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Editorial

# Controversies: Periodic discharges in critically ill patients –" urgent treatment is essential"

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## 1. Introduction

Clinicians typically treat nonconvulsive seizures in critically ill patients, but the optimal management of patients with EEG periodic discharges (PDs), is less clear. With cEEG (continuous or prolonged EEG) monitoring and management in critical or intensive care units (ICUs), the challenge of how to optimally treat patients with EEG patterns that lie along the ictal–interictal continuum (IIC), is of increasing importance. The American Clinical Neurophysiology Society (ACNS) classification of periodic patterns (Maciel and Hirsch, 2018; Hirsch et al., 2005) presently includes focal and generalized forms of PDs with varying morphology and frequency, and which along with different possible background patterns (varying in frequency, reactivity, continuity), challenge the clinician to come up with treatment strategies that will balance risk and benefit of various available treatment approaches and intensities.

The International Congress of Clinical Neurophysiology (ICCN) in Jakarta, Indonesia in 2024 took on this controversy in debate form, framed as **"Periodic discharges in critically ill patients – urgent treatment is essential"**.

The participants in this controversy have encapsulated their positions in the paper to follow, with Brandon Westover speaking in favor of the motion, and Peter Kaplan arguing against it, with Aatif Husain providing the moderating assessment.

The discussion should capture the contemporary clinical challenges now increasingly faced in the ICU, the problems in drawing firm conclusions, and directions that might be taken to answer these challenges.

## 2. For the proposition: "Periodic discharges in critically ill patients – urgent treatment is essential." Dr. Brandon Westover

### GPDs (sometimes) need urgent treatment

My focus is on whether GPDs (generalized periodic discharges) need urgent treatment. Sometimes they do. I'll start with a brief history of what we know about GPDs and then move on to some confusions that are often used to justify decisions not to treat patients with GPDs.

**A brief history of GPDs**

GPDs were first described in 1950 at the 75th American Neurological Association meeting by Foley et al. (1950). They noted waves in hepatic coma that resembled activity seen with petit mal epilepsy: generalized periodic epileptiform discharges (GPEDs). In a 1955 paper, Bickford and Butt (1955) described the same discharges—which they dubbed "triphasic waves." Initially, these GPDs were believed to be specific to hepatic encephalopathy, but we now know they occur in a wide range of conditions: metabolic derangements, medication-induced encephalopathy, withdrawal from ethanol or barbiturates, cerebral carcinomatosis, anoxic brain injury, and more.

**The ictal–interictal–injury continuum**

GPDs are considered part of the "ictal–interictal–injury continuum," an idea popularized by Chong and Hirsch in 2005. They showed various rhythmic and periodic EEG patterns arrayed along two axes: one representing how "seizure-like" they look on EEG, and the other representing their potential to cause secondary neuronal injury. GPDs occupy a large space on that chart: in some cases, they resemble seizures and cause harm, while in others, they do not.

Factors that push GPDs more toward the seizure + harm end of the spectrum include a higher frequency of discharges and a higher "burden" (i.e., the proportion of the recording they occupy), and perhaps their degree of "spikiness". When GPDs are higher in frequency and more prevalent, they are more seizure-like and more likely to cause harm.

**Confusion #1: "Nonconvulsive status epilepticus vs. toxic metabolic encephalopathy"**

One common rationale for not treating GPDs is the idea that they reflect toxic metabolic encephalopathy (TME) rather than nonconvulsive status epilepticus (NCSE). This is an incoherent distinction because these concepts belong to different categories:

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- **Toxic metabolic encephalopathy** describes an *etiology*: something is causing encephalopathy—like a metabolic derangement or toxic exposure.
- **Nonconvulsive status epilepticus**, meanwhile, is an *EEG pattern* that is not tied to any specific underlying cause. This EEG pattern can be triggered by toxins, metabolic derangements, structural injuries, or occur spontaneously.

