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The Aporetic Dialogues of Modena on Gender Differences: Is It All About Testosterone? Episode IV: Love

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ABSTRACT

This is the fourth and last episode of a series of four discussions on the differences between males and females in apparently non-andrological fields. You will read the transcript of discussions that actually took place at the Endocrinology Unit in Modena, Italy, in the form of the aporetic dialogues of ancient Greece. In this episode, the role of testosterone in gender differences in approaches to love will be explored. The discussants were divided into two groups: Group 1, which supports the thesis of a predominant role of testosterone, and Group 2, which opposes it. The first group argued that endogenous testosterone could shape approaches to love, regardless of psychological predispositions or sociocultural context. The second group highlighted the multifactorial nature of love, pointing to other hormonal and non-hormonal influences, such as neurotransmitters, cortisol, and sociological and psychological factors. In the end, an expert professor of endocrinology, acting as a referee, sought to resolve the aporia: Are the two theories equivalent, or is one superior?

1 | Introduction

This is the fourth article in a series dedicated to exploring the role of testosterone in determining gender differences in various fields. In the previous articles, we explored the role of testosterone in determining different attitudes in males compared with females in crime [1], empathy [2], and mathematics [3]. This episode will address the discussion of whether testosterone plays a role in determining different male and female behaviors in lovemaking, considering different—though not all—aspects of love, from falling in love to betrayal.

2 | Methodology

The discussion was carried out according to the scheme of the Socratic aporetic dialogue: The question of the definition or explanation of a phenomenon is posed and then discussed, without necessarily reaching a truth. Aporetic dialogues typically end in aporia, a state of puzzlement by way of the equality of opposite reasonings. The discussants could discover that the opposing reasons only apparently balance each other and therefore identify the most promising theory, or that the two theses are equivalent, so the investigation must take a new turn or stop.

Francesca Paglia (F.P.) introduced the topic, defining which aspects of love can be scientifically investigated and introducing evidence in support of gender differences in the way of loving.

The discussants were subdivided into two groups: Group 1 in favor of a prominent role of testosterone in determining such gender difference, and Group 2, which claimed that factors other than testosterone were responsible. The dialogue took place as a seminar event open to public.

Carmela Perri (C.P.) and Valentina Griseta (V.G.) tried to demonstrate that the evident gender differences in this context are due only to the effect of testosterone (Group 1). On the other hand, Daniele Renda Livraghi (D.R.L.) and Leonardo Dalla Valentina (L.D.V.) attempted to dismantle their thesis and to demonstrate that other hormonal, social, cultural, and anthropological factors also come into play (Group 2).

Cesare Carani (C.C.), full professor in endocrinology with particular interest in andrology and sexual behavior, had the role of commenting on the data, functioning as a referee and, in the end, deciding whether one of the two theories was successful or whether the two were equivalent.

The discussion was also open to questions or comments from the audience made up of endocrinologists and residents, biologists, biotechnologists from the Endocrinology Unit of Modena and residents from the school of Psychiatry (audience).

The organization of the dialogue and the collection of the data presented was managed and supervised by Giulia Brigante (G.B.), based on an idea by Manuela Simoni (M.S.).

No patient or participant consent was required for this study. No Clinical Study Registration Number was required for this study.

3 | The Aporetic Dialogue

F.P.: Before starting the debate, it is necessary to define the boundaries of the battlefield. The topic of Love is extremely broad, and we risk losing focus on what we want to explore.

There are numerous definitions of Love. The Treccani encyclopedia defines it as "the desire to bring good to the object of love and to seek its company" [4]. Shakespeare's dramatic definition uses the oxymoron: "It is a pleasure that displeases; it is a displeasure that pleases." ChatGPT provides a rather nebulous and vague definition, preferring the use of synonyms such as "affection, respect, concern, and desire." Finally, the team of psychologists who wrote the article "Love Is Not an Emotion" [5] precisely argues that love is not a feeling but rather a physiological impulse whose lack causes a clinical situation called Love Withdrawal Syndrome. Moving on to semantics, the ancient Greeks used eight different words to describe love: Eros (sexual passion); Philia (deep friendship); Ludus (playful love); Agape (altruistic love); Pragma (realistic love); Philautia (self-love); Storge (friendship-based love); and Mania (obsessive love). We will focus on romantic love and the types of love that refer to Greek definitions.

Having clarified the meaning of what we will discuss, the spontaneous question arises: Why love each other if reproducing is enough to maintain the species? Various anthropological studies on evolution suggest that love arises from necessity, as an adaptive response to isolation, anxiety, and stress caused by negative social interactions such as fights or food competition [6, 7]. The coping mechanism in response resides precisely in positive social interactions, which are then reinforced by social rewards with a reduction in anxiety.

What we call "attachment" may have arisen from physiological solutions to simplify survival and reproduction-related problems. Therefore, love is an innate feeling, regulated by a complex neurohormonal system [8].

From a scientific point of view, love can be divided into three temporally consequential phases: (1) desire, (2) attraction, and (3) attachment [9].

The first step, desire, is described as a craving for sexual gratification, characterized by increased energy and focused attention on a mating partner. This phase is characterized by sensations of excitement, desire for emotional union with the potential partner. The second is the attraction phase, which appears to be independent of bonding and sexual intercourse. The hypothesis is that attraction is a basic emotion that shares some neurobiological substrates with fear and anxiety, an altered mental state with intrusive thoughts about the partner [10]. This seems to have an evolutionary purpose: to push the individual to become more impulsive, to overcome fear and neophobia, and to willingly accept being close to a stranger. Finally, attachment keeps two individuals together for a long period.

