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Letter to the editor

Physical therapy improves lower limb muscle strength but not function in individuals with amyotrophic lateral sclerosis: A case series study

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Dear Editor

Amyotrophic lateral sclerosis (ALS) is characterized by degeneration of upper and lower motor neurons. Initial muscle weakness usually occurs in isolated muscles and is followed by progressive weakness and functional limitations. ALS has no cure, although a few agents can inhibit the progression of symptoms [1,2]. Therefore, individuals with ALS must maintain activities of daily living (ADL) as much as possible with symptomatic treatments.

Exercise for mild to moderate muscle weakness in patients with ALS may be effective for maintaining or improving muscle strength and ADL [1]. However, we have few reports on the effects of exercise in patients with ALS and the results of interventions for muscle strength are inconsistent [3–6]. Thus, the relationship between the severity of ALS and the effectiveness of exercise is unclear and the effect size of exercise is also unclear. Here, we investigated the short-term effects of physical therapy on lower-limb muscle strength in individuals with ALS.

This study was approved by the Osaka University Medical Hospital ethical committee. In accordance with provisions of the ethical committee, the research plan was published (http://www.hosp.med.osaka-u.ac.jp/research/data/rehabilitation1.pdf) and informed consent was not required. Personal information was anonymized.

We included 10 individuals with ALS who were admitted to the Osaka University Medical Hospital and underwent physical therapy from April 2015 to December 2016. ALS was diagnosed according to the Awaji criteria [7]. Eligibility criteria were the ability to walk 10 m or more without an assistive device and no use of respiratory assistance during the daytime.

Physical therapy was performed daily on weekdays for about 30 min in general. Muscle strengthening exercises for lower limbs were performed with weights and a machine in the closed kinetic chain position. Additionally, respiratory, gait and stair-climbing exercises were performed. Muscle strengthening exercises were usually performed for about half of the session and other exercises were performed during the other half. Exercise intensity was moderately adjusted based on the individual's fatigue, as evaluated by the modified Borg scale (5/10) for lower limbs. The duration of physical therapy was 2 to 3 weeks.

In addition to knee extension muscle strength, gait (gait score) and stair climbing (stair-climbing score), which are subscales of the ALS functional rating scale-revised (ALSFRS-R) [8], were evaluated at the start and end of physical therapy. The scales are rated from 0, cannot do to 4, normal ability. Scale scores are summed, for a total score of 0, worst, to 48, best condition. Spasticity measured by the modified Ashworth scale was rated from 0, no increase in muscle tone, to 4, affected part(s) rigid in flexion or extension.

Knee extension muscle strength was measured 3 times by using a hand-held dynamometer (μ-Tas F-1, ANIMA, Japan) as described [9] and calculated as mean of the 3 knee extension muscle strength measures × lower-leg length/body weight; the standardized scores were separated into stronger and weaker limbs for each individual. On the basis of the average knee extension muscle strength value for a healthy person (1.3 Nm/kg) [10] (normal value), the knee extension muscle strength value was classified as above normal (AN) and below normal (BN) for the 20 limbs at the start of therapy. Improvement in knee extension muscle strength value at the end of physical therapy was calculated as knee extension muscle strength (end of therapy)–knee extension muscle strength (start of therapy)/knee extension muscle strength (start of therapy) × 100 as previously described [6].

Statistical analysis involved the Wilcoxon signed-rank test used to examine differences in knee extension muscle strength, gait score and stair-climbing score between the start and end of therapy with EZR v1.35 (Saitama Medical Center, Jichi Medical University, Saitama, Japan). $P < 0.05$ was considered statistically significant.

The mean (SD) ALSFRS-R total score was 41.0 (4.6) (Table 1). For all participants, the ALSFRS-R total score was > 30, and for 8, it was > 40. For 5 individuals, the gait score was 4 and for 2, the stair-climbing score was 4. No individual exhibited cramps and scores for spasticity on the modified Ashworth scale were 1 or > 1. Moreover, no individual discontinued or reduced the intensity of the physical therapy; no adverse events were observed.

Knee extension muscle strength significantly improved for both stronger and weaker limbs ($P < 0.01$), although gait and stair-climbing scores did not significantly improve (Table 2). Mean (SD) improvement rates were 8.9% (12.4) for AN limbs and 31% (31.5) for BN limbs (Table 3).

To our knowledge, this is the first report showing improved muscle strength significantly in individuals with ALS. In ALS, muscle weakness progresses faster because motor neuron degenerates rapidly. Collateral sprouting reaches the limit as motor neurons degenerate. Residual motor neurons that dominate over the muscle fibers several times more than normal motor neurons get overloaded; thus, muscles become functionally close to limits, even during ADL [1] and eventually lose their response to

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Table 1
Demographic and medical information for individuals with amyotrophic lateral sclerosis (ALS) undergoing physical therapy of lower limbs ($n = 10$).

