Study of the translocation mechanism of octopamine in the dopamine transporter. New insights from molecular simulation studies.

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A different *monoaminergic system (*MS) of fundamental importance in invertebrates compared with mammals is the ***octopaminergic system***, which exerts and regulates different central and peripheral processes by specific receptors and transporters. Despite the abundant information available on the functions of octopamine and their receptors in insect physiology, differences associated at octopamine re-uptake process in this neural system remain unexplored. Using AutoDock 4.0 (1) dopamine (DA) and octopamine (OA) were evaluated in the crystal structure of Drosophila melanogaster DAT (PDBid: 4XP1). The complex DAT/ligand was inserted into a POPC membrane, solvating with water model TIP3. The PBC and NPT ensemble was used to perform MD calculations for 20 ns using NAMD 2.6 (2). Finally steered molecular dynamics simulations fixed the center of mass of the ligands and a constant velocity protocol was employed, with a pulling velocity of 0.0001 Å/timestep, for 40 ns and SMD spring constant to each system was 4 Kcal/mol/Å2. Thus, force profile determination to DA and OA crossing DAT were obtained using steered molecular dynamics simulations. Our computational results show a similar profile to both substrates in DAT.

References.

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