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An Attempt to Understand the Biology of Gender and Gender Dysphoria: A Christian Approach

The recent rise in the number of transgender individuals has perplexed many. A study of possible biological origins of gender dysphoria presents a complex picture. In some cases, prenatal hormonal imbalance may cause early-onset and persistent gender dysphoria. In contrast, late-onset cases are associated with a high incidence of comorbidities such as trauma, depression, and autism. In such cases, social isolation and an impaired body image may make individuals susceptible to social media suggestions of gender dysphoria. Moreover, affirmative counseling without addressing underlying comorbidities can strengthen this misperception, further moving these individuals along a trajectory toward transition. Care must be taken when considering early transition, given the fact that childhood gender dysphoria frequently desists. One must balance sparing a child from the distressing sexual changes of puberty with beginning transition in someone who might otherwise have desisted. Recent studies of perception suggest that it is a top-down predictive, "best guess" process. Although these "guesses" are continuously modified by sensory experience, they can persist; they might also apply to some cases of gender dysphoria. While some people have managed to detransition back to their natal gender, we should not assume that this is possible with everyone. As Christians, we need to examine each case individually, removing the stigma and supporting them through this distressing condition.

Keywords: gender dysphoria, gender incongruence, Waddington's landscape, puberty blockers, desistance, comorbidities, body perception, aromatase, integrity, disability, diversity

The recent dramatic increase in both the number of cases and the prominence of transgender individuals in our culture raises many questions. Responses from churches have been mixed, from outright condemnation to enthusiastic acceptance. How do we as Christians navigate this issue? One of the blessings of the American Scientific Affiliation that founded this journal is that it is an organization that values both science and scripture. It also recognizes that there

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may be differences of opinion within its members, so I expect that not everyone will agree with my conclusions, and I am open to correction as new evidence emerges. Since this is a rapidly evolving field, there often are not clear answers, and there can be vigorous disagreement. New findings may change perspectives. Unfortunately, the complexity of this topic and space limitations force me to oversimplify on occasion. Sadly, this issue is highly polarized, even in the scientific literature. Often the language itself is value-laden, which is well meaning but can be unhelpful for clarity. Moreover, every case is different, so generalizing can lead to mischaracterizations.

The Biology of Sex and Gender

As we begin, we first need to distinguish sex and gender. *Sex* refers to one's biological sex, which is genetically determined and usually causes both body and brain to be male or female. *Gender* refers to one's internal perception that one is male or female. This can conflict with sex in gender incongruence or vary in people who identify as gender-fluid. Determining sex of the body is relatively straightforward in most cases (with exceptions, discussed below), but when we look at brain development, our conclusions are by necessity more tentative. Gender is more difficult to study because it is based on self-reporting.

The usual pattern of development is as follows. Males have a Y chromosome, which contains the *sry* gene. Around six weeks into embryonic development, this gene is activated, which causes an embryonic structure called the genital ridge to develop into testes. These testes then produce testosterone, which stimulates the development of the male internal and external reproductive organs. Females lack the *sry* gene, so ovaries develop instead, along with the female internal and external reproductive organs before birth and secondary sexual characteristics at puberty.

What about the brain? The classical model for explaining sexual behaviors is that there is a twostage process. The *organization* stage occurs before birth, while *activation* occurs at puberty. In the organization stage, neural pathways in boys and girls develop differently under hormonal influence. These different neural pathways result not only in different behaviors during childhood, but also in different sexual behaviors in adolescence.¹ Our understanding is that the brain is masculinized by testosterone and possibly other hormones, including estrogen, while development of a female brain is the default pathway.²

In contrast, Brown University Professor Emerita and sex researcher Anne Fausto-Sterling has proposed a dynamic systems framework for gender/ sex³ development that is entirely based on conditioning.⁴ Fausto-Sterling describes three phases of a child's gender/sexual identity. In the first phase (<15 months), the child is exposed to different stimuli, depending on their sex, which has an impact on brain development. From 15 to 18 months, there is this fluid period in which one's sense of gender/sex is developing but not yet apparent. After 18 months, the child has developed their sense of gender/sex and begins to act accordingly. While I agree that there are environmental contributions to brain development, including sexual functions, they are not the only factors. It is striking that Fausto-Sterling never mentions prenatal hormonal influences, dismissing those who argue for biological underpinnings of gender. Yet, these environmental influences that Fausto-Sterling describes are set in a context of previous brain development *in utero*, under the influence of different sex hormones. Surely, they also have an influence on gender! I will address these hormonal effects later in this article.

GLOSSARY

- **Gender incongruence**: incongruence between one's biological sex and one's gender. May be present with or without dysphoria
- **Gender dysphoria**: the sense of distress resulting from gender incongruence
- **FtM**: Female-to-Male transgender person or transition
- **MtF**: Male-to-Female transgender person or transition
- **Binary**: understanding sex and gender to be either male or female
- **Nonbinary**: allowing for a spectrum of sex and/ or gender to be intermediate between male and female
- **Passing**: the ability of someone to be in public without others knowing that they are transgender
- **Puberty blockers**: GnRHa (gonadotropinreleasing hormone agonists), used to suppress sex hormone production and prevent the child from entering puberty. Originally developed to treat precocious puberty, these are used to suppress puberty in the Dutch protocol or to stop endogenous testosterone production in MtF individuals
- **WPATH**: World Professional Association for Transgender Health
- **USPATH**: United States Professional Association for Transgender Health
- APA: American Psychological Association

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Nevertheless, Fausto-Sterling's emphasis on the dynamic nature of sex and gender development is helpful, as it avoids a rigid essentialist understanding of gender. She also applies Waddington's epigenetic landscape model to gender/sex development. Waddington's landscape is a helpful way to understand the dynamic and stepwise nature of embryonic development.⁵ As an organism develops, cells progressively adopt cell fates by making developmental decisions. Waddington's model is that of balls rolling down an uneven slope, choosing different paths to descend, and thus ending in different places (fig. 1).



