Psychological Medicine, 1998, **28**, 655–663. Printed in the United Kingdom
© 1998 Cambridge University Press

Morphometry in schizophrenia revisited: height and its relationship to pre-morbid function

P. NOPOULOS,[1] M. FLAUM, S. ARNDT AND N. ANDREASEN

From the Mental Health Clinical Research Center, Department of Psychiatry and Department of Preventive Medicine, University of Iowa Hospitals and Clinics, University of Iowa College of Medicine, Iowa, USA

ABSTRACT

Background. Morphometry, the measurement of forms, is an ancient practice. In particular, schizophrenic somatology was popular early in this century, but has been essentially absent from the literature for over 30 years. More recently, evidence has grown to support the notion that aberrant neurodevelopment may play a role in the pathophysiology of schizophrenia. Is the body, like the brain, affected by abnormal development in these patients?

Methods. To evaluate global deficit in development and its relationship to pre-morbid function, height was compared in a large group ($N = 226$) of male schizophrenics and a group of healthy male controls ($N = 142$) equivalent in parental socio-economic status. Patients in the lower quartile of height were compared to those in the upper quartile of height.

Results. The patient group had a mean height of 177·1 cm, which was significantly shorter than the mean height of the control group of 179·4 ($P < 0{\cdot}003$). Those in the lower quartile had significantly poorer pre-morbid function as measured by: (1) psychosocial adjustment using the pre-morbid adjustment scales for childhood and adolescence/young adulthood, and (2) cognitive function using measures of school performance such as grades and need for special education. In addition, these measures of pre-morbid function correlated significantly with height when analysed using the entire sample.

Conclusions. These findings provide further support to the idea that abnormal development may play a key role in the pathophysiology of schizophrenia. Furthermore, this is manifested as a global deficit in growth and function resulting in smaller stature, poorer social skills, and deficits in cognitive abilities.

INTRODUCTION

The idea that the psyche and the soma go hand in hand dates back centuries. Aristotle was among the first group of writers to point out the relationship between mind and physiognomy (Ciocco, 1936). In regard to schizophrenia, a book published by Kretschmer in Germany in 1921 (later published in English) (Kretschmer, 1925), launched at least a decade of work on the issue of somatic habitus or body type and psychiatric disease. Later criticized for its lack of reliability and inconsistent findings, research on the issue of body constitution and schizophrenia has largely been ignored since that time. Although many of the early studies had conflicting findings with regards to body shape or type, they frequently found one variable that was abnormal in the schizophrenic population – height was reduced in the patient sample.

A review of the older literature on somatology of the schizophrenic patient was done by Barbara Betz in 1942. She obtained data from a review article published by Pearl & Ciocco in 1934 on the constitution of heart disease where they listed, in rank order, the stature of 66 separate groups of males with various medical diagnosis (cancer, heart-valve disease, flat foot, haemorrhoids, etc.), as well as two groups of 'healthy'

[1] Address for correspondence: Dr Peg Nopoulos, University of Iowa Hospitals and Clinics, Department of Psychiatry, 2887 JPP, 200 Hawkins Drive, Iowa City, Iowa 52242, USA.

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press

Table 1. *Literature review of stature in males in schizophrenia*

Mean height (cm) or schizophrenic males, in relation to comparison groups of males as compiled from the literature*

Rank	Group	Mean height	*N*	Author, year
1	US Army officers with valvular heart disease†	177·52	19	Reed & Love, 1933
21	US Army officers (random sample)	174·85	720	Reed & Love, 1933
39	Normal, healthy males	173·05	272	Pearl & Miner, 1927
63	Schizophrenia	169·45	125	Burchard, 1916
64	Draft recruits with defective physical development	169·09	12393	Davenport & Love, 1921
65	Nephritis and hypertension	167·86	15	Draper, 1924
66	Schizophrenia	168·7	100	Kolle, 1925
67	Schizophrenia	167·6	150	Wells, 1938
68	Schizophrenia	167·0	100	Henckel, 1924
69	Draft recruits underweight	166·37	12129	Davenport & Love, 1921
70	Schizophrenia	165.3	100	Kolle, 1926
71	Gastric and duodenal ulcer‡	164·28	30	Draper, 1924
72	Schizophrenia	160·5	100	Matecki & Szpidbaum, 1927
73	Schizophrenia	160·2	25	Shaw, 1925

* Adapted from Betz, 1942 and Pearl & Ciocco, 1934.
† Group from the Pearl & Ciocco sample of 66 groups with the highest mean stature.
‡ Group from the Pearl & Ciocco sample of 66 groups with the lowest mean stature.

controls (US army officers and a sample of normal males). To this list, Betz then added the mean stature of seven groups of males with schizophrenia, compiled from the literature, and rank ordered them again, raising the total number of separate groups to 73. Results from a subgroup of the larger sample of 73 are presented in Table 1. All of the schizophrenic groups ranked in the lowest one-fifth of the series.

