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# Sex Differences in Normal Fetuses and Infants: A Commentary

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Sex differences in normal fetuses and infants: A commentary

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### Abstract

Sex differences in infants warrant attention, not because they clarify the extent to which such differences reflect Nature or Nurture, but because studying them is likely to illuminate the origins of sex differences later in life and thereby yield manipulations that could influence the development of important competences. It is not yet clear how male and female infants come to differ. Testosterone is influential, but because of the complexity of the developmental systems in which it operates, its effects are not straightforward: testosterone does different things in different contexts. We should not expect simple explanations invoking hormone exposure to satisfactorily answer our questions about the origins of sex differences, but standardizing protocols to allow meaningful meta-analyses would help bring coherence to the research literature in this domain.

### Sex differences in normal fetuses and infants: A commentary

Interest in sex differences in infancy is driven partly by the desire to learn how males and females differ before socialization. However, socialization begins at birth because adults have different perceptions of and expectations for male and female babies (Stern & Karraker, 1989). Because people treat boys and girls differently, it is impossible to tease apart biological and sociocultural contributions to sex differences appearing after birth.

Nonetheless, the findings that *newborn* girls are “significantly more cuddly than boys” (Benenson, Philippoussis, & Leeb, 1999, p. 338) and that “female neonates expressed more facial features of pain” (Guinsburg et al., 2000, p. 130) cannot reflect social influences. (In some other studies of neonatal sex differences [e.g., Nagy, Kompagne, Orvos, & Pal, 2007], coders were not blind to the sex of observed infants; results from such studies are uninterpretable.) Still, neonates’ characteristics always reflect the influence of nonsocial environmental factors. Fetuses develop in uterine environments that vary with fetal sex, so newborns’ characteristics likely reflect these environments. In fact, males and females develop in amniotic fluid that differs, at some gestational ages, in concentrations of molecules involved in intercellular communication and embryogenesis, namely, hormones and possibly some cytokines. As Constantinescu and Hines (2012) report, male and female fetuses are exposed to differing concentrations of testosterone, and although the findings on other hormones and cytokines have not yet been as conclusively established, various laboratories have found male versus female prenatal environments to differ in concentrations of angiogenin (Poggi, Spong, Ghidini, & Ossandon, 2004), interleukin 5 (Chow et al., 2008), and leptin (Bugatto et al., 2010; Helland, Reseland, Saugstad, & Drevon, 1998). Because leptin, angiogenin, and testosterone influence birth weight, vascularization, and neural characteristics, respectively, they could influence many phenotypic

differences between newborn boys and girls, thereby influencing infants' postnatal social experiences. Thus, even behaviors in babies just several hours old are not more purely "biological" than are older children's behaviors. Currently, we are just beginning to understand what makes male and female neonates differ, but it is clear that sex-typical characteristics at birth emerge from complex processes involving interactions between differing male and female genomes and uterine environments.

What should concern us is not whether sex differences are caused more by Nature or Nurture, but rather how we can influence the development of specific competences. Consider, for example, that there are gender differences in spatial skills (Halpern, 2011) that are influenced by experience (Hoffman, Gneezy, & List, 2011) and that are essential for success in engineering and technology professions. Women are underrepresented in these fields (Hill, Corbett, & St. Rose, 2010), and their diminished presence in such lucrative occupations is one reason women earn less than men on average (American Association of University Women, 2011; Ryle, 2011). Understanding the origins of spatial skills *in a way that allows us to influence their development* could ultimately enable women's movement into these profitable professions. Parents routinely construct children's environments to provide tools that help them thrive (for example, literacy); thoughtful parents would also likely use knowledge about how to help boys and girls develop skills traditionally seen as strengths of the other gender if those skills would increase their children's fulfillment.

Studying sex differences in infants is worthwhile because "infants [might] have sex-linked dispositions that represent 'seeds' of later behavior" (Alexander & Wilcox, 2012, p. 400). If so, it might be most effective to influence sex differences in adults via manipulations implemented in infancy. By identifying early-appearing sex differences that might be

components of later-emerging sex differences, Alexander and Wilcox (2012) have provided a valuable service.

