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Inflammation in schizophrenia with metabolic syndrome

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after 1 or 14 days differentiation for MGLs and at day 0 (hiPSC stage) and after 10, 14 and 18 days of differentiation for NPCs. qPCR demonstrated MGLs expressed microglia signature genes (*TMEM119, CX3CR1 and MERTK*) after 14d differentiation, whilst NPCs after 20d differentiation expressed *Pax6* and *Zeb2*. One-way ANOVA analysis of *IFNgR1* (NPCs p=0.79, Eta2=0.12; MGLs p=0.73, Eta2= 0.10), *IFNgR2* (p=0.33, Eta2=0.34; MGLs p=0.80, Eta2= 0.07), *TNFaRSF1A* (NPCs p =0.1, Eta2=0.53; MGLs p=0.83, Eta2= 0.06) and *IL6ST* (gp130; NPCs p=0.09, Eta2=0.54; MGLs p=0.77, Eta2= 0.083) confirmed that transcripts for these receptors were expressed from day 0, and did not change with increasing differentiation time across both cell types. *IL6R (gp80)* expression in MGLs was also present from day 0 with no differences across all time-points (1-way ANOVA: p=0.25, Eta2=0.37). In contrast, *IL6R (gp80)* gene expression in NPCs significantly differed across time-points (1-way ANOVA $F_{(3,8)}$=227; p=<0.001; Eta2= 0.99). Post-hoc testing (Bonferroni) confirmed significantly reduced expression of IL6R mRNA in NPCs after 10, 14 and 18 days of differentiation (all p=<0.001).

Collectively, these data confirm that hiPSC-derived NPCs and MGLs express receptor transcripts for cytokines implicated in MIA, with the exception of IL6R in NPCs. These data suggest a hypothesis that MGLs are responsive to exogenous IL-6 stimulation, but NPCs are not. Confirmation of receptor signal transduction following IL-6 stimulation (phosphorylation of STAT3), expression of its downstream genes and cytokine secretion is underway to confirm this using western blot, qPCR and cytokine arrays respectively. The outcome of these experiments will confirm whether a neuron-microglia co-culture system is required to study the neurodevelopmental effects specific to IL-6.

No conflict of interest

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Inflammation in schizophrenia with metabolic syndrome: features of the cytokine spectrum

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Background: The incidence of metabolic syndrome (MetS) in schizophrenia is two times higher than in the general population and amounts up to 58% [1]. The use of antipsychotics leads to metabolic disorders that complicate the course of the underlying disease and reducing the quality of life [2,3]. Antipsychotics are associated with an increased risk for several physical diseases, including obesity, dyslipidemia, diabetes mellitus, which ultimately contribute to an increased risk for cardiovascular disease [4]. It has been suggested that the effects of inflammatory mediators causally contribute to the pathophysiology of schizophrenia and diabetes that accompanies the disorder. Several studies have delivered evidence for specific cytokine alterations in schizophrenia [5].

Objective: The aim of the study is to investigate characteristics of cytokines spectrum in patients with schizophrenia with and without metabolic syndrome.

Methods: This study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki 1975; 2013), established for experiments involving humans. After obtaining approval of the study protocol, suitable participants were recruited from psychiatric hospitals. Complex clinical examination of 136 patients with schizophrenia (ICD-10: F20) was carried out (50.35% males и 49.65% females). The average age – 35.66±10.17 years. All patients received long-term antipsychotic treatment. Patients were divided into two groups: 48 with MetS and 88 without MetS according to IDF-criteria (2005). The cytokine concentrations were determined on a MAGPIX analyzer (Luminex, USA) using xMAP® Technology with a panel HCYTMAG-60K-PX41 (Merck, Germany) on the base The Core Facility "Medical Genomics" (Tomsk NRMC). The multiplex kit includes 41 cytokines: sCD40L, IL-9, EGF, IL-10, Eotaxin, IL-12 (p40), FGF-2, IL-12 (p70), Flt3, IL-13, Fractalkine, IL-15, G-CSF, IL-17A, GM-CSF, IP-10, GRO, MCP-1, IFNα2, MCP-3, IFNγ, MDC, IL-1α, MIP-1α, IL-1β, MIP-1β, IL- 1Ra, PDGF-AA, IL-2, PDGF-AB/BB, IL-3, RANTES, IL-4, TGFα, IL-5, TNFα, IL-6, TNFβ, IL-7, (LTA), IL- 8, VEGF-A. Differences were considered significant at p<0.05.

