Dermatoglyphics and abnormal palmar flexion creases as markers of early prenatal stress in children with idiopathic intellectual disability

A. Rosa, B. Gutiérrez, A. Guerra, B. Arias & L. Fañanás
Laboratori d’Antropologia, Facultat de Biologia, Universitat de Barcelona, Barcelona, Spain

Abstract

A number of studies have shown the importance of dermatoglyphics as markers of prenatal disturbance in developmental disorders of unknown origin. Genetic and non-genetic factors are involved in the aetiology of intellectual disability (ID), although the cause remains unknown in up to 50% of cases. The aim of the present study was to analyse dermatoglyphic traits and abnormal palmar flexion creases as markers of environmental prenatal stress in children with idiopathic ID (IID) using a case-control study design. Three dermatoglyphic variables, which have been reported as altered in other congenital disorders, were considered were studied in a sample of 62 children with IID (IQ < 70) and 75 healthy controls (IQ > 70): (1) fingerprint patterns; (2) total a–b ridge count (TABRC); and (3) abnormal palmar flexion creases (APFCs). More arches, the simplest fingerprint pattern, and more radial loops, an unusual pattern, were found in IID cases in comparison to controls ($\chi^2 = 9.26; P = 0.02$), with especially marked differences in boys ($\chi^2 = 6.5; P = 0.0008$). A significant increase of APFCs was also found in the affected children ($\chi^2 = 28.52; P < 0.00$; odds ration = 3.86, 95% confidence interval = 1.77–8.47). For TABRC, the differences between IID cases and controls failed to reach the conventional level of significance. These findings suggest that environmental factors acting early in development, or mechanisms involving an interaction of genotype and environment could be involved in the aetiology of some cases of ID.

Keywords brain development, dermatoglyphics, environment, palmar flexion creases, prenatal risk factors

Introduction

Intellectual disability (ID) is a life-long disability and the most common neurological handicap in childhood. It can be defined in a number of ways; for example, by IQ, neurological functioning, social adaptation or behavioural competence, or by any combination of these (Kiely 1987). Epidemiological studies of ID generally report its prevalence by degree of intellectual impairment. Thus, the prevalence of moderate and severe ID (IQ < 50) has been estimated at 1.3–2 per 1000 and that of mild ID (IQ = 50–70) at 3.7–5.9 per 1000 (Frost 1977; Fishbach et al. 1982) in the general population.

The role of many factors in the aetiology of ID (e.g. chromosomal abnormalities, genetic metabolic disorders, and pregnancy complications such as maternal infection, exposure to toxins and radia-
tion, perinatal hypoxia, and postnatal infections) has been demonstrated. However, the causes in a high percentage of cases remain unknown (McLaren & Bryson 1987; Hou et al. 1998). The aetiology is partially dependent on the level of ID. Mild ID is generally idiopathic, but both severe and profound ID are more commonly of genetic origin. Additionally, labour-delivery complications (LDCs) have been suggested as being responsible in a high proportion of cases. Nevertheless, many authors have suggested that LDCs merely represent a secondary consequence of pre-existent abnormality in the foetus (Goodman 1987).

In cases of idiopathic ID, there is substantial evidence for a biological basis to brain abnormalities. Enlarged ventricles, similar to findings in schizophrenia, have been reported in 75% of children with ID of unknown origin (Prassopoulos et al. 1996).

Although dermatoglyphic characteristics have high but varying levels of heritability depending on the particular trait (Holt 1968), one part of their morphology is determined by intrauterine environmental influences acting early in the prenatal period and its embryology has been well established (Babler 1991; Kimura 1991). The development of the ridges begins with the formation of pads in the fingers, and the interdigital, hypothenar and thenar areas of the embryo’s palm during the second month of intrauterine life. Epidermal ridges appear on the surface of the hands after the regression of the pads by the end of the fourth foetal month, when significant and critical growth of another ectodermal derivative, the brain, is also taking place (Rakik 1988). After this period, dermatoglyphic patterns remain unchanged. The presence of abnormalities in dermatoglyphics constitutes fossilized evidence of a prenatal insult that has occurred in the second trimester of prenatal life or before (Schaumann & Alter 1976; Babler 1991).

