MRI detection of human motor unit fasciculation in Amyotrophic Lateral Sclerosis.

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Introduction

Amyotrophic lateral sclerosis (ALS), a progressive degenerative motor system disorder, has an incidence in the US of over 6,000 individuals per year. ALS is characterised by fasciculation; random and irregular muscle twitching produced by the involuntary activation of individual skeletal motor units. Fasciculation is a promising biomarker for earlier disease diagnosis, since it occurs before motor unit death has occurred. DWI studies in healthy muscle often show spontaneous, transient signal voids postulated to be micro-movement of muscle (1), which we further hypothesise represent firing of individual motor units and as such could provide a novel and sensitive biomarker of fasciculation in patients. In this study we aimed to characterise the ability of DWI to detect motor unit activity in healthy subjects and apply the technique to study fasciculation in patients with ALS.

Methods

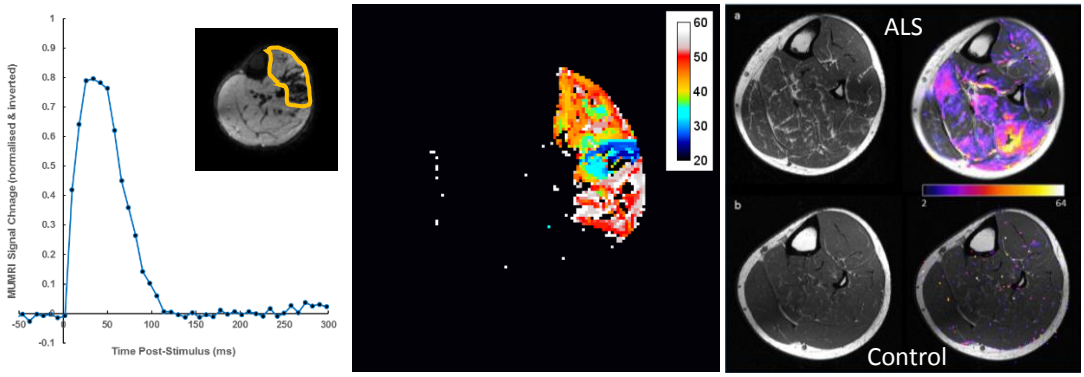
All measurements were made using a 3T Philips Achieva scanner with a FlexM coil pair placed around the leg. Scans used a SW-DWI sequence with 1.5 mm resolution and 7.5-10 mm thick axial slices (TR/TE=1000/36ms).

Characterisation of DWI sensitivity to motor unit activity was performed using electrical stimulation of the peroneal nerve with scan acquisition gated and timed relative to the stimulus. The temporal dynamics of the DWI response (-10 to 200 ms) and b value dependence (0 to 300 smm^{-2}) were determined and compared to known muscle twitch characteristics. Motor unit distribution was assessed using incremented nerve simulation (50μA steps).

Spontaneous DWI measured activity was assessed in 4 patients with ALS and 4 healthy controls using a 6 slices SE-DWI sequence and time series data collected over 3 minute intervals. Fasciculation events (signal voids) were counted on each slice at each time point and compared between groups. All studies had ethical approval and all subjects provided written, informed consent.

Results

An example dynamic curve of the DWI signal following a single electrical nerve simulation pulse is shown (*left*). The response reaches a peak change around 40-50 ms and then returns to baseline by ~120 ms. This matches well to the literature data on muscle twitch dynamics (2). Increasing nerve stimulus current causes an expanding area of signal void as successive motor units reach threshold for activation (*middle panel* where colour indicates image frame where each pixel activates), again matching expected behaviour of motor units.



ALS patients showed high numbers of spontaneous fluctuations (99.1/minute, range 26-161) while control subjects showed only occasional events (7.7/minute, range 4.3-9.7) as illustrated (*right*).

Discussion

Our data demonstrate that DWI acquisitions are highly sensitive to micro muscle contraction caused by firing of motor units – we therefore refer to this method of motor unit MRI (MUMRI) – and our observations define a new (non-diffusion) contrast mechanism for DWI scans. High numbers of fasciculation were detected in ALS patients despite some having no evidence of clinical fasciculation, suggesting MRI is potentially more sensitive than current routine clinical assessment.

References

1) Steidle, G. et al, NNR in Biomed, 2015. **28**(7): p. 801-810. **2)** Leitch, M. et al, J Neurophysiol, 2015. **114**(2): p. 1083-1089.

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