Supplementary Materials

Table S1. Search Terms.

Term Group	Search String
Final Search	(estrogen* OR estradiol OR oestrogen* OR aromatase OR ERα OR ERβ OR ESR1 OR ESR2) AND (aggress* OR violen* OR dominan* OR antisocial OR conduct disorder OR impulsiv* OR hostil* OR territorial*) AND (preclinical OR clinical OR trial OR cohort OR cross-sectional OR case-control OR animal OR rodent OR human OR male OR female)

Table S2. Preclinical studies.

Study	Study Design	Sample Size	Sample Age	Study Length	Measurement Tool(s)/Outcome Measures	Outcome(s)
Agrimi et al., 2024	Animal Study	~ 20–40 (groups ≈ 10 each)	Adult females (8–12 weeks old)	2–4 weeks	Behavioral tests (elevated plus maze, open-field test), Western blot and immunohistochemistry for hippocampal ERβ protein expression, plasma corticosterone assay	Reiterated male aggression ↓ hippocampal ERβ expression and ↑ anxiety-like behavior in females; findings suggest chronic social stress disrupts estrogen-mediated neuroprotection in the hippocampus
Albert et al., 1992	Animal Study	N/R	Adult female rats	6-8 weeks	Aggression was measured in resident–intruder tests, recording frequency and intensity of attacks, bites, and on-top behaviors to form a composite aggression score. Hormone levels were manipulated via implants (testosterone, estradiol, progesterone) and confirmed via serum assays.	Estradiol and testosterone maintained aggression after ovariectomy, while high progesterone levels suppressed it. When progesterone declined, aggression increased despite falling estradiol and testosterone, suggesting that progesterone moderates hormone-dependent aggression rather than directly drives it.
Albert, Jonik & Walsh, 1990	Animal Study	36 female rats	Adult	~1 month	T+E implants; Food competition; Resident–Intruder Test	Combined T+E implants increased aggression to levels of intact females; hormones act synergistically to promote aggression.
Asher et al., 2013)	Non-Randomized Experimen	48 adult females distributed into small social groups.	Adult female rhesus monkeys; specific ages not	Four 1-week estradiol/placebo treatment blocks separated by 2-week	Ovariectomy and estradiol replacement, social status classification (dominant vs subordinate), serotonin transporter	Estradiol-induced changes in central monoamines were altered by both social subordination and 5-HTT genotype, with subordinate and s-variant females

	tal Animal Study (OVX macaques)		provided in abstract.	washout periods; total experimental sequence spans several months.	(5-HTT) genotype, central monoamine concentrations measured from cerebrospinal fluid or brain tissue.	showing different monoaminergic responses compared with dominant and l/l females, supporting gene–environment–hormone interactions in stress-related neurochemistry.
Burmeister et al., 2007	Animal Study	n = 18	Adult males	>3 weeks of status observation prior to tissue collection	Quantitative PCR (qPCR) — mRNA levels of AR-α, AR-β, ER-α, ER-βa, ER-βb, GnRH1, and GnRH-R1 relative to 18S rRNA; gonadosomatic index (GSI); two-way ANOVA and multiple regression analysis	Dominant males had significantly higher mRNA expression of AR-α, AR-β, ER-βa, and ER-βb in the anterior brain compared to subordinates; ER-α did not differ by status in the brain; all anterior brain steroid receptors positively correlated with GnRH1 expression; AR-α, AR-β, ER-βa, and ER-βb in the anterior brain positively correlated with GSI; pituitary ER-α positively correlated with GSI; no status differences detected in posterior brain or testes — suggests dominant males may have enhanced steroid sensitivity in the anterior brain
Cologer-Clifford et al., 1999	Animal Study	~130 total; per group n = 5–15	50–60 days old	~5 weeks	Resident-Intruder Aggression Test (composite score: biting attacks + lateral threats + tail rattling), Motor Behavior Index (locomotion + rearing)	Androgenic stimulation (DHT/R1881) permitted broad serotonergic inhibition of aggression; estrogenic stimulation (DES) was restrictive — only high-dose combined 5-HT1A + 5-HT1B treatment reduced aggression; testosterone showed an intermediate pattern; high-dose CGS12066B effects on aggression were nonspecific due to concurrent motor impairment
Compaan et al., 1994	Animal Study	n = 10/selection line (SAL and LAL) for behavioral and aromatase assays; n = 9–10 pooled samples for kinetic analyses	14 weeks	~1 month	Resident-Intruder Aggression Test (attack latency score, ALS); In vitro aromatase activity (AA) assay (tritiated water method) in POA, VMH, amygdala (Am left and right), and parietal cortex (CTX); Kinetic analysis (Km, Lineweaver-Burk); Spearman Rank correlation; MANOVA	Nonaggressive LAL males had significantly higher POA aromatase activity than aggressive SAL males despite lower circulating testosterone; POA AA was positively correlated with attack latency (i.e., inversely correlated with aggressiveness); no significant strain differences in VMH or amygdala AA; area-specific distribution differed between strains (LAL: POA > VMH; SAL: VMH > POA); amygdala showed highest AA in both strains; aromatase Km was similar

						between strains, suggesting enzyme properties were unaltered by selection
Compaan et al., 1994b	Animal Study	n = 9–12 fetuses/group per embryonic day; n = 8–11 neonates/group; n = 5–7 pooled plasma samples (fetuses); n = 4–6 pooled plasma samples (neonates); n = 26–28 SAL and 12–14 LAL mothers	Embryonic days 17 and 18 (E17, E18); postnatal day 1	~2–3 days	In vitro aromatase activity (AA) assay (tritiated water method) in POA, AH, amygdala (Am), and parietal cortex (CTX); Testosterone RIA (pooled plasma); Body weight and brain weight; Spearman Rank correlation; ANOVA; MANOVA	No significant strain differences in POA AA on E17, E18, or day 1; LAL fetuses showed significant POA AA increase from E17 to E18 (correlated with brain weight), but SAL did not; SAL neonates had significantly higher amygdala AA than LAL neonates; SAL showed Am > POA+AH AA at day 1, while LAL showed no difference between areas; LAL fetuses tended to have higher plasma T prenatally, but SAL neonates had significantly higher plasma T at day 1; results suggest prenatal AA is T-independent while neonatal amygdala AA may be T-dependent
Clipperton-Allen et al., 2011	Animal Study	32-48	8-10 weeks old	3-4 weeks	Resident–Intruder Test, ethological behavior scoring, ERα agonist PPT administration	ERα activation increased sex-typical agonistic behavior in gonadectomized mice, minimal effects in intact mice
Cunningham & McGinnis, 2007	Animal Study	32	Adult male mice	9 weeks	The study used behavioral observations in a hidden-neighbor olfactory test to record aggression (attacks, threats, dominance) and sexual behaviors (mounts, intromissions, ejaculations) in male rats.	Pubertal AAS exposure increased aggression toward unreceptive females and caused persistent sexual mounting toward obstructed receptive females, indicating frustration-induced persistence rather than heightened aggression.
Cushing et al., 2008	Animal Study	31 (12 MeA-ERα, 19 controls)	60–70 days (adult males)	~3 weeks post-transfection before behavioral testing	AAV transfection; Alloparental Behavior Test; Partner Preference Test	Overexpression of ERα in the medial amygdala inhibited prosocial behavior; treated males showed more aggression and sexual behavior toward pups; low MeA ERα required for male prosociality.
Davis et al., 2003	Animal Study	78	Adult female mice	N/R	Resident Intruder Agression Test, Hormone Assays (Enzyme Immunoassay, Radioimmunoassay)	Compared to female control mice, tested female mice showed a decrease in expression of progesterone and progesterone:testosterone ratio, with no change in expression of testosterone, estradiol, corticosterone, estradiol:progesterone ratio, and

						estradiol:testosterone ratio, for both agressive and non-aggressive test mice
Davies et al., 2016)	Observational Field Study (wild cooperatively breeding mammals)	Multiple adult males and females sampled repeatedly; exact N per sex/status class reported in article tables, but not in abstract-only access.	Adult meerkats of known sex and social status; precise ages not given in the abstract.	Longitudinal sampling across multiple breeding seasons and reproductive states; spans months to years in the field.	Serial sampling of plasma androgens, estradiol, and other hormones; assignment of sex, dominant vs subordinate status, reproductive state (pregnant, lactating, etc.); behavioral and reproductive metrics such as mating opportunities and breeding success.	Dominant females showed unusually high androgen levels relative to many mammalian species, and hormone profiles differed by sex, status, and reproductive condition, highlighting a “masculinized” endocrine phenotype in dominant females of this cooperatively breeding species.
Dombret et al., 2020	Animal Study	48	2-5 months old	1 year	Behavioral tests, qPCR, and immunohistochemistry.	Neural ERβ deletion reduced social interaction, increased anxiety- and depressive-like behaviors, lowered oxytocin and serotonin-related gene expression, and decreased hippocampal neurogenesis.
Drea, 2007	Observational Longitudinal Animal Study	22 reproductively intact adults: 10 females and 12 males.	Reproductively intact adult ring-tailed lemurs; exact ages in years not specified in abstract.	Four annual cycles of observation and sampling, i.e., data collected across multiple seasons over several years.	Behavioral observations of aggression and dominance, measurement of circulating steroids (e.g., androgens, estrogens) across breeding and non-breeding seasons.	Females were socially dominant and showed aggressive behavior patterns and steroid profiles that in some respects resembled males, supporting partial hormonal “masculinization” of dominant females and seasonal modulation of both aggression and hormone secretion.
Fadem et al., 1989	Animal Study (hormone manipulation in castrated males)	N/R in accessible abstract; original Hormones and Behavior article must be checked for exact N.	Adult male opossums; specific age not reported in abstract.	Castration followed by hormone replacement and behavioral testing; exact duration in weeks not reported in abstract.	Hormone manipulations (castration; testosterone or estradiol replacement), quantification of chest and flank/hip scent marking, observation of precopulatory behavior, female aggression toward males.	Castration reduced chest and flank/hip marking; testosterone, but not estradiol, restored chest marking; both testosterone and estradiol increased flank/hip marking; females were most aggressive toward testosterone-treated males, indicating androgen-dependent control of specific scent-marking and social behaviors.
Faruzzi et al., 2005)	Animal Study (hormone manipulation after social defeat)	Abstract describes ovariectomized females assigned to hormone conditions; full N per group is not explicitly stated in the abstract and	Adult female Syrian hamsters; specific ages not provided.	Ovariectomy followed by a 3-week hormone replacement period, then four 5-min defeat trials and a conditioned defeat	Ovariectomy with Silastic capsule implants containing estradiol, testosterone, progesterone, dihydrotestosterone, or no hormone; social defeat paradigm (four encounters with a larger aggressive female); conditioned defeat test with a smaller	Females receiving estradiol or testosterone showed significantly lower submissive behavior after defeat than females given progesterone, dihydrotestosterone, or no hormone, indicating that specific gonadal steroids reduce submissive responding to social defeat in females.

