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**An electrophysiological approach to the diagnosis of neurogenic dysphagia; implications for botulinum toxin treatment.**

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## ABSTRACT

*Objectives:* Botulinum toxin (BTX) injection into the cricopharyngeal (CP) muscle has been proposed for the treatment of neurogenic dysphagia due to CP hyperactivity. We aimed to find out whether an electrophysiological method exploring oropharyngeal swallowing could guide treatment and discriminate responders from non-responders, based on the association of CP dysfunction with other electrophysiological abnormalities of swallowing.

*Methods:* We examined patients with different neurologic disorders: Parkinson's Disease, progressive supranuclear palsy, multiple system atrophy-Parkinson variant, multiple system atrophy- Cerebellar variant, stroke, multiple sclerosis, and ataxia-telangiectasia. All patients presented with clinical dysphagia, and with complete absence of CP muscle inhibition during the hypopharyngeal phase of swallowing. Each patient underwent clinical and electrophysiological investigations before and after treatment with BTX into the CP muscle of one side (15 units of BOTOX®, Allergan). Clinical and electrophysiological procedures were performed in a blind manner by two different investigators. The following electrophysiological measures were analysed: 1) duration of EMG activity of suprahyoid/submental muscles (SHEMG-D); 2) duration of Laryngopharyngeal mechanogram (LPM-D); 3) duration of the inhibition of the CP muscle EMG activity (CPEMG-ID); and 4) interval between onset of EMG activity of suprahyoid/submental muscles and onset of Laryngopharyngeal mechanogram (I-SHEMG-LPM).

*Results:* Two months after treatment, 50 % of patients showed significant improvement. Patients with prolonged or reduced SHEMG-D values and prolonged I-SHEMG-LPM values did not respond to BTX. Therefore, we identified values for which BTX had no effect (warning values).

*Conclusions:* Our electrophysiological method can recognize swallowing abnormalities which may affect the outcome of the therapeutic approach to dysphagia with BTX treatment.

## INTRODUCTION

Traditionally, deglutition has been described as a series of four phases that relate to the passage of the bolus through specific anatomic structures: oral preparatory, oral, pharyngeal, and oesophageal. The physiology of swallowing implies the interaction of sensory and motor functions and the interaction of voluntary and involuntary aspects. Recent studies suggest that swallowing is best understood as a single behaviour with four components that must act in an integrated manner if swallow success has to be achieved; these studies have also underlined the importance of sensation and of sensory-motor integration.<sup>1</sup>

Dysphagia, impairment in swallowing, is a frequent symptom in patients with many different neurological disorders, which can further complicate their clinical management, and adversely affect their quality of life and their outcome. Epidemiological studies have found that clinical dysphagia is present in up to a third of patients with stroke and in 50% of patients with Parkinson's Disease (PD).<sup>2,3</sup> Objective studies of swallowing in PD have shown an even higher frequency of swallowing abnormalities than subjective survey studies. Several investigators have reported abnormalities on modified barium swallow test in 75 to 97% of PD patients tested.<sup>4-6</sup>

Although any one phase of swallowing can be involved, dysphagia due to incomplete relaxation and defective opening of the upper esophageal sphincter (UES) is a frequent abnormality in these patients.<sup>3,7-13</sup> UES opening is a complex interaction between neural control and biomechanical events related to adjacent structures. Patients with UES dysfunction have difficulty passing the bolus into the esophagus. This results in hypopharyngeal retention with consequent aspiration of food or liquid into the airways.<sup>1</sup>

The use of botulinum toxin (BTX) has recently been expanding to encompass neurogenic dysphagia. Although no data from blinded randomized trials are available on the effect of BTX, several case series studies have shown the efficacy of BTX injection into the cricopharyngeal (CP)

muscle (the main component of the UES), but yet some patients do not respond to BTX treatment,<sup>7-10</sup> and reliable markers predicting BTX treatment response are lacking.

At present, videofluoroscopic swallowing study or fiberoptic endoscopic evaluation of swallowing are the mainstay of the diagnosis and clinical assessment of dysphagia. They can evaluate the anatomy and physiology of the swallowing process, assess swallowing safety, identify patterns of impaired swallowing and their consequences, confirm the patient's symptoms, and assess the efficacy of compensatory manoeuvres, or rehabilitation procedures. However, neither videofluoroscopy nor endoscopy can provide information about the pathophysiological process underlying the observed abnormality of the CP muscle. They cannot distinguish between insufficient opening from inadequate relaxation due to altered neurophysiologic control of the muscle tone, and that from stenosing fibrosis, or from other organic cause, when there is no abnormality of the lumen outline.

