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O-METHYLATION OF N-OLEOYL-DOPAMINE IN VIVO

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In previous experiments we showed, that N-oleoyl-dopamine (OLDA), a novel oleic derivative of dopamine, diminishes the respiratory response to hypoxia in a dopamine-like manner. However, the dopaminergic system, although essential, is but one pathway involved in OLDA action. The molecule also is a TRPV1 (vanilloid) receptor ligand, so the question arises whether methylation to an *O*-methylated derivative, which may have more facilitatory docking properties to the TRPV1 structure, would occur in vivo. In the current study we attempted to determine the presence of *O*-methyl-*N*-oleoyl-dopamine (*O*-Me-OLDA), a reaction product, in the rat brain after intrarterial injection of OLDA in a dose of 40 mg/kg dissolved in 0.3 ml of DMSO, using a HPLC/MS method. One hour after the injection, the rats were sacrificed and brain homogenates made. We positively identified *O*-Me-OLDA in the assay. Therefore, we herein report that OLDA undergoes the process of methylation in vivo, which yields *O*-Me-OLDA. Moreover, in additional *in vitro* experiments using commercially available catechol-*O*-methyltransferase (COMT), the main enzyme in the metabolism of dopamine, we showed that methylation of OLDA *via* COMT is possible. We therefore submit that OLDA enters the metabolic pathways of dopamine giving a possibly bioactive compound with both dopamine- and vanilloid-like properties.