Journal of the Neurological Sciences 361 (2016) 128–130

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Clinical short communication

Relative preservation of finger flexion in amyotrophic lateral sclerosis☆,☆☆,★,★★,☆☆☆,★★★

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ARTICLE INFO

Article history:
Received 25 June 2015
Received in revised form 15 November 2015
Accepted 17 December 2015
Available online 21 December 2015

Keywords:
Clinical neurology
Neuromuscular
ALS
Motor neuron disease
Clinical sign
Upper-limb weakness
Finger flexion
Finger extension

ABSTRACT

A characteristic pattern of intrinsic hand muscle involvement—known as the split hand sign—is typical of ALS; differential involvement of forearm muscles has not been examined systematically.
After observing that finger-flexion was often preserved in ALS, despite severe weakness of finger-extension, we assessed the relative involvement of these two muscle groups in a cohort of patients with ALS.
We found finger-flexion to be relatively preserved, when compared with finger-extension, in patients with ALS. In many cases finger-flexion is only minimally affected, even when finger-extension is totally paralyzed.
The reasons for this predilection are unclear, but may be similar to those underlying the split-hand sign. Nevertheless, the discrepancy may provide another useful clinical clue in patients presenting with distal upper-limb weakness.

1. Introduction

Neuromuscular diseases may be recognized by a characteristic pattern of muscle weakness; examples include: distal upper-limb weakness in multifocal motor neuropathy [1], oculobulbar involvement in myasthenia gravis [2], finger flexor and quadriceps predilection in sporadic inclusion body myositis [3] and sparing of the quadriceps in hereditary inclusion body myopathy [4].

Advanced amyotrophic lateral sclerosis (ALS) is characterized by sparing of extra-ocular and sphincter muscles—no other voluntary muscle group is spared consistently in late disease [5,6]. The split hand sign describes preferential involvement of lateral intrinsic hand muscles, with relative sparing of medially placed muscles [7–12]. We observed that in the early stages of ALS, finger-flexion (FF) was often unaffected in patients with pronounced weakness of finger-extension (FE) (video clip). This led us to assess the relative involvement of these two muscle groups on a systematic basis.

2. Methods

Muscle strength of patients visiting our ALS clinic between 2009 and 2013 was assessed using the MRC scale for muscle strength (by MG). MRC grade 4 was subdivided into 4+, 4 and 4−. We collected data from patients with suspected, possible, probable or definite ALS, but limited analysis to patients eventually diagnosed with probable or definite ALS, according to revised El Escorial Criteria [13]. Data analysis was retrospective, using data in our ALS database.

For each of the muscle groups (FF and FE) muscle force was graded separately in each upper-limb. We then determined the first occasion on which moderate or severe weakness was present (MRC < 4) in each tested muscle group. Muscle strength at that time-point was compared to the strength of the ipsilateral antagonist muscle group at the same time-point, yielding a data-pair. The upper-limbs of each patient were analyzed separately, thus each patient could provide between 0

☆ Dr. Ari Shemesh reports no disclosures.
☆☆ Dr. David Arkadir reports no disclosures.
★ Dr. Marc Gotkine reports no disclosures.
★★ A.S. had substantial contributions to the conception and design of this work, the acquisition and interpretation of the data, drafting the work and final approval of the submitted version.
☆☆☆ D.A. had substantial contributions to the conception and design of this work, the interpretation of the data, drafting the work and final approval of the submitted version.
★★★ M.G. had substantial contributions to the conception and design of this work, the acquisition and interpretation of the data, drafting the work and final approval of the submitted version.

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http://dx.doi.org/10.1016/j.jns.2015.12.028
0022-510X/

and 4 data-pairs for analysis. Our institutional review board approved the study.

3. Results

A total of 346 patients fulfilling ALS diagnostic criteria provided data for our analysis; this corresponds to a total of 1384 potential data-pairs (692 for each muscle group). Data from these patients yielded 312 data-pairs due to FE-MRC falling below 4, whereas 157 data-pairs were captured due to FF-MRC falling below 4. In all cases in which weakness FF-MRC was <4, ipsilateral FE was either as weak or weaker (Fig. 1, upper section). Conversely, whenever FE-MRC was <4, FF was either as strong or stronger (Fig. 1, lower section). These results were highly significant (McNemar's test, $P<0.001$). In 62.8% (196/312) of cases of MRC-FE ≤ (−) 4, the strength of ipsilateral FF was preserved or only mildly affected (≥4). This pattern was preserved, even when upper-limbs with increased tone were excluded from analysis (data not shown).

