Structural and functional neuroimaging in Myoclonus-Dystonia

Beukers, R.J.

Citation for published version (APA):
Beukers, R. J. (2011). Structural and functional neuroimaging in Myoclonus-Dystonia

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)
Chapter 8

Myoclonus-Dystonia and Spinocerebellar Ataxia type 14 presenting with similar phenotypes: trunk tremor, myoclonus and dystonia

Elisabeth M.J. Foncke¹, Richard J. Beukers¹, Cees C. Tijssen², Johannes H.T.M. Koelman¹ and Marina A.J. Tijssen¹

¹Department of Neurology and Clinical Neurophysiology, Academic Medical Centre, University of Amsterdam, The Netherlands.
²Department of Neurology, St. Elisabeth Hospital, Tilburg, the Netherlands.

Adapted from Parkinsonism and Related Disorders 2010; 16(4):288-289.
Abstract

We describe three genetically confirmed Myoclonus-Dystonia (M-D) patients and one spinocerebellar ataxia type 14 (SCA14) patient, presenting with a combination of trunk tremor, multifocal myoclonus and axial dystonia as predominant clinical features. We suggest that in patients with this M-D phenotype, without a mutation in the DYT-11 gene, SCA14 should be considered.
M-D and SCA 14; similar phenotypes

Introduction

M-D is a movement disorder characterized by myoclonic jerks and dystonic movements and/or postures of the upper body, often dramatically responding to alcohol and associated with psychiatric symptoms. M-D is autosomal dominantly inherited and frequently caused by mutations in the epsilon-sarcoglycan gene (SGCE) on chromosome 7q21 (DT-11). Spinocerebellar ataxia type 14 is also inherited autosomal dominantly. It is caused by mutations in the protein kinase C gamma gene (PRKCG) on chromosome 19q. The classical phenotype is a slowly progressive isolated cerebellar syndrome evolving after the age of 20 and extrapyramidal features such as (multifocal) myoclonus and dystonia, but not trunk tremor, have been reported in several SCA14 patients.

Here, we present three genetically confirmed M-D patients from one family and a single genetically confirmed SCA14 patient with comparable phenotypes.

Patients

Patients 1 and 2 are identical twin brothers. Patient 1, the index patient of the recently described M-D family by Foncke et al., developed myoclonus of the leg in early childhood. Dystonia of the trunk was noted in his teens. He was treated for recurrent depression and suffered from alcohol abuse. On neurological examination, age of 45 years, rhythmic movements of the trunk were noted especially during walking and in the upright position. In addition, torsion dystonia of the trunk and dystonia of the feet were present, along with myoclonic jerks of the hands, legs, and trunk. Polymyographic examination showed a 6 to 7 Hz. tremor of the paraspinal muscles, alternating with a tremor of the rectus abdominis muscles when standing (Figure 1) and walking. In supine position, the tremor was absent.
Structural and functional neuroimaging in Myoclonus-Dystonia

**Figure 1:** Surface EMG in an M-D patient.

![Surface EMG recordings from the M-D index patient in the standing position. Rhythmic alternating activity is seen in the lumbar (L4) paraspinal (PSP), and rectus abdominis (rectus abd) muscles with a frequency of 6-7 Hz.](image)

His identical twin brother presented with a quite similar clinical picture and electrophysiological findings. Interestingly, the torsion of his body was opposite to the torsion of his twin brother. Patient 3, the father of the twins, has deceased but was clinically described in 1974 by Korten et al. with a trunk tremor and myoclonus of the neck, trunk, and arms.\(^7\)

Sequence analysis of the *SGCE* gene revealed a two-base pair deletion in exon 5 (619_620delAG), resulting in a frame shift and premature protein truncation (Arg207fsX215) in these twins and 32 other family members.\(^6\) Based on the genetic studies in this family the father was likely to be carrier of the same mutation.

