BI-06 Endocrine life course: puberty to old age

Introduction: The Tri-Layered Framework of the Endocrine Life Course

To understand how men and women can best live together—whether in couples, families, organisations, or societies—it is necessary to strip away both the biological determinism of the past and the biological denialism of the present. The human endocrine life course is not a static binary but a dynamic, lifelong trajectory of hormonal divergence and convergence. To examine this trajectory with analytical rigour, this report adopts a tripartite framework, separating the human experience into three distinct but interacting layers.

First is the physiological layer: the measurable, objective reality of circulating hormones, neural receptor densities, and morphological brain changes. Second is the behavioural layer: the statistical manifestation of these biological realities in human action, emotion, and cognition. Crucially, behavioural sex differences are characterised by overlapping Gaussian distributions. Knowing a group average offers almost zero predictive power regarding any single individual. Finally, there is the cultural layer: the highly variable social scaffolding that either amplifies, dampens, or redirects underlying physiological and behavioural dispositions.

By tracing the endocrine life course from the silent hormonal surges of infancy through the dramatic divergence of puberty, the reproductive years, the neuroplastic crucible of parenthood, and the eventual hormonal convergence of old age, we can establish a robust foundation for understanding human sex differences. This understanding is grounded in peer-reviewed primary literature, systematic meta-analyses, and a strict adherence to separating what is known about statistical averages from what can be said about individuals.

Childhood: Mini-Puberty and the Transition to Adrenarche

It is a common misconception that childhood, prior to adolescence, is an endocrinologically dormant period devoid of sex differences. In reality, early human development features an initial, transient awakening of the hypothalamic-pituitary-gonadal (HPG) axis, followed years later by the independent maturation of the adrenal glands.

The Physiological Layer: Early HPG Activation

At birth, the sudden withdrawal of suppressive placental oestrogens triggers a rebound activation of the HPG axis in both sexes, a phase termed "mini-puberty"[1]. In male infants, a surge in luteinising hormone (LH) and follicle-stimulating hormone (FSH) leads to a dramatic peak in testosterone between one and three months of age. Serum testosterone reaches 100–400 ng/dL (3.5–13.9 nmol/L), levels comparable to early or mid-puberty in adolescent males[1]. This transient androgen exposure stimulates penile growth, testicular descent, and a massive proliferation of Sertoli cells, laying the physiological architecture for future

spermatogenesis. The fetal Leydig cells undergo apoptosis, and the system subsides to undetectable prepubertal levels by six months of age[1].

In female infants, the physiological profile is markedly different. The LH/FSH ratio diverges significantly from males, with FSH levels rising higher and remaining elevated much longer—often up to three or four years of age[2]. This drives fluctuating, cyclical levels of oestradiol that stimulate transient ovarian follicular maturation, breast tissue development, and uterine growth[1]. After this window, the HPG axis turns itself off, remaining dormant until true puberty[6].

Following the quiescence of mini-puberty, a second, distinct endocrine event occurs approximately two years prior to the onset of central puberty: adrenarche. Adrenarche involves the maturation of the zona reticularis of the adrenal cortex, leading to the secretion of dehydroepiandrosterone (DHEA) and its sulfate (DHEAS)[7]. This process is independent of the gonadal axis and provides the first significant exposure to weak androgens in both sexes, driving the early development of pubic hair (pubarche) and changes in body odour.

The Behavioural and Cultural Layers

The behavioural consequences of mini-puberty remain a subject of intense scientific debate. The central hypothesis posits that this postnatal testosterone surge contributes to the secondary masculinisation of the developing brain, influencing later play behaviour, spatial cognition, and potentially the development of autistic traits. However, longitudinal evidence linking postnatal hormones to behaviour is mixed and frequently fails to replicate.

