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Minor physical anomalies in bipolar I and bipolar II disorders – Results with the Méhes Scale

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ABSTRACT

Minor physical anomalies (MPAs) are external markers of abnormal brain development, so the more common appearence of these signs among bipolar I and bipolar II patients can confirm the possibility of a neurodevelopmental deficit in these illnesses. The aim of the present study was to investigate the rate and topological profile of minor physical anomalies in patients with bipolar I and – first in literature – with bipolar II disorders compared to matched healthy control subjects. Using a list of 57 minor physical anomalies (the Méhes Scale), 30 bipolar I and 30 bipolar II patients, while as a comparison 30 matched healthy control subjects were examined. Significant differences were detected between the three groups comparing the total number of minor physical anomalies, minor malformations and phenogenetic variants and in the cases of the ear and the mouth regions. The individual analyses of the 57 minor physical anomalies by simultaneous comparison of the three groups showed, that in the cases of furrowed tongue and high arched palate were significant differences between the three groups. The results can promote the concept, that a neurodevelopmental deficit may play a role in the etiology of both bipolar I and bipolar II disorders.

1. Introduction

The neurodevelopmental hypothesis of schizophrenia was formed in the late 80 s (Weinberger., 1986; Murray and Lewis, 1987) and since it has became widely accepted. The fact that there are many clinical and neurobiological similarities between schizophrenia and bipolar I and II disorders has lead some authors to conceptualize the etiology of both schizophrenia and bipolar disorders in terms of an aberrant neurodevelopment (Nasrallah, 1991, 1997; Palomo et al., 2002). The idea is that during prenatal periods, various genetic and environmental factors can lead to structural and functional brain changes, that increase the risk of disease later in the life of the individual. The hypothesis for aberrant neurodevelopment in bipolar disorders gets support from different evidences (Sivkov et al., 2013). Obstetric complications (Done et al.,1991), prenatal influenza infection (Machon et al., 1997), prenatal famine (Brown et al., 2000), urban (Marcelis et al., 1998) and winter (Torrey et al., 1997) birth precede the onset of bipolar disorder. Lower IQ (David et al., 1997), delayed attainment of developmental milestones (van Os et al., 1997), emotional problems and interpersonal difficulties (Cannon et al., 2002) have been implicated as premorbid neurobehavioral precursors in children who develop bipolar disorder in later life. In regard to bipolar I and II disorders, the neurodevelopmental alternative of etiology has also got a few underpinnings from structural neuroimaging studies (Sanches et al., 2008; Hozer and Houenou, 2016), however the evidence in favor of a neurodevelopmental basis for bipolar I and II disorders is more controversial than in the case of schizophrenia.

Minor physical anomalies (MPAs) are insignificant errors of morphogenesis which have a prenatal origin and may bear major informational value. The presence of minor physical anomalies is a sensitive physical indicator of embryonic development. Since both the central nervous system and the skin derived from the same ectodermal tissue in utero, minor physical anomalies may be external markers of abnormal brain development. Minor physical anomalies are considered to develop during the first and/or early second trimester of gestation (Pinsky, 1985; Méhes, 1988; Tényi et al., 2004, 2009, 2015) and represent potentially valuable indices of disturbances in early neurodevelopment. Once formed they persist into adult life and are readily

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detected on visual examination of the particular body area. As we (Trixler et al., 1997, 2001; Trixler and Tényi, 2000; Tényi et al., 2009, 2015; Hajnal et al., 2016) and others (Akabaliev and Sivkov, 2007) have discussed earlier, differences and contradictions between studies on minor physical anomalies among adults and children with different neuropsychiatric disorders, may be associated, partly, with the problems in the use of the Waldrop-scale for the detection of these signs. The Waldrop-Scale has poor internal consistency due to the heterogeneity of the anomalies in terms of location, character and time of prenatal development (Akabaliev and Sivkov, 2007). The Waldrop-scale contains only 18 minor physical anomalies (Waldrop and Goering, 1971) while in pediatric literature more than 50 anomalies have been listed (Pinsky, 1985; Méhes, 1988). An other basic problem with the Waldrop-scale that it makes no distinction between minor malformations, which arise during organogenesis and phenogenetic variants, which appear after organogenesis (Pinsky, 1985; Méhes, 1988; Trixler and Tényi, 2000). A clear distinction between morphogenetic events developing during and after organogenesis is needed. Minor malformations are always abnormal and are qualitive defects of embryogenesis, which arise during organogenesis. All malformations are developmental field defects and usually they are all-or-none anomalies. In contrast phenogenetic variants are quantitative defects of final morphogenesis and arise after organogenesis. Using a list of minor physical anomalies containing 57 minor signs collected by Károly Méhes (1988), previously we have studied the prevalence of minor physical anomalies in patients with schizophrenia, bipolar affective disorder, alcohol dependence, Tourette syndrome and major depression (Trixler et al., 1997, 2001; Tényi et al., 2004, 2015; Csábi et al., 2008), and recently the list and detailed definitions has become also acceptable for researchers, who wish to adapt our suggested modifications for the investigation of minor physical anomalies (Trixler et al., 2001).

