



Are tetranucleotide microsatellites implicated in neuropsychiatric diseases?

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Abstract. Expecting the significant breakthrough in the diagnosis of complex disorders of neuropsychiatry background, intensive efforts are undertaken to establish genetic markers associated with these disorders. Association of di-, tri- or tetranucleotide repeats with neurological disorders has been reported earlier in different populations. We have examined association between schizophrenia and polymorphism of several tetranucleotide genetic markers from different chromosome positions, including those being candidate in main psychiatric diseases. Results of statistical comparative analysis between neuropsychiatric patients from Poland and their regionally matched healthy subjects are presented. © 2005 Elsevier B.V. All rights reserved.

Keywords: Association study; STR polymorphism; Neuropsychiatric disorder; Poland

1. Introduction

Despite strong evidence for association between neuropsychiatric diseases and genetic inheritance, up till now the nature of the genes responsible for these disorders remains unknown. Microsatellites abundant and widespread throughout the genome have special importance in linkage and association studies [1]. Although the biological function of these sequences is scarcely known, their involvement in a process of recombination and transcription has been reported [2]. The implication of TCTA sequence polymorphism in TH01 locus on quantitative expression of hydroxylase tyrosine gene was documented [3]. The aim of the study was a statistical comparative analysis between neuropsychiatric patients from Poland and their regionally matched healthy subjects. The analysis included

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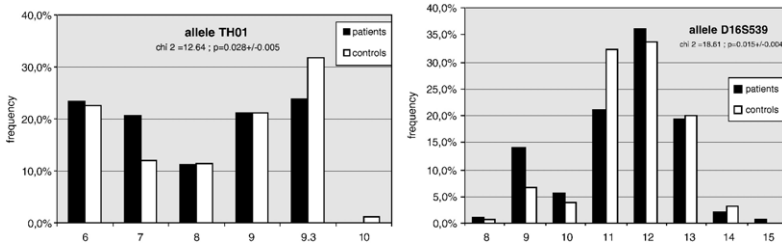


Fig. 1. Allele frequencies of TH01 and D16S539 loci in schizophrenic patients and controls.

14 tetranucleotide genetic markers from different chromosome positions, including those being candidate in main psychiatric diseases.

2. Materials and methods

Ninety patients affected by schizophrenia and 350 control subjects took part in the study. The neuropsychiatric patients were diagnosed by two psychiatrists according to the DSM-IV criteria. The control were recruited from among healthy individuals after the age of 45 with negative family history of psychiatric disorders. Bioethics Committee of Medical University in Lodz gave its assent to the research with the decision No. RNN/03/03/KB. Genomic DNA was isolated by the salt extraction procedure. Amplification of investigated markers: TH01, D5S818, D13S317, D8S1179, D21S11, D7S820, CSF1PO, D19S433, VWA, TPOX, D18S51, D3S1358, D16S539, D2S1338, FGA was carried out using set of primers included in the Identifiler kit according to the User's Manual (Applied Biosystems). Fluorescent detection was performed on the ABI Prism 377 sequencer with standard LIZ 500 using Gene Scan version 3.7. Distributions of alleles were compared using RXC program created by G. Carmody.

3. Results

Statistically significant differences in distribution of alleles in 4 out of 14 of investigated systems were reported between the neuropsychiatric subjects and the control sample from the same Polish region (see Figs. 1 and 2).

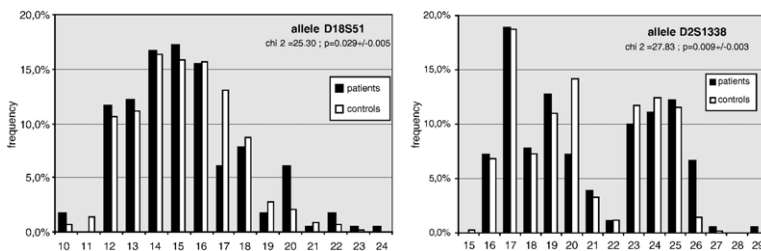


Fig. 2. Allele frequencies of D18S51 and D2S1338 loci in schizophrenic patients and controls.

4. Discussion

When patients and controls from Poland were compared a statistically significant overall difference in allele distribution was observed. Significantly higher frequency of 7 allele and significantly lower frequency of 9.3 allele in TH01 locus was found in patients than in controls. Our research is in agreement with the results obtained by Jönsson et al. [4] and at variance with Meloni et al. [5]. Similarly to TH01 locus in D16S539 locus, the shortest alleles are significantly more often in patients as compared with controls.

Contrary to that, the longest alleles with the highest number of tandem repetitions i.e. 20–24 in D18S51, and 26–29 in D2S1338 were detected significantly more often in patients than in controls. There is an analogy with expansion of trinucleotide repeat sequences in the genome as a risk factor in major psychiatric disorders [6].

In conclusion, the association displayed between polymorphism of 4 out of 14 investigated STR markers and neuropsychiatric disorders needs further investigation in larger samples of patients.

Acknowledgements

This work was supported by the Grant of Medical University of Lodz, Poland, No. 502-11-107. The authors thank Dr. Galecki from the Department of Psychiatry and Neurosis Disorders with Crisis Intervention Ward, Medical University of Lodz for collection of blood samples and psychiatric diagnosis.

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