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Original Article

Which Occurs First in Patients with Type 2 Diabetes Mellitus? Central or Peripheral Neuropathy

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ABSTRACT

Objective: To study the central and peripheral neuropathy by electrophysiological tests in type two diabetes mellitus patients (DM-2) before symptomatic peripheral neuropathy.

Methodology: DM-2 (n=30) and age- and sex-matched (n=30) healthy subjects (controls) with normal bilateral sural sensory nerve action potentials (SNAPs) were selected after informed written consent. Their 16-channel EEG records were transformed using Fast Fourier Transformation (FFT). EEG power spectra obtained were log-transformed and compared using student's t-test.

Results: DM-2 without symptoms of peripheral neuropathy had low amplitudes of bilateral sural SNAPs in comparison to the controls though they were above the normal cut-off values of ≥ 4 μV. In EEG, DM-2 had more beta power ($p<0.05$) at midline Fz (24.77±11.58 vs. 12.26±11.55,), Cz (33.04±19.41 vs. 17.65±19.51,), and Pz (30.34±16.54 vs. 16.13±15.57,) and at other sites (Fp2, F8, F4, C4, T4, T6, P4, O2, Fp1, F7, F3, C3, T3, T5, P3, and O1) during eyes-close condition. Similar differences in beta power were seen in eyes-open condition. The delta power was more ($p<0.05$) in DM-2 during eyes-close condition at midline Fz (64.64±34.54 vs. 47.37±22.47), Cz (73.87±45.07 vs. 51.73±25.58), and Pz (66.13±36.84 vs. 44.15±19.68) and at other sites (Fp2, F8, C4, P4, O2, Fp1, F7, T3, T5, O1). Similar differences in delta power were seen in eyes-open condition. Alpha activities were more ($p<0.05$) in DM-2 at some sites during eyes-open condition.

Conclusion: Diffuse central neuropathy occurs along with the peripheral neuropathy in DM-2 as measured by the electrophysiological tests.

Keywords: Type 2 diabetes mellitus, Peripheral neuropathy, Central neuropathy

INTRODUCTION

Diabetes mellitus (DM) is one of the most common metabolic disorders associated with chronic complications such as nephropathy, angiopathy, retinopathy, autonomic neuropathy, and peripheral neuropathy.[1] These complications result from a complex interaction of direct and indirect metabolic consequences of insulin deficiency and additional genetic and environmental factors.[2]

Involvement of peripheral and autonomic nervous systems frequently encounters in DM. However, there is a paucity of data regarding central neuropathy in DM. Neurochemical, electrophysiological, structural and neurobehavioral levels have demonstrated manifestations of DM-2 cerebral disorders. Probably alterations in cerebral blood supply and metabolic derangements play a role, as they do in the pathogenesis of DM-2 neuropathy. Furthermore, recurrent episodes of hypoglycemia and poor metabolic control also affect the brain.[1]

Some reports claim central neuropathy in DM based on evoked potentials. However, central neuropathy in DM particularly before symptomatic peripheral neuropathy has received much less attention.

Electrophysiological tests for diagnosing disorders of peripheral nervous system include nerve conduction studies (NCS), and electromyography.[3] EEG measures electrical

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activity of the brain and is a noninvasive tool with excellent temporal resolution and quite useful as a prognostic tool in disorders of the central nervous system (CNS).[1]

Our aim is to study the central and peripheral neuropathy by EEG and NCS respectively in DM-2 before symptomatic peripheral neuropathy. Hence, we believe that this study shades light on the central and peripheral neuropathy in DM-2 before they show symptoms of peripheral neuropathy.

