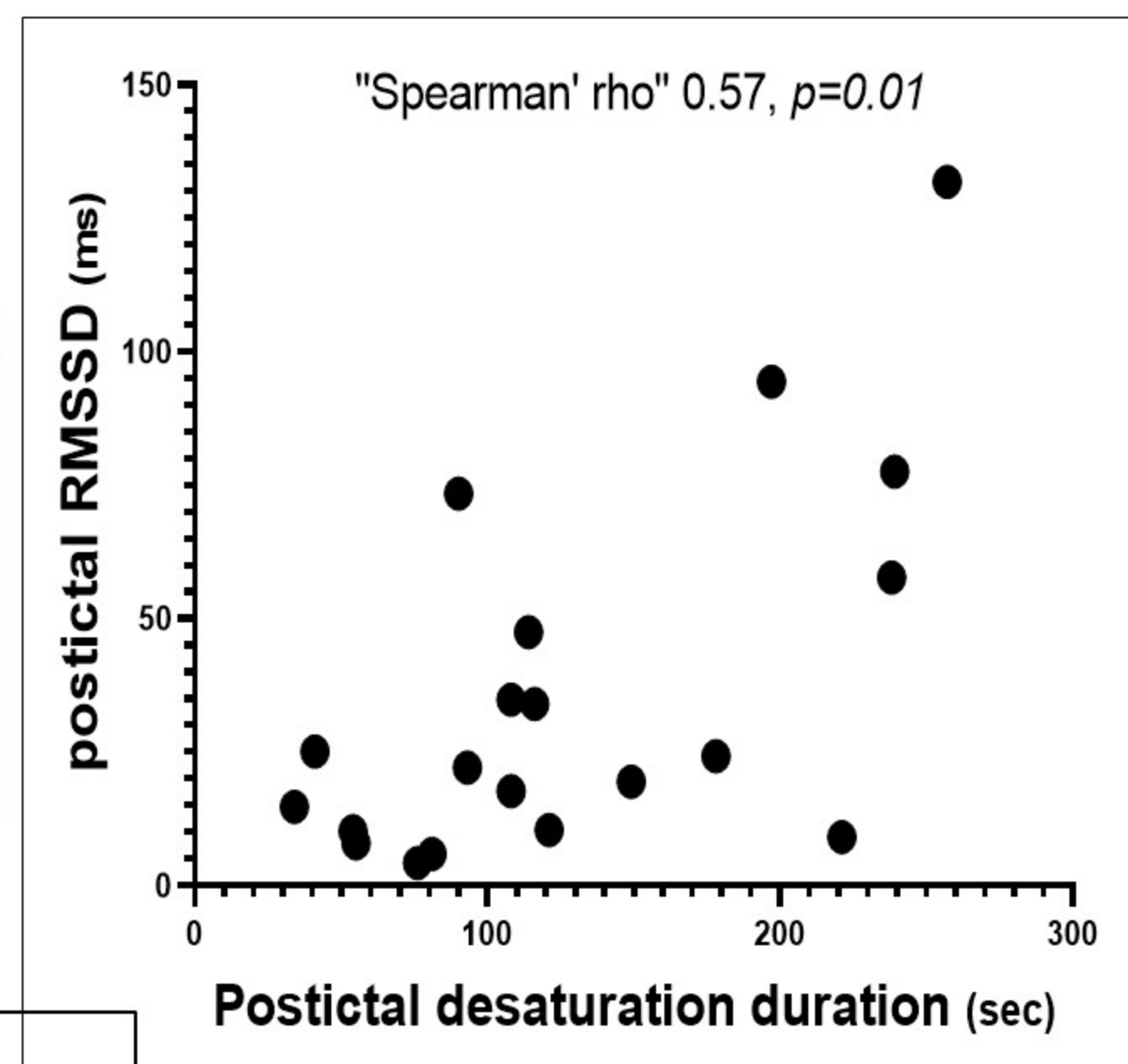


**Fig 2. Correlation between postictal desaturation duration and postictal RMSSD**

Postictal RMSSD was correlated with:

Postictal **hypercapnia duration** ( $r=0.281$ ;  $p=0.04$ )

Postictal **nadir SpO<sub>2</sub>** ( $r=-0.313$ ;  $p=0.01$ )



**Fig 3. Correlation between interictal HCVR and postictal RMSSD**

**Patients with low interictal HCVR slope had evidence of greater postictal parasympathetic activity (Fig. 3).**

**Table 1. Postictal RMSSD as dependent variable:**

Variable	Mean Ratio	95%CI	p-value
<b>Univariate</b>			
Age, year	1.02	(1.00-1.05)	0.15
Gender, <i>n</i>	1.58	(0.71-3.54)	0.27
Duration epilepsy, year	1.02	(0.99-1.05)	0.25
Number AEDs, <i>n</i>	0.71	(0.42-1.21)	0.15
Postictal hypercapnia duration, sec	1.00	(1.00-1.00)	<b>0.01</b>
Postictal rise in TcCO <sub>2</sub> , mmHg	1.09	(0.98-1.21)	0.13
Postictal nadir SpO <sub>2</sub> , %	0.98	(0.96-1.00)	<b>0.03</b>
Postictal desaturation duration, sec*	1.01	(1.00-1.01)	<b>0.01</b>
HCVR, L/min/mm Hg*	0.64	(0.47-0.90)	<b>0.01</b>
<b>Multivariate</b>			
HCVR, L/min/mm Hg*	0.74	(0.55-1.01)	<b>0.04</b>
Postictal desaturation duration, sec*	1.01	(1.00-1.01)	<b>0.01</b>

Abbreviations: AEDs, antiepileptic drugs; TcCO<sub>2</sub>, Transcutaneous carbon dioxide; SpO<sub>2</sub> peripheral oxygen saturation; HCVR, hypercapnic ventilatory response.

\*Mean ratio for RMSSD is per unit increase in HCVR and postictal desaturation duration, respectively.

**Postictal desaturation duration and interictal HCVR were positively and negatively associated, respectively, with postictal RMSSD (Table 1).**

## Conclusions

In patients with medically refractory epilepsy, low interictal HCVR was correlated with high HRV after GCS. This may reflect variable serotonergic modulation of autonomic function.

Low central CO<sub>2</sub> chemosensitivity and high parasympathetic activity may increase the risk of severe respiratory depression, bradycardia, and SUDEP after GCS.

## Funding

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