Beyond the apples-and-oranges conceptual confusion, some people mistakenly assume these two "diagnoses" necessarily involve different underlying mechanisms or arise from different etiologies. However, it is well known that metabolic derangements and toxic exposures can cause both clinical and electrographic seizures; they are by no means "protective" against seizures. Moreover, computational models suggest the same underlying mechanism can produce smooth transitions along the full spectrum of findings, from normal to periodic discharges, to high-frequency discharges that would be considered unequivocal electrographic seizures.

**Confusion #2: "Triphasic waves are GPDs that don't need treatment"**

A key study by Foreman et al.,(2016) investigated how reliably experts can identify and manage GPDs. They collected EEG data from 20 patients with GPDs and asked 11 experienced ICU EEG specialists to review the recordings. The results were revealing:

- The experts generally agreed on whether or not an EEG contained GPDs.
- However, they did **not** agree on whether the GPDs should be described as "triphasic waves."
- Even more strikingly, there was poor agreement on the appropriate management (i.e., whether to give antiseizure medications), the underlying etiology, and whether or not the patient was likely to have seizures or a good outcome.

In other words, the belief that triphasic waves—and by extension certain types of GPDs—are easily recognized and can be confidently asserted to require no treatment is undermined by the fact that even highly experienced EEG readers frequently cannot agree on these points.

**Confusion #3: "Triphasic waves don't respond to antiseizure medications"**

Another confusion is that GPDs with a "triphasic" morphology reflect a benign pattern that does not respond to antiseizure medications. Dr. Kaplan believes that experts like him can distinguish these "metabolic" GPDs from "ictal" patterns using visual analysis of the EEG alone. But the data do not support this.

A retrospective study by O'Rourke et al. (2016) took 64 patients with encephalopathy and triphasic waves and examined whether they improved clinically after receiving benzodiazepines or non-sedating antiseizure medications. About 20 % of the benzodiazepine group and 40 % of the non-sedating antiseizure group showed clinical improvement. Metabolic profiles did not predict who would respond.

Although this was a retrospective observational study, it's the best evidence available. It suggests that so-called "triphasic waves," which are traditionally considered benign, do sometimes respond to antiseizure therapy—and at a much higher rate than one might expect. Thus, there is no clear reason to manage GPDs and GPDs with triphasic morphology differently based on visual appearance alone (even if experts could reliably tell them apart).

**Confusion #4: "GPDs don't cause harm; only seizures do"**

Another confused justification for categorically not treating GPDs is the belief that they don't cause harm. But again, the evidence we have suggests otherwise. A study by Claassen and colleagues (2017) found that periodic discharges—generalized or lateralized—appear to cause decreased brain tissue oxygen when their frequency is higher (although the relationship may be bidirectional: decreased tissue oxygen à GPDs, and GPDs à further exacerbate tissue hypoxia). GPDs also appeared worse than LPDs (lateralized periodic discharges) at lower frequencies, possibly because GPDs involve more brain tissue.

A study by Vespa et al. (2016) used cerebral microdialysis monitoring to show that periodic discharges (including GPDs) were associated with elevated lactate-to-pyruvate ratios, suggesting GPDs cause cellular injury. More recent work by Chen, Zafar, and colleagues (2023) indicates that a higher "burden" of epileptiform activity, including GPDs, increases the probability of poor outcomes. And a separate analysis by Parikh et al. (2023) found a causal relationship between epileptiform burden (including GPDs) and worse neurological outcomes.

So, whether we call them seizures or not, evidence suggests that GPDs can be physiologically harmful.

**Confusion #5: "We can rely on reactivity to tell "ictal" from "non-ictal" GPDs"**

Dr. Kaplan and colleagues have suggested that "ictal" GPDs are nonreactive to stimulation, while GPDs that react or can be modulated by external stimulation are not seizures and do not need treatment. Essentially, this is a new variation on the old claim that the visual inspection of the EEG alone can be used to determine which patients with GPDs will benefit from treatment with antiseizure medication.

