Limb dystonia including writer’s cramp

Limb dystonia can occur in primary dystonias or as a complication in neurodegenerative diseases e.g. Huntington’s disease, Wilson’s disease or Parkinson syndromes or other diseases like structural brain damage, peripheral trauma or drug-induced. Any muscle group under voluntary control can be affected, dystonic muscle overactivity can occur during rest, be aggravated by movement, or occur only during voluntary movement (action dystonia). If the dystonia is triggered by a specific task, it is called “task-specific” dystonia and affects mostly the hand. As task-specific dystonia causes most disability and is the greatest therapeutic challenge, this summary will focus mainly on this form of limb dystonia. Exercises with a repetitive movement pattern such as writing, typing or playing musical instruments are predestinated to this type of dystonia (1). Co-contraction of agonist and antagonist muscles lead to abnormal postures and movements sometimes associated with tremor or myoclonic jerks. This leads to disability in occupations with repetitive fine motor tasks. The underlying pathophysiology why some individuals develop such a task-specific dystonia and others not, despite of maybe excessive overuse of the hand remains unclear. Safety and efficacy of botulinum toxin has been well established during decades of use (2).

Pathophysiology

Numerous studies in task-specific dystonias have shown abnormalities within the basal ganglia and its circuits, decreased inhibition at various levels of the sensorimotor system, abnormal plasticity and impaired sensorimotor processing (3). MRI-based volumetric techniques have shown changes in the basal ganglia, thalamus and gray matter of the sensorimotor cortex (4). Functional imaging such as fMRI or PET scan show increased activity in the contralateral sensorimotor cortex, premotor areas and ipsilateral cerebellum during dystonic movements and decreased activity in the primary sensorimotor cortex and supplementary motor areas in resting state (5). Impaired sensorimotor integration and defects in temporal and spatial discrimination was shown by studies in focal hand dystonia (6, 7, 3). Increased plasticity could be found in the brain of patients with task specific dystonia (8), however it remains unclear whether increased plasticity cause dystonia or the reverse. Due to its task-specificity limb dystonia can easier be investigated separately from other movements with brain imaging or transcranial magnetic stimulation and impaired inhibition of various types was shown (9). Deficient reciprocal inhibition at a spinal level could be shown by stimulation of la afferent nerves of agonist muscles in EMG (10), impaired intracortical, transcallosal and surround inhibition by transcranial magnetic stimulation techniques (11,12). Dystonic movements are mainly induced by complex tasks such as writing (writer’s cramp) or playing an instrument (musician’s cramp). These activities require integration of sensory input with complex patterns of motor inhibition and activation. A lot of evidence suggests an abnormal sensory processing in dystonia (13). It’s not yet clear which trigger factor can cause a disturbance of this system. Peripheral trauma is one observed trigger although only in low percentage of patients with writer’s cramp or musician’s cramp report a trauma.
(1) and sensory complaints can precede the onset of the dystonia (14). High-frequency muscle vibration can induce focal dystonia by stimulation of muscle spindles (tonic vibration reflex) (15). Repetitive motor activities induced dystonia in nonhuman primate models (16) and fMRI studies in patients with hand dystonia show a broadening of sensory fields (17).

The various aspects of the pathophysiology are integrated in the basal ganglia as inputs from cortical regions, thalamic nuclei and the cerebellum are involved in dystonia. A dysfunction within the indirect pathway is suggested as leading to dystonia, however the relation to the sensory system and the differentiation between the different types of dystonia is not clear yet (3,18).

Phenomenology

Writer’s cramp was first already described in the 18th century as symptom of overuse and as a psychogenic symptom, historical details can be read in the publication of Sheehy and Marsden 1982 (19). They evaluated a large series of patients with different types of occupational dystonias and suggested an organic cause. They divided writer’s cramp in 3 subtypes: “Simple” (task specific), “dystonic” (also other tasks than writing affected) and “progressive” (task specific in the beginning, later non-task specific). The dystonic and the progressive form are also called “complex” writer’s cramp. In a Mayo Clinic study the prevalence was assessed 69 per million persons (21). In a small percentage a family history can be found (20), in early-onset writer’s cramp a secondary generalization was found or writer’s cramp was a manifestation of DYT1 dystonia (22,23). Simple writer’s cramp affects females and men equally whereas the progressive and dystonic forms affect more men (22). Usually the start is between 20 and 50 years. Controversially to musician’s cramp in Sheehy’s and Marsden’s group of patients the majority did not have a job requiring extensive writing tasks. However, the beginning is usually gradually during periods of intensive writing with muscle tension and spasms in the hand- or forearm muscles leading to abnormal posturing of the limb. Patients are often unable to hold a pen. Additionally tremor or myoclonic jerks can occur. Sometimes a sensory trick like often seen in cervical dystonia can alleviate symptoms by lightly touching the forearm (24).

