Contribution of growth phases to adult size

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Summary. Based on the data of the First Zurich Longitudinal Growth Study we investigate how interindividual differences in adult size arise in the variables leg height, sitting height and standing height, arm length, biliac width and bihumeral width. Specifically, we are also interested in the question of whether across sexes and variables the same growth phases and the same parameters are predictive for achieving a certain adult size. A rather complex pattern emerges, demonstrating that regulation of growth is not the same for boys and girls and moreover is not the same for the six anthropometric variables studied. Prepubertal growth is characterized by its intensity (average velocity) and by its duration. Whereas duration has by itself no appreciable influence on adult size, prepubertal intensity determines adult size to a high degree across all variables and both sexes. The intensity of prepubertal growth determines adult size to a larger degree for boys than for girls. For a given size at the end of the prepubertal period, a small duration enhances the chance of obtaining a large adult size. Compared with prepubertal growth, the amount of variance of adult size explained is small for pubertal parameters, and—with respect to linear measures—significant for girls only. A small duration of prepubertal growth is in the following mainly compensated by a stronger pubertal spurt (PS), to a varying degree across variables. The overall picture which emerges indicates that sitting height—and to a lesser extent bihumeral width—develop in a more irregular fashion than the variables biliac width and leg height.

1. Introduction

In this paper we want to investigate to what extent various growth processes—prepubertal or pubertal—are important in determining variation in adult size in measures of length (legs, trunk, arms and height) and measures of breadth (biliac and bihumeral diameter). Moreover, we would like to investigate whether boys and girls, and different variables, rely on similar mechanisms in order to reach their adult size. In addition, we hope to shed some light on the interplay between intensity and duration of prepubertal and pubertal growth, and between prepubertal and pubertal growth. There are evidently numerous ways to achieve an identical adult size in a given anthropometric variable, and the question is whether some regulatory mechanisms are predominant.

We expect the correlations of distance attained at successive ages with adult size to get larger as age increases, since an increasing portion of adult size is determined at each successive age and there remains less uncertainty about further growth. We also expect higher correlations for girls than for boys at prepubertal ages, since at any fixed age, girls have reached a higher percentage of adult distance and have a shorter period of further growth, due to their earlier pubertal spurt (PS). Due to their more advanced bone age, girls are also biologically more mature at the same chronological age. Surprisingly, distinctly higher correlations for boys in all variables from late infancy till the onset of puberty have been consistently found (Tanner, Healy, Lockhart et al. 1956, Tanner and Whitehouse 1982, Molinari, Gasser, Largo et al.)
1995). We would like to examine this finding further and, if possible, find an explanation for it.

The PS is a prominent feature of the growth process and of sex differences in growth (Sheehy, Gasser, Molinari et al. 1999). The question then arises if and how the PS explains variation in adult size, and, on the other hand, if and how it compensates for prepubertal growth. Previous studies for height showed surprisingly little correlation between any of the variables timing, duration and intensity of the PS and adult size (Tanner, Whitehouse, Marubini et al. 1976, Largo, Gasser, Prader et al. 1978, Gasser, Mueller, Koehler et al. 1985). We characterize the PS by its age of peak of velocity, its duration and its intensity. The increment during the adolescent period was subdivided into an ‘increment due to level’—the prepubertal velocity level, extrapolated into puberty—and a ‘contribution due to the spurt’ (see figure 1). A problem associated with all these parameters is that they can only be determined from individually estimated velocity and acceleration curves with a certain amount of error. Inevitably, this tends to camouflage the magnitude of true relationships (‘errors-in-variables’ problem).

We have decided to subdivide prepubertal growth into the following periods:

- from conception to 1 month (age of our first measurement)
- from 1 month to 1.5 years
- from 1.5 years to 6 years
- and from 6 years to the onset of the PS ($T_6$)

Previous results for height (Gasser et al. 1985) indicate that sizeable positive correlations between the average velocity from 1.5 to 6 years and adult size should arise. Within the prepubertal period, and from the prepubertal to the pubertal period, we expect some regulatory interactions between the various growth phases. It is, for example, well known that there is a small negative correlation for height between size reached at 1 month and the increment from 1 month to 1.5 years, reflecting the regulation of the transition from intrauterine growth to the individual genetic track (Smith, Truog, Rogers et al. 1976). It is not clear how the increments from 1 month to 1.5 years and from 1.5 years to 6 years influence subsequent growth processes. It is, however, plausible to conjecture that the timing of the PS and/or the size of the contribution due to the spurt is related to the average velocity in the period from 6 years to the onset of the PS ($T_6$).

One might conjecture that an increment contributing on the average a large percentage to adult size would also explain a large part of the variance of adult size. While this is plausible, there is no compelling statistical or biological reason for this to be true.

The four linear variables and the two widths studied develop in markedly different ways prepubertally and pubertally (see Sheehy et al. 1999 and references therein). This does, however, not necessarily imply that the relationships between different phases of growth, and of these phases with adult size, will also show a different pattern across the six variables. It could well be the case that similar regulatory mechanisms prevail for the different parts of the body, where some ‘master genes’ steer growth in various body dimensions in a similar way. The literature is scarce on this subject and almost non-existent for variables other than height. The trunk and the legs develop in all growth phases quite differently (Sheehy et al. 1999) and the variable ‘height’ is thus composed of two heterogeneous growth components. For this reason, we will in this biologically oriented paper pay more attention to sitting
height and leg height than to height, despite the fact that height is of central interest clinically.