Electrophysiological investigations of oropharyngeal swallowing can detect CP muscle abnormalities during swallowing; they can characterize the dysfunction of CP muscle relaxation, as well as other abnormalities of the propulsive oral phase, of the interval between the oral and the pharyngeal phases, and of the duration of the pharyngeal phase of swallowing.<sup>13,14</sup>

In this study of patients with clinical dysphagia, and incomplete relaxation with defective opening of the UES our aims were: 1) to assess the efficacy of BTX injection into the CP muscle when absence of its inhibitory pause is observed on electromyography (EMG); and 2) to find out if our electrophysiological investigation could predict the efficacy of BTX, and discriminate responders from non-responders to the treatment, based on the association of CP dysfunction with other electrophysiological abnormalities of the oropharyngeal phase of swallowing.

## MATERIAL AND METHODS

### *Population*

The main characteristics of our patients are summarized in table 1. We studied 34 patients with clinical dysphagia, and incomplete relaxation and defective opening of the UES confirmed by EMG evaluation. None of our patients had a Zenker's diverticulum at the endoscopic investigation of the pharyngeal and esophageal tracts.

Patients with PD were all examined during the "on" phase of the levodopa response cycle. We decided to study PD patients in the "on" phase because we wanted to assess the entity of swallowing problems in the real life context. These patients were advised to take their L-dopa therapy in a way to provide maximum protection during meal time, as L-dopa should reduce oral and pharyngeal swallowing impairment as well as enhance upper extremities function.

Patients with stroke were examined between 12 and 17 months after onset of disease, when all stroke symptoms had stabilized.

Dysphagia severity was assessed based on the patient's subjective complaint or problem and quantified with a simple rating scale, the dysphagia severity score (DSS).<sup>12,13</sup> Briefly, DSS is graded as follows: 0 (absence of dysphagia), when there are not subjective difficulties in the swallowing of liquids or solids; 1 (mild to moderate dysphagia), when the patient experiences a feeling of something getting stuck while swallowing, or has to cough during or after swallowing, or has to cut food finely and to avoid certain difficult-to-particulate foods, or has to swallow liquids in small sips; 2 (severe dysphagia), when serious nutritional problems are present with need of a feeding tube. The main advantages of this scale reside in its utility in the clinical assessment of the level of swallowing safety, and in the fact that its 3 well separated levels make it highly specific for detecting changes after interventions. We considered as responders those patients in whom a reduction of at least 1 degree in DSS was observed.

### *Electrophysiological studies*

The method applied was described previously.<sup>13,14</sup> For the investigation, an electromyograph Key-point Medtronic (Skovlunde, Denmark) was used. Simultaneous electrokinesiographic recording from 3 channels was performed (fig.1). The first channel recorded the EMG activity of suprahyoid/submental muscles (a muscle complex consisting of the mylohyoid, the genioglossus, and the ventral belly of the digastric) using two surface electrodes applied to the skin over the suprahyoid region at an interelectrode distance of 30 mm. This activity marks the beginning of the propulsive action of the tongue in the oral phase of swallowing and continues throughout the pharyngeal phase of swallowing.<sup>15</sup> The second channel recorded the EMG activity of the CP muscle using a coaxial needle-electrode inserted through the skin at the level of the cricoid cartilage, 1.5 cm posterior to its palpable lateral border, in the posteromedial direction. At rest, this muscle shows tonic activity related to its function as a muscular sphincter, since it is a major contributor to the functional area known as the upper esophageal sphincter (UES); such EMG activity disappears completely (inhibitory pause), for a brief time, during the hypopharyngeal phase of swallowing. Opening of the UES was defined as the EMG inhibitory pause of CP muscle when the EMG signal amplitude was below 50  $\mu$ V.

EMG signals from both, first and second channels were bandpass filtered between 100 Hz and 2 kHz and then rectified. The third channel recorded the mechanogram obtained from a piezoelectric transducer detecting the deformations produced by pharyngolaryngeal structures during the pharyngeal phase of swallowing. In particular, the transducer marks the time of elevation-retroflexion, and return to the rest position of the epiglottis. This transducer consisted of a rectangular strip with a triangular rubber button in the centre of the strip applied to the skin over the cricothyroid membrane, and kept in place by adhesive tape wrapped around the neck. It showed a linear force-to-signal ratio for forces ranging from 0.1 to 300 g; its signals were bandpass filtered between 0.01 and 30 Hz. For each channel the signal sampling rate was 20 kHz.

Each patient was examined while seated with the head in a natural position, and had to swallow a small volume of water (3 ml) introduced into his/her mouth with a disposable syringe without needle.

