Further Evidence That Congenital Dermatoglyphic Abnormalities Are Associated With Psychosis: A Twin Study

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Abstract

The presence of abnormal palmar flexion creases (APFC) and dermatoglyphic ridge dissociation (RD) may constitute enduring evidence of a prenatal insult that occurred before the third trimester of intrauterine life. We examined these dermatoglyphic abnormalities in a twin study of psychotic disorders. RD and APFC were analyzed in a monozygotic (MZ) twin sample from the Maudsley Hospital in London (11 normal control pairs, 16 pairs concordant for psychosis, 9 pairs discordant for psychosis, 1 concordant triplet, and 1 triplet with one affected member). The risk of either RD or APFC was 44 percent in affected twins and 20 percent in nonaffected twins (odds ratio = 3.25, 95% confidence interval: 1.03–10.31; one-sided p = 0.023). In the group of MZ twins discordant for psychosis, discordance for RD or APFC always paralleled discordance for psychosis (one-sided p = 0.078), suggesting the operation of nongenetic factors. The results confirm previous work suggesting the possibility that nongenetic factors early in pregnancy contribute to the liability to develop psychosis in later life.

Keywords: Dermatoglyphic abnormalities, ridge dissociation, palmar flexion creases, neurodevelopment, twins, psychosis.
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Dermatoglyphics are the patterned traceries of the epidermal ridges on fingers and palms. Palmar and finger dermatoglyphics are formed on the surface of the hand early in intrauterine life. This period, the second trimester of pregnancy, coincides with a critical period of central nervous system development, when neuronal cell migration to the cerebral cortex takes place (Rakic et al. 1988). During this period, dermatoglyphic morphology can be influenced by environmental factors interfering with intrauterine development, but after this period dermatoglyphics remain unchanged and thus appear to constitute enduring evidence of prenatal insult.

Two congenital dermatoglyphic malformations—RD and APFC—carry special interest for research in disorders that are hypothesized to be congenital. A variety of unusual PFC and forms of RD have been associated with (1) congenital disorders due to intrauterine exposure to environmental factors such as viruses and teratogenic agents, (2) fetal alcohol syndrome, (3) craniofacial syndrome, (4) rubella and toluene embryopathy, and (5) congenital syndromes that share clinical features, such as low birth weight, growth retardation, and mental retardation (Schaumann and Alter 1976; Schaumann and Kimura 1991).

Several independent studies have reported dermatoglyphic changes, especially in ridge counts, in (1) psychiatric patients compared with controls from the general population (Raphael and Raphael 1962; Mellor 1968; Fañanás et al. 1990; Turek 1990; Fañanás et al. 1996b; Gutiérrez et al. 1998); and (2) twin studies (Bracha et al. 1992; Davis and Bracha 1996b). Twin studies are of particular interest in this type of investigation because they can distinguish between genetic and nongenetic mechanisms, or suggest a mechanism of genotype-environment interaction, whereby an environmental insult enhances the expression of genetic liability (Van Os and Marcelis 1998).

In three previous MZ twin studies, the frequencies of congenital dermatoglyphic abnormalities were examined in pairs of twins discordant or concordant for schizophrenia. Bracha and colleagues (1991) studied MZ twins discordant for schizophrenia or delusional disorder and found higher scores of selected dysmorphological hand anomalies in the affected co-twin. Van Os and coworkers (1997) reported higher risk of APFC and RD in MZ affected compared with MZ nonaffected twins. These results were recently replicated in the National Institute of Mental Health twin sample, where in addition it was found that

discordance for psychosis in MZ twins was strongly associated with discordance for these dermatoglyphic anomalies (Rosa et al. 2000*a*). The aim of the present study was to explore the presence of the same anomalies in a new, independent sample of twins concordant and discordant for psychosis.

Method

Sample. The sample consisted of MZ twin pairs who had agreed to participate in the Maudsley Twin Study. The patient sample consisted of 11 control pairs (14 male and 8 female), 16 pairs concordant for psychosis (28 male and 4 female), 9 pairs discordant for psychosis (14 male and 4 female), as well as one concordant set of triplets and another set of triplets with one affected member. The mean age was 34.9 years (standard deviation = 9.8). Zygosity determination was based on all available information, including analysis of genetic markers in 42 percent of pairs. Agreement between zygosity determination by genetic markers and by resemblance information was 95 percent. The *DSM–III–R* (American Psychiatric Association 1987) diagnostic distribution in the 45 individuals affected by a psychotic disorder was schizophrenia 71 percent ($n = 32$), schizophreniform disorder 13 percent ($n = 6$), and (schizo)affective/atypical psychosis 16 percent ($n = 7$). (See Cardno et al. 1999 for further detail about the sample.)