An argument given for this is that absence status epilepticus is clearly ictal, and its EEG pattern is nonreactive. However, the reasoning is not reasonable, and the comparison is not valid. Absence status epilepticus has a genetic origin, typically occurs in the outpatient ambulatory setting, and is very different from subclinical NCSE in critically ill patients. Moreover, reactivity *per se* can indeed be seen in association with seizures. Certain epilepsies are *provoked* by stimulation (reflex epilepsies), while in ICU patients we often see SIRPIDs (Stimulus-Induced Rhythmic, Periodic, or Ictal Discharges— i.e. seizures or periodic discharges that are provoked by stimulation. The latest ACNS ICU EEG terminology (Hirsch et al., 2021) even includes patterns that terminate with stimulation ("ST" patterns). So, there is simply no good basis to use reactivity alone to decide who does and does not need treatment.

**An empirical approach: the "TOAST" method**

These confused ideas about whether GPDs are "ictal" or "benign" are not very useful. The approach I recommend—echoed by the Salzburg criteria and the 2021 ACNS ICU EEG terminology —is the "TOAST" approach: **Trial Of Antiseizure drug Therapy**.

In short:

1. If you see GPDs between 1–2.5 Hz or > 0.5–1 Hz with additional features ("+" modifiers or fluctuation), consider an empirical trial of antiseizure medications.
2. If the EEG improves and the patient shows clinical improvement, then it's subclinical seizures or nonconvulsive status epilepticus. In the ICU setting, clinical improvement in response to treatment is effectively what we *mean* by seizures or nonconvulsive status.

Crucially, the diagnosis is not based on EEG alone but on an empirical trial to see if the patient gets better. Right now, that's the best strategy we have, supported by much of the evidence I've mentioned.

**Conclusion**

I'm against deciding the need for antiseizure therapy solely on how GPDs "look." The debate about whether GPDs are "nonconvulsive status vs. toxic-metabolic encephalopathy" is based on false and confused dichotomy. These are not mutually exclusive and are not even in the same category. Also, so-called triphasic waves are not automatically benign; evidence shows that many patients clinically benefit from treatment, and experts can't even reliably agree on whether a waveform is "triphasic." Finally, I reject the idea that we can label GPDs "ictal" or "non-

ictal" by visual analysis or simple reactivity tests.

If we define "ictal" to mean "causes harmful or unwanted clinical symptoms that can be reversed by antiseizure medication," then the only reliable way to figure that out is to administer a treatment trial and look for clinical (and EEG) improvement. Perhaps one day we'll have a better way to identify which GPDs are harmful, but it will come through empirical research, not mere opinion. Until then, "TOAST" is the most logical, evidence-based approach we have.

## 3. Against the proposition: "Periodic discharges in critically ill patients – urgent treatment is essential". Peter W. Kaplan

In this debate on "Periodic discharges in critically il patients: "urgent treatment is essential" I start with the **definitions**, or terms of this debate.

For **periodic discharges (PDs)**, I used the concept of "focal or generalized synchronous or asynchronous discharges, generalized periodic discharges (now GPDs), and now possibly generalized rhythmic delta activity (GRDA)," many terms that were originally described by Chatrian et al. (1964) and by Brenner and Schaul (1990). Such periodic discharges were a transient phenomenon that typically resolved in days to about a week. For the term **critically ill** used in the debate title: does this always imply patients in intensive care units (often in coma), or conversely awake patients but possibly with marked organ failure, electrolyte, infectious or unstable vital signs?

The decision to treat these patients may include decisions on intubation and a "do not resuscitate" (DNR) order. In making these decisions, the level of consciousness and the likely overall prognosis are important in calculated risk versus potential benefit. Regarding **urgent treatment** – does this imply **immediate** high intensity and aggressive treatment? **Essential** might be interpreted as "important," or "absolutely necessary," or "applied to all patients."

With this preamble, the challenge in the **stated title of this debate** is not whether just **some** patients should have treatment, but **all** patients. If it is **essential**, it should be done **now** and likely in an ICU. It would seem, therefore on the face of it, to include all patients after cardiac arrest with GPDs but possibly without brain stem function and absent cortical N20 responses on median nerve SSEPs.

If there are **exceptions** to these stipulations, then the authors of **pro and con** positions will merely stake out different ends of the playing field as their territory to make their points.