We analysed the following electrophysiological measures:

1) duration of EMG activity of suprahyoid/submental muscles (SHEMG-D); 2) duration of the laryngopharyngeal mechanogram (LPM-D); 3) duration of the inhibition of the cricopharyngeal muscle EMG activity (CPEMG-ID); and 4) interval between onset of EMG activity of suprahyoid/submental muscles and onset of laryngopharyngeal mechanogram (I-SHEMG-LPM). Signals were triggered when signal amplitude of suprahyoid/submental muscle EMG activity was equal to or greater than 50  $\mu$ V. Recordings obtained from ten successive swallowing acts were stored and the average value of each electrophysiological measure was evaluated.

Since all patients initially presented with absence of CP muscle inhibition, they all received a BTX injection into the CP muscle. This procedure was carried out while monitoring the EMG activity of the muscle using a needle electrode-cannula with the characteristics of a monopolar electrode. This electrode was inserted in the neck at the level of the cricoid cartilage in the same way described above; a surface electrode (reference electrode) was applied ipsilaterally over the middle line of the clavicle. In each patient 15 units of BTX (BOTOX®, Allergan), diluted 5.0 units/0.1ml, were injected into the CP muscle of one side (stroke patients received the injection on the paretic side).

We performed unilateral injection because injecting bilaterally could have increased the risk of aspiration. In fact, not only is BTX effecting CP muscle relaxation during the hypo-pharyngeal phase of swallowing. BTX is also reducing CP muscle resting tone. The loss of CP muscle sphincter function would increase the risk of food reflux from the oesophagus, with consequent post-deglutition aspiration into the airways. Furthermore, we chose the unilateral injection because the treatment with BTX into the CP muscle exposes to objective risks of contamination of nearby muscles involved in laryngeal and vocal cord motility. Diffusion of the toxin to such muscles could

paralyse them and bilateral injection could lead to greater severity of the side-effects due to the diffusion of the drug, with serious consequences for the patient.

In each patient, both clinical and electrophysiological evaluations were repeated 2 months after treatment. Clinical and electrophysiological procedures at baseline and after BTX treatment were performed in a blind manner by two different investigators, one performing the clinical assessments while the other the electrophysiological studies; the two-month assessments were performed without knowledge of preceding BTX injection.

#### *Statistical analyses*

Analyses were performed using Stata version 10 (Stata Corp, College Station, Tex).

Student's t-test, Mann-Whitney U-test, or Fisher exact test was used to compare the clinical, electrophysiological, and demographic differences between responders and non-responders. To compare DSS before and after treatment, we used extended McNemar test. For all analyses, the significance level was set at  $p = 0.05$ .

Electrophysiological measures were compared at baseline, and cut-off levels for each measure were identified on the graphical analysis (they represent the extreme non-outlier points in the box plots) in order to establish "warning values" that could be used to predict responders or non-responders to BTX treatment. Using the presence of a 'warning value' as a diagnostic test, able to detect the non-response to the BTX, we calculated the positive predictive value (PPV), that is the probability for a subject to be a non-responder given that he is test-positive, i.e. he has a 'warning value' at baseline. In the same way, we calculated the negative predictive value (NPV), that is the probability for a subject to be a responder given that he is test-negative, i.e. he does not have a 'warning value' at baseline.

#### *Ethics*

The research protocol was approved by the Ethics Committee of our Institute. All patients gave written informed consent to all the procedures of the study.

## RESULTS

Patients' characteristics and changes in DSS after BTX treatment are summarized in table 1.

Responder and non-responder patients were homogeneous in relation to age, gender, and DSS (table 2).

Following the electrophysiological procedures used and the dose of BTX injected into the CP muscle, we did not observe any worsening of dysphagia or any other side effects, like vocal cord dysfunction, in any of our patients, neither did any patient complain of other problems.

Two months after BTX treatment, 50% of patients had a significant improvement of dysphagia (lower DSS,  $p < 0.001$ ) (table 2). In these patients, the electrophysiological study showed the normal pause of the EMG activity of the CP muscle (fig.1). None of the responders with severe dysphagia (DSS: 2) became symptom-free (DSS: 0). Eleven patients showed a DSS improvement from 1 to 0, and 6 patients from 2 to 1. On the other hand, the remaining 50% of patients did not show any significant change in dysphagia severity (table 2). In 13 of these patients the electrophysiological study showed a pause of the EMG activity of the CP muscle, whereas in the other 4 patients the absence of EMG pause of the CP muscle persisted as before treatment.

Table 3 summarises the median values and interquartile ranges of the electrophysiological measures at baseline and two months after BTX treatment.

Since all our patients presented with complete absence of CP muscle inhibition, we did not have any CPEMG-ID value at baseline. After treatment, we observed recovery of this measure in both groups; although we obtained a larger increase for responders than for non-responders, the median CPEMG-ID was not significantly different between the two groups ( $p = 0.105$ ).

