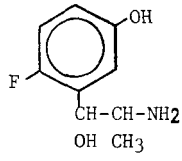
FALSE NEUROTRANSMITTERS; PROS AND CONS AS PET TRACERS

D.M. Wieland, M.E. Van Dort, D.L. Gildersleeve
University of Michigan, Division of Nuclear Medicine, Ann Arbor, MI 48109 USA

The false neurotransmitter 6-[^{18}F]fluorometaraminol (FMR) has recently been synthesized in our laboratory and validated as a heart agent that selectively maps adrenergic nerve density (1). FMR mimics the neuronal uptake, vesicular storage and impulse-stimulated release of norepinephrine (NE). The concentration of FMR in heart tissue, like endogenous NE itself, reflects the integrity of the neuron itself, not postsynaptic adrenergic receptor density.



6-FLUOROMETARAMINOL

Despite FMR's potential in detecting neuronal damage in the diseased heart, the clinical utility of FMR may be problematical: 1) FMR is synthesized by electrophilic fluorination; the low specific activity achieved by this process renders FMR doses needed for heart imaging precariously close to pharmacological levels. 2) The metabolic refractoriness of FMR simplifies the tissue signal and the blood input function for PET kinetic analysis but limits assessment of the "enzymatic health" of the neuron.

This presentation will review our recent efforts in evaluating the suitability of a number of sympathomimetic amines for probing discrete aspects of the peripheral adrenergic nerve complex. This includes: 1) [^{3}H]labeled amines which are both neuronally specific but share NE's susceptibility to monoamine oxidase; ie. meta-octopamine and phenylephrine; 2) SAR studies aimed at determining the minimum structural features necessary for neuronal uptake and storage; 3) synthetic routes to no-carrier-added [^{18}F]labeled sympathomimetic amines; 4) [^{11}C]labeled amines that can be used in conjunction with [^{18}F]fluorodeoxyglucose to assess neuronal metabolic function.

1. Mislankar, S.G., Gildersleeve, D.L., Wieland, D.M., Massin, C.C., Mulholland, G.K., Toorongian, S.A., J. Med. Chem., Feb, 1988.