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BIRTH ORDER AND ANDROPHILIC MALE-TO-FEMALE TRANSSEXUALISM IN BRAZIL

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Summary. Previous research has indicated that biological older brothers increase the odds of androphilia in males. This finding has been termed the *fraternal birth order effect*. The *maternal immune hypothesis* suggests that this effect reflects the progressive immunization of some mothers to male-specific antigens involved in fetal male brain masculinization. Exposure to these antigens, as a result of carrying earlier-born sons, is hypothesized to produce maternal immune responses towards later-born sons, thus leading to female-typical neural development of brain regions underlying sexual orientation. Because this hypothesis posits mechanisms that have the potential to be active in any situation where a mother gestates repeated male fetuses, a key prediction is that the fraternal birth order effect should be observable in diverse populations. The present study assessed the association between sexual orientation and birth order in androphilic male-to-female transsexuals in Brazil, a previously unexamined population. Male-to-female transsexuals who reported attraction to males were recruited from a specialty gender identity service in southern Brazil (n = 118) and a comparison group of gynephilic non-transsexual men (n = 143) was recruited at the same hospital. Logistic regression showed that the transsexual group had significantly more older brothers and other siblings. These effects were independent of one

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another and consistent with previous studies of birth order and male sexual orientation. The presence of the fraternal birth order effect in the present sample provides further evidence of the ubiquity of this effect and, therefore, lends support to the maternal immune hypothesis as an explanation of androphilic sexual orientation in some male-to-female transsexuals.

Introduction

Androphilia refers to sexual attraction and arousal towards adult males whereas *gynephilia* refers to sexual attraction and arousal towards adult females. Numerous studies have shown that older brothers increase the odds of androphilia in later-born males. The observed increase in odds is typically between 15 and 50% per older brother (e.g. Blanchard & Bogaert, 1996; Blanchard *et al.*, 1998; Blanchard & Lippa, 2007). This phenomenon has been termed the *fraternal birth order effect.* This effect is most easily demonstrated when the mean number of older brothers is elevated among androphilic, compared with gynephilic, males and the mean sum of other siblings (i.e. older sisters + younger brothers + younger sisters) is similar across these groups. If the mean sums of other siblings are not similar, or if there are other large demographic differences between groups, statistical corrections are sometimes needed to see the effect (e.g. Blanchard, 2014).

The best-developed explanation of the fraternal birth order effect is the *maternal immune hypothesis* (Blanchard & Bogaert, 1996; Bogaert & Skorska, 2011). This hypothesis argues that antigens from male fetuses' cells enter maternal circulation during pregnancy, promoting an immune response to these male-specific antigens. This immune response would, in turn, produce long-lasting effects on the brain of the male fetus, preventing its neurons from making a male-typical pattern of connections, resulting in attraction towards men rather than women. In its general form, the maternal immune hypothesis does not specify which male-specific proteins are most likely to be involved. Based on considerations like tissue distribution and prenatal expression, it has been conjectured (see Blanchard *et al.*, 2002; Blanchard, 2004) that two likely proteins are PCDH11Y (Blanco *et al.*, 2000) and NLGN4Y (Jamain *et al.*, 2003). As noted by Blanchard (2008), the maternal immune hypothesis does not challenge the long-standing theory that sexual orientation is primarily influenced via prenatal sex hormone exposure; rather, it proposes that sexual orientation in the human male brain is influenced by two systems: one driven by prenatal sex hormones and a supplementary system driven by male-specific proteins under direct genetic control.

Several lines of research support the plausibility of the maternal immune hypothesis. To begin with, fetal cells and fetal molecular material have been found in maternal circulation during early pregnancy and postpartum, a phenomenon called microchimerism (Lo *et al.*, 1996; O'Donoghue *et al.*, 2004; Gammil *et al.*, 2010). Further evidence points to a specific T-cell-mediated immune response towards antigens arisen from the Y-chromosome, called male antigens (HY) (Piper *et al.*, 2007; Khan & Baltimore, 2010; Lissauer *et al.*, 2012; Dierselhuis *et al.*, 2014) as well as polymorphisms to minor histocompatibility complexes (Christiansen *et al.*, 2012), which might play a significant role in the maternal immune response to male fetuses. Additional evidence shows higher prevalence of male fetus miscarriages in women with a supposedly more HY-reactive

HLA (Hiby *et al.*, 2008; Nielsen *et al.*, 2009), and the number of sons a woman has throughout life has been associated with age-linked inflammation (Marttila *et al.*, 2015), thus providing further evidence of a male-specific maternal immune response.

