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*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):*

Boiko, A. S., Kornetova, E. G., Ivanova, S. A., & Loonen, A. (2017). Potential biomarkers of tardive dyskinesia: A multiplex analysis of blood serum. S945-S946. Abstract from 30th ECNP Congress - Paris 2017, .

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# Potential Biomarkers Of Tardive Dyskinesia: A Multiplex Analysis Of Blood Serum

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## Introduction

Long-term antipsychotic treatment of schizophrenia is associated with the emergence of tardive dyskinesia (TD), a motor syndrome consisting of involuntary and hyperkinetic movements [1]. Pathogenesis of this drug-induced movement disorder is not yet fully established, but may be connected to oxidative stress-related indirect pathway neurotoxicity [2]. Dysregulations in immune, hormonal and neurotrophic systems have been postulated to be one of the mechanisms underlying this form of neurotoxicity [3, 4]. Principle aims of translational psychiatric research are searching for biomarkers which can be used to diagnose pathological biochemical processes and to identify molecular targets for treatment as well as development of pharmacogenetic approaches to personalize this therapy.

## Aims

The aim is to study potential endocrine, neurotrophic and immunological markers of tardive dyskinesia in the blood serum of patients with schizophrenia with antipsychotic therapy.

## Methods

After obtaining approval of the study protocol by the local ethical committee, suitable participants were recruited from psychiatric hospitals. All subjects gave informed consent after proper explanation of the study. TD was assessed cross-sectionally by the use of the Abnormal Involuntary Movement Scale (AIMS) [1, 5]. The concentrations of cortisol, brain-derived neurotrophic factor (BDNF), prolactin, cytokines (tumor necrosis factor (TNF $\alpha$ ), interleukin 1 (IL-1 $\beta$ ), interleukin 3 (IL-3), interleukin 6 (IL-6), interferon gamma (INF- $\gamma$ ) and S100 $\beta$ ) were measured in blood serum using the MILLIPLEX<sup>®</sup> MAP panels (Merck, Darmstadt, Germany) by the multiplex analyzer MAGPIX (Luminex, USA). Statistical analyses were performed using SPSS software for Windows. Results were expressed as median and quartile intervals (Me [Q<sub>1</sub>; Q<sub>3</sub>]) or mean and standard deviation (M $\pm$ SD). Differences were considered significant at  $p \leq 0.05$ .

## Results

In total 180 patients with schizophrenia, 128 males and 52 females (age 39.2 $\pm$ 12.1 years), receiving long-term antipsychotic treatment were included. These patients were divided into two groups: 71 patients with tardive dyskinesia and 109 patients without this movement disorder. A significant ( $p=0.04$ ) decrease in BDNF concentration was observed in patients with TD (1.9 [1.01; 2.99] ng/ml) in comparison to patients without TD (2.66 [1.29; 3.89] ng/ml) (Fig.1). An increase ( $p=0.05$ ) of the serum IL-6 level of patients with TD (5.69 [3.55; 7.4] pg/ml) was detected relative to patients without TD (4.69 [2.82; 6.13] pg/ml) (Fig.2). In addition, a statistical trend ( $p=0.06$ ) of increased serum S100 $\beta$  concentration was found in TD patients (85.29 $\pm$ 5.53 ng/L) compared to patients without this side effect (75.14 $\pm$ 2.81 ng/L) (Fig.3). No other significant differences were established concerning the other assayed biomarkers.

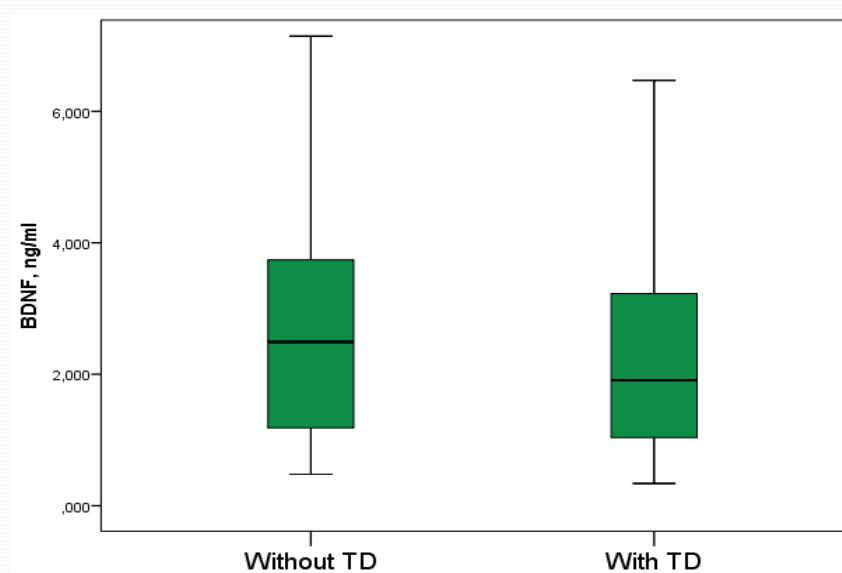


Fig.1. Concentration of BDNF in the blood serum of patients with schizophrenia (Me [Q<sub>1</sub>; Q<sub>3</sub>]).

