10. These items were selected from the Brief Psychiatric Rating Scale [J. E. Overall and D. R. Gorham, *Psychol. Rep.* **10**, 799 (1962)]; the Bunney-Hamburg rating scale [W. E. Bunney, Jr., and D. A. Hamburg, *Arch. Gen. Psychiatry* **9**, 280 (1963)], and an amphetamine interview rating scale used at the National Institute of Mental Health.
11. The sign test was chosen because these individual scales do not meet the conditions for parametric tests. A paired *t*-test was used for the sum of the eight rating measures because the sum more nearly approximates parametric conditions.
12. In these nonblind patients, the following doses of naloxone were administered on consecutive days: D.C. 2, 4, and 6 mg; Z.L. 0.8, 1.2, and 2.0 mg.
13. We thank L. Drake, J. Rayner, and H. Brightman for administrative and manuscript help.

11 January 1977; revised 30 March 1977

Androgen Concentration in Motor Neurons of Cranial Nerves and Spinal Cord

Abstract. *After injection of [^{3}H]dihydrotestosterone, a major testosterone metabolite, radioactivity is concentrated in nuclei of certain cells in the midbrain, pons, medulla oblongata, cerebellum, and spinal cord. While there is some overlap between androgen and estrogen target neuron distribution, certain motor neurons appear to be selectively labeled by androgen; in contrast, estrogen localization prevails in sensory neurons. These results may help to explain why male sexual behavior in some rodents is not fully activated with dihydrotestosterone alone but in addition requires estradiol, a testosterone metabolite.*

The central action of androgen on the modulation of reproductive functions is thought to be mediated through the preoptic-hypothalamic region (*1*). Androgen target neurons have been detected in this region (*2*). In addition, target sites for androgen have been identified in extrahypothalamic sites, such as the septum, the amygdala, the hippocampus, and the epithalamus (*3*). This study was undertaken to search for and anatomically define androgen target cells in the lower brainstem and spinal cord. Isotopically labeled 5α-dihydrotestosterone (DHT) was used because it is a major metabolite of testosterone, which is found in the brain and not converted to estradiol (*4*). Androgen-concentrating cells were found to be widely distributed in the lower brainstem, that is, midbrain, pons, and medulla oblongata, and in the spinal cord, with a preferential localization of androgen in motor neurons of cranial nerves and of the spinal cord.

Adrenal glands and testes were surgically removed from two 60-day and two 26-day-old male Sprague-Dawley rats. After 96 hours the animals were injected intravenously with [1,2-^{3}H]dihydrotestosterone (5α-androstan-17β-ol-3-one) (44 c/mmole). The adult rats were injected with 1.0 μg and the immature rats with 2.0 μg of labeled DHT per 100 g of body weight. The animals were killed 1 hour afterward. Midbrain, pons, medulla oblongata with cerebellum, and different segments (cervical, thoracic, and lumbar) of the spinal cord were dissected, mounted on tissue holders, and frozen in liquefied propane (−180°C). Serial frozen sections (4-μm thickness) were cut in a wide-range cryostat (Harris Manufacturing Co., North Billerica, Massachusetts) and dry- or thaw-mounted on slides coated with photographic emulsion (Kodak NTB-3). After autoradiographic exposure for 5 to 15 months, slides were photographically processed and stained with methylgreen pyronin (*5*).

Cells with radioactivity concentrated in the nucleus were found in areas of the midbrain, pons, medulla oblongata, cerebellum, and spinal cord of all animals studied (Fig. 1). The topographic distribution of labeled cells appears to be similar in brains of adult and immature male rats; possible quantitative differences cannot be excluded. The labeled cells are mainly neurons but include certain ependymal and subependymal cells in the region of the fourth ventricle and spinal canal. Ependymal and subependymal cells with concentrations of radioactivity in the nucleus are most apparent in the collicular recess organ (*6*) and the area postrema. Accumulation of radioactivity is also seen in the lumen of blood vessels and ventricles. This is consistent with the presence of sex steroid–binding proteins in plasma and suggests transport of androgens through the cerebrospinal fluid.