Implicit in our study is the concept of an adult target size: this would reflect the ideal individual size, governed by genetics, and achieved under ideal environmental conditions. The actual adult size measured is composed of target size minus some individual random component due to various disturbances during the growth process. That adult height is mainly determined by polygenic inheritance has been proved in a large number of studies starting with Galton (see Luo, Albertsson–Wikland and Karlberg 1998 for a recent study): the correlation between midparent height and adult height was consistently around 0.6, leading to a heritability of 0.83, leaving little room for environmental factors and for gene–environment interaction. Further, the characteristics of the PS are also largely under genetic control, as shown by twin studies (Sharma 1983, Hauspie, Bergman, Bielicki et al. 1994). Clearly, for an individual, characteristics of the PS are important in determining adult size. However, the large number of genes involved in determining these traits leads to a very variable interplay between these characteristics and adult size when examined across individuals. For example, the age of peak velocity varies over a range of about 4 years in a normal population. Thus, due to genetic heterogeneity across individuals, the percentage of variance explained in adult size by, for example, pubertal characteristics may be small. Using correlation and regression methods we are, however, able to identify those growth mechanisms which are important for a large number of subjects for reaching target size.

2. **Subjects and methods**

We give here a relatively concise summary of the relevant facts. Readers who need more details are referred to earlier papers (Gasser, Kneip, Binding, et al. 1991a; Gasser, Kneip, Ziegler et al. 1991b; Sheehy et al. 1999).

2.1. **Subjects**

Within a prospective, multicentre longitudinal study participation of 160 girls and 161 boys was achieved. Children with a disease hampering growth, and children who missed more than two visits, or two successive ones, were excluded from further analysis. This resulted in samples of 112 girls and 120 boys.

2.2. **Measurements**

Visits to the paediatric hospital took place at 1, 3, 6, 9, 12, 18 and 24 months and then annually up to age 9 for girls and age 10 for boys. Half-yearly visits continued until height increased by less than 0.5 cm per year. Yearly measurements continued till the increment in height was less than 0.5 cm in 2 years, but at least until age 18. Visits had to occur in certain intervals around the above ages; since the exact days of these visits are available, the latter were used in statistical analysis.

Height and sitting height were measured with a Harpenden stadiometer, and leg height was obtained as the difference. Arm length was measured with a tape, but the quality of the data was degraded by rounding to the full centimetre, consequently also degrading statistical accuracy. Bihumeral and biiliac width were measured with callipers. It is clear in retrospect that biacromial width would have been the better measurement for shoulder width, since bihumeral width is influenced by the presence of soft tissue. The longitudinal analysis of bihumeral width is also made more difficult by the fact that measurements did not start at 1 month for all children.
Up to 2 years we have data for this variable only on a subset of 47 girls and 58 boys, and only after 6 years do we have data on the full sample. In the statistical analysis we used as many children as were available at a given age when dealing with specific questions (e.g. for correlations during the PS, this would be the full sample).

2.3. Methods

As mentioned previously, measurements are available at ages scattered around the ages given by the study protocol. In order to obtain data for any desired age, kernel estimators were applied to estimate continuously individual distance, velocity and acceleration curves (Gasser, Mueller, Koehler, Molinari and Prader 1984; Sheehy et al. 1999).

To characterize the PS, the following ages have been determined from the acceleration curve:

- $T_6$: Age of minimal velocity (= zero acceleration) prior to the PS (‘onset of PS’)
- $T_7$: Age of maximal acceleration during the PS
- $T_8$: Age of peak velocity (= zero acceleration) during the PS (‘timing of PS’)
- $T_9$: Age of maximal deceleration at the end of the PS (‘end of PS’)

Note that $T_6$ is synonymously the duration of prepubertal growth. The distances, velocities and acceleration at these ages have also been determined; $T_9 - T_6$ is considered to be a measure of the duration of the PS and acceleration at $T_7$ to be a measure of its intensity. The age $T_9$ can be considered as a surrogate for the total postnatal growth period (on average between 95 and 98% of adult distances are reached at this age, see Sheehy et al. 1999).

The prepubertal growth period from 1 month till $T_6$ has been subdivided at ages 1.5 and 6 years. The demarcation at 1.5 years was made since various findings suggest that the transition from intrauterine growth to the individual genetic track is completed by 1.5 years (Smith et al. 1976, Gasser et al. 1991a, b). We chose 6 years as the next age since it subdivides about equally the period from 1.5 years to the onset of the PS.

While maximal acceleration is a good measure of the intensity of the PS since it characterizes the upsurge to peak velocity, it would not be an adequate measure of intensity prepubertally. For prepubertal growth periods, we use average velocity over a given period as a measure of intensity—this makes sense because of the more gradual growth over these years. Note that the increments in the phases from 1 month to 1.5 years and from 1.5 years to 6 years are proportional to the average velocity in these phases so that increment and average velocity lead to identical correlations (the average velocity is defined to be the increment in a phase divided by the length of that phase). This is true since the phases are determined by chronological ages. The third increment from 6 years to the onset of the PS ($T_6$) has an extra source of randomness in that the endpoint $T_6$ varies inter-individually (and is, moreover, estimated with some error). Thus this increment does not reflect individual growth velocity and it is thus important to compute the individual average velocity from 6 years to $T_6$. Correlations of growth velocity in this period with adult size are much higher than the correlations for the corresponding increments, indicating the greater relevance of intensity as a measure of underlying growth processes.

