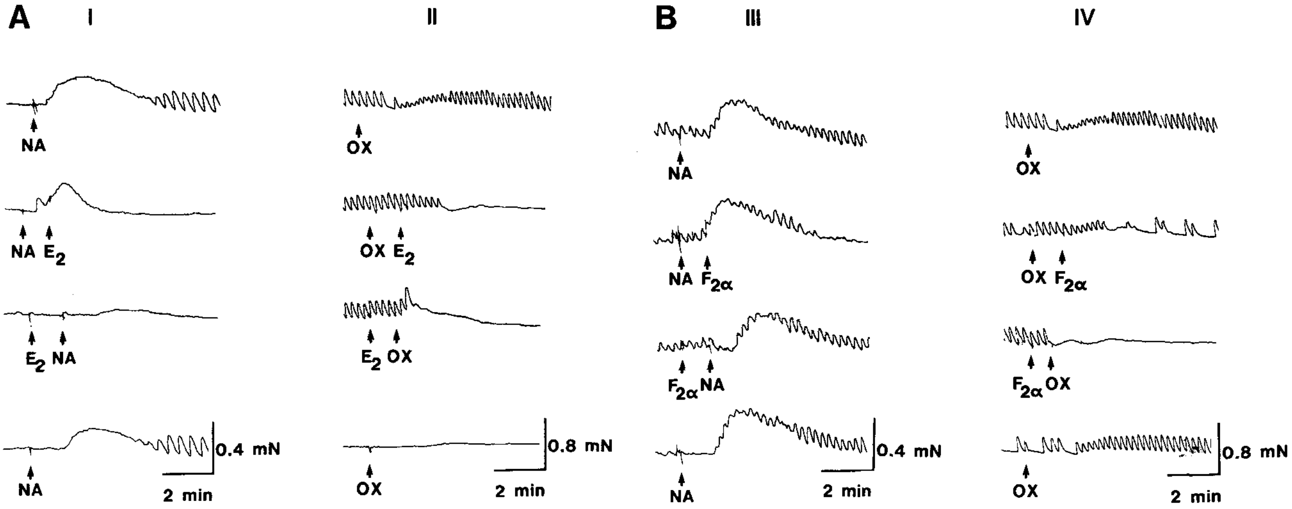

Effects of PGE_2 (A) and $PGF_{2\alpha}$ (B) on the stimulation by noradrenaline and oxytocin of cervical smooth muscle activity. The excitatory action of noradrenaline (NA 10^{-6} M, I) was reduced and that of oxytocin (OX, 100 mU/ml, II) abolished by PGE_2 (10^{-7} g/ml). $PGF_{2\alpha}$ (10^{-6} g/ml) did not influence the effects of noradrenaline (10^{-6} M, III) but inhibited the stimulatory action of oxytocin (100 mU/ml, IV). Flow rate was kept at approximately 1 ml/min. Calibration as indicated. The tracings shown represent continuous recordings from four experiments (I–IV). Tracings II and IV are registrations in the same cervical strip. The initial stimulation by oxytocin is shown in the upper panel.

PGE_2 and $PGF_{2\alpha}$ may contribute to cervical maturation at term not only by reducing the formation of collagen[7] but also by relaxing the smooth muscle.

Previous studies in this laboratory have documented the stimulatory action of noradrenaline on the cervical musculature and the relative predominance of α-adrenoceptors in the cervix of nonpregnant as well as early pregnant women[8]. Moreover, it was demonstrated that the blockage of prostaglandin synthesis by 5,8,11,14-eicosatetraynoic acid (ETYA) reduced both the spontaneous activity and the response to noradrenaline, suggesting that the effects of catecholamines may be mediated or modulated by PG products. Since PGE_2 and $PGF_{2\alpha}$ inhibit cervical muscle activity, the previously demonstrated effect of ETYA may be due to an inhibition of the formation of an arachidonic acid metabolite with an inherent excitatory action. Oxytocin also stimulated cervical contractile activity, though at concentrations higher than those required in the isthmus and corpus[10]. The observed inhibition by PGE_2 of the contractile responses to noradrenaline and oxytocin may be of physiological relevance. Its mechanism, however, remains to be studied.

