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NUCLEAR SEX AND BODY-BUILD IN SCHIZOPHRENIA

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A recent survey on body-build has shown that schizophrenics differ markedly from normal subjects with regard to the biacromial diameter and the androgyny score. Groups of patients of both sexes were found to have a much lower (more female) androgyny score and a smaller biacromial diameter than did groups of normal men and women (Rey and Coppen, 1959). The androgyny score is obtained by the formula:

$$3 \times \text{biacromial diameter (cm.)} - 1 \times \text{bi-iliac diameter (cm.)}$$

The androgyny score for normal individuals has been shown to have a normal distribution for each sex, with a mean of 90.1 (S.D. 4.7) for men and of 78.9 (S.D. 4.6) for women (Tanner, 1951). The androgyny score enables effective discrimination to be made between the sexes. Out of 409 men and women examined by Tanner (1951) only 12% were misclassified on the basis of the androgyny score.

The biacromial diameter and the androgyny score are closely related to sexual development (Rey and Coppen, 1959). Moreover, it has been found that anatomical males with chromatin-positive cells have smaller biacromial diameters than normal subjects (Raboch, 1957; Coppen and Cowie, 1960).

There are grounds for believing that some connexion may exist between anomalies of nuclear sex and mental

disorders. Thus Pasqualini *et al.* (1957) described a number of individuals with Klinefelter's syndrome who showed hypokinesia and timidity from an early age. They were usually idle, slept too much, lacked vital interests, and were shy, restrained, and had few friends. They were of low intelligence with a mean I.Q. of 81. In line with this last observation Ferguson-Smith (1958, 1959) found that just over 1% of male patients in a mental deficiency hospital and 1.2% of educationally subnormal male children had chromatin-positive Klinefelter's syndrome. These percentages greatly exceed that of 0.26% reported by Moore (1959) in an unselected group of newborn male infants.

Taking all these facts into consideration, it is not unreasonable to suspect that there may be changes in nuclear sex associated with schizophrenia. However, as many schizophrenics have a normal physique and as the classification of schizophrenia may well include heterogeneous groups of patients, it seems likely that if anomalies of nuclear sex occurred in this condition they would be found in patients with a female type of body-build.

In the present investigation male schizophrenics with an androgyny score characteristic of normal women were selected from a schizophrenic population for the examination of nuclear sex. A similar examination was carried out with a group of female schizophrenics with significantly reduced androgyny scores, as it is known that women with gonadal dysgenesis frequently have anomalies of physique and often lack sex chromatin (Grumbach *et al.*, 1955).

The Investigation

We examined 100 male and 100 female mental hospital patients with a diagnosis of chronic schizophrenia. In every case the biacromial and bi-iliac diameters were measured with a Martin anthropometer. The androgyny scores for patients of both sexes are shown in the Chart. The mean androgyny scores for both the male and the female

Distribution of androgyny score in schizophrenic patients and normal subjects.

*In receipt of a grant from the Medical Research Council.

groups were greatly reduced when compared with values obtained from groups of normal men and women. The mean androgyny score of the female schizophrenics was 76.1 (S.D. 5.5) and that of the male schizophrenics was 86.2 (S.D. 5.4). The figures obtained are in accordance with previous findings in the case of schizophrenic patients (Rey and Coppen, 1959).

From the total number of patients, three groups were selected on the basis of their androgyny scores. One group consisted of 6 male patients with an androgyny score of 89 or over, within the range for normal men. A second group of 16 men had androgyny scores less than 82, approximately the mean score for normal women. A third group consisted of 20 female patients whose androgyny score was under 72. Androgyny scores of this order are much lower than those found in normal women. It was thought that if any of the women lacked sex chromatin they would most likely be found in this group whose body-build showed the greatest deviation from normal.

A scraping of buccal mucosa and a smear of capillary blood from the ear were taken from each of the patients in these groups. Assessment of nuclear sex was carried out according to the method of Moore and Barr (1955) and Davidson and Smith (1954).

The results are set out in detail in Tables I-III. In spite of the wide deviation from normal of the androgyny scores, no anomalies of nuclear sex were discovered.

The estimation of androgyny scores was considered to be a good screening device for selecting patients likely to show inconsistencies between anatomical and

