Understanding Dystonia: A Summary of the Basics

Olivia Chisholm [1]

[1] Neurology Department John Hunter Hospital

Dystonia is a neurological movement disorder characterised by abnormal and involuntary twisting movements and postures. It comes in many forms and can affect various parts of the body. Dystonia is seen in children and adults as a standalone condition, or as one part of a complex disease. Dystonia can be caused by genetic mutations, specific medications, environmental and chemical factors, or, as in the majority of cases, the cause is unknown. There is currently no cure or disease modifying agent for dystonia, so treatments are aimed at managing symptoms and maintaining quality of life. The treatment options for dystonia include invasive surgeries, medications, botulinum toxin and non-pharmaceutical therapies. Dystonia is often a misunderstood and misdiagnosed disorder, which makes diagnosis difficult. The diagnosis of dystonia is usually made by a Neurologist who specialises in Movement Disorders. Research is ongoing to better understand the disorder and aims to find more effective and efficient treatments, and ultimately a cure for dystonia.

Dystonia is a neurological movement disorder that causes sustained or irregular involuntary muscle contractions resulting in involuntary, abnormal twisted movements and postures which often cause pain (Albanese et al., 2013). The condition typically occurs in repetitive and patterned movements, with or without tremor in the affected region(s) of the body (Albanese et al., 2013). Dystonia can affect any region of the body, can present differently from person to person and affects individuals of any age, gender, race, or ethnic background (Grutz & Klein, 2021).

Dystonia is believed to be the result of damage or abnormalities to several areas of the brain, including the basal ganglia, cortical region and cerebellum, all of which are responsible for the coordination of movement. In dystonia, neurotransmitters from the affected part of the brain send abnormal signals, which then result in the unusual posture or position in the affected region of the body (Bautista et al., 2020).

The diagnosis of dystonia is typically made by a neurologist who specialises in movement disorders. Examinations used in the diagnosis of dystonia include a comprehensive physical assessment and medical history, laboratory tests including urine and blood samples, and genetic testing if required. Other radiological examinations such as magnetic resonance imaging (MRI) and electroencephalogram (EEG) scans may be necessary to diagnose acquired dystonia or rule out other conditions or disorders (Albanese et al., 2019).

The classification of dystonia has had a chequered past. The first use of the term dystonia, did not appear until 1911, with Oppenheim's description of "*dystonia musculorum deformans*" that he saw in four children he examined (Oppenheim, 1911). In the same year, a paper by Flateau and Sterling (1911) changed dystonia to their preferred term "*progressive torsion spasms*". However, the term dystonia has survived, although the classification has been revised over the years (Albanese et al., 2019).

Dystonia comes in many forms. It can be a standalone condition, or it can be one part of many other complex diseases. Focal dystonia is the most common type of dystonia observed. For this type of dystonia, to date no cause has been established (Comella, 2018). Thus, it is referred to as *idiopathic dystonia*. However, dystonia can be caused by genetic mutations and abnormalities (*genetic dystonia)* (Comella, 2018). *Acquired dystonia* refers to dystonia that is the result of a traumatic brain injury such as a stroke or hypoxia. Acquired dystonia can also be caused through exposure to certain chemicals such as manganese and cyanide, heavy metals, for example mercury and lead, or due to medication reactions, for example particular neuroleptics and antidepressants (Comella, 2018; Quartarone & Ruge, 2018).

Questions or comments about this article should be directed to Olivia Chisholm

Email address: olivia.chisholm@health.nsw.gov.au

DOI: 10.21307/ajon-2021-009

According to Albanese et al., (2013), classifying the various types of dystonia remains difficult, and there are many factors that should be considered including age of onset of dystonia, region(s) of the body affected by dystonia, the pattern of dystonia and any accompanying features.

Due to the many different factors that make classification of dystonia difficult, it is a condition that is often undiagnosed or misdiagnosed (Comella, 2018). As a result, there are no reliable statistics on the number of individuals living with dystonia in the general population of Australia at this time.