The wide distribution of androgen-concentrating cells (*7*) is striking. Throughout the reticular formation in the mesencephalon, pons, and medulla oblongata, moderate to strong concentration of radioactivity is seen in neurons of different sizes and shapes (Fig. 1c). Androgen appears to be specifically concentrated in motor neurons in nuclei of cranial nerves and in motor neurons of the spinal cord (Fig. 1, b and d and Fig. 2). Androgen is also concentrated in the

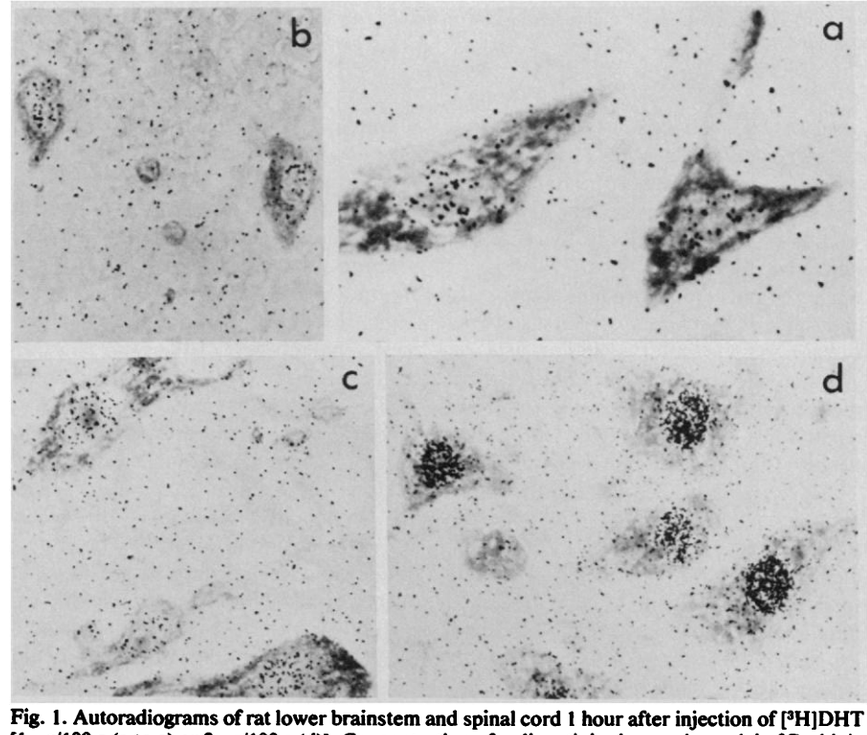

Fig. 1. Autoradiograms of rat lower brainstem and spinal cord 1 hour after injection of [^{3}H]DHT [1 μg/100 g (a to c) or 2 μg/100 g (d)]. Concentration of radioactivity is seen in nuclei of Purkinje cells (a), motor neurons of the seventh nerve (b), neurons of the reticular formation (c), and α-motor neurons in lamina IX of the thoracic segment of the spinal cord (d). Exposure times were 360 days (a), 290 days (b), 330 days (c), and 300 days (d). Stained with methylgreen pyronin (× 520).