It is desirable to decompose the adolescent gain into two components, one reflecting the gain due to the PS (‘growth due to spurt’) and one due to some type of
continuation of the pre-adolescent velocity level. In figure 1 the decomposition of growth of sitting height during the pubertal period into a contribution due to spurt and level for a typical child is given (the prepubertal increments are also shown). While this decomposition is somewhat arbitrary, some foundation for such a decomposition can be found in the two-component shape-invariant model with interaction proposed by Stuetze, Gasser, Molinari et al. (1980) and in the endocrinological literature. The prepubertal velocity level at $T_6$ is continued until $T_8$. Then, when acceleration becomes negative, prepubertal growth is reduced by a ‘switch-off’ function of sinusoidal shape (note that pubertal growth starts to decrease at the same age). An evaluation and an exact description of this approach will be presented in a forthcoming note.

In assessing the relationship between certain characteristics of growth and adult size, and interrelationships between different phases of growth, multiple linear regression was the principal method of analysis, rather than correlation tables. The predictive power of a regression model can be quantified by the squared multiple correlation coefficient $R^2$. Since the addition of further variables automatically increases $R^2$, some adjustment for the number of variables is needed. We will always tabulate such an adjusted coefficient, $R^2_{\text{adj}}$. To choose an appropriate subset of predictors, we computed regression models for all possible subsets of variables. The final choice of model was made according to the principles of maximizing $R^2_{\text{adj}}$ while at the same time ensuring that the model is parsimonious, biologically plausible and is consistent across the six variables and the two sexes.

Longitudinal pubertal parameters—the age of onset of the PS or maximal acceleration being examples—have been determined from individually fitted velocity and acceleration curves. Such parameters are inevitably subject to estimation errors (called ‘errors in variables’ $\varepsilon_i$ in the statistical literature). Thus, when the

![Figure 1. Illustration of the decomposition into increments (example: velocity curve for sitting height for a boy). Increments from 1 month to 1.5 years (white), from 1.5 to 6 years (dotted), from 6 years to $T_6$ (white), for the adolescent component due to the basic velocity level (diagonal lines) and for the adolescent component due to the spurt (dark grey).](image-url)
true individual age of peak velocity for subject number $i$ is $T_{8i}$, we have only an approximation $\hat{T}_{8i} = T_{8i} + \varepsilon_i$. The errors in variables lower the correlations (called ‘attenuated correlations’). Consider the correlation between the ideal $T_{8i}$ and some other variable $Y_i$ (say adult distance):

$$r(T_{8i}, Y_i) = \frac{\text{Cov}(T_{8i}, Y_i)}{\sqrt{\text{Var}(T_{8i})} \cdot \text{Var}(Y_i)}$$

While the numerator remains unchanged when going from $T_{8i}$ to $\hat{T}_{8i}$ (this holds under standard assumptions), the denominator is inflated by the extra variance due to the errors $\varepsilon_i$ ($\text{Var}(\hat{T}_{8i}) = \text{Var}(T_{8i}) + \text{Var}(\varepsilon_i)$). Note that correlations that are close to zero are hardly affected by errors in variables.

Statistical considerations indicate that the estimation error for age of maximal acceleration $T_7$ is considerably less than for $T_6$. In fact when trying to predict the onset of the PS from prepubertal growth parameters replacing $T_6$ by $T_7$—as a surrogate parameter of onset—brought clearer results.

3. Results

3.1. Correlations of cross-sectional distance reached with adult size

Figure 2 shows the correlation of distance reached, at successive ages, with adult distance. The curves are slightly smoothed. The general pattern is similar for all variables: there is a sharp increase in the first 2–3 years (from about $r = 0.4$ at 1 month), followed by a more gradual, almost linear increase until puberty. Then a dip occurs at the average age of peak velocity followed by a steep increase to $r = 1$.

![Figure 2. Correlations of distance reached at chronological ages with adult distance for boys (solid line) and girls (dashed line).](image-url)
Prepubertally, girls show distinctly lower correlations, contrary to our expectations. To explain this surprising sex difference, an analysis of further aspects of growth proved to be necessary (see Discussion).

Substantial differences in the size of correlations across variables can be seen. These differences are rather stable across age. Correlations are highest for biiilac width, followed by legs, and are lowest for bihumeral width and sitting height.

When plotting correlations at developmental ‘ages’ \((T_1 - T_9)\), the dip at puberty disappears (see figure 3 for height), and similarly in terms of bone age. Note that ages \(T_1 - T_4\) characterize the timings of the mid-growth spurt analogous to \(T_6\) to \(T_9\) for the PS (for details see Sheehy et al. 1999). No details are given, since these timings are not used otherwise in this paper.

3.2. Dependence of adult size on pubertal and prepubertal growth

The PS results in the most dramatic changes in size after infancy, and intuitively, one would therefore presume that some of its characteristics would correlate well with adult size. A detailed analysis shows that this is not the case. A regression of adult size on four pubertal parameters (age of peak velocity, maximal acceleration, duration of the PS (= \(T_9 - T_6\)) and contribution due to spurt) was performed (table 1). For all four measures of length a statistically significant relationship was found only for girls. The size of the adjusted multiple squared correlations is, however, not large, even when considering that their size is attenuated due to errors in variables (see Subjects and Methods). For the two width measures significant regressions were found for both sexes, and \(R_{adj}^2\) was again larger for girls than for boys. For arm length, leg and standing height, the age of peak velocity \((T_8)\) is the most important predictor, while for sitting height, biilac and bihumeral width the most important predictor is the contribution due to the PS. A later PS and/or a larger PS lead to a larger adult size.

