

# Seizures and hyperexcitable EEG patterns in primary intraventricular hemorrhage

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# Presenter disclosure information

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Seizures, periodic discharges and rhythmic patterns  
in primary intraventricular hemorrhage

FINANCIAL DISCLOSURE:

Nothing to disclose.

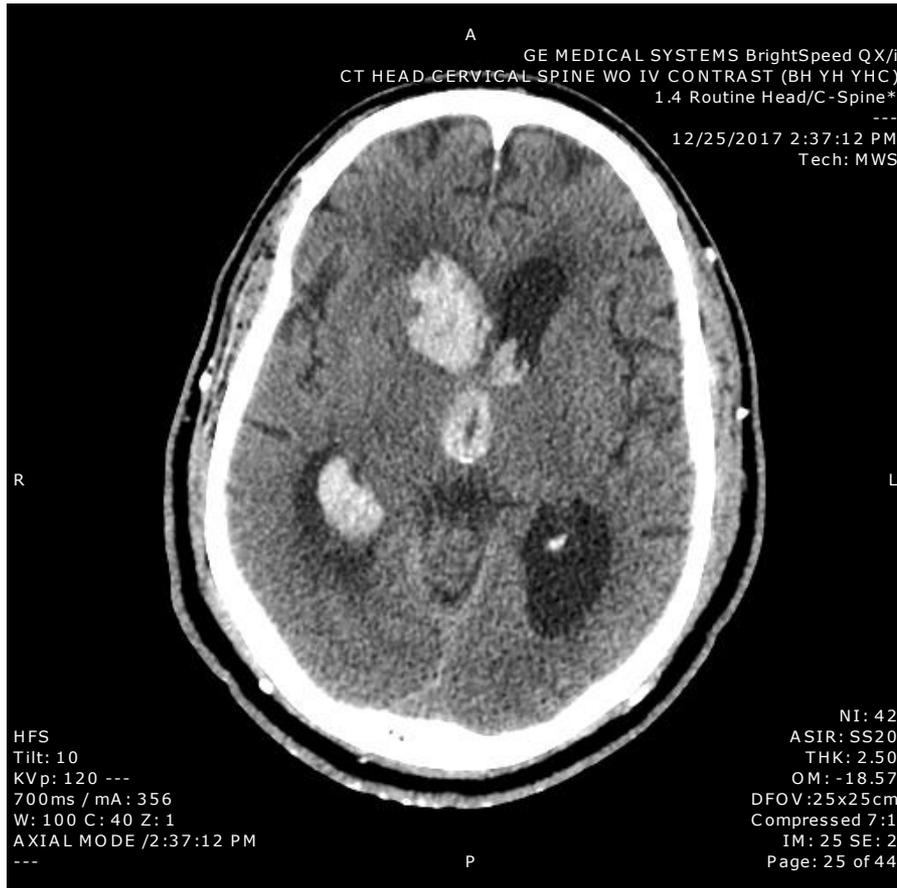
UNLABELED/UNAPPROVED USE DISCLOSURE:

None.

# Faculty disclosure information

- LJ Hirsch
  - **Research Grant- modest:** Eisai, Upsher-Smith.
  - **Honoraria – modest:** Neuropace.
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- CB Maciel, KN Sheth, EJ Gilmore: Nothing to disclose.

# Background



- Primary intraventricular hemorrhage (pIVH) uncommonly presents with seizures
- EEG data on seizures and periodic and rhythmic patterns (PRPs) in neurocritically ill patients with intracranial hemorrhage, specifically in
  - Intracerebral
  - Subdural and
  - Subarachnoid hemorrhage

Marti-Fabregas J, et al. 1999  
RodriguezRuiz A, et al. 2017  
Gaspard N, et al. 2013  
Chong DJ 2005  
Claassen J, et al. 2007  
Rudzinski LA, et al. 2011  
Maciel CB, et al. 2016  
Witsch J, et al. 2017

**RHYTHMIC OR PERIODIC PATTERNS**

All patterns recorded must consist of main term # 1 followed by #2, with modifiers added as appropriate.

