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ORIGINAL ARTICLE

Coaching of lifestyle recommendations improves sensory neurophysiological parameters in neuropathies related to glycemic disorder or metabolic syndrome. A pilot study

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KEYWORDS
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Metabolic syndrome;
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Summary
Objectives. — Metabolic abnormalities, such as, glycemic disorders and metabolic syndrome (GDMS) are one of the main causes of peripheral neuropathies. The objective of this study was to evaluate the impact of adding specific coaching care (CC) to standard care (SC) of therapeutic education based on lifestyle recommendations for neuropathies associated with GDMS.

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Peripheral neuropathy;
Quantitative sensory testing;
Therapeutic education

Methods. — This prospective randomized study included two groups of four patients (SC vs. CC) with examiners blinded to group allocation. The SC group had one day of therapeutic education on lifestyle measures (physical activity and diet recommendations) followed by only one phone call of reinforcement. The CC group received an additional weekly phone call of reinforcement for 3 months. Clinical, biological and neurophysiological variables were compared between the two groups at baseline and for the percentage of change at 3 months.
Results. — All patients (4 men and 4 women) had diabetes or pre-diabetes, which was associated with metabolic syndrome in 5 cases. There was no difference on any variable at baseline, but at 3 months, Mann-Whitney test showed a difference ($P = 0.0008$) between the two groups regarding the sensory neurophysiological variable, which deteriorated in the SC group (median: −6.0%) and improved in the CC group (median: +12.4%). No significant difference was observed between the two groups for the other variables at 3 months.
Conclusion. — The weekly coaching of recommendations for lifestyle measures over a period of three months allows an improvement of GDMS neuropathies, at least in terms of sensory aspects, as evidenced by neurophysiological assessments.

Introduction

Peripheral neuropathy is a common condition related to various causes, e.g., inflammatory, genetic, neoplastic, paraneoplastic, infectious or metabolic conditions. The neuropathy secondary to metabolic disorders presents as a chronic, distal, symmetric, length-dependent poly-neuropathy [13]. This condition, mostly observed in subjects over the age of 40 years, may be disabling due to neuropathic pain, balance difficulties, distal sensory impairment and motor deficits, leading to a significant alteration in quality of life [6].

The two most frequent metabolic disorders that cause chronic axonal polyneuropathies are diabetes mellitus and metabolic syndrome, which concern 400 million persons with diabetes and two billion overweight people [8,18]. Recently, the risk of poly-neuropathy associated with pre-diabetic states has been highlighted [10,20,35], especially regarding painful small fiber neuropathy [27]. The metabolic syndrome is a condition that has been also been associated with the previously termed chronic idiopathic axonal poly-neuropathy [32].

Apart from symptomatic treatment of pain and rehabilitation, the control of metabolic abnormalities is a valuable approach for preventing the development of neuropathies associated with glycemic disorders or metabolic syndrome (GDMS), or, for promoting their recovery [4,12,16,19]. Lifestyle changes, including increase of physical activity and diet recommendations, constitute the basis of this prevention [30,31]. Indeed, exercise programs improve balance and proprioception in patients with diabetic polyneuropathies [29], as well as, reducing pain and improving cutaneous sensory reinnervation [25,26,28,34].

However, adherence to these objectives may be limited outside a definite program defined in therapeutic trials.

We designed a trial to determine whether adding specific coaching to a standard therapeutic education of patients for lifestyle recommendations could be beneficial for patients with GMS-associated neuropathy.

