Anogenital Distance (AGD), Penile Growth, and Masculine Behaviour: Evidence for Independent Neurobehavioral Effects of Foetal Versus Postnatal Androgen Exposure in Boys

Vickie Pasterski[1,2], Carlo L Acerini[1], David B Dunger[1], Ken K Ong[1,3], Ieuan A Hughes[1], Ajay Thankamony[1], and Melissa Hines[2]

[1]Department of Paediatrics, University of Cambridge, UK; [2]Department of Psychology, University of Cambridge, UK; [3]MRC Epidemiology Unit, University of Cambridge, UK

Abstract

This report makes three major contributions to research aimed at understanding the impact of androgens on human neurobehavioral development. First, it provides the first demonstration that early postnatal androgen elevation, or mini-puberty, contributes to neurobehavioral sexual differentiation in boys, independent of prenatal androgen exposure. Second, it provides the first evidence linking AGD at birth to subsequent gender related behavior in humans. Third, it suggests that AGD at birth and penile growth from birth to 3 months provide inexpensive and non-invasive measures of androgen exposure prenatally and during mini-puberty, respectively, that could be used more broadly to investigate androgenic influences on human development.

Background

Early periods of prenatal and postnatal (mini-puberty) androgen production[1] are necessary for formation of the external genitalia in early embryonic development and further growth after birth[2]. At the same time, neural plasticity is high as the human brain develops through gestation and into early infancy[3]. Though these parallel processes have been characterized, potential behavioral consequences, in humans, have not.

These distinct aspects of physical development reflecting androgen exposure at different times may provide a methodology for separating effects of prenatal and early postnatal androgen exposure on human behavior. AGD, measured as the distance from the anus to the scrotum in males and to the vagina in females[4], may be a marker of androgen exposure during early fetal development. In humans, AGD is strongly sexually dimorphic, with boys having nearly twice the AGD of girls at birth, and appears to be sensitive to changes in fetal androgens[4].

Postnatally, penile growth could provide a measure of androgen exposure during mini-puberty. Evidence from rats has shown that while initial formation of the male external genitalia takes place early in embryonic development, a further period of penile growth reflects late gestational and early neonatal influences of androgens[5]. A population study of boys has shown that serum T, measured in blood, correlated with penile growth in length from birth to 3 months of age[6].

The aim was to assess neurobehavioral effects of the postnatal surge in androgens, prospectively, while controlling for potential confounding influences, such as androgen exposure prenatally.

Acknowledgements

Research supported by the European Union Framework V Programme, World Cancer Research Fund International, Mothercare Foundation, Newlife Foundation for Disabled Children and Medical Research Council (UK). We also thank the Wellcome Trust Clinical Research Facility and the National Institute for Health Research – Biomedical Research Centre Cambridge.

Method

Participants were 81 typically developing boys. Mothers were recruited from the maternity unit of Cambridge University Hospital.

Anthropometrics for penile length, AGD, weight, and body length were taken at birth, and at 3, 12, 18, and 24 months of age. Penile length was measured from the lower edge of the pubic bone to the tip of the penis, excluding the foreskin and avoiding erection. AGD was measured from the center of the anus to the junction of smooth perineal skin and rugated scrotal skin.

Gender-typical behavior was measured at 3-4 years of age using the Preschool Activities Inventory (PSAI),[7] a standardized 24-item parent-report instrument that assesses children's gender-typed play preferences. High scores are more masculine.

Results

Regression analysis. Table 1 shows results from three multiple regression models, with PSAI as the outcome variable. Model 1, including only AGD and penile length at birth, approached significance, and AGD on its own was significant as a predictor. When penile growth from 0 to 3 months was added in Model 2, both the model and R^2 change were significant. Finally, Model 3 shows that when penile growth in 3 subsequent periods and growth in body length from 0 to 12 months were added, penile growth in the first 3 months remained the primary predictor of male-typical behavior, with AGD at birth continuing to account for unique variance.

Analysis of Variance. Figure 1 shows a 3(growth period) X 3(tertiles for PSAI) repeated measures ANOVA. Boys in the top 33% for masculine behavior had the greatest increase in penile length in the period from 0 to 3 months.

Table 1. Regression statistics using physiological markers / growth to predict masculine behavior measured using the Pre-School Activities Inventory (PSAI).