		must be taken from the full text.		test the following day.	non-aggressive intruder; scoring of submissive, aggressive, social, and nonsocial behaviors.	
Floody & Pfaff, 1977	Animal Study	32	2-3 months old	several weeks	Behavioral observation of aggression (attack latency, number of bites, duration of aggressive postures) during resident–intruder tests	Aggression peaked during diestrus and was lowest during estrus. Ovariectomized females showed reduced aggression, which was restored by testosterone and partially by estradiol. Findings indicate that fluctuations in ovarian hormones regulate female aggression.
Ghiraldi et al., 1993	Animal Study	175	60-70 days	3-4 days	Aggression was measured through the number of lunges and attacks in a resident–intruder test, combined into a composite aggression score, alongside nursing behavior observations and hormonal manipulations.	Ovariectomy accelerated the onset of postpartum aggression, while estrogen replacement suppressed it, indicating that declining estrogen levels following birth facilitate maternal aggression in mice.
Haug & Brain, 1983	Animal Study	Exp 1: 160, Exp 2: 360	7 weeks	9-10 weeks	Aggression was measured in the home cage by recording the latency to the first biting attack (in seconds) and the total number of biting attacks directed toward lactating female intruders.	Castration increased aggression toward lactating females, while both testosterone and estradiol implants significantly reduced attack frequency and latency, and dihydrotestosterone had no effect, indicating that aromatization of testosterone to estradiol is required for its inhibitory action on aggression.
Hashikawa et al., 2017	Animal Study	Varies by experiment (e.g., fiber photometry N≈6; electrophysiology 103 neurons from 5 mice; behavioral cohorts across multiple groups)	Adult mice (2–12 months depending on experiment; virgin and lactating females)	Acute experiments (minutes–weeks depending on protocol; viral incubation 1–3 weeks; behavioral tests ~10–20 min sessions)	- c-Fos immunohistochemistry (neural activation) - Fiber photometry (GCaMP6f calcium activity) - Optogenetics (ChR2 activation) - Chemogenetics (hM4Di inhibition via CNO) - Behavioral assays (resident–intruder aggression tests, investigation, mating behaviors) - Electrophysiology recordings	VMHvl Esr1+ neurons are active during female aggression and mating. Inhibition reduces aggression. Activation induces aggression. Identified two distinct VMHvl subregions: one for aggression, one for mating. Demonstrates VMHvl is necessary and sufficient for female aggression.
He et al., 2012	Animal Study	40	2-3 months old	4-6 weeks	Aggression was assessed using a resident-intruder test, while serum testosterone and estradiol levels were measured by ELISA, and	Castrated males showed increased aggression, reduced testosterone, increased estradiol, decreased AR and ERβ expression in several brain regions,

					brain androgen and estrogen receptor expression was analyzed using immunohistochemistry and qPCR.	and increased ERα expression in the anterior hypothalamus.
Hilakivi-Clarke et al., 1996	Animal Study	Rats: n=12 (6 LF, 6 HF). Mice: n=16 (LF n=7, HF n=9).	3-month-old	3 weeks diet+housing; aggression test (rats 10 min; mice 5 min); mice bled 3 days post-test for E2	Latency to first aggressive encounter, observation, food intake/body weight, Serum E2 (mice; RIA)	HF groups showed shorter latencies and longer durations of aggression vs LF (rats: median latency 55 s vs 190 s; median duration 151 s vs 70 s; both sig.
Hilakivi-Clarke et al., 1997	Animal Study	31–34 (Exp 1), 97 (Exp 2)	7 weeks	2–4 days	Resident–Intruder Test; RIA for E2/T	Ethanol increased E2 levels overall; aggressive mice showed E2 decrease; altered E2:T ratio linked to ethanol-induced aggression.
Hume & Wynne-Edwards, 2005	Animal Study (Male Hamsters)	Experiment I: 22 castrated males, 21 sham controls. Experiment II: 6 castrated, 4 sham males.	80–120 days (adult, sexually mature)	From gestation day 7 to 12 days post-birth (~3–4 weeks total)	Serum testosterone and estradiol were quantified using validated radioimmunoassays (RIA). Paternal behavior was assessed with a standardized pup displacement test measuring contact, retrieval, and latency, and aggression was tested using a resident–intruder paradigm. Reproductive success was evaluated by pup survival, pup weight, and male weight change during parental care.	Castration dramatically reduced testosterone and estradiol levels, confirming testes as primary source of estradiol. Paternal responsiveness and reproductive success were unaffected by castration; males continued retrieving pups and caring for litters. However, territorial aggression toward intruder males was reduced, with castrated males attacking less and fleeing more often. Testicular androgens and estradiol are critical for male aggression but not necessary for paternal care in this biparental species.
Juntti et al., 2010	Animal Study	N/R	N/R	N/R	Resident-Intruder Aggression Test	Androgen receptor mutant mice were less agressive compared to control mice; only significant difference was in time fighting (not number of attacks)
Kramer et al., 2007	Animal Study	8-12	Adult male hamsters	8-10 weeks	The study used photoperiod manipulation, resident–intruder aggression testing, and immunocytochemistry for ERα and c-Fos to assess hormonal sensitivity and neural activation in aggression-related brain regions.	Short photoperiods increased ERα expression and neural activation in aggression centers, suggesting that seasonal aggression arises from heightened neural sensitivity to estrogen rather than elevated hormone levels.

Krzywkowski et al., 2020	Animal Study	Calcium imaging: n=4–12 per experiment; cFos TRAP: n=3–6 per group; Optogenetics: n=3–7 per group	Adult males (9–15 weeks for subordinate BALB/c intruders; exact age of experimental mice not reported)	Social defeat conducted over 1–2 days; context re-exposure 24 hours post-defeat; optogenetic testing pre- and post-defeat with ~2 days between sessions	In vivo microendoscopic calcium imaging (GCaMP6s, VMHvl), Resident-Intruder Aggression Test, Social Defeat Test, cFos TRAP-tagging immunohistochemistry, Optogenetic activation of Esr1+ neurons (ChR2), Linear Discriminant Analysis of neuron ensemble activity	VMHvl neurons encoded a generalized social threat state active during defeat, risk assessment, and flight; social defeat induced context-specific neural encoding (distinct home vs. defeat chamber populations) absent before defeat; ~50% overlap in cFos+ neurons activated by aggression and defense; social defeat but not repeated aggression remodeled VMHvl ensemble activity; optogenetic activation of Esr1+ VMHvl neurons elicited freezing, flight, and reduced social interaction after but not before social defeat, demonstrating experience-dependent functional plasticity
Lee et al., 2014	Animal Study	ChR2 activation: n=14–33 per intruder type; eNpHR3.0 silencing: n=3–17; c-Fos: n=3–5 per group; calcium imaging: n=35–60 cells	2–4 months old	2–5 weeks of behavioral testing post-surgery (1–2 sessions/week); 2–4 week recovery post-injection	Resident-Intruder Aggression Test, Optogenetic Activation (ChR2, 473 nm) and Silencing (eNpHR3.0, 593 nm) of Esr1+ VMHvl neurons, c-Fos Immunohistochemistry, In vitro Whole-Cell Patch-Clamp, Two-Photon Calcium Imaging (GCaMP6s), In vivo Extracellular Electrophysiology	Optogenetic activation of Esr1+ (but not Esr1−) VMHvl neurons was sufficient to elicit attack in >87% of ChR2-expressing males; weaker stimulation promoted mounting and close investigation toward both males and females; increasing stimulation intensity within a single trial could shift behavior progressively from investigation to mounting to attack; optogenetic silencing interrupted ongoing attack within ~3 s in ~60% of trials and blocked approach-to-attack transitions; the behavioral shift correlated with the number and activity level of recruited Esr1+ neurons, suggesting a scalable population-coding mechanism for social behavior progression
Liu et al., 2022	Animal Study	n=15–21 per group	8–10 weeks at start of virgin state; tested longitudinally over ~9–10 week lactation cycle	~9–10 weeks	scRNA-seq Act-seq, Resident-Intruder Aggression Test, Optogenetic Activation (ChR2) and Silencing (eNpHR3.0) of VMHvl α (Esr1+,Npy2r−) and β (Npy2r+) cells, Fiber Photometry (GCaMP6m), Lordosis Behavior Scoring, Ultrasonic Vocalization	scRNA-seq identified two distinct VMHvl Esr1+ subtypes: α cells (Esr1+,Npy2r−) active during mating; β cells (Npy2r+) active during aggression; activation of α cells promoted lordosis in estrus and diestrus virgins and inhibited maternal aggression; activation of β cells evoked fierce attack even in naturally nonaggressive virgin females, and

					Recording, No-Contact Interaction Test, Urine Preference Test	converted mating to aggression; longitudinal within-subject recordings showed β cells dramatically and reversibly increased responsiveness to social cues during the lactating state, while α cell responsiveness was unchanged, supporting a model in which state-dependent changes in relative β-cell activity drive the switch from sexual receptivity to maternal aggression
Mayer et al., 1990	Animal Study	Exp 1: 23, Exp 2: 45, Exp 3: 65, Exp 4: 38	70-120 days	~22 days	Intruder test	EB injected females on day 16 are as aggressive as prepartum femalea, wheras oil-injected are nonaggressive; prolonged E/P/EB treatment increases home-cage aggression and the likelihood of maternal aggression,
Merritt et al., 2018	Animal Study	Experiment 1: 1 WS male, 12 WS females, 5 TS males, 13 TS females (n=31 total); Experiment 2: same birds as Experiment 1	Adult	~20 minutes per trial (behavioral observation T10–T30 post-administration); at least 48h washout between trials; Experiment 2 conducted at least 1 week after Experiment 1	Aggression Assay (attacks and time near opponent during visual interaction), Egr-1 Immunohistochemistry (TnA, PVN, rPOM, VMH, BSTm), Plasma E2 Radioimmunoassay	Oral E2 administration rapidly increased attacks and time spent near opponent in WS but not TS birds within 20 minutes, suggesting morph-dependent differential sensitivity to E2 consistent with nongenomic mechanisms; E2 decreased Egr-1 immunoreactivity in nucleus taeniae of the amygdala (TnA) regardless of morph; plasma E2 levels were elevated equally in both morphs, confirming the behavioral difference was not due to differential E2 absorption
Michopoulos et al., 2011)	Non-Randomized Experimental Animal Study (OVX macaques)	37 adult females housed in eight small social groups.	Adult female rhesus monkeys; specific ages not provided in the article text excerpt.	Four 1-week treatment conditions (e.g., vehicle vs estradiol) separated by 2-week washout periods; total protocol spans several months.	Ovariectomy and estradiol treatment, social status classification (dominant vs subordinate), serotonin transporter (5-HTT) genotype, behavioral observations (prosocial, anxiety-like, and aggressive behaviors), serum oxytocin concentrations.	Prosocial and anxiety-like behavioral effects of estradiol, as well as serum oxytocin responses, differed by social status and 5-HTT genotype, with subordinate and s-variant females showing altered estradiol responsiveness relative to dominant and l/l females.
Mountoufaris et al., 2023	Animal Study	Behavioral experiments: n=11 per group	8–12 weeks	At least 4 weeks post-surgery recovery before	Resident-Intruder Aggression Test, Fiber Photometry (GCaMP8s bulk calcium), Microendoscopic Single-	CRISPR/Cas9 co-disruption of Oxtr/Avpr1a in VMHvlEsr1+ neurons significantly reduced attack frequency, duration, and

