ISSN 0253-9756 Acta Pharmacol Sin 中国药理学报 1999 Oct; 20 (10): 884 – 888
http://www.simm.ac.cn; www.chinainfo.gov.cn/periodical

Comparison of 12-chloroscoulerine enantiomers on animal behavior to dopamine receptors[1]

CHEN Li-Juan, ZHOU Qi-Ting, DONG Zhao-Jun, YU Lei-Ping, JIN Guo-Zhang[2]
(*Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 200031, China*)

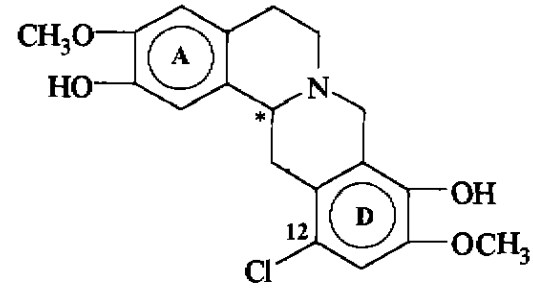
KEY WORDS 12-chloroscoulerine; *l*-stepholidine; apomorphine; dopamine D_1 receptors; Sch23390; radioligand assay; stereotyping; catalepsy; locomotion

ABSTRACT

AIM: To compare the pharmacological characteristics of 12-chloroscoulerine (CSL) enantiomers to dopamine (DA) receptors. **METHODS**: Radioligand receptor binding assay with calf striatum and behavioral tests of mice or rats were used. **RESULTS**: In the competitive binding assay, the affinities (K_i) of *l*-CSL to D_1 and D_2 receptors were 5.7 nmol·L^{-1}, while those of *d*-CSL for D_1 and D_2 receptors were 135 and 9150 nmol·L^{-1}, respectively. The K_i of *dl*-CSL to D_1 and D_2 recptors were 8.9 and 9.6 nmol·L^{-1}, respectively, which were slightly weaker than that of *l*-CSL. In the behavioral experiments, CSL enantiomers 5 – 60 mg·kg^{-1} antagonized the stereotypy induced by apomorphine in rats, and 5 – 150 mg·kg^{-1} produced catalepsy. The enantiomers 10 – 60 mg·kg^{-1} reduced the mice jumping behavior induced by amphetamine + levodopa. *l*-CSL 10 – 80 mg·kg^{-1} antagonized the spontaneous locomotor activity of normal or amphetamine-treated mice. **CONCLUSION**: CSL enantiomers are antagonists to DA receptors: *l*-CSL > *dl*-CSL > > *d*-CSL.

INTRODUCTION

dl-12-Chloroscoulerine (*dl*-CSL), a potent analog of tetrahydroprotoberberines (THPB), shares an isoquinoline structure with two OH groups at C_2 and C_9 and chlorine at C_{12} position. *d*-CSL has the potent affinities to dopamine (DA) D_1 and D_2 receptors[1]. Its activities are similar to that of *l*-stepholidine (SPD)[2-5], a leading compound of THPB. SPD shows DA receptors antagonistic action in the behavioral studies on stereotypy and catalepsy, but it displays the DA agonist action on the contralateral rotation in the 6-OHDA-lesioned rats[5-6]. Thus *dl*-CSL has also the dual action on DA receptors and it is very similar to SPD[7-10]. *l*-Tetrahydropalmatine (*l*-THP), another analog of THPB, is a DA receptor antagonist, while the *d*-THP enantiomer is a prototype of DA depletor[8,9]. Based on the differential actions of THP enantiomers to DA receptors, it is suggested that the *l*-CSL enantiomer should be a more potent DA receptor antagonist or/and agonist than *d*-CSL enantiomer. The present study aimed at the comparative study of CLS enantiomers to DA receptors.



Chemical structure of CSL enantiomers

MATERIALS AND METHODS

Drugs and reagents SPD (mp 163℃, $[\alpha]_D$ – 440° in pyridine) was isolated from *Stephania intermedia* LO; *dl*-CSL, *l*-CSL (mp 161 – 162 ℃, $[\alpha]_D^{11.5}$ – 223.19°, $CHCl_3$, C 0.14), *d*-CSL (mp 161

[1] Project supported by the National Natural Science Foundation of China, No 39130091, 39670853, and the State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, No K016.
[2] Correspondence to Prof JIN Guo-Zhang.
Phn 86-21-6431-1833, Ext 402. Fax 86-21-6437-0269.
E-mail gzjin@server.shcnc.ac.cn
Received 1999-06-01 Accepted 1999-07-06

