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Role of cannabinoid CB1 receptors in the proconvulsant effect of Apelin-13 on penicillin-induced epileptiform activity

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Epilepsy is a widespread neurological disorder. Many neurotransmitters, neuropeptides and neuromodulators have a significant role in the epileptic activity. Apelin-13 and cannabinoid CB1 receptor agonist and antagonist have an effect in the penicillin model of epilepsy. The relationship between apelin and epilepsy, and the apelin-cannabinoid relationship in epilepsy is still not well understood. Thus, this study focuses on the relationship between apelin-13 and CB1 receptor in experimental model of epilepsy. Penicillin injection was given intracortically (i.c.) for the development of epileptic seizures. Ninety-one male Wistar rats were divided into 13 groups. CB1 receptor agonist ACEA (7.5 µg, intracerebroventricularly, icv) and antagonist AM-251 (0.25 µg and 0.125 µg, icv) were administered to three different groups, two different doses of apelin-13 (5 µg and 15 µg, icv) were applied and the interactions between these five groups of substances were evaluated. Both apelin-13 (15 µg) and AM-251 (0.25 µg) raised the spike frequency of epileptiform activity separately. Application of apelin-13 + AM-251 also increased the spike frequency of epileptiform activity beginning in the 30 min after apelin-13 application. When the non-effective dose of AM-251 and the effective dose of apelin-13 were administered together, epileptic activity increased in the 20 min. ACEA reduced the epileptiform activity starting in the 50th min. apelin-13 and ACEA administration in effective doses decreased epileptiform activity. The non-effective doses of AM-251, apelin-13 and effective dose of ACEA decreased the epileptiform activity in the 50 min. Application of non-effective doses of apelin and AM-251 together does not induce any additional proconvulsant activity, and CB1 receptor agonist, ACEA reversed the proconvulsant activity of apelin-13. These results suggest that they utilize different receptors to begin their own effects by increasing intracellular Ca^{2+} in epilepsy. Considering that apelin-13 is an endogenous substance known for its neuroprotective properties, the proconvulsant effect of apelin-13 in the presented study is remarkable.

Keywords: Brain electrocorticograhy, Cannabinoid CB1 receptor agonists, Epilepsy, Neuromodulators