Though very few studies have been done in more modern times, the finding of schizophrenic patients being somewhat smaller in stature is a consistent finding over time and even across nations: in 1942, Betz found a group of 193 women with schizophrenia to be significantly smaller than controls. In 1972, Singer *et al.* reported that a group of 411 Chinese patients with schizophrenia were smaller in stature than controls and, in 1976, Kemali *et al.* reported that a group of 219 Italian patients with schizophrenia were significantly shorter than controls. In addition, at least two articles have evaluated height differences within subtypes of schizophrenia: in 1968, Pivnicki & Christie reported height across subtypes of schizophrenia with simple subtype the smallest < hebephrenic subtype < catatonic subtype < paranoid subtype, and that all groups, with the exception of the paranoid type, were smaller than a comparison group of patients with manic depressive illness. Similarly, Houston & Bloom (1975) reported that stature was lower for males with chronic schizophrenia compared with controls, but acute schizophrenics were not smaller than controls.

In more recent years, the measurement of height has been collected, usually to control for overall body or brain size in brain imaging studies in schizophrenia. Though often not highlighted in the study, several samples, including previous ones from our own laboratory, have shown that patients, on average, tend to be shorter than controls (Hauser *et al.* 1989; Andreasen *et al.* 1990; Bogerts *et al.* 1993; Flaum *et al.* 1995).

Though measurement of body proportion and shape may not be a reliable or germane measure to schizophrenia, there is good reason to believe that overall stature or height may be. One reason is that there now appears to be an abundance of evidence to support the notion that aberrant neurodevelopment may play a role in the pathophysiology of schizophrenia. Support from this comes not only from brain findings (Akbarian *et al.* 1993; Nopoulos *et al.* 1995, 1996, 1997), but also from studies showing abnormal social skills (Walker & Lewine, 1990) and cognitive dysfunction (Jones *et al.* 1994) in pre-schizophrenic children.

Several studies have reported that the birthweight of patients with schizophrenia is significantly lower than their well siblings (Lane & Albee, 1966; Woerner *et al.* 1971; Torrey, 1977), patients with affective psychosis (Rifkin *et al.* 1994), or normal controls (McNeil *et al.* 1993). In addition, poor pre-morbid social adjustment

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press

in schizophrenia has been shown to be predicted by low birth weight (Foerster *et al*. 1991; Rifkin *et al*. 1994) giving further credence to the notion that those patients who manifest early signs of growth delay go on to have other deficits.

To investigate the notion of a global deficit in growth and function, we studied height in a large group of patients with schizophrenia compared with a sample of healthy controls. Stature was then evaluated in relation to a variety of phenomenological variables, including measures of pre-morbid motor, cognitive, and social function, as well as post-morbid measures of illness severity. It was hypothesized that the patient group would be shorter than the controls and that those patients whose stature was most affected would manifest the poorest pre-morbid function and more severe illness.

METHOD

To eliminate the confound of sex on height and on phenomenological variables of the illness, we limited the sample to males only. In addition, we limited the sample to those males at least 21 years of age, as it has been shown that the epiphyseal plate does not fully close until about age 21 (Greisheimer, 1950), and thus long bone growth is still possible in males up to then. The patient sample (N = 226) consisted of consecutive admissions to the University of Iowa Mental Health Clinical Research Center in-patient unit. All patients were diagnosed as having DSM-III-R schizophrenia by consensus of at least three research psychiatrists. Height was measured at the time of admission by a research nurse and recorded in centimetres.

Demographic and pre-morbid measures

Each patient's demographic information, as well as past and current symptom history, was obtained using the Comprehensive Assessment of Psychiatric History (CASH) (Andreasen *et al*. 1992), a semi-structured interview that embeds a variety of measures that are relevant to the study of schizophrenia. All possible sources of information were used to complete the CASH – patient interview, interview with informant (usually mother) and medical records. Parental socioeconomic status was derived from the Hollingshead scale (Hollingshead & Redlich, 1958). This scale ranged from 1 (families of wealth, education, top-rank social prestige) to 5 (unskilled and semi-skilled workers; elementary education).

