Early Life Stress Modulates Sexual Orientation via Oxytocin and Arginine Vasopressin

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Abstract

Although interactions between environmental and biological factors could affect sexual orientation, little is known about whether early life stress (ELS) may alter sexual orientation by modulating sex hormone levels. We investigated the potential role of two sex hormones: oxytocin (OT) and arginine vasopressin (AVP), in sexual orientation changes induced by ELS. The 89 adult men participants were divided into heterosexual (n = 32) and gay/bisexual (n = 57) groups. Sexual orientation, mental health, and the serum levels of OT and AVP were evaluated. The results indicated that gay/bisexual men experienced more ELS with lower OT and AVP levels. Animal study also demonstrated that ELS resulted in decreased OT and AVP levels and a preference for same-sex in male mice which could be reversed via intraperitoneal OT/AVP treatment. Summarily, individuals with ELS are susceptible to sexual orientation changes and OT/AVP could ameliorate it, which extend the underlying mechanisms of ELS-induced sexual orientation changes.

Main

Sexual orientation is a fundamental aspect of human social behavior that has garnered significant attention since its emergence in the 1860s\(^1\). Individuals are typically classified as heterosexual, homosexual, or bisexual, based on their sexual behavior or identity. Non-heterosexual individuals, who represent a sexual minority, experience a higher prevalence of sexually transmitted infections and face more pronounced mental health challenges compared to their heterosexual counterparts\(^2\). Within the non-heterosexual community, gay and bisexual men are of particular interest due to their elevated rates of HIV incidence, suicidal ideation, and behaviors\(^3\). The criminalization of same-sex behavior in certain jurisdictions exacerbates the discrimination and health risks encountered by non-heterosexual individuals\(^4\). Moreover, gay and bisexual men often demonstrate early adoption of emerging "club drug" trends, underscoring the necessity of investigating the underlying mechanisms of sexual orientation, particularly within this demographic.

The differences in sexual orientation rates across nations and the consistency of opposite-sex attraction imply that environmental factors (e.g., upbringing and social experiences) and biological factors (e.g., prenatal hormones and genetic variations) interact to determine human sexual orientation\(^5\). Childhood trauma, including neglect, abuse, household dysfunction, other stressors, is a critical environmental factor for non-heteronormative\(^6\). Childhood trauma has been consistently associated with a range of chronic somatic diseases, including heart disease, cancer, and diabetes. It should also be noted that childhood trauma is linked to a higher risk of psychiatric disorders, including depression, non-suicidal self-injury and suicidality, bipolar disorder, schizophrenia, and post-traumatic stress disorder\(^7\). Recent studies have also linked sexual preference to a higher incidence of childhood trauma in sexual minorities\(^8\), pointing to potential correlations with sexual preference and mental health issues. Our previous studies in mice suggested that early life stress can impact on sexual preference, further highlighting a potential link between childhood trauma and sexual orientation\(^9,10\). We theorize that strong correlations exist among childhood trauma, sexual preference, and mental health issues. However, the underlying mechanism of childhood trauma-induced sexual orientation change remains unclear, and biological factors related to sexual orientation require further investigation.

Researchers have largely focused on neural correlates, genes, hormones, maternal immune responsivities and neuroendocrine systems in exploring the biological basis of sexual orientation\(^11,12\). Among these factors, sex
hormones have been found to be involved in the development of sexual orientation. Studies have indicated that perinatal levels of androgens or estrogens may influence gender nonconformity and sexual orientation. For example, males prenatally exposed to diethylstilbestrol (DES) were more likely to identify as bisexual or gay, while DES-exposed females were less likely to report being bisexual or lesbian. In recent years, researchers have also been looking into the neuropeptides oxytocin (OT) and arginine vasopressin (AVP), which are involved in regulating social behavior and cognition, including emotional regulation, social decision-making, sexual orientation, and partner preferences. Notably, AVP and OT may impact corticotropin-releasing factor function, potentially serving as key mediators of stress-induced adrenocorticotropic secretion. Antagonists of vasopressin increased stress hormone levels in the early postnatal period, indicating a strong association between VP and stress hormones. However, to date, there is no direct evidence that explores the role of OT and AVP in childhood trauma-induced sexual orientation changes.

