Results

BODY WEIGHT AND BLOOD GLUCOSE LEVEL OF EXPERIMENTAL RATS

Streptozotocin induced diabetic adult and old rats showed a significant (p<0.001) decrease in body weight after 10 days compared to their respective control. Insulin induced hypoglycaemia in adult and old diabetes (D+IIH) and control (C+IIH) rats showed no significant change in the body weight compared to their respective control (Table-1, 2; Fig-1, 2).

Diabetic adult and old rats showed a significant (p<0.001) increase in blood glucose compared to their respective control. There was a significant (p<0.001) decrease in blood glucose level of D+IIH and C+IIH adult and old rats compared to their respective diabetic and control rats (Table-3; Fig-3). Insulin administration to diabetic adult and old rats decreased blood glucose level significantly (p<0.001) below 50mg/dL after 3 hours and in control adult and old rats after 1 hour. The decreased glucose level reversed to diabetic level after 5 hours and control level after 2 hours respectively (Fig-4, 5).

CIRCULATING INSULIN LEVEL IN THE PLASMA OF CONTROL AND EXPERIMENTAL ADULT AND OLD RATS

Diabetic adult and old rats showed a significant (p<0.001) decrease in circulating insulin level compared to their respective control. There was a significant (p<0.001) increase in circulating insulin level of D+IIH and C+IIH adult and old rats compared to their respective diabetic and control rats. The adult and old C+IIH rats showed a significant (p<0.01) and (p<0.001) increase respectively in circulating insulin level compared to the respective D+IIH group (Table-4; Fig-6).
TRIIODOTHYRONINE (T3) CONTENT IN SERUM OF CONTROL AND EXPERIMENTAL ADULT AND OLD RATS

Diabetic adult and old rats showed a significant (p<0.001) decrease in T3 content compared to their respective controls. There was a significant increase in T3 content in adult (p<0.01) and old (p<0.001) D+IIH compared to their respective control rats. Also, the T3 content increased significantly (p<0.001) in D+IIH adult and old rats compared to their respective diabetic rats. The C+IIH adult and old rats showed significant (p<0.001) increase in the T3 content compared to their respective diabetic and control rats. The old C+IIH rats showed a significant (p<0.001) increase in T3 content compared to the old D+IIH group (Table-5; Fig-7).

GLUTAMATE CONTENT IN DIFFERENT BRAIN REGIONS AND PANCREAS OF CONTROL AND EXPERIMENTAL ADULT AND OLD RATS

Cerebral Cortex

Glutamate content in the cerebral cortex was significantly (p<0.001) increased in diabetic, D+IIH and C+IIH adult rats compared to control adult rats. In old experimental rats the glutamate content in the cerebral cortex was significantly increased in diabetic (p<0.01), D+IIH (p<0.001) and C+IIH (p<0.001) rats compared to control old rats. There was a significant (p<0.001) increase in glutamate content of D+IIH and C+IIH adult and old rats compared to their respective diabetic rats. The adult and old C+IIH rats showed a significant (p<0.001) increase in the glutamate content compared to the respective D+IIH group (Table-6; Fig-8).
Results

Cerebellum

Glutamate content in the cerebellum was significantly (p<0.001) increased in diabetic, D+IIH and C+IIH adult and old rats compared to their respective control group. The adult D+IIH group showed a significant (p<0.001) increase in glutamate content compared to diabetic adult rats. The adult and old C+IIH rats showed a significant (p<0.001) increase in the glutamate content compared to the respective diabetic and D+IIH group (Table-7; Fig-9).

Hippocampus

Glutamate content in the hippocampus was significantly (p<0.001) increased in diabetic, D+IIH and C+IIH adult and old rats compared to their respective control group. The adult and old D+IIH group showed a significant (p<0.001) and (p<0.01) increase respectively in glutamate content compared to diabetic adult and old rats. The adult and old C+IIH rats showed a significant (p<0.001) increase in the glutamate content compared to the respective diabetic group. Also, a significant increase in glutamate content in hippocampus was observed in the adult (p<0.001) and old (p<0.01) C+IIH rats compared to the respective D+IIH group (Table-8; Fig-10).

