Supplemental material

Figure S1

Participants in the MEDON study

T1DM with painful DPN (n=20)	T1DM with **probable** painless DPN (n=20)	T1DM without DPN (n=20)	Healthy controls (n=20)
DN4 score ≥ 4	DN4 score < 4	DN4 score < 4	DN4 score < 4
	VPT > 25V	VPT ≤ 25V	VPT ≤ 25V

Participants included in the resting-state fMRI study

T1DM with painful DPN (n=20)	T1DM with **confirmed** painless DPN (n=19)	T1DM without DPN (n=19)	Healthy controls (n=20)
DN4 score ≥ 4	DN4 score < 4	DN4 score < 4	DN4 score < 4
	VPT > 25V	VPT ≤ 25V	VPT ≤ 25V
	Abnormal peripheral NCS	Normal peripheral NCS	Normal peripheral NCS

Analysed

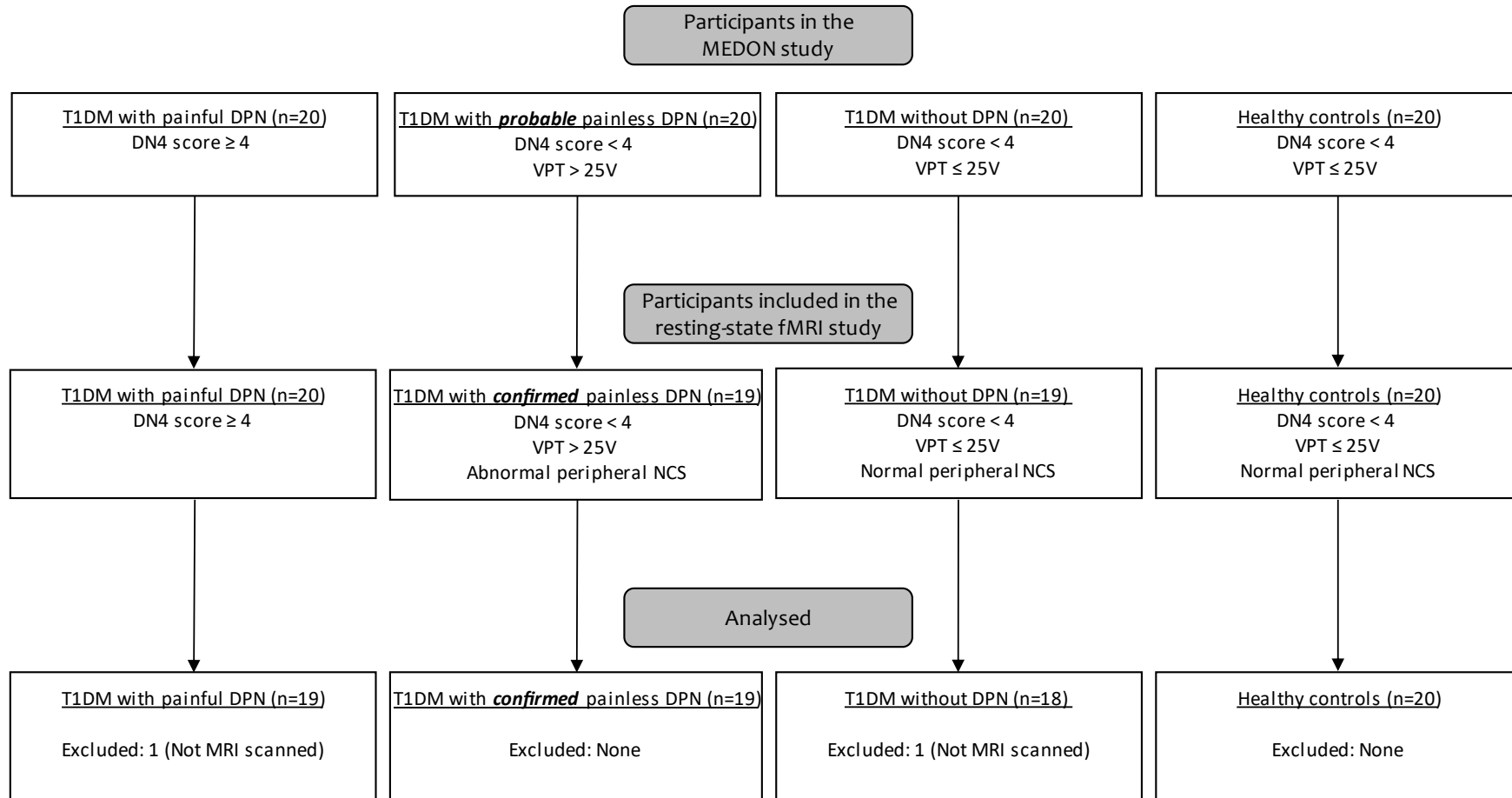| T1DM with painful DPN (n=19)	T1DM with **confirmed** painless DPN (n=19)	T1DM without DPN (n=18)	Healthy controls (n=20)
Excluded: 1 (Not MRI scanned)	Excluded: None	Excluded: 1 (Not MRI scanned)	Excluded: None

Figure S1: Overview of included participants.
Abbreviations: DN4, Douleur Neuropathique 4 Questions, DPN: diabetic peripheral neuropathy, fMRI: functional magnetic resonance, MEDON: Methods of Early Detection of diabetic peripheral Neuropathy, MRI: Magnetic resonance imaging, NCS: Nerve conduction study, NRS: Numeric rating scale, T1DM: type 1 diabetes mellitus, VPT: Vibration perception threshold.

