

Unilateral Topical Cortical Application of Penicillin: Electrographic Aspects

A New Complement to an Old Model

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Abstract. In 7 cats 800 IU of penicillin were applied diffusely over one hemisphere on the exposed neocortex. After 40 min all animals showed bilateral and synchronous burst discharges with a higher amplitude at the hemisphere where the penicillin had been applied. These data fill a gap in the literature concerning feline generalized penicillin epilepsy, in which penicillin is applied bilaterally on the exposed neocortex.

Introduction

Bilateral topical application of penicillin has been used for a long time as a model of generalized epilepsy. The role of cortical and sub-cortical structures in the genesis of the bursts in this model has been extensively studied [1, 7, 9, 14-17, 24, 25], and the role of the corpus callosum in the propagation of the generalized discharges is now firmly established [12, 19, 21-23].

Unilateral localized topical application of convulsant drugs has been widely used as a means of creating focal epileptic activity [2, 3, 13, 18, 26]. The appearance of mirror foci and the role of the cerebral commissures in its pathogenesis has also been determined [20].

Nevertheless, unilateral diffuse topical application of penicillin has never been reported. We have carried out experiments with unilateral topical application of penicillin under well controlled conditions.

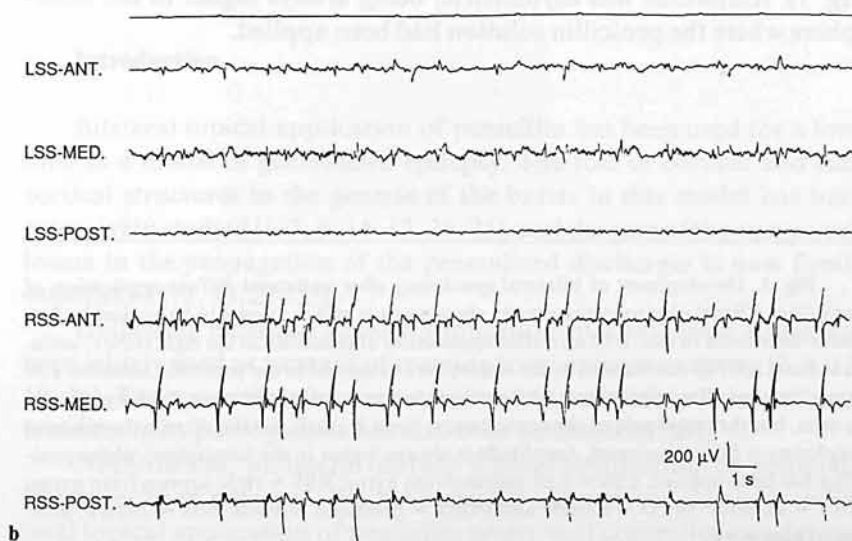
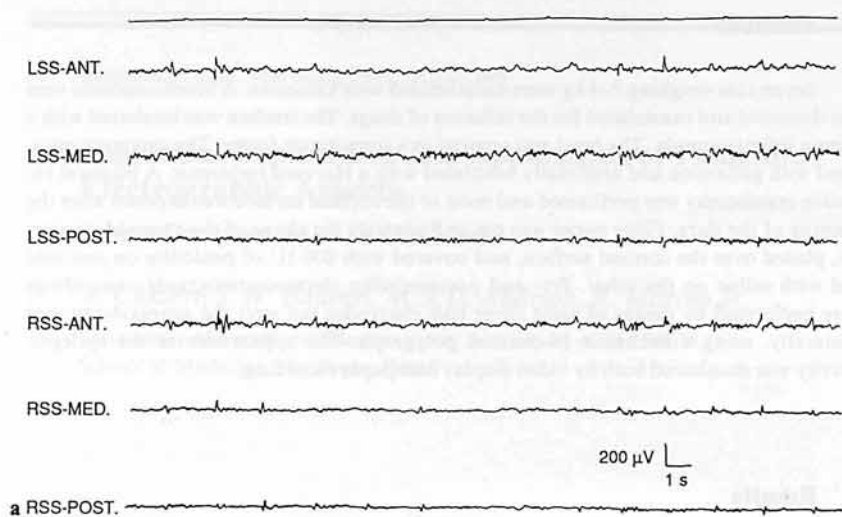
Methods