– 162 ℃, $[\alpha]_D^{11.5}$ + 222.53°) were synthesized in Shanghai Institute of Materia Medica. [^{3}H] Sch23390 (3071 GBq nmol · L^{-1}, Radiochemical Center, Amersham), [^{3}H] spiperone (592 GBq mmol · L^{-1}, radiochemical centre, Amersham); Sch23390 (RBI), *d*-amphetamine (Amp, BDH), levodopa (Sigma), haloperidol (Hal. Haipu Pharmaceutic Factory, Shanghai, China), apomorphine hydrochloride (Shenyang First Pharmaceutic Factory, China), and clozapine (Clo, Shanghai Pharmaceutic Factory, China) were used.

Animals Sprague-Dawley (SD) rats (♂, 210 g ± *s* 42 g) and Kun Ming species mice (♂, 19 g ± 2.6 g, Grade Ⅱ, Shanghai Experimental Animal Center, China, Certification No 005 by Animal Management Committee, Chinese Academy of Sciences) were used.

Receptor binding assay Calf striatal membrane protein was prepared as previous report[1]. [^{3}H]Sch 23390 and [^{3}H]spiperone were used for binding assay respectively to D_1 and D_2 receptors[10-11]. The K_d values of D_1 and D_2 receptors were 1.65 and 0.48 nmol · L^{-1}, the receptors densities (B_{max}) were 907.8 and 125.7 pmol · L^{-1}/g protein, respectively, and Hill number (n_H) were 0.91 and 0.99[1], respectively.

Rat stereotypy Rats were placed in the observing cages for 20 min before drug treatment to adapt to a new environment. After ip apomorphine (Apo) 5 mg · kg^{-1} 3 – 5 min, the stereotypy induced by Apo was observed, and CSL enantiomers were given (ip) 15 min after Apo. The 4-grade scoring system[12] for gnawing, licking, rearing, sniffing and vigorous movements without purpose were scored. The effect of CSL enantiomers was assessed by the antagonism to Apo-induced stereotypy.

Rat catalepsy[13] The catalepsy of rats was measured as followed: rats' front paws were put on wood cylinder 9 cm high, and hind paws on the ground. The time of its still posture remained after drug was recorded as the catalepsy criteria scored.

Jumping behavior in mice The jumping behavior in mice was elicited by amphetamine (Amp, ip) 10 mg · kg^{-1} + levodopa (ip) 200 mg · kg^{-1} 15 min after the injection. The mice started to jump almost immediately following levodopa injection. Tested compounds such as *l*-CSL, *d*-CSL, Hal, Clozapine (Clo) were given (ip) 5 min before Amp respectively. The effects of the compounds were evaluated by a "jumping medium number"[14] of mice.

Spontaneous locomotor activity of mice[15] Every group of 9 mice was tested for separately 3 times in the photocell boxes. Amphetamine (Amp, ip) 10 mg · kg^{-1} was injected by followed *l*-CSL, or Clo with 5 min apart, the spontaneous motor activity of grouped mice was recorded automatically on the basis of light beam interrupted by mice during a 5-min period. The drug tested groups and control group were compared parallely.

RESULTS

Affinities of CSL enantiomers Results showed that CSL enantiomers had the different affinities to dopamine D_1 and D_2 receptors. The affinity of *l*-CSL was the most potent one among CSL enantiomers. The K_i value of *l*-CSL was at 5.7 nmol · L^{-1} (Tab 1) to both dopamine D_1 and D_2 receptors, which were 24 and 1605 times stronger than that of *d*-CSL to D_1 and D_2 receptors respectively. The K_i values of *dl*-CSL was 8.9 and 9.6 nmol · L^{-1} to D_1 and D_2 receptors, respectively. And the D_2 activity was more active than that of *l*-SPD, of which D_1 activity was similar to that of *dl*-CSL. The potency order was *l*-CSL > *dl*-CSL > > *d*-CSL (Tab 1).

Tab 1. Affinities of CSL enantiomers to dopamine receptors.

