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Dopamine receptors

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Introduction

Dopamine (DA) is an important neurotransmitter. It is a catecholamine belonging to the group of monoamines, i.e. possessing a single amine (-NH_2) group. As other catecholamines, such as norepinephrine (noradrenaline) and epinephrine (adrenaline), it contains a nucleus of catechol (a benzene ring possessing two hydroxyl groups) and a side chain of ethylamine (see Fig. 1). DA is directly used in therapeutic for its effects on the cardiovascular and renal systems. Strategies to modulate DA transmission or to act on DA receptors directly are also used for treatment of central dysfunction, such as schizophrenia, Parkinson's disease and hyperprolactinemia. It is thought also that DA play a critical role in various functions, including motor activity, cognition, motivation, emotion, drug addiction and other pathological conditions.

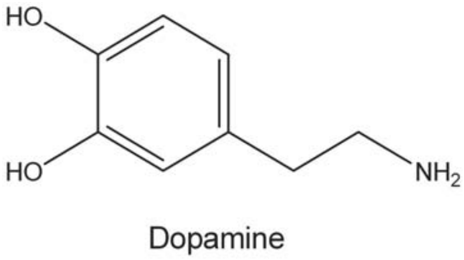

Figure 1.
Molecular structure of Dopamine (DA)

DA synthesis and degradation

Blaschko was the first to propose that DA was a precursor for norepinephrine and epinephrine synthesis[1]. Then, Carlsson and collegues proposed that DA had an independent role in addition to its precursor role[2]. They made the observation that DA was present in large quantities in the basal ganglia and was involved in the Parkinson-like symptoms occurring following the administration of reserpine, a catecholamine-depleting drug. The precursor for all catecholamine synthesis is tyrosine, an aromatic amino acid. The first step is the hydroxylation of L-tyrosine to L-3,4-dihydroxyphenylalanine (L-DOPA). This reaction is catalyzed by the enzyme called tyrosine hydroxylase (TH, or tyrosine 3-monooxygenase)[3]. Tyrosine hydroxylase is the rate-limiting enxyme in the catecholamine synthesis. α-methyl-*p*-tyrosine (AMPT) is a TH inhibitor, that will deplete both central and peripheral catecholamines. The formation of DA from DOPA occurs by DOPA decarboxylation by the enzyme called aromatic L-amino acid decarboxylase (AADC). Inhibitors of AADC are 3-hydroxybenzyl-hydrazine (NSD 1015) and α-methyl-dopa-hydrazine (carbidopa). Once synthetized DA can be converted to norepinephrine by the enzyme called dopamine β-hydroxylase (DBH). DA can also be stored in neuronal vesicule. The transport of DA occurs through monoamine vesicular transporter that can be inhibited by drugs such as tetrabenazine or reserpine. Reserpine has been used as an antihypertensive agent, but its use has been limited because of its sedating effects. The release of DA in the synapse occurs through vesicular exocytosis. After its release, DA will act on target DA receptors (see below) and will be inactivated. The main inactivation process is through reuptake that will occur through dopamine transporter (DAT)[4,5]. Drugs that inhibit the DAT, such as cocaine, produce strong elevation of DA levels. There are also enzymatic degradative pathways that are involving catechol-O-methyltransferase (COMT) and monoamine oxydase (MAO) that will not be developed here.

DA receptors

It has long been thought that only two receptor subtypes, the D1 and D2 receptors family, which were initially defined on the basis of their distinct transduction mechanisms and pharmacological profiles[6,7], were mediating the pleiotropic actions of dopamine. At the time, it was recognized that the target of antiparkinsonian drugs and of antipsychotic drugs was the D_2 receptor and D_2 receptor gene was the first to be cloned among dopamine receptors[8,9]. Almost at the same time of the cloning of the dopamine D_1 receptor (DRD_1)[10-13], three novel dopamine receptor subtypes were identified, the DRD_3[14], the DRD_4[15] and DRD_5[16]. The DRD_1 and DRD_5 belong to the D1-family, whereas the DRD_2, DRD_3 and DRD_4 belong to the D2-family. The main characteristics of D1 vs D2 families are presented in Table 1. The D1-like receptors are intronless genes that stimulate the enzyme adenylyl cyclase increasing the production of the second messenger cAMP, whereas the D2-like genes are with exons and classically produces the opposite effect on cAMP formation. The situation is far more complex *in vivo*, as it is clear that those receptors can dimerize and there are evidence that DRD_1 and DRD_3 can have synergistic effects[17]. Moreover, the heteromers can have specific transduction pathways that could be of importance when analyzing downstream effects of DA receptors stimulation[18,19].