Methods

Patients

The patients included in this study were referred by general practitioners or specialists to the neuromuscular outpatient clinic of the Department of neurology of Henri-Mondor university hospital for the investigation of peripheral neuropathy. All patients diagnosed as having a distal poly-neuropathy associated with GDMS were proposed to be included in this study, who received local ethical committee agreement and were registered (ClinicalTrials.gov Identifier: NCT01465620). All patients signed informed consent before inclusion in the study. Diagnosis of poly-neuropathy was based on the combination of neuropathic symptoms, signs, and abnormal electro-diagnostic studies [1]. Patients were evaluated with a standard protocol to exclude other causes of acquired poly-neuropathy including paraneoplastic, hereditary sensory neuropathy, amyloid neuropathy, alcohol intoxication, neurotoxic drugs, vitamin B12 deficiency, cryoglobulinemia, infection by hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), IgM monoclonal gammopathy with or without positive anti-myelin associated glycoprotein (MAG) antibodies, POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome, polyarteritis nodosa or other types of necrotizing vasculitis, definite connective tissue disease and sicca complex syndrome, evidence of a systemic autoimmune disease assessed by at least one of the following serologic abnormalities: positive rheumatoid factor (titer $\geq$ 1:160), positive antinuclear antibody (titer $\geq$ 1:160), positive SS-A or SS-B antibody.

The diagnosis of GDMS-associated polyneuropathy was defined according the following criteria:

- clinical manifestations of symmetrical distal sensory symptoms, such as, tiredness, weakness, tightness, pins

and needles sensations, and a chronic evolution of at least six months;
- nerve conduction study abnormalities characterized by distal sensory nerve action potential (SNAP) amplitude reduction (below normal limit according to our laboratory standards) for at least two of the four nerves usually explored at the lower extremities (i.e. both superficial peroneal and sural nerves);
- no identifiable cause other than the GDMS.

Medication and drug regimen

Patients were asked not to change their symptomatic treatment or their disease-modifying drugs for a three-month period.

Neurophysiological evaluation

Nerve conduction studies were performed with a Keypoint machine (Natus Neuro France, Paris, France) and quantitative sensory testing was performed with a TSA-II machine (Medoc, Ramat Yishai, Israel) as previously reported [21] using normative data established in the laboratory.

Metabolic evaluation

Glucose metabolism abnormalities (glycemic disorders) were classified as follows:

The diagnosis of diabetes was based on the following results [3]: HbA1c $\geq$ 6.5%; or fasting plasma glucose $\geq$ 126 mg/dL (7.0 mmol/L) with fasting defined as no caloric intake for at least 8 h; or 2-hour plasma glucose $\geq$ 200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water); or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose $\geq$ 200 mg/dL (11.1 mmol/L).

The diagnosis of pre-diabetes was based on the following results [3]: fasting plasma glucose from 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (impaired fasting glucose); or 2-hour plasma glucose in the 75-g OGTT from 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (impaired glucose tolerance); or HbA1c from 5.7% to 6.4%.

Metabolic syndrome

The metabolic syndrome was defined by the presence of a minimum of three out of five criteria based on the following measures [2]:

- elevated waist circumference with men > 94 cm or women > 80 cm;
- elevated triglycerides $\geq$ 150 mg/dL (1.7 mmol/L) (drug treatment for elevated triglycerides was an alternate indicator);
- reduced HDL-cholesterol (HDL-C) $\leq$ 40 mg/dL (1.0 mmol/L) in men or $\leq$ 50 mg/dL (1.3 mmol/L) in women (drug treatment for reduced HDL-C was an alternate indicator);
- elevated blood pressure with systolic $\geq$ 130 and/or diastolic $\geq$ 85 mmHg (antihypertensive drug treatment in a patient with a history of hypertension was an alternate indicator);
- elevated fasting glucose $\geq$ 100 mg/dL (drug treatment of elevated glucose was an alternate indicator)

Study design

Randomization

Eligible patients were randomly assigned in a 1:1 ratio into two study groups, i.e. standard care (SC) only (control group) and SC plus phone coaching care (CC), which were stratified with regard to NTSS-6 score in order to investigate a clinical effect (< 6 or $\geq$ 6).

