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Is Sexuality a Choice? An Analysis of the Facts and Factors that Influence One's Sexual Orientation

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Philadelphia College of Osteopathic Medicine
Graduate Program in Biomedical Sciences
School of Health Sciences

**Is Sexuality a Choice? An Analysis of the Facts and Factors that Influence One's
Sexual Orientation**

A Capstone in Neurobehavioral Science by Brandon Scott Hodges
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ABSTRACT

Sexual orientation is often viewed as the sex or gender to which one is attracted to; however, it is not that simple. Also, though many believe the default is for one to be attracted to the opposite sex and any other claim of sexual attraction is a choice; that is not true. Sexual orientation is the result of a complex combination of one's genes, environment, and hormones. As a result, not only is sexuality not a choice, but just as there are so many different colors, there are so many different sexual orientations beyond heterosexual, such as homosexual, bisexual, and pansexual, just to name a few. At the end of the day, sexual orientation is more like a giant web of endless possibilities as opposed to merely heterosexual or a sliding scale between heterosexual and homosexual.

Furthermore, though one's sexuality is fluid, meaning it can change over time and this fluidity has to occur naturally. As a result, expecting someone to simply stop their attraction as if they were turning off a switch or expecting conversion therapy to change their attraction is futile. In this review, the objective is to explore the science behind sexual orientation by analyzing research papers on the topic. This review will pay particular attention to examining "Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior", since it is the first study to find the existence of multiple "gay genes" and quantify the extent to which genes influence one's sexuality. The review will also examine similar papers as well as papers focusing on the environmental and hormonal influences on one's sexual orientation.

Moreover, the review will analyze the results of some of the research methods and strategies used in these papers, such as twin-studies, animal studies, longitudinal studies,

and surveys. By the end of this review, the facts and analysis should support the hypothesis that sexual orientation is the result of a complex combination of one's genes, environment, and hormones. Also, the facts and analysis should create a clear picture that one's sexual orientation is not a choice, nor is living a non-heterosexual lifestyle.

INTRODUCTION

The Lesbian, Gay, Bisexual, Trans, Queer, Intersex (LGBTQI)+ community refers to individuals who identify as not heterosexual, aka straight. In other words, LGBTQI+ individuals are more than just individuals who are not attracted to or not solely attracted to the opposite sex. LGBTQI+ is an umbrella term that refers to any individual whose identity differs from society's assumption that heterosexuality is the default, normal, or preferred sexual orientation, aka a heteronormative world view. Furthermore, the LGBTQI+ can also refer to individuals whose identify differs from the assumption that all men are masculine, all women are feminine, and that there are only two sexes (Flores et al. 2017).

Historically speaking, LGBTQI+ individuals have existed for as long as there has been life on this planet and have reached across all demographic barriers (such as economic, racial, sex, religious, etc.). For example, historical records describe art that shows LGBTQI+ individuals in ancient societies such as Ancient Greece and Ancient Rome (Wyatt, 2016). Researchers have even found LGBTQI+ individuals in other species, specifically, researchers have observed same-sex behavior in over 450 different species such as dogs, cats, chimpanzees, and giraffes. Despite homosexuality being observed in hundreds of species, homophobia (a prejudice or dislike of gay people) is ironically only found in one species; humans (Fraïssé & Barrientos, 2016).

The reason homophobia is found in humans is due to a variety of factors, the most prominent being in many cultures and religions, homosexuality is condemned. For example, in Christianity, the bible refers to homosexuality as a sin and an abomination