Within the CASH, the modified Pre-morbid Adjustment Scale (PAS) was used to evaluate social and interpersonal function prior to the onset of illness. Adapted from the Pre-morbid Asocial Adjustment Scale developed by Gittelman-Klein & Klein (1969), the modified version in the CASH has been shown to have good inter-rater and test–retest reliability (Gupta *et al*. 1995). The pre-morbid period was dichotomized into childhood (6–12 years) and adolescence (13–21 years), and ended 1 year prior to the first psychiatric contact or 1 year prior to the onset of characteristic florid symptoms, whichever came first.

Also within the CASH, school performance was measured by two variables: average grades (1–5 scale; the higher the number, the better the average grades) and education problems (1–5 scale; the higher the number, the fewer problems, such as being held back or needing special education).

Symptom and cognitive measures

Phenomenological measures, such as age of onset, duration of illness, number of previous hospitalizations and total duration of hospitalizations, were obtained from the CASH. Current symptoms were recorded as worst in the past month using the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984) and the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) within the current section of the CASH. Several factor analytical studies of the SANS/SAPS have indicated three independent symptom dimensions: psychosis, disorganization and negativity (Miller *et al*. 1993; Andreasen *et al*. 1995*a*, *b*). Global scores for each of the three dimensions were calculated from the SANS/SAPS. Past symptoms were obtained from the past history section of the CASH, again using global SANS/SAPS scores from the three dimensions of pathology.

Cognitive assessment was performed using a comprehensive battery designed to test a wide variety of functions. The entire battery was administered to patients when they were deemed clinically stable. This was done typically while patients were on their current medication

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press

regimen and prior to a 3 week medication washout. However, if the patient was admitted with no neuroleptic exposure, the testing was done prior to medication treatment. This analysis used only the Full Scale IQ from the WAIS-R.

The normal control sample ($N = 122$) was obtained from the community via newspaper advertisement. They were screened for any personal or family history of psychiatric illness. In addition, they were screened and eliminated if they had a history of, or were currently positive for, substance abuse.

All subjects gave written informed consent.

Statistical analysis

Paired t tests were used to evaluate height between patient and control groups. The entire patient sample was segmented to construct two extreme groups for comparison: the upper quartile of height ($N = 62$; 'tall') and lower quartile of height ($N = 61$; 'small'). Paired t tests were used to evaluate differences in pre-morbid and morbid measures between the extreme height groups. Since we had *a priori* hypotheses that the patient group would be smaller and that the smaller patients would have the poorest pre-morbid function and more severe illness, one-tailed tests were used.

For those variables that showed a significant difference between the 'small' patients *versus* the 'tall' patients, additional correlation analysis was performed on the entire sample using non-parametric methods.

RESULTS

The two groups were initially tested for differences in parental socio-economic status, since differences in nutrition and health may be related to social class and may have a direct effect on biological developmental variables, such as height. The patient group did not differ significantly from the control group in parental socioeconomic status ($t = 1{\cdot}23$, $P < 0{\cdot}23$). Moreover, the two extreme groups of patients (upper quartile of height *v.* lower quartile of height) also did not differ with regard to parental socio-economic status ($t = 1{\cdot}24$, $P < 0{\cdot}22$).

The mean height of the schizophrenic sample was 177·1 cm (S.D. = 7·98). This is significantly shorter than the mean height of the controls,

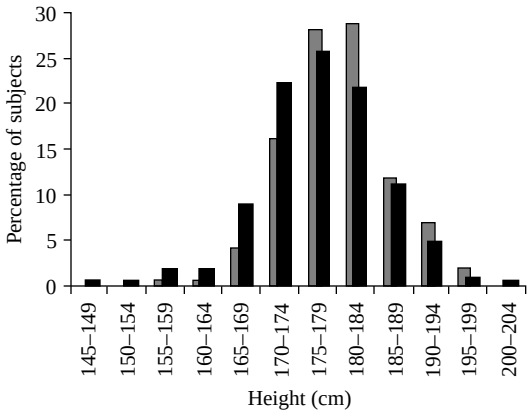


FIG. 1. Frequency distribution of height in patient (■) and control (▨) groups.

