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Epidemiological, clinical and genetic aspects of adult onset isolated focal dystonia in Ireland

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Background: Adult onset idiopathic isolated focal dystonia presents with a number of phenotypes. Reported prevalence rates vary considerably; well-characterized cohorts are important to our understanding of this disorder.

Aim: To perform a nationwide epidemiological study of adult onset idiopathic isolated focal dystonia in the Republic of Ireland.

Methods: Patients with adult onset idiopathic isolated focal dystonia were recruited from multiple sources. Diagnosis was based on assessment by a neurologist with an expertise in movement disorders. When consent was obtained, a number of clinical features including family history were assessed.

Results: On the prevalence date there were 592 individuals in Ireland with adult onset idiopathic isolated focal dystonia, a point prevalence of 17.8 per 100 000 (95% confidence interval 16.4–19.2). Phenotype numbers were cervical dystonia 410 (69.2%), blepharospasm 102 (17.2%), focal hand dystonia 39 (6.6%), spasmodic dysphonia 18 (3.0%), musician's dystonia 17 (2.9%) and oromandibular dystonia six (1.0%). Sixty-two (16.5%) of 375 consenting index cases had a relative with clinically confirmed adult onset idiopathic isolated focal dystonia (18 multiplex and 24 duplex families). Marked variations in the proportions of patients with tremor, segmental spread, sensory tricks, pain and psychiatric symptoms by phenotype were documented.

Conclusions: The prevalence of adult onset idiopathic isolated focal dystonia in Ireland is higher than that recorded in many similar service-based epidemiological studies but is still likely to be an underestimate. The low proportion of individuals with blepharospasm may reflect reduced environmental exposure to sunlight in Ireland. This study will serve as a resource for international comparative studies of environmental and genetic factors in the pathogenesis of the disorder.

Introduction

Dystonia, characterized by sustained or intermittent muscle contractions causing abnormal repetitive

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movements and postures [1], is the third most frequent movement disorder. Primary dystonia refers to pure dystonia with no additional neurological signs other than tremor; adult onset isolated focal dystonia (AOIFD) is the commonest form of primary dystonia [2]. Although predominantly a sporadic disorder, up to 25% of AOIFD patients have a family member affected [3–5] and it is now considered autosomal

dominant in inheritance with markedly reduced penetrance [4,6]. Although a number of genes implicated in primary dystonia have recently been identified [7–13] its pathogenesis remains elusive.

Adult onset isolated focal dystonia presents as a number of phenotypes including cervical dystonia (CD), focal hand dystonia (FHD), blepharospasm (BSP), spasmodic dysphonia (SD) and oromandibular dystonia (OMD). Owing to its heterogeneous clinical presentation and poor recognition by physicians, AOIFD is under-reported. Studies of the epidemiology of dystonia are often methodologically flawed, mixing primary focal, generalized and secondary causes of dystonia. Prevalence rates of primary dystonia range from 30 cases per million to 7320 per million [14–19]. Prevalence estimates of AOIFD (formerly adult onset primary torsion dystonia) range from 20 to 137 cases per million [16,17,20–23]. Genetic heterogeneity and variation in environmental exposures are possible explanations for this wide range [24,25]. Blepharospasm, for example, is more prevalent in studies from lower latitudes with high solar insolation [23,24,26–31]. Environmental exposures, sex and age at onset may interact with as yet unidentified genetic variants to influence phenotype and penetrance [32–34].

Improved understanding of pathogenesis and genetic causation requires well characterized patient cohorts. Thus the aim of this study was to determine comprehensively from multiple sources the clinical features, inheritance patterns and epidemiology of AOIFD in the Irish population for the first time.

Participants and methods

Participant recruitment: sources

There is currently no centralized, nationwide database of dystonia patients in Ireland. A database of patients attending a dystonia/botulinum toxin clinic in St Vincent's University Hospital, Dublin, has been established since 2001. In addition, patients with AOIFD were recruited from six neurology clinics and three ophthalmology clinics in hospitals throughout Ireland between 2011 and December 2014. These clinics are the principal specialist tertiary referral centres for neurology and ophthalmology in Ireland and were selected in an attempt to include all diagnosed dystonia patients. All consultant neurologists, ophthalmologists, neurophysiologists and botulinum toxin injection clinics, in both public and private practice, were repeatedly canvassed over a 5-year period (2010–2014) for participant recruitment. Members of the research team attended these clinics regularly and met

with patients, or, following consent, patients were referred to the research team for participation by their treating physician. In addition, the self-help group, Dystonia Ireland, advertised the survey to their members.

