Minor Physical Anomalies, Dermatoglyphic Asymmetries, and Cortisol Levels in Adolescents With Schizotypal Personality Disorder

Dana Davis Weinstein, Ph.D., Donald Diforio, M.A., Jason Schiffman, B.A., Elaine Walker, Ph.D., and Robert Bonsall, Ph.D.

Objective: A relationship between schizotypal personality disorder and schizophrenia has been documented in behavioral genetic studies, and there are similarities in the cognitive deficits and brain abnormalities associated with these disorders. Adolescents with schizotypal personality disorder are of particular interest because the postpubertal period is a critical one for the development of a DSM axis I disorder. It is likely that some schizotypal adolescents will remain stable over time, some will improve, and a subgroup will develop schizophrenia. This study tested the hypotheses that, like schizophrenic patients, schizotypal adolescents manifest an elevated rate of minor physical and dermatoglyphic anomalies, both of which suggest prenatal neurodevelopmental abnormalities. Cortisol release is also of interest because of evidence that the hypothalamic-pituitary-adrenal axis may influence the behavioral expression of vulnerability to schizophrenia. Method: Minor physical anomalies, dermatoglyphic asymmetries, and salivary cortisol levels were measured in three groups of adolescents: 20 with schizotypal personality disorder, 20 with other personality disorders, and 26 with no disorder. Assessments began at noon, and four saliva samples were obtained at hourly intervals. Results: The schizotypal personality disorder group showed more minor physical anomalies and dermatoglyphic asymmetries than the normal comparison group and higher cortisol levels than both of the other groups. Group differences in cortisol level were most pronounced at the beginning of the evaluation. Cortisol level and age were positively correlated. Conclusions: The findings support the assumption that schizotypal personality disorder is associated with perturbations in fetal neurodevelopment and, under some circumstances, a heightened cortisol response. (Am J Psychiatry 1999; 156:617–623)

Research has documented genetic links between schizophrenia and schizotypal personality disorder (1–3). Other investigations have demonstrated that subjects with schizotypal personality disorder manifest cognitive impairments (4), brain abnormalities (5), and premorbid deficits (6, 7) similar to those associated with schizophrenia. Notable among the last mentioned are marked increases in interpersonal and thought abnormalities during adolescence (6).

The features of schizotypal personality disorder parallel the prodromal signs of schizophrenia and have been shown to occur in preadolescents and adolescents (8–11). It is assumed that a subgroup of persons with schizotypal personality disorder will progress to schizophrenia. Speculations on the factors that potentiate this progression involve both psychosocial stress and perinatal complications (12–16).

This article presents initial results from a study intended to document the development of schizotypal personality disorder and identify predictors of psychotic symptoms. The focus is on adolescence, assuming that the pubertal period is associated with neurodevelopmental processes that can trigger the expression of latent vulnerabilities.

In the first evaluation, a primary goal was to verify risk status through the assessment of vulnerability markers, particularly physical indicators. Minor physical anomalies are physical characteristics known to be associated with developmental disorders (17, 18). Pa-
tients with schizophrenia have more minor physical anomalies than other psychiatric patients and normal subjects (19–22), and minor physical anomalies are related to earlier onset of the illness (23). Dermatoglyphic abnormalities are also associated with developmental disorders (24–27), and differences in right- and left-hand finger ridge counts (“fluctuating dermatoglyphic asymmetries”) are elevated in schizophrenia (28–30).

Dysmorphic signs originate during fetal development, primarily during the second trimester (17, 18, 26, 27). Both genetic and prenatal factors contribute to minor physical anomalies and fluctuating dermatoglyphic asymmetries. We are not aware of any report documenting minor physical anomalies or fluctuating dermatoglyphic asymmetries in schizotypal personality disorder; however, the fact that subjects with schizotypal personality disorder manifest brain abnormalities similar to those observed in schizophrenia (5) suggests that they would also show morphologic signs of neurodevelopmental deviation. Thus, it was hypothesized that schizotypal personality disorder would be associated with increased minor physical anomalies and fluctuating dermatoglyphic asymmetries.

