Effects of 3-aminopyridine-induced seizures on platelet eicosanoid synthesis

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Abstract:
We investigated the influence of recurrent epileptic seizures on the arachidonic acid (AA) cascade in platelets and brain microvessels, using [14C]AA as a tracer substrate and chromatographic determination. The recurrent epileptic seizures of male Wistar rats were induced every second day with 3-aminopyridine (3-AP, 25 mg/kg ip) for two weeks. In the chronic 3-AP model, the earlier epileptic insults resulted in a decreased incidence of limbic seizures and higher survival rate at later administration of 3-AP. After 3-AP treatment, the formation of lipoygenase products was unchanged, but the total amount of cyclooxygenase (COX) metabolites was decreased both in platelets and brain microvessels. The reduction in COX-mediated eicosanoid synthesis after recurrent seizures was due to the decreased synthesis of vasodilator and vasoconstrictor COX metabolites. In platelets, the 3-AP-treatment reduced the synthesis of vasodilator prostacyclin (PGI2), prostaglandin E2 (PGE2) and 12-L-hydroxy-5,8,10-heptadecatrienoic acid (12-HHT), while the synthesis of prostaglandin D2 (PGD2) remained unchanged. In isolated brain capillaries, the PGD2, PGE2 and 12-HHT synthesis was decreased after recurrent seizures. As for the vasoconstrictor COX metabolites, both platelets and brain microvessels synthesized significantly lesser amount of prostaglandin F2α (PGF2α) and thromboxane A2 (TxA2) upon 3-AP administration. Our results indicate that platelets and isolated brain capillaries synthesize significantly lesser amount of COX metabolites after chronic 3-AP treatment. The decreased conversion of AA into different COX products may play a role in the neuroprotective/preconditioning adaptation of the brain against subsequent seizures.

Key words: seizure, platelets, eicosanoids, 3-aminopyridine, prostaglandins, brain microvessels