MATERIALS AND METHODS

The present study was a cross-sectional comparative study. Based on the inclusion and exclusion criteria, 30 (23 male and seven female) DM-2 and 30 (23 male and seven female) age- and sex-matched controls were selected from local population using convenient sampling technique. DM-2 were newly diagnosed or follow-up cases without any clinical evidence of peripheral neuropathy and all of them were on oral hypoglycemic medication including sulphonylureas and metformin. The controls had no symptoms of any disease, normal on clinical examination, normal fasting blood glucose (FBG), age- and sex-matched, and were not on any medication and without any clinical evidence of infectious, systemic, metabolic, and neuropsychiatric illnesses.

All the subjects were acquainted with laboratory setting, study design, and recording procedures. Procedures were explained to them; informed written consents were taken, and they were interviewed with standard questionnaires. Before recording different parameters, their health status was assessed based on detailed medical history and physical examination and documented using a standard case history sheets. The recent reports of FBG, post-prandial blood sugar (PPBG), and glycated hemoglobin (HbA_1C) of DM-2 were noted and FBG of controls were assessed.

Their weight, height, systolic blood pressure (SBP), diastolic blood pressure (DBP), and respiratory rate (RR) were measured using standard tools and methods. BMI was calculated from standard formula, i.e., BMI = weight kilogram (kg)/height (m^2). Heart rate (HR) was calculated from the electrocardiogram (ECG) using the standard limb lead I connected to Nihon Kohden-Neurofax: optiplex GXMT 5120. Arterial oxygen saturation (SaO_2) was monitored using Pulse Oximeter (OLV-1100/1200 series, Nihon Kohden).

Temperature of the laboratories was maintained at 26 ± 2ºC. They were advised to relax and their comfort was maintained before and during the recording procedures. Latencies, conduction velocities, and amplitudes of bilateral sural SNAPs were recorded by antidromic method using Digital Nihon Kohden machine (NM-4205, H636, Japan) and its accessories. Table 1 shows the normal cut-off values considered for sural SNAP.

Table 1. Normal values for sural SNAP. [4]

Nerve	Onset latency	Nerve conduction velocity	Amplitude
Sural	≤ 4.2 ms @ 14 cm	≥ 42 m/sec	≥ 4 µV

Table 2. Anthropometric, FBG, and cardio-respiratory variables of DM-2 and controls

Variables	Mean ± SD		p value
	DM-2 (n=30)	Controls (n=30)	
Age (years)	53.20±2.66	53.03±2.77	0.814
Weight (Kg)	63.90±5.89	65.77±6.03	0.230
Height (cm)	166.1±6.14	168.12±6.96	0.239
BMI (Kg/m^2)	23.19±1.83	23.21±1.40	0.964
FBG (mg/dl)	175.17 ± 54.49	91.00 ± 11.24	**0.001**
SBP (mmHg)	119.94±5.55	119.34±5.62	0.679
DBP (mmHg)	74.14±4.04	72.80±3.35	0.169
HR (beats/min)	79.77±5.92	80.84±6.73	0.517
RR (breaths/min)	13.57±1.74	13.84±1.84	0.566
SaO_2 (%)	97.44±1.08	97.34±1.07	0.718

Kg = Kilogram, Kg/m^2 = kilogram per square meter, cm = centimeter, mg/dl = milligram per deciliter, mmHg = millimeter of mercury, min = minute

Table 3. Variables of bilateral sural SNAPs in DM-2 and controls

Variables	Sides	Mean ± SD		p value
		DM-2	Control	
Latency (ms)	Left	2.49 ± 0.35	2.34 ± 0.44	0.134
	Right	2.51 ± 0.40	2.37 ± 0.34	0.141
Conduction Velocity (m/s)	Left	55.93 ± 5.34	59.62 ± 9.24	0.064
	Right	56.47 ± 7.68	60.30 ± 8.45	0.072
Amplitude (µV)	Left	13.09 ± 3.61	15.69 ± 4.50	**0.016**
	Right	12.24 ± 4.44	14.83 ± 4.38	**0.027**

After recording bilateral sural SNAPs, each subject with normal sural SNAPs was taken to EEG lab for recording EEG. After 10 minutes of rest, 16-channel EEG (Figure 1) was recorded by digital EEG machine (Nihon Kohden-Neurofax: optiplex GXMT5120) during eyes-close and eyes-open conditions for 3 minutes each in a quiet, relaxed environment, in supine position.

