

## RESEARCH PAPER

# Sun exposure is an environmental factor for the development of blepharospasm

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**ABSTRACT**

**Background** Adult-onset isolated focal dystonia may present with various phenotypes including blepharospasm and cervical dystonia. Although inherited in an autosomal dominant manner with a markedly reduced penetrance, environmental factors are considered important in disease penetrance and expression. We observed a marked variation by latitude in the reports of the frequency of patients with blepharospasm relative to those with cervical dystonia; we hypothesised that sun exposure is an environmental risk factor for the development of blepharospasm in genetically susceptible individuals.

**Methods** From published clinic cohorts and epidemiological reports, the ratio of the number of cases of blepharospasm to cervical dystonia (phenotype case ratio) at each study site was analysed with regard to latitude and measures of annual insolation. Meta-regression analyses of the phenotype case ratio to these environmental factors were performed.

**Results** The phenotype case ratio in 15 eligible study sites over 41° of latitude demonstrated a statistically significant inverse association with latitude ( $p=0.0004$ ,  $R^2=53.5\%$ ). There were significant positive associations between the phenotype case ratio and quarter-one (January–March) insolation ( $p=0.0005$ ,  $R^2=53\%$ ) and average annual insolation ( $p=0.003$ ,  $R^2=40\%$ ).

**Conclusion** The increase in the blepharospasm: cervical dystonia case ratio with decreasing latitude and increasing insolation suggests that sunlight exposure is an environmental risk factor for the development of blepharospasm (rather than cervical dystonia) in individuals genetically susceptible to adult-onset dystonia.

**INTRODUCTION**

Dystonia is a movement disorder, characterised by “sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.”<sup>1</sup> Adult-onset idiopathic isolated focal dystonia (AOIFD), the most common form of dystonia, is inherited in an autosomal dominant manner with a reduced penetrance of 12–15%;<sup>2–3</sup> phenotypes include cervical dystonia, blepharospasm, focal hand dystonia, spasmodic dysphonia, oromandibular dystonia and task-specific dystonia. Evidence from studies of affected sib-pairs<sup>4</sup> and multiplex families<sup>5–6</sup> indicates that the same presumed genetic mutation may cause different phenotypes. Environmental factors may influence disease penetrance and phenotype expression.<sup>7–9</sup> Patients with cervical dystonia, compared with their

unaffected siblings, have a history of more frequent car accidents with hospital attendance;<sup>10</sup> anterior segment eye disease has been suggested to be a risk factor for blepharospasm,<sup>11</sup> whereas coffee drinking appears protective.<sup>12</sup> Cervical dystonia appears to be the most frequent phenotype in northern Europe, whereas blepharospasm seems more frequent in southern Europe. We hypothesised that higher sunlight exposure, causing increased spasm of the orbicularis oculi muscles, might be an environmental risk factor for blepharospasm. There are few population-based prevalence studies of blepharospasm; thus, we analysed published clinic cohorts of patients with AOIFD to examine the relationship between the frequency of cervical dystonia and blepharospasm presentations of AOIFD with regard to latitude and sunlight exposure in the country of origin.

**PARTICIPANTS AND METHODS****Study population**

We searched PubMed and MEDLINE for publications using the search terms “blepharospasm”, “cervical dystonia”, “environmental risk”, “dystonia”, “epidemiology”, “incidence” and “prevalence”. Our inclusion criteria were publications that reported numbers of patients with cervical dystonia and blepharospasm from the same clinic or study sample population. Three authors screened full texts to identify study eligibility. We included only studies that were published in English; the references of all eligible studies were searched to ensure that no study was missed. Only studies that included and differentiated clearly both patients with primary cervical dystonia and blepharospasm were included in our analysis. Exclusion criteria were studies reporting patient numbers which did not separate secondary dystonias or dystonia-plus syndromes and studies that reported prevalence rates without stipulating raw patient numbers. In each study, we excluded patients listed as having “cranial dystonia” (oromandibular dystonia, spasmodic dysphonia and Meige's syndrome) because not all cranial dystonia includes symptoms of blepharospasm. For each study site, we calculated the phenotype ratio of the number of patients with blepharospasm to total cervical dystonia and blepharospasm cases.

