Assessment of autonomic dysfunction in patients with multiple sclerosis

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ABSTRACT

Background: Multiple sclerosis can cause an extensive multiplicity of clinical features including those related to the involvement of the autonomic nervous system. Aim of work: to detect autonomic disturbances in the cardiovascular system, gastrointestinal tract, and sweating function in patients with multiple sclerosis. Methodology: 39 patients with definite multiple sclerosis were subjected to R-R interval variability, heart rate variability (HRV) in 24 hours ECG recording, sympathetic skin response (SSR) to assess the central sympathetic pathway, and scintigraphy to assess gastric emptying. Results: postural hypotension was more detected in patient group with a statistically significant lower percent of R-R interval variability with deep breathing, but no statistically significant difference was detected regarding HRV in 24 hours ECG recording. On performing SSR, the amplitude but not the latency showed marked affection in patients compared to control. Though the mean T½ of gastric emptying was slower in patient group; yet, the difference between the two groups was not statistically significant. Conclusions: autonomic function assessment showed quite a large percent of abnormalities especially in the context of SSR, come next the abnormalities of cardiovascular reflexes in respect mainly to deep breathing. As for gastric motility assessment, though the statistical significance was not achieved, yet gastric emptying was clearly slower in patients than control. (Egypt J. Neurol. Psychiat. Neurosurg., 2004, 41(1): 221-234).

INTRODUCTION

Though autonomic dysfunction is frequently observed in patients with multiple sclerosis, yet, clinical studies showed contradictory findings regarding frequency and type of abnormalities in autonomic function tests¹. Disorders of autonomic functions in multiple sclerosis include those of cardiovascular system², sudomotor neuraxis³, urological function⁴, gastrointestinal tract (GIT)⁵, sexual⁶, respiratory⁷, and pupillary function⁸.

Central disturbances in MS can lead to profound alterations in cardiovascular control manifested by cardiac arrhythmias, myocardial infarction, and lability of arterial blood pressure⁹. Though impairment of cardiovascular autonomic reflexes has been described in MS; yet, the exact site of autonomic cardiovascular abnormalities in MS patients is not well defined¹⁰,¹¹. However, such impairment reflects dysfunction of reflex pathways located within the central nervous system; the demyelinating plaques may damage the vasomotor centres in the brainstem or interfere with autonomic nervous
system descending fibres in the spinal cord\textsuperscript{12,13}. Assessment of cardiovascular autonomic functions include assessment of adrenergic (sympathetic) function mainly comprises blood pressure responses to change in posture, Valsalva manoeuvre, and pressor stimuli; and for cardiovagal (parasympathetic) innervation comprises heart rate responses to standing, deep breathing, and Valsalva manoeuvre (Valsalva ratio)\textsuperscript{14}.

Moreover; few reports documented gastrointestinal autonomic dysfunction in multiple sclerosis in form of gastroparesis and bowel dysfunction\textsuperscript{5,15}, and it seems that gastroparesis complicating multiple sclerosis may a more frequent problem than previously recognized. Furthermore; prevalence of bowel dysfunction in patients with multiple sclerosis has been reported to range between 41\% and 68\% in different studies\textsuperscript{5,16}. In multiple sclerosis either the storage function or the elimination function of faeces might be impaired, however, impairment of both functions is not uncommon\textsuperscript{17}. Assessment of gastrointestinal, and bowel motility could be achieved by scintigraphy (Radionuclide technique), radiography after ingested contrast “barium meal”\textsuperscript{18}, ultrasonography\textsuperscript{19}, manometric studies “both gastroduodenjejunal, and anorectal”\textsuperscript{20}, breath 13-CO\textsubscript{2} study\textsuperscript{21}, and anorectal electromyography\textsuperscript{22}.

In addition, another autonomic function impairment in multiple sclerosis is that related to sudomotor neuraxis, which comprises thermoreceptors, afferent pathway, central processing, central sympathetic pathways, preganglionic and postganglionic fibers, and the eccrine sweat glands. Abnormalities of thermo-regulation in MS include hypothermia\textsuperscript{23}, anhidrosis\textsuperscript{24}, and hyperhidrosis\textsuperscript{25}. Assessment of sudomotor function includes evoked electrodermal activity (Sympathetic Skin Response) (SSR)\textsuperscript{26}, Thermoregulatory Sweat Test (TST)\textsuperscript{27}, and Quantitative Sudomotor Axon Reflex Test (QSART)\textsuperscript{3}.