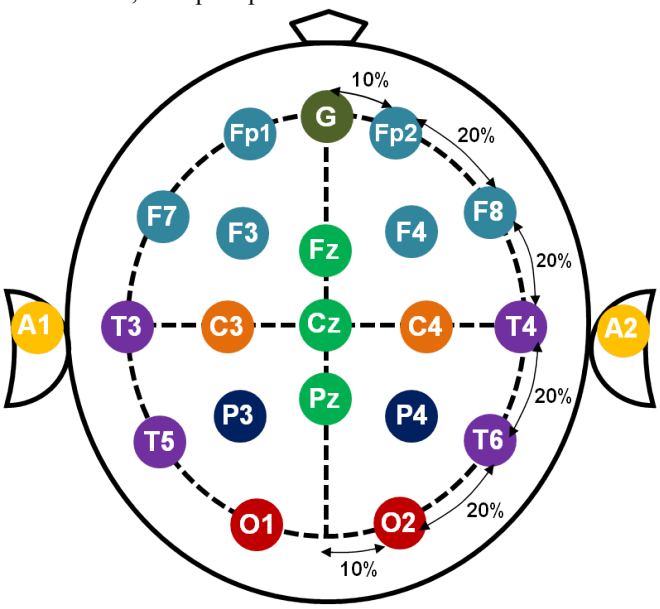

Figure. 1. International 10-20 common average reference system for EEG electrode placement.

Table 4. EEG power spectra of DM-2 (n=30) and controls (n=30) during eyes-close condition

