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Psychedelics promote plasticity by directly binding to BDNF receptor TrkB

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Supplementary Table 3. Simulated systems. The table lists the variants of TM TrkB dimers embedded in POPC-CHOL lipid membranes, mole percentage of cholesterol (ρ_{CHOL}), the number of POPC (N_{POPC}) and cholesterol (N_{CHOL}) molecules in a membrane, the number of independent simulation repeats (N_{sim}), and the simulation length per repeat (t_{sim}). "WT", "Y433F.homo", and "V437A.homo" refer in respective order to the wild-type and homozygous Y433F and V437A variants of a TrkB TM dimer (residues 427-459). LSD, LSD^+: psychoactive (+)-LSD (in a 5R,8R configuration) in a neutral and protonated form. PSI, PSI^+: psilocin in a neutral and protonated form. Lisuride, Lisuride+: lisuride in a neutral and protonated form. CAR: cabergoline in a neutral form (pKa = 6.22). DHE: dihydroergotamine in a neutral form (pKa = 6.75).

System name	Protein variant	Drug type	ρ_{CHOL} (mol%)	N_{POPC}	N_{CHOL}	N_{sim}	t_{sim} (μs)
System 1#	WT	LSD	20	112	28	100	1
System 2▽	WT	LSD	20	112	28	20	2
System 3▽	WT	LSD^+	20	112	28	20	2
System 4▽	WT	PSI	20	112	28	20	2
System 5▽	WT	PSI^+	20	112	28	20	2
System 6▽	WT	Lisuride	20	112	28	20	2
System 7▽	WT	Lisuride$^+$	20	112	28	20	2
System 8▽	WT	CAR	20	112	28	20	2
System 9▽	WT	DHE	20	112	28	20	2
System 10▽	Y433F	LSD	20	112	28	20	2
System 11▽	V437A	LSD	20	112	28	20	2
System 12▽	Y433F	LSD^+	20	112	28	20	2
System 13▽	V437A	LSD^+	20	112	28	20	2
System 14▽	Y433F	PSI^+	20	112	28	20	2
System 15▽	V437A	PSI^+	20	112	28	20	2
System 16†	WT	LSD	20	112	28	1	0.06
System 17†	Y433F	LSD	20	112	28	1	0.06
System 18†	V437A	LSD	20	112	28	1	0.06
System 19†	WT	LSD^+	20	112	28	1	0.06
System 20†	Y433F	LSD^+	20	112	28	1	0.06
System 21†	V437A	LSD^+	20	112	28	1	0.06
System 22†	WT	PSI	20	112	28	1	0.06
System 23†	WT	PSI^+	20	112	28	1	0.06
System 24†	Y433F	PSI^+	20	112	28	1	0.06
System 25†	V437A	PSI^+	20	112	28	1	0.06
System 26†	WT	Lisuride	20	112	28	1	0.06
System 27†	WT	Lisuride$^+$	20	112	28	1	0.06
System 28†	WT	CAR	20	112	28	1	0.16
System 29†	WT	DHE	20	112	28	1	0.06
System 30§	WT	-	40	90	60	10	1
System 31§	WT	LSD	40	90	60	10	1
System 32§	WT	LSD^+	40	90	60	10	1
System 33§	WT	PSI^+	40	90	60	10	1
System 34§	WT	Lisuride$^+$	40	90	60	10	1

Simulations to explore LSD binding site and mode.

▽ Simulations to optimize the binding modes of each drug in the wild type and mutated TM TrkB dimers.

† FEP/HREX (free energy) simulations to estimate the drug binding affinities.

§ Simulations to explore the effect of cholesterol and the drugs on the conformation of the protein.