Now the question is: do human males and females act differently in this complex process called love? In the book *Anatomy of Love*, Helen Fisher addresses various aspects of love, highlighting how there are evident gender differences in behavior during the initial stages of courtship and how analogies can be found within the animal kingdom [11]. Indeed, her studies reveal a universal model of flirting, particularly by the female gender. The movement sequences of potential partners were studied through video recordings, then analyzed by anthropologists and behavioral psychologists. Women flirt with the same sequence of expressions in the jungles of the Amazon, in the salons of Paris, as well as in the lands of New Guinea. In the first phase—the distance approach—the woman smiles, raises her eyebrows, and widens her eyes to gaze intently. She tilts her head down and to the side. These sequential flirtatious gestures are so distinctive that some anthropologists are convinced they are innate, an artifact of human female courtship that evolved centuries ago to signal sexual and/or romantic interest.

Some of these movements can be found in animals as well: Female opossum shakes their head to attract attention; albatrosses shake their heads and snap their beaks; turtles extend and retract their heads. Instead, the male uses a different gesture, puffing out the chest, mainly aimed at appearing bigger and standing tall with pride. Among animals, codfish flare out their fins; snakes, frogs, and toads inflate their bodies; and cats and pigeons fluff up.

The second flirting phase is the one called grooming talk. In animals, grooming refers to the act of cleaning or combing the fur of another individual, breaking the barrier of physical contact. The analogies with human behavior are, for example, leaning forward, resting an arm toward the other, and moving one's foot closer. It has been observed that it is usually the woman who initiates touch first, lightly brushing her hand against her suitor's body in the most informal but calculated possible way. The third and last flirting phase is characterized by the synchronized movement of the two individuals. Over time, potential lovers seem to move

until their shoulders are aligned and their bodies face each other. They move in a coordinated manner; when he lifts his glass, she lifts hers while looking deeply into each other's eyes. In this last part, there do not seem to be gender differences [11].

After these initial courtship stages, do men and women love differently? In an old but interesting study, strong gender differences were found analyzing the results of a questionnaire administered to 800 students from the University of Miami [12]: Males are more erotic and ludic, whereas females more pragmatic, storgic, and manic in their attitudes toward love.

However, analyzing love with mathematical–statistical models is really complicated, as it is a very complex phenomenon. Although aware of the questionability of the choice, we have tried to bring out a possible gender difference by studying some indirect social indicators of the way of loving of Italian males and females [13]. In 2019, nearly 40% of women reported having had only one sexual partner in their lifetime, compared with 22% of men. This gender gap remains similar up to six partners. Beyond that threshold, men clearly outnumber women: Overall, 25% of men versus 9% of women reported having had more than 10 sexual partners. Considering the Italian Pornhub audience, 30% of women use the site, compared with 71% of men. The trend remains similar in Spain, France, and Germany. Data regarding the percentage of young adults who distinguish love and sex show a narrowing of the gender gap over time, with more and more women believing that sex can be separated from love. Currently, about 80% of men and 77% of women believe that love and sex can be separated. Finally, in response to the question "How important is romance in a relationship to you?", most men stated that romance is essential and that they cannot feel love without romance, surpassing women. For women, romance appears to gain importance as the relationship develops; only 7% of men considered it unimportant, compared with 11% of women.

M.S.: How has love changed in the age of social media, where physical contact—and thus the second phase of courtship—is somehow avoided?

F.P.: Indeed, although online dating sites increase the chances of finding a partner, it has been observed that the frequency of first dates often increases [14]. Maybe because there is a greater variety of choices, and thus competition for a partner is much less perceived.

M.S.: Do animals experience love?

F.P.: First, it is necessary to define what we mean by love in the animal world. If we mean having a single partner and a long-term relationship, a distinction must be made between sexual monogamy and social monogamy. If we consider love as social monogamy, staying together lifelong and caring for offspring, yes, it exists in animals. However, this does not necessarily correspond to sexual monogamy, as even in species of mice that are considered monogamous, the partners may have sexual relations with other individuals [15].

C.P. (Group 1): I hope Francesca has convinced you that men and women love differently. I am in the team that supports a main role of the testosterone in inducing this difference.

I want to start citing a study on 65 young men, aged between 19 and 21 years [16]. They were asked to fill in a questionnaire about their way of loving. This is a paper-and-pencil questionnaire that assesses attitudes toward love, merging perceptions of one's current, recent, or hypothetical partner with general attitudes about love [17]. Participants respond to each statement with true or false answers, providing categorical data. Then the percentage of true responses is calculated and correlated with biological parameters. Respondents must be instructed to consider their current partner when answering; if they do not have one, they should reflect on their most recent partner. For those who have never experienced love, the guidelines suggest they answer based on their beliefs about what would be true. After completing the questionnaire, the enrolled men were divided into six subgroups based on their love attitudes: romantic love (Eros); playful love (Ludus), which does not involve emotional engagement; practical love (Pragma); love that slowly grows out of friendship (Storge), which therefore lacks passionate foundations; altruistic love (Agape), based on the concept of self-sacrifice for the other and mutual help; and obsessive love (Mania). Participants were also tested for plasma testosterone levels, their prenatal testosterone exposure and their androgen receptor sensitivity. Circulating testosterone was negatively correlated with romantic love and altruistic love. Lower prenatal testosterone exposure, corresponding to a higher ratio between the index and ring finger length (2D:4D digit ratio) [18], was positively correlated with romantic love. Finally, the androgen receptor was genetically analyzed, focusing on the number of CAG repeats in Exon 1 of the gene: Fewer repeats correspond to higher androgen sensitivity. They found that the number of CAG repeats, representing the sensitivity of the androgen receptor, did not correlate significantly with any of the love styles. Taking together, these results clearly indicate that as testosterone increases, the aptitude for a romantic way of experiencing love decreases.

