Masseter Muscle Volume Correlates with Disease Duration in Adults with Myotonic Dystrophy Type 1 (DM1)

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BACKGROUND

- Myotonic dystrophy type 1 (DM1) is a highly variable, multisystem condition and the most common form of muscular dystrophy in adults.
- Recent advances in understanding the genetic and molecular basis of DM1 have driven the development of potential therapies and, more recently, the first clinical trials in human subjects.
- There is therefore a growing need to define objective measures of DM1 disease severity for use in the context of clinical trials.

AIMS

This study sought to explore the clinical correlations of masseter muscle volume, imaged during standard MRI brain sequences, in a cohort with adult-onset DM1. The masseter muscle was selected as it is easy to identify, and is less subject to disuse atrophy compared with the limb muscles.

METHODS

- 46 individuals with adult-onset DM1 and 20 age-matched controls were recruited as part of the DM1-Neuro study.
- Participants completed self-reported symptom questionnaires, including the Myotonic Dystrophy Health Index (MDHI), DM1-ActivC, Fatigue and Daytime Sleepiness Scale, Beck Depression Inventory and McGill Pain Scale.
- DM1-affected participants were genotyped for CTG repeat length by SP-PCR, allowing estimation of modal (MAL) and progenitor (ePAL) allele length.
- Those with no contra-indications underwent a single brain MRI. Masseter volume was measured in male participants only leaving 17 affected and 12 control participants for analysis.
- T1-weighted 3D images were loaded to a viewer (ITK-SNAP v3.6.0) and the left masseter muscle manually segmented in an axial plane by a blinded rater (Figure 1). Four scans scored by an independent rater were found to be highly consistent (p = 0.003; Adj R^2 = 0.990). Masseter muscle volume was corrected for lean body mass (LBM); corrected masseter volume (cMV) = masseter muscle volume (mm3)/LBM.

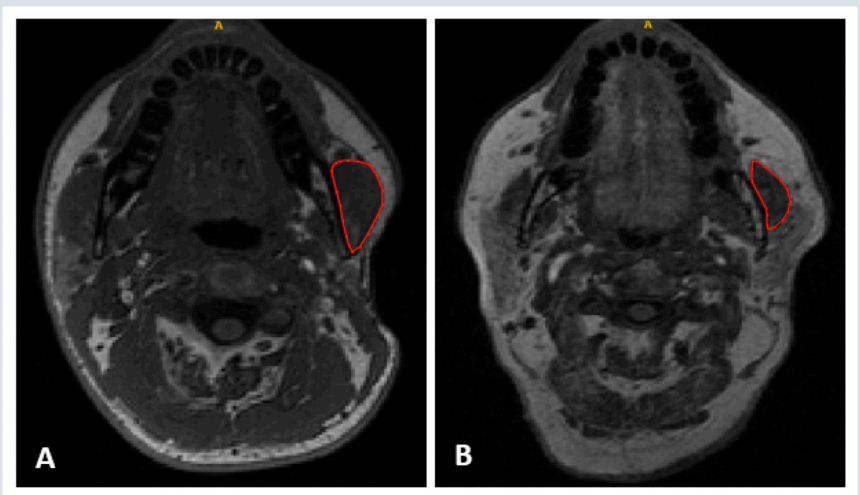

Figure 1. MRI scans at the same level for a control participant (A) and DM1-affected participant (B). Generalised muscle atrophy with extensive fatty infiltration is seen in the affected participant.

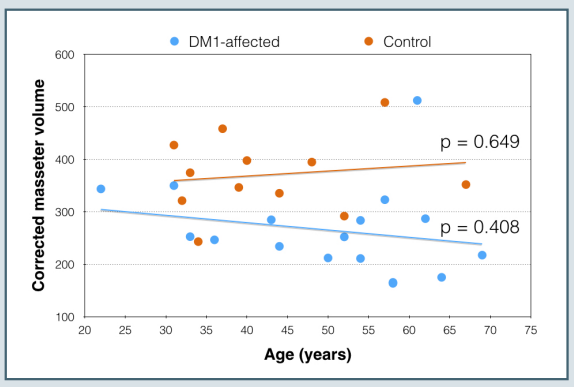

Figure 2. Trend towards decreasing cMV with increasing age in DM1-affected participants.