Pancreas

Glutamate content in the pancreas was significantly (p<0.001) increased in diabetic, D+IIH and C+IIH adult and old rats compared to their respective control group. The adult and old D+IIH group showed a significant (p<0.001) and (p<0.01) increase respectively in glutamate content compared to diabetic adult and old rats. The adult and old C+IIH rats showed a significant (p<0.001) increase in the glutamate content compared to the respective diabetic and D+IIH group (Table-9; Fig-11).
GLUTAMATE AND NMDA RECEPTOR CHANGES IN THE BRAIN
REGIONS AND PANCREAS OF CONTROL AND EXPERIMENTAL ADULT
AND OLD RATS

Cerebral Cortex

Scatchard analysis of glutamate receptors using [3H]Glutamate against glutamate

Scatchard analysis of [3H]glutamate against glutamate in cerebral cortex of adult and old diabetic, D+IIH and C+IIH groups of rats showed a significant (p<0.001) increase in B_max compared to their respective control rats. D+IIH and C+IIH adult and old rats showed a significant (p<0.001) increase in B_max compared to the respective diabetic group. Both adult and old C+IIH rats showed a significant (p<0.001) increase in B_max compared to the respective D+IIH rats. There was no significant change in K_d in all experimental groups in both adult and old rats (Table-10, 11; Fig-12, 13).

Scatchard analysis of NMDA receptors using [3H]MK801 against MK801

Scatchard analysis of [3H]MK801 against MK801 in cerebral cortex of adult rats showed a significant increase in B_max in diabetic (p<0.05), D+IIH (p<0.001) and C+IIH (p<0.001) rats compared to control rats. In the old cerebral cortex there was a significant (p<0.001) increase in the B_max in diabetic, D+IIH and C+IIH rats compared to the control group. Both adult and old D+IIH and C+IIH rats showed a significant (p<0.001) increase in B_max compared to the respective diabetic rats. There was a significant increase in B_max in adult (p<0.01) and old (p<0.001) C+IIH rats compared to the respective D+IIH rats. A significant (p<0.001) increase in K_d was observed in
the old C+IIH rats compared to old control, diabetic and D+IIH rats (Table-12, 13; Fig-14, 15).

**Real-Time PCR analysis of NMDAR1 receptors**

The Real-Time PCR analysis in the cerebral cortex showed a significant (p<0.001) increase in the expression of NMDAR1 receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant increase in expression of NMDAR1 receptors in adult (p<0.001) and old (p<0.01) D+IIH rats compared to the respective diabetic rats. Both adult and old C+IIH rats showed a significant (p<0.001) increase in expression of NMDAR1 receptors compared to the respective diabetic and D+IIH rats (Table-14, 15; Fig-16, 17).

**Real-Time PCR analysis of NMDA2B receptors**

The Real-Time PCR analysis in the cerebral cortex showed a significant (p<0.001) increase in the expression of NMDA2B receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant (p<0.01) increase in expression of NMDA2B receptors in adult and old D+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) increase in expression of NMDA2B receptors in both adult and old compared to the respective diabetic rats. Also, a significant increase in the expression of NMDA2B receptors was observed in adult (p<0.05) and old (p<0.01) C+IIH rats compared to the respective D+IIH group (Table-16, 17; Fig-18, 19).
**Real-Time PCR analysis of mGluR5 receptors**

The Real-Time PCR analysis in the cerebral cortex showed a significant (p<0.001) increase in the expression of mGluR5 receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant (p<0.001) increase in expression of mGluR5 receptors in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) increase in expression of mGluR5 receptors in both adult and old rats compared to the respective D+IIH rats (Table-18, 19; Fig-20, 21).

**Real-Time PCR analysis of GLAST glutamate transporter**

The Real-Time PCR analysis in the cerebral cortex showed a significant (p<0.001) decrease in the expression of GLAST glutamate transporter mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant decrease in expression of GLAST glutamate transporter in adult (p<0.01) and old (p<0.001) D+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) decrease in expression of GLAST glutamate transporter in both adult and old rats compared to the respective diabetic and D+IIH rats (Table-20, 21; Fig-22, 23).