The SHEMG-D at baseline was significantly longer in the non-responder than in the responder group ( $p = 0.005$ ); the same trend was present after treatment and the difference between the responder and the non-responder group was statistically relevant ( $p = 0.04$ ).

The median LPM-D at baseline was similar in both groups ( $p = 0.480$ ) but after treatment a sharper median decrease was observed in the responders compared to the non-responders ( $p < 0.001$ ).

The median value of I-SHEMG-LPM was significantly higher in the non-responder group, both at baseline ( $p < 0.001$ ) and after treatment ( $p < 0.001$ ).

The descriptive analysis of the electrophysiological measures at baseline showed significant differences between the responders and the non-responders for two measures: SHEMG-D and I-SHEMG-LPM. The graphical analysis of the distribution of SHEMG-D and I-SHEMG-LPM at baseline highlighted the following ‘warning values’: less than 1,000 ms and more than 1,680 ms for SHEMG-D; and more than 300 ms for I-SHEMG-LPM (fig.2).

We observed that the frequency of patients with ‘warning values’ at baseline for both measures, SHEMG-D and I-SHEMG-LPM, was significantly higher in the non-responders than in the responders (88.2% and 64.7% vs. 0% and 5.9%,  $p < 0.001$ ). The same result was observed after treatment: the frequency of patients with ‘warning values’ for both measures, SHEMG-D and I-SHEMG-LPM, was significantly higher in the non-responders than in the responders (82.4% and 70.6% vs. 5.9% and 5.9%,  $p < 0.001$ ).

The PPV for SHEMG-D was 100.0%; the PPV for I-SHEMG-LPM was 91.7%; the PPV for SHEMG-D plus I-SHEMG-LPM was 94.1%. The NPV for SHEMG-D was 89.5%, the NPV for I-SHEMG-LPM was 72.7%; the NPV for SHEMG-D plus I-SHEMG-LPM was 94.1%.

## DISCUSSION

In this study we examined the efficacy of BTX treatment in patients with symptomatic dysphagia when absence of CP muscle relaxation was present alone or in association with other abnormalities of oropharyngeal swallowing.

The CP muscle is a major contributor to the functional area known as UES. Adequacy of UES opening depends on the degree of preservation of the pharyngeal swallowing response and on hyolaryngeal traction.<sup>16-18</sup> An optimal assessment of failed CP muscle relaxation is obtained applying an electrophysiological method in which needle-EMG recording of this muscle is carried out during rest and swallowing.<sup>12-14</sup>

All patients submitted to BTX treatment in our study showed absence of the EMG pause of the CP muscle during the hypopharyngeal phase of swallowing. However, our electrophysiological method revealed, in several patients, other abnormalities such as prolonged or reduced SHEMG-D, prolonged LPM-D, and increased I-SHEMG-LPM. Fifty percent of our patients were responders; in these patients CP-ID absence was observed alone or together with prolonged LPM-D. In our non-responder patients (the remaining 50%), besides CP-ID absence, we observed SHEMG-D values exceeding, in most cases, both lower and upper limits of the responders, and I-SHEMG-LPM values exceeding, in most cases, the upper limits of the responders.

BTX treatment was able to completely restore swallowing function in responders with mild to moderate dysphagia, but not in those with severe dysphagia, who only improved to the mild/moderate degree on the DSS. A too low dose of BTX or the unilateral injection may explain our results. However, since the CP muscle spreads posteromedially to join the contralateral muscle, even a unilateral injection should give a good response.

Since our study included only a limited number of patients for each neurological disease, we cannot attempt to provide predictive data based on disease entity or duration. On the other hand, in a previous report of parkinsonian syndromes we observed that I-SHEMG-LPM prolongation is typical of PD dysphagia, and CP-ID absence characterizes most of MSA-P and PSP patients.<sup>13</sup> These observations have been confirmed in the present study; in fact, all MSA-P patients, 6 out of 9 PSP patients, but only 2 out of 7 PD patients responded to BTX (table 2). This suggests that CP hyperactivity is the main finding of dysphagia in both MSA-P and PSP, whereas it is often associated with other abnormalities in PD dysphagia.

When the only abnormality is the absence of CP muscle relaxation, BTX treatment is likely to be effective for dysphagia. This suggests that the success of this treatment has a high degree of probability when swallowing abnormalities are due exclusively to a dysfunction of the neural mechanisms influencing changes in neurogenic tone of the CP muscle during swallowing, as

observed in lesions involving some specific inhibitory activities of the 'central swallowing pattern generator' of the brainstem.<sup>16,19,20</sup>

In our study, LPM-D prolongation did not appear to have significant effect on the efficacy of BTX treatment. This measure includes both the infrahyoid-submental muscle activity which pulls up and holds up the larynx, and the passive forces which pull the larynx down; the latter are due to the viscous-elastic properties of the laryngopharyngeal structures and to gravitational forces.<sup>1,21,22</sup>

Therefore, LPM-D also depends on physical and anatomical characteristics of the subject examined.

