Supplemental Methods e-1.

Predicted methylation:

The predicted methylation model used here is taken from a prior publication and derived from a large cohort of FSHD1 (n=186) and healthy controls (n=254).[9] A linear mixed effects model was used to determine the relationship between log transformed CpG methylation (chromosomes 4q and 10q) and repeat array sizes, with a random effect per family. The predicted methylation for FSHD1 individuals can be calculated by the formula: [intercept + F1 X $\log_2$(4S) + F2 X $\log_2$(4L) + F3 X $\log_2$(10S) + F4 X $\log_2$(10L) + gender].[9] 4S = chromosome 4 D4Z4 region short allele; 4L = chromosome 4 D4Z4 region long allele; 10S = chromosome 10 D4Z4 region short allele; 10L = chromosome 10 D4Z4 region long allele.

Quantitative myometry:

Measurement of maximum voluntary isometric contraction (kg-force) was done with a digital force gauge (the QMA system, Gainsville, GA). Testing required that the joint at which the movement occurs is placed in a 90˚ position and the force transducer is attached perpendicular to the joint at a 90˚ angle with the help of an adjustable cuff and inelastic strap attached to a metal frame. Knee extension was tested twice for 3-5 seconds while the patient was coached vigorously. Predicted values for knee extensor strength were derived from a large normative database adjusting for gender, age, and height as previously described.[e2] Percent predicted of normal = 100 X (predicted strength-observed strength)/predicted strength.

Supplemental Table e-1. Clinical Severity Score description of scoring.[e1]

Score	Description
0.5	Facial weakness
1	Mild scapular involvement without limitation of arm abduction; no awareness of disease symptoms is possible
1.5	Moderate involvement of scapular and arm muscles or both (arm abduction >60° and strength ≥3 in arm muscles); no involvement of pelvic and leg muscles
2	Severe scapular involvement (arm abduction < 60° on at least one side); strength < 3 in at least one muscular district of the arms; no involvement of pelvic and leg muscles.
2.5	Tibioperoneal weakness; no weakness of pelvic and proximal leg muscles
3	Mild weakness of pelvic and proximal leg muscles or both (strength ≥4 in all these muscles); able to stand up from a chair without support
3.5	Moderate weakness of pelvic and proximal leg muscles or both (strength ≥3 in all these muscles); able to stand up from a chair with monolateral support
4	Severe weakness of pelvic and proximal leg muscles or both (strength < 3 in at least one of these muscles); able to stand up from a chair with double support; able to walk unaided
4.5	Unable to stand up from a chair; walking limited to several steps with support; may use wheelchair for most activities
5	Wheelchair bound

Supplemental e-References

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