

# Evolution of Gastric Electrical Features and Gastric Emptying in Children with Duchenne and Becker Muscular Dystrophy

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- OBJECTIVES:** Although muscular dystrophy (MD) affects primarily striated muscles, smooth muscle cells of the gastrointestinal tract may also be involved. We recorded gastric electrical activity and gastric emptying time (GET) in children with MD at initial presentation and at 3-yr follow-up in order to detect gastric motor abnormalities and study their evolution along the clinical course.
- METHODS:** Twenty children with MD (median age: 4.6 yr; range age: 3–7 yr) were investigated by means of ultrasonography, for measuring GET, and by electrogastrography (EGG); 70 children served as controls.
- RESULTS:** Ten patients had Duchenne muscular dystrophy (DMD) and 10 Becker muscular dystrophy (BMD). GET was significantly more delayed in MD patients (DMD, median: 195 min; range 150–260 min; BMD, median: 197 min; range: 150–250 min) than in controls (median: 150 min; 110–180 min;  $p < 0.05$ ); it markedly worsened at the follow-up in DMD (median: 270 min; range 170–310 min;  $p < 0.001$  vs controls) but not in BMD patients (median: 205 min; 155–275 min;  $p < 0.05$  vs DMD). Baseline EGG showed a significantly lower prevalence of normal rhythm and significantly higher prevalence of dysrhythmias in both groups of patients as compared to controls (% of normal rhythm: DMD  $66.7 \pm 8.2$ , BMD  $67.2 \pm 11.5$ , controls  $85.3 \pm 7.2$ ,  $p < 0.001$ ; % of tachygastria: DMD  $28.4 \pm 8.0$ , BMD  $29.8 \pm 12.3$ , controls  $10.6 \pm 5.1$ ,  $p < 0.001$ ; % of dominant frequency instability coefficient: DMD  $36.1 \pm 6.0$ , BMD  $33.2 \pm 2.9$ , controls  $17.9 \pm 7.1$ ,  $p < 0.001$ ); furthermore, no difference in fed-to-fasting ratio of the dominant EGG power was found between the two groups and controls (DMD  $2.84 \pm 1.27$ , BMD  $2.82 \pm 0.98$ , controls  $3.04 \pm 0.85$ , ns). However, at the follow-up no significant change in the prevalence of normal rhythm and dysrhythmias occurred in both groups (ns vs baseline values), whereas only DMD patients showed a marked reduction in fed-to-fasting power ratio ( $0.78 \pm 0.59$ ;  $p < 0.001$  vs controls and BMD;  $p < 0.05$  vs baseline), which correlated with the progressive neuromuscular weakness occurring in DMD subjects ( $r, 0.75$ ;  $p < 0.001$ ).
- CONCLUSIONS:** In children with MD, there is an early abnormality in gastric motility that is due to deranged regulatory mechanisms, whereas contractile activity of smooth muscle cells seems to be preserved. At the follow-up, DMD patients exhibited a progressive failure in neuromuscular function, which was accompanied by a gastric motility derangement with worsening in GET and in EGG features suggesting an altered function of gastric smooth muscle cells.

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## INTRODUCTION

Muscular dystrophies (MD), a group of inherited disorders with progressive striated muscle weakness as the most prominent feature, classically include Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) (1). The former is an X-linked lethal disease caused by mutations of the dystrophin gene, localized on the X chromosome at the Xp21 locus, the protein product of which, dystrophin, has

a critical role in maintaining muscle structure and function (2–4). It affects approximately 1 in every 3,300–4,000 live male births with loss of independent ambulation occurring at approximately 10 yr of age (1). BMD is very similar to DMD, with a genetic defect at the same locus; however, it progresses at a much slower rate (5, 6). The two forms are usually classified as dystrophinopathies (1).

Although striated muscles are typically affected, involvement of gastrointestinal smooth muscle has also been

recognized (7, 8). Gastric emptying delay and/or acute gastrointestinal dilatation have been shown to characterize the clinical course of MD (9, 10). Interestingly, gastroparesis and gastric distension can promote gastroesophageal reflux and cause nutritional disturbances because of delayed delivery of nutrients into the small intestine (11).

We aimed at recording gastric motility in a group of children with MD in order to detect gastric motor abnormalities and study their evolution in relation to the course of the neuromuscular disease. Gastric motility was recorded through ultrasound measurement of gastric emptying time (GET) and electrogastrography (EGG). Recordings were performed at baseline and after a 3-yr follow-up in all subjects.

## METHODS

Twenty children with a recent diagnosis of MD (median age: 4.6 yr; range: 3–7) were referred to our unit from the Department of Neurophysiopathology of the Faculty. The diagnosis of MD was based on clinical, electrophysiological, histological, and genetic findings. All drugs affecting the gastrointestinal motility had been stopped 1 wk before the study. The study was approved by the ethical committee of the University of Naples “Federico II,” and an informed written consent was obtained from all the parents.