The persisting contraction of the CP muscle during the hypopharyngeal phase of swallowing represents an obstacle to the smoothness of the laryngopharyngeal excursion, and it increases its duration (LPM-D). In the responders, BTX treatment led to a significant reduction of LPM-D.

The results of our study indicate that both abnormal reduction and increase of SHEMG-D are associated with inefficacy of BTX treatment. The EMG activity of the suprahyoid/ submental muscles indicates the propulsive action of the tongue and the pharyngeal phase of swallowing, including the elevation of the epiglottis.<sup>15,23</sup> In particular, the suprahyoid/ submental muscle group are considered to be the most important factor responsible for elevating the larynx.<sup>1,23</sup> The abnormal reduction of SHEMG-D reflects an insufficient activation of the suprahyoid/ submental muscles during the propulsive oral phase and the pharyngeal phase. This abnormality can be associated to hypokinesia of the oropharyngeal phase in parkinsonian syndromes,<sup>13</sup> or to a deficit of the oropharyngeal phase in other disorders of the Peripheral and Central Nervous Systems. A poor activation of suprahyoid/ submental muscles may fail to trigger the normal pharyngeal phase of deglutition.<sup>1,15,23</sup>

SHEMG-D prolongation can be due to either bradikinetik mechanisms, as observed in parkinsonian syndromes,<sup>13</sup> or to incoordination in the activity of pulling up the larynx, as observed in brainstem or cerebellar lesions.<sup>25,26</sup> SHEMG-D prolongation may represent a compensatory phenomenon which intervenes when the 'phasic activity' of these muscles, which is necessary to efficiently pull up the laryngopharyngeal structures, is missing. In other words, the deficit of force of the

suprahyoid/ submental muscles for triggering the swallow reflex tends to be corrected by a prolonged activity of these muscles.

We found that also I-SHEMG-LPM prolongation was associated with inefficacy of BTX treatment. I-SHEMG-LPM indicates the transition between the oral and the pharyngeal stages of swallowing; it is also called the 'pharyngeal delay time'.<sup>24</sup> I-SHEMG-LPM prolongation can be observed in different neurological disorders, such as parkinsonian syndromes,<sup>13</sup> multiple sclerosis,<sup>25</sup> and stroke.<sup>22,26</sup> Several mechanisms can increase I-SHEMG-LPM. An inappropriate planning of the voluntary swallowing activity related to a dysfunction of the cortical-subcortical loops connecting the basal ganglia to the premotor and supplementary motor areas of the frontal cortex, as found in parkinsonian syndromes;<sup>13</sup> a dysfunction of the brainstem interneurons involved in the programming and coordination of the swallowing sequence, as observed in disorders like stroke, and multiple sclerosis;<sup>22,25,26</sup> or a cerebellar dysfunction, with disruption of accuracy of movement and harmonious actions, both leading to a dysfunction of time-related neural control.<sup>27</sup> I-SHEMG-LPM prolongation, can in itself be responsible for dysphagia. In particular, it has been linked to aspiration, which is the entry of food or liquid into the airways below the level of the true vocal cords.<sup>22,24,25</sup>

In conclusion, our study indicates that the electrophysiological evaluation of oropharyngeal swallowing can recognize swallowing abnormalities which may interfere with the outcome of the therapeutic approach to dysphagia with BTX treatment. Electrophysiological evidence of isolated CP hyperactivity predicts good response to BTX. In this case the treatment can be appropriately used, when expected to be successful, saving on cost and patients' expectations.

A preliminary evaluation of oropharyngeal swallowing, applying this electrophysiological method, can be a useful screening tool for choosing strategies for treatment of dysphagia.

In the future we will need to verify if higher doses of BTX or bilateral injection can make patients with severe dysphagia due to CP hyperactivity symptom-free.

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#### REFERENCES:

