Transsexuality: Sexual Identity and the Brain.

Summary of a research article and critique of a popular press article.

By: Adriana Felisa Chávez De la Peña

Univesity of California Santa Barbara

Exchange Abroad Program

Psychology 137

October 30, 2014

Abstract

Here I present a summary for non-experts in neuroscience (which means I might be explaining a few concepts and ideas more than the original authors did) of a scientific article that shows that a specific part of the brain, called the central subdivision of the bed nucleus of the stria terminalis (BSTc), shows to be smaller in transsexuals from-male-to-female than it appears to be in ordinary men that are well identified with their gender (either if they are heterosexual or homosexual), a finding that turns out to be even more interesting because ordinary women show the same smaller size pattern when compared with men; according to the observational evidence provided by the authors, this size pattern can’t be explained by changes occuring during their adult lives but by an alteration in the organizational pattern that occured in response to sexual hormones during their early development. Then, I present a brief critique of a popular press article that tries to summarize these findings in a more attractive, and thus understandable, way to a more general audience.

*Keywords*: transsexuality, sex identity, sex-dimorphisc brain structures

Transsexuality: Sex Identity and the Brain

Summary of a research article and critique of a popular press article.

**Summary of the article ‘A sex difference in the human brain and its relation to transsexuality’**

Zhou, Hofman, Gooren and Swaab (1995) start their article by pointing out that, because most of the transexuals report to feel like they were born in the wrong body (men that feel like women and vice-versa), in some cases since they were children, the purpose of their research was to determine if that verbally reported feeling could be related to a difference in their brain when compared with ordinary people. According to the authors, previous studies trying to find a biological correlation to the ‘I was born the wrong sex’ feeling reported by transsexual people have failed to demonstrate any particular difference in terms of their genes, gonads, genitalia and hormonal levels.

Studies made with experimental animals show that the same gonadal hormones that play a role in typically-sexual behaviors and the sexual changes asociated with puberty are also involved in the early development of a sex-dimorphic organization of the body, from the genitalia to the brain. So, this lead Zhou et al. (1995) to the hypothesis that maybe, even if those gonadal hormones could have done a ‘good job’ at promoting the growth of the right genitalia according to genetic sex, they might have failed at some point in the development of a well sex-identity-adapted brain. Thus, the key question was: Is there any difference between the brains of transsexual people and the brains of people who don’t report any dissonance with their sexual identity?

In order to answer this question, Zhou et al. (1995) decided to focus their attention in the hypothalamus because many previous studies had already collected evidence of anatomical differences in this structure in relation to genetic sex and sexual orientation in humans, so it looked like an appropiate candidate to start studying the biological basis of sexual identity which seems to be impaired in transsexual people.

Zhou et al (1995) collected data from the brains of six dead male-to-female transsexuals during eleven years to compare the size of four different areas of the hypothalamus to see if they could find any differences between their brains and the brains of three non-transsexual groups of reference (Heterosexual men, homosexual men, and presumably-heterosexual women). They analyzed the data of four different hypothalamic nuclei: the paraventricular nucleus (PVN), the sexually dimorphic nucleus (SDN), the suprachiasmatic nucleus (SCN), and the bed nucleus of the stria terminalis (BST). However, they only presented the data of their findings in the BST since the other areas did not show any difference between groups.

The BST had already been tested in the field of sexual behavior research in rats, and it had shown to play a role in male sexual behavior and in the regulation of gonadotrophins releasing. The BST has estrogen and androgen receptors, it seems to work as a major aromatization center during rat development and it does present a sex-dimorphic difference in terms of its size and cell number, which has been linked to the influence of gonadal steroids during early development.

The functional aspects of BST in relation to sexual behavior had not been tested in humans yet, but it had already been found that a caudal part of the BST (called the BNST-dspm) is larger in men than women (2.5 times bigger). Zhou et al. (1995) looked for a sex-dimorphic pattern in another section of the BST, the BSTc (the ‘c’ stands for ‘central subdivision’), which is known to have somatostatin cells and innervations of the vasoactive intestinal polypeptide (VIP) that could be used to determine its volume across the transsexual group and the three groups used as a reference.

The main finding shown by Zhou et al. (1995) is that the volume of the central subdivision of the bed nucleus of the stria terminalis (the BSTc), which is bigger in men than women independently of their sexual orientation (44% bigger in heterosexual men and 62% bigger in homosexual men), is significantly smaller in male-to-female transsexuals than in any of the men reference groups (52% of the BSTc size found in heterosexual men and 46% of the BSTc of homosexual men) and even slightly smaller than the women´s BSTc tend to be (but this slight difference doesn’t reach a statistical significance).

