increase in [^{3}H]casein synthesis, whereas in the presence of antiserum to receptor no increase was observed. Essentially the same results were obtained when γ-globulin fractions isolated either from control or antiserum to the receptor were used. These results suggest that the inhibitory factor in the serum was due to the presence of antibodies. However, direct studies indicated that the specific binding of [^{125}I]oPRL to explants was reduced by 85 to 90 percent in the presence of antiserum to the receptor (*7*). These findings also demonstrate that the antiserum did not bind or destroy prolactin. The above observations taken together indicate that the antibodies to the receptor block the biological action of prolactin by blocking receptor sites, rendering them inaccessible to the hormone.

To demonstrate that the inhibitory effect of the antiserum was specifically limited to prolactin-mediated effects, two additional experiments were performed (Fig. 3). When transport of [^{14}C]aminoisobutyric acid (AIB) was measured in mammary explants cultured in a manner similar to that used for the determination of [^{3}H]casein synthesis, it was observed that insulin alone stimulated the uptake of [^{14}C]AIB transport, a finding that was observed previously (*8*). Addition of either control guinea pig serum or antiserum to the receptor did not influence the effect of insulin. However, the addition of prolactin to the medium containing control serums caused a further 50 percent stimulation of the uptake of [^{14}C]AIB above that observed in the presence of insulin plus serum. The prolactin-dependent portion of the [^{14}C]AIB transport was completely abolished on the addition of antiserum to the receptor.

Cellular metabolism, as reflected by the oxidation of [1-^{14}C]glucose in the cultured mammary explants, was not impaired by the addition of antiserum to the receptor (Fig. 3B). This observation shows that the antiserum selectively blocks the action of prolactin without any effect on insulin-mediated actions such as amino acid transport and oxidation of [1-^{14}C]glucose in the same tissue. The inhibition of prolactin action by the antiserum is thus specific and is not due to a general inhibition of membrane-mediated functions or due to a "toxic" effect of the antiserum on mammary cells.

Our results support the hypothesis that the membrane structures which bind prolactin are essential for mediating several actions of this hormone. Thus by definition, these structures are receptors for prolactin. The immunological approach used in our study may also be extended to elucidate receptor functions in intact animals as well as to locate putative target organs for prolactin.

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7. Mammary explants were cultured in medium containing only insulin and hydrocortisone in the presence of antiserum to receptor or control serum. About 5×10^5 count/min (0.5 ng) of [^{125}I]oPRL was added to each dish. For each determination of binding of [^{125}I]prolactin, two dishes contained only [^{125}I]prolactin and two dishes contained the same amount of [^{125}I]-prolactin plus 10 μg of unlabeled prolactin. After incubation for 10 hours, explants were weighed and washed twice with ice-cold medium, and the radioactivity was determined. Specific binding refers to the amount of [^{125}I]prolactin bound to explants in the absence of unlabeled prolactin minus that found in the presence of unlabeled hormone. Similar inhibition of binding of [^{125}I]prolactin to explants was observed 1 day and 4 days after the explants had been exposed to antiserums to receptors.
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Morphine-Induced Rotation in Naive, Nonlesioned Rats

Abstract. *In rats injected with morphine in the midbrain reticular formation, pronounced ipsilateral rotation behavior was elicited by mild auditory and visual stimuli. The frequency of occurrence and rate of rotation were dose-dependent. This effect was site specific and drug specific; other drugs (except heroin) failed to induce this behavior. Naloxone potentiated the morphine rotation. Pretreatment with drugs that either potentiated or attenuated the morphine rotation indicated involvement of the noradrenergic and cholinergic systems and excluded a role for the dopaminergic system. No analgesia was observed after morphine microinjection in this site; thus, the hyperresponsivity to mild auditory and visual stimuli and concurrent analgesia previously seen in animals with morphine microinjections in the periaqueductal gray matter appear to be dissociable effects of morphine, and site specific.*

Morphine, a potent analgesic opiate, has a wide spectrum of physiological and behavioral effects, including analgesia, hypothermia, respiratory depression, stimulation of locomotor activity, and euphoria; repeated administrations lead to development of tolerance and drug-seeking behavior. Cessation of morphine administration after repeated administrations leads to another behavioral syndrome, "abstinence," characterized by irritability, weight loss, increased intestinal motility, wet shakes, ear blanching, teeth chattering, and so forth. It seems probable that different sites in the central nervous system mediate these diverse effects of morphine and that different neurochemical systems underlie the different effects observed.