		(constitutive system); fiber photometry: n=16 control, n=13 experimental; CRISPRoscopy: n=5 control, n=7 experimental		behavioral testing; behavioral testing sessions ~15–20 min (male-male) and ~10 min (male-female)	Unit Calcium Imaging (CRISPRoscopy), Ex vivo 2-Photon Calcium Imaging, recurrent Switching Linear Dynamical Systems (rSLDS) Modeling, Autocorrelation Half-Width (ACHW) Analysis, Linear SVM Decoders, Choice Probability Analysis	probability without affecting sniffing, mounting, or locomotion; fiber photometry revealed reduced bulk VMHvlEsr1 activity during attack and sniffing; single-unit CRISPRoscopy showed modest reductions in activity and behavioral tuning but preserved population-level decoding of intruder sex and behavior; critically, co-disruption eliminated the line attractor (replaced by a trivial point attractor) and severely shortened persistent neural activity (ACHW), identifying neuropeptidergic OXT/AVP signaling as necessary for attractor dynamics and the persistent internal state of aggressiveness
Nakata et al., 2018	Animal Study	28	8-10 weeks old	Around 4 weeks	Agonistic behavior test, tube test, urine marking, corticosterone assay, gene expression	ERβ knockout males failed to form stable hierarchies, showed less aggression and dominance, altered social signaling, higher stress
Nyby et al., 1992	Animal Study	Exp1: n≈43 (SEPTUM 9, MPO 9, AHA 8, VMH 7, TSIL 5, BSIL 6). Exp2: n=55 (MPOTP 9, MPOE2 10, SEPTUMTP 9, SEPTUME2 9, TPSIL 9, BSIL 9).	Adult male mice	~1 week post-implant to start; testing across ~2–3+ weeks; aggression, ultrasound, marking, copulation scheduled on staggered days; histology within 48 h after last test	ultrasonic mating vocalizations interval counts, UV-visualized grid counts, observation, histology tests	Exp1 (T): MPO T restored high ultrasonic vocalizations; urine marking increased with MPO/AHA/VMH (not septum); mounting rare (MPO only); aggression largely absent. Exp2 (TP/E2): TP effective only in MPO for ultrasounds & marking; E2 effective in MPO and septum for ultrasounds & marking (robust). Brain implants rarely restored mounting/aggression; systemic T/TP (TSIL/TPSIL) restored all male-typical behaviors. Seminal vesicles small in brain-only groups → minimal systemic leakage.
Ogawa et al., 1998	Animal Study (Mice)	6–16 per group, depending on experiment (ERKO, heterozygous, and wild-type female mice).	Adult female mice (exact age not specified)	Approximately 3–4 weeks total (1 week post-ovariectomy recovery, 2 days hormone priming, followed by several weeks of behavioral testing)	Behavioral assays included: sexual behavior test (lordosis, rejection, pre-receptive posture), resident–intruder aggression test, and pup retrieval (parental behavior) test. Physiological measures included hormone treatments (estradiol, progesterone) and ERα	ERα knockout (ERKO) females showed absence of lordosis and reduced pre-receptive sexual behaviors, increased aggression toward female intruders, and reduced parental behavior with high rates of infanticide. These behavioral differences persisted after gonadectomy, indicating that ERα gene expression is

					immunocytochemistry for receptor localization. Light/dark transition tests assessed anxiety and activity.	essential for normal female reproductive, aggressive, and parental behaviors, likely through both developmental and adult neural mechanisms.
Olvera-Ramos et al., 2021	Animal Study	Experiment 1: n = 16 confronted, n = 12 non-confronted; Experiment 2: n = 10/group (ovariectomized, ovariectomized + E2, ovariectomized + P4, sham)	48–70 days old at start	Experiment 1: 15 days mating before testing; Experiment 2: ~30 days mating + 30 days post-surgery before testing	Resident-Intruder Aggression Test (attack latency, total attack time, offensive and defensive behavior frequencies); ELISA (plasma E2 and P4); Spearman correlations; Kruskal-Wallis and Mann-Whitney U tests	87.5% of females displayed territorial aggression in Experiment 1; 100% in all groups in Experiment 2; attack latency and total attack time did not correlate with E2 or P4; ovariectomy, E2 replacement, and P4 replacement did not affect aggression parameters; post-confrontation E2 was significantly higher in confronted vs. non-confronted females, suggesting aggression itself may trigger E2 release from a non-ovarian source; territorial aggression in female dwarf hamsters is independent of ovarian steroid hormones
Patisaul & Bateman, 2008	Animal Study	N/R	N/R	N/R	Elevated Plus Maze Test, Resident-Intruder Paradigm	Males neonatally treated with DPN (ERβ agonist), BPA, and EQ made significantly fewer open arm entries and spent less time in open arms compared to controls, indicating increased anxiety; DPN and EQ treated males showed significantly more aggressive bouts; only DPN treated males showed significantly more attacks--neonatal ERβ activation by endocrine active compounds can increase both anxiety and aggression in adult males
Pazol et al., 2004	Animal Study (Female pigtail macaques)	6 ovariectomized adult female macaques	Adult females (exact age not specified)	Sequential 1-week hormone treatments with 3-week washout periods	Behavioral observation of sexual initiation, aggression, self-scratching (anxiety measure), and locomotion; serum hormone assays for E2, P4, and MPA.	Estradiol alone increased sexual behavior; adding natural progesterone (P4) did not block this effect, but adding medroxyprogesterone acetate (MPA) suppressed sexual initiation and increased aggression and anxiety behaviors. MPA antagonized estrogen's positive behavioral effects.
Rines et al., 1984	Animal Study	N/R	5 months - 21 months	N/R	Sexual Behaviour Test, Resident-Intruder Agression Test	Fetal female mice developing between two male mice have higher levels of testosterone (2M) compared to mice not

						fetally developed beside male mice (0M); 0M mice were more responsive to male mice sexual advances and inseminated earlier compared to 2M mice; when treated with testosterone, young 2M mice displayed more agression compared to young 0M mice, but both old 0M and 2M mice were highly agressive
Sandhu et al., 2019	Animal Study	8-12	Adult male mice	6 weeks	Behavioral tests of aggression, social interaction, and odor preference were combined with c-Fos mapping in key social behavior circuits to evaluate the effects of dietary phytoestrogen depletion.	Mice fed a low-phytoestrogen diet showed reduced aggression, impaired sociability, and decreased neural activation in estrogen-sensitive brain regions, demonstrating that dietary estrogens modulate male social behavior through central neural pathways.
Scordalakes et al., 2004	Animal Study	Behaviour Tests: 40 Immunocytochemistry: 70	N/R	N/R	Resident-Intruder Aggression Test, Immunocytochemistry	Female WT mice, and male ERa KO and male double knockout (ERa and AR) mice showed did not show aggression during the resident-intruder test when given 17b-estradiol (E2) before the testing, but male WT and androgen receptor KO mice did show agression - E2 acts through ERa receptor to mediate agression in male mice
Simon & Gandelman, 1978	Animal Study	N/R	65 days	N/R	Resident-Intruder Aggression Test (olfactory bulbectomized male stimulus); proportion fighting, latency to aggression, attack ratio score	Adult EB alone failed to induce aggression in ovariectomized females; neonatal priming with either TP or EB was required for adult estrogen to activate aggression; the critical organizational window closed between postnatal Day 6 and Day 12; absence of fighting in non-primed females was not due to competing sexual behavior
Simon et al., 1985	Animal Study	N/R	N/R	N/R	The study used hormone implants (testosterone, dihydrotestosterone, methyltrienolone, estradiol, diethylstilbestrol, or vehicle) in ovariectomized adult female mice and assessed male-typical aggression through standardized behavioral aggression tests.	Androgen treatments, but not estrogen treatments, induced significant male-typical aggressive behavior in female mice, demonstrating that androgens, not estrogens, mediate this form of aggression.

Spiteri et al., 2010	Animal Study	52	N/R	N/R	Light/Dark Choice Test, Social Recognition Test, Resident-Intruder Aggression Test, Immunocytochemistry	Reduced ERa expression in posterodorsal amygdala of female rats reduced social recognition and reduced anxiety in the light/dark test, reduced ERa expression in the ventromedial nucleus of the hypothalamus of female rats resulted in enhanced aggression against juvenilles but not adults, social recognition was unaffected
Svare et al., 1975	Animal Study	N/R	Pregnant primiparous and multiparous mice	N/R	Resident Intruder Agression Test	Administering estradiol benzoate to lactating mice that previously showed aggression towards male intruders were now less aggressive in testing (reduced time fighting)
Toda et al., 2001	Animal Study	~100	Neonatal to 12–16 weeks	~12–16 weeks postnatal	Resident–Intruder Test; E2 supplementation	ArKO males lacked aggression; neonatal E2 restored aggression if initiated within 3 days of birth; estrogen critical for organizing male aggression.
Toufexis et al., 2007	Animal Study	128	Adult male and female mice	3-4 weeks	Fear learning was measured using fear-potentiated startle (FPS) responses during an AX+, BX– discrimination paradigm, assessing excitatory (fear) and inhibitory (safety) learning after treatment with estrogen or selective ERα/ERβ agonists.	Estrogen does not enhance fear directly but impairs the inhibition of fear in females, likely due to opposing effects of ERα and ERβ activation, revealing a potential mechanism for sex differences in emotional learning and anxiety disorders.
Trainor & Marler, 2001	Animal Study	~66	3–6 months	4 weeks post-surgery	Resident–Intruder Test; Paternal Behavior Test; Serum T assay	Testosterone maintained paternal behavior; aggression not reduced by castration; paternal care and aggression positively correlated.
Trainor et al., 2006	Animal Study	Behaviour Tests: 39 Immunocytochemistry: 21	N/R	N/R	Resident-Intruder Agression Test, Immunocytochemistry	Presence of ERa immunactivity in the lateral septum, ventral bed nucleus of the stria terminalis, and anterior hypothalamus in CD-1 mice is positively correlated with agressive behaviour; in aromatase-inhibited male mice, agression was reduced
Trainor et al., 2007	Animal Study	N/R	4-8 months	N/R	Immunocytochemistry, qPCR, Resident-Intrudent Agression Test	P. polionotus was more agressive than P. maniculatus; agression was increased in short days for both species during the

