CONCLUSION

Our findings demonstrate that alterations of 5-HT_{1A} and 5-HT_{2C} receptor function and gene expression in the brain stem, cerebral cortex and hypothalamus play an important role in the sympathetic regulation of insulin secretion during pancreatic regeneration. Though many reports are there implicating the functional interaction between brain 5-HT and the sympathoadrenal system, the involvement of specific receptor subtypes in regulating sympathoadrenal system during pancreatic regeneration has not given emphasis. We observed an increased 5-HT content and downregulation of 5-HT_{1A} and 5-HT_{2C} receptors in the cerebral cortex, brain stem and hypothalamus. RT-PCR analysis confirmed the receptor data in the brain regions. The relationship between 5-HT receptors and adrenal catecholamine release is much more homogenous. Thus, downregulation of 5-HT_{1A} or 5-HT_{2C} receptor leads to decreased adrenomedullary catecholamine release. Plasma NE and EPI levels of different experimental groups were in accordance with the functioning of the 5-HT_{1A} and 5-HT_{2C} receptors. These relationship between the serotonergic and the sympathoadrenal system lead in turn to a control of insulin release. In addition, receptor binding studies and RT-PCR analysis revealed that during pancreatic regeneration 5-HT_{1A} and 5-HT_{2C} receptors were up regulated in pancreatic islets. This suggests a stimulatory role for 5-HT_{1A} and 5-HT_{2C} receptors in islet cell proliferation i.e., the up regulation of this receptor facilitates proliferation. Insulin secretion study showed that 5-HT_{1A} receptor agonist, 8-OH DPAT was stimulatory to insulin secretion at lower concentration and inhibitory at higher concentration. Mesulergine blocked the insulin secretary potential at all concentrations. *In vitro* DNA synthesis studies revealed that 5-HT_{1A} receptor agonist, 8-OH DPAT inhibited DNA synthesis at higher concentration and stimulated DNA synthesis at lower concentration. 5-HT_{2C} receptor antagonist, mesulergine inhibited the pancreatic islet DNA synthesis.

Also, 8-OH DPAT and mesulergine enhanced the mitogenic effect mediated by EGF and TGFβ1. Thus, we conclude that brain and pancreatic 5-HT_{1A} and 5-HT_{2C} receptor gene expression modulates pancreatic endocrine function and islet cell proliferation during pancreatic regeneration. This will have immense clinical significance in the therapeutic applications of diabetes.