Intuitively then, certain aspects of prepubertal growth should be important in predicting adult size. First, the duration of prepubertal growth \((T_6)\) shows negligible to small, and mostly statistically not significant positive correlations. Next we evaluate the predictive power of successive growth increments in the prepubertal

![Figure 3. Correlations of distance reached at longitudinal ages with adult distance for boys (solid line) and girls (dashed line) for height.](image-url)
period for adult size. The increments are computed from conception to 1 month, from 1 month to 1.5 years, from 1.5 years to 6 years, and from 6 years to the onset of the PS ($T_6$). Table 2 gives the adjusted percentage of variance explained ($R_{adj}^2$) by using these four prepubertal increments in a linear regression model where $y$ equals adult size (percentage of distance reached at $T_6$ is given for comparison). The increment from 1.5 to 6 years has the highest predictive power followed by size at 1 month for biliac width, sitting height and arm length and by the increment from 6 years until $T_6$ for legs and standing height. Notice that on the one hand the percentage of distance reached is usually slightly lower for boys than for girls, while the percentage of variance explained by prepubertal growth is much smaller for girls than for boys. Across variables, the percentage of variance explained is surprisingly low for sitting height and rather high for biliac width and leg height. All regressions reach significant $p$-values: $p < 0.0001$.

The sum of the four increments of table 2 is the size reached at the onset of the PS ($T_6$). A regression with the latter variable as single predictor of adult size leads to a smaller variance explained compared with the multiple regression with the increments (this can also be deduced from table 3). Despite the lack of a (univariate) association between $T_6$, the length of prepubertal growth, and adult size, we computed also a bivariate regression with the size at $T_6$ and with $T_6$ as predictive variables. Interestingly, given the size at $T_6$, the age at $T_6$ has a highly significant influence on adult size (all $p < 0.0001$). As to be expected a large size at $T_6$ leads to a larger adult size, whereas for a given size at $T_6$, a short prepubertal growth period $T_6$ is associated with a larger adult size. This surprising finding needs some

Table 1. Regression of $y =$ adult size on $x =$ four pubertal parameters (timing, intensity, duration and contribution of the PS) for $n = 120$ boys and $n = 112$ girls. Tabulated are adjusted squared multiple correlation coefficients $\times 100(= R_{adj}^2)$ for statistically significant regressions and $p$-values (ns = not significant).

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further statistical analysis which can be found in the Discussion. The variance explained of adult size by the two predictors is about the same as for the four increments of table 2 (see table 3). The additional variance explained when incorporating $T_6$ as a variable in addition to size at $T_6$ ranges typically between 10 and 20%.

### 3.3. Dependence of pubertal growth on prepubertal growth

Our first objective is to assess whether prepubertal growth of low intensity and/or of short duration is compensated by a large contribution due to the adolescent spurt. Among all five prepubertal parameters (size at 1 month, increment from 1 month to 1.5 years, increment from 1.5 years to 6 years, average velocity from 6 years to the onset of the PS, the duration of prepubertal growth = $T_6$) the regression model with the two parameters $x_1 = T_6$ and $x_2 =$ average velocity from 6 years to $T_6$ was consistently an adequate model for all six variables and both sexes, and always highly significant as seen from the $p$-values (table 4). For most anthropometric variables, the duration of prepubertal growth ($T_6$) was a much better predictor of the increment due to the spurt than average intensity prior to the PS. A short duration and a low intensity are always associated with a larger increment due to the PS. For linear measures, the most striking feature is the contrast between the large $R^2$ (adjusted) for leg height as opposed to the small one for sitting height. Sex differences are inconsistent. However, both measures of width show much greater $R^2$ for boys, with a strikingly large value for bhumeral width.

As a next step we want to evaluate the usefulness of prepubertal parameters in forecasting the timing of the onset of the PS (for reasons given in Methods we used $T_7$, age of maximal acceleration, as a surrogate parameter for $T_6$, the onset of the

| Table 3. Regression of $y =$ adult size on $x =$ two prepubertal parameters (size achieved at $T_6$ and $T_6$) for $n = 120$ boys and $n = 112$ girls. Tabulated values are adjusted squared multiple correlation coefficients $\times 100(= R^2_{adj})$, that part of $R^2_{adj}$ due to $T_6(= \Delta R^2_{adj}(T_6))$ and $p$-values. |
| --- | --- | --- | --- | --- | --- | --- |
| $R^2_{adj}$ | Sex | Bihumeral width | Biliac width | Sitting height | Standing height | Leg height | Arm length |
| m | 68 | 85 | 66 | 80 | 79 | 73 |
| $\Delta R^2_{adj}(T_6)$ | m | 34 | 17 | 19 | 13 | 16 | 24 |
| f | 46 | 62 | 51 | 63 | 67 | 63 |
| $\Delta R^2_{adj}(T_6)$ | f | 11 | 11 | 13 | 11 | 21 | 10 |
| p-value | m | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 |
| f | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 |

