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Original Article

External Anal Sphincter Fatigability: An Electromyographic and Manometric Study in Patients With Anorectal Disorders

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Background/Aims

External anal sphincter (EAS) plays an important role in fecal and gas voluntary continence. Like every muscle, it can be affected by repeated efforts due to fatigability (physiological response) and/or fatigue (pathological response). No standardized fatiguing protocol and measure method to assess EAS fatigability has existed. The aim is to test a simple, standardized protocol for fatiguing and measuring EAS fatigability and fatigue to understand better the part of EAS fatigability in the pathophysiology of fecal incontinence.

Methods

Patients with anorectal disorders evaluated with anorectal manometry were included. They had to perform 10 repetitions of maximum voluntary contraction (MVC) of 20 seconds. Measurement was made with an anorectal manometry catheter and a surface recording electromyography (EMG). The primary outcome was the difference in EMG root mean square between the first and the last MVC. Secondary outcomes were differences in other EMG and manometry parameters between the first and the last MVC. Difficulties and adverse effects were recorded.

Results

Nineteen patients underwent the fatiguing protocol. All patients completed the entire protocol and no complications were found. No difficulty was declared by the examiner. A significant decrease in root mean square was found between the first and last MVC (0.01020 ± 0.00834 mV vs 0.00661 ± 0.00587 mV; $P = 0.002$), in maximum anal pressure area under the curve of continuous recordings of anal pressure and mean and total EMG power ($P < 0.05$).

Conclusions

This protocol is simple and minimally invasive to measure EAS fatigue and fatigability. We highlighted a fatigue of EAS in many patients with anorectal disorders.

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Key Words

Anal sphincter; Electromyography; Fecal incontinence; Manometry; Muscle fatigue

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Introduction

The anal canal is the final part of the digestive tube. Its muscular part is composed of anal sphincter which can be divided into the internal anal sphincter and external anal sphincter (EAS). Its role is to ensure fecal continence during rectal contraction and/or increase in intra-abdominal pressures during efforts. The internal sphincter is made of smooth muscle under involuntary autonomic control whereas the EAS consists of skeletal muscle whose contraction can be voluntarily elicited. Histologically, type I fibers are mainly present in the EAS[1] and then type IIa fibers. Type I fibers are muscle fibers characterized by an oxidative metabolism so that they can contract slowly but can maintain the contraction for a long time.[2]

In patients with nervous system diseases, constipation and incontinence are frequent. Constipation generally results from a prolonged transit time and can be exacerbated by treatments (such as analgesics or anticholinergics), lack of mobility, and diet. Additionally, anorectal dyssynergia can increase defecation difficulties. Incontinence can result from different mechanisms. In patients with supraconal lesions, strong rectal contractions and pronounced rectoanal inhibitor reflex could increase the risk of fecal incontinence. On the contrary, patients with conal lesions have an interruption in the reflex arch between the spinal cord and the EAS, leading to a flaccid rectal wall. Moreover, the lack of voluntary control of the EAS may increase the risk of incontinence in both cases. Finally, in patients with cauda equina lesions or polyneuropathy, the lack of sensibility and the altered control of voluntary contraction of the EAS participate in the mechanism of incontinence.[3]

In order to understand the cause of these anorectal disorders, several technologies have been developed. Some reviews have recently listed the different explorations which can be used for the evaluation of anorectal disorders.[4,5] First of all, anorectal manometry (standard, 3 dimension high-resolution or associated with electromyography [EMG]) is a direct measure of pressures in rectum, internal anal sphincter, and EAS during diverse tests and so helps to find abnormality in anorectal synergy. High-resolution manometry is a recent tool that shows dynamic measures of the anal canal during different efforts. It is now only used for exploration of anorectal disorders as no standardized techniques exist.[6,7] Defecography (with X-ray or MRI) is a tool showing anatomic modifications during defecation. It permits to see particularly recto-anal asynchronism. Nevertheless, it does not give any information concerning muscle strength quantification. EMG is also used to explore anorectal disorders. Needle EMG is particularly used to find muscle denervations whereas surface EMG gives a global reflection of muscle activity. Finally, motor and sensory evoked potentials are techniques exploring nervous conduction ways but not muscle activity. It is a second line exploration to understand anorectal disorders in people for whom the rest of the examination is normal.

