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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 [^{14}C]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 lipoxygenase 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 (PGI_2), prostaglandin E_2 (PGE_2) and 12-L-hydroxy-5,8,10-heptadecatrienoic acid (12-HHT), while the synthesis of prostaglandin D_2 (PGD_2) remained unchanged. In isolated brain capillaries, the PGD_2, PGE_2 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 $F_{2\alpha}$ ($PGF_{2\alpha}$) and thromboxane A_2 (TxA_2) 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/preconditional adaptation of the brain against subsequent seizures.

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