Age (years), mean (SD)	61.9 (11.7)
Sex (male: female)	9:1
Site of onset (upper limb: lower limb: bulbar)	4:1:5
Treatment	Riluzole + edaravone ($n = 4$), Riluzole ($n = 2$), none ($n = 4$)
Respiratory assistance	BIPAP during nighttime ($n = 6$), None ($n = 4$)
Time since disease onset (months), mean (SD)	30.6 (31.3)
Duration of physical therapy (days), mean (SD)	17.9 (3.6)
%FVC (%), mean (SD)	68.8 (19.4)
MRC sum score, mean (SD)	45.7 (7.1)
ALSFRS-R, mean (SD)	41.0 (4.6)

ALSFRS-R: ALS Functional Rating Scale-Revised, BIPAP: bilevel positive airway pressure, FVC: forced vital capacity, MRC: Medical Research Council.

Table 2
Knee extension muscle strength, gait score and stair climbing score at the start and end of physical therapy ($n = 10$).

		Start	End	*P* value
Knee extension muscle strength (Nm/kg)[a]	Stronger limbs	1.40 (0.73)	1.59 (0.68)	0.0059
	Weaker limbs	1.19 (0.64)	1.38 (0.61)	0.0098
Gait score		3.50 (0.53)	3.60 (0.52)	1.00
Stair-climbing score		2.90 (0.74)	3.10 (0.57)	0.35

Data are mean (SD).
[a] See text for calculation of knee extension muscle strength value.

Table 3
Knee extension muscle strength at the start and end of therapy and improvement for AN and BN limbs.

	Start	End	Improvement (%)
AN limbs ($n = 9$)	1.92 (0.51)	2.06 (0.45)	8.9 (12.4)
BN limbs ($n = 11$)	0.78 (0.15)	1.01 (0.24)	31 (31.5)

On the basis of the average KEMS value for a healthy person (1.3 Nm/kg) [9] (normal value), the KEMS value was classified as above normal (AN) and below normal (BN) at the start of therapy.

exercise. All our participants were ambulatory and did not need an assistive device, and the mean (SD) ALSFRS-R score was 41.0 (4.6), representing mild disease severity. Therefore, the response to physical therapy was sustained in our participants and the effects of physical therapy could exceed the progression of symptoms during the intervention. Regarding the physiological mechanism of muscle strength, muscle hypertrophy occurs 1 to 2 months after starting muscle-strengthening exercises and recruitment precedes muscle hypertrophy [11]; thus, we considered the effect of this recruitment in our participants. However, we could not determine which factors had a strong influence.

The gait and stair-climbing scores did not improve, even though knee extension muscle strength improved. Five patients had a gait score of 4, so a ceiling effect might explain the lack of improvement in gait. However, the stair-climbing score did not change significantly either. The improvement in knee extension muscle strength might be insufficient to improve function such as gait and stair climbing. However, disease progression is fast with ALS and whether exercise improved gait function or ADL for about 1 month in previous studies was unclear [2,6]. Therefore, whether a longer intervention period can improve muscle strength further and improve function and ADL remains to be studied.

Improvement was better for limbs with BN than AN values for knee extension muscle strength. Muscle weakness with ALS is caused by disease progression and disuse [1]. Even ambulatory individuals with ALS need to adapt to a more sedentary lifestyle to accommodate for the difficulties and risks associated with ambulation and a variety of symptoms such as muscle weakness [6]. Therefore, knee extension muscle strength being lower at the start of therapy for BN than AN limbs might be due to muscle weakness with disuse. Lunetta et al. [2] reported that exercise for individuals with ALS could improve muscle weakness due to disuse. Therefore, with physical therapy, knee extension muscle strength may recover to normal values in ambulatory individuals with ALS without the use of an assistive device. However, the motor unit number is not correlated with muscle strength because of collateral sprouting in individuals with ALS at an early stage [12]. Thus, muscle strength is normal, but the muscle itself might not be normal, which might explain the better improvement for BN than AN limbs. Thus, improving knee extension muscle strength fully may be difficult for AN limbs. In a study of moderate-intensity physical therapy in ambulatory patients with spinal and bulbar muscle atrophy [13], patients with low function showed improvement, with no change in patients with high function. The authors suggested that the exercise intensity might be insufficient for individuals with high function. Further studies are required to determine whether improvements over normal values can be obtained.

In this study, the sample size was very small and the selection for disease type and sex may have been biased. The duration of the acquired effects needs to be studied further.

Physical therapy for ambulatory individuals with ALS who do not use an assistive device could improve knee extension muscle strength but not functions such as gait and stair climbing. The physical therapy may help improve muscle weakness due to disuse. The response to physical therapy in such ambulatory individuals can be sustained. Physical therapy to achieve normal strength before gait impairment occurs is necessary.

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Disclosure of interest

The authors declare that they have no competing interest.

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