The New Atlantis
A Journal of Technology & Society

Part Three

Gender Identity

The concept of biological sex is well defined, based on the binary roles that males and females play in reproduction. By contrast, the concept of gender is not well defined. It is generally taken to refer to behaviors and psychological attributes that tend to be typical of a given sex. Some individuals identify as a gender that does not correspond to their biological sex. The causes of such cross-gender identification remain poorly understood. Research investigating whether these transgender individuals have certain physiological features or experiences in common with the opposite sex, such as brain structures or atypical prenatal hormone exposures, has so far been inconclusive. Gender dysphoria—a sense of incongruence between one's biological sex and one's gender, accompanied by clinically significant distress or impairment—is sometimes treated in adults by hormones or surgery, but there is little scientific evidence that these therapeutic interventions have psychological benefits. Science has shown that gender identity issues in children usually do not persist into adolescence or adulthood, and there is little scientific evidence for the therapeutic value of puberty-delaying treatments. We are concerned by the increasing tendency toward encouraging children with gender identity issues to transition to their preferred gender through medical and then surgical procedures. There is a clear need for more research in these areas.

As described in Part One, there is a widely held belief that *sexual orientation* is a well-defined concept, and that it is innate and fixed in each person—as it is often put, gay people are "born that way." Another emerging and related view is that *gender identity*—the subjective, internal sense of being a man or a woman (or some other gender category)—is also fixed at birth or at a very early age and can diverge from a person's biological sex. In the case of children, this is sometimes articulated by saying that a little boy may be trapped in a little girl's body, or vice versa.

In Part One we argued that scientific research does not give much support to the hypothesis that sexual orientation is innate and fixed. We will argue here, similarly, that there is little scientific evidence that gender identity is fixed at birth or at an early age. Though biological sex is innate, and gender identity and biological sex are related in complex ways, they

are not identical; gender is sometimes defined or expressed in ways that have little or no biological basis.

Key Concepts and Their Origins

To clarify what is meant by "gender" and "sex," we begin with a widely used definition, here quoted from a pamphlet published by the American Psychological Association (APA):

> *Sex* is assigned at birth, refers to one's biological status as either male or female, and is associated primarily with physical attributes such as chromosomes, hormone prevalence, and external and internal anatomy. *Gender* refers to the socially constructed roles, behaviors, activities, and attributes that a given society considers appropriate for boys and men or girls and women. These influence the ways that people act, interact, and feel about themselves. While aspects of biological sex are similar across different cultures, aspects of gender may differ.[1]

This definition points to the obvious fact that there are social norms for men and women, norms that vary across different cultures and that are not simply determined by biology. But it goes further in holding that gender is wholly "socially constructed"—that it is detached from biological sex. This idea has been an important part of a feminist movement to reform or eliminate traditional gender roles. In the classic feminist book *The Second Sex* (1949), Simone de Beauvoir wrote that "one is not born, but becomes a woman."[2] This notion is an early version of the now familiar distinction between sex as a biological designation and gender as a cultural construct: though one is born, as the APA explains, with the "chromosomes, hormone prevalence, and external and internal anatomy" of a female, one is socially conditioned to take on the "roles, behaviors, activities, and attributes" of a woman.

Developments in feminist theory in the second half of the twentieth century further solidified the position that gender is socially constructed. One of the first to use the term "gender" as distinct from sex in the social-science literature was Ann Oakley in her 1972 book, *Sex, Gender and Society*.[3] In the 1978 book *Gender: An Ethnomethodological Approach*, psychology professors Suzanne Kessler and Wendy McKenna argued that "gender is a social construction, that a world of two 'sexes' is a result of the socially shared, taken for granted methods which members use to construct reality."[4]

Anthropologist Gayle Rubin expresses a similar view, writing in 1975 that "Gender is a socially imposed division of the sexes. It is a product of

the social relations of sexuality."[5] According to her argument, if it were not for this social imposition, we would still have males and females but not "men" and "women." Furthermore, Rubin argues, if traditional gender roles are socially constructed, then they can also be *de*constructed, and we can eliminate "obligatory sexualities and sex roles" and create "an androgynous and genderless (though not sexless) society, in which one's sexual anatomy is irrelevant to who one is, what one does, and with whom one makes love."[6]

The relationship between gender theory and the deconstruction or overthrowing of traditional gender roles is made even clearer in the works of the influential feminist theorist Judith Butler. In works such as *Gender Trouble: Feminism and the Subversion of Identity* (1990)[7] and *Undoing Gender* (2004)[8] Butler advances what she describes as "performativity theory," according to which being a woman or man is not something that one *is* but something that one *does*. "Gender is neither the causal result of sex nor as seemingly fixed as sex," as she put it.[9] Rather, gender is a constructed status radically independent from biology or bodily traits, "a free floating artifice, with the consequence that *man* and *masculine* might just as easily signify a female body as a male one, and *woman* and *feminine* a male body as easily as a female one."[10]

This view, that gender and thus gender identity are fluid and plastic, and not necessarily binary, has recently become more prominent in popular culture. An example is Facebook's move in 2014 to include 56 new ways for users to describe their gender, in addition to the options of male and female. As Facebook explains, the new options allow the user to "feel comfortable being your true, authentic self," an important part of which is "the expression of gender."[11] Options include *agender*, several *cis-* and *trans-* variants, *gender fluid*, *gender questioning*, *neither*, *other*, *pangender*, and *two-spirit*.[12]

Whether or not Judith Butler was correct in describing traditional gender roles of men and women as "performative," her theory of gender as a "free-floating artifice" does seem to describe this new taxonomy of gender. As these terms multiply and their meanings become more individualized, we lose any common set of criteria for defining what gender distinctions mean. If gender is entirely detached from the binary of biological sex, gender could come to refer to any distinctions in behavior, biological attributes, or psychological traits, and each person could have a gender defined by the unique combination of characteristics the person possesses. This *reductio ad absurdum* is offered to present the possibility that defining gender too broadly could lead to a definition that has little meaning.

Alternatively, gender identity could be defined in terms of sex-typical traits and behaviors, so that being a boy means behaving in the ways boys typically behave—such as engaging in rough-and-tumble play and expressing an interest in sports and liking toy guns more than dolls. But this would imply that a boy who plays with dolls, hates guns, and refrains from sports or rough-and-tumble play might be considered to be a girl, rather than simply a boy who represents an exception to the typical patterns of male behavior. The ability to recognize exceptions to sex-typical behavior relies on an understanding of maleness and femaleness that is independent of these stereotypical sex-appropriate behaviors. The underlying basis of maleness and femaleness is the distinction between the reproductive roles of the sexes; in mammals such as humans, the female gestates offspring and the male impregnates the female. More universally, the male of the species fertilizes the egg cells provided by the female of the species. This conceptual basis for sex roles is binary and stable, and allows us to distinguish males from females on the grounds of their reproductive systems, even when these individuals exhibit behaviors that are not typical of males or females.

To illustrate how reproductive roles define the differences between the sexes even when behavior appears to be atypical for the particular sex, consider two examples, one from the diversity of the animal kingdom, and one from the diversity of human behavior. First, we look at the emperor penguin. Male emperor penguins provide more care for eggs than do females, and in this sense, the male emperor penguin could be described as more maternal than the female.[13] However, we recognize that the male emperor penguin is not in fact female but rather that the species represents an exception to the general, but not universal, tendency among animals for females to provide more care than males for offspring. We recognize this because sex-typical behaviors like parental care do not define the sexes; the individual's role in sexual reproduction does.

