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Current Opinion in Neurobiology

The early postnatal period, mini-puberty, provides a window on the role of testosterone in human neurobehavioural development

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Experimental research in non-human mammals indicates that testosterone exposure during early periods of rapid brain development has enduring influences on brain and behaviour. These influences are exerted when testosterone is higher in developing males than females, and the affected characteristics are those that differ by sex. Testosterone is higher in males than in females from about weeks 8 to 24 of human gestation and then again during early infancy, and both of these periods are times of rapid brain development. Substantial evidence suggests that testosterone prenatally influences human neurobehavioral development. Emerging evidence suggests that the early postnatal period is important too. This early postnatal period could provide a window for studying testosterone interacting with experience to shape human gender development.

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Current Opinion in Neurobiology 2016, **38**:69–73

This review comes from a themed issue on **Neurobiology of sex**

Edited by **Barry J Dickson** and **Catherine Dulac**

For a complete overview see the Issue and the Editorial

Available online 9th March 2016

http://dx.doi.org/10.1016/j.conb.2016.02.008

0959-4388/Published by Elsevier Ltd.

Introduction

Thousands of studies of non-human mammals have documented the important role of testicular hormones in sexual differentiation of the brain and of behaviour. These studies have shown that testosterone, and hormones produced from testosterone, exert enduring masculinizing and defeminizing effects during early sensitive periods of rapid brain development. The sensitive periods correspond to times when testosterone is higher in developing male than female animals, and, in many species, these periods occur prenatally as well as during early postnatal life. The characteristics that are affected by testosterone during these early sensitive periods include a range of behaviours that differ on average for male and female animals, as well as aspects of brain structure that differ by sex (see [1,2] for reviews). This review outlines what we know about similar influences of testosterone on human development. It concludes that: 1. Testosterone, prenatally, influences human gender development; 2. Recent evidence suggests that testosterone during the early postnatal period of mini-puberty also influences human gender development; 3. This early postnatal period could provide an accessible window for studying the influence of testosterone in interaction with experience on human neurobehavioral development.

Testosterone during early human development

In humans, testosterone is higher in male than in female foetuses prenatally, particularly from about week 8 to 24 of gestation, and this difference appears to be maximal from about week 8 to 16 of gestation [3]. Testosterone is again higher in boys than in girls from about week 4 to 24 postnatal, and this difference appears to be maximal from about week 4 to 12 postnatal [4,5••]. This early postnatal period of testosterone elevation is sometimes referred to as mini-puberty.

Human gendered behaviour

The behaviours that differ by sex in humans, and that thus might be influenced by testosterone during these early sensitive periods, can be referred to as gender-typical or gendered behaviours [2]. They include children's gender-typical play (toy and activity) preferences, as well as a person's direction of erotic interest (sexual orientation), and sense of self as male or female (gender identity) [6]. Although some other behaviours differ to some extent for men and women or girls and boys, these three (gender-typical childhood play behaviour, sexual orientation and gender identity) appear to show the largest differences [6]. To put them in a familiar context, the gender differences in play behaviour are similar in size to the sex difference in height, and the gender differences in sexual orientation and gender identity are many times larger than the sex difference in height. In contrast, gender differences in other behaviours, such as autistic traits, and expressive vocabulary in very young

children, are typically less than half the size of the sex difference in height (Figure 1) [6].