which was 179·4 cm (S.D. = 6·99); $t = 2{\cdot}76$, $P < 0{\cdot}003$. Fig. 1 displays the distribution of height for both the patient and control groups. As can be seen visually, as well as by statistical methods (Shapiro–Wilk W test for normality), both groups were normally distributed: controls $W = 0{\cdot}981$, $P = 0{\cdot}488$; patients $W = 0{\cdot}984$, $P = 0{\cdot}568$. The patient group was shifted slightly to the left with controls outnumbering patients in the upper half of the distribution and patients outnumbering controls in the lower half of the distribution. To test whether the two distributions were different from one another, a Kolmogorov–Smirnov D statistic was done. This showed marginal significance ($D = 0{\cdot}145$, $P < 0{\cdot}05$). However, since this difference can be caused by a mean shift, the two distributions were centred and re-tested. Once the averages were lined up (i.e. centred), the D statistic was no longer significant ($P > 0{\cdot}12$). Finally, an F test shows no significant difference ($P > 0{\cdot}08$) in the variances between the two groups.

The pre-morbid variables between the two extreme groups within the patient's sample were then analysed, as shown in Table 2. All pre-morbid measures of social and cognitive function were significantly poorer in the 'small' patient group, including pre-morbid adjustment (both childhood and adolescence/young adult), education performance, and education problems. This indicates that the 'small' had significantly more dysfunction in social and cognitive skills prior to the onset of their illness.

In contrast to the pre-morbid measures, all of the post-morbid or current measures of illness

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press

Table 2. *Comparison of pre-morbid measures between the 'small' patients and the 'tall' patients*

	N	Mean (S.D.)	*t*	*P*
Childhood Pre-morbid Adjustment Scale (ages 6–12)				
Lower quartile	61	4·08 (2·4)		
Upper quartile	60	3·05 (2·2)	2·46	< 0·008
Adolescence and young adulthood (ages 13–21)				
Lower quartile	61	5·93 (2·7)		
Upper quartile	60	4·90 (2·5)	2·16	< 0·015
Education performance				
Lower quartile	61	2·87 (1·0)		
Upper quartile	59	2·56 (0·83)	1·81	< 0·04
Education problems				
Lower quartile	61	1·77 (1·0)		
Upper quartile	59	1·31 (0·67)	2·94	< 0·000

Table 3. *Comparison of post-morbid measures between the 'small' patients and the 'tall' patients*

	N	Mean (S.D.)	*t*	*P*
FSIQ				
Lower quartile	43	87 (10·9)		
Upper quartile	43	90 (8·0)	1·4	< 0·09
Age of onset				
Lower quartile	62	22·6 (6·3)		
Upper quartile	60	22·5 (4·3)	0·09	< 0·461
Duration of illness (months)				
Lower quartile	62	137 (114)		
Upper quartile	60	132 (98)	0·25	< 0·40
Number of previous hospitalizations				
Lower quartile	51	7·14 (14)		
Upper quartile	46	6·47 (6·3)	0·29	< 0·38
Negative symptoms (current)				
Lower quartile	62	12·1 (3·8)		
Upper quartile	60	12·8 (3·3)	1·03	< 0·15
Psychotic symptoms (current)				
Lower quartile	62	6·6 (2·3)		
Upper quartile	60	6·0 (2·4)	1·5	< 0·07
Disorganized symptoms (current)				
Lower quartile	62	5·5 (3·2)		
Upper quartile	60	5·5 (3·0)	0·03	< 0·49
Negative symptoms (past)				
Lower quartile	48	12·41 (3·1)		
Upper quartile	49	13·22 (3·1)	1·29	< 0·10
Psychotic symptoms (past)				
Lower quartile	58	7·46 (1·9)		
Upper quartile	56	6·87 (2·6)	1·37	< 0·086
Disorganized symptoms (past)				
Lower quartile	58	6·81 (3·7)		
Upper quartile	56	6·57 (3·5)	0·35	< 0·35

severity did not show any significant difference between the 'small' and the 'tall' patient groups (see Table 3). Contrary to our hypothesis, the 'small' group did not seem to manifest more severe illness, as measured by age of onset, total number of previous hospitalizations, cognitive function (FSIQ), or any of the symptom measures. There was, however, a trend for the 'small' group to have lower FSIQ ($P < 0·09$) and to have more psychotic symptoms both currently ($P < 0·07$) and in the past ($P < 0·086$).

