Natural Course of Myoclonus-Dystonia in Adulthood: Stable Motor Signs But Increased Psychiatry

Myoclonus-dystonia (M-D) is a rare hyperkinetic movement disorder characterized by upper body–predominant myoclonus and dystonia.[1] A large proportion of cases are caused by autosomal-dominant inherited mutations in the *SGCE* gene. In addition to the motor manifestations, psychiatric disorders are frequently reported.[2] Several studies have suggested that they may form a primary component of the M-D phenotype.[3,4] This study represents the first long-term follow-up study of both motor and psychiatric symptomatology in adults with M-D (*SGCE* mutation), providing further insights into the natural history of M-D and enabling more prognostic information.

Methods

Manifesting adult carriers with a mutation in the *SGCE* gene were included, whose baseline data were collected in the Netherlands, Belgium, and the United Kingdom and reported previously.[2,3,5]

Regarding motor signs, both at baseline and follow-up, Burk Fahn Marsden Dystonia Rating Scale (BFMDRS) and Unified Myoclonus Rating scale (UMRS) were used to objectively assess motor sign severity. Psychiatric comorbidity and quality of life were evaluated using the same (or highly comparable) questionnaires at baseline and follow-up.

Results

Of the 63 adult M-D patients recruited in the original studies, 27 patients were able to participate in this follow-up assessment. An overview of body distribution and severity scales of motor signs at baseline and follow-up examination can be found in Table 1. No age-distinctive pattern in the scores was observed. See Table 1 for the prevalence of psychiatric disorders and scores of severity scales. No associations between changes in motor symptoms and psychiatric symptom severity, quality of life, and demographic information were found.

TABLE 1. Demographics, motor symptoms, and psychiatric comorbidities

Total number of patients	27		
Sex M/F	11/16		
Age at onset dystonia (range)	8 (1–40)		
Age at onset myoclonus (range)	7 (1–17)		
Oral medication for motor symptoms	6 (22%)		
Antidepressant			
SSRI	4 (13%)		
SNRI	2 (7%)		
TCA	1 (3%)		
Botulinum neurotoxin injections	3 (11%)		
Motor symptoms	**Baseline examination**	**Follow-up examination**	***P***
Age (SD)	44.6 (14.3)	55.2 (14.4)	
Number of patients with:			
Dystonia	23 (85%)	25 (93%)	0.625[a]
Myoclonus	22 (81%)	24 (89%)	0.500[a]
Body distribution			
Dystonia (n = 21)			
— Upper limbs	5 (24%)	18 (86%)	**< 0.001**[a]
— Lower limbs	2 (10%)	5 (24%)	0.250[a]
— Neck	18 (86%)	19 (90%)	1.000[a]
— Trunk	5 (24%)	8 (38%)	0.453[a]
Myoclonus (n = 22)			
— Upper limbs	20 (91%)	20 (91%)	1.000[a]
— Lower limbs	1 (5%)	7 (32%)	0.070[a]
— Neck	8 (36%)	16 (73%)	**0.008**[a]
— Trunk	6 (27%)	15 (68%)	**0.012**[a]
All patients			
BFMDRS, n = 24 (range)	3.5 (0–20)	6.6 (0–17.5)	0.203[b]
UMRS, n = 24 (range)	2.3 (0–12)	3.7 (0–12)	0.140[b]
Patients with mutation inherited via paternal line			
BFMDRS, n = 19 (range)	4.0 (0–20)	7.0 (1–17.5)	0.198[b]
UMRS, n = 19, (range)	5.2 (0–12)	5.4 (0–12)	0.260[b]
Psychiatry	**Baseline examination n = 26**	**Follow-up examination n = 6**	***P*[a]**
Any psychiatric disorder	16 (62%)	20 (77%)	0.219
Depression	7 (27%)	13 (50%)	0.070
Panic disorder	6 (23%)	12 (46%)	**0.031**
Social phobia	6 (23%)	4 (15%)	0.688

(Continues)

Key Words: follow-up, myoclonus-dystonia, nonmotor symptoms

***Correspondence to:** Marina A.J. Tijssen. Department of Neurology, University Medical Center Groningen, Hanzeplein 1, 9700RB Groningen, The Netherlands; E-mail: m.a.j.de.koning-tijssen@umcg.nl

Relevant conflicts of interest/financial disclosures: M.T. and E.T. received funding from the Dystonia Medical Research Foundation (DMRF). All other authors report no disclosures. None of the authors have potential conflicts of interest to be disclosed.

Funding agencies: This study was supported by the Dystonia Medical Research Foundation (DMRF).