Figure 1. Illustration of Waddington's landscape. The ball rolls down the "developmental" hill, making successive pathway decisions along the way. Depending on which path is chosen, the cell/organ/individual will adopt a different fate.

There is a usual pattern but there is also an element of chance and variability, as the pathways that are chosen can be affected by the environment. Moreover, there is also increasing stability as the pathway is chosen. In brain development, these developmental changes primarily involve the formation and refinement of synaptic connections and epigenetic regulation of gene expression, which presumably result in sex-typical behaviors. It is not difficult to imagine variability in the behaviors that are expressed, and to what degree, depending on which pathways were chosen. Note that this is an oversimplified explanation of a very complex process involving many interacting neural pathways and many types of behaviors. There may be differences between the sexes, due to hormones and other influences, but there is also much overlap in behaviors and preferences.

Before proceeding further, we need to be clear that gender is not how one acts, as male or female; it is how one senses oneself to be. I frequently see references to gender as a social construct,6 which seems to me to be a confusion of gender roles versus gender perception. To be sure, one's gender would affect how one acts-for example, mannerisms, clothing, choice of friends-but they follow from one's gender and are not equivalent to them. Gender roles are largely socially constructed but gender *identity* is not. As an example of this confusion, Meredith Meyer and Susan Gelman argue against gender essentialism on the basis that it forces children to stereotypical behaviors depending on their gender, which can lead to power inequality.⁷ To be sure, rigid stereotypes of sex-specific behaviors are neither necessary nor helpful, but they do not change one's gender. We also need to distinguish gender from sexual orientation. The former is inwardly focused, the latter outwardly focused. Moreover, gender incongruence does not need to entail a particular sexual orientation. Although these are distinct, it is possible that the two may be conflated by someone wondering whether they have gender incongruence (see below).

Development of Gender

What do we know about the biological basis for gender? The organization/activation model used to describe sexual behaviors was originally developed and studied in rodents, but gender obviously cannot be measured in animals, as gender is one's *internal* sense of whether one is male or female. Moreover, since it cannot be objectively measured, gender is difficult to study. Still, there are indications of a role of biology in gender development.⁸

It is becoming more apparent that, despite our increasing knowledge of the anatomy and circuitry of the brain, we do not have a good understanding of the higher-order processing in processes like gender perception. As described by Matthew Cobb, there are numerous models describing how the brain works, including anatomy, circuitry, brain waves, and neurotransmitters, but none of them accurately describes how we think, let alone how we perceive gender.⁹ The tools available to study human brain activity are far too crude to analyze complex neural pathways and synaptic rearrangements, which are key to understanding brain function.¹⁰ Thus, we are limited to looking for correlations. In this section, I will look at different ways to study the brain and

look for correlations with gender incongruence to help us detect possible biological causes. An important caveat is that as we search for possible causes of gender incongruence, there are likely to be multiple causes, so we must avoid generalizations.

Biology of Gender—Anatomy

Is one's gender apparent in one's brain anatomy and altered in gender incongruence? There are regions of the brain that are sexually dimorphic, that is, they differ in size between males and females. Could studies in transgender brains help us understand their role in gender? Indeed, numerous studies suggest that some of these regions in transgender individuals were intermediate or closer to their gender identity than their natal sex.11 However, these findings must be interpreted with caution. While these regions are sexually dimorphic, there is considerable overlap and mosaicism between males and females, that is, there is not a clear relationship between the sex of the individual and the anatomy of these regions.¹² Since these are postmortem studies, the number of samples is low, and there is variability between individual subjects.13 Moreover, due to the plasticity of the brain, it is also possible that individuals who lived according to their identified gender may have had corresponding changes in brain anatomy as a result. Finally, we do not know how these structures may function in gender identity.

Biology of Gender—Brain Function

If not anatomically, might gender incongruence be apparent in brain activity instead? One of the models for brain function that Cobb describes is a circuitry model. In this model, brain functions are not localized to a specific region, but using a wiring metaphor, brain functions result from different regions communicating with each other in a circuit. Such a circuit could differ between the sexes. Consistent with this model, there are differences in the cortex and gray matter between males and females, and individuals suffering from gender dysphoria display an intermediate pattern.¹⁴

Gender incongruence is often accompanied by comorbidities. One study found a high incidence of trauma, including anxiety, depression, family conflict, parental mental illness, separation, and bullying.¹⁵ Autism rates are high in transgender people, but it is not clear if there is a common cause or a cause-and-effect relationship.¹⁶ Gender incongruence may hinder psychological development of people with autism, thus amplifying the disorder. Alternatively, autism and accompanying social deficits might make it difficult for children to develop a sense of gender (reminiscent of Fausto-Sterling's dyad model of gender/sex development, described above). In addition to autism, gender dysphoria symptoms are also seen in schizophrenia¹⁷ and an increased incidence of gender variance was also seen in children of both sexes with ADHD.¹⁸

Biology of Gender-Hormones

The strongest case for a biological cause of gender is that of hormonal regulation. As mentioned above, exposure to testosterone in the fetal brain masculinizes it, while absence of testosterone results in a female brain. There are multiple indications of an important role for sex hormones in gender development and alterations in this hormonal milieu could result in gender incongruence.¹⁹

- In a study of female patients with congenital adrenal hyperplasia (CAH), where high levels of androgens ("male-acting" hormones) are produced, a large proportion declared a male identity despite being raised as females.²⁰
- In a study examining androgen insensitivity, where males have testes and testosterone but have defective receptors and physically develop as females, all (11/11) patients with complete androgen insensitivity identified as females, whereas most (11/14) patients with partial androgen insensitivity identified as males, despite having a female phenotype.²¹ This strongly suggests that even a small response to testosterone can affect one's perception of gender.
- Polycystic ovary syndrome (PCOS) is accompanied by high levels of androgens in the blood. A study on female-to-male (FtM) transgender individuals found a high proportion (39%) of PCOS in these patients.²²
- High levels of fetal testosterone may also contribute to gender dysphoria in girls but not in boys, which is consistent with the extreme male brain theory of autism.²³
- Prenatal exposure to diethylstilbestrol (DES, a nonsteroidal synthetic estrogen prescribed to prevent miscarriage) causes sexual abnormalities, and there are links to gender incongruence in females as well.²⁴