Like dysmorphic signs, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis can result from prenatal insults (31, 32). It has been shown that HPA dysregulation is associated with schizophrenia, as well as with mood disorders and some other psychiatric syndromes (33, 34). It has therefore been suggested that the HPA axis acts as a nonspecific moderating system that can potentiate the expression of a variety of disorders and mediate the effects of stress on symptom expression (34–37). A neural mechanism for this effect in schizophrenia is indicated by evidence that cortisol augments mesolimbic dopamine activity and is correlated with symptom severity (34). It is thus plausible that the HPA axis plays a role in potentiating the prodromal expression in individuals at risk. In this study we tested the hypothesis that schizotypal personality disorder is associated with heightened cortisol release.

**METHOD**

The study groups were 20 subjects (eight of whom were female) who met the DSM-IV criteria for schizotypal personality disorder, 20 subjects (seven female) who met the DSM-IV criteria for another axis II disorder or conduct disorder (the group with other personality disorders), and 26 subjects (nine female) who did not meet criteria for any axis II disorder (the normal comparison group). At the initial evaluation, no subject met diagnostic criteria for an axis I disorder.

Subjects were recruited from the community by means of announcements directed to parents. The announcements described the diagnostic criteria for schizotypal personality disorder in lay terms and indicated that assessments of children who manifested such problems were being conducted for research purposes at Emory University. (The advertisement stated that the child was eligible if he or she was "experiencing problems in at least two of the following areas: social relationships, unusual ideas or behavior, emotional reactions or fears.") As expected, this recruitment procedure yielded a large number of responses from parents, and their children showed a broad range of severity and chronicity of behavioral problems. A screening interview was conducted by telephone. It was first determined whether the child met the study exclusion criteria (i.e., no medical or neurologic conditions or mental retardation); then the parent was briefly interviewed about the child’s behavior. In addition to identifying potential subjects with schizotypal personality disorder, the screening also served to identify subjects with other axis II disorders for inclusion in the comparison group. Some respondents described symptoms that suggested disorders other than schizotypal personality disorder, whereas others described normal adolescent behavior. Children who seemed likely to meet criteria for inclusion in one of the diagnostic groups were scheduled for assessment. As required by university research guidelines, parents were informed that they would be provided with feedback on the results of the assessment.

The normal comparison group comprised children who did not meet criteria for an axis I or axis II disorder. Some were drawn from respondents to the announcement (N = 20), and others were adolescents whose parents had listed them in the University Research Registry (N = 6). (The registry contains names of children whose parents registered them as infants for developmental studies. Only one of the six participants drawn from this registry had participated in any previous research, and that was a study of childhood attitudes.) The fact that most of the normal subjects were recruited in the same manner as the other two groups afforded some control for any biases produced by the recruitment method. No differences between the registry subjects and the other normal comparison subjects in demographic or clinical characteristics were revealed.

The mean age was 14.2 years (SD = 1.2) for the schizotypal personality disorder group, 14.7 years (SD = 2.2) for the other personality disorders group, and 13.9 years (SD = 1.6) for the normal comparison group. Analysis of variance revealed a significant difference among the groups in mean age (F = 5.26, df = 2, 65, p < 0.01), with the normal comparison group being younger than the other groups. There were no group differences in sex or race (schizotypal personality disorder group: 17 Caucasian and three African American subjects; other personality disorders group: 17 Caucasian and three African American; normal comparison group: 23 Caucasian, one Hispanic, and two African American).

The diagnostic evaluation included the following: the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II) (38) questionnaire and interview, the SCID—Patient Version (SCID-P) (39) psychotic screen (and the complete SCID-P II indicated), and the Beck Depression Inventory (40). The Beck inventory was administered to obtain information for ruling out axis I mood disorder. In addition to these measures, information was obtained from parents in order to enhance the validity of the diagnoses. Parents were interviewed and completed a child behavior checklist.

It should be noted that we included subjects with schizoid and paranoid personality disorders in the other personality disorders group, rather than the schizotypal personality disorder group, for the analyses reported here. This decision was based on evidence from several family studies indicating that only the rate of schizotypal personality disorder is elevated in the relatives of probands with schizophrenia (41). However, we also conducted the data analyses comparing all subjects with cluster A personality disorders with the group that had other personality disorders and the normal comparison group. The results, described below, are consistent with the inference drawn from the family studies.