OT and AVP play a crucial role in regulating social and reproductive behaviors and have been implicated in the pathogenesis of neuropsychiatric disorders, including autism, schizophrenia, bipolar disorder, and major depressive disorder. In clinical research, OT has been found to dose-dependently modulate chemosensory decoding of sexual cues in both heterosexual and homosexual men. Additionally, studies have found higher levels of OT during ejaculation or orgasm, suggesting that OT may modulate sexual arousal. AVP has been found to enhance human cognition of sexual stimuli and regulate partner preference in male and female prairie voles. Moreover, blocking AVP signaling in the ventral pallidum has been linked to significantly reduced male opposite-sex preference and enhanced female opposite-sex preference and estrus, highlighting the strong associations between AVP and behavioral symptoms of sex preference. Hence, we speculate that OT and AVP may have the potential to target and modulate sexual orientation.

Based on previous studies, we propose that childhood trauma is associated with sexual orientation, and that OT and AVP play prominent roles in this process. In this study, we aimed to explore the link between childhood trauma and sexual orientation, and clarify the role of OT or AVP in sexual orientation. An initial analysis of the mental state and childhood trauma experience, as well as serum OT and AVP levels, was conducted on a sample of 32 heterosexual and 57 gay/bisexual men. Subsequently, animal studies were undertaken to investigate how OT and AVP might contribute to sexual orientation in relation to childhood trauma. The outcomes of this study will provide a robust experimental foundation for further investigations into the pathogenesis of childhood trauma-induced changes in sexual orientation, as well as present fresh opportunities for research into sexual orientation disorders.

Results

Gay/bisexual men experienced higher levels of childhood trauma compared with heterosexual men

A total of 32 heterosexual men and 57 gay/bisexual men were included in the analysis. Table 1 shows the basic characteristics and information of participants. Overall, the groups differed according to their sexual orientation. Gay/bisexual men experienced more childhood trauma and had lower good interparental relationship rates than heterosexual men (c² = 27.44, p < 0.001; c² = 18.51, p < 0.001; Table 1 and Fig. 1A-1B). These results suggest a correlation between sexual orientation and childhood trauma. To validate this conjecture, we posted the CTQ on the two clusters. Table 2 shows the scores from the CTQ questionnaires.
Emotional abuse ($t_{87} = 2.692, p = 0.0052$), physical abuse ($t_{87} = 2.349, p = 0.0211$), sexual abuse ($t_{87} = 2.797, p = 0.0017$), and the total score ($t_{87} = 2.981, p = 0.0024$) were all significantly higher in gay/bisexual men than in heterosexual men (Table 2). The above results strongly suggest that gay/bisexual men exert significant childhood trauma compared with heterosexual individuals and confirm that childhood trauma is an environmental factor of sexual orientation.

In addition, we analyzed psychiatric symptoms in relation to sexual orientation. Data from the SCL-90 showed that gay/bisexual men have significant symptoms of mental health issues, such as depression and anxiety, compared with heterosexual individuals (Table S1).

**Serum OT and AVP levels were decreased in gay/bisexual men compared with heterosexual men**

To verify whether the OT and AVP level change between heterosexual men and gay/bisexual men, pretreatment serum samples were available from 82 participants, of whom 30 were heterosexual men and 52 were gay/bisexual men. Compared to heterosexual men, the levels of OT and AVP in serum among gay/bisexual men were significantly lower ($t_{80} = 3.218, p = 0.002; t_{80} = 4.036, p < 0.0001$; Fig.1C-1D). The inverse relationship between the Kinsey score and serum OT and AVP levels was demonstrated by a scatter plot with fitted lining ($r = -0.2837, p = 0.0098; r = -0.3158, p = 0.0041$ Fig.1E-1F). These results suggest that OT and AVP may be involved in the development of sexual orientation. Thus, we conjectured that increasing the serum OT or AVP levels may be helpful in altering sexual orientation induced by childhood trauma. To test this hypothesis, we first conducted experiments using male mice to determine whether ELS have effect on sex preference in male mice.

