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Potential biomarkers of tardive dyskinesia

Boiko, A.S.; Kornetova, E.G.; Ivanova, S.A.; Loonen, A.J.M.

Published in:
European Neuropsychopharmacology

DOI:
[10.1016/S0924-977X\(17\)31674-7](https://doi.org/10.1016/S0924-977X(17)31674-7)

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):

Boiko, A. S., Kornetova, E. G., Ivanova, S. A., & Loonen, A. J. M. (2017). Potential biomarkers of tardive dyskinesia: A multiplex analysis of blood serum. *European Neuropsychopharmacology*, 27(Supplement 4), S945-S946. [https://doi.org/10.1016/S0924-977X\(17\)31674-7](https://doi.org/10.1016/S0924-977X(17)31674-7)

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Conclusions: To our knowledge, this is the first study using the 36-item version of the WHODAS scale, of a population 100% diagnosed with schizophrenia treated with PP1M. Overall, most of this patient population did not have or had only mild disability with a perception of their quality of life in line with this level of functionality.

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Disclosure statement: Berta Herrera and Marta García-Dorado are full-time employees of Janssen-Cilag S.A. Miguel Vega Piñero has worked as a speaker and/or advisor and/or research in initiatives and projects promoted by AB- Biotics, Astra-Zeneca, Elli Lilly, Juste, Lundbeck, Otsuka, Pfizer, and Janssen. Sergio Arques Egea has declared that in the last three years has worked as a speaker and/or advisor and/or research in initiatives and projects promoted by Otsuka, Lundbeck, Pfizer, Servier, Rovi, GlaxoSmithKline, Ferrer and Janssen. PICTURE study was sponsored by Janssen Cilag S.A.

P.3.d.027 Food craving evolution in schizophrenic patients starting treatment with clozapine

M. Garriga^{1*}, A. Mallorqui¹, L. Serrano¹, M. Salamero¹, E. Vieta¹, M. Bernardo¹, C. Garcia-Rizo¹ ¹*Hospital Clinic of Barcelona, Psychiatry and Psychology, Barcelona, Spain*

Background: The use of second generation antipsychotics (SGAs) has been the basis of the psychopharmacological treatment since 1960. Among them, clozapine is specially useful for treatment resistant psychosis. However, clozapine and olanzapine are related to the development of metabolic syndrome and weight gain as the most important adverse events related.

Some non conclusive hypothesis have arisen regarding the underlying mechanism of these adverse events in SGA. Amongst them, there is reference in the literature that pointed some increase in food craving for specific nutrients with a high caloric content (e.g., carbohydrates,...) might be involved [1,2].

Aims: To assess the food craving evolution of in those schizophrenic patients starting clozapine treatment during a 18 week period of follow up.

Methods: An observational prospective study of 18 weeks of follow up was performed in a Spanish sample of schizophrenic patients that attend to our Clozapine Unit to initiate treatment. Patients were asked to participate and agree in signing informed consent. The local ethical committee (Hospital Clinica of Barcelona) approved the study.

Anthropometric measures and semi-structured interviews of dietary habits were performed. Food craving was assessed through a validated scale in Spanish: the Food Craving Inventory (FCI-SP) [3]. All measures were performed at the beginning of

clozapine treatment (baseline), at week 8 and at week 18 of treatment.

A factorial analyses was used in order to classify different nutrient components in our sample. Mixed lineal model also evaluate the evolution of food craving through time [4]. SPSS v.19 software was used for statistics.

Results: A sample of 15 patients with schizophrenia was evaluated. The 42% of the sample presented >7% of weight increase at week 8.

The factorial analysis of the FCI-SP classified the different nutrients in three categories:

1. simple carbohydrates (e.g. processed sugar, fruit, dairy) – trans fat (e.g. fast food);
2. complex carbohydrates (e.g. breads, vegetables, nuts, legumes) – proteins (e.g., eggs, meat, fish);
3. saturated fat (e.g. fatty meat, butter).

At 8 weeks of clozapine treatment there is only a significant evolutive increase for nutrients of the “complex carbohydrates – proteins” group ($p = 0.041$). Of those patients that presented >7% of weight increase, there was no association between the evolution of weight and the three different nutrient groups evolution in terms of craving.

