Influence of (-)-Sulpiride and YM-09151-2 on Stereotyped Behavior in Chicks and Catalepsy in Rats

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Accepted September 1, 1986

Abstract—In this paper, the effects of three antipsychotic agents using the avian species laboratory model are described. d-Amphetamine (2-5 mg/kg, s.c.) dose-dependently antagonized catalepsy induced by haloperidol (0.25 mg/kg, i.p.), YM-09151-2 (0.02-0.04 mg/kg, i.p.) and (-)-sulpiride (20-40 mg/kg, i.p.) in rats. (-)-Sulpiride (10-40 mg/kg, i.p.) dose-dependently antagonized apomorphine (0.125 mg/kg, s.c.)-induced stereotyped behavior in young chicks. Similarly, YM-09151-2 (0.04 mg/kg, i.p.) antagonized apomorphine (0.125 mg/kg, s.c.)-induced stereotyped behavior in young chicks. (-)-Sulpiride (40 mg/kg, i.p.) significantly antagonized apomorphine (0.25 mg/kg, s.c.)-induced stereotyped behavior in 6 week old chicks. Parachlorophenylalanine (PCPA, 300 mg/kg, i.p.) significantly reduced the intensity of stereotyped behavior induced by apomorphine (0.125 mg/kg, s.c.) in young chicks. However, (-)-sulpiride (40 mg/kg, i.p.) did not significantly influence the effect of PCPA on apomorphine-induced stereotyped behavior. Similarly, catalepsy induced by (-)-sulpiride (40 mg/kg, i.p.), haloperidol (0.25 mg/kg, i.p.) and YM-09151-2 (0.04 mg/kg, i.p.) in male rats was profoundly suppressed by PCPA (300 mg/kg, i.p.). The present results indicate that apomorphine-induced stereotyped pecking in young (4-6 day old) chicks may serve as a suitable laboratory model for testing potential antipsychotic drugs. In addition, the data indicates that endogenous 5-hydroxytryptamine mechanisms may be involved in the genesis of drug-induced catalepsy in rats.

According to Borenstein and his colleagues (1), sulpiride is a potent blocker of apomorphine-induced emesis in dogs, while Niskanen and his co-workers (2) reported that sulpiride blocks rotation induced by d-amphetamine or apomorphine in rats with unilateral lesions of the substantia nigra. However, Trabucchi and his co-workers (3) reported that sulpiride, unlike typical neuroleptics, failed to block catecholamine-induced stimulation of adenylate cyclase. In 1983 however, Terai and his colleagues (4) reported that YM-09151-2 was an antagonist of D2 receptors but not adenylate cyclase-dependent D1 receptors. Furthermore, Collard (5) and Borenstein et al. (1) accumulated data which clearly indicate that sulpiride is an effective anti-psychotic agent which causes extrapyramidal symptoms occasionally. It is therefore apparent from both preclinical and clinical profiles of sulpiride that it is an "unusual" or "atypical" neuroleptic. This situation indicates that the mechanisms of action of neuroleptics are not yet fully understood.

In the present study, two experimental models of psychosis were employed (viz: catalepsy test in male albino rats and apomorphine-induced stereotyped pecking in cockerels) for comparative purposes. It is possible that the apparent differences between the substituted benzamides and the typical neuroleptics might partly be related to the poor penetration of the benzamides into the brain (6). Therefore, the effects of (-)-sulpiride and YM-09151-2 on apomorphine-induced stereotyped behavior in young chicks (lack functional blood-brain barrier, ref. 7)
and cockerels were studied.

**Materials and Methods**

**Catalepsy in rats:** Male albino rats (Wistar strain which were inbred in our Animal House) about two to three months old, weighing 200±50 g, were used for all the stereotyped behavioral studies reported in this project. The rats had free access to both food and water. Catalepsy was assessed using essentially the method of Costall, Hui and Naylor (8). All the experiments were conducted in a quiet air-conditioned room with an ambient temperature of 24±2°C. Catalepsy was induced by intraperitoneal injection of haloperidol (0.25 mg/kg).

Animals were normally housed in the same cage, but for the measurement of catalepsy, they were placed in individual (screened) perspex cages (25 cm x 25 cm x 15 cm) equipped with a horizontal bar (1 cm perspex dowel fitted 6 cm high and 8 cm long). Thirty min were allowed before drug treatment for adaptation to the new environment.