Rotation behavior has been reported (*1*) in morphine-dependent animals during naloxone-precipitated abstinence after various pretreatments involving alterations in the dopaminergic system. Typically, rotation behavior occurs after administration of dopamine agonists and antagonists in animals with lesions of the nigro-neostriatal pathway, and it is currently the focus of intensive investigations as an animal model for extrapyramidal malfunction (which occurs in such disorders as Parkinsonism). The results of these studies implicated primarily the dopaminergic system, although there were indications that serotoninergic and cholinergic mechanisms were also involved (*2*). Thus, the finding that rotation behavior was precipitated during morphine withdrawal in lesioned or pretreated rats suggested the involvement of dopaminergic mechanisms in the phenomenon of morphine dependence.

We report here the occurrence of pronounced rotation behavior following intracerebral microinjection of morphine in naive, nonlesioned rats. Following microinjection of morphine in the midbrain reticular formation (MRF), rats responded to previously neutral stimuli, such as auditory and visual ones, by a burst of "pivots" (rapid rotations) on the ipsilateral hind leg. The rate of rotation, often greater than 2 per second, was at least several times that reported to follow ad-

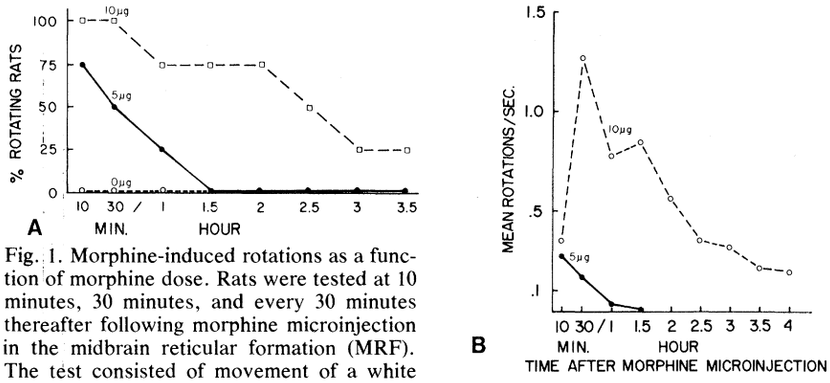

Fig. 1. Morphine-induced rotations as a function of morphine dose. Rats were tested at 10 minutes, 30 minutes, and every 30 minutes thereafter following morphine microinjection in the midbrain reticular formation (MRF). The test consisted of movement of a white cloth above the animal's head for 1 minute, during which 360° rotations were counted. Half of the animals were injected in the left MRF, the other half in the right MRF; all rotations were ipsilateral to the side of injection and were of type 3 (see text). (A) Frequency of rotators as a function of morphine dose. The 0-μg group, injected with the vehicle (Ringer solution) alone, showed no rotation; the 5-μg group showed a moderate level, and the 10-μg group showed 100 percent rotation. All rats were subsequently tested with a standard dose of 20 μg in the MRF and ascertained to be type 3 rotators. (B) Rotation speed as a function of morphine dose. The 0-μg group showed no rotations, the 5-μg group showed moderate speed, and the 10-μg group showed considerable speed (with some rotating more than twice a second).

ministration of dopamine agonists and antagonists in animals with unilateral nigro-neostriatal lesions (*3*), and without exception occurred ipsilateral to the side of morphine microinjection.

Three types of rotatory behavior were observed: (type 1) curvature of the body into an inverted "J" shape (without completion of a 360° rotation); (type 2) "loose" 360° rotations by ambulating or running around the perimeter of a circular container; and (type 3) "tight" 360° rotations, using one leg as a pivotal point. In more than 50 rats with morphine microinjection in the MRF, type 3 rotations, always ipsilateral to the side of injection, were observed without exception. Types 1 and 2 were also occasionally, but not invariably, observed in these animals.

Adult male albino Wistar rats were implanted with a double-legged cannula; the legs, separated by 1.0 to 1.5 mm, served as guide cannulas. These were made of 30-gauge stainless steel tubing (outer diameter, 0.30 mm) and the tip of one of the legs was aimed at a point 3 mm dorsal to the intended site. The intended site was 0.2 mm posterior to intra-aural zero, 9.25 mm below skull surface, and 1.0 to 1.5 mm lateral to the midline (with incisor bar set 5.0 mm above intra-aural zero). The other leg of the cannula allowed for control injections to be made in the adjacent site 1.0 to 1.5 mm away, to see if morphine microinjections at this other site would result in the same behavior. The injection needle, made of 35-gauge stainless steel tubing (outer diameter, 0.13 mm), was calibrated under a microscope (× 7) to ensure that it extended precisely 3 mm beyond the tip of the guide cannula. The microinjection technique has been described in detail elsewhere (*4*). At least 1 week elapsed after surgery before any testing was conducted.