Subsequently, I wondered in which phase of the relationship testosterone might play a prominent role. At the beginning of the relationship, the main phases of mating are male–male competition and partner attraction [19]. In a study conducted at the Harvard University, morning salivary testosterone was measured between 10:00 and 10:20 AM on 122 graduates [20]. Participants completed a questionnaire about their relationships and were divided into four groups: married with children, married without children, involved in a monogamous romantic relationship but not married, and single. The committed men (first three groups) had testosterone levels 21% lower than single men, and married men with children had testosterone levels 48% lower than singles but also 27% lower than married men without children and those in committed but unmarried relationships. There was no difference between the latter two groups, so the state of being a husband does not affect per se testosterone levels, or vice versa. Taking together, these results indicate that men in committed romantic relationships have lower testosterone levels than unpaired men. Additionally, these data suggest that the key factor is being in a relationship, rather than marital status. This is the first evidence directly supporting the idea that long-term pair bonds, and not only marriage, are important predictors of male testosterone levels. The data also support the notion that fatherhood may be linked to lower testosterone levels, although the small sample of fathers prevented meaningful conclusions.

Now I will present one of the few studies evaluating testosterone in females [21]. A questionnaire on their relationship status was administered to the enrolled subjects, determining six groups: single, with casual encounters, with more stable encounters, in monogamous relationships, cohabiting, and married. The most interesting result is that, differently from men, testosterone levels do not change as the commitment invested in the relationship increases. It is important to underline that half of the enrolled women were taking hormonal contraceptives that can reduce serum testosterone levels. Finally, all subjects provided information about their satisfaction and fulfillment within the relationship, and there was no correlation between these aspects and salivary testosterone levels.

To confirm the role of testosterone in determining a certain type of love in men, I want to show you the results of studies that analyze the possible relationship between this steroid and betrayal, the main cause of divorce in Western civilization [22]. In this study [23], 224 men between 40 and 75 years old, all involved in a stable, long-term monogamous relationship, were considered. A total of 212 were heterosexual, 2 homosexual, 8 bisexual, and 1 asexual. They were asked if they had ever cheated on their partner, and 37.5% said yes. Interestingly, higher salivary testosterone levels were observed in unfaithful men compared with faithful ones. Moreover, there was a positive correlation between salivary testosterone levels and the frequency of cheating on.

The same effect of testosterone is confirmed in another study conducted in North America [24]. The enrolled men and women were divided into four groups: single, involved in a monogamous relationship, involved in a polyamorous relationship (thus having multiple emotionally involved partners), and finally, those having a polyamorous lifestyle (multiple partners without emotional involvement). Again, men involved in monogamous relationships had significantly lower salivary testosterone levels than all the other groups. Additionally, there was a trend of increasing testosterone levels in polyamorous men even compared with singles. And here we add an interesting finding regarding women: Those involved in polyamorous relationships had higher testosterone levels.

Finally, I considered a society where polygamy is culturally accepted. In this African study, a sample of 81 men from rural villages in Senegal was considered [25]. They were divided into single, monogamously married with children, and polygamously married with children. They could have up to four wives, as imposed by the Islamic religion. Additionally, the wives were asked to evaluate the husband's commitment to family care, both for the partner and the offspring. For each participant, four salivary samples were taken over two consecutive days, in the morning and in the afternoon. Both monogamous and polygamous men exhibited higher morning salivary testosterone levels when they invested less time and effort in family care. An interesting detail is that before the age of 50, higher testosterone levels were observed in polygamous husbands compared with monogamous ones. This is consistent with what was seen in Western polyamorous subjects. However, after the age of 50, this trend is lost and even reversed. The authors speculate that this is because after the age of 50, partner choice no longer considers attraction or male–male competition, aspects where testosterone is very important, but rather socio-economic factors. The fact that testosterone levels in polygamous men become significantly lower than in monogamous men remains an open and unresolved question. Two hypotheses have been proposed: Polygamous men have lower testosterone levels because of the higher number of children, or having more partners could accelerate senescence [25].

D.R.L. (Group 2): Thank you for sharing these data, but I think that they are limited in primis by the small sample size and the measurement of salivary testosterone with unreliable methods. You did not convince me that it is all testosterone's fault. I think I have enough data to demonstrate that other substances are responsible for the different ways of loving of males compared with females.

First of all, the most common manifestations experienced by someone in love are euphoria, "butterflies in the stomach," palpitations, loss of appetite, hyperhidrosis, fixation, and the constant search for the partner. Actually, they are expressions of the activity of certain monoaminergic neurohormones operating within the central nervous system (CNS): dopamine, norepinephrine, and serotonin [26].