**MAIN TERMS**

1. **Generalized (G) OR Lateralized (L) OR Bilateral Independent (BI) OR Multifocal (Mf)**

Additional localizing information:

For **L**: Specify unilateral or bilateral asymmetric; and lobe(s) most involved or hemispheric

For **BI** or **Mf**: Specify symmetric or asymmetric; and lobe(s) most involved or hemispheric in both hemisphere

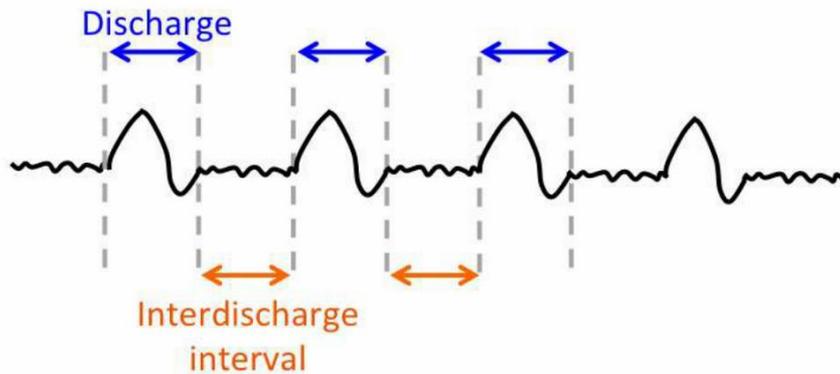
For **G**: Specify frontally predominant, occipitally predominant, midline predominant or “truly” generalized

2. **Periodic Discharges (PDs) OR Rhythmic Delta Activity (RDA) OR Spike-Wave (SW; includes sharp-wave and polyspike-wave)**

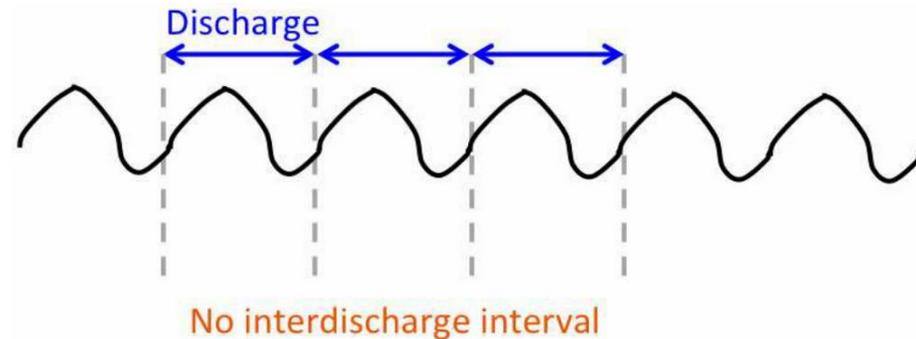
*NOTE 1: A pattern can qualify as rhythmic or periodic as long as it continues for at least 6 cycles (e.g. 1/s for 6 seconds, or 3/s for 2seconds).*

*NOTE 2: If a pattern qualifies as both GPDs and RDA simultaneously, it should be coded as GPDs+ rather than RDA+ (see modifier 8 below)*

Hirsch LJ, et al. 2013



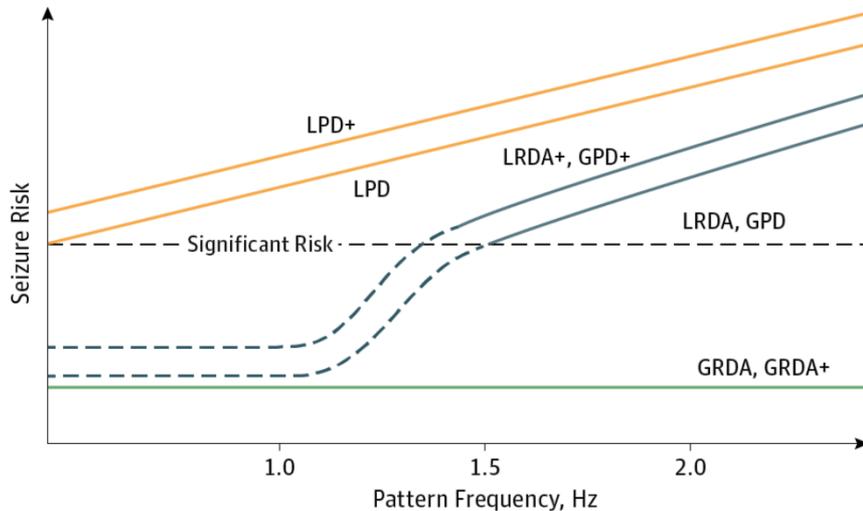
Periodic discharges (PDs)



Rhythmic delta activity (RDA)

