

INVITED REVIEW of Raymond et al., “Increased birth rank of homosexual males: Disentangling the older brother effect and sexual antagonism hypothesis.” Prepared by Ray Blanchard, Ph.D., Department of Psychiatry, University of Toronto

It is my pleasure to accept the invitation from bioRxiv to review the preprint by Raymond et al. entitled “Increased birth rank of homosexual males: Disentangling the older brother effect and sexual antagonism hypothesis.” I am not personally acquainted with Professor Raymond or any of the other authors and I am comfortable that I can review the document impartially. I had a brief email exchange with Professor Raymond some time ago, in which he asked me for a copy of a data set (which I provided), and that is basically all the interaction I remember.

Studies of samples consisting of homosexual and heterosexual men have found that homosexual subjects tend to have more older brothers and to have larger families (i.e., larger sibships). These associations could arise in different ways: (1) Homosexual men have more older brothers because they come from larger families, or (2) Homosexual men have larger families because they have more older brothers. It is also possible that (3) these two observed associations arise independently from the operation of separate underlying mechanisms. The primary goal of Raymond et al.’s study is to determine which of these possibilities is most likely.

TERMINOLOGY

The association between higher numbers of older brothers and higher odds of homosexuality has sometimes been called the FBOE (fraternal birth order effect); the present authors called it the older brother effect (OBE). The association between larger family sizes and higher odds of homosexuality has sometimes been called the female fecundity effect (FFE); the present authors call it the sex-antagonistic effect (AE).

It might be noted that these labels have different relations to the phenomena that they denote. The terms FBOE, OBE, and FFE are purely descriptive and theoretically neutral. In contrast, the term AE is related to the theory that the decreased fertility of homosexual men is offset by an increased fertility in their female relatives (including their mothers). It is possible that this theory arose as an auxiliary hypothesis to reconcile findings of a probable genetic influence on homosexuality with the observation that homosexuality confers a reproductive disadvantage. It would have been my preference that the authors used the relatively atheoretical term FFE rather than AE for the sake of conceptual consistency. I do not, however, feel strongly enough to recommend that the authors search-and-replace all instances of AE with FFE, because this might entail identifying and re-writing additional relevant sentences in the text, and these could easily be missed in the re-write of a longish manuscript.

SIGNIFICANCE OF THE RESEARCH

This study is important to research on the developmental origins of sexual orientation for at least two related reasons. First, the FBOE/OBE and FFE/AE are potential clues to biological

influences on sexual orientation. They could lead – and, in the case of the FBOE/OBE, already have led – to laboratory research on the origins of homosexuality (Bogaert et al., 2018). It is therefore important to establish with survey data which, if either, of these phenomena is reliable and genuine (i.e., non-artifactual), because laboratory research is relatively expensive, labor-intensive, and time-consuming. One would expect laboratory scientists to be more willing to undertake research on the biological underpinnings of these phenomena if the phenomena themselves have been shown to be reproducible.

Second, statistically disentangling parameters of sibship composition (including the OBE and the AE) is difficult and fraught with potential hidden problems. It is therefore desirable to approach such analyses with a variety of different statistical methods, each based on its own sound mathematical-statistical logic, with the goal of obtaining convergent conclusions. The present authors have developed such a set of novel statistical tools to investigate the reliability of the OBE and the AE and to investigate whether one is an artifact of the other.

The remainder of my review will consist of more specific comments and suggestions. The manuscript appears to have been carefully prepared and well-reasoned. My relevant expertise is in the content area of OBE research rather than mathematical statistics, and this will be reflected in the topics on which I offer comments or suggestions. Some of my comments are in the nature of opinions or asides rather than specific suggestions for additions, deletions, or modifications to the manuscript. I recognize that practically all authors do some amount of cherry-picking the data that they cite or the conclusions that can be drawn from them. This is often necessary for clear exposition and does not necessarily imply any deceitfulness on the part of the author. Thus, I do not expect the authors to pick up on everything that I write, but there are some observations that I would like to make somewhere, and this review presents an opportunity for doing that.

COMMENTS ON THE INTRODUCTION

On page 4, the authors write, “it is still unclear whether the OBE is universal. The OBE is not always found, even in some large samples.”

It is easy to make too much of failures to detect an OBE in specific individual samples, even large ones. The OBE is a weak effect (in the statistical sense) perhaps because it shares influence on sexual orientation with numerous other factors, including multiple inherited genes. Thus, researchers will have low statistical power to detect it.

