

Expression profile of microRNAs associated with Alzheimer's disease in patients with type 2 diabetes mellitus

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Circulating microRNAs may serve as early biomarkers of neurodegeneration in patients with type 2 diabetes mellitus

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS								
Type 2 diabetes mellitus (T2DM) and Alzheimer’s disease (AD) are prevalent chronic disorders representing leading causes of morbidity and mortality worldwide (1,2). Increasing evidence indicates that T2DM is a major risk factor for AD due to shared pathophysiological mechanisms, particularly insulin resistance, which contributes to impaired neuronal signaling, tau hyperphosphorylation, amyloid-β accumulation, and neurodegeneration (3). MicroRNAs (miRNAs) are key post-transcriptional regulators of gene expression. Recent evidence shows that specific circulating miRNAs modulate these shared pathways (e.g., insulin signaling, neuroinflammation), making them ideal molecular bridges and promising non-invasive biomarkers to link T2DM and AD pathogenesis (4,5). This study aimed to characterize the expression profile of AD-associated miRNAs in patients with T2DM.	Study design: Cross-sectional comparative study. Participants (total n=132): Controls (n=60), T2DM (n=60), AD (n=12), stratified by age: Group A (30-59 years) and Group B (≥60 years). Assessments: Clinical history, anthropometric measurements, biochemical parameters, cognitive assessment (Mini-Mental State Examination), insomnia assessment (Athens Insomnia Scale), depression assessment (Beck Depression Inventory), and blood sample collection. microRNAs quantification by qRT-PCR: Total RNA was extracted from serum samples. miR-146a-5p, miR-148a-3p, and miR-181a-5p were quantified by qRT-PCR (2^{^-ΔΔCt} method). Bioinformatics analysis: Target gene prediction (miRDB) and pathway enrichment (ShinyGO, FDR <0.05). Statistical analysis: Normality was assessed using Shapiro-Wilk test. Group comparisons used Student's t-test/Mann-Whitney U (two groups) or ANOVA-Tukey/Kruskal-Wallis-Holm (multiple groups). Significance was set at p < 0.05.	Serum microRNAs expression miR-146a-5p Reduced expression was observed in T2DM-A and T2DM-B compared with their age-matched CTRL groups (p < 0.05). miR-148a-3p Lower expression was detected in T2DM-A compared with CTRL-A (p < 0.05), while no significant differences were observed in older participants. miR-181a-5p Lower expression was observed in T2DM-B and AD compared with CTRL-B (p < 0.01). Bioinformatics analysis A) Predicted target genes A: miR-146a-5p: 488 genes B: miR-148a-3p: 839 genes C: miR-181a-5p: 1,408 genes B) Enriched KEGG pathways <table><tr><th>microRNAs</th><th>Main enriched KEGG pathways</th></tr><tr><td>miR-146a-5p</td><td>Herpes simplex virus 1 infection</td></tr><tr><td>miR-148a-3p</td><td>PI3K-Akt signaling pathway, Insulin signaling pathway, FoxO signaling pathway, Endocrine resistance, Focal adhesion, Proteoglycans in cancer, MicroRNAs in cancer</td></tr><tr><td>miR-181a-5p</td><td>Insulin resistance, Insulin signaling pathway, Neurotrophin signaling pathway, Long-term potentiation, Cellular senescence, Circadian rhythm, cGMP-PKG signaling pathway, Axon guidance, cAMP signaling pathway</td></tr></table>	microRNAs	Main enriched KEGG pathways	miR-146a-5p	Herpes simplex virus 1 infection	miR-148a-3p	PI3K-Akt signaling pathway, Insulin signaling pathway, FoxO signaling pathway, Endocrine resistance, Focal adhesion, Proteoglycans in cancer, MicroRNAs in cancer	miR-181a-5p	Insulin resistance, Insulin signaling pathway, Neurotrophin signaling pathway, Long-term potentiation, Cellular senescence, Circadian rhythm, cGMP-PKG signaling pathway, Axon guidance, cAMP signaling pathway	This study identifies a differential pattern of expression of miRNAs associated with AD in patients with T2DM treated with antihyperglycemic drugs, suggesting a possible modulatory and protective effect against neurodegeneration.
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