

## THE ROLE OF HORMONES AND INFLAMMATORY MARKERS IN COGNITIVE FUNCTIONING OF SCHIZOPHRENIC PATIENTS

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### SUMMARY

**Background:** In the literature we can find evidence that immunological processes are involved the alterations of cognition in schizophrenic patients. Another factor, which may have an impact on cognitive domains in this clinical group are hormones.

**Objective:** The objective of this review was to explore studies, in which the role of both immunological and endocrine factors on cognitive functions in schizophrenia are analyzed.

**Methods:** The search of papers covering this topic in PubMed and Google Scholar was performed.

**Results:** The studies focusing on this co-relation are not numerous. The role such hormones like cortisol, insulin and sex hormones may be important in the immunomodulatory processes influencing cognition in schizophrenia.

**Conclusions:** More studies are necessary to confirm these possible co-relations.

**Key words:** immunological processes – hormones -, cognitive functions - schizophrenia

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### Introduction

The immunopathogenesis of schizophrenia was postulated already in the 90-ties (Holden et al. 1997). Since then a number of publications have appeared to support this hypothesis (Muller & Schwarz 2006, Na et al. 2014, Bedrossian et al. 2016, Dickerson et al. 2016, Krysta et al. 2017, Karanikas 2011, Suvisaari & Mantere 2013). Levels of interleukins IL-2 and IL-4, IL-6 and other inflammatory markers were found to be increased of schizophrenic patients (Watanabe et al. 2008, Muller 2017). In the literature we can also find evidence for the co-relations of immunological processes and cognition in schizophrenia. In their systematic review Ribeiro-Santos et al. (2014) proposed that such factors like microglial activation, monoaminergic imbalance, brain abnormalities and the kynurenine pathway may be possible mechanisms leading to cognitive impairment in this psychiatric disorder (Ribeiro-Santos et al. 2014). Dunne et al. (2017) suggested that the level of anti-inflammatory cytokines like Interleukin-10 may be correlated with social cognition in schizophrenia (Dunne et al. 2017). Another group of literature reports focus on the influence of serum hormone levels and cognitive functioning in schizophrenia (Bratek et al. 2015, Moore et al. 2013, Li et al. 2015, Halari et al. 2004). Yuan et al. (2016) in a study involving first episode schizophrenia patients found that testosterone and estradiol may protect cognitive function against recession (Yuan et al. 2016). It is possible that some changes in sex hormone levels in men and women suffering from schizophrenia may lead to certain differences in cognitive functioning

(Bozikas et al. 2010, Krysta et al. 2013). According to other research reports a co-relation can be found between cortisol levels and cognition (Havelka et al. 2016). The objective of this review was to explore studies, in which the role of both immunological and endocrine factors on cognitive functions in schizophrenia are analyzed.

### Hormones and inflammatory markers and cognition in schizophrenia

Chiappelli et al. (2015) performed a study, in which they measured how cognitive deficits might be related to abnormalities in stress response. The participants of their study were tested with a battery of neurocognitive tests. They found that acute cortisol response was inversely correlated with processing speed, and the post-stress Interleukin-6 response was significantly and negatively correlated with working memory. Another observation from this study was an exacerbated immune response to stress in schizophrenic patients, which typically is suppressed in healthy controls. One of the conclusions they draw is that dysregulated cortisol-immune interactions, which is observed in the post-stress Interleukin-6 response, is linked to cognitive abnormalities in schizophrenia (Chiappelli et al. 2016). Dickinson and Harvey (2008) draw the attention to the link of type 2 diabetes and chronic inflammation to impaired cognitive performance in schizophrenia. They propose a hypothesis that insulin resistance interacting with inflammatory processes may be associated with cognitive deficits in schizophrenic patients (Dickinson

& Harvey 2008). An empirical basis for this can be an observation that an association between diabetes and cognitive functioning in schizophrenia was found in earlier studies (Dickinson et al. 2008). Observations from research results indicate that the use of estrogenic drugs may mimic the anti-inflammatory activity of 17beta-estradiol and have a beneficial effects against neurodegeneration (Pozzi et al. 2006). Weickert et al. (2016) in their study observed that the impact of sex hormones on cognitive functioning in schizophrenia may be different that in healthy controls. They discuss a possible role anti-inflammatory effects of oestrogen in the treatment of cognitive deficits (Weickert et al. 2016)

## Conclusions

Clinical reports show benefits from augmenting antipsychotic treatment with estrogens or selective estrogen receptor modulators. Different mechanism of action of these drugs are discussed (Bratek et al. 2016). Although the literature data referring to the role of hormones and inflammatory markers is not very rich, we have some observations that some hormones, like estrogen may have and anti-inflammatory effects, which may be advantageous in the treatment of cognitive deficits (Weickert et al. 2016). The role of other hormones, like cortisol is also very important, as it is observed that the stress response resulting in inflammatory markers response schizophrenia may be linked to cognitive abnormalities in schizophrenia. However due to limited literature data the above conclusions must be cautious and more research studies are necessary to confirm these possible co-relations.

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## Contribution of individual authors:

Krysta K and Krzystanek M designed the concept of the manuscript and performed the search,

Cubala WJ and Wiglusz MS derived and analysed the data.

Jakuszkowiak Wojten K, with Czarnowska-Cubala M, Szarmach J and Włodarczyk A wrote the manuscript in consultation with Janas-Kozik M.

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