In accordance with standard procedures, the SCID-II questionnaires were completed first, and responses were used as a guide for interviews that were conducted by doctoral students in psychology (D.W., D.D.) who had had systematic training in administering the SCID. Interviews were videotaped to establish interrater reliability. Axis II diagnoses (kappa > 0.80). Discrepancies were resolved by consensus.

Consistent with previous reports, there was a high rate of comorbidity, and some subjects with schizotypal personality disorder also met the criteria for another axis II disorder (e.g., avoidant, borderline, paranoid personality disorder). Diagnoses in the other personality disorders group were as follows: dependent, N = 4; obsessive-compulsive, N = 4; paranoid, N = 3; schizoid, N = 3; borderline, N = 3;
conduct disorder, N=6; passive-aggressive, N=5; and not otherwise specified, N=2. (The total number of diagnoses exceeds the number of subjects in the other personality disorders group because of comorbidity.) For each subject, ratings for the nine schizotypal personality disorder symptoms on the SCID-II were summed to yield a total schizotypal personality disorder symptom score. Separate positive and negative symptom scores were also derived.

As expected, a number of the participants had taken a psychotropic medication, usually prescribed by a pediatrician in response to parental concerns about the child’s behavior. Of these, 14 had taken medication within the past month: in the schizotypal personality disorder group, five had taken methylphenidate, and two had taken antidepressants; in the other personality disorders group, three had taken methylphenidate, and two had taken antidepressants; in the normal comparison group, two had taken methylphenidate. The rate of stimulant medication in the total study group, 15%, is about double the rate (7%) for this age range in the Atlanta metropolitan area. The prescription of stimulant medication to a subgroup of the schizotypal personality disorder subjects is consistent with research showing substantial attentional problems in both schizotypal personality disorder and schizophrenia (2, 4).

Evaluations were scheduled to begin at noon. Parents and children were informed that it was necessary for the subjects to avoid taking any psychotropic medications or caffeine products beginning the day before the evaluation. After complete description of the study to the subjects, written informed consent was obtained from the parents and from the children. The subjects then completed the SCID-II questionnaire and the Beck inventory. Examiners provided assistance when needed. After completion of the questionnaires, the clinical interviews were conducted; then the measures described below were administered.

Minor Physical Anomalies

Morphology of six body regions was examined with the use of the Waldrop and Halverson scale (18). The following anomalies were scored: head—fine electric hair, hair whoirs, large or small head circumference (measured by positioning a tape measure over the points on the forehead and occiput that gave the maximal circumference); eyes—epicanthal fold, hypertelorism; mouth—high-steepened or flat and narrow palate, furrowed tongue, tongue with smooth/rough spots; ears—asymmetrical ears, low-seated ears, adherent earlobes, malformed ears, soft and pliable ears; hand—markedly or slightly curved fifth finger, single transverse palmar crease; feet—third toe longer than or equal to the second, webbed toes, large gap between first and second toes. Each anomaly was scored as present or absent, and a point was assigned for each one scored as present.

Minor physical anomalies were assessed blind to the subject’s psychiatric history and current symptoms. The examiners were two research assistants who underwent systematic training in the administration of the Waldrop and Halverson scale. Training included observation of videotaped examinations as well as practice evaluations with normal subjects and psychiatric patients. Thirteen subjects received multiple independent assessments of minor physical anomalies. Reliability was determined by means of Cohen’s kappa for pairs of examiners, including the two research assistants and the first author. An overall kappa of 0.68 was obtained.

We used the modified Waldrop and Halverson (18) scoring criteria described by Green et al. (19, 20). Published norms, adjusted for age and sex, were used in scoring head circumference (42) and canthal distance (43) as being one or two standard deviations beyond the mean. Item scores were summed to yield a total score.

Dermatoglyphics

Handprints were obtained with the use of a colorless ink method (24). Fingertips were rolled on ink-sensitive paper to produce a clear print.

