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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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#### ACCEPTED MANUSCRIPT

- 1 QUANTIFICATION OF CELL-FREE DNA IN BLOOD PLASMA AND DNA DAMAGE
- 2 DEGREE IN LYMPHOCYTES TO EVALUATE DYSREGULATION OF APOPTOSIS
- 3 IN SCHIZOPHRENIA PATIENTS
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#### 11 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
- 17 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
- 21 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.

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

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#### 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.

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