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Sex Chromosome Aneuploidy and Anthropometry: A New Proportionality Assessment Using the Phantom Stratagem

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Reported anthropometric data on 121 subjects with 47,XYY, 47,XXY, 47,XXX, and 45,X aneuploidies were compared to those from 578 male and female control subjects by use of a single, unisex reference person ("phantom"). Subjects and controls were geometrically scaled to a standard stature of 170.18 cm, thus eliminating variance due to height. Deviations of anthropometric variables from specified phantom values were expressed as standard z-scores. By comparing z-scores of individual aneuploidy classes with those of their controls, further differences in proportionality came to light. The stratagem disclosed a systematic proportionality pattern between subjects and controls which appeared to be related to each specific sex chromosome aneuploidy. The phantom stratagem for proportional growth assessment appears to merit further use in genetic investigations where individual differences in size and shape confound the analysis of anthropometric data.

Key words: aneuploidy, anthropometry, proportionality, sex chromosomes, 47,XYY, 47,XXY, 47,XXX, 45,X

INTRODUCTION

Human growth is affected by various environmental and genetic factors which result in the morphologic diversity characteristic of normal individuals. Jost [1972] established that sexual differentiation is a sequential and ordered process: genetic sex, established at conception, determines gonadal sex, which, in turn, regulates phenotypic sex development. During embryonic development, the gonads inherently tend to become ovaries, and a female phenotype develops during the fetal stage. However, in the presence of the Y-linked gene product H-Y antigen, the gonads form testes, which, during fetal development, secrete the hormones necessary to produce a male phenotype [Ohno, 1976].

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Some individuals have an abnormal number of sex chromosomes, resulting in departures from normal sexual dimorphic development. Stature and arm span are affected by particular developmental abnormalities which occur with respect to longitudinal bone growth and thickness of articular cartilage. This paper deals with four types of aneuploidy: 47,XYY; 47,XXY, Klinefelter syndrome; 47,XXX; and 45,X, Ullrich-Turner syndrome. In consecutive newborn babies, the incidence of sex chromosome aneuploids was found to be 1/1,000 for 47,XYY, 47,XXY, and 47,XXX, and 1/8,000 for 45,X [Hamerton et al, 1975]. Most reports on these disorders are clinical. They reveal very little about the overall effect of sex chromosome aneuploidy on gross human morphology, ie, the weight, breadths, and proportional contribution of body segments to stature and arm span.

Ross [1976] suggests that the "most important work in science . . . is the novelty of new conclusions which do not come from the factual data but from the inference." Inferential models can help human biologists find new ways of looking at the chaos of data regarding shape and proportionality. If the facts can be linked symbolically, they can be understood and explained in new ways, and new questions can be formulated. This paper reports the application of such an inferential model to existing data, with the objective of understanding how abnormal numbers of X and Y chromosomes affect human proportionality. For the purposes of the present investigation, it is assumed that the degree of proportional difference between subjects with sex chromosome aneuploidy and control subjects is related to the overall effect exerted on bone growth by the atypical genotype during the prenatal and postnatal periods.

METHODS

Ross and Wilson's stragagem [1974] for proportional growth assessment was applied to anthropometric data reported in two separate studies of chromosome abnormalities [Milne et al, 1974; Eiben et al, 1974]. The reported mean values were used to give a visual representation of each aneuploidy body type (Fig. 1). In addition to the data on the aneuploidy subjects, each study presented anthropometric data on control groups which were used by the original authors for direct comparison with the sex chromosome aneuploidy group.

The reported age distributions for the subjects and their controls are summarized in Table I. The subjects reported by Milne et al [1974], were drawn from the Registry of Abnormal Karyotypes in the Medical Research Council's Clinical and Population Cytogenetics Unit at Edinburgh. Data were available on twenty-seven of the twenty-nine 47,XYY subjects. Roughly half of these were in mental hospitals and a third were in penal institutions. There were fifty 47,XXY subjects, almost all of whom were found in subfertility clinics or in mental hospitals. There were twenty-six 47,XXX subjects, and almost all were in mental hospitals. The sixteen 45,X subjects reported by Eiben et al [1974] had been identified in clinical practice and were subsequently confirmed by karyotyping.