(Loue, 2020). Another reason homophobia exists is that many people do not know that much about the LGBTQI+ community and what they do know are mostly stigmas and outdated, false information. The final reason homophobia exists is because LGBTQI+ individuals are a minority, with statistically only 2%-10% of most populations identifying as not heterosexual. As a result, LGBTQI+ individuals are subjected to similar judgment, criticism, and disparity as other minorities (Dessel et al. 2017). It should be noted this small percentage (2%-10%) of people identifying as LGBTQI+ is mostly believed to be due to the fact many individuals are afraid to come out and identify as LGBTQI+ for fear of being ostracized or discriminated against in their community. For example, many LGBTQI+ individuals are scared they will not be accepted if they come out, especially by their loved ones; some individuals have even been exiled, and some children have been kicked out of their house (Giannobile et al. 2016). Furthermore, LGBTQI+ individuals are subjected to severe persecution and violence; for example, the Orlando shooting at a gay nightclub in 2016 was not only considered a hate crime, but it was the worst shooting in American history at the time even though there have been so many shootings of different populations (Stonehem, 2016). Moreover, LGBTQI+ individuals in many countries do not have the right to marry, they fear their marriage will not be recognized in other parts of the world such as in Africa, it is harder for LGBTQI+ to adopt, and they fear their children or parental rights may be taken away. In many places, LGBTQI+ individuals not only have decreased protections but in many cases no protections under the law, especially in cases of discrimination and overall fundamental civil rights that everyone else has (Kaufman & Compton, 2020).

Despite all of the homophobic disadvantages, the number of LGBTQI+ individuals have been increasing over time, especially with the younger generations. This increase is due to the work of LGBTQI+ organizations, LGBTQI+ culture appearing in media, science improving our understanding about sexuality, people (especially children) being educated about the LGBTQI+ relations, and society promoting diversity and acceptance. In short, this increase in LGBTQI+ individuals is not because there are necessarily more LGBTQI+ individuals, but rather more individuals are more comfortable with coming out in recent years due to the positive change in laws and public opinion of the LGBTQI+ community (Jones, 2021). Unfortunately, despite society's changing view as well as the historical, statistical, and scientific evidence to the contrary, there still has not been a study that has confidently been able to suggest that one's sexual orientation is not a choice.

BACKGROUND

In the scientific community, sexual orientation has long been disputed to be caused by various factors such as biological, genetic, environmental, choice, or physical or mental defects. Furthermore, due to the complexity of factors for sexual orientation behavior, there have only been a limited number of studies on the subject. There have only been a small number of reliable conclusions drawn from those studies. The findings that have been gathered from these previous studies (mostly family studies and twin studies) suggest that one's sexual orientation is at least partially genetically influenced,

although the attempts to determine what specific genes contribute to same-sex behavior have been mostly unsuccessful until recently (Bailey et al. 2016).

What makes the paper “Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior” so unique is it is the largest study for same-sex behavior to date, and the data has been gathered from multiple countries and organizations. Furthermore, the study identifies factors, specifically genetic factors, that are primarily responsible for contributing to same-sex behavior. The study also asks whether genes influence same-sex attraction, same-sex behavior, and non-heterosexual identity the same in males and females as well as whether sex hormones contribute to same-sex behavior?

Researchers conducted a Gene-Wide Association Study (GWAS) to address the previously stated questions. A GWAS is a method that scans biomarkers, in this case, single nucleotide polymorphisms (SNPs), in the genome of many individuals that express a particular phenotype. Usually, a GWAS is used to detect possible diseases, and researchers can use the genetic associations found in GWASs to better treat and cure individuals with the phenotype. For example, GWASs have helped identify variations that contribute to one’s risk for diseases such as obesity, Crohn’s, heart, and Parkinson’s disease. Basically, a GWAS is good at finding associated genetic variations, which can serve as a useful guide to help lead researchers to at-risk regions of the genome (Ganna et al. 2019).

