

Writing tremor: Should we look for a TOR1A mutation

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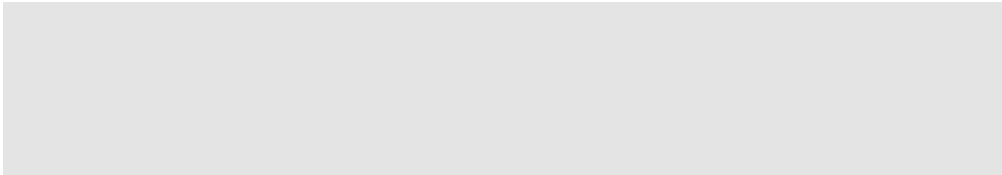
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Letter to the Editor

Writing tremor: Should we look for a *TOR1A* mutation?

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Dear Editor,

Three forms of dystonic tremor syndrome have been described [1]. Dystonic tremor corresponds to tremor observed in a body region affected by dystonia; it is usually a postural, kinetic, focal tremor, with an irregular amplitude and a variable frequency. Secondly, tremor associated with dystonia is present in a body region not affected by dystonia but is associated with dystonia in another body region. Lastly, dystonia gene-associated tremor corresponds to isolated tremor observed in patients with a mutation known to cause dystonia; dystonic posture is sometimes observed over the course of the disease. The latter entity is the most challenging to diagnose; for example, it can be difficult to differentiate from essential tremor [2]. Primary writing tremor is different in that no causal mutation was demonstrated in this disorder [3].

Here, we report on a family with two affected members (Fig. 1). The index case (II:3) presented with generalized dystonia from the age of 10 onwards. A *TOR1A* mutation (c.907delGAG) was identified. His brother (II:5) presented with mild, progressive writing difficulties from the age of 42 onwards (in 1990). After an initial consultation in 1999, writing tremor with jerky pronosupination developed over the next 13 years (Video 1). The wrist flexion seen on the video suggests dystonia, but a compensatory measure cannot be ruled out: the patient stated that his wrist was flexed in some conditions and extended in other conditions, in order to effectively control the tremor (Video 2). Apart from these features, the patient's clinical status was normal. Patient II:5 had the same *TOR1A* mutation as the index case. Various non-surgical treatments failed to relieve the patient's symptoms. The patient was lost to follow-up in 2013 but consulted again in September 2016. The clinical situation had changed dramatically; we observed marked dystonic flexion of the right wrist, associated with an irregular, postural, kinetic tremor of both hands (Video 3). Surprisingly, the patient's writing had not worsened. Polymyographic electromyography ruled out essential tremor and myoclonus.

It cannot be determined whether, at the onset of the disease, patient II:5 presented with dystonic tremor or isolated tremor (dystonia gene-associated tremor). Indeed, although dystonia gene-associated tremor is a classical concept, cases are very rare. Isolated head tremor (in the presence or the absence of dystonic posture of the neck) has been reported in families with an *ANO3* mutation (DYT24) [4]. Upper limb tremor was described in a patient with an *SGCE* mutation [5]. In other publications, dystonia gene-associated tremor has not been clearly proven. For example, the patient described by Caceres-Redondo et al. (*TOR1A* mutation) [6] presented with a postural tremor of upper limb, but it is unclear whether it was strictly isolated at onset or associated to a dystonia. In Markova et al.'s [7] description of a family with *TOR1A* mutation, the member with isolated hand tremor lacked a molecular diagnosis. Erro et al. [8] described a family whose members suffered from primary writing tremor and dystonia - showing that tremor can indeed be an isolated feature of dystonia. However, no mutations were found (DYT1 was ruled out).

Furthermore, the clinical presentation of patient II:5 was remarkable for a DYT1 dystonia: late onset (42 years old, whereas DYT1 dystonia typically presents in childhood or adolescence); mild phenotype (a focal, task-specific dystonic tremor); and slow course (the patient's dystonic posture became worse more than 20 years after the onset) [9]. In view of the late onset, a linkage to chromosome 18p (DYT7) could have been considered [10]; patients with this defect can present with writer's cramp and tremor. To reduce the risk of late diagnosis, it is essential to record a detailed family history for patients with writing tremor. As soon as an impairment was observed in patient II:5, a history of dystonia in the sibship pointed us towards a diagnosis of dystonic tremor rather than another cause of writing tremor (such as primary writing tremor).

In summary, screening for mutations (especially a *TOR1A* mutation or a *SGCE* mutation) should be considered in patients with writing tremor when there is a family history of dystonia. However, it should be borne in mind that all forms of genetically determined dystonia may present with tremor of the hand. Lastly, in patients with dystonia gene-associated writing tremor, dystonia may occur after several decades.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jns.2017.09.048>.

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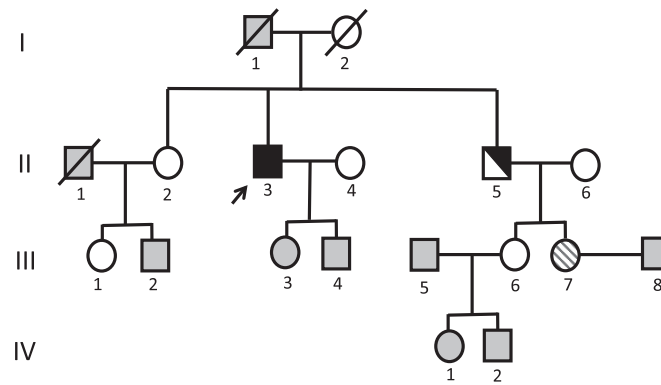


Fig. 1. Pedigree of the study family. Filled symbols: generalized dystonia and *TOR1A* mutation. Half-filled symbols: writing tremor and *TOR1A* mutation. Hatched symbols: asymptomatic, with a *TOR1A* mutation. Grey symbols: asymptomatic, *TOR1A* status unknown. Unfilled symbols: asymptomatic, no *TOR1A* mutation. Arrow: proband.

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