| Table 4. Regression of $y =$ increment due to pubertal spurt on two prepubertal parameters ($T_6$ and average velocity from 6 years to $T_6$) for $n = 120$ boys and $n = 112$ girls (for bhumeral width $n = 58$ and $n = 47$). Tabulated values are adjusted squared multiple correlation coefficients $\times 100(= R^2_{adj})$ for statistically significant regressions and $p$-values. |
| --- | --- | --- | --- | --- | --- | --- |
| $R^2_{adj}$ | Sex | Bihumeral width | Biliac width | Sitting height | Standing height | Leg height | Arm length |
| m | 69 | 31 | 11 | 16 | 36 | 43 |
| f | 29 | 13 | 12 | 20 | 48 | 22 |
| p-value | m | < 0.0001 | < 0.0001 | 0.0004 | 0.001 | < 0.0001 | < 0.0001 |
| f | < 0.0001 | 0.0002 | 0.0004 | < 0.0001 | < 0.0001 | < 0.0001 |
PS). The simple regression model with average velocity from 6 years to $T_6$ (age of onset of the PS) as the only predictor was selected as outlined in Methods (table 5). A low prepubertal intensity is associated with a long prepubertal duration. Here, again, a most striking feature is the contrast between leg and sitting height. The $R^2$ (adjusted) for sitting height is sizeable and highly significant, while that for leg height is not significant. For widths, only biiliac width shows a significant but relatively weak association.

### 3.4. Regulatory mechanisms within prepubertal growth

Next, we examined the influence of increments prior to 6 years on the average velocity in the interval between 6 years and $T_6(= y)$. Again a discrepant pattern emerged between sitting height (not significant) and leg height (highly significant) (table 6). Biiliac width displays moderate squared correlations (adjusted) which are highly significant, whereas correlations for bihumer width are negligible and not significant. The association is such that a high intensity in early childhood is associ-

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**Table 5.** Regression of $y = $ onset of the PS (resp. $T_7$ as a surrogate) and $x = $ average velocity from 6 years to $T_6$ for $n = 120$ boys and $n = 112$ girls (for bihumer width $n = 58$ and $n = 47$). Tabulated values are adjusted squared correlation coefficients $\times 100(= R^2_{adj})$ for statistically significant regressions and $p$-values (ns = not significant).

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**Table 6.** Regression of $y = $ average prepubertal velocity from 6 years to $T_6$ and $x = $ average velocity from 1.5 to 6 years for $n = 120$ boys and $n = 112$ girls (for bihumer width $n = 58$ and $n = 47$). Tabulated are adjusted squared correlation coefficients $\times 100(= R^2_{adj})$ for statistically significant regressions and $p$-values (ns = not significant).

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
<th>Bihumer width</th>
<th>Biiliac width</th>
<th>Sitting height</th>
<th>Standing height</th>
<th>Leg height</th>
<th>Arm length</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R^2_{adj}$</td>
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<td>--</td>
<td>32</td>
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<td>$&lt; 0.0001$</td>
<td>$&lt; 0.0001$</td>
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</tbody>
</table>

**Table 7.** Regression of $y = $ average velocity from 1 month to 1.5 years and $x = $ size at 1 month for $n = 120$ boys and $n = 112$ girls (for bihumer width $n = 58$ and $n = 47$). Tabulated values are adjusted squared correlation coefficients $\times 100(= R^2_{adj})$ for statistically significant regressions and $p$-values (ns = not significant).

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
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<th>Biiliac width</th>
<th>Sitting height</th>
<th>Standing height</th>
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<tbody>
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</tbody>
</table>
ated with a high intensity in later childhood. Boys show a consistently stronger prepubertal regulation than girls.

Lastly, we studied the relationship between size at 1 month and the increment between 1 month and 1.5 years (table 7). Mostly small and always negative correlations were found.

4. Discussion

4.1. Correlation of distance reached at a given age with adult size

The general pattern of correlations across age has a meaningful biological interpretation: the sharp increase in correlations after birth can be associated with the change from intrauterine growth to the individual genetic track (Smith et al. 1976; this period of sharp increase lasts for about 1.5 years for sitting and standing height, and somewhat longer for other variables). The slow linear increase in correlation afterwards, until the onset of the PS, can be explained by the steadily increasing percentage of adult size reached with increasing age. The dip occurring at the average age of peak velocity is clearly due to the large interindividual variability in the timing of puberty. This variability has as a consequence that the substantial gain in size due to the PS occurs at different chronological ages for different children which in turn lowers correlations. Not surprisingly, the dip disappears when using developmental ages (see figure 3).

These findings are consistent with the literature (e.g. Tanner et al. 1956, Tanner and Whitehouse 1982). Plausible arguments lead to the hypothesis of higher correlations for girls and not for boys. Surprisingly, the results show clearly the contrary. That prepubertal growth has a more distinct regulatory function for boys is, however, corroborated by different and by more refined analysis, see, for example, sections 4.2 and 4.6. One gets some insight into this sex difference by decomposing the correlation in the following way:

\[ r(D(t), D_{\text{adult}}) = s_t/s_{\text{adult}} + s_{\text{adult} - t}/s_{\text{adult}} \cdot r(D(t), D_{\text{adult}} - D(t)) \]

where \( D(t) \) is distance at age \( t \), \( D_{\text{adult}} \) is adult distance, \( s_t \) is standard deviation of \( D(t) \), \( s_{\text{adult}} \) is the standard deviation of \( D_{\text{adult}} \), and \( s_{\text{adult} - t} \) is the standard deviation of \( (D_{\text{adult}} - D(t)) \).

