

Population-Based Prevalence of Myotonic Dystrophy Type 1 Using Genetic Analysis of Statewide Blood Screening Program

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Study Question

Is the prevalence of CTG expansions in the *DMPK* gene in patients with myotonic dystrophy type 1 higher than previously reported?

What Is Known and What This Paper Adds

Myotonic dystrophy type 1 is caused by CTG expansion ≥ 50 repeats in the *DMPK* gene, and has an estimated prevalence of 0.5–2 people per 10,000 individuals in the general population. However, this is likely an underestimate due to a cross-section of the population who may be pauci-symptomatic or pre-symptomatic. This investigation's results suggest that the actual prevalence is up to 5 times higher than previously estimated.

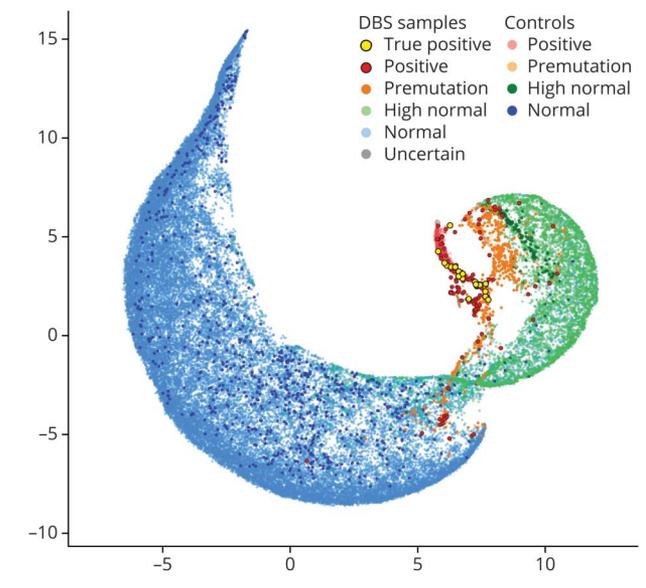
Methods

For this cross-sectional study, the investigators analyzed genetic data from 50,382 babies consecutively born at hospitals throughout the state of New York between December 2013 and April 2014 who underwent dried blood spot collection through the state's Newborn Screening Program. The investigators conducted melt curve analysis of the blood spots, and 4 blinded reviewers independently reviewed melt curve morphologies to identify samples with possible CTG expansions in the *DMPK* gene. To determine whether flagged samples actually contained CTG expansions, the investigators conducted further testing with a repeat-primed PCR procedure involving capillary electrophoresis, and they regarded the presence of ≥ 50 CTG repeats as a positive result. The primary outcome was the overall prevalence of CTG expansions in the *DMPK* gene.

Results and Study Limitations

Overall, the investigators detected 24 samples with ≥ 50 CTG repeats in the *DMPK* gene. This represents a prevalence of 4.76 cases per 10,000 births (95% CI, 2.86–6.67) or 1 case for every 2,100 births. The investigators also detected 96 samples with expansions from 35–49 CTG repeats, with the resulting

Figure Clustering and Variability of Blinded Review of Melt Curves From DBS Samples



prevalence for such shorter repeat expansions being 19.1 cases per 10,000 births or 1 case for every 525 births. These pre-mutation carriers represent the risk pool for further expansion in subsequent generations. The present study's limitations include a lack of data concerning clinical features and a focus on a single US state, which may limit generalizability.

Study Funding and Competing Interests

This study was funded by the Myotonic Dystrophy Foundation. Some authors report receiving consulting fees, committee appointments, and funding from healthcare companies; receiving funding from US government agencies; and receiving royalties for the use of clinical indices. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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