The implication of taking up this challenge is that **if** one cannot safely suppress or abolish PDs with a greater chance of good than harm, then "the treatment might be worse than the cure." Since treatment is mandated to occur in this frequently transient condition and often requires greater resources in possibly ill-equipped settings, then the answer is **no**: urgent treatment **cannot** be mandated in **all** patients with PDs.

The cardinal clinical approach to each patient must be "first do no harm;" the intentions cannot just be good, but the risk–benefit calculations must be undertaken individually.

What is clear in this debate is that a diagnosis of PDs derives from an EEG being performed, and perforce, correctly interpreted. Is there poor or good background activity? Is the underlying etiology chronic, or acute and evolving? Benign? Devastating? Do the discharges represent the end stage of actual seizures? As per the debate stipulations, the PDs are *per se* not seizures but does the EEG interpreter include rhythmic theta/delta patterns without epileptiform features? All these factors might play into the acuity, severity, and urgency of the clinical presentation.

Some GPD patterns have "identical bursts," a type with a universally poor prognosis (Hofmeijer et al., 2014) and in which treatment is futile. Would low voltage metronomic blunted transients warrant aggressive treatment? Do all triphasic waves with a known encephalopathy possibly from lithium or baclofen toxicity warrant such an approach? And what if the EEG shows a flat background with GPDs in a patient without brainstem reflexes, and possibly absent cortical SSEP responses. The chance of a favorable prognosis is effectively zero – why treat?

What of an elderly, frail, and critically ill patient who would not tolerate aggressive treatment or may be DNR? Or a post cardiac arrest patient in coma with minimal brainstem function? The guiding consideration is not that "in principle PDs are bad for the brain and our treatment is correspondingly safe" but the balancing of the overall risk–benefit in the individual frail or elderly person, or when the outcome is highly likely to be futile.

Treatment in clinical situations is always prospective with unknown outcome, but the effects of PDs are also unknown in the individual, hence the need for clinical judgment in every case, and not the universal mandate to treat all.

Outcome also depends on the experience of the EEG interpreter and the resources available (considering the actual and not the ideal, highly sophisticated academic center). One study of ictal states in hospital ICU settings showed that there was a **low** involvement of a neurologist (Walder et al., 2002)!

Will a patient with Lennox-Gastaut syndrome with frequent, chronic, interictal periodic discharges benefit from anesthetic suppression of PDs, if non-sedating antiseizure agents fail?

Animal models that might inform us are imperfect. We know that high frequency spikes are associated with neuronal injury, but occasional spikes or intermittent bursts of activity are not (Lowenstein et al., 1991).

Nonconvulsive seizures or status are an imperfect example of PDs but may shed some light as "a more intense equivalent of PDs." Jirsch and Hirsch (2007) noted that "in contrast to convulsive status, there is less robust evidence that ICU NCSE-NCSz [nonconvulsive seizures] are destructive." "Instances of permanent dysfunction after prolonged NCSE without any alternate acute brain insult are in the realm of case reports, and […] very prolonged [seizures]." Vespa et al. (2003) using multivariate analysis showed that "the neurologic status and patient age were much greater predictors of outcome than […] seizures."

In treating rhythmic and periodic EEG patterns after cardiac arrest, Ruijter et al. (2022) found that treating such activity in comatose patients after cardiac arrest **did not** alter outcome, while Ng et al. (2014) found that treating periodic patterns also **did not improve** clinical outcome in patients with impaired consciousness.

Even Neuron Specific Enolase in the DeGiorgio study inconsistently showed a high marker level (thought to reflect greater brain damage) in some patients with good outcome and conversely, low levels in some who did poorly (DeGiorgio et al., 1999).

Regarding treatment of refractory SE with pentobarbital, propofol or midazolam – agents used in treating PDs – Claassen et al. (2002) showed a poor outcome (50 % mortality) **regardless** of agent used or titration goal (e.g. seizure or background suppression). Treatment was frequently complicated by hypotension and the ultimate outcome was the same, with complications including refractory metabolic acidosis, cardiac failure, rhabdomyolysis, and renal failure.