For instance, while prenatal testosterone (measured via amniotic fluid) has been correlated with later autistic traits, postnatal testosterone measured during mini-puberty does not show the same predictive power. In the Cambridge Human Imaging and Longitudinal Development (CHILD) study, Auyeung and colleagues (2023, *Molecular Autism*) investigated salivary testosterone at two and six months of age in a prospective cohort (N = 87). The study found no significant association between log-transformed testosterone levels during mini-puberty and autistic traits at 18 months of age, as measured by the Quantitative Checklist of Autism in Toddlers (Q-CHAT)[9]. Conversely, other studies have found weak associations between salivary testosterone during the peak of mini-puberty (1–3 months) and smaller expressive vocabulary at 18–30 months, though these effects are heavily moderated by environmental factors[10].

Culturally, the near-equality of prepubescent boys and girls in size, strength, and cognitive capability means that the strict gender segregation often observed in childhood play is driven more by socialisation, peer-group dynamics, and prenatal organizational effects than by concurrent circulating hormones. The physiological hardware remains mostly quiescent until the onset of true puberty, creating a period of relative endocrine parity.

Puberty: Divergence, KNDy Neurons, and the Secular Trend

Puberty marks the permanent divergence of male and female endocrine profiles, transforming the physiological landscape and initiating profound behavioural and morphological changes.

The Physiological Layer: The Kisspeptin Trigger and Environmental

Disruptors

The mystery of how the dormant HPG axis is reawakened at puberty has been largely solved over the past two decades with the discovery of the *KISS1* gene and its peptide product, kisspeptin. Kisspeptin is now recognized as the master gatekeeper of pubertal onset[11].

In the arcuate nucleus of the hypothalamus, specialised neurons co-express kisspeptin, neurokinin B, and dynorphin (collectively termed KNDy neurons). Neurokinin B facilitates the synchronized firing of these neurons, while dynorphin A inhibits them, creating a pulsatile rhythm[13]. When this neural pulse generator activates, kisspeptin is released and binds to the GPR54 (KISS1R) receptor on Gonadotropin-Releasing Hormone (GnRH) neurons, triggering the pulsatile release of GnRH and initiating the cascade of puberty[11]. The sensitivity of the gonadotropic system to kisspeptin is extraordinarily high; loss-of-function mutations in *KISS1* or *GPR54* result in profound hypogonadotropic hypogonadism, permanently stalling puberty, while activating mutations cause precocious puberty[12].

Currently, there is a heavily debated secular trend of earlier pubertal onset, particularly regarding thelarche (breast budding) in girls, which has dropped from an average age of 16-17 a century ago to under 13 today[15]. While increased childhood adiposity—which increases peripheral aromatisation of androgens to oestrogens and elevates leptin levels—is acknowledged as a primary driver, significant attention is being paid to Endocrine-Disrupting Chemicals (EDCs)[16].

Systematic reviews highlight that synthetic chemicals such as Bisphenol A (BPA), phthalates, perfluoroalkyl substances (PFAS), and certain phenols (e.g., 2,5-dichlorophenol) can act as xenoestrogens or anti-androgens[15]. Evidence suggests that higher exposure to specific phenols correlates with earlier menarche in girls (hazard ratio of 1.10; 95% CI: 1.01-1.19)[15]. However, meta-analyses point out that these findings are highly heterogeneous, dependent on the timing of exposure (prenatal versus postnatal), and sometimes yield contradictory results. Critics of the EDC hypothesis note the lack of replication in boys, where EDCs like phthalates have been tentatively but inconsistently linked to delayed pubarche[19]. An expert panel reviewing American pubertal data from boys concluded that data were insufficient to confirm a secular trend toward earlier male puberty[20]. Thus, the exact contribution of EDCs relative to obesity remains an open and highly contested question.

The Behavioural Layer: Meta-Analyses and the Gender Similarities Hypothesis

The hormonal deluge of puberty drives sexually dimorphic behaviour, but the extent of this divergence is frequently exaggerated in popular culture. To separate signal from noise, rigorous psychological science relies on meta-analyses and the calculation of effect sizes, typically measured by Cohen's d (where $d \leq 0.2$ is small, 0.5 is medium, and ≥ 0.8 is large). When evaluating effect sizes, it is vital to distinguish between averages and individuals; even a medium effect size implies massive overlap between the male and female distributions, rendering individual prediction impossible.