						resident-intruder test; P. polionotus had significantly more ERa immunoreactive cells than P. maniculatus; both species exposed to short days had significantly more ERa immunoreactive cells compared to long days; no signficant interaction between photoperiod and species
Trainor et al., 2008	Animal Study	16	N/R	8 weeks	Resident-Intruder Aggression Test, Immunocytochemistry	Male reproductively-unresponsive mice housed in short-day photoperiods exhibited higher levels of agression compared to males housed in long-day photoperiods; males injected with estradiol showed greater levels of aggression in both short and long day periods - only significant for short day
Trives et al., 2025	Animal Study	Chemogenetics: n = 9–13 (hM4Di) and n = 10–11 (mCherry); Egr1 IHC: n = 5–7 naive and n = 4–11 experienced; Retrograde tracing: n = 33 AroCre males	>8 weeks	~6–7 weeks total	Resident-Intruder Aggression Test (attack number, duration, tail rattling, latency); Sexual Behavior Test (anogenital investigation, mount latency, mount time, ejaculation latency, proportions mounting/intromitting/ejaculating); Chemogenetic inhibition (hM4Di + CNO); Egr1 immunohistochemistry (activity proxy in BNSTpr, MeApd, VNO, mPOA, VMH, Arc, DMH); CAV2 retrograde tracing (Aro+ projections to mPOA)	Chemogenetic inhibition of BNSTpr Aro+ neurons in experienced males robustly reduced aggression (4–10 fold reduction in attacks, duration, tail rattling) but had limited effect on sexual behavior (only ejaculation latency significantly increased); social experience induced a behavior-specific 7.5-fold increase in Egr1+ cells in MeApd after sexual behavior but not aggression; VNO Egr1 increased 1.9-fold after sexual behavior but not aggression; mPOA Egr1 increased after both behaviors; MeApd Aro+ neurons projecting to mPOA showed specific activation after sexual but not aggressive experience
Tsuda et al. (2014)	Animal Study	8-12	Adult mice	10 weeks	Behavioral tests assessing social interaction and aggression (e.g., social interaction test, resident–intruder test); gene expression analysis of estrogen receptor β.	Neonatal maternal separation altered social and aggressive behavior in adulthood. Effects differed by sex and genotype: ERβ knockout mice showed altered social investigation and reduced aggression compared to wild-type mice, indicating that early-life stress and ERβ both modulate social behavior development.

Unger et al., 2015	Animal Study	Ablation males: n = 14 controls, n = 15 aroCre/IPIN; DREADD males: n = 20 aroCre/IPIN; Ablation females: n > 7 aroCre/IPIN, n > 14 controls (separate cohorts for mating and maternal behavior); Aggression comparison: n = 7 controls per sex	Adult mice	4 weeks post-surgery recovery before behavioral testing	Resident-Intruder Aggression Test (latency to attack and tail rattle, number of attacks, attack pattern); Mating Behavior Test (sniffing, mounting, intromission, receptivity index); Maternal Behavior (pup retrieval, latency); Courtship Vocalization Test; Urine Marking Test; Elevated Plus Maze; Food-Finding Test; Locomotion; Body weight; Circulating testosterone; Caspase-3-mediated targeted ablation (AAV-Cre-dependent); DREADD-Gi chemogenetic silencing (CNO); Cre-dependent activation (DREADD-Gq)	Ablation or chemogenetic silencing of MeApd aromatase+ neurons in males increased latency to attack and tail rattle and reduced attack number, without affecting mating, courtship vocalization, urine marking, or locomotion; ablation in lactating females reduced number of maternal attacks without affecting mating, pup retrieval, fertility, or locomotion; activation of MeApd aromatase+ neurons did not alter behavior; maternal and intermale aggression differ qualitatively (bite targets, pattern) but share dependence on MeApd aromatase+ neurons; aromatase+ MeApd neurons regulate aggression in a modular manner in both sexes
Villalon Landeros et al., 2012	Animal Study (Mice)	10–14 per group for behavior; 7–11 per group for brain analyses	Adult males, 3–6 months old	~6 weeks photoperiod acclimation + 10 days recovery + acute behavioral testing	Resident–intruder aggression test (bites, latency); immunohistochemistry for ERα and pERK in BNST, VMH, MPOA, MEA; plasma THF-diol levels by LC-MS/MS.	On cardboard bedding, estrogen inhibition (fadrozole) increased aggression, but on corncob bedding this effect disappeared. Corncob bedding reduced ERα-positive cells in BNST and VMH, suppressed pERK in social behavior circuits, and increased THF-diols suggesting bedding materials can block estrogen-dependent modulation of aggression.
vom Saal et al., 1983	Animal Study	n=20/30 per group	Fetuses (day 17 gestation); adults at ~90 days and ~200 days	16-day aggression testing period per experiment; overall study spans fetal to adult life (~200 days)	Radioimmunoassay (estradiol, testosterone, progesterone in amniotic fluid and blood); Resident-Intruder Aggression Test (sustained biting attack); Male Sexual Behavior Test (mounts and intromissions with receptive female); Female Sexual Behavior Test (elicited mounting and lordosis by stud male); Seminal vesicle weight (testosterone sensitivity index)	OM males (developed between two female fetuses) had significantly higher amniotic fluid estradiol than 2M males (developed between two male fetuses), with no difference in testosterone; OM intact males showed more mounts and intromissions than 2M males; neonatally castrated OM males were less sensitive to testosterone-induced aggression than 2M males and had lighter seminal vesicles; OM males were more responsive to estrogen/progesterone-induced female sexual behavior (lordosis/elicited mounting); results suggest prenatal

						estradiol differentially organizes sexual behavior versus aggression circuits
Wang et al., 2019	Animal Study	Sample sizes varied by experiment, for example fiber photometry recordings included 6 mice, optogenetic inhibition included approximately 10–12 mice per group, and other experiments used multiple cohorts depending on the method	Adult male mice (>10 weeks old) were used	Individual experiments were acute or short-term, including 10–20 minute behavioral sessions, with some protocols involving repeated exposure over up to 12 days	Behavioral analysis included social interaction assays with aggressive and non-aggressive intruders, quantification of defensive behaviors (dashing, upright posture, freezing), and video-based scoring; neural activity was measured using c-Fos immunohistochemistry and fiber photometry (GCaMP6f calcium signals); optogenetic activation and inhibition were used to assess causal effects of VMHvl Esr1+ neurons on behavior	VMHvl Esr1+ neurons were strongly activated during active social defense behaviors, particularly in the anterior VMHvl, and showed minimal activity during passive behaviors such as freezing. Optogenetic inhibition of these neurons impaired the ability of mice to defend against aggressors, while activation induced defensive behaviors and sometimes aggression. The findings demonstrate that VMHvl Esr1+ neurons are necessary and sufficient for active conspecific defense and reveal functional differences between anterior and posterior VMHvl regions
Wei et al., 2023	Animal Study	Varies by experiment: n = 5–15 per group	8–16 weeks	N/R	Fiber photometry (GCaMP6f Ca^{2+} imaging), Resident-Intruder Aggression Test, Four-Cup Social Interaction Test, Chemogenetic manipulation (hM4Di/hM3Dq + CNO), Optogenetic activation/inhibition (ChR2/stGtACR2), Immunohistochemistry (c-Fos), Patch-clamp slice recording, Real-Time Place Preference Test (RTPP)	cMPOAEsr1 cells responded preferentially during male-male (not female) interactions; their activity correlated with opponent resource-holding potential (RHP), increasing after social defeat by a stronger opponent; chemogenetic inhibition of cMPOAEsr1 cells increased aggression in aggressive males; chemogenetic activation nearly abolished intermale aggression; optogenetic activation of the cMPOAEsr1–VMHvl pathway suppressed ongoing attacks; optogenetic inhibition promoted attacks toward both male and female intruders, and toward previously dominant opponents; cMPOAEsr1 cells primarily provide inhibitory input to VMHvlEsr1 glutamatergic cells
Williamson et al., 2019	Animal Study	96	7-9 weeks	2 weeks	Agonistic behaviors were observed daily over 14 days to determine social hierarchy formation and stability.	Plasma corticosterone and estradiol levels, along with VMH/mPOA gene expression (ERα, ERβ, OTR, PR, OPRM1, GnRH), were measured to assess neuroendocrine correlates of dominance.

Wu et al., 2009	Animal Study	N/R	10-24 weeks	N/R	Resident-Intruder Aggression Test	Aromatase is important in activating male-specific aggression - aggressive behaviour elicited by AR mutant males given testosterone and neonatally estrogen-exposed females
Xu et al., 2021	Animal Study	80	Adult hamsters	N/R	Handling Bag Test, Neutral Arena Measurements (Resdient Intruder Test), Enzyme Immunoassay, RT-PCR	Female hamsters had the highest agressive performance (low-intensity agression) in proestrus, then estrus, and lowest in metestrus and dioestrus; agression decreased significantly during estrus if encounter was a male; estradiol concentration was highest in estrous and lowest in metestrus and dioestrus, ER2 expression in hypothalamus is lowest in proestrus and highest in metestrus and dioestrus - both estradiol andER2 mRNA in hypothalamus were associated with agression
Zha et al., 2025	Animal Study	Behavioral KO: n=16 per group; testosterone assay: n=9–11; retrograde tracing: n=4–6 per sex/genotype; electrophysiology: n=10–15 neurons from 3–4 mice; chemogenetic activation: n=4–9 per group; PIL fiber photometry: n=6; PIL chemogenetic inhibition: n=13–18	2–4 months at surgery	~4 weeks	Resident-Intruder Aggression Test, Retrograde Rabies Virus Tracing (RV-GFP), Optogenetic-assisted ex vivo Electrophysiology (oIPSC/oEPSC, paired-pulse ratio, whole-cell patch-clamp), Chemogenetic Activation (HM3D/CNO) and Inhibition (HM4D/CNO) of VMHvl neurons, Fiber Photometry (GCaMP6s in PIL), c-Fos Immunostaining, Testosterone ELISA, Open Field Test	Developmental SF1-Cre-mediated VMHvl Esr1 deletion (~40% reduction) significantly reduced male aggression without affecting testosterone, social investigation, or mating; estrogen-treated Esr1 knockout females failed to develop male-typical aggression; retrograde tracing revealed male-specific increases in inputs from LSv, BNST, MeA, PA, and PIL to VMHvl Esr1+ neurons; electrophysiology confirmed altered LSv→VMHvl synaptic connectivity and increased PIL→VMHvl connectivity in KO males; PIL neurons were activated during attack and required for aggression; KO males showed reduced VMHvl intrinsic excitability (halved maximum firing rates) and failed to mount attack upon chemogenetic activation; adult-onset Esr1 deletion did not alter input wiring, demonstrating a developmental-critical-period requirement for Esr1 in establishing male aggression circuits

Table S3. Clinical studies.