Conclusions: Our patients on clozapine treatment presented a significative increase for an specific group of nutrients (“complex carbohydrates – proteins”). There is evidence of these changes early in the treatment (week 8), but they do not seem to be related with weight gain.

Larger samples with a longitudinal follow up would aloud clinicians to better clarify this hypothesis. However, the presented results would help in the elaboration of targeted interventions in adequate programs of diet and weight gain control of patients on SGA.

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P.3.d.028 Potential biomarkers of tardive dyskinesia: a multiplex analysis of blood serum

A.S. Boiko^{1*}, E.G. Kornetova², S.A. Ivanova¹, A.J.M. Loonen³ ¹*Mental Health Research Institute, Tomsk National Research Medical Center of the Russian Academy of Sciences, Laboratory of Molecular Genetics and Biochemistry, Tomsk, Russia;* ²*Mental Health Research Institute, Tomsk National Research Medical Center of the Russian Academy of Sciences, Department of Endogenous Disorders, Tomsk, Russia;* ³*University of Groningen, Groningen Research Institute of Pharmacy, Groningen, The Netherlands*

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.

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 α), interleukin 1 (IL-1 β), interleukin 3 (IL-3), interleukin 6 (IL-6), interferon gamma (INF- γ) and S100 β were measured in blood serum using the MILLIPLEX[®] 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 [Q1; Q3]) 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 ± 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). 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). In addition, a statistical trend ($p = 0.06$) of increased serum S100 β concentration was found in TD patients (85.29 ± 5.53 ng/L) compared to patients without this side effect (75.14 ± 2.81 ng/L). No other significant differences were established concerning the other assayed biomarkers.

Conclusions: 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.

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P.3.d.029 Antidepressant augmentation of antipsychotics in schizophrenia: a systematic review, meta-analysis and metaregression analysis

B. Galling^{1*}, C.U. Correll² ¹Charité Universitätsmedizin, Department of Child and Adolescent Psychiatry, Berlin, Germany; ²The Zucker Hillside Hospital, Psychiatry Research, Glen Oaks, USA

Introduction: Despite a considerable increase in our understanding of schizophrenia due to numerous basic and clinical research studies over the last decades, the etiology and pathophysiology remain rather unclear [1] and medications that effectively treat all dimensions of symptoms are lacking [2]. In particular, all currently approved medications for schizophrenia act via modulation of the dopamine system [3] and treat positive symptoms, agitation, and aggression, while the functionally important domains of negative symptoms and cognitive dysfunction remain relatively unaddressed. This fact has stimulated the search for extra-dopaminergic neurotransmitter modulation to address not only positive symptoms, but also other domains of schizophrenia [1].

Several lines of evidence implicate dysfunction in the serotonergic (5-HT) system in the pathophysiology of psychosis, suggesting an alternate treatment target, specifically a potential role for serotonergic agents, which includes most classes of antidepressants [4,5].

Methods: Systematic PubMed/MEDLINE/PsycINFO/Cochrane Library search from database inception until 07/20/2015, for randomized, double-blind, efficacy-focused trials comparing adjunctive antidepressants vs placebo to antipsychotics in schizophrenia.

Two independent investigators extracted data in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for a random effects meta-analysis to calculate standardized mean differences (SMD) or risk ratios (RRs) $\pm$ their 95% confidence intervals (CIs) for continuous and categorical outcomes, respectively.

Co-primary outcomes were overall symptom reduction and study-defined response. Secondary outcomes included all-cause and specific-cause discontinuation, psychopathology and adverse effects. Pre-specified subgroup and meta-regression analyses (for all studies combined and for blinded studies reporting last-observation-carried-forward (LOCF) data separately).

Data Extraction: Data were extracted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard by two independent investigators.

Results: In a random-effects meta-analysis of 48 studies ($n = 2192$, duration = 10.2 ± 7.6 weeks), antidepressant augmentation outperformed placebo regarding total symptom reduction (studies = 28, $n = 1249$, standardized mean difference (SMD) = -0.36 ,