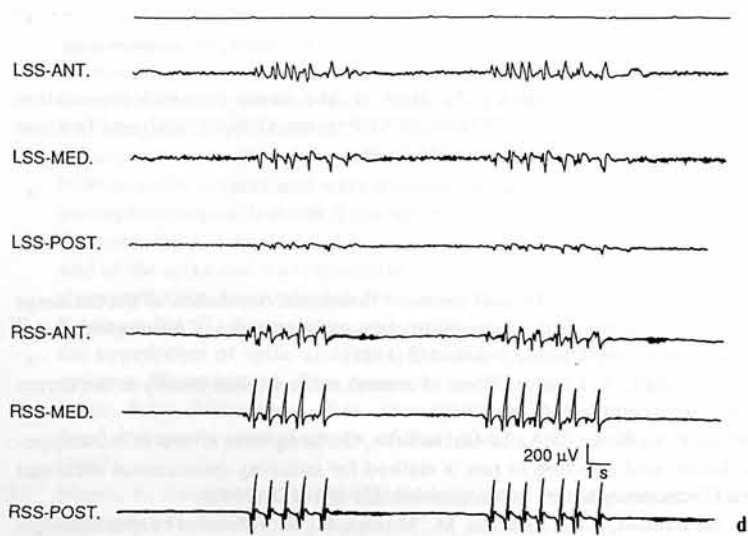
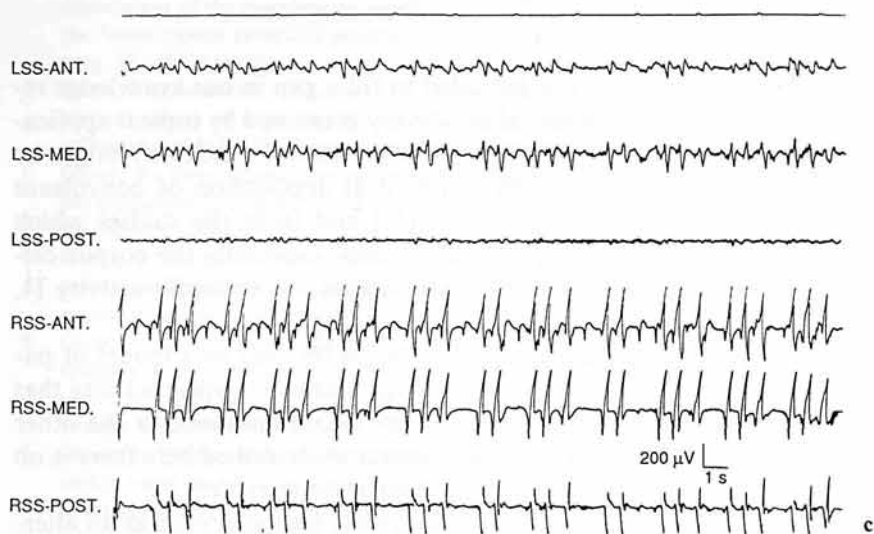
Seven cats weighing 2–4 kg were anesthetized with ketamine. A brachioradialis vein was dissected and cannulated for the infusion of drugs. The trachea was intubated with a human infant cannula. The head was secured in a stereotactic frame. The cats were paralyzed with gallamine and artificially ventilated with a Harvard respirator. A bilateral extensive craniotomy was performed and most of the cortical surface was exposed after the opening of the dura. Filter paper was cut to fit exactly the shape of the exposed neocortex, placed over the cortical surface, and covered with 800 IU of penicillin on one side and with saline on the other. Pre- and postpenicillin electrocorticographic recordings were performed by means of eight silver ball electrodes put over the suprasylvian gyri bilaterally, using a Beckman 16-channel polygraph. The appearance of the epileptic activity was monitored both by video display and paper recording.

Results

Basal electrocorticography disclosed only spikes evoked by ketamine anesthesia in cats. After 10 min unilateral burst activity in the hemisphere subjected to the penicillin solution occurred in 5 animals. After 30 min initial bilateral synchrony could be seen, but the amplitude of the contralateral burst was very small. After 40 min the epileptic activity was fully developed and bilateral synchrony was evident (fig. 1). Amplitude was asymmetric, being always higher in the hemisphere where the penicillin solution had been applied.