There is another, different reason that researchers should go into OBE research with the assumption of low statistical power. This relates to the maternal immune hypothesis (MIH), the notion that the OBE reflects the progressive immunization of some mothers to Y-linked antigen by each succeeding male fetus and the concomitantly increasing effects of anti-male antibody on sexual differentiation in the brain in each succeeding male fetus. On this view, live-born older brothers are most likely a proxy for maternal immunization to Y-linked antigens of fetal origin. If the MIH is essentially correct, then older brothers may be quite fallible as a proxy. One does

not know how many live-born sons did *not* expose their mothers to immunogenic amounts of Y-linked antigen, and one does not know how many miscarried (and perhaps never detected) male fetuses *did* expose their mothers to Y-linked antigen.

If any authors want to make the point that the universality of the OBE has not been fully demonstrated, they might do better to point out that nearly all the research has been carried out on subjects of European or Asian descent. There is little research on subjects of sub-Saharan African descent.

On pages 4–5, the authors also write, “the OBE is sometimes described from samples which are not comparable. For example, several meta-analyses . . . attempting to demonstrate an OBE in homosexual men across multiple studies include data from transexuals, pedophiles, hebephiles, or gender-dysphoria individuals As these different situations are drawn from highly non-representative populations . . . and are not necessarily the result of similar determinants as those for homosexuality, or could represent extreme values from a continuum, considering them could introduce some biases.”

Writers who make this criticism never point out that the compared homosexual and heterosexual groups were matched on the variable that distinguished them from standard samples; that is, homosexual pedophiles were compared with heterosexual pedophiles, homosexual transexuals were compared with heterosexual transexuals, and so on. In general, the homosexual group has been shown to report more older brothers than its heterosexual control group.

Thus, one could just as easily cite the findings from special groups as evidence for the broad applicability of the OBE. In practice, the atypicality of the groups is generally given as a reason for dismissing the findings out of hand, either because the writer wants to argue for the need of more research or because the writer would like to dismiss all evidence for the OBE in any way that he or she can.

COMMENTS ON THE METHOD AND RESULTS

Raymond et al. have thoroughly explicated the statistics they used (or developed) for their study. As I previously indicated, I will not attempt to critique their methodological innovations, because I have no particular expertise in mathematical statistics and there are plenty of other people who do. I can, however, compare their findings with those obtained in other, recently published analyses of homosexual and heterosexual males.

Prior to 2021, a variety of statistical approaches had been used in studies of the FBOE/OBE and FFE/AE. An emerging standard for investigating the FBOE/OBE was a logistic regression model, in which the criterion variable was the subject’s sexual orientation, dichotomously coded as heterosexual or homosexual, and the predictor variables were the subject’s numbers of older brothers, older sisters, younger brothers, and younger sisters. This approach had some drawbacks and limitations, which caused Blanchard and Lippa (2021) and Ablaza et al. (2022) to develop

new statistical procedures, which were different from each other and also different from the procedures used by Raymond et al. Because these studies used completely different methods to approach the same questions, it is useful to consider how Raymond et al.'s conclusions compare with those of the other two studies.

Raymond et al. agree with Blanchard and Lippa and Ablaza et al. in two ways: All three studies found positive evidence of an OBE (FBOE) and no evidence for an AE (FFE). Raymond et al. disagree with Blanchard and Lippa and Ablaza et al. in one way: Raymond et al. found no evidence for an OSE (SBOE), whereas both Blanchard and Lippa and Ablaza et al. did find evidence for such an effect. Thus, the study by Raymond et al. helps to clarify which topics within this research area most require further investigation.

COMMENTS ON THE DISCUSSION

I do not understand some of the remarks by Raymond et al. regarding prior research on the OSE (called the SBOE by other authors), that is, the possible existence of a positive correlation between a subject's number of live-born older sisters and his odds of being homosexual. On pages 23–24, Raymond et al. wrote, “Thus, the report, in a recent meta-analysis, of a widespread OSE in addition to the OBE (Blanchard and Lippa, 2020), should be treated with caution, as we have shown how an apparent OSE is generated when only OBE is acting (fig. 1). . . . This sampling bias does not rule out the action of a genuine OSE in population data, but any claim for an OSE, or for any additional sibling effect, should first control for the sampling bias generated by OBE. . . . We thus conclude that there is, to date, no conclusive support for an OSE in empirical data. The only exception is perhaps from Ablaza et al. (2022), although their new regression method, using several highly correlated variables, requires a formal validation.”