**Exposure to ELS decreased heterosexual preference in male mice at adulthood**

The present experiment investigated the influence of early life trauma on sexual orientation in male mice at adulthood. Developmental mice were exposed to chronic unpredictable mild stress (CUMS) during PND22 to PND35 (weaning-stress) or PND 35 to PND 49 (puberty-stress), followed by a series of behavioral tests during adulthood. Social interaction test (SIT) was performed to evaluate social interaction. One-way ANOVA of data from the SIT showed that social interaction varied dramatically among groups ($F_{2,23} = 7.225 p = 0.0037$, Fig. 2B). Post-hoc Dunnett’s multiple comparisons test showed that, compared with the control group, the weaning-stress (W-S) group showed a significant decrease in social interaction ($p = 0.003$). The sniffing time remained constant among the groups ($F_{2,23} = 1.674, p = 0.21$; Fig. S1B). The sexual preference test (SPT) and bedding preference test (BPT) were conducted to assess sexual orientation. One-way ANOVA of data from the SPT and BPT showed that either the sexual preference index or the bedding preference index varied dramatically among groups ($F_{2,23} = 5.944 p = 0.0083, F_{2,20} = 6.649 p = 0.0058$ Fig. 2C-2D). Post-hoc Dunnett’s multiple comparisons test showed that compared with the control group, either the sexual preference index or bedding preference index noticeably decreased in the W-S group ($p = 0.0021, p = 0.0352$). However, puberty-stress (P-S) group only decreased bedding preference index in the BPT compared than in the control group ($p = 0.0064$). There was no difference in sniffing time between the groups in the SPT and BPT ($F_{2,23} = 0.6623 p = 0.5252, F_{2,20} = 1.029 p = 0.3756$, Fig.S1C-1D). The above results suggested that exposure to ELS decreased heterosexual preference.
and social interaction in male mice in adulthood, we further investigated whether ELS has an effect on behavioral symptoms of anxiety and whether ELS-induced lower opposite-sex preferences is associated with OT or AVP levels.

**Exposure to ELS increased anxiety-like behavior in male mice at adulthood**

Since gay/bisexual individuals experience more behavioral health issues, such as anxiety, we then explored whether ELS could increase anxiety-like behavior in adulthood in male mice. We first evaluated the effects of ELS on the body weight of the mice. Body weight did not differ significantly among groups (Fig. S1A). Mice were then performed in the open field test (OFT) and novelty-suppressed feeding test (NSF) to assess anxiety-like behavior. In the OFT, there was no difference in the exploration time in the center and locomotion activity in each group ($F_{2,23} = 3.208, p = 0.059; F_{2,23} = 1.191, p = 0.322$ Fig. 2E-2F). This showed that neither W-S nor P-S had any adverse effects on the spontaneous activity of the mice. One-way ANOVA analysis of the NSF data revealed a significant effect of ELS ($F_{2,23} = 12.444, p < 0.0001$, Fig. 2G). Post-hoc Dunnett's multiple comparisons test showed that, compared with the control group, the latency to feeding time was extended in the W-S group ($p < 0.0001$). Total feed intake did not differ among the groups ($F_{2,24} = 0.501, p = 0.613$; Fig. 2H). There was no difference between P-S and control group in the NSF. These results show that ELS, especially the W-S stage, can affect the sexual orientation and anxiety levels of male mice in adulthood.

**Exposure to W-S decreased serum levels of OT and AVP in male mice at adulthood**

As W-S has a significant effect on adult sexual orientation in mice, we examined the effects of W-S on the serum levels of OT and AVP. After behavioral testing, the serum levels of OT and AVP were analyzed. Compared with the control group, the W-S group exhibited decreased OT and AVP levels in the serum by ELISA ($t_{14} = 4.488, p = 0.0005, t_{14} = 3.227 p = 0.0061$, Fig. 2I-2J). Based on these observations, we next examined the role of OT and AVP in ELS-induced the change of sexual orientation.

**Intraperitoneal injection of OT reverses the lower opposite-sex preferences induced by stress during weaning period in male mice**

