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Gonads and strife: Sex hormones vary according to sexual orientation for women and stress indices for both sexes

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ABSTRACT

This study assessed sexual orientation and psychobiological stress indices in relation to salivary sex hormones as part of a well-validated laboratory-based stress paradigm. Participants included 87 healthy adults that were on average 25 years old who self-identified as lesbian/bisexual women ($n = 20$), heterosexual women ($n = 21$), gay/bisexual men ($n = 26$), and heterosexual men ($n = 20$). Two saliva samples were collected fifteen minutes before and fifteen minutes after exposure to a modified Trier Social Stress Test to determine testosterone, estradiol, and progesterone concentrations via enzyme-immune assaying. Mean sex hormones were further tested in association to stress indices related to cortisol systemic output (area under the curve with respect to ground) based on ten measures throughout the two-hour visit, allostatic load indexed using 21 biomarkers, and perceived stress assessed using a well-validated questionnaire. Results revealed that lesbian/bisexual women had higher overall testosterone and progesterone concentrations than heterosexual women, while no differences were found among gay/bisexual men in comparison to heterosexual men. Lesbian/bisexual women and heterosexual men showed positive associations between mean estradiol concentrations and allostatic load, while gay/bisexual men and heterosexual women showed positive associations between mean testosterone and cortisol systemic output. In summary, sex hormone variations appear to vary according to sexual orientation among women, but also as a function of cortisol systemic output, allostatic load, and perceived stress for both sexes.

1. Introduction

Exploration into the neurobiological correlates of sexual orientation has had a controversial history. Early research reflected homosexuality's classification as a mental illness until 1973, at which time the American Psychiatric Association removed it from its diagnostic manual (Friedman and Downey, 1994). Biological explanations of non-heterosexual behavior have often hypothesized a dysregulation of sex-specific hormone profiles, resulting in anomalies in the organizational and activational effects of these hormones on the neurodevelopment of circuitry underlying species-specific sexual behavior. Animal models involving prenatal androgen deficits, for example, were first believed to cause male homosexuality (Phoenix et al., 1959), while prenatal androgen overabundance presumably resulted in female homosexuality. Our study endeavours to show that such sex hormone differences assumed to be attributable to sexual orientation are also modulated by unexplored stress phenomena.

Advances in behavioral neuroscience has led to the introduction of sophisticated genetic models involving non-functional androgen receptors, further allowing researchers to characterize the relation-

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ship between androgens, the masculinization of the rodent brain, and sexual behavior (Zuloaga et al., 2008). Guided by this literature, perturbations in the human prenatal environment during a critical period (between 10 to 22 weeks gestation) might expose the human fetus to androgen imbalances that have the potential to alter structure and function of key neuroanatomical regions implicated in human sexuality (Ellis and Ames, 1987). While this early exposure of androgens to the developing brain is understood to affect post-natal sex/gender, sexual orientation, and related behaviors, the literature has been inconclusive and thus reflects the multifactorial nature of human sexuality.

Several human studies during the 1970s using analytes extracted from either urine, serum, or plasma revealed that men belonging to a sexual minority showed higher testosterone (Brodie et al., 1974; Doerr et al., 1976; Tourney and Hatfield, 1973), lower testosterone (Brodie et al., 1974; Kolodny et al., 1972; Kolodny et al., 1971; Loraine et al., 1971; Loraine et al., 1970; Pillard et al., 1974; Rohde et al., 1977; Stahl et al., 1976), no differences in testosterone (Barlow et al., 1974; Birk et al., 1973; Doerr et al., 1973; Jaffee et al., 1980), higher estrogen (Doerr et al., 1973; Doerr et al., 1976), or lower estrogen (Evans, 1972) when compared to heterosexual controls. Likewise, among sexual minority women compared to age-matched heterosexual controls, studies have reported lower estrogen (Loraine et al., 1971; Loraine et al., 1970), higher testosterone (Loraine et al., 1971; Loraine et al., 1970), no differences in testosterone (Downey et al., 1987), and no differences in estrogen or progesterone (Griffiths et al., 1974; Seyler et al., 1978). Similarly for gonadotropins, studies reporting elevated luteinizing hormone concentrations among sexual minority men (Kolodny et al., 1972) and women (Loraine et al., 1971) have been matched by an abundance of research failing to show differences in luteinizing hormone, follicle stimulating hormone, as well as prolactin (Friedman and Frantz, 1977; Jaffee et al., 1980; Kolodny et al., 1971; Parks et al., 1974).

