Poster number: **EP.1177**

SODIUM-GLUCOSE CO-TRANSPORTER INHIBITOR DAPAGLIFLOZIN ATTENUATES COGNITIVE DEFICITS IN STREPTOZOTOCIN INDUCED SPORADIC ALZHEIMER'S RAT MODEL

Ayse Nur Hazar-Yavuz[1], Sila Yildiz[1], Rumeysa Keles,[1,2], Muhammet Emin Cam[1], Levent Kabasakal[1]

[1]Marmara University, Faculty of Pharmacy, Department of Pharmacology, Istanbul-Turkey [2]Sakarya University, Faculty of Medicine, Department of Pharmacology, Sakarya-Turkey

BACKGROUND

In Alzheimer's disease (AD), amyloid beta aggregates and hyperphosphorylated tau protein in brain are the triggers of oxidative and inflammatory damage and consequently cause synaptic dysfunction and neuronal death. In addition, Type 2 Diabetes Mellitus (T2DM) is associated with AD and it has been shown that several drugs from both groups are effective in the other. The effects of sodium-glucose co-transporter (SGLT) 2 inhibitors are unknown in AD. It has shown that SGLT2 inhibitors improve cognitive functions in diabetic rats associated with improvements in diabetic status and molecular docking studies have shown that SGLT inhibitors also inhibit acetylcholinesterase. In this study, the effects of dapagliflozin with unknown effects on AD were investigated with tests evaluating cognitive functions on rats in intracerebroventricular (icv) streptozotocin (STZ)-induced Alzheimer's model.

METHODS

24 rats were divided into 3 groups:
- Control Group
- STZ Group
- STZ+Dapagliflozin Group

Therapy:
- Distilled water
- 10 mg/kg/rat Dapagliflozin

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22

STZ ADMINISTRATION

STZ was given bilaterally icv injection in 5 µl citrate buffer at a dose of 3 mg/kg under ketamine/xylazine anesthesia in STZ and STZ+Dapagliflozin Groups.
Citrate buffer was administered bilaterally under anesthesia in same volume in Control Group.

In OFT test, the squares crossed was used for assess mobility of rats.

OPEN FIELD TEST (OFT)

PASSIVE AVOIDANCE (PA) TEST

PA test, two consecutive days were applied to acquisition and retrieval.

NOVEL OBJECT RECOGNITION TEST (NORT)

The NORT consisted of three-minute trials twice separated by an intertrial interval of one hour. Exploration of novel and familiar objects was defined if rats licked, sniffed or touched the object.

MORRIS'S WATER MAZE (MWM) TEST

MWM training was performed on 18th, 19th, 20th and 21st days.
MWM prob test was performed on 22nd day.

RESULTS

OPEN FIELD TEST

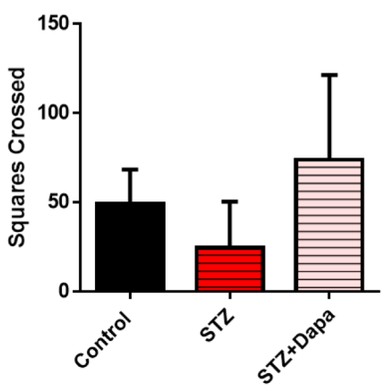


Figure 1: Squares crossed of rats in OFT. Values are expressed in Mean ± SEM (n=8). One-way ANOVA with Tukey post test was performed using GraphPad Prism version 6.05 for Windows.