While the malignancy of NCSz remains debated, severe outcomes in critically ill patients (Yaffe and Lowenstein, 1993) are more affected by other factors: the underlying etiology, the length of ICU stays, and intercurrent infections. They noted that understanding of the optimal management of patients with SIRPIDs and PDs "is in its infancy."

The **prognosis** with PDs depends largely on the cause and clinical situation, and it varies from minimal to maximal, from the awake to the comatose, from old stroke as a cause of PDs, to a new devastating stroke. The agents used have known adverse effects. With propofol syndrome there is lactic acidosis, rhabdomyolysis, acute renal failure, liver failure, and death. Barbiturates may suppress immune function and predispose to infections. In a study of propofol and barbiturates in refractory status epilepticus, Parviainen et al. (2007) noted the large proportion of patients who died after nonprocedural sedation. Hypotension occurs with barbiturates and propofol.

There is no prospective, randomized study comparing different

anesthetics on mortality or survival. Sutter et al. (2017) noted that treatment of SE with IV anesthetic drugs had a higher proportion of infection and risk of death compared to those not receiving IV anesthetic drugs.

Closer to home are the data in humans on intravenous agents in patients with periodic discharges which reflect the few studies available in humans. Ng et al. (2014) found that in the 111/4246 who had PDs, the administration of abortive therapy was an independent risk factor for poor outcome, concluding that treatment of PDs did not independently improve clinical outcome.

There is an iceberg of hidden danger in interpreting even first rank studies (Ioannidis, 2009). Pitrou et al. (2009) and Ioannidis 2009 have addressed these issues. In the Pitrou et al. (2009) report on adverse events in randomized trials, such events were "neglected, restricted, distorted and silenced." Pitrou et al. (2009) evaluated 133 trials published in high-impact factor journals and found suboptimal reporting of adverse effects even in top medical journals. Some trials provided no information on harms. Severity was undefined or vaguely defined in others, and half of the trials reported no information on withdrawal of patients owing to harms. Fewer than 20 % reported reasons why patients withdrew owing to adverse events, information of prime clinical relevance. As both articles have emphasized, single trials are usually underpowered to detect differences in harms, hence automatic reassurance statements that "no significant differences were found" are misleading. "…where clear conflicts of interest operate, [investigators are] trying to hide bothersome risks under the carpet. Distortion can happen not only in the trial reports themselves, but also in the accompanying literature that comments on the trial results through editorials, expert reviews and even biased guidelines that focus on effectiveness and neglect or distort harms."

"In an environment where effectiveness benefits are small and shrinking, the randomized trial agenda may need to reprogram its whole mission, including its reporting, toward better understanding of harms."

In conclusion, our comments speak to whether to mandate an intensive treatment for all to all hospitals with an ICU (even resource poor or understaffed facilities), who may have challenges with EEG interpretation and availability at night, or the availability of continuous studies. And many hospitals will not transfer care.

What we know at present is that outcome is not demonstrably better across the board in the critically ill. Prospective, adequately powered studies are insufficient, and animal studies are not applicable. Adverse effects are known, and morbidity in studies are often underestimated.

Should all hospitals (often without a neurologist trained in reading critical care EEGs) have to approach all PDs as warranting "essential and urgent treatment?" One study (Ng et al. 2014) put the proposition to the test in patients with impaired consciousness by looking at all patients who had periodic discharges on their EEG for (a) mortality, (b) functional status, and (c) resolution of EEG pattern. Of the 4246 patients, 111 (2.6 %) had periodic EEG patterns and 64 met inclusion criteria, and the authors found that treatment of periodic EEG patterns did not improve clinical outcome of patients with impaired consciousness!

I hold the position that the presence of periodic discharges should not mandate treatment decisions but rather be addressed in the context of the patient's clinical situation.

