

dicates (i) that the host's prey run has been successful and (ii) that a prey item is stored and hence can be stolen. Small prey are never wrapped, but instead are held in the chelicerae and therefore are not available to the kleptoparasites.

The results of the behavior experiments suggest that the kleptoparasites indeed read the vibratory pattern of their host's prey-catching sequence and that they use the information it contains to adjust their stealing behavior accordingly. The host has certain "antiparasitic" behaviors—such as searching for stolen prey or abandoning its present web site for another—which are detrimental to the kleptoparasites (4). By monitoring the host's movements, a kleptoparasite can reduce the likelihood of being perceived; for example, it avoids moving on the orb when the host is inactive at the hub and most sensitive to vibrations in its web. In addition, an ability to evaluate the vibratory pattern enables the kleptoparasite to adjust its pillaging to the availability of prey packets and consequently allows it to conserve energy.

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8. The Fotonic Sensor (KD 45A, Mechanical Tech.) requires adjacent pairs of light sources and receivers in order to detect the amount of light reflected by a foil. Minute translocations of the threads were displayed very well but the sensor did not allow the recording of large translocations. A piezocrystal from a recorder cartridge [C. Wallcott, *J. Exp. Biol.* **40**, 535 (1963)] or a dynamic microphone was fitted with a bristle touching the web; in this setup, the signals were altered by inertia and large translocations were damped away.
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12. The signals for 20 experimental setups were recorded on a Pacal FM tape recorder and displayed on a Gould 4000 storage oscilloscope from which the photographs were taken. The frames housing the spiders (*N. clavipes*: 100 by 100 by 20 cm; *A. argentata*: 30 by 40 by 20 cm) stood on thick felt padding. In several setups, control measurements were taken from the frame at the same time that recordings were being made. During the recording of vibrations, no kleptoparasites were kept in the webs and live houseflies were presented as prey in the lower part of the web, 20 cm off the hub. No air currents were present.
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14. The web of an *Argiope* female is wide-meshed with high elasticity (40 cm in diameter, 30 radii, 40 spiral turns). This contrasts with the web of the *Nephila* female which is fine-meshed, tightly woven (55 cm in diameter, 150 radii, 160 spiral turns) and which gets additional tension through guy threads connecting the hub with a surrounding space web.
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## Pharmacologic Effects in Man of a Potent, Long-Acting Dopamine Receptor Agonist

**Abstract.** Single-dose administration of pergolide mesylate (100 to 400 micrograms) results in a dose-related inhibition of prolactin secretion which persists for more than 24 hours. During multiple-dose administration of pergolide, plasma prolactin concentrations remain markedly reduced (greater than 80 percent) and gradually return to control levels several days after drug administration is discontinued.

Dopamine receptor agonists inhibit prolactin secretion and are clinically effective in the treatment of amenorrhea and galactorrhea (1). They are also useful in the treatment of Parkinson's disease when administered either alone or in combination with L-dopa (2). Two dopamine receptor agonists of the ergoline class that have been extensively investigated in animals and man are  $\alpha$ -bromocriptine and lergotril. These drugs can reduce serum prolactin concentrations in normal volunteers and patients with hyperprolactinemia at doses of about 2 to 2.5 mg (3); however, the

duration of their effectiveness is only about 6 to 8 hours after the administration of a single dose.

In this report we describe the clinical pharmacology of pergolide mesylate, (8 $\beta$ )-8-[(methylthio)methyl]-6-propylergoline, a potent ergoline with a long duration of action.

Eight normal, healthy male volunteers aged 28 to 47 years participated in this study. The volunteers were given an oral and written explanation of the study design and the associated hazards, and they gave their informed consent. They were hospitalized on a clinical research

ward throughout the entire study period.

Initial single-dose studies were designed so that we could increase the dose of pergolide cautiously and evaluate its safety and pharmacologic effects. Five of the volunteers participated in this phase of the study. For several days the subjects were given placebo medication; then a dose of 50  $\mu$ g of pergolide was given orally to one of the subjects instead of the placebo. On specific days thereafter, pergolide was substituted in increasing doses (50 to 400  $\mu$ g) for placebo medication in the four other subjects. At the higher doses, pergolide caused pronounced uncomfortable symptoms, including nausea, emesis, and nasal stuffiness. These adverse effects occurred 30 to 60 minutes after drug administration and lasted for up to 4 hours (4). The drug also produced dose-dependent decreases in plasma prolactin concentrations (5) that persisted for more than 24 hours (see Fig. 1).

