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Testosterone and Aggression: Berthold, Birds and Beyond

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Abstract

Berthold's classic study of domesticated roosters in 1849 demonstrated that testicular secretions are necessary for the normal expression of aggressive behaviour. Although this conclusion is undoubtedly correct, field studies of wild songbirds have yielded important modifications and limitations of Berthold's original hypothesis. For example, studies of the North American song sparrow (*Melospiza melodia*) during the breeding season reveal that not only does testosterone increase aggression, but aggressive interactions also increase plasma testosterone levels. Furthermore, in winter, nonbreeding song sparrows have low plasma testosterone levels but are very aggressive, and castration of nonbreeding song sparrows does not decrease aggression. Interestingly, an aromatase inhibitor (fadrozole) does decrease male aggression in the nonbreeding season, and the effects of fadrozole can be rescued with oestradiol. In winter, dehydroepiandrosterone (DHEA) from the periphery can be metabolised within the brain to supply oestradiol to specific neural circuits. Additionally, oestradiol might be synthesised *de novo* from cholesterol entirely within the brain. These mechanisms may have evolved to avoid the 'costs' of circulating testosterone in the nonbreeding season. Recent studies in tropical birds, hamsters, and humans suggest that these neuroendocrine mechanisms are important for the control of aggression in many vertebrate species.

Keywords

3β-HSD; aromatase; AVT; bird; BNST; brain; c-fos; dehydroepiandrosterone; DHEA; oestradiol; oestrogen; neurosteroid; season; songbird; stress; vasotocin; ZENK oestradiol; oestrogen

Studies in birds have contributed greatly to understanding the neuroendocrine regulation of aggression (1–7). The first study of hormones and aggressive behaviour was conducted in roosters in the 19th Century. More recently, field studies of wild songbirds have been central in unravelling hormone-behaviour relationships across seasons and habitats. Free-living animals are often more aggressive and generally have higher circulating hormone levels than captive animals (8–10). In addition, testing conditions in the laboratory can have large unexpected effects on behaviour, particularly when animals are forced to interact in constrained spaces. For these reasons, field studies can be an important complement to laboratory studies. Combined field–laboratory approaches in birds have produced novel

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insights into the social regulation of testosterone levels, the expression of aggression during the nonbreeding season, and the ‘costs’ of elevated circulating testosterone levels (4).

Berthold’s capons

The study of hormones and aggression, and of hormones in general, can be traced back to the classic experiment of Arnold Berthold in 1849 (11). He removed the testes of immature male chickens (the castrated animals are called capons) and found a decrease in some secondary sex characteristics (comb, wattles) and male-typical behaviours (11). Capons did not crow, did not try to mate with females, and did not fight aggressively with other males. Importantly, Berthold also transplanted testes into capons. When a testis was transplanted, these subjects showed normal aggressive behaviour and secondary sex characteristics. If the transplanted testis was removed, then the animal behaved as a capon. Upon dissection, Berthold found that the transplanted testis had established new vascular connections. Berthold concluded that the testes release a substance into the blood which affects behaviour and morphology. Thus, from its very beginning, the study of hormones and aggression was focused on gonadal secretions.

In seasonally breeding birds, the gonads grow before the breeding season and regress after the termination of breeding. Circulating sex steroids also fluctuate, generally with high levels during the breeding season and basal or nondetectable levels during other periods of the annual cycle (e.g. molt, nonbreeding season) (12). In many avian species, territorial behaviour shows a similar seasonal pattern: animals are territorial in spring, but gregarious and form flocks in autumn and winter (13, 14). However, there are also many avian species in which territorial aggression is expressed in the nonbreeding season, when circulating sex steroids are low (15).

Aggressive behaviour in birds

Our knowledge of the natural history, behaviour, social systems, and seasonal reproductive patterns of birds is by far greater than for other classes of vertebrates. There are approximately 9000 species of birds living in diverse habitats, from the tropical rainforest to the arctic tundra (16). Approximately 5300 species belong to the order Passeriformes (‘perching birds’), which is composed of the oscine suborder (‘true songbirds’) and the suboscine suborder (e.g. antbirds, flycatchers). There is a rich variety of social organisations, from colonial to strictly territorial, permitting comparative studies of aggression and physiological mechanisms (15, 17, 18). Many birds are terrestrial and diurnal, making their behaviour relatively easy to observe in the field. Moreover, in some species, animals return to the same territories year after year, facilitating long-term behavioural studies of individuals.

For example, Margaret Morse Nice (19) carried out pioneering studies of song sparrows (*Melospiza melodia*), a common North American songbird, by marking animals with unique combinations of colour bands and conducting detailed behavioural observations, following individuals for several years. She described territorial interactions, including postures and vocalisations (19). Song sparrows use songs, specific threat postures, feather ‘puffing’, wing

'waving' and physical contact during conflicts. Nice also described seasonal patterns of territorial behaviour and the development of aggression in juveniles. Importantly, she incorporated these behavioural observations into a larger context, including weather and population ecology. Similar data are available for many other avian species in which the neuroendocrinology of aggression has been investigated, such as European robins (*Erithacus rubecula*) (9), European starlings (*Sturnus vulgaris*) (20), red-winged blackbirds (*Agealius phoenecius*) (21), spotted antbirds (*Hylophylax naevioides*) (22) and Lapland longspurs (*Calcarius lapponicus*) (23). Such extensive behavioural and natural history data provide significant advantages when studying the neuroendocrine mechanisms of aggressive behaviour.