**Sunlight exposure**

We determined coordinates (longitude, latitude) for each region under study using Google Maps (<http://>

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maps.google.com). We then used data from the US National Aeronautics and Space Administration (NASA) Surface Meteorology and Solar Energy (SSE) V.6.0 database for the climatological data. These data are obtained from the NASA Langley Research Center Atmospheric Science Data Center SSE web portal supported by the NASA LaRC POWER Project (<http://power.larc.nasa.gov>). These satellite-based and model-based products have been shown to be accurate enough to provide reliable solar and meteorological resource data over regions where surface measurements are sparse or non-existent, and offer two unique features—the data are global and, in general, contiguous in time. This database provides solar insolation values for the entire globe based on data collected from 1983 to 2005 (<http://eosweb.larc.nasa.gov/sse/>). The monthly average insolation is available for every  $1 \times 1^\circ$  grid of latitude and longitude. Solar insolation is a measure of the electromagnetic energy from the sun received for a given surface area on earth at a given time, expressed in kWh/m<sup>2</sup>/day. The solar insolation is associated with the earth–sun relationship (angle of the sun's rays and the day's length), absorption by clouds and atmospheric aerosols, and reflection into space by snow, ice and desert sand (<http://eosweb.larc.nasa.gov/sse/>). The pattern of monthly solar insolation varies predominantly with latitude, and locations at or near the equator will show the least monthly variation throughout the year, while locations near  $90^\circ$  from the equator (North and South Poles) have the most variation.

### Statistical analysis

A mixed effects meta-regression model was fitted to the logit of the phenotype ratio (proportion of blepharospasm cases to total number of cases of blepharospasm plus cases of cervical dystonia), with the latitude and then the solar insolation of the study location being included as moderators in the model. The model was fitted in R V.3.1.1 using the package metafor V.1.9.3.

## RESULTS

### Analysis set

Of 25 reports selected after screening by three neurologists (AM, SOR, MH), 15 were deemed to be suitable for inclusion (table 1). Reasons for excluding 10 reports were: studies of a single AOIFD phenotype (3 reports), only prevalence rates published (1), cohorts which did not separate patients with secondary dystonias from patients with primary dystonia only (2), a study of segmental dystonia (1), studies reporting cranial dystonia without reference to numbers of patients with pure blepharospasm (2) and non-English publication (1).

The 15 studies analysed came from Europe (11 studies<sup>13–23</sup>), Japan (2 studies<sup>24–25</sup>), India (1 study<sup>26</sup>) and USA (1 study;<sup>27</sup> table 1); all were from the northern hemisphere covering a latitude of  $41^\circ$  (Reykjavik, Iceland at  $64.1^\circ$  to Kolkata, India at  $22.6^\circ$ ). Most (13 studies) were service-based except for two epidemiological surveys in northern England<sup>13</sup> and India.<sup>26</sup> For each study, the numbers of patients with the phenotypes of interest, the ratio of cases with blepharospasm to cervical dystonia cases and blepharospasm cases combined (the phenotype ratio), the latitude of the study site, average annual and quarter-one (January–March) insolation at each study site are listed in table 1.

### Meta-regression analysis

*Blepharospasm: cervical dystonia phenotype case ratio versus latitude*—In a mixed effects meta-regression, a statistically significant inverse association between the phenotype case ratio and latitude was identified; the coefficient of latitude in a model for logit (proportion blepharospasm) was:  $-0.08$ , 95% CI ( $-0.12$  to  $-0.03$ ),  $p=0.0004$  (table 2). The  $R^2$  value for this association was 53.5%. This indicates evidence of a decreasing proportion of blepharospasm cases with increasing latitude. This effect is illustrated in the plot of proportion of cases versus latitude in figure 1.