Courtesy of Emily Gilmore

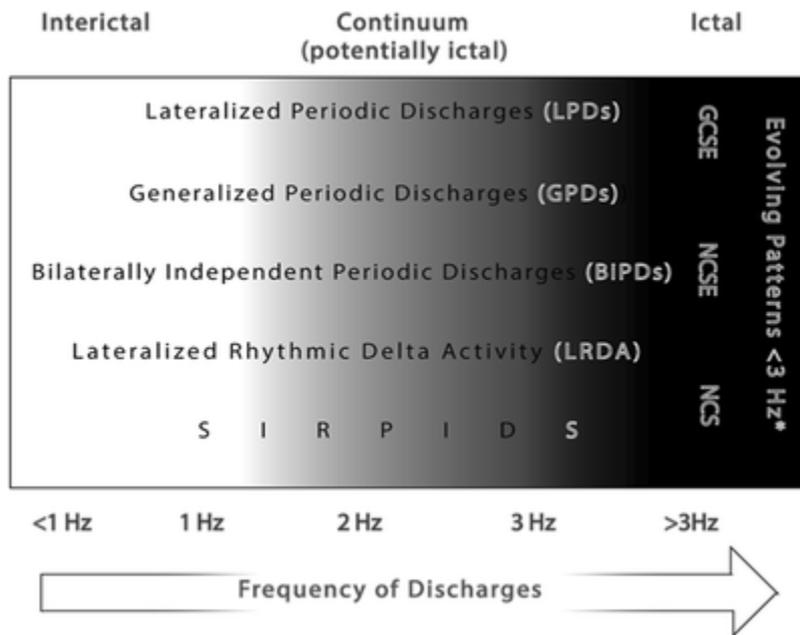
# Hyperexcitable EEG patterns



- Any PD's, SW or RDA, including modifiers, except for GRDA
- Associated with an increased risk for seizures

RodriguezRuiz A, et al. 2017

# Ictal-Interictal continuum (IIC)



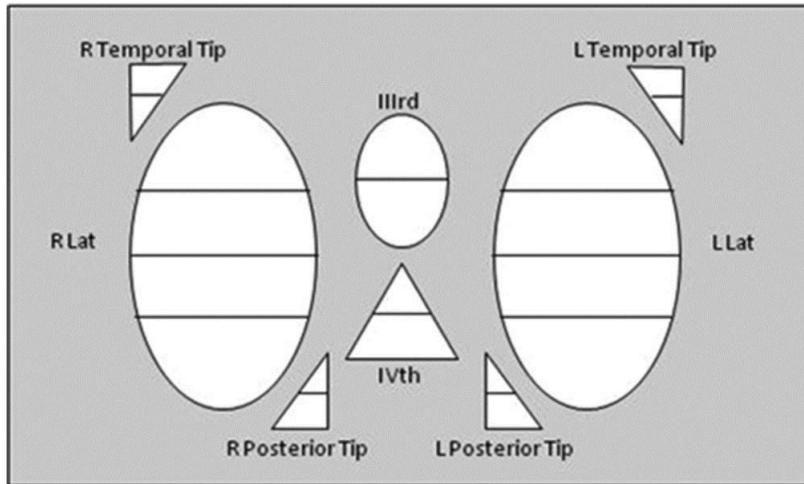
Sivaraju A, et al. 2016

- Periodic or rhythmic patterns, typically  $> 1 < 2.5$  Hz
  - LRDA, PDs and/or SW
- Patterns can be lateralized, generalized, bilaterally independent or stimulus-induced
- Not meeting criteria for definite electrographic seizures

# Study Design & Methods

- Retrospective review of pIVH patients with cEEG as part of their routine clinical care at YNHH 1/2013-12/2016
- Recorded data
  - Demographics
  - cEEG indication
  - IVH extent by mGS, hydrocephalus and EVD location
  - Antiseizure medication use prior and during recording
- EEG data
  - Duration of cEEG monitoring
  - Electrographic vs. clinical seizures
  - Periodic and rhythmic patterns (PRPs), including IIC and GRDA, by location and morphology

# Modified Graeb Score



	Scores:	Enter "1" if Expanded
R Temporal Tip:	—	—
R Lateral:	—	—
R Posterior Tip:	—	—
L Temporal Tip:	—	—
L Lateral:	—	—
L Posterior Tip:	—	—
3rd:	—	—
4th:	—	—
Sum each column:	—	—
Total Score:	—	—