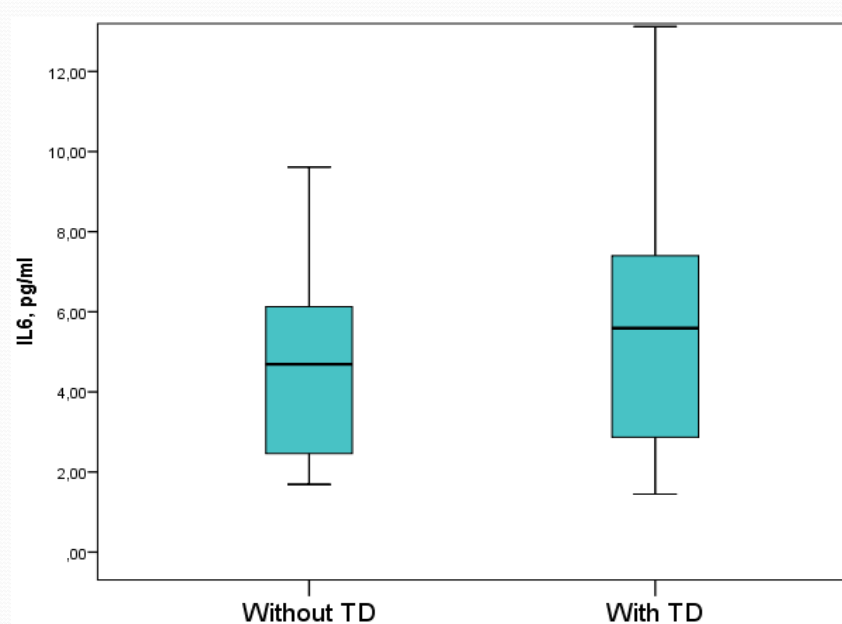


Fig.2. Concentration of IL-6 in the blood serum of patients with schizophrenia (Me [Q<sub>1</sub>; Q<sub>3</sub>]).

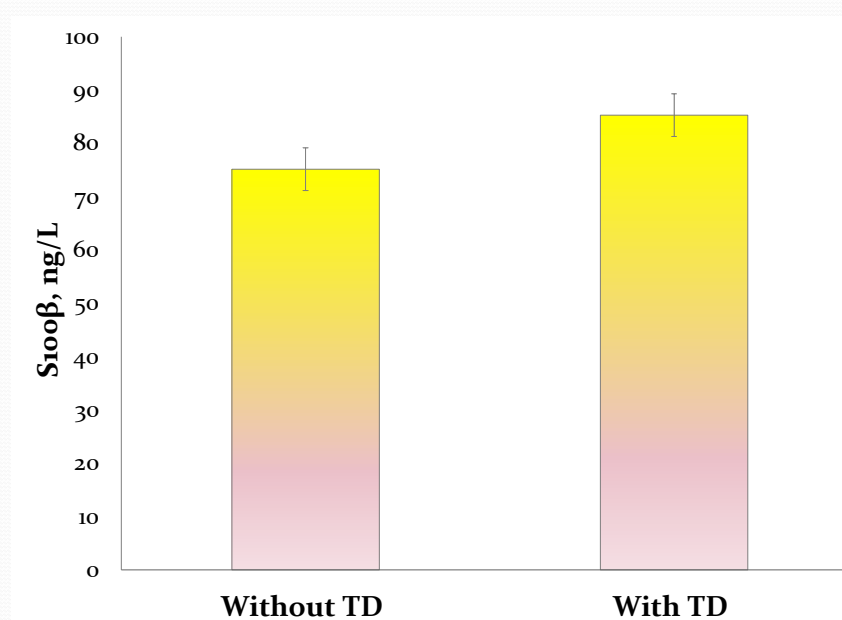


Fig.3. Concentration of S100 $\beta$  in the blood serum of patients with schizophrenia (M $\pm$ SD).

## Discussion

The biological processes that might play a role in the development of TD are not confined to the human brain per se. Hormonal and immune systems are also involved, which may be related to these systems being closely interrelated. Furthermore, these parameters may provide information about risk factors of the movement disorder. Identifying markers that can be used as diagnostics or predictors of treatment response in people with tardive dyskinesia will be an important step towards being able to provide personalized treatment.

There is no potential conflict of interest.

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