Multiple-dose studies were conducted after we had established a range of safe doses. Placebo medication was administered to five subjects for the first 7 days. Pergolide was administered orally for the next week. The initial dose of medication was administered as a single 250- $\mu$ g dose. In only one of the subjects was this dose well tolerated without uncomfortable side effects, and this dose was continued in this individual for the entire week. However, for the remaining four subjects, who experienced nausea (and emesis in two subjects) and nasal stuffiness, the daily dose was reduced to 150  $\mu$ g. This dose was continued for the next 4 days, after which the subjects were given a 250- $\mu$ g dose for the final 2 days. Tolerance developed to the adverse effects of pergolide in all five subjects, as evidenced by the failure of the 250- $\mu$ g dose to produce any significant side effects on days 6 and 7 of the study.

The concentration of prolactin in the plasma of all subjects was measured by radioimmunoassay (6). The prolactin concentration was unaffected by the placebo medication, whereas after a single dose of pergolide the concentration was markedly reduced. This suppression lasted at least 24 hours, at which time the next dose of the drug was administered. The long-term administration of pergolide (for 7 days) resulted in a significant decrease in plasma prolactin concentration (greater than 80 percent) ( $P < .01$ ) (Fig. 2). In some subjects the plasma prolactin was reduced to concentrations at or below the limit of detection of the method (that is, 0.5 ng/ml). In one of the five subjects the plasma prolactin was only slightly reduced after pergolide adminis-

tration. However, the initial concentration of prolactin in this subject before pergolide administration was very low (1.4 to 2.0 ng/ml); the concentration after administration was 1.1 to 1.6 ng/ml. In contrast, the prolactin concentrations in the remaining subjects were reduced from mean control values (at 8 a.m.) of 9.5 ng/ml (range 5.1 to 12.7 ng/ml) to a mean of 1.0 ng/ml (range 0.5 to 2.4 ng/ml).

After completion of the 7-day course of drug administration, plasma prolactin concentrations remained suppressed for at least an additional 3 days, after which they returned to the concentrations in

control subjects receiving placebo and then temporarily exceeded these levels (that is, they showed a rebound effect).

In contrast to the marked effect that pergolide had on the concentrations of plasma prolactin, this drug had no significant effect on the concentrations of plasma luteinizing hormone (LH), follicle-stimulating hormone (FSH), growth hormone, cortisol, and thyroid-stimulating hormone (TSH). Thus it appears that pergolide, at the doses used, was specific in inhibiting the secretion of prolactin, although other endocrinologic effects cannot be excluded since only two time periods were used in this investigation.

Studies with lergotril and  $\alpha$ -bromocriptine indicated that postural hypotension occurred after the initial doses were administered. In the present study we monitored the blood pressure of all subjects. Although some subjects did experience clinical symptoms of postural hypotension, such as lightheadedness on standing, there were only minimal decreases in systolic and diastolic blood pressure (about 10 to 15 mm-Hg) when subjects were lying down or standing. Moreover, there was no significant difference between the blood pressure of subjects receiving the placebo and of subjects receiving the drug.

Our results demonstrate that in man pergolide produces a marked lowering of plasma prolactin concentration and that this effect is of long duration. Pergolide in high doses produces nausea and emesis, effects related to its dopamine receptor stimulating properties and shared by other drugs in this pharmacologic class. In animals, pergolide induces turning behavior in rats with 6-hydroxydopamine-induced lesions of the substantia nigra, decreases serum prolactin concentrations in rats treated with reserpine, decreases dopamine turnover in rat brain, and produces stereotyped hyperactivity (7). These effects indicate that, pharmacologically, pergolide is a dopamine receptor agonist. The currently used dopamine agonists of the ergoline type (lergotril and  $\alpha$ -bromocriptine) are effective in a variety of disease states, including Parkinson's disease, amenorrhea and galactorrhea, and acromegaly. Pergolide appears to be more potent and its effects are of a greater duration than the previously studied ergoline dopamine agonist; therefore, it may be useful in diseases associated with dopamine deficiency at the receptor site.