Classifications of dystonia

Cervical dystonia (CD) is the most common form of focal dystonia. Cervical dystonia is an 'umbrella term' for dystonia that affects muscles in the head and neck. Dystonia where the neck is pushed to one side is called *laterocollis.* Dystonia where the chin is tilted to one side is called *torticollis*, *anterocollis* is where the head is pushed forward, and *retrocolis* where the head is pushed back. Tremor is a common feature in CD. Individuals can have one or more forms of cervical dystonia. (Jost et al., 2020; McCambridge & Bradnam, 2021).

Writer's cramp is a task-specific dystonia where abnormal posturing can occur in the fingers, hand and often forearm while writing (Todt et al., 2021). *Benign essential blepharospasm* is dystonia of the eyelids which induces twitching, excessive blinking and often involuntary closure of the eyes (Byun et al., 2019; Soikas et al., 2019). *Oromandibular dystonia* is dystonia affecting the lower half of the face, including the masticatory muscles, muscles in the jaw, the tongue, lips, soft palate and pharnyx (Britton et al., 2020).

Dystonia - Parkinsonism is the term used for genetic disorders where both features of dystonia and parkinsonism, bradykinesia, rigidity and tremor, occur concurrently (Weissbach et al., 2021). The severity of dystonia and parkinsonism can vary in each individual. Examples of this disorder include some forms of dopa-responsive dystonia, rapid onset dystonia-parkinsonism disorder, Wilson's disease, some variants of juvenile Huntington's disease and some variants of infantile parkinsonism- dystonia disorder (Herzog et al., 2021; Ng et al., 2021).

Myoclonus - dystonia is another collective term for mostly genetic disorders that include myoclonus and features of dystonia. Often in these disorders, myoclonic jerks occur in the neck and upper limbs and dystonia presents as abnormal posturing of the forearm and hands, as well as the presence of cervical dystonia. The lower limbs are much less affected (Blackburn & Parnes, 2021; van der Veen et al., 2019).

Dopamine responsive dystonia is another umbrella term applied to genetic forms of dystonia, where the symptoms improve with the administration of dopaminergic medications, such as levodopa. In this form of dystonia, the symptoms begin in the lower limbs and later progress to the upper limbs. Abnormalities in gait are common. (Dong et al., 2020; Lee et al., 2018).

Dystonia can be drug induced. For example as seen in *tardive drug induced dystonia*, which is caused from long term use of neuroleptic medications. Alternatively, *acute dystonic reactions* may be seen following the use of antipsychotics, antiemetics and antidepressant medications (Krause et al., 2022).

Management of Dystonia

Unfortunately, at the present time, there is neither cure nor disease modifying treatment that can slow down or change the course of dystonia. The focus of the treatment for dystonia is based on the concept of symptomatic management and enhancing quality of life (Bledsoe et al. 2020). Thus, the treatment of dystonia is categorised into four main areas including medications, neurotoxins, neuromodulation and rehabilitation.

Medications for the treatment of dystonia must be individualised. Dopaminergic medications used for Parkinson's disease such as levodopa, dopamine agonists and monoamine oxidase inhibitors (MAOIs) can be effective in the treatment of dystonia particularly in types such as dopa-responsive dystonia (DRD), myoclonus dystonia or rapid-onset dystonia Parkinsonism (Pirio et al., 2017). Responses may vary depending on the condition and levodopa-induced dyskinesia may occur as a side effect (Bledsoe et al. 2020).

Tetrabenazine is a medication that is effective against tardive dystonia and anticholinergic medications, for example benzhexol and benztropine, are most effective in treating generalised dystonia (Jinnah, 2020). Baclofen, a medication more commonly used to

treat spasticity, has been effective in treating idiopathic and tardive dystonia (Pirio et al., 2017). Benzodiazepines such as diazepam and clonazepam, are used as second or third -line agents for management of dystonia (Bledsoe et al. 2020).