Even other sex-typical biological traits, such as chromosomes, are not necessarily helpful for defining sex in a universal way, as the penguin example further illustrates. As with other birds, the genetics of sex determination in the emperor penguin is different than the genetics of sex determination in mammals and many other animals. In humans, males have XY chromosomes and females have XX chromosomes; that is, males have a unique sex-determining chromosome that they do not share with females, while females have two copies of a chromosome that they share with males. But in birds, it is females, not males, that have and pass on the sex-specific chromosome.[14] Just as the observation that

male emperor penguins nurture their offspring more than their partners did not lead zoologists to conclude that the egg-laying member of the emperor penguin species was in fact the male, the discovery of the ZW sex-determination system in birds did not lead geneticists to challenge the age-old recognition that hens are females and roosters are males. The only variable that serves as the fundamental and reliable basis for biologists to distinguish the sexes of animals is their role in reproduction, not some other behavioral or biological trait.

Another example that, in this case, only appears to be non-sex-typical behavior is that of Thomas Beatie, who made headlines as a man who gave birth to three children between 2008 and 2010.[15] Thomas Beatie was born a woman, Tracy Lehuanani LaGondino, and underwent a surgical and legal transition to living as a man before deciding to have children. Because the medical procedures he underwent did not involve the removal of his ovaries or uterus, Beatie was capable of bearing children. The state of Arizona recognizes Thomas Beatie as the father of his three children, even though, biologically, he is their mother. Unlike the case of the male emperor penguin's ostensibly maternal, "feminine" parenting behavior, Beatie's ability to have children does not represent an exception to the normal inability of males to bear children. The labeling of Beatie as a man despite his being biologically female is a personal, social, and legal decision that was made without any basis in biology; nothing whatsoever in biology suggests Thomas Beatie is a male.

In biology, an organism is male or female if it is structured to perform one of the respective roles in reproduction. This definition does not require any arbitrary measurable or quantifiable physical characteristics or behaviors; it requires understanding the reproductive system and the reproduction process. Different animals have different reproductive systems, but sexual reproduction occurs when the sex cells from the male and female of the species come together to form newly fertilized embryos. It is these reproductive roles that provide the conceptual basis for the differentiation of animals into the biological categories of male and female. There is no other widely accepted biological classification for the sexes.

But this definition of the biological category of sex is not universally accepted. For example, philosopher and legal scholar Edward Stein maintains that infertility poses a crucial problem for defining sex in terms of reproductive roles, writing that defining sex in terms of these roles would define "infertile males as females."[16] Since an infertile male cannot play the reproductive role for which males are structured, and an infertile

female cannot play the reproductive role for which females are structured, according to this line of thinking, defining sex in terms of reproductive roles would not be appropriate, as infertile males would be classified as females, and infertile females as males. Nevertheless, while a reproductive system structured to serve a particular reproductive role may be impaired in such a way that it cannot perform its function, the system is still recognizably structured for that role, so that biological sex can still be defined strictly in terms of the structure of reproductive systems. A similar point can be made about heterosexual couples who choose not to reproduce for any of a variety of reasons. The male and female reproductive systems are generally clearly recognizable, regardless of whether or not they are being used for purposes of reproduction.

The following analogy illustrates how a system can be recognized as having a particular purpose, even when that system is dysfunctional in a way that renders it incapable of carrying out its purpose: Eyes are complex organs that function as processors of vision. However, there are numerous conditions affecting the eye that can impair vision, resulting in blindness. The eyes of the blind are still recognizably organs structured for the function of sight. Any impairments that result in blindness do not affect the purpose of the eye—any more than wearing a blindfold—but only its function. The same is true for the reproductive system. Infertility can be caused by many problems. However, the reproductive system continues to exist for the purpose of begetting children.

There are individuals, however, who are biologically "intersex," meaning that their sexual anatomy is ambiguous, usually for reasons of genetic abnormalities. For example, the clitoris and penis are derived from the same embryonic structures. A baby may display an abnormally large clitoris or an abnormally small penis, causing its biological sex to be difficult to determine long after birth.

The first academic article to use the term "gender" appears to be the 1955 paper by the psychiatry professor John Money of Johns Hopkins on the treatment of "intersex" children (the term then used was "hermaphrodites").[17] Money posited that gender identity, at least for these children, was fluid and that it could be constructed. In his mind, making a child identify with a gender only required constructing sex-typical genitalia and creating a gender-appropriate environment for the child. The chosen gender for these children was often female—a decision that was not based on genetics or biology, nor on the belief that these children were "really" girls, but, in part, on the fact that at the time it was easier surgically to construct a vagina then it was to construct a penis.

The most widely known patient of Dr. Money was David Reimer, a boy who was not born with an intersex condition but whose penis was damaged during circumcision as an infant.[18] David was raised by his parents as a girl named Brenda, and provided with both surgical and hormonal interventions to ensure that he would develop female-typical sex characteristics. However, the attempt to conceal from the child what had happened to him was not successful—he self-identified as a boy, and eventually, at the age of 14, his psychiatrist recommended to his parents that they tell him the truth. David then began the difficult process of reversing the hormonal and surgical interventions that had been performed to feminize his body. But he continued to be tormented by his childhood ordeal, and took his own life in 2004, at the age of 38.

David Reimer is just one example of the harm wrought by theories that gender identity can socially and medically be reassigned in children. In a 2004 paper, William G. Reiner, a pediatric urologist and child and adolescent psychiatrist, and John P. Gearhart, a professor of pediatric urology, followed up on the sexual identities of 16 genetic males affected by cloacal exstrophy—a condition involving a badly deformed bladder and genitals. Of the 16 subjects, 14 were assigned female sex at birth, receiving surgical interventions to construct female genitalia, and were raised as girls by their parents; 6 of these 14 later chose to identify as males, while 5 continued to identify as females and 2 declared themselves males at a young age but continued to be raised as females because their parents rejected the children's declarations. The remaining subject, who had been told at age 12 that he was born male, refused to discuss sexual identity.[19] So the assignment of female sex persisted in only 5 of the 13 cases with known results.

This lack of persistence is some evidence that the assignment of sex through genital construction at birth with immersion into a "gender-appropriate" environment is not likely to be a successful option for managing the rare problem of genital ambiguity from birth defects. It is important to note that the ages of these individuals at last follow-up ranged from 9 to 19, so it is possible that some of them may have subsequently changed their gender identities.

Reiner and Gearhart's research indicates that gender is not arbitrary; it suggests that a biological male (or female) will probably not come to identify as the opposite gender after having been altered physically and immersed into the corresponding gender-typical environment. The plasticity of gender appears to have a limit.

What is clear is that biological sex is not a concept that can be reduced to, or artificially assigned on the basis of, the type of external genitalia

alone. Surgeons are becoming more capable of constructing artificial genitalia, but these "add-ons" do not change the biological sex of the recipients, who are no more capable of playing the reproductive roles of the opposite biological sex than they were without the surgery. Nor does biological sex change as a function of the environment provided for the child. No degree of supporting a little boy in converting to be considered, by himself and others, to be a little girl makes him biologically a little girl. The scientific definition of biological sex is, for almost all human beings, clear, binary, and stable, reflecting an underlying biological reality that is not contradicted by exceptions to sex-typical behavior, and cannot be altered by surgery or social conditioning.

In a 2004 article summarizing the results of research related to intersex conditions, Paul McHugh, the former chief of psychiatry at Johns Hopkins Hospital (and the coauthor of this report), suggested:

> We in the Johns Hopkins Psychiatry Department eventually concluded that human sexual identity is mostly built into our constitution by the genes we inherit and the embryogenesis we undergo. Male hormones sexualize the brain and the mind. Sexual dysphoria—a sense of disquiet in one's sexual role—naturally occurs amongst those rare males who are raised as females in an effort to correct an infantile genital structural problem.[20]

We now turn our attention to transgender individuals—children and adults—who choose to identify as a gender different from their biological sex, and explore the meaning of gender identity in this context and what the scientific literature tells us about its development.

Gender Dysphoria

While biological sex is, with very few exceptions, a well-defined, binary trait (male versus female) corresponding to how the body is organized for reproduction, *gender identity* is a more subjective attribute. For most people, their own gender identity is probably not a significant concern; most biological males identify as boys or men, and most biological females identify as girls or women. But some individuals experience an incongruence between their biological sex and their gender identity. If this struggle causes them to seek professional help, then the problem is classified as "gender dysphoria."