Field endocrinology and the challenge hypothesis

While Berthold's study in captive chickens was important for demonstrating that hormones affect aggressive behaviour, field studies of wild birds were central in showing that aggressive interactions can influence hormone levels. Early avian endocrinologists focused on domesticated species, such as chickens, but ethologists focused on the behaviour of free-living birds. These two approaches were combined in studies of wild songbirds by Wingfield *et al.* (1, 24). Initially, laboratory studies demonstrated that long photoperiods stimulate testis growth and increase plasma testosterone levels in sparrows. However, in subsequent field studies, the temporal pattern of testosterone titres differed from laboratory studies, and testosterone concentrations were higher in wild-caught sparrows (8). These two differences suggested that nonphotoperiodic information (e.g. male–male interaction) was critical for testosterone secretion.

As mentioned previously, song sparrows are a common North American songbird (25). In a migratory population in New York State, USA, plasma testosterone levels in males are very high in early spring, when males are aggressively establishing territories (8). After pairing with females, plasma testosterone levels in males decline, even though photoperiod is increasing at this time. These data raised the hypothesis that aggressive male–male interactions stimulate testosterone secretion. This hypothesis was tested experimentally. In the field, territorial males were given either long-term subcutaneous testosterone implants or empty implants in spring (26). Testosterone-treated males were more aggressive, as measured by simulated territorial intrusions (STI) using taped song playback. The immediate neighbours of testosterone-treated males had higher circulating testosterone levels than the immediate neighbours of control subjects, suggesting that cues from aggressive males stimulate testosterone secretion (26). In a separate field experiment, free-living males were exposed to a STI using both song playback and a live caged decoy for up to 120 min (27). The visual and auditory cues provoked an aggressive response. In addition, plasma testosterone levels were significantly higher in males exposed to STIs than controls.

Laboratory studies built upon these field experiments. Breeding male song sparrows were captured in the field and brought into captivity. After interaction with a novel male conspecific, plasma testosterone titres were elevated. However, interaction with a novel heterospecific male had no effect (28). In addition, laboratory experiments demonstrated that rapid changes in plasma testosterone can occur within only 10 min of STI (28).

These results and studies in many other avian species led to the formulation of the 'challenge hypothesis' (24). This hypothesis states that plasma testosterone levels and aggression are positively correlated during periods of social instability, or challenge, such as establishment of territorial boundaries or attempts at territory takeover. During such periods, aggressive interactions are more frequent, leading to high testosterone concentrations. By contrast, during times of social stability, status or boundaries are maintained by social inertia, and plasma testosterone levels are lower. Under such stable conditions, aggression and plasma testosterone may not be correlated. This hypothesis has been examined in a wide variety of avian and nonavian species (6, 29).

It may be advantageous to limit testosterone titres during the breeding season because high circulating testosterone levels incur 'costs' (30). Chronic systemic testosterone treatment can increase metabolic rate (31) and decrease body mass and fat stores in birds (26, 32). In addition, testosterone treatment suppresses immune function in some species of birds (33, 34). These costs of high circulating testosterone are likely to be most evident in studies performed in the field, where food is not available *ab libitum* and parasites are more abundant. Importantly, field studies have shown that testosterone treatment can reduce male parental care (35, 36). In many bird species, biparental care is important, or even obligatory, for offspring survival.

Territorial aggression in nonbreeding song sparrows

While Berthold's study was important for understanding the role of gonadal steroid hormones, field studies of nonbreeding birds have been useful for examining the role of nongonadal steroids in regulating aggression (15, 37). During the autumn and winter, many birds are in nonbreeding condition, which is generally characterised by regressed gonads, regressed secondary sex characteristics (e.g. cloacal protuberance), and basal or nondetectable plasma sex steroid levels. Often, nonbreeding birds abandon exclusive territories in favour of flocks. However, some species aggressively defend territories during the nonbreeding season, even if plasma testosterone is basal at this time (14, 15). Although the physiological regulation of breeding territoriality has been the focus of numerous studies (1), the proximate mechanisms underlying nonbreeding territoriality have received less attention.

In Washington State, USA, song sparrows (*Melospiza melodia morphna*) are sedentary. Males are territorial during the spring (breeding season), when plasma testosterone is high (37, 38). After breeding, the animals molt their feathers (August to September). During the molt, plasma testosterone levels are basal, gonads are partially regressed, and aggression is greatly reduced. Following completion of the molt, there is a resurgence of territorial aggression in the autumn (nonbreeding season). Plasma testosterone remains nondetectable during the autumn, and the testes and cloacal protuberance are completely regressed (15, 38, 39). Further, agonistic interactions between males do not increase circulating testosterone in autumn (38, 40). Plasma 17β-oestradiol (E_2), 5α-dihydrotestosterone (5α-DHT), androstenedione (AE), and oestrone concentrations are also basal in males during the nonbreeding season (15, 38). Importantly, castration does not decrease aggressive behaviour in nonbreeding song sparrows (41), in contrast to Berthold's capons.

The above data raised the hypothesis that aggression is independent of testosterone and other sex steroids in the nonbreeding season. This hypothesis was tested in three field experiments by treating wild male song sparrows with pharmacological inhibitors of aromatase, with or without an androgen receptor (AR) antagonist. The aromatase enzyme catalyses the conversion of testosterone to E_2 and is critical for the expression of male aggressive behaviour in reproductive contexts (42). First, a combined treatment of an aromatase inhibitor (ATD) and an AR antagonist (flutamide) decreases nonbreeding aggression in free-living males after 30 days (43). Second, chronic treatment with fadrozole, a more potent and specific aromatase inhibitor than ATD, strongly decreases nonbreeding aggression within 10 days (Fig. 1). The effects of fadrozole are rescued by E_2 replacement (Fig. 1) (44). Fadrozole did not affect body condition or plasma corticosterone levels, indicating that the animals were not affected in a nonspecific manner (44). Third, acute fadrozole treatment reduces some aspects of autumnal aggression within only 24 h (45). Taken together, these results indicate that sex steroids, particularly oestrogens, are necessary for the expression of male territorial aggression in the nonbreeding season, even though sex steroids are nondetectable in plasma and castration has no effect.