Fatigability and fatigue are 2 different concepts: fatigability is physiological due to a normal decrease of muscular contraction following maintained or repeated efforts; fatigue is pathological with lack of resistance, endurance, and contraction capacities of muscle in various conditions. Thus, fatigue is commonly reported as a decrease in muscular response to a stimulus. Its causes are numerous but they are classified as central and peripheral. Central fatigue is the consequence of all that can affect the nervous message from cerebral cortex to the spinal junction between the first and second motoneurons.[8] Peripheral fatigue is due to muscle or second motoneuron lesions.[9] On the other hand, fatigability is the normal physiological muscle response to a fatigue exercise.[10]

In skeletal muscle study, many protocols have been developed to evaluate and quantify fatigability. The majority of the studies have been conducted using repetitive maximal or submaximal voluntary contractions. Moreover, imposed contractions can be made during exercise with the help of peripheral nerve stimulation or with transcranial magnetic stimulation.[11] For measuring this fatigability, there are also many tools. Indirectly, fatigue and fatigability can be evaluated by means of dynamometers which measure the global muscular strength at rest and following efforts. Fatigue can also be directly quantified by global and kinetic surface EMG[12] especially by means of mathematical treatment of the EMG signal (area under the curve [AUC], spectral analysis, mean power frequency, and root mean square [RMS]).

Anal sphincter has already been studied. Parks et al[13] measured the first electrical activity of EAS in 1962 with EMG and demonstrated that its contraction lasted approximately 1 minute. Many manometric studies have been done but no uniformed protocol or measure method has been standardized.[14,15] Fatigue rate index (FRI) has been developed by Marcello et al[14] It is derived from the fatigue rate (FR) calculated on manometry for a sustained contraction. FRI (minutes) = (squeeze pressure–resting pressure [mmHg])/(−FR [mmHg/minute]). This is at this day, the most used tool to study EAS fatigability.[16-18]

The primary aim of this study is to test a simple, routine reproducible protocol to evaluate and quantify EAS fatigue and fatigability. The secondary aim is to study the correlation between the level of fatigability and the symptoms reported by the patients.

Materials and Methods

Study Design

This prospective study was approved by the local ethics review board, registration number 2018-A01644-51, and all participants provided written informed consent before their inclusion in this observational study. This study was registered on clinicaltrials.gov: NCT04067453. Participants were recruited in a Neuro-urology department. They underwent anorectal manometry in order to investigate bowel disorders such as constipation, recto-anal dyssynergia, and fecal incontinence.

Participants

The inclusion criteria were: age over 18, anorectal disorders (constipation and/or fecal incontinence), presence of an EAS selective command at the digital rectal examination. The exclusion criteria were: impossibility to understand simple orders in order to contract and maintain EAS contraction. Participants were recruited between August 1st and October 31st, 2019.

Before manometric and EMG evaluation, patients were asked to answer questions about their symptoms and their medical or surgical history. Questionnaires were filled by patients and results were collected: Bristol scale, Cleveland score, neurogenic bowel dysfunction (NBD), Urinary Symptoms Profile, Fatigue Impact Scale, and Anticholinergic Drug Scale. The other data collected were: age, gender, weight, body mass index, and treatment at the moment of the examination.

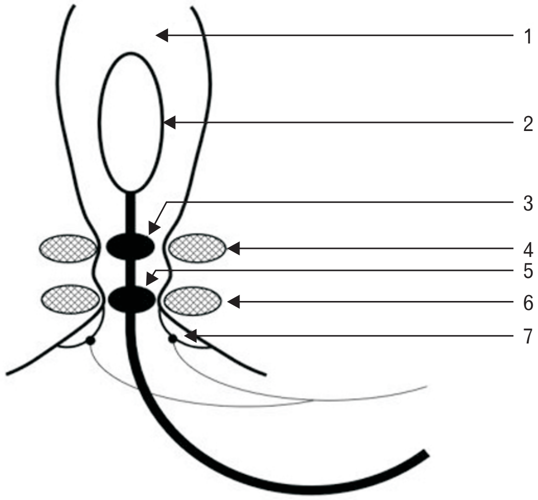

Figure 1. Scheme of installation procedure. 1, rectum ampulla; 2, intrarectal distending balloon; 3, pressure sensor regarding the internal anal sphincter; 4, internal anal sphincter; 5, pressure sensor regarding the external anal sphincter; 6, external anal sphincter; 7, surface electromyography electrode.