Some male children raised as females, as described in Reiner and colleagues' 2004 study, came to experience problems with their gender

identity when their subjective sense of being boys conflicted with being identified and treated as girls by their parents and doctors. The biological sex of the boys was not in question (they had an XY genotype), and the cause of gender dysphoria lay in the fact that they were genetically male, came to identify as male, but had been assigned female gender identities. This suggests that gender identity can be a complex and burdensome issue for those who choose (or have others choose for them) a gender identity opposite their biological sex.

But the cases of gender dysphoria that are the subject of much public debate are those in which individuals come to identify as genders different from those based on their biological sex. These people are usually identified, and describe themselves, as "transgender."*

According to the fifth edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*), gender dysphoria is marked by "incongruence between one's experienced/expressed gender and assigned gender," as well as "clinically significant distress or impairment in social, occupational, or other important areas of functioning."[21]

It is important to clarify that gender dysphoria is not the same as gender nonconformity or gender identity disorder. Gender nonconformity describes an individual who behaves in a manner contrary to the gender-specific norms of his or her biological sex. As the *DSM-5* notes, most transvestites, for instance, are not transgender—men who dress as women typically do not identify themselves as women.[22] (However, certain forms of transvestitism can be associated with late-onset gender dysphoria.[23])

Gender identity disorder, an obsolete term from an earlier version of the *DSM* that was removed in its fifth edition, was used as a psychiatric diagnosis. If we compare the diagnostic criteria for gender dysphoria (the current term) and gender identity disorder (the former term), we see that both require the patient to display "a marked incongruence between one's

* A note on terminology: In this report, we generally use the term *transgender* to refer to persons for whom there is an incongruity between the gender identity they understand themselves to possess and their biological sex. We use the term *transsexual* to refer to individuals who have undergone medical interventions to transform their appearance to better correspond with that of their preferred gender. The most familiar colloquial term used to describe the medical interventions that transform the appearance of transgender individuals may be "sex change" (or, in the case of surgery, "sex-change operation"), but this is not commonly used in the scientific and medical literature today. While no simple terms for these procedures are completely satisfactory, in this report we employ the commonly used terms *sex reassignment* and *sex-reassignment surgery*, except when quoting a source that uses "gender reassignment" or some other term.

experienced/expressed gender and assigned gender."[24] The key difference is that a diagnosis of gender dysphoria requires the patient additionally to experience a "clinically significant distress or impairment in social, occupational, or other important areas of functioning" associated with these incongruent feelings.[25] Thus the major set of diagnostic criteria used in contemporary psychiatry does not designate all transgender individuals as having a psychiatric disorder. For example, a biological male who identifies himself as a female is not considered to have a psychiatric disorder unless the individual is experiencing significant psychosocial distress at the incongruence. A diagnosis of gender dysphoria may be part of the criteria used to justify sex-reassignment surgery or other clinical interventions. Furthermore, a patient who has had medical or surgical modifications to express his or her gender identity may still suffer from gender dysphoria. It is the nature of the struggle that defines the disorder, not the fact that the expressed gender differs from the biological sex.

There is no scientific evidence that all transgender people have gender dysphoria, or that they are all struggling with their gender identities. Some individuals who are not transgender—that is, who do not identify as a gender that does not correspond with their biological sex—might nonetheless struggle with their gender identity; for example, girls who behave in some male-typical ways might experience various forms of distress without ever coming to identify as boys. Conversely, individuals who do identify as a gender that does not correspond with their biological sex may not experience clinically significant distress related to their gender identity. Even if only, say, 40% of individuals who identify as a gender that does not correspond with their biological sex experience significant distress related to their gender identity, this would constitute a public health issue requiring clinicians and others to act to support those with gender dysphoria, and hopefully, to reduce the rate of gender dysphoria in the population. There is no evidence to suggest that the other 60% in this hypothetical—that is, the individuals who identify as a gender that does not correspond with their biological sex but who do not experience significant distress—would require clinical treatment.

The *DSM*'s concept of subjectively "experiencing" one's gender as incongruent from one's biological sex may require more critical scrutiny and possibly modification. The exact definition of gender dysphoria, however well-intentioned, is somewhat vague and confusing. It does not account for individuals who self-identify as transgender but do not experience dysphoria associated with their gender identity and who seek psychiatric care for functional impairment for problems unrelated to their

gender identity, such as anxiety or depression. They may then be mislabeled as having gender dysphoria simply because they have a desire to be identified as a member of the opposite gender, when they have come to a satisfactory resolution, subjectively, with this incongruence and may be depressed for reasons having nothing to do with their gender identity.

The *DSM-5* criteria for a diagnosis of gender dysphoria in children are defined in a "more concrete, behavioral manner than those for adolescents and adults."[26] This is to say that some of the diagnostic criteria for gender dysphoria in children refer to behaviors that are stereotypically associated with the opposite gender. Clinically significant distress is still necessary for a diagnosis of gender dysphoria in children, but some of the other diagnostic criteria include, for instance, a "strong preference for the toys, games, or activities stereotypically used or engaged in by the other gender."[27] What of girls who are "tomboys" or boys who are not oriented toward violence and guns, who prefer quieter play? Should parents worry that their tomboy daughter is really a boy stuck in a girl's body? There is no scientific basis for believing that playing with toys typical of boys defines a child as a boy, or that playing with toys typical of girls defines a child as a girl. The *DSM-5* criterion for diagnosing gender dysphoria by reference to gender-typical toys is unsound; it appears to ignore the fact that a child could display an *expressed* gender—manifested by social or behavioral traits—incongruent with the child's biological sex but without *identifying* as the opposite gender. Furthermore, even for children who do identify as a gender opposite their biological sex, diagnoses of gender dysphoria are simply unreliable. The reality is that they may have psychological difficulties in accepting their biological sex as their gender. Children can have difficulty with the expectations associated with those gender roles. Traumatic experiences can also cause a child to express distress with the gender associated with his or her biological sex.

Gender identity problems can also arise with intersex conditions (the presence of ambiguous genitalia due to genetic abnormalities), which we discussed earlier. These disorders of sex development, while rare, can contribute to gender dysphoria in some cases.[28] Some of these conditions include complete androgen insensitivity syndrome, where individuals with XY (male) chromosomes lack receptors for male sex hormones, leading them to develop the secondary sex characteristics of females, rather than males (though they lack ovaries, do not menstruate, and are consequently sterile).[29] Another hormonal disorder of sex development that can lead to individuals developing in ways that are not typical of their genetic sex include congenital adrenal hyperplasia, a condition that can

masculinize XX (female) fetuses.[30] Other rare phenomena such as genetic mosaicism[31] or chimerism,[32] where some cells in the individual's bodies contain XX chromosomes and others contain XY chromosomes, can lead to considerable ambiguity in sex characteristics, including individuals who possess both male and female gonads and sex organs.

While there are many cases of gender dysphoria that are not associated with these identifiable intersex conditions, gender dysphoria may still represent a different type of intersex condition in which the primary sex characteristics such as genitalia develop normally while secondary sex characteristics associated with the brain develop along the lines of the opposite sex. Controversy exists over influences determining the nature of neurological, psychological, and behavioral sex differences. The emerging consensus is that there may be some differences in patterns of neurological development in- and ex-utero for men and women.[33] Therefore, in theory, transgender individuals could be subject to conditions allowing a more female-type brain to develop within a genetic male (having the XY chromosomal patterns), and vice versa. However, as we will show in the next section, the research supporting this idea is quite minimal.