In 2005, Janet Shibley Hyde published a landmark paper in the *American Psychologist* titled

"The Gender Similarities Hypothesis." Reviewing 46 major meta-analyses comprising hundreds of studies, Hyde demonstrated that 78% of reported psychological sex differences had effect sizes in the close-to-zero ($d \leq 0.10$) or small ($0.11 < d < 0.35$) range[21]. Cognitive abilities, communication styles, and leadership effectiveness showed near-total overlap between the sexes.

However, this hypothesis has prominent critics. Evolutionary psychologists, such as Archer (2004) and Davies & Shackelford, argue that Hyde's methodology obscures large, biologically driven differences in specific domains related to sexual selection and reproductive competition[24]. Two domains stand out robustly in the literature as exceptions to the Gender Similarities Hypothesis:

Psychological /Cognitive Domain	Representative Meta-Analysis	Sample Size (N)	Effect Size (d)	Interpretation of Distributions
General Intelligence / Math	Hyde et al. (1990)	> 3,000,000	$\leq$	Near-total overlap; functionally identical averages.
Verbal Ability	Hyde & Linn (1988)	> 1,400,000	0.11	Near-total overlap; slight female advantage.
3D Mental Rotation	Voyer et al. (1995)	> 10,000	0.94	Significant divergence post-puberty; robust male advantage[26].
Direct Physical Aggression	Archer (2004)	9,760	$0.60 -$	Moderate to large divergence peaking in young adulthood[27].

The sex difference in 3D mental rotation (e.g., the Vandenberg Mental Rotation Test) is large and highly replicable, emerging post-puberty and heavily influenced by organisational

androgen exposure[26]. Similarly, Archer's comprehensive meta-analysis demonstrated that men engage in significantly more direct physical aggression than women, a difference that peaks between the ages of 20 and 30, coinciding with peak testosterone and reproductive competition[25].

The Cultural Layer: Scaffolding Biological Divergence

Culture invariably acts upon the divergence of puberty. Because boys gain substantial upper-body muscle mass under the influence of testosterone, and girls undergo fat redistribution and menarche under the influence of oestradiol, cultures universally construct gender roles around these emerging physical realities. While physiological aggression differences exist, cultures can either tightly constrain male violence through strict legal and social sanctions or channel it into socially acceptable avenues such as competitive sports or militarization[24]. The cultural layer dictates the acceptable expression of the underlying physiological hardware.

The Reproductive Years: Cyclical Hormones, Sleep, and Stress

During the reproductive years, the endocrine milieu of men and women stabilises into distinct patterns: a relatively steady state of testosterone in men (subject to diurnal rhythms) and a 28-day cyclical fluctuation of oestradiol and progesterone in women.

The Physiological Layer: The Estrobolome and Hippocampal Plasticity

The female brain is highly sensitive to the cyclical fluctuations of the menstrual cycle. Precision neuroimaging studies utilizing dense longitudinal sampling have revealed that endogenous oestradiol and estrone concentrations significantly correlate with changes in bilateral hippocampal volume. Sacher et al. (2023, *npj Women's Health*) demonstrated that in the high-oestradiol pre-ovulatory phase, women show increased hippocampal grey matter volume and enhanced structural neuroplasticity[30]. Behaviourally, this translates into measurable fluctuations in cognition; for instance, women in their high-oestradiol phase demonstrate more rapid category learning and exception processing than during low-oestradiol phases, driven by oestradiol's impact on pattern separation pathways in the hippocampus[31].

This systemic hormonal regulation is intricately linked to the gut microbiome through the "estrobolome"—the collection of enteric microbial genes encoding enzymes like β-glucuronidase and sulfatase. When the liver conjugates oestrogens to render them biologically inactive for biliary excretion, the estrobolome deconjugates them in the gut[33]. This allows free, active oestrogens to be reabsorbed into the enterohepatic circulation. Dysbiosis in the gut microbiome can alter this reabsorption rate, leading to systemic oestrogen dominance or deficiency. This continuous homeostatic equilibrium within the gut-vagina axis has profound downstream effects on female reproductive diseases, including endometriosis, and potentially influences the risk of hormone-receptor-positive breast cancers[34].