Let's start with dopamine. I have brought here the results of a study conducted on prairie voles (*Microtus ochrogaster*), small rodents known for being monogamous [27]. In these mammals, the establishment of a pair bond is a consequence of the mating phase. Following copulation, the partners tend to share the nest and take care of the offspring together. The bond between partners is so strong that, if one of the two partners dies, the surviving vole generally shows no interest in seeking another life companion [28]. Previous studies highlighted the presence of a dopaminergic spike in the nucleus accumbens during copulation, a key element for the pair bond of prairie voles [29]. On the basis of this evidence, the authors attempted to artificially reproduce this phenomenon. Some female voles were placed in two different scenarios: In one case, they were left in contact with a male for the 24 h necessary for copulation, with video monitoring; in the other, contact was limited to 6 h, ensuring that the two animals did not have sexual intercourse. The female vole was then placed in a multi-compartment system composed of three interconnected rooms: The female was in the central room, and the males from the previous scenarios were in the lateral rooms. In this standard model, the female seemed to express a sexual preference, seeking the male with whom copulation had occurred over the one with whom she had only shared the room. To verify the role of dopamine as the primary driver of this behavior, the female was intrathecally injected with a dopaminergic agonist and a dopaminergic antagonist before the short exposure (6 h without copulation) to one male and the long exposure (24 h with copulation) to the other male, respectively. In both cases, the female showed a preference for the non-copulating partner, supporting the importance of dopamine levels in the establishment of the pair bond [27].

The importance of dopamine also emerges from trials conducted on humans using functional magnetic resonance imaging (fMRI). Administering affective stimuli to subjects in the phase of falling in love, such as viewing photos or listening to voice recordings of their partner, elicits the activation of certain subcortical dopaminergic circuits: the right ventral tegmental area implicated in sensations of pleasure, arousal, and goal-directed behaviors;

and the caudate nucleus, a center for the integration of multiple sensory stimuli, also involved in goal-directed behavior. This suggests that love constitutes more than just a feeling: It is a primordial impulse, scarcely controllable and, like hunger and thirst, subject to the control of more ancient neural circuits [9, 30].

Let's now focus on serotonin. I want to start from a study in which 30 subjects (17 females and 13 males) in love for less than 6 months were compared with 20 subjects (10 females and 10 males) with untreated obsessive–compulsive disorder (OCD) and 20 healthy controls (10 females and 10 males) without documented organic or psychiatric comorbidities [31]. The analysis of the study population showed that the platelet serotonin transporter, a fairly reliable model of central serotonin dynamics [32, 33], was similarly reduced in both the subjects in love and the OCD subjects compared with healthy controls. However, reevaluation of the same subjects 1 year after the start of the relationship showed a leveling of this expression pattern compared with healthy controls, without gender differences [31].

In another report, Marazziti and Stahl reported the case of a 22-year-old man, an excellent academic and football player in a second-division team [34]. The young man, with a family history of OCD, exhibited obsessive–compulsive symptoms characterized by excessive attention to order and symmetry only when he fell in love. The onset of symptoms coincided with his first crush and was managed by his father, a general practitioner, with selective serotonin reuptake inhibitors (SSRIs), as recommended by guidelines [35]. Despite an improvement in psychiatric symptoms, the young man experienced sexual side effects, such as erectile dysfunction and decreased libido, which became increasingly severe and led to the end of the relationship. After a similar episode treated unsuccessfully with sertraline, the young man fell in love with another girl. Remembering the adverse sexual effects previously experienced during SSRI, he decided not to take any medication other than benzodiazepines. The result was a progressive worsening of the disorder, affecting not only his personal life but also his relationships with his partner and loved ones. The young man was eventually taken to a specialized center, where treatment with pregabalin was initiated [34]. Love shares some behavioral aspects with OCD and can, therefore, act as a trigger for the manifestation of this disorder in susceptible individuals.

An interesting study showed a gender-specific pattern of blood serotonin levels during the phase of falling in love. Women exhibit a higher basal serotoninergic tone compared with men [36], partly attributable to the stimulating effect of estrogen on biosynthetic pathways and activity of this neurotransmitter in the CNS [37, 38]. However, I must admit that the study has several limitations, including the small sample size and the analysis of peripheral serotonin levels, which do not fully reflect central dynamics.

Finally, I want to convince you that testosterone is not responsible for a more violent way of loving by citing another, not insignificant aspect. Recent evidence indicates that testosterone exerts immunomodulatory effects in the brain, regulating the stress response via the hypothalamic–pituitary–adrenal axis and modulating the expression of genes and proteins involved in neuroinflammatory processes, with potential implications for the prevention of mood disorders. Zuloaga et al. [39] demonstrated that testosterone regulates behavioral and neuroendocrine stress responses via direct actions on androgen receptors and modulation of gene and protein expression in key brain regions, which may contribute to its protective effects against mood disorders [40].

C.C. (referee): One aspect that deserves further investigation is the difference between infatuation and love. The first 6 months of a relationship indeed cause biochemical changes that subsequently disappear. The continuation of the relationship involves endorphins and catecholamines. Therefore, I invite you to study these changes in the future, also considering the changes in society, as the way young people communicate is also different.

Instead, considering the sexual sphere and the role of estrogen in modulating serotonin tone, do you have any idea of the role of serotonin in the reduction of sexual desire in women undergoing estrogen treatment?

