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B.5 SEIZURE THRESHOLD TO KAINIC ACID IN INFANT RATS IS MARKEDLY DECREASED BY CORTICOTROPIN RELEASING HORMONE.

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RATIONALE: Corticotropin releasing hormone (CRH) is a direct convulsant *in vivo*, and a neuroexcitant *in vitro*. Both effects are more pronounced in the immature brain. Mechanisms of CRH-induced neuronal activation are unclear, but may involve increased calcium influx. This study examined whether CRH-induced seizures facilitated the action of kainic acid, a glutamate-receptor mediated convulsant.

METHODS: i). A preliminary experiment (n=27) established the threshold dose of kainate (intraperitoneal) in 12 day old rats. ii). Kainate threshold dose was then administered to three groups: naive controls (n=8), sham-infused cannula-carrying controls (n=3) and CRH-treated (n=8). The CRH group received 0.75 μ m CRH into the lateral ventricles, via a cannula, twice daily on postnatal days 10 and 11, resulting in sustained (4-6 hours) seizures. Presence, latency and duration of kainate-induced seizures were measured on day 12, 14 hours subsequent to the final CRH infusion.

RESULTS: Threshold kainate dose (0.2 mg/kg) produced no seizures in 2 naive controls, and short-term automatisms (10.8 ± 1.2 min, after a 69.7 ± 7 min latency) in six. No motor seizures occurred in naive or sham-infused controls. CRH- infused rats developed automatisms followed by prolonged (114 ± 26 min) seizures, within 30.1 ± 4 min of kainate injection. This approximated seizures in naive rats given 1.0 mg/kg of kainate.

CONCLUSION: Exposure to CRH-induced status epilepticus lowers kainic acid seizure threshold in infant rats about five-fold. Whether this is a direct effect of the peptide or a result of CRH-induced severe seizures is under investigation.

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