The 290 controls for the 47,XYY and 47,XXY subjects were selected from males in general practice and from male blood donors. In order to minimize size differences, the controls for 47,XXY subjects were matched for stature. The 124 controls for the 47,XXX subjects were selected from female blood donors, none of whom had a stature less than 154.4 cm. The 164 controls for the 45,X subjects were selected from fertile females who were seen for termination of pregnancy.

Since the total incidence of sex chromosome aneuploidy in live born children is in the order of three to, four per thousand, the accidental inclusion of abnormal sex chromo-

some aneuploids in the control groups was an unlikely event. Each syndrome and control group had the same measurement protocol; therefore, it was unlikely that differences between groups were attributable to systematic measurement error.

Table II shows mean values reported for each type of aneuploidy and its control group, for nine selected anthropometric variables (stature, weight, sitting height, sub-ischial height, arm span, bi-acromial width, transverse chest width, bi-iliac width, and anterior-posterior chest depth). These values were translated into proportionality z-values by relating them to a single unisex reference person or phantom (Fig. 2). This was done by application of the following general formula which geometrically scaled the syndrome and control subjects to phantom stature and located the adjusted value in a normally distributed population with mean and standard deviation of P and S, respectively:

$$\left[Z = \frac{1}{S} \left(v \frac{170.18}{h} \right)^{d} - P \right]$$

where:

Z is a proportionality value as a standard z-score.

v is any anthropometric variable.

S is the phantom standard deviation for the given variable as shown in Table III.

170.18 cm. is the phantom height constant.

h is the subject's obtained height.

d is a dimensional exponent (1 for all heights, lengths, breadths, girths, and skinfold thicknesses; 2 for all area values; and 3 for all weights and volumes). And

P is the phantom value for the given variable as shown in Table III.

Height-adjusted aneuploidy classes are illustrated in Figure 3.

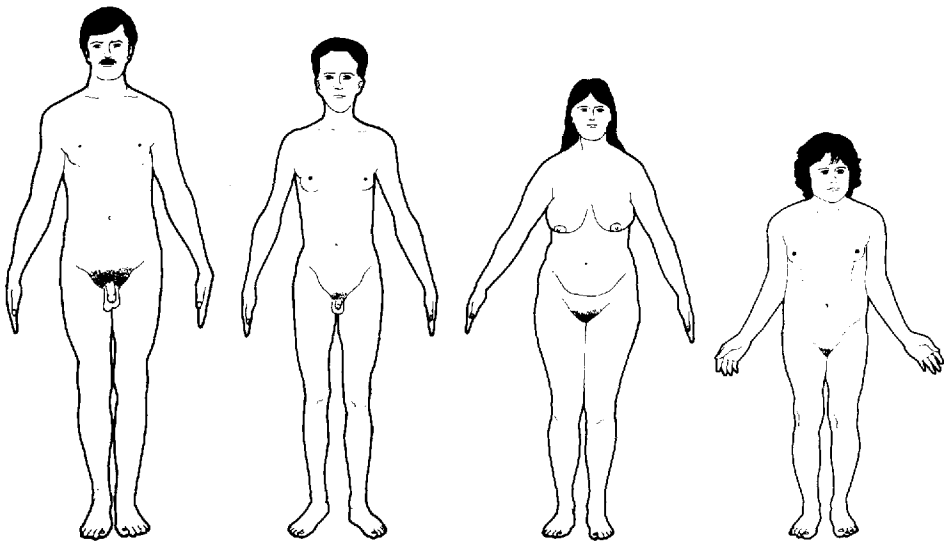

Fig. 1. Pictorial representations of 47,XYY, 47,XXY, 47XXX, and 45,X phenotypes depicting absolute mean values of anthropometric variables.

RESULTS

The aneuploidy subject and control z-values for each variable thus obtained are summarized in Table IV. A z-value of 0.00 indicates that the obtained measure for a particular variable was proportionally the same as that of the phantom. A z-value greater than 0.00 indicates the measure was proportionally larger; a negative value indicates it was proportionally smaller.