**Table 1** The regions (or cities), country of origin and the references to the publications included in this analysis

Study location (reference)	(a) Blepharospasm cases (N)	(b) Cervical dystonia cases (N)	Phenotype ratio (a/a+b)	Average annual insolation (kWh/m <sup>2</sup> /day)	Quarter-one (January–March) insolation (kWh/m <sup>2</sup> /day)	Latitude (degrees north)
Reykjavik, Iceland <sup>14</sup>	9	33	0.21	2.09	0.7	64.1
Oslo, Norway <sup>15</sup>	24	66	0.27	2.46	1.09	59.9
Amsterdam, the Netherlands <sup>16</sup>	97	432	0.18	3.02	1.62	52.4
Northern England, UK <sup>13</sup>	219	566	0.25	2.54	1.37	52.2
London, UK <sup>17</sup>	102	424	0.19	2.72	1.5	51.5
Lille, France <sup>18</sup>	58	75	0.44	2.91	1.67	50.6
Munich, Germany <sup>19</sup>	41	72	0.36	3.15	2.04	48.1
Belgrade, Serbia <sup>20</sup>	23	72	0.24	3.57	2.34	44.8
Rochester, Minn, USA <sup>27</sup>	1	5	0.17	3.73	2.64	44
Rome, Italy <sup>21</sup>	128	118	0.52	4.65	3.07	41.9
Foggia, Italy <sup>22</sup>	32	24	0.57	4	2.62	41.5
Segovia, Spain <sup>23</sup>	24	5	0.83	4.39	3.06	40.9
Akita, Japan <sup>25</sup>	122	33	0.79	3.42	2.64	39.7
Kyoto, Japan <sup>24</sup>	49	34	0.59	3.63	2.66	35
Kolkata, India <sup>26</sup>	3	2	0.6	4.67	4.95	22.6

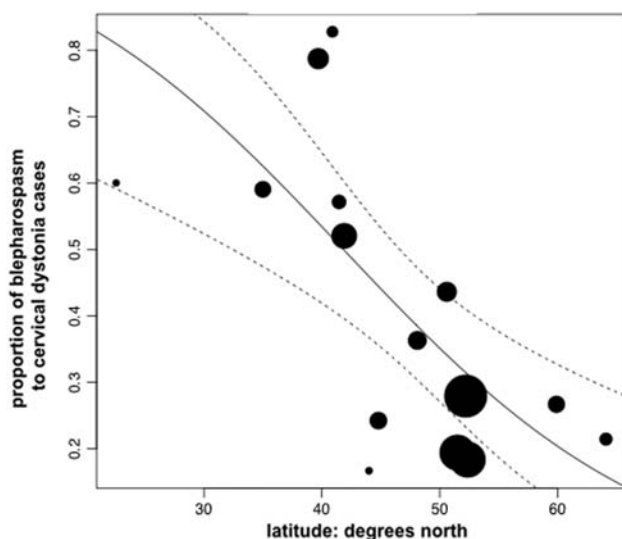
The sites are ordered by descending latitude. The number of (a) blepharospasm and (b) cervical dystonia cases reported in each study are given. The phenotype ratio for each study site was calculated from the number of blepharospasm cases divided by the total number of cervical dystonia plus blepharospasm cases. For each study site, the average annual solar insolation (insolation is a measure of electromagnetic energy from the sun received for a given surface area at a given time, expressed as kWh/m<sup>2</sup>/day), quarter-one (January–March) insolation and latitude in degrees north are given (the three independent variables of interest in this analysis).

**Table 2** The meta-regression analysis results for the three independent variables of interest (latitude (degrees), average annual insolation as kWh/m<sup>2</sup>/day, and quarter-one (January–March) insolation (kWh/m<sup>2</sup>/day)) with the blepharospasm:cervical dystonia phenotype ratio as the dependent variable

Meta-regression analysis of the blepharospasm:cervical dystonia ratios reported at 15 sites by latitude, average annual insolation and quarter-one (January–March) insolation					
Variable	Coefficient	SE	p Value	CI	R <sup>2</sup> (%)
Latitude	−0.08	0.02	0.0004	−0.12 to −0.03	53.5
Average annual insolation	0.81	0.27	0.003	0.28 to 1.35	40
Quarter-one insolation	0.75	0.22	0.0005	0.33 to 1.18	53

Coefficients, SEs, p values and CIs are shown. p Values<0.05 are considered to be statistically significant.

