saw. Clarification of the mechanisms underlying variable expressivity in neurodevelopmental movement disorders, a prerequisite for improved patient care, will require further study.[7]

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Data Availability Statement

Detailed clinical information are available upon reasonable request.

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Reply to: "Heterogeneous Phenotypic Evolution in *ANO3*-Related Dystonia Due to the Recurrent p.Glu510Lys Variant"

We thank Indelicato and colleagues for reporting the phenotypic evolution of an additional patient with early-onset combined dystonia carrying the *ANO3* variant c.1528G > A (p.Glu510Lys)[1] and for highlighting the need to unravel the mechanisms underpinning the heterogeneous expressivity of neurodevelopmental movement disorders. These rare conditions are often misdiagnosed, emphasizing the necessity to approach them in a multidisciplinary setting where neurologists, pediatricians, geneticists, and other professionals could share their knowledge and experience. It is crucial to report even single patients affected by rare genetic syndromes to allow the characterization of clinical phenotypes and define prognostic aspects such as response to treatments. The latter has become increasingly relevant given the recognized importance of underlying genetic causes in predicting motor outcomes, for instance, following deep brain stimulation (eg, DYT-*TOR1A*, DYT-*KMT2B*).[2,3] Furthermore, these clinical cases highlight the general lack of longitudinal cohort studies to report the natural history of rare and ultrarare movement disorders, even well-known ones (eg, myoclonus dystonia due to *SGCE* mutations), and their potential phenotypic evolution into more complex movement disorders or syndromes, including significant motor (eg, β-propeller protein-associated neurodegeneration that is fairly static until the second decade) or psychiatric manifestations (as in our DYT-*ANO3* case[4]), which can impact on patient's quality of life and raise the need for a multidisciplinary approach also for therapeutic purposes. It needs to be recognized that the motor and nonmotor phenotypes in genetic dystonia may change in parallel to the evolving brain, from childhood to elderly life, when anatomical/

Key Words: *ANO3*, anoctamin, chorea, dystonia, DYT24, myoclonus

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neurophysiological modifications related to development and aging could modulate or complicate the phenomenology.[5]

It is also essential to underline the importance of having longitudinal video documentation of such complex clinical cases, in which patients are evaluated based on a series of standard tasks, including those required for the assessment of dystonia, allowing a more precise definition of the evolution of such complex patients.[6] In the near future, deep learning-based algorithms will potentially help improve the accuracy and reliability of diagnosis and prediction results by integrating clinical features, genetic results, neuroimaging/video, and kinematic recordings.[7]

Rowing somehow against the current, we would like to emphasize the need to publish case reports and case series of patients with such rare genetic disorders and encourage continuous efforts for a more comprehensive clinical characterization of their natural history.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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