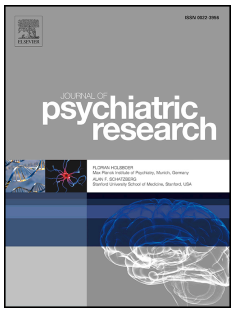
Accepted Manuscript



Quantification of cell-free DNA in blood plasma and DNA damage degree in lymphocytes to evaluate dysregulation of apoptosis in schizophrenia patients

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PII: S0022-3956(16)30224-2

DOI: 10.1016/j.jpsychires.2016.12.006

Reference: PIAT 3019

To appear in: *Journal of Psychiatric Research*

Received Date: 16 August 2016

Revised Date: 18 November 2016

Accepted Date: 1 December 2016

Please cite this article as: Ershova ES, Jestkova EM, Chestkov IV, Porokhovnik LN, Izevskaya VL, Kutsev SI, Veiko NN, Shmarina G, Dolgikh O, Kostyuk SV, Quantification of cell-free DNA in blood plasma and DNA damage degree in lymphocytes to evaluate dysregulation of apoptosis in schizophrenia patients, *Journal of Psychiatric Research* (2017), doi: 10.1016/j.jpsychires.2016.12.006.

QUANTIFICATION OF CELL-FREE DNA IN BLOOD PLASMA AND DNA DAMAGE DEGREE IN LYMPHOCYTES TO EVALUATE DYSREGULATION OF APOPTOSIS IN SCHIZOPHRENIA PATIENTS

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Abstract

Oxidative DNA damage has been proposed as one of the causes of schizophrenia (SZ), and *post mortem* data indicate a dysregulation of apoptosis in SZ patients. To evaluate apoptosis *in vivo* we quantified the concentration of plasma cell-free DNA (**cfDNA** index, determined using fluorescence), the levels of 8-oxodG in cfDNA (immunoassay) and lymphocytes (**FL1-8-oxodG** index, flow cytometry) of male patients with acute psychotic disorders: paranoid SZ (total N=58), schizophreniform (N=11) and alcohol-induced (N = 14) psychotic disorder, and 30 healthy males. **CfDNA** in SZ (N=58) does not change compared with controls. In SZ patients. elevated levels of 8-oxodG were found in cfDNA (N =58) and lymphocytes (n = 45). The main sources of cfDNA are dying cells with oxidized DNA. Thus, the **cfDNA/FL1-8-oxodG** ratio shows the level of apoptosis in damaged cells. Two subgroups were identified among the SZ patients (n=45). For *SZ-1* (31%) and *SZ-2* (69%) median values of **cfDNA/FL1-8-oxodG** index are related as 1:6 ($p < 0.0000001$). For the patients with other psychotic disorders and healthy controls, **cfDNA/FL1-8-oxodG** values were within the range of the values in *SZ-2*. Thus, apoptosis is impaired in approximately one-third of SZ patients. This leads to an increase in the number of cells with damaged DNA in the patient's body tissues and may be a contributing cause of acute psychotic disorder.

Keywords: schizophrenia, cell- free DNA, cfDNA, oxidized DNA, 8-oxodG, lymphocytes

Highlights

- Cell-free DNA quantity (**cfDNA**) was determined for the first time in plasma of SZ patients.
- A high level of 8-oxodG was found in cell-free DNA of SZ patients.
- A high level of 8-oxodG (**FL1-8-oxodG**) was found in SZ lymphocytes.