Three assistants were trained to use the scoring procedures described by Holt (25). An image enhancer was used to enlarge each print, and the number of dermal ridges was determined for each fin-
RESULTS

Minor physical anomalies. Table 1 presents the group means and standard deviations for minor physical anomalies; there was a significant difference among the groups (Kruskal-Wallis $\chi^2=5.45$, df=2, $p<0.05$). The subjects with schizotypal personality disorder had significantly higher minor physical anomalies scores when compared with the normal subjects ($U=144.5$, $z=2.26$, $p<0.02$), but in the comparison with the other personality disorders group, the difference did not reach significance ($U=133$, $z=1.43$, $p=0.07$). The other personality disorders group and the normal comparison group were not significantly different. Although there is no standard cutoff for total number of minor physical anomalies, it is noteworthy that 37% (N=7) of the schizotypal personality disorder group, 11% (N=2) of the other personality disorders group, and 4% (N=1) of the normal comparison group exceeded a score of 3. (A similar but attenuated pattern of differences was obtained when the cluster A group was compared with the other personality disorders group and the normal comparison group.)

Fluctuating dermatoglyphic asymmetries. The means and standard deviations for fluctuating dermatoglyphic asymmetries by diagnostic group are also presented in Table 1; there was a significant overall difference among the groups (Kruskal-Wallis $\chi^2=2.76$, df=2, $p<0.05$). The schizotypal personality disorder group showed higher scores than the normal comparison group ($U=147$, $z=1.59$, $p<0.05$) but not the other personality disorders group (U=144.5, z=0.54, p=0.58). The subjects with other personality disorders and the normal comparison subjects did not differ. (As with minor physical anomalies, comparison of the cluster A group with the other groups yielded a similar but attenuated pattern of findings.)

For the entire study group, the correlation (Pearson r) between minor physical anomalies and fluctuating dermatoglyphic asymmetries was modest but significant ($r=0.23$, df=62, $p<0.05$).

Cortisol. For each subject, the average of the four cortisol assays was derived. Figure 1 presents the mean values, across groups, by age. Figure 1 includes data from three subjects who underwent the assessment but were not assigned to a diagnostic group because they were under 12 years of age (two were 10 years old, and one was 11) and may not have comprehended the questionnaires. These subjects are included in figure 1 to broaden the age range. Also, the 16- to 18-year range is collapsed because there were relatively few subjects at each of these ages (three at 16 years, six at 17 years, and four at 18 years).

Across groups, there was a positive relation between cortisol and age ($r=0.48$, df=62, $p<0.001$). When coefficients were computed separately for the groups, the same relationship was observed for the other personality disorders group ($r=0.61$, df=17, $p<0.01$) and the normal comparison group ($r=0.45$, df=23, $p<0.05$) but not the schizotypal personality disorder group ($r=0.14$, df=18, $p=0.27$).

ANCOVA, controlling for age, revealed a significant difference among the groups in mean cortisol level ($F=4.19$, df=2, 62, $p<0.02$). The schizotypal personality disorder group had a higher overall mean cortisol concentration than the normal comparison group ($F=3.90$, df=1, 43, $p<0.05$) and the other personality disorders group ($F=5.00$, df=1, 37, $p<0.02$). For the total study group, mean cortisol level was modestly correlated with total schizotypal personality disorder symptoms ($r=0.26$, df=62, $p=0.01$) and negative symptoms ($r=0.23$, df=62, $p=0.03$) but not positive symptoms ($r=0.15$, df=62, $p=0.10$).