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Testosterone and eye-brain asymmetry for copulation in chickens

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Summary. Asymmetry of eye function has been demonstrated in the young chicken. Precocious copulation following intramuscular treatment with testosterone can be elicited by presentation of an appropriate stimulus to the left eye, but not to the right eye.

Key words. Eye-brain asymmetry; lateralization; copulation; testosterone; monocular testing; chickens.

Young, male chicks are known to display a precocious form of adult copulation following treatment with testosterone[1]. We have now found that the elevation in copulation which follows this treatment with testosterone is evident in monocularly tested chickens only on presentation of the stimulus to the left eye, but not the right. Lack of copulation in untreated males tested binocularly appears to be due to right-eye (left hemisphere) dominance, and testosterone shifts the dominance to the left eye (right hemisphere). This indicates that androgen treatment during development can alter functional asymmetry of the brain.

Based on previous reports of testosterone's effect on the neuronal development of sexually dimorphic structures, Geschwind and Behan[2] have speculated that testosterone may play a major role in the development of brain asymmetry and so account for differences in functional brain asymmetries observed between human males and females. Although Geschwind and Behan cite possible instances of testosterone influencing structural brain asymmetries there have been few direct demonstrations that the presence of testosterone may lead to, or influence, asymmetry of brain function.

Using unilateral intrahemispheric injections of monosodium glutamate we have previously demonstrated that the chicken has brain asymmetry for a number of behaviors including the control of attack and copulation[3]. Since these behaviors are known to be androgen dependent[1], we decided to investigate the influence of testosterone on asymmetry. Brain asymmetry was investigated by using monocular testing. This technique takes advantage of the fact that avian visual pathways decussate completely[4] such that information entering each eye is processed largely by the contralateral hemisphere.

Materials and methods. On day 2 of post-hatch life male Leghorn-Australorp chickens were injected i.m. with testosterone oenanthate (25 mg in 0.1 ml of oil; Schering) and controls received 0.1 ml of the oil vehicle. These chickens were housed in groups of four until day 5 when they were moved to individual cages which visually isolated each chicken from the others. Food, water and warmth were available ad libitum. On day 5 one eye of each chick was occluded with a cone-shaped patch of adhesive, zinc oxide tape (Leukoplast, FRG). Half of the testosterone-treated chicks had their left eyes occluded and half their right. The controls were subdivided similarly. There were 11 or 12 chicks in each group. In this experiment, copulation was tested daily from days 6–18 of life with the original eyepatches remaining on until day 14 when they were removed and the opposite eye was occluded. Another experiment was conducted to examine the effects of prior binocular experience of the test situation and compared monocularly tested chicks to binocularly tested couterparts. The standard test for copulation uses the moving hand as a stimulus[1,3]. The hand, held with the palm downwards, was moved gently back and forth at the chickens chest and then held close to the floor. Copulatory behavior on the hand was scored using a ranking procedure, ranging from zero for no mounting to 10 for circling, treading and pelvic thrusting. The data collected was analyzed by Analysis of Variance using simple main effects and trend analysis where appropriate.

Results and discussion. Those chicks treated with testosterone and tested with occlusion of the right eye (i.e. using the left-eye system, LES) showed a significant linear increase in copulation over days 6–14 of life ($F_{1,10} = 13.4$, $p \leq 0.001$), the magnitude of this increase being equivalent to that reported previously for binocularly-tested, testosterone-treated males (fig. 1). When this group had their eyepatches reversed on day 14 so that they were now using their right-eye system (RES), the copulation scores dropped dramatically and remained low throughout the rest of the testing period ($F_{1,10} = 53.9$, $p \leq 0.001$); for a comparison of scores for the 4 days prior to patch reversal with the 4 days after patch reversal).

The group treated with testosterone but tested using their RES from days 6–14 showed no such significant increase in copulation ($F_{1,11} = 1.02$, $p \geq 0.05$) and had copulatory performances significantly below those of the chicks tested using their LES ($F_{1,21} = 10.7$, $p \leq 0.05$). However, after reversal of the eyepatches on day 14 so that this group was now using their LES, an increase in copulation did occur. The scores for the 4 days after eyepatch reversal (LES) were significantly greater than those for the previous 4 days (RES) ($F_{1,11} = 12.3$, $p < 0.01$; fig. 1).