CSL enantiomers	K_i/nmol · L^{-1}	
	D_1	D_2
Sch23390	0.28	–
Haloperidol	–	0.14
l-SPD	8.6	80
l-CSL	5.7	5.7
dl-CSL	8.9	9.6
d-CSL	135	9150

CSL enantiomers antagonized APO-induced stereotyped behavior The stereotypy in rats induced by Apo 5 mg · kg^{-1} was markedly reduced after ip injection of CSL enatiomers 5 – 60 mg · kg^{-1}. The effect of *l*-CSL was the most potent one among CSL

ISSN 0253-9756 Acta Pharmacol Sin 中国药理学报 1999 Oct; 20 (10)
E-mail aps@server.shcnc.ac.cn Phn/Fax 86-21-6474-2629

enantiomers. At the dose of *l*-CSL 5 – 40 mg·kg^{-1}, the stereotypy was obviously reduced ($P < 0.01$) or abolished in a dose-dependent manner. Although *d*-CSL 40 – 60 mg·kg^{-1} also reduced stereotypy, but its antagonistic action was equal to that of *l*-CSL 5 mg·kg^{-1}. Thus, the potency of *l*-CSL was about 12 times more potent than that of *d*-CSL (Tab 2).

Tab 2. Blockaded effect of CSL enantiomers on Apomorphine-induced stereotyped behavior rats (n = 6), $\bar{x} \pm s$. $^aP > 0.05$, $^bP < 0.05$, $^cP < 0.01$ *vs* Apo.

Drugs	Dose/mg·kg^{-1}	Score
Apo	5	3.0 ± 0.6
Apo + NS	5	3.3 ± 0.5^a
Apo	5	3.5 ± 0.6
Apo + Hal	1	0^c
Apo	5	3.6 ± 0.5
Apo + *l*-CSL	5	1.6 ± 1.5^c
Apo	5	2.8 ± 0.4
Apo + *l*-CSL	10	1.3 ± 0.8^b
Apo	5	3.2 ± 0.4
Apo + *l*-CSL	20	0.5 ± 0.5^c
Apo	5	3.6 ± 0.5
Apo + *l*-CSL	40	0^c
Apo	5	3.5 ± 0.6
Apo + *dl*CSL	20	1.5 ± 1.1^c
Apo	5	3.0 ± 0.6
Apo + *dl*CSL	40	0.8 ± 0.7^c
Apo	5	3.5 ± 0.8
Apo + *d*CSL	40	1.8 ± 1.0^c
Apo	5	3.3 ± 0.8
Apo + *d*CSL	60	1.5 ± 1.4^c

CSL enantiomers evoked catalepsy in rats

The results showed that normal saline (NS) group did not display any cataleptic effect, while haloperidol (Hal) had very profound cataleptic efgect at the 1 mg·kg^{-1} and lasted for a long time (455 ± 37 min). However, *l*-CSL exhibited its cataleptic effect with a dose-dependent manner at the range of 5 – 80 mg·kg^{-1}, but it was far weaker against Hal. The cataleptic effect of *dl*-CSL enantiomer was slightly weaker than the same doses of *l*-CSL enantiomer. And the cataleptic effect of *d*-CSL at the 150 mg·kg^{-1} was also weaker than that of *l*-CSL 5 mg·kg^{-1}(Tab 3).

Tab 3. CSL enantiomers evoked catalepsy in rats. $n = 6$, $\bar{x} \pm s$.

Drugs	Dose/ mg·kg^{-1}	Time of appearance catalepsy/ min	Retaining time of catalepsy/ min	Score
NS		–	–	0
Hal	1	9.5 ± 1.2	455 ± 37	5.0 ± 0.0
l-CSL	5	4.1 ± 2.3	8.0 ± 5.9	2.7 ± 1.6
l-CSL	10	3.8 ± 1.8	12.8 ± 4.7	3.6 ± 0.5
l-CSL	20	2.9 ± 2.1	18.2 ± 7.1	4.2 ± 0.8
l-CSL	40	3.0 ± 1.5	22.2 ± 7.9	4.6 ± 0.8
l-CSL	80	2.5 ± 1.0	46 ± 10	5.0 ± 0.0
dl-CSL	5	5.7 ± 2.2	3.0 ± 3.0	1.6 ± 1.4
dl-CSL	10	10.5 ± 3.5	8.0 ± 4.0	3.3 ± 1.8
d-CSL	150	12.6 ± 1.6	3.1 ± 2.8	1.6 ± 1.0

CSL enantiomers blocked mice jumping behavior induced by amphetamine plus levodopa

Mice in saline group did not show any jumping. When the mice were ip Amp 10 mg·kg^{-1} + levodopa 200 mg·kg^{-1}, the jumping was revealed vigorously with 340 times in one hour. This jumping behavior was profoundly reduced or abolished by Hal 1 mg·kg^{-1} and Clo 5 mg·kg^{-1}(Tab 4). The jumping behavior was also reduced by *l*-CSL at the dose range of 10 – 60 mg·kg^{-1} and *d*-CSL 40 mg·kg^{-1}, and the jumping numbers were reduced from 340 times in one hour of control to 151 – 67 times and 121 times respectively. These results indicate that *l*-CSL and *d*-CSL have antagonistic action on DA receptors.

