The Influence of Glucagon-Like-Peptide-1 Receptor Single Nucleotide Polymorphisms on Gastric Emptying Rate in Caucasian Men- A Pilot

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Gastric emptying is the rate-limiting step in the absorption of nutrients in the small intestine. The emptying rate of a glucose solution has been shown to be highly variable between individuals[1]. The gastrointestinal hormone glucagon-like peptide-1 which is prominently secreted following carbohydrate ingestion, has been shown to exert inhibitory effects on gastric emptying rate[2]. Previous work has shown an influence of glucagon-like peptide-1 receptor (GLP-1R) genetic variation on gastric emptying rate in mice[3]. This pilot study investigated the effect of GLP-1R single nucleotide polymorphisms (SNPs) on the rate of gastric emptying in humans.

Forty-eight healthy non-smoking UK Caucasian males aged 18-35 yr (mean ± SD age 23 ± 5 yr, height 178.2 ± 6.9 cm, weight 75.82 ± 11.24 kg, BMI 23.9 ± 3.3, body fat 19.0 ± 6.2%) took part in this investigation. Following an overnight fast, participants completed a single experimental trial involving the ingestion of 595 ml of a 6% glucose solution containing 100 mg¹³C sodium acetate. Gastric emptying rate of the solution was measured by ¹³C breath test whereby breath samples were collected at baseline and 10 min intervals for 60 min. A venous blood sample was obtained from each participant for genetic analysis. Twenty-eight haplotype-tagging (Tag) SNPs in the GLP-1R locus incorporating 10,000bp upstream and downstream of the major transcription initiation site and the last exon, respectively, were identified from the HapMap database. Twenty-seven SNPs were successfully genotyped using Sequenom MassARRAY iPLEX GOLD analysis. Gastric emptying results were analysed by genotype and phenotype using Kruskal-Wallace and Wilcoxon statistical tests, respectively. Values are median [quartiles].

A significant effect of genotype on time of maximum emptying rate (Tlag) was seen for neighbouring SNPs rs742764 and rs2254336. For SNP rs742764, Tlag was faster in genotype CC compared to genotype TT and TC (35 [30-36] vs. 41 [37-46] and 41 [39-45] min; P<0.01). For SNP rs2254336, Tlag was slower in genotype AA compared to genotype TT and TA (43 [39-49] vs. 36 [34-41] and 39 [35-42] min; P<0.05). An effect of phenotype was also seen for SNP rs2254336 where Tlag was slower in homozygotes of the major allele A compared to participants with the minor allele T (43 [39-49] vs. 39 [34-41] min; P<0.05). Further effects of phenotype were seen for SNP rs2268657 where Tlag was faster in homozygotes of the major allele A compared to participants with the minor allele G (37 [34-39] vs. 41 [37-45] min; P<0.05) and for SNP rs9283907 where half emptying time (T½) was slower in homozygotes of the major allele G compared to participants with the minor allele A (67 [59-82] vs. 55 [53-61] min; P<0.05).
The results of this study suggest that gastric emptying rate may be influenced by SNPs within the GLP-1R gene. Replication of this pilot study in larger cohorts is required to confirm the contribution of GLP-1R gene variation to gastric emptying rate.