Lifestyle recommendations—Standard Care

All patients underwent a one-day therapeutic education for diet and physical activity counseling for metabolic and diabetic patients in a specialized clinical ward. This consisted of an individual interview with a physician, a specialized nurse and a dietetic specialist. Then, the patient, in a group session, was informed about cardiovascular risk factors and lifestyle changes. Finally, individual objectives (biological, dietetic, physical activity, smoking addiction) were finalized with the patient by the specialized team.

Phone coaching—Coaching care

Phone coaching was performed by one of us (SNWT) as follows: the physician and the patient had weekly 5 minute phone meetings to evaluate the adherence to the lifestyle recommendations. Then, the physician reinforced encouragement to follow diet recommendations and to perform some form of physical activity for at least 30 minutes a day.

Analyzed variables

The following variables were analyzed at baseline and 3 months (M3) after SC of CC:

- clinical score variables: SF-12 Physical and Mental Health Composite Scores (PCS and MCS) [33], mean pain score on a 0—10 visual analogue scale (VAS), Neuropathy Total Symptom Score-6 (NTSS-6) [5], and Inflammatory Neuropathy Cause and Treatment group score (INCAT), and Overall Disability Sum Score [23]
- anthropometric measurement variables: body weight (Kg) and waist circumference (cm);
- blood pressure variables: systolic and diastolic blood pressures (mmHg);
- glycemic biological variables: fasting glycemia (mmol/L) and glycated hemoglobin (HbA1c (%));
- lipid biological variables: HDL and LDL-cholesterol and triglyceride levels (mg/dL);
- motor neurophysiological variables: distal compound muscle action potential (CMAP) amplitude (mV), motor nerve conduction velocity (MNCV) at the leg (m/s), and F-wave latency (ms) for peroneal and tibial nerves (results were averaged from measurements made for both nerves of each lower limb);
- sensory neurophysiological variables: distal SNAP amplitude (μV), sensory nerve conduction velocity (SNCV) at the ankle (m/s) for superficial peroneal and sural nerves

(results were averaged from measurements made for the nerves of both lower limbs), and detection thresholds for vibratory (VDT, in μm), warm (WDT, in °C), and cold (CDT, in °C) stimuli applied on the dorsum of the foot (results were averaged from measurements made for both limbs).

The examiner physician was blinded to the study group allocation for all the patients.

Statistical analysis

The primary objective was the improvement from baseline to M3 of the clinical variable NTSS-6. Secondary objectives were improvement from baseline to M3 of the other clinical, biological, or neurophysiological markers. We determined that 40 patients would be needed to detect a treatment effect at 3 months, assuming an improvement of 2.29 points in the NTSS-6 score in the CC vs. the SC group with a two-sided test and a significance level of 5%.

Baseline data were compared between the two groups for each variable using the nonparametric Mann-Whitney test. The effect of the intervention (SC vs. CC) was analyzed by grouping the percentages of improvement into the seven categories of variables described above: clinical scores, anthropometric measurements, blood pressure, glycemic or lipid biological variables, and motor or sensory neurophysiological variables. The percentages of change from baseline to M3 were calculated by the formula: $100 \times [(M3 - Baseline)/Baseline]$ for variables for which an increase in values represents an improvement and $-100 \times [(M3 - Baseline)/Baseline]$ for variables for which a decrease in values represents an improvement.

The overall percentages of change were compared for the seven categories of grouped (composite) variables between patients in the SC control group and patients in the CC group using the nonparametric Mann-Whitney test (Prism software, GraphPad, La Jolla, CA, USA). The level of P value significance was set at $P < 0.05$.

Results

Patients

For this study, 42 patients were screened, but only 11 entered the study and subsequently underwent randomization. However, only 8 patients (4 men and 4 women, aged 65 ± 9 [mean $\pm$ SD]) completed the study and were analysed between baseline and M3. One patient was lost to follow-up (randomized in the SC group), one patient retracted his consent (SC group), and one patient was secondarily excluded due to the occurrence of renal failure (CC group).

These patients had a diabetic ($n = 6$) or a pre-diabetic ($n = 2$) state and 5 had a metabolic syndrome. Demographic features are presented in Table 1.