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- Genetic studies have identified particular variants of the testosterone and androgen receptors that correlate with an increased incidence of gender dysphoria.²⁵
- Exposure to endocrine disruptors such as bisphenols A and F might also have an effect.²⁶

Greg Eilers's situation is another clue to the role of sex hormones in gender.²⁷ Eilers suffered lifelong gender dysphoria, which resulted in his resigning his position as a pastor, to transition to a woman. As a result of taking estrogen for his transition, his dysphoria resolved, and he sensed himself as a man again. His identifying as a man is dependent on continuing to take estrogen.28 While it may seem surprising that taking a "female" hormone such as estrogen would resolve his dysphoria, it should be noted that estrogen is not strictly a "female" hormone, as it is present in male brains, being converted from testosterone by the enzyme aromatase.²⁹ Aromatase is expressed in many tissues, including nonreproductive organs, and plays a variety of roles, not just in reproduction.³⁰ Estrogen in the brain is involved in many functions, including cognition.³¹ One might speculate that blocking testosterone and increasing estrogen normalized Eilers's estrogen levels, which were possibly perturbed by prenatal exposure to DES.

Kayo Takahashi et al. found that levels of aromatase in different brain regions correlate with personality traits.³² Although gender was not specifically addressed in this study, it should be noted that levels of aromatase are decreased in autism, a common comorbidity in gender incongruence.³³ Though we do not understand *how* hormones regulate gender, it seems clear that hormonally regulated gene expression plays a role in at least some cases of gender incongruence.

To summarize, there are many biological factors that may play a role in contributing to gender incongruence but none of these is well understood. The above examples either increase the possibility of gender incongruence or play a more definitive role in a subset of cases.

Are Sex and Gender Binary, or a Spectrum?

The above discussion implies that both sex and gender are binary. One is either one or the other. Yet there are arguments that both sex and gender are nonbinary, and even a spectrum.³⁴ The development of one's sex that is described above occurs in most cases. However, sometimes the usual developmental pathway is not followed. Such cases are collectively called disorders of sexual development (DSDs) and occur in roughly 1 in 100 live births.³⁵ This is a broad category, and the incidence of genital anomalies is much lower, at 1 in 4,500 births.³⁶ Other DSDs include androgen-insensitivity syndrome (described above), or gene mutations in the developmental pathways, which result in intermediate phenotypes. Still other DSDs result from a chromosomal abnormality, such as Turner (XO) or Klinefelter (XXY) syndromes, where the sex is apparent, but normal sexual development does not occur.

The existence of DSDs seems to be the exception that proves the rule of sex being binary. These conditions are a result of a developmental *disorder*, not normal variance. As Christians, we must acknowledge that people with these conditions exist, and we must love and support them. However, that does not mean that biological sex exists on a spectrum.

The binary nature of gender is more difficult to assert because the issues are more complex. First, gender is difficult to define because it is entirely self-reported. While one's experience of gender may be very real for those suffering from gender dysphoria, there are no objective criteria for assessing gender, and studies that are done to assess gender need further development to improve reliability.37 It seems that most cases of gender dysphoria involve a gender binary, but assuming a developmental process of gender formation, one can certainly imagine exceptions to this pattern.³⁸ Note that, as mentioned earlier, we must still distinguish between variations in sex-typical behaviors and one's gender. Just because someone has preferences that do not conform to most others of that person's sex, does not mean they are nonbinary, let alone transgender.

Recent Increases in Gender Dysphoria

It is difficult to determine the frequency of gender dysphoria. The number of reported cases is rising, but reliable diagnosis of the condition is difficult. Estimates range from 0.5 to 1.3%,³⁹ although one recent study had roughly 10% of high school respondents claim to be gender-diverse.⁴⁰ More recently, however, the number of adolescents, particularly girls, with gender dysphoria presenting to clinics has increased considerably, with a lesser increase in boys

and in adults of both sexes.⁴¹ There are several possible explanations for these changes.

One possibility is better diagnosis. With the increased prominence and social acceptance of LGBT individuals in our culture,42 more people are aware of gender incongruence, may see themselves also having this condition, and present to gender clinics. The increased use of the internet, and particularly social media, makes information on gender dysphoria readily available. Mark Yarhouse and Julia Sadusky, citing Hacking, describe a "looping effect," where the naming of a condition (like gender dysphoria) results in an increase in the number of people identifying with that condition, which in turn increases the number of institutions and experts who deal with it.43 This is not meant to invalidate gender dysphoria, but it does provide a possible explanation for its relatively sudden increased prominence.

The increased study of gender dysphoria has presumably also resulted in better evaluation criteria for diagnosis. One study carefully examined this possibility for the Swedish population from 2005 to 2015 but found similar results to those reported recently: a slight increase in diagnoses in both sexes aged 18–30; and a several-fold increase in females aged 10–17, but no corresponding increase in males of that age.⁴⁴ It is not clear why the incidence of gender dysphoria is higher in adolescent girls. One possible explanation is that the social consequences of transitioning are higher for boys than girls, thus suppressing the number of cases in boys.⁴⁵ However, if the dysphoria persists, then one would expect a later increase in boys, which is not seen.