D.R.L. (Group 2): Thank you for this question that gives me the opportunity to talk about female sexual desire, an often-overlooked aspect in women. Estrogens certainly have a modulating role in serotoninergic tone, increasing it [41]. And serotonin has a negative effect on sexual desire [42]. According to the consensus of the International Society for the Study of Women's Sexual Health (ISSWSH), the basis of hypoactive desire lies in a prevalence of inhibitory neural circuits (serotonin, endocannabinoids, prolactin, opioids) over excitatory ones (dopamine, norepinephrine, oxytocin, vasopressin). In fact, there are some drugs, other than sex steroids, that modulate these mechanisms, such as flibanserin or bupropion [43]. Returning to testosterone, let me comment on its role in female sexual desire as well. Numerous pieces of evidence in the literature support the primary influence of testosterone on sexual desire in both sexes [44]. The guidelines of major scientific societies regarding hypoactive sexual desire disorder (HSDD) in women recommend the use of testosterone off-label [45]. For example, the transdermal testosterone formulation (300 mcg) specific for HSDD was withdrawn from the market a few years ago, although the specific reason (poor marketability or lack of efficacy?) is unknown [46]. In Italy, only injectable testosterone propionate is indicated for "sexual performance difficulties, decreased desire" in its technical sheet, although the usage modalities are rather vague and do not mention the duration of such treatment [47].

Audience: As shown by D.R.L., the use of pharmacological treatments, both hormonal and non-hormonal, employed in men to improve aspects of sexuality in women has largely yielded unsuccessful results. Sildenafil and other vasoactive substances have not worked, nor has testosterone [48], with supporting data being unclear and of very weak evidence. Although testosterone administration in males guarantees a significant improvement in libido [49], it provides minor assistance in alleviating discomfort related to sexual, romantic, and emotional life in females [48]. It is therefore very difficult, especially in this field, to identify a single factor, whether a hormone or a neurotransmitter, as the cause of any gender differences. The real challenge is to recognize the quantitative impact of small changes in these substances observed in animals and presumably present in humans, as well as their gender-specific contributions to the aspects of love and sexuality illustrated so far.

C.C. (referee): I would like to draw your attention to the importance of estrogens in the male sexual sphere by describing the case of a patient followed at the Endocrinology Unit of Modena, Italy, for aromatase deficiency [50]. This rare condition is characterized by upper normal or slightly elevated androgen levels in the context of estrogen deficiency and continuous height growth due to the absence of estrogen-dependent epiphyseal growth plate fusion. The patient was initially treated with high doses of testosterone without achieving epiphyseal closure. After 6 months of estrogen therapy, bone growth completely ceased. Moreover, there were also benefits in terms of libido. A similar case involved an Argentine subject, also affected by aromatase deficiency [51], and estrogen treatment induced a drastic improvement in sexual desire. This highlights the importance of the correct balance of androgens and estrogens for male sexuality.

L.D.V. (Group 2): In this regard, I would like to present the results of a crossover study conducted on subjects with Complete Androgen Insensitivity Syndrome with 46, XY karyotype, phenotypically female, treated with high doses of testosterone or estrogens to study the effects on sexual desire [52]. The most significant improvements were observed following androgen treatment, and these improvements were lost upon switching to estrogen therapy. Among the possible hypotheses, the authors suggested either an insufficient estrogen dosage or the presence of extrareceptoral pathways through which testosterone exerts its effects.

V.G. (Group 1): Although D.R.L. brought interesting data on the undeniable role of neurotransmitters in falling in love, he did not convince me that these are responsible for the different ways of loving of the two genders. C.P. has already shown strong data supporting the role of testosterone in partner selection and cheating.

Audience: C.P. showed data demonstrating a correlation between serum testosterone levels and some aspects of love. None of these data, which were also limited by the salivary dosage of the steroid, demonstrate a causal link.

V.G. (Group 1): Yes, it is true. In fact, I will add some more data from studies on the effect of exogenous testosterone on the way of loving.

In a study, the authors treated heterosexual men with testosterone gel or a placebo in a double-blind manner [53]. Three hours after administration, corresponding to the testosterone serum peak, they were shown a series of images of naked women taken from the web. Initially, the images were blurred, and the men were asked to choose whether to wait a few seconds and then view the clear image for 3 s or to view it immediately but only for 1 s. The subjects who chose to wait were mainly in the placebo group. This study indicates not only higher sexual desire in subjects with higher testosterone, which would be almost obvious, but also greater impulsivity. In this case, the cause–effect relationship becomes evident because it is not viewing a sexual image that increases testosterone, but the externally given testosterone seems to cause greater impulsivity.

I will show the results from another study on heterosexual men treated with testosterone or placebo in a double-blind manner [54]. Three hours after administration of 150 mg of AndroGel topical gel, they were asked to choose the face they preferred for a short-term relationship between two female faces, very similar to each other, one more feminine and one more masculinized. Subsequently, there was a second experiment with the same underlying mechanism: They had to choose between two images, one more feminine and the other more masculinized, but this time selecting the one they preferred for a long-term relationship. The group treated with testosterone chose far fewer feminine faces for long-term relationships. This difference was not confirmed in the placebo group. The authors attribute this to the acute rise in testosterone that makes men more interested in short-term relationships than in long-term ones, so that women's characteristics in this context could be less important for them. This seems to suggest a role for testosterone in regulating not only infatuation but also planning for love relationships.

Now I hope I have convinced you that there is a causal link between increased testosterone and love choices, at least in men. Let's move on to a model of female hyperandrogenism: polycystic ovary syndrome (PCOS). PCOS-affected women with manifest clinical hyperandrogenism have higher scores regarding sexual desire in response to erotic-visual stimuli, such as watching a man exercise, being close to an attractive man, or watching a muscular person [55]. So, androgens could have a role in directing sexual desire also in females.