In testing for catalepsy, each animal was gently held with the hand, across its shoulders and along the animals' back. The animals were slowly moved towards the bar, the hind limbs at all times contacting the cage floor while the front limbs were level with the bar. The front limbs were placed over the bar with the hind limbs approximately 6 cm behind. The experimenter ensured that the rat maintained the position for 2–3 sec before slowly and cautiously withdrawing the supporting hand to the rear of the animal to avoid distraction. The animals were tested for catalepsy once every 10 min to determine the onset of catalepsy.

Catalepsy was assessed by converting the values obtained in minutes to scores as follows: 0.1–2.5 min = score 1, 2.6–5.0 min = score 2, 5.1–10.0 min = score 3, 10.1–20.0 min = score 4 and 20.1 and over = score 5. This scoring system eliminates the need to observe animals for an indefinite period of time by providing a “cut off” point at score 5. Animals were observed continuously to determine the intensity of catalepsy per min for conversion to a score as indicated above. The scoring system is in accordance with that reported by Costall, Hui and Naylor (8).

**Stereotyped behavior in chicks and cocks:** Four to six day old chicks and 6 week old cocks weighing 35±5 g and 250±30 g, respectively, were used. The cockerels and cocks (Ranger strain) were obtained from Arewa Agricultural Enterprises, Ltd., Zaria. Six chicks were used to study each of the drugs used in this project. Two chicks were used per experiment. Each experiment was repeated three times.

The recording of stereotyped behavior was done in accordance with the method of Osuide and Adejoh (9). The stereotyped behavior was recorded by technical assistants who were unaware of the drug injected into the different groups of chicks and cocks.

Interaction studies for the standard neuroleptic drug (haloperidol) were obtained by pretreating 3 sets of chicks with haloperidol (0.25 mg/kg, i.p.) prior to the administration of apomorphine (0.125 mg/kg, s.c.) 5 min later. The same stereotyped behavioral parameters as before were observed and recorded. Such studies were immediately preceded by a control experiment using apomorphine alone to verify its stability. For interaction studies involving YM-09151-2 and (-)-sulpiride, a control for apomorphine alone was obtained in the same manner as for haloperidol.

After injection, each set of chicks was placed in a cage containing food and water and observed for 30 min.

**Preparation of test drugs:** Sulpiride (20 mg) was suspended in 20 ml of 3% v/v Tween 80. This preparation was used to study the dose-dependent effect of the drug in rats. Both YM-09151-2 and haloperidol solutions were prepared in a similar way to sulpiride. d-Amphetamine sulphate was dissolved in physiological saline. Haloperidol (Janssen Pharmaceutica, 0.25 mg/kg), YM-09151-2 (Yamanouchi Pharmaceutical, Ltd.; 0.01–0.04 mg/kg) and (-)-sulpiride (Ravizza, Italy; 20–40 mg/kg) were administered intraperitoneally, while d-amphetamine (Smith Kline and French, 1–5 mg/kg) was administered subcutaneously. Apomorphine HCl (British Drug Houses, Ltd.; 0.125 mg/mg) was freshly prepared each day by dissolving in recently boiled physiological saline. Sodium metabisulphite (British Drug
Houses, Ltd.; 1% w/w) was used as an antioxidant. Apomorphine was injected subcutaneously. The pretreatment time with each of the test drugs, prior to the administration of either apomorphine or d-amphetamine was 5 min. The doses mentioned in this paper refer to the salts of the drugs. The pretreatment times were established in our laboratory from preliminary studies.

Statistical analysis: The data was analyzed using the Mann-Whitney U-test.

Results

Influence of d-amphetamine on haloperidol-induced catalepsy in rats: Haloperidol (0.25 mg/kg, i.p.) induced catalepsy within 10 min of injection. The effect lasted for over 2 hr. d-Amphetamine (2–4 mg/kg, s.c.) antagonized haloperidol-induced catalepsy dose-dependently. Thus, the intensity of catalepsy was reduced by 2–4 mg/kg, while 5 mg/kg of d-amphetamine completely antagonized haloperidol-induced catalepsy (Table 1).

Influence of d-amphetamine on YM-09151-2-induced catalepsy in rats: YM-09151-2 (0.02–0.04 mg/kg, i.p.) induced catalepsy within 30 min of injection. The cataleptogenic effect of YM-09151-2 was apparently dose-dependent. d-Amphetamine (2.5 mg/kg, s.c.) reduced the intensity and delayed the onset, but the duration of catalepsy was unaffected. However, 5 mg/kg, s.c. of d-amphetamine completely antagonized YM-09151-2-induced catalepsy (Table 2).