Logically, the first term is an increasing function of \( t \). Sex differences for this term are small. As to the second term, the factor \( r(D(t), D_{\text{adult}} - D(t)) \) is decisive in determining \( r(D(t), D_{\text{adult}}) \), while the first factor has only a small modifying influence. In this way we see that differences in cross-sectional correlations are directly related to differences in correlations between size achieved and size still to be gained. Figure 4 shows the correlations \( r(D(t), D_{\text{adult}} - D(t)) \) from 0 to 9 years for sitting height and biliac width (legs and arms are similar to the latter). The correlations between size achieved at a given age with the size still to be gained are positive for biliac width and quite a bit higher for boys than for girls. Thus, growth is a more uniform process over the years for boys. For sitting height, correlations at a young age are positive for boys and zero for girls, and at a later age they are zero for boys and even negative for girls. The latter implies that the growth of sitting height proceeds by some ‘up-and-down regulation’ for girls.

We have also investigated whether differences in tracking behaviour between boys and girls could be a contributing factor to the above sex difference. Tracking measures the regularity of the growth process (see Goldstein 1981 and a forthcoming note). While our analysis indicates that tracking is better for boys than for girls—
favouring higher correlations—this does not seem to be the determining factor for the sex differences in the cross-sectional correlations.

Variables differ substantially with regard to the size of cross-sectional correlations, but not in the general pattern across age. Biliac width and legs have a high correlation and sitting height and bihumeral width a low one. Evidently, the regulation of growth is not homogeneous in different parts of the body. Unfortunately, we have no convincing biological explanation for why this is so. However, it is in line

Figure 4. Correlations of distance reached at age $t$ with increment between age $t$ and age 20 for boys (solid line) and girls (dashed line). (a) Biliac width, (b) sitting height.
with figure 4 and the formula given above: for biiliac width or leg height, children who have already achieved a relatively big size at a given age, tend to have a relatively big increment in the future. On the other hand, for sitting height after age 4 the size achieved for boys has no relationship at all with the further increment and for girls a relatively large size achieved even indicates a small future increment. Thus, growth is a more uniform, steady process for legs and biiliac width and follows a more chaotic pattern for sitting height.

4.2. The influence of prepubertal increments on adult size

A multiple regression of adult size on the four prepubertal increments (until 1 month, from 1 month to 1.5 years, from 1.5 to 6 years—the most important period—and from 6 years to $T_6$) led to some interesting results (and quite similar for average intensity in these epochs). When we compare the percentage variance of adult size explained for boys with that for girls, we see that these increments predict adult size much better for boys. This cannot be explained by the percentage of distance reached at the onset of the PS which is approximately the same for both sexes.

Across variables there exist large differences in the predictive power of prepubertal increments. For example, for boys the variance explained is 82% for biiliac width and 62% for sitting height, while the percentage of distance reached at $T_6$ is 78% for biiliac and 82% for sitting height. At present we have no biological explanation—for example, in terms of differential bone growth—for this discrepancy. Statistical artefacts and differences in measurement error can be excluded as an explanation.

These findings about differences across variables and sexes are in line with those for cross-sectional correlations (section 4.1), but they offer a more complete picture of the predictive importance of prepubertal growth.

It is interesting that the duration of the prepubertal period ($T_6$) by itself has no influence on adult size for any of the six variables in good accordance with the results of Tanner et al. (1976) (but see also section 4.4). However, in a bivariate regression with size reached at $T_6$ and $T_6$ as predictors of adult size, the duration of prepubertal growth ($T_6$) became a highly significant factor. For an identical prepubertal size, a short duration enhances the chance to reach a relatively large adult size. This is in line with clinical growth predictions where an early maturing boy at age 8 (size 140 cm and bone age 10) has a Bayley–Pinnean prediction of 187.4 cm, while a late maturer at age 12 (size 140 cm and bone age 10 as well) has a prediction of only 172.4 cm (Prader 1984). Trying to explain this fact, we computed correlation between $T_6$ and the increment due to the level of the PS and also with the duration of the PS. Both were significantly negative. That an early onset of the PS ($T_6$) leads to a higher contribution due to level is logical: given the size at $T_6$ a short duration has to be compensated by a higher prepubertal velocity, and this velocity is continued into puberty. Furthermore, a short prepubertal duration is also associated with a larger contribution due to the pubertal peak (table 4 and section 4.4). Thus, both adolescent components help to enhance adult size for those with an early $T_6$. This is at least partly due to the fact that the PS can last longer when it starts early, as shown by the negative correlations between $T_6$ and duration of the PS. These findings underline that a multivariate analysis can lead to qualitatively different conclusions: univariately, the small, mostly insignificant correlations between $T_6$ and adult size were always positive which is intuitively plausible.
4.3. The influence of pubertal parameters on adult size

For linear measures, the most prominent feature is that pubertal parameters (intensity, duration, timing and contribution due to the PS) have a significant influence on adult size for girls only; for boys the influence is completely negligible. It is surprising that the PS plays a more important regulatory role for girls while its size is more important for boys (Sheehy et al. 1999). While the values for variance explained by the regression are relatively small (table 1), they are attenuated somewhat by the errors in estimating pubertal parameters. Legs show again a stronger association with adult size than the trunk, as was the case for prepubertal parameters. The negligible (for boys) to modest (for girls) dependence of adult size on the PS is in accordance with clinical findings: for children with a gonadal dysfunction there is no PS but still a normal adult height.