To examine whether the finding of poor pre-morbid function in the small patient group is a finding that is specific to schizophrenia, or if this is a generalized phenomenon, we conducted further analysis on the control sample. 'Pre-

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press

Table 4. *Correlations between height and phenomenological measures*

Height	Childhood pre-morbid adjustment	Adolescent pre-morbid adjustment	Education performance	Education problems
r	−0·181	−0·174	−0·155	−0·224
P	0·007	0·009	0·020	0·000
N	221	221	222	221

morbid' or childhood function of the control group was not available; however, at the time of enrolment into our study, controls were given a neuropsychological battery and thus adult intelligence quotients were available (FSIQ). Because childhood cognitive function should indeed be highly correlated with adult FSIQ, the FSIQ was considered a proxy for childhood cognitive function in the control group. The control group was divided into extreme categories of height with the lower quartile representing the 'small' group ($N = 42$) and the upper quartile representing the 'tall' group ($N = 43$). The mean FSIQ of the small group (112·1, S.D. = 13·4) was not significantly different than that of the tall group (113·1, S.D. = 12·2, $P = 0{\cdot}706$. Furthermore, Spearman correlations using the entire group of controls showed no relationship between height and FSIQ ($r = 0{\cdot}018$, $P = 0{\cdot}84$), whereas there was a significant correlation between FSIQ and height in the patient sample ($r = 0{\cdot}146$, $P = 0{\cdot}03$).

In an effort to verify the differences in phenomenological variables between groups, all measures that showed significant difference between the extreme groups were correlated to height using the entire sample. These results are presented in Table 4. All four of the pre-morbid functioning variables from the *t* test analysis that showed significant differences between the extreme groups were correlated with height: (1) pre-morbid psychosocial adjustment score (both childhood and adolescence/young adult section) was negatively correlated with height, suggesting that the smaller the child, the poorer the social adjustment; (2) education performance was negatively correlated with height, indicating that the smaller the child, the lower the grades; and (3) education problems were also negatively correlated with height, showing that the smaller the child, the more difficulty he/she had with school. It is important to note that the correlations, though statistically significant, are quite small and account for only a small portion of the variance in height. However, as the correlations were all in the expected direction, this analysis appears to support the *t* test analysis of the extreme groups for the pre-morbid variables.

DISCUSSION

These findings provide further support to the notion that developmental factors may play a role in the pathophysiology of schizophrenia. There appears to be a global disturbance of growth and development that may begin very early, but also extends beyond the intrauterine period into infancy, childhood, and even through adolescence, manifesting in overall smaller stature in adulthood compared to healthy controls. In addition to deficits in size, there are accompanying deficits in social skills and cognitive abilities. This relationship between small stature and cognitive abilities does not appear to be a universal phenomenon seen in the general population, as indicated by the lack of relationship between FSIQ and height in our control sample. The differences in the patient extreme group comparison were most prominent during the pre-morbid period. After onset of the illness, the 'small' group of patients did not appear to manifest a greater degree of severity of illness, though they showed consistent trends toward having more psychotic symptoms.

Analysis of the distribution of height in patient and control groups suggests that the smaller stature in the patient population is not a phenomenon specific to only a subgroup of patients. Instead, there is a distributional shift downwards, consistent with a uniform effect. Though the notion that schizophrenia represents a heterogeneous group of patients (and possibly a variety of aetiologies) has been popular, the current data are supportive of other studies of biological markers of schizophrenia that argue against a subgroup phenomenon. For example, Daniel *et al.* (1991) pooled data from 671 patients, 205 medical controls and 160 healthy volunteers, and found no bimodal distribution in VBR among the patients, supporting the notion that ventricular enlargement is not specific to a subgroup of patients. Lane & Albee

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press

(1966) studied dysmorphic facial features in a sample of 174 patients and 80 matched controls and once again found a uniform distribution shift upward in abnormal facial features in the patients, rather than a distribution supportive of a subgroup effect.

These findings are supportive of the earlier anthropometry literature, from as early as 1916, that schizophrenic patients were somewhat smaller (Burchard, 1916). In addition, they support the more recent literature on the implications of lower birth weight in patients with schizophrenia and, in particular, the studies by Foerster *et al*. (1991) and Rifkin *et al*. (1993), which showed an association between lower birth weight and poor childhood social and cognitive function.

