

FFT-P1 KAKO DIJABETES TIP 2 UTIČE NA TRANSKRIPTOM PREFRONTALNOG KORTEKSA: SAZNANJA IZ MODELA DIJABETESA TIP 2 KOD STARIJIH ŽENKI PACOVA

K. Jezdić, J. Ivanović, V. Todorović, T. Stanković, A. Santrač, J. Arandelović Ilić

Univerzitet u Beogradu – Farmaceutski fakultet, Beograd, Srbija

Žene srednjih godina nalaze se na prekretnici kada je reč o zdravlju mozga i riziku od neurodegenerativnih oboljenja, a ovu ranjivost dodatno mogu pogoršati česta metabolička stanja kao što je dijabetes tipa 2 (T2D). Alchajmerova bolest je češća u ovoj populaciji nego kod muškaraca, a pojedini podaci ukazuju i na veću učestalost kognitivnog propadanja kod žena nego kod muškaraca sa T2D. Uprkos tome, postoje ograničeni dokazi o molekularnim mehanizmima u mozgu kod žena, i u kliničkim i u prekliničkim istraživanjima, uključujući transkriptomsko profilisanje prefrontalnog korteksa (pfc), regije mozga uključene u kognitivne funkcije. Zbog toga smo modelovali T2D kod ženki pacova i sprovedi analizu transkriptomike u pfc.

Starije ženke Sprague-Dawley pacova hranjene visokomasnom dijetom i tretirane niskom dozom streptozotocina predstavljale su T2D grupu, dok je kontrolna grupa (CTRL) dobijala standardnu dijetu i odgovarajući rastvarač. Sekvenciranje ukupne RNK je sprovedeno na tkivu pfc iz eksperimentalnih grupa, uz naknadnu kontrolu kvaliteta, normalizaciju i analizu diferencijalno eksprimiranih gena (DEG), kao i analizu molekularnih puteva u KEGG bazi podataka u internet alatu GeneCodis 4.

U pfc, prvih deset molekularnih puteva na osnovu DEGs u T2D grupi u poređenju sa CTRL odnosilo se na bazalne transkripcione faktore, sekreciju pankreasa, aldosteronom regulisanu reapsorpciju natrijuma, apsorpciju minerala, sekreciju insulina, degradaciju lizina, sintezu tiroidnih hormona, varenje i apsorpciju ugljenih hidrata, metabolizam glicerofosfolipida i reapsorpciju bikarbonata u proksimalnim tubulima.

Ovi podaci upućuju da žene ne bi trebalo zanemarivati u ovakvim istraživanjima, jer naši rezultati sugerišu T2D-indukovane promene na nivou hormona, elektrolita i metabolizma na nivou pfc.

Zahvalnica

Ovo istraživanje je podržano od strane Fonda za nauku Republike Srbije, 10203, pod nazivom: "Translational road to elucidate the effects of GLP-1 receptor agonist treatment on adipose tissue-brain axis function in cognitive processes in diabetes type 2 with concomitant obesity – CoD-GOAT".

FFT-P1 HOW DOES DIABETES TYPE 2 AFFECT PREFRONTAL CORTEX TRANSCRIPTOME: INSIGHTS FROM DIABETES TYPE 2 MODEL IN AGING FEMALE RATS

K. Jezdić, J. Ivanović, V. Todorović, T. Stanković, A. Santrač, J. Arandelović Ilić

University of Belgrade – Faculty of Pharmacy, Belgrade, Serbia

Middle-aged women are at a crossroads in terms of their brain health and risk of neurodegenerative disorders, and this vulnerability may be further exacerbated by common metabolic conditions such as diabetes type 2 (T2D). Alzheimer's disease is more prevalent in this population compared with men, and some data also suggest higher prevalence of cognitive decline in females versus males with T2D. Nevertheless, there is limited evidence on the underlying brain molecular mechanisms in females in both clinical and preclinical research, including transcriptomic profiling of the prefrontal cortex (pfc), as brain region involved in cognitive functions. Therefore, we modeled T2D in female rats and performed transcriptomic analysis of the pfc.

Middle-aged female Sprague-Dawley rats fed by high-fat diet and treated with low-dose streptozotocin were selected as T2D group, while control group (CTRL) received control diet and was treated by solvent. Bulk RNA sequencing was performed on pfc tissue from the respective experimental groups, followed by quality control, normalization, and differential expression analysis. Pathway enrichment analysis based on KEGG database was then conducted in GeneCodis 4 web tool.

In pfc, the top 10 significantly enriched pathways in T2D females vs CTRL females were to basal transcription factors, pancreatic secretion, aldosterone-regulated sodium reabsorption, mineral absorption, insulin secretion, lysine degradation, thyroid hormone synthesis, carbohydrate digestion and absorption, glycerophospholipid metabolism, and proximal tubule bicarbonate reclamation.

These findings suggest that females should not be neglected in research, as our insights implicate hormone-related, electrolyte, and metabolic mechanisms in T2D-associated pfc changes.

Acknowledgement

This research was supported by the Science Fund of the Republic of Serbia, 10203, titled: "Translational road to elucidate the effects of GLP-1 receptor agonist treatment on adipose tissue-brain axis function in cognitive processes in diabetes type 2 with concomitant obesity – CoD-GOAT."