EEG Electrode Sites	Groups	Delta, μV^2 Mean ± SD	P value	Theta, μV^2 Mean ± SD	p value	Alpha1, μV^2 Mean ± SD	p value	Alpha2, μV^2 Mean ± SD	P value	Beta, μV^2 Mean ± SD	P value
Fz	DM-2	64.64±34.54	**0.015**	24.89±15.31	0.760	75.47±126.78	**0.041**	27.50±39.95	0.093	24.77±11.58	**0.001**
	Controls	47.37±22.47		22.42±11.72		29.47±19.02		15.09±12.58		12.26±11.55	
Cz	DM-2	73.87±45.07	**0.007**	29.11±17.55	0.944	85.87±142.6	0.115	38.51±54.79	0.169	33.04±19.41	**0.001**
	Controls	51.73±25.58		29.06±17.79		39.41±23.93		21.77±20.15		17.65±19.51	
Pz	DM-2	66.13±36.84	**0.002**	25.04±17.08	0.732	67.10±81.24	0.551	60.64±96.54	0.208	30.34±16.54	**0.001**
	Controls	44.15±19.68		23.04±13.65		51.20±41.48		31.25±31.60		16.13±15.57	
Fp2	DM-2	64.28±33.53	**0.049**	14.62±09.43	0.643	51.07±90.61	0.103	18.42±28.30	0.147	19.22±09.03	**0.001**
	Controls	50.09±30.95		14.32±06.44		20.16±12.65		10.20±07.84		08.97±07.68	
F8	DM-2	38.09±39.83	**0.013**	05.22±03.94	0.771	19.24±36.99	0.255	07.16±10.61	0.130	07.06±03.26	**0.001**
	Controls	18.74±11.37		04.80±02.25		9.29±12.37		03.90±02.97		03.88±03.58	
F4	DM-2	16.20±07.67	0.192	05.71±03.53	0.563	14.83±22.58	0.495	08.77±09.68	0.701	12.81±08.88	**0.001**
	Controls	14.05±07.23		06.22±04.15		09.96±08.00		06.51±04.81		09.31±13.16	
C4	DM-2	26.06±21.27	**0.007**	10.72±09.61	0.311	47.36±88.40	0.597	24.25±47.70	0.810	14.94±09.27	**0.001**
	Controls	15.94±10.91		08.14±06.07		28.65±24.29		18.07±20.16		08.83±09.98	
T4	DM-2	44.72±23.03	0.053	14.60±10.11	0.921	50.59±89.26	0.083	18.62±27.54	0.126	23.91±18.48	**0.001**
	Controls	34.26±17.60		13.95±07.51		20.36±14.09		10.58±08.98		10.35±09.40	
T6	DM-2	46.93±27.27	0.071	18.00±12.37	0.808	54.97±90.91	0.133	30.29±38.79	0.414	24.52±14.15	**0.001**
	Controls	36.20±17.07		18.22±11.57		25.88±16.38		19.84±17.24		13.03±12.40	
P4	DM-2	47.26±24.01	**0.004**	16.97±11.33	0.946	47.74±68.17	0.562	46.69±70.77	0.342	23.56±14.77	**0.001**
	Controls	32.45±16.36		16.98±11.33		35.31±26.53		29.47±31.35		12.76±11.69	
O2	DM-2	49.91±32.56	**0.004**	20.70±17.59	0.812	73.31±120.14	0.836	58.98 ±101.19	0.784	25.31±15.44	**0.001**
	Controls	32.67±18.45		18.00±12.31		67.81±75.99		46.62±53.86		14.81±14.74	
Fp1	DM-2	76.85±37.24	**0.016**	16.76±09.64	0.8752	50.70±86.22	0.059	17.85±20.89	0.050	23.28±15.98	**0.001**
	Controls	54.95±32.45		15.26±05.61		19.84±12.24		09.72±06.93		09.36±07.66	
F7	DM-2	36.60±38.70	**0.005**	06.03±03.57	0.583	18.90±33.90	0.096	06.86±08.29	0.071	08.26±05.01	**0.001**
	Controls	18.35±13.47		05.14±02.12		08.16±07.60		03.55±02.24		03.80±03.62	
F3	DM-2	16.60±11.32	0.559	05.29±03.68	0.2525	14.61±25.38	0.498	09.84±11.54	0.250	13.21±09.25	**0.001**
	Controls	13.86±05.82		05.96±03.53		10.01±09.00		05.86±04.36		07.02±07.82	
C3	DM-2	22.59±16.28	0.118	08.32±08.73	0.798	51.93±103.25	0.389	22.97±42.67	0.532	13.33±07.45	**0.001**
	Controls	17.12±10.11		06.80±04.21		30.69±29.82		15.94±16.45		07.64±07.62	
T3	DM-2	54.24±38.18	**0.009**	14.41±08.25	0.679	45.72±77.75	0.055	16.52±18.68	0.066	20.85±12.75	**0.001**
	Controls	33.40±16.41		12.59±04.96		17.56±12.00		09.10±06.91		09.31±08.64	
T5	DM-2	41.53±20.88	**0.018**	16.80±11.37	0.848	49.74±72.39	0.153	27.78±32.56	0.262	23.40±13.10	**0.001**
	Controls	30.55±12.28		15.38±08.12		27.29±22.91		17.34±16.23		11.46±11.10	
P3	DM-2	39.49±17.94	0.061	14.57±08.51	0.691	50.22±68.16	0.332	45.87±69.73	0.281	22.43±11.72	**0.001**
	Controls	31.30 ±12.00		13.46±08.58		37.13±34.92		27.16±26.01		11.63±10.87	
O1	DM-2	46.56±25.20	**0.002**	15.13±12.29	0.762	85.19±174.84	0.485	55.86 ±120.55	0.466	21.23±11.43	**0.001**
	Controls	29.14±12.77		13.24±09.98		52.47±52.35		32.12±31.00		11.02±10.04	