Fig. 1. Development of bilateral synchrony after unilateral diffuse application of penicillin. **a** Basal electrocorticography showing only spikes known to be evoked by ketamine anesthesia in cats. **b** 10 min after application of penicillin to the right cortex; unilateral burst activity can be seen in the hemisphere subjected to the penicillin solution. **c** 30 min after penicillin application; bilateral synchronous spike and wave discharges could be seen, but the amplitude of the contralateral burst is small. **d** After 40 min the bilateral synchrony is fully developed. Amplitude is always higher in the hemisphere where penicillin has been applied. LSS = Left suprasylvian gyrus; RSS = right suprasylvian gyrus; ANT = anterior; MED = middle and POST = posterior. Vertical bars = 200 μ V; horizontal bars = 1 s.





Discussion

The present study was intended to fill a gap in our knowledge regarding the model of bilateral synchrony generated by topical application of penicillin [6, 8, 10]. This diffuse bilateral synchrony might be anticipated from prior studies with focal application of convulsant drugs and mirror foci appearance [20] and from the studies which clearly implicate the cerebral commissures, especially the corpus callosum, in the interhemispheric propagation of epileptic activity [4, 27-29].

The final electrographic picture might be used as a model of pathology where a diseased hemisphere generates epileptic activity that spreads, presumably through the cerebral commissures, to the other hemisphere, although in the experimental set described here there is no anatomical lesion, but only a physiological derangement.

Complete [5] or partial [11] callosotomy has been used as an alternative for hemispherectomy in some cases with hemispheric pathology and bilateral generalized epileptic activity. The present model will be suitable to study the effects and possible benefits of this kind of functional intervention in candidates for hemispherectomy. The behavioral correlates of this particular kind of bilateral synchrony should also be studied.

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References

- 1 Avoli, M.; Gloor, P.: The effects of transient functional depression of the thalamus on spindles and on bilateral synchronous epileptic discharges of feline generalized penicillin epilepsy. *Epilepsia* 22: 443-452 (1981).
- 2 Carrea, R.; Lanari, A.: Chronic effect of tetanus toxin applied locally to the cortex of the dog. *Science* 137: 342-343 (1962).
- 3 Cavalheiro, E.A.; Riche, D.A.; Le Gal la Salle, G.: Long-term effects of intrahippocampal kainic acid injection in rats: a method for inducing spontaneous recurrent seizures. *Electroenceph. clin. Neurophysiol.* 53: 581-589 (1982).
- 4 Cukiert, A.; Baumel, S.W.; Andrioli, M.; Marino, R., Jr.: Effects of corpus callosum