Procedure

During the protocol, patients were placed on their left lateral side. The day before the examination, they had a rectal enema in order to empty the rectum. Empty rectum was verified at the beginning of the protocol with a digital rectal examination. All manometries (Latitude equipment, Laborie Medical Technologies, Williston, VT, USA) were realized by the same doctor, in a specific place, with calm. The procedure was explained, any questions responded, and written consent to perform manometry and participate in the study was obtained. A flexible anorectal catheter with 3 air-charged microballoons (T-doc, pressure sensors; Laborie Medical Technologies) was used. The catheter was connected to a PC polygraph system (Solar GI Manometry; Laborie Medical Technologies) used to calculate time and pressure parameters. It was a disposable closed system, with no perfusion at all. The catheter was inserted within the rectum through the anus. A non-anaesthetizing lubricant was used to avoid any pain and/or local injury. The most external balloon was positioned in the distal part of the anal canal. The other pressure sensor was in the upper part of the anal canal and the distending balloon in the rectal ampulla (Fig. 1).

Surface EMG electrodes (Kendall H135SG; CardinalHealth, Dublin, OH, USA) were disposed on the anal margin (Fig. 1). The electromyographic signal obtained during the protocol was recorded on Biopac 2 system software (Biopac Systems Inc, Goleta, CA, USA) and treated on the Acknowledge software (Biopac Systems Inc). The good positioning of the contact electrodes was controlled on the investigator screen by asking the patient to perform a

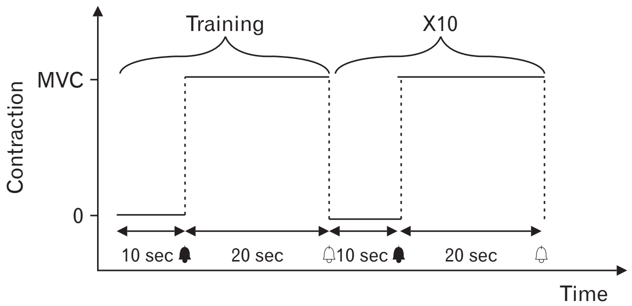

Figure 2. Scheme of the fatiguing protocol and instructions given to the patients. Black bells show the sound signal given to the patient to begin the maximal voluntary contraction (MVC). White bells show the sound signal given to the patient to end the MVC.

voluntary anal contraction.

The fatiguing protocol consisted of 10 maximal voluntary contractions (MVC) of 20 seconds (one third of the maximum time possible previously demonstrated[13] with 10 seconds of resting between the MVCs. Before the protocol, the patients had a training MVC. A sound signal was made at the beginning and the end of each MVC (Fig. 2).

For each MVC, manometric and electromyographic signals were recorded. The manometric signal obtained on the EAS was recorded and processed on the Manufacturing Management System software (MMS USA Inc, Dover, NH, USA). For each MVC, the peak of contraction, the FR, the FRI and the AUC were analyzed. In order to calculate the FRI, the mean slope during the contraction was directly calculated by the polygraph, and the resting value was calculated as the mean value during the resting period before the MVC. Movement artifacts were removed from the EMG recordings by applying a high pass filter of 5 Hz (second-order bidirectional Butterworth). A notch filter (50 Hz and its harmonics 100 Hz, 200 Hz, second-order bidirectional Butterworth,) was applied to remove power line noise. The amplitude variability of EMG was estimated by the RMS, which reflects the averaged intensity during muscle contraction. The mean frequency, the total power, and the mean power were also determined using Fast Fourier Transformation for each MVC.