For measures of width—in contrast to linear measures—the $R^2$'s (adjusted) are significant for boys, but they are still smaller than for girls. When taking into account the errors in variables for pubertal parameters, their influence on the adult size of the two widths is relatively strong. This is in line with the fact that the PS for width shows both a strong intensity and a long duration compared with linear measures (Gasser et al. 1991a, b, Sheehy et al. 1999). It seems intuitive that a stronger PS plays a greater regulatory role than a weaker PS.

The most influential variables are the timing and the contribution due to the PS, with the effect that a later and/or a larger PS lead to a greater adult size.

For girls, the prepubertal period leaves a substantial percentage of variation in adult size unexplained by the growth process. The significant predictive power of pubertal parameters corrects somewhat for this lack of association and shows clearly that a different growth regulation is effective in boys and girls.

4.4. The influence of prepubertal parameters on the contribution due to the PS

The prepubertal parameters with an appreciable influence on the PS are the average velocity from 6 years to the onset of the PS ($T_6$) and the duration of prepubertal growth (= $T_6$), and of the two parameters duration is much more important. A short duration and/or a small prepubertal intensity are compensated by a more pronounced PS.

For legs the increment due to the PS depends substantially on these parameters, and this contrasts sharply to sitting height, where, while significant dependence is found, it is, however, of modest practical importance. Thus, the prepubertal development of legs has not only a relatively large influence on adult size, but also on the contribution due to the pubertal spurt. This is difficult to explain biologically, but phenomenologically it should be noted that the percentage contribution due to prepubertal growth is very large for legs. For linear measures, sex differences are inconsistent.

For measures of width, the pubertal spurt of boys depends to a much higher degree on prepubertal growth than that of girls—even for biiliac width. For boys the percentage of variance explained (69%) is truly impressive for bihumeral width, and shows that the PS is not only relatively large in size (Gasser et al. 1991b) but has also an important compensating function for the intensity and duration of prepubertal growth.
4.5. The influence of prepubertal growth intensity on the duration of the prepubertal period

The duration of the prepubertal period depends for certain variables on the intensity of growth from 6 years till $T_6$, but not on growth intensity prior to 6 years. Interestingly, this association is strong for sitting height and negligible for legs. Comparing this with the Discussion in section 4.4, we see that for legs, a small prepubertal growth intensity is compensated by a larger increment due to the PS while for sitting height it is compensated by a longer prepubertal growth period.

4.6. Associations between prepubertal growth parameters

A high growth intensity in early childhood entails a relatively high growth intensity from 6 years to the onset of the PS for legs and biliac width, but not for sitting height and bihumeral width. On seeing the relatively large influence of prepubertal growth on adult size for legs and biliac width (sections 4.1 and 4.2) and less so for sitting height and bihumeral width, one might draw the conclusion that prepubertal growth for legs and biliac width is governed by a stronger, more uniform regulatory mechanism than that for sitting height and bihumeral width, contrasting growth in the upper and the lower parts of the body. In table 7 one sees correlations squared between size at one month and growth intensity till 1.5 years. These negative correlations reflect the regulatory role of postnatal growth when changing from intrauterine to extrauterine growth. This has been repeatedly noted in the literature (Smith et al. 1976, Bergman and Bergman 1986).

4.7. Aspects of genetic regulation

Adult size is mainly determined by polygenic autosomal inheritance, whereas environmental factors are of minor influence in developed countries (see Hauspie et al. 1994 and literature cited therein). The characteristics of the PS, such as timing or peak height velocity are also largely under genetic control. Thus, generally speaking, the tempo and the intensity of the growth process are mainly determined by genetic factors. Different genes are probably responsible for tempo and intensity, and for different ages.

That adult size, and many aspects of growth are genetically determined—clearly at an individual level—does not imply that large correlations need arise, since the growth process and its genetics can be quite diverse from child to child even when they reach a similar adult size. What we can detect in a sample are those regulatory mechanisms that are relatively homogeneous in the sample. Let us illustrate this with a simple model. If the velocity curve $v_i(t)$ for individual number $i$ is of the form $v_i(t) = c_i v(t)$, where $v(t)$ is a hypothetical average velocity curve, then the correlations of increments with adult size would be 1 (the genes would here select $c_i$). An important violation of this naive model consists of a highly variable growth tempo, which would rather need a function of individual tempo $h_i(t)$ instead of chronological age $t$ (i.e. $c_i v(h_i(t))$ instead of $c_i v(t)$). Furthermore, the whole growth process consists of at least two sub-processes—pubertal and prepubertal growth—with distinct hormonal regulation. These two facts leave a lot of room for phenomologial and genetic diversity, lowering inevitably correlations across a sample. That intensity is modulated via a factor $c_i$—independent of age—is clearly also an oversimplification.