The aim of this work was to detect autonomic disturbances in the cardiovascular system, gastrointestinal tract, and sweating function in patients with multiple sclerosis; also, to find a relation between the detected autonomic dysfunctions and the site of MS plaques on the MRI, and to relate different autonomic tests with demographic and clinical data.

**SUBJECTS AND METHODS**

**Subjects:** This study was conducted on 39 patients with definite multiple sclerosis, according to criteria proposed by Poser et al.\textsuperscript{28}, they were 23 females and 16 males, with age range between 19 to 47 years with a mean age of 32±8.6 years. The study also included age and gender matched 20 healthy control subjects.

**Patients selection:** patients with relapsing remitting (RR-MS) [n=27], secondary progressive (SP-MS) [n=7], and primary progressive (PP-MS) [n=5] were included. Most patients were in acute relapse or showed disease progression by clinical evidence.

**Exclusion Criteria:** patients with possible causes of dysautonomia like those with endocrinal disorders as diabetes; patients with collagen vascular diseases, or those with cardiovascular illness; and patients with history of drug intake that may affect autonomic function e.g. anticholinergic medications.

**Methods:**
All patients included in the study were subjected to the following:
A. Clinical Evaluation: including history taking, neurological examination, and assessment of the clinical disability using the Kurtzke Multiple Sclerosis Rating Scales; “Expanded Disability Status Scale” (EDSS)²⁹.

B. Radiological Assessment: magnetic resonance imaging (MRI) of the brain and the spinal cord; [cervical and upper dorsal parts]. The following pulse sequences were obtained: T1- and T2-weighted spin echo images, PD and FLAIR images. Verification of the site of the plaques was interpreted by a specialized neuroradiologist to be correlated with autonomic dysfunction.

C. Evoked potential studies: visual, short latency somatosensory, and brainstem evoked potential studies using four-channel Schwartser apparatus.

D. Assessment of Autonomic Function:
   a. Clinical Evaluation:
      - Questionnaire for autonomic symptoms according to Low and Zimmerman³⁰.
      - Assessment of blood pressure response to change in posture was done according to Mohoek et al.¹³. A fall of systolic blood pressure of 20 mmHg or more and/or diastolic pressure of 10 mmHg was considered abnormal according to definitions of Adams and Victor³². This procedure assesses sympathetic function¹⁴.
   b. Electrophysiological Studies:
      - R-R interval variation was assessed in response to normal breathing, deep breathing to assess vagal function¹⁴, Valsalva manoeuvre to assess both sympathetic and vagal functions mainly vagal¹⁴, and lastly in response to standing up to assess mainly vagal function¹⁴, using Keypoint® Software version 3.00; the Interval program. Recording: two surface electrodes were placed over the radial pulse, one in each arm. Analysis: an epoch of one minute was analysed. A plot of R-R intervals versus time was displayed on-line on the computer screen. R-R interval variation in response to normal and deep breathing; the following algorithm is used: \([\text{RR (max)} - \text{RR (min)}] \times 100 / \text{RR (mean)}\). Valsalva ratio: automatically calculated as follows: the ratio of the longest R-R interval after the manoeuvre to the shortest R-R interval during the manoeuvre. A ratio of 1.2 or greater has been taken as normal³³. Heart rate response to standing: using computer analysis, the 30:15 ratio was automatically calculated, by dividing length of longest R-R interval at beat 30 after standing by length of shortest R-R at beat 15 after standing. Ratios less than 1.03 were considered abnormal according to Ewing et al.³⁴.

   - Heart Rate Variability (HRV) in 24 hours ECG Recording:
      The time domain method was used; this method determines the intervals between successive normal QRS complexes. In a continuous ECG record, each QRS complex is detected, and the normal-to-normal (NN) intervals (that is all intervals between adjacent QRS complexes “RR”). Calculation was performed using statistical methods, to detect the standard deviation of the NN interval (SDNN), which provides a measure of heart rate variability over a range of frequencies and reflects all the cyclic components responsible for variability in the period of recording³,³⁵.
- **Sympathetic skin response (SSR)** to assess the central sympathetic pathway.