*Blepharospasm: cervical dystonia phenotype case ratio versus measures of insolation*—There was a statistically significant positive association between the phenotype case ratio and average annual insolation; coefficient of annual insolation in a model for logit (proportion blepharospasm) was: 0.81, 95% CI (0.28 to 1.35),  $p=0.003$ . The  $R^2$  value for this association was 40% (table 2). In this model, for a 1-unit change in insolation, there was predicted to be an 18.7% increase in the proportion of blepharospasm cases. When insolation was analysed in quarters, using forward stepwise regression the quarter-one insolation (January–March) had an  $R^2=53\%$ , approaching that of latitude; of all measures of insolation, these 3 months correlated best with an increase in proportion of blepharospasm (table 2). The relationship between quarter-one insolation and blepharospasm is illustrated in figure 2. There was strong correlation between insolation and latitude ( $r=-0.86$ ), indicating that a multivariate



**Figure 1** The association between the blepharospasm:cervical dystonia phenotype ratio and latitude (degrees). Circles show data from each of the study centres 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% CIs for the mean association back transformed to the original scale.

model including both may be inappropriate; the model for latitude ( $R^2=53.5\%$ ) had a similar fit to that of quarter-one insolation ( $R^2=53\%$ ) but a better fit than average annual insolation ( $R^2=40\%$ ).

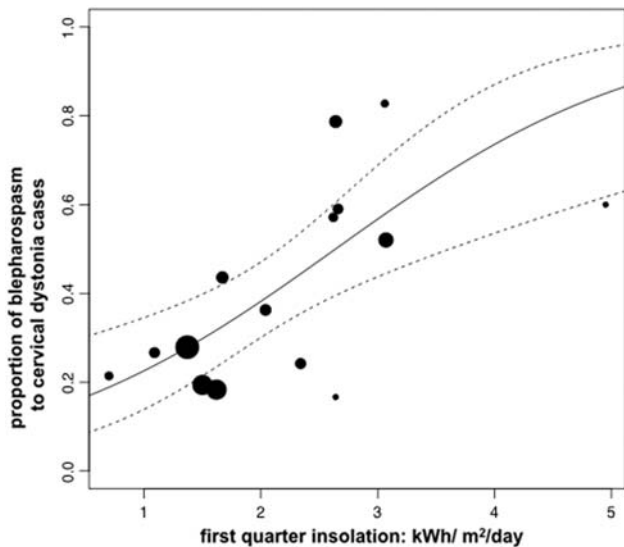
## DISCUSSION

In this meta-regression analysis, we have found that, over  $41^\circ$  of latitude in the northern hemisphere, decreasing latitude and increasing sunlight exposure intensity were both directly associated with the relative frequency of AOIFD presenting as blepharospasm compared with cervical dystonia. We postulate that, in a given population of individuals carrying a genetic predisposition for AOIFD, sunlight is an environmental risk factor for the development of blepharospasm rather than cervical dystonia. It might be reasonably hypothesised that the relationship between increased blepharospasm frequency and sunlight exposure is secondary to chronically increased orbicularis oculi muscle spasm due to more intense sunlight at lower latitudes. Patients with blepharospasm report photosensitivity and some find relief with tinted spectacles.<sup>28</sup> Environmental studies in blepharospasm have shown that eye symptoms are reported more frequently prior to onset<sup>11</sup> and tend to be more prevalent in the year prior to onset of spasms.<sup>8</sup> Diseases of the anterior ocular segment (blepharitis, conjunctivitis) have been shown to be significantly related to blepharospasm, but not other ocular diseases such as glaucoma and cataracts.<sup>7</sup> Excessive blinking caused by dry eye symptoms (xerophthalmia) is associated with Meige's syndrome as well as blepharospasm.<sup>29</sup> The hypothesis of a double-hit in the pathogenesis of blepharospasm, demonstrated in an animal model, may be of particular relevance.<sup>30</sup>