Furthermore, the widespread use of oral contraceptives (OCs) introduces exogenous synthetic hormones that alter both brain structure and behaviour. Systematic reviews by Pletzer et al.

(2019) indicate that OCs abolish the natural cyclical changes in brain morphology. Crucially, the effects depend on the specific formulation: anti-androgenic progestins are associated with larger grey matter volumes in the hippocampus and fusiform face area compared to androgenic progestins[36].

Sleep Architecture and the Menstrual Cycle

Sleep architecture demonstrates notable physiological sex differences during the reproductive years. Women generally experience longer total sleep time, shorter REM sleep duration, and a higher proportion of slow-wave sleep (SWS) and spindle density than men[38]. Progesterone, which peaks during the luteal phase of the menstrual cycle, acts as a respiratory stimulant and promotes SWS[38].

However, women consistently report significantly poorer subjective sleep quality and suffer from higher rates of insomnia than men[38]. This paradox is partially explained by female neurobiology maintaining a lower arousal threshold during non-REM sleep[38]. This lower threshold is likely an evolutionary adaptation related to infant monitoring, making women more susceptible to environmental disturbances and leading to fragmented sleep architecture.

Interestingly, when transgender men (assigned female at birth) undergo gender-affirming testosterone therapy, their sleep architecture shifts within three months to match cisgender male patterns, including decreased SWS and increased REM sleep duration, confirming the direct modulatory role of androgens on sleep[39].

The Behavioural Layer: Stress Responses and the Dual-Hormone Hypothesis

The interaction between the Hypothalamic-Pituitary-Adrenal (HPA) axis (stress) and the HPG axis (reproduction) yields significant sex differences. A highly cited consensus review by Kudielka and Kirschbaum (2005, *Biological Psychology*) examined responses to the Trier Social Stress Test (TSST), a standardized psychosocial stressor involving public speaking and mental arithmetic[41].

They found a robust, replicable effect: men exhibit a significantly higher physiological cortisol output (measured via salivary assay) in response to acute psychosocial stress than women[41]. Paradoxically, women consistently report higher *subjective* feelings of stress, anxiety, and distress in response to the exact same stimuli[41].

In men, the behavioural output of testosterone is heavily moderated by the HPA axis, a concept known as the Dual-Hormone Hypothesis. Meta-analyses indicate that baseline testosterone only predicts status-seeking, dominance, and risk-taking behaviours when cortisol levels are low. When cortisol is high (indicating acute stress or social defeat), the association between testosterone and dominance behaviour is abolished or reversed[44]. This interaction ensures that aggressive or status-seeking behaviour is suppressed during times of systemic threat, optimizing survival.

The Cultural Layer: Navigating Cyclical Realities

Culturally, the female menstrual cycle has historically been medicalised or stigmatised. However, separating the physiological reality of cyclical emotional fluctuations from cultural expectations is difficult. While Premenstrual Syndrome (PMS) has a definitive physiological

basis—linked to the rapid drop in progesterone and its neuroactive metabolites like allopregnanolone—cultural narratives often exaggerate the extent to which hormonal cycles impair female rationality. Cognitive testing demonstrates preserved executive function across the cycle[31], proving that cultural assumptions often outpace physiological facts.

Pair-Bonding and Conflict: Oxytocin, Vasopressin, and Testosterone

Living together requires the continuous navigation of trust, resource allocation, and conflict. The neuroendocrine regulation of these social dynamics involves a delicate interplay of oxytocin, vasopressin, and testosterone.

Oxytocin: Initial Attachment and Parochial Altruism

During the initial stages of romantic attachment, partnered individuals display significantly higher levels of circulating oxytocin compared to single individuals, facilitating early pair-bond formation[45]. In the context of established romantic couples, oxytocin buffers the HPA axis against social stress. Ditzen et al. (2009, *Biological Psychiatry*) utilised a conflict-discussion paradigm with 47 couples. They found that intranasal oxytocin administered prior to a marital conflict significantly increased positive communication behaviours (e.g., eye contact, self-disclosure) and lowered salivary cortisol levels compared to a placebo, effectively facilitating conflict resolution[47].