Tab 4. Effect of CSL on *l*-dopa induced jumping behavior in Amp-treated mice. $n = 9 – 14$.

Drugs	Dose/ mg·kg^{-1}	Jumping/No·h^{-1}
Amp 10 + *l*-dopa	200	340 (198 – 409)
Amp 10 + *l*-dopa + Hal	1	0 (0 – 8)
Amp 10 + *l*-dopa + Clo	2.5	124 (3 – 432)
Amp 10 + *l*-dopa + Clo	5	0 (0 – 63)
Amp 10 + *l*-dopa + *l*-CSL	10	151 (45 – 405)
Amp 10 + *l*-dopa + *l*-CSL	30	135 (16 – 324)
Amp 10 + *l*-dopa + *l*-CSL	60	67 (0 – 226)
Amp 10 + *l*-dopa + *d*-CSL	40	121 (34 – 382)

Inhibition of *l*-CSL on amphetamine-induced spontaneous locomotor activity in mice

Amphetamine (Amp) augmented the spontaneous

locomotor activity of mice by inducing the release of DA from DA nerve endings. After Amp 10 mg·kg^{-1}, the spontaneous locomotor activity (680 ± 99 times in 5 min) in mice was twice as that of NS group (329 ± 137), during the observing period of 5 – 10 min, as a hyperactive response. At the doses of 10, 20, 40, and 80 mg·kg^{-1} of *l*-CSL, both the normal activity (NS) and the Amp-hyperactive response were rapidly inhibited with a dose-response dependent manner. The peak activity was at 15 – 20 min after ip *l*-CSL but lasted for only about 20 – 30 min, except at high dose (80 mg·kg^{-1}) which lasted for about 3 h (Tab 5). In contrast to *l*-CSL, the low dose of Clo 1.25 mg·kg^{-1} remarkably inhibited the Amp-hyperactive response and the peak effect was on 3 h, then slowly recovered for a long period, even more than 8 h. Apparently, the effect of Clo prolonged quite more than that of *l*-CSL.

DISCUSSION

In the present work, the affinities to dopamine D_1 receptors of *l*-CSL, *dl*-CSL and *l*-SPD were active at the same level (K_i, 5.7 – 8.9 nmol·L^{-1}), but to D_2 receptors, *l*-CSL and *dl*-CSL were more potent (K_i, 5.7 – 9.6 nmol·L^{-1}) than *l*-SPD (K_i, 80 nmol·L^{-1}). Obviously, the Cl on C_{12} of D ring of *l*-CSL increase the negative electronic charges on the D ring. Thus, it may enhance the affinity of *l*-CSL to dopamine D_1 and D_2 receptors against *l*-SPD, particularly to D_2. As to optical enantiomers of CSL to D_1 receptors affinity, *d*-CSL enantiomer (K_i, 135 nmol·L^{-1}) was weaker than *l*-CSL. Furthermore, the affinity of *d*-CSL enantiomer to D_2 recptors was quite weaker (K_i, 9150 nmol·L^{-1}) than *l*-CSL. Therefore, *l*-CSL enantiomer is really more potent one in the CSL enantiomers, while *d*-CSL is a less active enantiomer or inactive one to D_2 receptors. This action of CSL enantiomers is very similar to that of THP enantiomers[16]. In other works, the *l*-enantiomer of THPB is active, and *d*-enantiomer is less active or inactive. The reason of different effects of THPB enantiomers to DA receptors has been explained by stereo and quantum chemistry in 1996[17-18].

In the behavioral tests for DA receptor functions such as anti-seterotypy and catalepsy-induced in rats, anti-jumping and anti-locomotor activity in mice, all the enatiomers of CSL exhibited the antagonistic action on DA receptors, in which the *l*-enantiomer was the most potent one. Nevertheless, it has been demonstrated that *l*-CSL possesses the agonistic action to D_1 receptors by rotational behavior in 6-OHDA-lesioned rats, GTP regulation of R_H binding sites of *l*-CSL to D_1 receptors, and augmentation of adenylate cyclase activity in rat striatum (Chen LJ, *et al*, unpublished data). All these results indicate that *l*-CSL possesses the intrinsic activity to D_1 receptors, and is D_1 agonist in the supersensitivity of D_1 receptors.