Gene-Wide Association Study General Methods

After deciding on the method, the researchers began to gather biological data. They collected data from a cohort of research participants from 23andMe from western countries (predominately the United States) and the Biobank in the United Kingdom (UK). The study included about 500,000 participants (both male and female). The 23andMe sample had approximately 70,000 participants and was comprised of 23andMe customers who consented to participate in research as well as who chose to complete a survey about sexual orientation. The UK Biobank sample had 400,000+ participants and was composed of a genotyped sample of UK residents aged 40-70. In total, the researchers used data from genotyped individuals from five cohorts who provided self-reported information. Informed consent was received from all individuals participating in the studies, which their local research ethics committee then approved. It is important to note that the researchers dropped individuals from the study whose biological sex and self-identified sex did not match. In other words, they did not include any transgender or intersex individuals. The researchers acknowledge that this is an important limitation to their study that they hope will be addressed in future studies. Also, additional experiments and analyses were done in the study, but this paper focuses on those related to the GWAS. Furthermore, in this study, the researchers performed four GWASs, each focusing on different variables (Ganna et al. 2019).

Standard Quality Control Check

Before the researchers performed their GWAS, they had to perform a standard quality control check. They did this by assessing whether same-sex sex behavior clustered in families in a way that was consistent with genetic influences of the phenotype of same-sex behavior. In other words, the researchers examined if there was a correlation between the presence of same-sex behavior in families and the genetic influences on same-sex behavior. After the standard quality control check, the researchers began the GWAS (Ganna et al. 2019).

What the researchers determined for the standard quality control check was, among the pairs of individuals in the UK Biobank that were related at the level of first cousins or closer, the more closely related individuals were more were to display same-sex behavior consistently. The researchers estimated this broad-sense heritability to be 32.4%, which means that genes contribute 32.4% to the trait's heritability. This finding was consistent with the estimates of previous smaller twin studies (Ganna et al. 2019).

RESEARCH STRATEGIES

All of the references in this paper were retrieved via Refworks and Google Scholar. The research strategies used in this paper were an analysis of several papers concerning LGBTQI+ individuals such as twin-studies, population and demographic studies, longitudinal studies, and surveys. This review also examines papers focusing on the environmental and hormonal influences on one's sexual orientation. Furthermore, this paper conducted a heavy examination of the paper "Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior". The review focused on "Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior" because it was the first study to quantify the extent to which genes influence one's sexuality as well as find the existence of multiple "gay genes". Furthermore, this paper analyzes the results of some of the research strategies and methods in these papers. Following the analysis of the papers a review was done with much of it being left open ended in the hopes it will be expanded on by future studies.

RESULTS AND DISCUSSION

Gene-Wide Association Study Experiment 1

For GWAS experiment 1, the researchers performed a GWAS in the UK Biobank sample to identify genetic variants, which were largely SNPs associated with same-sex behavior. They also performed a GWAS in the sample from 23andMe to increase the results' power and generalizability. The researchers then estimated the genetic correlation between different heritable traits to determine how consistent the genetic influences were on same-sex behavior between the two samples. Finally, the researchers then meta-analyzed the two sample sets using a Multi-Trait Analysis of GWAS (MTAG), which is an analysis that models the genetic correlations to determine the meta-analytic weights of the two samples (Ganna et al. 2019).

Regarding the GWAS experiment 1, in the UK Biobank sample, 4.1% of males and 2.8% of females reported engaging in same-sex behavior with higher rates among younger participants. In the 23andMe sample, about 18.57% of participants reported engaging in same-sex behavior (additional information about the demographics was not discussed). Also, the unusually high number of individuals reporting same-sex behavior in the 23andMe sample was believed to be because individuals who engaged in same-sex behavior were assumed to be more likely to participate the sexual orientation survey (Ganna et al. 2019).

Concerning their estimation of genetic correlation between different heritable traits, the researchers found the genetic correlation was high between same-sex behavior and was also high between 28 different traits in the UK Biobank and 23andMe samples;

however, there were a few differences. For example, in females, the genetic correlations between same-sex behavior and anorexia were in opposite directions in the UK Biobank and 23andMe data; in other words, they were positively and negatively correlated, respectively (Ganna et al. 2019).