Influence of d-amphetamine on sulpiride-induced catalepsy in rats: (−)-Sulpiride (20–40 mg/kg, i.p.) induced weak catalepsy. The onset was 60 min, while the duration of catalepsy was relatively short (about 30 min). In addition, unlike haloperidol and YM-09151-2, the rats were profoundly sedated by sulpiride. d-Amphetamine (1 mg/kg, s.c.) effectively blocked sulpiride-induced catalepsy. In fact, hyperactivity of the animals was observed within 5 min. of injection of d-amphetamine (1 mg/kg, s.c.) into sulpiride-pretreated rats (Table 3).

Influence of (−)-sulpiride and PCPA on apomorphine-induced stereotyped behavior in 4–6 day old cockerels: Apomorphine (0.125 mg/kg, s.c.) induced stereotyped fighting, pecking at non-food materials, self and each other. Haloperidol (0.25 mg/kg, i.p.) significantly antagonized apomorphine-induced stereotyped behavior (Table 4). PCPA (300 mg/kg, i.p.) significantly (P<0.05) reduced

| d-Amp (mg/kg) | Post-injection time (min) | Catalepsy score Median±range |
|---------------|--------------------------|------------------------------|
| 0             | 10                       | 1.78 ±1.20                  |
| 0             | 30                       | 2.61 ±1.18                  |
| 0             | 60                       | 2.46 ±0.60                  |
| 0             | 120                      | 1.5 ±0.40                   |
| 2.0           | 10                       | 0.87*±0.36                  |
| 2.0           | 30                       | 1.32*±0.26                  |
| 2.0           | 60                       | 0.91*±0.30                  |
| 2.0           | 120                      | 0.63*±0.19                  |
| 4.0           | 10                       | 0.45*±0.12                  |
| 4.0           | 30                       | 0.50*±0.20                  |
| 4.0           | 60                       | 0.66*±0.11                  |
| 4.0           | 120                      | —                            |
| 5.0           | 30                       | —                            |

In Tables 1–3, catalepsy was assessed by converting the value obtained in minutes to a score: 0.1–2.5 min =score 1, 2.6–5 min =score 2, 5.1–10 min =score 3, 10.1–20 min =score 4, 20.1 min or above =score 5. Haloperidol (0.25 mg/kg) was administered to all the rats. *Is significantly different from the controls (same dose of haloperidol) at the level of P<0.001, Mann Whitney U-test. d-Amp: d-amphetamine, n=10 rats per dose. The sign "—" in all the Tables refers to "no observable effect".
the intensity of stereotyped behavior induced by apomorphine (0.125 mg/kg, s.c.) in chicks. However, PCPA (300 mg/kg, i.p.) did not alter the influence of sulpiride on apomorphine-induced stereotypy in any significant manner (Table 4).

Table 2. Effect of d-amphetamine on catalepsy induced by YM-09151-2 using rats

| YM-09151-2 (mg/kg) | d-Amp | Post-injection time (min) | Catalepsy score Median±range |
|-------------------|-----------------|--------------------------|-----------------------------|
| 0.02              | 0               | 60                       | 0.65 ±0.04                  |
| 0.02              | 0               | 120                      | 1.83 ±0.08                  |
| 0.04              | 0               | 60                       | 2.86 ±0.1                   |
| 0.04              | 0               | 120                      | 5.0 ±0.81                   |
| 0.02              | 2.5             | 60                       | 0.17*±0.03                  |
| 0.02              | 2.5             | 120                      | 0.68*±0.2                   |
| 0.04              | 2.5             | 60                       | 0.65*±0.02                  |
| 0.04              | 2.5             | 120                      | 1.1*±0.2                    |
| 0.04              | 5               | 120                      | —                          |

*Is significantly different from the controls (same dose of YM-09151-2) at the level of P<0.001, Mann Whitney U-test. d-Amp: d-amphetamine; YM-09151-2: cis-N-(1-benzyl-2-methyl-pyrrolidine-3-yl)-5-chloro-2-M. n=10 rats per dose.