However, oxytocin is frequently misrepresented in popular culture as a simple "cuddle hormone." The physiological reality is far more nuanced. Oxytocin facilitates social bonding and trust, but it does so selectively. In a seminal study by De Dreu et al. (2010, *Science*), 480 male participants engaged in intergroup economic games (the Intergroup Attacker-Defender Contest) after receiving intranasal oxytocin[49]. The researchers found that oxytocin significantly increased "parochial altruism"—it enhanced cooperation and defensive protection of in-group members, while simultaneously increasing preemptive, coordinated aggression against perceived out-groups[50]. Oxytocin does not promote universal love; it promotes tribal cohesion.

Vasopressin: The Genetics of Marital Instability

Arginine vasopressin, a closely related neuropeptide, plays a critical role in male pair-bonding and mate guarding. Walum et al. (2008, *PNAS*) investigated the *AVPR1A* gene in 552 Swedish twin pairs and their spouses. They found that a specific genetic variant in the promoter region, the RS3 334 allele, was highly predictive of marital instability[52].

Men homozygous for the 334 allele were twice as likely to report a recent marital crisis or threat of divorce compared to non-carriers (34% vs 15%), and their wives reported significantly lower marital satisfaction[53]. While statistically significant, the effect size was modest ($d = 0.27$ to 0.38)[53]. This reinforces the principle that while genetics and endocrinology provide a probabilistic nudge toward certain attachment styles, they do not dictate individual destiny.

Testosterone: Debunking the Empathy Deficit

A highly publicised claim in the early 2010s was that testosterone actively destroys human

empathy. This originated from a study by van Honk et al. (2011, *PNAS*), which administered exogenous testosterone to 16 women and reported a significant impairment in their ability to read emotions via the "Reading the Mind in the Eyes Test" (RMET)[54].

However, this represents a prime example of why replication and sample sizes matter in behavioural endocrinology. Subsequent studies by Nadler et al. (2019) utilising sample sizes 15 to 25 times larger (N > 400) definitively failed to replicate van Honk's findings. In rigorous, preregistered, double-blind, placebo-controlled trials on men, exogenous testosterone administration had *no* significant effect on cognitive empathy[55]. The scientific consensus has shifted: while baseline testosterone correlates weakly with status-seeking, the claim that testosterone acts as a direct, acute inhibitor of human empathy is entirely unsupported by properly powered modern literature[55].

Parenthood: The Neuroplasticity of Mothers and Fathers

The transition to parenthood constitutes one of the most profound periods of adult neuroplasticity and endocrine alteration in the human life course, fundamentally rewiring both men and women to prioritise offspring survival.

The Physiological Layer: Maternal Brain Remodelling and Postpartum Depression

Pregnancy exposes the female brain to unprecedented surges in sex steroids. Progesterone levels increase 10- to 15-fold, and a woman experiences more oestrogen exposure during a single pregnancy than throughout her entire non-pregnant life[56].

In a groundbreaking prospective study, Hoekzema et al. (2017, *Nature Neuroscience*) used MRI to scan the brains of first-time mothers (N=25) before conception and postpartum, comparing them to fathers, nulliparous women, and childless men[56]. The results were dramatic and robustly replicated. Pregnancy induced highly consistent reductions in grey matter volume specifically within the default mode network (DMN)—regions subserving social cognition and "Theory of Mind" (e.g., the precuneus, anterior and posterior midline, and bilateral temporal cortex)[56]. This volume reduction is not a loss of function, but rather a targeted synaptic pruning and maturation process that fine-tunes the brain for maternal attachment, akin to the pruning seen during adolescent puberty. The degree of grey matter reduction highly predicted the mother's postnatal attachment to her infant, and these changes persisted for at least two to six years postpartum[56].