Given the behavioural effects of aromatase inhibitors, studies examined the regional and seasonal differences in song sparrow brain aromatase. *In situ* hybridisation reveals that aromatase mRNA is highly expressed in the song sparrow brain, in both spring and autumn (Fig. 2). Multiple brain regions contain aromatase mRNA: preoptic area, ventromedial nucleus of the hypothalamus, nucleus taeniae of the amygdala (Tn), bed nucleus of the stria terminalis (BnST), and caudomedial nidopallium (implicated in song perception) (39). In addition, a biochemical assay was used to measure androgen-metabolising enzyme activities in several brain regions during spring, molt and autumn. Aromatase activity in the ventromedial telencephalon dissection (includes Tn) is specifically reduced during molt, matching seasonal changes in aggression (39). Aromatase activity in the diencephalon, however, is high only during spring. The activity of brain 5β-reductase, which inactivates testosterone (46), is not elevated during molt, and thus, cannot explain the low aggression at this time. Overall, these results suggest that changes in aromatase activity may regulate seasonal changes in aggression, consistent with other studies in birds (42, 47).

The androgen substrate for brain aromatase in the nonbreeding season was unclear, because plasma levels of aromatisable androgens (testosterone and AE) are basal at this time. One candidate, dehydroepiandrosterone (DHEA), is considered an ‘inert’ androgen precursor and does not bind with high affinity to intracellular androgen receptors or oestrogen receptors (48). However, DHEA can be converted into active sex steroids within tissues that express the appropriate enzymes, such as the brain (Fig. 3A). Across the annual cycle, circulating DHEA levels are specifically reduced during the molt, when song sparrows show reduced aggressiveness (40). Interestingly, in the nonbreeding season, circulating DHEA is detectable and several-fold higher than plasma testosterone and E_2 (Fig. 3B) (40).

In the nonbreeding season, circulating DHEA might originate from the adrenals or regressed testes. In autumn birds, DHEA levels are higher in adrenal and testicular tissue than in plasma, but restraint stress (30 or 60 min) and GnRH treatment do not increase circulating

DHEA levels (40, 49). It is unlikely that circulating DHEA originates from the brain in autumn, because DHEA levels are not higher in jugular plasma than brachial plasma (49).

A subsequent field experiment examined the effects of DHEA treatment in the autumn. Treatment of wild nonbreeding song sparrows with physiological levels of DHEA increases territorial singing (but not other territorial behaviours) (50). In addition, DHEA treatment increases the size of the song nucleus HVC by approximately 50% in adult birds (50). These data may help understand why song nuclei growth is not affected by castration in some species and why song nuclei growth can occur before full gonadal development in spring (51, 52). Importantly, DHEA treatment does not stimulate the growth of a peripheral secondary sex characteristic (cloacal protuberance) (50).

Further studies examined the neural mechanisms by which DHEA might affect territorial behaviour. Arginine vasotocin (AVT) is a neuropeptide homologous to arginine vasopressin in mammals. AVT neurones in the extended amygdala (medial amygdala and BnST) are involved in the regulation of social behaviour in birds (4, 53). These neurones project to many regions, including the lateral septum, nucleus accumbens and periaqueductal grey. The lateral septum receives AVT input from the BnST and contains AVT receptors. Importantly, septal AVT infusions inhibit overt physical aggression in territorial songbirds (4). In captive breeding song sparrows, immediate early gene (ZENK, also known as egr-1) expression in the medial BnST shows a selective increase after STI (54). Moreover, infusion of an AVT antagonist into the lateral ventricle abolishes this ZENK response (54). These data suggest that AVT acts within the medial BnST to modulate neural responses to social stimuli.

The effects of DHEA on AVT within this ‘social behaviour network’ (55) were examined in nonbreeding song sparrows (56). Captive nonbreeding male song sparrows were given a DHEA synthesis inhibitor (YM116), with or without DHEA replacement. Subjects were then exposed to a STI or control. Multiple forebrain regions show an up-regulation of c-fos or ZENK in response to STI (56). Surprisingly, among the subjects exposed to STI, aggressive behaviour is negatively correlated with c-fos or ZENK expression in several areas of the hypothalamus and lateral septum (56). In addition, plasma DHEA levels are negatively correlated with c-fos expression in the medial BnST (Fig. 4A) (56). Plasma DHEA levels are positively correlated with AVT-immunoreactive neurone number in the medial BnST (Fig. 4B) (J. Goodson, A. Evans and K. Soma, unpubl. data). It remains to be determined whether the DHEA-induced increase in AVT-immunoreactive neurone number reflects increased synthesis or decreased release of AVT. Nonetheless, it is notable that DHEA influences this population of AVT neurones, given their effects on territorial behaviour and song (57). A testable hypothesis is that DHEA acts on the medial BnST to: (i) inhibit neuronal activation in response to STI and (ii) decrease transport or release of AVT. In this way, DHEA could reduce a ‘brake’ on aggression.

Additional studies examined DHEA metabolism in song-bird brain. An *in vitro* biochemical assay was used to measure the conversion of [^{3}H]-DHEA to [^{3}H]-AE and [^{3}H]-oestrogens by the sequential activities of 3β-HSD and aromatase (Figs 3A and 5) (58, 59). In captive adult zebra finches (*Taeniopygia guttata*), brain homogenates metabolise [^{3}H]-DHEA to [^{3}H]-AE, which is in turn aromatised to [^{3}H]-oestrogens (Fig. 5) (58). Trilostane, a 3β-HSD

inhibitor, abolishes the production of [^{3}H]-AE and [^{3}H]-oestrogens, whereas fadrozole, an aromatase inhibitor, reduces [^{3}H]-oestrogens but not [^{3}H]-AE. The song sparrow brain can also convert DHEA to androgens and oestrogens, with highest levels of 3β-HSD activity in the diencephalon and telencephalon (K. Soma, D. Wacker, J. Wingfield, B. Schlinger, unpubli. data). Importantly, seasonal studies show that neural DHEA metabolism is highest in the nonbreeding season (K. Soma, D. Wacker, J. Wingfield, B. Schlinger, unpubl. data).