In contrast to the current findings, a recent meta-analysis of brain and cranial size in schizophrenia also evaluated height and found no relationship to diagnosis (Ward *et al*. 1996). However, the Ward meta-analysis may have been confounded by gender. The meta-analysis compiled brain imaging studies that had measured brain ($N = 27$ studies), intracranial ($N = 18$ studies), or extracranial size ($N = 8$ studies). Within that pool of studies, 17 reported height information, and a secondary meta-analysis was performed. However, in six of the 17 studies, samples were unbalanced for gender, yet height was reported as a mean patient value, rather than separated for each gender. Further, in five of these six studies, the percentage of male patients was greater than the percentage of male controls. For example, in the study of Grove *et al*. (1991), the patient sample was 77% male and the mean height reported for the entire patient sample was 177·2 cm. The control sample was 47% male and the mean control sample height was reported at 172 cm. Since males are taller than females on average, mean height values for groups unbalanced in gender would seriously confound any diagnostic effect on stature. In particular, the mean patient height would often be artificially elevated in many of the studies, as the percentage of male patients exceeds the percentage of male controls.

The aetiology of height is multifactorial, with strong genetic factors, but also environmental factors, such as disease and nutrition, playing a substantial role. The patient and control groups did not differ significantly in parental socio-economic status. Therefore, the shorter stature among the patients is not likely to be due to differential environmental influences between the two groups. It is also important that our control group was not obtained epidemiologically and, therefore, could possibly contain an ascertainment bias. However, this would not account for the differences in height seen within the patient group in relation to pre-morbid factors.

What factors could lead to a global and sustained delay in development? In the context of schizophrenia, both environmental and genetic factors have been implicated. Moreover, many of the 'environmental' insults proposed to cause abnormal development later manifested as schizophrenia are typically early insults such as viral infection (Mednick *et al*. 1994), maternal malnutrition (Susser *et al*. 1996), Rh incompatibility (Hollister *et al*. 1996) and birth injury (Cannon *et al*. 1989). These factors would play a large part in the determination of intrauterine growth and may be a determinant in the reported findings of decreased birth weight in schizophrenic babies. However, as is implicated by the current study, it is not intrauterine growth alone that is delayed. At least for some patients, growth appears to be delayed through the time in which adult stature is obtained (for males, sometime prior to age 21). Therefore, intrauterine environmental factors cannot be the only process affecting growth.

What factors would be affecting the growth of pre-schizophrenic children? As mentioned earlier, height is determined by some combination of genetics and environment. Since our patient and control sample is not different in parental socio-economic status, this reduces some of the differential effects of environment during childhood. This suggests that genetic factors may play an important role in the global developmental deficit. Many congenital/genetic syndromes are associated with short stature. Moreover, in the majority of these syndromes there is also cognitive dysfunction, the most notable example being Down's syndrome (Jones, 1997). Generally speaking, schizophrenia may have much in common with a syndrome such as Down's: a developmental syndrome initially manifested as global growth development with early cognitive deficits and later neuropsychiatric syndromes. For Down's, the later neuro-

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press

psychiatric syndrome is typically dementia, while for 'developmental schizophrenia', it is psychosis. The genetics of schizophrenia, however, are far from being as straightforward as for other genetic syndromes such as Down's. In fact, the validity of the distinction between 'familial' and 'sporadic' schizophrenia has recently been called into question, as the two groups are hard to distinguish from one another (Roy & Crowe, 1994). To understand more fully the aetiology of a global deficit in growth, future studies will need to address the issue of the impact of either pre- or perinatal complications and family history on pre-morbid function and adult stature.

This research was supported in part by NIMH grants MH31593, MH40856 and MHCRC 43271, the Nellie Ball Trust Fund, Iowa State Bank and Trust Company, Trustee; and a Research Scientist Award, MH00625.

REFERENCES

Akbarian, S., Bunney, W., Potkin, S., Wigal, S., Hagman, J., Sandman, C. & Jones, E. (1993). Altered distribution of nicotinamide-adenine dinucleotide phosphate-diaphorase cells in frontal lobe of schizophrenics implies disturbance of cortical development. *Archives of General Psychiatry* **50**, 169–177.

Andreasen, N. C. (1983). *The Scale for the Assessment of Negative Symptoms* (*SANS*). The University of Iowa: Iowa City, Iowa.

Andreasen, N. C. (1984). *The Scale for the Assessment of Positive Symptoms* (*SAPS*). The University of Iowa: Iowa City. Iowa.