Patients were questioned in relation to a possible family history of dystonia and there was further detailed questioning in order to identify family members with possible symptoms of any neurological condition or movement disorder. Consenting relatives living in Ireland of index patients who were reported, or suspected, to have a movement disorder by history were visited and examined by a member of the research team and, with further consent, were videotaped for later clinical analysis by two consultant neurologists (SO'R and MH). Multiplex and duplex families were evaluated in this way and detailed pedigree diagrams were drawn up and stored.

Diagnostic criteria

Patients, aged 20 years or more, were diagnosed with AOIFD and phenotyped by a consultant neurologist with expertise in movement disorders [1]. Those with secondary dystonia, primary with onset prior to 20 years of age or with DYT1 dystonia were excluded (no other genetic testing was systematically used).

Prevalence date

The prevalence date was 31 December 2014 and all data refer to patients identified who were alive on that date. Prevalence rate calculations were based upon the total number of AOIFD patients; limited de-identified patient data (sex, date of birth, phenotype) provided by clinicians were included in prevalence calculations for those who did not consent to use of their full clinical information in the study.

Methods

Anonymised, encrypted data were collected, both prospectively at recruitment and retrospectively, through a combination of medical record review and patient history, following written informed consent. Data were entered in a dichotomous fashion in a database. Missing information was a result of either incomplete data in medical notes or patients who did not consent to full participation in this study. Those patients with AOIFD who did not consent to use of their data are included in the overall numbers in the study but their clinical information is not.

Data collected included current age, sex, phenotype, site at onset of initial dystonic symptoms, presence of

spread of symptoms (but not time of spread as this was a retrospective study), age at symptom onset, presence of a sensory trick, coexisting upper limb tremor and pain. Patients were routinely questioned regarding a family history of any movement disorder. Patients were reported to have a family history of clinically confirmed dystonia if family members were assessed by a neurologist and given a clear diagnosis of dystonia. Patients who reported a relative with symptoms consistent with dystonia but who had not been assessed by a neurologist were referred to as having a family history of possible dystonia. A positive psychiatric history was based on a diagnosis documented in the medical notes and/or verbal report from a patient of a confirmed diagnosis of a psychiatric disorder by another physician.

DYT1 testing was performed only in patients with onset before 28 years or in patients with another affected family member with onset before 28 years of age; no other genetic testing was performed.

Statistical analysis

The point prevalence and age/sex-specific prevalence rates of AOIFD in the Republic of Ireland were calculated using population data acquired from the 2011 National Census (www.cso.ie/en/census/census2011reports). Patient characteristics were analysed using ANOVA and the Kruskal–Wallis test. The relationship between categorical variables was assessed using the chi-squared test. *Post hoc* analysis for ANOVA was carried out using Fisher's least significant difference (LSD). For all tests the type I error rate was set at 0.05, without correcting for multiple comparisons. Statistical analyses were carried out using SPSS (IBM SPSS statistics version 20).

Ethics

Ethical approval for this work was granted by the Ethics and Medical Research Committees, St Vincent's University Hospital, Dublin, and by ethics committees at all participating centres.

Results

Participants recruited

In all, 592 AOIFD patients who were alive on the prevalence date were identified. Of these, 507 patients consented for use of their data to calculate age/sex-specific prevalence rates; for 375 participants there was a full dataset available for clinical characteristics analysis.

Prevalence of AOIFD in Ireland

From the most recent census of the Republic of Ireland (Census 2011) the total population was 4 588 252 (3 325 821 $\geq$ 20 years of age). The point prevalence of AOIFD in those over the age of 20 years on 31 December 2014 (592 patients) was 0.0178% (17.8 per 100 000; 95% confidence interval 16.4–19.2). Overall point prevalence was twice as high in women as in men (0.021% vs. 0.0093%). The highest point prevalence in women was 58.4 per 100 000 in the 65–69 year age group; in men the highest point prevalence was 37.9 per 100 000 in the age group $\geq$ 85 years (with a relatively small population denominator) (Table S1 and Fig. 1). The age/sex-specific prevalence rates for each 5-year period are graphically displayed in Fig. 1, which indicates clearly the overall predominance of women except in the 20–34 year quinquennia.