A controversial explanation of social contagion was first proposed by Lisa Littman, who described transitioning in clusters of friends, often encouraged by YouTube videos and other social media.⁴⁶ This phenomenon of rapid onset gender dysphoria (ROGD) was picked up by others, including the popular press, in both the US and the UK.⁴⁷ The Littman paper was critiqued on methodological grounds,⁴⁸ but the phenomenon exists,⁴⁹ and an explanation for the higher rates in this segment of the population remains elusive. A similar phenomenon involved an increase in Tourette's-like tics, which was linked to the viewing of TikTok videos of Tourette's syndrome by teenage girls and young women during the COVID-19 pandemic.⁵⁰

What might be the role of environmental factors such as social media on gender? The possible perturbance of Waddington's epigenetic landscape was described earlier in the context of gender development in the fetus (the organization stage). Can it also function in adolescence, to provide an explanation for late-onset gender dysphoria? Fausto-Sterling discussed brain plasticity in the context of child development, but the dramatic changes in the brain that occur during puberty,⁵¹ with the rise in the levels of sex hormones, may also occasion further changes in brain organization and behavior. Intrinsic stressors, such as depression or eating disorders, or extrinsic stressors, such as family trauma or social isolation, may contribute to instability in the epigenetic landscape and contribute to gender dysphoria.52

The Process of Transitioning

Transitioning is a big step to take and must not be taken lightly. Transitioning can (but does not necessarily) involve multiple steps in the progression: psychotherapy, hormone treatments, nongenital surgery, and genital surgery. The later stages are also costly and largely irreversible (but see below). Even with the extensive surgeries and lifelong hormone treatments, it can be difficult to "pass" as a member of the opposite sex. Despite these concerns, many deem the process to be essential, to relieve them of the dysphoria they experience. Which treatments that are done, and in what order, can depend on the individual. Many transition socially and hormonally but do not go further. Social transitioning can involve changes in hair and clothing, name change, and coaching to modify mannerisms and speech to the desired gender.

The World Professional Association for Transgender Health (WPATH) has laid out guidelines to determine if a patient is ready for surgery:

- Patient's gender dysphoria is persistent and well documented.
- Patient has the capacity to make a fully informed decision and consent for treatment.
- Patient is the legal age of majority in a given country.
- Patient's medical or mental health comorbidities, including any psychiatric disorders, are "reasonably well controlled" (for chest surgery) or "well controlled" for genital surgery. Obviously,

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surgery should not be performed on actively psychotic patients.⁵³

The initial steps include confirmation that the patient meets the criteria for gender dysphoria, assessment by mental health professionals, psychotherapy, and social transition for at least three months before hormone therapy is initiated.⁵⁴ Although these guidelines are clear, these are just guidelines, and they may not always be followed.⁵⁵ A culture of gender "affirmation" may be encouraging transition instead of using it as a last resort when other options have been exhausted.

Hormone treatments are the next step in transitioning. Gonadotropin-releasing hormone analogs (GnRHa) act on the pituitary to suppress the release of luteinizing hormone and follicle-stimulating hormone, which in turn prevents the production of estrogen in females and testosterone in males. GnRHa drugs were originally developed to treat precocious puberty but are also used off-label in this context. Female-to-male (FtM) patients receive testosterone, administered in various ways, sometimes with GnRHa or the less cost-prohibitive progestin to suppress endogenous estrogen production. Male-tofemale (MtF) patients require GnRHa and estrogen, which can be associated with more adverse events, including blood clots. In the US, the diuretic spironolactone is commonly used off-label instead of GnRHa because it also blocks the effect of testosterone and is much less expensive. However, it also blocks the activity of aldosterone (sodium/potassium balance) in the kidney for which it was originally developed, so patients need to be closely monitored for adverse effects.56 WPATH guidelines call for the individual to be on hormone treatments for a year before surgery.⁵⁷

Reviews of studies on the effects of hormone treatments on gender dysphoria, quality of life, and psychological functioning found mixed results.⁵⁸ One recent review found a lack of high-quality randomized clinical trials to assess the safety of hormone use in trans women.⁵⁹ Yet another study found that testosterone therapy in trans men resulted in an increased body mass index (BMI) and decreased high-density lipoprotein ("good" cholesterol),⁶⁰ while a different study found increased occurrence of acute cardiovascular events in trans people of both sexes.⁶¹

While hormone treatments do alter facial shape and body contours, nongenital surgery can also modify the outward appearance to help the individual "pass" as the opposite sex in public. In MtF cases, this includes hair removal, voice modification surgery, and facial feminization surgery. Other surgeries include body contouring by fat redistribution (the particulars depend on the desired sex) and mastectomy. Genital surgery in both MtF and FtM cases removes the testes or ovaries, which means the individual needs to take sex hormones for life and will be infertile.

While the goal of genital surgery in FtM patients is to produce a phallus that can become erect, allow standing urination, and have both tactile and erogenous sensation, none of the available surgeries can accomplish this goal.62 There are two main options for FtM genital surgery. Metoidioplasty is the least complicated and involves enlargement of the clitoris through hormone therapy and using local skin and tissues to construct a penis and scrotum, which will have testicular prostheses. While metoidioplasty maintains sensation and allows standing urination, the neo-phallus is small and generally does not allow penetrative sex. The alternative is phalloplasty, in which tissue is grafted from elsewhere in the body (forearm, back, leg, or groin). This procedure is more technically challenging and complex. While phalloplasty results in an anatomically sized neo-phallus and allows for standing urination, erogenous sensation is poor or lacking. Penetrative sex is possible only if an inflatable prosthesis is included or if bone or cartilage are included in the graft. This latter option means the neo-phallus is permanently rigid, which can cause other complications. In all cases of phalloplasty, the donor site is considerably altered. Despite these challenges, genital surgery is reported to have a high level of satisfaction.63 This is most likely because it resolves the dysphoria in gender incongruence.