**Cerebellum**

**Scatchard analysis of glutamate receptors using [3H]Glutamate against glutamate**

Scatchard analysis of [3H]glutamate against glutamate in cerebellum of adult and old diabetic, D+IIH and C+IIH groups of rats showed a significant (p<0.001) increase in $B_{max}$ compared to their respective control. D+IIH and C+IIH adult and old rats showed a significant (p<0.001) increase in $B_{max}$ compared to the respective
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diabetic group. Both adult and old C+IIH rats showed a significant (p<0.001) increase in $B_{\text{max}}$ compared to the respective D+IIH rats. The $K_d$ showed a significant (p<0.01) increase in adult diabetic, D+IIH and C+IIH groups of rats compared to control adult rats. The D+IIH and C+IIH groups of adult rats showed a significant (p<0.001) increase in $K_d$ compared to diabetic adult rats. Also, the C+IIH adult rats showed a significant (p<0.01) increase in $K_d$ compared to D+IIH adult rats (Table-22, 23; Fig-24, 25).

Scatchard analysis of NMDA receptors using $[^3H] MK801$ against MK801

Scatchard analysis of $[^3H] MK801$ against MK801 in cerebellum of adult and old rats showed a significant (p<0.001) increase in $B_{\text{max}}$ in diabetic, D+IIH and C+IIH rats compared to their respective control rats. D+IIH and C+IIH adult and old rats showed a significant (p<0.001) increase in $B_{\text{max}}$ compared to the respective diabetic group. Both adult and old C+IIH rats showed a significant (p<0.001) increase in $B_{\text{max}}$ compared to the respective D+IIH rats. There was no significant change in $K_d$ in all experimental groups in both adult and old rats (Table-24, 25; Fig-26, 27).

Real-Time PCR analysis of NMDAR1 receptors

The Real-Time PCR analysis in the cerebellum showed a significant (p<0.001) increase in the expression of NMDAR1 receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant (p<0.001) increase in expression of NMDAR1 receptors in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. Both adult and old C+IIH rats showed a significant (p<0.001) increase in expression of NMDAR1 receptors compared to the respective D+IIH rats (Table-26, 27; Fig-28, 29).
Real-Time PCR analysis of NMDA2B receptors

The Real-Time PCR analysis in the cerebellum showed a significant (p<0.001) increase in the expression of NMDA2B receptor mRNA in adult diabetic, D+IIH and C+IIH rats compared to control adult rats. The Real-Time PCR analysis in the cerebellum showed a significant increase in the expression of NMDA2B receptor mRNA in old diabetic (p<0.05), D+IIH (p<0.001) and C+IIH (p<0.001) rats compared to control old rats. There was a significant (p<0.01) increase in expression of NMDA2B receptors in adult D+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant increase in expression of NMDA2B receptors in both adult (p<0.01) and old (p<0.001) compared to the respective diabetic rats. Also, a significant (p<0.01) increase in the expression of NMDA2B receptors was observed in adult and old C+IIH rats compared to the respective D+IIH group (Table-28, 29; Fig-30, 31).

Real-Time PCR analysis of mGluR5 receptors

The Real-Time PCR analysis in the cerebellum showed a significant (p<0.001) increase in the expression of mGluR5 receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant (p<0.001) increase in expression of mGluR5 receptors in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) increase in expression of mGluR5 receptors in both adult and old rats compared to the respective D+IIH rats (Table-30, 31; Fig-32, 33).
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**Real-Time PCR analysis of GLAST glutamate transporter**

The Real-Time PCR analysis in the cerebral cortex showed a significant (p<0.001) decrease in the expression of GLAST glutamate transporter mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant (p<0.001) decrease in expression of GLAST glutamate transporter in both adult and old D+IIH rats compared to the respective diabetic rats (Table-32, 33; Fig-34, 35).