If high insolation-induced orbicularis ocular spasm in a genetically predisposed individual is an environmental risk factor for dystonic blepharospasm, then it might be classified as an overuse phenomenon. Overuse as a pathogenetic factor is seen in musicians' and focal hand dystonia;<sup>31–34</sup> it is also a factor in an animal model of dystonia.<sup>35</sup> Musicians' dystonia occurs in approximately 1% of highly trained musicians; the risk is higher with the more intensively used hand and with instruments requiring maximal fine motor skills.<sup>34</sup> A dose–response effect relationship has been shown in focal hand dystonia; increased writing hours per day, particularly in the year preceding onset, is a significant environmental risk factor, suggested to be related to maladaptive plasticity when motor training is pushed to extremes.<sup>32</sup> The alternative conclusion, that low sunlight exposure at high latitudes is a risk factor for cervical dystonia, is possible but seems biologically implausible.

There are a number of limitations to our study. There is variation in the patient numbers reported in different regions; however, the weighted nature of our analysis takes account of the fact that the larger studies have more influence on the effect estimate than smaller studies. A limitation of meta-analysis in general is the differences in data collection methods between study sites. Our primary concern was with proportions of blepharospasm and cervical dystonia reported in each study. This might have been affected by referral bias; neurologists and ophthalmologists treat different proportions of blepharospasm. Healthcare-seeking patterns are also important; in areas where specialist botulinum toxin services exist, awareness and specialist referral would be greater. Other differences in case ascertainment included population-based surveys versus electronic medical record or clinic record reviews. While the analysis of data obtained using differing collection methods from predominantly European countries is not ideal, pure epidemiological studies worldwide are few and would not be sufficient to

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**Figure 2** The association between the blepharospasm:cervical dystonia phenotype ratio and quarter-one insolation measured as kWh/m<sup>2</sup>/day. 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% CIs for the mean association back transformed to the original scale.

support this novel hypothesis. It is probable that many cases of blepharospasm go undiagnosed and it is noteworthy that diagnostic criteria differed across studies.

Dystonia is considered to be a primary basal ganglia disorder with secondary cortical manifestations;<sup>36</sup> putaminal enlargement is found in blepharospasm,<sup>37</sup> and thalamic hypermetabolism is reported in patients with blepharospasm with photophobia compared with patients with blepharospasm without photophobia and control subjects.<sup>38</sup>

An underlying hypothesis is that disease penetrance and phenotypic expression, in an individual who has inherited susceptibility gene(s) for AOIFD, depend on the nature and duration of the environmental exposure. Environmental risk factors for cervical dystonia include trauma,<sup>7–10</sup> but no relationship has been found between head trauma and blepharospasm or other cranial phenotypes.<sup>39</sup> Similarly, scoliosis, which has been associated with cervical dystonia,<sup>40</sup> has been shown not to be a risk for blepharospasm.<sup>41</sup> The links between sun intensity, increased orbicularis oculi spasm and blepharospasm are pathophysiological plausible.

In summary, we hypothesise that sunlight intensity is a risk factor for development of blepharospasm and, in this manner, may represent an overuse phenomenon. We would recommend further prospective collaborative studies including population-based surveys between centres of divergent latitudes, examining other factors, including age of onset, to investigate this observation further.

**Contributors** AM contributed in the study design, drafting of the manuscript, review of the literature, and performed preliminary statistical analyses. LW contributed in the study design, critique of the manuscript and review of the available literature. OK and JSB contributed in the study design, critique of the manuscript and review of the literature. IB and EM contributed in the study design, review of the literature and drafting of the manuscript. SOR oversaw the project and contributed in the critique of the manuscript. RBR contributed in the study design and review of the manuscript, and oversaw the project. CW provided statistical expertise and contributed in review of the manuscript. MH contributed in the study design, generation of the hypothesis and critique of the manuscript, and oversaw the project.

