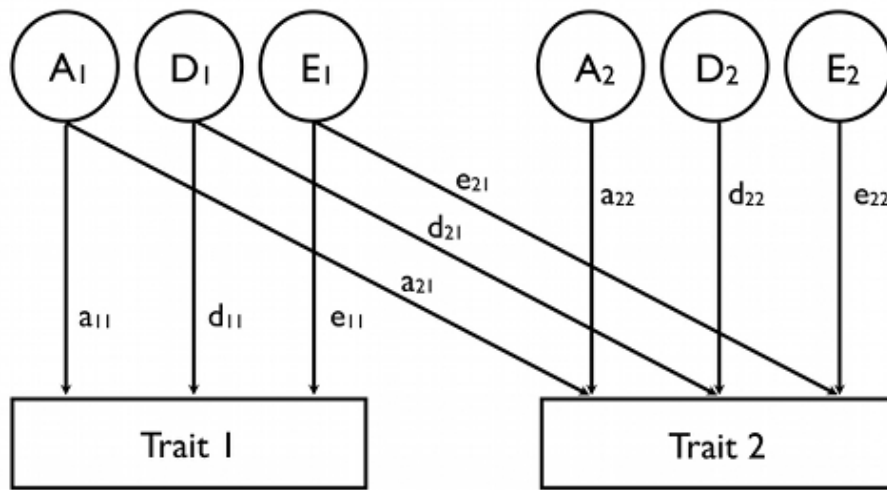


Supplemental Data - Methods



Supplemental Figure 1. The bivariate ADE model. The aim of the bivariate ADE model is to estimate simultaneously the contributions of (non) additive genetic and environmental factors that explain variance in two traits, and that explain the covariance between the two traits.

Drawn here is the diagram for only one of the twins. For i in $\{1,2\}$, A_i represents the additive genetic factor acting on trait i . D_i represents the dominant genetic factor acting on trait i .

Likewise, E_i represents the unique environmental factor acting on trait i . The diagram for the other twin is exactly the same but omitted here due to limitations of space. The two diagrams

for the twins are connected through the assumptions that follow from the twin model: for monozygotic twins, the factors A_1 for twin 1 and twin 2 are fully correlated ($r=1.0$); and

likewise for A_2 , D_1 and D_2 , because they share (almost) the same genetic makeup. For

dizygotic twins, the correlations between factors A_1 (and A_2) for twin1 and twin 2 are by definition equal to 0.5, whereas the correlations between factors D_1 (and D_2) for twin1 and

twin 2 are by definition equal to 0.25. These constraints can be used to estimate the path

coefficients such that the total variance of trait 1 $(a_{11})^2 + (d_{11})^2 + (e_{11})^2$, the total variance of

trait 2 $(a_{21})^2 + (d_{21})^2 + (e_{21})^2 + (a_{22})^2 + (d_{22})^2 + (e_{22})^2$ and the covariance between the two traits

$((a_{11} * a_{21} + d_{11} * d_{21}))$ for monozygotic twins and $(0.5 (a_{11} * a_{21}) + 0.25 (d_{11} * d_{21}))$ for dizygotic

twins) are best fitted to the data. The additive and dominant genetic effects were combined to

compute broad heritability of the individual traits as $((a_{11})^2 + (d_{11})^2) / ((a_{11})^2 + (d_{11})^2 + (e_{11})^2)$

for trait 1 and $((a_{21})^2 + (d_{21})^2 + (a_{22})^2 + (d_{22})^2) / ((a_{21})^2 + (d_{21})^2 + (e_{21})^2 + (a_{22})^2 + (d_{22})^2 + (e_{22})^2)$
for trait 2. Further, a (broad sense) genetic correlation between the broad sense genetic factors
was computed as $(a_{11} * a_{21} + d_{11} * d_{21}) / (\sqrt{((a_{11})^2 + (d_{11})^2)} * \sqrt{((a_{21})^2 + (d_{21})^2 + (a_{22})^2 + (d_{22})^2)})$.

Supplemental Table 1. Twin correlations for hormone levels (a), Tanner stages in boys (b), and Tanner stages in girls (c) for all monozygotic (MZ) and dizygotic (DZ) pairs. Data are presented as correlation (number of complete pairs).

a. Hormone levels

	LH 9	FSH 9	E2 9	T 9	LH 12	FSH 12	E2 12	T 12
MZ girls	0.73 (25)	0.45 (25)	0.65 (25)	0.67 (24)	0.72 (20)	0.60 (20)	0.84 (20)	0.46 (20)
DZ girls	0.02 (21)	0.17 (21)	0.72 (21)	0.40 (19)	0.46 (14)	0.31 (16)	0.57 (16)	0.08 (16)
MZ boys	0.76 (23)	0.87 (23)	0.87 (22)	0.59 (23)	0.91 (20)	0.95 (20)	0.56 (20)	0.79 (19)
DZ boys	0.37 (22)	0.13 (22)	0.39 (22)	0.14 (19)	0.53 (17)	-0.07 (17)	0.35 (17)	0.62 (15)
DOS boy-girl	0.51 (19)	0.42 (19)	0.26 (20)	0.22 (20)	0.21 (15)	0.28 (15)	0.16 (15)	0.32 (15)

b. Tanner stages in boys *

	Tanner-P 12	Tanner-T 12	Tanner-PH 12
MZ boys	0.45 (18)	0.89 (15)	0.87 (18)
DZ boys	0.49 (15)	0.48 (12)	0.74 (16)

c. Tanner stages in girls *

	Tanner-B 12	Tanner-PH 12
MZ girls	0.94 (19)	0.90 (17)
DZ girls	0.72 (17)	0.23 (17)

MZ= monozygotic; DZ= dizygotic; DOS= dizygotic opposite sex; E2= estradiol; T= testosterone; Tanner-P= penis development; Tanner-T=testes development; Tanner-PH= pubic hair development; Tanner-B= breast development.