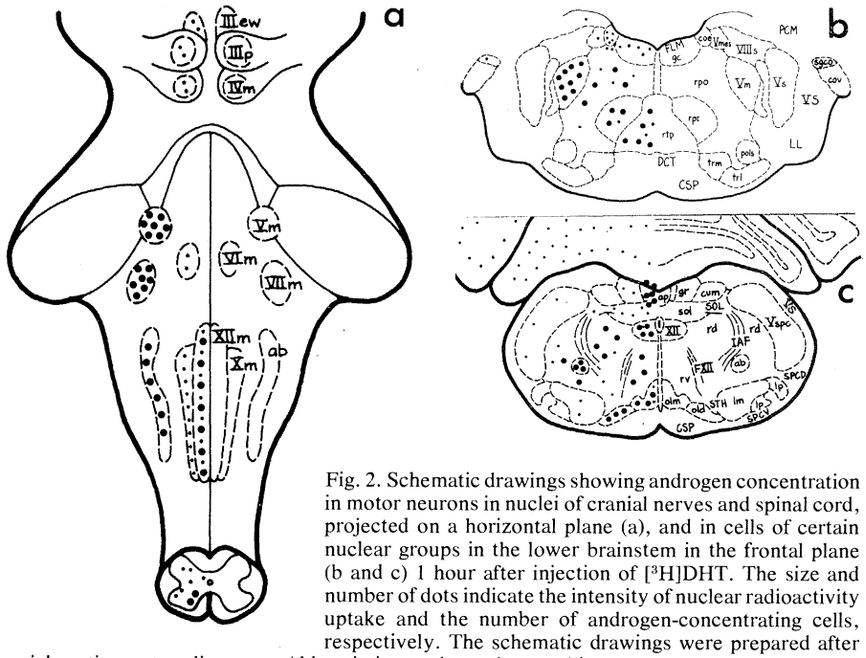

Fig. 2. Schematic drawings showing androgen concentration in motor neurons in nuclei of cranial nerves and spinal cord, projected on a horizontal plane (a), and in cells of certain nuclear groups in the lower brainstem in the frontal plane (b and c) 1 hour after injection of [^{3}H]DHT. The size and number of dots indicate the intensity of nuclear radioactivity uptake and the number of androgen-concentrating cells, respectively. The schematic drawings were prepared after serial-section autoradiograms. Abbreviations: *ab*, nucleus ambiguus; *ap*, area postrema; *coe*, nucleus coeruleus; *cov*, nucleus cochlearis ventralis; *CSP*, tractus corticospinalis; *cum*, nucleus cuneatus medialis; *DCT*, decussatio corporis trapezoidei; *FLM*, fasiculus longitudinalis medialis; *FXII*, fibrae nervi hypoglossi; *gc*, griseum centrale; *gr*, nucleus gracilis; *IAF*, fibrae arcuatae internae; *LL*, lemniscus lateralis; *LM*, lemniscus medialis; *lp*, nucleus reticularis lateralis parvocellularis; *old*, nucleus olivaris accessorius dorsalis; *olm*, nucleus olivaris accessorius medialis; *PCM*, pedunculus cerebellaris medius; *pols*, nucleus paraolivaris superior; *rd*, nucleus reticularis dorsalis medullae oblongatae; *rpc*, nucleus reticularis pontis caudalis; *rtp*, nucleus reticularis tegmenti pontis; *rv*, nucleus reticularis ventralis medullae oblongata; *sgco*, substantia gliosa cochlearis; *sol*, nucleus tractus solitarii; *SOL*, tractus solitarius; *SPCD*, tractus spinocerebellaris dorsalis; *SPCV*, tractus spinocerebellaris ventralis; *STH*, tractus spinothalamicus; *trl*, nucleus trapezoides lateralis; *trm*, nucleus trapezoides medialis; *Vm*, nucleus motorius nervi trigemini; *Vmes*, nucleus tractus mesencephali nervi trigemini; *Vs*, nucleus sensibilis nervi trigemini; *VS*, tractus spinalis nervi trigemini; *IIIew*, nucleus Edinger-Westphal; *IIIp*, nucleus oculomotorius principalis; *IVm*, nucleus trochlearis; *Vspc*, nucleus caudalis tractus spinalis nervi trigemini; *Vm*, nucleus motorius nervi trigemini; *VIm*, nucleus abducens; *VIIIm*, nucleus vestibularis medialis; *Xm*, nucleus dorsalis motorius nervi vagi; and *XIIm*, nucleus hypoglossus.

cerebellar connections of the somatomotor system, with labeling of neurons in the different portions of the pontine nuclei and the accessory olivary nuclei, as well as of Purkinje cells of the cerebellum (Figs. 1a and 2c).