In a subset of women, the rapid withdrawal of these neuroactive steroids at birth triggers Postpartum Depression (PPD). In a major pharmacological breakthrough, Deligiannidis et al. (2023, *JAMA Psychiatry*) published a Phase 3, double-blind, randomized controlled trial (the SKYLARK study, N=150) on zuranolone, an oral neuroactive steroid and positive allosteric modulator of the $GABA_A$ receptor[61]. Zuranolone directly targets the neural networks dysregulated by the postpartum crash of allopregnanolone. The trial demonstrated a rapid, significant reduction in depressive symptoms by day 15 (HAM-D score difference of -4.2;

$d = 0.56$), leading to its FDA approval as the first rapid-acting oral treatment for PPD, replacing standard SSRIs which take weeks to take effect[62].

The Physiological Layer: The Endocrine Preparation of Fathers

Fathers do not experience pregnancy, but their endocrine systems undergo highly reliable, evolutionarily conserved shifts upon cohabitation and active parenting. In a landmark longitudinal study (N=683) in the Philippines, Gettler et al. (2011, *PNAS*) tracked men transitioning from single, non-fathers to partnered fathers over 4.5 years. The study definitively proved that while high baseline testosterone predicts initial mating success, the transition to active, involved fatherhood causes a precipitous, statistically massive drop in waking and evening testosterone[65].

Furthermore, fathers show elevated levels of oxytocin and prolactin compared to non-fathers. Functional neuroimaging reveals that fathers who engage in heavy direct childcare exhibit increased neural activation in the ventral tegmental area (VTA) and the temporoparietal junction (TPJ) when viewing their children, mirroring the maternal caregiving network[65].

Culturally, societies that encourage active paternal involvement facilitate these endocrine shifts. The Gettler study highlights that testosterone drops most significantly in men who spend more than three hours a day in direct childcare[66]. Therefore, cultural mandates regarding paternity leave directly influence the physiological pair-bonding and caregiving capacity of fathers.

Convergence: Menopause, Andropause, and Later Life

As the reproductive years wane, the distinct male and female endocrine trajectories undergo a gradual convergence, though the physiological mechanisms of decline differ fundamentally between the sexes.

The Physiological Layer: Menopause, VMS, and the Timing Hypothesis

Menopause is characterized by the total depletion of ovarian follicles and a precipitous crash in circulating oestradiol. Deprived of oestrogen's inhibitory negative feedback, the KNDy neurons in the hypothalamus undergo massive hypertrophy and become radically overactive[69]. This hypersensitizes the brain's thermoregulatory center in the median preoptic nucleus, triggering the sudden, inappropriate heat-dissipation responses known as Vasomotor Symptoms (VMS), or hot flashes[71]. VMS affect up to 80% of women, persisting for a median of 7.4 years, and cause severe disruptions to sleep architecture, exacerbating age-related cognitive fatigue and depression[70].

A major breakthrough in treating VMS without exogenous hormones is fezolinetant, an oral neurokinin-3 receptor (NK3R) antagonist. By blocking the neurokinin B signals that overstimulate KNDy neurons, fezolinetant restores hypothalamic homeostasis. Phase 2b and 3 trials (e.g., VESTA and SKYLIGHT) have shown it significantly reduces the frequency (by up to 93%) and severity of hot flashes within days, providing a vital alternative for women with contraindications to Hormone Replacement Therapy (HRT)[72].

For women utilizing HRT, the medical consensus is defined by the "timing hypothesis." The Early versus Late Intervention Trial with Estradiol (ELITE), published by Hodis et al. (2016, *NEJM*;

N=643), settled a decade of controversy sparked by the earlier Women's Health Initiative (WHI)[76].