Patient 4 developed myoclonic jerks of the trunk, arms and head around the age of 13 years with progressive worsening up to the age of 25 years. Since the age of 15 years, the patient noted progressive difficulties with walking. Neurological examination at the age of 54 years, showed multifocal myoclonus predominantly located distally in the arms but also more proximal in the arms and in the trunk, increasing with action and mild cervical dystonia. A trunk tremor was present during walking and in the upright position. In addition, a slight gait-ataxia was
M-D and SCA 14; similar phenotypes

noted without signs of limb-ataxia. Clonazepam has a beneficial effect on his symptoms. Magnetic resonance imaging revealed diffuse cerebellar atrophy. On electrophysiological examination, a tremor of 5 to 6 Hz was found in the paraspinal muscles when sitting (Figure 2) and standing. In supine position, the tremor was absent. The patient’s father had gait problems, as did his grandmother on father’s side. The patient’s son has complaints of fine motor skills and his daughter experienced a period of jerky movements around the age of three years. Screening for the DYT-11 mutation was negative. Further genetic testing for the SCA’s revealed a Gly118Asp mutation in the *PKRCG* gene. Genealogic investigations revealed that the patient is linked to a previously described Dutch SCA14 pedigree.4

Figure 2: Surface EMG in a SCA14 patient

![Surface EMG in a SCA14 patient](image)

Figure legend: Surface EMG recordings from the SCA14 patient in the sitting position. Note the rhythmic activity in the left and right lumbar (L4) paraspinal muscles with a frequency of 5-6 Hz.

**Discussion**

Trunk tremor is a rare movement disorder, reported as isolated manifestation of dystonia or as part of a cerebellar axial postural tremor, essential or orthostatic tremor.8-10 The features of the trunk tremor in the two M-D patients show similarities to the trunk tremor described by Rivest and Marsden8 as isolated manifestation of dystonia: “lying down they are still, but as they sit, stand or walk they oscillate about their pelvis”. The clinical picture also fits well in the general definition of dystonic tremor established as a mainly postural/kinetic tremor in an extremity or body part that is affected by dystonia and usually not seen during complete rest, with irregular amplitudes and variable frequency (usually below 7 Hz).10 A positive effect of the anticholinergic drug trihexyphenidyl (up to 6 mg daily) on the trunk tremor in the M-D patients supports the idea of a dystonic tremor. In patients with the M-D phenotype, trunk myoclonus is highly predictive for the DYT-11 mutation11, but a trunk tremor has, to our knowledge, not been previously reported.
Structural and functional neuroimaging in Myoclonus-Dystonia

The postural trunk tremor of the SCA 14 patient could be considered part of the cerebellar features which are common in SCA 14 patients.\textsuperscript{3,4} The patients cerebellar atrophy on the MRI and ataxic gait support this hypothesis. The axial tremor described in relation to cerebellar pathology has a frequency of 5 Hz, is usually more regular than the dystonic tremor and disappears with action.\textsuperscript{9} This is in contradiction with the irregular tremor and the absence of the tremor in supine position in our patient. Therefore, we suggest that the trunk tremor in the SCA14 patient should be classified as a dystonic tremor.

The multifocal myoclonus and axial dystonia in the M-D patients are consistent with the classical phenotype of M-D [1]. The SCA14 patient also exhibited multifocal myoclonus combined with mild cervical dystonia. Myoclonus or dystonia, as a presenting feature of SCA14 have been described in two Dutch and a Japanese pedigree.\textsuperscript{3-5} Trunk tremor has been reported in one patient of another Japanese pedigree.\textsuperscript{12} Our patient appeared to be linked to one of the Dutch SCA14 families.\textsuperscript{4} At presentation, ataxia was very mild and not relevant for the patient, but in the course of his disease, the gait ataxia became more manifest.

In conclusion, the combination of trunk tremor, myoclonus and dystonia can be part of the phenotypic spectrum of both DYT-11 and SCA 14 mutations. We suggest that in patients with the M-D phenotype tested negative for DYT-11, SCA 14 should be considered, especially when ataxia is described or noted in other family members and MRI scan of the brain shows cerebellar atrophy.
M-D and SCA 14; similar phenotypes

References