Table 1:
Summary of dopamine receptor subtypes

	Receptor subfamily				
	D1-like		D2-like		
	D_1	D_5	D_2	D_3	D_4
Gene[a]	DRD1	DRD5[b]	DRD2	DRD3	DRD4
Human chromosome	5q35.1	4p15.2	11q23	3q13.3	11p15.5
Structural information	Intronless	Intronless	7 exons[c]	7 exons[c]	4 exons[c]
Number of aminoacids[d]	446 (h) 446 (r)	477 (h) 475 (r)	D_{2L}: 443 (h), 444 (r) D_{2S}: 414 (h), 415 (r)	400 (h) 446 (r)	387-515[e] (h) 386 (r)
Signal transduction mechanisms[f]	cAMP (+) $[Ca^{2+}]_I$ (+ or 0)	cAMP (+)	cAMP (-) $[Ca^{2+}]_I$ (+/-) K^+ outward curr. (+) AA release (+)	cAMP (-), Ca^{2+} curr. (-) (-) MAP kinase (+) K^+ outward curr. (+)	cAMP (-), Ca^{2+} curr. (-) K^+ outward curr. (+) AA release (+)

[a] Nomenclature recommended by the Human Genome Organization; [b] Two pseudogenes have been identified; [c] Number of exons in the coding sequence; [d] h, human; r, rat; [e] The D_4 receptor contains a highly variable sequence, see text.; [f] +, stimulation; -, inhibition; 0, no effect; curr., currents.

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Use of DA ligands in therapeutics

The use of ligands modulating DA transmission has been already reviewed elsewhere and will be only briefly introduced here[20].
In neurology, Parkinson's disease is induced by the death of dopamine neurons in the substantia nigra. A therapeutic strategy consists at compensating for this DA depletion. The first strategy has been to use the dopamine precursor, 3,4-dihydroxyphenylalanine (L-DOPA)[21,22]. The use of D2-like agonists such as apomorphine, pramipexole, ropinirole, piribedil, rotigotine, and the ergot alkaloids pergolide, bromocriptine and cabergoline is also effective to attenuate the clinical symptoms of Parkinson's disease[23-26]. Restless leg syndrome is also treated successfully with dopamine agonists ligands[27]. Schizophrenia is a severe mental health disorder that is related to DA dysfunction[28,29]. Ligands effective to treat schizophrenia are blocking D2-like receptors[30]. It appears that the antipsychotic effect is not mediated by the blockade of the DRD_4, since selective DRD_4 antagonists were ineffective in schizophrenics[31,32]. The respective role of DRD_2 vs DRD_3 in antipsychotic efficacy remains to be tested by selective ligands[33]. The use of DRD_3 ligands has been proposed as a novel strategy for treatment of drug dependence[34] and notably nicotine dependence[35-37], but no validation has been performed yet in humans. It is thought also that DA be involved in other psychiatric disorders. Notably, its involvement in Attention-Deficit Hyperactivity Disorder is suspected because the drugs (such as methylphenidate) that are used for treatment of this condition are increasing DA transmission[38]. The role on the periphery should not be overlooked. And DA receptor may participate to some form of arterial hypertension[39].

