Introduction

Previous studies suggested that susceptibility to schizophrenia is based at least to some extent on genes [1]. However, evolution of the disease is believed to depend on interaction between the genetic factors and physical, psychological and psychosocial factors, which have not been completely described yet [2]. To distinguish between the morphologic and metabolic changes in the brain of schizophrenic patients caused by the genetic predisposition and by the disease itself, monozygotic twins were studied.

MR relaxometry revealed consistent changes in T1 [3] and T2 [4,5] relaxation times due to schizophrenia. Prolonged T2 relaxation times were found in white matter, cortex [4], and also in basal ganglia [5]. We examined both healthy monozygotic twins and concordant and discordant monozygotic twins by MR relaxometry to confirm or rule out the genetic contribution to relaxation time alteration in the basal ganglia, thalamus, and white matter.

Methods

We scanned 3 discordant monozygotic twins (age 35.7±9.4 years), 1 pair of concordant schizophrenic twins (age 22 years) and 5 healthy individuals (all from twins, age 36.2±9.3 years). The schizophrenic patients met DSM-III-R criteria for schizophrenia as determined by an interview with theStructured Clinical Interview for DSM-III-R (SCID). The patients are adjusted on standard maintenance neuroleptic medication.

We used a Siemens Magnetom Vision imager 1.5 T with a standard head coil. T2 was obtained using a CPMG sequence with 16 echoes (echo-spacing TE=22.5 ms, repetition time TR=3000 ms), T1 using saturation recovery, repetition time varied from 100 up to 1500 ms, echo time TE=22 ms. As the T1 measurement takes substantially longer time, it suffers more often from motion artefacts and was not successfully completed for all the subjects. In both measurements, a 5 mm thick tilted axial slice through the basal ganglia was chosen.

Relaxation maps were calculated using three-parameter fit both for T1 and T2. Relaxation time values were then obtained from the basal ganglia, thalamus, and white matter.

The protocol was approved by the ethics committee of our institution, and the patients and controls were in detail informed about the examination.

Results

We observed an increase of T1 and T2 of all schizophrenic subjects compared to the control group of healthy subjects in the basal ganglia, thalamus, and white matter. We found that the schizophrenic subjects differ in T1 and T2 also from their healthy siblings, which do not differ from control group.

In the discordant twins, statistically signifant increase of T2 (paired T-test, p<0.002) in all evaluated structures in the schizophrenic patients was found compared to their healthy siblings (see Table). Similar trend we observed for T1, nevertheless lack of T1 data does not enable meaningful statistical analysis.

No difference was found between schizophrenic patients from discordant and concordant twins.

Discussion

Although the brain symmetry or asymmetry of discordant twins is still broadly discussed, we found no trend or regularity in symmetry.

Higher values of T1 and T2, which we found in schizophrenic subjects compared to healthy ones, are in agreement with previously published results [3-5]. Significant prolongation of the relaxation times in case of schizophrenic patients from discordant twins compared to their healthy siblings can indicate the origin of the disease. It confirms the hypothesis that although the susceptibility to schizophrenia is to some extent based on genetic factors, more important than inherited predispositions are other factors, such as obstetric complications, physical, psychological or psychosocial factors.

The effect of the medication should be discussed, because changes were reported from PET and MRI studies in the basal ganglia due to the influence of neuroleptics. Bartokiz et al. in [6] reported greater variability of caudate nucleus T2 values (which we also observed, see Tab.) and T2 relaxation time shortening possibly due to iron deposition caused by corrupted metabolism in basal ganglia. Nevertheless this trend in T2 is in the opposite direction than the observed changes, thus the influence of the medication has only minor, if any, effect.

Although the mechanism, which is responsible for the increase of the relaxation times, remains unexplained yet, the increase seems to be a consequence of the disease, not an expression of its cause.

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References


T2 values (in ms) in the discordant twins and the control healthy group

<table>
<thead>
<tr>
<th>Nucleus</th>
<th>Schizophren. Siblings (from discordant twins)</th>
<th>Healthy Siblings (from discordant twins)</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Globus</td>
<td>75.4±5.5</td>
<td>69.9±4.7</td>
<td>68.6±1.9</td>
</tr>
<tr>
<td>Pallidus</td>
<td>87.8±6.6</td>
<td>82.7±3.4</td>
<td>79.3±1.6</td>
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<td>Putamen</td>
<td>95.8±9.0</td>
<td>89.8±1.1</td>
<td>86.4±1.9</td>
</tr>
<tr>
<td>Caudate</td>
<td>88.8±7.2</td>
<td>83.6±1.3</td>
<td>82.2±1.6</td>
</tr>
<tr>
<td>Nucleus</td>
<td>81.2±6.9</td>
<td>75.7±0.8</td>
<td>77.4±1.4</td>
</tr>
</tbody>
</table>

A Twin Study in Schizophrenia: Preliminary Relaxometry Results

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