In addition, the fraternal birth order effect does indeed appear to be prenatal in origin. First, relatively low birth weight provides a marker of prenatal exposure to a maternal immune response (for review, see VanderLaan *et al.*, 2015) and androphilic males who have older brothers exhibit lower birth weights (Blanchard & Ellis, 2001; Blanchard *et al.*, 2002; VanderLaan *et al.*, 2015). Hence, even at the time of birth, there seems to be a physical marker of sexual orientation (i.e. birth weight) that is related to the number of older brothers. Second, Bogaert (2006) examined the association between male sexual orientation and biological siblings (i.e. born from the same mother) and non-biological siblings (i.e. adoptive, step or paternal half-siblings). Whether and how long probands were reared with these siblings was also considered. Biological older brothers significantly predicted male sexual orientation regardless of whether or how long probands were reared with these brothers. In contrast, the remaining sibling categories, including non-biological older brothers, did not.

By virtue of suggesting that the fraternal birth order effect is prenatal in origin, the maternal immune hypothesis posits mechanisms that have the potential to operate in any situation where a mother gestates a male fetus in more than one pregnancy. As such, one would predict the fraternal birth order effect to be nearly ubiquitous – with the exception of populations where people do not have older brothers (e.g. China: Xu & Zheng, 2015). One approach for establishing the ubiquity of this effect has been to examine a variety of sample types. To date, the fraternal birth order effect has been documented in university and community convenience samples, national probability samples, clinical samples of male-to-female transsexuals, clinical samples of men who are primarily attracted to prepubescent or pubescent children, clinical samples of natal male children and adolescents who are likely to be androphilic as adults, and archival samples of men interviewed decades ago (for reviews, see Blanchard, 1997, 2004; Bogaert & Skorska, 2011; VanderLaan *et al.*, 2014; Blanchard & VanderLaan, 2015). In addition, this effect has been documented in several countries (e.g. Canada: Blanchard & Bogaert, 1996; Italy: Camperio Ciani *et al.*, 2004; The Netherlands: Schagen *et al.*, 2012; Samoa: VanderLaan & Vasey, 2011; Spain: Gómez-Gil *et al.*, 2011; Turkey: Bozkurt *et al.*, 2015; UK: King *et al.*, 2005; USA: Schwartz *et al.*, 2010).

Despite the consistency with which the fraternal birth order effect has been observed, there has been debate regarding its ubiquity and, by extension, the role of maternal immune factors in the development of male sexual orientation. Some studies failed to replicate this effect, raising scepticism about its importance (e.g. Currin *et al.*, 2015; Frisch & Hviid, 2006; Kashida & Rahman, 2015). Other research reported that androphilic males show elevations in older brothers and older sisters, raising the question of whether the male sexual orientation difference in birth order is specific to older brothers (e.g. King *et al.*, 2005).

Blanchard and VanderLaan (2015) addressed both of these challenges. First, their re-analyses of the data presented by Frisch and Hviid (2006) and Kashida and Rahman (2015), respectively, indicated that the fraternal birth effect was, in fact, evident in these samples. Further, they noted that failures to replicate (Type II error) are to be expected in some proportion of studies, as is the case with any true effect. Second, they explained

that number of older brothers tends to be correlated positively with number of older sisters. Thus, although one would expect to observe older sister effects in some proportion of samples, older sister effects should not be observed as consistently as older brother effects. Indeed, Blanchard and VanderLaan (2015) presented a meta-analysis showing that only the older brother effect was reliably associated with male sexual orientation across previously published studies.

An additional means of continuing to evaluate the reliability and ubiquity of the fraternal birth order effect is to examine birth order in relation to male sexual orientation in previously unexamined populations. The present study did so by comparing numbers of older brothers and numbers of other siblings in a sample of Brazilian male-to-female transsexuals who are attracted to men vs a comparison group of non-transsexual gynephilic men.