Trial Name	Sample Demographics	Timing of HRT Initiation	Primary Cardiovascular Outcome	Interpretation
WHI (2002)	Average age > 60[77]	Late (>10 years post-menopause)	Increased risk of stroke / cardiac events	Estrogen on established atherosclerotic plaques is pro-thrombotic[78].
ELITE (2016)	Stratified by age / time since menopause	Early (< 6 years post-menopause)	Significantly slower progression of atherosclerosis (carotid intima-media thickness)[79]	Estrogen protects healthy endothelium; the "critical window" is early menopause[78].
ELITE (2016)	Stratified by age / time since menopause	Late (> 10 years post-menopause)	No cardiovascular benefit; identical to placebo[76]	Confirms WHI; late initiation misses the therapeutic window[80].

The ELITE trial definitively proved that initiating HRT *early* provides cardiovascular and neuroprotective benefits, while late initiation poses risks[76].

The Physiological Layer: Andropause and the EMAS Criteria

Unlike the sudden ovarian failure in women, men experience a slow, steady decline in testosterone production of roughly 1% per year after age 30, due to declining Leydig cell function. The concept of "andropause" or late-onset hypogonadism (LOH) is frequently exaggerated by commercial clinics.

The European Male Ageing Study (EMAS), published by Wu et al. (2010, *NEJM*; N=3369), established strict criteria for LOH, requiring both physiologically low serum testosterone (<300 ng/dL) and the presence of three specific sexual symptoms (erectile dysfunction, loss of morning erections, and low libido)[83]. Using these strict criteria, true LOH affects only 2.1% of men in their 40s to 70s[83]. The fatigue and low mood commonly attributed to "low T" in older men are more frequently the result of obesity, visceral fat accumulation, and general

cardiovascular decline[83].

The Behavioural and Cultural Layers: Post-Reproductive Convergence

In later life, the behavioural and cultural profiles of men and women converge. As testosterone slowly declines in men and oestrogen vanishes in women, the stark behavioural dimorphism driven by reproductive competition softens. Culturally, postmenopausal women in many societies gain status and authority, moving out from under the restrictive norms of peak reproductive age. Relationships between older couples often transition from intense romantic and competitive dynamics into deeply companionate, egalitarian bonds, supported by stable oxytocinergic networks and a lifetime of shared neurocognitive attunement.

Summary of Robust Findings

1. Infants experience a transient 3-to-6-month activation of the HPG axis ("mini-puberty"), producing pubertal-level testosterone in boys and fluctuating oestradiol in girls, though postnatal behavioural impacts remain unproven.
2. The onset of true puberty is uniformly driven by the activation of hypothalamic KNDy neurons, which release kisspeptin to stimulate GnRH pulsatility.
3. Across 46 meta-analyses, 78% of psychological sex differences show small or near-zero effect sizes, proving men and women are overwhelmingly more alike than different on average.
4. Two domains show robust, large sex differences contrary to the gender similarities hypothesis: 3D mental rotation (favouring males, $d = 0.94$) and direct physical aggression (favouring males, peaking in the 20s).
5. Men exhibit higher physiological cortisol responses to acute psychosocial stress (e.g., TSST), while women consistently report higher subjective psychological distress.
6. Pregnancy induces massive, permanent structural pruning in the female brain's Theory of Mind networks, optimizing neural circuitry for infant attachment.
7. Transitioning to active, involved fatherhood causes a precipitous, long-term decline in male waking testosterone and an increase in oxytocin, preparing the male brain for caregiving.
8. Oxytocin promotes in-group trust, bonding, and conflict de-escalation, but it actively drives parochial altruism and coordinated out-group defensive aggression.
9. The claim that exogenous testosterone acutely impairs cognitive empathy has been definitively debunked by large-scale, pre-registered replication failures.
10. Hormone Replacement Therapy provides neuroprotective and cardiovascular benefits if initiated within 6 years of menopause (the ELITE timing hypothesis), while non-hormonal NK3R antagonists (fezolinetant) are now proven to safely halt vasomotor symptoms.

Contested or Open Questions

1. **Endocrine-Disrupting Chemicals (EDCs):** Do environmental chemicals (phthalates, BPA) play a major causal role in the secular trend of earlier female puberty, or is childhood obesity and peripheral aromatisation the overwhelming primary driver?
2. **The Estrobolome and Pathology:** To what exact degree do gut microbiome dysbiosis

and the resulting altered reabsorption of free oestrogens directly cause endometriosis and hormone-receptor-positive breast cancers?