All patients had symmetric sensory deficits of superficial and proprioceptive sensibility assessed by alteration of vibratory (measured by a 128 Hz tuning fork), light-touch, or pinprick sensation in the feet. Three patients in each group had limited motor deficits affecting intrinsic foot muscles, but that did not impair walking capacities.

Table 1 Demographic features.

	Standard care	Coaching care
Age (years)	64 ± 9	66 ± 10
Sex (women/men)	2/2	2/2
Diabetes	3	3
Pre-diabetes state	1	1
Metabolic syndrome	2	3
Disease course (years)	3.3 ± 2.6	1.6 ± 0.5
Height (cm)	175 ± 11.7	171 ± 8.5

Analyzed variables

Detailed results (mean $\pm$ SD) observed at baseline and M3 regarding the seven categories of variables (clinical scores, anthropometric measurements, blood pressure, glycemic or lipid biological variables, and motor or sensory neurophysiological variables) are presented in Tables 2–6.

Mann-Whitney test did not show any difference between the two groups at baseline ($P > 0.05$). In contrast, we found a difference ($P = 0.0008$) between the two groups regarding the overall percentage of change at M3 for the sensory neurophysiological grouped (composite) variable, which worsened in the control group (median: −6.0%) and improved in the coached group (median: +12.4%) (Fig. 1). No significant difference was observed between the two groups regarding the overall percentage of change at M3 for the other grouped (composite) variables (Fig. 1), with median percentages of improvement or worsening less than 10%.

Discussion

In the present study, we show that a three-month period of coaching of patients with GDMS-associated neuropathies for lifestyle modifications can result in an improvement of sensory neurophysiological parameters combining large and small nerve fiber assessment. The improvement was limited to sensory parameters without changes in motor nerve conduction parameters. This result is fully in accordance with a recent study [16] that showed an improvement of sural sensory nerve conduction velocity, but not of motor nerve conduction parameters in a group of patients with diabetic poly-neuropathy who performed an aerobic training exercise, compared to a control group of non-exercised patients. Although the majority of previous studies in GDMS neuropathies have focused on the prevention of degradation of neurophysiological parameters through glycemic equilibrium (review in [9]), few have focused on the impact of lifestyle changes on improvement [4,12,16,19].

There are some arguments suggesting that, in this context, the improvement of glycemic balance is more relevant in type 1 diabetic neuropathies than in type 2 diabetic neuropathies [9]. These data support the idea that the control of various aspects of the metabolic syndrome (i.e. dyslipidemia, hypertension, obesity) should be associated with the control of glycemia in order to prevent the development of neuropathies associated with type 2 diabetes. Thus, a global change in lifestyle in patients with GDMS neuropathies

Table 2 Clinical variables.

	Standard care		Coaching care	
	Baseline	Month 3	Baseline	Month 3
SF-12 physical	41.8 ± 11.8	39.7 ± 9.2	36.8 ± 3.1	43.4 ± 8.9
SF-12 mental	37.9 ± 11.8	47.0 ± 15.2	38.2 ± 8.1	40.3 ± 12.8
NTSS-6 a	1.7 ± 1.6	0.9 ± 1.8	1.2 ± 1.4	1.3 ± 1.0
NTSS-6 b	1.4 ± 1.8	1.2 ± 0.4	0.8 ± 1.1	0.5 ± 1.2
NTSS-6 c	1.1 ± 1.3	0.3 ± 0.5	0.5 ± 0.6	0.4 ± 0.9
NTSS-6 d	1.7 ± 1.9	1.7 ± 1.9	NA	NA
NTSS-6 e	1.1 ± 1.2	1.9 ± 1.4	1.7 ± 1.2	1.9 ± 1.1
NTSS-6 f	1.3 ± 1.6	1.6 ± 1.4	1.2 ± 1.1	0.9 ± 1.1
NTSS-6 Total	8.3 ± 6.8	6.4 ± 5.8	5.6 ± 2.3	4.7 ± 2.3
Mean pain VAS	7.8 ± 1.8	7.7 ± 2.5	4.2 ± 1.6	4.0 ± 3.8
INCAT score	3.5 ± 1.9	2.3 ± 1.3	5.3 ± 1.5	4.5 ± 2.0

VAS: Visual analogue scale; NA: Not available; NTSS: Neuropathy total symptom score-6; INCAT score: Inflammatory neuropathy cause and treatment group overall disability sum score.