Tab 5. Effects of *l*-CSL on the spontaneous locomotor activity of mice. $\bar{x} \pm s$. $n = 3$ times (9 mice). $^cP < 0.01$ *vs* NS. $^fP < 0.01$ *vs* Amp + NS.

Compound	Dose/ mg·kg^{-1}	Locomotor activities (after ip) activity No./5 min 5 – 10	15 – 20	30 – 35	60 – 65	90 – 95	120 – 125	180 – 185
NS	–	329 ± 137	367 ± 137	385 ± 118	462 ± 157	500 ± 79	485 ± 53	469 ± 81
l-CSL	10	23 ± 36^c	231 ± 34^c	291 ± 61^c	539 ± 99	430 ± 63^c	461 ± 22	474 ± 61
*l*CSL	20	9 ± 15^c	18 ± 18^c	300 ± 134^c	411 ± 135	501 ± 121	430 ± 126^c	437 ± 95
l-CSL	40	14 ± 26^c	7.8 ± 6.4^c	76 ± 73^c	337 ± 172^c	442 ± 101	378 ± 98^c	412 ± 53
l-CSL	80	2 ± 2^c	2 ± 2^c	8 ± 5^c	134 ± 120^c	188 ± 90^c	398 ± 14^c	423 ± 92
Amp + NS	–	680 ± 99	745 ± 44	702 ± 51	672 ± 51	598 ± 74	687 ± 100	548 ± 92
Amp + *l*-CSL	10	70 ± 26^f	257 ± 67^f	743 ± 66	757 ± 86	703 ± 109	603 ± 47	379 ± 25
Amp + *l*-CSL	20	91 ± 149^f	46 ± 25^f	607 ± 219	834 ± 86	671 ± 147	648 ± 157	684 ± 52
Amp + *l*-CSL	40	15 ± 27^f	5 ± 9^f	153 ± 24^f	766 ± 61	544 ± 176	666 ± 116	492 ± 78
Amp + *l*-CSL	90	1 ± 2^f	5 ± 8^f	239 ± 151^f	470 ± 165^f	608 ± 136	449 ± 308^f	374 ± 125^f
Amp + Cloz	1.25	216 ± 55^f	209 ± 37^f	182 ± 6^f	142 ± 84^f	151 ± 58^f	63 ± 32^f	57 ± 42^f

*Amp 10 mg·kg^{-1}

ISSN 0253-9756 Acta Pharmacol Sin 中国药理学报 1999 Oct; 20 (10)
E-mail aps@server.shcnc.ac.cn Phn/Fax 86-21-6474-2629

Recently, it has been found that *l* – SPD, *dl*-CSL and *l*-CSL had the protection of striatal injury by ischemia and MPP^+-lesion (Jin GZ, *et al*, unpublished data, 1999).

Taken together, CSL enantiomers have the antagonsitic (D_2)-agonistic (D_1) dual action, which is very similar to that of SPD.