Study	Study Design	Sample Size	Sample Age	Study Length	Measurement Tool(s)/Outcome Measures	Outcome(s)
Aluja & García, 2007	Cross-sectional human study	89 male inmates	19–46 years (mean 27.7 ± 5.7)	One-time data collection (questionnaires + blood sampling)	Hormones: Plasma total testosterone (TT), free bioavailable testosterone (BT), sex hormone-binding globulin (SHBG), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) measured by radioimmunoassay (RIA) and immunoradiometric assay (IRMA). Aggressiveness: Buss–Durkee Hostility Inventory (BDHI) subscales (assault, verbal, indirect aggression). Antisocial Personality: Aluja Antisocial Personality Disorder Scale (AAPDS), validated against DSM-III criteria. Penal status (sentenced, recidivist) collected through prison records.	Aggressiveness correlated positively with SHBG (r = 0.39, p < .001) and total testosterone (r = 0.29, p < .01), but this testosterone correlation disappeared when controlling for SHBG, suggesting SHBG mediates the relationship. Inmates high in antisocial personality traits and recidivists had elevated SHBG levels. Free testosterone was unrelated to aggression or antisocial scores.
Aluja & Torrubia, 2004	Cross-sectional human study	30 healthy adult males	aged 21–40 years; mean = 27.9 ± 4.9	Single time point (cross-sectional blood draw and personality assessment)	Blood samples collected three times (8:00–9:00 AM) and pooled; radioimmunoassay (RIA) for LH, FSH, estradiol (E_2), total testosterone (TT), sex hormone-binding globulin (SHBG), and calculation of the free androgen index (FAI). Personality assessed with the Buss–Durkee Hostility Inventory (BDHI) and Sensation-Seeking Scale Form V (SSS-V).	No significant correlations between aggressiveness-hostility and hormone levels. Testosterone and free androgen index were positively correlated with Sensation Seeking, especially after controlling for LH and SHBG. High sensation seekers had higher TT and FAI values, while aggressive subjects had higher SHBG and TT. Suggests testosterone relates more strongly to sensation seeking than to aggressiveness in healthy men.
Bagatell et al., 1994	Randomized double blind (Human)	48 healthy young men divided into five treatment groups (n ≈ 9–10 per group)	20–40 years (mean age not reported)	4-week baseline + 6-week treatment + 4-week recovery period (14 weeks total)	Serum testosterone (T) and estradiol (E_2) assays; behavioral questionnaires assessing sexual desire, fantasies, intercourse, masturbation, aggression, and relationship satisfaction (validated items from the Dyadic	Suppression of gonadal steroids via GnRH antagonist (Nal-Glu) significantly decreased sexual desire, fantasies, intercourse frequency, and masturbation within 4–6 weeks, all of which recovered post-treatment. Partial testosterone replacement (50 mg/week) maintained normal sexual

					Adjustment Scale, Personality Research Form, and standard sexual history inventories).	behavior, while estradiol depletion had minimal behavioral effect. Aggression showed a non-significant increase during hypogonadism. Overall, physiological testosterone is essential for maintaining sexual behavior in men, whereas estradiol plays a limited role.
Bernhard et al., 2021	Cross Sectional Study	360 adolescents	9-18 years	N/A	Salivary cortisol, alpha-amylase, testosterone, dehydroepiandrosterone-sulfate (DHEA-S), estradiol, progesterone, oxytocin, and arginine-vasopressin	When accounting for interactions between neuroendocrine systems, a male-specific sex hormone factor (testosterone/DHEA-S) predicted male CD, while estradiol and a stress-system factor (cortisol/alpha-amylase) interacting with oxytocin predicted female CD. Estradiol, progesterone, and oxytocin partly explained associations between early environmental risk and CD.
Blake et al., 2017	Non-randomized cohort study	98 women	mean age= 22.19 years, SD of age= 4.43 years, range: 18 to 36 years. 75% of participants were from ages 18 to 24 years old.	3 to 5 weeks (avg. is 4 weeks)	hormone pre-screening questionnaire, clothes buying task, 1 saliva sample per session; Using Inquisit 4.0.4.0, a Single Category Implicit Association Task (SC-IAT), then a 2nd SC-IAT about associations w/ self and sexual availability; then questionnaires assessing mate value, self-reported assertiveness, and sociosexual orientation.	The zero-order effect of progesterone on self-reported assertive behavior demonstrated that self-reported assertive behavior was only marginally negatively predicted by progesterone. When controlling for other hormone predictors, estradiol was found to have a significant positive effect on self-report assertive behavior and implicit perceived volitional control of one's actions while progesterone significantly had the opposite effect on both. Implicit assertiveness was marginally positively predicted by the zero-order effect of estradiol and not by that of progesterone. When controlling for all hormone effects, the effect of estradiol was larger, positive, and statistically significant.
Björn et al., 2009	Randomized controlled trial	106 women	Mean age was 51.8 years (range was 39 to 61 years)	4 years; 3 trials within those 4 years; each trial lasting for a 2-month period	estradiol valerate (E2), The Cyclicity Diagnoser (CD) scale, interviews, Karolinska Scales of Personality (KSP), T score tests, Chi-square test, SPSS	When comparing women with PMS history to women who had the highest negative mood scores during the addition of progestin to estrogen, significant co-variation was found. Both of those groups reported feeling more indirect aggression and lower life & childhood satisfaction. Women with PMS history differed from those with no PMS history in personality characteristics as those

						with PMS also had greater anxiety, muscular tension & lack of impulse control compared to those without PMS. Women who had the highest negative mood scores during the addition of progestin to estrogen also had a greater aim to avoid monotony & greater irritability & somatic anxiety.
Brambilla et al., 2010	Non randomized Cohort Study	15 psychologically and physically healthy women	Mean age = 27.3 ± 2.6 years	One menstrual cycle	Hormones: Plasma estradiol, progesterone, and free testosterone measured via immunochemiluminescence assay. Aggressiveness: Buss–Durkee Rating Scale (BDHI) assessing global aggressiveness and subscales (verbal aggression, suspiciousness, resentment).	Hormonal levels varied significantly across the menstrual cycle (Estrogen and Progesterone rose mid-cycle, FT unchanged). Global aggressiveness did not differ across phases, but estradiol correlated positively with verbal aggression (follicular phase) and resentment (premenstrual phase), while progesterone correlated negatively with suspiciousness and resentment (luteal phase). Hormonal fluctuations (Δ values) also showed negative associations with verbal aggressiveness and resentment.
Cadena-Molina et al., 2025	Non-Randomized Case–Control (Human) Study	49 males total; 28 young offenders and 21 university controls.	Young adult men 18–24 years; mean age approximately 20 years in both groups.	Single assessment; cross-sectional sampling at one time point.	Serum total testosterone measured by immunoassay, demographic and behavioral information (criminal status, type of offense, substance use, etc.), comparison of hormone levels between offenders and controls.	Young offenders had higher mean serum testosterone than controls, and higher testosterone was associated with violent offending, supporting a link between elevated androgens and antisocial or aggressive behavior in young men.
Cashdan, 2003	Non-Randomized Cross-Sectional (Human Behavioral Study)	30 women	19–26 years	2-4 weeks	Serum hormone assays; Competition Diary	High androgens (especially androstenedione) associated with verbal competition; estradiol negatively correlated with physical competition.
Christiansen & Winkler, 1992	Cross-sectional human study	114 healthy adult	ages 18–38 years, mean = 26.4 ± 4.7	Field data collection during summer 1987 (one-time assessments)	Physical aggression: Interview and physical inspection of scars/wounds to classify men as “violent” or “nonviolent.” Hormones: Serum testosterone, dihydrotestosterone (DHT), estradiol (E_2), and salivary	No mean differences in hormone levels between violent and nonviolent men. Among aggressive men, DHT, salivary testosterone, and Tsal/Tser ratio were positively correlated with frequency of violent behavior ($r \approx 0.33$, $p < .05$). Violent men showed greater physical robustness (broader facial and body

					testosterone measured using radioimmunoassay (RIA). Anthropometry: 50 body and head measurements (robustness indices). Alcohol use: 24-hour self-reported intake (beer). Acculturation: Structured interview (language, clothing, religion, travel, employment, education).	measurements). Alcohol consumption was positively associated with violent behavior, while acculturation was unrelated. This signifies that androgens (especially DHT and free testosterone) and alcohol jointly contribute to physical aggression.
DeSoto et al., 2003	Non-randomized cohort study	Study 1: 226 women; Study 2: 57 women; Study 3: 17 women in experimental group, 29 women in the control group	Study 1: mean age=19 years; Study 2: mean age=20.1 years	4 weeks	Study 1: Personality Assessment Inventory—Borderline Features Scale (PAI-BOR), A separate questionnaire about menstrual cycle/period and birth control; Study 2: Saliva collection, the PAI-BOR; Study 3: the PAI-BOR	Fluctuations in estrogen level may impact borderline personality disorder (BPD) symptoms. BPD symptoms most commonly occurred in women using oral contraceptives and in conditions of elevated estrogen during the menstrual cycle. The variation in estrogen levels was found to be a significant predictor of the presence of BPD symptoms, even when statistically controlling for an increase in negative affect. After starting pill use (which increases estrogen levels), it was found that BPD symptoms significantly worsened in women who had already had high levels of BPD before they even entered the trial.
Eisenlohr-Moul et al., 2015	Non-randomized cohort study	40 women	18 to 30 years old	4 weeks	a trait version of the PAI-BOR, saliva sample, the SCID-II, BSL-23, MSI-BPD, PANAS, SSES, Rumination-Reflection Questionnaire, Anger Rumination Scale, UPPS-P Impulsivity scale	Estrogen fluctuations at ovulation and in the luteal phase influence BPD trait expression in at-risk women. Only in cases of high P4, was there a significant negative association between E2 deviation and outcomes (emotion-related impulsivity, greater perseverance, and fewer relationship difficulties) such that lower-than-usual levels of E2 appeared deleterious and higher-than-usual levels of E2 appeared protective, especially among women who scored +1 SD high in BPD trait features. The association of higher-than-usual E2 with fewer relationship difficulties only occurred when P4 was high. Higher-than-usual E2 predicted lower negative affect, general rumination, lack of perseverance and identity disturbance

						among women high in trait BPD features.
Eriksson et al., 2003	Non-Randomized Case-Control	N = 84 (40 AGG+ men with history of alcohol-related aggression; 44 AGG− controls)	AGG+: 42.9 ± 1.8 years; AGG−: 39.7 ± 1.5 years	~2-week recruitment and data collection period per participant (no longitudinal follow-up)	Plasma oestradiol, total and free testosterone (radioimmunoassay); ethanol (gas chromatography), Revised Conflict Tactics Scale (CTS2; Straus et al., 1996), Michigan Alcoholism Screening Test (MAST).	- Oestradiol positively correlated with emotional negotiation (empathy-related) and psychological aggression. - Testosterone correlated positively with physical assault and injury (violent aggression) in AGG+ men. - Oestradiol may counteract testosterone-related physical aggression and promote empathic negotiation. - Suggests oestradiol as a moderating or protective factor in alcohol-related aggression.
Flegr et al., 2012	Non-randomized cross-sectional study	100 male and 93 female military personnel	mean age 27.9 years & standard deviation of 7.9 years in men; mean age 29.2 years & standard deviation of 7.3 years in women	N/A	Meili selective memory test, TOPP – Test of attention and short term memory, N-70, OD-1, BDI (Buss-Dürker Inventory) w/ a 5-grade scale from “absolutely agree” to “absolutely disagree”, The Wiener Matrizen-Test WMT, OTIS, serum samples, Statistica 6.1 and SPSS 16.0	Estradiol had a significant positive correlation with psychopathology in men and negativism in women as well as a significant negative correlation with phobia in women. Its correlation with psychopathology in males is present because in males, estradiol is synthesized from testosterone.
Finkelstein et al., 1997	Randomized clinical trial	49 (35 males, 14 females)	13–17 years	Total ≈ 12 months (8 treatment periods × 3 months each; alternating hormone and placebo phases)	Modified Olweus Multifaceted Aggression Inventory (OMAI); serum and urine hormone assays (testosterone, estrone sulfate, LH, FSH)	Administration of exogenous sex steroids (testosterone for boys; conjugated estrogen for girls) significantly increased self-reported physical aggression and aggressive impulses but not verbal aggression. Effects were dose-dependent up to mid-level exposure, then plateaued. Both sexes showed similar behavioral changes.
Geniole et al., 2013	Randomized controlled trial	107 men, 101 women	Mean age= 20 years, Standard deviation of age= 2.5 years, age range: 18 to 37 years	Test sessions were approximately 60 min long and conducted between 12:00 p.m. and 6:00 p.m. to minimize variation in hormones related to diurnal rhythms.	The Psychopathic Personality Inventory — Revised (PPI-R), The Point Subtraction Aggression Paradigm (PSAP), Suspicion check (questions after PSAP), reward allocation paradigms (measure antagonistic behaviors), endocrine measures (2 saliva samples), statistical analyses	When examining changes in hormones as predictors of antagonistic behavior, it was found that only the third step was significant in men, meaning men with greater increases in testosterone and men in the share a sum of money condition were more likely to be antagonistic than men with lesser increases in testosterone and men in the decide the honorarium condition and this relationship occurred independently of co-

