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Amyotrophic Lateral Sclerosis: An Analysis of the Electromyographic Fatigue of the Masticatory Muscles

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Abstract: Amyotrophic lateral sclerosis is a chronic degenerative disease that affects motor neurons, thereby promoting functional changes in the human body. The study evaluated the electromyographic fatigue threshold of the masseter and temporal muscles of subjects with amyotrophic lateral sclerosis. A total of eighteen subjects were divided into two groups: amyotrophic lateral sclerosis (n=9) and disease-free control (n=9). The groups were equally divided according to gender (7 males, 2 females). The fatigue threshold was analysed using median frequencies obtained during the 5-second window (initial [IP], mid [MP], and final [FP] periods) of electromyographic signalling of the masseter and temporal muscles bilaterally, with reduction in muscle force during maximal voluntary dental clenching. Significant difference ($p<0.05$) in the left temporal muscle: IP ($p=0.05$) and MP ($p=0.05$) periods was demonstrated. The amyotrophic lateral sclerosis group showed a decrease in median frequency of the electromyographic signal of the masseter and temporal muscles compared to the control group. Amyotrophic lateral sclerosis promotes functional impairment of the stomatognathic system, especially at the electromyographic fatigue threshold of the masticatory muscles.

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Introduction

Amyotrophic lateral sclerosis is an adult-onset neurodegenerative disease that affects the upper and lower neuromotor system at the bulbar, cervical, thoracic, and lumbar levels (van Es et al., 2017). It prevents correct functionality of the skeletal striated musculature, leading to progressive muscle atrophy and paralysis (Martin et al., 2020; Wobst et al., 2020; Peters et al., 2021; Goutman et al., 2022).

Subjects who develop amyotrophic lateral sclerosis have a clinical picture of fasciculation, progressive muscle weakness, and muscle deterioration. Changes start at the extremities, usually unilaterally. Difficulties in speaking and performing voluntary movements may also be observed (Gonçalves et al., 2018). However, sensory function and intellectual capacity remain unaffected (Gonçalves et al., 2018).

The incidence of amyotrophic lateral sclerosis is not fully established and reported rates vary, depending on the studied population (Zapata-Zapata et al., 2019). Annually, the worldwide incidence is approximately 1 to 2.6 cases per 100,000 subjects, and the prevalence is 6 cases per 100,000 (Talbott et al., 2016).

Voluntary muscle activities involve mechanisms controlling the cerebral cortex and the formation of cross-bridges of myosin with actin filaments, resulting in muscle fiber contractions (Kawai and Jin, 2021). When assessing muscle activities, voluntary muscle fatigue stands out (Berchicci et al., 2013) that is induced by sustained contractions. Contractions is a determinant function of muscle performance (Oliveira et al., 2017; Akagi et al., 2020) and observational studies have provided evidence demonstrating fatigue in subjects with Amyotrophic lateral sclerosis (Nazemi et al., 2016; de Carvalho et al., 2019).

Muscular imbalances resulting from chronic degenerative diseases can be evaluated by specific methods using surface electromyography, which analyses biomechanical effects from the muscular fatigue process (Wanshi Arnoni et al., 2019). However, the electromyographic fatigue threshold of masticatory muscles in subjects with amyotrophic lateral sclerosis has not been identified so far.

In this study, the electromyographic fatigue threshold of the masseter and temporal muscles of subjects with amyotrophic lateral sclerosis was investigated. The null hypothesis to be tested is that there will be no difference between the groups.

Material and Methods

Study design

The study was approved by the local ethics committee (process # 13071913.3.3001.5419). All subjects were given written and verbal information before participating and gave their written consent.

A post hoc sample size calculation was conducted with $\alpha = 0.05$ and a power of 99%. For the main outcome: median values of the median frequency in the fatigue condition for the left temporal muscle (mean of initial periods, disease-free control group = 144.12 [24.58] and amyotrophic lateral sclerosis group = 183.10 [51.33]), an effect size of 0.96 was determined. The minimal sample size obtained

Table 1 – Comparison of body mass index and age (years) between amyotrophic lateral sclerosis group (ALSG) and disease-free control group (CG) using Student's *t*-test (p<0.05)

	Groups		
	ALSG	**CG**	**P-value**
Age	43.50 (4.50)	43.30 (4.90)	0.97
Body mass index	20.68 (1.53)	21.38 (1.46)	0.74

was 18 volunteers (9 in each group). Sample size calculation was performed with the G* Power software (v.3.1.9.2, Franz Faul, Universität Kiel, Germany).

We evaluated subjects with ALS (amyotrophic lateral sclerosis) who attended the Department of Neurosciences and Behavioral Sciences, Ribeirão Preto, São Paulo, Brazil. From an initial cohort of thirty subjects with amyotrophic lateral sclerosis, nine subjects with the disease (mean age [SD – standard deviation] = 43.5 [4.5] years) were selected for the amyotrophic lateral sclerosis group on the basis of the eligibility screening criteria.