Patient with no other findings on EEG except periodic discharges who are unlikely to benefit from aggressive treatment, and in whom adverse risks outweigh benefit:

- Post cardiac arrest patients with EEGs showing identical bursts
- Post cardiac arrest patients with minimal or no brainstem function
- Awake Lennox-Gastaut patients with known interictal PDs, and not having clinical seizures
- Patients with absent SSEP N20s post cardiac arrest, after 48–72 h
- Fragile elderly patients with occasional PDs in underserved and resource poor hospitals
- Clinical settings where continuous or frequent EEGs, and adequately trained EEGers are not available at all, over the weekends or at night

We might all agree that certain patients with PDs may be given a trial with safe doses of non-sedating antiseizure drugs and/or low doses of benzodiazepines, but beyond that, much is in contention. I join with Brandon in looking to a better way to identify which GPDs are harmful. Better, larger, blinded, and randomized prospective studies are the ideal, but at least studies with a combination of most of these elements are needed.

## 4. Moderator – Aatif M. Husain

Whether periodic discharges (PDs) should be aggressively treated has been debated for decades. At the 1996 annual meeting of ACNS, a debate titled "Which EEG patterns of status epilepticus warrant emergent treatment" took place. The central question was whether generalized periodic epileptiform discharges (GPEDs), as they were then called, should be aggressively treated. David Treiman argued the "pro" side, while Frank Sharbrough argued the "con" side (Treiman, 1997; Sharbrough, 1997). I was fortunate to witness that debate firsthand, having presented a paper at the same meeting discussing the etiology and relationship of GPEDs with status epilepticus (Husain et al., 1999).

In that debate, Treiman noted that GPEDs were the final of five electrographic stages of status epilepticus (Treiman et al., 1990). Consequently, he argued that GPEDs should be treated aggressively, like earlier stages of status epilepticus. Conversely, Sharbrough (1997) argued that GPEDs were simply a manifestation of severe brain injury, which could be due to status epilepticus or another cause such as cardiac arrest (Lothman, 1990). Given the extensive nature of the brain injury, Sharbrough contended that aggressive treatment was both futile and potentially dangerous.

Both Treiman and Sharbrough presented valid arguments. Indeed, the paper my colleagues and I presented noted that GPEDs were more likely to be associated with status epilepticus when discharge amplitude was higher, duration longer, and inter-GPED amplitude higher (Husain et al., 1999). Poor prognosis (death) was noted when the patient was older, had a more depressed mental status, and exhibited lower inter-GPED amplitude. While some patients with GPEDs seemed to be in a late stage of status epilepticus, others had poor prognoses despite optimal treatment. The debate ended in what seemed like a draw, with both experts presenting compelling points but neither side fully convincing the audience.

Since that debate, considerable research has explored the clinical significance and management of GPEDs and other PDs (Sully and Husain, 2018). One key advancement has been the recognition that not all GPEDs are "epileptiform." Consequently, the updated terminology now refers to these discharges as "generalized periodic discharges" (GPDs), deliberately removing the presumption of an epileptic origin from the name (Hirsch et al., 2021). Nearly 30 years after the Treiman and Sharbrough debate, I had the opportunity to moderate a new debate on the same topic between two current thought leaders, M. Brandon Westover and Peter W. Kaplan, at the ICCN in 2024. Have the past three decades resolved the question whether aggressive treatment should be pursued for (all) GPDs and other PDs?

Westover, advocating for the "pro" side, argued that PDs are part of the ictal-interictal-injury spectrum (IIIS). He emphasized that some GPDs, including those with triphasic morphology, should not automatically be assumed to be of toxic-metabolic origin and dismissed as non-epileptic. Citing evidence that some GPDs may cause brain injury, Westover stressed that visual analysis alone should not dictate treatment decisions. He recommended that if GPDs are between 1–2.5 Hz or >0.5–1 Hz with additional features (such as "+" modifiers and fluctuation), they should be given a trial of antiseizure medications (ASMs). Signs of clinical improvement should be sought, and if they occur alongside EEG improvement, the GPD pattern was likely epileptiform

and should be treated aggressively. Conversely, if clinical improvement does not occur, further treatment may not be warranted.

