Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

Supplementary Table S4: Statistical analysis clinical characteristics pure small fiber neuropathy patients

Variable	No Variant	Variant	SCN9A	SCN10A	SCN11A	Main comparison (alpha < 0.05)	Post-hoc analyses (alpha < 0.0083)					
						No variant vs. variant	*SCN9A vs no variant*	*SCN10A vs no variant*	*SCN11A vs no variant*	*SCN9A vs. SCN10A*	*SCN9A vs. SCN11A*	*SCN10A vs. SCN11A*
TTT (total abnormal)	932/1000 (93.2%)	122/132 (92.4%)	52/57 (91.2%)	41/42 (97.6%)	28/32 (87.5%)	0.741	0.587*	0.518*	0.274*	0.237*	0.717*	0.159*
IENFD (total abnormal)	327/1003 (32.6%)	50/132 (37.9%)	23/57 (40.4%)	17/42 (40.5%)	9/32 (28.1%)	0.226	0.226	0.287	0.594	0.990	0.249	0.270
Abnormal pain sensation (total)	224/407 (55.0%)	33/52 (63.5%)	11/21 (52.4%)	7/12 (58.3%)	15/19 (78.9%)	0.249	0.811	0.821	0.040	0.741	0.079	0.253*
Erythromelalgia (total present)	265/1004 (26.4%)	43/132 (32.6%)	25/57 (43.9%)	7/42 (16.7%)	10/32 (31.3%)	0.133	0.004	0.159	0.540	0.004	0.243	0.140
Itch (total present)	117/1004 (11.7%)	13/131 (9.9%)	5/56 (8.9%)	4/42 (9.5%)	4/32 (12.5%)	0.559	0.534	0.810*	0.782*	1.000*	0.718*	0.720*
Cramps (total present)	166/1004 (16.5%)	25/131 (19.1%)	8/56 (14.3%)	8/42 (19.0%)	9/32 (28.1%)	0.463	0.658	0.668	0.085	0.528	0.114	0.467
Positive family history (total)	225/916 (24.6%)	41/121 (33.9%)	19/53 (35.8%)	13/38 (34.2%)	9/30 (30.0%)	0.027	0.066	0.178	0.497	0.872	0.588	0.712
Increase of pain by warmth (total)	178/576 (30.9%)	33/73 (45.2%)	18/37 (48.6%)	6/17 (35.3%)	9/19 (47.4%)	0.014	0.025	0.700	0.128	0.359	0.928	0.463
Increase of pain by cold (total)	245/541 (45.3%)	36/64 (56.3%)	14/29 (48.3%)	13/19 (68.4%)	9/16 (56.3%)	0.096	0.753	0.047	0.386	0.169	0.608	0.458
Increase of pain by exercise (total)	470/661 (71.1%)	62/91 (68.1%)	25/36 (69.4%)	19/29 (65.5%)	18/26 (69.2%)	0.559	0.831	0.517	0.836	0.736	0.986	0.769
Increase of pain by rest (total)	271/408 (66.4%)	38/57 (66.7%)	14/23 (60.9%)	14/18 (77.8%)	10/16 (62.5%)	0.971	0.584	0.316	0.745	0.248	0.918	0.457*
NPS1 (total score 4 or higher)	709/800 (88.6%)	98/112 (87.5%)	47/50 (94.0%)	29/35 (82.9%)	21/26 (80.8%)	0.727	0.240	0.282*	0.213*	0.152*	0.114*	1.000*
NPS2	692/803 (86.2%)	101/112 (90.2%)	46/50 (92.0%)	32/37 (86.5%)	22/24 (91.7%)	0.243	0.242	0.957	0.761*	0.486*	1.000*	0.694*
NPS3	692/818 (84.6%)	99/113 (87.6%)	45/50 (90.0%)	32/37 (86.5%)	21/25 (84.0%)	0.401	0.300	0.755	1.000*	0.738*	0.470*	1.000*
NPS4	589/763 (77.2%)	82/111 (73.9%)	36/50 (72.0%)	24/35 (68.6%)	21/25 (84.0%)	0.439	0.399	0.237	0.423	0.733	0.251	0.174
NPS5	452/817 (55.3%)	68/116 (58.6%)	28/52 (53.8%)	23/38 (60.5%)	16/25 (64.0%)	0.504	0.835	0.528	0.390	0.528	0.399	0.781
NPS6	548/816 (67.2%)	79/113 (69.9%)	36/52 (69.2%)	23/36 (63.9%)	19/24 (79.2%)	0.558	0.757	0.683	0.216	0.600	0.368	0.206
NPS7	350/818 (42.8%)	58/117 (49.6%)	19/53 (35.8%)	23/38 (60.5%)	16/25 (64.0%)	0.166	0.322	0.031	0.035	0.020	0.020	0.781
NPS9	730/769 (94.9%)	101/105 (96.2%)	46/47 (97.9%)	33/35 (94.3%)	21/22 (95.5%)	0.575	0.723*	0.697*	1.000*	0.573*	0.539*	1.000*
NPS10a	673/769 (87.5%)	95/109 (87.2%)	42/48 (87.5%)	32/36 (88.9%)	21/24 (87.5%)	0.915	0.997	1.000*	1.000*	1.000a	1.000*	1.000*
NPS10b	653/773 (84.5%)	89/106 (84.0%)	41/47 (87.2%)	28/35 (80.0%)	20/23 (87.0%)	0.891	0.611	0.477	1.000*	0.375	1.000*	0.725*
SFN-SIQ1 (total score 2 or higher)	681/840 (81.1%)	91/113 (80.5%)	38/50 (76.0%)	28/35 (80.0%)	24/27 (88.9%)	0.891	0.377	0.874	0.305	0.663	0.173	0.491*
SFN-SIQ2	535/839 (63.8%)	72/117 (61.5%)	29/51 (56.9%)	22/38 (57.9%)	20/27 (74.1%)	0.639	0.320	0.462	0.272	0.922	0.135	0.179
SFN-SIQ3	507/842 (60.2%)	69/114 (60.5%)	32/52 (61.5%)	17/35 (48.6%)	20/26 (76.9%)	0.949	0.850	0.169	0.086	0.232	0.174	0.025
SFN-SIQ4	574/845 (67.9%)	78/117 (66.7%)	33/52 (63.5%)	23/37 (62.2%)	22/27 (81.5%)	0.784	0.504	0.463	0.136	0.900	0.099	0.095
SFN-SIQ5	543/843 (64.4%)	80/119 (67.2%)	34/53 (64.2%)	28/38 (73.7%)	17/27 (63.0%)	0.547	0.969	0.242	0.877	0.336	0.917	0.356
SFN-SIQ6	673/844 (79.7%)	98/118 (83.1%)	42/52 (80.8%)	33/38 (86.8%)	22/27 (81.5%)	0.398	0.858	0.284	0.824	0.445	0.939	0.729*
SFN-SIQ7	595/840 (70.8%)	81/118 (68.5%)	35/52 (67.3%)	26/38 (68.4%)	20/27 (74.1%)	0.625	0.588	0.749	0.715	0.911	0.535	0.621
SFN-SIQ8	567/838 (67.7%)	77/117 (65.8%)	33/52 (63.5%)	25/38 (65.8%)	18/26 (69.2%)	0.689	0.531	0.809	0.866	0.820	0.614	0.773
SFN-SIQ9	587/841 (69.8%)	82/117 (70.1%)	34/52 (65.4%)	26/37 (70.3%)	21/27 (77.8%)	0.949	0.502	0.951	0.373	0.628	0.256	0.502
SFN-SIQ10	662/844 (78.4%)	91/116 (78.4%)	36/51 (70.6%)	30/38 (78.9%)	24/26 (92.3%)	0.998	0.189	0.940	0.088	0.373	0.030	0.181*
SFN-SIQ11	771/834 (92.4%)	108/116 (93.1%)	46/50 (92.0%)	35/38 (92.5%)	26/27 (96.3%)	0.801	0.786*	0.761*	0.714*	1.000*	0.652*	0.636*
SFN-SIQ12	626/843 (74.3%)	88/118 (74.6%)	38/52 (73.1%)	27/38 (71.1%)	22/27 (81.5%)	0.941	0.850	0.659	0.397	0.832	0.407	0.336
SFN-SIQ13	732/839 (87.2%)	97/118 (82.2%)	44/52 (84.6%)	29/38 (76.3%)	23/27 (85.2%)	0.132	0.583	0.052	0.768*	0.320	1.000*	0.378
						Independent T-Test						
Mean age (in years ± SD)	52.22 ± 12.990	51.26 ± 14.506	48.74 ± 15.202	53.48 ± 13.204	52.47 ± 14.728	0.468#	0.095#	0.541	0.917	0.109	0.264	0.758
Mean debut age (in years ± SD)	46.03 ± 14.457	45.84 ± 15.483	42.12 ± 16.722	48.74 ± 13.895	48.09 ± 14.340	0.884	0.091#	0.235	0.428	0.040	0.093	0.846
VAS maximal (± SD)	77.52 ± 21.833	78.26 ± 18.610	79.76 ± 18.337	77.03 ± 19.095	78.00 ± 19.305	0.754	0.534	0.903	0.918	0.548	0.726	0.857