Clinical expression of neuromuscular involvement was classified according to the criteria of Hoffman *et al.* (12), modified by Comi *et al.* (13). The patient’s status has been defined as: grade I = asymptomatic (elevated serum creatine kinase and/or calf hypertrophy); grade II = mild (patients reported fatigue, and/or myalgia and cramps, and/or frequent falling, or patients showing abnormal gait, toe walking, slow running, all in the absence of a positive Gower’s sign); grade III = moderate (patients reporting any of the previous symptoms and signs, with a positive Gower’s sign); grade IV = severe (inability to rise without assistance and/or less than three-fifths strength in proximal muscle groups and/or severe muscle wasting); and grade V = wheelchair bound.

Children and parents were interviewed at the beginning of the study according to a standard questionnaire to define the presence and the severity of dyspeptic symptoms experienced during the 2 wk prior to the study (14). The evaluated symptoms were: abdominal (epigastric and mesogastric) pain, early satiety or anorexia, feeling of abdominal fullness (or bloating), regurgitation (or vomiting or heartburn). Symptoms were scored as follows: 0 = absent; 2 = occasionally (1–3 days per week), slight; 4 = occasionally (1–3 days per week), moderately severe, 6 = often (>3 days per week), markedly severe. Anorexia or early satiety were scored on the basis of the percentage of daily caloric intake during the week before starting the study as related to the ideal caloric intake (0 = 75–100%; 2 = 50–75%; 4 =  $\geq$ 25–50%; 6 = <25%). A global dyspeptic symptom score was calculated as the sum of the four individual symptom scores, with a maximum value of 24.

**Table 1.** Test Meals Administered for Different Age Group\*

| Age (year) | Bread (g) | Raw Ham (g) | Butter (g) | Fruit Juice (ml) |
|------------|-----------|-------------|------------|------------------|
| 3–6        | 60        | 35          | 5          | 180              |
| >6–9       | 80        | 40          | 7.5        | 210              |
| >9–12      | 100       | 45          | 10         | 240              |
| >12        | 120       | 50          | 12.5       | 270              |

\*Caloric content: bread 290 kcal/100 g; Parma ham 268 kcal/100 g, butter 758 kcal/100 g; fruit juice 56 kcal/100 ml.

Gastric motility was recorded after an overnight fast by simultaneous measurements of GET and gastric electrical activity (GEA). Subjects received a mixed solid-liquid meal based on the caloric intake at breakfast for children of different age groups (Table 1). The GET was measured by ultrasonography of the gastric antrum using a real-time apparatus with a 5-MHz linear array transducer applied with minimal compression. Scanning was performed by the same operator in the fasting state and every 30 min for the first postprandial hour and at 15-min intervals afterwards, while the patients sat at a 30° angle to the horizontal plane of the examination couch (14). The cross-section of the gastric antrum was measured at the level of a sagittal plane passing through the superior mesenteric vein taken as a point of reference. At this level, the cross-section of the gastric antrum has an elliptic shape and its area was calculated using the following formula:  $\pi \times A \times B / 4$  (cc; A, longitudinal diameter; B, anteroposterior diameter). The stomach was considered empty when the antral area returned to the baseline value without food particles in its lumen and persisted unchanged for at least 30 min (15).

Recording of GEA was performed by EGG, *i.e.*, by placing two Ag-AgCl bipolar surface electrodes (Commed Andover Med, Haverill, MA) on the epigastric skin, after reducing cutaneous impedance by a skin preparation paste (OmniPrep, D.O. Weaver, Aurora, CO). One active electrode was located on the ventral midline between the xiphoid process and umbilicus, after sonographic localization of the antrum; the second active electrode was located on the left of first active electrode, 30° cephalad, just below the costochondral margin, in the midclavicular line. A reference electrode was placed in the left iliac fossa. The EGG was recorded for 1 h during fasting and 1 h after the test meal. The electrodes were connected to a 96 KB portable battery operated recorder (Synectics-Medtronic Medical, Milan, Italy). All recordings were done at the sampling frequency of 4 Hz; high and low cutoff frequencies were set at 0.01 and 0.5 Hz, respectively. The signals were digitized and processed by means of an appropriate software program (Synectics-Medtronic Medical, Milan, Italy). The EGG signals were subjected to running spectral analysis. In this technique, spectra were obtained as follows: every 64 s a power spectrum was computed from the preceding 256 s of the EGG time signal to which a Hamming window has been applied to reduce the leakage (16); this procedure generates a series of overlapping spectra graphed as running spectra and makes both frequency and time analysis possible (17).