There is little or no radioactivity concentrated in nuclei of sensory nerves, such as the acoustic, vestibular, and trigeminal nuclei. In the nucleus tractus mesencephali nervi trigemini, small labeled cells are occasionally seen between the large unlabeled neurons. There are also labeled cells in the locus coeruleus, the nucleus tractus solitarii, the area postrema, and various raphe nuclei. Furthermore, labeled cells are seen throughout the central gray of the aqueduct and the fourth ventricle, with highest accumulation in the region of the collicular recess. Concentrations of radioactivity are not seen in neurons of the nucleus interpeduncularis, nucleus ruber, nucleus olivaris superior, and nuclei trapezoides medialis and lateralis.

In the spinal cord, androgen target neurons are found in the ventral horn in laminae IX and X as well as in the dorsal horn, especially the nuclei dorsalis and proprius dorsalis, as well as in the nuclei intermediomedialis and lateralis. Highest concentrations of radioactivity are seen in α-motor neurons in the ventral horn in lamina IX of the lumbar and lower thoracic segments (Fig. 1d).

The results of the autoradiographic studies indicate the existence of androgen target cells not only in the diencephalon (*7*), but also in many regions of the lower brainstem and spinal cord. The involvement of components of the motor system is most conspicuous. The effects of testosterone appear to be mediated all or in part through its androgenic and estrogenic metabolites. The individual and cooperative action of the metabolites of testosterone, DHT, and estrogen have been demonstrated in different species (*8*); however, the mechanisms of action remained to be clarified. The results of our localization studies suggest that DHT is an activator of certain motor systems. Activation of sensory structures seems to be mediated mainly by estrogen since [^{3}H]estradiol localizes preferentially in brainstem regions associated with sensory functions (*6*, *9*). The absence (*10*) of estrogen concentration and the presence of androgen concentration in motor neurons in conjunction with the absence (*10*) of androgen concentration and the presence of estrogen concentration in sensory neurons in the lower brainstem and spinal cord (*9*, *11*) indicate that estrogen and androgen have different and complementary anatomical sites of action in these regions.

The anatomical substrate defined here appears consistent with behavioral observations regarding the effects of testosterone on the stimulation of copulatory behavior. Myelencephalic and spinal areas have been implicated in the mediation of copulatory reflexes, which are capable of functioning after separation from more rostral parts of the central nervous system (*12*). Sexual reflexes in male rats in which the spinal cord is transected at midthoracic level are also modulated by varying systemic levels of androgen (*12*, *13*). Copulatory behavior in castrated mature male rats can be induced by testosterone or a combined treatment with its estrogenic and androgenic metabolites, while treatment with DHT or estradiol alone is not fully effective (*8*, *14*). In guinea pigs and monkeys, however, DHT appears to be as effective as testosterone in activating sexual behavior (*8*). Our autoradiographic results support the concept that in the male rat both androgen and estrogen are required for a full activation and maximal behavioral responses by acting on different neural systems.

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24 September 1976

Stereopsis in the Falcon

Abstract. *Stereoscopic depth perception is demonstrated in the falcon, a nonmammalian with binocular vision. This result complements recent physiological evidence for binocular interaction in the bird visual system, and suggests that stereopsis may be a general attribute of vertebrate vision and not an exclusive product of mammalian evolution.*

Binocular vision, present whenever an animal's eyes view a common segment of visual space, provides the horizontally disparate stimulation considered to be essential for the relative perception of depth known as stereopsis (*1, 2*). Stereopsis, known for more than 100 years to exist in humans, provides a compelling rationale for the evolution of mechanisms designed to promote binocularity, such as yoked eye movements and semidecussation of the optic tract, which are present in mammalian visual systems and are particularly well developed in primates. The apparent absence of these mechanisms in nonmammalians, which have independent eye movements and complete decussation of the optic tract, supports the hypothesis that binocular vision and the attendant capacity for stereopsis have been products of mammalian evolution and indeed may be defining characteristics of primates (*3–5*).