A) DRD_1

Initially, in the absence of selective radioligands, the distribution of dopamine receptors in the brain has been assessed by *in situ* hybridization. DRD_1 mRNA are the most abundant, expressed in all dopaminergic neuron-projecting areas of the nigrostriatal and mesolimbocortical pathways[40]. DRD_1 receptor mRNA are also detected in hypothalamus and thalamus. In other regions where D1-like binding sites are detected, such as the substantia nigra, no DRD_1 mRNA is found, suggesting that this receptor is present on afferences. This was later confirmed by using a selective antibody allowing the localization of the protein[41,42]. The DRD_1 mRNAs prominently segregate in distinct striatal neuronal populations, expressing the substance P/dynorphin- and the DRD_3[43-45]. The DRD_1 localization and its postsynaptic function critically depend on the dopamine tone, the receptor being internalized after challenge by DRD_1 agonists or following elevation of dopamine levels induced by psychostimulant drugs administration[46,47].
Various agonists and antagonists for studying DRD_1 are available (see Fig. 2). Several agonists belong to the family of 1-phenyltetrahydrobenzazepines. The most used DRD_1 agonist is called SKF 38393 and is a partial DRD_1 agonist (as SKF 82526). SKF 81297 is a full D_1 receptor agonist (6-Chloro-2,3,4,5-tetrahydro-1-phenyl-1*H*-3-benzazepine hydrobromide). SKF 82958 is another DRD_1 agonist. The classical DRD_1 antagonist is called SCH 23390[48]. A brominated analog has also been developed and is called SKF 83566[48]. It should be noted that currently there is no ligands that can discriminate between DRD_1 and DRD_5. Therefore, the use of mutant mice is useful to delineate what is respective contribution of DRD_1 vs DRD_5 in the effects of D1-like ligands. It is possible that the use of D1 ligands could have some utility for treatment of Parkinson's disease or possibly drug addiction[49-51]. However, few studies have been conducted and no clear conclusions can be drawn at this point of the utility of D1 ligands in therapeutics.

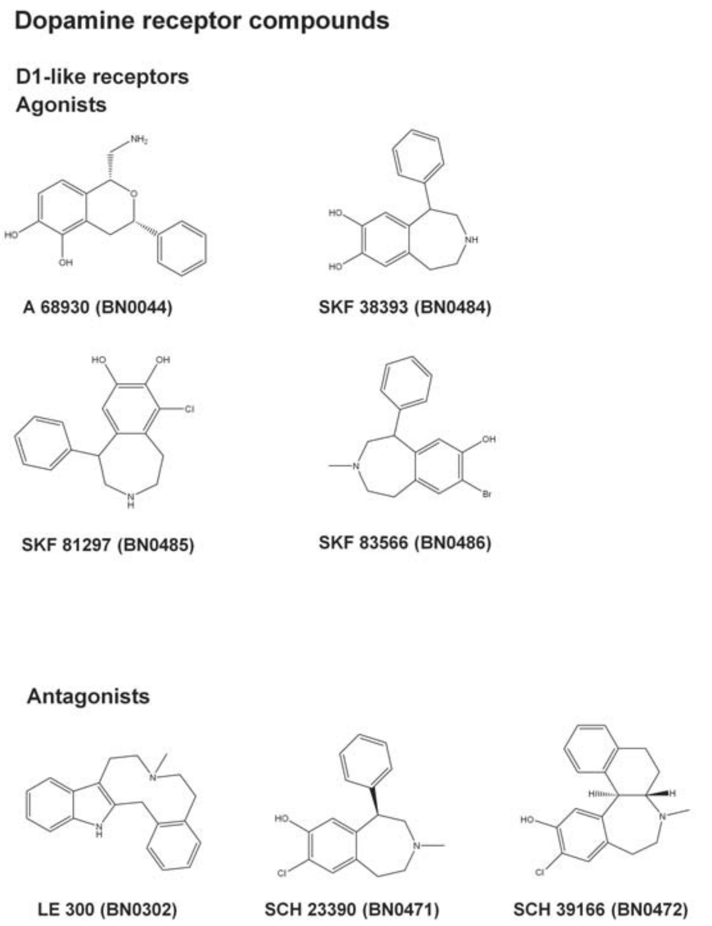

Figure 2.
Structures of some Dopamine D1-like agonists and antagonists (Bold text denotes compound available from BIOTREND with catalogue numbers).