Winter territoriality may be dissociated from plasma testosterone because of the high costs of circulating testosterone at this time (Fig. 6). Although interference with parental care is an important cost of high plasma testosterone in the breeding season, the main costs of circulating testosterone during the nonbreeding season are likely energetic costs. The nonbreeding season has reduced food supply and low ambient temperatures (60). Testosterone treatment increases basal metabolic rate (31) and decreases fat stores (33), which are important for surviving winter storms. In addition, treatment with testosterone, but not DHEA, suppresses the immune system of nonbreeding song sparrows (33). Testosterone treatment can also stimulate reproductive behaviour, which is inappropriate during winter (61). These various effects help explain why testosterone treatment reduces over-winter survival in some avian species (62–64). Thus, neuroendocrine mechanisms may have evolved to support aggression in nonreproductive contexts, while circumventing the costs of high circulating testosterone (13).

The above studies are consistent with the hypothesis that in nonbreeding song sparrows, circulating DHEA (from the adrenals or another peripheral organ) is metabolised within the brain to provide sex steroids to neural circuits controlling aggression (Fig. 7C). An alternative hypothesis is that DHEA and E_2 are ‘neurosteroids’, synthesised *de novo* from cholesterol in the brain (Fig. 7D) (65). Either mechanism would reduce the exposure of peripheral tissues and other brain regions to testosterone and E_2. Several studies suggest that neurosteroids are synthesised in the avian brain, although less is known regarding physiological functions (66–70). Current studies in song sparrows are addressing these hypotheses by measuring DHEA, testosterone and E_2 directly in brain tissue. In addition, ongoing experiments are examining the effects of STI on steroid levels in plasma and specific brain regions.

Neuroendocrine control of aggression in other species

Birds

Such neuroendocrine mechanisms are not particular to song sparrows and may be present in many other avian species. For example, several species that breed in the tropics defend territories year-round and have very low levels of circulating sex steroids throughout the year (71, 72). One case is the spotted antbird in the Central American rainforest. In this species, both sexes sing and aggressively defend territories year-round (73). Spotted antbirds have basal plasma testosterone and E_2 levels, even during the breeding season, except for transient increases during territorial encounters (74). Combined treatment with an aromatase inhibitor (ATD) and an AR antagonist (flutamide) decreased male aggressive vocalisations (songs and ‘snarls’) in the breeding season, even though plasma testosterone was nondetectable in control subjects (75).

In the nonbreeding season, male and female spotted antbirds show high levels of territorial aggression towards same-sex intruders (22). Relative to plasma concentrations of testosterone and E_2 (low or nondetectable), plasma concentrations of DHEA are elevated in males and females. In males, plasma DHEA levels are positively correlated with aggressive vocalisations and/or the duration of territorial intrusions (22). Future studies will continue to explore the endocrine regulation of male and female aggression in this species. In tropical species facing many parasites, immune function may be particularly important (76), favouring the evolution of endocrine mechanisms which avoid the immunosuppressive effects of high circulating testosterone.

Moreover, winter territoriality is not uncommon in the temperate zone. For example, field studies have documented nonbreeding territoriality in mockingbirds (*Mimus polyglottus*) (77), willow tits (*Parus montanus*) (78), European robins (*Erithacus rubecula*) (9, 79), European stonechats (*Saxicola torquata*) (80) and red grouse (*Lagopus lagopus*) (81). In these species, except for red grouse, circulating testosterone levels are basal during the autumn and winter. Other species are not territorial *per se* during the nonbreeding season, but may nonetheless express aggression. For example, nonbreeding European starlings (*Sturnus vulgaris*) compete for night roosting sites, and castration does not decrease aggression in this context (20). Given the diversity of behaviour in avian species, there may be diverse neuroendocrine control mechanisms as well.

Rodents

Recent studies of mammals reveal some striking similarities to research on birds (6). Syrian hamsters (*Mesocricetus auratus*) and Siberian hamsters (*Phodopus sungorus*) show high levels of territorial aggression under short (winter) photoperiods, when the gonads are regressed and circulating testosterone levels are basal (82, 83). Melatonin administration increases aggression in long-day Siberian hamsters, and evidence suggests that adrenocortical hormones mediate the effects of melatonin on aggression (84). Unlike laboratory rats and mice, hamsters secrete DHEA and DHEA-sulphate (DHEA-S) from the adrenal cortex (85, 86), and ongoing studies are testing the hypothesis that adrenal DHEA supports aggression in nonbreeding hamsters (6).

Humans

Studies suggest a role for DHEA in human aggressive behaviour as well. In prepubertal children, plasma testosterone levels are relatively low, but during adrenarche (approximately 7 years), circulating DHEA and DHEA-S levels begin to rise. In a study of prepubertal boys (8–12 years), circulating testosterone and DHEA-S levels were measured in normal controls and boys with conduct disorder, who were severely aggressive (87). Plasma testosterone levels were low and did not differ between controls and subjects with conduct disorder. In contrast, plasma DHEA-S levels were 50% higher in subjects with conduct disorder (87). Plasma DHEA-S (but not testosterone) levels were positively correlated with individual aggression ratings. Similar data have been reported in additional studies (88–90). Other research has examined children with congenital adrenal hyperplasia (CAH), who have clinically high levels of DHEA-S. Adolescent CAH females are more aggressive than

controls (91). In a case report, treatment of a CAH male with a P450c17 inhibitor reduced DHEA-S levels and aggressive behaviour (92).