**Technique:**
A Nihon Kohden 2 channels EMG and evoked potential system, the band pass was 0.5 Hz (low filter) and 5 KHz (high filter). Stimulating electrodes: a bipolar stimulator surface electrode was applied to the median nerve at the wrist of the upper limb, and to the planter surface at the mid foot of the lower limb contralateral to the site of recording. Recording electrodes: applying of surface disk electrodes 1 cm diameter stainless steel as follows; in the upper limb: the active electrode was placed over the second palmar interspace 3 cm proximal to the first web space and the reference electrode over the pulp of the middle finger. In the lower limb: the active electrode was placed over the second plantar interspace in the midfoot and the reference electrode at the pulp of the second toe. Test execution: in the upper limbs: the recording was from the right side and the stimulation was to the left side and vice versa in the lower limbs. The intensity of the simulation was 20 mA, with duration of 0.2 msec; and the interstimulus interval was more than 30 seconds to avoid habituation of the response. More than one response was elicited (on the average 4 responses) to check reproducibility. The response with the largest amplitude was taken.

**Interpretation:** According to the cut off values produced by logistic regression analysis; latency was considered prolonged if it exceeded 1.88 second in the upper limb and 2.77 seconds in the lower limb; amplitude was considered small if it was less than 0.66 mV in upper limb and 0.447 in the lower limb. Absent response was considered if no consistent voltage change was seen after 4 or more trials.

c. **Scintigraphy**

**Study principles:** measurement of the disappearance of radioactivity from the field of view of a detector positioned adjacent to the stomach.

**Radiopharmaceutical:** patients were requested to fast for a minimum 4 hours, and then 2 mCi (75 MBq) 99m Tc colloid was mixed with a scrambled egg (labeled meal).

**Imaging protocol:** using a large field of view Gamma camera with dual detectors, patient was placed in the semi-recumbent position with the two camera heads located anteriorly and posteriorly. Serial digital images at 15 minutes intervals were acquired immediately after the patient finished ingesting the meal. Acquisition of images continued for 2 hours. Expression of the results: based on visual analysis for the disappearance slope of the gastric emptying curve was implemented. The scoring system was a 5 point scale where: (1) definite slow descent in the disappearance slope (almost plateau); (2) slow descent in the disappearance slope; (3) normal descent in the disappearance slope (linear descent); (3) fast descent in the disappearance slope; (4) definite fast descent in the disappearance slope (very steep).

**Statistical Methods:**
Data management and statistical analyses were done using the Statistical Analysis
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System. Harvard graphics were used for figures drawing, numeric variables were summarized as means and standard deviations. To test differences between cases and controls, the non-parametric Mann-Witney test was used, which is equivalent to the t-test, to be used in case of small sample size. Logistic regression was used to elicit cut off values. P-values less than 0.05 was considered significant.

RESULTS

A. Cardiovascular system:

* Postural hypotension and blood pressure measurement after standing

The frequency of patients who experienced symptoms of postural hypotension, throughout the course of the disease, were 16 patients (41%), where 10 patients (62.5%) had mild symptoms (grade 1); 4 (25%) had moderate symptoms (grade 2); and 2 patients (12.5%) showed severe symptoms (grade 3).

The range of change in both systolic blood pressure (SBP), and diastolic blood pressure (DBP) on switching from lying to standing position was higher in patient group when compared to that of control group with a statistical significant difference (P<0.05), as shown in Table (1).

* Neurophysiological Tests

1. Heart rate variability (HRV) in 24 hours recording (n=35).

On comparing the components of HRV: SDNN, SDNN-i, SDANN-i, r-MSSD, and pNN50, between patients and control groups, no statistically significant difference was detected (P>0.05).

2. R-R interval variability with:

Normal breathing (Respiratory sinus arrhythmia) (n=35)

The mean percent of R-R interval variability with normal breathing in patients compared to controls showed no statistically significant difference (P = 0.173).

Deep breathing (n=35)

Regarding the change in heart rate after deep breathing, 19 patients (54.2%) of 35 patients showed an increase in HR of less than 10 beats/minute or even showed a decrease in HR, any of which considered an abnormal response, Table (2).