EEG data acquisition and analysis

EEG waveforms were reduced and analyzed by using *Focus* software *version (1.1)*. Initial visual inspection of the records was done on computer screen for artifacts due to eyes-blink, and detectable eyes and body movements. Three artifact-free five-second epochs were selected from just before the end of first, second and third minutes of EEG records during eyes-close and eyes-open conditions. FFT was applied on these data to decompose EEG waveforms into sine wave components in terms of respective frequencies. These components were used to estimate spectral power for frequency in the ranges of delta (0.5-4.0 Hz), theta (4.0-7.0 Hz), alpha1 (7.0-10.0 Hz), alpha2 (10.0-13.0 Hz), and beta (13.0-32.0 Hz) bands. The spectral power for each band thus obtained for different regions of the brain (as provided by the selected montage) was exported to Microsoft Excel worksheet files for further analysis. The powers from three epochs were averaged for each subject. All the data from the DM-2 and controls were collected and compared.

Table 5. EEG power spectra of DM-2 (n=30) and controls (n=30) during eyes-open condition

EEG Electrode Sites	Groups	Delta, μV^2 Mean ± SD	p value	Theta, μV^2 Mean ± SD	p value	Alpha1, μV^2 Mean ± SD	p value	Alpha2, μV^2 Mean ± SD	P value	Beta, μV^2 Mean ± SD	p value
Fz	DM-2	59.54±35.00	**0.019**	21.17±12.74	0.376	23.09±22.55	0.052	21.05±33.72	**0.002**	20.53±10.33	**0.001**
	Controls	42.11±20.26		22.22±09.46		14.76±12.16		07.08±05.50		10.13±09.49	
Cz	DM-2	66.13±27.39	**0.009**	22.79±13.08	0.210	26.44±27.06	0.091	27.83±43.19	**0.005**	26.66±17.98	**0.001**
	Controls	48.53±21.14		27.05±15.72		18.45±16.53		09.75±08.49		13.61±14.01	
Pz	DM-2	58.68±29.35	**0.014**	20.78±19.11	0.934	32.78±47.57	0.063	40.38±74.48	**0.021**	25.01±13.9	**0.001**
	Controls	43.25±17.32		18.82±09.41		20.04±25.15		13.69±14.55		12.93±13.55	
Fp2	DM-2	60.56±64.15	**0.016**	17.08±15.86	0.995	16.42±17.15	**0.030**	14.35±22.37	**0.002**	20.21±13.72	**0.001**
	Controls	33.56±16.81		13.66±06.41		09.35±07.18		05.12±03.84		08.45±06.93	
F8	DM-2	25.49±24.09	0.151	04.39±03.35	0.470	05.80±06.70	**0.024**	04.94±07.84	**0.003**	08.27±06.18	**0.001**
	Controls	17.50±17.78		04.32±02.06		02.94±02.42		01.80±01.20		03.80±03.63	
F4	DM-2	16.82 ±0 9.97	0.183	04.56±02.85	0.109	06.35±06.82	0.251	07.21±10.36	0.173	12.44±08.59	**0.005**
	Controls	13.04±06.78		05.47±02.81		04.90±04.17		03.82±02.84		09.85±12.93	
C4	DM-2	20.96±14.74	0.051	07.86±08.57	0.604	16.98±27.54	0.081	16.82±29.44	**0.044**	14.14±09.56	**0.001**
	Controls	15.20±10.27		06.50±04.54		09.65±13.60		06.04±06.29		07.39±07.96	
T4	DM-2	44.27±31.26	**0.028**	12.87±09.49	0.513	14.80±14.92	**0.041**	14.14±23.03	**0.004**	28.21±27.52	**0.001**