A rhythmic activity of 2.0–4.0 cpm is defined as normal frequency range. The parameters measured were (i) percentage of time with normal gastric electrical rhythm; (ii) percentage of time with dysrhythmic episodes (lasting at least 2 min) and absence of normal electrical rhythm. Dysrhythmias include bradygastria when the spectrum has a dominant peak in the 0.5–2.0 cpm range; tachygastria, when the dominant peak is in the 4.0–9.0 cpm range; (iii) fed-to-fasting power ratio of the dominant EGG frequency (power was calculated on a linear scale); and (iv) percentage of the dominant frequency instability coefficient (DFIC), this is a measure of the dominant frequency change over the EGG recording period. The raw EGG signal was visually inspected to verify that no artifacts were present in any recording period. Periods containing these motion artifacts were deleted before computer analysis. The portions of EGG signals recorded during the ultrasound scanning periods were excluded from analysis. Measurement of GET and GEA as well as clinical assessment was repeated after 3 yr by the same baseline investigator group.

Seventy healthy children without gastrointestinal symptoms (median age: 5.6 yr; range: 3–14) were recruited during the study and served as controls. For all of them, parents

completed a detailed questionnaire to assess demographic data and clinical history. To be included as controls, subjects had to show (i) absence of gastrointestinal symptoms, (ii) no history of prior gastrointestinal surgery or drug administration during the previous 6 months, and (iii) no history of peptic ulcer disease, food allergy, and functional bowel disorder. Controls underwent measurement of GET and GEA and received the same test meal given to the patients.

Results analyzed using the Mann-Whitney U-test were used to compare independent samples and the Wilcoxon signed rank test for relative samples. A *p*-value < 0.05 was required for significance. Different parameters were correlated with the Spearman's rank correlation coefficient. Data were expressed as median value and ranges and as mean  $\pm$  SD.

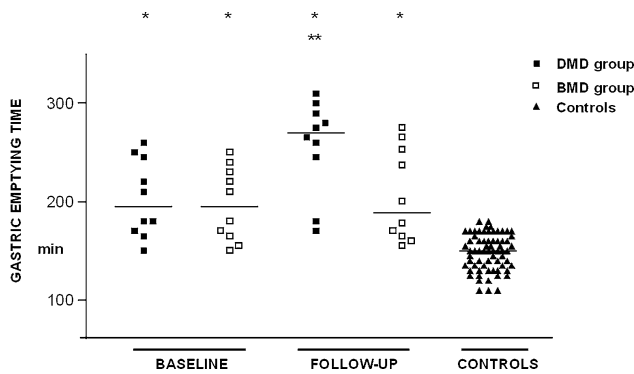
## RESULTS

Table 2 summarizes demographic and clinical data of the patients investigated: 10 patients had DMD (median age: 4.2 yr; range: 3–6 yr) and 10 BMD (median age: 5.0 yr; range: 4–7 yr). At the first presentation, the neuromuscular status in the