Several environmental factors such as hypoxia, viral infections and delaying growth factors may modify the symmetry and size of the pad, modifying the future dermatoglyphic patterns and number of ridges (Mulhivill & Smith 1969).

Babler (1978) showed the relationship between embryonic stress and the presence of the simplest digital patterns. In the above study, more arches and, in consequence, lower ridge counts were associated with spontaneous abortion when cases were compared with elective abortions. Likewise, the association between dermatoglyphic abnormalities and maternal exposure to a range of environmental agents such as rubella, cytomegalovirus and alcohol has been well documented (for review, see Schaumann & Alter 1976).

The a–b ridge count (ABRC) has similarly shown a high degree of morphological variability related to environmental factors, and consequently, has been considered particularly suitable in the investigation of developmental disorders of idiopathic origin. The ABRC has been found to differentiate between cases of schizophrénia and normal controls (Turek 1990; Fañanás et al. 1990, 1996; Fearon et al. 2001), and to be sensitive to exposure to rubella in pregnancy (Schaumann & Alter 1976). In both cases, low ridge count values have been demonstrated in exposed individuals.

The association between Down’s syndrome and abnormal palmar flexion creases (APFCs) is probably the best documented (Plato et al. 1973; Borbolla et al. 1980; Rajangam et al. 1995). However, APFC patterns have also been found with increased frequency in individuals with developmental defects caused by intrauterine exposure to adverse environmental factors, mainly infectious agents (Schaumann & Kimura 1991).

Environmental factors such as rubella (Purvis-Smith & Menser 1968), prenatal toxaemia, hypertension (Davies & Smallpeice 1963) and intrauterine methadone exposure (Dar et al. 1977) have also been associated with APFCs. A significant increase in Sydney lines and a large number of arches have been found in the fingers of victims of sudden infant death syndrome (Wilber et al. 1993). Previous studies have reported an association between unusual creases and schizophrenia in affected individuals (Bracha et al. 1991; Van Os et al. 1997; Rosa et al. 2000).

Although a large number of dermatoglyphic variables can be analysed as indirect markers of prenatal stress, some are particularly relevant to the investigation of congenital disorders, including: (1) simplification of finger patterns, as measured by the relative number of arches; (2) a decrease in the number of lines in the second interdigital area (the ABRC); and (3) abnormalities in the palmar flexion creases.
The aim of the present work was to conduct a case-controlled study that examined the above-mentioned variables in children with ID of idiopathic origin. The hypothesis was that dermatoglyphic abnormalities would be more prevalent in these children than in the control sample because an environmental factor had affected early intrauterine development in a subgroup of children affected by idiopathic ID.

**Subjects and methods**

**Subjects and sample collection**

In order to recruit a representative sample of children with ID, all the special education schools of l’Hospitalet de Llobregat, a typical metropolitan area of Barcelona, were invited to participate in the present study. The three special schools of the area were Alpi, Escorça and Estel. Parents were invited to join in the study and gave informed written consent for the inclusion of their children.

All subjects with ID had karyotype blood testing in clinical records. Only those subjects with no evidence of a chromosomal abnormality or genetic metabolic disorder were included in the study, and they were defined as non-genetic ID or idiopathic cases (IGID).

Out of the 85 children with ID attending the three special schools, only 23 children (27.1%) had a chromosomal abnormality (i.e. Down’s syndrome, fragile-X syndrome, West syndrome, Filippo syndrome, Cornelia de Lange syndrome or genetic metabolic disorders). Because the objective was to study children with ID of idiopathic origin, these children were excluded. Thus, the final sample consisted of 62 children with no evidence of a genetic cause for their ID.

