Neurochemical characteristics of epileptogenic lesions: PET experience

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A number of radiopharmaceutical tracers have been applied to the study of epilepsy. This talk will focus on the use of the tracer alpha[^{11}C]methyl-L-tryptophan ([^{11}C]AMT) imaged with positron emission tomography. Our rationale for applying this tracer, which had been developed to measure serotonin (5HT) synthesis, in epilepsy patients was based on evidence implicating serotonergic mechanisms in epileptogenesis. The levels of 5-HT and its metabolite 5-HIAA had been reported to be higher in actively spiking temporal cortex, as compared to nonspiking cortex, and immunohistochemical studies had suggested serotonergic hyperinnervation in patients with focal cortical dysplasia. We have reported increased uptake of [^{11}C]AMT in epileptogenic tubers in approximately one-half of patients with tuberous sclerosis complex (TSC) and medically intractable epilepsy. To our surprise, biochemical studies of tissue obtained at surgery performed for seizure control demonstrated that the increase in [^{11}C]AMT uptake in cortical tubers did not represent increased serotonin synthesis. Resected tissues (epileptogenic tuber with high [^{11}C]AMT uptake, non-epileptogenic tuber with low uptake, adjacent cortex) were analyzed for tryptophan hydroxylase (TPH) activity, 5HIAA, 5HTP and quinolinic acid. Cortical tissue and tubers with low [^{11}C]AMT uptake contained measurable amounts of 5HT, 5HIAA, and tryptophan, but only tryptophan was detected in the tubers with high [^{11}C]AMT uptake. Furthermore, tryptophan hydroxylase activity was very low in the epileptogenic tuber. In contrast, quinolinic acid, a tryptophan metabolite of the kynurenine pathway, was 5-fold higher in the epileptogenic tubers than in non-epileptogenic tuber. It is pertinent that quinolinic acid is a convulsant through its action as an agonist at N-methyl-D-aspartate receptors, and this suggests a role for quinolinic acid in facilitating epileptogenesis in patients with TSC. The significance of these results with regard to application of [^{11}C]AMT in seizures secondary to brain tumors and non-lesional epilepsy will also be discussed.

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session 34