Parkinsonism and Related Disorders xxx (2015) 1–10

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Review

Non-motor symptoms in genetically defined dystonia: Homogenous groups require systematic assessment

K.J. Peall [a, c, 1], A. Kuiper [a, 1], T.J. de Koning [a, b], M.A.J. Tijssen [a, *]

[a] Department of Neurology, University of Groningen, Groningen, The Netherlands
[b] University of Groningen, University Medical Center Groningen, Department of Genetics, Groningen, The Netherlands
[c] Institute of Psychological Medicine and Clinical Neurosciences, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, UK

ARTICLE INFO

Article history:
Received 14 May 2015
Received in revised form
8 June 2015
Accepted 6 July 2015

Keywords:
Dystonia
Genetics
Non-motor symptoms

ABSTRACT

Introduction: Dystonia is a movement disorder involving sustained or intermittent muscle contractions resulting in abnormal movements and postures. Identification of disease causing genes has allowed examination of genetically homogenous groups. Unlike the motor symptoms, non-motor characteristics are less clearly defined, despite their impact on a patient's quality of life. This review aims to examine the evidence for non-motor symptoms, addressing cohort size and methods of assessment in each study.
Methods: A systematic and standardised search strategy was used to identify the published literature relating to psychiatric symptoms, cognition, sleep disorders, sensory abnormalities and pain in each of the genetically determined dystonias. Studies were divided according to cohort size, method of assessment and whether comparison was made to an appropriate control group.
Results: Ninety-five articles were identified including reported clinical histories (n = 42), case reports and smaller case series (n = 12), larger case series (n = 23) and case-control cohorts (n = 18). Psychiatric symptoms were the most frequently investigated with anxiety, depression and Obsessive–Compulsive disorder being most common. Cognitive impairment involved either global deficits or isolated difficulties in specific domains. Disturbances to sleep were most common in the dopa-responsive dystonias. Sensory testing in DYT1 cases identified an intermediate subclinical phenotype.
Conclusion: Non-motor symptoms form an integral component of the dystonia phenotype. However, future studies should involve a complete assessment of all symptom subtypes in order to understand the frequency and gene-specificity of these symptoms. This will enable early symptom identification, appropriate clinical management, and provide additional outcome measures in future clinical trials.
© 2015 Elsevier Ltd. All rights reserved.

1. Introduction

Dystonia is a hyperkinetic movement disorder characterized by sustained or intermittent muscle contractions resulting in abnormal movements and postures. Identification of disease causing genes in dystonia has allowed for extensive phenotyping of their motor characteristics, a summary of which can be seen in Table 1.

More recently greater emphasis has been placed on co-existent non-motor features including psychiatric symptoms, cognitive impairment, sleep disorders and abnormalities in sensory perception with several papers suggesting that these non-motor symptoms have a larger impact on an individual's quality of life than that of their motor symptoms. The majority of studies in this area to date have involved mixed groups of focal dystonias, with several suggesting an increased rate of psychiatric symptoms. One study, using standardised diagnostic tools, found an excess of panic disorder and agoraphobia in those with spasmodic torticollis, with over half reporting onset of these symptoms prior to their movement disorder [1].

The identification of disease causing genes has allowed examination of genetically homogenous groups, facilitating a more complete understanding of the disorder phenotype. This paper systematically reviews the most up-to-date evidence for non-motor symptoms in the genetically determined dystonias. We

* Corresponding author. Department of Neurology, University Medical Center Groningen, Groningen, The Netherlands.
E-mail addresses: PeallKJ@cardiff.ac.uk (K.J. Peall), a.kuiper@umcg.nl (A. Kuiper), t.j.de.koning@umcg.nl (T.J. de Koning), m.a.j.de.koning-tijssen@umcg.nl (M.A.J. Tijssen).
[1] These authors contributed equally to the manuscript.

http://dx.doi.org/10.1016/j.parkreldis.2015.07.003
1353-8020/© 2015 Elsevier Ltd. All rights reserved.

Please cite this article in press as: K.J. Peall, et al., Non-motor symptoms in genetically defined dystonia: Homogenous groups require systematic assessment, Parkinsonism and Related Disorders (2015), http://dx.doi.org/10.1016/j.parkreldis.2015.07.003

Table 1
Genotype and motor phenotypic characteristics of the genetically determined dystonias.