In the first study, 12 cannula-implanted (but otherwise naive) rats were randomly assigned to three groups, the first group receiving no morphine (Ringer solution only) and the second and third groups receiving 5 and 10 μg of morphine, respectively. The injection was always 0.5 μl, infused at a rate of 0.1 μl per 15 seconds by a Hamilton microliter syringe driven by a motor-operated micrometer controlled by a timer. After the injection, the needle was kept in place for another 45 seconds to allow the surrounding tissue to absorb the drug. Each subject was then tested at 10 minutes, 30 minutes, and every 30 minutes thereafter, until the animal ceased to respond. Each animal was placed in a large individual plastic container (60 cm high and 45 cm in diameter), and the test consisted of the experimenter ("blind" as to group assignment of each rat) waving a white cloth above the animal's head for 1 minute, during which the number of rotations (type 3) were counted. Figure 1 shows that the morphine-induced rotation was dose-dependent. (All rats were subsequently tested with a standard test dose of 20 μg of morphine in 0.5 μl of Ringer solution and ascertained to be rotators of the type 3 kind.) Typically, the rats would show a burst of five or six pivots (type 3 rotation), always ipsilateral to the side of injection, with the rotations gradually slowing and then stopping for an interval, followed by another burst of pivots, with a subsequent quiescent period, and so forth. The rotation began about 10 to 15 minutes after microinjection, and with time the number of rotations per burst decreased and the quiescent periods between bursts increased. The rotation behavior usually lasted for 2 to 3 hours, but in some animals as long as 8 hours. The burst of rotation could be elicited by any slight auditory stimulus (such as a whisper, or even the faint sound of a distant door closing), or any movement in the visual field of the animal.

The specificity of this effect of morphine was tested in two ways. First, to ascertain the anatomic specificity of the effect, morphine (20 μg) was injected in the control site, using the other leg of the cannula in the same animals. At this site, type 3 rotation was never observed after morphine microinjection. Second, to ascertain drug specificity, other pharmacological agents were injected in the MRF site. Microinjection of heroin (20 μg) resulted in pronounced type 3 rotation; however, levorphanol (40 μg), dextrorphan (20 μg), methadone (40 μg), chlorpromazine (10 μg), dopamine (50 μg), noradrenalin (50 μg), carbachol (10 μg), and atropine (10 μg) all failed to induce type 3 rotation. (Each drug was tested in at least four rats.) Interestingly, after microinjection of chlorpromazine, a catecholaminergic blocker, some animals showed contralateral curvature (type 1). Naloxone given either systemically (20 mg/kg intraperitoneally) or intracerebrally (20 μg in the MRF) either 10 minutes before or after the morphine microinjection (20 μg in the MRF) failed to block, but rather potentiated, the effect of morphine in inducing rotation.

What are the neurochemical events underlying this morphine-induced rotation? To test the possibility that morphine-induced rotation is related to the rotatory behavior following application of dopamine agonists and antagonists in animals with unilateral disruption of the nigro-neostriatal pathway (and consequent bilateral asymmetry in dopaminergic neurotransmitter levels), eight rats were pretreated with either 1 or 3 mg per kilogram of the dopaminergic blocker pimozide, given intraperitoneally 4 hours before the morphine microinjection (20 μg in the MRF). However, this pretreatment failed to block the morphine-induced type 3 rotation. Pretreatment with dopamine (50 μg in the MRF) also failed to affect the subsequent morphine-induced rotation.

Similarly, the alpha and beta noradrenergic blocking agents phentolamine (either 1 or 3 mg/kg given intraperitoneally 0.5 hour before) and propranolol (1 or 3 mg/kg given intraperitoneally 2 hours be-

fore) failed to affect the subsequent morphine-induced rotation. Pretreatment with noradrenalin (50 μg in the MRF), however, attenuated the subsequent morphine-induced rotation. Pretreatment with carbachol (10 μg in the MRF) potentiated and with atropine (10 μg in the MRF) attenuated the morphine-induced rotation. These results suggest that the mechanism underlying morphine-induced rotation is different from that following application of dopaminergic agonist or antagonist in unilaterally nigroneostriatal lesioned animals, and involves a complex interaction between cholinergic and noradrenergic mechanisms (5).

