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Effects of yohimbine on novel open field exploration of mice

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The effects of the anxiogenic compound yohimbine on exploration of a novel open field was investigated. The drug had no effect on latency to enter the open field but produced a marginally significant increase in number of open field entries. The results suggest that yohimbine may have behavioral stimulant and/or anticonflict properties under some testing conditions. Such effects may limit its usefulness as a research tool for the study of anxiety.

Although various forms of conspecific agonistic encounters (e.g., resident-intruder or isolation-induced aggression) provide clear evidence for the antiaggressive actions of drugs (see, e.g., Olivier, 1981), additional behavioral measures are needed to determine whether these effects are mediated by anxiolytic or anxiogenic properties. During previous investigations of the potent antiaggressive compound fluprazine, we (Kemble, Thornton, & Schultz, 1987) found that drug treatment strongly inhibited entry into a novel open field, which presumably reflected a drug-induced anxiogenic effect. If this interpretation is correct, then this simple exploratory behavior might provide a convenient and sensitive tool for the detection of anxiogenic effects in other aggression-modulating drugs as well. In the present experiments, the effects of yohimbine on novel open field exploration were investigated. A substantial body of data demonstrate anxiogenic properties of yohimbine in a variety of test situations (see, e.g., Charney, Heninger, & Redmond, 1983; Davis, Redmond, & Baraban, 1979; File & Johnson, 1987; Harris & Newman, 1987; Tsuda, Ida, & Tanaka, 1988). Drug treatment with yohimbine might therefore be expected to inhibit open field exploration as well.

METHOD

Subjects

The subjects were 24 experimentally naive male CD-1 mice weighing 30.0–49.2 g at the time of testing. All mice were individually housed for 8 days prior to testing with ad-lib access to Purina Lab Chow and water. The mice were randomly assigned to weight-balanced groups (N = 8), which received 0.5-mg/kg (*low*) or 2.0-mg/kg (*high*) dosages of yohimbine or an equivalent volume of isotonic saline (control). All drugs were administered by intraperitoneal injection.

Apparatus and Procedure

The apparatus and procedure were similar to those described previously (Kemble et al., 1987). Briefly, the mice were confined in a 15×9×9 cm lightproof startbox, which was constructed entirely of black Plexiglas and had a 9×9 cm guillotine door at one end. The startbox communicated with a 46×36×30 cm open field via a 5-cm-diam opening. Two walls and the ceiling of the open field were of clear Plexiglas, while the remaining walls and floor were of flat gray plywood. The open field was brightly illuminated by a 170-W incandescent bulb suspended 55 cm above the open field floor. Entrances into the open field were detected by a photocell placed 10 cm in front of the startbox door. Latencies were timed by an electronic timer with .01-sec accuracy. The observer and all programming equipment were located in an adjacent sound-attenuating cubicle.

Immediately after drug or saline treatment, the mice were placed in the startbox. Thirty minutes later, the startbox door was opened, and latency to enter the open field and number of entries into the open field were recorded during a 10-min test.

RESULTS AND DISCUSSION

Although the mean entrance latencies of both low (M = 37.7 sec) and high (M = 27.7 sec) yohimbine-treated groups were lower than control values (M = 78.1 sec), the elevated control mean was due primarily to a single aberrant (318-sec latency) control mouse. Analysis of variance failed to suggest any reliable group differences [$F(2,21) = 1.64, p > .10$]. Yohimbine treatment (low, M = 63.4; high, M = 64.1) did produce a marginally significant elevation [$F(2,21) = 2.98, .10 > p > .05$] of open field entries over control (M = 40.5) levels, however.

In view of yohimbine's rather robust anxiogenic effects (see, e.g., Charney et al., 1983; Davis et al., 1979; Harris & Newman, 1987; Tsuda et al., 1988), including suppression of maze exploration in rats (File & Johnson, 1987), its failure to inhibit novel open field exploration was somewhat unexpected. It is possible, of course, that this relatively simple test is insensitive to the anxiogenic effects of some drugs. If so, however, it is difficult to understand why other simple responses such as social investigation (Guy & Gardner, 1985) are not similarly affected by this drug. Alternatively, however, some investigators have reported that yohimbine increases nonreinforced (Huang, Messing, & Sparber, 1987; Sanger, 1988) and even punished (Sepinwall & Cook, 1981) leverpressing. The latter findings suggest that behavioral stimulant and/or anticonflict effects may override yohimbine's anxiogenic

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effects in some testing situations. The present results are consistent with such an interpretation and suggest that yohimbine may be of limited value as a research tool for the study of anxiety.

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