Table 3. Effect of d-amphetamine on catalepsy induced by (-)-sulpiride using rats

| (-)-Sulpiride (mg/kg) | d-Amp | Post-injection time (min) | Catalepsy score Median±range |
|-----------------------|-------|--------------------------|-----------------------------|
| 20                    | 0     | 90                       | 0.5 ±0.2                    |
| 20                    | 0     | 120                      | 0.17±0.03                   |
| 40                    | 0     | 30                       | 0.73±0.09                   |
| 40                    | 0     | 120                      | 1.1 ±0.4                    |
| 20                    | 1.0   | 90                       | —                           |
| 20                    | 1.0   | 120                      | —                           |
| 40                    | 1.0   | 30                       | —                           |
| 40                    | 1.0   | 120                      | —                           |

n=10 rats per dose.

Table 4. Effect of (-)-sulpiride, haloperidol and PCPA on apomorphine-induced stereotypy using 4-6 day old chicks

| Apo (mg/kg) | (-)-Sulpiride (mg/kg) | Hal (mg/kg) | PCPA | Pecking at cage floor Median±range | Pecking at own body Median±range | Pecking at each other Median±range |
|-------------|-----------------------|-------------|------|-----------------------------------|---------------------------------|----------------------------------|
| 0.125       | 0                     | 0           | 0    | 492 ±150                          | 35.0 ±10                        | 203 ±48                          |
| 0.125       | 20                    | 0           | 0    |                                  |                                 |                                  |
| 0.125       | 20                    | 0           | 0    | 435**±60                          | 18.0**±5                        | 100**±25                         |
| 0.125       | 40                    | 0           | 0    |                                  |                                 |                                  |
| 0.125       | 40                    | 0           | 0    | 55*±10                            | 6.3*±1.0                        | 31*±9                            |
| 0.125       | 0                     | 0           | 0.25 |                                  |                                 |                                  |
| 0.125       | 0                     | 0.25        | 0    |                                  |                                 |                                  |
| 0.125       | 0                     | 0.25        | 300  | 24*±8                             | 18.0*±10                        | 3*±1.9                           |
| 0.125       | 40                    | 0           | 300  |                                  |                                 |                                  |
| 0.125       | 0                     | 0           | 300  | 175*±30                           | 72.0*±26                        | 105*±32.0                        |
| 0.125       | 40                    | 0           | 300  | 130*±50                           | 41 ±9                           | 90*±20.0                         |

* and ** are significantly different from their controls. P<0.001 and P<0.01, Mann Whitney U-test, respectively. The number of animals used per study was 6, and the observation period was 30 min. Apo, Hal and PCPA are abbreviations for apomorphine, haloperidol and parachlorophenylalanine, respectively.
Influence of YM-09151-2 on apomorphine-induced stereotyped behavior in 4–6 day old cockerels: YM-09151-2 (0.01–0.04 mg/kg, i.p.) dose-dependently antagonized apomorphine-induced stereotyped behavior (Table 5).

Influence of haloperidol and (-)-sulpiride on apomorphine-induced stereotypy in 6 week old cocks: Haloperidol (0.25 mg/kg, i.p.) effectively blocked the stereotyped behavior induced by apomorphine (0.25 mg/kg, s.c.) on all the three parameters of stereotypy studied in this project. On the other hand, (-)-sulpiride (40 mg/kg, i.p.) antagonized pecking of self and partner, but pecking of the cage floor was unaffected (Table 6).

Effect of PCPA on catalepsy induced by

**Table 5.** Effect of YM-09151-2 on apomorphine-induced stereotypy using 4–6 day old chicks

| Apo (mg/kg) | YM-09151-2 | Pecking at cage floor Median ± range | Pecking at own body Median ± range | Pecking at each other Median ± range |
|------------|------------|-------------------------------------|------------------------------------|-------------------------------------|
| 0.125      | 0          | 482 ± 150                           | 35 ± 10                            | 203 ± 48                            |
| 0          | 0.01       |                                    |                                    |                                    |
| 0.125      | 0.01       | 125 *± 20                           | 19 ± 8                             | 110 ± 40                            |
| 0          | 0.02       |                                    |                                    |                                    |
| 0.125      | 0.02       | 200 *± 60                           | 14 *± 4                            | 21 *± 6                             |
| 0          | 0.04       |                                    |                                    |                                    |
| 0.125      | 0.04       |                                    |                                    |                                    |

*Is significantly different from the controls (same dose of apomorphine) at the level of P<0.001, Mann-Whitney U-test. Apo: Apomorphine. The number of animals used per study was 6, and the observation period was 30 min.