Andreasen, N. C., Ehrhardt, J. C., Swayze, V. W., Alliger, R. J., Yuh, W. T. C., Cohen, G. & Ziebell, S. (1990). Magnetic resonance imaging of the brain in schizophrenia: the pathophysiology significance of structural abnormalities. *Archives of General Psychiatry* **47**, 35–44.

Andreasen, N. C., Flaum, M. & Arndt, S. (1992). The Comprehensive Assessment of Symptoms and History (CASH): an instrument for assessing psychopathology and diagnosis. *Archives of General Psychiatry* **49**, 615–623.

Andreasen, N. C., Arndt, S., Alliger, R., Miller, D. & Flaum, M. (1995*a*). Symptoms of schizophrenia: methods, meanings, and mechanisms. *Archives of General Psychiatry* **52**, 341–351.

Andreasen, N. C., Arndt, S., Miller, D., Flaum, M. & Nopoulos, P. (1995*b*). Correlational studies of the Scale for the Assessment of Negative Symptoms (SANS) and the Scale for the Assessment of Positive Symptoms (SAPS): an overview and update. *Psychopathology* **28**, 7–17.

Betz, b. (1942). Somatology of the schizophrenic patient. *Human Biology* **14**, 21–47.

Bogerts, B., Lieberman, J., Ashtari, M., Bilder, R., Degreef, G., Lerner, G., Johns, C. & Masiar, S. (1993). Hippocampus–amygdala volumes and psychopathology in chronic schizophrenia. *Biological Psychiatry* **33**, 236–246.

Burchard, E. (1916). Physique and psychosis. An analysis of the postulated relationship between bodily constitution and mental disease syndrome. In *Comprehensive Psychological Monographs*, pp. 73. Johns Hopkins Press: Baltimore.

Cannon, T., Mednick, S. A. & Parnas, J. (1989). Genetic and perinatal determinants of structural brain deficits in schizophrenia. *Archives of General Psychiatry* **46**, 883–889.

Ciocco, A. (1936). The historical background of the modern study of constitution. *Bulletin of the Institute of the History of Medicine* **4**, 23–36.

Daniel, D., Goldberg, T., Gibbons, R. & Weinberger, D. (1991). Lack of bimodal distribution of ventricular size in schizophrenia: a Gaussian mixture analysis of 1056 cases and controls. *Biological Psychiatry* **30**, 887–903.

Flaum, M., Swayze, V. W. I., O'Leary, D. S., Yuh, W. T. C., Ehrhardt, J. C., Arndt, S. V. & Andreasen, N. C. (1995). Effects of diagnosis, laterality, and gender on brain morphology in schizophrenia. *America Journal of Psychiatry* **152**, 704–714.

Foerster, A., Lewis, S. W., Owen, M. J. & Murray, R. M. (1991). Low birth weight and a family history of schizophrenia predict poor premorbid functioning in psychosis. *Schizophrenia Research* **5**, 13–20.

Gittelman-Klein, R. & Klein, D. F. (1969). Premorbid asocial adjustment and prognosis in schizophrenia. *Journal of Psychiatric Research* **7**, 35–53.

Greisheimer, E. M. (1950). *Physiology and Anatomy*. Lippincott: Philadelphia.

Grove, W. M., Lebow, B. S. & Medus, C. (1991). Head size in relation to schizophrenia and schizotypy. *Schizophrenia Bulletin* **17**, 157–161.

Gupta, S., Rajaprabhakaran, R., Arndt, S., Flaum, M. & Andreasen, N. C. (1995). Premorbid adjustment as a predictor of phenomenological and neurobiology indices in schizophrenia. *Schizophrenia Research* **16**, 189–197.

Hauser, P., Dauphinais, D., Berrettini, W., DeLisi, L. E., Gelernter, J. & Post, R. M. (1989). Corpus callosum dimensions measured by magnetic resonance imaging in bipolar affective disorder and schizophrenia. *Biological Psychiatry* **26**, 659–668.

Hollingshead, A. B. & Redlich, F. C. (1958). *Social Class and Mental Illness*. John Wiley & Sons: New York.

Hollister, J. M., Laing, P. & Mednick, S. A. (1996). Rhesus incompatibility as a risk factor for schizophrenia in male adults. *Archives of General Psychiatry* **53**, 19–24.

Houston, B. K. & Bloom, L. J. (1975). Constitutional factors, stature, and chronic schizophrenia. *Journal of Clinical Psychology* **31**, 26–29.