**Table 2.** Demographic and Clinical Data

| Patient No. | Age at           |                     | Disease in Family | Presenting Features   | Gastrointestinal Symptoms                |  |
|-------------|------------------|---------------------|-------------------|---|--|--|
|             | Diagnosis (year) | Dystrophin Analysis |                   |   | Baseline                                 | Follow-up  |
| 1           | 3                | Absent              | No                | Frequent falling, slow running, GS neg                        | Asymptomatic                             | Asymptomatic                                     |
| 2           | 3.7              | Absent              | Yes               | Difficult climbing stairs, GS neg                             | Asymptomatic                             | Asymptomatic                                     |
| 3           | 3.7              | Absent              | Yes               | Frequent falling, poor running, GS pos                        | Asymptomatic                             | Asymptomatic                                     |
| 4           | 4.1              | Absent              | Yes               | Frequent falling, GS neg                                      | Asymptomatic                             | Anorexia, vomiting, fullness                     |
| 5           | 4.5              | Absent              | Yes               | Toe walking, frequent falling, GS pos                         | Asymptomatic                             | Anorexia, vomiting, fullness                     |
| 6           | 4.8              | Absent              | No                | Difficult climbing stairs, slow running, toe walking, GS pos  | Abdominal pain, fullness                 | Regurgitation, vomiting, early satiety, anorexia |
| 7           | 4.8              | Absent              | No                | Slow running, frequent falling, GS pos                        | Fullness, early satiety                  | Vomiting, fullness, mesogastric pain, anorexia   |
| 8           | 6.3              | Absent              | No                | Fatigue and myalgia, poor running, difficult climbing, GS pos | Abdominal pain, fullness, anorexia       | Fullness, vomiting, anorexia, mesogastric pain   |
| 9           | 4.1              | Absent              | No                | Difficult climbing, frequent falling, GS pos                  | Regurgitation, epigastric pain, anorexia | Regurgitation, epigastric pain, anorexia         |
| 10          | 3.3              | Absent              | Yes               | Frequent falling, slow running, GS neg                        | Asymptomatic                             | Asymptomatic                                     |
| 11          | 4.3              | Abnormal            | No                | HyperCKemia   | Abdominal pain                           | Abdominal pain                                   |
| 12          | 4                | Reduced             | Yes               | HyperCKemia   | Asymptomatic                             | Asymptomatic                                     |
| 13          | 5.5              | Abnormal            | No                | Difficult climbing, GS neg                                    | Fullness, anorexia                       | Vomiting, anorexia                               |
| 14          | 4.1              | Reduced             | Yes               | HyperCKemia   | Asymptomatic                             | Asymptomatic                                     |
| 15          | 4.8              | Reduced             | No                | HyperCKemia   | Asymptomatic                             | Asymptomatic                                     |
| 16          | 6.7              | Abnormal            | Yes               | Frequent falling, poor running, GS pos                        | Fullness, early satiety                  | Fullness, anorexia, vomiting                     |
| 17          | 4.1              | Reduced             | Yes               | HyperCKemia   | Asymptomatic                             | Asymptomatic                                     |
| 18          | 5.2              | Reduced             | No                | HyperCKemia   | Asymptomatic                             | Asymptomatic                                     |
| 19          | 7                | Abnormal            | No                | HyperCKemia   | Asymptomatic                             | Asymptomatic                                     |
| 20          | 3.7              | Reduced             | Yes               | HyperCKemia   | Asymptomatic                             | Asymptomatic                                     |

GS: Gower's sign, CK: creatine phosphokinase.



**Figure 1.** GET in patients with DMD and BMD and in controls. \**p* < 0.001 versus controls, \*\**p* < 0.001 versus baseline. Horizontal bars indicate median value.

DMD patients ranged between grade II (4 patients) and grade III (6 patients). Eight BMD patients were asymptomatic: they had been referred to the Neurophysiology Department because of elevated serum creatine kinase levels, detected during routine clinical tests, or as relatives of patients with BMD; of the two remaining BMD patients, one was classified as grade II, and one as grade III. After 3 yr, most DMD patients exhibited a marked impairment in the neuromuscular functional capacity: two were classified as grade II, six as grade IV, and two were at wheelchair bound stage. In contrast, in the BMD group seven patients remained unchanged, one was classified as grade II, one as grade III, and one as grade IV.

Dyspeptic symptom score did not statistically differ in the two groups at baseline (DMD: 5.2 ± 4.23; BMD: 4.8 ± 4.7; ns); however, at the follow-up it significantly worsened only in the DMD group (11.6 ± 3.62; *p* < 0.01 vs baseline; BMD group 5.4 ± 4.11; ns vs baseline), and DMD patients had a significantly higher symptomatic score than BMD patients (*p* < 0.01).

GET ranged from 110 to 180 min (median value: 150 min) in controls, whereas it did not differ at baseline between the two groups (DMD: 195 min, range: 150–260; BMD: 197 min, range: 150–250; ns); however, it was significantly more prolonged in patients than in controls (*p* < 0.05). At the follow-up, GET significantly worsened in the DMD group (270 min, range: 170–310; *p* < 0.05 vs baseline), but it did not statistically change in the BMD group (205 min, range: 155–275; ns vs baseline) (Fig. 1).

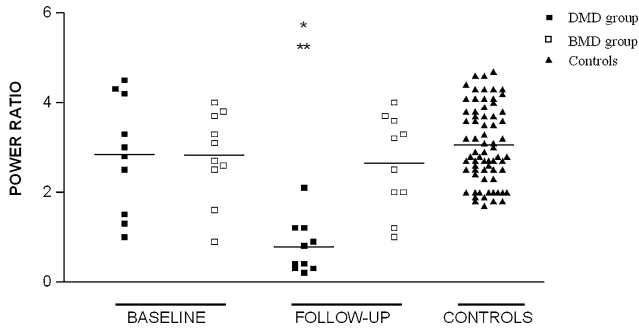
Results of baseline and follow-up EGG recordings are reported in Table 3. Baseline gastric electrical variables did not differ between the two patient groups, but a significantly higher prevalence of gastric electrical dysrhythmias and a lower prevalence of normal electrical rhythm were detected in both groups of patients as compared to controls. Both groups of patients also exhibited a significantly higher percentage of DFIC than controls, whereas no statistical difference in fed-to-fasting power ratio was found between the two groups and the controls (Fig. 2). Figures 3 and 4 show examples of electrogastrographic running spectral analysis from a control child and from a DMD patient at baseline. At the follow-up, no significant change in the percentage of normal rhythm, tachygastria, and DFIC occurred in both groups; there was, however, only the DMD group exhibited a significant decrease in fed-to-fasting power ratio; the latter at the follow-up was significantly lower in the DMD group than in the BMD group (Fig. 2). Figure 5 shows an example of EGG running spectral analysis from a DMD patient at the follow-up.