REFERENCES

1 Chen LJ, Xi Y, Pang DW, Zhou QT, Jin GZ. Effect of *dl*-2-chloroscoulerine on brain dopamine receptors. Acta Pharmacol Sin 1996; 17: 185 – 9.
2 Jin GZ. (–)-Tetrahydropalmatine and its analogues as new dopamine receptor antagonists. Trends Pharmacol Sci 1987; 8: 81 – 2.
3 Zhang XX, Jin GZ. (–)-Stepholidine vs 12-chloroscoulerine enantiomoers on firing activity of substantia nigral dopamine neurons. Acta Pharmacol Sin 1996; 17: 18 – 22.
4 Xu SX, Yu LP, Han YR, Chen Y, Jin GZ. Effects of tetrahydroprotoberberines on dopamine receptor subtypes in brain. Acta Pharmacol Sin 1989; 10: 104 – 10.
5 Huang KX, Sun BC, Jin GZ. (–)-Stepholidine: a dopamine receptor antagonist shows agonistic effect on rotational behavior in 6-hydroxydropamine-lesioned rats. Acta Pharmacol Sin 1992; 13: 17 – 22.
6 Jin GZ, Huang KX, Sun BC. Dual action of (–)-stepholidine on dopamine receptors subtypes after substantia nigra lesion. Neurochem Int 1992; 20 (Suppl): 175 – 8.
7 Dong ZJ, Chen LJ, Jin GZ, Creese I. GTP regulation of (–)-stepolidine binding to R_H of D_1 dopamine receptors in calf striatum. Biochem Pharmacol 1997; 14: 227 – 32.
8 Xu SX, Jin GZ, Yu LP, Liu GX, Lu WW, Fang SD. Brain dopamine depleted by *d*-tetrahydropalmatine. Acta Pharmacol Sin 1987; 8: 207 – 12.
9 Huang KX, Fang SD, Jin GZ, Dong XW. Fluorescence-histochemical evidence for dopamine depletion in nigrostriatal system by d-tetrohydropalmatine. Chin J Physiol Sci 1988; 4: 19 – 24.
10 Creese I, Schneider R, Snyder SH. [^{3}H]-spiroperidol labels dopamine receptors in pituitary and brain. Eur J Pharmacol 1977; 46: 377 – 81.
11 Billard W, Ruperto V, Crosby G, Iorio LC, Barnett A. Characterization of the binding of ^{3}H-SCH23390, a selective D_1 receptor antagonist ligand, in rat striatum. Life Sci 1984; 35: 1885 – 93.
12 Costall B, Naylor RJ. The role of telencephalic dopaminergic systems in the mediation of apomorphine-stereotyped behaviour. Eur J Pharmacol 1973; 24: 8 – 24.
13 Christensen AV, Arnt J, Svendsen O. Animal models for neuroleptic-induced neurological dysfunction. In: Usdin E, Carlsson A, Dahlstrom A, Engel J, editors. Catecholamines part C: Neuropharmacology and central nerve system — therapeutic aspects. New York: Anan R Liss Inc; 1984. p 99 – 109.
14 Fielding S, Lal H. Behavioral actions of neuroleptics In: Iversen LL, Iversen SD, Snyder SH, editors. Hand book of psychopharmacology; vol 10. Neuroleptics and shizophrenia. New York: Plenum Press; 1978. p 91 – 128.
15 Pycock C, Dawbarn D, O'shaughnessy C. Behavioral and biochemical changes following chronic adminstration of *L*-dopa to rats. Eur J Pharmacol 1982; 79: 201 – 15.
16 Jin GZ, Xu SX, Yu LP. Different effects of enantiomers of tetrhydropalmatine on dopaminergic system. Sci Sin [B] 1986; 29: 1054 – 64.
17 Tang Y, Chen KX, Jiang HL, Jin GZ, Ji RY. Molecular modeling of interatctions between tetrahydroprotoberberines and dopamine receptors. Acta Pharmacol Sin 1996; 17: 8 – 12.
18 Xuan JC, Lin GD, Jin GZ, Chen Y. Relevance of stereo and quantum chemistry of four tetrahydroprotoberberines to their effects on dopamine receptors. Acta Pharmacol Sin 1988; 9: 197 – 205.

氯代斯阔任旋光异构体作用于多巴胺受体对动物行为的比较[1]

陈丽娟, 周启霆, 董兆君, 俞蕾平, 金国章[2]
(中国科学院上海药物研究所, 上海 200031, 中国)

关键词 12-氯代斯阔任; 左旋千金藤立定; 阿朴吗啡; 多巴胺 D_1 受体; Sch 23390; 放射配体测定; 刻板; 强直性木僵; 穿梭活动

目的: 比较氯代斯阔任(CSL)旋光异构体对 DA 受体的作用特性. **方法**: 采用小牛纹状体 DA 受体结合分析和小鼠、大鼠的行为实验. **结果**: *d*-CSL 对 D_1 和 D_2 受体的 K_i 值分别是 135 和 9150 nmol·L^{-1}, 而 *l*-CSL 对 D_1 和 D_2 的亲和力(K_i)均为 5.7 nmol·L^{-1}, 分别为 *d*-CSL 的 24 倍和 1605 倍. *dl*-CSL 对 D_1 和 D_2 受体的 K_i 值分别为 8.9 和 9.6 nmol·L^{-1}, 比 *l*-CSL 稍弱. 大鼠刻板活动和木僵实验、小鼠的跳跃和自发活动实验均证明 CSL 旋光异构体对 DA 受体有阻滞作用. **结论**: CSL 旋光异构体为 DA 受体阻滞剂的作用特性, 其作用强度为: *l*-CSL > *dl*-CSL > > *d*-CSL.

(责任编辑 李 颖)