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The importance of the reproducibility of oropharyngeal swallowing in amyotrophic lateral sclerosis. An electrophysiological study

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HIGHLIGHTS

- Electrophysiological evaluation of swallowing reproducibility in ALS using mathematical algorithms.
- Reproducibility of both the oral and pharyngeal phases of swallowing is markedly reduced in ALS.
- Electrophysiological study of swallowing is useful for management of swallowing abnormalities in ALS.

ABSTRACT

Objective: To investigate electrophysiologically the reproducibility of oropharyngeal swallowing in patients with ALS.
Methods: We enrolled 26 ALS patients, both with and without clinical signs of dysphagia, and 30 age-matched controls. The reproducibility of the electrophysiological signals related to the oral phase (electromyographic activity of the submental/suprahyoid muscles) and the pharyngeal phase (laryngeal-pharyngeal mechanogram) of swallowing across repeated swallows was assessed. To do this we computed two similarity indexes (SI) by using previously described mathematical algorithms.
Results: The reproducibility of oropharyngeal swallowing was significantly reduced both in patients with and in those without clinical signs of dysphagia, with more marked alterations being detected in the dysphagic group. The SI of both phases of swallowing, oral and pharyngeal, correlated significantly with dysphagia severity and disease severity.
Conclusions: In ALS different pathophysiological mechanisms can alter the stereotyped motor behaviors underlying normal swallowing, thus reducing the reproducibility of the swallowing act. A decrease in swallowing reproducibility could be a preclinical sign of dysphagia and, beyond a certain threshold, a pathological hallmark of oropharyngeal dysphagia.
Significance: Electrophysiological assessment is a simple and useful tool for the early detection of swallowing abnormalities, and for the management of overt dysphagia in ALS.

1. Introduction

Oropharyngeal dysphagia is one of the most frequent and critical clinical symptoms of amyotrophic lateral sclerosis (ALS). It has a severe impact on the patient's quality of life and invariably leads to malnutrition, dehydration and a high risk of aspiration pneumonia (Kasarskis et al., 1996; Kühnlein et al., 2008). Swallowing difficulties may appear at any stage of the disease, and typically have a progressive course, albeit with unpredictable changes over time. Not uncommonly, dysphagia is diagnosed only when swallowing function is already significantly impaired; this diagnostic delay can be attributed, in part, to the fact that adaptation mechanisms initially compensate for the relatively slow deterioration of bulbar function.

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On these bases, it seems reasonable to argue that swallowing function should be routinely evaluated in all patients with ALS, whether or not they have clear symptoms of dysphagia. Indeed, early recognition of swallowing dysfunctions, and identification of the underlying pathophysiological mechanisms, are fundamental to ensure early and targeted treatment strategies that could prevent severe complications and delay the need for percutaneous endoscopic gastrostomy (Barbiera et al., 2006; Kühnlein et al., 2008; Andersen et al., 2012).

As reported in the literature, there exist several procedures for assessing swallowing function in ALS; these include videofluoroscopy (VF), used alone or in conjunction with manometry (Briani et al., 1998; Higo et al., 2002,2004; Kawai et al., 2003; Goeleven et al., 2006), fiberoptic endoscopic evaluation of swallowing (FEES) (Leder et al., 2004; Ruoppolo et al., 2013), and oropharyngoesophageal scintigraphy (Fattori et al., 2006). Videofluoroscopic swallow evaluation is considered the most sensitive technique for detecting dysphagia, and it has also been shown to be capable of detecting preclinical abnormalities in non-dysphagic ALS patients who later develop swallowing problems (Briani et al., 1998; Kawai et al., 2003; Goeleven et al., 2006). However, VF is not always available, involves irradiation exposure, and adds to the evaluation costs and personnel requirements of the evaluation; these drawbacks make it unsuitable for use in regular follow-up assessments.

Electrophysiological assessment, on the other hand, is a non-invasive method that allows reliable and easily repeatable investigation of the physiological and pathological aspects of oropharyngeal swallowing (Ertekin et al., 1995; Perlman et al., 1999; Vaiman et al., 2004). In a recent study, we described a new electrophysiological approach for non-invasive evaluation of oropharyngeal swallowing (Alfonsi et al., 2015). In particular, we evaluated, in normal subjects, the reproducibility of the electrophysiological signals related to the oral and pharyngeal phases of swallowing by calculating a similarity index (SI) across repeated swallowing acts. In accordance with the concept that the act of swallowing is characterized by stereotyped motor behaviors modulated by different bolus properties (Jean, 2001), we recorded a high overall reproducibility of both the oral phase and the pharyngeal phase of swallowing in physiological conditions.

