

Dopamine

Overview: Dopamine receptors (nomenclature as agreed by NC-IUPHAR Subcommittee on Dopamine Receptors, see Schwartz *et al.*, 1998) are commonly divided into D₁-like (D₁ and D₅) and D₂-like (D₂, D₃ and D₄) families, where the endogenous agonist is dopamine. Quinpirole is an agonist with selectivity for D₂-like receptors.

Nomenclature	D ₁	D ₂	D ₃	D ₄	D ₅
Other names	D _{1A}	–	–	–	D _{1B}
Ensembl ID	ENSG00000184845	ENSG00000149295	ENSG00000151577	ENSG00000069696	ENSG00000169676
Principal transduction	G _s , G _{olf}	G _{i/o}	G _{i/o}	G _{i/o}	G _s
Selective agonists	R(+)-SKF81297, R(+)-SKF38393	–	PD128907	PD168077, A412997 (Moreland <i>et al.</i> , 2005)	–
Selective antagonists	SCH23390, SKF83566, SCH39166	Raclopride, domperidone	S33084 (9.6, Millan <i>et al.</i> , 2000), nafadotride (9.5), (+)-S14297 (8.7, Millan <i>et al.</i> , 1994), SB277011 (7.5, Reavill <i>et al.</i> , 2000)	L745870 (9.3), U101958 (8.9, Schlachter <i>et al.</i> , 1997), L741742 (8.5)	–
Probes	[³ H]-SCH23390 (0.2 nM), [¹²⁵ I]-SCH23982 (0.7 nM)	[³ H]-Raclopride, [³ H]-spiperone	[³ H]-7-OH-DPAT, [³ H]-PD128907, [³ H]-spiperone	[³ H]-NGD941 (5 nM, Primus <i>et al.</i> , 1997), [¹²⁵ I]-L750667 (1 nM, Patel <i>et al.</i> , 1996), [³ H]-spiperone	[¹²⁵ I]-SCH23982 (0.8 nM) [³ H]-SCH23390 (0.5 nM)

The selectivity of many of these agents is less than two orders of magnitude. [³H]-Raclopride exhibits similar high affinity for D₂ and D₃ receptors (low affinity for D₄), but has been used to label D₂ receptors in the presence of a D₃-selective antagonist. [³H]-7-OH-DPAT has similar affinity for D₂ and D₃ receptors, but labels only D₃ receptors in the absence of divalent cations. The pharmacological profile of the D₅ receptor is similar to, yet distinct from, that of the D₁ receptor. The splice variants of the D₂ receptor are commonly termed D_{2S} and D_{2L} (short and long). The *DRD4* gene encoding the D₄ receptor is highly polymorphic in humans, with allelic variations of the protein from amino acid 387 to 515.

Abbreviations: (+)-7-OH-DPAT, (+)-7-hydroxy-2-aminopropylaminotetralin; (+)-S14297, (+)-7-(N,N-dipropylamino)-5,6,7,8-tetrahydronaphtho(2,3b)dihydro-2,3-furane; L741742, 5-(4-chlorophenyl)-4-methyl-3-(1-[2-phenethyl]piperidin-4-yl)isoxazole; L745870, 3-[[4-(4-chlorophenyl)piperazin-1-yl]methyl]-1H-pyrrolo[2,3-b]pyridine; L750667, iodinated L745870; NGD941, 2-phenyl-4(S)-(4-[2-pyrimidinyl]-[piperazin-1-yl]-methyl)-imidazole dimaleate; PD128907, R-(+)-trans-3,4,4a,10b-tetrahydro-4-propyl-2H,5H-[1]benzopyrano [4,3-b]-1,4-oxazine-9-ol; PD168077, N-methyl-4-(2-cyanophenyl)piperazinyl-3-methylbenzamide; R(+)-SKF38393, R-(+)-7,8-dihydroxy-1-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine; R(+)-SKF81297, R-(+)-6-chloro-7,8-dihydroxy-1-phenyl-2,3,4,5-tetrahydro-1H-benzazepine; S33084, (3aR,9bS)-N[4-(8-cyano-1,3a,4,9b-tetrahydro-3H-benzopyrano[3,4-c]pyrrole-2-yl)-butyl] (4-phenyl)benzamide; SB277011, trans-N-(4-[2-[6-cyano-1,2,3,4-tetrahydroisoquinolin-2-yl]ethyl]cyclohexyl)-4-quinolininecarboxamide; SCH23390, 7-chloro-8-hydroxy-3-methyl-5-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine; SCH23982, 8-iodo-2,3,4,5-tetrahydro-3-methyl-5-phenyl-1H-3-benzazepine; SCH39166, (-)-trans-6,7,7a,8,9,13b-hexahydro-3-chloro-2-hydroxy-N-ethyl-5H-benzo[d]naphtho-(2,b)azepine; SKF83566, (-)-7-bromo-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-3-benzazepine; U101958, 3-isopropoxy-N-methyl-N-(1-[phenylmethyl]-4-piperidinyl)-2-pyridinylamine