The rotation behavior following morphine microinjection in the MRF appears to have two components: (i) a heightened arousal, with the rat being hyper-responsive and making vigorous "runs" to escape from previously neutral auditory and visual stimuli, and (ii) an impaired ability to move the ipsilateral hind limb, so that the net effect is a pivot, or rotation. [We observed that the ipsilateral fore and hind limbs were often hypotonic and showed a loss of placing reflex (6).]

Circus movement and head turning have been reported following MRF lesions; these were contralateral to the side of lesion (7). Electrical stimulation in the ventromedial MRF elicited an ipsilateral turning of the head and body (8); however, contralateral turning has also been reported. This rotatory behavior, however, appears to be of a different kind, more similar to type 2, than the bursts of rapid rotations with one leg as a pivotal point seen in our studies. Thus, it seems unlikely that the effect of morphine here is similar to that of electrical stimulation.

Hyper-responsivity to previously neutral, mild auditory and visual stimuli was previously reported (9) following morphine microinjections in the midbrain periaqueductal gray matter (PAG). The hyper-responsivity took the form of explosive bursts of repetitive, rapid leaps, sometimes as high as 60 cm. In contrast, morphine microinjection into the MRF resulted in animals oriented in a horizontal (rather than vertical) plane, and the rotating animals never exhibited any leaps. Nevertheless, the hyper-responsivity to mild stimuli seen following morphine microinjection in both the PAG and the MRF suggests a common neural pathway or mechanism of action for this stimulatory action of morphine. Since the MRF is known to be an "activating" system, it is not surprising that the morphine action here is to lower the threshold for sensory-motor systems. In the PAG-injected animals, the hyper-responsivity to previously neutral auditory and visual stimuli was accompanied by a profound analgesia to painful stimuli (pinches, pinpricks, and hot and cold stimuli). However, in the MRF-injected animals, no analgesic action of morphine could be detected. Thus, the two effects of morphine, hyper-responsivity to mild stimuli and analgesia to painful stimuli, appear to be dissociable effects of morphine, and site specific.

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Falcon Visual Acuity

Abstract. *Grating acuity, the ability to resolve high-contrast square-wave gratings, was measured in a falcon and in humans under comparable conditions. This behavioral test of falcon acuity supports the common belief that Falconiformes have superb vision—the falcon's threshold was 160 cycles per degree, while the human thresholds were 60 cycles per degree. Falcon acuity, however, was much more dependent on luminance, declining sharply with decreases in luminance.*

The belief that falcons and hawks possess extraordinary visual acuity is deeply ingrained in language and thought. It arises in part from reports of awesome feats of visual prowess based on casual observation under national conditions. More substantial evidence is provided by the anatomy of eye and retina, where a number of features facilitating acuity are present. The most notable of these is a cone density substantially greater than in the human retina (*1–3*), which implies visual acuity superior to that of humans, yet provides no basis for quantitative prediction. Recently R. Shlaer (*4*) succeeded in measuring retinal image quality in a live bird, the African serpent eagle, and conservatively deduced that its visual resolution would be 2 to 2.4 times greater than that of humans. Shlaer noted that a more definitive answer requires behavioral testing.

We report here a behavioral test of falcon visual acuity under conditions that permit direct comparison with human acuity; to the best of our knowledge this is the first such test. Our subject was an American kestrel (*Falco sparverius*), a small falcon (approximately 125 g) possessing the essential attributes of larger Falconiformes. The bird was born in the wild and donated to us at about 3 weeks of age. It was reared in our laboratory under conditions afforded a pet. These conditions made the bird, which we named Wulst, quite tame and facilitated testing.

The method of testing was the classic two-choice discrimination task, where correct and incorrect stimulus pairs are presented simultaneously and the animal selects one member of the pair by moving toward it. Our version of the method required the bird to fly 1.8 m from a starting platform to one of two perches located under 1° square stimulus windows. Selection of the window containing the correct stimulus resulted in a food reward; selection of the incorrect stimulus yielded nothing. The correct stimuli were vertically oriented square-wave gratings transilluminated for 100 percent contrast, while the incorrect stimuli were blank fields of the same mean luminance as the grating (*5*).

We trained Wulst to make discriminations by gradually introducing more complex components of the task after simpler ones had been mastered. The first step was to train him to fly from the starting platform to the perches and then return. Choice discrimination was introduced by presenting a coarse grating