Throughout the study, there was a significant inverse correlation between fed-to-fasting power ratio and GET both in patients and controls (*r* = −0.83; *p* < 0.001) (Fig. 6). In all patients, we found a significant inverse correlation between neuromuscular weakness and fed-to-fasting power ratio (*r*, −0.75; *p* < 0.001) (Fig. 7) as well as a significant correlation between neuromuscular weakness and GET (*r* = 0.76; *p* < 0.001) (Fig. 8).

**Table 3.** Neuromuscular Grade, Clinical Score, Electrogastrographic Variables, and GET at Baseline and after 3 Yr in Children with DMD and BMD as Compared to the Controls

| Variables                       | DMD            |                    | BMD            |                | Control Group  |
|---------------------------------|----------------|--------------------|----------------|----------------|----------------|
|                                 | Baseline       | Follow-up          | Baseline       | Follow-up      |                |
| Neuromuscular grade (mean ± SD) | 2.6 ± 0.51*    | 3.8 ± 1.03*,†      | 1.3 ± 0.67     | 1.6 ± 1.07     | –              |
| Clinical score (mean ± SD)      | 5.2 ± 4.23     | 11.6 ± 3.62*,†     | 4.8 ± 4.7      | 5.4 ± 4.11     | –              |
| EGG Variables (mean ± SD)       |                |                    |                |                |                |
| % 3 cpm                         | 66.7 ± 8.2‡    | 63.1 ± 7.2‡        | 67.2 ± 11.5‡   | 67.2 ± 13.7‡   | 85.3 ± 7.2     |
| % tachygastria                  | 28.4 ± 8.0‡    | 34.03 ± 6.9‡       | 29.82 ± 12.3‡  | 30.6 ± 12.3‡   | 10.6 ± 5.1     |
| % bradygastria                  | 4.9 ± 4.8      | 2.6 ± 1.8          | 2.8 ± 2.8      | 2.3 ± 3.3      | 4.2 ± 2.9      |
| % DFIC                          | 36.1 ± 6.0‡    | 36.0 ± 8.3‡        | 33.2 ± 2.9‡    | 29.5 ± 12.3‡   | 17.9 ± 7.1     |
| Fed-to-fasting power ratio      | 2.84 ± 1.27    | 0.78 ± 0.6†,‡,§    | 2.82 ± 0.98    | 2.65 ± 1.06    | 3.04 ± 0.85    |
| GET (minutes; median and range) | 195¶ (150–260) | 270¶, ** (170–310) | 197¶ (150–250) | 205¶ (155–275) | 150¶ (110–180) |

\**p* < 0.01 versus BMD group.  
 †*p* < 0.01 versus baseline.  
 ‡*p* < 0.001 versus controls.  
 §*p* < 0.001 versus BMD group.  
 ¶*p* < 0.05 versus controls.  
 \*\**p* < 0.05 versus BMD group.



**Figure 2.** Fed-to-fasting ratio of the EGG dominant power (PR) in patients with DMD and BMD and in controls. \* $p < 0.001$  versus controls. \*\* $p < 0.001$  versus baseline. Horizontal bars indicate mean value.

**DISCUSSION**

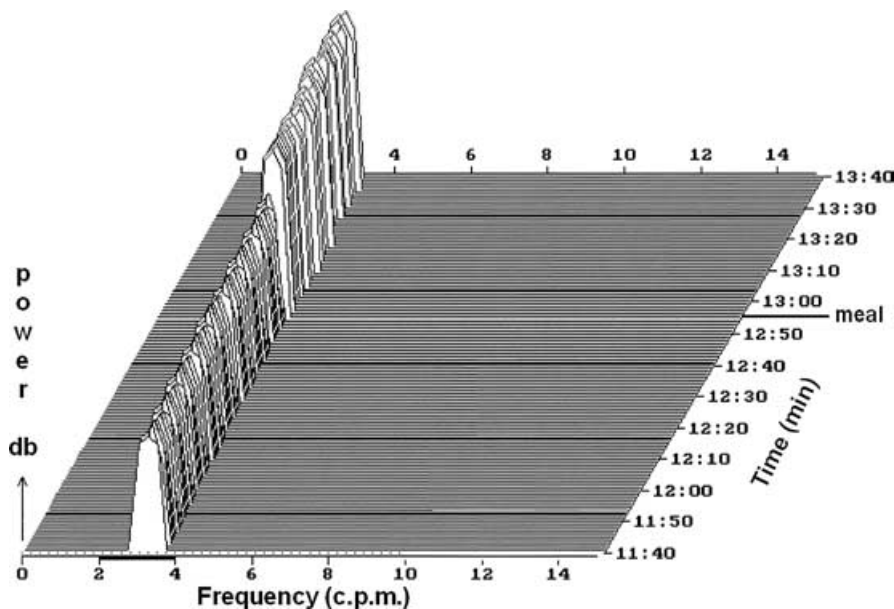
The study shows that children with MD exhibit gastric motor abnormalities at the initial phases of the disease. The study also shows that in DMD patients a worsening of gastric motor activity parallels a progressive derangement of neuromuscular function during the course of the disease.