B) DRD_2

As DRD_1, DRD_2 mRNA is also abundantly expressed in all dopaminergic terminals areas[52,53]. DRD_2 expression in the brain is dependent upon dopamine inputs, being increased after denervation in 6-hydroxydopamine (6-OHDA)-lesioned rats[54] or 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-intoxicated monkeys[55], or after chronic treatment with antipsychotic drugs[56]. D_2 receptor mRNAs prominently segregate in the enkephalin-containing neurons[43], but there is also some co-localization with DRD_1[57].
In contrast with DRD_1 mRNA, DRD_2 mRNA is less abundant in cortical areas, but highly expressed in the dopamine cell bodies of the substantia nigra and ventral tegmental area. Studies with DRD_2 KO mice demonstrate that DRD_2 is a major functional presynaptic autoreceptor controlling phasic dopamine neuron activity[58-60] and evidence indicates that the short D_{2S} variant serves autoreceptor functions[61-63].
In contrast to DRD_1, many DRD_2 ligands are available in therapeutics. Bromocriptine and apomorphine are widely used as D_2 agonists. Bromocriptine is used for treatment of hyperprolactinemie (as prolactine levels are controlled by dopamine transmission in the pituitary gland) and apomorphine has been used to induce vomiting in case of drug overdosage. The classicals antipsychotic drugs (haloperidol, raclopride, sulpiride) are all blocking DRD_2 receptors. Most D_2 antagonist do not discriminate well between DRD_2 and DRD_3. L741626 is a preferential DRD_2 receptor antagonist (3-[4-(4-chlorophenyl)-4-hydroxyperidin-l-yl]methyl-1*H*-indole).

C) DRD_3

In marked contrast with DRD_1 and DRD_2, the localization of DRD_3 is restricted to certain dopamine terminal areas. The DRD_3 is expressed in the most ventral parts of the striatal complex (nucleus accumbens) and in other limbic areas[14,53]. DRD_3 are expressed at lower levels in the dorsal striatum and various cortical areas, including the frontal cortex, of non-human primates[64] and humans[65,66], but the dorsal striatum is almost entirely devoid of DRD_3 expression in rodents. The DRD_3 are also found in the islands of Calleja, which are small neuronal structures embedded in the nucleus accumbens and olfactory tubercle, the cerebellum and other brain areas (see[45,67]). One important aspect of DRD_3 localization is that it is expressed on dopaminergic neurons[45] and that its expression is controlled by Brain Derived Neurotrophic Factor (BDNF) (see[68-70]). In 6-OHDA-lesioned rat, DRD_3 receptor expression is decreased in the shell of the nucleus accumbens of the denervated side[68]. D_3 receptor density is also decreased in a non-human primate model of Parkinson's disease, i.e. in MPTP-treated monkeys[64] or in patients suffering from this disease[71]. Those changes are opposite to those described with DRD_2, and likely due to the deprivation of BDNF. D_3 receptor mRNA and protein are also elevated in the post-mortem brain of human cocaine overdose fatalities[72,73]. Interestingly, BDNF and DRD_3 expressions increases following various drugs exposure, suggesting that BDNF-DRD_3 pathway may be implicated in drug addiction processes[70,74-77].