Thus, the standard rise in copulation expected after testosterone treatment of male chicks can be elicited from chicks using their LES, but not from those using their RES. It is unlikely that the lower level of copulation in testosterone-treated chickens tested using their RES results from a general lack of responsiveness, since previous studies have reported superior visual learning performance in chicks using their RES[5] and not their LES. As there is complete decussation of optic nerve fibers in the avian brain, our data suggests that copulation is preferentially activated by pathways in the right side of the brain. Nordeen and Yahr[6] have recently demonstrated asymmetry for sexual behavior in the rat hypothalamus: unilateral implants of estradiol into the left side were reported to decrease lordosis and have no effect on mounting, while implants into the right side had no effect on lordosis but increased mounting. In contrast to this latter report and also to previous reports of asymmetry of another androgen-dependent behavior (viz. singing) in the avian brain[7,8] our study has detected an asymmetry evident at the perceptual level of the system, and therefore one likely to be manifest in behavior of the

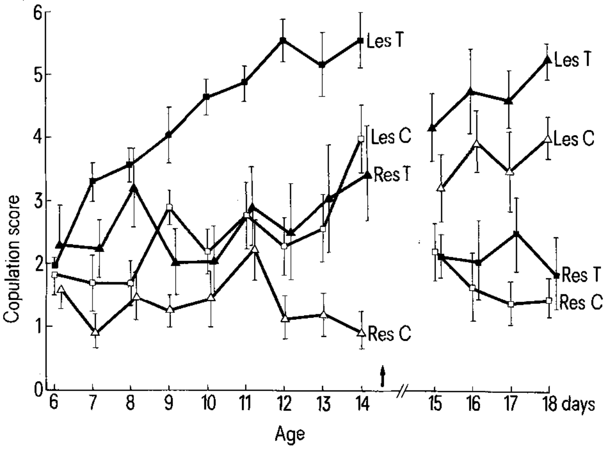

Figure 1. Mean copulation scores (±SE) for male chickens tested daily. The solid and open symbols indicate testosterone-treated and control groups respectively. The solid squares represent testosterone-treated animals initially tested using their left-eye system (LES T), and the solid triangles represent testosterone-treated animals tested using their right-eye system (RES T). After reversal of the eyepatches on day 14, the original LES T group becomes the RES T group and vice versa. Similarly for the oil-treated control groups which are represented by the open symbols, squares for those tested using their LES (LES C) and triangles for those tested using the RES (RES C).

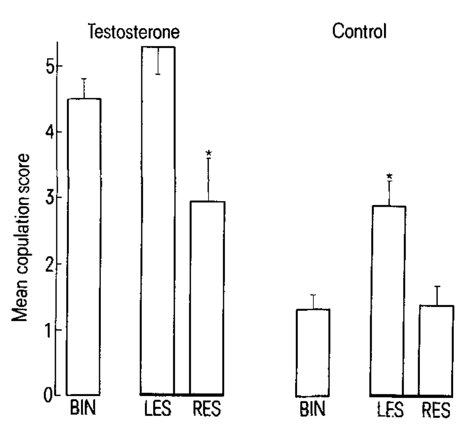

Figure 2. Copulation scores of testosterone-treated and control chicks as a function of eye use during testing. Each bar represents the mean and SE of copulation scores between days 11 and 14 of life inclusively. The binocular group for each condition is labeled BIN, while groups tested monocularly are labeled LES and RES to indicate birds tested using the left-eye system and right-eye system respectively. The asterisks indicate groups which differ significantly ($p \leq 0.05$) from their respective binocularly tested counterparts.

whole animal. The presence of an asymmetry detectable as a left-right eye difference could mean that the position of a stimulus in space relative to the bird may influence its likelihood of eliciting a copulatory response. Alternatively, the bird may overcome the eye asymmetry by having a mechanism which ensures that it will turn its head to view any copulatory stimulus with both eyes. In either case, it may be expected to influence the pattern of courtship display behavior, such as the direction of circling during waltzing.

