Dopamine receptors genes polymorphisms in Parkinson patients with levodopa-induced dyskinesia
Pozhidaev, I.; Alifirova, V.M.; Freidin, M.B.; Zhukova, I.A.; Fedorenko, O.Y.; Osmanova, D.Z.; Mironova, Y.S.; Wilffert, B.; Ivanova, S.A.; Loonen, A.J.M.

Published in:
European Neuropsychopharmacology

DOI:
10.1016/S0924-977X(17)31129-X

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2017

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Syndrome Scale (PANSS). There were no significant correlations between chlorpromazine equivalent dosage or treatment duration and the level of HERV-K methylation.

**Summary of results:** There was no significant difference in the level of HERV-K methylation between first-episodic schizophrenia patients and healthy controls (40.33 ± 4.85 vs. 40.95 ± 4.10%, p = 0.192). However, there was a negative correlation between the level of HERV-K methylation and PANSS positive symptoms score (r = −0.352, p = 0.017). Linear regression analysis revealed that HERV-K methylation level was a negative predictor of the severity of positive symptoms (B = −0.378, t = −2.688, p = 0.010) after co-varying for chlorpromazine equivalent dosage. HERV-K methylation level was not associated with scores of other PANSS subcales.

**Conclusion:** Our results provide preliminary evidence that HERV-K methylation is not related to schizophrenia susceptibility. However, the level of HERV-K methylation might be associated with the severity of positive symptoms. Future studies in larger samples are required to confirm results of this study.

**Reference**


**P.1.a.025 Dopamine receptors genes polymorphisms in Parkinson patients with levodopa-induced dyskinesia**

I. Pozhidaev1*, V.M. Alifirova2, M.B. Freidin3, I.A. Zhukova2, O.Y. Fedorenko1, A.Z. Osmanova1, Y.S. Minnova2, B. Wilfert4, S.A. Ivanova1, A.M. Loonen5  
1Mental Health Research Institute, Molecular Genetics and Biochemistry, Tomsk, Russia; 2Siberian State Medical University, Neurology and Neurosurgery, Tomsk, Russia; 3Research Institute for Medical Genetics, Laboratory of Population Genetics, Tomsk, Russia; 4Groningen Research Institute of Pharmacy, Pharmacotherapy and Clinical Pharmacology, Groningen, The Netherlands; 5Groningen Research Institute of Pharmacy, Pharmacotherapy in Psychiatric Patients, Groningen, The Netherlands

**Introduction:** Long-term levodopa treatment of Parkinson’s disease (PD) is frequently complicated by spontaneously occurring involuntary muscle movements called levodopa-induced dyskinesia (LID). LID are a substantial barrier to effective symptomatic management of Parkinson’s disease (PD), as up to 45% of L-DOPA users develop LID within 5 years [1]. The exact pathological mechanism of this complication has not yet been elucidated. A lot of studies nowadays which approved complex genetic nature of LID. And these genes are involved not only for oxidative stress, but in drug metabolism too [2–4].

**Objective:** This study aimed to investigate a possible contribution of polymorphic variants of DRD1, DRD2, DRD2/ANKK1, DRD3, DRD4 genes in the development of LID in PD patients.

**Methods:** 212 patients with Parkinson’s disease on levodopa therapy were investigated. Dyskinesia was measured by using Abnormal Involuntary Movement Scale (AIMS). DNA extraction and fluorogenic 5’-exonuclease TaqMan genotyping assays were conducted according to standard protocols and blind to clinical status of the subjects. Genotyping was carried out on 28 SNPs of dopamine receptors (rs4532, rs936461, rs6275, rs1801028, rs4245147, rs134655, rs6277, rs1076560, rs2283265, rs179997, rs6279, rs1076562, rs2734842, rs2734849, rs11721264, rs167770, rs3773678, rs963468, rs7633291, rs2134655, rs9817063, rs324035, rs1800828, rs167771, rs6280, rs1587756, rs3758653, rs11246226) on the MassARRAY® Analyzer 4 (Agena Biosciencis) using the set SEQUENOM Consumables iPLEX Gold 384. SPSS software was used for statistical analysis. Statistical significance of the association testing was established using permutations. P-value <0.05 after permutations was considered statistically significant.

**Results:** Patients in our cohort demonstrated typical PD demographics, with a mean age of onset of 60.04 ± 9.46 years, a mean disease duration of 9.79 ± 5.57 years. Dyskinesia was reported in 57 (26.9%) patients. The distribution of genotypes of studied genes corresponded to the Hardy-Weinberg equilibrium. We found that 5 polymorphisms (rs4245147, rs6275, rs2734842, rs6279, rs1076562) are significantly associated with LID. All these polymorphisms are located in DRD2 gene. In logistic regression models adjusted for the covariates, such as age, gender and duration of disease only one of the studied markers was associated with LID (rs4245147). Odds ratio for carriers of the genotype TT is 1.73 [95% CI: 1.12–2.70], which indicates the predisposing effect of this genotype on the development of dyskinesia. Polymorphisms in the dopamine receptors genes play significant role in the therapy response to L-DOPA as well as in various of its adverse effects. We hypothesized that single nucleotide polymorphisms in DR genes may result in a clinical phenotype contributing to an increased risk of LID. This appears to be especially true for rs4245147 of the DRD2 gene. Hence, this gene polymorphism is a good candidate for studying (genetic) biomarkers predicting the risk of developing this movement disorder.

**Conclusion:** Rs4245147 polymorphism of the DRD2 gene is a putative component of a set of biomarkers predicting the vulnerability to develop dyskinesia.

**References**


**P.1.a.026 Association between polymorphisms of the PCDH15 gene and schizophrenia in Korean population**

Y. Choi1*, W. Kang1, E. Kim2, J. Kim1  
1School of Medicine, Kyung Hee University, Department of Neuropsychiatry, Seoul, South-Korea; 2Nowon Eulji Medical Center, Eulji University, Department of Neuropsychiatry, Seoul, South-Korea

**Objective:** Protocadherin 15 (PCDH15) gene, which encodes a member of the cadherin superfamily that plays a crucial role in hair cell sensory transduction and contributes to neural development