According to this findings, even if there is no direct evidence that can prove that BST also plays a role in sexual behavior in humans, as has been proved in rats, the sex- dimorphic size pattern in the BSTc, along with the previously described differences per sex found in the BNST-dspm, might be enough reason to start thinking about this nucleus as involved in sexual and reproductive behaviors in humans. Furthermore, even if there is nothing like an accepted animal model for studying alterations in gender identity, BST might be a good place to start working on it: it has shown to be sexually-dimorphic and is not influenced by sexual orientation (because findings between homosexual and heterosexual men remained statistically the same), and therefore it is compatible with the fact that transsexuals can be sexually attracted to people from the same, or opposite, gender than that to which they identify.

There might be alternative explanations for the BSTc size difference found in the article; most of them, as outlined in the next paragraphs, suggest that it might be due to changes in hormonal levels during adult life and not because of an alteration during early development. In that way, the BSTc size differences found in transexual people would reflect their condition’s lifestyle (hormonal treatments, for example) and not explain the ‘I felt like I was born the wrong sex’ reported from childhood.

The first evidence Zhou et al. (1995) provide to negate the infuence of variations in hormonal levels during adulthood in the BSTc size is that two of the women they studied were in a postmenopausal condition (which means that they had lower blood levels of estrogen), and a third one, a 46-year-old woman that had to deal for almost one year with a tumour of the adrenal cortex (causing higher levels of androstenedione and testosterone in blood), still fall in the normal range according to the general population of women.

Now, talking specifically about the transsexual group, it could be said, since all of them were having a hormonal treatment with estrogen (one of the most typically- female hormones), that the fact that their BSTc’s size seems to be smaller than men and more alike to women could be due to its administration, rather than a genuine per se feeling of being ‘the wrong sex’. However, two of the six transsexuals whose hypothalamus were examined stopped taking their hormone treatment 15 and 3 months before death because of a medical condition (one of them developed a problem with her prolactin levels going too high and the other one because of sarcoma), and both of them had a small BSTc. Furthermore, one of the men included in the reference group had a feminizing adrenal tumour that caused him to produce higher levels of estrogen in his blood than what’s normal in men, and he still had a big BSTc.

Another very specific feature of the transsexual group that could potentialy affect the BSTc size by hormonal level, is that all of them had a lack of androgens (a typically-male kind of hormone), because five of them had been orchidectomized, which means that one or both of their testis had been removed. The only transsexual included in the study who wasn’t orchidectomized had a BSTc size ranged just in the middle of the scores of the rest of the transsexuals. Furthermore, when they analyzed two men that were orchidectomized because of cancer of the prostate, both of them showed a very large BSTc, in the high end of the normal male range.

Independently of the fact of being orchidectomized or not, all of the transsexuals in this study were taking an antiandrogen compound, cyproterone acetate (CPA), which also contributes to the decrease of androgens in their blood steam. The authors deny this its influence on what they found because two of the six transsexuals who stopped taking CPA either ten or two years before death, yet their BSTc was still small.

Another piece of evidence that supports the idea that BSTc size is established since early development comes from studies with animals in which the neonatal gonadectomy of male rats and the androgenization of female rats, both procedures that alter the sex hormone release during development of the very first sex-dimorphic features as part of their organizational effects, do affect the number of neurons in the BST and, therefore, suppress the sex-dimorphic size pattern. Also, in the present study, the size of the BSTc in the transsexual group did not differ in any statistically-significant way whether they were early-onset or late-onset transsexuals, so the difference in size in relation to the ordinary men was established with independence of the age they realized they weren’t confortable with the sex into which they were born.

Zhou et al. (1995) also included particular features of the subjects that conformed to either of the groups with a brief explanation about why they should not be pointed out as alternative explanations of their findings. Thus, even if the transsexual group were older than the men groups of reference (between 10 and 13 years older in general), the authors find no correlation between the BSTc size and age between their scores. And, even if the lack of sexual orientation influence could have been previously established by the fact that no statistically-significant size difference was found between homosexual and heterosexual men, they also found that there was no correlation between the BSTc size and the sexual orientation of the transsexuals in the study (they all were male-to-female transsexuals but they still could be attracted to men or women).

And, finally, speaking about the characteristics of the groups of reference, it was convenient that they included two heterosexual women and three heterosexual men who also presented AIDS but all kept showing the same size patterns within the range.

In summary, this article provides evidence of a sex-dimorphic size pattern in a very specific part of the hypothalamus that appears to be female-sized in male-to-female transsexuals. The main finding is that BSTc size differences are not due to hormonal changes in adulthood and are not influenced by sexual orientation. Therefore, the ultimate conclusion that the findings in this article provide together with the previous research done with animals, is that gender identity, whether in normal or altered conditions, might have its basis in the interaction between the early development of the brain and the organizational action of sex hormones.