In the first place, the study by Blanchard and Lippa (2021) was not a meta-analysis but a reanalysis of a single large data set. It is possible that Raymond et al. are confusing the study by Blanchard and Lippa (2021) with the study by Blanchard, Beier, Gómez Jiménez, Grundmann, Krupp, Semenyna, and Vasey (2021), which did use meta-analysis, and which also found evidence for an OSE/SBOE, albeit using a completely different methodology.

It is possible that Blanchard and Lippa's finding of an OSE is wrong but it is not possible that it is artifactual. In other words, it is possible that Blanchard and Lippa's finding was simply the result of sampling error (virtually always and everywhere a possibility) but it is not possible that the observed correlation between live-born older sisters and homosexuality was the artifactual result of a correlation between live-born older brothers and homosexuality. That is because Blanchard and Lippa's investigation of the OSE was carried out on a subset of subjects who had no older brothers.

Blanchard and Lippa (2021) reasoned that mothers can be immunized by male fetuses, whether these fetuses are subsequently delivered as live-born infant boys or are miscarried. They further reasoned that the number of live-born girls a man's mother delivered before him should correlate

with the number of male fetuses that she miscarried before him. Thus, one should observe very slightly higher rates of homosexuality in men who had one or more older sisters but no older brothers compared with men who had no older siblings of either sex. That is exactly what Blanchard and Lippa (2021) found.

As far as I can see, the research design of Blanchard and Lippa (2021) is pretty clean, and the results cannot be explained as an artifact of older brothers, because none of the subjects had any older brothers. It is noteworthy that they found that one older sister increased the odds of homosexuality by 12% and two or more older sisters increased the odds of homosexuality by 39%. Furthermore, the one subsequent published study that also made a preplanned attempt to detect an OSE did detect one (Ablaza et al., 2022) and the magnitude of the OSE was similar.

In summary, I think that Raymond et al. should refine their conclusion, in the Abstract, for example, that “An OSE seems to result from a sampling bias in presence of OBE, and is likely to be artefactual.” There is little question that the correlation between live-born older brothers and homosexuality does produce an artifactual correlation between live-born older sisters and homosexuality, but Raymond et al. have been too quick to dismiss evidence from other studies that a small correlation between live-born older sisters and homosexuality may remain after one has excluded the effect of live-born older brothers.

On page 23, the authors wrote, with regard to prior research, that “the generation of various ad hoc statistics to test various hypotheses has added to the confusion.” I think the authors should be careful about throwing around “ad hoc” as a pejorative. One could argue that the statistical procedures they developed for their own study are just as “ad hoc.”

On page 27, as elsewhere in the manuscript, the authors state their important conclusion that “After controlling for the confounding effect of the OBE on fertility in families of heterosexuals and homosexuals, we have found no direct association between higher maternal fertility and male homosexual orientation, i.e. no support for genetic factors increasing fertility of females and increasing at the same time the probability that any given son is homosexual.” This is an important conclusion, because the balancing selection hypothesis of homosexuality has long been a favorite of evolutionary psychologists, evolutionary biologists, and geneticists.

I think it adds to their study rather than detracting from it to point out that other authors have also reached the conclusion that homosexual men do not come from larger sibships than heterosexual men when birth order is taken into account. The study by Blanchard (2012), while not particularly sophisticated with regard to methodology, included the historically important interview data collected by Alfred Kinsey and his associates. The conclusion reached by Blanchard (2012) was not supported by Rieger et al. (2012), but it was supported by Ablaza et al. (2022).

MISCELLANY

I have two comments regarding Table 1. First — and this is important — the group labels are reversed for the homosexual and heterosexual subjects in the study by Blanchard and Lippa (2007). Second, In Table 1, the data for the homosexual and heterosexual subjects in each study are given in random order: Sometimes the data for the homosexuals are given first and sometimes the data for the heterosexuals are given first. I think it would be highly desirable to make this consistent between studies.

The section headed “Aggregated family data” on page 19 could be made easier to follow. One has to go back to page 11 to see that male birth rank is computed as $OB/N + 1$ and female birth rank is computed as $OS/N + 1$. Reminders of these formulas could easily be given in parentheses on page 19. Similarly, it might be helpful to remind the reader somewhere that the X-axes in Figure 2 are actually Fertility/2.

On page 8, Raymond et al. state “In a meta-analysis, when data are restricted to families with only one or only two sons, no AE is found (Blanchard et al., 2020b), although this analysis includes a paper retracted since then.” They need to report what paper was retracted. (I haven’t heard anything about it.) This is surely not a secret; there is a whole website called Retraction Watch. This is important information for future authors who need to review the literature or perform meta-analyses on it.

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