- 1) **Cichero J**. Applied Anatomy and physiology of the normal swallow. In: Dysphagia. Foundation, Theory and Practice. Julie A Y Cichero and Bruce E Murdoch Eds. Chichester: John Wiley & Sons, Ltd, 2006.
- 2) **Hamdy S**, Aziz Q, Rothwell JC, et al. Explaining oropharyngeal dysphagia after unilateral hemispheric stroke. *Lancet* 1997; **350**:686-692.
- 3) **Pfeiffer RF**. Gastrointestinal function in Parkinson's disease. *Lancet Neurol* 2003; **2**: 107-116.
- 4) **Logemann JA**, Blonsky ER, Boshes B. Editorial: dysphagia in parkinsonism. *JAMA* 1975; **231**: 69-70
- 5) **Stroudley J**, Walsh M. Radiological assessment of dysphagia in Parkinson's disease. *Br J Radiol* 1991; **64**: 890-893
- 6) **Bird MR**, Woodward MC, Gibson EM, Phyland DJ, Fonda D. Asymptomatic swallowing disorders in elderly patients with Parkinson's disease: a description of findings on clinical examination and videofluoroscopy in sixteen patients. *Age Aging* 1994; **23**: 251-254
- 7) **Schenider I**, Thumfart WF, Potoschig C, Eckel HE. Treatment of dysfunction of the cricopharyngeal muscle with botulinum A toxin: introduction of a new, noninvasive method. *Ann Otol Rhinol Laryngol* 1994; **103**: 31-35.
- 8) **Haapaniemi JI**, Laurikainen EA, Pulkkinen J, et al. Botulinum toxin in the treatment of cricopharyngeal dysphagia. Review of the use of botulinum in treating proximal dysphagia. *Dysphagia* 2001; **16**: 171-175.

- 9) **Ahsan SF**, Meleca RJ, Dworkin JP. Botulinum toxin injection of the cricopharyngeus muscle for the treatment of dysphagia. *Otolaryngol Head Neck Surg* 2000; 122(5): 691-695.
- 10) **Blitzer A**, Sulica L. Botulinum Toxin: Basic Science and Clinical Uses in Otolaryngology. *Laryngoscope* 2001; **111**: 218-226.
- 11) **Restivo DA**, Palmeri A, Marchese-Ragona R. Botulinum toxin for cricopharyngeal dysfunction in Parkinson's disease. *N Engl J Med* 2002; **346**: 1174-1175.
- 12) **Merlo IM**, Occhini A, Pacchetti C, Alfonsi E. Not paralysis, but dystonia causes stridor in multiple system atrophy. *Neurology* 2002; **58**: 649-952.
- 13) **Alfonsi E**, Versino M, Merlo IM, et al. Electrophysiologic patterns of oral-pharyngeal swallowing in parkinsonian syndromes. *Neurology* 2007; **68**: 583-590.
- 14) **Ertekin C**, Pehlivan M, Aydogdu I, et al. An electrophysiological investigation of deglutition in man. *Muscle Nerve* 1995; **18**: 1177-1186.
- 15) **Logemann JA**. Evaluation and treatment of swallowing disorders. 2<sup>nd</sup> ed. Austin, TX: ProED, 1998.
- 16) **Sivarao DV**, Goyal Ray K. Functional anatomy and physiology of the upper esophageal sphincter. *Am J Med* 2000; **108**: 27S-37S.
- 17) **Mu L**, Sanders I. The innervation of the human upper esophageal sphincter. *Dysphagia* 1996; **11**: 234-238.
- 18) **Mu L**, Sanders I. Neuromuscular organization of the human upper esophageal sphincter. *Ann Otol Rhinol Laryngol* 1998; **107**: 734.
- 19) **Cook IJ**, Dodds WJ, Dantas RO, et al. Opening mechanism of the human upper esophageal sphincter. *Am J Physiol Gastrointest Liver Physiol* 1989; **257**: G748-G759.
- 20) **Kahrilas PJ**, Dodds WJ, Dent J, Logemann JS, and Shaker R. Upper esophageal sphincter function during deglutition. *Gastroenterology* 1988; **92**: 52-62.

- 21) **Williams RB**, Pal A, Brasseur JG, Cook IJ. Space-time pressure structure of pharyngo-esophageal segment during swallowing. *Am J Physiol Gastrointest Liver Physiol* 2001; **281**: G1290-G1300.
- 22) **Bass NH**. The Neurology of swallowing. In: *Dysphagia. Diagnosis and Management*. 3rd Edition. Michael E. Groher Ed. Philadelphia: Butterworth-Heinemann, 1997.
- 23) **Vaiman M**, Eviatar E, Segal S. Evaluation of normal deglutition with the help of rectified surface electromyography records. *Dysphagia* 2004; **19**:125-132.
- 24) **Kim Y**, McCullough GH, Asp CW. Temporal measurements of pharyngeal swallowing in normal populations. *Dysphagia* 2005; **20**: 290-296.
- 25) **Abraham SS**, and Yun PT. Laryngopharyngeal dysmotility in multiple sclerosis. *Dysphagia* 2002; **16**: 69-74.
- 26) **Crary MA**, and Baldwin BO. Surface Electromyographic characteristic of swallowing in dysphagia secondary to brainstem stroke. *Dysphagia* 1997; **12**: 180-187.
- 27) **Schmahmann JD**. Disorders of the cerebellum: ataxia, dysmetria of thought, and the cerebellar cognitive affective syndrome. *J Neuropsychiatry Clin Neurosci* 2004; **16**: 367-378.