Conclusions

Songbirds are outstanding model systems for studying the regulation of aggressive behaviour by sex steroids (7). Field experiments in birds have been central to understanding the effects of agonistic interactions on circulating steroid levels and the role of steroid hormones in aggression during the nonbreeding season. Insights from avian studies into the neuroendocrinology of aggression will continue to be of broad relevance to a variety of vertebrate species.

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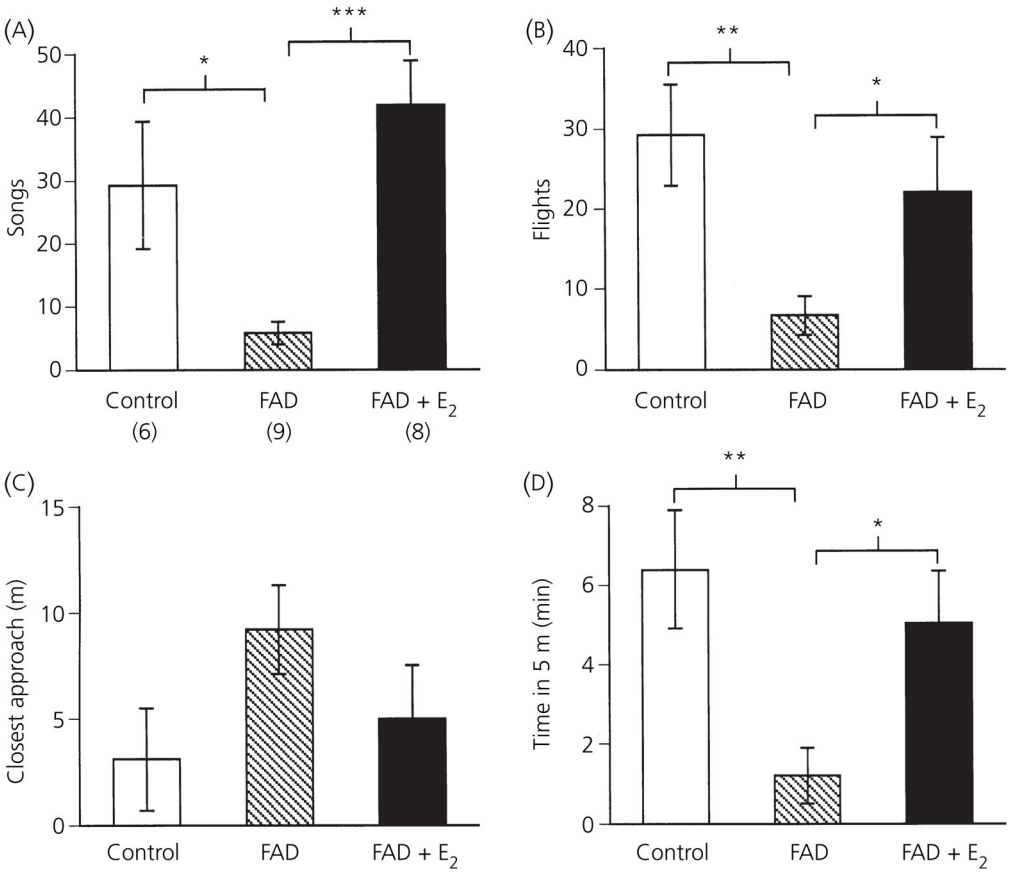

Fig. 1.

Effects of the aromatase inhibitor fadrozole (FAD) and 17β-oestradiol (E_2) on territorial aggression of nonbreeding male song sparrows in the field. Males were challenged with a simulated territorial intrusion (STI, live decoy and song playback) for 10 min. Singing (A), rapid flights (B), close approaches (C), and time spent near the decoy (D) are typical aggressive responses in this species. Sample sizes are in parentheses, and asterisks indicate significant differences between groups. Redrawn from data in (44).

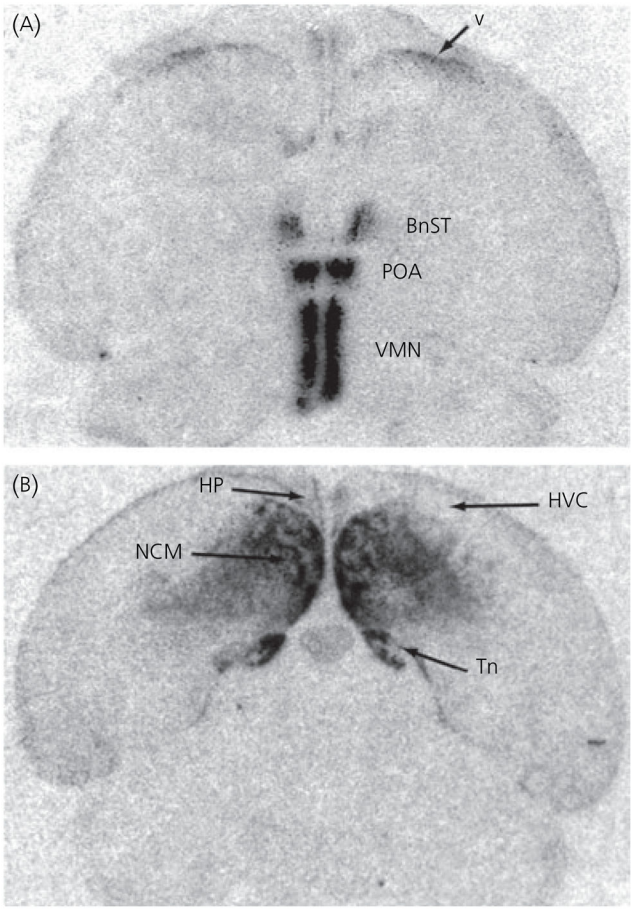

Fig. 2.