* Because of lack of variation in Tanner stages in 9-year-old boy and girls, correlations were computed for age 12 only.

Supplemental Results

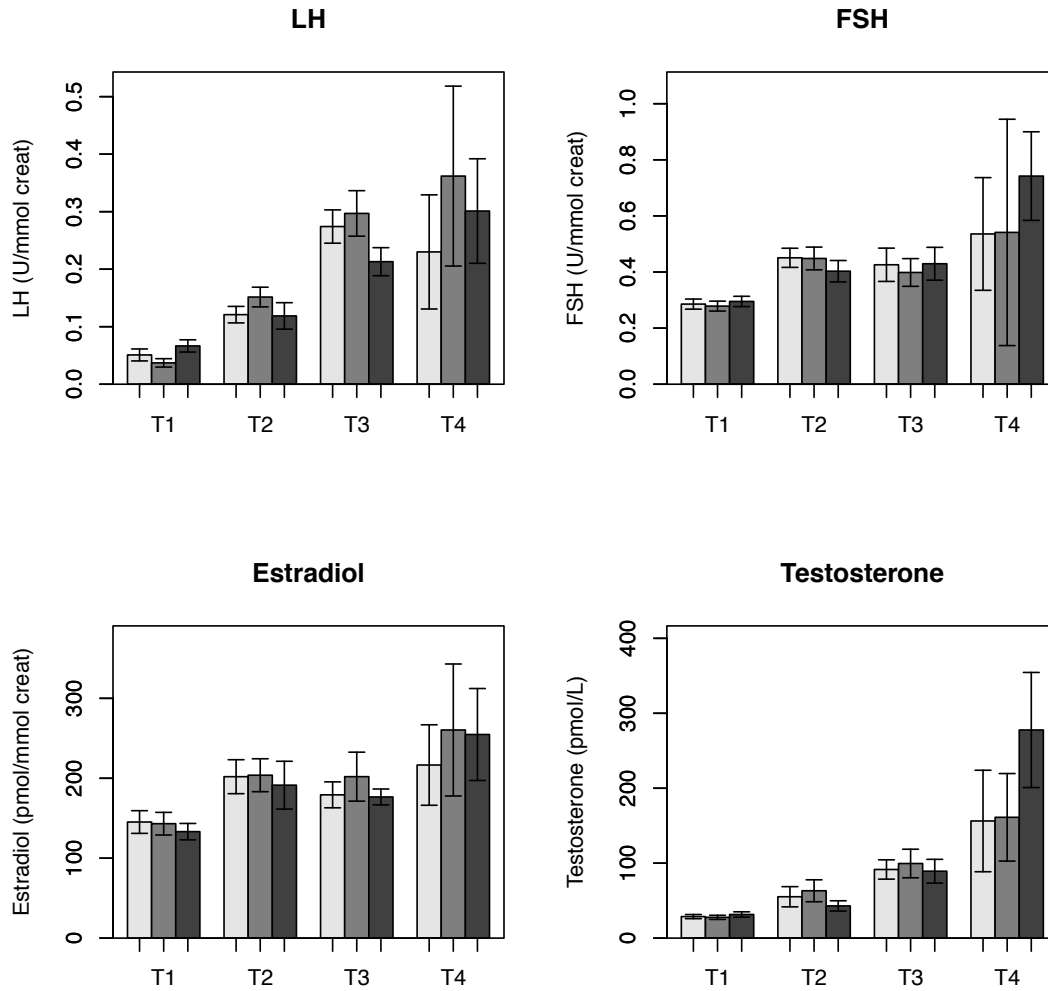
Supplemental Table 2. Unstandardized variance components for genetic, common environmental and unique environmental influences on hormone levels at age 9 and 12 in boys and girls.

Boys		Model ^a	Genetic Variance ^a	Common Environmental Variance	Environmental Variance
Age 9	LH	ADE	0.080	-	0.017
	FSH	ADE	0.059	-	0.007
	E2	ACE	0.071	0.013	0.014
	T	ADE	0.071	-	0.040
Age 12	LH	ADE	0.182	-	0.014
	FSH	ADE	0.067	-	0.004
	E2	ACE	0.027	0.006	0.022
	T	ADE	0.107	-	0.030
Girls		Model ^a	Genetic Variance ^a	Common Environmental Variance	Environmental Variance
Age 9	LH	ADE	0.075	-	0.032
	FSH	ADE	0.031	-	0.041
	E2	ACE	0.001	0.032	0.018
	T	ADE	0.086	-	0.033
Age 12	LH	ADE	0.143	-	0.076
	FSH	ADE	0.029	-	0.022
	E2	ACE	0.032	0.014	0.011
	T	ADE	0.036	-	0.032

E2= estradiol; T= testosterone, - = not modeled.

^a Based on twin correlations, an ACE model was fitted for estradiol in boys and girls, and all Tanner scales in both boys and girls. For the other variables, an ADE model was fitted. Column 4 contains an estimate of additive genetic variance in the case of an ACE model, and an estimate of additive + non-additive genetic variance in the case of an ADE model.

Supplemental Figure 2. Normative hormone levels of 9 and 12-year-old boys categorized according to Tanner stages (T1 – T4). Light grey: penis development; medium grey: testes development; dark grey: pubic hair development. Error bars represent standard error.



Supplemental Figure 3. Normative hormone levels of 9 and 12-year-old girls categorized according to Tanner stages (T1 – T5). Light grey: breast development; medium grey: pubic hair development. Error bars represent standard error.

