405. Corticotropin-releasing Hormone Receptor Antagonist Is Effective for Febrile Seizures in the Infant Rat

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Febrile seizures (FS) are a common, age-specific entity observed in 3 to 5% of infants and young children. Despite the frequency of FS, the mechanisms and potential endogenous convulsants involved in their generation are poorly under-stood. Corticotropin-releasing hormone (CRH) is a neuro-peptide, inducing age-specific seizures when administered into the cerebral ventricles of infant rats in picomolar amounts. Endogenous CRH, found in the hypothalamus and limbic system, has been found to participate in certain mecha-nisms of hyperthermia. We tested the hypothesis that endog-enous CRH may contribute to febrile seizures in an infant rat paradigm. Infant rats ($n = 43$) were implanted with a chronic cannula in the lateral cerebral ventricle (icv) on post-natal day 9. On day 10, α-helical-(9-41)-CRH, a competitive antagonist of the CRH receptor, was infused icv (0.9×10^{-9} mol) to half the animals. Hyperthermia was induced 30 min-utes later to 2 rats at a time, 1 of which was treated and the other used as a control. Seizure onset was assessed by an investigator blinded to treatment; rectal temperature was measured immediately (Thermistor probe, Omega Engi-neering, Stamford, CT). Mean temperature at onset of FS was 43.16°C + 0.46 for controls, and 44.47°C + 0.46 for rats pretreated with CRH antagonist ($p < 0.05$). CRH antag-onist increased temperature required for hyperthermic sei-zures in infant rats by 1.31 °C. In the same paradigm, phe-nobarbital raised FS-inducing temperature by 1°C, while phenytoin did not affect seizure threshold, similar to effects on FS in human infants (Olson JE, Scher MS, Holtzman D. Effects of anticonvulsants on hyperthermia-induced seizures in the rat pup. Epilepsia 1984;25:96–99). We conclude that CRH antagonist may be effective for human FS, via alteration of CRH-mediated convulsive mechanisms. (Supported by NS28912.)