In a critical review of the literature, Meyer-Bahlburg concluded that findings were overall inconsistent among sexual minority men (Meyer-Bahlburg, 1977). By contrast, about one-third of participating sexual minority women manifested elevated androgen levels while otherwise showing no endocrine abnormalities (Meyer-Bahlburg, 1979). Importantly, methodological differences between studies rendered comparisons and any final conclusions difficult. This body of human research did not support the neurohormonal hypothesis of sexual orientation (Banks and Gartrell, 1995). Meyer-Bahlberg acknowledged that some early researchers were rightfully cautious in their conclusions (Meyer-Bahlburg, 1977). In particular, the inconsistencies in observed HPG-axis patterns might not be the primary cause of sexual minority orientation, but rather a secondary consequence related to unmeasured factors such as psychosocial stress (Kolodny et al., 1972; Meyer-Bahlburg, 1979).

Stress researchers during the 1970s began showing that psychological factors could modulate the HPG-axis. For example, a longitudinal study among military men undergoing stressful training revealed that plasma testosterone levels were lowest during the earlier novice phase compared to the later senior phase (Kreuz et al., 1972). This paralleled the pioneering work of Mason who systematically studied stressful situations (e.g., parachute jumping, air-traffic controlling) and identified key psychological determinants (e.g., novelty, uncontrollability) that activated stress responses (Mason, 1968). Unfortunately this knowledge was not applied to understanding the mixed HPG-axis literature on sexual orientation, despite speculation that psychosocial stress might be involved in study inconsistencies. Because sexual minorities are at an increased risk for stress-related pathologies due to stigma and discrimination (IOM, 2011; Meyer, 2003), it is highly probable that unique psychosocial contexts influence HPG-axis profiles and might confound the literature describing biological differences focusing purely on sexual orientation, identity, & behavior.

Advances in psychosocial and biological approaches to studying stress propelled an entire field of psychoneuroendocrine research aimed at identifying mechanisms of disease susceptibility. In particular, the development of laboratory-based stress induction paradigms have substantiated that the sexes differ in their stress response patterns of the stress hormone cortisol easily collected via saliva. Studies using the popular Trier Social Stress Test or TSST (Kirschbaum et al., 1993) consistently show that men mount a greater cortisol response than women of reproductive age (Kirschbaum et al., 1992). In turn, women show further attenuation when using oral contraceptives (Kirschbaum et al., 1995) or during the high estrogen (follicular) phase of their menstrual cycles as opposed to during the luteal phase (Kirschbaum et al., 1999).

Beyond sex differences in stress reactivity, research applying stress biomarkers are beginning to be used to understand how stigma affects the health and wellbeing of sexual minorities (Hatzenbuehler et al., 2013). Our group has recently provided novel evidence that sexual orientation modulates cortisol reactivity. Specifically, lesbian/bisexual women show higher post-stressor cortisol concentrations compared to heterosexual women, while gay/men show overall lower cortisol concentrations compared to heterosexual men after controlling for basal sex hormone concentrations (Juster et al., 2015). In addition to this, we found that sexual minority participants who had disclosed their sexual orientation to family and friends evidenced lower morning cortisol levels and less psychiatric symptoms than those who had not completely disclosed irrespective of sex (Juster et al., 2013b). These reports suggest that important psychosocial and behavioral factors may result in distinct biological signatures.

It remains unknown however, how circulating sex hormones in the context of the TSST paradigm vary as a function of one's sexual orientation, and how these associations are further modulated by stress phenomena. In the current study, we explored whether sexual minorities differ from same-sex heterosexual controls in terms of salivary testosterone, estradiol, and progesterone concentrations before and after exposure to the TSST. Guided by our previous reports showing that biopsychosocial stress is uniquely experienced between and within sexual orientations (Juster et al., 2015; Juster et al., 2016a; Juster et al., 2013b), we further assessed whether changes in sex hormones were associated with cortisol systemic output summarized using 10 measurements throughout the TSST, allostatic load indexed using 21 stress-related biomarkers, and finally perceived stress.

Given the mixed findings in the HPG-axis literature on sexual orientation and the lack of studies linked to stress indices, we did not hypothesize directionality of associations. We did, however, hypothesize that psychobiological stress indices would correlate with mean sex hormone concentrations beyond those associations attributable to sexual orientation.

2. Methods

2.1. Participants

Eighty-seven participants ages 18–45 ($M = 24.61 \pm 0.61\ SE$) identifying as lesbian or gay (8 women and 20 men), bisexual (13 women and 6 men), and heterosexual (20 women and 21 men) were recruited from Montreal as part of a broader research program (Juster et al., 2015; Juster et al., 2016a; Juster et al., 2013b). To equalize groups due to fewer lesbians and bisexual men, we combined lesbian/gay with bisexual individuals (20 women and 26 men) and contrasted them to heterosexuals (20 women and 21 men).