Supplemental table 1. 1-deoxydihydroceramide concentrations.

Deoxysphingolipids (pmol/100 µL)	Lean controls	Obese	Obese/T2D	Obese/T2D/DN	Spearman Correlation (CC, p-value)
C16:0 1-deoxydihydroceramide	0.23 ± 0.13	0.39 ± 0.27	0.46 ± 0.29*	0.53 ± 0.29**	0.47 <0.001
C18:0 1-deoxydihydroceramide	0.38 ± 0.23	0.79 ± 0.64	1.10 ± 0.80**	1.13 ± 0.58***	0.56 <0.001
C20:0 1-deoxydihydroceramide	0.49 ± 0.29	0.73 ± 0.44	1.03 ± 0.60**	1.14 ± 0.43***,†	0.52 <0.001
C22:0 1-deoxydihydroceramide	1.58 ± 1.10	1.66 ± 0.97	2.04 ± 1.37	2.46 ± 0.88*	0.35 0.002
C24:0 1-deoxydihydroceramide	1.58 ± 0.94	1.36 ± 0.86	1.66 ± 0.99	1.88 ± 0.85	0.17 0.15
C24:1 1-deoxydihydroceramide	0.93 ± 0.69	1.16 ± 0.69	1.49 ± 1.01	1.81 ± 0.85**	0.43 0.0001
Total 1-deoxydihydroceramides	5.19 ± 3.18	6.08± 3.40	7.79 ± 4.54	8.94 ± 3.23**	0.41 0.0002

* statistically significant compared to lean (Tukey-Kramer adjusted p value: *p<0.05, **p<0.01, ***p<0.001).

† statistically significant compared to obese (Tukey-Kramer adjusted p value: †p<0.05, ††p<0.01, †††p<0.001).

Supplemental table 2. Correlation of amino acids with individual 1-deoxydihydroceramide species

	Serine (µM)	Alanine (µM)	Alanine:Serine Ratio
Deoxysphingolipids (pmol/100 µL)			
C16:0 1-deoxydihydroceramide	-0.37, 0.001	0.49, <0.0001	0.63, <0.0001
C18:0 1-deoxydihydroceramide	-0.31, 0.007	0.41, 0.0003	0.49, <0.0001
C20:0 1-deoxydihydroceramide	-0.35, 0.002	0.47, <0.0001	0.56, <0.0001
C22:0 1-deoxydihydroceramide	-0.31, 0.006	0.44, <0.0001	0.54, <0.0001
C24:0 1-deoxydihydroceramide	-0.23, 0.045	0.35, 0.002	0.39, 0.0005
C24:1 1-deoxydihydroceramide	-0.26, 0.027	0.29, 0.011	0.40, 0.0006
Total 1-deoxydihydroceramides	-0.33, 0.004	0.45, <0.0001	0.54, <0.0001

Values are expressed as correlation coefficient (CC), p value, n=75.

Supplemental table 3. Correlation of individual 1-deoxydihydroceramide species and amino acids with neuropathy outcome measures

	MNSI-Q (n=75)	MNSI-E (n=75)	Sural Amplitude (n=73)	IENFD Leg (n=74)	IENFD Thigh (n=75)
Deoxysphingolipids (pmol/100 µL)					
C16:0 1-deoxydihydroceramide	0.29, 0.012	0.14, 0.219	-0.25, 0.032	-0.40, 0.0005	-0.23, 0.052
C18:0 1-deoxydihydroceramide	0.30, 0.008	0.11, 0.369	-0.27, 0.023	-0.42, 0.0002	-0.17, 0.149
C20:0 1-deoxydihydroceramide	0.37, 0.001	0.27, 0.018	-0.35, 0.003	-0.47, <0.0001	-0.30, 0.009
C22:0 1-deoxydihydroceramide	0.24, 0.04	0.15, 0.205	-0.25, 0.034	-0.28, 0.015	-0.15, 0.200
C24:0 1-deoxydihydroceramide	0.11, 0.336	0.04, 0.743	-0.10, 0.381	-0.079, 0.505	-0.10, 0.417
C24:1 1-deoxydihydroceramide	0.26, 0.023	0.18, 0.122	-0.30, 0.010	-0.36, 0.002	-0.26, 0.024
Total 1-deoxydihydroceramides	0.28, 0.016	0.16, 0.176	-0.28, 0.018	-0.34, 0.003	-0.21, 0.070

Values are expressed as correlation coefficient (CC), p value. MNSI-Q, Michigan Neuropathy Screening Instrument Questionnaire; MNSI-E, Michigan Neuropathy Screening Instrument Exam Score; IENFD, intraepidermal nerve fiber density.

Supplemental table 4. Comparison of total 1-deoxysphingolipids after adjusting for lactosylceramide concentrations

	Lean (n=19)	Ob (n=19)	Ob/T2D (n=18)	Ob/T2D/DN (n=19)
Deoxysphingolipids (pmol/100 µL)				
C16:0 1-deoxydihydroceramide	0.214 ± 0.040	0.386 ± 0.061	0.467 ± 0.069*	0.537 ± 0.070**
C18:0 1-deoxydihydroceramide	0.346 ± 0.074	0.788 ± 0.146	1.111 ± 0.190**	1.159 ± 0.139***
C20:0 1-deoxydihydroceramide	0.403 ± 0.086	0.730 ± 0.095	1.057 ± 0.147**	1.206 ± 0.105***,††
C22:0 1-deoxydihydroceramide	1.472 ± 0.298	1.658 ± 0.216	2.070 ± 0.337	2.549 ± 0.232†
C24:0 1-deoxydihydroceramide	1.475 ± 0.256	1.354 ± 0.192	1.687 ± 0.245	1.961 ± 0.214
C24:1 1-deoxydihydroceramide	0.758 ± 0.191	1.155 ± 0.151	1.530 ± 0.249	1.942 ± 0.204**,†
Total 1-deoxydihydroceramides	4.601 ± 0.894	6.071 ± 0.747	7.939 ± 1.125	9.404 ± 0.812**, †

Values are expressed as mean ± SD.

* statistically significant compared to lean (Tukey-Kramer adjusted p value: *p<0.05, **p<0.01, ***p<0.001).

† statistically significant compared to obese (Tukey-Kramer adjusted p value: †p<0.05, ††p<0.01, †††p<0.001).

‡ statistically significant compared to obese + T2D (Tukey-Kramer adjusted p value: ‡p<0.05, ‡‡p<0.01, ‡‡‡p<0.001).

§ statistically significant compared to obese + T2D + DN (Tukey-Kramer adjusted p value: §p<0.05, §§p<0.01, §§§ p<0.001).