Brain aromatase mRNA expression in a wild male song sparrow. (A) Aromatase mRNA in the bed nucleus of the stria terminalis (BnST), pre-optic area (POA), ventromedial nucleus (VMN) and near the lateral ventricle (v). (B) More caudally, high expression of aromatase mRNA in caudomedial nidopallium (NCM) and nucleus taeniae of the amygdala (Tn), and low expression in hippocampus (HP). A few cells in caudomedial HVC expressed aromatase. Modified from (39).

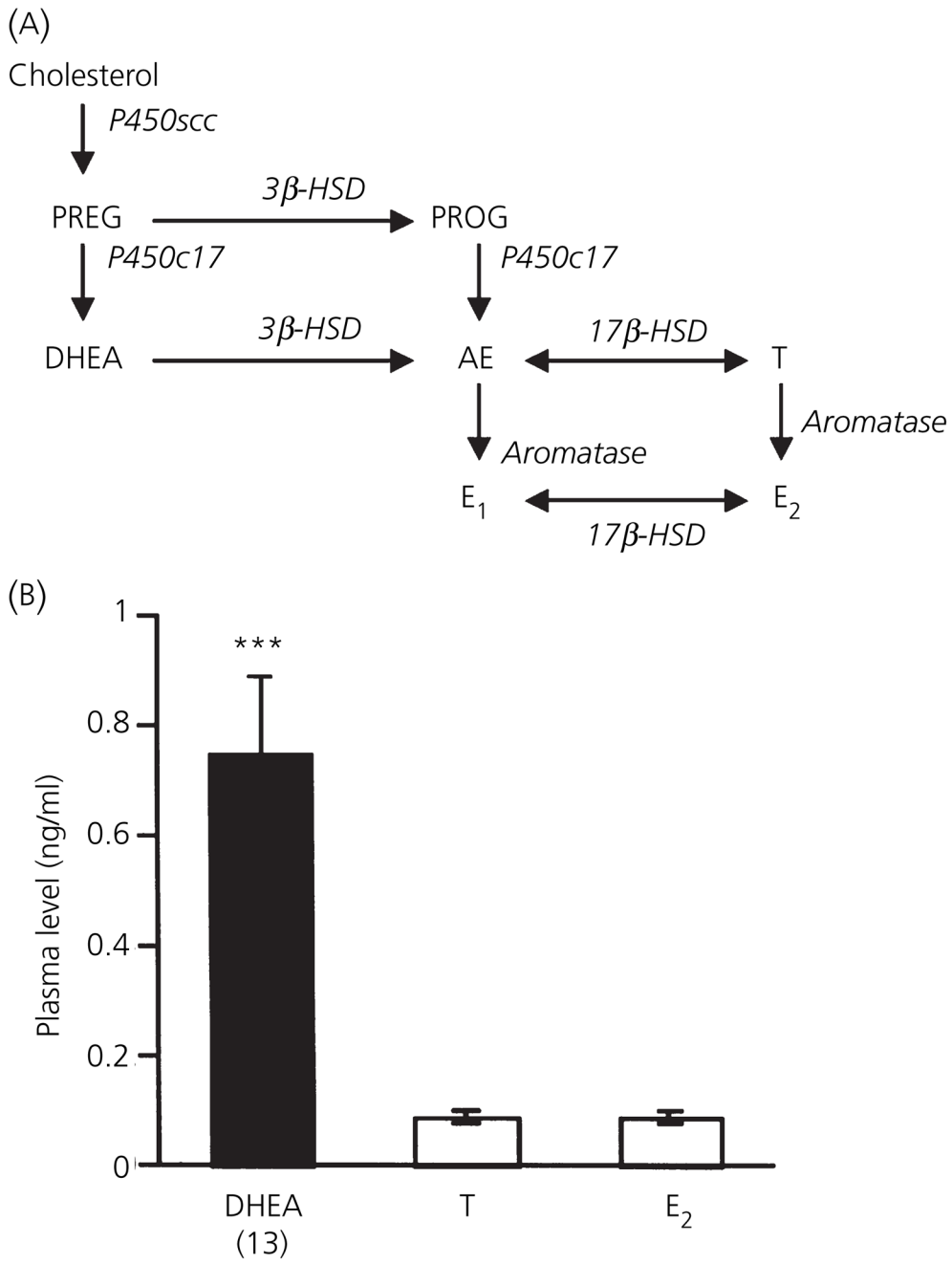

Fig. 3.

(A) A simplified diagram of sex steroid synthesis. Steroids: PREG, pregnenolone; PROG, progesterone; DHEA, dehydroepiandrosterone; AE, androstenedione; T, testosterone; E_1, oestrone; E_2, 17β-oestradiol. Enzymes: P450scc, Cytochrome P450 side chain cleavage; P450c17, Cytochrome P450 17α-hydroxylase/C17, 20 lyase; 3β-HSD, 3β-hydroxysteroid dehydrogenase/isomerase; 17β-HSD, 17β-hydroxysteroid dehydrogenase; Aromatase, Cytochrome P450 aromatase. (B) Levels of dehydroepiandrosterone (DHEA), testoterone, and E_2 (ng/ml) in brachial plasma from wild male song sparrows in the nonbreeding season. Redrawn from data in (40).

