Neurological soft signs in schizophrenia and mood disorders
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CHAPTER 7

NEGATIVE ASSOCIATION BETWEEN A HISTORY OF OBSTETRIC COMPLICATIONS AND THE NUMBER OF NEUROLOGICAL SOFT SIGNS IN FIRST-EPISTODE SCHIZOPHRENIC DISORDER.

Marco P.M. Boks, Jean-Paul Selten, Stuart Leask, Stynke Castelein, Robert J. van den Bosch.
SUMMARY

We examined the relationship between having a history of obstetric complications (OCs) and the number of neurological soft signs (NSS) in a group of 132 patients experiencing their first episode of psychosis. Contrary to our expectations we found a negative relationship between these two measures. It is possible that the patients with a history of OCs carry fewer susceptibility genes for schizophrenia and NSS than those without a history of OCs.

INTRODUCTION

There is compelling evidence of an increased number of NSS in first episode psychosis (Dazzan and Murray, 2002) and schizophrenia (Boks et al., 2000; Leask et al., 2002). Furthermore, some see OCs as risk factors for schizophrenia (see Cannon et al., 2002, although see also Crow, 2003). The observation that both NSS and OCs are associated with an increased ventricle to brain ratio (Wright et al., 2000; Owen et al., 1988) leads to the hypothesis that OCs might contribute to the development of NSS. Consequently, we tested the hypothesis that the presence of a history of OCs is related to a greater number of NSS in schizophrenia.

METHOD

We examined 132 consecutive first admissions for a first episode psychosis, including 92 patients with a diagnosis of a ‘schizophrenic disorder’ (DSM-IV: 295.x: schizophrenia, schizoaffective or schizoaffective disorder). The patients had been diagnosed with; schizophrenia (N=47), schizoaffective disorder (N=20), schizophreniform disorder (N=25), drug induced psychotic disorder (N=10), brief psychotic disorder (N=10), psychotic disorder not otherwise specified (N=7), mood disorder with psychotic features (N=9), delusional disorder (N=4). Eighty-three patients (63%) were male, the mean age was 25.9 years (SD 5.8). Thirty-two patients were not on antipsychotics. The other patients used; olanzapine (N=32), risperidone (N=31), pimozide (N=10), quetiapine (N=8), haloperidol (N=5), zuclopenthixol (N=5), sertindole (N=3), clozapine (N=2), perphenazine (N=2), penfluridol (N=1). The mean dosage in haloperidol equivalents was 4.1 mg (SD 3.4). Ten patients (8%) were left-handed, in 5 patients (4%) handedness was mixed. Seventeen patients (13%) had a history of head trauma.

After complete description of the study written informed consent was obtained. DSM IV diagnoses were established by means of the SCAN interview (Wing et al., 1990). Information on handedness and history of head trauma was assessed by a semi-structured interview. Six weeks after admission all patients underwent a standardized comprehensive neurological investigation, the Cambridge Neurological Investigation (Chen et al., 1995). Interrater reliability between three raters had been assessed in a random sample of 30 cases and was satisfactory (ICC 0.83). Previously we reported on significant increase in the number of NSS in patients versus healthy controls (Boks et al., 2004).
Obstetric complications

The biological mother completed a questionnaire on several pregnancy, labor-delivery and neonatal complications. We focused on the 10 OCs that had been shown to be significant risk factors for schizophrenia in the Cannon et al. meta-analysis (2002): diabetes in pregnancy, birth weight <2000 g and birth weight <2500 g separately, emergency caesarian section, congenital malformations, uterine atony, rhesus antagonism, asphyxia, bleeding in pregnancy, and preeclampsia.

We tested differences in the number of NSS between groups with or without OCs using an independent, two-tailed t-test. The analyses were conducted for the entire group, and for the schizophrenic disorder group and the other psychotic disorder group separately.

Table 1: Characteristics of the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Schizophrenic disorders</th>
<th>Other psychotic disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No OC</td>
<td>OC</td>
</tr>
<tr>
<td>N</td>
<td>62</td>
<td>30</td>
</tr>
<tr>
<td>Mean Age (SD)</td>
<td>26.1 (5.6)</td>
<td>26.2 (6.9)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>42 (68%)</td>
<td>20 (68%)</td>
</tr>
<tr>
<td>Not right handed (%)</td>
<td>5 (8.1%)</td>
<td>4 (13.3%)</td>
</tr>
<tr>
<td>Head trauma (%)</td>
<td>6 (9.7%)</td>
<td>5 (16.7%)</td>
</tr>
<tr>
<td>Dosage haloper. Eq (SD)</td>
<td>5.4 (3.5)</td>
<td>4.2 (2.3)</td>
</tr>
<tr>
<td>Total score NSS (SD)</td>
<td>10.3 (6.9)</td>
<td>7.3 (5.9)</td>
</tr>
<tr>
<td>High NSS (%)</td>
<td>35 (56%)</td>
<td>12 (40%)</td>
</tr>
</tbody>
</table>

RESULTS

Table 1 shows the characteristics of patients with a schizophrenic disorder and those with other psychotic disorders, divided into patients with and without OCs. There were no significant differences in age, sex and dosage of antipsychotics, history of head trauma or handedness between any of the subgroups.

Contrary to our hypothesis we found a significantly smaller number of NSS in the total group of patients with a history of OCs; 7.0 vs. 9.6 respectively (t=2.0 df =130 p=0.049). The same was found in the subgroup of schizophrenic disorder patients with a history of OCs (t=2.07 df=90 p=0.04). In the group of patients with other psychotic disorders the differences were not significant (t=0.704 df=37 p=0.48). To exclude the possibility that the differences in the dosage of antipsychotics accounted for the differences between patients with and without history of OCs we tested the differences between these groups with the dosage as a co-variate. For the entire group the differences no longer reached significance (F= 2.56 df=2 p=0.08). However in the schizophrenic disorder group the differences were amplified (F= 3.63 df=2 p=0.03).
This study finds a significant but negative relationship between the number of NSS and a history of OCs in first episode patients with a schizophrenic disorder. Strength of this study is its use of standardized neurological and diagnostic assessments. A limitation of this study is the use of maternal information on OCs. However, this is likely to lead to an overestimation of OCs in patients compared to healthy control subjects (Buka et al., 2000) and in our study we did not include controls.

To our knowledge there have been only 2 studies that addressed this topic. One was negative (Cantor-Graae et al., 1994). Another found a positive relationship between NSS and OCs in male schizophrenia patients, but not in female patients (Lane et al., 1996).

How to explain a negative association between a history of OCs and the number of NSS? Several studies have found that the number of NSS is strongly associated with a positive family history of schizophrenia (Ismail et al., 1998; Cantor-Graae et al., 2000). Consequently, it is possible that the patients with a history of OCs carry fewer genes for schizophrenia (and NSS), and ‘needed’ the further neurodevelopmental insult of OCs to develop schizophrenia.
ACKNOWLEDGEMENT

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