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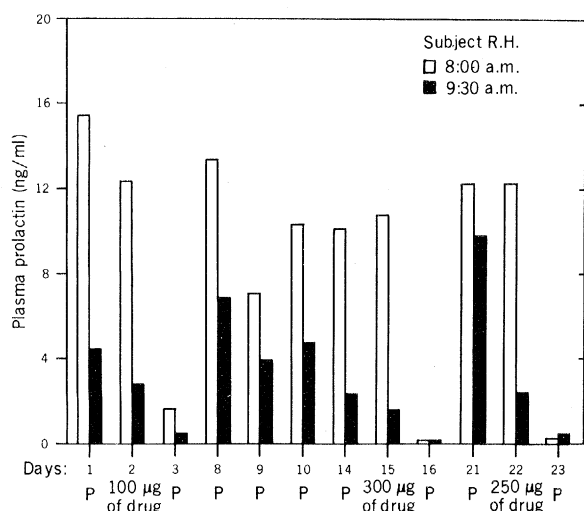


Fig. 1. The effect of single doses of pergolide mesylate on the plasma prolactin concentration. Values represent those from a typical subject to whom either placebo (P) or various doses of pergolide were administered. The prolactin values at 8:00 a.m. were obtained just prior to drug administration. Numbers above placebo or drug represent the day of study.

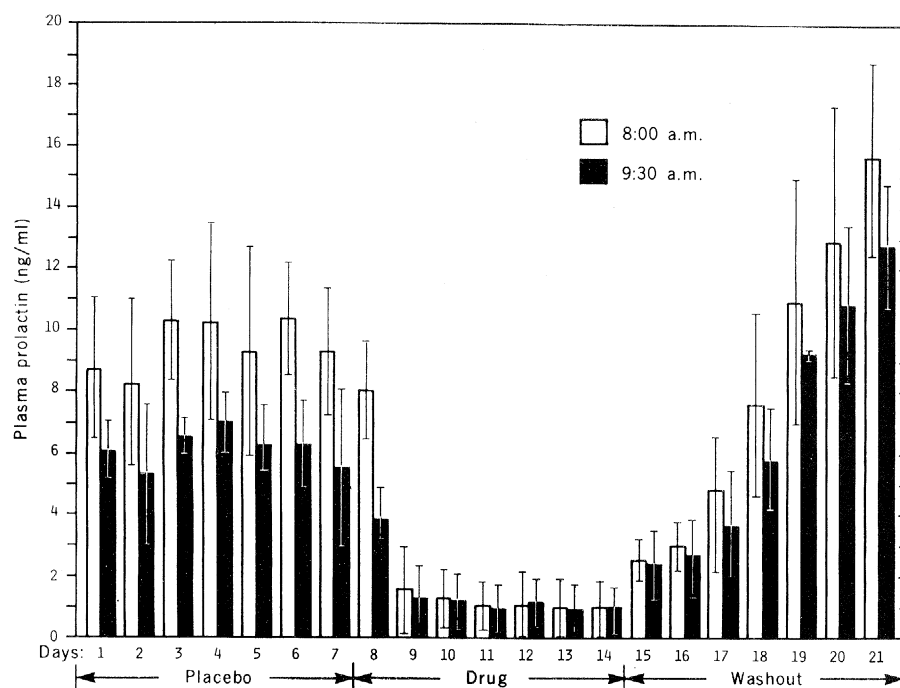


Fig. 2. The effect of multiple doses of pergolide mesylate on the plasma prolactin concentration. Placebo medication was administered for 7 days, followed by the administration of pergolide at an initial dose of 250 µg. In four of five subjects the dose was reduced to 150 µg for 4 days, followed by 250 µg for the remaining 2 days. The fifth subject received 250 µg daily for 7 days. No medications were administered after day 14 (washout). Values represent the mean  $\pm$  standard deviation for five subjects.

