Increased heart glucose uptake in Slc6a19 (-/-) mice appears to be independent of GLP-1 action

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Global loss of intestinal and renal neutral amino acid transporter SLC6A19 has been reported to improve glycaemic control in a mouse model, a desirable outcome in the treatment of type 2 diabetes. It is thought to arise through elevated levels of the metabolic hormones glucagon-like peptide-1 (GLP-1) and fibroblast growth factor 21 (FGF21) observed in Slc6a19 (-/-) mice. One phenotype relevant to glucose homeostasis in these Slc6a19 (-/-) mice is a significantly increased glucose uptake by the heart compared with wild type mice. It is postulated that this novel trait is mainly driven by the elevated postprandial level of circulating GLP-1. In this study, the mRNA and total protein levels of cardiac glucose transporters were characterized. Moreover, the effects of GLP-1 receptor activation by the agonist Exendin-4 on cardiac glucose transporter expression was also examined.

Our results indicate that levels of glucose transporter mRNAs and proteins in the hearts of Slc6a19 (-/-) mice were not significantly different when compared to wild type mice. Transcript levels of hexokinase-1 (Hk1), -2 (Hk2) and glucokinase (Gck) were also similar between Slc6a19 (-/-) mice and wild type mice. Administration of the agonist Exendin-4 to increase GLP-1 receptor activation unexpectedly reduced transcript and protein levels of the major cardiac glucose transporter GLUT4 in both wild type and Slc6a19 (-/-) mice. Collectively, these results suggest that the increased glucose uptake rate in hearts of Slc6a19 (-/-) mice is unlikely to be caused by higher levels of circulating GLP-1 and further research is required to uncover the underlying mechanisms of this important phenotype.