In the experiment, the mice's body weights remained stable between groups throughout the study (Fig. S1E). To investigate the acute and chronic effects of exogenously administered oxytocin (OT) on behavior, with mice receiving intraperitoneal injections of OT in two ways: during the CUMS procedure (OT-S group), or before each behavioral test (S-OT group). One-way ANOVA of data from the SIT showed that there was no difference among the groups in sniffing time ($F_{3,34} = 0.7332 p = 0.5394$, Fig.S1F). However, the social interaction index was difference among groups ($F_{3,34} = 2.881 p = 0.005$, Fig. 3B). Post-hoc analysis showed that the social interaction index was significantly reduced in the W-S group compared to that in the control group ($p = 0.044$). Compared to the W-S group, the social interaction index was improved in the OT-S group ($p = 0.034$). Results for SPT and BPT are similar. One-way ANOVA analysis showed significant differences among groups in the female sexual preference index in SPT and female bedding preference index in BPT ($F_{3,34} = 16.38, p < 0.0001, F_{3,34} = $
3.945 \( p = 0.0162 \) Fig. 3C-3D), while there was no difference among groups in sniffing time \((F_{3,34} = 0.9279 \ p = 0.4378, \ F_{3,34} = 2.438, \ p = 0.0814 \) Fig. S1G-1H). Post-hoc Dunnett’s multiple comparisons test showed that the W-S group demonstrated clear preference for the “male zone” in contrast to the control group in SPT and BPT \((p = 0.0002, \ p = 0.0043)\). Compared with W-S group, the OT-S group demonstrated clear preference for the “female zone” in SPT and BPT \((p < 0.0001, \ p = 0.0056)\). Only S-OT group in SPT showed clear preference for the “female zone” when compared with W-S group \((p < 0.0001)\). One-way ANOVA of data from the OFT showed that there was no difference among groups in the time spent in the center and total distance \((F_{3,34} = 0.8947 \ p = 0.4539, \ F_{3,34} = 0.7725 \ p = 0.5175, \) Fig. 3E-3F). This showed that neither stress nor OT administration had any adverse effects on the spontaneous activity of the mice. One-way ANOVA in FST revealed that intraperitoneal injection of OT improved stress-induced depression-like behavior \((F_{3,34} = 6.468, \ p = 0.0014; \ F_{3,34} = 2.82, \ p = 0.0535, \) Fig. 3G-3H). Post-hoc Dunnett’s multiple comparisons test showed that the W-S group had an increased immobility time compared to the control group \((p = 0.0365)\), and the immobility time in the S-OT group was lower than that in the W-S group \((p = 0.0479)\).

These results establish that OT produces anti-same sex preferences effect, as well as antidepressant- and anxiolytic effects. Importantly, OT can prevent ELS-induced same-sex preferences, highlight its prophylactic potential in altering sexual orientation.

**Intraperitoneal injection of AVP reverses the lower opposite-sex preferences induced by stress during weaning period in male mice**

In this experiment, body weight of the mice was unchanged between groups throughout the experiment (Fig. S1E). Similarly, mice receiving intraperitoneal injections of AVP in two ways: during the CUMS procedure (VP-S group), or before each behavioral test (S-VP group). In SIT, one-way ANOVA showed that the social interaction index was different among the groups \((F_{3,34} = 3.904 \ p = 0.017, \) Fig. 4B). Post-hoc analyses showed that compared with the control group, the social interaction index was decreased in the W-S group \((p = 0.048)\). The social interaction index was higher in AVP-S group compared to W-S group \((p = 0.024)\). There was no difference in sniffing time among the groups \((F_{3,34} = 0.796, \ p = 0.505, \) Fig. S1J). The results for the SPT and BPT were similar. One-way ANOVA results showed significant differences among groups in the female sexual preference index in SPT and female bedding preference index in BPT \((F_{3,34} = 11.595 \ p < 0.0001, \ F_{3,29} = 4.454 \ p = 0.0108 \) Fig. 4C-4D), while there was no difference among groups in sniffing time \((F_{3,34} = 1.445, \ p = 0.247; \ F_{3,29} = 0.869, \ p = 0.4684 \) Fig. S1K-1L). Post-hoc analyses showed that the W-S group demonstrated clear preference for the “male zone” in contrast to the control group in SPT and BPT \((p = 0.004, \ p = 0.0322)\). Compared with W-S group, the AVP-S group demonstrated clear preference for the “female zone” in SPT and BPT \((p < 0.0001, \ p = 0.0435)\). Compared with the W-S group, the S-AVP group also demonstrated a clear preference for the “female zone: in the SPT and BPT \((p < 0.0001 \text{ and } p = 0.0157, \text{ respectively})\). The mice were then evaluated using the OFT and FST for anxiety- and depression-like behaviors. In the OFT, there was no difference in exploring time in the center and locomotion activity between the group \((F_{3,34} = 1.464 \ p = 0.292, \ F_{3,34} = 0.932 \ p = 0.436 \) Fig. 4E-4F). This showed that neither stress nor AVP administration had any adverse effects on the spontaneous activity of the mice. One-way ANOVA in FST revealed that intraperitoneal injection of AVP improved stress-induced depression-like behavior \((F_{3,34} = 5.798, \ p = 0.003; \ F_{3,34} = 2.297, \ p = 0.045; \) Fig. 4G-4H). Post-hoc analyses showed
that the W-S group had an increased immobility time compared to the control group ($p = 0.015$), and the immobility time in the AVP-S group was lower than that in the W-S group ($p = 0.003$). These results establish that AVP produces anti-same sex preferences effect, as well as antidepressant- and anxiolytic effects. Importantly, AVP can prevent ELS-induced same-sex preferences, highlight its prophylactic potential in altering sexual orientation.