The next point is paternal love and how the relationship between partners and testosterone levels changes following childbirth. Several studies demonstrated that fathers have lower testosterone levels compared with non-fathers [56, 57], and a drop in testosterone is demonstrated following the birth of a child even within the same man [58]. First-time expectant couples were enrolled, and salivary testosterone was measured in both men and women at four time points during pregnancy. Three months after birth, they subjected both men and women to three different questionnaires, evaluating the partner support after the birth of the child, the help with household chores, and the childcare. Testosterone drops during pregnancy time in fathers, whereas it increases in mothers. Moreover, the most supportive fathers had lower testosterone levels during pregnancy, and its decline was more pronounced compared with less supportive fathers. Again, the same inverse correlation was found between testosterone levels and household chores in men. In this study, we see a cause–effect relationship because testosterone was measured before the child's birth, so it is clear that it could not have been influenced by how parents behaved after childbirth [57].

This aspect has been demonstrated in many animal studies. An interesting model comes from two species of hamsters, which have different behaviors toward their offspring: *Phodopus campbelli* typically have biparental care, so by both mother and father, whereas *Phodopus sungorus* typically have uniparental (maternal) care. Any difference in their testosterone level has been tested in males before meeting the female, during gestation, and in the days following birth [59]. After birth, they subjected hamsters to an experiment: They put the entire litter in a cage, all in one corner except one pup, which was placed in the opposite corner. At this point, the father was introduced into the cage, and the researchers calculated the time passed before the father reached the litter and if he eventually saw the lone pup, picked it up, and brought it to the others. *P. campbelli*, characterized by biparental care for the offspring, demonstrated shorter latency

before contact with the litter and more fathers who actually went to pick up the lone pup. Regarding testosterone, it dropped in *P. campbelli* from the last day before the birth of the pup to the day after birth. This drop is much less evident in *P. sungorus*, indicating a role of testosterone in father care for the offspring. Interestingly, testosterone tends to rise again in *P. campbelli* in the following days, probably due to a necessary greater aggressiveness of the hamster in defense of the litter.

Returning to humans, there is one last study in which salivary testosterone was measured in men and women from couples in a stable relationship [58]. Enrolled subjects completed a questionnaire evaluating satisfaction, commitment in the relationship, and the investment in the relationship. Both men and women had an inverse correlation between testosterone levels and relationship satisfaction and commitment. This correlation did not exist when investment was considered. The authors speculate that investment considers the entire story of the relationship, including the early stages, when testosterone levels are higher, as C.P. showed you before. Instead, satisfaction and commitment concern the current state of the relationship [58].

Audience: The decline in testosterone related to fatherhood struck me. What is the molecular mechanism through which this hormone is downregulated? I ask you to speculate on this, which seems almost like a negative feedback mechanism.

V.G. (Group 1): A proposed mechanism suggests that the stress associated with fatherhood may lead to an increase in cortisol levels, which inhibits testosterone production through the HPG axis. This mechanism could be advantageous for fathers by reducing aggression and facilitating childcare [60].

C.P. (Group 1): I think that evolutionary mechanisms must be considered too. Initially, the male's energy is invested in competition with other individuals of the same gender and in attracting a partner, and testosterone is crucial in this phase. Subsequently, the energy shifts toward parental care and the preservation of survival, preferring other molecules rather than testosterone.

M.S.: I hypothesize that this decline in testosterone comes from a reduction in gonadotropin secretion, resulting from a change in gonadotropin-releasing hormone secretion or pulsatility.

L.D.V. (Group 2): The studies presented by Group 1 support the role of testosterone in increasing impulsivity, sexual desire, and even the rate of infidelity. This led me to ask what happens to males who are born and grow up without testosterone.

An interesting study analyzed the psycho-relational lives of 13 patients with Kallmann syndrome, a genetically based hypogonadotropic hypogonadism, through questionnaires and interviews [61]. At the time of the study, all these patients were receiving hormone replacement therapy, with satisfactory male secondary sexual characteristics development, except for facial hair, and active relational life without sexual dysfunctions. Specifically, four of them were in stable relationships or married, seven had casual relationships, and only two avoided relationships altogether. However, none of these patients reported to have experienced feelings comparable to love. The questionnaires revealed that none described their relationships with the overwhelming and all-encompassing nature typical of romantic love. The interviews highlighted a certain emotional detachment, likened to that seen in arranged marriages. So, despite having normal testosterone levels and preserved sexual desire, none of them seem to have ever fallen in love. The authors proposed several hypotheses to explain this phenomenon. The first hypothesis, later revisited in a more recent article [62], suggests that the absence of male hormones during early life and puberty led to a less "masculine" development of the brain system. Additionally, each of these patients may have experienced discomfort, low self-esteem, and insecurity due to the lack of male sexual characteristics during puberty, a crucial time for forming social identity.

M.S.: Did you say that individuals with Kallmann syndrome do not fall in love?

L.D.V. (Group 2): Yes, this is what emerged from this study.

M.S.: But did they have relationships?

L.D.V. (Group 2): Yes, they did.

C.C. (referee): Are we talking about Kallmann patients treated or untreated?