Abnormalities of upper gastrointestinal motility and dyspeptic symptoms have previously been reported in DMD adult patients; however, they are rarely described in children with dystrophinopathies (7–10, 18). This is likely due to the invasiveness of methods recording intestinal motility, most of which require nasogastric intubation and the use of radiolabeled meals. In our study, gastric motility was assessed through noninvasive tools, such as real time ultrasonogra-

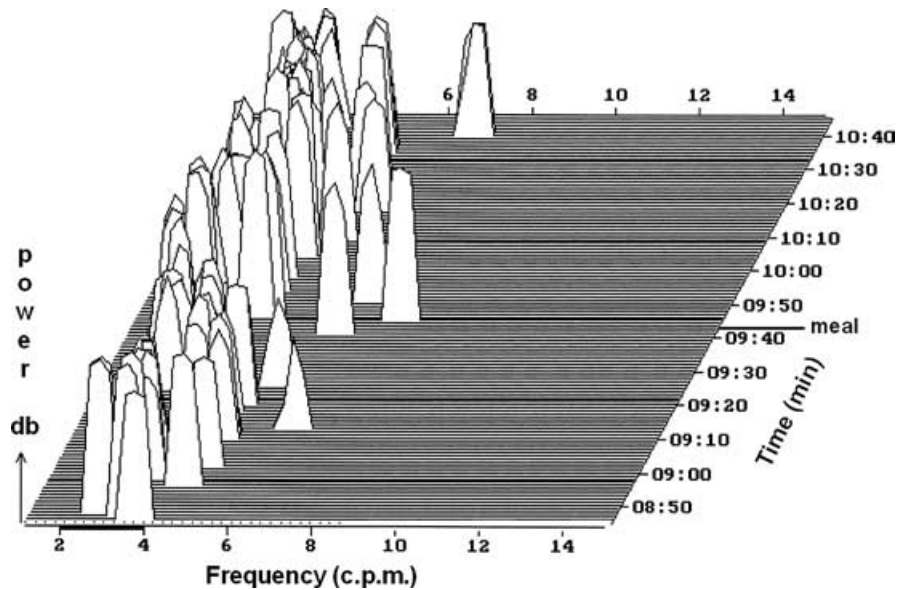
phy, which measures GET, and EGG, which records electrical activity of gastric smooth muscle cells through cutaneous electrodes placed on the epigastric skin. These methods have previously been validated by numerous studies in adult and pediatric patients with gastrointestinal motor abnormalities (19–26).

At baseline, the two groups of patients differed from controls for a delay in gastric emptying and for a higher prevalence of gastric dysrhythmias. The latter mainly consisted of periods of tachygastria with absence of normal 3-cpm activity and increased instability coefficient at the dominant EGG frequency, whereas a normal postprandial rise in the power ratio at the dominant frequency was observed. The increase in the power of the electrical signal after eating is a normal EGG feature and thought to be the electrical counterpart of a normal gastric motor response to the meal (27–29). Dysrhythmic episodes such as those detected in our patients at the initial assessment have previously been described in subjects with gastrointestinal motility disorders of neuropathic type (30, 31). Thus, gastric motility in the early phase of MD is characterized by a derangement in its regulatory mechanisms, whereas contractile activity of smooth muscle cells seems to be preserved.

Our results are supported by experimental observations showing that dystrophin can be identified in tissues other than striated muscles such as smooth muscle cells, enteric neurons, and interstitial cells of Cajal (32, 33). The latter are commonly viewed as specialized nonmyogenic nonneurogenic cells having a role both in triggering myogenic electrical activity (“pacemaker”) and in modulating inputs from enteric neurons to smooth muscle cells (34). Interestingly,



**Figure 3.** Example of a running spectral analysis from a control child. A regular 3-cpm activity is seen before and after the test meal. A clear increase in EGG dominant power is visible after meal ingestion. The x-axis indicates the frequency of the signal (cycles/min). The y-axis shows the time where the running spectral analysis represents consecutive segments of the EGG.