**Hippocampus**

**Scatchard analysis of glutamate receptors using [3H]Glutamate against glutamate**

Scatchard analysis of [3H]glutamate against glutamate in hippocampus of adult and old diabetic, D+IIH and C+IIH groups of rats showed a significant (p<0.001) increase in B<sub>max</sub> compared to their respective controls. D+IIH and C+IIH adult and old rats showed a significant (p<0.001) increase in B<sub>max</sub> compared to the respective diabetic group. Both adult and old C+IIH rats showed a significant (p<0.001) increase in B<sub>max</sub> compared to the respective D+IIH rats. There was no significant change in K<sub>d</sub> in all experimental groups in both adult and old rats (Table-34, 35; Fig-36, 37).

**Scatchard analysis of NMDA receptors using [3H]MK801 against MK801**

Scatchard analysis of [3H]MK801 against MK801 in hippocampus of adult and old rats showed a significant (p<0.001) increase in B<sub>max</sub> in diabetic, D+IIH and C+IIH rats compared to their respective control rats. D+IIH and C+IIH adult and old rats showed a significant (p<0.001) increase in B<sub>max</sub> compared to the respective diabetic group. Both adult and old C+IIH rats showed a significant (p<0.001) increase
in $B_{\text{max}}$ compared to the respective D+IIH rats. There was no significant change in $K_d$ in all experimental groups in both adult and old rats (Table-36, 37; Fig-38, 39).

**Real-Time PCR analysis of NMDAR1 receptors**

The Real-Time PCR analysis in the hippocampus showed a significant (p<0.001) increase in the expression of NMDAR1 receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant (p<0.001) increase in expression of NMDAR1 receptors in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. A significant increased expression of NMDAR1 receptors in adult (p<0.001) and old (p<0.05) C+IIH rats was observed compared to the respective D+IIH rats (Table-38, 39; Fig-40, 41).

**Real-Time PCR analysis of NMDA2B receptors**

The Real-Time PCR analysis in the hippocampus showed a significant (p<0.001) increase in the expression of NMDA2B receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant (p<0.001) increase in expression of NMDA2B receptors in old D+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) increase in expression of NMDA2B receptors in both adult and old compared to the respective diabetic rats. Also, a significant (p<0.001) increase in the expression of NMDA2B receptors was observed in old C+IIH rats compared to the D+IIH old rats (Table-40, 41; Fig-42, 43).
Results

Real-Time PCR analysis of mGluR5 receptors

The Real-Time PCR analysis in the hippocampus showed a significant (p<0.001) increase in the expression of mGluR5 receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The mGluR5 receptors showed a significant increase in expression of in both adult (p<0.001) and old (p<0.05) D+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) increase in expression of mGluR5 receptors in both adult and old compared to the respective diabetic rats. Also, a significant (p<0.001) increase in the expression of mGluR5 receptors was observed in old C+IIH rats compared to the D+IIH old rats (Table-42, 43; Fig-44, 45).

Real-Time PCR analysis of GLAST glutamate transporter

The Real-Time PCR analysis in the hippocampus showed a significant (p<0.001) decrease in the expression of GLAST glutamate transporter mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The GLAST glutamate transporter showed a significant decrease in expression of in both adult (p<0.01) and old (p<0.001) D+IIH rats compared to the respective diabetic rats. In C+IIH group GLAST glutamate transporter showed a significant decrease in expression of in both adult (p<0.01) and old (p<0.001) rats compared to the respective D+IIH rats (Table-44, 45; Fig-46, 47).

Pancreas

Scatchard analysis of glutamate receptors using [3H]Glutamate against glutamate

Scatchard analysis of [3H]glutamate against glutamate in pancreas of adult and old diabetic, D+IIH and C+IIH groups of rats showed a significant (p<0.001)
increase in $B_{\text{max}}$ compared to their respective control. D+IIH and C+IIH adult and old rats showed a significant ($p<0.001$) increase in $B_{\text{max}}$ compared to the respective diabetic groups. Both adult and old C+IIH rats showed a significant ($p<0.001$) increase in $B_{\text{max}}$ compared to the respective D+IIH rats. There was no significant change in $K_d$ in all experimental groups in both adult and old rats (Table-46, 47; Fig-48, 49).