Before inclusion in the study, the 62 cases were personally interviewed by an experienced psychiatrist (A.G.) who determined that they met the ICD-9 and DSM-IV criteria for ID (CPHA 1980; American Psychiatric Association (APA) 1987). By degree of intellectual impairment (ICD-9; CPHA 1980), there were 29 children (46.77%) with mild or moderate ID (IQ = 35–69), 28 (45.16%) with severe or profound ID (IQ < 34), and five children (8.07%) with unspecific ID. The term ‘unspecified ID’ refers to those cases in whom there was a strong presumption of ID, but whose intelligence level was unstable on a standard test.

Healthy children with normal IQ, assessed with the Raven Progressive Matrices (Raven 1960), from different schools within the same population were invited to participate in the study as a control sample. The controls were matched for age, sex and ethnic origin. Since ethnic variation is important in dermatoglyphic pattern, the children with ID and the controls were all Spanish and matched to the same geographical area on the basis of the birthplace of their four grandparents (Table 1).

**Dermatoglyphics**

Palm and fingerprints were taken using a non-inky method (Prints-kit, Printscan Verification Systems Ltd., Printscan Distributoships, UK). The dermatoglyphic variables analysed included: (1) fingerprint patterns (FPs); (2) total a–b ridge count (TABRC); and (3) abnormal palmar flexion creases (APFCs).

*Table 1* Demographic characteristics of the children with intellectual disability (ID) and controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Children with ID</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intellectual level</td>
<td>ID of idiopathic origin (IQ &lt; 70)</td>
<td>Healthy with normal IQ (IQ &gt; 70)</td>
</tr>
<tr>
<td>Source of sample</td>
<td>All the special schools in l’Hospitalet</td>
<td>State schools in Barcelona</td>
</tr>
<tr>
<td>Number (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>43 (69.4)</td>
<td>50 (66.7)</td>
</tr>
<tr>
<td>female</td>
<td>19 (30.6)</td>
<td>25 (33.3)</td>
</tr>
<tr>
<td>total</td>
<td>62 (100)</td>
<td>75 (100)</td>
</tr>
<tr>
<td>Mean age (± SD; years)</td>
<td>12.8 ± 3.38</td>
<td>13.13 ± 0.53</td>
</tr>
</tbody>
</table>

*A metropolitan area of Barcelona.

The standard types of FPs considered were: the arch (A), the radial loop (L_r), the ulnar loop (L_u) and the whorl (W) (see Fig. 1) (Cummins & Midlo 1943).

The ABRC is a measure of the second interdigital area of the hand (Fig. 2). It is calculated by counting the number of ridges between the triradius, ‘a’, at the base of the index finger and the triradius, ‘b’, at the base of the middle finger. The TABRC is determined by adding both left and right counts (for further details, see Fañanás et al. 1996).

The APFCs considered in the present study were the Simian line, the Sydney line, hypoplastic (i.e. very rudimentary) creases, and clear broken proximal and distal palmar creases (Fig. 3).

Dermatoglyphic and PFC analyses were conducted by one of the authors (A.R.) who was blind to the status of the subjects.

Statistical analysis

The chi-square test was used to test for differences between cases and controls for the qualitative variables (FPs and APFCs). Associations were expressed as odds ratio (ORs). The ORs and 95% confidence intervals (95% CIs) were calculated using the Epi Info computer program (Dean et al. 1990). When the chi-square test was not appropriate, Fisher’s exact test was used (Raymon & Rousset 1995). It was calculated with STRUC

Results

The distribution of finger ridge patterns in cases and controls is shown in Table 2. The frequencies of As, L_r$s$, L_u$s$ and Ws in fingers were first compared between the total sample of children with ID and
controls, and secondly, according to the sex of the individuals. The children with ID had a different distribution of FPs compared to controls ($\chi^2 = 9.26$, d.f. = 3, $P=0.026$). The differences consisted of an increase in As and Ls in children with IGID compared to controls. When differences were studied according to individual sex, the present authors only found these differences in males. Boys with ID presented with an increased frequency of As and Ls that was reflected in a decreased W frequency in the male sample ($\chi^2 = 16.50$, d.f. = 3, $P<0.001$).