Finally, the results of the MTAG showed that about 27,000 participants reported same-sex behavior. Overall, the GWAS 1 experiment results indicated that the genetic influences on same-sex behavior in the BioBank and 23andME samples are similar. Furthermore, the researchers were able to identify two genome-wide significant signals, in other words, two SNPs (rs1111497512q21.31 and rs102618577q31.2) for same-sex behavior (Ganna et al. 2019).

In regard to these loci, the researchers discovered the locus encompassing rs34730029-11q12.1 contains several olfactory receptor genes that were significantly associated with same-sex behavior. This SNP is correlated with a missense mutation in OR5A1 that has been known to have a substantial effect on the sensitivity to certain scents and has had several indications of being involved in sex hormone regulation. Although the underlying mechanism is unclear, this supports previous findings that there is a link between olfaction and reproductive function, such as in individuals with Kallmann syndrome. Furthermore, the other SNP (rs1111497512q21.31) is linked to male pattern balding and is near a gene relevant to sexual differentiation. As a result, the idea that sex-hormone regulation may be involved in the development of same-sex behavior is strengthened (Ganna et al. 2019).

Gene-Wide Association Study Experiment 2

For GWAS experiment 2, the researchers wanted to perform a sex-specific analysis to assess differences in females' and males' effects. In other words, the researchers conducted another GWAS, but this time the independent variables were sex (Ganna et al. 2019).

Concerning the GWAS experiment 2, the results suggested only a partially shared genetic architecture across the sexes. This is important because other studied traits show much higher genetic architectures across sex genetic correlations in the past. Furthermore, through this GWAS, the researchers were able to identify the two additional SNPs in males (rs28371400-15q21.3 and rs34730029-11q12.1), which showed no significant association in females. On the other hand, they found one SNP in females (rs13135637-4p14), which showed no significant association in males. These three SNPs were replicated in other independent samples in meta-analyzed replication datasets; however, they had minimal effects. For example, in the UK Biobank, males with a specific genotype had a 0.4% higher prevalence of same-sex behavior than those with a different genotype. Despite these small effects, these results are important because the researchers determined the contribution of all measured common SNPs aggregated together was estimated to be 8%-25% variation in male and females same-sex behavior. This finding is significant because it means that when added together, these SNPs contribute to 8-25% of same-sex behavior in males and females. These results suggest that same-sex behavior, like most complex human traits, is influenced by the small additive effects of many genetic variants, most of which cannot be detected at this study's

current sample size. Due to these results, the researchers also show that the degree each chromosome contributes to heritability in same-sex behavior is proportional to the chromosome's size (Ganna et al. 2019).

Furthermore, in contrast to previous linkage studies, the researchers found no excess of SNPs on the X-chromosome. It is important to note that all the SNPs measured, when combined, do not capture the entirety of family-based heritability. What is meant by this is the results from the GWAS suggest genes contribute 8%-25% to same-sex behavior, while other studies that use family-based methods of gathering data suggests genes contribute 32% to same-sex behavior. This suggests family heritability contributes to same-sex behavior about three times more than SNP-heritability. The study's research suggests the reasons behind this discrepancy are likely due to variants not captured by genotyping arrays, nonadditive genetic effects, and phenotypic heterogeneity (Ganna et al. 2019).

Gene-Wide Association Study Experiment 3

In their study, the researchers defined the primary phenotype as having or never having had a same-sex partner in order to maximize the sample size and increase the power to detect SNP associations; however, this failed to capture the multifaceted richness and complexity of human sexual orientation. As a result, to explore the consequences of this simplification (in other words, their primary phenotype), the researchers performed a third GWAS pursuing genetic analyses across different aspects of sexual orientation and behavior. Specifically, the researchers conducted a GWAS on participants that reported

same-sex behavior focusing on the proportion of same-sex partners/total sexual partners; a higher value indicated a higher proportion of same-sex partners. The UK Biobank and 23andMe variables were heritable and genetically correlated with each other, so the researchers used MTAG to meta-analyze across the two studies for subsequent analyses (Ganna et al. 2019).