Of the 78 individuals in the study, the measure of RD was available in 70, the measure of APFC in 66, and one or the other measure in 73. As in our previous investigations (Rosa et al. 2000*a*), the sample was a priori not confined to any particular diagnostic category for two reasons. First, dermatoglyphic abnormalities occur more frequently not only in schizophrenia and delusional disorder but also in bipolar disorder (Gutiérrez et al. 1998) and schizotypy (Fañanás et al. 1996*a*; Rosa et al. 2000*b*). Second, there is good evidence that affective and nonaffective psychotic diagnostic categories share to a large degree the liabilities arising from prenatal and developmental risk factors; such evidence argues against division along arbitrary diagnostic lines (Marcelis et al. 1998; Van Os et al. 1998; Brown et al. 2000).

Dermatoglyphic Measures. Palm and finger prints were taken with a noninky method (Prints-kit, Printscan Verification Systems Ltd.). The variables selected for the analysis included (1) presence of RD and (2) presence of APFC. RD, a well-delineated dermatoglyphic anomaly, refers to a short, broken segment of lines that cover the dermatoglyphic pattern areas in a disorganized way. Cummins and Midlo (1961) concluded that extreme RD is due to some fault in embryonic development that causes

failure of the ridge units to become consolidated (figure 1A).

APFC have been defined as variations in the basic configuration and appearance of the major palmar creases (Alter 1970). The categories of APFC used in the present study were the Simian Crease, the Sydney Line, very rudimentary creases, and clear broken proximal and distal palmar creases (figure 1B).

A.R., blind to the diagnosis, zygosity, and concordance status of the twins, conducted the dermatoglyphic analyses. This rater had extensive prior experience in rating similar data (Rosa et al. 2000*a*, 2000*b*).

Analyses. Two types of case-control analyses were carried out. In the first analysis, the rate of dermatoglyphic abnormalities in MZ affected and MZ unaffected twins was compared. MZ affected twins included (1) twins concordant for psychosis (including one set of concordant triplets) and (2) the affected co-twins of discordant pairs (including one affected member of a set of triplets). MZ unaffected twins were normal control twins and the unaffected co-twins of the discordant pairs. Effect sizes were expressed as odds ratios (ORs) from the case-control logistic regression analyses. Because the members of one twin pair cannot be considered independent statistically, a multilevel logistic regression procedure was carried out using the XTGEE procedure in Stata (StataCorp 1999), thus taking account of the fact that level 1 units (level of individual twins) were clustered into level 2 units (level of the pairs). This procedure gives correct estimates of standard errors that otherwise might be wrongly estimated. Multilevel or hierarchical regression analyses are commonly used in twin studies (Heitmann et al. 1997; Emery et al. 1998; Hur et al. 1998). All the multilevel analyses were adjusted for sex in view of the uneven sex distribution (see below).

The second analysis consisted of a pairwise comparison of affected versus nonaffected members of discordant pairs. To this end, a logistic regression analysis for matched pairs was carried out in the group of discordant pairs only. In this analysis, the triplet with one affected member was split up in two discordant pairs. Because this study explicitly sought to replicate the direction of a previously reported effect, one-sided *p* values are presented for two-sided confidence intervals.

Results

Affected Versus Nonaffected Twins. The proportion of women was 13 percent in affected twins and 34 percent in nonaffected twins ($\chi^2 = 4.8$, $df = 1$, two-sided $p = 0.028$). The risk of RD was 12 percent in the affected twins and 4 percent in nonaffected twins (adjusted OR from multilevel

Table 1. Presence of either APFC or RD in affected and nonaffected MZ twins

	APFC or RD, n (%)	No abnormalities, n (%)
Affected MZ twins	19 (44.2)	24 (55.8)
Nonaffected MZ twins	6 (20.0)	24 (80.0)

Note.—APFC = abnormal palmar flexion creases; MZ = monozygotic; RD = ridge dissociation. Odds ratio = 3.25, 95% confidence interval: 1.03–10.31; one-sided $p = 0.023$.

Figure 1. Anomalies considered in the present study: (A) second interdigital area of the palm showing ridge dissociation; (B) abnormal palmar flexion creases