Methods

Participants

Participants ($N = 261$) were recruited at the Hospital de Clínicas de Porto Alegre (HCPA) from 2008 to 2013. All male-to-female transsexual participants ($n = 118$) were at least 18 years of age and were patients of the Gender Identity Program (PROTIG) who met the DSM-IV-TR criteria for Gender Identity Disorder (GID; American Psychiatric Association, 2000). Prior to assessment by PROTIG, all had previously used hormonal medications without medical guidance, but none had undergone sex-reassignment surgery. Three individuals assessed by PROTIG were excluded from the present study because they evidenced psychotic symptoms that limited the ability to make an accurate diagnosis concerning GID. None had a disorder of sex development.

The comparison group of gynephilic men ($n = 143$) consisted of medication-free volunteers who had no current, past history, or first-degree family history of a major psychiatric disorder, dementia or mental retardation. The sample was collected from non-psychiatric medical patients and companions at the outpatient clinics at HCPA, aged 18 years old or greater.

Measures

Male-to-female transsexuals and men completed a questionnaire about their age, year of birth and numbers of biological older and younger brothers and sisters from the same biological mother. Information regarding the sexual orientation of transsexual patients was obtained during semi-structured interviews with a psychiatrist (patients attended group and/or individual medical appointments on a biweekly basis). On the basis of this clinical information, all transsexuals were categorized as sexually attracted towards men. For the comparison group of men, they were asked to self-report their sexual orientation identity. All men self-reported a heterosexual sexual orientation identity (i.e. gynephilia, sexual attraction towards women).

Ethics statement

This research was approved by the institutional research ethics review board at the Hospital de Clínicas de Porto Alegre (HCPA).

Results

Table 1 shows descriptive statistics regarding age, year of birth and numbers of older brothers and other siblings by group. Male-to-female transsexuals were significantly younger (Levene's test for equality of variances: $F = 35.53$, $p < 0.001$, two-tailed independent samples *t*-test, $t(231.71) = -5.48$, $p < 0.001$) and had significantly later years of birth (Levene's test for equality of variances: $F = 39.18$, $p < 0.001$, two-tailed independent samples *t*-test, $t(227.64) = 3.54$, $p < 0.001$). The correlation between age and year of birth was near perfect (two-tailed Pearson's $r = -0.99$, $p < 0.001$), indicating that these variables were redundant with respect to the information they provided. As such, only age was retained as a control variable when comparing groups on sibship composition.

Table 2 summarizes the results of a logistic regression examining group differences in sibship composition. Group membership was the criterion variable with the male-to-female transsexuals coded as 1 and the control men coded as 0. Predictors in the model included: age, number of older brothers, number of other siblings, the interaction between age and number of older brothers, and the interaction between age and number of other siblings. All predictors were first centred to reduce multicollinearity and then entered in the model simultaneously to identify the unique contribution of each variable to predicting group membership (i.e. male-to-female transsexuals vs men). Male-to-female transsexuals had significantly more older brothers and significantly more other siblings. In addition, there was a significant interaction between age and number of other siblings such that probands in the present sample who were younger and had larger numbers of other siblings were more likely to be male-to-female transsexuals.

Table 1. Descriptive statistics

	Male-to-female transsexuals ($n = 118$)		Gynephilic men ($n = 143$)	
	Mean	SD	Mean	SD
Age	30.14	8.28	38.02	14.58
Year of birth	1980.02	7.99	1974.98	14.58
Number of older brothers	0.92	1.21	0.74	0.99
Number of other siblings[a]	2.18	1.80	1.98	1.79

[a]Number of older sisters + younger brothers + younger sisters.

Table 2. Logistic regression predicting group membership

Predictor	*B*	SE	Wald's χ^2 ($df = 1$)	*p*-value	Odds ratio
Age	−0.073	0.014	26.02	<0.001	0.93
Number of older brothers	0.277	0.126	4.86	0.028	1.32
Number of other siblings[a]	0.221	0.091	5.94	0.015	1.25
Age × number of older brothers	0.018	0.013	1.99	0.158	1.02
Age × number of other siblings	−0.022	0.009	6.26	0.012	0.98

Group is the criterion variable with men coded as 0 and male-to-female transsexuals coded as 1.
[a]Number of older sisters + younger brothers + younger sisters.

