Confusion and SIRPIDs regress with parenteral lorazepam

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ABSTRACT – Stimulus-induced rhythmic, periodic or ictal discharges (SIRPIDs) are EEG epileptiform periodic discharges (PD) induced by arousal. SIRPIDs lie along an ictal-interictal continuum with debate regarding urgency of treatment. In a patient with SIRPIDs, aphasia and confusion, i.v. lorazepam during EEG resulted in improved level of consciousness, return of verbal interaction and regression of SIRPIDs. This suggests that some forms of SIRPIDs may be associated with an ictal confusional state.

Key words: SIRPIDs, periodic discharges, confusion, treatment, status epilepticus

Prolonged or continuous EEG monitoring (cEEG) in intensive care has increasingly revealed patients with subclinical seizures, non-convulsive status epilepticus (NCSE), and periodic epileptiform discharges (PDs). Conditions with PDs, including PLEDs, SIRPIDs and BIPLEDs, lie along an ictal-interictal continuum (Pohlmann-Eden et al., 1996; Chong and Hirsch, 2005; Hirsch et al., 2004) particularly when objective clinical correlates such as aphasia or confusion are noticed. In such cases, the risk-benefit of intensive AED treatment must be weighed (Kaplan, 1996). The spectrum of intensity of treatment (from no treatment through to parenteral anaesthetic agents with intubation and respiratory support) stems from the uncertainty that clinicians have regarding potential consequences of epileptic phenomena (periodic discharges, seizures or status epilepticus) (Drislane, 1999).

Many believe that mildly obtunded NCSE patients are at low risk for seizure-induced permanent neurological damage (Drislane, 1999; Kaplan, 1999), others project possible permanent brain damage from epileptic phenomena along the ictal-interictal spectrum (I-IS), including PDs (Handforth et al., 1994), independent of precipitating cause. Where SIRPIDs lie along the ictal-interictal continuum, and how damaging they may be, is not known. To determine if SIRPIDs respond to AEDs, we evaluated the EEG and clinical response to i.v. benzodiazepines and found an immediate clinical and EEG regression; a finding not previously reported.

Case report

A 65-year-old woman with diabetes mellitus on coumadin one month
after aneurysm surgery, fell and hit her head. On head CT she had a left frontal intracerebral haemorrhage, intraventricular extension, subfalcine herniation, and hydrocephalus. After placement of an intraventricular catheter, she was confused. EEG showed intermittent runs of epileptiform discharges over the left frontal region induced by noxious stimulation, at 1.2 Hz; SIRPIDs (figure 1). Background was at 7-9 Hz during arousal with marked diffuse polymorphic theta and delta activity. Anaesthetic agents were avoided as SIRPIDs regressed during drowsiness. cEEG over two days revealed repeated instances (>15) of SIRPIDs in the left frontal region after every arousal, but no independent progression to seizures.

**Figure 1.** A) EEG before noxious stimulation; there is diffuse theta activity without SIRPIDs. B) EEG with stimulation; left frontal SIRPIDs are present. C) EEG following lorazepam; SIRPIDs are markedly decreased despite arousal reflected by muscle artefact and clinical response to commands.
When awake, she was non-verbal and did not follow commands. Despite increases in levetiracetam and phenytoin, SIRPIDs persisted. The patient was given 1 mg of lorazepam, became more alert, opened her eyes spontaneously and visually tracked objects, responded by giving her name, followed simple limb and eye-closure commands and requested water. The clinical effect lasted 20 minutes before she became unresponsive to voice. The cEEG showed SIRPIDs. Ativan and levetiracetam were added, phenytoin was increased, and the following day EEG showed SIRPID regression with alertness. Twelve days later, occasional independent bifrontal discharges were recorded. At follow-up, she was partially aphasic with some single word verbalisation, but followed commands.

**Discussion**

This patient had SIRPIDs that regressed with *i.v.* lorazepam. Responsiveness and language improved *pari passu* with EEG improvement, suggesting that, in this case, SIRPIDs behaved like seizures, rather than interictal PDs, a finding not previously reported. The effect was transient suggesting that the underlying irritant (probably blood) remained epileptogenic. Despite addition of other AEDs, it was only after several days that the left frontal SIRPIDs finally abated. Further lorazepam was not given to avoid intubation. During the several days of SIRPIDs, the patient was arousable, opened her eyes, but could not follow commands or speak. The pathophysiology of SIRPIDs is poorly understood, but has many features associated with PDs. PDs exhibit characteristics of cortical/subcortical disturbance (Chatrian *et al.*, 1964; Gloor, 1968; Snodgrass *et al.*, 1989). SIRPIDs *in toto* have no specific cause, but reflect cortical “irritability” as seen with intra-cerebral and sub-arachnoid haemorrhage, ischaemia, infection, trauma, anoxia, or tumour (Hirsch *et al.*, 2004). Where SIRPIDs lie along the ictal-interictal continuum is unclear; they refer to stimulus-induced PDs. Our patient had SIRPIDs from intracranial haemorrhage. Without knowing how damaging SIRPIDs might be to neuronal structures, clinicians have given patients non-sedating AEDs, but hesitated to induce anaesthesia (personal communications). Whether intensive treatment of PDs results in greater harm than good is an unresolved debate. In striking a balance between risk and benefit, this case would suggest that SIRPIDs behave like seizures responding to benzodiazepines without recourse to anaesthesia. Our case suggests that SIRPIDs can behave like seizures or even electrographic status epilepticus. Alternately, seizure activity might have occurred at depth, but was not visible at the scalp surface until induced or propagated by stimulation (Jenssen *et al.*, 2011). The precise location of SIRPIDs on the ictal-interictal continuum warrants greater exploration on a case-by-case basis. A step-wise approach with increasing acuity of investigation and treatment is advocated (*e.g.* with SPECT or PET) (Claassen, 2009) to determine surrogates of neuronal activity and damage with increased SPECT perfusion. Although rCBF does not directly measure active seizures, studies suggest sensitivity for seizures of >90%, and conclude that a negative SPECT argues against seizures (Devous *et al.*, 1998). Additional reports of SIRPID regression with clinical improvement might strengthen the link between SIRPIDs and seizure activity. An EEG “improvement” with benzodiazepines is not specific to seizures, but concurrent clinical improvement would support such a link. What remains unclear is whether intensive, expeditious treatment and regression of SIRPIDs improves outcome. □

**Disclosure.**

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**References**


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