These results corroborate our conjecture that increasing the serum levels of OT and AVP may be helpful in correcting same-sex preferences induced by childhood trauma.

**Discussion**

Sexual orientation remains a contentious matter encompassing concerns pertaining to heightened susceptibility to certain ailments, such as HIV/AIDS, and psychological challenges encountered by individuals identifying as homosexual. In order to elucidate the determinants underlying individual homosexuality and address these concerns, our efforts have been directed towards exploring the influence of early-life distress and neuropeptides OT and AVP on sexual orientation. Within the present investigation, we have discovered notable psychological difficulties among gay/bisexual men, who have experienced greater instances of childhood trauma compared to their cisgender heterosexual counterparts. Moreover, our animal-based inquiries have demonstrated that adverse encounters in early life contribute to diminished preferences for individuals of the opposite sex. Additionally, our research has revealed lower serum levels of OT and AVP in gay/bisexual men when contrasted with heterosexual men, and has unveiled a negative correlation between the Kinsey score and serum levels of OT and AVP, respectively. These findings have also been corroborated by animal experiments, wherein OT and AVP have been observed to modulate sexual orientation in response to early-life stress. Thus, these results present novel prospects for comprehending the intricate interplay between childhood trauma and sexual orientation.

Individuals who identify as lesbian, gay, or bisexual have higher rates of childhood trauma compared to their heterosexual counterparts. A recent study conducted in the UK has shown that adolescents who belong to a sexual minority are more prone to experiencing various forms of bullying and victimization. Similarly, a nationally representative study involving 57,479 individuals in Denmark has found that non-heterosexual individuals report higher rates of adverse childhood experiences, which can lead to increased odds of mental health problems, especially among bisexual individuals. In line with these findings, our research has also shown that gay and bisexual men have experienced more traumatic childhood events compared to heterosexual men. In addition, the male mouse model of CUMS proved that ELS decreased the sexual preference of male mice to female mice but increased sexual preference in male mice. Therefore, our clinical findings and animal results suggest that adverse early life experiences may contribute to same-sex preference. Additionally, gay and bisexual individuals experience significant psychological distress, including anxiety and depression. Studies conducted on mice have also revealed that gay mice display more severe anxiety and depression behaviors than control mice. It follows that ELS can have adverse effects on individuals in adulthood, particularly in terms of sexual orientation and psychological problems. This highlights the importance of reducing the incidence of childhood traumatic events to promote heterosexual preference.

In 2013, Roberts et al. proposed a model linking childhood sexual abuse to an increase in homosexual orientation due to parental factors. However, this was challenged by Rind, who believed that homosexuality is not a pathology and exists widely in humans. As a result, the causal relationship between childhood stress and
sexual orientation remains unresolved. Effective treatment measures are necessary to assist sexual minority patients who have experienced childhood trauma and are troubled by their sexual orientation. As mentioned above, ELS exposure alters emotions and behaviors via neuropeptides OT and AVP. Women who experienced childhood abuse have lower concentrations of OT in cerebrospinal fluid, while parental divorce during childhood is associated with lower urinary OT concentrations in adulthood; furthermore, a recent study showed that AVP levels in infants are influenced by birth stress. This emerging evidence suggests that OT and AVP play significant roles in the experience of childhood trauma. Interestingly, OT and AVP have been verified to regulate sex preference in animal studies. Consistent with these studies, the present study indicates that serum levels of OT and AVP were lower in gay/bisexual men than in heterosexual men. This was exemplified by an inverse association between the Kinsey score and OT and AVP, which partly uncovers the relationship between childhood stress and sexual orientation. We further found that upregulated OT and AVP levels increase the same-sex preference index in ELS-exposed mice. Combined with population and animal data, this fully demonstrates that sexual orientation is related to OT and AVP.