Regarding the GWAS experiment 3, the researchers found little evidence for a genetic correlation between same-sex/total sexual partners' proportion among individuals reporting same-sex behavior with the same-sex behavior variable. These findings suggest there is no single continuum from opposite-sex to same-sex behavior. In other words, the results suggest that sexuality does not lie on single spectrum from strictly homosexual to heterosexual; it is more complicated than that (Ganna et al. 2019).

Gene-Wide Association Study Experiment 4

(Ganna et al. 2019). The researchers also examined the possibility of different genetic variants being responsible for the difference between heterosexual behavior and the varying degrees to which one may exhibit same-sex behavior within non-heterosexuals. To do so, they performed an additional GWAS on the UK Biobank data on the traits of participants whose total sexual partners were:

1. Less than a third same-sex.
2. Between a third and two-thirds same-sex.
3. More than a third same-sex.
4. Exclusively same-sex.

Concerning the GWAS experiment 4, the results indicated partly different genetic variants being responsible for the difference between heterosexual behavior and the varying degrees to which one may exhibit same-sex behavior within non-heterosexuals. Lastly, using additional measures from 23andMe, the researchers showed strong genetic correlations of same-sex behavior with factors assessing same-sex attraction, identity, and fantasies, which suggest that largely the same gene variants influence these different aspects of sexual orientation (Ganna et al. 2019).

Methods for Other Follow Up Experiments

By using summary statistics from the GWASs, the researchers explored the genetic correlations between same-sex behavior and 28 other relevant traits that they chose before the analysis. In particular, the researchers chose mental health traits because they are substantially heritable. The researchers also chose mental health traits because previous population surveys have shown an elevated risk of adverse mental health outcomes (such as depression, anxiety, or substance use) in sexual minority populations such as non-heterosexual populations (Ganna et al. 2019).

Regarding the other follow-up experiments, the researchers found several personality traits (loneliness and openness to experience), risky behaviors (smoking and cannabis use), and mental health disorders, which are significantly genetically correlated with same-sex behavior. They found in both sexes that same-sex behavior was positively genetically correlated with several mental health traits. The researchers emphasize that the causes of these genetic correlations are unclear and could be generated by any number

of factors such as prejudice against individuals engaging in same-sex behavior. Some associations were sex-specific, such as the genetic correlations with bipolar disorder, cannabis use, and how the number of sexual partners was significantly higher in females than in males (Ganna et al. 2019).

Conclusions

The conclusions were that the researchers performed a genome-wide association study on about 500,000 individuals and identified five loci that were significantly associated with same-sex behavior. The researchers established that the underlying genetic architecture is highly complex, and there is certainly no single “gay gene”. On the contrary, sexuality is the result of many loci with individually minor effects, spread out across the whole genome and partly overlapping in females and males. Added together, the sum of these SNPs contribute to the predisposition of same-sex behavior. Also, in aggregate, all SNPs account for only 8%-25% of same-sex behavior. Therefore, the findings can only explain genetic heritability at the population level and cannot meaningfully predict an individual’s sexual preference

Some additional conclusions were though the study focused on the genetic basis of same-sex sexual behavior, several of the results point to the importance of sociocultural context as well. For example, the researchers observed changes in the prevalence of reported same-sex behavior across time, which raises questions about how genetic and sociocultural influences on sexual behavior might interact. The researchers also observed different genetic influences on same-sex behavior in females and males,

which could reflect sex differences in hormonal influences on sexual behavior. For example, how testosterone vs. estrogen plays a part in one's sexual orientation. Finally, the researchers suggest that there is no single spectrum from opposite-sex to same-sex sexual behavior; sexuality is more complicated than that.

Some of the study's limitations are GWASs require a large sample size (in this case, about 500,000 participants), so it is hard to do, which is why it is not used more often. The researchers only studied participants of European descent and from a few Western countries; therefore, studies that have more extensive and more diverse samples will allow for greater insight into how these findings differ across different sociocultural contexts. Also, due to these limitations as well as the fact that the study does not include transgender or intersex individuals, the results are ultimately simplistic.