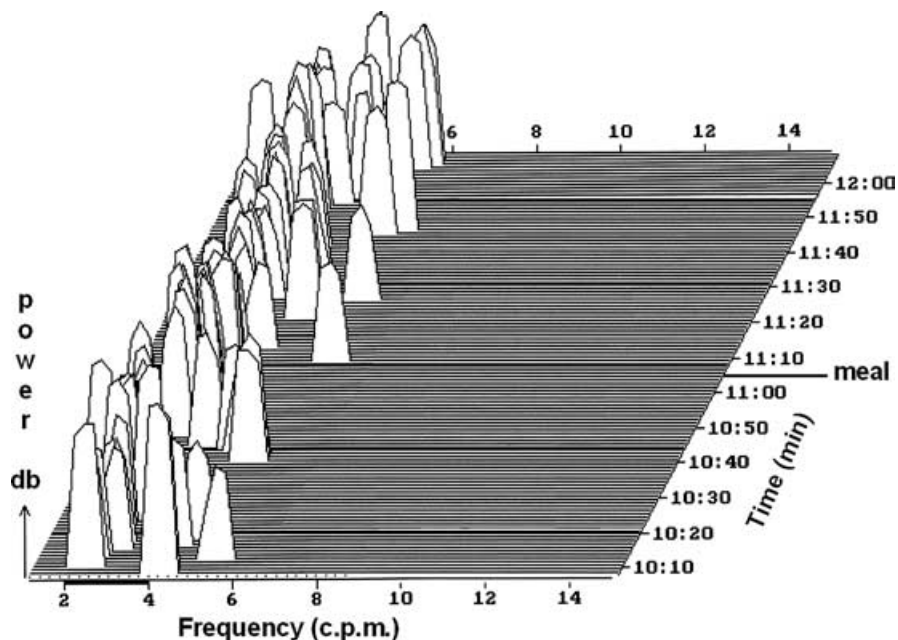


**Figure 4.** Example of running spectral analysis from a child with DMD at baseline. Clear episodes of tachygastric with a rate  $>4$  cpm are shown preprandially and postprandially. A normal increase in EGG dominant power is visible after the test meal. Analysis as in Figure 3.

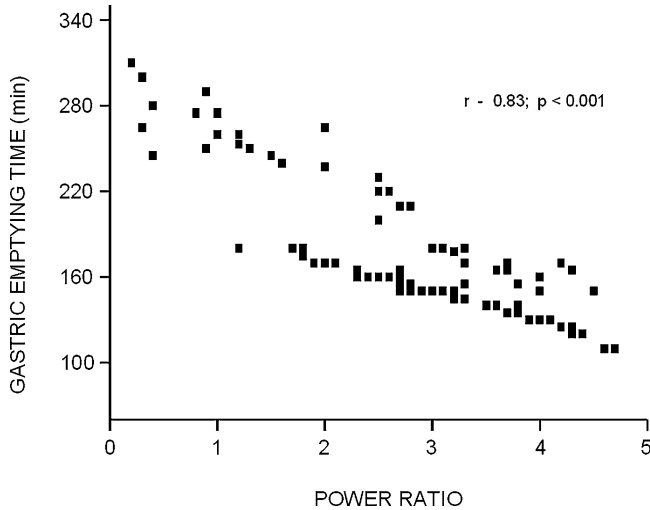
Vannucchi *et al.* have recently shown that in animal models of dystrophinopathies, such as the dystrophin-deficient mice (mdx), gastric electrical dysrhythmias occur and ultrastructural and electrophysiological alterations in interstitial cells of Cajal can be found (35).

At the follow-up EGG monitoring, the two patient groups did not differ for prevalence of episodes of dysrhythmias; however, DMD patients did not exhibit an increase in the postprandial power ratio as compared to BMD subjects. Fur-

thermore, measurement of GET showed a significant worsening only in the DMD patients. It is widely agreed that a failed increase of the EGG power in the postprandial state is an abnormal feature that usually reflects an antral mechanical hypomotility after meal (27–29). Interestingly, we documented in our patients a significant inverse correlation between the delay in gastric emptying and the degree of change in the fed-to-fasting EGG power ratio. Previous reports have highlighted the relationship between gastric emptying and