	Controls	28.18±14.00		13.02±06.52		09.53±08.87		05.17±04.83		16.34±22.09	
T6	DM-2	42.77±20.11	0.064	14.48±09.93	0.309	18.28±23.73	0.153	23.26±34.83	0.051	20.62±12.18	**0.001**
	Controls	33.07±15.29		16.59±09.83		13.21±11.60		09.79±08.35		11.14±11.01	
P4	DM-2	45.80±27.48	**0.013**	13.90±11.98	0.811	25.65±43.97	0.086	30.52±52.35	**0.048**	19.45±11.15	**0.001**
	Controls	31.21±15.12		13.57±06.91		15.79±20.73		11.78±11.35		10.42±10.71	
O2	DM-2	46.76±34.46	**0.049**	15.82±16.14	0.884	25.72±33.72	0.158	28.53±48.26	0.081	19.73±11.14	**0.001**
	Controls	33.71±21.47		14.68±09.04		16.81±17.48		13.68±14.87		09.93±08.65	
Fp1	DM-2	59.10±65.66	**0.032**	19.13±17.25	0.900	17.14±15.21	0.055	13.33±15.01	**0.001**	26.86±22.78	**0.001**
	Controls	35.38±21.89		15.52±08.04		10.25±06.78		05.67±03.57		09.32±08.05	
F7	DM-2	20.69±13.19	0.079	05.00±03.14	0.499	05.74±05.31	0.074	04.61±05.70	**0.008**	08.86±07.39	**0.001**
	Controls	15.90±14.34		05.05±02.17		03.34±02.05		01.98±00.95		04.01±04.39	
F3	DM-2	15.97±08.69	0.149	04.21±02.91	0.062	06.34±06.86	0.122	06.85±08.29	0.070	13.47±12.06	**0.001**
	Controls	12.80 ±0 6.45		05.45±03.22		04.47±03.92		03.91±03.37		07.48±08.87	
C3	DM-2	18.80±10.44	0.061	05.57±05.20	0.657	14.85±21.08	0.079	15.15±28.06	0.092	11.65±07.86	**0.001**
	Controls	14.06±06.58		05.43±02.99		06.44±06.32		05.69±06.35		06.55±06.91	
T3	DM-2	41.80±30.12	**0.012**	12.94±08.89	0.648	14.25±13.83	0.108	11.99±13.97	**0.002**	25.02±19.22	**0.001**
	Controls	27.47±18.98		12.26±04.73		09.02±07.95		04.87±03.19		10.26±09.13	
T5	DM-2	39.11±18.20	**0.003**	13.45±10.35	0.524	19.52±27.22	0.089	18.97±23.25	0.121	20.24±12.27	**0.001**
	Controls	27.41±11.69		14.09±07.76		11.63±10.14		10.24±10.59		09.77±09.78	
P3	DM-2	37.39±14.55	**0.035**	11.74±09.65	0.779	25.97±38.27	0.058	28.64±46.20	0.051	18.65±10.60	**0.001**
	Controls	29.75±12.20		11.12±04.99		13.48±15.52		12.46±13.87		08.82±08.69	
O1	DM-2	40.58±18.72	**0.006**	10.51±09.31	0.287	21.52±23.43	0.080	30.36±61.27	0.078	16.50±09.71	**0.001**
	Controls	28.33±14.22		11.35±05.78		11.83±11.05		10.81±11.24		07.80±06.71	

Statistical Analysis

The data obtained were exported to Statistical Package for the Social Sciences (SPSS *version 18*) and were tested for normal distribution. The data of age, weight, height, BMI, BP, HR, RR, SaO_2, blood sugar profile, and variables of bilateral sural SNAPs were normally distributed and expressed in terms of mean ± standard deviation. The data of EEG power spectra were non-normally distributed and hence subjected to log transformation and statistical analysis. The EEG power spectra were expressed as mean ± standard deviation. Unpaired t-test was used for comparison of all the variables between DM-2 and controls. A *p value* of < 0.05 was considered statistically significant.