Clinical characteristics of AOIFD patient population

Phenotypes

Of the total 592 patients, the most common phenotype was CD with 410 individuals (69.2%) followed by BSP 102 (17.2%), FHD 39 (6.6%), SD 18 (3.0%), musician's dystonia (MD) 17 (2.9%) and OMD six (1.0%) (Table 1). All phenotypes occurred more frequently in women except MD, which was more common in men, and FHD, which was approximately equal between the sexes (Table S1 and Fig. 1). All FHD patients had task-specific writer's cramp.

Figure 1 Histogram illustrating the age/sex prevalence of AOIFD (cases per 100 000 population) in men and women within 5-year age groups in the Irish population (women, pink bars; men, blue bars). This illustrates the overall predominance of women in each quinquennium except for the 20–34 years age groups.

Table 1 Clinical and demographic characteristics for each phenotype in the prevalence study

Phenotype	CD	BSP	FHD	SD	MD	OMD
Number of patients (592)	410	102	39	18	17	6
Female:male ratio	2.6: 1	3.1: 1	1.2: 1	5: 1	0.6: 1	5: 1
Number of patients with all data (375)	291	33	21	10	16	4
Mean age at onset (years) (SD)	45.4 (12.8)	56.1 (9.9)	38.9 (11.4)	47.0 (20.3)	31.7 (12.3)	65.3 (15.8)
Women: mean age at onset (years) (SD)	46.3 (12.1)	54.4 (10)	41.7 (11.8)	44.6 (20)	40	65.3 (15.8)
Men: mean age at onset (years) (SD)	43.7 (13.8)	61.5 (7.98)	35.9 (10.7)	69	31.3 (12.9)	N/A
Confirmed family history of dystonia (%)	17.2	18.2	9.5	30	0	25
Segmental spread (%)	13.7	33.3	19.0	33.3	0	50
Sensory trick (%)	59.5	21.2	4.8	0	0	25
Associated upper limb tremor (%)	16.8	0	23.8	20	0	0
Pain (%)	54.6	3.0	38.1	0	0	0
Psychiatric comorbidity reported (%)	23.4	33.3	9.5	10.0	25.0	33.3
Onset <30 years (%)	5.8	3.0	19.0	10.0	50	0

CD, cervical dystonia; BSP, blepharospasm; FHD, focal hand dystonia; MD, musician's dystonia; SD, spasmodic dysphonia; OMD, oro-mandibular dystonia.

The full cohort consists of 592 individuals with adult onset idiopathic isolated focal dystonia in Ireland on the prevalence date. However, full clinical characteristics could only be determined for 375 individuals. Patients with cervical dystonia were more likely to consent to use of their clinical data in this study (than other phenotypes). Note the tendency for an earlier mean age of onset in men (than women) in focal hand dystonia, musician's dystonia and cervical dystonia.

Associated clinical features in 375 (of 592) patients with full data

Age at onset

The oldest mean age at onset in our cohort occurred in patients with OMD (65.3 years), followed by BSP (56.1 years), SD (47.0 years), CD (45.4 years) and FHD (38.9 years) (Table 1). The data were submitted to a one-way ANOVA, which confirmed an overall significant difference in age of onset between the various sites of dystonia onset [$F(5, 369) = 11.6$; $P < 0.001$]. In Fisher's LSD *post hoc* analysis the same degree of statistical difference was again seen between all phenotypes except for BSP versus OMD, CD versus SD, SD versus FHD and FHD versus MD where difference in mean age of onset did not reach significance. A younger mean age of onset of dystonia in men versus women was found for all phenotypes except BSP and SD. In our CD cohort men were, on average, 3 years younger than women when they first developed symptoms with a mean age of onset of 43.7 years in men and 46.3 years in women (Table 1).

Other clinical features

A sensory trick was found in 59.5% of CD, 21.2% of BSP and 4.8% of FHD ($P < 0.0001$ across phenotypes, Kruskal–Wallis, 17.4% effect size). A proportion of CD, FHD and SD patients were noted to have a concomitant upper limb tremor [16.8%, 23.8% and 20%, respectively ($P = 0.041$ across groups, Kruskal–Wallis, 3.13% effect size)]. There was no significant influence of age of onset ($P = 0.396$) and sex ($P = 0.806$) on the occurrence of upper limb tremor.