Prenatal influences of testosterone on human behaviour

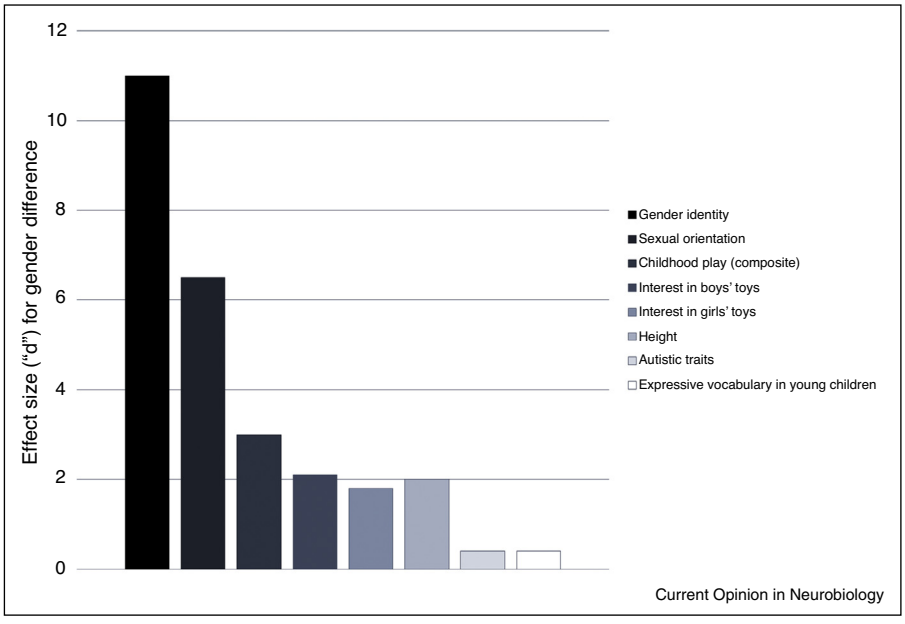
The available evidence suggests that testosterone prenatally influences human behaviours that show large gender differences. For instance, over a dozen studies from several independent research groups have found that girls exposed to unusually high concentrations of testosterone prenatally, because they have the genetic condition, congenital adrenal hyperplasia (CAH), show increased male-typical play behaviour and decreased female-typical play behaviour in childhood [7,8,9,10,11,12,13,14]. Several studies from independent research groups also suggest that females with CAH showed reduced heterosexual interest and reduced female-typical gender identity [8,10,14,15,16]. Studies of individuals with other genetic conditions that cause exposure to gender-atypical hormone concentrations prenatally are less numerous than studies of girls and women with CAH, but they also suggest that testosterone prenatally influences later gender-typical play behaviour, sexual orientation and gender identity [2].

The strongest evidence supporting early influences of testosterone on human gender development has come from studies of individuals with genetic conditions, such as CAH, and these conditions have other consequences that also could influence behaviour. It is difficult, therefore, to be completely confident that early testosterone abnormality is the responsible agent. Evidence from a range of conditions, each with different consequences in addition to testosterone abnormality, provides some convergent evidence that testosterone is responsible for the behavioural changes [2]. Nevertheless, evidence that normal variability in testosterone exposure prenatally relates to later gendered behaviour would be useful too. Studies attempting to provide such evidence have looked at testosterone measured in amniotic fluid or maternal blood during gestation, or in umbilical cord blood at birth. Studies have even looked at the ratio of the 2nd to the 4th digit of the hands as a proxy for prenatal androgen exposure, because this ratio differs on average in males and females. All these approaches to measuring prenatal androgen exposure have limited reliability, however, and, perhaps unsurprisingly, they have produced largely inconsistent results [2,17,18].

Early postnatal testicular activation: mini-puberty

The early postnatal period when testosterone is elevated in developing boys (mini-puberty) might provide an alternative, and more accessible, window on the effects of testosterone on human gender development. It is

Figure 1



Some, but not all, gender differences in human behaviour are large. The familiar sex difference in height is about 2.0 standard deviations (d) in magnitude. Some behavioural gender differences are as large, or larger, than the sex difference in height. Characteristics that show large differences include gender identity, sexual orientation, and children's gender-typical play styles, and toy interests (e.g., interest in dolls vs toy vehicles). In contrast, some behaviours that have been studied in relation to early postnatal testosterone exposure, such as autistic traits and expressive vocabulary in very young children, show substantially smaller gender differences (0.4 d) than that seen in height. (In the behavioural sciences, group differences of 0.8 d or greater are considered to be large, those of 0.5 d are considered to be of medium size, and those of 0.2 d are considered to be small [34].).