RESULTS

There were no statistically significant differences in age, weight, height, BMI, SBP, DBP, HR, RR, and SaO_2 among the groups. The mean FBG of controls was significantly less ($p<0.05$) than that of the DM-2 (Table 2). The mean PPBG and HbA_1C of DM-2 were 266.9 ± 86.74 mg/dl and 7.03 ± 1.15 % respectively. There were no significant differences in latencies and conduction velocities of bilateral sural SNAPs of DM-2 and controls. However, the amplitudes of bilateral sural SNAPs were reduced in DM-2 `in comparison to the controls (Table 3) though they were above normal cut-off values of ≥ 4 μV (Table 1).

EEG Characteristics

During eyes-close (Table 4): Beta activity was more in DM-2 at all electrodes. Similarly, DM-2 had more delta activity at midline (Fz, Cz, Pz), bilateral frontal (Fp1, Fp2, F7, F8), right central (C4), right parietal (P4), left temporal (T3, T5), and bilateral occipital (O1, O2) regions, and more alpha1 activity at midline frontal (Fz) region. *During eyes-open (Table 5):* Beta activity was more in DM-2 at all electrodes. Similarly, delta activity was more in DM-2 at midline (Fz, Cz, Pz), anterior frontal (Fp1, Fp2), bilateral temporal (T3, T4, T5), bilateral parietal (P3, P4), and bilateral occipital (O1, O2) regions. DM-2 had more alpha1 activity at right frontal (Fp2, F8), and right temporal (T4) regions, and more alpha2 activity at midline (Fz, Cz, Pz), bilateral frontal (Fp1, Fp2, F7, F8), right central (C4), bilateral temporal (T3, T4), and right parietal (P4) regions.

DISCUSSION

Our objective was to study the central and peripheral neuropathy by EEG and NCS respectively in DM-2 before they show the symptoms of peripheral neuropathy. Both the groups were comparable in terms of their age, weight, height, BMI, and all the cardio-respiratory variables. The FBG, PPBG, and HbA_1C % of DM-2 were suggestive of confirmed diabetes and FBG was normal in all the controls. DM-2 had no clinical evidence of sensory neuropathy. The latencies, conduction velocities, and amplitudes of their bilateral sural SNAPs were above the normal cut-off values of ≥ 4 μV. The latencies and conduction velocities of bilateral sural SNAPs in DM-2 were comparable with that in the controls. However, the amplitudes of bilateral sural SNAPs were low in DM-2 in comparison to the controls. Reduced amplitude is the primary abnormality associated with axonal loss. Comparing the amplitude of a potential with a normal control value is one of the best way to assess the amount of axonal loss. The typical pattern associated with axonal loss is one of reduced amplitudes with preserved latencies and conduction velocities. Sensory amplitudes often are low in demyelinating lesions. Reduced sensory amplitudes result from the normal processes of temporal dispersion and phase cancellation.[5] *EEG power spectra of delta activity* were more in DM-2 at most sites as compared to controls during both the eyes-close and eyes-open conditions. Our results are in the line of the result of Mooradian et al[6] who found DM-2 tended to have slower delta EEG power bands at all three recording sites Fz, Cz, and Pz during eyes-close and eyes-open conditions. Nevertheless, in their study they recorded the EEG activity from Fz, Cz, and Pz locations only. In our study, slowing (increased power of delta activity) was more in DM-2 at multiple sites during both the eyes-close and eyes-open conditions. Daniel et al[7] found that hyperglycemia (blood glucose >15 mmol/dl) was associated with slowing of all cognitive performance tests and an increased number of mental subtraction errors for DM.[7] Thus, our results are indicative of diffuse central neuropathy in DM-2 as indicated by EEG changes.