4. Discussion

This data demonstrates that FF is relatively preserved, when compared with FE, in patients who ultimately receive a diagnosis of ALS. Moreover, in many cases FF was only mildly affected, even when FE was paralyzed; this implies that this pattern of predilection is preserved until complete paralysis of the fingers occurs with disease progression. The difference between these muscle groups was present even when analysis was limited to upper-limbs without increased tone, arguing against the phenomenon being a manifestation of spasticity. The predilection may be due to differences in functional reserves—as the FF muscle group is physiologically more powerful than the FE group—or to different susceptibilities of the neuronal populations related to these two muscle groups.

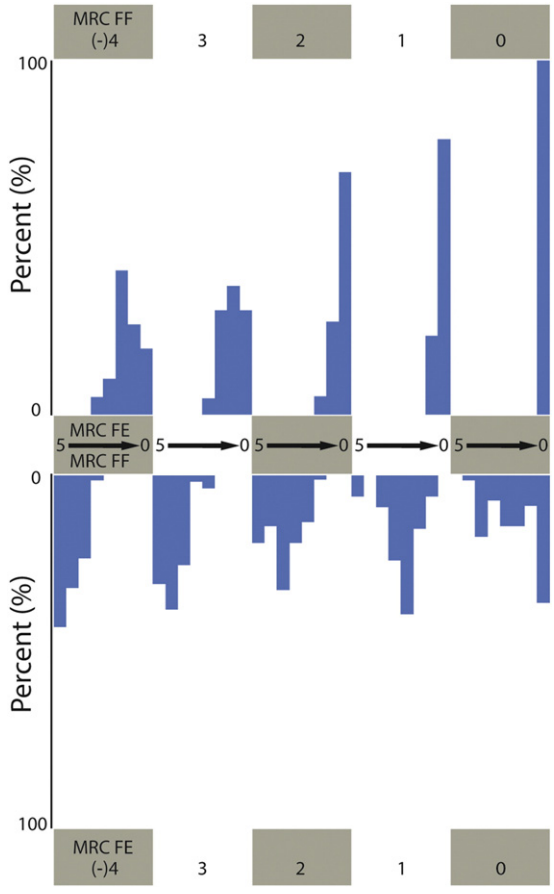

Fig. 1. Relative muscle force of finger flexors (FF) and extensors (FE) in ALS. The upper part of the figure presents the relative weakness of FE as FF weakness progresses. Strength was measured based on the MRC scale. The lower part of the figure presents a 'mirror image' - the relatively preserved strength of FF, compared to FE weakness.

The pathophysiological basis of the discrepancy between FF and FE may be similar to that underling the split hand sign. The APB and FDI muscles are more generously represented in the motor cortex than other intrinsic hand muscles, suggesting a cortical origin for the split hand sign [9]. More importantly, cortical hyperexcitability—a hallmark of ALS—is observed in all intrinsic hand muscles of patients, although most prominently in the APB and FDI muscles [14,15]. Furthermore, cortical excitability in healthy controls also follows a split hand pattern [16]; thus differential baseline cortical excitability is likely to be underlying the development of the split hand phenomenon. As such, it would be interesting to examine differences in cortical excitability parameters between muscles involved in FF compared to those involved in FE, in patients with ALS and healthy controls. We hypothesize that the correlates of cortical hyperexcitability will be most prominent when measured in FE muscles, compared to FF muscles, thus extending the pattern observed in the intrinsic hand muscles, to the forearm.

Finger flexion tasks are often chosen in fMRI studies on the basis of simplicity [17,18]. These studies demonstrate increased activation of areas usually involved in planning and initiation of movement [18] as well as subcortical structures [17], in patients with ALS. Increased activation observed during FF tasks in ALS seems less likely to be due to new synaptic connections and is probably related to enhanced recruitment of existing resources—a phenomenon which may be related to the increased effort needed to perform the tasks [19]. To our knowledge, no study has investigated how fMRI activation patterns change in ALS using separate FF and FE paradigms. Conclusions derived from paradigms focusing on a muscle group that is selectively preserved in ALS—namely FF—may not be able to be extrapolated to other muscle groups. For example, the increased cortical recruitment in FF paradigms could be related, in part, to the effort needed to modulate FF strength in the presence of disproportionally weak antagonist muscles.

Since completing this study, we have found this pattern to be a useful clinical clue, in patients presenting with undiagnosed progressive upper-limb weakness. Unlike preservation of eye movements, which is observed even in very advanced disease, the discrepancy between FF and FE can only be appreciated in earlier stages, before limb paralysis is complete; in this respect its clinical utility is similar to the split hand sign.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jns.2015.12.028.

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