

Letter to the Editor

## Autonomic Complications of Seizures and Migraines

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We read with interest the narrative review article by D'Agnano *et al.* [1] on the role of the autonomic nervous system (ANS) in epilepsy and migraine, and in particular, the section on the autonomic manifestations of seizures and migraine attacks. The authors concluded that ANS dysfunction is a common complication of migraine and seizures, that it is manifested by a wide range of symptoms, and that treatment of migraine and seizures should also include treatment of ANS manifestations [1]. The study is excellent, but has limitations that are of concern and should be discussed.

The first major point is that several autonomic manifestations of seizures were not considered in the review [1]. The first is Takotsubo syndrome (TTS), also known as stress cardiomyopathy, stunned myocardium, or broken-heart syndrome [2]. TTS is characterized by acute heart failure, which is thought to be due to overstimulation of autonomic cardiac innervation by endogenous or exogenous stress [2]. TTS that is related to seizures is thought to be the result of endogenous stress and the excess of catecholamines caused by the seizure [2]. However, TTS can be triggered not only by generalized seizures or status epilepticus, but also by focal seizures [3]. Therefore, it is likely that factors other than catecholamine storm are involved in the pathophysiology of seizure-related TTS.

A second autonomic manifestation of seizures not addressed in the review is neurogenic pulmonary edema (NPE) [4]. NPE is characterized by acute respiratory distress caused by acute, severe, central nervous system (CNS) compromise, manifested by pink, foamy sputum, pulmonary edema, bilateral radiographic opacities, PaO<sub>2</sub>:PiO<sub>2</sub> <200 mm Hg, acute CNS compromise with increased intracranial pressure, and rapid improvement within 48–72 hours unless alternative causes of shortness of breath are present [5]. Seizures are one of the most common triggers of NPE.

A third manifestation of ANS dysfunction during seizures that was not adequately addressed in the review is malignant cardiac arrhythmias [6]. These include supraventricular and ventricular tachycardia, bradycardia, pauses, torsades des pointes, ventricular fibrillation, and asystole. Since some of them may be responsible for sudden unexpected death in epilepsy (SUDEP), it is crucial to recognize this ANS manifestation of seizures and take preventive measures if necessary.

A fourth ANS manifestation of seizures is coronary spasm [7]. Although rarely reported, it can be a complication of seizures and manifest as acute coronary syndrome or myocardial infarction [7].

The fifth ANS manifestation of seizures not covered in the review is voiding of urine or stool during a seizure. Secessus alvi or urinae are common autonomic complications of particularly generalized seizures and are often the only evidence that a seizure has occurred.

Because seizures typically activate the sympathetic system, they increase heart rate and blood pressure, although parasympathetic activation or sympathetic inhibition may predominate in partial seizures [8]. Seizures may also weaken autonomic respiratory reflexes postictally, which may contribute to SUDEP [8].

The second major point is that the spectrum of ANS complications in migraine is also not complete. It is missing the fact that migraine sufferers with disabling attacks are prone to ANS dysfunction, particularly blood pressure dysregulation (e.g., reduced blood pressure fluctuation or increased resting diastolic blood pressure) [9].

Overall, the interesting study has limitations that call into question the results and their interpretation. Addressing these issues would strengthen the conclusions and could improve the status of the study. The spectrum of ANS manifestations of seizures and migraine is wider than expected and requires special attention because some of them, especially in seizures, can be fatal.

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Not applicable.

### Author Contributions

JF: design, literature search, discussion, first draft, critical comments, final approval.

### Ethics Approval and Consent to Participate

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## Conflict of Interest

The author declares no conflict of interest.

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