**Scatchard analysis of NMDA receptors using $[^3H]$MK801 against MK801**

Scatchard analysis of $[^3H]$MK801 against MK801 in pancreas of adult and old rats showed a significant ($p<0.001$) increase in $B_{\text{max}}$ in diabetic, D+IIH and C+IIH rats compared to their respective control rats. D+IIH and C+IIH adult and old rats showed a significant ($p<0.001$) increase in $B_{\text{max}}$ compared to the respective diabetic groups. Both adult and old C+IIH rats showed a significant ($p<0.001$) increase in $B_{\text{max}}$ compared to the respective D+IIH rats. There was no significant change in $K_d$ in all experimental groups in both adult and old rats (Table-48, 49; Fig-50, 51).

**Real-Time PCR analysis of NMDAR1 receptors**

The Real-Time PCR analysis in the pancreas showed a significant ($p<0.001$) increase in the expression of NMDAR1 receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The NMDAR1 receptor expression showed a significant ($p<0.001$) increase in both adult and old D+IIH and C+IIH rats compared to their respective diabetic rats. A significant ($p<0.001$) increased expression of NMDAR1 receptors in adult C+IIH rats was observed compared to the adult D+IIH rats (Table-50, 51; Fig-52, 53).
Results

Real-Time PCR analysis of NMDA2B receptors

The Real-Time PCR analysis in the pancreas showed a significant (p<0.001) increase in the expression of NMDA2B receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. There was a significant (p<0.001) increase in expression of NMDA2B receptors in old D+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) increase in expression of NMDA2B receptors in both adult and old compared to the respective diabetic rats. Also, a significant increase in the expression of NMDA2B receptors was observed in adult (p<0.001) and old (p<0.05) C+IIH rats compared to the respective D+IIH rats (Table-52, 53; Fig-54, 55).

Real-Time PCR analysis of mGluR5 receptors

The Real-Time PCR analysis in the pancreas showed a significant (p<0.001) increase in the expression of mGluR5 receptor mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The mGluR5 receptors showed a significant increase in expression of in both adult (p<0.001) and old (p<0.05) D+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) increase in expression of mGluR5 receptors in both adult and old compared to the respective diabetic rats. Also, a significant (p<0.01) increase in the expression of mGluR5 receptors was observed in old C+IIH rats compared to the D+IIH old rats (Table-54, 55; Fig-56, 57).

Real-Time PCR analysis of GLAST glutamate transporter

The Real-Time PCR analysis in the pancreas showed a significant (p<0.001) decrease in the expression of GLAST glutamate transporter mRNA in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The
GLAST glutamate transporter showed a significant decrease in expression of in both adult (p<0.05) and old (p<0.001) D+IIH rats compared to the respective diabetic rats. C+IIH rats showed a significant (p<0.001) decrease in expression of GLAST glutamate transporter in both adult and old compared to the respective diabetic rats. In C+IIH group GLAST glutamate transporter showed a significant decrease in expression of in both adult (p<0.001) and old (p<0.01) rats compared to the respective D+IIH rats (Table-56, 57; Fig-58, 59).

SECOND MESSENGER ASSAYS

**IP3, cGMP and cAMP content in the cerebral cortex of control and experimental adult and old rats**

The IP3 content in the cerebral cortex was significantly (p<0.001) increased in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The IP3 content showed a significant increase in both adult (p<0.05) and old (p<0.001) D+IIH rats compared to the respective diabetic rats. The C+IIH adult and old rats showed a significant (p<0.001) increase in the IP3 content when compared to their respective diabetic and D+IIH rats (Table-58, 59; Fig-60, 61).

The cGMP content in the cerebral cortex was significantly (p<0.001) increased in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The cGMP content showed a significant (p<0.001) increase in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. Also, C+IIH rats showed a significant increase in the cGMP in adult (p<0.01) and old (p<0.001) rats when compared to their respective D+IIH rats (Table-58, 59; Fig-60, 61).

The cAMP content in the cerebral cortex was significantly (p<0.001) increased in both adult and old diabetic, D+IIH and C+IIH rats compared to their
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The cAMP content showed a significant (p<0.001) increase in both adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. Also, C+IIH rats showed a significant (p<0.001) increase in the cAMP in adult and old rats when compared to their respective D+IIH rats (Table-58, 59; Fig-60, 61).