Discussion

The present study examined the fraternal birth order effect in Brazil, a previously unexamined population. Consistent with the maternal immune hypothesis and numerous previous studies conducted in other populations, Brazilian male-to-female transsexuals who reported sexual attraction towards men had significantly greater numbers of older brothers than a comparison group of gynephilic non-transsexual men. Importantly, this effect was independent of numbers of other siblings, thus providing further evidence of the unique contribution of older brothers to the development of same-sex sexual orientation among males.

In addition to documenting the fraternal birth order effect in the present sample, the odds ratio associated with this effect is noteworthy. Each additional older brother increased the odds of being in the male-to-female transsexual group by 32% (see Table 2). This value falls in the middle of the range of 15–50% reported previously (Blanchard & Bogaert, 1996; Blanchard *et al.*, 1998; Blanchard & Lippa, 2007) and is remarkably similar to the values of 33% reported for a Canadian sample (Cantor *et al.*, 2002) and 34% reported for a Samoan sample (VanderLaan & Vasey, 2011). Thus, across diverse populations, the fraternal birth order effect has been documented and each additional older brother contributes similarly to the odds of developing an androphilic sexual orientation in natal males. These patterns are consistent with the maternal immune hypothesis and suggest that the influence of older brothers on male sexual orientation development is ubiquitous.

It is less clear, however, whether older brothers, via maternal immune mechanisms, have a more general influence on male psychosexual development that includes the domains of gender behaviour and identity in addition to sexual orientation. Gay men tend to exhibit elevated cross-gender behaviour and identity during childhood (Bailey & Zucker, 1995; Rieger *et al.*, 2008) and report some female-typical characteristics during adulthood (for review, see Lippa, 2005). Also, as was the case with the present study, many studies documenting the fraternal birth order effect examined samples of natal males who exhibited marked cross-gender behaviour and identity (for review, see VanderLaan *et al.*, 2014). As such, some have suggested that fraternal birth order may not only relate to sexual orientation, but also to female-typical gender expression and identity, among androphilic natal males (Wampold, 2013; VanderLaan *et al.*, 2015).

To date, data bearing on this issue are limited. Two studies did not find associations between numbers of older brothers and female-typical characteristics among gay men (Bogaert, 2003; Rahman, 2005; although see VanderLaan *et al.*, 2015, for recent insights into why these studies may have not found such an effect). In four other studies, there was no fraternal birth order effect among clinical samples of natal males who exhibited marked cross-gender behaviour and identity but did not report predominant sexual attraction towards males (Blanchard & Sheridan, 1992; Blanchard *et al.*, 1996; Green, 2000; VanderLaan *et al.*, 2014). Thus, although further data are needed to address this issue, it appears that if the fraternal birth order effect and maternal immune hypothesis apply to variation in natal male gender expression as well as sexual orientation, then they probably only apply to natal males who exhibit both cross-gender characteristics and androphilic sexual orientation.

Apart from an older brother effect, two additional effects were observed in the present study. First, male-to-female transsexuals had greater numbers of siblings other

than older brothers. It is important to note that this effect was independent of the older brother effect discussed above. Furthermore, it is not uncommon for other sibling category effects to be observed in studies of birth order and male sexual orientation, although they are observed with less regularity than older brother effects (for review, see Blanchard & VanderLaan, 2015). As such, the presence of the other sibling effect in the present sample (Table 2) is not inconsistent with research on this topic, the fraternal birth order effect or the maternal immune hypothesis. Second, there was an interaction between age and number of other siblings in the prediction of group such that the transsexual probands were more likely to be younger and to have more other siblings. Such a finding has not been reported in the literature previously and there is no *a priori* reason to expect such a pattern. Unless this pattern is replicated in future studies, the most reasonable explanation is that this interaction effect was due to some form of sampling bias and is, therefore, unlikely to be theoretically meaningful.

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