Given our results one has to assume that the genetic regulation of growth depends to some extent on the sex chromosomes, even if adult size is inherited in an auto-
somal way (but note that an additional Y chromosome leads to about 13 cm additional height, and the loss of an X chromosome leads to stunted growth). The PS plays a regulatory role for adult size predominantly for girls, and only for girls with respect to length. Given the fact that the PS depends on the presence of sex hormones, this different steering mechanism might well be tied to sex chromosomes. The clear sex difference in the regulatory function of prepubertal increments depends probably also on sex chromosomes, directly or indirectly. Prader (1984) argues that the pattern of prepubertal velocity, and the concentration of hormones, makes it plausible that a decreasing peripheral growth response is responsible for the changes in velocity. It could be that girls are genetically more diverse in this respect or have a more variable peripheral reaction.

The genetic inheritance of characteristics of the PS makes their weak association with adult size a little surprising. A straightforward interpretation is that the genetic diversity with respect to intensity, timing and duration is too large to lead to consistent associations—in the sample—between PS characteristics and adult size. The large range of 4 years for the normal timing of the PS makes this plausible.

The different patterns of associations for different variables leads to the hypothesis that quite different genes are responsible for regulating growth in various body dimensions in detail, even if the overall regulation might be steered by some ‘master genes’.

4.8. Conclusions

The relative importance of the various growth phases and their corresponding parameters in determining adult size varies considerably between sexes and across anthropometric variables. Growth regulation is thus not a homogeneous phenomenon in different parts of the body, and neither for boys and girls. Consistent features are

- the large role played by prepubertal growth intensity and the unimportance of duration of prepubertal growth by itself in determining adult size;
- for a given size at the end of the prepubertal period its duration is negatively associated with adult size;
- prepubertal growth intensity is much more influential than pubertal growth in explaining variation in adult size. (This is true even when considering the fact that the influence of pubertal parameters is underestimated since these parameters can only be estimated with a considerable amount of statistical error.)

Other findings are as follows:

1. Interestingly, prepubertal growth plays a bigger role in determining adult size for boys than for girls, while pubertal growth is more important for girls than for boys. This is surprising since the PS is smaller in magnitude for girls, even in proportion to their smaller adult size (Sheehy et al. 1999).

2. We do not have a biological explanation as to why adult biiliac width and adult leg height are so much better explained by prepubertal growth intensity than sitting height and bihumeral width. While for bihumeral width, the PS explains a sizeable portion of the variability in adult size, this is not true for sitting height. Thus, for sitting height—i.e. mainly the growth of the spine—there is a surprisingly large portion of the variance of adult size which cannot
be explained by any of the approaches used here. It is, however, plausible that long-term regulation of the growth of long bones is more orderly than that of the spine which is made up of many components. Let us note, in this respect, that velocity is turned off sharply after the PS for the legs, while it is running out smoothly for sitting height for a prolonged period (Gasser et al. 1991a).

(3) When assessing the influence of prepubertal growth intensity on the onset of the PS and on the contribution due to the PS, we see again a rather complex pattern. Since pubertal growth has—at best—only a modest influence on adult size, the question arises whether it compensates either for a low intensity or a short duration of prepubertal growth. Indeed, a short duration has a sizeable association with a strong PS (except for sitting height, where it is weak), whereas prepubertal intensity is of modest importance for the PS. For sitting height, on the other hand, a low prepubertal growth intensity is related to a prolonged prepubertal growth period.

(4) A high intensity of growth in early childhood is associated with a relatively higher intensity in later childhood for legs and biiilia width, but not for sitting height and bhumeral width. These two variables seem to develop, again, in a more ‘chaotic’ way.

(5) Our results make it plausible that the regulation of growth—with respect to prepubertal and pubertal growth, and with respect to aspects of intensity and duration—is genetically quite diverse in a normal sample. The sex dependence of phenomenological regulation makes some participation of sex chromosomes probable. While there seems to exist a qualitatively similar genetic program for the different anthropometric variables, the detailed regulation seems to necessitate quite different genes.

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References


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Résumé. A partir des données de la Première Étude de Croissance Longitudinale de Zurich, on analyse comment se produisent les différences interindividuelles de taille adulte par les variables hauteur de la jambe, taille-assis, stature, longueur du bras, larges du biliaire et bihumaire. On est aussi plus particulièrement intéressé de connaître si en fonction du sexe et des variables, les mêmes phases de croissance et les mêmes paramètres sont prédicatifs d’une certaine taille adulte. Un modèle relativement complexe apparaît, démontrant que la régulation de la croissance n’est pas la même pour les garçons et pour les filles et qui plus est n’est pas la même pour les six variables anthropométriques étudiées. La croissance pré-pubertaire est caractérisée par son intensité (vitesse moyenne) et par sa durée. Alors que la durée n’a en elle-même aucune influence appreciable sur la stature adulte, l’intensité pré-pubertaire détermine de la taille adulte à un haut degré pour toutes les variables et dans les deux sexes. L’intensité de la croissance pré-pubertaire détermine la taille adulte dans une mesure plus forte chez les garçons que chez les filles. Pour une taille donnée à la fin de la période pré-pubertaire, une durée courte accroît les chances de réaliser une haute taille adulte. La part de variance de la taille adulte expliquée par les paramètres pubertaires comparés à la croissance pré-pubertaire est petite et pour ce qui concerne les mesures linéaires, uniquement significative pour les filles. Une courte durée de la croissance pré-pubertaire est à des degrés divers selon les variables, essentiellement compensée par la suite par une plus forte poussé pubertaire. Le panorama général qui émerge indique que la taille-assis et à un degré moindre la largeur bihumaire, se développent d’une manière plus irrégulière que la largeur biliaire et la longueur de la jambe.