## Scores for each ventricle

% of blood	R Temp Tip	R Lateral	R Post Tip	L Temp Tip	L Lateral	L Post Tip	IIIrd	IVth
None	0	0	0	0	0	0	0	0
≤ 25%	1	1	1	1	1	1	2	2
> 25% to ≤ 50%	1	2	1	1	2	1	2	2
> 50% to ≤ 75%	2	3	2	2	3	2	4	4
> 75% to 100%	2	4	2	2	4	2	4	4
Expanded	1	1	1	1	1	1	1	1

Morgan TC, et al. 2013

# Results

**Table 1. Demographic, radiologic and EEG data**

Characteristic N in (%) or median (IQR)	Entire group (N=11)	“Hyperexcitable group” (N=5)	“non- hyperexcitable group” (N=6)	p value
Age (years, IQR)	81(46-87)	80(59-84)	82(46-86)	0.26
Female, N (%)	7(64)	2(40)	5(83)	0.13
Hydrocephalus, N (%)	7(64)	5 (100)	2(33)	N/A
EVD, N (%)	7 (64)	5 (100)	2 (33)	-
mGS (IQR)	15(9-23)	17(12-22)	12(9-23)	0.28
Rhythmic and/or periodic patterns, N (%)	7 (64)	5	2	N/A
Electrographic seizures, N (%)	1 (9)	1(20)	0(0)	N/A
Monitoring duration in hours (IQR)	19 (12-156)	98(36-156)	18(12-38)	<b>0.007</b>
Monitoring sessions count, median (IQR)	1 (1-7)	5(1-7)	1(1-2)	0.08

# Results – EEG Data

**Table 2. Recorded EEG patterns**

Patient	Pattern							Antiseizure medication use	EVD location		Outcome (mRS)*			
	PDs (n=3)			RDA (n=5)			GSW		IIC	Seizures		I/L	C/L	
	LP D	LPD+R	BIPD+R	GPD+R	LRDA	LRDA+S	GRDA							
1		X		X								X	4	
2					X	X						X	4	
3	X									X	LEV/LAC/PHE	X	6	
4							X	X	X		LEV	X	X	5
5			X						X		LEV/ PHE	X	X	6
6							X							4
7							X							0

**Abbreviations:**

ASM – antiseizure medication, EVD – external ventricular drain, I/L and C/L – location of EVD ipsilateral or contralateral to EVD if patterns include a unilateral pattern.

\*mRS is a measure of disability ranging from 0 (no symptoms) to 6 (death).

PDs – periodic discharges, LPD (+R) – lateralized periodic discharges (+ rhythmicity), BIPD + R – bilateral independent periodic discharges (+ rhythmicity), GPD (+R) – generalized periodic discharges (+rhythmicity), RDA – rhythmic delta activity, LRDA (+S) – lateralized rhythmic delta activity (+sharps), GSW – generalized spike wave and/or sharp waves, IIC – ictal-interictal continuum. Note that GRDA is not a hyperexcitable pattern. LEV – levetiracetam, LAC – lacosamide, PHE – phenytoin

# Discussion

- In our cohort of patients with pLVH, 45% had hyperexcitable patterns and 9% electrographic seizures.
- Limitations include retrospective nature, sample size, potential selection bias and limited monitoring duration
- At present, all pLVH patients and impaired mental status and/or limited exam should be monitored with cEEG.
- Prophylactic ASM use is not currently recommended, but should be individualized, such as in patients with ICH
- Different hyperexcitable patterns confer varying seizure risk and may lead to hypoxia and metabolic crisis similar to seizures