On the other hand, a statistically significant difference in the “mean percent” of R-R interval variability with deep breathing was found on comparing patients to control group (P = 0.042), this is shown in Table (3).

Valsalva (n=33)

No statistically significant difference was found in the mean Valsalva ratio between patients and control groups (P=0.297). Twelve patients (36.4%) showed abnormal Valsalva ratio (<1.2), as shown in Figure (1).

Standing up (30:15 ratio) (n=32)

No statistically significant difference existed in the mean 30:15 ratio between patients and controls (P=0.395). However, 19 patients (59.3%), out of the 32 patients for whom the test was done, showed abnormal ratio (<1.03), as shown in Figure (2).

* Relation between clinical and neurophysiological findings of CVS

There was no statistically significant difference in the mean percent of heart rate change (R-R) on deep breathing, or the mean heart rate change with Valsava maneuver or after standing up between patients with and without postural hypotension.
* CVS autonomic dysfunction and MRI findings

Only patients with corpus callosum plaques showed a statistically significant difference in the mean change of SBP on standing, where the mean change was higher in patients with plaques in the corpus callosum (P=0.045). Otherwise, the rest of cardiovascular dysfunctions were not associated with a particular location either on MRI brain or spinal cord.

B. Sympathetic skin response (SSR):

The sympathetic skin response test in the upper limb was performed to the 39 patients, while one patient was missing when the test was carried out in the lower limb because of having edema of the lower limbs. In the upper limb, no statistically significant difference was found between patients and controls in latency (P=0.272) whereas a highly statistically significant decrease was found in amplitude of SSR in patients compared to controls (P<0.0001), as shown in Table (4).

In the lower limb, no statistically significant difference between patients and controls in the mean latency of the SSRs (P=0.252), but a highly statistically significant decrease in amplitude existed in patients compared to controls (P=0.009), as shown in Table (5), and Figure (3).

* SSR and disordered sweating

Only the mean amplitude in upper limb was lower in patients with hyperhidrosis when compared to those with no such complaint and the difference was statistically significant (P=0.014). Otherwise, no statistically significant difference was observed in the mean upper limb latency or median lower limb latency or amplitude in patients with and without hyperhidrosis.

* SSR and MRI

The median SSR latency in the lower limb was significantly statistically lower in patients with brainstem plaques compared to those with free brainstem (P=0.038). Otherwise, neither mean upper nor median lower limb latency or amplitude of SSR were statistically significantly different in patients with or without periventricular, centrum semiovale, corpus callosum, cerebellar or spinal cord lesions.

C. Gastrointestinal system:

* Gastric Emptying by Scintigraphy

Out of the 36 patients who performed gastric emptying test using scintigraphy, 14 patients (38.9%) showed slow curves (grade 1 & 2); 15 (41.7%) showed normal curves (grade 3); 7 (19.4%) showed fast curves (grade 4 & 5). Though the mean T½ of gastric emptying in patients was 92.2±266.5 minutes with a minimum of 13 and a maximum of 1590 minutes and the controls showed a mean of 31.3±12.6 minutes with a range of 19 – 66 minutes; yet, the difference between the two groups was not statistically significant (P=0.41)

* Gastric emptying T½ and GIT symptoms

The mean T½ was more in patients with constipation, nevertheless there was no statistically significant difference between patients with and patients without constipation (P=0.197). Also, though the mean T½ was lower in patients with fecal incontinence, yet, there was no statistically significant difference between those with and those without fecal incontinence (P=0.654).

* Gastric emptying T½ and MRI findings

There was no statistically significant difference in the mean T½ between patients with and without periventricular, centrum semiovale, corpus callosum, cerebellar, brainstem, or spinal cord plaques (P>0.05).
D. Relation between different autonomic tests and demographic and clinical data:
There was no statistically significant correlation between cardiovascular autonomic abnormalities, SSR abnormalities or gastric emptying abnormalities and the age of the patients; duration of the disease; number of attacks; or the EDSS. Also, no difference in the various autonomic tests existed between males and females or between the different types of MS.

