**Supplementary Table 1**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Intervention** | **PLA+NaCl** | **PLA+GIP** | **PLA+GLP-1** | **SU+NaCl** | **SU+GIP** | **SU+GLP-1** | **Interaction** |
| **Insulin** |
| ***HNF1A* mutation carriers**  |  |  |  |  |  |  |  |
|  Baseline (pM) | 24 ± 3 | 22 ± 2 | 24 ± 3 | 23 ± 3 | 24 ± 2 | 23 ± 2 |  |
| bsAUC0-60 min (nM × min) | 0.1 ± 0.1 | 1.0 ± 0.2\* | 0.6 ± 0.2 | 0.8 ± 0.3 | 2.5 ± 0.4\*†**§**‡ | 2.1 ± 0.4\*†**§**‡ | *P* = 0.0595 |
| bsAUC60-120 min (nM × min) | 1.2 ± 0.4 | 2.1 ± 0.5 | 2.8 ± 0.7 | 2.4 ± 0.6 | 5.1 ± 0.7\*†**§**‡ | 5.1 ± 0.8\*†**§**‡ | *P* = 0.0447 |
| bsAUC0-120 min (nM × min) | 1.3 ± 0.4 | 3.1 ± 0.6 | 3.4 ± 0.8 | 3.3 ± 0.8 | 7.7 ± 1.1\*†**§**‡ | 7.2 ± 1.1\*†**§**‡ | *P* = 0.0320 |
| **Non-diabetic controls** |  |  |  |  |  |  |  |
|  Baseline (pM) | 33 ± 6 | 41 ± 4 | 35 ± 5 | 36 ± 6 | 36 ± 5 | 42 ± 5 |  |
|  bsAUC0-60 min (nM × min) | -0.3 ± 0.4 | 1.3 ± 0.4 | 0.9 ± 0.5 | 0.8 ± 0.3 | 2.2 ± 0.6\* | 3.8 ± 0.9\*†**§** | *P* = 0.0936 |
|  bsAUC60-120 min (nM × min) | 3.0 ± 1.7 | 8.8 ± 2.4 | 11.7 ± 4.6 | 6.8 ± 2.6 | 17.2 ± 4.8 | 30.2 ±6.4\*†**§**‡ | *P* = 0.0215 |
|  bsAUC0-120 min (nM × min) | 2.7 ± 2.1 | 10.0 ± 2.7 | 12.6 ± 5.1 | 7.5 ± 2.8 | 19.4 ± 5.3 | 34.5 ±7.2\*†**§**‡ | *P* = 0.0196 |
| **Insulin:glucose** |
| ***HNF1A* mutation carriers**  |  |  |  |  |  |  |  |
|  Baseline (pM/mM)  | 3.4 ± 0.7 | 2.9±0.6 | 3.3 ± 0.6 | 3.0 ± 0.6 | 3.1 ± 0.5 | 3.1 ± 0.5 |  |
|  bsAUC0-60 min (pM/mM× min) | 0.9 ± 12 | 115±22\* | 71.5 ± 25 | 110 ± 28 | 303 ± 45\*†**§**‡ | 264 ± 43\*†**§**‡ | *P*=0.0729 |
|  bsAUC60-120 min (pM/mM× min) | 59.1 ± 32 | 151±54 | 218 ± 77 | 151 ± 51 | 425 ± 78\*†**§**‡ | 413 ± 92\*†**§**‡ | *P*=0.0065 |
|  bsAUC0-120 min (pM/mM× min) | 60.1 ± 33 | 266±69 | 289 ± 94 | 256 ± 70 | 728 ± 116\*†**§**‡ | 677 ± 129\*†**§**‡ | *P*=0.0065 |
| **Non-diabetic controls** |  |  |  |  |  |  |  |
|  Baseline (pM) | 6.9 ± 1.2 | 8.2 ± 0.9 | 7.1 ± 1.1 | 7.2 ± 1.1 | 7.3 ± 1.0 | 8.2 ± 1.0 |  |
|  bsAUC0-60 min (pM/mM× min) | -66 ± 92 | 268 ± 89 | 179 ± 103 | 161 ± 70 | 456 ± 132\* | 779 ± 179\*†**§** | *P*=0.0964 |
|  bsAUC60-120 min (pM/mM× min) | 275 ± 247 | 1001 ± 329 | 1450 ± 670 | 743 ± 340 | 2137 ± 630 | 3937 ± 907\*†**§** | *P*=0.0279 |
|  bsAUC0-120 min (pM/mM× min) | 208 ± 287 | 1269 ± 358 | 1629 ± 446 | 904 ± 312 | 2593 ± 716 | 4792 ± 705\*†**§** | *P*=0.0276 |
| **ISR** |
| ***HNF1A* mutation carriers** |  |  |  |  |  |  |  |
|  Baseline (pmol/kg/min) | 1.1 ± 0.1 | 1.0 ± 0.1 | 1.2 ± 0.1 | 1.1 ± 0.1 | 1.3 ± 0.1 | 1.8 ± 0.1 |  |
|  bsAUC0-60 min (pmol/kg) | 16 ± 8 | 39 ± 7 | 32 ± 7 | 33 ± 7 | 84 ± 14\*†**§**‡ | 75 ± 14\*† | *P*=0.1689 |
|  bsAUC60-120 min (pmol/kg) | 64 ± 13 | 82 ± 14 | 113 ± 17 | 95 ± 19 | 177 ± 23\*†**§** | 183 ± 23\*†**§** | *P*=0.0238 |
