Evaluation of T2 heterogeneity in patients with ALS

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Introduction

The focus of the study was to examine motor unit distribution in patients with ALS using T2 MRI and exercise. The neuromuscular system in ALS and other motor neuron diseases or nerve injuries may undergo a period of muscle denervation (with motor neuron death) followed by reinnervation. This would sustain muscle volume and muscle function during disease processes. Previously, a computer model of muscle denervation-reinnervation suggested that the resulting increased density of innervated cells within motor unit territories should result in increased heterogeneity of MRI –measured muscle T2 increase after moderate exercise (1,2). Therefore, the heterogeneity of muscle T2 was evaluated in patients with ALS compared to controls before and after moderate exercise.

Methods

Eleven subjects with probably or definite ALS (4 females, 62±7 [SD] yrs) were compared to nine healthy age matched controls (2 females, 59±9 yrs). The dorsiflexor maximal force (MVC) was measured with the ankle fixed at 120° using a custom exercise device. Following resting MRI (described below), subjects performed 2-3 minutes of dynamic dorsiflexion at a target load of ~30% MVC using resistive elastic tubing. Post exercise images were immediately acquired via a standard quadrature T/R extremity coil after the dynamic exercise. Dual standard spin echo images (TR=1500, TE1=24-30ms, TE2=60ms, Sl. Thick = 1.0 cm, 384x224 acquisition matrix) were collected at 3T MRI for all but 2 subjects in each group (2 CON and 2 ALS were tested at 1.5T). Fifteen axial images were acquired, which encompassed the largest CSA of the anterior compartment (AC). Analyses were done on the largest 3 slices. The muscle CSA was manually traced excluding visible fat and blood vessels using custom in-house software (Winvessel). All protocols were approved by the Institutional Review Board and Michigan State University and Mary Freebed Rehabilitation Hospital. Muscle T2, T2 change with exercise, the standard deviation of muscle T2 (T2SD, evaluated on a pixel-by-pixel basis) and exercise characteristics were compared using independent t-tests with significance at $p<0.05$; Pearson correlation coefficient was used to examine correlation between MVC and T2. ALS subjects were separated into 2 groups based on presence (ALST2+) or absence (ALST2-) of an exercise induced T2 response. Resting T2 for the medial gastrocnemius muscle (MG) was also compared between groups. Data are presented as mean ± SD.

Results

Resting and post exercise T2 images are shown in Fig.1. Initial inspection of the group mean exercise response for all ALS patients, suggested a bimodal T2 distribution post-exercise, which would indicate heterogeneity (Fig 2, All ALS). However, the T2 post-exercise reflects two distinct groups of ALS patients, those with an exercise T2 shift (ALST2+) and those without (ALST2-) (Fig.2). When comparing all ALS to controls, ALS had 50% smaller T2 change; this was attributed to the ALST2- group. Resting T2 was significantly higher for ALS vs. CON for AC and MG; this was also attributed to the ALST2- group (Table 1). The AC T2SD rest was significantly greater for all ALS vs. CON and greater in ALST2- vs. ALST2+; T2SD in AC post-exercise and in MG approached significance between ALS and CON ($p=0.051$, Table 1). MVC was greater in CON vs. all ALS and 50% higher in ALST2+ vs. ALST2- (Table 1). There was a significant negative correlation ($r=0.782$) between dorsiflexor MVC and resting AC T2 for ALS, but not CON.

Fig. 1: T2 images

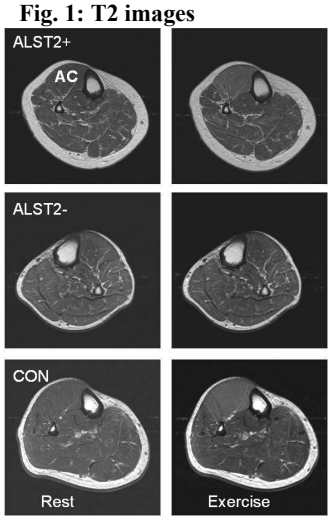
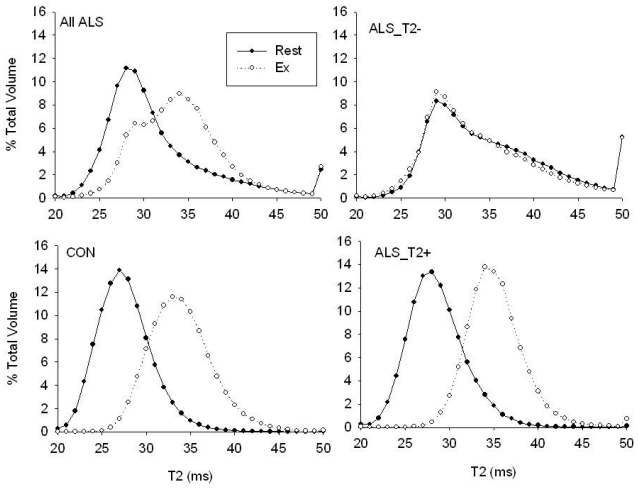


Table 1.

Values: mean ±SD	ALST2- (n=5)	ALST2+ (n=6)	All ALS (n=11)	CON (n=9)
MVC (N/cm²)	9.1±3.9	20.8±4.8*	15.5±7.4	23.9±3.9†
AC Rest T2 (ms)	35.6±5.0	28.7±1.4*	31.9±5.0	28.2±1.7†
AC T2SD Rest	6.2±4.1	3.3±0.6	4.6±3.0	2.6±0.5††
AC T2 Ex % change	-0.8± 2.5	20.4±11.3*	10.8±14	23.4±8.0†
AC T2SD Ex	6.0±3.3	3.4±0.4	4.6±2.5	2.8±0.5†
MG T2 Rest (ms)	41.9±6.9	34.0±3.5*	37.6±7.0	30.1±2.1†
MG T2SD Rest	4.97±1.53	3.71±1.09	4.28±1.40	3.30±0.65††

*ALST2- vs. ALST2+, $p<0.05$, †All ALS vs. CON, $p<0.05$, †† All ALS vs. CON, $p<0.06$

Fig. 2: T2 distribution before and after exercise



Discussion

Contrary to our hypothesis, exercise T2 heterogeneity was not observed in ALS compared to controls. Our findings suggest that reinnervation associated with ALS may not result in motor units that reflect fiber regrouping. Recent biopsy findings from ALS also support this conclusion (3). Exercise T2 responses were not evoked in half the ALS patients, whom also had weak muscle strength. Resting T2 and T2SD was elevated in both the AC and MG of ALS patients compared to controls. This elevation of resting T2 is suggestive of muscle denervation (4). Although exercise T2 heterogeneity was not observed, resting muscle T2 may be useful to evaluate the onset and recovery or progression of muscle denervation as well as the distribution of muscle denervation in ALS. Further studies on patients lacking an exercise T2 change may provide insight to clinical outcomes and disease progression.

References

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