Table 1. Population Characteristics

Characteristics	n = 19
Gender	
Women	12 (63)
Men	7 (37)
Age (yr)	55 (33-80)
Body mass index (kg/m²)	26.21 (19.90-45.00)
Abdominal surgery history	10 (53)
Gynecologic surgery or obstetric history	10 (53)
Pelvic-Floorrehabilitation history	7 (37)
Anorectal dyschesia	14 (74)
Anal incontinence	
Gas	3 (15)
Liquids	2 (11)
Feces	5 (26)
Bristol	3 (1-6)
NBD (/47)	7.4 (0.0-19.0)
Cleveland score (/15)	4.9 (0.0-13.0)
Fatigue impact Scale (/160)	76.8 (2.0-139.0)
Urinary symptom profile	
Incontinence (/9)	1.4 (0.0-9.0)
Overactivity (/21)	6.3 (0.0-13.0)
Low stream (/9)	2.6 (0.0-9.0)
Anticholinergic drug scale	1.2 (0.0-7.0)

NBD, neurogenic bowel dysfunction.
Data are presented as n (%) or median (range).

The primary outcome to measure fatigue and fatigability was the difference in electromyographic RMS between the first and the last MVC. Secondary outcomes were the differences in electromyographic and manometric data between the MVC. Secondary analyses related to patients' characteristics were performed. To assess the feasibility of the protocol, difficulties of recording, difficulties of realization and pain were listed.

Statistical Methods

Statistical analyses were performed with the R software for Windows (Rx64 3.6.1; R Foundation for Statistical Computing, Vienna, Austria). Descriptive data are presented as means with standard deviation for continuous data and as medians with range for ordinal data and data not normally distributed. A Wilcoxon paired test was performed for the comparison between quantitative data. Paired ANOVA tests and Spearman correlations were used for subgroup analysis.

Results

Patients Characteristics

Nineteen patients were included, 5 had fecal incontinence and 14 had anorectal dyssynergia. Their characteristics are summarized in Table 1. The etiology of fecal and urinary disorders was known for almost all patients: 4 multiple sclerosis, 2 Parkinson disease, 2

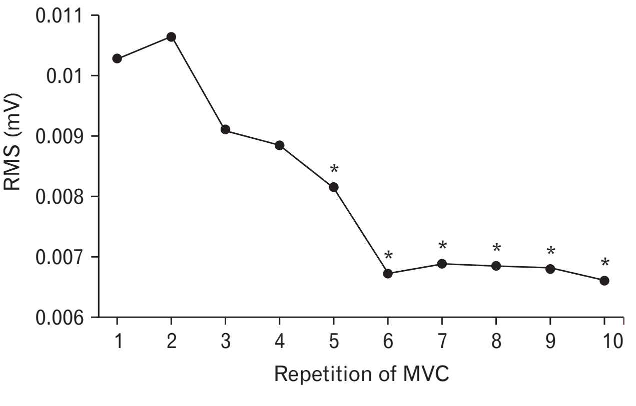

Figure 3. Evaluation of root mean square (RMS) at each RMS of maximum voluntary contraction (MVC). *Significative difference between the current and the first MVC.

neurologic central disease still unknown at the moment of the examination, 2 post-pelvic surgery urinary and anorectal disorders, 1 perineal pain, 1 glioblastoma, 1 amyloid neuropathy, 1 sarcoidosis, 1 scleroderma, 1 cervical ependymoma, 1 small fiber neuropathy, and 1 idiopathic anorectal disorder. All patients completed the entire protocol with no difficulty reported.

Primary Outcome

A significant decrease in EMG RMS was found between the first and the last MVC (0.0102 mV ± 0.00834 mV vs 0.00661 mV ± 0.00587, $P = 0.002$). A statistical difference between the first MVC and the others was observed from the fifth MVC ($P = 0.021$) to the 10th, and EMG RMS value seemed to be then stable from the sixth to the 10th MVC, with no significant difference ($P = 0.293$) (Fig. 3).

Besides, all patients completed the entire fatiguing protocol and it was well tolerated by them. It seemed reproducible because no complications occurred and there was not any difficulty in installation, measuring, and data collection for the examiner.

