



Indian Journal of Experimental Biology  
Vol. 62, November 2024, pp. 873-883  
DOI: 10.56042/ijeb.v62i11.4531

NISPR  
सीएसआईआर-निरूपर

## Probing the risk markers of mild cognitive impairment and Alzheimer's disease in alloxan-induced diabetic rats

Yogaraje Gowda C Varadaiah<sup>1,2</sup>, Senthilkumar Sivanesan<sup>1,3</sup>, Mathew D Howell<sup>4</sup>, Jayakumar Rajadas<sup>5</sup>, Suchitra Kavuri<sup>6</sup>, Rajagopalan Vijayaraghavan<sup>1</sup> & Kashinath RT<sup>7</sup>

<sup>1</sup>Department of Research and Development, Saveetha Institute of Medical and Technical Sciences, Thandalam, Chennai 602105, Tamil Nadu, India

<sup>2</sup>Department of Biochemistry, Bangalore Medical College & Research Institute, Bengaluru 560 002, Karnataka, India

<sup>3</sup>Department of Biosciences, Institute of Biotechnology, Saveetha Institute of Medical and Technical Sciences, Chennai 602105, India

<sup>4</sup>Department of Biomedical Sciences, Iowa State University, Ames, Iowa 50011, USA

<sup>5</sup>Stanford Advanced Drug Delivery and Regenerative Biomaterials Laboratory, Cardiovascular Institute, Stanford University School of Medicine, Stanford, CA 94304, USA

<sup>6</sup>Department of Biochemistry, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, India

<sup>7</sup>Department of Research and Development, Subbaiah Institute of Medical Sciences, NH-13, Purlu, Shivamogga 577222, Karnataka, India

Received 02 August 2023; revised 14 March 2024

Alzheimer's disease (AD) exemplifies a form of diabetes mellitus that selectively affects the brain. In this study we evaluated serum markers and genes linked to AD and investigated the possible link between AD and diabetes. We measured the serum levels of insulin, lactate, citrulline, argininosuccinate, homocitrulline, and AD-associated lipids (2,4-dihydroxybutanoic acid and sphinganine-1-phosphate). We used semi-quantitative reverse transcription polymerase chain reaction to determine the relative gene expression of *Rest*, *Bace1*, and *Rtn3* in the brain. Western blotting was used to determine the relative protein expression of REST, BACE1, and RTN3 in the brain. Serum from diabetic rats showed significantly higher levels of citrulline, homocitrulline, lactate, 2,4-dihydroxybutanoic acid, and sphinganine-1-phosphate, but lower levels of argininosuccinate and insulin compared with serum from control rats. At the gene level, *Bace1* and *Rest* were significantly increased, whereas *Rtn3* was considerably reduced in diabetic compared with control rat brains. At the protein level, BACE1 and RTN3 were significantly increased whereas REST was significantly reduced in diabetic compared with control rat brains. These findings indicate that hyperglycemia and insulin resistance in the brain may be the common element that connects urate turnover and alterations in neural regulatory genes.

**Keywords:** Amyloid, Urate turnover, Lactate, Serum markers, Gene