

INFULENCE OF SEX HORMONES AND INFLAMMATORY PROCESSES ON COGNITION IN SCHIZOPHRENIA

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SUMMARY

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

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

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

Results: Endocrine factors like: testosterone, estrogen, as well as immunomodulatory are observed to play a role in cognitive functioning in schizophrenia.

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

Key words: immunological processes - sex hormones - cognitive functions - schizophrenia

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INTRODUCTION

Cognitive deficits in schizophrenia are important symptoms, which may be mild to moderated are modestly related to negative symptoms (Keefe et al. 2006). There are different factors which may have an influence on neuropsychological functioning by schizophrenic patients. One of them is medication. According to a number of studies atypical antipsychotic drugs are regarded as being superior to the typical ones in terms of their impact of cognitive functions (Meltzer and McGurk 1999, Klasik et al. 2011). Another condition that may modify this domain in schizophrenia is drug abuse (Wobrock et al. 2013). In the literature we can also find reports focusing on the influence of serum hormone levels and cognitive functioning in schizophrenia (Bratek et al. 2015, Moore et al. 2013, Li et al. 2015). Yuan et al. (2016) in a study involving first episode schizophrenia patients found that testosterone and estradiol may protect cognitive function against recession. 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). 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, 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). The objective of this review was to explore studies, in which the role immunological and endocrine factors on cognitive functions in schizophrenia are analyzed.

METHODS

This review was focused on the impact of sex hormones and inflammatory processes on the cognitive functioning of schizophrenic patients. In order to achieve this result PubMed and Google scholar were searched (effective date 30.07.2019). During our search we used following terms: (cognitive functions (Title/Abstract) OR schizophrenia (Title/Abstract)) AND sex hormones (Title/Abstract) OR inflammatory markers OR memory OR attention OR neuropsychological symptoms OR AND (humans (MeSH Terms) AND English (lang).

RESULTS

Sex hormones and cognitive functions in schizophrenia

A number of research results show, that there is a correlation between the levels of sex hormones and the cognitive functioning in schizophrenic patients. According to Ko at al. (2006). there is an association between serum levels of estrogen and reduced performance in cognitive function, especially verbal performance and executive functioning in schizophrenic women of reproductive age. Yuan et al. (2016) observed that endogenous testosterone and estradiol are protective factors against the recession of cognitive functions in the first episode of schizophrenia. In another study, performed in the population of older female schizophrenic patients, it was found, that estrogen interacts with the dopaminergic system and in this way it affects cognition (Searles et al. 2018). In the study by Halari et al. (2004), which investigated the effects of serum levels of oestrogen, progesterone, testosterone and cortisol on neuropsychological functioning and psychopathology in schizophrenia

it was found that oestrogen and age was co-related with lower intensity of positive symptom scores, and in the analysis of differences between men and women, cortisol was associated with poor performance on information processing in men. Moore et al. (2013) analyzed the correlation between hormone levels (testosterone, estrogen, and prolactin), cognitive function and general symptoms of chronically ill male patients with schizophrenia or schizoaffective disorder. A correlation was found between circulating testosterone levels and the performance on verbal memory, processing speed, and working memory in examined subjects. Rubin et al. (2015) postulated that oxytocin, the level of which does not change during the menstrual cycle, may have a stronger positive impact on some cognitive domains than estrogens in schizophrenia. According to McGregor et al. (2017) the protective action of estrogens in schizophrenia, which affects also cognitive functioning, is correlated with the functional outcome of the disease. The results of the study by Gurvich et al. (2018) revealed that in females with schizophrenia, menstrual cycle irregularity predicted significantly poorer cognitive performance in the areas of psychomotor speed, verbal fluency and verbal memory.

Inflammatory markers and cognitive functions in schizophrenia

There is a group of research findings suggesting that inflammatory processes are associated with worse cognitive performance in schizophrenia. Possible mechanism of this process are: microglial activation, monoaminergic imbalance, brain abnormalities and the kynurenine pathway (Ribeiro-Santos et al. 2014). Negative associations between inflammatory markers and general cognitive abilities were found in the study by Hope et al. (2015). The role of peripheral inflammation might and cognitive deficits in schizophrenia and bipolar disorder were also discussed by Misiak et al. (2018). Kogan et al. (2018) found evidence that the increased inflammation is correlated with cognitive deficits and worse daily functioning in schizophrenic patients (Kogan et al. 2018). Dunne et al. (2017) found that the cytokines IL-10 and MDC are associated with the social cognition in schizophrenia. Bora et al. (2019) discussed the role of the elevated CRP and reduced BDNF levels in schizophrenia in the cognitive functioning in schizophrenia. According to the authors, due to small effect sizes of the observed correlations further studies are needed to confirm this phenomenon.

Implications for treatment

Clinical reports show benefits from augmenting anti-psychotic treatment with estrogens or selective estrogen receptor modulators. Different mechanism of action of these drugs are discussed (Bratek et al. 2016). Although literature data referring to the role of hormones and inflammatory markers is not very rich, we have obser-

vations 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).

CONCLUSIONS

Due to limited literature data the suggestions for the therapy of cognitive dysfunction in schizophrenia must be cautious and more research studies are necessary to confirm these possible co-relations.

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Krzysztof Krysta; design of the review, literature researches and analyses, interpretation of data, manuscript writing.

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