Secondary Outcomes

A significant decrease was found for the EAS EMG mean power, the EAS EMG total power, the anal sphincter pressure recorded during maximal contraction on manometry, the AUC of sustained anal sphincter contraction, and the manometric FRI between the first and the last MVC. A plateau was also reached at the sixth MVC, except for the FRI. No statistical difference was found for EMG mean frequency and manometry fatigue rate. These results are summarized in Table 2.

Secondary Analyses

Patients aged over 60 years had the highest fatigability (−0.0080 mV vs −0.0022 mV; $P = 0.024$) on EMG RMS than the youngest persons. Besides, no difference was found in the decrease in manometry peak between the first and the 10th MVC function with respect to the age of the participants ($P = 0.936$). The morphology of the EAS pressure recording curve depended on the age of the subject. In younger subjects, the manometry peak was maintained relatively well but the pressure decreased more and more rapidly with the onset of fatigue. In the elderly, a regular decrease in the peak was observed. An example of curve morphology in a young and an older subject is shown in Figure 4.

No fatigability difference was found according to gender and surgical or obstetric history. A correlation was demonstrated between importance of fatigability assessed by EMG RMS and NBD score (rho = 0.552; $P = 0.020$).

Table 2. Statistical Analyses of Primary and Secondary Outcomes on Difference Between First, Sixth, and 10th Repetition

Studied data	Δ1-10	*P*-value	Δ1-6	*P*-value	Δ6-10	*P*-value
EMG RMS (mV)	0.003667 (0.004747)	0.002	0.003566 (0.004476)	0.001	0.000101 (0.001167)	0.293
EMG mean power (V^2/Hz)	8.08×10^{-7} (1.42×10^{-6})	0.034	8.19×10^{-7} (1.34×10^{-6})	0.018	-1.18×10^{-8} (2.96×10^{-7})	0.351
EMG total power (V^2/Hz)	8.30×10^{-4} (1.40×10^{-3})	0.034	8.40×10^{-4} (1.30×10^{-3})	0.018	-1.20×10^{-5} (3.00×10^{-4})	0.351
EMG mean frequency (Hz)	0.14 (2.81)	0.381	0.94 (3.18)	0.343	−0.80 (3.26)	0.704
Manometry peak (mmHg)	15.90 (21.90)	0.011	15.60 (15.70)	< 0.001	0.32 (11.00)	0.487
Manometry AUC (mmHg)	161 (233)	0.006	103 (194)	0.037	58 (224)	0.264
Manometry FR (mmHg/min)	0.22 (1.44)	0.403	−0.07 (0.66)	0.646	0.30 (1.29)	0.604
Manometry FRI (min)	0.47 (2.35)	0.015	0.50 (1.46)	0.101	−0.03 (1.71)	0.069

Δx-y, difference between xth and yth maximal voluntary contraction; EMG, electromyography; RMS, root mean square; AUC, area under the curve; FR, fatigue rate; FRI, fatigue rate index.
Data are presented as mean (SD).
$P < 0.05$ was considered statistically significant.

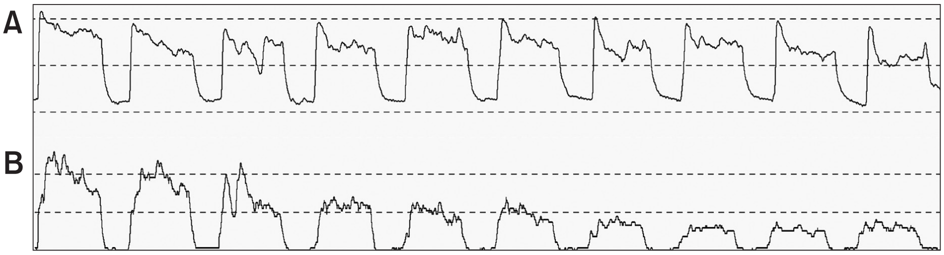

Figure 4. Manometry curves of pressure in external anal sphincter during the protocol. (A)It shows the recording of a 38-year-old patient. (B)It shows the recording of a 80-year-old patient. Abscissa represents time and ordinate represents pressure.