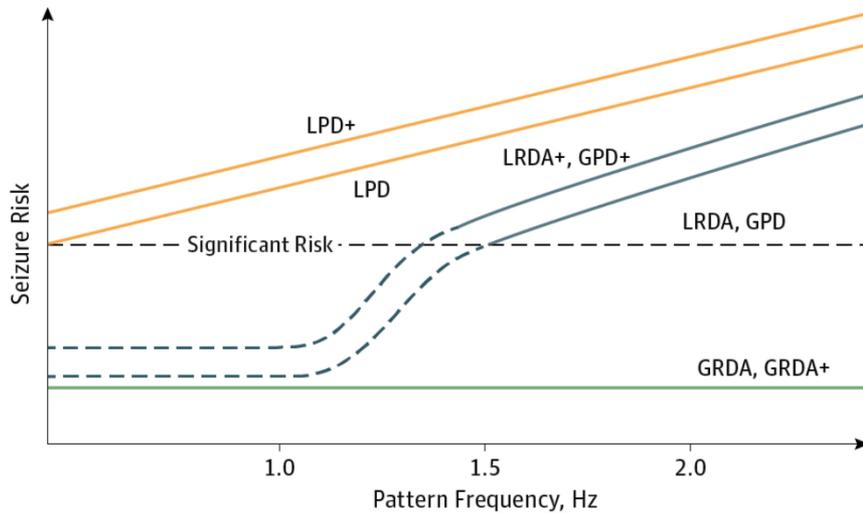
Gilmore EJ, et al. 2016

RodriguezRuiz A, et al. 2017

Witsch J, et al. 2017

Vespa P, et al. 2016

# Discussion – Evolving understanding of PRPs



- LPDs are associated with seizures at 1Hz, but LRDA + GPDs only  $\geq 1.5$  Hz

RodriguezRuiz A, et al. 2017

- In comatose SAH patients with intracranial EEG, PDs  $> 2$ Hz may be associated with brain tissue hypoxia
- In patients with severe TBI on intracranial EEG, PDs may trigger metabolic crisis similar to seizures

Witsch J, et al. 2017

Vespa P, et al. 2017

# Significance

- This is the first analysis to our knowledge to examine seizures and PRPs in a small cohort of patients with pIVH.
- Based on our data, PRPs are common in pIVH, but these findings need to be validated in a larger cohort.
- The relationship between seizures and PRPs with IVH volume, EVD location/complications and hydrocephalus is not well understood.
- Even in the absence of evidence of radiographic cortical and subcortical brain injury, occurrence of these patterns may increase metabolic demand, promote secondary brain injury and be associated with worse outcomes.

# Further areas of research

- Collect cEEG data on patients with pIVH, as a multicenter collaborative effort – CCEMRC
- Assess for predictors of seizures and PRPs
- Correlate EEG, including seizures, PRPs and degree of encephalopathy
  - with multimodal physiologic data
  - with functional outcome

# Thank you

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  - Emily J. Gilmore, MD/MS
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- Comprehensive Epilepsy Center, Yale University
  - Zubeda Sheikh, MBBS
  - Lawrence J. Hirsch, MD
- Division of Neurocritical Care, University of Florida
  - Carolina B. Maciel, MD

# References

- Marti-Fabregas J, Piles S, Guardia E, Marti-Vilalta JL: Spontaneous primary intraventricular hemorrhage: clinical data, etiology and outcome. *J Neurol* (1999) 246: 287-291
- Rodriguez Ruiz A, Vlachy J, Lee JW, Gilmore EJ, Ayer T, Haider HA, et al. for the Critical Care EEG Monitoring Research Consortium. Association of Periodic and Rhythmic Electroencephalographic Patterns with Seizures in Critically Ill Patients. *JAMA Neurol.* 2017;74: 181–188
- Gaspard N, Manganas L, Rampal N, Petroff OA, Hirsch LJ. Similarity of lateralized rhythmic delta activity to periodic lateralized epileptiform discharges in critically ill patients. *JAMA Neurol.* 2013; 70:1288-1295
- Chong DJ, Hirsch LJ. Which EEG patterns warrant treatment in the critically ill? Reviewing the evidence for treatment of periodic epileptiform discharges and related patterns. *J Clin Neurophysiol* 2005; 22:79-91
- Claassen J, Jette N, Chum F, Green R, Schmidt M, Choi H, et al. Electrographic seizures and periodic discharges after intracerebral hemorrhage. *Neurology* 2007; 69; 1356-1365
- Rudzinski LA, Rabinstein AA, Chung SY, Wong-Kisiel LC, Burrus TM, Lanzino G, et al. Electroencephalographic findings in acute subdural hematoma. *J Clin Neurophysiol.* 2011; 28:633-41
- Maciel CB, Gilmore EJ. Seizures and epileptiform patterns in SAH and their relation to outcomes. *J Clin Neurophysiol.* 2016; 33:183-95
- Witsch J, Frey HP, Schmidt JM, Velazquez A, Falo CM, Reznik M et al. Electroencephalographic periodic discharges and frequency-dependent brain tissue hypoxia in acute brain injury. *Jama Neurol.* 2017 March 01; 74:301-309
- Morgan TC, Dawson J, Spengler D, Lees KR, Aldrich C, Mishra NK, et al. The modified Graeb score: an enhanced tool for intraventricular hemorrhage measurement and prediction of functional outcome. *Stroke* 2013; 44: 635-41