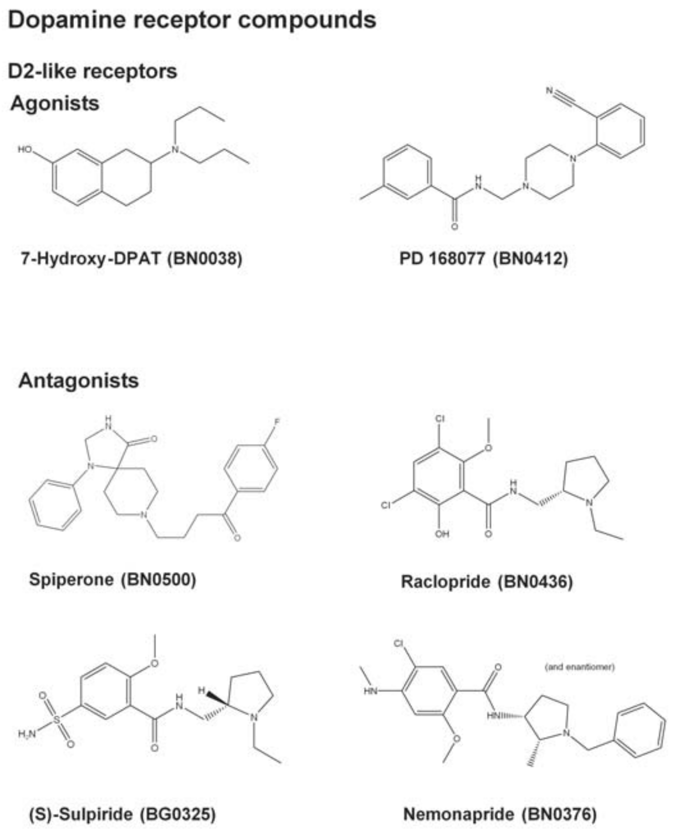

Figure 3.
Structures of some Dopamine D2-like agonists and antagonists (Bold text denotes compound available from BIOTREND with catalogue numbers).

There is no agonists that are highly selective for DRD_3 vs DRD_2. D_{2-3} receptor agonist quinpirole, PD 128907, pergolide and 7-OH-DPAT appears the most DRD_3 selective among the agonists (see Fig. 3). Recently, some selective DRD_3 antagonists have become available. Some of those antagonists have around 100 fold selectivity of DRD_3 vs DRD_2. The SB 277011-A has been one of the best characterized. It is a highly selective DRD_3 antagonist, with 100 folds higher affinity to DRD_3 than DRD_2[78]. Interestingly, there is no effect of DRD_3 blockade on spontaneous locomotion or stimulant-induced hyperlocomotion (up to 42.3 mg/kg SB-277011-A) and no induction of cataleptogenic effects or increase of plasma prolactin levels (up to 78.8 mg/kg SB-277011-A). This clearly demonstrates that DRD_3 vs DRD_2 are producing very different behavioural effects and that blocking DRD_3 may be producing less side-effects than blocking DRD_2. ST 198 is another DRD_3 antagonist that has been tested in non-human primates[79] and rodents[80]. NGB 2904 has been explored extensively in drug addiction models[81]. Several groups have recently reported the development of selective DRD_3 ligands (for example *R*- and *S-22* compounds recently discovered[82]). DDR_3 partial agonists have also been developed. Among those, BP 897 has been proposed to be useful for treatment of drug addiction[36,83]. It should be noted that at high doses, BP 897 is also acting as DRD_2 antagonist resulting in effects such as, disruption in the responding in nicotine discrimination test at the dose of 10 mg/kg, catalepsy at the dose of 12 mg/kg in rats, and DRD_2 occupancy with an ED_{50} of 15 mg/kg[74,83] and that BP 897 may also act on other targets[84]. But, clearly some of BP 897 effects are DRD_3 mediated since abolished in DRD_3-deficient mice[85], but BP 897 has been shown to be unable to modulate nicotine-taking or cue-induced reinstatement of nicotine seeking[37] and may not be as effective as initially thought.

D) DRD_4

DRD_4 mRNA is found in various brain regions at low density compared with DRD_1 or DRD_2. It is most abundant in retina[86], cerebral cortex, amygdala, hypothalamus and pituitary, but sparses in the basal ganglia, as assessed by RT-PCR and Northern blot[87]. This was confirmed by using higher resolution techniques, such as *in situ* hybridization[88-90] and immunohistochemistry[91]. These studies notably confirmed the presence of DRD_4 in both pyramidal and non-pyramidal cells of the cerebral cortex, particularly layer V, and in the hippocampus. In cerebral cortex and hippocampus, non-pyramidal cells are γ-aminobutyric acid (GABA)-producing neurons[91]. DRD_4 is also present in granule cells of the cerebellum[92].
At the discovery of the DRD_4, it has been reported that clozapine had a high affinity for DRD_4[15]. During the following years, there was a great interest at developing selective selective DRD_4 antagonists for the treatment of schizophrenia, as those compounds could retain antipsychotic efficacy without the side-effects induced by DRD_2 blockade. Those efforts have led to the clinical trials evaluating the efficacy of L-745,870 and sonepiprazole, two selective DRD_4 antagonists. Unfortunately, both trials were ineffective in schizophrenics[31-32]. Since that time, no clear use of DRD_4 ligands has emerged. Recent rodent studies have implicated the DRD_4 in emotional learning[93] and drug addiction (see[94] for review).