|  bsAUC0-120 min (pmol/kg) | 80 ± 19 | 121 ± 19 | 145 ± 22 | 127 ± 29 | 260 ± 35\*†**§** | 258 ± 34\*†**§** | *P*=0.0383 |

**Supplementary Table 1 (continued)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Intervention** | **PLA+NaCl** | **PLA+GIP** | **PLA+GLP-1** | **SU+NaCl** | **SU+GIP** | **SU+GLP-1** | **Interaction** |
| **ISR** |
| **Non-diabetic controls**  |  |  |  |  |  |  |  |
|  Baseline (pmol/kg/min) | 1.1 ± 0.2 | 1.3 ± 0.1 | 1.1 ± 0.1 | 2.2 ± 0.7 | 1.1 ± 0.2 | 1.5 ± 0.2 |  |
|  bsAUC0-60 min (pmol/kg) | -3 ± 15 | 39 ± 13 | 39 ± 16 | 54 ± 23 | 78 ± 22 | 125 ± 24\*†**§** | *P*=0.3967 |
|  bsAUC60-120 min (pmol/kg) | 92 ± 40 | 220 ± 44 | 284 ± 59 | 310 ± 86 | 386 ± 92 | 594 ± 100\*†**§**‡***||*** | *P*=0.2333 |
|  bsAUC0-120 min (pmol/kg) | 89 ± 51 | 259 ± 54 | 323 ± 73 | 364 ± 102 | 464 ± 111 | 720 ± 121\*†**§**‡ | *P*=0.2348 |
| **ISR:Glucose** |
| ***HNF1A* mutation carriers** |  |  |  |  |  |  |  |
|  Baseline (pmol/kg/min/mM) | 0.15 ± 0.02 | 0.14 ± 0.02 | 0.15 ± 0.03 | 0.14 ± 0.02 | 0.18 ± 0.02 | 0.17±0.03 |  |
|  bsAUC0-60 min (pmol/kg/mM) | 2.1 ± 1.2 | 4.2 ± 0.9 | 4.0 ± 1.1 | 3.7 ± 1.3 | 9.7 ± 1.5\*†**§**‡ | 8.4±1.5\*‡ | *P*=0.2166 |
|  bsAUC60-120 min (pmol/kg/mM) | 3.8 ± 1.4 | 5.1 ± 1.5 | 7.9 ± 2.2 | 5.6 ± 1.8 | 12.1 ± 2.3\*†‡ | 13.5±2.6\*‡ | *P*=0.0520 |
|  bsAUC0-120 min (pmol/kg/mM) | 5.8 ± 2.4 | 9.2 ± 2.2 | 11.9 ± 3.0 | 9.2 ± 3.0 | 27.8 ± 3.7\*†‡ | 21.9±3.9\*‡ | *P*=0.0874 |
| **Non-diabetic controls** |  |  |  |  |  |  |  |
|  Baseline (pmol/kg/min/mM) | 0.24 ± 0.03 | 0.33 ± 0.08 | 0.24 ± 0.02 | 0.29 ± 0.03 | 0.25 ± 0.03 | 0.34 ± 0.03 |  |
|  bsAUC0-60 min (pmol/kg/mM) | -0.9 ± 2.2 | 5.7 ± 3.7 | 8.4 ± 2.1 | 5.7 ± 2.3 | 16.3 ± 3.5\* | 20.4 ± 3.8\*†**§** | *P*=0.4305 |
|  bsAUC60-120 min (pmol/kg/mM) | 9.0 ± 3.4 | 23.8 ± 5.8 | 37.1 ± 11.6\*† | 21.7 ± 5.4 | 50.2 ± 10.1\*†‡ | 74.1 ± 10.9\*†**§**‡ | *P*=0.0660 |
|  bsAUC0-120 min (pmol/kg/mM) | 8.1 ± 5.0 | 29.5 ± 8.9 | 45.5 ± 8.2 | 27.4 ± 7.1 | 66.4 ± 13.2\*†‡ | 93.0 ± 13.7\*†**§**‡ | *P*=0.1322 |

Insulin, Insulin:glucose, ISR, ISR:glucose.All values are mean±SEM. A significant interaction describes a supra-additive of combining SU+GIP and/or SU+GLP-1. Symbols show significant differences between interventions: Asterisks (\*) significantly greater (*P*<0.05) than PLA+NaCl; Daggers (†) significantly greater SU+NaCl; Double daggers (‡) significantly greater than PLA+GIP; Paragraph (§) significantly greater than PLA+GLP-1; Parallel lines (||) significantly greater than SU+GIP. AUC, area under the curve; bsAUC, baseline subtracted area under the curve; HNF1A, hepatocyte nuclear factor 1-alpha; iAUC: incremental value area under the curve; ISR, insulin secretion rate; PLA, Placebo; SU, sulfonylurea.