N = 81	R^2	R^2 Change	F Change F	F Change *p*	Standardized Coefficients Beta	Standardized Coefficients t	Standardized Coefficients *p*
Model 1 ($p = .072, f^2 = 0.07$)†	.066	.066	2.72	.072			
AGD at birth					**.255**	**2.29**	**.025***
Penile length at birth					-.090	-0.81	.420
Model 2 ($p = .005^{**}, f^2 = 0.18$)†	**.154**	**.088**	**7.91**	**.006****			
AGD at birth					**.238**	**2.23**	**.029***
Penile length at birth					.054	0.46	.648
Δ Penile length birth to 3M					**.329**	**2.81**	**.006****
Model 3 ($p = .008^{**}, f^2 = 0.29$)†	.226	.072	1.66	.168			
AGD at birth					**.240**	**2.24**	**.028***
Penile length at birth					.121	0.92	.362
Δ Penile length birth to 3M					**.502**	**3.58**	**.001*****
Δ Penile length 3M to 12M					.297	1.81	.074
Δ Penile length 12M to 18M					.202	1.13	.264
Δ Penile length 18M to 24M					.239	1.63	.107
Δ Body length birth to 12M					-.107	-0.98	.332

$^{*}p \leq .05$, $^{**}p \leq .01$, $^{***}p \leq .001$
† Effect size is Cohen's $f^2 = R^2 / 1 - R^2$ (Cohen, 1988).
AGD is anogenital distance.
Δ signifies change in the parameter.

Penile Growth in the First 18 Months of Life & Later Masculine Behavior

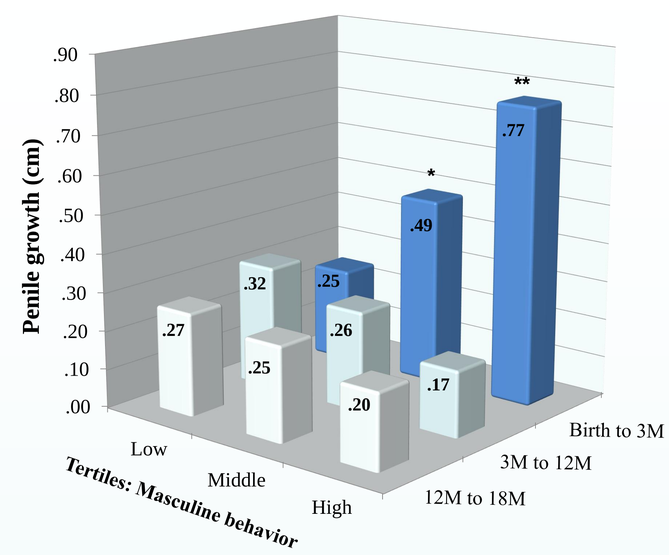

Figure 1. Penile growth across the first 18 months of life as a function of male-typical behavior measured using the Pre-school Activities Inventory (PSAI). Note that group differences were only significant for the period of Birth to 3 months. M = months.
* $p < .05$ compared to High and to Low; ** $p < .01$ compared to Low.

Conclusions

Using multiple linear regression, we demonstrated that penile growth between birth and 3 months, concurrent with mini-puberty, significantly predicted variance in masculine behavior assessed using a standardized measure of gender-typical behavior at 3- to 4 years old in a sample of 81 boys. Furthermore, when we controlled for other potential influences on gender-typical behavior and/or penile growth, e.g., variance in androgen exposure prenatally and body growth postnatally, the predictive value of penile growth in mini-puberty persisted. Also, while AGD at birth, but not thereafter, correlated with PSAI scores, penile length correlated with PSAI scores only at 3 months of age and older. Our findings suggest that independent associations of PSAI with AGD at birth and with penile growth during mini-puberty reflect prenatal and early postnatal androgen exposures respectively.

Such methodologies could provide more information on how early androgens relate to human development. Future studies might evaluate whether mini-puberty is important for additional human gender-related behaviors, including psychiatric disorders that differ by sex, such as depression, autism and eating disorders. In addition, these methods could be used to study interactions between early hormone exposures and other factors known to influence human gender development, such as postnatal socialization by parents or self-socialization based on cognitive understanding of gender.

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