About 25% of patients develop writer’s cramp on the contralateral side when this hand is used for writing instead. The severity is variable and disability is depending on individual requirements of the patients. In the worst case patients are no longer able to perform their job. About 40% of patients who begin with simple writer’s cramp develop complex cramps (22). Differential diagnoses of writer’s cramp are focal nerve entrapment syndromes, cervical root compression syndromes or soft-tissue disorders such as tendinitis. Rarely secondary forms due to structural cerebral lesions e.g. tumours, hemangiomas or multiple sclerosis or neurodegenerative diseases like Parkinson’s disease exist (19). The differentiation of primary writing tremor that is regarded a variant of essential tremor can be very difficult because compensatory muscle contractions can be confused with dystonic cramps. The diagnosis of primary writer’s cramp is usually clinically made by watching the patient writing and excluding other neurological signs and symptoms. Usually the cramp is
not present at rest, the writing is slow, stiff and jerky, the pen is hold abnormally, pain is present in 15% of cases (25). Often there is marked flexion of the proximal interphalangeal joint and hyperextension of the distal interphalangeal joint of the index finger, flexing of wrist, pronation of the forearm, exaggerated handgrip and an abnormal angle between pen and paper. In clinical unclear cases MRI of the brain or electrophysiological examination may be helpful, in younger patients Wilson’s disease or dopa-responsive dystonia or, when there is a positive family history, also DYT1 dystonia should be excluded (26).

Musician’s cramp is another very disabling condition. Newmark and Hochberg defined three patterns in their 59 observed instrumental musicians (27): The first is observed in pianists where involuntary flexion of the fourth and fifth digit occurs, the second pattern is observed in guitarists and consists of flexion or difficulty with extension of the third digit. In the third pattern involuntary flexion of digit four and five and extension of digit three occurs in clarinetists. A long list of other occupational limb dystonias exists affecting hands (typists, waiters, painters, milkers, metal workers,….) but also lower limbs (dancers, sewing-machine workers,….) (25). Other secondary focal limb dystonias are painful “Off”-dystonia in Parkinson’s disease affecting very often the leg (28) or dystonias due to structural brain lesions (1).

Conventional therapies

A wide range of drugs including anticholinergics, benzodiazepines, baclofen, valproate, neuroleptics, L-dopa, amantadine or tizanidine have been tried in writer’s cramp and other dystonias with poor results. For pallidal deep brain stimulation there is insufficient evidence. Physiotherapy, relaxation techniques and writing retraining, biofeedback or using mechanical aids have shown success but there is a lack of qualitative studies evaluating extent and duration of the effect (25,27).

Botulinum toxin

Botulinum toxin serotype A (BTX) is the current standard therapy for focal limb dystonia (2). The evidence supports a B level recommendation for the two formulations, Abobotulinum (Dysport®) and Onabotulinum (Botox®). For other available formulations, the Botulinum toxin A Incobotulinum (Xeomin®) and the serotype B Rimabotulinum (Myobloc®) no published studies in limb dystonia were identified (29). Open label studies with and without EMG guidance to inject the most active muscles reported a good response, most common side effect was muscle weakness. Cohen et al achieved functional improvement of 16 out of 19 patients with writer’s cramp lasting from 1-6 months (30), Rivest et al injected 44 Patients for a mean period of 12 month and reported significant improvement in 56% of treatment sessions (31). Randomized, double-blind, placebo-controlled studies have shown benefit of BTX in writer’s cramp and other focal dystonias (32,2,33). In musician’s cramp 50-69% patients reported improvement from BTX treatment in a case series, 36% reported long-term benefit (34,35).
The treatment should consist of several stages (1): Identification of overactive muscles, selection of overactive muscles for injection, choosing dose, injection and follow-up. An accurate clinical examination sometimes with palpation to identify the most active dystonic muscles during the dystonic movement is crucial to get a satisfying treatment result. Patients should avoid compensatory movements as they can mask the dystonia, dystonic overflow and compensatory are sometimes difficult to differentiate. Dystonia can develop gradually therefore a longer observation may be necessary. Sometimes mirror movements during writing with the not-affected hand can help to identify the most dystonic muscles. Patient’s sensation of involuntary muscle pushing into a certain direction also can help choosing the right muscle for injection. Sheean suggests injecting preferably the first muscle starting dystonic posturing for example for index finger flexion the flexor digitorum profundus or superficialis. Then other muscles can be added. This strategy can help evaluating treatment success and avoid injecting compensatory acting muscles. Dosage used in dystonia is usually smaller than in spasticity and to avoid weakness starting doses should be rather low. From the two available BTX formulations, 1 vial Dysport® (500 mu) is diluted with 2.5 ml saline and 1 vial Botox® (100mu) with 1ml saline. Injection can be supported by EMG and/or stimulation technical devices, as only anatomical guides cannot provide the exact position of the injection needle. Ultrasonography has gained a lot of attention during the last years. It allows non-invasive, real-time imaging of muscular structures. Small randomized studies suggest that ultrasound-guidance can improve therapeutic efficacy and reduce adverse effects of BTX therapy when compared to conventional placement. Ultrasound-guidance can help improving functionality in the forearm muscles in writer’s cramp and in selected leg muscles (36). Follow-up after about 3 weeks after the first injections is recommended, a video before treatment for comparison might be helpful to assess the clinical benefit and any side effect such as weakness.