Previously 11 publications of 9 studies (Alexander at al.,1992; 1994, Green et al., 1994; Torrey et al.,1994; Trixler et al., 2001; Kelly et al., 2004; Akabaliev et al., 2011, 2014; Sivkov et al., 2013; Goswami et al., 2011; Praharaj et al., 2012) were published on the prevalence of MPAs in bipolar affective disorder with mixed results, while other 6 studies (Lohr and Flynn, 1993; McGrath et al., 1995, 2002; Dean et al., 2006, 2007; Lloyd et al., 2008) reported on MPAs in affective disorders not distinguishing between specific diagnoses (schizoaffective disorder, bipolar disorders, major depression, mania, psychotic depression). The summary of these studies are presented on Table 1 and Table 2. A limitation of all of these studies, that there is no data available on the prevalence of MPAs using the distinction between bipolar I and bipolar II disorders.

The aim of the present study was to investigate the rate and topological profile of minor physical anomalies - using the Méhes-Scale to differentiate minor malformations and phenogenetic variants - in patients with bipolar I and – first in literature – with bipolar II disorder comparing them to normal control subjects. The following hypotheses have been tested: (1) Minor physical anomalies are more common in patients with bipolar I and bipolar II disorder compared to normal controls, (2) a higher rate of minor physical anomalies is found predominantly in the head and facial regions among bipolar I and bipolar II patients pointing at aberrant early (first and second trimester) brain development.

2. Material and methods

2.1. Study subjects

Using a list of 57 minor physical anomalies collected by Méhes (1988), 30 patients with the diagnosis of bipolar I disorder and 30 patients with the diagnosis of bipolar II disorder were included in the study. Patients with non-Hungarian ethnic origin were excluded from the study. As a comparison 30 healthy control subjects matched for sex, age and ethnic origin were also observed for minor physical anomalies. The gender distribution in the three groups was the same. Controls were excluded if they endorsed any personal or family history (in the first- or second-degree relatives) of psychotic disorders, mood disorders or any other neuropsychiatric disease. Controls with the family history of completed suicide were also excluded. In the bipolar groups family history for bipolar disorders and for other mood disorders were detected. In the bipolar I group among the relatives 12 bipolar I persons and 4 relatives with major depression were detected, while in the bipolar II group 2 bipolar I and 2 bipolar II persons and 7 relatives with major depression were found. Family history was based on reports from patients and relatives. The age of the bipolar I group was 52.3 ± 10.0 and in the bipolar II group 52.1 ± 14.1. The age of onset in the bipolar I group was 31.6 ± 6.4 and 36.7 ± 8.8 in the bipolar II sample. The duration of illness in the bipolar I group was 20.8 ± 8.3 and 15.8 ± 8.8 in the bipolar II group. The diagnoses of the patients were evaluated independently by two experienced psychiatrists according to the DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders, 2000). All available clinical information and data were obtained from structured clinical interviews.

2.2. Examination of minor physical anomalies

We have used the Méhes Scale for evaluation of minor physical anomalies, which includes 57 minor signs (Trixler et al., 1997, 2001; Tényi et al., 2009). Minor physical anomalies are connected to body regions for comparison and analysis of data. A clear differentiation between minor malformations and phenogenetic variants were introduced, the scale and detailed definitions were published earlier (Trixler et al., 2001). All participants gave informed consent, the study was performed in accordance with the Declaration of Helsinki as revised 1989, and was evaluated following institutional guidelines. Two

Table 1
Studies on MPAs in affective disorders not distinguishing between specific diagnoses.

Studies	Number of patients	Scale used
Lohr and Flynn (1993)	33 patients with mood disorders	Waldrop Scale
McGrath et al. (1995)*	31 patients with schizoaffective disorder, 24 patients with mania, 13 with unipolar major depression	Modified Waldrop Scale
McGrath et al. (2002)**	9 patients with psychotic depression, 21 patients with bipolar affective disorder, 10 patients with schizoaffective disorder	15 MPAs on the head and the face
Dean et al. (2006)*	60 patients with functional psychoses	Abridged version of the Lane Scale
Dean et al. (2007)*	51 patients with mania, 44 patients with depression with psychotic features	Abridged version of the Lane Scale
Lloyd et al. (2008)**	110 patients with affective psychoses	Abridged version of the Lane Scale

* studies reporting on a significantly higher total number of MPAs in patients as compared to controls.
** studies that found certain individual MPAs to be significantly more frequent in patients than in controls.