This article was the very first brain study that provided evidence of an actual difference in the brain associated with the transsexual condition, and it also provided some light on the idea of a well-established brain feature during early development that could come along with the discordance between genetic sex and sex identity reported by transsexual people. There is a high need for more investigation involving other brain areas because, according to this study, the differences found in the BSTc seem to be very local as the researchers were not able to find any contradictorial sex-dimorphic pattern in the transsexual group when they looked for it in the PVN, SCN and SDN. It is unclear if the discrepancy between the results might be due to the inherent features of those areas, such as the presence of specific receptors to sexual hormones and aromatase. This is why Zhou et al. (1995) closed their article by pointing out that they were then interested in the possible relation between: aromatase and sex hormone receptor distribution, on the one hand, and sexual orientation and gender on the other.

**Critique of the popular press article “Study links brain to transsexuality”**

In general, considering it is a press article that is not specifically directed to people with any kind of specialized knowledge, the Natalie Angier (1995) does a great job summarizing the content of the scientific article. She does not omit anything crucial and instead simplifies the description of the subjects, methods, and results well enough to be understandable for everybody. And actually she even added information not included in the referred article about the contribution of its findings to the scientific approach to transsexuality in relation to the brain and sexual identity.

Angier (1995) also makes a very-convenient and well-established distinction –between sexual orientation and sexual identity and which is their relation to the different sexual dimorphisms already found in the brain– that is really helpful to understanding what is the main subject of interest in the discussed article: that, in order to establish any direct relationship between a specific pattern of features that seems to be different between transsexuals and ordinary people as ‘transsexual determining’, first it has to be proved to be independent of sexual orientation and appear as somehow preserving the pattern regularly as a sex difference between ordinary men and women.

However, since the article is directed to a broader audience, whether they have any kind of knowledge in neuroscience or not, it has to present the information in an appealing way that can lead to the exaggeration of the implications of the found data. For example, Angier (1995) presents a mostly-fair approximate percentage in which men’s BSTc differs from women’s –she says ‘about 50 percent’ when talking about an actual difference of 44% for heterosexual men and 62% for homosexual men– but exaggerates the percentage when talking about the comparision involving the transsexuals group –she says BSTc in regular men is ‘almost 60% larger’ than in male-to-female-transsexuals when BSTc in transsexuals is actually just 52% of the size found in heterosexual men and 46% of homosexual men’s BSTc size– so, even if the data are presented in the same direction (‘smaller in transsexuals than in regular men’, ‘larger in men than women’), the percentages are manipulated presumably to keep the attention and interest of the audience.

Continuing with the idea of keeping people involved in the reading of the article, Angier (1995) does take a pretty big leap from what is said in the scientific article and what its presumable implications in real life are by saying that “the results raise tantalizing possibilities that transsexuals may in a sense be more female than females” (Angier, 1995).

However, this critical affirmation gets cancelled by the continious mentions the author does to some comments made by either scientists involved in neurobiological research (including the author of the referred article) or by people who are really involved in transsexuality as a topic of discussion (the editor of a the newsletter of the Intersex Society of North America, for example), which, in general, tends to attenuate the asumption that the findings of this article are intended to be the only truth about what’s really underlying that ‘born the wrong sex’ feeling reported by transsexual people as an altered sexual identity that could be reduced to an alteration in the organizational effects during development of certain sexual hormones that lead to a reduced size of the BSTc in relation to other genetic men who are comfortable with their sexual identities.

Speaking about the comments from other people involved at different levels with the transsexual condition that Angier (1995) included in her own article, it’s notable to see how it can go from the most trivial and sensationalist (For example,“these are astonishing data” is apparently the only important thing that the author found quotable from the neurobiologist Dr. Geert de Vries) to the most elaborated and enriching observations that provide new testing possibilities to the study of the sexual identity and its relation to brain development, such as those made by Dr. Roger Gorski, who did not appeal to changes in hormonal levels during adulthood as alternatives causes of the found results, which would imply that the lifestyle of transsexual people could be having an effect in the brain structure, but suggested that maybe the BSTc size can also be influenced by the wave of hormonal changes that occur during puberty, and thus it would not be a direct effect of an alteration in the organizational effect of hormones during early development but an effect of the person’s behavior during his or her first years of life, which would be consistent with the idea that many of the activational effects of the sex hormones in our body occur during puberty.

One last critique that should be done to this popular press article is that it doesn’t include any references and that it doesn’t specify how or where did Angier (1995) get the declarations quoted during the article nor how she knew that Zhou et al. (1995) were then collecting evidence from dead female-to-male transsexuals to see if they show a male-sized BSTc; the original article actually says that the authors were then interested in the study of the receptors of sex hormones and aromatase in relation to gender and sexual orientation.

References

Angier, N. (1995). Study links brain to transsexuality. *The New York Times*

Zhou, J. N., Hoffman, M. A., Gooren, L. J. G., & Swaab, D. F. (1995). A sex difference in the human brain and ints relation to transsexuality. *Nature*, 378, 68-70.