E. Relation between different autonomic tests:
A statistically significant increase in the median latency of SSR in the lower limb was found in patients with symptoms of postural hypotension when compared to those without such symptoms (P=0.004). On the other hand, no statistically significant difference in the mean upper limb nor the median lower limb latencies and amplitudes existed between patients with and without heart rate difference of less than 10 beats/min, 30:15 ratio < 1.03 or Valsalva ratio of <1.2.

Table 1. Postural Blood Pressure in patients & controls.

<table>
<thead>
<tr>
<th>Change in BP</th>
<th>Range (mmHg)</th>
<th>Mean (mmHg)</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls (n=20)</td>
<td>0 – 15</td>
<td>7</td>
<td>5</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Patients (n=36)</td>
<td>45 – 30</td>
<td>10</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls (n.20)</td>
<td>0 – 15</td>
<td>9.5</td>
<td>3.6</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Patients (n.36)</td>
<td>20 – 30</td>
<td>1.1</td>
<td>12.1</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Frequency of patients with abnormal change in HR after deep breathing.

<table>
<thead>
<tr>
<th>HR change</th>
<th>No. (n.35)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase of &lt; 10 beats/min</td>
<td>13</td>
<td>37.1</td>
</tr>
<tr>
<td>Decrease</td>
<td>6</td>
<td>17.1</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>54.2</td>
</tr>
</tbody>
</table>

Table 3. Mean RR variability % with deep breathing in patients & controls.

<table>
<thead>
<tr>
<th>Group</th>
<th>Range (%)</th>
<th>Mean (%)</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n.20)</td>
<td>14 - 288</td>
<td>123.8</td>
<td>68</td>
<td>0.042</td>
</tr>
<tr>
<td>Patients (n.35)</td>
<td>12-214</td>
<td>85</td>
<td>54.5</td>
<td></td>
</tr>
</tbody>
</table>
Fig. (1): Frequency of abnormal Valsalva ratio in patients.

Fig. (2): Frequency of abnormal HR response on standing in patients.

Table 4. Mean upper limb SSR latency and amplitude in patients and controls.

<table>
<thead>
<tr>
<th>UL SSR</th>
<th>Controls</th>
<th>Patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency mean (sec)</td>
<td>1.54±0.16</td>
<td>1.79±0.71</td>
<td>0.272</td>
</tr>
<tr>
<td>Latency range (sec)</td>
<td>1.22-1.79</td>
<td>1.18-5.09</td>
<td></td>
</tr>
<tr>
<td>Amplitude mean (mV)</td>
<td>1.61±0.73</td>
<td>0.37±0.33</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Amplitude range (mV)</td>
<td>0.5-3</td>
<td>0.03-1.35</td>
<td></td>
</tr>
</tbody>
</table>
**Table 5.** The SSR in lower limbs in patients and controls.

<table>
<thead>
<tr>
<th>LL SSR</th>
<th>Controls</th>
<th>Patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency mean (sec)</td>
<td>2.37±0.29</td>
<td>2.41±0.78</td>
<td>0.252</td>
</tr>
<tr>
<td>Latency range (sec)</td>
<td>1.90-2.84</td>
<td>1.38-5.2</td>
<td></td>
</tr>
<tr>
<td>Amplitude mean (mV)</td>
<td>0.63±0.58</td>
<td>0.26±0.27</td>
<td>0.009</td>
</tr>
<tr>
<td>Amplitude range (mV)</td>
<td>0.1-2</td>
<td>0.02-1.28</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. (3):** Comparison of mean amplitude in UL & LL between patients and controls (P< 0.0001, P=0.009).

