CNTF and endogenous psychoses?

Sir — Takahashi *et al.*[1] recently reported in *Nature Genetics* a null mutation in the human *CNTF* gene that is not causally related to neurological diseases. We have genotyped 352 unrelated Caucasian individuals (178 females, 174 males; mean age ± SD: 44.2 ± 17.2 years) for this mutation. The sample comprised 205 neurological patients, 41 healthy controls (well matched for age and sex) as well as 106 psychiatric inpatients.

We found a frequency of the mutant allele of 0.122 in the control group and of 0.144 in our patients with neurological diseases, confirming the previous results that the allele frequency is not significantly elevated in neurological patients. However, for psychiatric patients we found a significantly (chi-square test, $P < 0.05$) increased mutant allele frequency of 0.241. The distribution of the single genotypes in controls vs. neurological vs. psychiatric patients was as follows: normal: 75.6% vs. 72.7% vs 54.7%; heterozygote mutant: 24.4% vs 25.9% vs 42.5%; homozygote mutant: 0.0% vs 1.5% vs 2.8%.

More than 66% of our psychiatric patients suffered from endogenous psychoses such as schizophrenia, schizotypical and delusional disorders (ICD-10 F2) and mood affective disorders (ICD-10 F3). The three homozygous mutation carriers of the psychiatric group suffered from manic-depressive disorder, hypochondriacal depression and periodic catatonia, respectively. The latter represents a subtype of schizophrenic psychosis with considerable familial inheritance.

We conclude that a reduced level of neurotrophic factors may represent a predisposing factor which together with other noxae such as environmental effects or other genetic defects, might lead to disturbed development and function of the CNS. On the other hand it is possible that a disorder involving the lack of a neurotrophic disorder (such as *CNTF*) might underlie a specific subgroup of psychiatric diseases. Neurodevelopmental deficits, disturbances of the cell migration and dysconnections of neuronal and glial structures are possible pathomechanisms for psychiatric disorders, mainly psychoses[2–4]. Associations have been found between variants in another neurotrophic factor gene (*NT3*) and schizophrenia[5,6]. Our results support these findings. The fact that the mutations are found in healthy persons as well could be due to the strong pleiotropia and redundancy among neurotrophic factors[7].

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