Jones, K. L. (1997). Small stature. In *Smith's Recognizable Patterns of Human Malformation* (ed. D. W. Smith), pp. 88–137. W. B. Saunders Company: Philadelphia.

Jones, P., Rodgers, B., Murray, R. & Marmot, M. (1994). Child development risk factors for adult schizophrenia in the British 1946 birth cohort. *Lancet* **344**, 1398–1402.

Kemali, D., Polani, N., Polani, P. & Amati, A. (1976). A dermatoglyphic study of 219 Italian schizophrenic males. *Clinical Genetics* **9**, 51–60.

Kretschmer, E. (1925). *Physique and Character*. Harcourt, Brace & Co.: New York.

Lane, E. & Albee, G. (1966). Comparative birth weights of schizophrenics and their siblings. *Journal of Psychology* **64**, 227–231.

McNeil, T. F., Cantor-Graae, E. & Nordstrom, L. G. (1993). Head circumference in 'preschizophrenic' and control neonates. *British Journal of Psychiatry* **162**, 517–523.

Mednick, S. A., Huttunen, M. O. & Machon, R. A. (1994). Prenatal influenza infections and adult schizophrenia. *Schizophrenia Bulletin* **20**, 263–7.

Miller, D. D., Arndt, S. & Andreasen, N. C. (1993). Alogia, attentional impairment, and inappropriate affect: their status in the dimensions of schizophrenia. *Comprehensive Psychiatry* **34**, 221–226.

Nopoulos, P., Flaum, M. A., Andreasen, N. C. & Swayze, V. W. (1995). Gray matter heterotopias in schizophrenia. *Psychiatry Research: Neuroimaging* **61**, 11–14.

Nopoulos, P., Swayze, V. I. & Andreasen, N. (1996). Pattern of brain morphology in patients with schizophrenia and large cavum septi pellucidi. *Journal of Neuropsychiatry and Clinical Neurosciences* **8**, 147–152.

Nopoulos, P., Swayze, V., Flaum, M., Ehrhardt, J., Yuh, W. T. C. &

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press

Andreasen, N. C. (1997). Cavum septi pellucidi in normals and patients with schizophrenia as detected by MRI. *Biological Psychiatry* **41**, 1102–1108.

Pearl, R. & Ciocco, A. (1934). Studies on constitution II. Somatological differences associated with diseases of the heart in white males. *Human Biology* **6**, 651–713.

Pivnicki, D. & Christie, R. (1968). Body build characteristics in psychotics. *Comprehensive Psychiatry* **9**, 574–580.

Rifkin, L., Lewis, S., Stewart, A. & Murray, R. M. (1993). Small babies and schizophrenia. *British Journal of Psychiatry* **163**, 553–554.

Rifkin, L., Lewis, S., Jones, P., Toone, B. & Murray, R. (1994). Low birth weight and schizophrenia. *British Journal of Psychiatry* **165**, 357–362.

Roy, M. A. & Crowe, R. R. (1994). Validity of the familial and sporadic subtypes of schizophrenia. *American Journal of Psychiatry* **151**, 805–814.

Singer, K., Chang, P. & Hsu, G. (1972). Physique, personality and mental illness in the Southern Chinese. *British Journal of Psychiatry* **121**, 315–319.

Susser, E., Neugebauer, R., Hoek, H. W., Brown, A. S., Lin, S., Labovitz, D. & Gorman, J. M. (1996). Schizophrenia after prenatal famine: further evidence. *Archives of General Psychiatry* **53**, 25–31.

Torrey, E. F. (1977). Birth weights, perinatal insults, and HLA types: return to 'original sin'. *Schizophrenia Bulletin* **3**, 347–351.

Walker, E. & Lewine, R. J. (1990). Prediction of adult-onset schizophrenia from childhood home movies of the patients. *American Journal of Psychiatry* **147**, 1052–1056.

Ward, K., Friedman, L., Wise, A. & Schulz, C. (1996). Meta-analysis of brain and cranial size in schizophrenia. *Schizophrenia Research* **22**, 197–213.

Woerner, M. G., Pollack, M. & Klein, D. F. (1971). Birth weight and length in schizophrenics, personalty disorders, and their siblings. *British Journal of Psychiatry* **118**, 461–464.

https://doi.org/10.1017/S0033291797006417 Published online by Cambridge University Press