Results: Analysis of the results revealed a number of features of 10 cytokines from the studied spectrum. A significant increase in the concentration of Flt3L (p=0.007), IL-10 (p=0.036), MDC (p=0.004) and MCP-1 (p=0.01) is observed in schizophrenia patients with MetS compared to patients without it. However, lower levels of FGF-2 (p=0.023), GM-CSF (p=0.004), PDGF-AB/BB (p=0.027) and IL-2 (p=0.004)

were found in the same group of patients with MetS. An increase in TNFα and G-CSF is observed, but the differences are at the level of a statistical trend (p=0.06 and p=0.055, respectively). Spearman's correlation analysis was performed in groups of patients with schizophrenia to assess the relationship between cytokines. A distinctive feature of the group of patients with MetS is a smaller number of significant correlations relative to patients without MetS.

Conclusion: We identified an imbalance, dysregulation and disturbance of relationships in the cytokine spectrum in schizophrenia with MetS. A number of immune destructions are observed in patients with MetS, which worsen the functioning of patients and the course of the main mental disorder.

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Errors in the visual system and cognitive deficit in patients with schizophrenia

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Background: For a long, it has been believed that there were no marked sensory disturbances in schizophrenia, but subsequently higher values of the vision thresholds have been found in patients compared with healthy people, which led to an increase in experiments both in visual and in other modalities. It remains unclear where the failure occurs, at what stage of information transfer in sensory impairment. Are sensory dysfunctions independent, or is it a consequence of cognitive impairment, such as attention, memory, or thinking.

Methods: The study was conducted on the basis of the National Research Medical Center of Psychiatry and Neurology" named after V. M. Bekhterev. The study involved 37 patients with a diagnosis of F20 according to ICD criteria of 10, and 20 healthy subjects, men and women aged 18-45. Patients with schizophrenia, depending on their response to treatment, were divided into two groups: patients with manifestations of therapeutic resistance and non-resistant patients.

The study consisted of 3 parts:1. Determination of the differential threshold of the length of the length segment. 2. Motor analysis of the length segment. 3. A study of the cognitive functions of patients with schizophrenia using a battery of BACS tests. Incentives were presented on the computer screen: two identical segments, one located above the other, the distance between the segments 7.5 cm. The subjects did not know that the segments were the same. In each trial the upper shaft was the etalon and subject had to change the length of the lower shaft by pressing the keys "up" or "down". The task was to equalize the lengths of both central shafts. In the second part, the tracking task was used for sensorimotor responses.

Results: As a result of the study, a strong negative (and in the text positive, worse function - worse threshold) relationship was found between the magnitude of the error in estimating the length of the segments and the cognitive functions that were measured on the BACS scale both in the general group of patients (r = -0.84), so and in separate groups (for resistant r = -0.89, and for non-resistant r = -0.79). The worse the patient coped with the tasks "Tower of London" and "Encryption", the higher he had an error in assessing the size of two segments (r = -0.72, r = -7.52). A similar trend was noted in the tasks "Speech fluency", "Verbal memory", "Order of numbers" (r = 0.58, r = 0.57, r = 0.50). Connection evaluation results, the error value of the segments evaluation with the "Motor Test" turned out to be lower than the significance level (r = -0.22).

Conclusions: The relationships obtained in our studies support the hypothesis that differences in threshold values in the problem of distinguishing stimuli using the method of adjustment are consistent with the involvement of cognitive functions in the evaluation process, rather than an independent sensory impairment.

No conflict of interest

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Facial emotion recognition in first-episode psychosis: correlations with functionality and quality of life

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