						occurring changes in cortisol and estradiol. Women with lower baseline estradiol and those scoring higher in self-centered impulsivity were more aggressive than those with higher baseline estradiol and those scoring lower in self-centered impulsivity. Additionally, women using contraceptives were more aggressive than women not using contraceptives. The predictive effect of baseline estradiol did not differ between sexes.
Giegling et al., 2008	Non-randomized Case-control study	92 non-control individuals (53 males and 39 females); 312 control subjects (138 males and 174 females)	mean age was 51.8 (± 18.5; range: 19–86 years) for cases; mean age was 45.01 ± 14.92 years (range: 19–79) for controls	N/A	SCID I and SCID II, Basic Documentation for Suicidal Behavior, Intent Score Scale, STAXI, Questionnaire for Measuring Factors of Aggression, Family History Assessment Module, Illumina genotyping, chi-square, t-tests, Mann–Whitney U Test, MANCOVA, statistical software “R” package “haplo.score”	Strong linkage disequilibrium was observable between rs1913474 and rs1801132 and between rs722207 and rs974276. Singer marker analyses did not demonstrate the markers having any significant main effects on STAXI or FAF scores. Esr1 haplotype analyses showed that none of the three haplotypes were associated with FAF scores and only block 3 haplotypes had a putative association with Anger Control scores, especially the T-G-A-G haplotype. The gene variants rs1913474, rs1801132, and rs722207 were majorly involved and contributed to the association with Anger Control scores.
Górniak et al. (2025)	Non-randomized cross-sectional study (two studies).	Study 1: 183 women; Study 2: 269 women.	Study 1: mean 21.82 ± 2.31 years (range 18–30); Study 2: mean 22.02 ± 2.36 years (range 19–29).	Single assessment in the first 5 days of the menstrual cycle; morning blood draw (7:30–9:30 AM) followed by online psychological assessment.	Venous blood estradiol (ECLIA Elecsys Estradiol III); self-assessed estradiol; self-assessed attractiveness; NARQ; FFNI-SF.	(1) Across both studies, objectively measured estradiol was not significantly associated with grandiose narcissism, including its agentic facet. (2) In Study 1 only, estradiol showed small positive associations with neurotic narcissism and vulnerable narcissism, but these findings were not replicated in Study 2. (3) In both studies, higher agentic narcissism was associated with higher self-assessed estradiol. (4) In both studies, higher agentic narcissism was also associated with higher self-assessed attractiveness. (5) Self-assessed attractiveness was positively correlated with self-assessed estradiol.
Hall et al., 2005	Randomized controlled trial	27 men- 13 experimental	The experimental	8 weeks	the Rating Scale for Aggressive Behavior in the Elderly (RAGE),	There were no significant differences between the groups when examining the mean total

		group, 14 controls	group ranged from 63 to 84 years old, with mean age of 78.1 years and SD of 6.21 years. The control group ranged from 55 to 89 years old, with mean age of 78.8 years and SD of 9.64 years.		the Cornell Scale for Depression in Dementia (CSDD) and the Mini-mental State Examination (MMSE). Physical exam, biochemistry and serum hormone concentrations (at baseline and at 8 weeks). Concomitant psychotropic medication use was recorded and analyzed.	RAGE scores, the 21 individual RAGE variables and the means of the groupings of the variables into physical or verbal violence, with either no changes or improvement week-by-week. RAGE scores and baseline estrogen and testosterone concentrations were not correlated. Patch usage resulted in a significant rise in serum estrogen and no significant decrease in serum testosterone. When examining the mean scores in the estrogen group over time from patch removal (week 8) to 2 weeks post-removal aggressive behaviour rebounded and this rebound was approaching statistical significance.
Harrison et al., 2020	Cross-sectional	66	12–18 years (M = 15.73, SD = 1.45)	Per participant: ~4 hours across 2 sessions (same afternoon window; baseline → stressor ~55 min; +20 min post-stressor sample; +20 min recovery)	Hormones: Salivary 17β-estradiol, testosterone, cortisol (baseline and reactivity; solid-phase extraction + EIA; log10; fold-change composite). Psychopathy: PCL-YV total and four facets (interpersonal, affective, lifestyle, antisocial); inter-rater reliability reported. Stressor: Adapted TSST (speech + serial 7s). Covariates/Checks: Age, time-of-day random effects; confederate sex, setting, meds checks. Collaterals: ICU (youth), ICE-P (parent), SRO (offending).	Interactions among estradiol, testosterone, and cortisol reactivity relate to psychopathy. Two-way E2×T reactivity predicts higher psychopathy total and factor-1 facets (interpersonal, affective) when both E2 and T decreasepost-stressor. Three-way E2×T×cortisol reactivity predicts affective traits when all three increase post-stressor. Baseline hormones largely non-significant once modeled with interactions.
Kyomen et al., 1999	Randomized controlled trial	12 women and 2 men	The average age was 83.8 years. The standard deviation of age was 7.16 years. All patients were at least 60 years old	over a 4-week period	a physical & mental status exam, Mini-Mental State Exam (MMSE), Test for Severe Impairment (TSI) (weekly for checking cognitive function), Cornell Scale for Depression in Dementia (CSDD), a modified Katz Activities of Daily Living Scale (ADL),The Overt Aggression Scale (modified version)	When examining weekly Placebo vs. Estrogen differences, researchers found that differences were substantial for all weeks for Physical and Verbal Aggression including week 1, demonstrating that estrogen acts quickly and significantly impacts aggressive behavior in as little as 3 days of drug initiation. In all weekly comparisons for both Physical and Verbal Aggression, it was found that those in the Estrogen group had significantly lower scores on the Physical and Verbal Aggression Scales compared to those in

						the Placebo Group.
Lubke & Pause, 2014	Non-randomized cohort study	26 men & 25 women	mean age of 26.0 years; SD of age = 5.6 years; age range from 19 to 42 years old; the mean age did not differ with respect to gender	N/A	A two-alternative forced-choice single-staircase odor detection procedure; 0 to 10 scale for odors; language-free Self-Assessment Manikin (SAM), Saliva sampling and biochemical analysis of testosterone and 17-beta-estradiol; 2 x 2 ANOVA testing; correlational analyses; T tests; alpha level of $P < 0.05$ for all statistical testing	Testosterone levels did not affect female androstenone perception. For women with higher estradiol levels than the median, androstenone was rated significantly less pleasant and significantly more unpleasant, Women with lower estradiol levels than the median rated androstenone's pleasantness higher and androstenone's unpleasantness lower. This may be due to androstenone being a signal of reduced willingness for social cooperation and a greater likelihood to engage in extramarital sex, which are behaviours/traits associated with dominance and aggressiveness. This supports the theory that androstenone is a chemosensory signal of dominance and aggressiveness.
Inoff-Germain et al., 1988	Cross-sectional human study	60 participants (30 boys, 30 girls)	9–14 years (mean ≈ 12.3)	Single assessment visit (behavioral and hormonal data collected within 2–3 days)	Hormones: Luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T), estradiol (E_2), androstenedione, dehydroepiandrosterone (DHEA), and DHEA-sulfate (DHEAS), measured via radioimmunoassay (RIA) from three blood samples (mean values used). Behavioral aggression: Videotaped 45-min family interaction tasks (structured and unstructured) coded for nine variables: modulated anger, explosiveness, dominance, defiance, and anger toward parents. Coders were blind to hormone data.	In girls, higher estradiol and androstenedione levels were positively associated with observed aggression (anger, dominance, defiance toward parents). In boys, aggression was less strongly related to hormone levels; small effects noted for LH and DHEA. Sex-specific hormonal influences, with estradiol being a key predictor of aggressive behavior in girls during puberty.
Pajer et al., 2006	Cross Sectional Study	87 adolescents	15-17 years	N/A	Plasma was assayed for testosterone, estradiol, androstenedione, dehydroepiandrosterone (DHEA), dehydroepiandrosterone-sulfate	Girls with CD had significantly lower cortisol to DHEA ratios, but did not differ from NC girls on any other hormone variable. Girls with symptoms of aggressive CD had significantly higher mean free testosterone indexes, lower SHBG levels, and lower cortisol