As a way of surveying the biological and social science research on gender dysphoria, we can list some of the important questions. Are there biological factors that influence the development of a gender identity that does not correspond with one's biological sex? Are some individuals born with a gender identity different from their biological sex? Is gender identity shaped by environmental or nurturing conditions? How stable are choices of gender identity? How common is gender dysphoria? Is it persistent across the lifespan? Can a little boy who thinks he is a little girl change over the course of his life to regard himself as male? If so, how often can such people change their gender identities? How would someone's gender identity be measured scientifically? Does self-understanding suffice? Does a biological girl become a gender boy by believing, or at least stating, she is a little boy? Do people's struggles with a sense of incongruity between their gender identity and biological sex persist over the life course? Does gender dysphoria respond to psychiatric interventions? Should those interventions focus on affirming the gender identity of the patient or take a more neutral stance? Do efforts to hormonally or surgically modify an individual's primary or secondary sex characteristics help resolve gender dysphoria? Does modification create further psychiatric problems for some of those diagnosed with gender dysphoria, or does it typically resolve existing psychiatric problems? We broach a few of these critical questions in the following sections.

Gender and Physiology

Robert Sapolsky, a Stanford professor of biology who has done extensive neuroimaging research, suggested a possible neurobiological explanation for cross-gender identification in a 2013 *Wall Street Journal* article, "Caught Between Male and Female." He asserted that recent neuroimaging studies of the brains of transgender adults suggest that they may have brain structures more similar to their gender identity than to their biological sex.[34] Sapolsky bases this assertion on the fact that there are differences between male and female brains, and while the differences are "small and variable," they "probably contribute to the sex differences in learning, emotion and socialization."[35] He concludes: "The issue isn't that sometimes people believe they are of a different gender than they actually are. Remarkably, instead, it's that sometimes people are born with bodies whose gender is different from what they actually are."[36] In other words, he claims that some people can have a female-type brain in a male body, or vice versa.

While this kind of neurobiological theory of cross-gender identification remains outside of the scientific mainstream, it has recently received scientific and popular attention. It provides a potentially attractive explanation for cross-gender identification, especially for individuals who are not affected by any known genetic, hormonal, or psychosocial abnormalities.[37] However, while Sapolsky may be right, there is fairly little support in the scientific literature for his contention. His neurological explanation for differences between male and female brains and those differences' possible relevance to cross-gender identification warrant further scientific consideration.

There are many small studies that attempt to define causal factors of the experience of incongruence between one's biological sex and felt gender. These studies are described in the following pages, each pointing to an influence that may contribute to the explanation for cross-gender identification.

Nancy Segal, a psychologist and geneticist, researched two case studies of identical twins discordant for female-to-male (FtM) transsexualism.[38] Segal notes that, according to another, earlier study that conducted nonclinical interviews with 45 FtM transsexuals, 60% suffered some form of childhood abuse, with 31% experiencing sexual abuse, 29% experiencing emotional abuse, and 38% physical abuse.[39] However, this earlier study did not include a control group and was limited by its small sample size, making it difficult to extract significant interactions, or generalizations, from the data.

Segal's own first case study was of a 34-year-old FtM twin, whose identical twin sister was married and the mother of seven children.[40] Several stressful events had occurred during the twins' mother's pregnancy, and they were born five weeks prematurely. When they were eight years old, their parents divorced. The FtM twin exhibited gender-nonconforming behavior early and it persisted throughout childhood. She became attracted to other girls in junior high school and as a teenager attempted suicide several times. She reported physical abuse and emotional abuse at the hand of her mother. The twins were raised in a Mormon household, in which transsexuality was not tolerated.[41] The twin sister had never questioned her gender identity but did experience some depression. For Segal, the FtM twin's gender nonconformity and abuse in childhood were factors that contributed to gender dysphoria; the other twin was not subject to the same stressors in childhood, and did not develop issues around her gender identity. Segal's second case study also concerned identical twins with one twin transitioning from female to male.[42] This FtM twin had early-onset nonconforming behaviors and attempted suicide as a young adult. At age 29 she underwent reassignment surgery, was well supported by family, met a woman, and married. As in the first case, the other twin was reportedly always secure in her female gender identity.

Segal speculates that each set of twins may have had uneven prenatal androgen exposures (though her study did not offer evidence to support this)[43] and concludes that "Transsexualism is unlikely to be associated with a major gene, but is likely to be associated with multiple genetic, epigenetic, developmental and experiential influences."[44] Segal is critical of the notion that the maternal abuse experienced by the FtM twin in her first case study may have played a causal role in the twin's "atypical gender identification" since the abuse "apparently *followed*" the twin's gender-atypical behaviors—though Segal acknowledges "it is possible that this abuse reinforced his already atypical gender identification."[45] These case studies, while informative, are not scientifically strong, and do not provide direct evidence for any causal hypotheses about the origins of atypical gender identification.

A source of more information—but also inadequate to make direct causal inferences—is a case analysis by Mayo Clinic psychiatrists J. Michael Bostwick and Kari A. Martin of an intersex individual born with ambiguous genitalia who was operated on and raised as a female.[46] By way of offering some background, the authors draw a distinction between gender identity disorder (an "inconsistency between perceived gender identity and phenotypic sex" that generally involves "no discernible neuroendocri-

nological abnormality"[47]), and intersexuality (a condition in which biological features of both sexes are present). They also provide a summary and classification scheme of the various types of intersex disorders. After a thorough discussion of the various intersex developmental issues that can lead to a disjunction between the brain and body, the authors acknowledge that "Some adult patients with severe dysphoria—transsexuals—have neither history nor objective findings supporting a known biological cause of brain-body disjunction."[48] These patients require thorough medical and psychiatric attention to avoid gender dysphoria.

After this helpful summary, the authors state that "Absent psychosis or severe character pathology, patients' subjective assertions are presently the most reliable standards for delineating core gender identity."[49] But it is not clear how we could consider subjective assertions more reliable in establishing gender identity, unless gender identity is defined as a completely subjective phenomenon. The bulk of the article is devoted to describing the various objectively discernible and identifiable ways in which one's identity as a male or female is imprinted on the nervous and endocrine system. Even when something goes wrong with the development of external genitalia, individuals are more likely to act in accordance with their chromosomal and hormonal makeup.[50]

In 2011, Giuseppina Rametti and colleagues from various research centers in Spain used MRI to study the brain structures of 18 FtM transsexuals who exhibited gender nonconformity early in life and experienced sexual attraction to females prior to hormone treatment.[51] The goal was to learn whether their brain features corresponded more to their biological sex or to their sense of gender identity. The control group consisted of 24 male and 19 female heterosexuals with gender identities conforming to their biological sex. Differences were noted in the white matter microstructure of specific brain areas. In untreated FtM transsexuals, that structure was more similar to that of heterosexual males than to that of heterosexual females in three of four brain areas.[52] In a complementary study, Rametti and colleagues compared 18 MtF transsexuals to 19 female and 19 male heterosexual controls.[53] These MtF transsexuals had white matter tract averages in several brain areas that fell between the averages of the control males and the control females. The values, however, were typically closer to the males (that is, to those that shared their biological sex) than to the females in most areas.[54] In controls the authors found that, as expected, the males had greater amounts of gray and white matter and higher volumes of cerebrospinal fluid than control females. The MtF transsexual brain volumes

were all similar to those of male controls and significantly different from those of females.[55]

Overall, the findings of these studies by Rametti and colleagues do not sufficiently support the notion that transgender individuals have brains more similar to their preferred gender than to the gender corresponding with their biological sex. Both studies are limited by small sample sizes and lack of a prospective hypothesis—both analyzed the MRI data to find the gender differences and then looked to see where the data from transgender subjects fit.

Whereas both of these MRI studies looked at brain *structure*, a functional MRI study by Emiliano Santarnecchi and colleagues from the University of Siena and the University of Florence looked at brain *function*, examining gender-related differences in spontaneous brain activity during the resting state.[56] The researchers compared a single FtM individual (declared cross-gender since childhood), and control groups of 25 males and 25 females, with regard to spontaneous brain activity. The FtM individual demonstrated a "brain activity profile more close to his biological sex than to his desired one," and based in part on this result the authors concluded that "untreated FtM transsexuals show a functional connectivity profile comparable to female control subjects."[57] With a sample size of one, this study's statistical power is virtually zero.

