**Supplemental Table 1**

|  |  |  |
| --- | --- | --- |
| **Analyte** | **Dilution Factors** | **Lower Limit of Detection** |
| sAPPα | 2, 4 | 0.78 ng/mL |
| sAPPβ | 2, 4 | 0.78 ng/mL |
| sAPP total | 10, 20 | 0.39 ng/mL |
| Aβ(1-40) | 4, 8 | 1.56 pg/mL |
| Aβ(1-42) | 2, 4 | 1.56 pg/mL |
| ADAM-10 | 600, 1200 | 62.5 pg/mL |
| ADAM-17 | 2, 4 | 78.15 pg/mL |
| BACE-1 | 200, 800 | 0.25 ng/mL |

**Supplemental Table 2**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Analyte** | **FXS Average** | **TDC Average** | **p-value** | **Effect Size (d\*)** | **Sex\*Group p-value** |
| sAPPα (ng/mL) | 8.97 ± 5.09 | 17.10 ± 8.132 | \*0.0003 | 1.13 | 0.7979 |
| sAPPβ (ng/mL) | 7.58 ± 3.82 | 8.82 ± 3.36 | 0.1745 | 0.42 | 0.3411 |
| sAPP total (ng/mL) | 143.70 ± 64.98 | 173.50 ± 71.28 | 0.1148 | 0.45 | 0.5510 |
| Aβ(1-40) (pg/mL) | 130.20 ± 72.85 | 94.27 ± 40.69 | \*0.0169 | 0.70 | 0.2790 |
| Aβ(1-42) (pg/mL) | 14.02 ± 11.10 | 6.602 ± 6.090 | \*0.0098 | 0.85 | 0.6190 |
| ADAM-10 (ng/mL) | 512.676 ± 255.938 | 522.244 ± 248.440 | 0.5451 | 0.17 | 0.0701 |
| ADAM-17 (pg/mL) | 861.6 ± 737.5 | 704.5 ± 486.5 | 0.9658 | 0.01 | 0.6189 |
| BACE-1 (ng/mL) | 1274 ± 1523 | 1321 ± 1424 | 0.8716 | 0.04 | 0.5637 |

**Supplemental Table 3**

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **FXS** | **TDC** |
| **Enzyme** | **Metabolite** | **No.**  | **p-value** | **No.** | **p-value** |
| ADAM-10 |  |  |  |  |  |
|  | sAPPα | 24 | 0.185 | 24 | 0.912 |
| ADAM-17 |  |  |  |  |  |
|  | sAPPα | 15 | 0.612 | 19 | 0.176 |
| BACE-1 |  |  |  |  |  |
|  | sAPPβ | 17 | 0.794 | 20 | 0.923 |
|  | Aβ(1-40) | 20 | 0.794 | 22 | 0.275 |
|  | Aβ(1-42) | 18 | 0.999 | 17 | 0.923 |