L.D.V. (Group 2): This is the point. We are talking about Kallman patients undergoing successful replacement treatment. There should be another fascinating, but difficult to prove, theory: These patients are hyposmic, they cannot smell. This could lead to difficulties in the chemical pheromonal communication with the opposite sex. The evidence regarding pheromones in the animal kingdom is very strong, indicating their influence on attraction, mating, defense, protection of offspring, aggression [63]. The role of pheromones in humans is certainly different but not negligible.

M.S.: But pheromones do not have a smell, right?

L.D.V. (Group 2): Yes, pheromones do not have an odor perceptible to the human sense of smell [64]. However, talking about animals, the vomeronasal organ is located within the nasal cavities, and it is unclear whether the signals that reach the CNS are mediated solely by the vomeronasal organ or if the olfactory epithelium is also involved.

M.S.: Does the vomeronasal organ exist in humans?

L.D.V. (Group 2): In humans as in most primates, this anatomical structure is vestigial and the genes responsible for its synthesis are pseudogenes [65]. There are some studies showing that even in the absence of the vomeronasal organ—in knockout mice or those that have undergone surgical procedures blocking the pathways to the CNS—there is still a pheromonal effect. Thus, it could be possible that pheromones act through alternative pathways, not exclusively the vomeronasal organ.

Now, let's consider another study published in Nature in 2002 [66]. Using chromosomal engineering techniques and gene silencing, the authors created knockout mice for the Vr1 pheromone receptors. They observed that the absence of these receptors caused sex-specific behavioral changes. Specifically, females exhibited reduced aggression toward strangers when

defending their offspring, with no change in the time spent caring for their pups. Conversely, males did not show increased aggression but rather a reduction in sexual behaviors. Without pheromone receptors, the females were less aggressive in defending their offspring, whereas the males exhibited significantly reduced sexual drive, even though their testosterone levels were comparable to those of wild-type mice. This indicates that it was not just testosterone driving sexual desire in these mice.

In conclusion, these studies suggest that pheromones play a crucial role in animal gender-specific behavior, influencing both mating and aggression. While testosterone is important, it is not the only factor at play, highlighting the complexity of biochemical communication in determining these behaviors, at least in animals.

Audience: One of the major issues regarding pheromones is the difficulty in determining the threshold sensitivity to these substances. Additionally, I believe it is very challenging to understand what might happen in relation to substances whose targets of action are not well understood. From an olfactory pathway perspective, there are also scents that are difficult to interpret, and olfactory sensitivity varies from person to person [67]. Thus, methodologically, it is very challenging to ascertain anything definitive about these substances.

L.D.V. (Group 2): Regarding the issue of pheromone perception thresholds, in the previously mentioned study, a series of tests were conducted to determine the subjects' ability to perceive androstenedione [68]. Specifically, various olfactory tests with different substances were performed and 25% of subjects were anosmic to androstenedione.

Audience: From an evolutionary standpoint, I would argue that they are more evolved because olfactory systems are archaic and have been lost over the course of evolution.

L.D.V. (Group 2): Relevant to this point are the results of a study that considered patients deemed anosmic due to advanced nasal polyposis [69]. Each of these patients underwent tests with various odorous substances and two pheromones, one being androstenedione and the other an estrogen-derived pheromone. They observed that compared with controls, the anosmic patients could not perceive any odor except for the pheromone derived from estradiol. Specifically, only the female-derived pheromone showed hypothalamic brain activation as indicated by functional MRI in the same areas as the controls, despite the patients being anosmic and insensitive to all other odorous substances. Not all the pathways through which these molecules generate a central signal are fully understood. Some are mediated by the olfactory epithelium, but others clearly operate via parallel mechanisms.

What about the role of other molecules in regulating love and causing differences between genders? A double-blind, placebo-controlled crossover trial investigated the effects of intranasal oxytocin (OX) on sexual behavior [70]. Twenty-nine couples were asked to use intranasal oxytocin 35 min before sexual intercourse. The parameters assessed included heart rate, cortisol levels, and salivary amylase levels both before and after intercourse. Additionally, questionnaires evaluated classic sexual parameters, orgasm characteristics, post-orgasm experiences, and interaction between partners. OX has different effects depending on gender compared with the control group: Men experienced an increase in orgasm intensity, post-coital satisfaction, and sexual satiety after intercourse, whereas women only reported an increased sense of connection and empathy with their partner, as well as a greater ability to share sexual desires. This suggests a gender difference in response to the same stimulus. OX may act as an amplifier of perceptions, enhancing the intensity of whatever sensation the individual is experiencing at the time [26, 71].

F.P.: Thanks to all the discussants for presenting stimulating results. Now my task is to provide further food for thought. I would like to close the circle, seeking an answer to the question that emerged at the beginning of our discussion: Why to love when it would suffice to reproduce to sustain the species?

I start, apparently, from afar. As you all know, cardiovascular diseases are the leading cause of morbidity and mortality, accounting for nearly half of all deaths in Europe. However, there is a significant gender difference in cardiovascular mortality: in Europe, one in four men dies before the age of 75, compared with one in six women. This gender disparity is even more pronounced for deaths before the age of 65, with rates of 12% in men versus 5% in women [72]. The reasons for this gender-specific excess mortality are not fully understood. Epidemiological studies have shown lower morbidity and mortality rates for married men compared with their unmarried counterparts. Marriage could reduce stress and stress-related illnesses by mitigating the effects of stress on cardiovascular hyperreactivity and excessive sympathetic nervous system activity [72]. Another theory is that married men tend to engage in fewer self-destructive behaviors, such as drinking alcohol or smoking, and are less likely to neglect their health thanks to the care of their partner [72].