In 2013, Hsaio-Lun Ku and colleagues from various medical centers and research institutes in Taiwan also conducted functional brain imaging studies. They compared the brain activity of 41 transsexuals (21 FtMs, 20 MtFs) and 38 matched heterosexual controls (19 males and 19 females).[58] Arousal response of each cohort while viewing neutral as compared to erotic films was compared between groups. All of the transsexuals in the study reported sexual attractions to members of their natal, biological sex, and exhibited more sexual arousal than heterosexual controls when viewing erotic films that depicted sexual activity between subjects sharing their biological sex. A "selfness" score was also incorporated into the study, in which the researchers asked participants to "rate the degree to which you identify yourself as the male or female in the film."[59] The transsexuals in the study identified with those of their preferred gender more than the controls identified with those of their biological gender, in both erotic films and neutral films. The heterosexual controls did not identify themselves with either males or females in either of the film types. Ku and colleagues claim to have demonstrated characteristic brain patterns for sexual attraction as related to biological sex but did not make meaningful neurobiological gender-identity comparisons among the three cohorts. In

addition, they reported findings that transsexuals demonstrated psychosocial maladaptive defensive styles.

A 2008 study by Hans Berglund and colleagues from Sweden's Karolinska Institute and Stockholm Brain Institute used PET and fMRI scans to compare brain-area activation patterns in 12 MtF transgendered individuals who were sexually attracted to women with those of 12 heterosexual women and 12 heterosexual men.[60] The first set of subjects took no hormones and had not undergone sex-reassignment surgery. The experiment involved smelling odorous steroids thought to be female pheromones, and other sexually neutral odors such as lavender oil, cedar oil, eugenol, butanol, and odorless air. The results were varied and mixed between the groups for the various odors, which should not be surprising, since *post hoc* analyses usually lead to contradictory findings.

In summary, the studies presented above show inconclusive evidence and mixed findings regarding the brains of transgender adults. Brain-activation patterns in these studies do not offer sufficient evidence for drawing sound conclusions about possible associations between brain activation and sexual identity or arousal. The results are conflicting and confusing. Since the data by Ku and colleagues on brain-activation patterns are not universally associated with a particular sex, it remains unclear whether and to what extent neurobiological findings say anything meaningful about gender identity. It is important to note that regardless of their findings, studies of this kind cannot support any conclusion that individuals come to identify as a gender that does not correspond to their biological sex because of an innate, biological condition of the brain.

The question is not simply whether there are differences between the brains of transgender individuals and people identifying with the gender corresponding to their biological sex, but whether gender identity is a fixed, innate, and biological trait, even when it does not correspond to biological sex, or whether environmental or psychological causes contribute to the development of a sense of gender identity in such cases. Neurological differences in transgender adults might be the consequence of biological factors such as genes or prenatal hormone exposure, or of psychological and environmental factors such as childhood abuse, or they could result from some combination of the two. There are no serial, longitudinal, or prospective studies looking at the brains of cross-gender identifying children who develop to later identify as transgender adults. Lack of this research severely limits our ability to understand causal relationships between brain morphology, or functional activity, and the later development of gender identity different from biological sex.

More generally, it is now widely recognized among psychiatrists and neuroscientists who engage in brain imaging research that there are inherent and ineradicable methodological limitations of *any* neuroimaging study that simply associates a particular trait, such as a certain behavior, with a particular brain morphology.[61] (And when the trait in question is not a concrete behavior but something as elusive and vague as "gender identity," these methodological problems are even more serious.) These studies cannot provide statistical evidence nor show a plausible biological mechanism strong enough to support *causal connections* between a brain feature and the trait, behavior, or symptom in question. To support a conclusion of causality, even epidemiological causality, we need to conduct prospective longitudinal panel studies of a fixed set of individuals across the course of sexual development if not their lifespan.

Studies like these would use serial brain images at birth, in childhood, and at other points along the developmental continuum, to see whether brain morphology findings were there from the beginning. Otherwise, we cannot establish whether certain brain features caused a trait, or whether the trait is innate and perhaps fixed. Studies like those discussed above of individuals who already exhibit the trait are incapable of distinguishing between *causes* and *consequences* of the trait. In most cases transgender individuals have been acting and thinking for years in ways that, through learned behavior and associated neuroplasticity, may have produced brain changes that could differentiate them from other members of their biological or natal sex. The only definitive way to establish epidemiological causality between a brain feature and a trait (especially one as complex as gender identity) is to conduct prospective, longitudinal, preferably randomly sampled and population-based studies.

In the absence of such prospective longitudinal studies, large representative population-based samples with adequate statistical controls for confounding factors may help narrow the possible causes of a behavioral trait and thereby increase the probability of identifying a neurological cause.[62] However, because the studies conducted thus far use small convenience samples, none of them is especially helpful for narrowing down the options for causality. To obtain a better study sample, we would need to include neuroimaging in large-scale epidemiological studies. In fact, given the small number of transgender individuals in the general population,[63] the studies would need to be prohibitively large to attain findings that would reach statistical significance.

Moreover, if a study found significant differences between these groups—that is, a number of differences higher than what would be

expected by chance alone—these differences would refer to the average in a population of each group. Even if these two *groups* differed significantly for all 100 measurements, it would not necessarily indicate a biological difference among *individuals* at the extremes of the distribution. Thus, a randomly selected transgender individual and a randomly selected non-transgender individual might not differ on any of these 100 measurements. Additionally, since the probability that a randomly selected person from the general population will be transgender is quite small, statistically significant differences in the sample means are not sufficient evidence to conclude that a particular measurement is predictive of whether the person is transgender or not. If we measured the brain of an infant, toddler, or adolescent and found this individual to be closer to one cohort than another on these measures, it would not imply that this individual would grow up to identify as a member of that cohort. It may be helpful to keep this caveat in mind when interpreting research on transgender individuals.

In this context, it is important to note that there are no studies that demonstrate that any of the biological differences being examined have predictive power, and so all interpretations, usually in popular outlets, claiming or suggesting that a statistically significant difference between the brains of people who are transgender and those who are not is the cause of being transgendered or not—that is to say, that the biological differences determine the differences in gender identity—are unwarranted.

In short, the current studies on associations between brain structure and transgender identity are small, methodologically limited, inconclusive, and sometimes contradictory. Even if they were more methodologically reliable, they would be insufficient to demonstrate that brain structure is a cause, rather than an effect, of the gender-identity behavior. They would likewise lack predictive power, the real challenge for any theory in science.

For a simple example to illustrate this point, suppose we had a room with 100 people in it. Two of them are transgender and all others are not. I pick someone at random and ask you to guess the person's gender identity. If you know that 98 out of 100 of the individuals are not transgender, the safest bet would be to guess that the individual is not transgender, since that answer will be correct 98% of the time. Suppose, then, that you have the opportunity to ask questions about the neurobiology and about the natal sex of the person. Knowing the biology only helps in predicting whether the individual is transgender if it can improve on the original guess that the person is not transgender. So if knowing a characteristic of the individual's brain does not improve the ability to predict what group the patient belongs to, then the fact that the two groups differ at the mean is almost irrelevant.

Improving on the original prediction is very difficult for a rare trait such as being transgender, because the probability of that prediction being correct is already very high. If there really were a clear difference between the brains of transgender and non-transgender individuals, akin to the biological differences between the sexes, then improving on the original guess would be relatively easy. Unlike the differences between the sexes, however, there are no biological features that can reliably identify transgender individuals as different from others.

The consensus of scientific evidence overwhelmingly supports the proposition that a physically and developmentally normal boy or girl is indeed what he or she appears to be at birth. The available evidence from brain imaging and genetics does not demonstrate that the development of gender identity as different from biological sex is innate. Because scientists have not established a solid framework for understanding the causes of cross-gender identification, ongoing research should be open to psychological and social causes, as well as biological ones.