**Table 6.** Effect of haloperidol and (-)-sulpiride on apomorphine-induced stereotypy using 6 week old cocks

| Apo (mg/kg) | Hal (mg/kg) | (-)-Sulpiride | Pecking at cage floor Median ± range | Pecking at own body Median ± range | Pecking at each other Median ± range |
|------------|-------------|---------------|-------------------------------------|------------------------------------|-------------------------------------|
| 0.25       | 0           | 0             | 315 ± 55                            | 165 ± 45                           | 600 ± 70                            |
| 0          | 0.25        | 0             |                                    |                                    |                                    |
| 0.25       | 0.25        | 0             | 5 *± 2                              |                                    |                                    |
| 0          | 0           | 40            |                                    |                                    |                                    |
| 0.25       | 0           | 40            | 315 ± 40                            | 10 *± 5                            | 11 *± 6                             |

*Is significantly different from the controls (same dose of apomorphine) at the level of P<0.001, Mann-Whitney U-test. n=6 per dose and the observation period was 30 min. Hal and Apo are abbreviations for haloperidol and apomorphine, respectively.

**Table 7.** Effect of PCPA on catalepsy induced by (-)-sulpiride, haloperidol and YM-09151-2 using rats

| PCPA (mg/kg) | (-)-Sulpiride (mg/kg) | Hal (mg/kg) | YM-09151-2 | Post-injection time (min) | Catalepsy score Median ± range |
|-------------|-----------------------|-------------|------------|--------------------------|--------------------------------|
| 300         | 0                     | 0           | 0          | 0                        | 160                            |
| 0           | 40                    | 0           | 0          | 120                      | 1.1±0.4                        |
| 300         | 0                     | 0.25        | 0          | 120                      | 1.5±0.4                        |
| 0           | 0                     | 0.25        | 0          | 120                      | 0                              |
| 300         | 0                     | 0.04        | 0          | 120                      | 5.0±0.81                       |
| 300         | 0                     | 0.04        | 0          | 120                      | 1.0±0.01*                      |

*Is significantly different from the controls (same dose of YM-09151-2) at the level of P<0.001, Mann-Whitney U-test. Hal: Haloperidol. n=10 rats per dose.
(-)-sulpiride, haloperidol and YM-09151-2 using male rats: PCPA (300 mg/kg, i.p.) completely abolished catalepsy induced by (-)-sulpiride (40 mg/kg, i.p.) and haloperidol (0.25 mg/kg, i.p.). Similarly, catalepsy induced by YM-09151-2 (0.04 mg/kg, i.p.) was profoundly suppressed by PCPA (Table 7).

Discussion

Neuroleptic drugs are capable of inducing extrapyramidal effects in humans (10) and catalepsy in animals (11, 12) resulting from the blockade of the central dopaminergic system (13).

The present data show that haloperidol, YM-09151-2 and (-)-sulpiride induced catalepsy in rats. A cataleptic rat will maintain an imposed position for a length of time which has been considered to be a measure of the “intensity” of catalepsy (8). Haloperidol was used as a standard to compare the cataleptogenic effects of the other drugs (YM-09151-2, (-)-sulpiride) used in this project. Haloperidol (0.25 mg/kg) induced catalepsy in all the rats used with an onset of about 10 min and duration of more than 2 hr (Table 1). This finding agrees with the report of Costall et al. (8). However, in this study, a lower dose of haloperidol was found to be adequate for induction of catalepsy. This apparent difference may be related to strain and sex variations.

Sulpiride induced a relatively weak but dose-dependent cataleptogenic effect in rats compared to haloperidol on a weight basis. Similarly, all the doses of (-)-sulpiride used in this project were effectively antagonized by 1 mg/kg, s.c. of d-amphetamine. On the other hand, 5 mg/kg of d-amphetamine were required to block the cataleptogenic effect of haloperidol (0.25 mg/kg, i.p.). The apparent difference in the potencies of sulpiride and haloperidol might be related to the relatively poor penetration of sulpiride into the brain (14). It was also apparent from the data that d-amphetamine effectively blocked the weak cataleptogenic effect of sulpiride. These results essentially agree with those of Spano and co-workers (15) as well as Jenner and Marsden (16). These workers proposed that the mechanism of action of sulpiride may differ from classical neuroleptics since it is a weak blocker of d-amphetamine-induced hyperactivity.

