A novel method for measuring vibration perception thresholds (VPTs) shows an improvement in VPTs in type 1 diabetes patients with improved metabolic control.

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Aim

To investigate how vibration perception thresholds change in T1DM patients after changes in metabolic control

Background

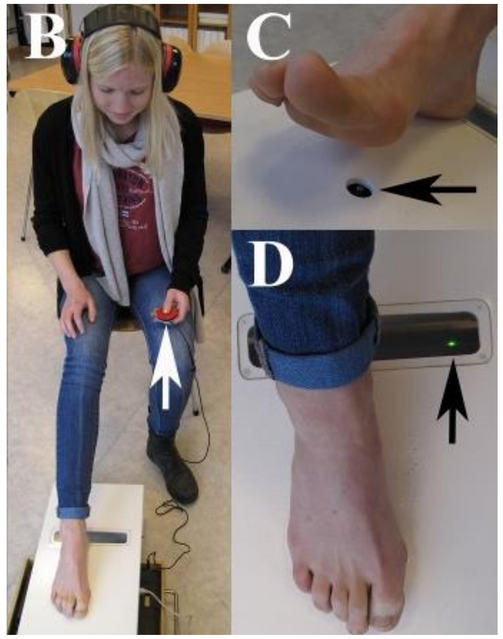
Established neuropathy is considered to be irreversible despite improvement in metabolic control[1]. Studies on reversibility are scarce but improvement of metabolic control has been shown to result in improvement in tests evaluating functional and structural measures of small diameter nerve fibres[2,3]. However, no such improvement has been presented for large diameter (i.e. myelinated) nerve fibres detected by vibration perception tests (using only one frequency) or electrophysiology.

Participants and Methods

A total of 125 patients were studied between 2015 and 2017. Vibration perception thresholds (VPTs) were determined at six frequencies (4, 8, 16, 32, 64 and 125 Hz) based on Multi-Frequency Vibrometry using VibroSense Meter (VibroSense Dynamics AB) in the sole of the foot - at the first metatarsal head (MT1) and at fifth metatarsal head (MT5) – at two different occasions (mean follow up time 1.6±0.3 years) in patients with type 1 diabetes (n = 125; 57 males, 68 females).
The mean VPTs for the right and left foot were calculated for each frequency. VPTs at baseline and at follow up were compared separately in the patients with lower HbA_{1c} (n=72) and with the same or higher HbA_{1c} at follow up (n=53). The significant p-value after multiple comparisons (n=24) was less than 0.002.

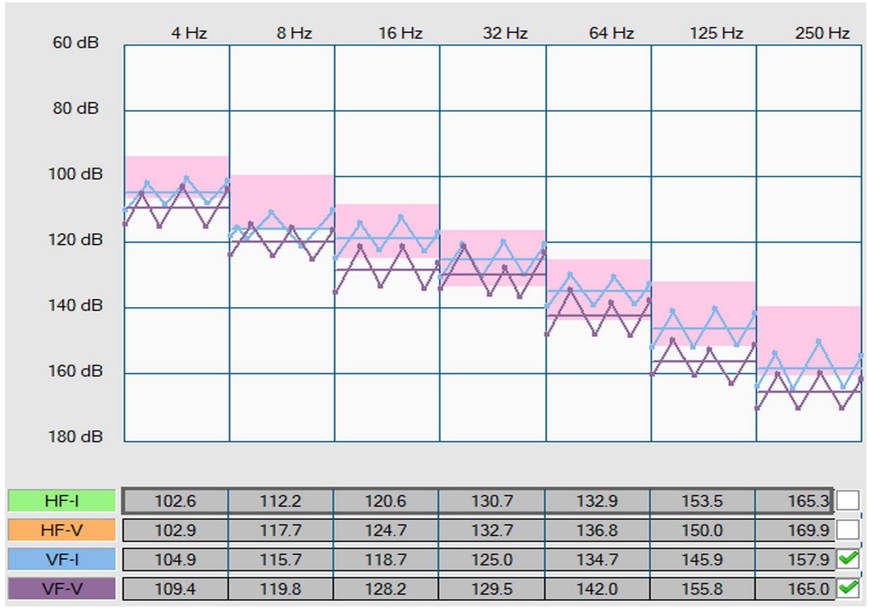
Baseline characteristics and follow up time according to HbA_{1c} group

	HbA_{1c} improved	HbA_{1c} not improved	p
N (males/females)	72 (32/40)	53 (25/28)	NS
Age (years)	46.8±16.3	48.2±16.4	NS
Duration (years)	17[10-32]	22[9-34]	NS
BMI (kg/m²)	**26.0±3.9**	**24.1±3.4**	**0.005**
Systolic Blood pressure (mmHg)	127.8±19.5	126.0±13.4	NS
Diastolic blood pressure (mmHg)	72.3±10.1	71.9±8.9	NS
Follow up time (years)	1.63±0.26	1.56±0.22	NS
Numbers are mean±SD or median[25th-75th quartile]			



The experimental set-up:
The subject is sitting with the leg and foot in a relaxed position (B). The investigated area (head of the first or fifth metatarsal bone) is placed on a vibrating probe protruding from a circular surround (C). The probe pressure is adjusted before start of the test, to get a pre-defined force on the skin at the investigated area, which is indicated by a green light (D). During the test the subject responds by pressing or releasing a response button attached to the device (arrow) (B) when a vibration is, or is not, perceived. The intensity of the vibration increases when the response button is released and decreases when the button is pressed. The result registers as a vibrogram (see right).
The person on the photo is ***not*** one of the subjects in the study.
Picture from Dahlin et. Al. Vibrotactile perception in finger pulps and in the sole of the foot in healthy subjects among children or adolescents.
PLoS One. 2015 Apr 2;10(3).