The proportional difference between subjects and controls was indicated by the difference in z-values obtained in each group as shown in Table V. These were obtained by finding the difference between the z-values shown in Table IV. For example, a body weight z-value of −0.253 for the 47,XYY subject and +0.611 for its 46,XY control resulted in a subject-control difference of −0.864, showing that 47,XYY subjects were proportionally lighter than their controls.

The subject-minus-control differences are displayed diagrammatically in Figure 4. For all measures except sub-ischial height, the 47,XYY subjects departed further from their controls in a negative direction than did any other of the syndrome subjects under discussion. This was interpreted as a general linearity with proportionally short arm span. The proportionally shorter sitting height and longer sub-ischial height were consistent with this impression. The 47,XXY subjects were somewhat more linear than their controls, but systematically less deviant than the 47,XYY subjects.

The 47,XXX subjects tended to be heavier than their controls, as indicated by the positive value for body weight. Compared to their controls, they had proportionally shorter sitting height and longer sub-ischial height. They were characteristically larger in bi-iliac width and markedly so in A-P chest depth. In considering A-P and transverse chest measures together, the 47,XXX subjects had an apparently rounder trunk than did their controls.

TABLE I

Age distributions of persons with sex chromosome abnormalities and with assumed 46,XX and 46,XY chromosome constitution

	AGE							
GROUP	10–	20–	30–	40–	50–	60–	70+	Total
47, XYY	4	7	7	3	6	2	–	29
47, XXY	3	13	6	12	10	2	4	50
47, XXX	1	4	4	4	6	5	2	26
45,X	mean age 21.3 yrs			range 15.2–32.3 yrs.				16
Men from general practice	–	22	25	28	27	–	–	102
Male blood donors	–	66	58	32	32	–	–	188
Female blood donors	–	56	25	22	21	–	–	124
Fertile female controls	mean age 27.0 yrs			range 16.9–44.2 yrs.				164

TABLE II

Comparative anthropometric mean values on 47,XYY, 47,XXY, 47,XXX, 45,X and control samples

	47, XYY N=27	46,XY control N=102	47,XXY N=50	46,XY control N=147	47,XXX N=47	46,XX control N=124	45, X N=16	46,XX control N=164
Stature (cm)	184.96	170.70	174.06	173.30	160.14	162.39	142.36	159.35
Weight (kg)	80.12	70.48	69.70	69.70	63.30	61.10	48.45	58.14
Sit height (cm)	95.81	90.81	90.15	91.72	84.09	86.88	76.88	84.97
Subischial ht. (cm)	89.15	79.91	83.91	81.55	76.05	75.51	65.48	74.38
Arm span (cm)	184.09	174.47	175.15	176.37	159.62	163.22	144.18	159.00
Biacromial (cm)	40.06	39.35	38.01	39.72	34.93	36.59	34.88	36.71
Trans. chest (cm)	28.93	28.15	26.74	28.12	24.75	25.88	25.13	26.41
Bi-iliac (cm)	29.64	28.77	28.94	28.77	29.05	28.57	30.64*	33.04*
A–P chest (cm)	21.66	21.63	20.78	20.98	20.07	18.55	16.83	16.78

* Bi-trochanteric (cm)

Compared to their controls, 45,X subjects were proportionally heavier, longer in trunk, shorter in legs, greater in arm span, bi-acromial width, and transverse and A-P chest measures. The bitrochanteric value substituted for the unavailable bi-iliac breadth showed them to be proportionally greater in hip width than their controls.

DISCUSSION

Figure 4 shows proportionality trends which might relate to differences in the number of X and Y chromosomes. When the groups are arranged according to their relative numbers of X and Y chromosomes, it becomes obvious that sitting height contributes less (and sub-ischial height more) to overall stature as the number of sex chromosomes and Y chromosomes increases. In fact, all body measurements, with the exception of transverse

