**SUPPLEMENTAL DATA**

***Nerve conduction studies***

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| --- | --- | --- | --- | --- | --- |
| **Motor NCS** | **Stimulation point** | **Record point** | **Latency (ms)** | **Amplitude (mV)** | **Velocity (m/s)** |
| *Right median* | Wrist | APB | 3,25 | 11,3 |  |
| Elbow |  | 8,70 | 10,4 | 45,9 |
| *Left common peroneal* | Ankle | EDB | 8,15 | \ |  |
| Head of fibula |  | 23,65 |  | 21,9 |
| *Right common peroneal* | Ankle | EDB | 3,75 | \ |  |
| Head of fibula |  | 18,35 | 0,2 | 22,6 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Sensory NCS** |  |  | **Latency (ms)** | **Amplitude (μV)** |
| *Right median* | wrist | 3rd digit | 3,10 | 9,8 |
| 4th digit | 3 | 8,3 |
| *Right ulnar* | wrist | 4th digit | 3,25 | 3,1 |
| 5th digit | 2,75 | 5,3 |
| *Right sural* | Lateral malleolus | calf | -- | -- |
| *Left sural* | Lateral malleolus | calf | -- | -- |

|  |  |
| --- | --- |
| **Nerve** | **Minimal Latency F-Wave (ms)** |
| *left common peroneal* | -- |
| *left tibial (knee)* | -- |
| *Right tibial (knee)* | -- |
| *Right common peroneal* | -- |
| *Right median* | 31,55 |

***Genetic screening - gene panel***

NGS was performed by in-house panel containing 45 CMT and HSAN-related genes including: APTX, ATL1, ATL3, ATP7A, CCT5, CLTCL1, CNTNAP1, DGAT2, DNAJC3, DNMT1, DST, FAM134B, FLVCR1, GBA, GBA2, GLA, HSD17B4, IFRD1, IKBKAP,  KIF1A, MPV17, NAGLU, NGF, NTRK1, PHYH, POLG, PRDM12, PRNP, RAB7, RFN170, RFN216, SACS, SCN10A, SCN11A, SCN9A, SETX, SPTLC1, SPTLC2, STUB1, TDP1, TECPR2, TRPA1, TTPA, TTR, WNK1.  Targeted sequencing was performed by multiplex PCR on a PGM Ion Torrent machine (Thermo Fischer Scientific) according to the manufacturer's protocol. Mean target coverage was >800 X; on average 93% of all targeted bases had coverage greater than 20X.

SPTLC1 (OMIM**\***605712) has long been associated with HSAN I (phenotype MIM number 162400). Dawkins and Bejaoui independently described the Cys133Trp and Cys133Tyr mutations in SPTLC1 in 20011,2, while Rautenstrauss reported a case of HSAN I associated with Cys133Arg genotype3. Bode et al. compared enzymatic properties of most known SPTLC1 and SPTLC2 mutants, providing basis for structure-function-phenotype correlations4.

1. Bejaoui K, Wu C, Scheffler MD, et al. SPTLC1 is mutated in hereditary sensory neuropathy, type 1. Nature Genetics. 2001;27:261–262.
2. Dawkins JL, Hulme DJ, Brahmbhatt SB, Auer-Grumbach M, Nicholson GA. Mutations in SPTLC1, encoding serine palmitoyltransferase, long chain base subunit-1, cause hereditary sensory neuropathy type I. Nature Genetics. 2001;27:309–312.
3. Rautenstrauss B, Neitzel B, Muench C, Haas J, Holinski-Feder E. Late onset hereditary sensory neuropathy type 1 (HSN1) caused by a novel p.C133R missense mutation in SPTLC1 Würzburg, Germany. 2009 Meeting of the Peripheral Nerve Society July 4-8, 2009. (290 of 381)
4. Bode H, Bourquin F, Suriyanarayanan S, et al. HSAN1 mutations in serine palmitoyltransferase reveal a close structure-function-phenotype relationship. Human Molecular Genetics. 2016;25:853–865

***Methodological details on untargeted lipidomics analysis***

Plasma samples (0.1 ml) were extracted using the Bligh-Dyer total lipid extraction protocol (Bligh EG, Dyer WJ (1959) A rapid method of total lipid extraction and purification. Canadian Journal of Biochemistry and Physiology 37:911–917 . doi: 10.1139/o59-099). After extraction, the apolar, lower phase was separated and dried under nitrogen. The samples were then re-dissolved in a 9:1 methanol:chloroform mixture (0.2 ml) and transferred to a glass vial for LC-MS/MS analysis that was conducted as described elsewhere (Basit A, Pontis S, Piomelli D, Armirotti A (2016) Ion mobility mass spectrometry enhances low-abundance species detection in untargeted lipidomics. Metabolomics: Official journal of the Metabolomic Society 12:50. doi: 10.1007/s11306-016-0971-3) on a Acquity UPLC system coupled with a Synapt G2 QToF mass spectrometer (both purchased from Waters, Milford, MA, USA).

All the solvents were purchased from Sigma Aldrich (Milano, Italy). Data analysis was performed by using MassLynx software (Waters).