In contrast to Alexander and Wilcox's (2012) focus on sex differences in postnatal behavior, Constantinescu and Hines (2012) focus on prenatal testosterone's contributions to such differences; both complementary approaches will ultimately yield increased understanding. However, both articles imply that we still know surprisingly little about this topic. Constantinescu and Hines's review suggests that the relationship between prenatal testosterone and postnatal behavior in normal children is far from established, but their review does not consider studies of atypical populations, such as offspring of females prescribed hormones during pregnancy or girls diagnosed with congenital adrenal hyperplasia. After a broader review, Alexander and Wilcox conclude that the evidence "supports the masculinizing effects of prenatal testosterone on social and cognitive behavior" (p. 400), and this is the general consensus (e.g., Hines, 2011). Studies of individuals developing in normal hormone environments, though, have yet to generate agreed-on understandings of the effects of prenatal sex hormone exposure.

One theme in both articles is the lack of replication of many studies in this domain. Additionally, some researchers find trends in the opposite direction of what others predict (Geangu, Benga, Stahl, & Striano, 2010), some find testosterone accounting for behavioral differences in only one sex or having opposite effects on males and females (Grimshaw, Sitarenios, & Finegan, 1995), and some find behavioral sex differences unrelated to prenatal testosterone exposure in either sex (Knickmeyer et al., 2005). No unambiguous pattern emerges from the studies that Constantinescu and Hines (2012) review; what is clear is that some sex differences appear to be independent of testosterone concentrations in amniotic fluid.

Why have these studies generated inconsistent results? All but two examined amniotic

testosterone, but Rodeck, Gill, Rosenberg, and Collins (1985)—the only study to examine the correlation between amniotic and fetal blood testosterone—reported no such correlation, so it should be unsurprising that amniotic testosterone is not related to postnatal behavior in an easily detectable way. Constantinescu and Hines (2012) discuss two studies that examined testosterone in maternal serum during gestation, and although the one study that looked (Gitau, Adams, Fisk, & Glover, 2005) found that this variable *is* correlated with fetal serum testosterone, it is impossible to draw firm conclusions from such limited data.

There are good reasons not to expect measures of testosterone in any fluid—amniotic, maternal serum, or even fetal blood—to be *clearly* associated with postnatal behavior. Testosterone's functionality is affected by several factors operating within developing person-environment systems, among which are the presence and concentration of testosterone receptors in the brain (without which testosterone is ineffectual) and of sex hormone binding globulin (which binds free testosterone, thereby reducing its bioavailability). Because testosterone can affect the brain only when it interacts (and does not interact) with specific molecules, its effects on behavior are not direct. Moreover, once testosterone reaches and binds with receptors, it has numerous effects, including altering cell numbers in specific brain structures, inducing outgrowth of axons and dendrites, supporting synaptogenesis, regulating cell death, and affecting axonal guidance and therefore neural connectivity (Hines, 2011; Simerly, 2002). Thus, testosterone does many things (as expected, given that it is evolutionarily ancient; Guerriero, 2009), and through its interactions with androgen receptors and a variety of molecular co-regulators, it is able to produce different effects in different cell types (Li & Al-Azzawi, 2009). Consequently, we ought not expect its effects on behavior to be straightforward; instead, we should understand testosterone to be a relatively nonspecific agent capable of contributing to

several effects in context-specific ways.

This conclusion is supported by the finding that testosterone can correlate with a competence *within* a sex, even if there is no sex difference in the competence (e.g., Finegan, Niccols, & Sitarenios, 1992; Grimshaw, Bryden, & Finegan, 1995; Jacklin, Wilcox, & Maccoby, 1988). When testosterone accounts for variation like this, it *seems* to have a direct causal role in the development of the competence. But where correlations exist within female populations (for example) even in the absence of sex differences in a competence, testosterone must not cause the competence in a context-independent way; otherwise, it would affect males, too, and a sex difference would be detectable because males are exposed to more testosterone. Of course, the findings in all three studies cited here could be spurious, but if they reflect real phenomena, we could understand them by acknowledging that testosterone is operating in different contexts in male and female bodies. But this would mean that references to testosterone alone will never yield satisfactory answers to questions about how male-typical or female-typical behaviors develop in either sex.

Constantinescu and Hines (2012) offer valuable suggestions for the future, including using large samples, studying the contents of maternal blood as well as amniotic fluid, controlling for variables like gestational age and time of day when samples are taken, and reporting null results. The latter will be critical for correctly interpreting meta-analyses of data in this domain. Such meta-analyses will be indispensable; without them, it will remain hard to contend with inconsistent results. Currently, meta-analyses might be premature, because existing studies are few, they have used varying behavioral outcome measures, and they have measured testosterone in different ways at different times (in gestation and diurnally). Our understanding of the development of sex differences will improve once researchers implement standardized



protocols that allow comparisons of results across studies.

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Author Note

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