Progranulin gene variability decreases the risk to develop Bipolar Disorder and Schizophrenia and plasma levels are decreased in patients with Bipolar Disorder

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Background

Mutations in the progranulin gene (GRN) are the most frequent cause of autosomal dominant frontotemporal lobar degeneration (FTLD). Age at disease onset, as well as clinical phenotypes associated with such mutations, are extremely heterogenous. Basing on the assumption that frontotemporal lobar degeneration (FTLD), schizophrenia and bipolar disorder (BD) might share common aetiological mechanisms, we analyzed genetic variation in the FTLD risk gene progranulin (GRN) in a German sample of patients with schizophrenia and BD as compared with age-, gender- and ethnicity-matched controls. Furthermore, we measured plasma progranulin levels in German BD patients as well as in Italian BD patients and matched controls1,2.

Methods

We analyzed genetic variation in the FTLD risk gene progranulin (GRN) in a German population of 508 patients with schizophrenia and BD as compared with 567 age-, gender- and ethnicity-matched controls. Furthermore, we measured plasma progranulin levels in 26 German BD patients as well as in 61 Italian BD patients and 29 matched controls.

Results

A significantly decreased allelic frequency of the minor versus the wild-type allele was observed for rs2879096 (23.2 versus 34.2%, P=0.001, OR:0.63, 95%CI:0.49-0.80), rs4792938 (30.7 versus 39.7%, P=0.005, OR:0.70, 95%CI: 0.55-0.89) and rs5848 (30.3 versus 36.8, P=0.007, OR: 0.71, 95%CI:0.56-0.91). Progranulin plasma levels were significantly decreased in BD patients, either Germans or Italians, as compared with controls (89.69:3.97 ng/ml and 116.14 5.80 ng/ml, respectively, versus 180,81:18.39 ng/ml P<0.01) and were not correlated with age.

Conclusions

Taken as a whole, GRN variability decreases the risk to develop BD and schizophrenia, and progranulin plasma levels are significantly lower in patients than in controls. Nevertheless, a larger replication analysis is needed to confirm these preliminary results.

References


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