Another agent used in the treatment of dystonia is botulinum toxin (BoNT) however, the approval for BoNT use for dystonia varies from country to country. In Australia, BoNT has been approved by the Pharmaceutical Benefits Scheme (PBS) for use in cervical dystonia, blepharospasm and spasmodic dysphonia (Bledsoe et al., 2020; Sy & Fernandez, 2021). Other classifications of dystonia that are treated with off-label BoNT include upper limb dystonic tremor, upper and lower limb dystonia and orofacial dystonia. The advantages of using BoNT is the localised effect it has on the affected area of the body, and avoidance of the many systemic side effects that may occur with oral medications (Bledsoe et al. 2020; Jinnah et al., 2020).

Invasive neuromodulation includes techniques such as ablation and deep brain stimulation (DBS) (Sy & Fernandez, 2021). Ablation refers to surgically induced scarring of the affected area of the brain that causes the dystonia, through methods such as thalamotomy and in more recent times, MRI guided high-intensity focused ultrasound (MRgFUS) (Bledsoe et al., 2020). DBS is the most commonly used invasive neurosurgical treatment for dystonia (Bledsoe et al., 2020; Pirio et al., 2017). The DBS target site most used for dystonia is the globus pallidus internus (GPi) (Bledsoe et al. 2020).

Research continues to try and better understand and treat dystonia. Over recent years, surgical treatment options for dystonia have increased due to the advances in neurosurgery (Bledsoe et al., 2020), and while both Deep Brain Stimulation (DBS) and BoTN have revolutionised dystonia treatment, they are not without their therapeutic limitations and are not suitable treatments for all patients (Galpern et al., 2014; Kilic-Berkmen et al., 2021).

Ongoing research aims to refine and increase the effectiveness of methods used to manage dystonia. By identifying similarities in the many forms of dystonia and comparing this to other movement disorders, research aims to understand more about dystonia and how to find more effective treatments (Downs et al., 2020; Galpern et al., 2014).

Due to the many types of dystonia, prognosis varies enormously. For instance, spreading of dystonia from one region to another, has a negative effect on prognosis. Other factors that affect prognosis include, the individual's response to medications and treatment, and whether individuals experience periods of partial or complete remission from dystonic symptoms (Mainka et al., 2019). In patients with an acquired dystonia, such as drug induced dystonia or dystonia secondary to brain injury, the prognosis depends on the cause of the dystonia, the underlying pathology and available treatment options (Liow et al., 2016; van Edmond et al., 2015)

Future directions for dystonia

Looking forward, while effective treatment may require a combination of current therapeutic approaches, new therapies are being developed. Investigations into the effectiveness of methods such as exercise therapy, yoga, music therapy, mindfulness, transcranial electrical stimulation (TES) and transcranial magnetic stimulation (TMS) continue. Further investigation into these methods through well-designed clinical trials are necessary to evaluate their safety, effectiveness and efficacy (Galpern et al., 2014).

Dystonia continues to present as a complex disease, while its disease classification continues to evolve over time. Although dystonia is often a misunderstood disease, ongoing research and clinical trials hope to better understand disease pathophysiology and identify more efficient and effective treatment options.

References

Albanese, A., Bhatia, K., Bressman, S.B., Delong, M.R., Fahn, S., Fung, V.S., Hallett, M., Jankovic, J., Jinnah, H.A., Klein, C., Lang, A.E., Mink, J.W., Teller, J.K. (2013). Phenomenology and classification of dystonia: a consensus update. *Movement Disorders.* 28(7), 863-73. https://doi.10.1002/mds.25475. Epub 2013 May 6. PMID: 23649720; PMCID: PMC3729880.

Albanese, A., Di Giovanni, M., & Lalli, S. (2019). Dystonia: diagnosis and management. *European Journal of Neurology*, 12(1), 5-17.

Albanese, A., Di Giovanni, M., Lalli, S. (2019). Dystonia: diagnosis and management. *European Journal of Neurology.* 26(1), 5-17. https://doi: 10.1111/ene.13762. Epub 2018 Aug 18. PMID: 30035844.

Bautista, C., Miravite, J., Coronel, H., Hunt, D., & Dallow, E. (2020). Evidence-Based Strategies for Care of the Patient with Movement Disorders and Deep Brain Stimulation. *American Association of Neuroscience Nurses*, 1-29.

