research is required to elucidate its contribution to the development of *in vivo* skeletal muscle IR and broader impact in this syndrome. **References:** (1) Stepto *et al., Hum Reprod* 2013 Mar;28(3):777–784. (2) Cassar *et al., Hum Reprod* 2016 Nov;31(11):2619–2631. (3) Corbould *et al., Am J Physiol-Endoc* 2005 May;88(5):E1047-54. (4) Stepto *et al., J Clin Endocrinol Metab*, 2019 Nov 1;104(11):5372–5381. (5) Raja-Khan *et al., Reprod Sci* 2014 Jan;21(1):20–31.

Diabetes Mellitus and Glucose Metabolism

DYSREGULATED METABOLIC RESPONSE

The Short-Term Impact of Roux-en-Y Gastric Bypass on Enteroendocrine Hormone Distribution and Density in Rhesus Macaques

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Roux-en-Y gastric bypass (RYGB) surgery results in profound weight loss and improvements in glucose homeostasis through a likely combination of malabsorption and changes in GI tract signaling. One component of GI tract signaling implicated in RYGB effects are enteroendocrine hormones, which are produced along the tract and regulate GI tract motility, pancreas exocrine and endocrine functions, including insulin release, and central nervous system control of feeding. While RYGB has been shown to cause post-prandial serum increases of several enteroendocrine hormones, the mechanism for how this occurs in the GI tract is still unknown. The current study examined GI tract tissue 13 weeks after RYGB or sham-surgery combined with pair-feeding (Sham/PF) in adult rhesus macaques. In situ hybridization analysis revealed no RYGB-induced changes compared to Sham/PF animals in the overall distribution of enteroendocrine hormones, with cholecystokinin (CCK) and glucose-dependent insulinotropic peptide (GIP) cells found predominantly in the proximal small intestine and preglucagon, encoding glucagon-like peptide-1 (GLP-1), and peptide tyrosine tyrosine (PYY) cells found predominantly in the ileum and colon. Immunohistochemistry was performed to further characterize the impact of RYGB on enteroendocrine cell density. No differences were observed in CCK cell densities in the proximal tract following RYGB, nor were there any differences in PYY and GLP-1 densities in the distal intestine. The only observed difference was an increase in serotonin and chromogranin A cell densities in the ileum of the RYGB group compared to the Sham/PF group. Serotonin has diverse actions from regulating GI tract motility to central nervous system signaling via the vagus nerve. Additional studies are planned to investigate how this up-regulation of serotonin may impact metabolic physiology after RYGB.

Diabetes Mellitus and Glucose Metabolism

DYSREGULATED METABOLIC RESPONSE

Use of Intranasal Insulin as Neuroprotection From Hyperglycemia in Rat Model of Extremely Preterm Infants

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Background: Hyperglycemia is common in extremely preterm infants (EPI) and is a risk factor for increased mortality and morbidity, including abnormal neurodevelopment. Hippocampus-mediated cognitive deficits are common in this population. In a rat model of insulinopenic hyperglycemia, abnormal neurochemistry in the hippocampus was found, with lactate, glutamate (Glu):glutamine (Gln) ratio lower and Phosphorylated Creatinine (PCr):Creatinine (Cr) higher. Intranasal insulin has been shown to improve cognitive function in animal models of Alzheimer's disease and type 2 diabetes mellitus, as well as in adult human studies of Alzheimer's disease. No study has previous investigated the use of intranasal insulin on preventing the long-term effects of hyperglycemia in the EPI population. **Objective:** To determine whether administration of intranasal insulin during early postnatal days would negate the effects of hyperglycemia on the developing hippocampus in neonatal rat model of streptozotocin (STZ)-induced hyperglycemia. **Design/Methods:** STZ (80mg/kg IP) was injected on postnatal day (P) 2, and littermates in the control group were injected with an equivalent volume of citrate buffer. STZ pups were randomized to intranasal insulin, 3U twice daily from P3-P6 (STZ + INS) or left untreated (STZ). Neurochemical profile (consisting of 20 metabolites, PCr:Cr and Glu:Gln ratios) of the hippocampus was evaluated using ultra-high-field (9.4 T) magnetic resonance spectroscopy (MRS) on P7 (acute effects) and P56 (long-term effects) compared with the control group (CON)(N=6/group). **Results:** Mean glucose values from P3-P6 were higher in STZ groups (STZ = 279.0 +/- 132.2 mg/dL, STZ+INS = 274.4 +/- 89.5 mg/dL, CONT = 128.4 +/- 15.1 mg/dL). The neurochemical profile was different at both P7 and P56. On P7, compared with the control, the taurine (Tau) was higher in the STZ groups ($p = 0.007$. At P56, PCr:Cr was higher in the STZ group compared to CONT and STZ+INS groups ($p = 0.04$). No difference noted between the STZ+INS and CONT groups. No other metabolites were altered. **Conclusion:** Neonatal hyperglycemia alters the acute and long-term neurochemical profile in the hippocampus of developing rats. The increase in PCr:Cr ratio in the STZ group indicates lower demand for ATP and PCr, secondary to decreased neuronal activity, which has been demonstrated in previous studies. PCr:Cr ratio of the STZ+INS group was no different than control, indicating that intranasal insulin reverses the negative effect on neuronal activity caused by neonatal hyperglycemia.

Diabetes Mellitus and Glucose Metabolism

DYSREGULATED METABOLIC RESPONSE

Young Adult LEW.1WR1 Rats Develop Dysregulated Islet Function and Impaired Liver Insulin Responses