Received: 25 February 2020; **Accepted:** 27 February 2020

Published online 25 March 2020 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.28033

TABLE 1. Continued

Psychiatry	Baseline examination n = 26	Follow-up examination n = 6	P^a
OCD	3 (12%)	6 (23%)	0.453
Alcohol dependence	3 (12%)	3 (12%)	1.000
GAD	3 (12%)	3 (12%)	1.000
Specific phobia	3 (14%)[3]	5 (23%)[3]	0.688
Agoraphobia	4 (33%)[4]	6 (50%)[4]	0.500
Hypomania	1 (10%)[6]	1 (10%)[6]	1.000
Psychosis	1 (10%)[6]	2 (20%)[6]	1.000
	n = 22	n = 22	P^b
YBOCS (range)	0.0 (0–14)	0.0 (0–12)	0.634
BDI (range)	5.0 (0–21)	7.5 (0–30)	**0.038**
BAI (range)	5.0 (0–24)	7.5 (0–45)	0.070
	n = 13	n = 13	P^c
QoL PC (SD)	44.8 (8.8)	45.2 (6.9)	0.875
QoL MC (SD)	38.8 (13.6)	43.0 (9.2)	0.193

The following statistical tests were used:
[a]McNemar test.
[b]Wilcoxon signed rank test.
[c]Paired-sample *t* test: [1]n = 9; [2]n = 5; [3]n = 22; [4]n = 12; [5]n = 7; [6]n = 10.
SSRI, selective serotonin reuptake inhibitor; SNRI, selective serotonin and noradrenalin reuptake inhibitor; TCA, tricyclic antidepressant; BFMDRS, Burke Fahn Marsden Dystonia Rating Scale; UMRS, Unified Myoclonus Rating Scale; OCD, obsessive compulsive disorder; GAD, generalized anxiety disorder; YBOCS, Yale Brown Obsessive Compulsive Scale; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; QoL PC, physical component of quality of life; QoL MC, mental component of quality of life.

Discussion

This is the first systematic long-term follow-up study of both motor and psychiatric manifestations in adult M-D patients. Despite the percentage of patients retested (27 of 63), the rarity of M-D makes our results valuable. Results of this study showed that in adulthood the course of dystonia and myoclonus is static and the prevalence of psychiatric comorbidities remains high. Specific psychiatric disorders, notably panic disorder and depression, became even more prevalent over time.

It appears that in adulthood severity of motor manifestations is relatively stable, but distribution lightly changed. At follow-up examination significantly more patients had dystonia in the upper limbs and more patients had myoclonus in the neck and trunk compared with baseline. This is consistent with previous findings.[6]

Comparable to the literature, psychiatric comorbidity was highly prevalent in our cohort. The prevalence of panic disorder doubled at follow-up compared with baseline and was accompanied by an increased score on the anxiety severity scale. Similar, but not statistically significant, findings were detected for depressive disorder. It is unlikely that our findings are because of an increase in age, as the prevalence of panic disorder and depression in the general population tends to decrease in the age group of our cohort.[7]

The relatively stable course of motor manifestations is in contrast with the increased prevalence of psychiatric comorbidity. Results highlight the need for more awareness and adequate treatment for psychiatric disorders in M-D patients. Simultaneously, adult patients can be reassured that their motor functioning will not deteriorate.

Acknowledgment: Authors want to thank A.M.M. van der Stouwe and M. Smit for scoring a part of the follow-up videos, A. Kuiper, J. van Zijl, H. Eggink, M. Coenen, A.L. Bartels, and J. Gelauff for helping with the collection of the data, and Z. Yilmaz for contacting the UK patients.

Elze R. Timmers, BSc,[1] Kathryn J. Peall, MD, PhD,[2] Joke M. Dijk, MD, PhD,[3] Rodi Zutt, MD, PhD,[1] Cees C. Tijssen, MD, PhD,[4] Bruno Bergmans, MD, PhD,[5,6] Elisabeth M. Foncke, MD, PhD,[3] and Marina A.J. Tijssen, MD, PhD[1*]

[1]*Department of Neurology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands*
[2]*Neuroscience and Mental Health Research Institute, Division of Psychological Medicine and Clinical Neurosciences, Cardiff University, Cardiff, Wales, United Kingdom*
[3]*Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands*
[4]*Department of Neurology, Elisabeth-TweeSteden Ziekenhuis, Tilburg, The Netherlands*
[5]*Department of Neurology, A.Z. Sint-Jan Brugge-Oostende AV, Bruges, Belgium*
[6]*Department of Neurology, Ghent University Hospital, Ghent, Belgium*

References

1. Roze E, Lang AE, Vidailhet M. Myoclonus-dystonia: classification, phenomenology, pathogenesis, and treatment. Curr Opin Neurol 2018; 31:484–490.
2. Peall KJ, Smith DJ, Kurian MA, et al. SGCE mutations cause psychiatric disorders: clinical and genetic characterization. Brain 2013;136:294–303.
3. van Tricht MJ, Dreissen YE, Cath D, et al. Cognition and psychopathology in myoclonus-dystonia. J Neurol Neurosurg Psychiatry 2012; 83:814–820.
4. Peall KJ, Dijk JM, Saunders-Pullman R, et al. Psychiatric disorders, myoclonus dystonia and SGCE: an international study. Ann Clin Transl Neurol 2015;3:4–11.
5. Foncke EM, Cath D, Zwinderman K, Smit J, Schmand B, Tijssen M. Is psychopathology part of the phenotypic spectrum of myoclonus-dystonia? A study of a large Dutch M-D family. Cogn Behav Neurol 2009;22:127–133.
6. Peall KJ, Kurian MA, Wardle M, et al. SGCE and myoclonus dystonia: motor characteristics, diagnostic criteria and clinical predictors of genotype. J Neurol 2014;261:2296–2304.
7. Lenze EJ, Wetherell JL. A lifespan view of anxiety disorders. Dialogues Clin Neurosci 2011;13:381–399.