Like the FtM situation, the goal of genital surgery in MtF patients in constructing a vagina that can achieve pleasurable penetrative sex has not been achieved. This surgery involves the removal of the penis and the construction of a vagina. There are two options for constructing a vagina, neither of which generates a surface that is designed for penetrative sex. The interior walls of the vagina contain an epithelium that can withstand abrasion (stratified squamous) but also provides lubrication for intercourse, due to the seeping of fluid through the epithelium in arousal (in addition to mucus produced by vestibular glands). A mucous vaginal

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interior can be accomplished by grafting part of the small or large intestine. These tissues contain mucusproducing cells, but they are designed for nutrient absorption, not to withstand abrasion. Instead, in most cases, skin from the penis and perineum is used to construct the vagina. This surface is better able to withstand abrasion but does not produce any liquids or mucus for lubrication. Moreover, the amount of skin is limited, and dilation is needed, more so if the patient received puberty blockers before transitioning, which prevents the normal enlargement of the penis during puberty. Not surprisingly, pain in intercourse is common. The construction of a clitoris with erogenous sensitivity and labia majora are more straightforward but constructing labia minora is more challenging.⁶⁴ Complications of the surgery are common and wide-ranging, often requiring secondary procedures.⁶⁵ Urinary complications are also common. Detransitioning surgery in cases of regret is possible after MtF transitions, resulting in a phallus that provided improved esthetic and psychological status.66 However, this surgery (phalloplasty) does not provide erogenous sensation.

More attention is now being paid to the needs of detransitioners.⁶⁷ Mental health usually improves after transition, particularly over time,⁶⁸ but some decide to detransition. While it is difficult to obtain accurate numbers, studies have suggested that the incidence of regret is low (approximately 1%⁶⁹ but may be higher⁷⁰) and is due to a variety of reasons.⁷¹ A reddit site exists to support detransitioners,⁷² and as more studies are done, it is hoped that the frequency and causes of detransitioning will be better understood.

Desistance and Early Transition

Another controversy in this field is the question of desistance, that is, children whose childhood gender dysphoria resolved in puberty or adolescence. Littman and Shrier suggested that many of the adolescent girls did not have genuine gender dysphoria, based on reports that most childhood gender dysphoria desists when the individual reaches puberty, with some having same-sex attraction instead.⁷³ This raises further questions about diagnosis and treatment.

Is there a difference between those cases that desist and those that persist? Are they qualitatively or quantitatively different? Clearly, if we can distinguish them, we can spare the desisters from irreversible treatments and proceed with the others. The criteria generally used to determine which cases are likely to continue are that the dysphoria is persistent, consistent, and insistent. These criteria are not that clear cut, however, given different personalities of these children, and there is considerable debate and a dearth of high-quality studies to provide clarity.⁷⁴

In one report, Steensma et al. studied 53 adolescents who had gender dysphoria, 24 of whom desisted, to see whether there were differences related to their psychosexual development.⁷⁵ Both groups were similar before puberty, being indifferent up to age 5 (which is inconsistent with other studies showing dysphoria at younger ages) but identifying with the other sex around age 6/7. The difference between persisters and desisters became apparent at puberty, starting around age 10. For persisters, the dysphoria intensified with the social and physical changes and the beginnings of sexual attraction that accompanied puberty, while the same changes resulted in dissipation of dysphoria in desisters. There was also a difference in the sense of gender of the two groups before they reached puberty. Those who persisted asserted that they were the opposite gender, whereas those who desisted wanted to be the opposite gender. A follow-up study by the same researchers also found that the intensity of the dysphoria was greater in the persisters than the desisters.⁷⁶ Despite this promising finding, others have not described a similar phenomenon; it remains unclear how reliably one can predict persistence or desistance.

Clearly, the question of desistance presents a dilemma for treatment.⁷⁷ Given that most children with gender dysphoria will desist, early transitioning will result in transitioning in someone who would not have otherwise persisted. The permanent nature of some aspects of transitioning, including hormone therapy, argues that unnecessary treatments should be avoided. Despite this concern, the WPATH and USPATH have issued a joint statement supporting treatment for children with gender dysphoria.⁷⁸

Another concern with treating gender dysphoria in children is the question of consent. Our brains undergo considerable development in puberty and adolescence, which has a profound impact on behavior.⁷⁹ Can a prepubescent, or even an adolescent understand well enough who they are, what the process of transitioning will be like, and what the final

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consequences will be (including loss of normal sexual function and fertility), to provide truly informed consent?

Moreover, what is the effect of counseling on a child's (or parent's) decision to transition? Concerns about "conversion therapy" are well founded; the consensus is that counseling cannot resolve genuine cases of gender dysphoria. However, given that gender *affirmation* is the prescribed approach to counseling,⁸⁰ how many children proceed along the pathway of transition when they do not have genuine gender incongruence?⁸¹ As mentioned above, there are significant comorbidities with gender dysphoria; is the counselor addressing them? If so, how?

On the other hand, waiting until puberty, known as "watchful waiting," can make transitioning more difficult, as the development of secondary sex characteristics (for example, bone structure, breasts, body hair) is more difficult to undo and makes it more difficult for the person to "pass" after transitioning. Additionally, the individual would experience an extended time of distress and further social consequences before transitioning.

The "Dutch protocol" involves treatment at the beginning of puberty, using GnRHa puberty blockers to delay puberty temporarily.82 As their name suggests, they can be used either at the beginning of puberty, or later in adolescence as part of the transitioning process. When administered at the beginning of puberty, the goal is to buy time for gender dysphoric children before the physical changes of puberty exacerbate their dysphoria. In addition, puberty blockers would eliminate the need for many surgical procedures to treat the irreversible secondary sex characteristics that develop in puberty. However, side effects include a reduction in height when accompanied by cross-sex hormones,⁸³ weight gain,⁸⁴ and reductions in bone density.⁸⁵ A further complication is that puberty blockers prevent the normal growth of the penis, providing insufficient skin for the construction of a neo-vagina from the penis should the person desire this surgery.⁸⁶