Berman, B. D., Groth, C. L., Sillau, S. H., Richardson, S. P., Norris, S. A., Junker, J., Bruggemann, N., Agarwal, P., Barbano, R. L., Espay, A. J., Vizcarra, J. A., Klein, C., Baumer, T., Loens, S., Reich, S. G., Vidailhet, M., Bonnet, C., Roze, E., Jinnah, H. A., Perlmutter, J. S. (2020). Risk of spread in adult-onset isolated focal dystonia: a prospective international cohort study. *Journal of Neurology, Neurosurgery & Psychiatry* ; 91 (3), 314-320. https://doi.10.1136/jnnp-2019-321794. Epub 2019 Dec 17. PMID: 31848221; PMCID:PMC7024047.

Blackburn, J., & Parnes, M. (2021). Tics, tremors and other movement disorders in childhood. *Current Problems in Pediatric and Adolescent Health Care*, *51*(3). https://doi.org/10.1016/j.cppeds.2021.100983

Bledsoe, I. O., Viser, A. C., & San Luciano, M. (2020). Treatment of Dystonia: Medications, Neurotoxins, Neuromodulation, and Rehabilitation. *Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics*, *17*(4), 1622–1644. https://doi.org/10.1007/s13311-020-00944-0

Britton, D., Alty, J., & Mannion, C. (2020). Oromandibular dystonia: a diagnosis not to miss. *Journal of Oral Maxillofacial Surgery*. *58*(5), 520-524 https://doi: 10.1016/j.bjoms.2020.02.018

Comella, C. (2018). Dystonia: Then and now. *Parkinsonism Related Disorders*, 46 (1), 66-69 https://doi: 10.1016/j.parkreldis.2017.06.025. Epub 2017 Jun 30. PMID: 28843401.

Diez-Fairen, M., Alvarez Jerez, P., Berghausen, J., & Bandres-Ciga, S. (2021). The Genetic Landscape of Parkinsonism-Related Dystonias and Atypical Parkinsonism-Related Syndromes. *International Journal of Molecular Sciences*, *22*(15). https://doi.org/10.3390/ijms22158100

Dong, H. Y., Feng, J. Y., Yue, X. J., Shan, L., & Jia, F. Y. (2020). Dopa-responsive dystonia caused by tyrosine hydroxylase deficiency: Three cases report and literature review. *Medicine, 99*(33), e21753. https://doi.org/10.1097/MD.0000000000021753

Downs, A.M., Roman, K. M., Campbell, S. A., Pisani, A., Hess, E. J., Bonsi, P. (2019) The neurobiological basis for novel experimental therapeutics in dystonia. *Neurobiol Dis*. Oct;130:104526. doi: 10.1016/j.nbd.2019.104526. Epub 2019 Jul 4. PMID: 31279827; PMCID: PMC6885011.

Flateau, E., & Sterling, W. (1911). *Progressiver Torsionspasms* bei Kindern. Z Gesamte *Neurol Psychiatr,* 7, 586-612

Galpern, W. R., Coffey, C. S., Albanese, A., Cheung, K., Comella, C. L., Ecklund, D. J., Fahn, S., Jankovic, J., Kieburtz, K., Lang, A. E., McDermott, M. P., Shefner, J. M., Teller, J. K., Thompson, J. L., Yeatts, S. D., & Jinnah, H. A. (2014). Designing clinical trials for dystonia. *Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics, 11*(1), 117–127. https://doi.org/10.1007/s13311-013-0221-6

Grutz, K., & Klein, C. (2021). Dystonia updates: definition, nomenclature, clinical classification, and etiology. *Journal of Neural Transmission*, 128, 395-404.