Table 3. Subgroup Analysis: Qualitative Factors Associated With Higher Fatigability

Patients characteristics	Δ1-10 RMS (10^{-3} mV)	*P*-value
Age		
≥ 60 yr	4.152 (4.653)	0.024
< 60 yr	3.918 (4.891)	
Gender		
Male	3.864 (4.170)	0.079
Female	3.667 (4.877)	
Gynecologic surgery or obstetric history		
Yes	3.667 (4.877)	0.951
No	6.110 (5.927)	
Abdominal surgery history		
Yes	3.667 (4.877)	0.768
No	3.401 (4.044)	
Perineal rehabilitation history		
Yes	4.151 (4.653)	0.727
No	2.900 (4.361)	
Anal Incontinence		
Yes	4.204 (4.285)	0.983
No	3.667 (4.878)	
Anorectal dyschesia		
Yes	3.667 (4.878)	0.584
No	4.077 (4.452)	

Δ1-10, difference between the first and the 10th contraction.
Data are presented as mean (SD).
$P < 0.05$ was considered statistically significant.

All results are summarized in Tables 3 and 4.

Discussion

This is the first study to develop a protocol to assess EAS fatigability, especially with mathematical EMG signal treatment. In our population, a significant difference was shown in EMG RMS after 10 MVCs, which reflects muscle fatigue or fatigability. Moreover, this difference appeared already at the fifth MVC and did not seem to increase significantly after the sixth MVC. Besides, the other outcomes assessing muscle fatigue or fatigability (EMG total and mean power, manometry AUC, and manometry peak of pressure) also showed consistent results with a significant decrease. Age over 60 years correlated with more severe fatigability.

Our results are consistent with previous studies in non-pathologic populations. Schabrun et al[11] showed a significant difference in pressure measured by manometry after 10 MVC repetitions in 10 healthy subjects, but there was no EMG measurement.

Influence of age on fatigue or fatigability can probably be explained by a change in muscle fibers with age, and particularly after menopause for women.[19,20] The presence of hormonal receptors on anal canal fibers induces a switch of histology from type IIa to type I with modification of hormonal secretions. Nockolds et al[21] showed an opposite relationship with greater fatigability in younger subjects. However, their evaluation was based on a single contraction by FR, and this correlation with age was not found in patients with fecal incontinence.

Table 4. Subgroup Analysis: Quantitative Factors Associated With Larger Fatigability

Patients characteristics	rho	*P*-value
BMI	0.449	0.571
NBD	0.552	0.020
Cleveland score	0.401	0.885
Fatigue impact Scale	0.343	0.152
Physical fatigue	0.158	0.526
Cognitive fatigue	0.310	0.204
Psychosocial fatigue	0.229	0.341
Urinary symptom profile		
Incontinence	0.050	0.845
Overactivity	0.071	0.794

BMI, body mass index; NBD, neurogenic bowel dysfunction score.
Spearman correlation. $P < 0.05$ was considered statistically significant.

We showed a correlation between importance of fatigue or fatigability and NBD scores. This could suggest a link between anorectal symptoms and EAS fatigue or fatigability. This relation had already been studied with contradictory results.[16-18,22,23] The heterogeneity of the results in the previous studies, can be explained by the absence of a standardized protocol or standard measurement for fatigability. Besides, none of these studies had explored fatigability with EMG. In our study, the heterogeneity of the population, the influence of neurologic diseases with a possible impact on muscle contractility, and the small number of subjects does not allow us to conclude on the explanatory mechanisms.

In our study, we propose a simple and minimally invasive protocol to assess EAS fatigability, usable in everyday evaluations and well tolerated by patients. Indeed, the exercise or effort required to induce fatigability varies greatly according to the published studies: 10 maximal contractions supported by TMS,[11] 3 maximal contractions then sustained contraction as long as possible,[24] 10 pelvic contractions followed by sustained contraction,[25] 6 cough efforts.[26] Understanding the instructions and dosing the intensity of the contractions are parameters that can complexify the protocol, especially since control on the anal sphincter is sometimes difficult to obtain.[27] In our procedure, the instruction was simple, requiring maximum contraction effort of regular duration with a rest time equal to half the contraction time. The interest and the value of the protocol are reinforced by consistent fatigue or fatigability results obtained with EMG and manometry, achieved at the same time. Moreover, we studied the 2 types of fibers of EAS. Manometry peak reflects the fast twitch type IIa fibers activity and EMG RMS reflects the slow twitch type I fibers activity. In our study, these 2 measures were significantly reduced between the first and 10th MVC showing we probably succeeded in fatiguing both types of fibers. The use of both techniques (EMG and manometry) helps to clarify the choice of evaluation method and measurement collected according to the aim of future studies.