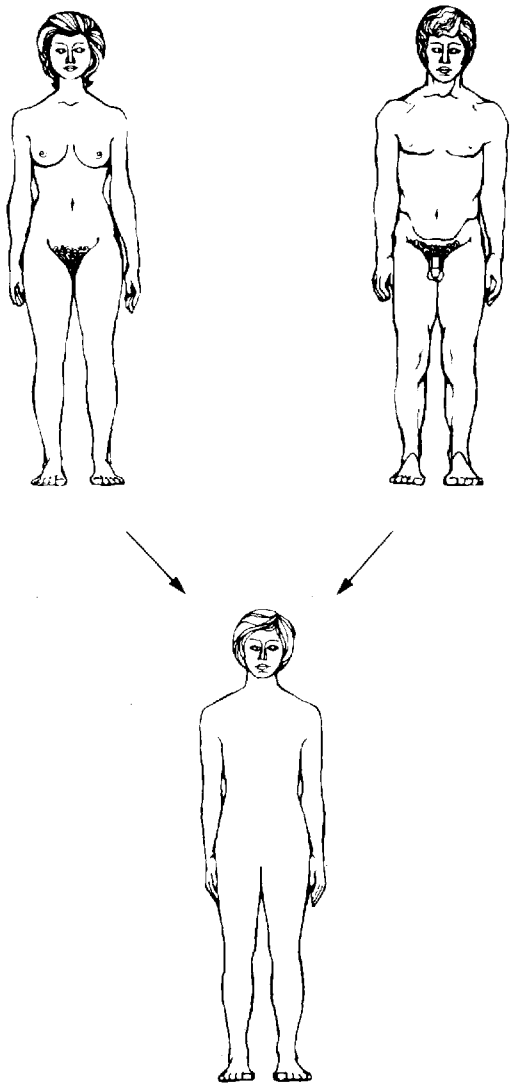

Fig. 2. The Phantom: A unisex reference person geometrically scaled to a standard stature of 170.18 cm with standard deviations based on a hypothetical universal population.

chest width, show similar relationships to the sex chromosomes. Bi-iliac width was not available on the 45,X subjects; however, the bitrochanteric width which was included seemed to indicate the same trend as noted above.

The authors of the original papers drew the following conclusions from their anthropometric assessment of patients with sex chromosome aneuploidy:
1) The 47,XYY subjects were significantly taller and heavier than the 46,XY controls; the observed proportionality differences were likely due to the differences in overall height.

TABLE III

Selected Phantom p and s values prescribed by Ross and Wilson (1974)

	p	s
Stature (cm)	170.18	6.29
Weight (kg)	64.58	8.60
Sit height (cm)	90.78	4.54
Subischial ht. (cm)	79.4	3.97
Arm span (cm)	173.03	4.30
Biacromial (cm)	38.04	1.92
Trans. chest (cm)	27.92	1.74
Bi–iliac (cm)	28.84	1.75
A–P chest (cm)	17.50	1.38
Bi-trochanteric (cm)	32.66	1.80

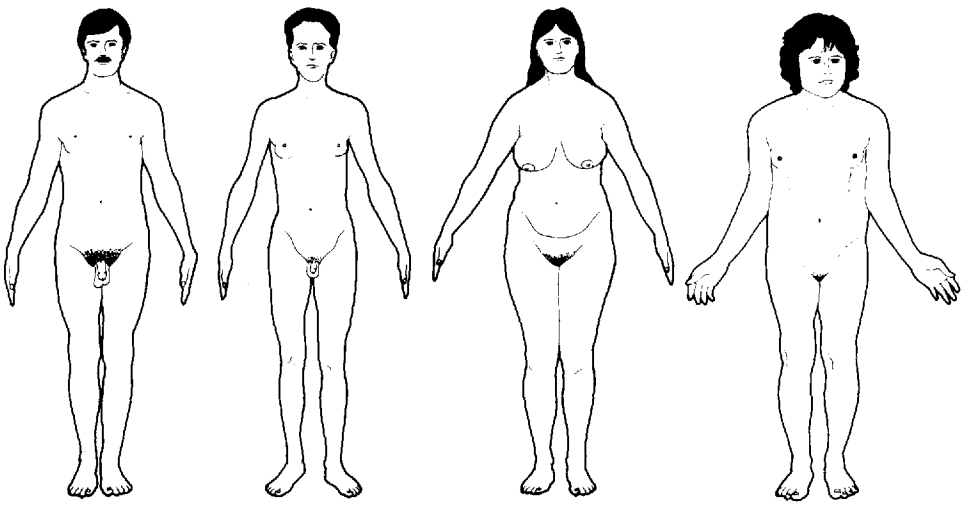

Fig. 3. Pictorial representations of 47 ,XYY, 47 ,XXY, 47 ,XXX, and 45 ,X phenotypes after adjustment of stature to reference height of 170.18 cm.