**IP3, cGMP and cAMP content in the cerebellum of control and experimental adult and old rats**

The IP3 content in the cerebellum was significantly (p<0.001) increased in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The IP3 content showed a significant (p<0.001) increase in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. The C+IIH adult and old rats showed a significant (p<0.001) increase in the IP3 content when compared to their respective D+IIH rats (Table-60, 61; Fig-62, 63).

The cGMP content in the cerebellum was significantly (p<0.001) increased in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The cGMP content showed a significant increase in adult (p<0.05) and old (p<0.01) D+IIH rats compared to the respective diabetic rats. The cGMP content showed a significant (p<0.001) increase in adult and old C+IIH rats compared to the respective diabetic rats. Also, C+IIH rats showed a significant increase in the cGMP in adult (p<0.01) and old (p<0.05) rats when compared to their respective D+IIH rats (Table-60, 61; Fig-62, 63).

The cAMP content in the cerebellum was significantly (p<0.001) increased in adult diabetic, D+IIH and C+IIH rats compared to control rats. The cAMP content was significantly increased in old diabetic (p<0.01), D+IIH (p<0.001) and C+IIH (p<0.001) rats compared to control rats. The cAMP content showed a significant increase in both adult (p<0.001) and old (p<0.01) D+IIH rats compared to the diabetic
The cAMP content showed a significant (p<0.001) increase in adult and old C+IIH rats compared to the respective diabetic rats. Also, C+IIH rats showed a significant increase in the cAMP in adult (p<0.001) and old (p<0.05) rats when compared to their respective D+IIH rats (Table-60, 61; Fig-62, 63).

### IP3, cGMP and cAMP content in the hippocampus of control and experimental adult and old rats

The IP3 content in the hippocampus was significantly (p<0.001) increased in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The IP3 content showed a significant increase in adult (p<0.01) and old (p<0.001) D+IIH rats compared to the respective diabetic rats. The C+IIH adult and old rats showed a significant (p<0.001) increase in the IP3 content when compared to their respective diabetic and D+IIH rats (Table-62, 63; Fig-64, 65).

The cGMP content in the hippocampus was significantly increased in adult diabetic (p<0.05), D+IIH (p<0.001) and C+IIH (p<0.001) rats compared to control adult rats. The cGMP content in the hippocampus was significantly (p<0.001) increased in old diabetic, D+IIH and C+IIH rats compared to control old rats. The cGMP content showed a significant increase in adult (p<0.01) and old (p<0.001) D+IIH rats compared to the respective diabetic rats. The cGMP content showed a significant (p<0.001) increase in adult and old C+IIH rats compared to the respective diabetic rats. Also, C+IIH rats showed a significant increase in the cGMP in adult (p<0.001) and old (p<0.05) rats when compared to their respective D+IIH rats (Table-62, 63; Fig-64, 65).

The cAMP content in the hippocampus was significantly (p<0.001) increased in adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. In the old D+IIH rats the cAMP content showed a significant (p<0.001) increase
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compared to the old diabetic rats. The cAMP content showed a significant (p<0.001) increase in adult and old C+IIH rats compared to the respective diabetic and D+IIH rats (Table-62, 63; Fig-64, 65).

IP3, cGMP and cAMP content in the pancreas of control and experimental adult and old rats

The IP3 content in the pancreas was significantly (p<0.001) increased in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The IP3 content showed a significant (p<0.001) increase in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. Also, C+IIH adult and old rats showed a significant (p<0.001) increase in the IP3 content when compared to their respective D+IIH rats (Table-64, 65; Fig-66, 67).

The cGMP content in the pancreas was significantly (p<0.001) increased in both adult and old diabetic, D+IIH and C+IIH rats compared to their respective control rats. The cGMP content showed a significant (p<0.001) increase in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. Also, C+IIH adult and old rats showed a significant (p<0.001) increase in the cGMP content when compared to their respective D+IIH rats (Table-64, 65; Fig-66, 67).