Table 3 Anthropometric and blood pressure variables.

	Standard care		Coaching care	
	Baseline	Month 3	Baseline	Month 3
Weight (Kg)	84.8 ± 8.5	82.1 ± 6.8	97.3 ± 34.0	94.6 ± 31.5
Waist circumference (cm)	103.8 ± 10.5	105.3 ± 8.3	107.9 ± 24.8	108.8 ± 24.9
Systolic BP (mmHg)	146.2 ± 20.5	134 ± 12.1	140.8 ± 13.0	135.2 ± 10.0
Diastolic BP (mmHg)	87.8 ± 3.8	85 ± 6.6	80.3 ± 4.6	77.6 ± 11.8

BP: blood pressure.

Table 4 Biological variables.

	Standard care		Coaching care	
	Baseline	Month 3	Baseline	Month 3
Fasting plasma glucose (mmol/L)	6.8 ± 2.0	4.3 ± 2.8	5.0 ± 3.0	5.2 ± 4.7
2-hour plasma glucose (mmol/L)	6.8 ± 0.7	4.7 ± 0.5	7.9 ± 0.3	5.3 ± 0.8
Creatinine (μmol/L)	81.2 ± 14.7	96.1 ± 18.2	97.4 ± 45.3	87.2 ± 33.7
HbA1c (%)	5.9 ± 0.6	6.1 ± 0.5	7.8 ± 1.0	7.0 ± 1.3
Triglycerides (mmol/L)	1.7 ± 0.6	1.6 ± 1.3	2.1 ± 1.4	1.5 ± 0.9
HDL-cholesterol (mg/dL)	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0.1	0.4 ± 0.1
LDL-cholesterol (mg/dL)	1.3 ± 0.4	1.2 ± 0.9	1.2 ± 0.4	1.2 ± 0.5

could potentially contribute much more benefit than simply normalizing glycemia.

These considerations conducted authors to investigate the effect of increase of physical activity in patients with GDMS neuropathies. In patients with type 2 diabetes, one study investigated the value of systematic physical activity with an aerobic exercise program during eight weeks and showed an improvement of the Michigan Diabetic Neuropathy Score [12]. Another study reported neuropathic symptom improvement, as well as histological signs of cutaneous reinnervation, after 10 weeks of aerobic and strengthening exercises [19]. As aforementioned, a recent study showed an improvement of sural sensory nerve conduction velocity in a group of patients with diabetic polyneuropathy who performed an aerobic training exercise [16]. Finally, increased nerve conduction velocities were found after a 12-week program of tai chi chuan in a series of 28 patients with type 2 diabetes [17]. Other data support the protective effect of physical exercise on diabetic nerves even for a longer term, with a follow-up of several years [4].

Our study shows that sensory nerve alterations can be reversible very rapidly (within 3 months) after lifestyle recommendations. This could relate to the fact that various features of the metabolic syndrome (glycemic disorders, dyslipidemia, or overweight) are associated with processes of microvasculopathy, inflammation and oxidative stress, which can cause neuropathy [22,24] and may vary rapidly.

Table 5 Motor neurophysiological variables.