TTT: temperature threshold testing; IENFD: intraepidermal nerve fiber density; SD: standard deviation; *Fisher exact test; #equal variances not assumed. The green shaded values are statistically significant.

One patient with both an *SCN9A* and *SCN11A* variant was excluded in the separate analysis.

NPS: neuropathic pain scale. NPS pain qualities: 1 = severity; 2 = sharpness; 3 = hotness; 4 = dullness; 5 = coldness; 6 = sensitivity; 7 = itchiness; 9 = unpleasantness; 10a = intensity deep pain; 10b = intensity surface pain. Each item is scored on an 11-point scale (0 = not applicable to the experienced pain and 10 = in the most severe form applicable to the experienced pain). An NPS score >3 is considered as a relevant pain quality.

SFN-SIQ: small fiber neuropathy inventory questionnaire. SFN-SIQ symptoms: 1 = altered sweating pattern; 2 = diarrhea; 3 = constipation; 4 = micturation problems; 5 = dry eyes; 6 = dry mouth; 7 = orthostatic dizziness; 8 = palpitations; 9 = hot flashes; 10 = sensitive skin legs; 11 = burning feet; 12 = intolerance for sheets; 13 = restless legs. The answer options of the SFN-SIQ include 'never = 1', 'sometimes = 2', 'often = 3' and 'always = 4'. A symptom is considered to be present when the score is >1.

VAS: visual analogue scale. VAS is ranging from 0-100 (0 = no pain and 100 = the worst possible pain).