Rates of pain varied across all six phenotypes ($P < 0.0001$, Kruskal–Wallis) with phenotype accounting for 15.8% of the variance. Pain was most prevalent in those with CD (54.6%; $P < 0.001$) and FHD (38.1%). On *post hoc* analysis the frequency of pain in CD and FHD remained significant compared to other phenotypes except for CD versus FHD ($P = 0.143$) and FHD versus OMD ($P = 0.142$).

Self-reported psychiatric symptoms requiring medical advice

Self-reported psychiatric symptoms requiring medical advice were common across all phenotypes but were most prevalent in BSP, CD and OMD although there were no statistically significant differences across the groups ($P = 0.248$, Kruskal–Wallis). Depression and anxiety were the most commonly reported psychiatric comorbidities. There was no significant association between pain and psychiatric comorbidity ($P = 0.210$).

Segmental spread

Spread of dystonic symptoms was most commonly seen in those with OMD (50%), BSP (33.3%) and SD (33.3%) with lower rates of 13.7% and 19% in CD and FHD ($P = 0.005$ across groups, Kruskal–Wallis, 4.42% effect size). This remained significant on *post hoc* (chi-squared) analysis between phenotypes for CD versus BSP ($P = 0.003$), CD versus OMD ($P = 0.040$), BSP versus MD ($P = 0.009$), SD versus MD ($P = 0.022$) and for MD versus OMD ($P = 0.004$). There was a significant correlation between segmental spread and the presence of upper limb tremor ($P < 0.001$). The mean age at onset of those who

experienced spread of their dystonia was 47.36 years (SD 13.19) versus those without spread at 45.4 years (SD 13.0) ($P = 0.291$). Disease duration had a significant impact on spread; patients without symptom spread had average disease duration of 14.4 years (SD 9.6) on the prevalence date, whilst those with spread of their dystonia had average disease duration of 19.9 years (SD 12.3; $P < 0.001$). Sex did not influence spread of dystonic symptoms ($P = 0.949$).

Family history

Some 134/375 (35.7%) patients with a full dataset reported a family history of a movement disorder; 62/375 (16.5%) had clinically confirmed AOIFD in a relative (Fig. 2). Eighteen multiplex families with three or more individuals affected with AOIFD and another 24 duplex families with two individuals affected were identified. Affected relatives deceased or living outside Ireland were identified and are included in the reporting of the frequency of a positive family history but were not included in other aspects of the epidemiological survey.

Genetic architecture

All of the 18 multiplex families had a possible autosomal dominant mode of inheritance with reduced penetrance. Mitochondrial inheritance was also a possible mode of transmission in 14 of these 18 pedigrees but many offspring had not yet reached the age for risk of onset of AOIFD. Phenotypic heterogeneity was observed within the pedigrees (Table 2). All affected members of 18 families (five multiplex, 13 duplex) had CD only, whilst seven families had CD and FHD and another six families had CD and SD. The mean age at onset in the CD patients with a clinically confirmed

family history of dystonia (41.8 years; SD 12.1) was 4.2 years earlier than the mean age of onset of sporadic CD patients (46.0 years; SD 12.7) [$F(1, 227) = 4.00$; $P = 0.047$, one-way ANOVA].

Discussion

Point prevalence rate

In this study the prevalence of AOIFD in Ireland has been determined following an intensive recruitment of eligible patients over a 5-year period. A point prevalence of 17.8 per 100 000 was calculated, similar to other service-based studies [21,22,35–37]. A recent meta-analysis of prevalence studies of primary dystonia estimated a prevalence rate of 16.43 per 100 000 (95% confidence interval 12.09–22.32) [19]; our point prevalence rate is remarkably similar. Through participation of all the neurology, specialist botulinum toxin and movement disorder outpatient clinical services in the country an attempt was made to limit the number of potentially missed cases. Service-based studies remain the most practical method of prevalence estimation; record linkage or door-to-door studies are limited by diagnostic inaccuracy, small denominators and over-ascertainment, with marked variation in prevalence estimates. Prevalence rates of AOIFD depend on expert neurological assessment but are also totally dependent on patient referral from primary

Table 2 Phenotypic composition of the 42 familial adult onset idiopathic isolated focal dystonia (AOIFD) pedigrees ascertained in the prevalence study from 42 consenting index cases (18 multiplex and 24 duplex pedigrees)

Phenotypes seen in pedigree	Number of multiplex pedigrees with phenotypes	Number of duplex pedigrees with phenotypes
CD only	5	13
FHD only	–	1
BSP only	–	1
CD + SD	5	1
CD + FHD	2	5
CD + BSP	2	–
CD + FHD + BSP	1	–
CD + UL dystonic tremor	1	–
CD + SD + OMD	1	–
CD + SD + CD + UL tremor	1	–
CD + axial dystonia	–	1
CD + BSP + OMD	–	1
CD + BSP + OMD + SD	–	1
Total	18	24

BSP, blepharospasm; CD, cervical dystonia; FHD, focal hand dystonia; OMD, oromandibular dystonia; SD, spasmodic dysphonia; UL, upper limb.