A

B

SIMIAN CREASE   SYDNEY LINE   RUDIMENTARY CREASES   BROKEN CREASES
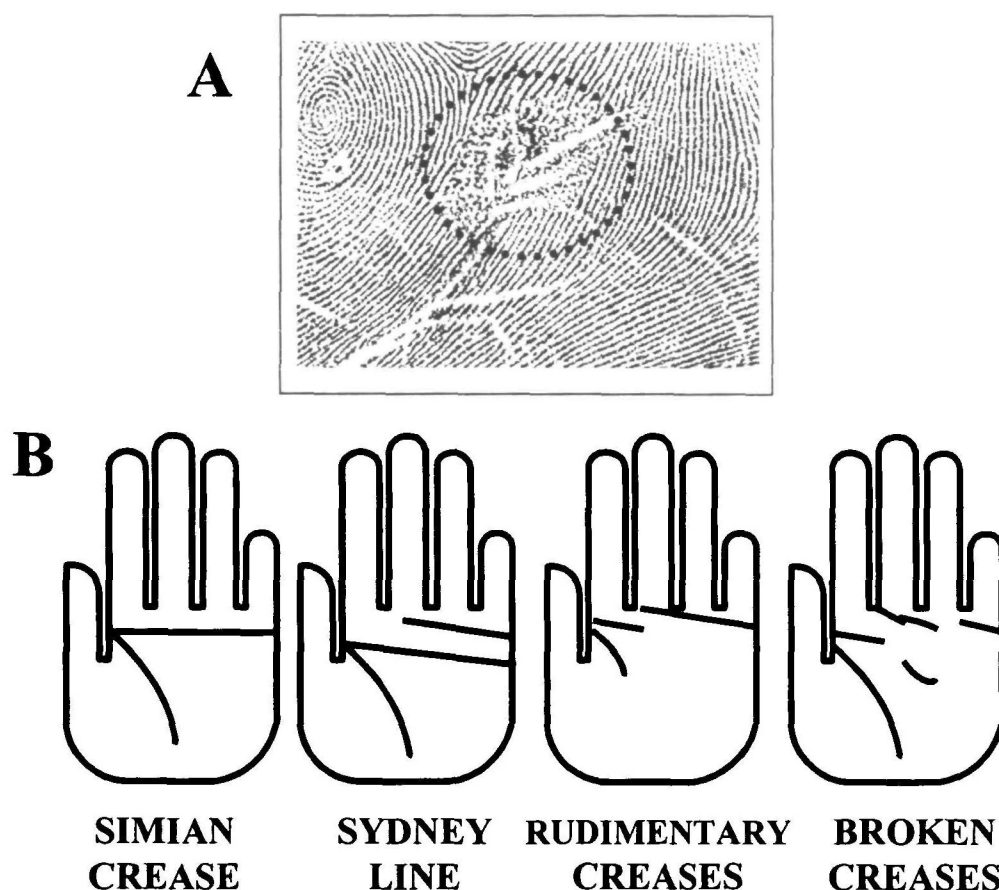
logistic regression 4.08; 95% confidence interval [CI]: 0.45–36.80; one-sided $p = 0.069$). The risk of APFC was 41 percent in affected twins and 19 percent in nonaffected twins (OR = 2.52; 95% CI: 0.74–8.58; one-sided $p = 0.10$). The risk of either exposure was 44 percent in affected twins and 20 percent in nonaffected twins (OR = 3.25; 95% CI: 1.03–10.31; one-sided $p = 0.023$).

Within-Pair Matched Comparison of Discordant Twins. In the sample of 11 discordant pairs (including the two pairs constructed from the triplet), 2 pairs were discordant for either RD or APFC. In both of these pairs,

the abnormality occurred in the affected twin. The OR for matched pairs for this result could not be calculated because of the zero denominator (OR = infinite). The one-sided p value associated with this result was $\chi^2 = 2.0$, $df = 1$, one-sided $p = 0.078$. There was no difference between the well co-twins of the discordant pairs and the control twins (OR = 1.11; 95% CI: 0.17–7.26; $p = 0.92$).

Discussion

We chose to include psychotic patients with a broad group of diagnoses. However, when we repeated the comparison

between affected and nonaffected twins considering only cases with a *DSM–III–R* diagnosis of schizophrenia or schizophreniform disorder, the effect size for the exposure of either APFC or RD remained unchanged (OR = 3.46; 95% CI: 1.10–10.90; one-sided p = 0.017).

Although the effect sizes were moderately large, the confidence intervals were very wide, indicating that the statistical resolution of the study remained limited because of the low prevalence of the abnormalities and the modest sample size.

The finding that APFC and RD occur more commonly in patients with psychosis has now been replicated in three independent twin samples. Although there was overlap in the investigators of the three studies, care was always taken to ensure that dermatoglyphic analyses were carried out entirely blind to diagnostic and concordance status. In addition, the within-pair comparisons in genetically identical twins who are discordant for psychosis in the current and one previous study (Rosa et al. 2000*a*) may suggest that the explanation for this finding is nongenetic. This, in combination with the knowledge that these dermatoglyphic abnormalities must develop during the first and second trimesters of pregnancy, implies that nongenetic factors early in pregnancy contribute to the liability to develop psychosis in later life.

The dermatoglyphic abnormalities in this and previous studies are in all likelihood a proxy variable for a true causal influence. To identify this influence, associations between dermatoglyphics and other variables need to be examined. One study suggested that dermatoglyphic abnormalities such as low ridge counts may be associated with enlarged cerebral ventricles (Van Os et al. 2000), but this finding remains to be replicated. It has been reported that prenatal hypoxic events, prenatal infections, prenatal maternal stress, and prenatal nutritional deficiency increase the risk for adult psychosis (Buka et al. 1993; Takei et al. 1995; Davis and Bracha 1996*a*, 1996*b*; Van Os and Selten 1998; Brown et al. 2000). These variables, therefore, constitute the most plausible candidates to investigate in relation to actual morphological proof of prenatal nongenetic influences. A related area of research involves the study of slight anatomical malformations known as minor physical anomalies (Green et al. 1994; Waddington et al. 1998). The structures involved in these malformations achieve their postnatal form by 16 to 17 weeks of gestation—that is, around the same time as dermatoglyphic measures. Thus, the simultaneous study of minor physical abnormalities and dermatoglyphic measures also has heuristic potential.

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