					(DHEA-S), sex hormone binding globulin (SHBG), and cortisol	to DHEA ratios than girls with non-aggressive CD. Girls with CD scored higher on the aggression questionnaire, but there was no association between general aggression and any hormone variable for the sample.
Popova et al., 2018	Cross-sectional human study	35 healthy male university students (14 Indian, 21 Ukrainian)	18–22 years	Single data collection session	Hormones: Serum testosterone and β-estradiol measured using enzyme-linked immunoassay (ELISA) kits. Aggression: Buss–Durkee Hostility Inventory (BDHI) and Eysenck Personality Questionnaire (EPQ) for physical and verbal aggression. Anthropometric marker: 2D:4D digit ratio measured by caliper.	Moderate positive but statistically insignificant correlations were observed between serum testosterone and physical aggressiveness (r = +0.39, p = .099) and between testosterone/estradiol ratio and aggression (r = +0.42, p = .072). Estradiol showed no significant associations. The 2D:4D ratio correlated positively but weakly with testosterone levels (r = +0.51, p = .004) in the overall group. Testosterone has only a modest relationship with aggression in young men, and the 2D:4D ratio is not a reliable biomarker of prenatal androgen exposure or adult aggressiveness.
Peper et al., 2015	Cross-sectional human study	258 participants (126 boys, 132 girls)	8–25 years (mean = 14.2 ± 3.8)	Single session including MRI, saliva sampling, and behavioral testing	Diffusion Weighted Imaging (DWI) on 3T Philips MRI to assess white matter integrity (FA, MD, RD, LD) across six fronto-temporal–subcortical pathways; salivary testosterone and estradiol assays via isotope dilution LC-MS/MS and ELISA; Buss–Perry Aggression Questionnaire (BPAQ) for total and subscale aggression (physical, verbal, anger, hostility).	Higher testosterone levels were linked to lower white matter integrity (higher MD, RD, LD) in fronto-temporal–subcortical pathways and increased expressive aggression (physical/verbal), particularly in boys. Higher estradiol in boys correlated with total and physical aggression, while in girls, aggression decreased with age. Lower white matter integrity was associated with greater verbal aggression, whereas increased connectivity was linked to higher hostility. Results suggest sex steroids modulate white matter connectivity and aggression across adolescence.
Peters & Eisenlohr, 2019	Systematic review synthesizing multiple studies (non-randomized cohort)	varying sample sizes; N=54 women, N=46 undergrads, N=57 undergrads, N=40	All patients at least 15 years old	4 weeks	cross-sectional diagnostic interviews and self-report measures; prospective daily assessments; retrospective self-reports of at baseline; The Carolina Premenstrual Assessment (C-PASS); psychosocial interventions, such	Most symptoms of Borderline Personality Disorder (BPD) are normally lowest around ovulation except for proactive aggression and some forms of impulsive behaviors which peak during ovulation. Preliminary evidence suggests ovarian hormones may exert strong effects on BPD symptom expression, and further research should be

		undergrads, N=14 women, N=15 women			as cognitive-behavioral therapy (CBT)	done to examine mechanisms and develop interventions. The cyclical increases in estrogen in humans has been shown to upregulate neural reward processing (replicated results from animal studies), resulting in enhanced cognitive resources, assertiveness, and reward drive at ovulation. Individuals with BPD experience all this combined with the context of negative cognitive biases that the world is hostile, dangerous and untrustworthy, which may result in higher levels of proactive aggression as it appears to be the most viable way to achieve goals effectively.
Peters et al., 2020	Non-randomized cohort study	15 females in the final sample	mean age of 32.16 years; range from 19 to 44	35 days	online screening questionnaire of SCID-BPD, Daily Record of Severity of Problems, State-Trait Anger Expression Inventory-2, Reactive-Proactive Aggression Questionnaire, urine luteinizing hormone (LH) tests	Anger/Irritability began significantly rising during the midluteal phase & significantly peaked in the perimenstrual phase. Levels of Reactive Aggression peaked in the midluteal phase, with significant contrasts with perimenstrual and follicular phases and in the perimenstrual phase was not elevated compared to the ovulatory phase. Proactive Aggression peaked during the ovulatory and follicular phases with lowest levels occurring in the perimenstrual phase. This suggests a generally protective effect of higher levels of estradiol during the ovulatory phase which may provide individuals with BPD greater ability to engage in premeditated and purposeful (versus reactive) action.
Ritter, 2003	Non-randomized cohort study	22 females and 22 males	mean female age= 21.6 years, standard deviation of female age= 2.45 years; mean male age= 22.3 years, standard deviation of male age= 2.11 years	approximately 4 weeks	The Aggression Questionnaire [Buss and Perry, 1992]-> to assess four different components of aggression (Physical and Verbal Aggression = Instrumental Component, Anger = Affective Component, and Hostility = Cognitive Component)	It was found that levels of physical aggression and verbal aggression in women were higher at menses than at the midluteal phase, with the differences in physical aggression levels during the two phases being significant while the differences in verbal aggression levels during the two phases were non-significant. Reporting of anger or hostility did not change across the menstrual cycle, which resulted in a significant sex-difference on reporting physical aggression between men and women

						at the midluteal phase but not at menses (men were used as a control group).
Stanton, S. J., & Schultheiss, O. C., 2007	Non randomized Cohort Study	49 F Participants	19.96 ± 0.27 years old	2 Days	Picture Story Exercise (PSE)/ Implicit Power Motiviation (n power) score, Dominance contest paradigm (Serial response task)/ Contest outcome (win vs lose), Personality Research Form (PRF)/ Self reported dominance and agression scales, Radioimmunoassay/Salivary estradiol and testosterone concentrations	Implicit power motivation was positively correlated with basal estradiol (R = 0.36, p < 0.01), particularly in single women, normally cycling women, and those with low measurement error. Following a dominance contest, estradiol responses were moderated by the interaction of implicit power motivation and contest outcome (B = 1.38, p = 0.01), with power-motivated winners showing increases and losers showing decreases. Implicit power motivation did not predict testosterone levels or changes, and self-report measures of dominance and aggression did not predict estradiol outcomes.
Tackett et al., 2015	Non-randomized cohort study	105 adolescents (55% females)	All participants were between the ages of 13 and 18 years old; mean age= 16.00 years, standard deviation of age= 1.29 years	N/A	DIPSI — Dimensional Personality Symptom Item Pool (DIPSI); CBCL — Child Behavior Checklist (CBCL—6-18); Hormone Assays — E2 (estradiol), T (testosterone), and C (cortisol) assays (saliva samples)	Greater levels of externalizing behaviours were found to be associated with high estradiol only under low cortisol and high levels of the personality traits of disagreeableness and emotional instability. This did not change even when controlling for testosterone concentrations. This matched with the dual-hormone hypothesis, which claims that adolescents with high estradiol and low cortisol concentrations have the greatest risk for externalizing problems if they also show high levels of pathological personality traits.
Takahashi et al., 2018	Non-randomized case-control study	10 females and 11 males	Two females (35 and 45 yrs old) and 2 males (36 and 35 yrs old); rest of them have unknown ages	N/A	positron emission tomography (PET) using 11C-cetrozole, MR image, PET Image Processing, Buss-Perry Aggression Questionnaire and Temperament and Character Inventory	Sex hormone levels in plasma had no effects on binding potential (BPND) values of 11C-cetrozole (aromatase concentration). In females, aggression scores were positively associated with BPND in the left amygdala. In contrast, data from male and combined data from male and female did not exhibit a significant association between aggression scores and BPND in the amygdala. BPND in the right amygdala was strongly negatively associated with novelty-seeking and persistence and strongly positively associated

						with cooperativeness and self-transcendence.
Talarowska et al., 2019	Non-Randomized Cross-Sectional (Human Clinical Study)	44 (31 women, 13 men)	20–60 years	N/R	MMPI-2; HAM-D; qPCR; ELISA	ERα expression correlated with paranoia and mania in women; ERβ correlated with anxiety in men; links between ERs and personality traits.
Treleaven et al. , 2013	Non-randomized Case-control study	122 non-control men; 1229 control group men	avg. age of 47.9 years for control; avg. age of 49.8 years for non-control group	4 months	survey of BFI (Big Five factor personality inventory)	Agreeableness was the only BFI personality trait that significantly differed across groups, with castrated individuals on supplementary estrogen scoring the highest, and the controls the lowest. The castrated individuals not on supplemental hormones scored higher on agreeableness, conscientiousness, and neuroticism and lower on openness and extroversion compared to the controls although these differences were not found to be statistically significant.
Vaillancourt et al., 2012	Cross-sectional genetic association study (human males)	188 male undergraduate students	Young adults (mean age not reported)	One-time sampling and measurement session	2D:4D digit ratio measured from hand images; ESR1 TA(n) repeat genotyping; self-reported physical aggression questionnaire.	Higher ESR1 TA repeat number correlated with higher (more feminized) left-hand 2D:4D ratios. Heterozygous men had lower physical aggression. This suggests ESR1 polymorphism influences both digit ratio and aggression through estrogen receptor–related pathways.
Vermeersch et al., 2008	Cross-sectional	298	Mean 14.3 y (SD≈0.6)	Single visit	Hormones: TT, TE2, SHBG, LH (immunoassays); calculated FT & FE2. Puberty: physician-rated Tanner (pubic hair + breast). Psychometrics: Aggressive (ART, 6 items, α=0.71) & Non-aggressive (NART, 21 items, α=0.83) risk-taking scales; Differential Association (peers' RT; 7 items, α=0.86). Menstrual phase from last menses date.	FE2 positively associated with NART and ART. Testosterone (FT/TT) not associated with ART/NART. Peer RT strongly associated with both outcomes. Cycle-phase: hormone-behavior links significant only mid-cycle—FE2→NART & ART. Interactions: FE2×peer RT significant mid-cycle; early-phase FE2×peer RT significant for ART. No effects late-phase.
Westberg et al., 2003	Genetic association study (non-randomized, case-control)	172 women	42 years old	N/A	waist/hip circumference ratio (WHR), Karolinska Scales of Personality (KSP), genotyping	Repeat was assoc. w/ neuroticism, psychoticism, & non-conformity. Suspicion, Indirect aggresion & irritability had significant associations w/ genotype. 40% of variation in the KSP subscales could be attributed to Psychic Anxiety. Subjects with

						the SS genotype differed from the rest wrt Psychic Anxiety.
Witte et al., 2008	Cross-sectional	33 (16 women, 17 men)	Mean 26.24 ± 5.5 years	Single visit (~half day): morning blood draw; aggression questionnaire; 90-min dynamic PET scan; structural MRI	Aggression: Questionnaire for Measuring Factors of Aggression. Imaging: PET with BPND quantified via SRTM2 in prefrontal, cingulate, limbic ROIs; MRI for coregistration. Hormones: Plasma SHBG, bioavailable testosterone, bioavailable 17β-estradiol. Covariates: Age, sex; radiochemical parameters checked.	Primary findings: Higher aggression associated with higher 5-HT$_1$A BPND in dorsolateral/ventromedial/orbitofrontal PFC and ACC; no effects in hippocampus/RN reach significance. More aggressive subjects showed lower SHBG; SHBG inversely correlated with 5-HT$_1$A BPND in frontal cortices, ACC/PCC, and amygdala. In women, testosterone positively associated with frontal/cingulate 5-HT$_1$A BPND. Interpretation: reduced downstream control via elevated postsynaptic 5-HT$_1$A in frontal regions, modulated by sex hormones.
Zoimkewicz et al., 2015	Non-Randomized Cross-Sectional (Human) Study	72	24-35 years	N/R	Trait Dominance-Submissiveness Scale (TDS), State and Trait Anxiety Inventory (STAI), Radioimmunioassay	Self-assessed social dominance (DSS) is negatively assoicated with free E2 and E2:T ratio, which is moderated by trait anxiety (moderately and highly anxious women, no relationship found with low-anxiety women - TAS)

Table S4. Risk of Bias — Randomized Controlled Trials (RoB 2). Cochrane Risk of Bias tool version 2 (RoB 2). Color-coded traffic-light format per Sterne et al. (2019). **Legend:** ✚ Low risk ? Some concerns — High risk

Study	Randomization process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of Reported Result	Overall
Bagatell et al., 1994	✚	✚	✚	?	✚	✚
Björn et al., 2009	✚	✚	✚	✚	✚	✚
Finkelstein et al., 1997	✚	✚	✚	?	✚	?
Geniole et al., 2013	✚	✚	✚	✚	✚	✚
Hall et al., 2005	✚	✚	✚	✚	✚	✚
Kyomen et al., 1999	✚	✚	✚	✚	✚	✚

Table S5. Risk of Bias — Cohort Studies (Newcastle-Ottawa Scale). Newcastle–Ottawa Scale (NOS) for cohort studies. Stars (★) indicate criteria met; blank = criterion not met. **Legend:** ★ = one star awarded; ★★ = two stars awarded (comparability domain); blank = criterion not met. Quality: High ≥ 7 stars; Moderate = 5–6 stars; Low ≤ 4 stars.