The means for the four cortisol samples are presented separately in Figure 2. All groups showed a decrease in cortisol across time. This reflects the afternoon portion of the diurnal decline. Although the decrease was significant across groups, it appeared more pronounced for the schizotypal personality disorder group.

| TABLE 1. Minor Physical Anomaly and Fluctuating Dermatoglyphic Asymmetry Scores of Adolescents With Schizotypal and Other Personality Disorders and of Normal Adolescents |
|---------------------------------|---------|---------|---------|
| Group                           | Minor Physical Anomaly Score | Mean | SD  | Fluctuating Dermatoglyphic Asymmetry Score | Mean | SD  |
| Schizotypal personality disorder (N=19) | 2.74 | 2.1     | 17.59 | 7.9     |
| Other personality disorders (N=19)   | 1.74 | 1.3     | 16.16 | 8.4     |
| Normal (N=26)                    | 1.25 | 1.1     | 11.57 | 4.5     |

| FIGURE 1. Mean Cortisol Levels, Averaged Across Four Saliva Samples, for All Study Subjects by Age Group |

Am J Psychiatry 156:4, April 1999
Group comparisons of the individual cortisol samples, controlled for age, revealed that the schizotypal personality disorder group had a higher time 1 cortisol level than the other personality disorders group (F = 3.39, df=1, 37, p = 0.04) and the normal comparison group (F = 4.79, df=1, 43, p = 0.02). Although the schizotypal personality disorder group exceeded the other groups at times 3 and 4, these differences were not significant when age was controlled.

Given that exposure to novelty can heighten cortisol levels (47, 48), the finding of greater group differences in time 1 cortisol concentrations suggests that subjects with schizotypal personality disorder are more responsive to the initial novelty of the assessment. When superimposed on the diurnal change, this results in a greater decline in cortisol values for the schizotypal personality disorder group. We indexed the magnitude of the linear change from the initial level by calculating the slope of the line relating cortisol values for each subject. The mean slope was 0.095 (SD = 0.026) for the schizotypal personality disorder group, 0.078 (SD = 0.030) for the other personality disorders group, and 0.080 (SD = 0.032) for the normal comparison group. A nonparametric test revealed an overall group difference in the slopes (Kruskal-Wallis χ² = 5.49, df = 2, p = 0.04). The subjects with schizotypal personality disorder had a significantly greater linear decline in cortisol release than the normal comparison group (U = 157.5, z = 2.27, p = 0.02), but the difference only approached significance in the comparison with the other personality disorders group (U = 131.5, z = 1.64, p = 0.05). There were no other significant group differences in cortisol slope.

In the entire study group, there was a positive correlation between fluctuating dermatoglyphic asymmetries and cortisol slope (r = 0.23, df = 58, p = 0.05), but the relation between fluctuating dermatoglyphic asymmetries and mean cortisol level only approached significance (r = 0.20, df = 58, p = 0.06). Minor physical anomalies were not correlated with mean cortisol level or cortisol slope.

**DISCUSSION**

These results provide further support for an etiologic link between schizotypal personality disorder and schizophrenia. The findings indicate that, like schizophrenia, schizotypal personality disorder is associated with an increase in minor physical anomalies and fluctuating dermatoglyphic asymmetries. Assuming that these abnormalities have prenatal origins, a disruption in fetal neurodevelopment may be involved in both disorders.

It also appears, however, that minor physical anomalies and fluctuating dermatoglyphic asymmetries are not specific to schizotypal personality disorder, since there was no significant difference between the schizotypal personality disorder group and the other personality disorders group on these variables. This is consistent with previous reports linking dysmorphic features with a range of mental disorders (17, 18).

Consistent with prediction, we also found that the subjects with schizotypal personality disorder manifested higher mean cortisol values than both of the other groups. It is noteworthy that the difference between groups was most pronounced when the first sample was obtained. This could reflect group differences in diurnal profile; however, it is also plausible that the schizotypal personality disorder group showed hyperresponsivity to the novelty of the context or procedures (48).

Our study also replicates the previously reported correlation of salivary cortisol level with age through adolescence (35). It is of interest that a recent longitudinal investigation of serum cortisol in 28 adolescents found no developmental change (49). These discrepancies may be due to differences in subjects' responses to blood versus saliva sampling or may reflect differential subject attrition based on sampling procedure (50, 51).

If the pubertal period is associated with an enhancement of HPA activity, this suggests a role for the HPA axis as a neuromodulator of the expression of preexisting vulnerabilities during adolescence. When computed separately by group, the correlations between age and cortisol level were significant only for the other personality disorders group and the normal comparison group. This may indicate that the pubertal increase in HPA activity began earlier in the schizotypal personality disorder group. Because these speculations are based on cross-sectional data, confirmation is needed from prospective research.

