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The role of electrical stimulation and lesioning of the anterior thalamic nucleus on kainic acid-induced focal cortical seizure

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Background and Objective: Electrical stimulation of the anterior nucleus of the thalamus (ANT) is receiving increased attention as a novel means of controlling intractable epilepsy.[1,2] Animal data supporting the anticonvulsant benefit of ANT stimulation has been obtained from systemic convulsant models.[1,2] We used a rat model of focal cortical seizures induced by intra-cortical kainic acid (KA) injection to interrogate the anticonvulsant effects of electrically stimulating the ANT. We tested the effects of both unilateral and bilateral electrical stimulation, and introduced lesioning of the ANT as a comparison procedure. To elucidate the mechanism underlying these anticonvulsant action, cerebral glucose metabolism following ANT electrical stimulation and lesioning was also examined.

Methods: Wistar rats were divided into five major groups of nine rats each: control, unilateral and bilateral ANT electrical stimulation, and unilateral and bilateral ANT lesioning. A stainless-steel chemitrode was inserted stereotactically into the left sensorimotor cortex (SMC) for KA injection and electroencephalography (EEG) recording. After KA injection, average clinical seizure frequencies in each group were measured. Local cerebral glucose utilization (LCGU) was measured using [^{14}C] 2-deoxyglucose autoradiography in the three groups of seven rats each: control, bilateral ANT stimulation and bilateral ANT lesioning.

Results: All control animals treated with KA alone developed focal cortical seizure status epilepticus. Unilateral ANT electrical stimulation and lesioning significantly reduced clinical seizure frequency, compared with control animals. Strikingly, no animals treated with bilateral ANT procedures demonstrated any obvious clinical motor seizures, although electroencephalographic seizure activities were observed in the SMC. LCGU was markedly increased in the SMC, caudate-putamen (CP), globus pallidus (GP), thalamus (ANT, central thalamus, entire posterior thalamus), mammillary body (MB), mammillothalamic tract (MTT) and midbrain tegmentum of control-group rats following KA injection. While, the LCGU in each structures in both ANT stimualtion and lesioning group were significantly decreased, compared with the control group.

Discussion: The finding that EEG foci remained active without clinically motor manifestations suggests that ANT stimulation or lesioning may impede the propagation of after-discharges from the focus to other regions of the brain. From an analysis of cerebral metabolic changes, we proposed functional anatomy in the KA-induced focal cortical seizure model. That is, when the motor cortex was initially activated by the KA intra-cortical injection followed by seizure-activity propagation from the motor cortex to the CP, GP, and thalamus, the cortico-thalamic circuit was driven via the thalamo-cortical pathway. Finally, when the MB and midbrain tegmentum were activated via the MTT, seizure activity from the brain stem was also initiated. The ANT is thought to function as a relay structure to amplify and synchronize seizure activities in these circuits. Furthermore, we suggest that the electrical stimulation and lesioning of the ANT may therefore act to inhibit the above-described functions of this anatomical structure.

Conclusion: Both electrical stimulation and lesioning of the ANT suppressed clinical focal cortical seizures induced by an intra-cortical KA injection. Additionally, an analysis of cerebral metabolic changes indicated that these procedures might suppress the function as amplifier and synchronizer of seizure activity.

References

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