Study	Design	Representativeness of Exposed Cohort	Selection of Non-Exposed Cohort	Ascertainment of Exposure	Outcome Not Present at Start	Comparability (max ★★)	Assessment of Outcome	Follow-Up Length	Follow-Up Adequacy	Score /9	Quality
Blake et al., 2017	Prospective Cohort	★	★	★	★	★		★	★	7/9	High
Brambilla et al., 2010	Prospective Cohort			★	★		★	★	★	6/9	Moderate
Eisenlohr-Moul et al., 2015	Prospective Cohort		★	★	★			★	★	7/9	High
DeSoto et al., 2003	Prospective Cohort	★	★	★			★	★	★	7/9	High
Lubke & Pause, 2014	Prospective Cohort	★	★	★	★		★	★	★	9/9	High
Peters & Eisenlohr, 2019	Prospective Cohort	★	★	★	★		★	★		7/9	High
Peters et al., 2020	Prospective Cohort	★	★	★	★			★	★	7/9	High
Ritter, 2003	Prospective Cohort	★	★	★	★		★	★	★	9/9	High
Stanton & Schultheiss, 2007	Prospective Cohort		★	★	★		★	★	★	7/9	High

[a] *A study can be awarded a maximum of one star per item except Comparability (max two stars).*

Table S6. Risk of Bias — Cross-Sectional Studies (Newcastle-Ottawa Scale). Newcastle–Ottawa Scale (NOS) adapted for cross-sectional studies. Ascertainment of Exposure can receive a maximum of two stars (★★); all other items max one star. **Legend:** ★ = one star awarded; ★★ = two stars awarded (comparability domain); blank = criterion not met. Quality: High ≥ 7 stars; Moderate = 5–6 stars; Low ≤ 4 stars.

Study	Representativeness of Sample	Sample Size	Non-Respondents	Ascertainment of Exposure (max ★★)	Comparability (max ★★)	Assessment of Outcome	Statistical Methodology	Score /9	Quality
Aluja & Torrubia, 2004	★			★★	★	★	★	5/9	Moderate
Aluja & García, 2007				★★	★	★	★	5/9	Moderate
Bernhard et al., 2021	★	★		★	★★	★	★	7/9	High
Cashdan, 2003	★			★★	★	★	★	6/9	Moderate
Christiansen & Winkler, 1992	★			★★	★	★	★	6/9	Moderate
Flegr et al., 2012	★		★	★★	★	★	★	8/9	High
Górniak et al., 2025				★★		★	★	4/9	Moderate
Harrison et al., 2020		★		★★	★	★	★	6/9	Moderate
Inoff-Germain et al., 1988	★			★★	★	★	★	6/9	Moderate
Pajer et al., 2006	★	★		★	★	★	★	6/9	Moderate
Peper et al., 2015	★	★		★★	★	★	★	7/9	High
Popova et al., 2018				★★	★	★	★	5/9	Moderate
Tackett et al., 2015	★			★★	★	★	★	6/9	Moderate

Talarowska et al., 2019				★★		★	★	4/9	Moderate
Takahashi et al., 2018				★★		★	★	4/9	Moderate
Vaillancourt et al., 2012				★★	★	★	★	5/9	Moderate
Vermeersch et al., 2008	★	★	★	★★	★	★	★	8/9	High
Witte et al., 2008				★★	★	★	★	5/9	Moderate
Ziomkiewicz et al., 2015	★		★	★★	★	★	★	7/9	High

[a] *Ascertainment of Exposure (max ★★): both stars awarded when a validated laboratory measurement tool was used (e.g., radioimmunoassay or ELISA for hormone quantification).*

Table S7. Risk of Bias — Case-Control Studies (Newcastle-Ottawa Scale). Newcastle–Ottawa Scale (NOS) for case-control studies. Case Definition can receive a maximum of two stars (★★). **Legend:** ★ = one star awarded; ★★ = two stars awarded (comparability domain); blank = criterion not met. Quality: High ≥ 7 stars; Moderate = 5–6 stars; Low ≤ 4 stars.

Study	Design	Case Definition (max ★★)	Representativeness of Cases	Selection of Controls	Definition of Controls	Comparability (max ★★)	Ascertainment of Exposure	Non-Response Rate	Score /8	Quality
Eriksson et al., 2003	Non-Randomized CC	★★		★		★	★	★	6/8	High
Giegling et al., 2008	Non-Randomized CC (Genetic Assoc.)	★★	★	★		★	★	★	7/8	High
Treleaven et al., 2013	Non-Randomized CC	★★	★	★		★	★	★	8/8	High
Westberg et al., 2003	Non-Randomized	★★	★	★		★	★	★	8/8	High

	CC (Genetic Assoc.)									
Cadena-Molina et al., 2025	Non-Randomized Case–Control (Human) Study	★★		★		★	★		5/8	**Moderate**

CC = Case-Control; Genetic Assoc. = Genetic Association Study.

Table S8. Risk of Bias — Preclinical Animal Studies (SYRCLE). SYRCLE Risk of Bias tool for animal studies (Hooijmans et al., 2014). Color-coded traffic-light format. N/A = not applicable (narrative review paper). **Legend:** ✚ Low risk ? Some concerns — High risk

Study	1. Sequence Generation	2. Baseline Characteristics	3. Allocation Concealment	4. Random Housing	5. Blinding (Performance)	6. Random Outcome Assess.	7. Blinding (Detection)	8. Incomplete Outcome Data	9. Selective Outcome Reporting	10. Other Sources of Bias	Overall Risk of Bias
Agrimi et al., 2024	?	?	—	—	—	?	?	✚	✚	?	—
Albert et al., 1990	?	—	?	—	—	?	—	✚	✚	?	—
Albert et al., 1992	?	✚	?	?	?	?	?	✚	✚	?	?
Burmeister et al., 2007	?	✚	?	?	?	?	✚	✚	✚	?	?
Clipperton-Allen et al., 2011	—	✚	?	?	?	—	?	✚	✚	?	?
Cologer-Clifford et al., 1999	?	✚	?	✚	?	?	?	✚	✚	?	?
Compaan et al., 1994	?	✚	?	?	?	?	✚	✚	✚	?	?

Cunningham & McGinnis, 2007	+	+	?	+	?	+	?	+	+	−	?
Cushing et al., 2008	?	?	?	?	?	−	+	−	?	−	−
Davis et al., 2003	?	+	+	+	?	+	?	+	+	?	?
Dombret et al., 2020	+	+	?	?	?	?	+	+	+	+	?
Floody & Pfaff, 1977	−	+	−	?	?	−	?	+	+	?	−
Ghiraldi et al., 1993	?	+	−	+	?	?	−	+	+	−	−
Hashikawa et al., 2017	?	?	?	?	?	?	+	+	?	?	?
Haug & Brain, 1983	−	+	−	?	?	−	?	+	+	?	−
He et al., 2012	?	+	?	?	−	?	−	+	+	?	?
Hilakivi-Clarke et al., 1996	?	−	?	?	−	−	?	+	?	+	−
Hilakivi-Clarke et al., 1997	?	+	?	?	?	?	?	+	+	?	?
Hume & Wynne-Edwards, 2005	?	+	?	?	?	?	+	+	+	?	?
Juntti et al., 2010	+	+	?	?	+	?	+	+	+	?	?
Kramer et al., 2008	?	+	−	+	?	?	−	+	+	−	−

Krzywkowski et al., 2020	?	+	?	?	?	?	+	+	+	+	?
Lee et al., 2014	?	+	?	?	?	?	+	+	+	+	?
Liu et al., 2022	?	+	?	?	?	?	?	+	+	+	?
Mayer et al., 1990	+	+	?	?	+	?	+	+	?	?	?
Merritt et al., 2018	+	+	?	?	?	?	+	+	+	+	?
Mountoufaris et al., 2023	?	+	?	?	?	?	+	+	+	?	?
Nakata et al., 2018	+	+	?	?	?	?	+	+	+	+	?
Nyby et al., 1992	?	?	?	?	?	−	+	−	?	−	−
Ogawa et al., 1998	?	+	?	?	?	?	+	+	+	?	?
Olvera-Ramos et al., 2021	?	+	?	?	?	?	?	+	+	?	?
Patisaul & Bateman, 2008	?	+	?	?	?	?	+	+	+	?	?
Pazol et al., 2004	?	+	?	?	?	?	?	+	+	?	?
Rines et al., 1984	?	−	+	?	?	+	?	+	+	?	?
Sandhu et al., 2019	?	+	−	+	?	?	−	+	+	−	−
Scordalakes et al., 2004	+	−	?	+	?	+	+	+	+	?	?

Simon & Gandelman, 1978	?	+	?	?	+	?	+	+	+	?	?
Simon et al., 1985	?	+	–	?	–	?	–	+	+	–	–
Spiteri et al., 2010	?	–	?	?	?	+	?	–	+	?	?
Svare et al., 1975	?	+	?	+	?	–	?	–	–	?	–
Toda et al., 2001	?	+	–	–	–	?	?	+	+	?	–
Toufexis et al., 2007	–	+	–	?	?	–	?	+	+	?	–
Trainor & Marler, 2001	?	+	–	?	–	?	–	+	+	?	–
Trainor et al., 2006	?	–	+	?	?	+	?	–	?	–	?
Trainor et al., 2007	?	–	+	?	+	+	+	–	+	?	–
Trainor et al., 2008	?	+	+	+	+	+	+	+	+	+	?
Trives et al., 2025	+	+	?	?	+	?	+	+	+	?	?
Tsuda et al., 2014	–	+	–	?	?	–	?	+	+	?	–
Unger et al., 2015	+	+	?	?	+	?	+	+	+	?	?
Villalon Landeros et al., 2012	?	+	?	?	?	?	?	+	+	?	?
vom Saal et al., 1983	?	+	?	?	?	?	?	+	+	?	?

Wang et al., 2019	?	?	?	?	?	?	+	+	?	?	?
Wei et al., 2023	+	+	?	?	+	?	+	+	+	?	?
Williamson et al., 2019	−	+	?	?	?	?	?	+	+	?	?
Wu et al., 2009	?	+	?	?	+	?	+	+	+	?	?
Xu et al., 2021	?	+	?	?	?	?	?	+	+	?	?
Zha et al., 2025	?	+	?	?	?	?	+	+	+	+	?

Items: 1 = Sequence Generation; 2 = Baseline Characteristics; 3 = Allocation Concealment; 4 = Random Housing; 5 = Blinding (Performance Bias); 6 = Random Outcome Assessment; 7 = Blinding (Detection Bias); 8 = Incomplete Outcome Data; 9 = Selective Outcome Reporting; 10 = Other Sources of Bias.

Table S-Ref. Complete Reference List of All 103 Analyzed Studies

Part A — Preclinical Studies (n = 64)

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