But recent neuroanatomical comparisons of the visual systems of mammals and nonmammals have revealed many similarities between the older vertebrate classes and the more recently evolved mammals (*6*). The bird visual system has received special scrutiny, and in the pigeon and the owl pathways have been identified that would permit extensive interaction between the eyes (*7, 8*)

We now report a behavioral demonstration of stereopsis in the falcon, a predatory nonmammalian with excellent acuity and with temporal foveae that provide binocular vision (*9, 10*). Our subject was an American kestrel (*Falco sparverius*), which was trained to select a stereoscopic form in a classic two-choice discrimination task. In this testing situation, the bird sits on a perch and views two displays enclosed in parallel alleys; flying to the correct display (the stereoscopic form) produces a food reward,

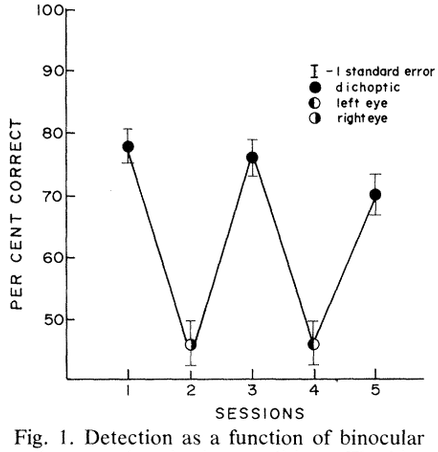

Fig. 1. Detection as a function of binocular and monocular viewing conditions. The binocular condition (●) refers to dichoptic or separate stimulation of each eye by the red and the green dot matrices. This is accomplished by placing red and green filters before the eyes and fulfills the requirement for stereoscopic presentation. The monocular conditions refer to stimulation of both eyes by only one dot matrix, either red or green. This is accomplished by placing filters of the same color, red or green, before the eyes. (◐) Stimulation by the left-eye matrix; (◑) stimulation by the right-eye matrix. The testing sessions, consisting of 25 trials each, were consecutive.

flying to the incorrect display (no stereoscopic form) produces no reward. The position of the correct stimulus is varied randomly so that chance performance would be 50 percent correct; performance significantly above chance would be evidence of successful discrimination (*11*).

The essential element in testing for stereopsis in animals is a stereopsis display that contains no monocular cues an animal might exploit through such strategies as alternately closing the eyes or making lateral head movements to obtain motion parallax information. A display free of monocular cues is provided by random element stereograms in which the left and right eye segments each consist of a matrix of thousands of minute dots (*12*). Disparity is introduced by displacing a subset of dots in one matrix. When both segments are viewed by an observer with stereopsis, the visual system detects the disparity and generates the perception of a stereoscopic form that has distinct edges and a palpable surface. When each segment is viewed alone or both are viewed by an observer without stereopsis, no trace of the form is visible—only a matrix of randomly ordered dots can be seen. We used random element stereograms consisting of large matrices of red and green dots generated on a modified color television receiver. When appropriate red and green filters are placed before the eyes the red and green dot matrices stimulate separate eyes, thereby fulfilling the conditions of stereoscopic viewing (*13*).

The falcon was trained to fly in the testing apparatus while wearing a kind of helmet-goggle device that placed filters before its eyes. The filters completely covered the field of view so that it was not possible to view the display without looking through the filters. Through a gradual series of steps we trained the bird to fly to the display containing the stereoscopic form, which was a vertical rectangle (1° by 3°) appearing in depth in front of the display background (that is, crossed disparity). During the initial stages of training, discrimination was aided by nonstereopsis information about the location and shape of the form. In the final stage of training, only stereopsis information was available. The stereograms were in the dynamic mode, in which all elements of the matrices were replaced every 16 msec by a random generator. The replacement produces a scintillating apparent motion of the elements because the spatial positions of individual elements change, but the clarity, shape, and depth of the stereoscopic form are not altered. Replace-