The cAMP content in the pancreas was significantly (p<0.001) increased in adult diabetic, D+IIH and C+IIH rats compared to adult control rats. The cAMP content significantly increased in old diabetic (p<0.001), D+IIH (p<0.05) and C+IIH (p<0.01) rats compared to old control rats. The cAMP content showed a significant (p<0.001) increase in adult and old D+IIH and C+IIH rats compared to the respective diabetic rats. The cAMP content showed a significant (p<0.001) increase in adult C+IIH rats compared to the adult D+IIH rats (Table-64, 65; Fig-66, 67).
Rotarod Performance of control and experimental groups of adult rats

Rotarod experiments showed a significant (p<0.001) decrease in the retention time on the rotating rod in adult diabetic, D+IIH and C+IIH rats group compared to control at 10 rpm, 25 rpm and 50 rpm. The D+IIH and C+IIH adult rats showed significantly (p<0.001) decreased retention time compared to adult diabetic group at 10 rpm, 25 rpm and 50 rpm. The C+IIH adult rats showed significantly (p<0.001) decreased retention time compared to adult D+IIH group at 10 rpm, 25 rpm and 50 rpm (Table-66; Fig-68).

Rotarod Performance of control and experimental groups of old rats

Rotarod experiments showed a significant (p<0.001) decrease in the retention time on the rotating rod in old diabetic, D+IIH and C+IIH rats group compared to control at 10 rpm, 25 rpm and 50 rpm. The D+IIH and C+IIH old rats showed significantly (p<0.001) decreased retention time compared to old diabetic group at 10 rpm, 25 rpm and 50 rpm. The C+IIH old rats showed significantly (p<0.001) decreased retention time compared to old D+IIH group at 10 rpm, 25 rpm and 50 rpm (Table-67; Fig-69).

CONFOCAL STUDIES

Cerebral Cortex

NMDAR1 receptor antibody staining in control and experimental groups of rats

The NMDAR1 receptor antibody staining in the cerebral cortex showed significant (p<0.001) increase in the NMDAR1 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of NMDAR1 receptors in the cerebral cortex of D+IIH and C+IIH rats group.
compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased NMDAR1 receptor expression compared to D+IIH rats (Table-68; Fig-70).

**NMDA2B receptor antibody staining in control and experimental groups of rats**

The NMDA2B receptor antibody staining in the cerebral cortex showed significant (p<0.001) increase in the NMDA2B receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of NMDA2B receptors in the cerebral cortex of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased NMDA2B receptor expression compared to D+IIH rats (Table-68; Fig-71).

**mGluR5 receptor antibody staining in control and experimental groups of rats**

The mGluR5 receptor antibody staining in the cerebral cortex showed significant (p<0.001) increase in the mGluR5 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of mGluR5 receptors in the cerebral cortex of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased mGluR5 receptor expression compared to D+IIH rats (Table-68; Fig-72).

**IP3 receptor antibody staining in control and experimental groups of rats**

The IP3 receptor antibody staining in the cerebral cortex showed significant (p<0.001) increase in the IP3 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of IP3 receptors in the cerebral cortex of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased IP3 receptor expression compared to D+IIH rats (Table-68; Fig-73).
Cerebellum

NMDAR1 receptor antibody staining in control and experimental groups of rats

The NMDAR1 receptor antibody staining in the cerebellum showed significant (p<0.001) increase in the NMDAR1 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of NMDAR1 receptors in the cerebellum of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased NMDAR1 receptor expression compared to D+IIH rats (Table-69; Fig-74).

NMDA2B receptor antibody staining in control and experimental groups of rats

The NMDA2B receptor antibody staining in the cerebellum showed significant (p<0.001) increase in the NMDA2B receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of NMDA2B receptors in the cerebellum of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased NMDA2B receptor expression compared to D+IIH rats (Table-69; Fig-75).

mGluR5 receptor antibody staining in control and experimental groups of rats

The mGluR5 receptor antibody staining in the cerebellum showed significant (p<0.001) increase in the mGluR5 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of mGluR5 receptors in the cerebellum of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased mGluR5 receptor expression compared to D+IIH rats (Table-69; Fig-76).
Results

IP3 receptor antibody staining in control and experimental groups of rats

The IP3 receptor antibody staining in the cerebellum showed significant (p<0.001) increase in the IP3 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of IP3 receptors in the cerebellum of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased IP3 receptor expression compared to D+IIH rats (Table-69; Fig-77).