	Standard care		Coaching care	
	Baseline	Month 3	Baseline	Month 3
Right peroneal CMAP amplitude (mV)	3.7 ± 3	5.3 ± 3.5	4.9 ± 2.5	5.2 ± 2.7
Left peroneal CMAP amplitude (mV)	3.7 ± 2.2	3.9 ± 2.5	4.9 ± 2.4	4.9 ± 1.9
Right tibial CMAP amplitude (mV)	3.6 ± 3.7	3.4 ± 3.8	6.4 ± 2.6	5.2 ± 1.8
Left tibial CMAP amplitude (mV)	4.1 ± 5.3	3.8 ± 4.9	8.9 ± 3.1	7.8 ± 2.9
Averaged CMAP amplitude (mV)	3.8 ± 3.4	4.1 ± 3.5	6.3 ± 2.0	6.0 ± 1.4
Right peroneal MNCV (m/s)	42 .0 ± 1.8	38.5 ± 3.9	40.5 ± 2.5	38.8 ± 5.1
Left peroneal MNCV (m/s)	39.8 ± 3.8	38.3 ± 2.2	42.8 ± 3.9	40.6 ± 4.3
Right tibial MNCV (m/s)	40.3 ± 3.8	37.3 ± 2.6	40.3 ± 4.9	39.0 ± 3.8
Left tibial MNCV (m/s)	38.7 ± 3.8	40.3 ± 3.4	40.3 ± 4.6	40.2 ± 4.3
Averaged MNCV (m/s)	40.3 ± 2.9	38.6 ± 2.4	41.3 ± 3.2	39.6 ± 3.6
Right peroneal F-wave latency (ms)	55.8 ± 2.5	57.5 ± 1.7	52.3 ± 3.3	54.9 ± 4.9
Left peroneal F-wave latency (ms)	60.4 ± 6.4	58.2 ± 0.2	54.0 ± 4.2	55.4 ± 4.6
Right tibial F-wave latency (ms)	64.0 ± 1.8	63.7 ± 3.4	59.9 ± 2.3	59.2 ± 1.2
Left tibial F-wave latency (ms)	63.2 ± 4.3	59.2 ± 1.2	57.7 ± 5.1	59.0 ± 6.4
Averaged F-wave latency (ms)	62.8 ± 4.4	60.2 ± 1.8	56.8 ± 3.7	57.4 ± 5.4

CMAP: Distal compound muscle action potential; MNCV: Motor nerve conduction velocity.

Table 6 Sensory neurophysiological variables.

	Standard care		Coaching care	
	Baseline	Month 3	Baseline	Month 3
Right peroneal SNAP amplitude (μV)	7.8 ± 2.6	6.8 ± 3.3	7.6 ± 3.4	9.6 ± 3.3
Left peroneal SNAP amplitude (μV)	8.5 ± 3.9	8.1 ± 3.1	8.4 ± 3.6	11.6 ± 3.4
Right sural SNAP amplitude (μV)	12.9 ± 11.4	12.4 ± 7.3	11.0 ± 4.3	11.9 ± 5.9
Left sural SNAP amplitude (μV)	12.8 ± 7.7	10.5 ± 6.6	11.1 ± 5.9	10.9 ± 4.8
Averaged SNAP amplitude (μV)	10.5 ± 5.6	9.4 ± 2.3	9.5 ± 3.6	11.0 ± 4.1
Right peroneal SNCV (m/s)	42.8 ± 2.5	45.8 ± 4.1	45.5 ± 7.5	43.4 ± 1.7
Left peroneal SNCV (m/s)	43.0 ± 3.8	41.0 ± 3.6	43.8 ± 5.6	44.0 ± 3.1
Right sural SNCV (m/s)	39.0 ± 7.4	44.0 ± 11.9	43.0 ± 6.8	43.0 ± 5.3
Left sural SNCV (m/s)	41.4 ± 7.3	41.8 ± 6.1	44.0 ± 9.8	44.2 ± 6.2
Averaged SNCV (m/s)	41.4 ± 2.8	43.1 ± 5.7	44.1 ± 6.5	43.7 ± 3.3
Right WDT (°C)	9.0 ± 4.6	11.7 ± 6.2	11.8 ± 5.6	11.6 ± 3.1
Left WDT (°C)	9.3 ± 4.6	9.8 ± 6.0	13.7 ± 4.4	10.4 ± 3.9
Right CDT (°C)	7.2 ± 3.8	7.6 ± 4.3	14.9 ± 14.0	11.6 ± 12.0
Left CDT (°C)	7.5 ± 4.0	18.0 ± 12.5	11.9 ± 13.6	16.2 ± 13.8
Averaged TDT (°C)	8.2 ± 3.2	11.8 ± 4.9	13.1 ± 7.7	12.4 ± 6.4
Right VDT (μm)	17.2 ± 6.1	18.6 ± 5.8	15.0 ± 10.1	20.3 ± 7.9
Left VDT (μm)	19.1 ± 7.8	17.9 ± 4.2	17.0 ± 8.7	19.6 ± 7.6
Averaged VDT (μm)	18.1 ± 6.7	18.3 ± 4.9	16.0 ± 9.4	20.0 ± 7.6