Studies of nonhuman primates have shown that maternal exposure to stress during pregnancy results in heightened cortisol release, hippocampal abnormalities, and an increase in fluctuating dermatoglyphic asymmetries and other dermatoglyphic abnormalities in offspring (see Walker and Diforio [34] for a review). Research has also linked schizophrenia to prenatal exposure of the mother to stress (52, 53). The present study showed a modest correlation between fluctuating dermatoglyphic asymmetries and cortisol slope. Presuming that the latter is an index of the HPA re-
sponse to novelty, this may reflect the influence of pre-
natal neurodevelopment on both cortisol response and 
fluctuating dermatoglyphic asymmetries.

It is of interest that negative, but not positive, symp-
tom ratings were correlated with cortisol level. Al-
though this might be taken as further support for the
notion that different neural processes underlie the two
symptom dimensions, such a conclusion would be pre-
mature, because this study excluded subjects whose
symptoms would meet criteria for an axis I disorder
and, by definition, restricted the range of symptoms.

A remaining issue is whether minor physical anomalies,
fluctuating dermatoglyphic asymmetries, and cor-
tisol level are predictive of clinical course in individuals
at risk for schizophrenia. As noted, recent studies indi-
cate that dermatoglyphic abnormalities are linked with
greater sensitivity to stress and that heightened cortisol
values are associated with poorer 6-month outcome in
clinic-referred children (37). Follow-up of the present
study group will allow us to determine whether there is
an interactive effect of morphologic abnormalities and
response to stress on clinical course.

The chief limitation of this study concerns the ab-
sence of outcome data. It is anticipated that some sub-
jects in the schizotypal personality disorder group will
continue to manifest the syndrome, some will improve,
and some will develop axis I disorders, including
schizophrenia. Follow-up of our study group will shed
light on this issue. In addition, we cannot generalize
the findings to adults with schizotypal personality dis-
order; it is possible that they are specific to early-onset
schizotypal personality disorder.

REFERENCES

1. Siever LJ, Silverman JM, Horvath TB, Klar H, Coccaro E,
   Keefe RS, Pinkham L, Rinaldi P, Mohs RC, Davis KL: In-
   creased morbid risk for schizophrenia-related disorders in re-
   latives of schizotypal personality disorder patients. Arch Gen
   Psychiatry 1990; 47:634–640

2. Siever LJ, Kalus OF, Keefe RS: The boundaries of schizo-

3. Kendler KS, Grueenberg AM, Strauss JJ: An independent anal-
   ysis of the Copenhagen sample of the Danish Adoption Study of
   Schizophrenia, II: the relationship between schizotypal per-
   sonality disorder and schizophrenia. Arch Gen Psychiatry
   1981; 38:982–984

   Cambridge, UK, Cambridge University Press, 1995

5. Cazzulo CL, Vita A, Giobbio GM, Dieci M, Sacchetti E: Cere-
   bral structural abnormalities in schizophreniform disorder and
   in schizophrenia spectrum personality disorders, in Schizo-
   phrenia Research: Advances in Neuropsychiatry and Psy-
   chopharmacology. Edited by Tammenga CA, Schulz SC. New

6. Walker E, Baum K, Diforio D: Developmental changes in the
   behavioral expression of vulnerability for schizophrenia, in Or-
   igins and Development of Schizophrenia: Advances in Exper-
   imental Psychopathology. Edited by Lenzonweger MF, Dvor-
   kin RH. Washington, DC, American Psychological
   Association, 1998, pp 469–491

7. Olin SS, Rain A, Cannon TD, Parnas J, Schulsingler F, Med-
   nick S: Childhood behavior precursors of schizotypal personal-
   ity disorder. Schizophr Bull 1997; 23:93–103

8. Wolff S, Townsend R, McGuire RJ, Weeks DJ: “Schizoid” per-
   sonality in childhood and adult life, II: adult adjustment and
   the continuity with schizotypal personality disorder. Br J Psy-
   chiatry 1991; 159:620–629

9. Asarnow JR, Ben-Meir S: Children with schizophrenia spec-
   trum and depressive disorders: a comparative study of pre-
   morbid adjustment, onset pattern and severity of impairment.


