

POINT

Raimondo D'Ambrosio and John W. Miller provide the following comment:

We welcome an open debate, but would like to correct several erroneous assertions. Dudek and Bertram claim that the events in fluid percussion injury (FPI) animals can occur in sham control animals and that they resemble sleep spindles or the alpha rhythm. However, in our hands, blinded observers never see these events in sham-injured animals, provided that appropriate care is taken not to injure the cortex during animal preparation (1–3). The electrographic features are easily distinguished from normal activities by their waveform and localization. Various behaviors occur during the electrical events including motion arrest, posturing, and automatisms; these behaviors are ictal because they are unvarying and reproducible. The electrographic and behavioral events are coincident as demonstrated by blinded cross-correlation analysis (3).

They also say that the electrographic discharges are different in waveform, duration, and frequency of occurrence from seizures in human posttraumatic epilepsy. This is incorrect—seizures in human posttraumatic epilepsy most often arise in the temporal and frontal lobes (4,5), and many frontal lobe seizures in this setting have electrographic discharges with waveforms and evolution that are similar to those in FPI rats (3,6–9). The authors emphasize the shorter seizures, but we have reported seizures as long as 89 seconds (2). If these longer events are conceded to be seizures, shorter events with a similar electrical signature and behavioral impact must also be seizures (3). The difference in seizure frequency is by design. It results from our optimization of the injury to yield seizure frequencies high enough to power preclinical studies with manageable number of animals (10). We can obtain animals with lower seizure frequencies by reducing the severity of FPI, but the model would then not be as useful for mechanistic and drug studies.

Finally, they assert that we have noted FPI seizures to be similar to absence seizures. We have never said this, and it is critical not to confuse FPI seizures, which model partial seizures, with absences. Rare idiopathic absence seizures may be seen

in both control and experimental animals, appearing about 5 months later than FPI-induced epilepsy, but these are easy to identify by their distinctive electrographic waveform and localization (2). Another important difference is that carisbamate, which potently controls absence seizures, is ineffective for FPI epilepsy (11).

Developing more effective treatments for epilepsy will require experimental models that reproduce the etiologies of human epilepsies. We believe that FPI represents one such model.

References

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