

EPIDEMIOLOGY & RISK FACTORS

Childhood Abuse Experiences and the COMT and MTHFR Genetic Variants Associated With Male Sexual Orientation in the Han Chinese Populations: A Case-Control Study



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ABSTRACT

Background: Although it is widely acknowledged that genetic and environmental factors are involved in the development of male homosexuality, the causes are not fully understood.

Aim: To explore the association and interaction of childhood abuse experiences and genetic variants of the catechol-O-methyltransferase (COMT) and methylenetetrahydrofolate reductase (MTHFR) genes with the development of male homosexuality.

Methods: A case-control study of 537 exclusively homosexual men and 583 exclusively heterosexual men was conducted, with data collected from March 2013 to August 2015. Data were analyzed using χ^2 tests and logistic regression models.

Outcomes: Sociodemographic characteristics, childhood abuse experiences, and polymorphisms of COMT at rs4680, rs4818, and rs6267 and MTHFR at rs1801133.

Results: More frequent occurrence of physical (adjusted odds ratio [aOR] = 1.78), emotional (aOR = 2.07), and sexual (aOR = 2.53) abuse during childhood was significantly associated with the development of male homosexuality. The polymorphisms of MTHFR at rs1801133 and COMT at rs4818 also were significantly associated with the development of male homosexuality in the homozygote comparisons (T/T vs C/C at rs1801133, aOR = 1.68; G/G vs C/C at rs4818, aOR = 1.75). In addition, significant interaction effects between childhood abuse experiences and the COMT and MTHFR genetic variants on the development of male homosexuality were found.

Clinical Translation: This is the first time that an association of childhood abuse, COMT and MTHFR genetic variants, and their interactions with development of male homosexuality was exhaustively explored, which could help provide new insight into the etiology of male homosexuality.

Strengths and Limitations: Because homosexual men are a relatively obscure population, it was impossible to select the study participants by random sampling, which could lead to selection bias. In addition, because this was a case-control study, recall bias was inevitable, and we could not verify causality.

Conclusions: Childhood abuse and the COMT and MTHFR genetic variants could be positively associated with the development of homosexuality. However, it remains unknown how these factors jointly play a role in the development of homosexuality, and more studies in different ethnic populations and with a larger sample and a prospective design are required to confirm our findings. **Qin J-B, Zhao G-L, Wang F, et al. Childhood Abuse Experiences and the COMT and MTHFR Genetic Variants Associated With Male Sexual Orientation in the Han Chinese Populations: A Case-Control Study. J Sex Med 2018;15:29–42.**

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Key Words: Male Sexual Orientation; Childhood Abuse; COMT; MTHFR; Gene Polymorphisms

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INTRODUCTION

Homosexuality describes the romantic or sexual attraction or behavior among members of the same sex, situationally or in an enduring disposition.¹ Differences in sexual orientation represent one of the most common human behavioral variations. For example, in China, approximately 96% of the sexually active

male population is predominantly heterosexual, and the remaining 4% is predominantly homosexual.² Although public attention to and scholarship on male sexual orientation has increased significantly during the past decade, little is known about the mechanisms underlying its development.

Psychoanalytic and other environment-based theories³ for the development of homosexuality emphasize social and family experiences; victimization has been the subject of a great deal of this interest. More and more evidence suggests that disparities exist between sexual minorities (ie, lesbian, gay, and bisexual groups) and their heterosexual counterparts. A widespread finding is that sexual minorities have a significantly higher prevalence rate of childhood victimization, such as physical or sexual abuse, parental neglect, or witnessing domestic abuse, before 18 years of age than their heterosexual contemporaries.^{4–11} Therefore, early exposure to traumatic events could contribute to the development of male sexual orientation later in life. However, most published research on disparities in childhood victimization among sexual minorities has focused mainly on lesbian, gay, and bisexual populations as a single group. Few studies have separately examined the association between childhood victimization and the development of male sexual orientation; further investigation is needed to understand how childhood victimization influences the development of male homosexuality.

Genetic and epidemiologic studies provide some evidence for a genetic component to male homosexuality. Several studies conducted within families^{12,13} and twins studies^{14,15} have shown that male homosexuality is at least partly heritable. Although some investigators have tried to locate genetic loci associated with homosexuality on chromosomes^{16–19} and genome-wide scans^{20–22} have been used to explore the inheritance of male homosexuality, the specific gene of male homosexuality has not been found. More powerful genetic studies will be required to find any relevant genes. Dopaminergic disturbance is believed to be involved in the development of sexual orientation, which has been extensively studied.^{23,24} A positive association between dopamine levels and the propensity toward male-male courtship behavior has been confirmed by animal model studies.^{25–28} Hence, genetic screening for the susceptibility to male homosexuality seems essential to investigate dopamine-related genes such as the catechol-O-methyltransferase (COMT) gene, which is involved in dopamine metabolism,²⁹ and the methylenetetrahydrofolate reductase (MTHFR) gene, which can affect COMT methylation and COMT function by influencing DNA methylation status.^{30,31}

Currently, it is generally agreed that genetic and environmental factors are involved in the etiology of male homosexuality, although the causes are not fully understood. In the present study, we conducted a case-control study with the following objectives: (i) to examine whether male homosexuals report more childhood abuse experiences, including physical, emotional, and sexual abuse, than male heterosexuals; (ii) to assess the possibility

that the COMT and MTHFR genes are the susceptibility genes of male homosexuality, and (iii) to analyze the interactions between childhood abuse experiences and the COMT and MTHFR genetic variants for male homosexuality.

METHODS

Recruitment of Study Participants

The main characteristics of the participants and research procedure have been described previously.^{1,32} Recruitment was conducted by the Shenzhen Center for Chronic Disease Control from March 2013 to August 2015. Shenzhen Center for Chronic Disease Control is responsible for the city's prevention, treatment, and management of chronic diseases and sexually transmitted diseases. Every year, some people will come to this center for health counseling, medical examination, or treatment of chronic diseases and sexually transmitted diseases. Eligible men were recruited for this study during health counseling or medical examination. A case-control design was performed in the present study. The convenience sample, driven mainly by the number of respondents, was used for the study. Homosexual men were identified as the case group, and healthy heterosexual men composed the control group. The study participants were recruited at 2 clinics from this center. Homosexual men were recruited from a gay clinic, which provides health guidance and the prevention, treatment, and management of sexually transmitted diseases for homosexual men. All homosexual men were tested for HIV and syphilis. Healthy controls were recruited after health counseling or medical examination in the health examination clinic. This study was approved by the institutional review board of the National Research Institute for Family Planning, and all study participants gave written informed consent.

Inclusion Criteria

Homosexual men were exclusively homosexual and were selected using the following criteria: self-identified as homosexual and engaging in same-sex sexual intercourse at least once in the past 6 months before recruitment. Controls were exclusively heterosexual and were selected using an adult health check, self-identified as heterosexual, and never participated in same-sex sexual intercourse. The participants were 18 to 55 years old. Participants (homosexual and heterosexual men) with a history of bisexuality, prostitution, and situational male-on-male sexual behavior (men who assessed that their history of male-on-male sexual behavior was induced by an environmental influence but have no desire for homosexual sexual behavior) were excluded. All participants were clinically examined by a psychiatrist to confirm they were genuinely and completely homosexual or heterosexual and not misrepresenting their sexuality. All participants were of Han Chinese descent. In addition, we excluded those men who reported a history of depression or other psychiatric disorders or were diagnosed with depression or a psychiatric illness when they were recruited into the study.

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