Transgender Identity in Children

In 2012, the *Washington Post* featured a story by Petula Dvorak, "Transgender at five,"[64] about a girl who at the age of 2 years began insisting that she was a boy. The story recounts her mother's interpretation of this behavior: "Her little girl's brain was different. Jean [her mother] could tell. She had heard about transgender people, those who are one gender physically but the other gender mentally." The story recounts this mother's distressed experiences as she began researching gender identity problems in children and came to understand other parents' experiences:

> Many talked about their painful decision to allow their children to publicly transition to the opposite gender—a much tougher process for boys who wanted to be girls. Some of what Jean heard was reassuring: Parents who took the plunge said their children's behavior problems largely disappeared, schoolwork improved, happy kid smiles returned. But some of what she heard was scary: children taking puberty blockers in elementary school and teens embarking on hormone therapy before they'd even finished high school.[65]

The story goes on to describe how the sister, Moyin, of the transgender child Tyler (formerly Kathryn) made sense of her sibling's identity:

> Tyler's sister, who's 8, was much more casual about describing her transgender sibling. "It's just a boy mind in a girl body," Moyin

> explained matter-of-factly to her second-grade classmates at her private school, which will allow Tyler to start kindergarten as a boy, with no mention of Kathryn.[66]

The remarks from the child's sister encapsulate the popular notion regarding gender identity: transgender individuals, or children who meet the diagnostic criteria for gender dysphoria, are simply "a boy mind in a girl body," or vice versa. This view implies that gender identity is a persistent and innate feature of human psychology, and it has inspired a gender-affirming approach to children who experience gender identity issues at an early age.

As we have seen above in the overview of the neurobiological and genetic research on the origins of gender identity, there is little evidence that the phenomenon of transgender identity has a biological basis. There is also little evidence that gender identity issues have a high rate of persistence in children. According to the *DSM-5*, "In natal [biological] males, persistence [of gender dysphoria] has ranged from 2.2% to 30%. In natal females, persistence has ranged from 12% to 50%."[67] Scientific data on persistence of gender dysphoria remains sparse due to the very low prevalence of the disorder in the general population, but the wide range of findings in the literature suggests that there is still much that we do not know about why gender dysphoria persists or desists in children. As the *DSM-5* entry goes on to note, "It is unclear if children 'encouraged' or supported to live socially in the desired gender will show higher rates of persistence, since such children have not yet been followed longitudinally in a systematic manner."[68] There is a clear need for more research in these areas, and for parents and therapists to acknowledge the great uncertainty regarding how to interpret the behavior of these children.

Therapeutic Interventions in Children

With the uncertainty surrounding the diagnosis of and prognosis for gender dysphoria in children, therapeutic decisions are particularly complex and difficult. Therapeutic interventions for children must take into account the probability that the children may outgrow cross-gender identification. University of Toronto researcher and therapist Kenneth Zucker believes that family and peer dynamics can play a significant role in the development and persistence of gender-nonconforming behavior, writing that

> it is important to consider both predisposing and perpetuating factors that might inform a clinical formulation and the development of

> a therapeutic plan: the role of temperament, parental reinforcement of cross-gender behavior during the sensitive period of gender identity formation, family dynamics, parental psychopathology, peer relationships and the multiple meanings that might underlie the child's fantasy of becoming a member of the opposite sex.[69]

Zucker worked for years with children experiencing feelings of gender incongruence, offering psychosocial treatments to help them embrace the gender corresponding with their biological sex—for instance, talk therapy, parent-arranged play dates with same-sex peers, therapy for co-occurring psychopathological issues such as autism spectrum disorder, and parent counseling.[70]

In a follow-up study by Zucker and colleagues of children treated by them over the course of thirty years at the Center for Mental Health and Addiction in Toronto, they found that gender identity disorder persisted in only 3 of the 25 girls they had treated.[71] (Zucker's clinic was closed by the Canadian government in 2015.[72])

An alternative to Zucker's approach that emphasizes affirming the child's preferred gender identity has become more common among therapists.[73] This approach involves helping the children to self-identify even more with the gender label they prefer at the time. One component of the gender-affirming approach has been the use of hormone treatments for adolescents in order to delay the onset of sex-typical characteristics during puberty and alleviate the feelings of dysphoria the adolescents will experience as their bodies develop sex-typical characteristics that are at odds with the gender with which they identify. There is relatively little evidence for the therapeutic value of these kinds of puberty-delaying treatments, but they are currently the subject of a large clinical study sponsored by the National Institutes of Health.[74]

While epidemiological data on the outcomes of medically delayed puberty is quite limited, referrals for sex-reassignment hormones and surgical procedures appear to be on the rise, and there is a push among many advocates to proceed with sex reassignment at younger ages. According to a 2013 article in *The Times* of London, the United Kingdom saw a 50% increase in the number of children referred to gender dysphoria clinics from 2011 to 2012, and a nearly 50% increase in referrals among adults from 2010 to 2012.[75] Whether this increase can be attributed to rising rates of gender confusion, rising sensitivity to gender issues, growing acceptance of therapy as an option, or other factors, the increase itself is concerning, and merits further scientific inquiry into the family dynamics

and other potential problems, such as social rejection or developmental issues, that may be taken as signs of childhood gender dysphoria.

A study of psychological outcomes following puberty suppression and sex-reassignment surgery, published in the journal *Pediatrics* in 2014 by child and adolescent psychiatrist Annelou L. C. de Vries and colleagues, suggested improved outcomes for individuals after receiving these interventions, with well-being improving to a level similar to that of young adults from the general population.[76] This study looked at 55 transgender adolescents and young adults (22 MtF and 33 FtM) from a Dutch clinic who were assessed three times: before the start of puberty suppression (mean age: 13.6 years), when cross-sex hormones were introduced (mean age: 16.7 years), and at least one year after sex-reassignment surgery (mean age: 20.7 years). The study did not provide a matched group for comparison—that is, a group of transgender adolescents who did not receive puberty-blocking hormones, cross-sex hormones, and/or sex-reassignment surgery—which makes comparisons of outcomes more difficult.

In the study cohort, gender dysphoria improved over time, body image improved on some measures, and overall functioning improved modestly. Due to the lack of a matched control group it is unclear whether these changes are attributable to the procedures or would have occurred in this cohort without the medical and surgical interventions. Measures of anxiety, depression, and anger showed some improvements over time, but these findings did not reach statistical significance. While this study suggested some improvements over time in this cohort, particularly the reported subjective satisfaction with the procedures, detecting significant differences would require the study to be replicated with a matched control group and a larger sample size. The interventions also included care from a multidisciplinary team of medical professionals, which could have had a beneficial effect. Future studies of this kind would ideally include long-term follow-ups that assess outcomes and functioning beyond the late teens or early twenties.

Therapeutic Interventions in Adults

The potential that patients undergoing medical and surgical sex reassignment may want to return to a gender identity consistent with their biological sex suggests that reassignment carries considerable psychological and physical risk, especially when performed in childhood, but also in adulthood. It suggests that the patients' pre-treatment beliefs about an ideal post-treatment life may sometimes go unrealized.

In 2004, Birmingham University's Aggressive Research Intelligence Facility (Arif) assessed the findings of more than one hundred follow-up studies of post-operative transsexuals.[77] An article in *The Guardian* summarized the findings:

> Arif…concludes that none of the studies provides conclusive evidence that gender reassignment is beneficial for patients. It found that most research was poorly designed, which skewed the results in favour of physically changing sex. There was no evaluation of whether other treatments, such as long-term counselling, might help transsexuals, or whether their gender confusion might lessen over time. Arif says the findings of the few studies that have tracked significant numbers of patients over several years were flawed because the researchers lost track of at least half of the participants. The potential complications of hormones and genital surgery, which include deep vein thrombosis and incontinence respectively, have not been thoroughly investigated, either. "There is huge uncertainty over whether changing someone's sex is a good or a bad thing," says Dr Chris Hyde, director of Arif. "While no doubt great care is taken to ensure that appropriate patients undergo gender reassignment, there's still a large number of people who have the surgery but remain traumatized—often to the point of committing suicide."[78]

The high level of uncertainty regarding various outcomes after sex-reassignment surgery makes it difficult to find clear answers about the effects on patients of reassignment surgery. Since 2004, there have been other studies on the efficacy of sex-reassignment surgery, using larger sample sizes and better methodologies. We will now examine some of the more informative and reliable studies on outcomes for individuals receiving sex-reassignment surgery.