**Table 6.** Frequency of symptoms of GIT dysfunction amongst patients.

<table>
<thead>
<tr>
<th>GIT symptom</th>
<th>No. (n.39)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>22</td>
<td>56.4</td>
</tr>
<tr>
<td>Fecal incontinence</td>
<td>15</td>
<td>38.5</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>2</td>
<td>5.1</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In our study the mean change in both systolic and diastolic blood pressure on switching from lying to standing position was higher in patient group when compared to that of control group with a statistical significant difference; and the HR response to standing showed abnormalities in 59.3% of patients; 54.2% of patients gave abnormal responses to deep breathing and 36.4% showed abnormal HR response to Valsalva manoeuvre. These findings go in accordance with Flachenecker et al.\textsuperscript{13}; and De Seze et al.\textsuperscript{36} who reported...
affection in all non-invasive cardiovascular tests when comparing patients to controls. On the contrary, Thomaides et al. elicited no difference between patients and controls regarding responses to deep breathing and to the Valsalva manoeuvre. However, in our study there was lack of significant difference in the mean 30:15 ratio between patients and controls, which might be rendered to the minimal support offered to some patients with moderate or relatively severe disability during standing, while the test requires the ability of the subject to stand up unsupported. Moreover, there was no statistically significant difference existed between patients and controls regarding assessment of heart rate variability (HRV) over 24 hours. In contrast to our study, Frontoni et al. used power spectral analysis in assessment of cardiovascular autonomic tests in patients with multiple sclerosis, the patients showed decreased spectrum total power when compared with controls. This contradiction could be due to the choice of different methods to assess the HRV, as in our study the time domain method was used not the spectral analysis.

In the current study, the observed different cardiovascular autonomic abnormalities did not show particular association with age or sex of the patients; duration of the disease; number of attacks or the EDSS. This goes in accordance with Anema et al. and Nasseri et al. In contrast to these observations, Vita et al. and Acevedo et al. showed a significant association between presence of cardiovascular autonomic dysfunction and clinical disability. In our study, only patients with corpus callosum plaques showed a statistically significant difference in the mean change of SBP on standing, where the mean change was higher in patients with plaques in the corpus callosum. Anema et al. found no indications for localization of the autonomic disturbances in the brainstem based on clinical and magnetic resonance imaging findings. On the contrary, Acevedo et al. showed a significant association between presence of autonomic dysfunction and MRI evidence of brainstem lesions. De Seze et al. emphasized that autonomic dysfunction was correlated with spinal cord cross-sectional area reduction but not with spinal cord hyperintensities, thus, autonomic dysfunction appears to more closely related to axonal loss, as demonstrated by spinal cord atrophy, than to demyelinating lesions.

Regarding GIT results; though the main symptoms of autonomic dysfunction in the GIT were related to the large bowel, yet the method used in this study to assess GIT motility was “gastric emptying by scintigraphy” because of its availability and its relatively simple performance. Its use was supported by the opinion of some authors that gastric emptying may be altered by small bowel or colonic dysfunction. In the present study, though the mean T½ of gastric emptying was more in patients than controls, yet the difference between the two groups was not statistically significant. This may be due to the smaller number of control subjects compared to patients. The results of our work, also, showed that the mean T½ was more in patients with constipation implying slower rate of gastric emptying and it was lower in patients with fecal incontinence indicating a faster rate of gastric emptying, nevertheless there was no statistically significant difference between patients with and patients without constipation or between those with and those without fecal incontinence. This can go in accordance with Chatterton, who stated that there is often a poor correlation between symptoms and the degree of emptying. Moreover; there was no statistically significant correlation between gastric
emptying abnormalities and the age of the patients; duration of the disease; or the number of attacks. In agreement with this, Minderhoud et al.\textsuperscript{43} found that bowel disturbances bore no relation to the age of the patient. There was also no particular association between the mean T½ and the MRI findings, which goes in agreement with Hawker and Frohman\textsuperscript{44}, who mentioned that constipation was not due to a specific neurological lesion in the CNS.

Concerning sudomotor functions, the main abnormality of the SSR in the present work was reduction in amplitude, rather than latency, in addition to the presence of completely absent responses in the lower limbs. In accordance with our findings; Gutrecht et al.\textsuperscript{45} noted SSR abnormalities only in amplitude in their study concerning MS patients. Hussein\textsuperscript{46}, reported that there was no statistically significant difference in the mean latency or amplitude of SSRs in upper limbs between patients and controls, though the amplitude was notably lower in patients than controls (P=0.06), also, she reported that 60\% of MS patients showed absent responses in their lower limbs. On the other hand and in contrast to our study, Elie and Louboutin\textsuperscript{47}, in their study of patients with MS, observed abnormally delayed palmar or plantar SSRs in 85\% of patients, whereas SSR amplitude was normal. Yokota et al.\textsuperscript{48}, mentioned that the great variability of the SSR amplitude renders it unreliable as an index of abnormality and considered the SSR to be abnormal only when it is absent. The significant reduction in amplitude in our study might be explained by what was stated by Ferguson et al.\textsuperscript{49}, who found, in addition to demyelination, axonal loss in acute MS as well as in chronic progressive types.