The TABRC results are shown in Table 3. Data on TABRC were available in 57 cases and 75 controls. Although children with ID had a lower mean TABRC, this finding failed to reach the conventional significance level (children with ID: mean = 76.42, SD = 11.96; controls: mean = 78.69, SD = 12.63; $t = 1.04$, d.f. = 130, $P=0.3$). The male cases showed a lower TABRC than the controls ($P=0.08$).

The distribution of abnormal palmar flexion creases in the samples is shown in Table 4. The present authors found a low frequency of normal PFCs in children with ID ($41.4\%$) compared to controls ($71.2\%$). The most frequent abnormality in cases and controls was hypoplasic creases ($34.1\%$ and $20.6\%$, respectively). The other abnormalities were less common than hypoplasic creases, but always more frequent in cases than in controls. When the distribution of the PFCs was compared in the two samples, the differences were statistically significant ($\chi^2 = 28.52; d.f. = 4; P<0.0001$). The same associations were observed in the male ($P<0.005$) and female groups ($P<0.005$).
When individuals were grouped according to the presence/absence of abnormal creases, APFCs were associated with an increased risk of ID ($\chi^2 = 14.07$, d.f. = 1, $P < 0.001$; OR $= 3.86$; 95% CI $= 1.77$–$8.47$).

**Discussion**

Studies of dermatoglyphics and PFCs are of aetiological interest in neurodevelopmental disorders (Kimura 1991). Although only a few previous dermatoglyphic studies in ID of idiopathic origin have been reported in the literature, most have been focused exclusively on ID related to chromosomal aetiology, especially Down’s syndrome. To the present authors’ knowledge, this is the first time that dermatoglyphic and APFCs have been analysed together in a sample of children with IGID. Wakita et al. (1998) studied the dermatoglyphics of a sample of subjects with severe ID using a multivariate analysis. The above authors’ results suggested that early intrauterine factors produced dermatoglyphic deviations in individuals with IGID compared to controls. However, the different approach...
used in the Wakita et al. (1998) study did not specify the deviations, and therefore, did not permit a comparison with the present findings.

In the present study, the main findings were that:
(1) there is a simplification of the dermatoglyphic and a high frequency of unusual patterns such as L's, especially in boys affected with idiopathic ID (IID); and (2) APFCs differentiate between cases and controls. For the ABRC, a lower number of ridges was found in children with ID, especially males, although the differences were not statistically significant. Probably the main reason for the lack of significance is the sample size and the small number of girls in the group of cases.

The first finding, i.e. dermatoglyphic simplification, has been described in spontaneous abortions which have shown no clinical indication of anatomical or morphological abnormalities, suggesting evidence of prenatal injury (Babler 1978).

The present authors found evidence that the association between AFP and IID was different in males and females since the effect was large and significant for the male prenatal growth is more affected by stress (Stinson 1985; Murray 1991). The main neurodevelopmental disorders (i.e. dyslexia, autism, stuttering, Asperger syndrome and severe ID) are all more common in males (Murray 1991).

The second result confirms that the percentages of abnormal palm creases were higher in children with ID compared to controls. The presence of APFCs was associated with a nearly fourfold increased risk for ID of idiopathic origin in this Spanish sample.

Although the present authors are conscious that they carried out a high number of statistical comparisons, they can be confident that the main associations found were not caused by chance because of the P-values obtained.

Since dermatoglyphic traits are known to complete development between the thirteenth and eighteenth weeks of gestational age, the results of the present study provide indirect evidence that some children with IID experience a time-specific and a time-limited exposure to stress factors during this early period of intrauterine life. However, other environmental or genetic factors could also have acted in different periods of brain development in some of these children.

Future case-control studies with large samples will allow the division of individuals into subsamples based on possible aetiological clues or risk factors for ID, which could shed more light on specific dermatoglyphic abnormalities for each subtype.

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