Hsieh, H.T., & Yeh, Y.W. (2020). Dose-Dependent Effects of Lithium Treatment on the Aggravation of Antipsychotic-Induced Pisa Syndrome. *Clinical Neuropharmacology*, *43*(3), 90–91. https://doi.org/10.1097/WNF.0000000000000388

Jinnah, H. A. (2020). Medical and Surgical Treatments for Dystonia. *Neurologic Clinics*, *38*(2), 325–348. https://doi-org.ezproxy.utas.edu.au/10.1016/j.ncl.2020.01.003

Jost, W. H., Tatu, L., Pandey, S., Sławek, J., Drużdż, A., Biering-Sørensen, B., Altmann, C. F., & Kreisler, A. (2020). Frequency of different subtypes of cervical dystonia: a prospective multicenter study according to ColCap concept. *Journal of Neural Transmission (Vienna, Austria : 1996)*, *127*(1), 45–50. https://doi-org.ezproxy.utas.edu.au/10.1007/s00702-019-02116-7

Kilic-Berkmen, G., Wright, L. J., Perlmutter, J. S., Comella, C., Hallett, M., Teller, J., Pirio Richardson, S., Peterson, D. A., Cruchaga, C., Lungu, C., & Jinnah, H. A. (2021). The Dystonia Coalition: A Multicenter Network for Clinical and Translational Studies.*Frontiers in neurology*, *12*, 660909. https://doi.org/10.3389/fneur.2021.660909

Krause, P., Kroneberg, D., Gruber, D., Koch, K., Schneider, G.-H., & Kühn, A. A. (2022). Long-term effects of pallidal deep brain stimulation in tardive dystonia: a follow-up of 5–14 years. *Journal of Neurology*, 1–6. https://doi.org/10.1007/s00415-022-10965-8

Liow, N.J.K., Gimeno, H., Lumsden, D.E., Marianczak, J., Kaminska, M., Tomlin, S., Lin. S.J.P.SM., (2016). Gabapentin can significantly improve dystonia severity and quality of life in children. *European Journal of Paediatric Neurology*, Volume 20, Issue 1:100-107.

Lee, W.W., Jeon, B., & Kim, R. (2018). Expanding the Spectrum of Dopa-Responsive Dystonia (DRD) and Proposal for New Definition: DRD, DRD-plus, and DRD Look-alike. *Journal of Korean Medical Science*, *33*(28), e184. https://doi.org/10.3346/jkms.2018.33.e184

Lu, H., Chiu Wa Lam, L., Ning, Y., Li, H.X., He, L., Zhang, C.-C., Eisinger, R., Pan, Y.-X., Wang, T., Sun, B.-M., Wu, Y.-W., & Li, D.-Y. (2019). Deep brain stimulation in post-traumatic dystonia: A case series study. *CNS Neuroscience & Therapeutics*, *25*(11), 1262. https://doi.org/10.1111/cns.13145

Mainka, T., Erro, R., Rothwell, J. A., Kühn, A. A., Bhatia, K. P., Ganos, C. (2019). Remission in dystonia – Systematic review of the literature and meta-analysis. *Parkinsonism & Related Disorders*, Volume 66,Pages 9-15.

McCambridge, A. B., & Bradnam, L. V. (2021). Cortical neurophysiology of primary isolated dystonia and non-dystonic adults: A meta-analysis. *European Journal of Neuroscience*, *53*(4), 1300. https://doi-org.ezproxy.utas.edu.au/10.1111/ejn.14987

Ng, A. R., Jamora, R. D. G., & Rosales, R. L. (2021). X-linked dystonia Parkinsonism: crossing a new threshold. *Journal of Neural Transmission (Vienna, Austria : 1996)*, *128*(4), 567–573. https://doi.org/10.1007/s00702-021-02324-0

Oppenheim, H. (1911). About a rare spasm disease of childhood and young age (Dysbasia lordotica progressive, dystonia musculorum deformans). (1911). *Neurologisce Centralblatt*, 30:1090-1107.

Pirio Richardson, S., Wegele, A. R., Skipper, B., Deligtisch, A., & Jinnah, H. A. (2017). Dystonia treatment: Patterns of medication use in an international cohort. *Neurology*, *88*(6), 543–550. https://doi-org.ezproxy.utas.edu.au/10.1212/WNL.0000000000003596

Prudente, C. N., Zetterberg, L., Bring, A., Bradnam, L., & Kimberley, T. J. (2018). Systematic Review of Rehabilitation in Focal Dystonias: Classification and Recommendations. *Movement disorders clinical practice*, *5*(3), 237–245. https://doi.org/10.1002/mdc3.12574