Table 2:
Dopamine receptor affinity for antagonists

Drug	Affinity K_i, nM Receptor subtype				
	D_1	D_2	D_3	D_4	D_5
Non selective:					
Amisulpride	>1,000	2.8	3.2	>1,000	>1,000
(+) Butaclamol	5	1	4.5	45	6.1
Chlorpromazine	35	5	4	16	33
Clozapine	35	145	238	29	343
Eticlopride	>10,000	0.1	0.25	25	>10,000
Flupentixol, cis	4	1.5	2.5	-	12
Fluphenazine	6	0.6	0.8	30	8
Haloperidol	150	2	5	6.5	170
Olanzapine	48	30	41	36	74
Pimozide	>10,000	3	4	30	-
Quetiapine	390	380	260	1,050	-
Raclopride	>50,000	1	1.2	2,100	-
Remoxipride	>10,000	588	1,600	3,200	-
Risperidone	560	6	11	16	560
Spiperone	380	0.08	0.4	0.1	2,400
Sulpiride	>10,000	38	60	280	>10,000
Thioridazine	34	7	8	10	300
YM-09151-2	2,600	0.05	0.09	0.13	-
D_1-/D_5-selective: (a)					
SCH 23390	0.4	1,400	1,450	2,910	0.5
D_2-selective:					
Domperidone	>10,000	0.9	13	90	-
L741,626	790	4	63	320	630
D_3- selective:					
BP 897	3,000	61	0.9	300	-
GR 103,691	-	24	0.4	81	-
GR 218,231	>1,000	63	1	10,000	-
Nafadotride	890	3	0.3	1,780	-
NGD 2904	>10,000	217	1.4	>5,000	>10,000
S 33084	500	32	0.3	2,000	1,300
SB-277011-A	>1,000	1,030	10.5	>1,000	>1,000
U 99194A	-	2,280	223	>10,000	-
D_4-selective:					
FAUC 213	5,500	>3,400	5,300	2.2	-
L745,870	-	1,210	2,300	3.4	-
L750,667	-	>1,700	>4,500	0.5	-
NGD 94-1	>10,000	2,230	>10,000	4	-
RBI-257	2,830	568	145	0.33	>10,000
U 101387	>8,000	1,820-5,000	>2,500	4-29	-

[a] Drugs that are selective for D_1 and D_5 receptors with respect to D_2, D_3 and D_4 receptors, but that do not distinguish D_1 from D_5 receptors.

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Therefore, it is possible that some psychiatric disorders may be improved by the use of DRD_4 ligands.
Various ligands are available. Among the DRD_4 antagonists: L745,870 and L-741,741[93,95]. PD 168,077 is a DRD_4 agonist[96-98] (see Fig. 3).

E) DRD_5

The distribution of DRD_5 has also been difficult to assess by *in situ* hybridization studies, because of the sequence similarities between DRD_5 and DRD_1 and the two DRD_5 pseudogenes[16]. Studies in rat showed that DRD_5 mRNA is restricted to the hippocampus, mammillary bodies and a thalamic nucleus initially identified as the anterior pretectal nucleus[99] and subsequently identified as the parafascicular nucleus[100]. Higher and more organized levels of DRD_5 mRNA expression were found in the human hippocampus, subicular complex and temporal cortex[89]. Immunohistochemical studies of the DRD_5 protein largely confirmed and extended *in situ* hybridization studies, but also showed significant differences between the localization of DRD_1 and DRD_5 receptors at cellular levels. Thus, in the cortical pyramidal cells, whereas DRD_1 are concentrated in dendritic spines, DRD_5 are more localized in dendritic shafts[101]. In the striatum, DRD_1 and DRD_5 are both present in medium-size spiny GABA-containing neurons, but only DRD_5 are present in large cholinergic interneurons[101]. At the ultrastructural level, DRD_1 are present on spines making asymmetrical, presumably non-dopaminergic synapses, whereas both DRD_1 and DRD_5 are present at small postsynaptic densities of symmetrical synapses typical of dopaminergic synapses[102]. Unfortunately at this point, no DRD_5 selective ligand is available.