TABLE IV

Proportionality mean values on 47, XYY, 47, XXY, 47, XXX, 45, X and control samples expressed as Phantom Z–scores

	47,XYY N=27	46,XY control N=102	47,XXY N=50	46,XY control N=147	47,XXX N=47	46,XX control N=124	45,X N=16	46,XX control N=164
Stature (cm)	184.96	170.7	174.06	173.3	160.14	162.39	142.36	159.35
Weight	–.253	+ .611	+.065	+.165	+1.324	+.668	+2.11	+.720
Sit height	–.578	–.054	–.581	–.157	–.312	+.059	+.240	+.000
Subischial ht.	+.661	+.067	+.665	+.172	+.357	–.067	–.283	+.000
Arm span	–.849	+.211	–.415	+.038	–.791	–.461	–.150	–.740
Biacromial	–.615	+.620	–.457	+.503	–.479	+.159	+1.90	+.600
Trans. chest	–.748	+.083	–1.021	–.176	–.930	–.459	+1.21	+.160
Bi–iliac	–.896	–.090	–.311	–.336	+1.16	+.629	2.20*	1.46*
A–P chest	+1.760	+2.945	+2.04	+2.248	+2.774	+1.406	+1.89	+.300

*Bi-trochanteric

TABLE V

Proportionality differences in 47,XYY, 47,XXY, 47,XXX, and 45,X from respective controls expressed as Phantom Z–scores

	Syndrome minus Control Z – Values			
	47,XYY	47,XXY	47,XXX	45,X
Weight	-.864	-.100	+ .656	+ 1.390
Sit height	-.524	-.424	-.371	+ .240
Subischial ht.	+.594	+.493	+.424	- .283
Arm span	-1.060	-.453	-.330	+ .590
Biacromial	-1.235	-.960	-.638	+1.300
Trans. chest	-.831	-.845	-.471	+1.050
Bi-iliac	-.806	+ .025	+.531	.745*
A–P chest	-1.185	-.207	+1.368	+1.590