The best documented example of the effect of marital relationships on health is the so-called widowhood effect: After the death of a spouse, men and women face a dramatically increased risk of death in the following months [73]. This effect is particularly pronounced for cardiovascular diseases and is gender-specific, being more evident in widowed men than in women. Beyond this "widowhood effect," two complementary explanations have been proposed: According to the "social causation" theory, being in a stable relationship encourages healthier behaviors and emotional stability, whereas the "social selection" theory suggests that individuals in better health are more likely to attract and maintain a partner. Together, these mechanisms may contribute to the observed association between love, health, and longevity [74].

Therefore, beyond the influence of hormones, we hope that from today onward, each of you will feel inspired to embrace love a little more!

G.B.: So, to conclude, I want to comment on some issues. First of all, we have come up against the difficulty of finding an all-encompassing and, at the same time, scientifically valid definition of what love is. The data presented so far confirmed that love has many facets and includes various aspects of the biopsychosocial life of the individual.

In the end, we decided to consider love in the way it is presented in scientific literature. Whether we like it or not, romantic love,

predominantly heterosexual, is considered. Moreover, we noticed that the vast majority of studies on love were conducted on males. Finally, I would try to answer the question of why to love when it suffices to reproduce to sustain the species. Somehow, love could be counterproductive from an evolutionary perspective. If I fall in love with my husband and I reproduce with him only, we are unlikely to have the number of children we would have if each of us had a more playful sexual attitude. Moreover, we have seen that the various phases of love, from falling in love to caring for offspring, are regulated by complex, redundant physiological mechanisms. And we know that when a system is redundant, it is because it is biologically important. For example, gonadotropins are two, and they are the only pituitary hormones to be two, because they regulate an essential biological phenomenon, reproduction. It is true that each gonadotropin regulates different functions, but it is a fact that evolutionarily we have moved in the direction of redundancy in the regulation of a function vital for the survival of the species. So, this enormous complexity of love is due to its important biological role for the individual and the species. Today I understood that love is essential to overcome the fear of the other on one side and the fear of loneliness on the other side. Although energetically very expensive, it is evident that loving helps to avoid being overwhelmed by fear, pain, and loneliness, which would probably be just as harmful as a reduction in reproductive capacity.

C.C. (referee): Thanks to both teams and to the audience for this interesting dialogue. I would give an equal score to both groups, because very important topics were addressed. The discussion of sexuality has somewhat stalled lately and is taken very much for granted, but today's discussion clarified that this topic is becoming increasingly important.

4 | Aporetic Conclusion

In conclusion, the nature of love and its gender-specific manifestations are influenced by a complex interplay of biological, psychological, and sociocultural factors. Although testosterone has been shown to play a significant role in shaping certain aspects of romantic and sexual behavior, particularly in males, it is not the sole determinant of how individuals experience and express love. The evidence presented highlights that testosterone levels are associated with differences in romantic attachment, sexual impulsivity, and even infidelity, particularly in men. However, these effects are not isolated; they are modulated by a broader neuroendocrine system involving neurotransmitters, such as dopamine, serotonin, and oxytocin, which also contribute to the emotional and behavioral dimensions of love.

The discussion revealed that although testosterone may drive certain gender-specific behaviors, such as male competitiveness and short-term mating strategies, other hormones and neurotransmitters are equally critical in fostering long-term attachment, emotional bonding, and relationship satisfaction. For instance, dopamine and oxytocin have been shown to play pivotal roles in pair bonding and emotional connection, whereas serotonin influences the obsessive and compulsive aspects often observed in the early stages of romantic love. Furthermore, the role of cortisol in modulating stress responses and its potential impact on testosterone levels during fatherhood underscores the intricate balance between hormonal systems.

Sociocultural factors also cannot be overlooked. The way love is experienced and expressed is deeply embedded in cultural norms, societal expectations, and individual psychological predispositions. For example, the rise of online dating and social media has altered traditional courtship behaviors, potentially influencing how individuals form and maintain romantic relationships. Additionally, the evolutionary perspective suggests that love, although seemingly counterproductive in terms of reproductive efficiency, serves as a crucial adaptive mechanism to reduce social isolation, anxiety, and stress, thereby promoting long-term pair bonding and parental investment.

In the end, the referee, Prof. Cesare Carani, concluded that both groups presented compelling arguments, and the aporia remains unresolved. Love is a multifaceted phenomenon that cannot be reduced to a single hormonal or neurochemical factor. Instead, it emerges from the dynamic interplay of testosterone, other hormones, neurotransmitters, and sociocultural influences. This complexity underscores the importance of recognizing that no single theory can fully explain the rich and varied experiences of human affection and attachment.

Author Contributions

Manuela Simoni had the idea of the discussion on this topic and the aporetic dialogue structure. Francesca Paglia, Leonardo Dalla Valentina, Valentina Griseta, Carmela Perri, and Daniele Renda Livraghi did the bibliographic research and created the data presentation under the supervision of Giulia Brigante. Cesare Carani, Manuela Simoni, Giulia Brigante, Francesca Paglia, Leonardo Dalla Valentina, Valentina Griseta, Carmela Perri, and Daniele Renda Livraghi discussed and commented on the data and wrote the article. Giulia Brigante submitted the article.

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Conflicts of Interest

The authors declare no conflicts of interest.

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