**Figure legend:**

Figure 1- Electrophysiological evaluation in a responder patient with PSP, before (top half) and after (bottom half) botulinum toxin (BTX) treatment. Upper trace: rectified EMG activity of suprahyoid/submental muscles; middle trace: rectified EMG activity of the cricopharyngeal muscle; and lower trace: mechanogram of pharyngolaryngeal structures. Vertical and horizontal thin bars indicate SHEMG duration (SHEMG-D), duration of the EMG inhibition of the CP muscle (CPEMG-ID), LPM duration (LPM-D), and interval between the onset of SHEMG and the onset of LPM (I- SHEMG-LPM). Absence of the EMG pause of the cricopharyngeal muscle activity can be seen at baseline (horizontal thick bar), while after treatment the EMG pause of the cricopharyngeal muscle activity is restored.

Figure 2- Box-plots of baseline measures I- SHEMG-LPM (a) and SHEMG-D (b). The “warning values” for SHEMG-D exceed both low and high values (less than 1000ms and more than 1680 ms); the “warning values” for I- SHEMG-LPM exceed high values (more than 300 ms).

Table 1 Patients characteristics and changes in dysphagia severity score after botulinum toxin treatment

Patients	Sex	Age	Disease	Disease duration (month)	DSS*		Response To BTX
	F/M	(yr)			Baseline	After BTX†	
1	F	44	MSA-P‡	26	1	0	yes
2	F	66	MSA-P	21	2	1	yes
3	M	60	MSA-P	38	1	0	yes
4	M	61	MSA-P	36	1	0	yes
5	F	68	MSA-C¶	32	2	2	no
6	M	78	PSP#	79	2	2	no
7	F	68	PSP	31	1	0	yes
8	F	70	PSP	49	2	1	yes
9	M	72	PSP	44	2	1	yes
10	M	61	PSP	25	1	0	yes
11	F	66	PSP	24	2	1	yes
12	F	66	PSP	60	1	0	yes
13	M	62	PSP	52	2	2	no
14	M	73	PSP	75	2	2	no
15	M	77	PD**	74	2	2	no
16	F	63	PD	55	1	0	yes
17	M	71	PD	124	2	2	no
18	F	57	PD	88	1	0	yes
19	F	64	PD	65	1	1	no
20	F	76	PD	97	2	2	no
21	M	68	PD	105	1	1	no

22	F	59	MS††	52	1	0	yes
23	F	39	MS	99	1	1	no
24	M	63	Stroke	8	2	1	yes
25	M	74	Stroke	48	1	1	no
26	M	77	Stroke	44	1	1	no
27	M	74	Stroke	39	2	2	no
28	M	77	Stroke	38	2	2	no
29	M	79	Stroke	11	1	0	yes
30	F	58	Stroke	9	1	1	no
31	F	82	Stroke	26	1	0	yes
32	F	69	Stroke	15	2	1	yes
33	F	55	Stroke	24	1	1	no
34	F	24	A-T‡‡	288	1	1	no

\*DSS: Dysphagia Severity Score (0: absent, 1: mild to moderate, 2: severe)

†BTX: Botulinum Toxin

‡MSA-P: Parkinson variant of multiple system atrophy

¶MSA-C: Cerebellar variant of multiple system atrophy

#PSP: progressive supranuclear palsy

\*\*PD: Parkinson's disease

††MS: multiple sclerosis

‡‡A-T: Atassia Telangiectasia

Table 2 Patients' characteristics at baseline and after botulinum toxin ( BTX ) treatment. Responders and non-responders are homogeneous in relation to age, gender and dysphagia severity .

	No. of patients	Age (yr) mean $\pm$ SD	Male/Female	DSS* baseline		DSS after treatment			P value
				No. (%) <sup>†</sup>		No. (%)			
				1	2	0	1	2	
All patients	34	65.3 $\pm$ 11.9	16/18	19 (55.9)	15 (44.1)	11 (32.4)	14 (41.2)	9 (26.5)	<0.001¶
Responders	17	65.1 $\pm$ 8.6	6/11	11 (64.7)	6 (35.3)	11 (64.7)	6 (35.3)	-	<0.001¶
Non-responders	17	65.6 $\pm$ 14.8	10/7	8 (47.1)	9 (52.9)	-	8 (47.1)	9 (52.9)	-
P value		0.900‡	0.303§	0.491§		<0.001§			

\* DSS: dysphagia severity score; 0: absent; 1: mild to moderate; 2: severe

† No. of patients and percentage of patients

‡ Student's *t*-test, and § Fisher exact test for comparing responders with non-responders