On the later days of testing a LES-RES asymmetry for copulatory behavior developed even in control male chicks which had not received testosterone treatment (fig. 1). The group using their LES had significantly higher scores than the group using their RES ($F_{1,22} = 11.74$, $p \leq 0.001$ for a comparison of RES and LES groups over the 4 days prior to eye-patch reversal on day 14). Indeed, the control group tested using their LES showed a significant linear increase in copulation from days 6–14 ($F_{1,11} = 6.99$, $p \leq 0.025$), while the group using their RES showed no significant change over this period ($F_{1,11} = 1.58$, $p \leq 0.05$). This could possibly be due to endogenous levels of androgen rising over the first 2 weeks of life and/or to prolonged monocular eye occlusion.

It is also possible that prolonged wearing of eyepatches may interact with testosterone treatment, since after eyepatch reversal there is no longer any difference between the testosterone-treated and control groups using their RES ($F \leq 1$). Thus, in testosterone-treated animals prior monocular experience using the eye dominant for copulation (i.e. LES) may have led to a suppression of any ability of testosterone to elevate copulation in the RES.

Asymmetry for copulation was also demonstrated in chicks which had prior binocular experience in the test situation. In the second experiment, a group of testosterone-treated chicks were tested binocularly on days 6 and 7 of life. On day 8 either the right or left eye was occluded and copulation was tested 3 h later (n = 16 per group). Copulation scores remained high in the LES group (the mean copulation score with SE was 5.8 ± 0.5 in the binocular test on day 7 and 5.3 ± 0.5 when using the LES on day 8) but dropped significantly in the RES group (5.6 ± 0.5 in the binocular test on day 7, which fell significantly to 2.7 ± 0.4 when using the RES on day 8).

A comparison of monocularly and binocularly tested chicks (see fig. 2) reveals that controls using their RES score at the basal levels characteristic of binocularly-tested controls; whereas testosterone-treated chicks using their LES have scores comparable to those found in testosterone-treated chicks tested binocularly. Therefore, when tested binocularly, the RES is dominant in control chicks and the LES is dominant in testosterone-treated chicks. That is, although a control chick possess the neural mechanisms which can activate copulation at least to some degree, when tested monocularly (fig. 1), a control with both eyes open does not copulate because the RES system is dominant. The action of testosterone is to reverse dominance from RES to LES thus disinhibiting, or activating, copulation. We have previously demonstrated that light experience prior to hatching can also alter brain asymmetry[3]. The final organization of brain asymmetry in the chicken must be dependent on an interaction between genetic, hormonal and environmental factors. While not underplaying the importance of hormonal influences on brain development, recognition of the interaction between these variables must caution us against explanations of brain asymmetry based solely on hormonal causes as implied by Geschwind and Behan[2] for sex differences in the human brain.

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Induction of the synthesis of thymidine kinase by aldosterone in the kidney of the immature male rat

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Summary. Thymidine kinase activity was studied in kidneys from immature male rats after administration of aldosterone. Kinetic studies showed that the enzyme activity reached its maximum level 24 h after aldosterone injection. That increase was specific for aldosterone and could be related to the synthesis of new molecules of enzyme.

Key words. Aldosterone; kidney; thymidine kinase activity.

Steroid hormones interact in their target organs after binding to cytoplasmic receptors. These are translocated into the nucleus and nuclear receptors interact on the acceptor sites of the chromatin. It is established that the activation of genes regulated by steroids is followed by the induction of the synthesis of specific proteins. Such a mechanism of action is probably applicable to aldosterone. In fact publications have shown that this steroid binds in the kidney, having cytoplasmic and nuclear receptors[5,6,7,13,15]. More recently, it was shown by autographic study that in the kidney, the receptors of aldosterone are exclusively localized in the nucleus[2,8,9]. These results suggest that this mineralocorticoid could regulate the activity of certain genes and induce the synthesis of specific proteins. Recently in our laboratory it has been shown that estrogen receptors specifically induce the synthesis of thymidine kinase in the uterus[1,10] and that the androgens produce same effect in the prostate (in preparation). These conclusions led us to investigate whether aldosterone might effect the induction of thymidine kinase in the kidney. The results obtained show that this hormone specifically induces the synthesis of this enzyme in the kidney.