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Streptozotocin Causes Blood–Brain Barrier and Astrocytic Dysfunction *In Vitro*

Sarah A Habib

Harvard Medical School-Brigham Women's Hospital, USA

Streptozotocin (STZ) is a famous naturally occuring alkylating agent and the most commonly used diabetogenic agent in diabetes research. STZ has a pronounced neurotoxic effect when injected into the cerebral ventricles (ICV) and also models many other features of Dementia and Alzheimer's disease. However, the mechanisms through which STZ induces its neurotoxicity are not well understood, and needs further investigation. In this study, we hypothesized that some of the neurotoxic effects of STZ could be due to direct activities on brain endothelial cells and astrocytes. These cells are key in forming and supporting the functions of the blood–brain barrier (BBB), respectively. To test this hypothesis, we characterized the changes induced by STZ either in cultures of human-induced pluripotent stem cell (iPSC)-derived brain endothelial-like cells (iBECs), which form an in vitro BBB model, or in primary human astrocytes. We found that STZ at a dosage of 5 mM caused a delayed reduction in the transendothelial electrical resistance (TEER) of iBECs at 7–11 days post-treatment, indicating induction of BBB leakage. Additionally, we observed significant increases in Iodine-131 labelled albumin leakage across the monolayer. Moreover, altered iBECs morphology, and reductions in tight junction proteins (TJPs) as Claudin-5 and Zonula Occludens (ZO-1), suggesting that STZ causes disruption of the BBB. We further found that the BBB glucose transporter -1 (GLUT-1) was reduced in iBECs, as was the total number of iBECs. In astrocytes, the 5 mM dose of STZ reduced the Glial Fibrillary Acidic Protein (GFAP) signal and the total number of cells, suggesting that STZ has an anti proliferative and/or toxic effects on astrocytes. Together, these findings would be able to support that STZ's neurotoxic effects could be due, in part, to its direct induction of toxic activities on brain endothelial cells and astrocytes, which have key role in the BBB structure and function.

Biography

Sarah Habib is an Assistant Lecturer in The British University in Egypt, she has completed her MD from Faculty of Pharmacy, Cairo University, Egypt. She is a last year PhD student in department of Biochemistry, Cairo University, Egypt. Currently, she is working in Biomedical Engineering department in Brigham and Women's Hospital, Harvard medical school funded by a Fulbright Fellowship program. Her work primarily focuses on rescuing degenerative diseases using mesenchymal stem cells in tissue regeneration, with the focus of her PhD study being the modelling of sporadic Alzheimer's disease and therapeutic interventions. She joined Shin Lab in October 2025 and is currently working on Colloidal hydrogel-mediated delivery of miRNA in limb ischemia.

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