All subjects with amyotrophic lateral sclerosis were medicated with riluzole. The potential drug interactions with caffeine, anti-inflammatory, tranquillizer, vasodilator, and antidepressants were explained, to avoid the reduction of drug potentiation. The diagnosis of the disease was confirmed by an experienced neurologist.

The disease-free control group (mean age [SD] = 43.3 [4.9] years) comprised of subjects with normal occlusion (Angle's class I), without temporomandibular disorder, with all permanent teeth (except third molars) who were matched by age, gender, and body mass index with the subjects in the amyotrophic lateral sclerosis group (Table 1). The groups were equally divided into males and females (7 males, 2 females).

The exclusion criteria included cognitive changes, necessity for ventilatory support, diseases of the anterior medullary horn, dementia, visual, autonomic, and sphincter disorders, temporomandibular disorders, absence of first permanent molars, and moderate to severe malocclusion. Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) questionnaire was used to determine the absence of temporomandibular disorders in both groups (Louca Jounger et al., 2017).

Analyses of the electromyographic signals were performed by a single trained professional. Intra-examiner calibration was performed for all analyses in this study. The reliability of the intra-rater was calculated via intra-class coefficient (ICC). Reliability was considered acceptable for electromyographic activity (ICC = 0.936).

Surface electromyography recordings

Surface EMG (electromyographic) activity recordings were performed using MyoSystem Br1_P84 electromyograph (Datahominis, Uberlândia, Minas Gerais,

Brazil) with four simple differential active sensors (Datahominis Ltda., Modelo DHT-easd; two 10-mm-long × 2-mm-wide silver chloride bars 10 mm apart). Input impedance of 1010 Ω/6, pf, bias current input of ±2 nA, common-mode rejection ratio of 110 dB at 60 Hz, and gain equal to ×20, was used to capture the electromyographic signals of the masseter and temporal muscles under the following conditions of the electromyographic fatigue threshold (Hz).

The sensors were positioned in the masticatory muscles by the same operator trained according to the Surface EMG for Non-Invasive Assessment of Muscles (SENIAM) recommendations (Hermens et al., 2000).The positioning point of the sensors was determined by dental clenching in maximum voluntary contraction, accompanied by digital palpation.

Fatigue threshold of the electromyographic signal was assessed using the median frequency spectrum. Muscle fatigue was determined by reduction of muscle force during maximal voluntary dental clenching (Gandevia, 2001; Di Palma et al., 2017).

The duration of maximum isometric contraction was measured. The case group had an average period of 29.48 ± 4.06 seconds, and the disease-free control group had an average period of 28.88 ± 5.01 seconds.

The signals were analogically amplified (1000× gain), filtered (0.02–2 kHz bandpass filter), and sampled by a 12-bit A/D converter board with a 4 kHz acquisition frequency. The processed electromyographic signals from the masseter and temporal muscles bilaterally, enabled the establishment of the raw signal that was used to derive median frequency values through the five-second window of the initial, mid, and final periods.

Statistical analysis

Data are presented as group mean values ± standard deviations (SD). The electromyographic data were tabulated and analyzed using the BM SPSS Statistics for Windows, version 22.0 (IBM SPSS, IBM Corp., Armonk, NY, USA). Data were submitted to Student's *t*-test ($p<0.05$).

Results

Table 1 shows a comparison of the data between the groups. No significant differences (95% confidence interval [CI]) were found between the groups in terms of age ($p=0.97$) and body mass index ($p=0.74$).

The median frequencies of the electromyographic signal of the masseter and temporal muscles bilaterally, during the initial (IP), mid (MP), and final (FP) periods were compared between the groups, as shown in Table 2. Statistical significance was demonstrated ($p\leq0.05$) in the left temporal muscle during the IP ($p=0.05$) and MP ($p=0.05$) periods. The amyotrophic lateral sclerosis group showed a decrease in the median frequency of the electromyographic signal of the masseter and temporal muscles compared to the control group.

Table 2 – Mean values, standard deviation, and statistical significance (p<0.05) of the median frequency spectrum (Hz) in the condition of electromyographic fatigue of the right masseter (MD), left masseter (ME), right temporal (TD), and left temporal muscles (TE): initial (IP), mid (MP), and final (FP) periods between amyotrophic lateral sclerosis (ALSG) and disease-free control (CG) groups

Muscles	Periods	Groups		P-value
		ALSG	CG	
RM	IP	139.12 ± 44.75	164.36 ± 48.03	0.26
	MP	135.63 ± 45.39	158.41 ± 43.83	0.29
	FP	132.41 ± 45.34	152.23 ± 41.81	0.34
LM	IP	130.60 ± 27.30	159.01 ± 49.36	0.15
	MP	120.72 ± 26.40	151.44 ± 42.34	0.08
	FP	116.65 ± 23.33	140.05 ± 41.69	0.16
RT	IP	138.32 ± 31.01	176.55 ± 50.77	0.07
	MP	133.20 ± 30.92	164.18 ± 44.99	0.10
	FP	126.55 ± 28.88	159.23 ± 48.72	0.10
LT	IP	144.12 ± 24.58	183.10 ± 51.33	0.05
	MP	138.15 ± 33.27	176.87 ± 46.07	0.05
	FP	139.25 ± 30.09	166.95 ± 40.51	0.11