The use of puberty blockers has proved to be controversial because they may also block desistance. In a study of 70 patients taking puberty blockers, none of them desisted (when a large proportion would be expected), although there were fewer emotional problems and depressive symptoms.⁸⁷ The reasons for the lack of desistance are unclear but may have been partly due to more-stringent selection criteria for inclusion in this study. Alternatively, if it is the changes in hormone levels per se that occur in puberty that are responsible for desistance, then it should not be surprising that puberty blockers would block desistance. It should be noted that the prefrontal cortex, which is responsible for cognition, does not mature until late in adolescence.⁸⁸ Jack Turban et al. claim that the use of puberty blockers in adolescents improves mental health and reduces suicidal ideation.⁸⁹ However, this conclusion has also been challenged, citing weak data and confounding factors such as comorbidities.90 In a systematic review, Lieke Vrouenraets et al. report disagreement on the use of puberty blockers, citing numerous areas in which our understanding is incomplete.91 A more recent (but small) study found little change in psychological function after use of puberty blockers.92

The treatment of gender-dysphoric children in the UK has been contentious, centering around the services provided by the Gender Identity Development Service (GIDS). It is claimed that these services are overwhelmed and that providers are unable to adequately judge the suitability of a patient to consent to puberty blockers.93 Indeed, former GIDS employees and others have compiled a book to protest perceived inappropriate services provided by GIDS.94 In response to a lawsuit filed by Keira Bell, who was prescribed GnRHa and transitioned to a male before detransitioning sometime later, the British High Court banned the prescription of puberty blockers to patients below the age of 16, citing their inability to provide truly informed consent.95 This ruling is being appealed, and the National Health Service (NHS) has announced an independent review of the gender identity services for children and young people.⁹⁶ Sweden does not initiate treatment for children under 16, and requires a court order to initiate treatment in children from 16 to 18.97 On the other hand, in the US, a recent survey of a listserv of providers of gender-affirming care found overwhelming support for medical interventions before age 18.98

Sensing One's Gender

In reading works by transgender authors, I am struck by the certainty with which they express their sense of gender, even though it is incongruent with their sex. This is not a matter of "determining" their gender; they just "know" what gender they

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are. They usually do not want this incongruence but feel helpless to change it. Consequently, it is entirely understandable that trans people want acceptance in our society because it is simply who they are. Thus, I disagree with well-meaning people who claim that gender is simply a matter of choice, and that sheer willpower can overcome it.

However, the scientific evidence I have described has not yet given a straightforward biological cause for gender incongruence. Hormonal factors that alter developmental trajectories seem to play a role, but it is not clear how this occurs. Moreover, the desistance data for childhood gender dysphoria, the recent increases in cases of gender dysphoria, and the common occurrence of comorbidities all argue against a single biological cause for this condition. Most likely, there are multiple causes, at least some of which involve perturbations in the hormonal milieu in utero. But might other cases involve a different cause, which may be more psychological in nature? I must be careful here not to imply a false dichotomy between biology and psychology. Clearly, psychological changes involve biological changes as well, but at this point an understanding of the basis of gender is beyond the reach of biology. Since my formal training is not in psychology, I must also present these ideas somewhat tentatively, but I find them intriguing and suggestive.

The neuroscientist Anil Seth recently gave a TED talk,99 further elaborating on his book Being You,100 in which he explains the research done by his group and others to describe how we interpret what we experience. Intuitively, one would think that the process is one of an analysis of our surroundings to construct a sense of reality, in a bottom-up fashion. However, such an approach would make us continuously a step behind in our assessment of our environment. Instead, Seth argues that our brains predict or generate our reality in a top-down manner, using sensory clues, and these "controlled hallucinations" are modified by continuous sensory input. Optical illusions demonstrate this phenomenon; our brains construct a reality that does not really exist. In the same way, our sense of self is constructed by a "best guess" of who we are, based on what our internal senses tell us.¹⁰¹ This internal sense is surprisingly malleable. The classic rubber hand illusion describes a procedure where tactile stimulation of a rubber hand in one's field of view coupled with simultaneous stimulation of one's real hand, which is hidden,

leads to a sense of ownership of the rubber hand as part of the body. $^{102}\,$

Seth goes on to explain how this predictive aspect of constructing reality also applies to our physiology. Our bodies' physiology often changes in anticipation of an action: for example, commencing digestion before we have started eating, or mobilizing energy reserves before a race. This phenomenon is called allostasis, in contrast to the better-known homeostasis. Homeostasis is inadequate because it is always a step behind, so it needs to be supplemented by the more-predictive allostasis.¹⁰³

How pervasive is this predictive aspect of interpreting reality? While not discussing gender, the social psychologist Jonathan Haidt made a similar argument a decade ago in his book *The Righteous Mind*, in which he shows how intuition *precedes* rationality, and that "explanations" are often *post hoc* rationalizations.¹⁰⁴ This phenomenon is also reminiscent of the difficulty of people to give up mistaken beliefs and conspiracy theories despite contrary evidence.

Could gender dysphoria be an example of people making incorrect assessments of their gender? This would not preclude biological contributions, such as hormones, but incorrect generation of one's identity may also occur in gender dysphoria. I hasten to add that I am not implying that gender dysphoria is something that people just "make up," as if it were easy to dispel this incongruence. Nonetheless, Seth's research, and our own personal experiences, indicate that we can easily be mistaken about what we think is reality. One would think that a misconception like that of gender would be easily corrected, simply by looking at one's own body. However, Seth cites other body ownership conditions such as phantom limb syndrome, asomatognosia, and xenomelia (the sense that an extremity does not belong to one's body and should be amputated¹⁰⁵) as persistent examples of disorders of our sense of self.¹⁰⁶ One could add anorexia and body dysmorphic disorder¹⁰⁷ to the list.

Several lines of evidence suggest that body misperception could lead to gender incongruence. It may seem surprising, but multiple studies indicate that our own sense of gender is not as fixed as we might expect.¹⁰⁸ Magnetic resonance imaging studies in both trans men and trans women found weaker structural and functional connections in regions of the brain that process their own body perception in

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the context of self.¹⁰⁹ In a different study, researchers used a variation of the rubber hand illusion to alter the subject's sense of gender.¹¹⁰ Subjects wore virtual reality goggles that presented a body of the opposite sex to theirs in place of where their body was. They then watched that body being stroked on the leg and abdomen, simultaneous to their own body being stroked in the same locations. After a few minutes of this activity, their sense of body ownership moved toward that of the opposite sex.