RECOMMENDATIONS FOR FUTURE STUDIES

My interpretations of the study are though this research has its limitations, it finally answers the question that sexual orientation is not a choice but instead results from a complex interaction of genetic, environmental, and hormonal factors. Overall, I believe the methods of this research distinguish it from similar studies and make its results more reliable. Furthermore, it paves the way for additional research by raising questions about how factors such as smell contribute to one's sexual orientation. For example, if heterosexual and non-heterosexual individuals have a difference in smell when it comes to pheromones.

While there have been many studies in the past that have looked at the effect of pheromones in human sexual attraction only a handful have looked into how pheromones might differ between heterosexual and non-heterosexual individuals. One such study, “Pheromones and Same-Sex-Sexual Behavior”, already begins to investigate an answer to how pheromones affect sexual orientation by expanding on the research of twin studies, family studies, and the study “Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior” (the GWAS study). By expanding the results of these studies, the researchers investigate how the loss of a gene function, specifically the transient receptor potential cation channel 2 (TRPC2) gene, was a determining factor in developing same-sex sexual behavior in some primates such as humans. Furthermore, the researchers determine that the TRPC2 gene could be related to one of the several olfactory genes that is strongly linked to the SNP loci identified in the GWAS study (rs34730029-11q12.1) (Ventura-Aquino & Paredes, 2020). Though the “Pheromones and Same-Sex-Sexual Behavior” study already makes advancements in

expanding the results of previous studies, it could further evolve by addressing the limitations of the GWAS study, such as analyzing the genes of transgender or intersex individuals. Furthermore, this study could evolve by doing an analysis of individuals from as many different demographics as possible and not limiting it to western or European countries.

Another study that could evolve through the results of the GWAS study and expanding on its limitations is the “Neurobiology of gender identity and sexual orientation” study. The study analyzes the balance between one’s gender identity, as well as sexual orientation and how major influences such as one’s early hormone environment can affect the harmony of them. The data was obtained through basic research in animals, biometric indications of androgens, and through the analysis of previous studies of the clinical conditions associated with sexual development disorders. The study results theorized that regarding gender identity and sexual orientation, more prenatal exposure to testosterone leads to more masculine individuals, and a lack of testosterone leads to more feminine individuals. Though the study was strong, the researchers recognized there were many exceptions to their theory that could not be resolved due to a lack of knowledge at the time. Furthermore, at the time of publishing, the study had many limitations due to a lack of understanding of which genes influence one’s sexual orientation or how the genes interact with each other (Roselli, 2018).

By incorporating the results of recent studies of sexual orientation, this study could address some of the unknown questions it could not answer before and overall evolve by overcoming some of its previous limitations. For example, if this study incorporates the five loci identified in the GWAS study, it can evolve by understanding which genes

influence one's sexual orientation. Also, the SNP (rs1111497512q21.31) identified in the GWAS study already strengthens the idea that sex hormone regulation may be involved in the development of same-sex behavior. As a result, the researchers can expand on this result of the GWAS study and their previous research by understanding how the rs1111497512q21.31 loci influences hormone regulation, especially testosterone.

Another interesting finding of the study was the suggestion that the number of older brothers influences the sexual orientation of males; in other words, the more older brothers a male has, the more likely he is to exhibit same-sex behavior. The study suggested that according to evidence this phenomenon is due to a maternal immune response that is triggered when enough male breeders have already been born (Roselli, 2018). There have been other studies in the past that have come to similar conclusions that the more heterosexual males born into a family, the more likely the next born male will exhibit same-sex behavior; however, the reason for this is unclear (Blanchard, 2017). Another way how this study could evolve would be to examine the reasoning of this phenomenon and why there are exceptions, such as an only child exhibiting same-sex behavior. Furthermore, it would be interesting to explore if the same phenomenon is true for females and non-binary individuals such as trans or intersex.

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