Figure 2 Flowchart illustrating the disposition of the total number of 592 ascertained patients with adult onset idiopathic isolated focal dystonia (AOIFD), the subgroup of 375 patients with full clinical details, the 62 patients with clinically confirmed familial AOIFD and the 19 patients with a family history of suspected AOIFD.

healthcare practitioners. For that reason our study is an underestimate of the true prevalence; many individuals with milder forms of FHD, for example, are unlikely to seek medical attention.

Prevalence of phenotypes: environmental effects?

Cervical dystonia was by far the most commonly observed phenotype. There was a relatively low prevalence of BSP compared to that reported from southern Europe [38], despite repeated determined efforts to recruit these patients through specialist ophthalmology clinics in all parts of Ireland. This low proportion of BSP is therefore considered not to be the result of referral bias but rather reflects a true low prevalence. Given the relatively high rate of immigration and emigration from Ireland over centuries it is unlikely that this represents a genetic isolate. It is hypothesized that it is a consequence of lower sunlight exposure in Ireland [24]. The ratio of BSP to total CD plus BSP patients ascertained in this study ($102/512 = 0.20$) is within the confidence limits of the ratio predicted from the average first quarter solar insolation reported in Ireland ($1.4 \text{ kWh/m}^2/\text{day}$) (see Fig. 3, derived from reference 24, Fig. 2).

Age-related sexual dimorphism of sex ratios in AOIFD

Overall in this study (as in other epidemiological reports) women were more frequently affected with AOIFD than men with the exception of an almost equal ratio in FHD and a male predominance in MD. The ratio of women to men affected with CD was 2.6:1 which is slightly higher than previously reported [15,21,29,39,40]. Men had an earlier mean age at onset in CD, FHD and MD than women; men were approximately 3 years younger at mean age of onset than women in our CD cohort. A younger age of onset in men has been demonstrated in other CD populations [40,41]; the reasons for this are not known. Theories include possible protective hormonal or genetic sex effects. Sexual dimorphism in the sex ratios of AOIFD phenotypes has been noted for many years with a male predominance in FHD and MD along with a steadily increasing female:male sex ratio with increasing mean age of onset in the phenotypes CD, BSP and OMD. Temporal discrimination thresholds show similar sexual dimorphism [42], a measure found to be abnormal in AOIFD patients [43–45] and their unaffected first-degree relatives. The sexual dimorphism seen in temporal processing of sensory stimuli in both healthy control subjects [42] and unaffected relatives of AOIFD patients [45] seems to parallel age-related sexual dimorphism of sex ratios observed in AOIFD.

Figure 3 This graph (derived from reference 24, Fig. 2) illustrates the association between the blepharospasm:cervical dystonia phenotype ratio (the ratio of the number of blepharospasm patients to the total number of cervical dystonia and blepharospasm patients) and quarter-one insolation measured as $\text{kWh/m}^2/\text{day}$ for study sites throughout the northern hemisphere. The ratio of blepharospasm to total cervical dystonia plus blepharospasm patients ascertained in the present study ($102/512 = 0.20$) (red filled circle) is within the confidence limits of the ratio predicted from the average first quarter insolation reported in Ireland ($1.4 \text{ kWh/m}^2/\text{day}$). The black circles show data from each of the studies with the diameter of the circles proportional to the square root of the total number of individuals in each study. The solid line is the fitted meta-regression back transformed from the logit scale. The dashed lines are the 95% confidence intervals for the mean association back transformed to the original scale.

Sensory tricks

The reported prevalence of sensory tricks was similar to that found in previous studies [28,46]. The physiology of such alleviating manoeuvres in dystonia has been suggested to involve modulation of abnormally increased facilitation [47,48]; detailed characterization of the neurophysiological mechanisms of such alleviating manoeuvres would contribute to increased understanding of sensorimotor integration in dystonia.