TABLE III.—*Females with Low Androgyny Score*

No.	Androgyny Score	Blood Chromatin			Blood Chromatin Assessment	+ Eosinophils	Mean Lobe Count	Buccal Mucosa Chromatin		Buccal Mucosa Chromatin Assessment	Overall Nuclear Sex Assessment
		Observed		Calc.				% Neg.	% Pos.		
		No. of Nodules	No. of Neutrophils								
1	69.9	8	120	33	+	0:5	—	74	26	+	Pos.
2	64.1	38	500	38	+	0:8	3:10	64	36	+	..
3	70.7	20	500	20	+	1:7	2:94	74	26	+	..
4	67.4	21	400	26	+	2:7	2:82	70	30	+	..
5	69.9	2	189	5+	+	0:0	2:84	70	30	+	..
6	65.4	8	320	13	+	2:20	3:06	78	22	+	..
7	71.0	20	500	20	+	1:4	2:96	70	30	+	..
8	67.2	5	300	8	+	0:2	2:94	77	23	+	..
9	71.4	42	500	42	+	1:5	3:1	78	22	+	..
10	69.3	21	500	21	+	4:29	3:26	78	22	+	..
11	71.7							77	23	+	..
12	71.9	10	500	10	+	0:5	2:5	62	38	+	..
13	67.6	25	500	25	+	0:10	3:32	69	31	+	..
14	70.1	9	500	9	+	0:8	2:78	76	24	+	..
15	69.9	11	500	11	+	2:46	3:23	75	25	+	..
16	69.3	15	500	15	+	0:3	3:2	81	19	+	..
17	69.9	17	500	17	+	0:4	2:92	73	27	+	..
18	65.3	23	500	23	+	0:5	3:26	83	17	+	..
19	68.6	25	500	25	+	1:12	3:32	63	37	+	..
20	67.3							62	38	+	..

chromosomal sex. It seems improbable, therefore, that nuclear-sex anomalies are associated in any significant degree with schizophrenia, or that they are responsible for the marked differences in body-build between schizophrenic patients and normal individuals.

Discussion

The possibility of an anomaly in nuclear sex associated with an abnormality of body-build in schizophrenics has been examined, but according to the methods used in this investigation there appears to be no significant relationship of this kind. Thus the striking difference in physique between schizophrenics and normal subjects remains unexplained on this basis. As the marked increase in width of the biacromial diameter occurs during the adolescent growth spurt under the influence of the sex hormones, it seems most likely that the abnormality in physique of schizophrenics is related to endocrinological abnormalities occurring at that time. This in turn may be genetically determined or produced by environmental disturbances during the period of the child's growth. The other possibility is that this narrow physique possessed by so many schizophrenics is not related to sexual development but rather to a general factor of "narrowness." This appears unlikely, as the other breadth measurement made during the examination of schizophrenics—the bi-iliac diameter—shows no significant deviation from normal (Rey and Coppen, 1959).

Summary

The primary aim of the present investigation was to examine schizophrenics for anomalies of nuclear sex. Abnormal mean androgyny scores and mean biacromial diameters had already been found in groups of schizophrenics. As these values appear closely related to sexual development, it was considered an economical screening method to select schizophrenics with highly abnormal androgyny scores for cytological examination. The deviations from normal of mean androgyny scores for both male and female schizophrenics were in accordance with previous findings.

Cytological examination failed to reveal anomalies of nuclear sex in 16 male and 20 female schizophrenics

TABLE I.—*Males with Normal Androgyny Score*

No.	Androgyny Score	Blood Chromatin		Blood Chromatin Assessment	+ Eosinophils	Mean Lobe Count	Buccal Mucosa Chromatin		Buccal Mucosa Chromatin Assessment	Overall Nuclear Sex Assessment
		Observed					% Neg.	% Pos.		
		No. of Nodules	No. of Neutrophils							
1	90.5	0	500	Neg.	0: 10	3:37	98	2	Neg.	Neg.
2	89.6	0	500	..	0: 37	2:97	97	3	..	..
3	91.4	0	500	..	0: 10	3:06	99	1	..	..
4	95.3	0	500	..	0: 7	2:89	97	3	..	..
5	91.6	0	500	..	0: 16	3:29	97	3	..	..
6	97.5	0	500	..	0: 2	3:11	98	2	..	..

TABLE II.—*Males with Low Androgyny Score*

No.	Androgyny Score	Blood Chromatin		Blood Chromatin Assessment	+ Eosinophils	Mean Lobe Count	Buccal Mucosa Chromatin		Buccal Mucosa Chromatin Assessment	Overall Nuclear Sex Assessment
		Observed					% Neg.	% Pos.		
		No. of Nodules	No. of Neutrophils							
1	78.5	0	500	Neg.	0:20	2:96	97	3	Neg.	Neg.
2	78.7	0	500	..	0:9	3:40	95	5	..	..
3	77.0	0	500	..	0:11	2:96	97	3	..	..
4	67.4	0	500	..	0:16	2:82	95	5	..	..
5	67.4	0	440	..	0:10	2:76	97	3	..	..
6	79.7	0	500	..	0:4	2:99	98	2	..	..
7	76.8	0	500	..	0:6	3:35	98	2	..	..
8	78.1	0	500	..	0:29	3:21	95	5	..	..
9	78.1	0	500	..	0:20	3:03	95	5	..	..
10	80.8	0	500	..	0:19	3:33	99	1	..	..
11	81.4	0	500	..	0:12	3:06	95	5	..	..
12	74.0	0	500	..	0:30	3:48	95	5	..	..
13	80.8	0	500	..	0:6	3:06	97	3	..	..
14	80.6	0	500	..	0:5	3:14	97	3	..	..
15	79.8	0	500	..	0:22	3:53	98	2	..	..
16	80.1	0	500	..	0:12	3:24	98	2	..	..

with a maximum deviation from normal with respect to the androgyny score.