* Bi-trochanteric

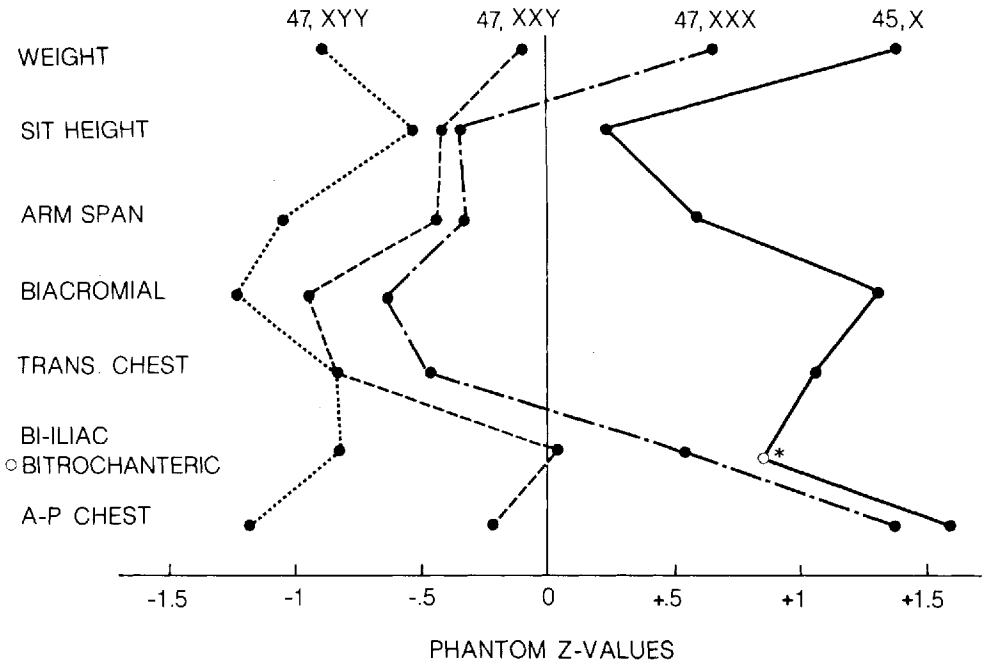

Fig. 4. Proportionality differences in z-scores: syndrome subjects' scores minus their respective controls' scores.

2) The 47,XXY subjects had reduced bi-acromial width, transverse chest, sitting height, and arm span, when compared with the 46,XY controls.
3) The 47,XXX subjects did not differ from the 46,XX controls.
4) The 45,X subjects had a proportionally longer trunk, longer arms, and greater breadths especially across the shoulders when compared with their 46,XX control group.

The present treatment of their data using the phantom stratagem showed the following:

1) The 47,XYY subjects differed proportionally from the 46,XY control group and that these differences were not merely a matter of difference in stature, as perhaps implied in the original report.
2) The 47,XXY subjects were proportionally smaller than the 46,XY control group in those ways already described.
3) The 47,XXX subjects had proportionally reduced sitting height, arm span, bi-acromial, and transverse chest widths; increased bi-iliac width, A-P chest, and sub-ischial height, when compared with the 46,XX control group.
4) The 45,X subjects were proportionally different from their controls in those ways already described.

The above anthropometric assessments describe adult samples. Although some pertinent data have been collected, comparable anthropometric data are not available for prepubertal males and females with sex chromosome aneuploidy. Without further evidence, it is not possible to know with certainty when the effects of sex chromosome aneuploidy are first manifested – at birth, in the prepubertal growth stage, or during adolescence as a result of gonadal dysfunction.

According to Brook et al [1974], the 45,X subject is short at birth and typically has a height velocity between the 10th and 25th centiles; thus, her subsequent short stature results from reduced intrauterine growth, low prepubertal growth rate, and the absence of an adolescent growth spurt. Neither estrogen replacement [Brook et al, 1974], nor growth hormone treatment [Tanner et al, 1971] affected ultimate stature in 45,X females. These observations provide evidence in support of the hypothesis that the growth failure in 45,X aneuploidy results from a genetic abnormality in the bone growth mechanism.

Birth lengths for 47,XYY subjects were greater than those of normal males, and mean prepubertal stature was at the 97th centile [Nielsen et al, 1971]. Schibler et al [1974] found that mean prepubertal stature in 47,XXY subjects was at the 75th centile, and that their increased stature was attributable to increased leg length, rather than to trunk length. Low levels of testes-secreted testosterone in 47,XXY subjects do not influence prepubertal growth, since normal stature and leg length occur in prepubertal anorchic boys [Aynsley-Green et al, 1976]. Later, during male adolescent growth, spurts in sitting height and leg length are largely independent: testosterone accelerates sitting height velocity, while growth hormone accelerates leg length velocity [Tanner et al, 1976].

Perhaps these apparent, consistent growth patterns of shortness in 45,X subjects, and tallness in 47,XYY and 47,XXY subjects result from abnormal functionings of a common control mechanism. Sex chromosome aneuploidy may result in an alteration of the bone growth mechanism by 1) a change in the sensitivity of the mechanism itself, or 2) prenatal gonadal dysfunction and altered endocrine control.

The new perspective afforded by the phantom stratagem in abnormal subject-control comparisons has brought to light a systematic pattern which seems to be related to each specific sex chromosome aneuploidy. However, since subjects included in each aneuploidy

sample were selected clinically, inferences about anthropometric characteristics of the population should be made with caution.

While the phenomena have not been fully elucidated, these findings invite further exploration. The phantom stratagem is a simple tool for the analysis of such data, and thus, is preferable to more complex statistical procedures. For example, Eiben et al [1974] used factor analysis to reach their conclusions, all of which were supported by the present method of data analysis, which is easier both to use and to understand.

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