SNAP: Distal sensory nerve action potential; SNCV: Sensory nerve conduction velocity; WDT: Detection threshold; CDT: Cold detection threshold; TDT; Thermal detection threshold; VDT: Vibration detection threshold.

The sensory neurophysiological changes observed in the CC group in the present study related to a composite variable. Because of the low statistical power due to the small sample, we were not able to distinguish between changes in SNAP amplitude versus SNCV, or between changes in sensory thresholds affecting large (VDT) versus small (WDT, CDT) sensory afferents. However, such a 'global' improvement may result from a distal sensory reinnervation process, as suggested by a study showing an increase in intraepidermal nerve fiber density after a supervised program of physical exercises in a series of patients with metabolic syndrome [26]. However, in a previously cited study [16], based on a larger sample (24 patients), exercise improved sural SNCV but not SNAP amplitude: these authors suggested that this improvement was more likely to be functional and related to better glucose control (fasting glucose level and HbA1c).

Our study shows that GDMS neuropathies can improve by changing lifestyle, combining diet recommendations and increase of daily physical activity, without the need for a heavily supervised program of sport and physical

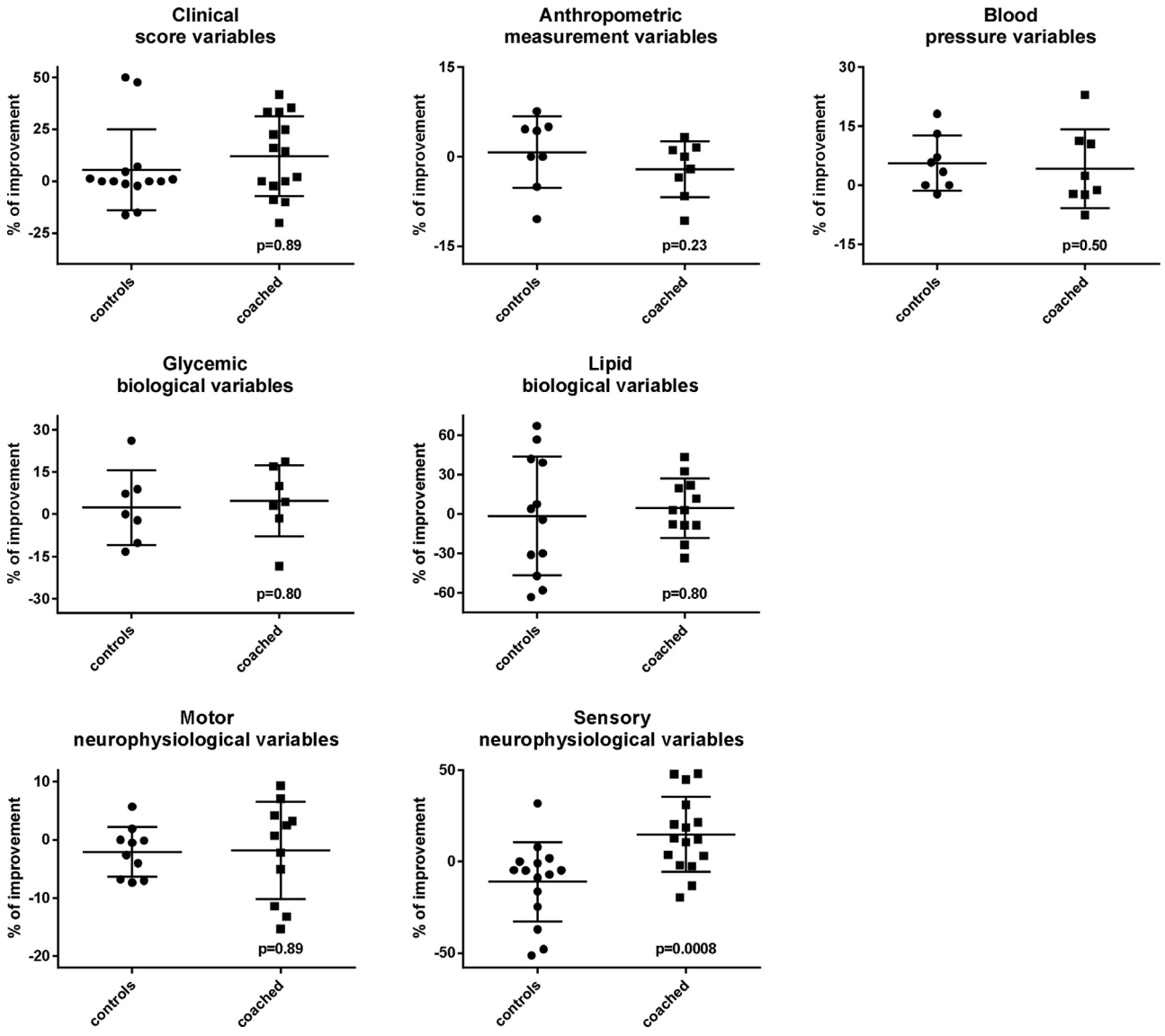

Figure 1 Scatter plots of clinical (including anthropometric and blood pressure), biological (glycemic and lipid) and neurophysiological (motor and sensory) changes from baseline to month 3 in control and coached patients.

rehabilitation. In fact, the adherence to the latter type of program may be low and difficult to sustain in the daily life outside a dedicated therapeutic trial, as has been shown for cardiac rehabilitation [11].