Conclusion

DA is an important neurotransmitter that is involved in major neurologic (Parkinson's disease) and psychiatric (Schizophrenia) disorders. It is likely that DA also plays a critical role in other disorders such as depression and drug addiction, but it has not been possible yet to find a clear use of DA ligands for those indications. The ligands that are currently used in therapeutics are mostly targeting the D2-family. It appears that targeting the D1-family could also have therapeutic utility, but this has not been explored yet enough. Notably, the use of partial agonists, could have some uti-lity and be better tolerated. The discovery that there are five dopamine receptor subtypes has suscited numerous studies aiming at the characterization of these receptor subtypes and of their physiological roles. Among the emerging role is the fact that DRD_3 appears to contribute to the motivational aspects and/or the effects of cues over behaviours. Much more remains to do in order to delineate the role of DRD_4 and DRD_5. The progress in developing highly selective DA ligands will allow in the next future delineate the role of those receptors in the brain and hopefully develop novel therapeutic tools.

Acknowledgment

Information on distribution of DA receptors and Tables 1 and 2 have been reproduced with permission from[103]. Sokoloff P., Leriche L. and Le Foll B. "Dopamine Receptors Structure, function and implication in psychiatric disorders." Chapter in Psychopharmacogenetics, P. Gorwood & M Hamon eds, Springer Science = Business Media, Inc., New York 2006, pp357-419 (With kind permission of Springer Science and Business Media).

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Dopamine receptor compounds

D1-like receptors (D_1, D_5)

Cat. No.	Product	Category
BN0044	A 68930 hydrochloride	Potent, selective D1-like agonist
BN0601	CY 208-243	Dopamine D_1 agonist
BN0185	Dihydrexidine hydrochloride	Selective D_1 agonist
BN0484	SKF 38393 hydrochloride	Selective D1-like partial agonist
BN0485	SKF 81297 hydrobromide	Selective D1-like agonist
BN0486	SKF 83566 hydrobromide	Potent, selective D1-like agonist
BN0487	SKF 83822 hydrobromide	Selective D1-like agonist
BN0488	SKF 83959 hydrobromide	D1-like partial agonist
BN0302	LE 300	Potent D_1 antagonist
BN0471	SCH 23390 hydrochloride	Potent, selective D1-like antagonist
BN0472	SCH 39166 hydrobromide	Potent, selective D1-like antagonist

D2-like receptors (D_2, D_3, D_4)

Cat. No.	Product	Category
BN0118	Bromocriptine mesylate	Selective D2-like agonist
BN0186	Dihydroergocristine mesylate	D2-like partial agonist, partial α agonist, 5-HT antagonist
BN0187	Dihydroergotamine mesylate	D2-like partial agonist, partial α agonist, 5-HT antagonist
BN0038	7-Hydroxy-DPAT hydrobromide	D_3 agonist
BN0410	(+)-PD 128907 hydrochloride	D_3 agonist
BN0412	PD 168077 maleate	High affinity, selective D_4 agonist
BG0545	Pergolide mesylate	D_1/D_2 agonist
BN0420	Piribedil hydrochloride	D2-like agonist
BN0636	(-)-Quinpirole hydrochloride	Selective D2-like agonist
BG0550	Ropinirole hydrochloride	Selective D2-like agonist
BN0446	Roxindole hydrochloride	D_2 agonist, affinity for 5-HT_{1A}, D_3/D_4, 5-HT uptake inhibitor
BG0560	Terguride	Partial D_2 agonist
BG0361	Amisulpride	Selective D_2/D_3 antagonist
BG0007	Acepromazine maleate	D2-like antagonist
BG0154	Clozapine	D_2/D_4 antagonist, 5-HT and muscarinic antagonist
BG0172	Domperidone	D_3 antagonist
BN0016	3'-Fluorobenzylspiperone maleate	D2-like ligand
BG0211	Haloperidol	D2-like antagonist, σ ligand
BG0253	Metoclopramide hydrochloride	D_2 antagonist, weak 5-HT_3 antagonist
BN0376	Nemonapride	Highly potent D2-like antagonist, 5-HT_{1A} agonist
BG0359	Opipramol dihydrochloride	D_2 antagonist, 5-HT antagonist and σ ligand
BG0551	Paliperidone	D_2 antagonist and 5-HT_2 antagonist
BG0381	Pimozide	Dopamine D_2 antagonist, high affinity 5-HT_7 ligand
BN0436	Raclopride	Selective D_2/D_3 antagonist
BG0386	Remoxipride hydrochloride	Selective D2-like antagonist
BG0309	Risperidone	D_2 antagonist and 5-HT_2 antagonist
BG0324	(RS)-Sulpiride	Selective D2-like antagonist
BG0325	(S)-(-)-Sulpiride	Selective D2-like antagonist
BN0500	Spiperone	Very potent D2-like antagonist, 5-HT_{2A} antagonist
BG0338	Tiapride hydrochloride	D2-like antagonist
BN0528	U 99194 maleate	Potent, selective D_3 antagonist