This malleability of self-perception extends to social media, which is a prominent means by which adolescents decide that they are trans.¹¹¹ Adolescents who feel isolated from their communities—recall that many cases of gender incongruence have significant comorbidities—can readily find a replacement community online, where social media influencers convince them that they are trans. Websites such as TrevorSpace are devoted to supporting LGBTQ adolescents.¹¹² While such information may be helpful for some, this information is not given by someone with a personal knowledge of them and their situation. Moreover, gender-affirming counseling, as opposed to watchful waiting, can likewise perpetuate and reify this misconception.

A common feature of early onset gender dysphoria is desistance upon reaching puberty. Could the development of secondary sexual characteristics provide enough of a corrective in some people to dissipate the gender dysphoria? What about those for whom it does not dissipate? A characteristic of gender dysphoria is the sense that one's sexual organs (for example, penis, breasts) do not belong to the body and greatly contribute to the dysphoria, which is reminiscent of xenomelia.¹¹³ Along these lines, a study of FtM transgender individuals found differences in brain activation by stimulation of a sexed body part (breast) versus a nonsexed body part (hand) between transgender individuals and controls, suggesting differences in neural representation of the body in gender dysphoria.¹¹⁴ Finally, a controversial proposal was made by Stephen Gliske, who suggested that gender dysphoria is a condition that involves the distress, social behavioral, and bodyownership networks (more on this below).¹¹⁵

Could it be that one's misperception of one's own gender is actually the *cause* of the dysphoria, leading one to see one's sexed body parts as not belonging to them? The rubber hand and the opposite-body illusions are fleeting and quickly resolved, but could a combination of hormonal and environmental conditions direct someone to a more robust gender dysphoria, one that cannot so easily be resolved? While this is beyond my area of expertise, I look forward to future studies, particularly collaborative work by Christians in biology and psychology, to provide clarity to this question.

Christian Perspectives

Having covered many potentially controversial aspects of the science of gender dysphoria and various treatments, we need to see how a Christian perspective can inform us on how to approach these controversies. Sadly, this topic has become highly polarized, and whatever position is taken by one will result in disappointment and possible hurt for others. Various denominations and individuals have expressed differing Christian perspectives on this topic.¹¹⁶ Space does not permit me to go into depth here, and a trained theologian might provide further insight, but allow me to make a few observations.

Although the Bible does not directly address transgender issues, we can nevertheless use scriptural guidelines to help us. First, as Christians who are called to love God above all and our neighbor as ourselves, we need to act in a manner that is consistent with scripture and in the person's best interest. All human beings are created in the image of God and deserve our love and care, particularly those who are suffering. To this end, one can appreciate the desire to destigmatize gender dysphoria. Moreover, assigned gender roles, whether by our culture or (mis)perceived biblical standards, can exacerbate the stress in someone who does not fit their gender stereotype.

Second, the binary of sex and gender are rooted in creation. Although he does not directly address gender dysphoria, Christopher West, in his book on Pope John Paul II's *Theology of the Body*, describes how the creational structure woven throughout scripture is one of (binary) complementarity and relationship.¹¹⁷ To list just a few examples, marriage and sexual union are depicted in the Garden of Eden (Gen. 2:23), the first sin marred that relationship (Gen. 3:12), an entire book of the Bible (Song of Songs) is about sex, Jesus's incarnation was a conception (Luke 1:35), his first miracle was at a wedding (John 2:11), and the church is the bride of Christ (Rev. 22:17). One

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of the most grievous sins is adultery (for example, Genesis 6, Exodus 32, and Numbers 25, not to mention the many references in the epistles). Idolatry is depicted as adultery: for example, consider the book of Hosea and also the Ten Commandments, in which both idolatry and adultery are prohibited. Moreover, one's sex is integral to one's identity, even after death. For example, biblical characters in the intermediate state (Samuel, Elijah, and Moses) or after resurrection (Jesus) retained their sex, apart from the body.

Despite this pattern of complementarity, however, there clearly are exceptions. Not all humans live in a complementary relationship. Some, either by choice or by circumstance, never marry. Indeed, Paul describes the ability to remain single as a gift from God (1 Cor. 7:7). But these are exceptions. Does being transgender or nonbinary also fall into the category of a legitimate exception to the pattern?

Yarhouse and Sadusky describe three approaches that Christians take toward transgender questions: the *integrity*, the *disability*, and the *diversity* approaches.¹¹⁸

The *integrity* approach holds that God created a binary of sex and gender. Any deviation from that binary is sin and the goals of treatment must be conformity of gender to one's biological sex. If that is not possible, then the dysphoria must be a burden to carry because of the Fall.¹¹⁹ The integrity position sometimes points to Deuteronomy 22:5, which is a prohibition of people wearing clothes of the opposite sex. However, it is argued that this verse is irrelevant to the transgender discussion because it refers to deception (avoiding or entering military service, or men gaining access to women's spaces) and does not apply to cross-dressing or gender dysphoria.¹²⁰ Cross-dressing by people with gender dysphoria is palliative, done to relieve distress, and not done for deception. While the attraction of the integrity position is that it takes scripture seriously and strives to live by what it says, those holding the integrity position are obliged to be careful to appreciate fully the possible biological causes of the condition and the inability of some people to relieve their dysphoria without transitioning. While there are some people who have detransitioned as part of their religious conversion,¹²¹ one cannot extrapolate from a few examples to all who suffer from gender dysphoria.

The *disability* (or disorder) approach likewise holds to a binary of sex and gender as rooted in creation, but recognizes that we live in a fallen world, and sometimes we need to make allowances for that fact. Sometimes sex and gender are incongruent, and the dysphoria cannot simply be wished away or endured. As was mentioned earlier, suicide rates in gender-dysphoric individuals are frighteningly high before (and after) transitioning. Suggesting that people can always just tough it out is insensitive and futile.