In our study, the complaint of hyperhidrosis was unexpectedly associated with small amplitude of the SSR, which tends to assess hypo- rather than hyperfunction of sweat glands. Actually, in our study we did not objectively measure sweat pattern and the information obtained from the patients in this regard may not be much reliable. In the present study, SSR latency in the lower limb was associated with plaques in the brainstem. Also, all the patients with absent responses, except one, had spinal cord plaques. In contrast, Gutrecht et al.\textsuperscript{45} found no correlation between MRI abnormalities of brainstem and the abnormalities of sweating. SSR was not correlated with the age of patients, which goes in accordance with Knezevic and Bajada\textsuperscript{26} who found no significant correlation between SSR latency or amplitude and age. Also, SSR was not correlated with duration of the disease, number of attacks, or the EDSS. In contrast, a high correlation between the degree of SSR impairment and the severity of disability caused by MS has been found by Gutrecht et al.\textsuperscript{45}. This contradiction may be explained as follows; the EDSS is mainly a measure of mobility of the MS patient, not only reflecting pyramidal tract involvement but also cerebellar as well as posterior column affection. Thus, the high EDSS not necessarily implies only pyramidal tract involvement, where a large portion of sudomotor fibers passes within. The descending sympathetic fibers, in addition to their path within the corticospinal tract, also descend along the anterior and posterior aspects of the lateral funiculus.\textsuperscript{50} A statistically significant difference in the median latency of SSR in the lower limb was found in patients with symptoms of postural hypotension when compared to those without such symptoms, which represents a logical relation as the impairment of either of them implies an impairment sympathetic function. In conclusion, besides the evident clinical symptoms of autonomic dysfunction in MS patients; objective tests showed a large
percentage of abnormalities especially in the context of SSR where more than 90% showed abnormal responses, come next cardiovascular reflexes abnormalities in respect to deep breathing, standing up, and Valsalva manoeuvre; lastly it was clearly evidenced that gastric emptying was slower in patients than controls.

REFERENCES


الملخص العربي

تقييم الخلل في الوظائف التلقائية في مرضى التصلب المتعذر

اشتملت الدراسة على 39 مريضاً بمرض التصلب المتعذر و 20 فرداً طبيعياً يمثلون المجموعة الضابطة. وقد أجريت لهم اختبارات قياس الخلل في الوظائف التلقائية في الجهاز الالتحالي في الجهاز الالتحالي و الالتحالي، و تقييم وظيفة الغدد العرقية من خلال اختبار الاستجابة السيميثرائية عن طريق الجلد، بالإضافة لقياس وظائف الجهاز الالتحالي. لذا إجراء الاختبار قياس التغير في معدل التنفس أثناء التنفس الطبيعي والتنفس العميق عند الوقوف وأثناء ممارسة طريقة فايرفلا وجد أن نسبة درجة التغير في معدل التنفس أثناء التنفس العميق أقل في المرضى من المجموعة الضابطة بشكل ذي دلالة إحصائية.

وقد تم عمل رسم القلب الكهربائي على مدى 24 ساعة لتسجيل درجة التغير الزمني الذي حدث من نبضة إلى نبضة ولم يتغير وجود رد فعل ضربة دلالة إحصائية بين المرضى والمجموعة الضابطة. وعند عمل اختبار الاستجابة السيميثرائية عن طريق الجلد، فقد تبين أن متوسط حجم الاستجابة كان أقل بدرجة ذات دلالة إحصائية في المرضى عن في المجموعة الضابطة، بينما لم يختلف متوسط كموم الاستجابة في المرضى والمجموعة الضابطة. وبصدام قياس معدل تغير المعدة باستخدام النظائر المشعة كان معدل التغير أبطأ في المرضى عن في المجموعة الضابطة ولكن ذلك لم يصل إلى درجة ذات دلالة إحصائية.