Discussion

To the authors' knowledge, this is the first study to examine the electromyographic fatigue threshold to determine the functional patterns in subjects with amyotrophic lateral sclerosis. When comparing subjects with amyotrophic lateral sclerosis with disease-free subjects, the null hypothesis of this study was rejected because there was a significant difference between the groups.

The identification of muscle fatigue through electromyographic evaluation has been evidenced by the phenomenon of decreased median frequency of the electromyographic signal (Oliveira et al., 2005; Wanshi Arnoni et al., 2019; Qi et al., 2020). Although muscle fatigue is a well-studied subject, no results were found in any studies regarding electromyographic fatigue threshold of the masseter and temporal muscles in subjects with amyotrophic lateral sclerosis. This made it difficult to compare our results with those of previous studies.

According to Wanshi Arnoni et al. (2019), the median frequency spectrum in the electromyographic signal of the masseter and temporal muscles is lower than that in the control group without degenerative diseases, such as osteoporosis (Imagama et al., 2019). Our results concur with the findings of the literature, where the spectrum of the median frequency of the masseter and temporal muscles in the initial, medium, and final periods were shown to be smaller in the amyotrophic lateral sclerosis group.

The observed reduction in the median frequency spectrum of subjects with amyotrophic lateral sclerosis may be explained by the relationship between production and control of muscle strength, which are processes resulting from the central and peripheral nervous systems. It is known that the median frequency spectrum is a sensitive variable, which is associated with changes in the pattern of muscle recruitment and the absence of speed of propagation of the action potential of muscle fibers, causing changes in the physiological muscle profile (Escorcio-Bezerra et al., 2018; Musarò et al., 2019).

In subjects with amyotrophic lateral sclerosis, the motor units that have lost innervation, return to innervation after a certain period, due to the axon collateral sprouting that occurs in the surviving motoneurons. This influences the characteristics of the muscle fibers, modifies the recruitment patterns of the muscle fibers, and the production of strength; thereby reducing the synchrony of activation of muscle fibers with polyphasic potentials (Martineau et al., 2018). Thus, the action potential of the motor unit increases in size and decreases in functionality, with reduced amplitude and duration.

In the analysis of the electromyographic fatigue between the groups during the initial, mid, and final periods, a significant difference was found only for the left temporal muscle in the initial and mid periods. This muscle presented higher values in the disease-free control group. The other muscles studied did not show a significant difference.

Neurons are cells that make up the central nervous system, polarized with an extended axon, facing, with the function of maintaining energy homeostasis and mitochondrial integrity (Lin et al., 2017). Chronic mitochondrial stress has been mentioned in the main neurodegenerative diseases, including amyotrophic lateral sclerosis (Xie et al., 2015). The decrease in the median frequency spectrum in amyotrophic lateral sclerosis during the initial, mid, and final periods of the electromyographic signal may be directly related to mitochondrial stress. In this study, long-term cumulative mitochondrial stress was not evaluated, which can lead to axonal accumulation of damaged mitochondria, promoting less efficiency (Xie et al., 2015).

Thus, there is a direct relationship between the motor neuron and the action potential of the muscle fiber. The possible changes in this dynamic process that results from the combination of depolarization and repolarization could compromise muscle efficiency and reduce the spectrum of the median frequency of the electromyographic signal of the skeletal striated muscle of subjects with amyotrophic lateral sclerosis.

The decreased of the median frequency spectrum of the electromyographic signal in subjects with amyotrophic lateral sclerosis can also be explained by the interruption of blood flow, with a lack of nutrients and oxygen in the skeletal muscles that subjects with degenerative disease may present as clinical signs (Tanaka et al., 2003).

This study is important for determining the morphology and function of humans, especially the skeletal striated muscles of subjects with amyotrophic lateral sclerosis because it shows that disease alters the standard electromyographic. Therefore, the clinical relevance lies in the fact that longer dental procedures could take place in subjects with degenerative disease, as long as the dentist is careful to respect the functional conditions of the masticatory muscles that can fatigue more easily, when compared to groups without the disease.

This study has several limitations. First, the sample size is small. Second, significant differences between the groups and monitoring of the subjects longitudinally would provide more information. However, in this study, the electromyographic analysis was performed for only a single time point.

Conclusion

The authors of this study suggest that amyotrophic lateral sclerosis promotes functional impairment of the stomatognathic system; in particular, in the electromyographic fatigue threshold of the masticatory muscles.

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