- stimulation of the morphology, synchrony and frequency of the epileptic bursts in the feline topical penicillin generalized epilepsy model. *Stereotact. Funct. Neurosurg.* 52: 18-25 (1989).
- 5 Gates, J.R.; Maxwell, R.; Leppik, I.E.; Gumnit, R.J.: Electroencephalographic and clinical effects of total corpus callosotomy; in Reeves, Epilepsy and the corpus callosum, pp. 315-328 (Plenum Press, New York 1985).
 - 6 Gloor, P.: Generalized cortico-reticular epilepsies. Some considerations on the pathophysiology of generalized bilaterally synchronous spike and wave discharge. *Epilepsia* 9: 249-263 (1968).
 - 7 Gloor, P.; Testa, G.: Generalized penicillin epilepsy in the cat: effects of intracarotid and intravertebral pentilenotetrazol and amobarbital injections. *Electroenceph. Clin. Neurophysiol.* 36: 499-515 (1974).
 - 8 Gloor, P.; Quesnay, L.F.; Zumstein, H.: Pathophysiology of generalized penicillin epilepsy in the cat: the role of cortical and subcortical structures. II. Topical application of penicillin in the cerebral cortex and to subcortical structures. *Electroenceph. Clin. Neurophysiol.* 43: 79-94 (1977).
 - 9 Gloor, P.; Pellegrini, A. and Kostopoulos, G.K.: Effects of changes in cortical excitability upon the epileptic bursts in generalized penicillin epilepsy of the cat. *Electroenceph. Clin. Neurophysiol.* 46: 274-289 (1978).
 - 10 Gloor, P.: Generalized epilepsy with spike and wave discharge: a reinterpretation of its electrographic and clinical manifestations. *Epilepsia* 20: 571-588 (1979).
 - 11 Huck, F.R.; Radvany, J.; Avila, J.O.; Pires de Camargo, C.H.; Marino, R., Jr.; Ragozzano, P.C.; Riva, D.: Anterior callosotomy in epileptics with multiform seizures and bilateral synchronous spike and wave EEG pattern. *Acta Neurochir., suppl.* 30, pp. 127-135 (1980).
 - 12 Isaacson, R.L.; Schwartz, H.; Persoff, N.; Pinson, L.: The role of the corpus callosum in the establishment of areas of secondary epileptiform activity. *Epilepsia* 12: 133-146 (1971).
 - 13 Kopellof, L.M.; Chusid, J.G.; Kopellof, N.: Chronic experimental epilepsy in *Maca mulatta*. *Neurology* 4: 218-227 (1954).
 - 14 Kostopoulos, G.; Gloor, P.; Pellegrini, A. and Siatitsas, I.: A study of the transition from spindles to spike-and-wave discharge in feline generalized penicillin epilepsy: EEG features. *Exp. Neurol.* 73: 43-54 (1981).
 - 15 Kostopoulos, G.; Gloor, P.; Pellegrini, A.; Gotman, J.: A study of the transition from spindles to spike and wave discharge in feline generalized penicillin epilepsy: microphysiological features. *Exp. Neurol.* 73: 55-77 (1981).
 - 16 Kostopoulos, G.; Avoli, M.; Pellegrini, A.; Gloor, P.: Laminar analysis of spindles and of the spike and wave discharge of feline generalized penicillin epilepsy. *Electroenceph. Clin. Neurophysiol.* 53: 1-13 (1982).
 - 17 Kostopoulos, G.: Potentiation and modification of recruiting responses precedes the appearance of spike and wave discharges in the feline generalized penicillin epilepsy. *Electroenceph. Clin. Neurophysiol.* 53: 467-478 (1982).
 - 18 Louis, E.D.; Williamson, P.D.; Darcey, T.M.: Experimental models of chronic focal epilepsy: a critical review of four models. *Yale J. Biol. Med.* 60: 255-272 (1987).
 - 19 Mares, P.: Symmetrical epileptogenic foci in the cerebral cortex of immature rat. *Epilepsia* 14: 422-435 (1973).

- 20 Morrel, F.: Secondary epileptogenic lesions. *Epilepsia* 1: 536-560 (1959).
- 21 Musgrave, J.; Gloor, P.: The role of the corpus callosum in bilateral interhemispheric synchrony of spike and wave discharge in feline generalized penicillin epilepsy. *Epilepsia* 21: 369-378 (1980).
- 22 Mutani, R.; Durelli, L.: Mechanisms of interactions of asymmetrical foci in the neocortex. *Epilepsia* 21: 549-556 (1981).
- 23 Ottino, C.A.; Meglio, M.; Rossi, G.F.; Tercero, E.: An experimental study of the structures mediating bilateral synchrony of epileptic discharges of cortical origin. *Epilepsia* 12: 299-311 (1971).
- 24 Pellegrini, A.; Musgrave, J.; Gloor, P.: Role of afferent input of subcortical origin in the genesis of bilaterally synchronous epileptic discharges of feline generalized penicillin epilepsy. *Exp. Neurol.* 64: 155-173 (1979).
- 25 Quesnay, L.F.; Gloor, P.: Generalized penicillin epilepsy in the cat: correlation between electrophysiological data and distribution of 14-C penicillin in the brain. *Epilepsia* 19: 35-45 (1978).
- 26 Shinozaki, H.; Konishi, S.: Action of several antihelminthics and insecticides on rat cortical neurons. *Brain Res.* 24: 368-371 (1970).
- 27 van Wagenen, W.P.; Herren, R.Y.: Surgical division of commissural pathways in the corpus callosum. *Archs Neurol. Psychiat.* 44: 740-789 (1940).
- 28 Wada, J.A.: Anterior 2/3 callosal bissection: comparative observations in animals and man; in Engel, *Fundamental mechanisms of human brain function*, pp. 259-266 (Raven Press, New York 1987).
- 29 Wilson, D.H.; Reeves, A.; Gazzaniga, M.; Culver, C.: Cerebral commissurotomy for control of intractable seizures. *Neurology* 72: 708-715 (1977).