¶ Extended McNemar test for comparing DSS before and after BTX treatment

Table 3 Quantitative evaluations of electrophysiological measures at baseline and 2 months after Botulinum Toxin (BTX) injection

	Responders n=17	Non Responders n=17	*P value
SHEMG-D (ms)			
Baseline, median (IQR)†	1450 (1200-1500)	2790 (1485-2980)	0.005
After treatment, median (IQR)	1325 (1300-1620)	2866 (1320-3185)	0.040
SHEMG-D variation after treatment, median	↑‡25	↑30	
LPM-D (ms)			
Baseline, median (IQR)	3100 (2245-3850)	3321 (2994-3890)	0.480
After treatment, median (IQR)	2300 (2100-2750)	3487 (3115-3690)	<0.001
LPM-D variation after treatment, median	↓§425	↓63	
I-SHEMG-LPM (ms)			
Baseline, median (IQR)	120 (100-190)	440 (180-510)	<0.001
After treatment, median (IQR)	118 (100-150)	480 (240-541)	<0.001
I-SHEMG-LPM variation after treatment, median	↑5	↑30	
CPEMG-ID (ms)			
Baseline, median (IQR)	0 (0-0)	0 (0-0)	
After treatment, median (IQR)	380 (250-420)	195 (110-400)	0.105
CPEMG-ID variation after treatment, median	↑380	↑195	

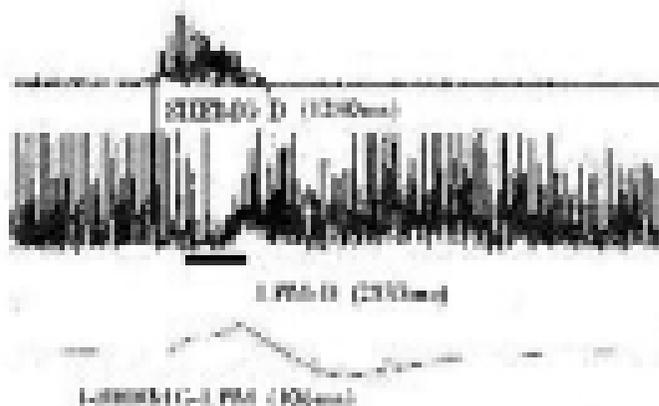
\*P value was obtained by Mann-Whitney U-test

†(IQR) = interquartile range

‡ ↑ = median increase

§ ↓ = median decrease

Control



500  $\mu$ V

200  $\mu$ V

50  $\mu$ V

Control signal after 1000 sweeps



500  $\mu$ V

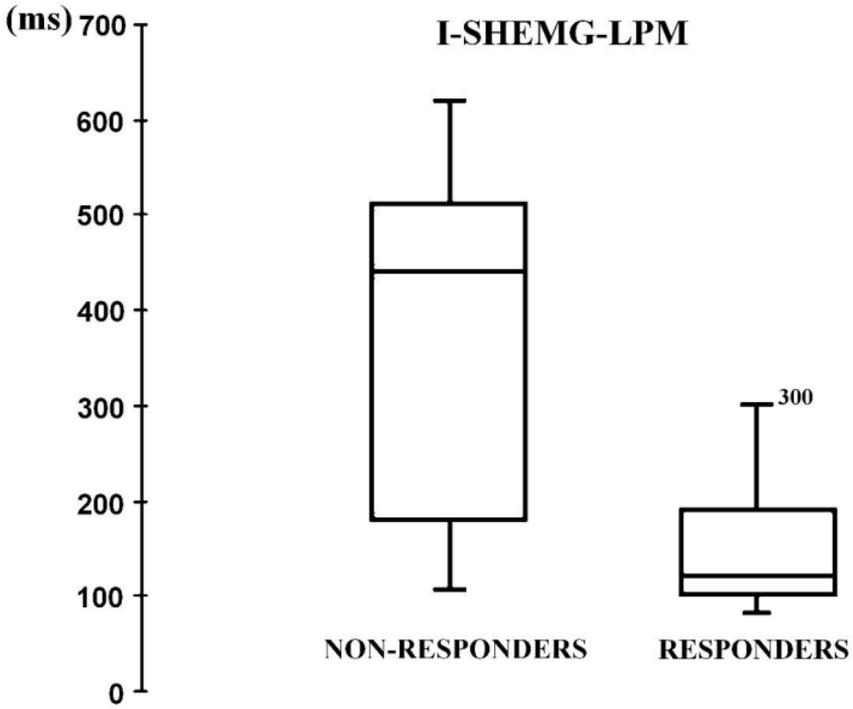
200  $\mu$ V

50  $\mu$ V

20  $\mu$ V

(a)

**I-SHEMG-LPM**



(b)

**SHEMG-D**