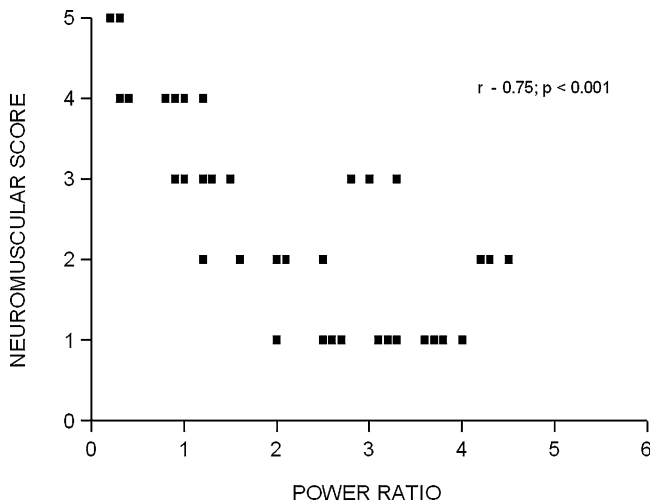


**Figure 5.** Example of running spectral analysis from a child with DMD after a 3-yr follow-up. Episodes of tachygastric are seen as in Figure 4. After the test meal, there was no apparent change in EGG dominant power. Analysis as in Figure 3.

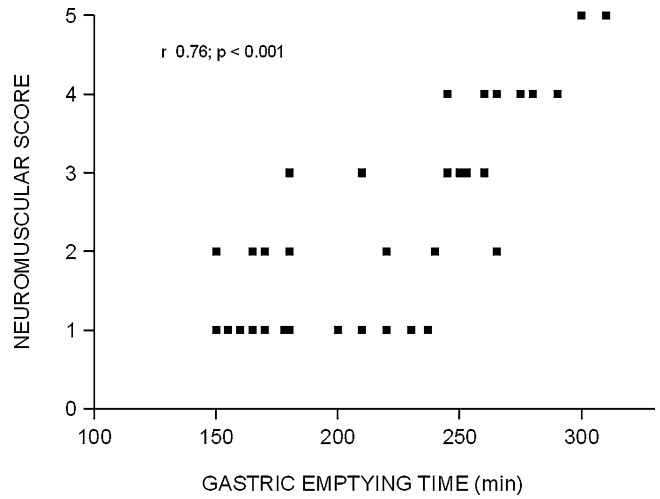


**Figure 6.** Significant inverse correlation between fed-to-fasting ratio of the EGG dominant power and GET in control subjects and in both groups of patients with dystrophinopathies.

changes in postprandial EGG power. A defective or absent increase in fed-to-fasting power ratio has been shown to significantly correlate with a delay in gastric emptying in children with severe gastroesophageal reflux disease (22) as well as in children with insulin-dependent diabetes and poor metabolic control (14). This has also been recognized in children with functional dyspepsia and no organic or inflammatory disease (36). A close relationship between a lack of postprandial rise in EGG power and delayed gastric emptying has also been proved in adults with unexplained nausea and vomiting (37, 38). It has been suggested that this EGG feature may highly predict an abnormal gastric emptying in subjects with upper gastrointestinal complaints, particularly if EGG and GET are measured concomitantly (38–40). Thus, both mechanical and EGG features detected in DMD patients at the



**Figure 7.** Significant inverse correlation between fed-to-fasting ratio of the EGG dominant power and neuromuscular score in both groups of patients with dystrophinopathies.



**Figure 8.** Significant correlation between GET and neuromuscular score in both groups of patients with dystrophinopathies.

follow-up recording were consistent with a deranged function of smooth muscle cells of the stomach. It is of interest that pathological changes in intestinal smooth muscle cells similar to those observed in skeletal muscle have been reported in autopsic studies in patients with DMD (9, 10). Thus, it is conceivable that progressive degenerative changes in skeletal muscle as well as in intestinal smooth muscle cells, usually observed in DMD but not in BMD patients, may underlie a worsening in neuromuscular function and in gastric motility, respectively. This view is supported by the significant correlation between neuromuscular weakness and gastric emptying delay found in our patients; it is also remarkable that a significant inverse correlation between neuromuscular weakness and the EGG fed-to-fasting power ratio was documented in our patients.

In conclusion, our study indicates that in children with dystrophinopathies the gastrointestinal tract is an early target of the disease expression. In DMD, progressive neuromuscular worsening is accompanied by a gastric motor activity derangement that is characterized by EGG features suggesting an altered function of gastric smooth muscle cells. Noninvasive tools such as EGG and gastric ultrasonography may provide useful methods for detecting abnormalities in gastric motor activity and revealing the underlying pathophysiology. Early detection of abnormal gastric motility in MD children is of clinical significance since foregut motor abnormalities predispose both to gastroesophageal reflux that carries a high risk of pulmonary aspiration and to gastric emptying delay. The latter in turn promotes reflux and causes malnutrition because of delayed delivery of nutrients into the small bowel.

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