Further Reading

- Bjorklund A, Dunnett SB (2007). Dopamine neuron systems in the brain: an update. *Trends Neurosci* 30: 194–202.
- Bjorklund A, Dunnett SB (2007). Fifty years of dopamine research. *Trends Neurosci* 30: 185–187.
- Carlsson A, Carlsson ML (2008). Adaptive properties and heterogeneity of dopamine D₂ receptors – pharmacological implications. *Brain Res Rev* 58: 374–378.
- De Mei C, Ramos M, Iitaka C, Borrelli E (2009). Getting specialized: presynaptic and postsynaptic dopamine D₂ receptors. *Curr Opin Pharmacol* 9: 53–58.
- Giorgioni G, Piergentili A, Ruggieri S, Quaglia W (2008). Dopamine D₅ receptors: a challenge to medicinal chemists. *Mini Rev Med Chem* 8: 976–995.
- Hoebel BG, Avena NM, Rada P (2007). Accumbens dopamine–acetylcholine balance in approach and avoidance. *Curr Opin Pharmacol* 7: 617–627.
- Horowski R (2007). A history of dopamine agonists. From the physiology and pharmacology of dopamine to therapies for prolactinomas and Parkinson's disease – a subjective view. *J Neural Transm* 114: 127–134.
- Iversen SD, Iversen LL (2007). Dopamine: 50 years in perspective. *Trends Neurosci* 30: 188–193.
- Joyce JN, Millan MJ (2007). Dopamine D₃ receptor agonists for protection and repair in Parkinson's disease. *Curr Opin Pharmacol* 7: 100–105.
- Le Foll B, Gallo A, Le Strat Y, Lu L, Gorwood P (2009). Genetics of dopamine receptors and drug addiction: a comprehensive review. *Behav Pharmacol* 20: 1–17.
- Marsden CA (2006). Dopamine: the rewarding years. *Br J Pharmacol* 147: S136–S144.
- Ohara K (2007). The n-3 polyunsaturated fatty acid/dopamine hypothesis of schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry* 31: 469–474.
- Redgrave P, Gurney K (2006). The short-latency dopamine signal: a role in discovering novel actions? *Nat Rev Neurosci* 7: 967–975.

- Rollo CD (2009). Dopamine and aging: intersecting facets. *Neurochem Res* **34**: 601–629.
- Rolls ET, Loh M, Deco G, Winterer G (2008). Computational models of schizophrenia and dopamine modulation in the prefrontal cortex. *Nat Rev Neurosci* **9**: 696–709.
- Schwartz J-C, Carlsson A, Caron M, Scatton B, Civelli O, Kebabian JW et al. (1998). Dopamine receptors. In: Girdlestone D (ed.). *The IUPHAR Compendium of Receptor Characterization and Classification*. IUPHAR Media: London, pp. 141–151.
- Scott L, Aperia A (2009). Interaction between N-methyl-D-aspartic acid receptors and D1 dopamine receptors: an important mechanism for brain plasticity. *Neuroscience* **158**: 62–66.
- Stanwood GD (2008). Protein-protein interactions and dopamine D2 receptor signaling: a calcium connection. *Mol Pharmacol* **74**: 317–319.
- Thomas MJ, Kalivas PW, Shaham Y (2008). Neuroplasticity in the mesolimbic dopamine system and cocaine addiction. *Br J Pharmacol* **154**: 327–342.
- Wood MD, Wren PB (2008). Serotonin-dopamine interactions: implications for the design of novel therapeutic agents for psychiatric disorders. *Prog Brain Res* **172**: 213–230.

References

- Millan MJ et al. (1994). *Eur J Pharmacol* **260**: R3–R5.
- Millan MJ et al. (2000). *J Pharmacol Exp Ther* **293**: 1048–1062.
- Moreland RB et al. (2005). *Pharmacol Biochem Behav* **82**: 140–147.
- Patel S et al. (1996). *Mol Pharmacol* **50**: 1658–1664.
- Primus RJ et al. (1997). *J Pharmacol Exp Ther* **282**: 1020–1027.
- Reavill C et al. (2000). *J Pharmacol Exp Ther* **294**: 1154–1165.
- Schlachter SK et al. (1997). *Eur J Pharmacol* **322**: 283–286.