3. **Postnatal vs. Prenatal Androgens:** Does the testosterone surge during male "mini-puberty" permanently organize brain architecture for later sex-typical behaviour, or is behavioural dimorphism almost entirely programmed prenatally?
4. **Oral Contraceptives and the Brain:** Do the structural brain changes induced by androgenic versus anti-androgenic oral contraceptives have lasting functional consequences on female mood, stress resilience, and mate preference after discontinuation?
5. **Female Status Seeking:** What is the precise role of oestradiol, relative to testosterone, in driving female status-seeking and competitive behaviour, and does the "dual-hormone hypothesis" (testosterone interacting with cortisol) apply similarly across both sexes?

Most Important Sources to Read in Full

Author & Year	Publication	Title & Significance
Hyde, J. S. (2005)	*American Psychologist*	*The gender similarities hypothesis.* The foundational meta-analytic proof that men and women are cognitively and psychologically vastly more similar than different.
Archer, J. (2004)	*Review of General Psychology*	*Sex differences in aggression in real-world settings: A meta-analytic review.* Provides the definitive evolutionary counter-balance to Hyde, detailing physical divergence.
Hoekzema, E., et al. (2017)	*Nature Neuroscience*	*Pregnancy leads to long-lasting changes in human brain structure.* The groundbreaking MRI study proving how motherhood physically rewires social cognition networks.

Gettler, L. T., et al. (2011)	*PNAS*	*Longitudinal evidence that fatherhood decreases testosterone in human males.* The definitive proof of male biological adaptability to caregiving.
Hodis, H. N., et al. (2016)	*New England Journal of Medicine*	*Vascular Effects of Early versus Late Postmenopausal Treatment with Estradiol.* The ELITE trial that proved the "timing hypothesis" for HRT.
De Dreu, C. K. W., et al. (2010)	*Science*	*The neuropeptide oxytocin regulates parochial altruism in intergroup conflict among humans.* Critically nuances the "cuddle hormone" myth.
Wu, F. C., et al. (2010)	*New England Journal of Medicine*	*Identification of late-onset hypogonadism in middle-aged and elderly men.* The EMAS study defining the true, rare nature of clinical andropause.
Kudielka, B. M., & Kirschbaum, C. (2005)	*Biological Psychology*	*Sex differences in HPA axis responses to stress: a review.* The benchmark review on how men and women process physiological versus psychological stress.

Implications for Living Together

When applying endocrine science to the structuring of families, workplaces, and societies, we

must strictly avoid the naturalistic fallacy: the erroneous belief that what is biologically "natural" is therefore morally "good" or socially mandated. Human biology provides a set of predispositions, not a straitjacket.

For couples and families, understanding the physiological transitions of parenthood should breed profound mutual empathy. A mother's brain undergoes intense, involuntary structural pruning to prioritise infant survival, making her highly sensitive to social threats. Simultaneously, a father's biology is entirely capable of shifting away from competition and toward nurturing caregiving, provided the culture and his partner allow him to spend time in direct childcare, which actively lowers his testosterone. Recognizing these shifts allows couples to view postpartum friction as an expected endocrine adaptation rather than a personal failing.

In the workplace and broader society, Hyde's Gender Similarities Hypothesis should be the guiding operational principle. Because the psychological distributions of men and women overlap almost entirely, any policy or organizational structure that restricts roles based on biological sex relies on statistically flawed assumptions. However, recognizing the physiological reality of the menstrual cycle, the sleep disruptions of menopause, and the neurocognitive burden of early motherhood is not sexism; it is biological realism. Accommodating these physiological truths—through flexible working arrangements, adequate medical leave for postpartum depression, and menopause support—does not hinder female competence. Rather, it optimizes the environment so that the overwhelming cognitive equality between the sexes can be fully realized. Men and women live together best when they acknowledge the profound physiological journeys their bodies undertake, while refusing to let those journeys dictate the limits of their individual potential.

Works cited

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