Table S1

	T1DM with painful DPN n=19	T1DM with painless DPN n=19	T1DM without DPN n=18	Healthy controls n=20	*P*-value
Quantitative sensory testing					
Thermal sensory limen (°C)	26.5(21.2-38.9)[A]	32.0(24.0-42.8)[A]	14.7(11.5-20.0)[B]	12.9(4.9-23.6)[B]	<0.001*
Cold perception threshold (°C)	2.7(0.0-13.2)	0.0(0.0-3.6)	4.9(0.0-13.9)	5.8(0.0-17.0)	0.070
Warm perception threshold (°C)	49.1(45.8-50.0)	49.8(47.0-50.0)	47.6(42.9-49.0)	46.6(43.5-49.8)	0.020*
Mechanical pain threshold (mN)	212.9(79.6-689.4)[A]	264.4(44.1-739.3)[A]	57.6(23.0-123.5)[B]	42.4(20.8-119.1)[B]	<0.001*
Mechanical pain sensitivity (NRS)	20.8(7.6-33.9)	20.0(8.0-29.0)	16.6(10.7-28.1)	14.3(8.4-23.6)	0.825
Wind-up ratio	2.8(2.2-2.9)	2.2(1.8-3.1)	2.3(1.7-2.7)	2.2(1.8-2.7)	0.530
Pressure pain threshold (kPa)	312.7(237.8-349.1)[A]	366.7(258.5-522.7)[A,B]	454.0(366.7-545.5)[B]	427.5(344.3-590.8)[B]	0.009*

Table S1. Quantitative sensory testing data. Data are presented as median(interquartile range). The overall *p*-values are presented. Statistical differences between groups are denoted with A, B, and C, where groups including similar letters (such as for thermal sensory limen where the groups T1DM with painful DPN and T1DM with painless DPN are denoted with A) indicate no statistical differences, and groups not including similar letters (such as for thermal sensory limen where T1DM with painful DPN is denoted with A and T1DM without DPN is denoted with B) indicate pairwise statistical differences. * Indicates significant difference.

Abbreviations: DPN: diabetic peripheral neuropathy, NRS: Numeric rating scale, T1DM: type 1 diabetes mellitus.

Table S2

	Thalamus R-SMC,SFG L (-10, 0, 66)	Mean Thalamus L-SMC, SFG L (-14,-2,66 and -14,0,66)	PostCG R-PostCG R (12, -40, 70)	PostCG R-PreCG,PostCG L(-34, -24, 52)	PostCG R-PreCG,PostCG R(40, -20, 40)	PostCG L-PreCG, PostCG L(-34,-22,52)	PostCG L-PostCG R(40,-32,40)
Sural nerve amp	r= 0.377, p=0.004**	r= 0.526, p<0.001***	r= 0.282, p=0.035*	r= 0.301, p=0.024*	r= 0.321, p=0.016*	r= 0.271, p=0.043*	r= 0.355, p=0.007**
Sural nerve CV	r= 0.376, p=0.004**	r= 0.529, p<0.001***	r= 0.274, p<0.041*	r= 0.431, p<0.001***	r= 0.423, p=0.001**	r= 0.385, p=0.003**	r= 0.440, p=0.001**
Peroneal nerve amp	r= 0.476, p<0.001***	r= 0.564, p<0.001***	r= 0.346, p=0.009**	r= 0.421, p=0.001***	r= 0.362, p=0.006**	r= 0.428, p=0.001**	r= 0.411, p=0.002**
Peroneal nerve CV	r= 0.436, p=0.001***	r= 0.563, p=0.001***	r= 0.374, p=0.005**	r= 0.467, p<0.001***	r= 0.384, p=0.003**	r= 0.468, p<0.001***	r= 0.457, p<0.001***
Cold detection threshold	r= 0.377, p=0.004**	r= 0.369, p=0.005**	r= 0.242, p=0.073	r= 0.419, p<0.001***	r= 0.319, p=0.017*	r= 0.318, p=0.017*	r= 0.411, p=0.002**
Warm detection threshold	r= -0.586, p<0.001***	r= -0.451, p<0.001***	r= -0.436, p=0.001***	r= -0.443, p=0.001***	r= -0.380, p=0.004**	r= -0.307, p=0.021*	r= -0.504, p<0.001***
DN4 score	r= -0.401, p=0.002**	r= -0.530, p<0.001***	r= -0.449, p<0.001***	r= -0.475, p<0.001***	r= -0.422, p=0.001**	r= -0.473, p<0.001***	r= -0.446, p=0.001**
NRS peak pain	r= -0.385, p=0.003**	r= -0.498, p<0.001***	r= -0.340, p=0.010*	r= -0.396, p=0.003**	r= -0.342, p=0.010*	r= -0.437, p=0.001**	r= -0.379, p=0.004**
NRS average pain	r= -0.413, p=0.002**	r= -0.571, p<0.001***	r= -0.327, p=0.014*	r= -0.346, p=0.009**	r= -0.345, p=0.009**	r= -0.440, p=0.001**	r= -0.351, p=0.008**

Table S2. Correlation between ROI connectivity and peripheral and pain measurements.

Abbreviations: Amp: Amplitude, CV: Conduction velocity, DN4: Douleur Neuropathique 4 Questions, L: Left, PostCG: Postcentral gyrus, PreCG: Precentral gyrus, NRS: Numeric rating scale, R: Right, ROI: Region of interest, SFG: Superior frontal gyrus, SMC: Supplementary motor cortex.