A meta-analysis of 24 studies showed that depression was associated with hyperglycemia in both type 1 diabetes mellitus (DM-1) and DM-2.[8] In a prospective population-based similar study of 2764 Japanese men, those with major depressive disorder (MDD) or depressive symptoms were at a higher risk of developing DM-2.[9]

In our study, we did not assess cognitive functions and depressive symptoms of the patients. However, the patients with DM are twice as likely to have depression[10, 11] that will also negatively affect cognitive function and daily activities. DM-2 also has an increased incidence of Alzheimer's disease[12-14] and increased incidence of vascular dementia.[15,16] This might be one of the reasons for increased delta activity in DM-2 in our study. *EEG power spectra of beta activity* were more in DM-2 as compared to controls during both the eyes-close and eyes-open conditions at all sites. Our results are in the line of the result of Gibbs et al[17] who found mixed slow and fast frequencies and some intermingled spiking in patients with elevated blood sugar levels. [17] Beta waves (>13/sec) are usually seen, especially on the frontal and central areas, in tense and anxious patients. [18] Anxiety disorders are also highly prevalent in DM-2. [19] The prevalence of anxiety and depression symptoms in DM was more than double the general population estimates. [20] Khan et al[21] in their study, done in 889 DM-2, identified that 57.9% had anxiety and 43.5% were positive for depression.[21] Peyrot and Rubin[22] studied 634 patients in an outpatient DM education program and reported depression and anxiety in 41.3% and 49.2% of the patients respectively. They concluded that DM is associated with an increased risk of psychological disturbance, particularly those with more DM-2-related complications. [22]

EEG power spectra of alpha2 activity was more in DM-2 during eyes-open condition at Fz, Cz, Pz, C4, T4, P4, Fp1, F7, and T3. Increased alpha2 power activity contradicts the increase in faster activities. However, to explore our observations, further study is required. Alpha rhythm is the classical EEG correlate for a state of relaxed wakefulness best obtained with the eyes closed. Eye opening, other afferent stimuli, and mental activities temporarily block the posterior alpha rhythm. [23] Occasionally, an increase in abundance of alpha activity occurs with eyes-open instead of decrease. This reversal is a "paradoxical effect" or "paradoxical alpha", which occurs mostly with eyes-open in response to stimulation following a brief period of drowsiness. [24]

EEG power spectra of alpha1 activity were more in DM-2 at Fz during eyes-close condition and at Fp2, F8, and T4 during eyes-open condition.

Our results are in the line of the result of Duffy et al[25] who suggested that the bilateral slowing of the alpha rhythm might be seen in metabolic, toxic, and infectious encephalopathy of diverse etiology.[24] It is also a consistent finding in patients with dementia irrespective of the underlying cause. The degree of slowing often parallels alteration in the mental status of the patient.[25]

CONCLUSION

DM-2 had more beta, delta, and alpha bands in EEG indicative of central neuropathy, which appeared before symptomatic peripheral neuropathy. Although DM-2 did not show symptoms of peripheral neuropathy, they had reduced amplitudes of bilateral sural SNAPs as compared to controls. Based on the result of our study and the available literatures, we believe that diffuse EEG changes occur in DM-2 along with reduction in amplitudes of bilateral sural SNAPs.

Therefore, we conclude that diffuse central neuropathy occurs along with the peripheral neuropathy in DM-2 as measured by the electrophysiological tests.

It appears prudent for the clinician to at least carefully assess cerebral functions in all DM-2 and take into account the possibility of CNS impairments before they develop symptoms of peripheral neuropathy when planning the management of these patients.

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What this study adds:

1.What is known about this subject?

Diabetes mellitus (DM) is associated with chronic complications such as nephropathy, angiopathy, retinopathy, autonomic neuropathy, and peripheral neuropathy. However, there is a paucity of data regarding central neuropathy in DM. Some reports claim central neuropathy in DM based on evoked potentials. However, central neuropathy in DM particularly before symptomatic peripheral neuropathy has received much less attention.

2. What new information is offered in this study?

Diffuse central neuropathy occurs along with the peripheral neuropathy in DM-2 as measured by the electrophysiological tests.

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