YM-09151-2 showed cataleptogenic activity with a quick onset of action compared to sulpiride. YM-09151-2 induced catalepsy in all the rats used in this project. The onset of catalepsy (20–40 min) induced by YM-09151-2 (0.04 mg/kg, i.p.) is longer when compared to that of haloperidol (0.25 mg/kg i.p., 10 min). Apparently, YM-09151-2 is a more potent cataleptogenic agent than haloperidol on a weight basis. Since YM-09151-2 and haloperidol are conventional D2 antagonists, their potent cataleptogenic effects may be partly due to blockade of dopamine D2 receptors. However, the possible involvement of dopamine D1 receptors in the genesis of dopamine-induced stereotypy cannot be ignored since it has been reported recently (17) that SCH 23390 (D1 antagonist) effectively blocked dopamine-induced stereotypy.

As shown in Table 2, d-amphetamine blocked the cataleptogenic activity of YM-09151-2 in rats. The blockade was statistically significant vis-à-vis the number of rats that showed catalepsy (P<0.001). d-Amphetamine (2.5–5 mg/kg, s.c.) completely blocked the cataleptogenic effect of YM-09151-2 (0.02 and 0.04 mg/kg, i.p.). Unlike sulpiride, YM-09151-2 had no sedative effect on the rats, but it induced a state of behavioral calmness in all the animals used.

Table 4 shows that haloperidol (0.25 mg/kg, i.p.) effectively antagonized apomorphine-induced stereotyped pecking in young chicks. All the parameters of the stereotyped pecking observed in this project were profoundly blocked by haloperidol. Similarly, (-)-sulpiride significantly antagonized apomorphine-induced stereotyped behavior in young chicks. The antagonism of apomorphine-induced stereotyped effect by sulpiride is not surprising since both drugs have been claimed to act at the adenylate cyclase independent or D2 receptors (16, 18). The present data however, indicates that haloperidol is far more potent on a weight basis than sulpiride. Such an observation agrees essentially with that of Wazer and his
co-workers (14). Similarly, the data obtained with the chick model agrees with that of the rat model of psychosis.

Since according to Leysen and his colleagues (19), spiroperidol (originally claimed to be a highly specific dopaminergic antagonist) exhibited significant activity for serotonin receptors, PCPA was therefore tested on apomorphine-induced stereotyped behavior. The present findings show that apomorphine induced stereotypy was significantly reduced by pretreatment with PCPA (300 mg/kg, i.p.). Similarly, PCPA (300 mg/kg, i.p.) reduced the intensity of haloperidol-induced catalepsy in rats. The result suggests that endogenous serotoninergic mechanisms may exert a positive influence on apomorphine-induced stereotyped behavior in chicks and drug-induced catalepsy in rats. However, sulpiride did not influence the effect of PCPA on apomorphine stereotypy in any significant manner.

The results shown in Table 6 indicate that haloperidol (0.25 mg/kg, i.p.) effectively antagonized apomorphine stereotypy in 6 week old cocks (possesses functional blood-brain barrier unlike the younger cockerels, ref. 6). Similarly, (-)-sulpiride (40 mg/kg, i.p.) antagonized apomorphine stereotypy in adult cocks, but to a lesser extent compared to haloperidol. It is noteworthy that the antagonistic effect of sulpiride against apomorphine in both young cockerels and adult cocks apparently compare favorably. Thus, the difficulty of penetration of sulpiride into the brain (6) may not be a major factor in the avian species, vis-à-vis its antagonism of apomorphine-induced stereotypy.

Another benzamide derivative (YM-09151-2 at the dose of 0.04 mg/kg, i.p.) significantly antagonized apomorphine-induced stereotyped pecking in young chicks. The present results indicate that YM-09151-2 is about five times more potent on a weight basis than haloperidol. According to Jenner, Theodorou and Marsden (20), YM-09151-2 selectively antagonized adenylate cyclase independent dopamine receptors or D2 dopamine receptors. Thus, stereotyped pecking in chicks (like catalepsy in rats) may be mediated via activation of D2-dopamine receptors.

The data accumulated in this project indicate that apomorphine-induced stereotyped pecking in young chicks may serve as a suitable laboratory model for testing potential antipsychotic drugs. In addition, serotoninergic mechanisms may enhance stereotyped behavior in chicks and rats.

Acknowledgements: I am grateful to Ravizza, Italy ((-)-sulpiride) and Yamanouchi Pharmaceutical Limited, Japan (YM-09151-2) for their generous gifts of drugs. I am also indebted to Dr. Ben Oyejola and Mr. J.E.A. Imoni for statistical analyses and technical assistance, respectively. Finally, I sincerely thank Dr. Ibrahim Abdu-Aguye for typing the manuscript.

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