Segmental spread

The observed rate of segmental spread was, as expected, highest in OMD and BSP [49]. Although data on time elapsed from symptom onset to segmental spread was not recorded, our findings of increased disease duration in those who developed segmental spread is in line with other studies reporting age as an independent factor for spread [50].

Tremor

Upper limb tremor occurred in association with AOIFD in 16.8% and 20% of CD and SD patients respectively. Overall rates of tremor reported (both dystonic tremor and tremor associated with dystonia), vary considerably and range from 10% to 85% [26,51,52]. In a large Italian dystonia cohort there was an overall prevalence of tremor at 16.7%, but only 5.8% with upper limb tremor [26]. Tremor was reported in almost 24% of the FHD patients; it is suspected that this is an artefact of referral bias. Overall FHD is likely to be under-ascertained in a service-based epidemiological survey. Patients with FHD and associated tremor are more likely to be referred by general practitioners whereas FHD patients without tremor are less likely to be recognized in the community.

Pain

The high rates of pain and coincident psychiatric conditions highlight the overall burden of dystonia and the importance of screening for these in the clinical setting and employing a multidisciplinary approach to treatment of AOIFD. Interestingly there was no statistically significant relationship observed between the two, indicating that the processes involved in their development are independent of each other.

Genetic aspects

Sixty-two patients who had another family member with a confirmed diagnosis of AOIFD were identified, representing 16.5% of our cohort. None of these patients had a secondary or identifiable genetic cause for their dystonia. This is probably an underestimation of the proportion of familial cases; in a further 19 patients a family history of dystonia was deemed suspicious but could not be confirmed for a number of reasons (refusal to participate, living abroad). A family history of dystonia in these remaining 19 patients cannot be confirmed; Leube and colleagues suggest that patient report is likely to significantly underestimate actual rates of dystonia amongst family members [6]. Reported rates of family history of dystonia in seemingly sporadic AOIFD vary from 26.1% [53], 18% [6] to 9.1% [28]. The patterns of inheritance observed in this study would support an autosomal dominant transmission of genes predisposing to dystonia, with reduced penetrance. Although some of the multiplex pedigrees might appear to support a mitochondrial inheritance pattern, many of the probands' offspring had not yet

reached the age at which the disorder would be penetrant. Evidence from abnormal temporal discrimination thresholds in unaffected first-degree relatives of patients with AOIFD would also support an autosomal dominant inheritance with reduced penetrance [44,45]. Further understanding of the patterns of disease penetrance, including the influence of gender, in AOIFD will add to our knowledge of the aetiopathology of this multifactorial condition. The CD patients were not sub-divided with regard to the presence or absence of head tremor and the observation that patients with tremulous CD, compared to those without head tremor, are more likely to be familial cannot be confirmed [54].

An earlier age at onset in patients with a confirmed family history of dystonia could be indicative of as yet undiscovered genetic variants with higher penetrance. However, more probably, an increased awareness of the condition in relatives of affected patients and identification of asymptomatic affected relatives by the research team prior to seeking medical attention may also have contributed to the finding of an earlier age at onset in familial cases.

Limitations

This was a service-based study and therefore is probably an underestimate of the true prevalence of AOIFD, as it does not take into account those who have not sought medical attention or have not attended a specialist. There may also be a referral bias as patients were recruited mainly through neurology, botulinum toxin and ophthalmology outpatient clinics, with perhaps an underestimate in particular of the prevalence of SD as ear, nose and throat clinics were not routinely included in our recruitment process. Full clinical information was missing or not included due to lack of full consent in 217/592; as a result the prevalence of clinical characteristics described in Table 1 is open to error. However, this is considered unlikely as 375 patients represent a significant cohort and the prevalence rates are similar to, or greater than, those reported elsewhere.

Conclusion

The clinical characteristics of a large population of patients with primary AOIFD are described and, for the first time in an Irish population, prevalence data are reported. Detailed characterization of disease with identification of patient subgroups based on phenotype, age at onset, mode of inheritance and other clinical features is vital to inform future genetic studies and guide research.

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Disclosure of conflicts of interest

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Point prevalence of adult onset isolated focal dystonia (AOIFD) in Ireland for men and women by age groups in quinquennia illustrating the effects of age and gender on the age/sex-specific point prevalence rates.

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