Pancreas

NMDAR1 receptor antibody staining in control and experimental groups of rats

The NMDAR1 receptor antibody staining in the pancreas showed significant (p<0.001) increase in the NMDAR1 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of NMDAR1 receptors in the pancreas of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased NMDAR1 receptor expression compared to D+IIH rats (Table-70; Fig-78).

NMDA2B receptor antibody staining in control and experimental groups of rats

The NMDA2B receptor antibody staining in the pancreas showed significant (p<0.001) increase in the NMDA2B receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of NMDA2B receptors in the pancreas of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased NMDA2B receptor expression compared to D+IIH rats (Table-70; Fig-79).
mGluR5 receptor antibody staining in control and experimental groups of rats

The mGluR5 receptor antibody staining in the pancreas showed significant (p<0.001) increase in the mGluR5 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of mGluR5 receptors in the pancreas of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased mGluR5 receptor expression compared to D+IIH rats (Table-70; Fig-80).

IP3 receptor antibody staining in control and experimental groups of rats

The IP3 receptor antibody staining in the pancreas showed significant (p<0.001) increase in the IP3 receptor in diabetic, D+IIH and C+IIH rats group compared to control. There was significant (p<0.001) increased expression of IP3 receptors in the pancreas of D+IIH and C+IIH rats group compared to diabetic rats. The C+IIH rats showed significant (p<0.001) increased IP3 receptor expression compared to D+IIH rats (Table-70; Fig-81).

CALCIUM IMAGING

Effect of 10^{-5}M Dopamine, 10^{-5}M Sulpiride on calcium release from Pancreatic Islets in the presence of 1mM, 4mM and 20mM Glucose

Dopamine at 10^{-5} M significantly (p<0.001) inhibited calcium release from the pancreatic islets in the presence of 1 mM glucose. Dopamine D_2 receptor antagonist sulpiride at 10^{-5} M significantly (p<0.001) reversed the inhibition from the pancreatic islets in the presence of 1 mM glucose (Table-71; Fig-82). In the normoglycaemic condition, 4mM glucose, 10^{-5} M dopamine significantly (p<0.001) increased the calcium release. Dopamine D_2 receptor antagonist sulpiride at 10^{-5} M significantly
Results

(p<0.001) inhibited the calcium release from the islet cells in the presence of $10^{-5}$ M dopamine (Table-72; Fig-83). In the hyperglycaemic condition, 20 mM glucose, $10^{-5}$ M dopamine significantly (p<0.001) increased the calcium release. Dopamine D$_2$ receptor antagonist sulpiride at $10^{-5}$ M significantly (p<0.001) inhibited the calcium release from the islet cells in the presence of $10^{-5}$ M dopamine (Table-73; Fig-84).

Effect of $10^{-5}$M glutamate, $10^{-5}$M MK801 on calcium release from Pancreatic Islets in the presence of 1mM, 4mM and 20mM Glucose

Glutamate at $10^{-5}$M significantly (p<0.001) increased calcium release from the pancreatic islets in the presence of 1mM glucose. NMDA receptor antagonist MK801 at $10^{-5}$ M significantly (p<0.001) inhibited the release from the pancreatic islets in the presence of 1 mM glucose (Table-74; Fig-85). In the normoglycaemic condition, 4 mM glucose, $10^{-5}$ M glutamate significantly (p<0.001) increased the calcium release. NMDA receptor antagonist MK801 at $10^{-5}$ M significantly (p<0.001) inhibited the calcium release from the islet cells in the presence of $10^{-5}$ M glutamate and 4 mM glucose (Table-75; Fig-86). In the hyperglycaemic condition, 20 mM glucose, $10^{-5}$ M glutamate significantly (p<0.001) increased the calcium release. NMDA receptor antagonist MK801 at $10^{-5}$ M significantly (p<0.001) inhibited the calcium release from the islet cells in the presence of $10^{-5}$ M glutamate 20 mM glucose (Table-76; Fig-87).