Two different experimental protocols were used in animal experiments to assess the roles of OT and AVP. We adopted administration during ELS and administration after ELS to prove the prevention and treatment effects of OT and AVP. The findings indicated that OT and AVP possess preventive and ameliorating effects on the reduction in the rate of heterosexual preference induced by ELS. Correspondingly, Bales et al. have also demonstrated that the low to medium dose of intranasal OT reduces same-sex partner preference in males. Furthermore, we observed that the OT inhibitor reduced the preference rate of male mice for female bedding in BPT (figure not shown). This provides further evidence that the level of OT is closely associated with sexual orientation. In conclusion, OT and AVP might be potential molecular mechanisms that partially elucidate the link between early life stress and the alteration of sexual orientation.

Nevertheless, the present work has certain limitations. Firstly, the small sample size and grouping of gay and bisexual men may have obscured the subtle distinctions between homosexual and bisexual individuals. Bisexual individuals have a higher likelihood of psychiatric disorders compared to non-bisexual individuals, which implies that future studies should replicate our findings with a larger and more diverse sample. Secondly, our study only included male mice, and there appear to be gender differences in the effect of OT and AVP on social behavior. OT’s ability to accelerate sex preference is more pronounced in females, while AVP is more crucial for regulating male social cognition. Thus, the effects of OT or AVP treatment on behaviors in females need further investigation.

**Conclusion**

In summary, this study uncovered the underlying mechanism of sexual orientation involving both environmental and biological factors. Our results suggest a partial causal relationship between childhood trauma and sexual preference, and OT and AVP treatment can help ameliorate the reduced rate of heterosexual preference in male mice caused by ELS. Future research should concentrate on the role of OT and AVP in sexual minorities who wish to change their sexual orientation and the mechanisms underlying these disparities.

**Methods**
Participants and mice

Participants were recruited from the local Centers for Disease Control (CDC). Upon a 5-minute study explanation, eligible participants were completed the semi-structured in-depth interview, a self-made general questionnaire, Kinsey scale, childhood trauma questionnaire (CTQ) and symptom checklist 90 (SCL-90) at the local CDC. A total of 89 participants were recruited, of which 32 were heterosexual and 57 were gay/bisexual.

Two-week-old male ICR mice were purchased from Beijing Vital River Laboratory Animal Technology Co. Ltd. They were provided food and water ad libitum and housed under a conventional 12-h dark /12-h light cycle at a constant temperature of 21–22°C and 55–60% humidity. The mice were kept in the laboratory animal center and subjected to chronic unpredictable mild stress (CUMS) after one-week acclimatization. Behavioral tests were conducted after mice reached sexual maturity.

All procedures are detailed in the Supplement data.

Data availability

The data generated during this study are made available from the corresponding author upon reasonable request.

References

7. Nelson CA, Bhutta ZA, Harris NB, Danese A, Samara M. Adversity in childhood is linked to mental and physical health throughout life. bmj. 2020;371.


Tables

Table 1. Sample Descriptive Statistics According to Sexual Orientation
<table>
<thead>
<tr>
<th>Information</th>
<th>Heterosexual men</th>
<th>Gay/Bisexual men</th>
<th>t/χ²</th>
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<td>32</td>
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<td>Demographic</td>
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<td>Age(years),mean (SD)</td>
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<td>26.42(5.65)</td>
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<td>Unemployed,%</td>
<td>3.13</td>
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<td>Sexual Orientationa</td>
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<td>Behavioral</td>
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<td>Smokers, %</td>
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<tr>
<td>Siblings,%</td>
<td>68.75</td>
<td>80.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inteparental Relationship</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very good,%</td>
<td>93.75</td>
<td>49.12</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Generally,%</td>
<td>6.25</td>
<td>24.56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not too well,%</td>
<td>0.00</td>
<td>26.32</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Comparison of Childhood Trauma Questionnaire (CTQ) scores between Heterosexual and Gay/Bisexual men