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**Competing interests** None declared.

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## REFERENCES

- Albanese A, Bhatia K, Bressman SB, *et al.* Phenomenology and classification of dystonia: a consensus update. *Mov Disord* 2013;28:863–73.
- Waddy HM, Fletcher NA, Harding AE, *et al.* A genetic study of idiopathic focal dystonias. *Ann Neurol* 1991;29:320–4.
- Leube B, Kessler KR, Goecke T, *et al.* Frequency of familial inheritance among 488 index patients with idiopathic focal dystonia and clinical variability in a large family. *Mov Disord* 1997;12:1000–6.
- Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? *Brain* 2007;130:1183–93.
- Brancati F, Defazio G, Caputo V, *et al.* Novel Italian family supports clinical and genetic heterogeneity of primary adult-onset torsion dystonia. *Mov Disord* 2002;17:392–7.
- O’Riordan S, Raymond D, Lynch T, *et al.* Age at onset as a factor in determining the phenotype of primary torsion dystonia. *Neurology* 2004;63:1423–6.
- Defazio G, Berardelli A, Abbruzzese G, *et al.* Possible risk factors for primary adult onset dystonia: a case-control investigation by the Italian Movement Disorders Study Group. *J Neurol Neurosurg Psychiatry* 1998;64:25–32.
- Martino D, Defazio G, Alessio G, *et al.* Relationship between eye symptoms and blepharospasm: a multicenter case-control study. *Mov Disord* 2005;20:1564–70.
- Tanner K, Roy N, Merrill RM, *et al.* Case-control study of risk factors for spasmodic dysphonia: a comparison with other voice disorders. *Laryngoscope* 2012;122:1082–92.
- Molloy A, Kimmich O, Williams L, *et al.* An evaluation of the role of environmental factors in the disease penetrance of cervical dystonia. *J Neurol Neurosurg Psychiatry* 2015;86:331–5.
- Defazio G, Abbruzzese G, Aniello MS, *et al.* Environmental risk factors and clinical phenotype in familial and sporadic primary blepharospasm. *Neurology* 2011;77:1–11.
- Defazio G, Martino D, Abbruzzese G, *et al.* Influence of coffee drinking and cigarette smoking on the risk of primary late-onset blepharospasm: evidence from a multicentre case control study. *J Neurol Neurosurg Psychiatry* 2007;78:877–9.
- Butler AG, Duffey PO, Hawthorne MR, *et al.* An epidemiologic survey of dystonia within the entire population of northeast England over the past nine years. *Adv Neurol* 2004;94:95–9.
- Asgeirsson H, Jakobsson F, Hjalton H, *et al.* Prevalence study of primary dystonia in Iceland. *Mov Disord* 2006;21:293–8.
- Le KD, Nilsen B, Dietrichs E. Prevalence of primary focal and segmental dystonia in Oslo. *Neurology* 2003;61:1294–6.
- Groen J, Kallen M, de Warrenburg B, *et al.* Phenotypes and genetic architecture of focal primary torsion dystonia. *J Neurol Neurosurg Psychiatry* 2012;83:1006–11.
- Soland V, Bhatia K, Marsden D. Sex prevalence of focal dystonias. *J Neurol Neurosurg Psychiatry* 1996;60:204–5.
- Dhaenens CM, Krystkowiak P, Douay X, *et al.* Clinical and genetic evaluation in a French population presenting with primary focal dystonia. *Mov Disord* 2005;20:822–5.
- Castelon Konkiewitz E, Trender-Gerhard I, Kamm C, *et al.* Service-based survey of dystonia in Munich. *Neuroepidemiology* 2002;21:202–6.
- Pekmezovic T, Ivanovic N, Svetel M, *et al.* Prevalence of primary late-onset focal dystonia in the Belgrade population. *Mov Disord* 2003;18:1389–92.
- Defazio G, Gigante A, Abbruzzese G, *et al.* Tremor in primary adult-onset dystonia: prevalence and associated clinical features. *J Neurol Neurosurg Psychiatry* 2013;84:404–8.
- Papantonio AM, Beghi E, Fogli D, *et al.* Prevalence of primary focal or segmental dystonia in adults in the district of Foggia, southern Italy: a service-based study. *Neuroepidemiology* 2009;33:117–23.
- Sempere AP, Duarte C, Coria F, *et al.* Prevalence of idiopathic focal dystonia in the province of Segovia, Spain. *J Neurol* 1994;241:5124.
- Matsumoto S, Nishimura M, Shibasaki H, *et al.* Epidemiology of primary dystonias in Japan: comparison with Western countries. *Mov Disord* 2003;18:1196–8.
- Sugawara M, Watanabe S, Toyoshima I. Prevalence of dystonia in Akita Prefecture in Northern Japan. *Mov Disord* 2006;21:1047–9.
- Das SK, Banerjee TK, Biswas A, *et al.* Community survey of primary dystonia in the city of Kolkata, India. *Mov Disord* 2007;22:2031–6.
- Nutt JG, Muentner MD, Aronson A, *et al.* Epidemiology of focal and generalized dystonia in Rochester, Minnesota. *Mov Disord* 1988;3:188–94.
- Patel N, Jankovic J, Hallett M. Sensory aspects of movement disorders. *Lancet Neurol* 2014;13:100–12.