Quartarone, A., & Ruge, D. (2018). How Many Types of Dystonia? Pathophysiological Considerations. *Frontiers in Neurology*, *9*. https://doi.org.ezproxy.utas.edu.au/10.3389/fneur.2018.00012

Simonyan, K., Barkmeier-Kraemer, J., Blitzer, A., Hallett, M., Houde, J. F., Jacobson Kimberley, T., Ozelius, L. J., Pitman, M. J., Richardson, R. M., Sharma, N., & Tanner, K. (2021). Laryngeal Dystonia: Multidisciplinary Update on Terminology, Pathophysiology, and Research Priorities. *Neurology*, *96*(21), 989–1001. https://doi.org/10.1212/WNL.0000000000011922

Siokas, V., Kardaras, D., Aloizou, A.-M., Asproudis, I., Boboridis, K. G., Papageorgiou, E., Hadjigeorgiou, G. M., Tsironi, E. E., & Dardiotis, E. (2019). BDNF rs6265 (Val66Met) Polymorphism as a Risk Factor for Blepharospasm. *Neuromolecular Medicine*, *21*(1), 68–74. https://doi.org/10.1007/s12017-018-8519-5

Sy, M. A. C., & Fernandez, H. H. (2021). Dystonia and leveraging oral pharmacotherapy. *Journal of Neural Transmission: Translational Neuroscience, Neurology and Preclinical Neurological Studies, Psychiatry and Preclinical Psychiatric Studies*, *128*(4), 521–529. https://doi-org.ezproxy.utas.edu.au/10.1007/s00702-021-02339-7

Tambirajoo, K., Furlanetti, L., Hasegawa, H., Raslan, A., Gimeno, H., Lin, J.-P., Selway, R., & Ashkan, K. (2021). Deep Brain Stimulation of the Internal Pallidum in Lesch-Nyhan Syndrome: Clinical Outcomes and Connectivity Analysis. *Neuromodulation : Journal of the International Neuromodulation Society*, *24*(2), 380–391. https://doi.org/10.1111/ner.13217

Tödt, I., Baumann, A., Knutzen, A., Granert, O., Tzvi, E., Lindert, J., Wolff, S., Witt, K., & Zeuner, K. E. (2021). Abnormal effective connectivity in the sensory network in writer's cramp. *NeuroImage: Clinical*, *31*. https://doi.org/10.1016/j.nicl.2021.102761

van der Veen, S., Zutt, R., Klein, C., Marras, C., Berkovic, S. F., Caviness, J. N., Shibasaki, H., de Koning, T. J., & Tijssen, M. A. J. (2019). Nomenclature of Genetically Determined Myoclonus Syndromes: Recommendations of the International Parkinson and Movement Disorder Society Task Force. *Movement Disorders : Official Journal of the Movement Disorder Society*, *34*(11), 1602–1613. https://doi.org/10.1002/mds.27828

van Egmond, M. E, Kuiper A., Eggink, H. et al. (2015). Dystonia in children and adolescents: a systematic review and a new diagnostic algorithm. *Journal of Neurology, Neurosurgery & Psychiatry*, 86:774-781.

Weissbach, A., Saranza, G., & Domingo, A. (2020). Combined dystonias: clinical and genetic updates. *Journal of Neural Transmission*, *128*(4), 417–429. https://doi.org/10.1007/s00702-020-02269-w

Woo, K.A., Kim, H.J., Yoo D., Choi, J.H., Shin, J., Park S, Kim, R., Jeon, B. (2020). Patient-reported responses to medical treatment in primary dystonia. *J Clin Neurosci*, May;75:242-244.

Zarucchi, A., Vismara, L., Frazzitta, G., Mauro, A., Priano, L., Maestri, R., Bergna, A., & Tarantino, A. G. (2020). Efficacy of Osteopathic Manipulative Treatment on postural control in Parkinsonian patients with Pisa syndrome: A pilot randomized placebo-controlled trial. *NeuroRehabilitation*, *46*(4), 529–537. https://doi.org/10.3233/NRE-203068

10-11 November 2022
ANNA Conference
'Diving into Neuroscience Nursing – Just Keep Swimming'