11. Wolff S: “Schizoid” personality in childhood and adult life, III:

12. Cantor-Graae E, McNeil TF, Torrey EF, Quinn P, Bowler A,
    Sjöstrom K, Rawlings R: Link between pregnancy complica-
    tions and minor physical anomalies in monozygotic twins dis-
    cordant for schizophrenia. Am J Psychiatry 1994; 151:1188–
    1193

13. Walker E, Gale S: Neurodevelopmental processes in schizo-
    phrenia and schizotypal personality disorder, in Schizotypal
    Personality. Edited by Raine A, Lencz T, Mednick SA. Cam-
    bridge, UK, Cambridge University Press, 1995, pp 56–75

14. Norman RM, Malla AK: Stressful life events and schizophre-
    nia, I: a review of the research. Br J Psychiatry 1993; 162:
    161–166

15. Norman RM, Malla AK: Stressful life events and schizophre-
    nia, II: conceptual and methodological issues. Br J Psychiatry
    1993; 162:166–174

16. Cannon TD, Mednick SA, Parnas J: Genetic and perinatal de-
    terminants of structural brain deficits in schizophrenia. Arch
    Gen Psychiatry 1989; 46:883–889

17. Smith DW: Recognizable Patterns of Human Malformation:
    Genetic, Embryologic and Clinical Aspects. Philadelphia, WB
    Saunders, 1976

18. Waldrop MF, Halverson CF: Minor physical anomalies and
    hyperactive behavior in young children, in Exceptional Infant:
    Studies in Abnormalities. Edited by Helmuth J. New York,
    Brunner/Mazel, 1971, pp 343–380

19. Green MF, Bracha HS, Satz P, Christenson CD: Preliminary evi-
    dence for an association between minor physical anomalies
    and second trimester neurodevelopment in schizophre-

20. Green MF, Satz P, Christenson C: Minor physical anomalies in
    schizophrenia patients, bipolar patients, and their siblings.
    Schizophr Bull 1994; 20:433–440

21. Guy JD, Majorski LV, Wallace CJ, Guy MP: The incidence of
    minor physical anomalies in adult male schizophrenics.
    Schizophr Bull 1983; 9:571–582

22. Lohr JB, Flynn K: Minor physical anomalies in schizophrenia
    and mood disorders. Schizophr Bull 1993; 19:551–556

23. Green MF, Satz P, Soper HV, Kharabi F: Relationship be-
    tween physical anomalies and age at onset of schizophrenia.
    Am J Psychiatry 1987; 144:666–667

24. Cummins H, Midlo C: Finger-prints, Palms and Soles: An In-
    troduction to Dermatoglyphics. New York, Dover Publications,
    1961

25. Holt SB: The Genetics of Dermal Ridges. Springfield, III,
    Charles C Thomas, 1968

26. Purvis-Smith SG, Menser MA: Genetic and environmental in-
    fluences on digital dermatoglyphics in congenital rubella. Pe-

27. Schaumann B, Alten M: Dermatoglyphics in Medical Disor-

28. Markow TA, Gottesman II: Fluctuating dermatoglyphic asym-

29. Markow TA, Wandler K: Fluctuating dermatoglyphic asym-
    metry and the genetics of liability to schizophrenia. Psychiatry
    Res 1986; 19:323–328

30. Meguro CS: Dermatoglyphic evidence of fluctuating asymme-
    try in schizophrenia. Br J Psychiatry 1992; 160:467–472

    and Nonhuman Primates: Biosocial Determinants. Basel,
    Switzerland, S Karger, 1995

32. Clarke AS, Wittiner DJ, Abbott DH, Schneider ML: Long-term
    effects of prenatal stress on HPA axis activity in juvenile
    rhesus monkeys. Dev Psychobiol 1994; 27:257–269
47. Hennessy MB, Mendoza SP, Mason WA, Mobegh GP: Endocrine sensitivity to novelty in squirrel monkeys and til monkeys. Physiol Behav 1995; 57:331–335