Non-selective

Cat. No.	Product	Category
BG0043	R-(-)-Apomorphine hydrochloride	Non-selective dopamine agonist
BG0173	Dopamine hydrochloride	Dopamine agonist
BG0198	Fluphenazine	Potent D_1/D_2 antagonist
BG0337	Thioridazine hydrochloride	Non-selective dopamine antagonist

Related Radioligands

Cat. No.	Product	Category
ART-0808	[^{3}H]-R-(-)-Apomorphine hydrochloride	Non-selective dopamine agonist
ART-0519	[^{3}H]-Clozapine	D_2/D_4 antagonist, 5-HT and muscarinic antagonist
ART-0651	[^{3}H]-Cocaine	Dopamine uptake inhibitor
A3-AI-062	[^{125}I]-Dihydroergocryptine	Dopamine agonist
ART-0235	[^{3}H]-Levodopa	Dopamine precursor
ART-1401	[^{3}H]-FLB-457	D_2antagonist
ART-1198	[^{3}H]-MFZ 2-12	Dopamine transporter
ART-0849	[^{3}H]-MPP^+ acetate	Neurotoxin
ART-0150	[^{3}H]-MPP^+ iodide	Neurotoxin
ART-0811	[^{3}H]-R-(-)-N-Propylnorapomorphine hydrochloride	Non-selective dopamine agonist
ART-0425	[^{3}H]-Tyramine hydrochloride	Dopamine transporter

Dopamine receptor modulators/ metabolism

Cat. No.	Product	Category
BG0026	Amantadine hydrochloride	Dopamine releaser
BG0103	Benserazide hydrochloride	L-aromatic amino acid decarboxylase inhibitor
BG0117	Bupropion hydrochloride	Adrenergic, 5-HT and dopamine transport inhibitor
BG0127	Carbidopa	L-aromatic amino acid decarboxylase inhibitor
BG0405	(R)-(-)-Deprenyl hydrochloride	MAO-B inhibitor
BG0500	Fusaric acid	Dopamine β-hydroxylase inhibitor
BN0219	GBR 12783 dihydrochloride	Potent, selective dopamine uptake inhibitor
BN0220	GBR 12909 dihydrochloride	Selective dopamine uptake inhibitor, potent σ ligand
BN0221	GBR 12935 dihydrochloride	Selective dopamine uptake inhibitor
BN0222	GBR 13069 dihydrochloride	Potent dopamine uptake inhibitor
BG0214	Hydralazine hydrochloride	MAO-A/MAO-B inhibitor
BN0274	Indatraline hydrochloride	Potent dopamine (monoamine) uptake inhibitor
BG0419	Levodopa	Dopamine precursor
BG0252	α-Methyldopa	L-aromatic amino acid decarboxylase inhibitor
BG0261	Moclobemide	MAO-A inhibitor
BP0181	MSH release inhibiting factor	Increases brain dopamine levels, α-MSH inhibitor
BN0422	Pirlindole mesylate	MAO-A inhibitor
BN0516	Tetrindole mesylate	MAO-A inhibitor
BN0515	Tetrabenazine	Potent vesicular monoamine uptake inhibitor
BN0679	L-3,4-Dihydroxyphenylalanine methyl ester hydrochloride	Antiparkinsonian agent and precursor to L-DOPA
BN0709	MPTP hydrochloride	Dopaminergic neurotoxin
BN0710	6-Hydroxydopamine hydrobromide	Catecholaminergic neurotoxin

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