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4. After the administration of  $^{14}\text{C}$ -labeled pergolide, total radiation in plasma reached its peaked concentration at 1 to 2 hours, indicating that the drug was absorbed during this period of pharmacologic activity (A. Rubin *et al.*, unpublished observations).

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## Genetic Variance in Nonverbal Intelligence: Data from the Kinships of Identical Twins

**Abstract.** *The multiple relationships within kinships of adult monozygotic twins permit incisive analyses to be made of genetic and environmental effects on behavioral traits. Data from families of 65 monozygotic twin pairs yield evidence of genetic variance on the Block Design Test, a nonverbal measure of general intelligence.*

A comparison of mental ability of foster children with that of their biological and their adoptive parents was first reported in 1924 (1), and 1 year later H. J. Muller presented the first case report of intellectual resemblance in monozygotic (MZ) co-twins who had been separated in infancy (2). In the succeeding half-century, studies of adopted children and separated identical twins have had a central role in research on genetic and environmental determinants of cognitive abilities. The resultant data have generated a continuing controversy (3), and its resolution may require new research designs.

The families of adult identical twins provide a new paradigm of particular promise for behavior-genetic study (4). In this report we describe the paradigm and illustrate its application.

In Fig. 1 the multiple parent-offspring relationships found within families of adult identical twins are diagrammed. Children in each of the nuclear families derive half their genes from a twin parent, those genes being identical with genes of the parent's twin sister or brother (the children's "twin aunt" or "twin uncle"). Since the children and the twin aunt or uncle do not live in the same households, their relationship is somewhat comparable to that between foster children and their biological mother or father. In this way, studies of children of MZ twins provide a parallel to studies of adopted children, with two important advantages: (i) There is no disruption of the nuclear family milieu; the children are reared by their biological parents in their

own homes. (ii) In adoption studies biological fathers are rarely available for study (5); the relationship of nephew or niece to twin uncle parallels that of foster children to their biological father.

The environmental covariance of a nephew or niece and the twin aunt or uncle will be markedly less than that of a parent and child living in a common household. It may not be zero, however, because MZ twins may select or create similar postmarital environments. An estimate of such effects can be obtained from the resemblance of nephew or niece to the spouse aunt in kinships of male twins and to the spouse uncle in kinships of female twins. In the absence of assortative mating, the children share neither genes nor a household environment

with the spouse aunt or uncle, and any behavioral resemblance would therefore suggest an environmental covariance common to all members of the kinship.

Because their twin parents have identical sets of nuclear genes, children of MZ twins are genetically related to one another as half-siblings; socially, they are reared as cousins in separate homes. Further, in contrast to conventional half-siblings resulting from divorce, death of a parent, or illegitimacy, MZ half-siblings are expected to be of the same age and size. Accordingly, offspring of MZ twins afford a unique human parallel to methods employed in animal genetics, where controlled matings of sires to multiple dams yield estimates of genetic, environmental, and maternal effects from a nested analysis of variance of the full- and half-sib progeny. Better still, half-sib progeny occur with equal frequency among maternal and paternal MZ twins, providing a balanced research paradigm that cannot be achieved in lower animals even with controlled matings. To illustrate the paradigm, we here present a study in which it is applied to the Block Design Subtest of the Wechsler Intelligence Scales.

Wechsler's Block Design Test is an adaptation of one introduced in 1923 by Kohs (6), who presented evidence that results from his test correlated highly with results from the Stanford Binet but, unlike the Binet, had only a modest relation to level of education. Research with Wechsler's adaptation supports Kohs's assertion that the block test provides a measure of general intelligence. Across a wide age range, block design is highly related to the general factor common to all Wechsler subtests (7); it is the most reliable of the nonverbal subtests, and no

Fig. 1. Parent-offspring relationships in families of identical twins. (A) The offspring of identical twin mothers comprise a maternal half-sibship who genetically relate to their twin aunt as closely as they do to their own mother. (B) In the absence of assortative mating, offspring in a paternal half-sibship share neither common genes nor a common environment with their spouse aunt. In a parallel manner, offspring of identical twin brothers genetically relate to their twin uncle as closely as they do to their own father but offspring in a maternal half-sibship share neither common genes nor a common environment with their spouse uncle.

