No association between genetic variants at the *ASCT1* gene and schizophrenia or bipolar disorder in a German sample

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Altered glutamatergic neurotransmission is considered a potential etiological factor of schizophrenia (SCZ) and affective disorders. The gene *ASCT1 (SLC1A4)* coding for a Na^+-dependent neutral aminoacid transporter is a member of the glutamate transporter superfamily and is located on 2p13–14, a region showing linkage to both SCZ and bipolar disorder (BD). *ASCT1* can thus be considered a candidate gene for both disorders. In a German sample, we tested for association between *ASCT1* and both SCZ and BD. Allele and haplotype frequencies, however, did not differ between cases and controls. Recent findings on the associations between brainderived neurotrophic factor (BDNF) and SCZ and between *G72/G30* and BD suggest that SCZ patients with a history of major depressive episodes (MDE) outside psychotic episodes and BD cases with a history of persecutory delusions constitute genetically distinct subgroups of these disorders. Thus, we hypothesized that restricting case definition to those 95 SCZ individuals with MDE and to those 107 BD patients with a history of persecutory delusions might clarify the relationship between BD, SCZ and *ASCT1*. However, these stratification approaches did not yield any significant association either. Allele and haplotype frequencies did not differ between cases and controls. Our results do not support an association of the *ASCT1* gene with BD or SCZ in the German population. *Psychiatr Genet* 16:233–234 © 2006 Lippincott Williams & Wilkins.

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Summary

Altered glutamatergic neurotransmission is considered a potential etiological factor of schizophrenia (SCZ) and affective disorders. The gene *ASCT1 (SLC1A4)* coding for a Na^+-dependent neutral amino acid transporter is a member of the glutamate transporter superfamily and is located on 2p13–14, a region showing linkage to both SCZ and bipolar disorder (BD) (Camp *et al.*, 2001; Liu *et al.*, 2003). *ASCT1* can thus be considered a candidate gene for both disorders.

In a German sample, we tested for association between *ASCT1* and both SCZ and BD (according to Diagnostic and Statistical Manual of Mental Disorder-IV). Samples were as follows: for SCZ, 330 patients (44% female, 56% male, age 35.8 ± 11.8); for BD, 306 patients (53% women, 47% men, age 42.4 ± 13.3 years); 319 population-based controls (CON, 58% women, 42% men, age 49.2 ± 15.5 years). In addition to single nucleotide polymorphisms rs2075209, rs1064512, rs3732062 and rs759458, we identified and genotyped a short tandem repeat (STR) ~11 kb downstream of the last exon (STR-SLC1A4-11, primers: forward 5′-CCCTGCAGATGATTCTGATACC-3′, reverse 5′-CCGTAATCCCAGTTACTCAGGA-3′). Genotypes were in Hardy–Weinberg equilibrium. Power to detect an effect at genotype relative risks of 1.3–1.5 was moderate to good (45–90%).

Allele and haplotype frequencies did not differ between cases and controls. Minor allele frequencies of the single nucleotide polymorphisms were as follows (for SCZ, BD and CON, respectively): rs2075209 (A/G), A = 0.170, 0.171, 0.186; rs1064512 (C/G), C = 0.062, 0.079, 0.077; rs3732062 (C/T), C = 0.157, 0.158, 0.169; rs759458 (A/G), A = 0.245, 0.258, 0.247. STR-SLC1A4 showed eight different alleles. Recent findings from our group on the associations between brain-derived neurotrophic factor and SCZ and between *G72/G30* and BD suggest that SCZ patients with a history of major depressive episodes outside psychotic episodes and BD cases with

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a history of persecutory delusions constitute genetically distinct subgroups of these disorders (Schulze *et al.*, 2005; Schumacher *et al.*, 2005). Thus, we hypothesized that restricting case definition to those 95 SCZ individuals with major depressive episodes and to those 107 BD patients with a history of persecutory delusions might clarify the relationship between BPAD, SCZ and *ASCT1*. These stratification approaches, however, did not yield any significant association either. Our results do not support an association of the *ASCT1* gene with BD or SCZ in the German population.

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