As far back as 1979, Jon K. Meyer and Donna J. Reter published a longitudinal follow-up study on the overall well-being of adults who underwent sex-reassignment surgery.[79] The study compared the outcomes of 15 people who received surgery with those of 35 people who requested but did not receive surgery (14 of these individuals eventually received surgery later, resulting in three cohorts of comparison: operated, not-operated, and operated later). Well-being was quantified using a scoring system that assessed psychiatric, economic, legal, and relationship outcome variables. Scores were determined by the researchers after performing interviews with the subjects. Average follow-up time was approximately five years for subjects who had sex change surgery, and about two years for those subjects who did not.

Compared to their condition before surgery, the individuals who had undergone surgery appeared to show some improvement in well-being, though the results had a fairly low level of statistical significance. Individuals who had no surgical intervention did display a statistically significant improvement at follow-up. However, there was no statistically significant difference between the two groups' scores of well-being at follow-up. The authors concluded that "sex reassignment surgery confers no objective advantage in terms of social rehabilitation, although it remains subjectively satisfying to those who have rigorously pursued a trial period and who have undergone it."[80] This study led the psychiatry department at Johns Hopkins Medical Center (JHMC) to discontinue surgical interventions for sex changes for adults.[81]

However, the study has important limitations. Selection bias was introduced in the study population, because the subjects were drawn from those individuals who sought sex-reassignment surgery at JHMC. In addition, the sample size was small. Also, the individuals who did not undergo sex-reassignment surgery but presented to JHMC for it did not represent a true control group. Random assignment of the surgical procedure was not possible. Large differences in the average follow-up time between those who underwent surgery and those who did not further reduces any capacity to draw valid comparisons between the two groups. Additionally, the study's methodology was also criticized for the somewhat arbitrary and idiosyncratic way it measured the well-being of its subjects. Cohabitation or any form of contact with psychiatric services were scored as equally negative factors as having been arrested.[82]

In 2011, Cecilia Dhejne and colleagues from the Karolinska Institute and Gothenburg University in Sweden published one of the more robust and well-designed studies to examine outcomes for persons who underwent sex-reassignment surgery. Focusing on mortality, morbidity, and criminality rates, the matched cohort study compared a total of 324 transsexual persons (191 MtFs, 133 FtMs) who underwent sex reassignment between 1973 and 2003 to two age-matched controls: people of the same sex as the transsexual person at birth, and people of the sex to which the individual had been reassigned.[83]

Given the relatively low number of transsexual persons in the general population, the size of this study is impressive. Unlike Meyer and Reter, Dhejne and colleagues did not seek to evaluate the patient satisfaction after sex-reassignment surgery, which would have required a control group of transgender persons who desired to have sex-reassignment surgery but did not receive it. Also, the study did not compare outcome

variables before and after sex-reassignment surgery; only outcomes after surgery were evaluated. We need to keep these caveats in mind as we look at what this study found.

Dhejne and colleagues found statistically significant differences between the two cohorts on several of the studied rates. For example, the postoperative transsexual individuals had an approximately three times higher risk for psychiatric hospitalization than the control groups, even after adjusting for prior psychiatric treatment.[84] (However, the risk of being hospitalized for substance abuse was not significantly higher after adjusting for prior psychiatric treatment, as well as other covariates.) Sex-reassigned individuals had nearly a three times higher risk of all-cause mortality after adjusting for covariates, although the elevated risk was significant only for the time period of 1973–1988.[85] Those undergoing surgery during this period were also at increased risk of being convicted of a crime.[86] Most alarmingly, sex-reassigned individuals were 4.9 times more likely to attempt suicide and 19.1 times more likely to die by suicide compared to controls.[87] "Mortality from suicide was strikingly high among sex-reassigned persons, including after adjustment for prior psychiatric morbidity."[88]

The study design precludes drawing inferences "as to the effectiveness of sex reassignment as a treatment for transsexualism," although Dhejne and colleagues state that it is possible that "things might have been even worse without sex reassignment."[89] Overall, post-surgical mental health was quite poor, as indicated especially by the high rate of suicide attempts and all-cause mortality in the 1973–1988 group. (It is worth noting that for the transsexuals in the study who underwent sex reassignment from 1989 to 2003, there were of course fewer years of data available at the time the study was conducted than for those transsexuals from the earlier period. The rates of mortality, morbidity, and criminality in the later group may in time come to resemble the elevated risks of the earlier group.) In summary, this study suggests that sex-reassignment surgery may not rectify the comparatively poor health outcomes associated with transgender populations in general. Still, because of the limitations of this study mentioned above, the results also cannot establish that sex-reassignment surgery causes poor health outcomes.

In 2009, Annette Kuhn and colleagues from the University Hospital and University of Bern in Switzerland examined post-surgery quality of life in 52 MtF and 3 FtM transsexuals fifteen years after sex-reassignment surgery.[90] This study found considerably lower general life satisfaction in post-surgical transsexuals as compared with females who had at least one

pelvic surgery in the past. The postoperative transsexuals reported lower satisfaction with their general quality of health and with some of the personal, physical, and social limitations they experienced with incontinence that resulted as a side effect of the surgery. Again, inferences cannot be drawn from this study regarding the efficacy of sex-reassignment surgery due to the lack of a control group of transgender individuals who did not receive sex-reassignment surgery.

In 2010, Mohammad Hassan Murad and colleagues from the Mayo Clinic published a systematic review of studies on the outcomes of hormonal therapies used in sex-reassignment procedures, finding that there was "very low quality evidence" that sex reassignment via hormonal interventions "likely improves gender dysphoria, psychological functioning and comorbidities, sexual function and overall quality of life."[91] The authors identified 28 studies that together examined 1,833 patients who underwent sex-reassignment procedures that included hormonal interventions (1,093 male-to-female, 801 female-to-male).[92] Pooling data across studies showed that, after receiving sex-reassignment procedures, 80% of patients reported improvement in gender dysphoria, 78% reported improvement in psychological symptoms, and 80% reported improvement in quality of life.[93] None of the studies included the bias-limiting measure of randomization (that is, in none of the studies were sex-reassignment procedures assigned randomly to some patients but not to others), and only three of the studies included control groups (that is, patients who were not provided the treatment to serve as comparison cases for those who did).[94] Most of the studies examined in Murad and colleagues' review reported improvements in psychiatric comorbidities and quality of life, though notably suicide rates remained higher for individuals who had received hormone treatments than for the general population, despite reductions in suicide rates following the treatments.[95] The authors also found that there were some exceptions to reports of improvements in mental health and satisfaction with sex-reassignment procedures; in one study, 3 of 17 individuals regretted the procedure with 2 of these 3 seeking reversal procedures,[96] and four of the studies reviewed reported worsening quality of life, including continuing social isolation, lack of improvement in social relationships, and dependence on government welfare programs.[97]

The scientific evidence summarized suggests we take a skeptical view toward the claim that sex-reassignment procedures provide the hoped-for benefits or resolve the underlying issues that contribute to elevated mental health risks among the transgender population. While we work to stop maltreatment and misunderstanding, we should also work to study

and understand whatever factors may contribute to the high rates of suicide and other psychological and behavioral health problems among the transgender population, and to think more clearly about the treatment options that are available.

Part Three: Gender Identity

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40. Segal, "Two Monozygotic Twin Pairs Discordant for Female-to-Male Transsexualism," 350.

41. *Ibid.*, 351.

42. *Ibid.*, 353–354.

43. *Ibid.*, 354.

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45. *Ibid.*, 355. Emphasis in original.