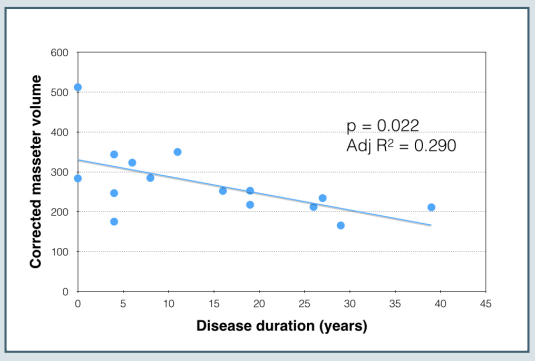

Figure 3. Significant inverse correlation of cMV with disease duration.

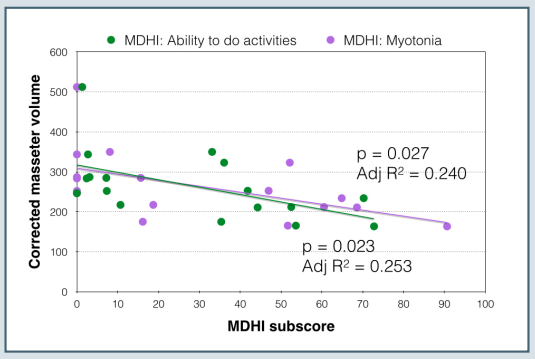

Figure 4. Significant inverse correlations with MDHI sub-measures of myotonia and ability to do activities.

RESULTS

- Mean cMV was significantly lower in DM1-affected participants when compared with controls (p = 0.001). Lean body mass was also significantly reduced in the affected cohort (p = 0.002), consistent with generalised muscle atrophy.
- A trend towards decreasing cMV with increasing age amongst affected participants was identified which did not reach statistical significance (p = 0.408, Adj R^2 = -0.018) but this model improved with in multivariate analysis including (log) ePAL (p = 0.182; Adj R^2 = 0.104). This trend was not present in the control participants (Figure 2).
- A significant inverse correlation of cMV was observed with disease duration (p = 0.022, Adj R^2 = 0.290) suggesting cMV may be a good marker of primary disease process (Figure 3).
- A trend towards correlation of cMV with MDHI sub-measures of a motor theme was demonstrated; correlations with myotonia (p = 0.027, Adj R^2 = 0.240) and ability to do activities (p = 0.023, Adj R^2 = 0.253) sub-scores reached statistical significance (Figure 4).
- These findings suggest that cMV may correlate to some extent with symptoms of direct clinical relevance to patients. No significant correlations were identified with other self-reported symptom questionnaires (Table 1).

	P Value	Adjusted R^2
Age	0.408	-0.018
(log)ePAL	0.158	0.070
MAL	0.219	0.039
Disease Duration	0.022	0.290
MDHI Ability to do Activities	0.023	0.253
MDHI Myotonia	0.027	0.240
MDHI Mobility	0.100	0.113
MDHI Upper Extremity	0.058	0.167
DM1ActivC©	0.260	0.023

Table 1. Linear regression analysis of corrected masseter volume against other study measures.

CONCLUSIONS

- cMV is reduced in males with adult-onset DM1, and correlates with disease duration and some self-reported muscle symptoms in a clinically and genetically well characterised cohort.
- This suggests that cMV has potential as a marker of disease severity. Thus meaningful objective outcome data regarding both the central and peripheral effects of DM1 could be gained from a single brain MRI.
- Sample size was small, therefore further analysis of the masseter muscle in larger mixed gender cohorts using additional imaging modalities is warranted.

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