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CORTISONE AND SKIN SENSITIVITY TO TUBERCULIN IN RETICULOSES

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There have been several reports on the effect of cortisone and corticotrophin on skin sensitivity to tuberculin in a variety of diseases but not in malignant diseases of lymphoreticular tissue. Excluding tuberculosis and sarcoidosis, most workers have found that sensitivity is reduced by systemic cortisone (Carey *et al.*, 1950; Long and Favour, 1950; Lovell *et al.*, 1953), although a variable response was reported by Sulzberger *et al.* (1951). Truelove (1957) noted, however, that the Mantoux reaction became positive in 20 out of 24 patients with various diseases during treatment with prednisolone and cortisone.

In sarcoidosis Citron and Scadding (1957) reported that 57% of the patients were insensitive to 100 tuberculin units (T.U.) of purified protein derivative (P.P.D.) and that half of these became sensitive when cortisone was injected with the tuberculin. This was not just a local effect, as systemic cortisone had a similar action (Pyke and Scadding, 1952). The same occurred in patients suffering from tuberculosis who had been desensitized to P.P.D., and Citron and Scadding concluded that, since the result in sarcoidosis was identical with that in desensitized patients with tuberculosis, there was a causal relationship between tuberculosis and sarcoidosis in the patients they investigated.

Patients with malignant disease of lymphoreticular tissue form another group frequently insensitive to tuberculin (Hoyle *et al.*, 1954). The purpose of this study was to determine the effect of cortisone on tuberculin sensitivity in such patients in order to ascertain whether those who were insensitive responded in the same way as Citron and Scadding's patients with sarcoidosis.

Selection of Cases

Three groups of patients, totalling 297, have been studied: (1) 138 patients with reticuloses (aged 18–76); (2) 43 patients with carcinoma (aged 35–77); and (3) 116 controls (aged 18–78).

The term "reticulosis" is used to include all primary malignant diseases of lymphoreticular tissue. These have been classified under the headings of Hodgkin's disease, reticulum-cell sarcoma, multiple myelomatosis, lymphosarcoma (including lymphoid follicular reticulosis or Brill-Symmers disease), chronic lymphatic leukaemia, myeloproliferative syndromes (including chronic myeloid leukaemia, myelosclerosis, myelofibrosis, and polycythaemia rubra vera), and acute leukaemia (including acute erythromyelosis).

In the patients with carcinoma the primary sites included breast, bronchus, bladder, kidney, liver, pharynx, stomach, and thyroid.

The controls consisted of patients suffering from diseases unrelated to any form of malignant or reticulo-endothelial disorders. These included ischaemic heart disease, cerebrovascular disease, chronic rheumatic heart disease, hypertension, a variety of infections (excluding tuberculosis), ulcerative colitis, senile osteoporosis, pernicious anaemia (treated), iron-deficiency anaemia, rheumatoid arthritis, osteoarthritis, prolapsed intervertebral disk, epilepsy, peptic ulceration, diabetes mellitus, obesity, malabsorption syndromes, cirrhosis hepatitis, and anxiety neurosis.

Technique

The technique used was very similar to that of Citron and Scadding (1957). The P.P.D. was supplied by the Ministry of Agriculture and Veterinary Research Laboratory, Weybridge (0.00002 mg. of P.P.D. is equivalent to 1 T.U.). Dilutions containing 10 T.U. and 100 T.U. in 0.05 ml. were prepared every four weeks and stored at 4° C. Just prior to injection this was mixed with 0.05 ml. of physiological saline (without preservative) to make a final dilution in 0.1 ml. The injection of tuberculin plus cortisone was prepared by mixing 0.05 ml. of the appropriate P.P.D. solution with 0.05 ml. of cortisone acetate suspension containing 1.25 mg. of cortisone acetate.

On admission each patient received an intradermal injection of 10 T.U. into one arm, and 10 T.U. plus cortisone into the other arm. Those who were negative to these were tested with 100 T.U. with and without cortisone.

TABLE I.—Results of Testing with Tuberculin Alone

Disease	No. of Patients	Sensitive to				Insensitive to 100 T.U.		Significance Tests
		10 T.U.		100 T.U.		No.	%	
		No.	%	No.	%			
Reticuloses:								$\chi^2 = 20.11$ d.f. = 8 P < 0.01
Hodgkin's disease	40	2	5	16	40	22	55	
Reticulum-cell sarcoma ..	9	2	22	1	11	6	67	
Multiple myelomatosis ..	16	7	44	4	25	5	31	
Lymphosarcoma ..	12	5	42	2	16	5	42	
Chronic lymphatic leukaemia ..	15	7	47	1	6	7	47	
Myeloproliferative syndromes	28	10	36	10	36	8	28	
Acute leukaemia	18	5	28	4	22	9	50	
Total ..	138	38	27.5	38	27.5	62	45	$\chi^2 = 50.9$ d.f. = 2 P < 0.001
Controls	116	82	71	20	17	14	12	
Carcinoma ..	43	18	42	17	40	8	18	