- 29 Tsubota K, Fujihara T, Kaido M, *et al.* Dry eye and Meige's syndrome. *Br J Ophthalmol* 1997;81:439–42.
- 30 Schicatanò EJ, Basso MA, Evinger C. Animal model explains the origins of the cranial dystonia benign essential blepharospasm. *J Neurophysiol* 1997;77:2842–6.
- 31 Frucht SJ, Fahn S, Greene PE, *et al.* The natural history of embouchure dystonia. *Mov Disord* 2001;16:899–906.
- 32 Roze E, Soumare A, Pironneau I, *et al.* Case-control study of writer's cramp. *Brain* 2009;132:756–64.
- 33 Hallett M, Lin P. The pathophysiology of focal hand dystonia. *J Hand Ther* 2009;22:109–14.
- 34 Altenmüller E, Jabusch HC. Focal dystonia in musicians: phenomenology, pathophysiology and triggering factors. *Eur J Neurol* 2010;17:(Suppl 1): 31–6.
- 35 Byl NN, Merzenich MM, Jenkins WM. A primate genesis model of focal dystonia and repetitive strain injury: I. Learning-induced dedifferentiation of the representation of the hand in the primary somatosensory cortex in adult monkeys. *Neurology* 1996;47:508–20.
- 36 Berardelli A, Rothwell JC, Hallett M, *et al.* The pathophysiology of primary dystonia. *Brain* 1998;121:1195–212.
- 37 Etgen T, Mühlau M, Gaser C, *et al.* Bilateral grey-matter increase in the putamen in primary blepharospasm. *J Neurol Neurosurg Psychiatry* 2006;77:1017–20.
- 38 Emoto H, Suzuki Y, Wakakura M, *et al.* Photophobia in essential blepharospasm—a positron emission tomographic study. *Mov Disord* 2010;25:433–9.
- 39 Martino D, Defazio G, Abbruzzese G, *et al.* Head trauma in primary cranial dystonias: a multicentre case-control study. *J Neurol Neurosurg Psychiatry* 2007;78:260–3.
- 40 Defazio G, Abbruzzese G, Girlanda P, *et al.* Primary cervical dystonia and scoliosis: a multicentre case control study. *Neurology* 2003;60:1012–15.
- 41 Martino D, Defazio G, Abbruzzese G, *et al.* Are non-genetic triggers for dystonia type-specific? A study exploring scoliosis in blepharospasm. *Mov Disord* 2007;22:576–8.



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