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## **Brief report**

## Impaired vibrotactile sense at low frequencies in fingers in autoantibody positive and negative diabetes

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#### ABSTRACT

Vibration thresholds in index and little finger pulps in subjects with autoantibody [GADA, IA-2A and/or ICA] positive and negative diabetes 20 years after diagnosis were higher than in age-matched controls at low frequencies (8 and 16 Hz), irrespective of HbA1c values, indicating selective impairment of Meissner's corpuscles and/or their innervating axons.

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Neuropathy develops earlier in type 1 [1] than in type 2 diabetic rats [2], but data in humans are conflicting. Disturbed vibrotactile sense depends on definition and type of subjects as well as upon evaluated extremity [3-6]. Autoimmune activity [presence of islet antibodies: glutamic acid decarboxylase antibodies (GADA), islet cell antibodies (ICA) and IA-2A antibodies] in type 1 diabetes predicts beta-cell failure, whereas beta-cell damage is less pronounced in autoantibody negative type 2 diabetes [7], but its potential long term influence on vibrotactile sense, presently examined in subjects with autoantibody positive and negative diabetes, is unknown.

#### Materials and methods

Consecutive adult subjects with diabetes diagnosed 1985-1987 (age >15 years; n = 233) were followed up. After 20 years 50/118 survivors [7] were examined with respect to vibrotactile sense, length, weight, blood pressure, blood samples, type of diabetes treatment and complications. Subjects were regarded as islet autoantibody positive if they had one or more types of antibodies (GADA, IA-2A and ICA) at onset. Vibrotactile thresholds in index and little finger pulps, reflecting median and ulnar nerve function, respectively, at

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Table 1 – Characteristics and vibration thresholds of autoantibody positive (AB+) and negative (AB-) patients with diabetes compared with control subjects from two previous studies [3,4]. Values are from present follow up if not otherwise stated.

Autoantibodies at onset	Positive (AB+) (n = 15)	Negative (AB-) (n = 35)	Control AB+ (n = 25)	Control AB– (n = 28)	Kruskal– Wallis	P-value control vs AB+	P-value control vs AB–	P-value AB+ vs AB–
	51 [18]	69 [16]	52 [12.3]	74 [2]	<0.0001	0.45	0.02	0.001
Age (years)	51 [18] 7/8	12/23		74 [2] 0/28	0.0001	0.45	0.02	0.51
Gender (F/M) BMI			12/13 NA		0.004	NA	0.49	0.046
	23.4 [5.2]	26.9 [7.3]		27.2 [4.3]				
C-peptide (nmol/l)	0.03 [0]	0.7 [0.6]	NA	1.54 [0.8]	<0.0001	NA	<0.0001	<0.0001
HbA1c at onset (%)	11.1 [2.3]	8.5 [3.9]	NA	NA	-	NA	NA	0.02
HbA1c at onset (mmol/mol)	97 [25]	69 [42]	NA	NA	-	NA	NA	0.02
HbA1c <sup>a</sup> (%)	8.3 [2.4]	7.8 [2.0]	5.3 [0.6]	5.5 [0.5]	< 0.0001	<0.0001	<0.0001	0.1
HbA1c <sup>a</sup> (mmol/mol)	67 [26]	61 [21]	34.3 [6.5]	36.4 [5.2]	< 0.0001	<0.0001	<0.0001	0.1
HbA1c <sup>b</sup> (%)	9.6 [2.4]	8.1 [2.2]	NA	NA	-	NA	NA	0.02
HbA1c <sup>b</sup> (mmol/mol)	82 [27]	64 [24]	NA	NA	-	NA	NA	0.02
HDL (mmol/l)	1.3 [0.5]	1.1 [0.4]	NA	1.2 [0.4]	0.02	NA	0.17	0.01
LDL (mmol/l)	3.0 [0.6]	2.3 [1.4]	NA	3.0 [1.4]	0.002	NA	0.001	0.01
LDL/HDL ratio	2.2 [1.2]	1.9 [1.4]	NA	2.4 [1.4]	0.08	NA	0.03	0.58
Cholesterol (mmol/l)	4.6 [0.5]	4.0 [1.5]	NA	5.0 [1.1]	0.0004	NA	0.0002	0.06
Triglycerides (mmol/l)	0.8 [0.4]	1.3 [0.8]	NA	1.5 [1.1]	0.0002	NA	0.34	0.001
SBP (mm Hg)	140 [29]	150 [20]	NA	NA	-	NA	NA	0.03
DBP (mm Hg)	80 [4]	80 [15]	NA	NA	_	NA	NA	0.69
Hypertension	5 (33%)	24 (69%)	0 (0%)	NA	<0.0001	0.002	NA	0.02
Angina pectoris	1 (6.7%)	7 (20%)	0 (0%)	NA	0.04	0.19	NA	0.24
Stroke	0 (0%)	3 (9%)	0 (0%)	NA	0.16	0.99	NA	0.24
Diabetes treatment	, ,	,	,					
Diet Diet	0 (0%)	13 (37.1%)	0 (0%)	0 (0%)				
OHA	` '	` '		` '		_	-	_
	0 (0%)	17 (48.6%)	0 (0%)	0 (0%)		- <0.0001°	- <0.0001°	- 0.00040
Insulin	15 (100%)	5 (14.3%)	0 (0%)	0 (0%)	-	<0.0001	<0.0001	<0.0001°
Clinical diagnosis								
Clinical diagnosis	8/7	3/32	NA	NA	-	-	-	-
(T1D/T2D)								
Vibration thresholds								
Pathology <sup>c</sup> at least one finger	5 (33%)	17 (49%)	4 (16%)	9 (32%)	-	0.35	0.18	0.32
Pathology <sup>c</sup> in four fingers	1 (6.7%)	7 (20%)	0 (0%)	4 (14%)	-	0.19	0.55	0.24
Right index finger	Positive (AB+)	Negative (AB-)	Control AB+	Control AB-	Kruskal–Wallis	P-value control vs AB+	P-value control vs AB–	P-value AB+ vs AB–
8 Hz	107 [6.0]	111 [7.0]	105 [3.0]	108 [12.6]	0.0003	0.19	0.07	0.03
16 Hz	115 [5.3]	117 [10.0]	112 [2.5]	114 [10.8]	0.001	0.001	0.05	0.51
32.5 Hz	118 [4.0]	118 [6.0]	115 [5.3]	121 [10.4]	0.312	0.10	0.40	0.72
64 Hz	110 [7.5]	114 [9.0]	113 [9.0]	116 [7.6]	0.03	0.24	0.07	0.18
125 Hz	110 [7.3]	117 [16.0]	108 [9.3]	116 [13.0]	0.03	0.62	0.08	0.12
250 Hz	125 [18.0]	128 [18.0]	118 [9.3]	127 [16.9]	0.004	0.10	0.28	0.03
500 Hz	140 [17.5]	143 [19.0]	135 [12.5]	146 [20.4]	0.001	0.22	0.14	0.17
500 122	1.0 [17.0]	110 [15.0]	100 [12.0]	1.0 [20.1]	0.001	V.22	0.11	0.17

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