Our study has several limitations. First, we have no control group without pathology or symptoms to compare their EAS fatigability with our population. This limitation is due to the design of the study since the population was recruited on the need for an anorectal manometry, less acceptable in an asymptomatic population. That is why our results cannot differentiate between physiological and pathological fatigue. Another limit is the absence of other control skeletal muscles. In an ex vivo animal study, Poortmans and Wyndaele[28] compared fatigability of perineal muscles and skeletal muscle, measuring the contraction force after repeated electrostimulation to induce fatigue. They reported a higher fatigability in perineal muscles with a drop of the contraction force of 33% for the iliococcygeus while the soleus maintained a contraction force of 85% for the same electrostimulation protocol.[28] Nevertheless, our study population had mainly neurologic disease and this could distort the results obtained on skeletal muscles. Our small sample and the variability in pathologies did not permit us to highlight subgroup differences, due to a lack of power. Finally, other phases would be necessary to validate this protocol as a standardized one, with for example a reproducible phase, or a responsiveness assessment after therapeutic options.

Several perspectives exist. First, several fatigability protocol designs could also be tested, including modulating the resting time between each MVC, known to influence muscle fatigue.[28] However, the one proposed in our study is fast and effective in fatiguing the EAS. Secondly, the use of a standardized protocol could make it possible to assess the effectiveness of a pelvic floor rehabilitation program, either in comparison with another, or to verify the effectiveness in the patient by showing a reduction in fatigability. On the other hand, knowledge of this rapid fatigability of the EAS should make it possible to adapt rehabilitation protocols. Intensive training on a muscle that is too fatigued is unlikely to be effective. Many studies have shown the benefit of a long rest period between each muscle contraction on the increase in strength, suggesting a greater difficulty in strengthening the muscle when it is fatigued.[29-31] The benefit of a short interval on endurance gain is more controversial.[31] Time to get back to basal measures have also not been studied in our study and further work is needed to be done in this way, especially since animal studies seem to show a different behavior of EAS compared to other skeletal muscles.[28] The muscle strengthening protocols in rehabilitation of the EAS must therefore adapt to this need for sufficient rest time according to the fatigue induced by the MVC. Finally, it could also be interesting to assess correlation between a more intense fatigability and symptoms, particularly anal incontinence.

In conclusion, this procedure with repetitive MVC is feasible, simple, and minimally invasive for fatiguing EAS in patients with anorectal disorders. The quantification of this fatigue and fatigability by EMG RMS with surface electrode sampling is efficient, but we highlighted fatigability of EAS on many electromyographic and manometric outcomes after 10 MVC. Age over 60 correlated with a higher fatigability.

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Conflicts of interest: None.

Author contributions: Study conception and design: Matthieu Grasland, Claire Hentzen, Nicolas Turmel, Camille Chesnel, Gérard Amarenco, Audrey Charlanes, Samer Sheikh-Ismael, Camille Pouyau, Camille Leroux, and Frédérique Le Breton; acquisition of data: Matthieu Grasland, Camille Pouyau, and Camille Leroux; analysis and interpretation of data: Matthieu Grasland, Claire Hentzen, Camille Chesnel, Audrey Charlanes, Samer Sheikh-Ismael, Camille Leroux, Camille Pouyau, and Gérard Amarenco; drafting of manuscript: Matthieu Grasla, Claire Hentzen, Nicolas Turmel, Camille Chesnel, Audrey Charlanes, and Audrey Charlanes; and critical revision: Claire Hentzen, Gérard Amarenco, and Samer Sheikh-Ismael.

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