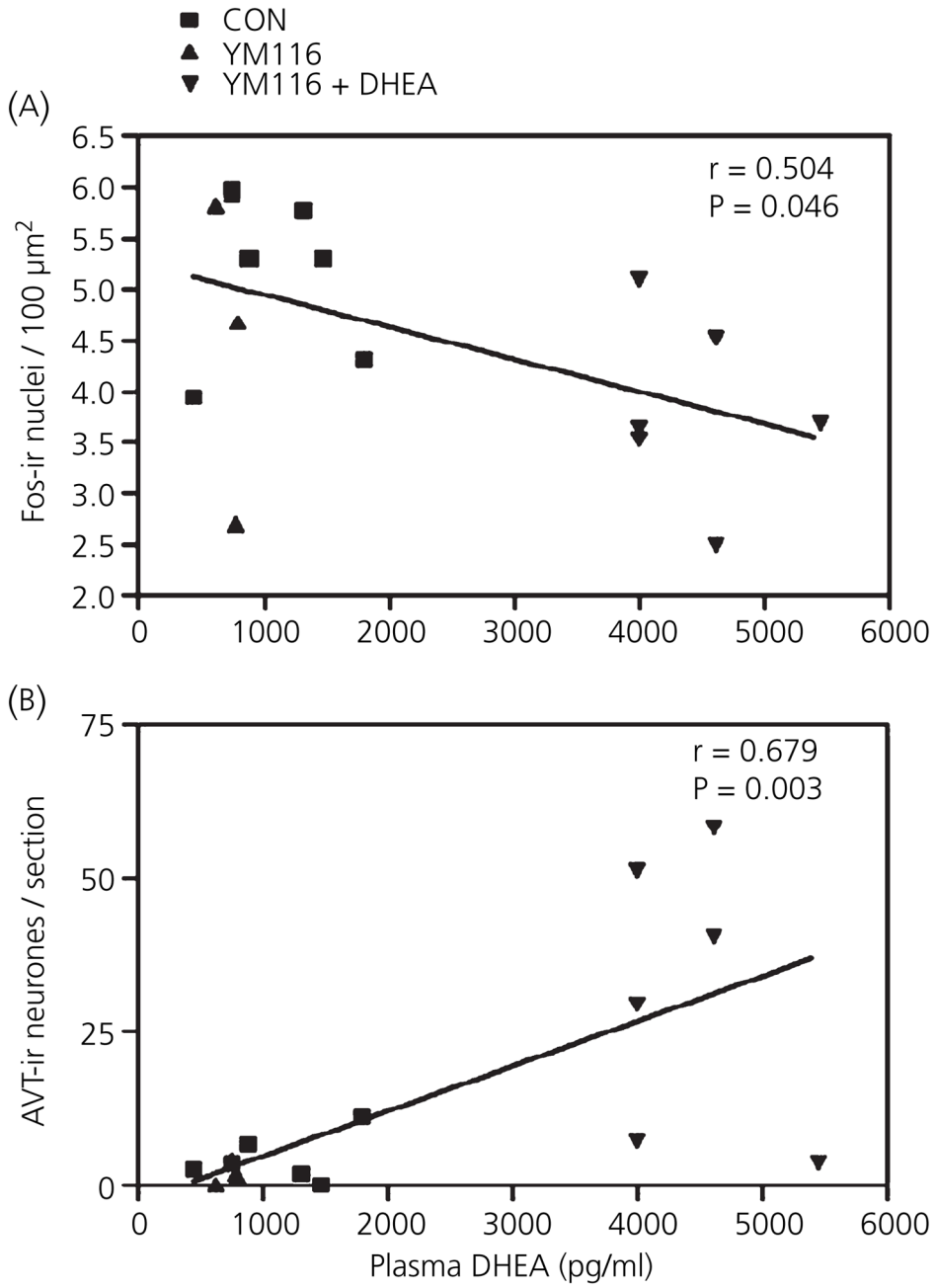

Fig. 4.

(A) Correlation between plasma dehydroepiandrosterone (DHEA) levels (pg/ml) and Fos immunoreactive (ir) nuclei in the medial bed nucleus of the stria terminalis (BnST). Redrawn from data in (56). (B) Correlation between plasma DHEA levels (pg/ml) and the number of arginine vasotocin (AVT)-ir neurones in the medial BnST. AVT-ir neurone counts are shown as the number of neurones per 40-µm coronal section. For both (A) and (B), subjects received one of three treatments: control (n = 6), YM116 (a DHEA synthesis inhibitor) (n = 4), or YM116 + DHEA (n = 6).

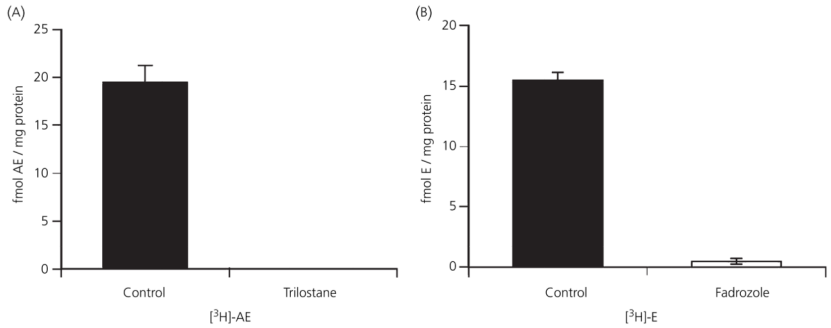

Fig. 5.

In vitro metabolism of [^{3}H]-dehydroepiandrosterone (DHEA) to (A) [^{3}H]-androstenedione (AE) and (B) [^{3}H]-oestrogens (E) by zebra finch brain homogenates. (A) Metabolism of [^{3}H]-DHEA to [^{3}H]-AE was abolished by trilostane, a 3β-HSD inhibitor. (B) Metabolism of [^{3}H]-DHEA to [^{3}H]-E was greatly reduced by fadrozole, an aromatase inhibitor. Similar data were obtained using song sparrow brain homogenates. Modified from (58).