[1]Coppini et. Al. Established diabetic neuropathy seems irreversible despite improvements in metabolic and vascular risk markers--a retrospective case-control study in a hospital patient cohort. Diabet Med. 2006 Sep;23(9):1016-20.
[2]Tavakoli te.al. Corneal confocal microscopy detects improvement in corneal nerve morphology with an improvement in risk factors for diabetic neuropathy. Diabet Med. 2011 Oct;28(10):1261-7.
[3]Smith et. al. Lifestyle intervention for pre-diabetic neuropathy. Diabetes Care. 2006 Jun;29(6):1294-9.



HF-I	102.6	112.2	120.6	130.7	132.9	153.5	165.3
HF-V	102.9	117.7	124.7	132.7	136.8	150.0	169.9
VF-I	104.9	115.7	118.7	125.0	134.7	145.9	157.9
VF-V	109.4	119.8	128.2	129.5	142.0	155.8	165.0

Vibrogram. The pink area is normal range defined as mean±1.6xSD adjusted for age and sex. Blue line: left MT1, purple line: left MT5. (lines for right foot not shown). Numbers below are the VPTs for each frequency.

Results

VPTs and HbA_{1c} at baseline and at follow up according to HbA_{1c} group

	HbA_{1c} improved			HbA_{1c} not improved		
	baseline	follow up	p[a]	baseline	follow up	p[a]
HbA_{1c} (mmol/mol)	**65.9±11.5**	**56.9±11.0**	**<0.00001**	**56.6±10.3**	**62.0±11.3**	**<0.00001**
MT1 4 Hz (Db)	97.0[90.5-107.0]	95.9[90.8-101.8]	0.05	92.6[88.1-102.0]	94.5[88.5-101.8]	0.65
MT1 8 Hz (Db)	101.7[97.1-115.5]	101.8[95.6-112.1]	0.003	98.1[95.1-110.0]	101.4[94.6-109.5]	0.72
MT1 16 Hz (Db)	108.8[104.0-122.0]	110.0[103.0-118.5]	0.09	106.9[102.9-118.6]	108.1[102.3-115.7]	0.87
MT1 32 Hz (Db)	117.3[111.4-130.6]	117.8[111.8-126.3]	0.06	116.0[111.2-128.1]	118.7[111.9-123.9]	0.98
MT1 64 Hz (Db)	**128.7[116.8-140.1]**	**124.4[111.0-135.0]**	**0.0002**	125.5[115.9-136.3]	123.4[113.5-133.2]	0.03
MT1 125 Hz (Db)	134.7[120.8-145.8]	131.0[113.1-147.2]	0.011	135.2[118.3-144.9]	131.2[117.1-143.7]	0.008
MT5 4 Hz (Db)	**98.4[92.2-107.5]**	**94.9[88.1-103.0]**	**0.0005**	97.2[91.2-102.7]	93.4[87.3-101.8]	0.05
MT5 8 Hz (Db)	104.3[98.4-115.4]	103.0[95.1-111.7]	0.003	103.4[97.6-113.0]	102.1[95.9-109.2]	0.21
MT5 16 Hz (Db)	**111.5[105.1-120.3]**	**108.6[102.6-119.7]**	**0.0005**	111.5[105.9-119.7]	109.6[103.0-114.1]	0.11
MT5 32 Hz (Db)	118.2[113.1-130.8]	116.7[109.6-128.4]	0.006	118.6[113.1-129.4]	118.5[113.2-124.7]	0.11
MT5 64 Hz (Db)	**126.2[117.2-139.7]**	**121.8[109.8-134.8]**	**0.00001**	126.3[119.1-136.4]	125.9[114.8-133.0]	0.004
MT5 125 Hz (Db)	**133.6[119.3-143.3]**	**128.0[114.5-141.6]**	**0.0002**	131.1[119.1-146.6]	130.9[118.8-142.8]	0.10

[a]Significant after Bonferroni correction for multiple comparisons (n=24) if p <0.002; Db=decibel. (Wilcoxon signed rank test). Numbers are mean±SD for the HbA1c, median[25th-75th percentile] for the VPTs.

Conclusions

Lowering HbA_{1c} in patients with type 1 diabetes can improve VPTs, suggesting a reversible effect on nerve function by improved metabolic control. The use of the non-invasive method Multi Frequency Vibrometry to assess early changes in nerve function can further motivate patients with diabetes to adhere to a strict treatment strategy.