NOVEL OBJECT RECOGNITION TEST

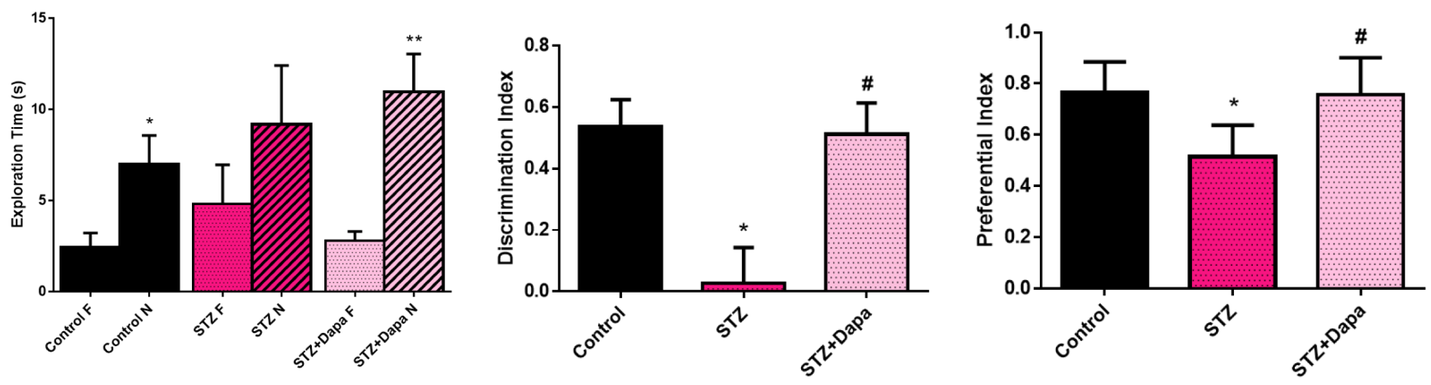


Figure 2: Exploration time (a), discrimination index (b) and preferential index (c) of rats in NORT.
a: Values are expressed in Mean ± SEM (n=8). One-way ANOVA with unpaired t test was performed using GraphPad Prism version 6.05 for Windows; *p<0.05 in comparison with control group and **p<0.01 in comparison with STZ group.
b: Values are expressed in Mean ± SEM (n=8). One-way ANOVA with Tukey post test was performed using GraphPad Prism version 6.05 for Windows; *p<0.05 in comparison with control group and #p<0.05 in comparison with STZ group.
c: Values are expressed in Mean ± SEM (n=8). One-way ANOVA with Tukey post test was performed using GraphPad Prism version 6.05 for Windows; *p<0.05 in comparison with control group and #p<0.05 in comparison with STZ group.

PASSIVE AVOIDANCE TEST

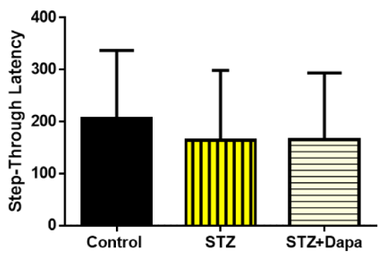


Figure 3: Step-through latency of rats in PA test. Values are expressed in Mean ± SEM (n=8). One-way ANOVA with Tukey post test was performed using GraphPad Prism version 6.05 for Windows.

MORRIS'S WATER MAZE TEST

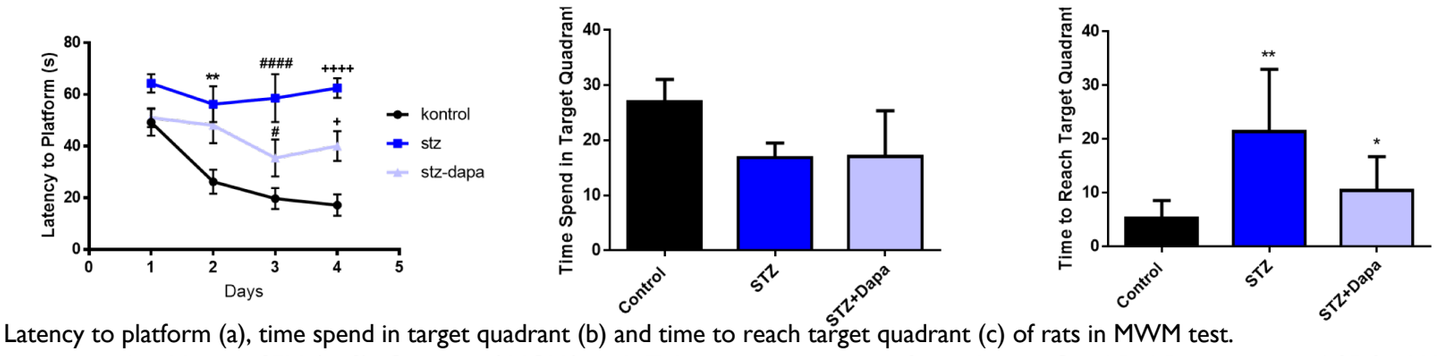


Figure 4: Latency to platform (a), time spend in target quadrant (b) and time to reach target quadrant (c) of rats in MWM test.
a: Values are expressed in Mean ± SEM (n=8). One-way ANOVA with Tukey post test was performed using GraphPad Prism version 6.05 for Windows; **p<0.01, ####p<0.0001, ++++p<0.0001 in comparison with control group and #p<0.05, +p<0.05 in comparison with STZ group.
b: Values are expressed in Mean ± SEM (n=8). One-way ANOVA with Tukey post test was performed using GraphPad Prism version 6.05 for Windows.
c: Values are expressed in Mean ± SEM (n=8). One-way ANOVA with Tukey post test was performed using GraphPad Prism version 6.05 for Windows; **p<0.01 in comparison with control group and *p<0.05 in comparison with STZ group.

CONCLUSIONS

According to the results, we have found that SGLT2 inhibitor dapagliflozin, which had not previously been studied in AD, improved cognitive functions in STZ-induced AD rats by enhancing NORT and MWM test.

Experimental process was approved by MU Local Committee on Animal Research Ethics (Protokol number: 38.2018.mar)