

Neuro-endocrinology

BRIEFINGS

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SUMMARY

Why are there sex differences in human behaviour, and why do some of us behave in sex-typical ways, whereas others do not? For instance, why are some girls “tomboys”, preferring to play with boys and boys’ toys? Similarly, why do people differ in sexual orientation, with some interested in partners of the opposite sex, while others are interested in partners of the same sex? Testosterone during prenatal development appears to be part of the answer.

SEX HORMONES AND HUMAN DESTINY

Hormones direct sexual development

Both XX and XY embryos are originally bi-potential in regard to phenotypic sex, but information on the Y chromosome sets the foetal testes into action; by week 8 of gestation, they are producing androgens, including testosterone, at similar levels to adult males. In contrast, the foetal ovaries produce little testosterone. Consequently, there is a large sex difference in testosterone during human gestation. Testosterone acts prenatally on androgen receptors in the rudimentary external genitalia to produce penis and scrotum rather than clitoris and labia. Receptors for testosterone and other androgens are also present in the developing brain and hormones sculpt brain develop-

ment, thus altering behaviour across the lifespan. Initial evidence for these effects came from experimental research in rodents. Exposing female animals to testosterone during early development produced adults who behaved like males, and removing testosterone from developing males had the opposite effect. These effects appeared to occur because testosterone, and hormones produced from it, direct basic processes of brain development in rodents, determining whether certain neurons live or die, which neural regions they connect with anatomically and which neurochemicals they express. Similar behavioural effects of early hormone manipulations were demonstrated in other species, including non-human primates, suggesting that human sex-related behaviour might also relate to testosterone during early life.

Vervet monkeys contacting sex-typed toys. Left: female with doll; Right: male with car.

Reprinted from Alexander & Hines, *Evolution and Human Behavior* (2002) 23: 467-479.



Toy choices

The strongest evidence that early androgen exposure influences human behaviour comes from studies of childhood play. Girls exposed to high levels of androgen prenatally, because they have the genetic disorder, congenital adrenal hyperplasia (CAH), show increased interest in toys usually preferred by boys, such as vehicles and weapons, and reduced interest in toys usually preferred by girls, such as dolls. They also show increased interest in boys' activities and in playing with boys. Normal variability in testosterone exposure prenatally also has been linked to subsequent childhood behaviour. For instance, mothers of girls with highly feminine behaviour have lower testosterone levels during pregnancy than mothers of highly masculine girls. Testosterone measured in amniotic fluid also predicts male-typical behaviour in childhood.

Findings linking children's sex-typed toy preferences to prenatal testosterone exposure challenge the perspective that girl-typical and boy-typical preferences arise purely from social factors. Non-human primates also show sex differences in toy preferences similar to those seen in humans, suggesting that the different object preferences of girls and boys are part of our evolutionary heritage.

Adult behaviour

Prenatal hormones also have been linked to sexual orientation. Most women exposed prenatally to high levels of testosterone, because they have CAH, are heterosexual, however, as a group they show reduced heterosexual interest and increased erotic interest in same-sex partners. In addition, these changes in sexual

“Non-human primates also show sex differences in toy preferences similar to those seen in humans ...”

orientation are stronger in women with the more severe form of CAH than in those with the less severe form, suggesting a dose-response relationship. Other behaviours that have been linked to testosterone prenatally include core gender identity (sense of self as male or female), physical aggression, and empathy. Women with CAH also have been observed to exhibit more male-typical neural functioning in response to negative facial emotions in the amygdaloid nucleus, a brain region that is known to contain receptors for androgen, and which has been linked to aggression and been found to be influenced by androgen exposure during early development in other mammals.

Hormones and psychiatric outcomes

Some psychiatric conditions are sex-linked, suggesting a role for prenatal hormone exposure. For instance, autistic spectrum conditions (ASC) and learning disabilities are more common in boys than in girls, while depression shows the opposite sex-linked pattern. Prenatal androgen exposure has been linked to some psychological traits that are also linked to ASC, such as empathy. However, individuals exposed to high levels of androgen because of CAH appear not to be at increased risk of ASC. Pervasive developmental disorders, such as ASC, may be one area

where direct genetic effects involving X-linked genes are more important than sex hormones.

Nature plus nurture

Sex hormones and the sex chromosomes are not the only factors influencing the development of human sex-related behaviour. For instance, children model the behaviour of others of the same sex, and when told that certain things are “for girls” or “for boys”, they show interest in what they have been told is for their own sex. What is surprising is that, to some extent, sex differences and individual differences in childhood play and in erotic interests and other sex-linked behaviours are inborn. Testosterone sculpts the brain prenatally to predispose individuals to show particular behavioural propensities postnatally, propensities that can then be augmented or inhibited by postnatal experience.

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