One potential concern regarding Westover's position is that although he advocates against relying solely on visual analysis of GPDs to determine treatment, his practical recommendations do involve visual assessments such as frequency, morphology, and evolution of discharges. Furthermore, he emphasizes clinical improvement as a marker of treatment success. However, in critically ill patients with complex medical conditions, clinical improvement may be difficult to detect, and potentially treatment may mitigate neuronal injury even without obvious clinical signs of recovery.

Kaplan, presenting the "con" side, cautioned against treating all GPDs as a single entity. He emphasized that clinical context is crucial in determining how to manage GPDs, citing research that shows prognosis is often dictated by the underlying etiology rather than treatment itself. Kaplan also highlighted recent literature showing that ASMs and anesthetic treatments can result in complications and prolonged ICU stays, particularly without close collaboration with a neurologist and clinical neurophysiologist.

However, Kaplan's position leaves the audience facing continued uncertainty about GPD management. While acknowledging that the importance of clinical context is vital, practical guidance on managing GPDs remains less clear. Kaplan also suggests that treatment approaches may vary depending on available resources. While this is certainly true in practice, it raises the question: should there not be an optimal treatment strategy for all patients, regardless of setting?

Like the Treiman and Sharbrough debate, Westover and Kaplan's debate concluded in a draw. Both delivered eloquent, evidence-supported arguments. They highlighted remarkable advancements in our understanding of GPDs over the past three decades while also emphasizing the gaps that remain. Key takeaways include:

1. GPDs are not a uniform EEG pattern. A nuanced management approach is essential.
2. GPDs are not a benign EEG finding and likely contribute to neuronal injury. The extent of this injury beyond what is already being caused by the underlying condition and whether treatment alters prognosis remain unclear.
3. When GPDs are identified, involving a neurologist and clinical neurophysiologist in patient management is critical. Telemedicine or patient transfer may be necessary.
4. Clinical context and logical decision-making remain central to interpreting EEG findings and recommending treatment. "If it looks like a duck, walks like a duck, and quacks like a duck, it is probably a duck." For instance, GPDs in a patient resuscitated after prolonged cardiac arrest with no brainstem reflexes and a very suppressed background may not warrant aggressive treatment.
5. Simply looking at the morphology of GPDs and assuming an etiology and hence possible futility of treatment of the GPDs with ASMs, is unwise. For example, assuming that GPDs with triphasic morphology are always linked to toxic-metabolic encephalopathy may be incorrect. Indeed, many toxic-metabolic states can still increase the risk of seizures.
6. The principle of "*primum non nocere*" (first, do no harm) applies when treating GPDs aggressively. Even in advanced ICUs, use of high doses of ASMs and anesthetic agents can cause complications that exacerbate brain injury and lead to worse outcomes and longer ICU and hospital stays.
7. The TOAST method provides a practical approach for assessing GPDs, emphasizing the importance of observing additional "+" modifiers or evolution, both of which may suggest epileptic potential.
8. Evaluating clinical improvement is key when determining ASM efficacy. When clinical improvement occurs alongside EEG resolution of GPDs, the assumption of an epileptic etiology is reasonable. In these situations, treating continuing GPDs more aggressively may be appropriate. However, at times clinical improvement in critically ill patients may be difficult to discern. In these cases, unequivocal improvement of the GPDs with ASMs may also suggest an epileptic etiology.
9. Frequent reassessment of patients with GPDs is crucial. As clinical information evolves, GPD recategorization may be needed. They may change from possibly related to epileptic etiology to not epileptic or vice versa.
10. Future research will continue to help better understand when and how aggressively GPDs should be treated. As the use of artificial intelligence continues to advance, its value in analysis of the GPDs beyond the obvious morphology and clinical context may further lead to improved recommendations.

Westover and Kaplan are to be commended on their excellent reviews and advocacy of their stated positions on the treatment of GPDs. While clear answers are elusive, as they often are in clinical medicine, they have provided a roadmap that can help clinicians manage this challenging diagnostic finding. Certainly, the next debate will shed even more light on this topic, and hopefully it will not take 30 more years!

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

Data will be made available on request.

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