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## Biochemical Pharmacology

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Blood-brain barrier and neuronal membrane transport of 6-[18F]fluoro-L-DOPA<sup>1</sup>Randa E. Yee<sup>a</sup>, David W. Cheng<sup>a</sup>, Sung-Cheng Huang<sup>a</sup>, Mohammad Namavari<sup>a</sup>, Nagichettiar Satyamurthy<sup>a</sup>, Jorge R. Barrio<sup>a</sup>

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## Abstract

The transport of 6-[<sup>18</sup>F]fluoro-L-3,4-dihydroxyphenylalanine ([<sup>18</sup>F]FDOPA) across the blood-brain barrier (BBB) and neuronal membranes was compared with that of L-3,4-dihydroxyphenylalanine (L-DOPA) in rats. The carotid injection method was used as a direct measurement of [<sup>18</sup>F]FDOPA, 1-[<sup>14</sup>C]-L-DOPA, and 3-[<sup>14</sup>C]-L-DOPA transport across the BBB, while isolated nerve terminals were used to examine neuronal membrane transport of [<sup>3</sup>H]-L-DOPA. [<sup>18</sup>F]FDOPA appeared to use the same large neutral amino acid carrier for BBB transport as L-DOPA and L-phenylalanine. **In addition, carbidopa [L-α-hydrazino-α-methyl-β-(3,4-dihydroxyphenyl)propionic acid] was found not to have direct interference with the transport carrier on the BBB, but indirectly inhibited aromatic L-amino acid decarboxylase (AAAD) activity in brain endothelium by depletion of pyridoxal phosphate, a necessary cofactor of the enzyme.** In striatal and cortical synaptosomes, [<sup>3</sup>H]-L-DOPA uptake was inhibited by non-radioactive L-DOPA, FDOPA, and 6-fluoro-L-*meta*-tyrosine (6-FMT). The inhibition was significantly greater in terminals isolated from the striatum than in those from the cerebral cortex. FDOPA, 6-FMT, and L-DOPA equally inhibited the neuronal transport of [<sup>3</sup>H]-L-DOPA. This suggests that FDOPA and 6-FMT compete with L-DOPA at similar transport sites at the neuronal membrane.

## Keywords

AAAD; Brain uptake index; L-DOPA; Carbidopa; Synaptosomes

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<sup>1</sup> **Abbreviations:** AAAD, aromatic L-amino acid decarboxylase; BBB, blood-brain barrier; BUI, brain uptake index; carbidopa, L-α-hydrazino-α-methyl-β-(3,4-dihydroxyphenyl)propionic acid; L-DOPA, L-3,4-dihydroxyphenylalanine; FDA, 6-fluorodopamine; [<sup>18</sup>F]FDOPA, 6-[<sup>18</sup>F]fluoro-L-3,4-dihydroxyphenylalanine; 4-[<sup>18</sup>F]FMT, 4-[<sup>18</sup>F]fluoro-L-*meta*-tyrosine; 6-[<sup>18</sup>F]FMT, 6-[<sup>18</sup>F]fluoro-L-*meta*-tyrosine; MeAIB, α-(methylamino)isobutyric acid; MPTP, 1-methyl-1,2,3,6-tetrahydropyridine; PD, Parkinson's disease; PET, positron emission tomography; and PLP, pyridoxal phosphate.

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