Comment on: “Clinical Management of Seizures in Newborns: Diagnosis and Treatment”

Eugenio Grillo

Published online: 5 October 2013
© Springer International Publishing Switzerland 2013

In their narrative review on management of neonatal seizures, Van Rooij et al. [1] acknowledge that there are controversies about how aggressive we should be in managing neonatal seizures. Nevertheless, they state that “as a consequence of the growing body of evidence that neonatal seizures per se contribute to adverse neurodevelopmental outcome, clinicians are more focused on treatment of neonatal seizures” [1]. In the reference cited at the end of this paragraph, a Cochrane systematic review on treatment of neonatal seizures, the authors, Booth and Evans, did not mention a growing body of evidence but that “in the literature, there remains a body of opinion that seizures should be treated because of the concern that seizures in themselves may be harmful, although this is only supported by relatively low-grade evidence” [2]. After this statement, Booth and Evans cited an American nationwide survey of neonatologists on the management of neonatal seizures [3] and one paper on animal models [4].

The seizure-induced adverse neurodevelopmental outcome notion has been repeated as a mantra, based more on the “body of opinion” and less on the “body of evidence”. This notion is so widespread that this situation has imposed a reversal of burden of proof. However, designing clinical studies is extremely difficult or even impossible, considering

that you will never know if more refractory seizures are the cause or just a marker of more severe brain insult and worse outcome. Evidence supporting seizure-induced adverse neurodevelopmental outcome comes from animal or in vitro models, which are far from emulating a real clinical scenario of seizures coming from an intrinsically dysfunctional brain, considering that, in these models, an external agent such as pilocarpine, kainic acid, fluorothyl, electrical stimulation, hyperthermia, inflammation inductors, or hypoxia-ischemia, among others, are added to the experiment [4–6].

The account for the electrical phenomenon per se damaging neurons could be false, and the old precept of non-maleficence is being disregarded on this issue, both in newborns and in older patients. Van Rooij et al. also mention that animal experiments have suggested that some antiepileptic drugs could contribute to apoptosis, which is even more concerning.

Conflict of interest None.

References

1. van Rooij LG, van den Broek MP, Rademaker CM, de Vries LS. Clinical management of seizures in newborns: diagnosis and treatment. *Paediatr Drugs*. 2013;15(1):9–18.
2. Booth D, Evans DJ. Anticonvulsants for neonates with seizures. *Cochrane Database Syst Rev* 2004(4):CD004218.
3. Massingale TW, Buttross S. Survey of treatment practices for neonatal seizures. *J Perinatol Off J Calif Perinatal Assoc*. 1993;13(2):107–10.
4. Levene M. The clinical conundrum of neonatal seizures. *Arch Dis Child Fetal Neonatal Ed*. 2002;86(2):F75–7.
5. Pitkanen A, Kharatishvili I, Karhunen H, Lukasiuk K, Immonen R, Nairismagi J, et al. Epileptogenesis in experimental models. *Epilepsia*. 2007;48(Suppl 2):13–20.
6. Auvin S, Pineda E, Shin D, Gressens P, Mazarati A. Novel animal models of pediatric epilepsy. *Neurother J Am Soc Exp Neurother*. 2012;9(2):245–61.

The authors’ reply to this letter can be found under doi:[10.1007/s40272-013-0055-z](https://doi.org/10.1007/s40272-013-0055-z).

E. Grillo
Department of Pediatrics, Hospital Universitário, Universidade Federal de Santa Catarina, Campus Universitário, Trindade, Florianópolis, SC 88040-970, Brazil

E. Grillo (✉)
Department of Neurology,
Hospital Infantil Joana de Gusmão, Rua Rui Barbosa 152,
Agrônômica, Florianópolis, SC 88025-301, Brazil
e-mail: eugeniogrillo@gmail.com