Our study stresses the interest of therapeutic education and coaching in the management of GDMS neuropathies, but presents several limitations. First, the number of patients included was very small and a larger study should be obviously designed to confirm these preliminary findings. Second, we did not find a significant clinical improvement after CC, including on the NTSS-6 score, which was our primary endpoint. Third, although CC proved its effect on neurophysiological sensory parameters, we have no evidence of the real efficiency of this coaching to modify daily lifestyle habits. Fourth, patients were recruited from an expert setting, and the results cannot be generalized to primary care. Finally, the duration of the follow-up was limited to three months, and one can only speculate on the long-term efficacy of coaching on clinical and neurophysiological parameters, but also on the observance of changes in lifestyle habits, including physical activity level and calorie intake.

Indeed, changes in lifestyle habits are able to improve metabolic biological parameters and to reduce cardiovascular risks [7,15], but the best strategy for long-term efficiency remains to be defined [14,30].

Conclusion

The preliminary results of this pilot study performed in a small series of patients with GDMS suggest that coaching the therapeutic education on lifestyle measures (physical activity and diet recommendations) can rapidly improve GMS-associated neuropathy, especially its sensory aspects, at least on neurophysiological grounds. Whether

this approach can provide sustained benefits in the long term, on both sensory and motor fibers, also on meaningful clinical features and ameliorate the prognosis of such type of neuropathy remains to be confirmed in a larger series of patients.

Disclosure of interest

The authors declare that they have no competing interest.

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