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Minor physical anomalies in schizophrenia and bipolar affective disorder

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Abstract

Objective. The prevalence of minor physical anomalies (MPAs) (prenatal errors of morphogenesis) was evaluated in patients with schizophrenia and bipolar affective disorder.

Method. A new modification of the Waldrop-scale was used to detect the presence or absence of 57 MPAs in 30 patients with schizophrenia, 30 with bipolar disorder, and in 30 matched normal controls.

Results. Patients with schizophrenia compared to normal controls had significantly higher rates of three minor malformations (furrowed tongue, flat occiput, primitive shape of ears) and those of one phenogenetic variant (wide distance between toes 1 and 2), and they also had a significantly higher rate of one minor malformation (primitive shape of ears), as compared to patients with bipolar disorder. In patients with bipolar disorder, furrowed tongue was significantly more common than in controls.

Conclusions. These results support an 'early' neuro-developmental model of schizophrenia.

Keywords: Neuro-development; Minor physical anomalies; Clinical stigmata; Schizophrenia and bipolar affective disorder

1. Introduction

Minor physical anomalies (MPAs) or informative morphogenetic variants (IMVs) are mild, clinically and cosmetically insignificant errors of morphogenesis which have a prenatal origin and may bear major informational value for diagnostic, prognostic, and epidemiological purposes (Pinsky, 1985). Many different terms have been used to describe them: e.g. minor congenital anomalies, minor malformations (MM), minor physical anomalies, and each of them refer to a mixture of familiar anthropometric variants, minor deformities, dysplasias and malformations (Méhes, 1988). Pinsky (1985) proposed the collective term IMV, but in the psychiatric literature MPA is generally accepted.

The presence of MPAs is a sensitive physical indicator of embryonic development. They are of value to the clinical morphologists as they serve as indicators of altered morphogenesis that occurred early in gestation. Since both the central nervous system and the skin are derived from the same ectodermal tissue in utero, MPAs may be external markers of abnormal brain development.

Opitz (1985) urged a clear distinction between morphogenetic events developing during and after organogenesis based on the report of the International Working Group (Spranger et al., 1982). According to his recommendations MM are always abnormal, they

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are qualitative defects of embryogenesis and arise during organogenesis. All malformations are developmental field defects and usually they are all-or-none anomalies. The use of physical morphology is based on studies which have shown that minor anomalies are true deviations from normal (Spranger et al., 1982; Opitz, 1985).

In contrast, phenogenetic variants (PV) are quantitative defects of final morphogenesis and arise after organogenesis. Morphologically PV are the exact equivalents of normal anthropometric variants (Spranger et al., 1982; Opitz, 1985). Individually MPAs may represent the extreme of a normal trait, or may be a dysmaturity, or the exact equivalent of a normal variant in another family (Opitz, 2000).

With the distinction of MM and PV, data on the ratio of MPAs developing during and after organogenesis, could be obtained. The change in the development during pregnancy resulted in the production of the MPAs which is assumed to have either caused or contributed to the development of schizophrenia or bipolar disorder. Several studies have shown an excess of MPAs in patients with schizophrenia (Gualteri et al., 1982; Green et al., 1989; O'Callaghan et al., 1991; Lohr and Flynn, 1993; McGrath et al., 1995; Lane et al., 1997; Trixler et al., 1997; Buckley, 1998; Griffiths et al., 1998; Ismail et al., 1998) and a few in patients with affective disorders (Lohr and Flynn, 1993; Green et al., 1994; Lohr et al., 1997) compared to controls. Differences between studies may be associated, partly, with the problems in the use of the Waldrop-scale. This scale includes MM arising during organogenesis, and PV appearing after organogenesis without distinction (Trixler et al., 1997; Trixler and Tényi, 2000). A clear distinction between morphogenetic events appearing during and after organogenesis is strongly needed (Opitz, 1985).

Recent research focusing on the neuro-developmental etiology of schizophrenia and affective disorders clearly requires such a distinction, as this may yield a clue to the time and nature of the supposed genetic or epigenetic change. The Waldrop-scale contains only 18 MPAs (Waldrop and Goering, 1971; Waldrop et al., 1978), while in recent paediatric literature more than 50 MPAs have been listed (Feingold and Bossert, 1974; Méhes, 1985, 1988; Merlob, 1994). The growing amount of research on markers of an aberrant neurodevelopment in both schizophrenia and bipolar affective disorder (Gutiérrez et al., 1998; Buckley, 1998) has not produced unequivocal findings. While Green et al. (1994) were not able to demonstrate a significantly higher rate of minor physical anomalies among bipolar patients, Lohr et al. (1997) have published a significantly higher rate in unipolar depression as compared to controls.

The aim of the present study was to investigate the rate and topological profile of minor physical anomalies in a group of patients with schizophrenia and bipolar affective disorder. The following hypotheses have been tested: (1) MPAs are more common in patients with schizophrenia as well as with bipolar affective disorder than in normal subjects; (2) a higher rate of MPAs is found predominantly in the head and facial regions in patients with schizophrenia and bipolar affective disorder than in normal subjects; (3) there is at least partial similarity between the MPA profiles of patients with schizophrenia and those with bipolar affective disorder.

2. Material and method

Using a list of MPAs containing 57 minor signs collected by Méhes (Méhes, 1985, 1988) 30 consecutively admitted patients with schizophrenia, 30 with bipolar affective disorder and 30 healthy controls matched based on sex, age and ethnical origin were evaluated. All items in the Waldrop-scale except for head circumference and longer third toe were included in this list. A clear differentiation between MM and PV were introduced (see Appendix A).

All patients gave informed consent; the study was performed in accordance with the Declaration of Helsinki and was evaluated following institutional guidelines. Three examiners, one unaware and two aware of the diagnoses, investigated all the patients and controls separately. Interrater reliability was tested and the kappa coefficient was $>75\%$. The diagnoses of the patients were done independently by two experienced psychiatrists according to DSM-IV. Only those meeting DSM-IV criteria unanimously were considered for the study. The examination of minor physical anomalies was done qualitatively (present or absent) without scores being used, but where it was