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49. *Ibid.*

50. *Ibid.*, 1503–1504.

51. Giuseppina Rametti *et al.*, "White matter microstructure in female to male transsexuals before cross-sex hormonal treatment. A diffusion tensor imaging study," *Journal of Psychiatric Research* 45, no. 2 (2011): 199–204, http://dx.doi.org/10.1016/j.jpsychires.2010.05.006.

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53. Giuseppina Rametti *et al.*, "The microstructure of white matter in male to female transsexuals before cross-sex hormonal treatment. A DTI study," *Journal of Psychiatric Research* 45, no. 7 (2011): 949–954, http://dx.doi.org/10.1016/j.jpsychires.2010.11.007.

54. *Ibid.*, 952.

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56. Emiliano Santarnecchi *et al.*, "Intrinsic Cerebral Connectivity Analysis in an Untreated Female-to-Male Transsexual Subject: A First Attempt Using Resting-State fMRI," *Neuroendocrinology* 96, no. 3 (2012): 188–193, http://dx.doi.org/10.1159/000342001.

57. *Ibid.*, 188.

58. Hsaio-Lun Ku *et al.*, "Brain Signature Characterizing the Body-Brain-Mind Axis of Transsexuals," *PLOS ONE* 8, no. 7 (2013): e70808, http://dx.doi.org/10.1371/journal.pone.0070808.

59. *Ibid.*, 2.

60. Hans Berglund *et al.*, "Male-to-Female Transsexuals Show Sex-Atypical Hypothalamus Activation When Smelling Odorous Steroids, *Cerebral Cortex* 18, no. 8 (2008): 1900–1908, http://dx.doi.org/10.1093/cercor/bhm216.

61. See, for example, Sally Satel and Scott D. Lilenfeld, *Brainwashed: The Seductive Appeal*

of Mindless Neuroscience, (New York: Basic Books, 2013).

62. An additional clarification may be helpful with regard to research studies of this kind. Significant differences in the means of sample populations do not entail predictive power of any consequence. Suppose that we made 100 different types of brain measurements in cohorts of transgender and non-transgender individuals, and then calculated the means of each of those 100 variables for both cohorts. Statistical theory tells us that, due to mere chance, we can (on average) expect the two cohorts to differ significantly in the means of 5 of those 100 variables. This implies that if the significant differences are about 5 or fewer out of 100, these differences could easily be by chance and therefore we should not ignore the fact that 95 other measurements failed to find significant differences.

63. One recent paper estimates that 0.6% of the adult U.S. population is transgender. See Andrew R. Flores *et al.*, "How Many Adults Identify as Transgender in the United States?" (white paper), Williams Institute, UCLA School of Law, June 30, 2016, http://williamsinstitute.law.ucla.edu/wp-content/uploads/How-Many-Adults-Identify-as-Transgender-in-the-United-States.pdf.

64. Petula Dvorak, "Transgender at five," *Washington Post*, May 19, 2012, https://www.washingtonpost.com/local/transgender-at-five/2012/05/19/gIQABfFkbU_story.html.

65. *Ibid.*

66. *Ibid.*

67. American Psychiatric Association, "Gender Dysphoria," *DSM-5*, 455. Note: Although the quotation comes from the *DSM-5* entry for "gender dysphoria" and implies that the listed persistence rates apply to that precise diagnosis, the diagnosis of gender dysphoria was formalized by the *DSM-5*, so some of the studies from which the persistence rates were drawn may have employed earlier diagnostic criteria.

68. *Ibid.*, 455.

69. Kenneth J. Zucker, "Children with gender identity disorder: Is there a best practice?," *Neuropsychiatrie de l'Enfance et de l'Adolescence* 56, no. 6 (2008): 363, http://dx.doi.org/10.1016/j.neurenf.2008.06.003.

70. Kenneth J. Zucker *et al.*, "A Developmental, Biopsychosocial Model for the Treatment of Children with Gender Identity Disorder," *Journal of Homosexuality* 59, no. 2 (2012), http://dx.doi.org/10.1080/00918369.2012.653309. For an accessible summary of Zucker's approach to treating gender dysphoria in children, see J. Michael Bailey, *The Man Who Would Be Queen: The Science of Gender-Bending and Transsexualism* (Washington, D.C.: Joseph Henry Press, 2003), 31–32.

71. Kelley D. Drummond *et al.*, "A follow-up study of girls with gender identity disorder," *Developmental Psychology* 44, no. 1 (2008): 34–45, http://dx.doi.org/10.1037/0012-1649.44.1.34.

72. Jesse Singal, "How the Fight Over Transgender Kids Got a Leading Sex Researcher Fired," *New York Magazine*, February 7, 2016, http://nymag.com/scienceofus/2016/02/fight-over-trans-kids-got-a-researcher-fired.html.

73. See, for example, American Psychological Association, "Guidelines for Psychological Practice with Transgender and Gender Nonconforming People," *American Psychologist* 70 no. 9, (2015): 832–864, http://dx.doi.org/10.1037/a0039906; and Marco A. Hidalgo *et al.*, "The Gender Affirmative Model: What We Know and What We Aim to Learn," *Human Development* 56 (2013): 285–290, http://dx.doi.org/10.1159/000355235.

74. Sara Reardon, "Largest ever study of transgender teenagers set to kick off," *Nature* 531, no. 7596 (2016): 560, http://dx.doi.org/10.1038/531560a.

75. Chris Smyth, "Better help urged for children with signs of gender dysphoria," *The Times* (London), October 25, 2013, http://www.thetimes.co.uk/tto/health/news/article3903783.ece. According to the article, in 2012 "1,296 adults were referred to specialist gender dysphoria clinics, up from 879 in 2010. There are now [in 2013] 18,000 people in treatment, compared with 4,000 15 years ago. [In 2012] 208 children were referred, up from 139 the year before and 64 in 2008."

76. Annelou L. C. de Vries *et al.*, "Young Adult Psychological Outcome After Puberty Suppression and Gender Reassignment," *Pediatrics* 134, no. 4 (2014): 696–704, http://dx.doi.org/10.1542/peds.2013-2958d.

77. David Batty, "Mistaken identity," *The Guardian*, July 30, 2004, http://www.theguardian.com/society/2004/jul/31/health.socialcare.

78. *Ibid.*

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80. *Ibid.*, 1015.

81. See, for instance, Paul R. McHugh, "Surgical Sex," *First Things* (November 2004), http://www.firstthings.com/article/2004/11/surgical-sex.

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83. Cecilia Dhejne *et al.*, "Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden," *PLOS ONE* 6, no. 2 (2011): e16885, http://dx.doi.org/10.1371/journal.pone.0016885.

84. 95% confidence interval: 2.0–3.9.

85. 95% confidence interval: 1.8–4.3.

86. MtF transsexuals in the study's 1973–1988 period showed a higher risk of crime compared to the female controls, suggesting that they maintain a male pattern for criminality. That study period's FtM transsexuals, however, did show a higher risk of crime compared to the female controls, perhaps related to the effects of exogenous testosterone administration.

87. 95% confidence intervals: 2.9–8.5 and 5.8–62.9, respectively.

88. *Ibid.*, 6.

89. *Ibid.*, 7.

90. Annette Kuhn *et al.*, "Quality of life 15 years after sex reassignment surgery for transsexualism," *Fertility and Sterility* 92, no. 5 (2009): 1685–1689, http://dx.doi.org/10.1016/j.fertnstert.2008.08.126.

91. Mohammad Hassan Murad *et al.*, "Hormonal therapy and sex reassignment: a systematic review and meta-analysis of quality of life and psychosocial outcomes," *Clinical Endocrinology* 72 (2010): 214–231, http://dx.doi.org/10.1111/j.1365-2265.2009.03625.x.

92. *Ibid.*, 215.

93. 95% confidence intervals: 68–89%, 56–94%, and 72–88%, respectively.

94. *Ibid.*

95. *Ibid.*, 216.

96. *Ibid.*

97. *Ibid.*, 228.