<table>
<thead>
<tr>
<th>Item</th>
<th>Heterosexual men (n=32), mean(P25, P75)</th>
<th>Gay/Bisexual men (n=57), mean(P25, P75)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional Abuse</td>
<td>5.00(5.00-6.00)</td>
<td>6.00(5.00-9.50)</td>
<td>0.0052</td>
</tr>
<tr>
<td>Emotional Neglect</td>
<td>7.50(5.00-10.00)</td>
<td>9.00(5.00-15.00)</td>
<td>0.0867</td>
</tr>
<tr>
<td>Physical Abuse</td>
<td>5.00(5.00-5.00)</td>
<td>6.00(5.00-7.00)</td>
<td>0.0021</td>
</tr>
<tr>
<td>Physical Neglect</td>
<td>6.50(5.00-8.75)</td>
<td>9.00(7.00-9.50)</td>
<td>0.3693</td>
</tr>
<tr>
<td>Sexual Abuse</td>
<td>5.00(5.00-5.00)</td>
<td>6.00(5.00-7.50)</td>
<td>0.0017</td>
</tr>
<tr>
<td>Total scores</td>
<td>41.50(37.50-46.75)</td>
<td>47.00(41.50-55.50)</td>
<td>0.0024</td>
</tr>
</tbody>
</table>

Figures
Figure 1

Serum OT and AVP levels were decreased in gay/bisexual men induced by childhood trauma compared with heterosexual men

(A) Gay/bisexual men exert more early life trauma experience and (B) lower ratio of good interparental relationship. (C) Serum levels of OT in heterosexual men and gay/bisexual men. (D) Serum levels of AVP in heterosexual men and gay/bisexual men. (E) Correlation of Kinsey score with OT levels. (F) Correlation of Kinsey score with AVP levels. Data represent mean ± SEM. Data are presented as mean ± SEM; *p < 0.05, **p < 0.01, ***p < 0.001 versus the heterosexual men.
Figure 2

Early life stress, especially during weaning, reduces sexual preference in male mice and with a decrease in serum oxytocin and arginine vasopressin

(A) Timeline of ELS and behavioural tests. (B) In the SIT, social interaction index in W-S was decreased relative to CON. (C) In the SPT, preference index to female mice in W-S was decreased relative to CON. (D) In the BPT, preference index to female mice in W-S and P-S were decreased relative to CON. (E-F) In the OFT, the time spent in center and total distance were without affecting by early life stress. (G) In the NSF, the latency to feeding time in W-S group was increased relative to CON. (H) In the NSF, total food intake was no changed among groups. (I-
J) The OT and AVP levels in the serum were decreased in mice of W-S relative to CON. Data represent mean ± SEM. Data are presented as mean ± SEM; *p < 0.05, **p < 0.01, ***p< 0.001 versus the CON group.

Figure 3

Intraperitoneal injection of OT reverses the lower opposite-sex preferences induced by stress during weaning period in male mice

(A) Schematic illustrating intraperitoneal injection and behavioural test timeline. (B) Intraperitoneal injection of OT restored ELS-induced decreased social interaction index in the SIT. (C) Intraperitoneal injection of OT restored
ELS-induced decreased female sexual preference index in the SPT. (D) Intraperitoneal injection of OT restored ELS-induced decreased female sexual preference index in the BPT. (E) In the OFT, there was no difference among groups in the time spent in the center. (F) In the OFT, there was no difference among groups in total distance. (G) Intraperitoneal injection of OT restored ELS-induced increased immobility time in the FST. (H) There was no difference among groups in latency to floating time in FST. Data represent mean ± SEM. Data are presented as mean ± SEM; *p < 0.05, **p < 0.01, ***p < 0.001 versus the CON group. #p < 0.05, ##p < 0.01, ###p < 0.001 versus W-S group.

Figure 4
Intraperitoneal injection of AVP reverses the lower opposite-sex preferences induced by stress during weaning period in male rats.

(A) Schematic illustrating intraperitoneal injection and behavioural test timeline. (B) Intraperitoneal injection of AVP restored ELS-induced decreased social interaction index in the SIT. (C) Intraperitoneal injection of AVP restored ELS-induced decreased female sexual preference index in the SPT. (D) Intraperitoneal injection of AVP restored ELS-induced decreased female sexual preference index in the BPT. (E) In the OFT, there was no difference among groups in the time spent in the center. (F) In the OFT, there was no difference among groups in total distance. (G) Intraperitoneal injection of AVP restored ELS-induced increased immobility time in the FST. (H) Intraperitoneal injection of AVP restored ELS-induced decreased latency to floating time in the FST. Data represent mean ± SEM. Data are presented as mean ± SEM; *p < 0.05, **p < 0.01, ***p < 0.001 versus the CON group. #p < 0.05, ##p < 0.01, ###p < 0.001 versus W-S group.

Supplementary Files

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- Supplementarydata.docx