POSSIBLE ROLE OF TGF-B PATHWAYS IN SCHIZOPHRENIA

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MOGUĆA ULOGA TGF-B SIGNALNIH PUTEVA U SHIZOFRENIJI

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ABSTRACT

The phenomenological uniqueness of each patient with schizophrenia is determined by complex symptomatology, particularly the overlapping of symptoms and their prominence in certain phases of this mental disorder. Establishing biological markers is an important step in the further objectivisation and quantification of schizophrenia. Identifying the cytokine profiles that precede a psychotic episode could direct the strategies for relapse prevention and be useful in predicting disease progression and treatment response. In the context of inflammation, TGF-β exerts potent anti-inflammatory and immunosuppressive functions by inhibiting pro-inflammatory cytokine synthesis, but it can also have pro-inflammatory functions through its stimulatory effects on inflammatory Th17 cells. It has been shown that the T helper cell type-1 and type-17 responses are reduced and type-2 response is increased in patients with schizophrenia. Both data from the literature and our results also indicate the presence of an anti-inflammatory response through production of the TGF-β regulatory cytokine. A meta-analysis of plasma cytokine alterations suggested that TGF-β is the state marker for acute exacerbation of schizophrenia, and we showed that TGF-β can also be a valuable marker for psychosis. Hyperactivity of TGF-β signalling pathways in schizophrenia may be both a neuroprotective mechanism and a possible therapeutic target.

Keywords: *schizophrenia, biomarkers, TGF-β, neuroplasticity*

SAŽETAK

Konstelacija simptoma opservirana kod svakog pacijenta sa shizofrenijom je jedinstvena i može se menjati progresijom bolesti. Aktuelni pokušaji objektivizacije i kvantifikacije u shizofreniji obuhvatili su i istraživanja bioloških markera ovog poremećaja. Određivanje specifičnih citokinskih profila u prodromalnoj fazi poremećaja može usmeriti nove strategije prevencije relapsa i biti od koristi u predviđanju toka bolesti i odgovora na terapiju. U kontekstu inflamacije, TGF-β ispoljava snažnu antiinflamatornu i imunosupresivnu aktivnost sprečavanjem sinteze proinflamatornih citokina, ali može imati i proinflamatornu ulogu stimulacijom inflamatornih Th17 ćelija. Pokazano je da su imunski odgovori tipa-1 i tipa-17 oslabljeni i tip-2 odgovor pojačan kod pacijenata sa shizofrenijom. Podaci iz literature i naši rezultati ukazuju i na antiinflamatorni odgovor u shizofreniji sekrecijom regulatornog citokina TGF-β. Meta- analiza studija, koje su određivale plazmatske nivoe citokina pacijenata sa shizofrenijom, ukazala je na TGF-β kao marker pogoršanja shizofrenije, a naši rezultati takođe pokazuju da TGF-β može biti koristan marker psihoze. Hiperaktivnost TGF-β signalnih puteva u shizofreniji može biti neuroprotektivni mehanizam i potencijalni terapijski cilj.

Ključne reči: *Shizofrenija, biomarkeri, TGF-β, neuroplastičnost*

INTRODUCTION

The phenomenological uniqueness of each patient with schizophrenia is determined by complex symptomatology, particularly the overlapping of symptoms and their prominence in certain phases of this mental disorder (1). Different approaches to evaluating and characterising schizophrenia can lead to misunderstandings among clinicians and researchers (2).

To address this problem, reliable diagnostic criteria have been defined (3, 4). Additionally, clinical assessment scales are used to evaluate the severity of illness and the degree of treatment response. New diagnostic criteria should account for the knowledge gained over the past 20 years, especially in the field of neurobiology of mental disorders (5). Establishing biological markers is an important step in

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