Disorder	OMIM number	Gene	Inheritance	Typical motor phenotype
DYT1	605204	GAG deletion of *Torsin A*	AD with reduced penetrance (~30%)	Ranging from mild focal dystonia to more severe generalized forms
DYT2	224500	Not identified	Probable AR	Lower limb predominant dystonia with generalization in some cases
DYT3 X-Linked Dystonia-Parkinsonism	313650	*TAF-1*	X-Linked	Initial focal/segmental dystonia with subsequent generalisation. Levodopa unresponsive parkinsonism becomes evident in the later stages
DYT4 Whispering Dysphonia	602662	*TUBB4*	AD	Craniocervical and laryngeal dystonia with subsequent generalisation
DYT5a Autosomal Dominant Dopa-Responsive Dystonia/Segawa Syndrome	600225	*GCH1*	AD with reduced penetrance	Initial lower limb dystonia with subsequent generalization Diurnal fluctuation. parkinsonism, dystonic tremor
DYT5b Autosomal Recessive Dopa-Responsive Dystonia	191290	*TH*	AR	Hypokinesia, rigidity and encephalopathy
DYT5b Autosomal Recessive Dopa-Responsive Dystonia	182125	*SPR*	AR	Diurnal fluctuation, ataxia and myoclonus
DYT6	609520	*THAP1*	AD (~60% penetrance)	Adult onset, predominantly craniocervical and laryngeal torsion dystonia.
DYT7	602124	Not identified	Unknown	Focal dystonia typically blepharospasm, cervical or involving the hands
DYT8 Paroxysmal Non-Kinesigenic Dyskinesia 1	609023	*MR-1*	AD	Intermittent episodes (10 min–1 h) Dystonia, chorea, ballism, blepharospasm
DYT10 Episodic Kinesigenic Dyskinesia	614386	*PRRT2*	AD (incomplete penetrance)	Intermittent episodes of isolated dystonia or in combination with chorea, athetosis, ballism.
DYT11 Myoclonus Dystonia	604149	*SGCE*	AD (reduced penetrance due to maternal imprinting)	Myoclonus (trunk and upper limbs) and dystonia (cervical & writer's cramp)
DYT12 Rapid-Onset Dystonia-Parkinsonism	182350	*ATP1A3*	AD (reduced penetrance)	Sudden onset dystonia, developing in a raustro-caudal pattern and gait instability
DYT13	607671	Not identified	AD	Idiopathic torsion dystonia with predominant upper body and cranio-cervical involvement
DYT15 Myoclonus Dystonia	607488	Not identified	Possible AD	Myoclonic dystonia of the trunk and upper limbs
DYT16	603424	*PRKRA*	AR	2 forms: 1) generalised dystonia, 2) dystonia-parkinsonism
DYT17	612406	Not identified	AR	Primary focal torsion dystonia spreading to involve a segmental or generalized pattern
DYT18 GLUT1 Deficiency Syndrome 2	138140	*SLC2A1*	AD	Dyskinetic, predominantly lower limb dystonic episodes triggered by exercise or hunger
DYT20 Paroxysmal Non-Kinesigenic Dyskinesia 2	611147	Not identified	AD	Intermittent dystonia involving the hands and feet
DYT21	614588	Not identified	AD (incomplete but high penetrance)	Focal dystonia, predominantly involving the eyes and neck
DYT23	614860	Not identified	AD	Adult onset cervical dystonia with head and limb tremor
DYT24	610110	*ANO3*	AD	Adult-onset cervical dystonia with laryngeal involvement, upper limb tremor and myoclonus
DYT25	139312	*GNAL*	AD	Adult-onset focal dystonia, typically involving the neck progressing to involve the face, larynx, trunk and limbs

Key: AD: Autosomal Dominant, AR: Autosomal Recessive.

have also sought to evaluate the strength of this evidence by means of cohort size, methods of assessment and whether comparison to an adequate control group has been employed.

2. Methods

We performed a systematic search of the PUBMED database. The search strategy included the key words “non-motor”, “psychiatry”, “psychiatric”, “mental disorders”, “cognition”, “sleep”, “behavioral”, “pain” and “sensory perception” in conjunction with each of the known genes as well as their DYT value. The reference lists of each relevant study were checked for further appropriate articles. There was no restriction on year of publication but only those published in English and in peer-reviewed journals until January 2015 were included. Published articles were divided according to the number of cases included and the presence or absence of a control group. These subgroups included: case reports ($n = 1$), smaller case series ($n < 5$), larger case series ($n \geq 5$) and case-control studies. Articles were further grouped based on method of assessment, either reported clinical history or standardized method of assessment. This later group included either assessment by a specialist in that field (e.g. psychiatrist) or use of validated, systematic and standardized questionnaires. Where no published material was identified the disorder is not discussed in further detail. To enable greater clarity of study findings, motor affected mutation carriers are referred to as Manifesting Carriers (MC), mutation carriers with no motor symptoms as Non-Manifesting Carriers (NMC) and those without mutations as Non-Carriers (NC).

3. Results

A total of 95 published articles were identified. These included

Please cite this article in press as: K.J. Peall, et al., Non-motor symptoms in genetically defined dystonia: Homogenous groups require systematic assessment, Parkinsonism and Related Disorders (2015), http://dx.doi.org/10.1016/j.parkreldis.2015.07.003

Download English Version:

https://daneshyari.com/en/article/10744877

Download Persian Version:

https://daneshyari.com/article/10744877

Daneshyari.com