In the present study we evaluated the SI in ALS patients with and without clear symptoms of dysphagia as assessed by clinical examination and FEES. Our first aim was to investigate whether evaluation of the reproducibility of oropharyngeal swallowing, along with other classical electrophysiological measures such as the oropharyngeal interval and the duration of the electromyographic activity of the submental/suprahyoid muscles, might provide useful information on functional aspects of swallowing in ALS. Our second aim was to evaluate whether electrophysiological assessment could reveal swallowing abnormalities in non-dysphagic ALS patients when compared to age- and sex-matched healthy controls. Were this found to be the case, electrophysiological assessment might become a useful tool in the routine evaluation of oropharyngeal swallowing in patients with ALS, even at the initial stage of the disease.

2. Subjects and methods

2.1. Subjects

Twenty-six patients (11 female, 15 male; mean age = 61 ± 12 years, ranging from 32 to 80 years) with a diagnosis of definite or probable ALS according to the El Escorial criteria (Brooks et al., 2000), and 30 age- and sex-matched healthy controls (15 female, 15 male; mean age = 60 ± 9 years, ranging from 39 to 74 years) were enrolled in the study. The patients were consecutively recruited at first presentation or in the course of routine, three-monthly check-ups at the neurology clinic of the C. Mondino Institute of Neurology Foundation (Pavia, Italy). They had a mean Revised ALS Functional Rating Scale (ALSFRS-R) (Cedarbaum et al., 1999) score of 35 ± 5, and a mean disease duration of 19 ± 14 months. Eleven patients had a predominantly bulbar onset (8 bulbar and 3 bulbospinal) of the disease, while the other 15 had a spinal onset. Among patients with spinal onset of the disease, an electromyography (EMG) exam performed at the time of the evaluation revealed signs of denervation of bulbar muscles only in one subject (cricothyroid and thyroarytenoid muscles, with no involvement of the tongue).

All except for 4 patients were on treatment with riluzole. Other drugs used were antidepressants (4 patients), baclofen (2 patients), quinine (1 patient), diazepam (1 patient) and phenytoin (1 patient).

In all the patients, swallowing function was evaluated by a multidisciplinary team composed of a neurologist, a speech-language pathologist and an otorhinolaryngologist with experience in swallowing dysfunction. FEES was performed by the otorhinolaryngologist in each patient; the examination allows direct visualization of the oropharynx and larynx during swallowing. It was performed using liquid (3–5 cc), fruit jelly (3–5 cc), and solid (cracker) boluses. The patients were assessed for the following signs of dysphagia: spillage, penetration, aspiration, retention and piecemeal deglutition; impairment of swallow function was computed by Penetration/Aspiration Scale scores (Rosenbek et al., 1996). The Dysphagia Outcome and Severity Scale (DOSS) (O'Neil et al., 1999) was used to rate the functional severity of dysphagia based on clinical findings and FEES examination. On this basis, the patients were divided into two groups: those with and those without signs of dysphagia (Table 1). All patients were able to ingest orally. The exclusion criteria for both patients and control subjects were the presence of diabetes, intercurrent illness, odynophagia of any cause, esophageal and gastroenterological diseases, or neurological diseases (other than the motor neuron disease in the patient group).

The research protocol was approved by the Ethics Committee of the C. Mondino National Institute of Neurology. All the patients gave their informed consent to all the study procedures.

Table 1
Demographics and clinical characteristics of the subjects enrolled.

	Dysphagic ALS patients (n = 16)	Non-dysphagic ALS patients (n = 10)	Healthy controls
Sex (F/M)	7F/9M	4F/6M	15F/15M
Mean age (years) ± SD	64 ± 8	57 ± 15	60 ± 9
Onset (bulbar, B; bulbospinal, BS; spinal, S)	6 B; 3 BS; 7 S	2 B; 8 S	–
Disease duration (months) ± SD	17 ± 14	22 ± 13	–
Mean ALSFRS-R score ± SD	33 ± 4	38 ± 3.6	–
Mean DOSS score ± SD	3.6 ± 1.3	7 ± 0	–
Mean PAS score ± SD	3.0 ± 1.2	1.3 ± 0.5	–

ALSFRS-R: ALS Functional Rating Scale-Revised. DOSS: Dysphagia Outcome and Severity Scale. PAS: Penetration/Aspiration Scale.