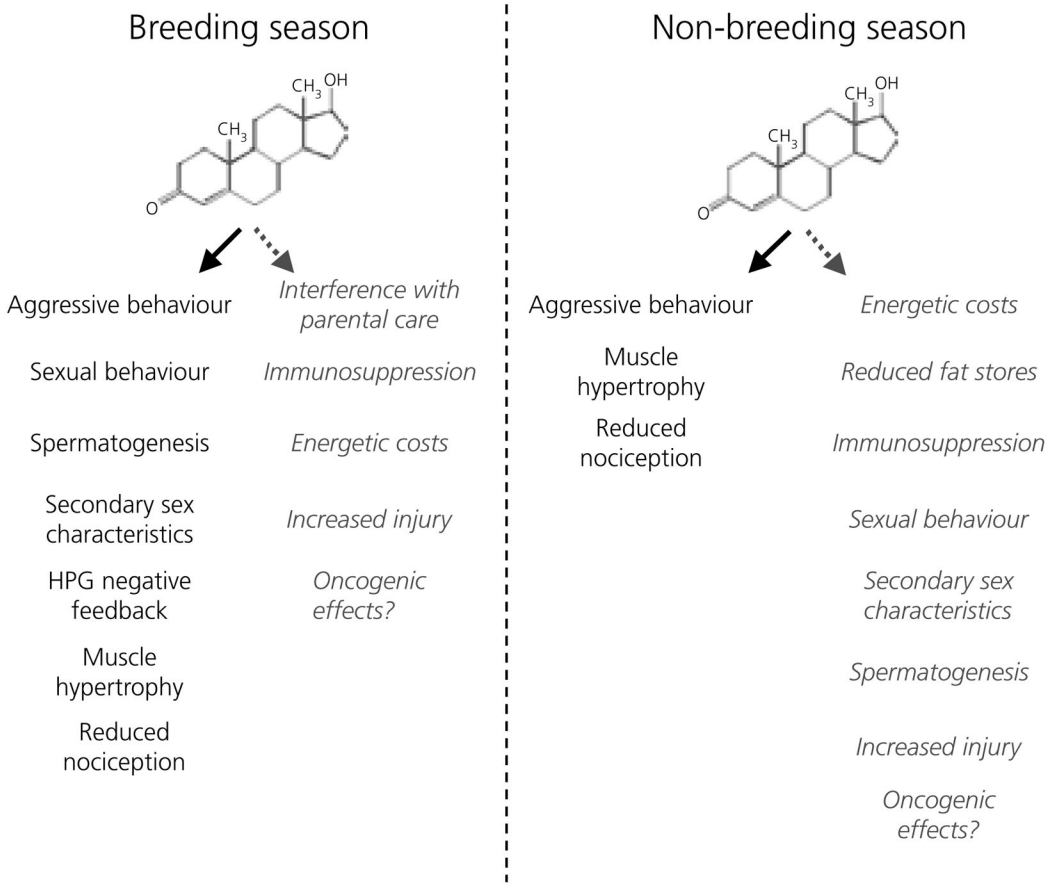

Fig. 6.

Actions and costs of high circulating testosterone in the breeding season and nonbreeding season. Actions are in black, and potential costs are in red. In the breeding season, a major cost of high circulating testosterone is interference with parental care. In the nonbreeding season, interference with parental care is not an issue, but a major cost of high circulating testosterone is increased energy expenditure. Modified from (13).

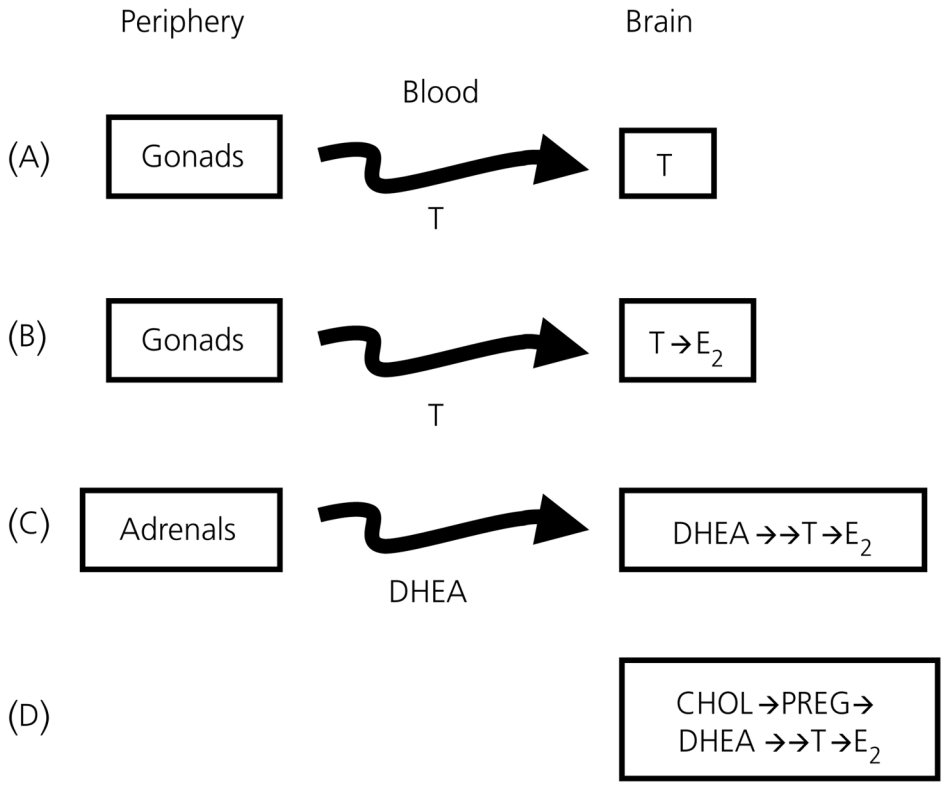

Fig. 7.

Pathways by which steroids could affect aggression. (A) Gonadal testosterone (T) acts directly on the brain; (B) gonadal T is converted locally to 17β-oestradiol (E_2); (C) adrenal DHEA is converted locally to T and/or E_2; (D) neurosteroids are produced locally in the absence of gonadal and adrenal steroid production. Modified from (6).