The *diversity* approach holds that while the sex/gender binary in creation are descriptive, they are not prescriptive. A spectrum of sex and gender are welcome, not as a disability but as part of the diversity in creation.¹²² This position is consistent with the WPATH and APA standards of care, which describe gender incongruence as an aspect of diversity, not pathology.¹²³ Austen Hartke has made the comparison with eunuchs, who are outside the male/ female norm but are welcomed in the church (Acts 8:35ff).¹²⁴ The attraction of this position is the evident love and concern that it holds for those who suffer from gender dysphoria. However, depathologizing a condition like gender incongruence (which this approach and WPATH and APA do) may also be unhelpful, if the treatment for it is so radical that it involves loss of fertility, disfiguring surgery, and lifelong hormone treatments.

How do we deal with situations that do not conform to the usual pattern? The integrity and disability approaches argue that we should maintain a holistic view of ourselves, where possible, maintaining consistency between gender and sex. The body is not irrelevant. Many transgender people instinctively agree, and this explains why they undergo hormonal treatments and surgeries to relieve their dysphoria and align their gender and sex. The challenge is in knowing what should be changed when there is incongruence. Do we maintain a conservative approach, doing only as much as is needed to relieve the dysphoria (if that is possible), or is the goal a full transition?

Can we get guidance by comparing transitioning for gender dysphoria to other health conditions? It is not comparable to same-sex attraction. We do not encourage someone who is same-sex attracted to act on those impulses because the Bible forbids *any* sex outside of marriage. The fact that there is a biblical

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prohibition indicates that it is possible to withstand these temptations (1 Cor. 10:13). Alternatively, a possible comparison may be someone with cancer. We generally support cancer treatments that may require the removal of a body part or the use of chemotherapeutic drugs that will affect one's quality of life because these treatments achieve the greater goal of saving the patient's life. A still closer (but rare) comparison may be xenomelia, described above, in which a body part is felt not to belong to the body and therefore must be amputated. In both cases, there is the prospect of body-altering surgery on an individual who is otherwise physically and psychologically healthy but has this particular psychological trauma. By making an analogy to gender dysphoria, a case has been made in favor of amputation for xenomelia.125

On the other hand, Monique Robles, publishing in a Catholic bioethical journal, argues that transition "violates the body-soul union, disregards the principle of totality and integrity, and debases the dignity of humanity."¹²⁶ While there may be some merit to the arguments, one must also consider that, in this broken world, transitioning may be making the best of a difficult situation.

Final Thoughts

How did we go from a time when people with gender dysphoria were shunned from society, to today when sex changes are celebrated? The pendulum has now shifted to the point that any questioning of the legitimacy of gender dysphoria is met with vehement opposition.

Gliske's article proposing a scientific basis for gender incongruence was withdrawn by the journal, in part because of claims that it was disrespectful and pathologized gender dysphoria.¹²⁷ When Ryan Anderson's book *When Harry Became Sally* critiqued this cultural shift,¹²⁸ it received considerable opposition from the LGBT community (it is still not available for purchase on Amazon).

Carl Trueman in *The Rise and Triumph of the Modern Self* traces the importance of one's personal identity, from Rousseau, through Nietzsche, Sartre, de Beauvoir, Freud, to the present day.¹²⁹ There isn't space in this article to outline his arguments, but clearly the tide has shifted when it comes to our understanding of sex and gender. Even the secular community is raising concerns. Blaire White and Buck Angel, both trans people, express their fears on YouTube about indiscriminate transitioning of children and adolescents,¹³⁰ and sex researcher Debra Soh also voices concerns in her book *The End of Gender*.¹³¹

For many, gender incongruence/dysphoria is a very real condition, which causes considerable distress in those who suffer from it. In many cases, the underlying causes are not well understood. Full understanding and accurate diagnosis remain a challenge, as does finding a standard path for treatment.

As Christians, we cannot ignore this condition, either in our churches or from our task in the society at large. As agents of restoration, we are called to do what we can to help those suffering from gender dysphoria. This is no small task, however; it requires collaborative efforts by people trained in different fields, including biology, psychology, social work, philosophy, and theology. In addition, we must look to both science and scripture to guide us in these investigations. While we recognize that in this life we may make only small beginnings in that task, we can look forward to the time when Christ will return to make all things new.

Notes

¹Arthur P. Arnold, "The Organizational-Activational Hypothesis as the Foundation for a Unified Theory of Sexual Differentiation of All Mammalian Tissues," *Hormones and Behavior* 55, no. 5 (May 2009): 570–78, https://doi.org/10.1016/j.yhbeh.2009.03.011; Jo-Anne Finegan, Betty Bartleman, and P. Y. Wong, "A Window for the Study of Prenatal Sex Hormone Influences on Postnatal Development," *The Journal of Genetic Psychology* 150, no. 1 (March 1989): 101–12, https://doi.org/10.1080/00221325.1989.9914580.

²Katherine A. O'Hanlan, Jennifer C. Gordon, and Mackenzie W. Sullivan, "Biological Origins of Sexual Orientation and Gender Identity: Impact on Health," Gynecologic Oncology 149, no. 1 (April 1, 2018): 33-42, https://doi .org/10.1016/j.ygyno.2017.11.014; Julie Bakker, "The Role of Steroid Hormones in the Sexual Differentiation of the Human Brain," Journal of Neuroendocrinology 34, no. 2 (2021): e13050, https://doi.org/10.1111/jne.13050; and Julie Bakker and Michael J. Baum, "Role for Estradiol in Female-Typical Brain and Behavioral Sexual Differentiation," Frontiers in Neuroendocrinology 29, no. 1 (January 2008): 1-16, https://doi.org/10.1016/j.yfrne.2007.06.001. The situation is more complicated in rodents, on whom most studies have been done, where testosterone in the brain is converted to estrogen by the enzyme aromatase. Although aromatase is also found in the human brains, the importance of estrogen in human brain sexualization is unclear.

³Fausto-Sterling uses the term gender/sex to indicate the interconnectedness of sex and gender, which I welcome.

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