REVIEW

Task-specific dystonia: pathophysiology and management

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Katherine Butler,5 Mark Edwards6

ABSTRACT
Task-specific dystonia is a form of isolated focal dystonia with the peculiarity of being displayed only during performance of a specific skilled motor task. This distinctive feature makes task-specific dystonia a particularly mysterious and fascinating neurological condition. In this review, we cover phenomenology and its increasingly broad-spectrum risk factors for the disease, critically review pathophysiological theories and evaluate current therapeutic options. We conclude by highlighting the unique features of task-specific dystonia within the wider concept of dystonia. We emphasise the central contribution of environmental risk factors, and propose a model by which these triggers may impact on the motor control of skilled movement. By viewing task-specific dystonia through this new lens which considers the disorder a modifiable disorder of motor control, we are optimistic that research will yield novel therapeutic avenues for this highly motivated group of patients.

INTRODUCTION
Skilled movement, particularly of the hand, represents the pinnacle of motor development in humans. Through practice, some of us can achieve remarkable feats of dexterity leading to output of great beauty and societal impact. However, in a small proportion of people, a deficit of motor control specific to a motor skill emerges, which is called task-specific dystonia. Although focal in nature, these disorders are hugely disabling. For example, in musicians, the development of dystonia frequently terminates a professional career which is rich with a broader approach. As such, it would be reasonable that a broad definition of task-specific dystonia includes loss of motor control confined to a specific motor skill. This could include tremor and be with or without an evident abnormal posture.

PHENOMENOLOGY
Symptoms can be very subtle at the start of task-specific dystonia. At first, there may be only a perceived loss of dexterity with nothing obvious on examination of the affected body region. In other patients, even the thought of performing the affected motor skill initiates dystonic posturing. Furthermore, presentation can be exceptionally task-specific, exemplified by a fascinating case series in which difficulty in writing was seen for only a single letter or number (these cases were all linked by the need to repetitively write the said character under stressful situations). Musicians have among the most subtle forms of the disorder, as any deterioration in motor control, no matter how minuscule, may be critical to performance. Initially, loss of control can be for discreet types of movement required only during certain sections of particular pieces (e.g., intricate fast individuated finger movements required for scale-like runs, or playing octaves on the piano in which the 1st and 5th finger need to strike the keyboard in synergy). Pain is usually not a dominant feature of task-specific dystonia, despite the previous use of the word ‘cramp’ to describe these symptoms.

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Task-specific dystonia typically progresses insidiously over weeks to months, and a subsequent abnormality of posture becomes apparent in most cases. Fluctuations in symptoms are common but remissions are rare. A significant proportion of patients who initially only have dystonia for a specific task later report difficulty with other fine motor skills. For example, in the hand, spread to tasks such as buttoning clothes or typing on a keyboard has been documented in approximately one half of the hand, spread to tasks such as buttoning clothes or typing on technology and working life. For example, one of the change, as it has historically, in response to the evolution of technology and working life. For example, in

Differential Diagnosis

Task-specific dystonia (or isolated dystonia of the limb which is non-task-specific) may be the presenting feature of the hereditary dystonias (such as DYT1) or isolated generalised/segmental dystonias, however, with time, the more extensive distribution of the disorder is defined. In such cases, early imaging excludes the infrequent possibility that the dystonia is caused by a focal lesion. Occasionally, task-specific dystonia is symptomatic of an alternative neurological condition, such as Parkinson’s disease, spinocerebellar ataxias, or pantothenate kinase-associated neurodegeneration. Motor skill learning is complex, with multiple sensorimotor and cognitive domains recruited, and therefore, it is not surprising that specific tasks can be preferentially affected at the start of a neurodegenerative disorder. In major injury, such as significant stroke, the deficit in skilled movement will be dwarfed by the grosser motor deficit. However, in degenerative disease, it is possible for patients to present with an initial apparently isolated deficit of motor control affecting a motor skill, but over time for this to develop into a more generalised motor impairment. These people do not have task-specific dystonia. Myotonia can cause an abnormality of posture and pain brought on by movement, and is another rare disorder to keep in mind. Postural abnormalities during tasks involving exertion or gross body movement may be related to exercise-induced movement disorders such as GLUT-1 deficiency.

The range of motor impairments seen in performing artists are varied, and a subclassification in musicians has recently been proposed which may have utility for classification of other types of task-specific dystonia (table 1). Within this classification, overuse syndromes are perhaps the most difficult to distinguish from task-specific dystonia. Both result in an impairment of motor function after repetitive task performance. Classically overuse syndromes are painful, whereas dystonia is not, and symptoms often generalise to all movements of the hand, not just a specific skilled movement.

Risk Factors

Stratification of risk factors has mostly been systematically studied in musicians’ dystonia, due to the existence of specialist clinics with large numbers of patients and good availability of control musician data. Most of the identified risk factors in this specialist group have also been reported anecdotally in other

Figure 1  Writing dystonia. (A) Dystonic posturing of the index finger and the participant finds it difficult to maintain the nib on the page. For a limited time writing is possible by gripping the pen and all fingers as shown in (B). A spiral figure from a patient with writing dystonia and coexisting tremor (C). Task-specific tremor sits awkwardly outside established diagnostic frameworks. There is no consensus whether these patients can be well defined as a dystonia variant, an essential tremor variant, a unique entity in its own right, or an amalgamation of these.
types of task-specific dystonia, but there is a relative paucity of case-controlled studies.

Genetic factors
An influence of genetic risk factors is suggested by the preponderance for males to develop task-specific dystonia (4M:1F in musicians’ dystonia), and a positive family history of task-specific dystonia in a proportion of cases. A multicentre genome-wide association study has identified arylsulfatase G as a locus which may confer risk for task-specific dystonia of the hand (although independent confirmations are still needed to validate this result). One needs to be cautious about causality in this situation, as, though the genetic makeup of the individual may confer susceptibility to dystonia, it will also, in part, define the motor ability and aptitudes necessary for specific features of the affected task (such as the unique audiomotor interactions required for learning and performing music).

Environmental factors
Environmental risk factors really segregate task-specific dystonia from the other dystonias. The specific demands of the tasks, the parameters of task reproduction and non-task-related factors can all impact on motor physiology.

Specific tasks requirements
It seems that the greater the departure of the task from the inherent ability of the limb, the greater the risk of developing dystonia. This influence of task ‘difficulty’ is exemplified by dystonias in performing artists or competitive sports in which the body is pushed to the very extremes of its spatiotemporal capacity. The probability of developing musicians’ dystonia depends on the instrument played (guitarists and pianists have the highest risk of developing dystonia), and dystonia preferentially involves the hand engaged in the more complex motor task. For example the right hand is more commonly involved in keyboard players where this hand typically carries the greater technical burden. The converse is seen in bowed instruments where the left hand carries the greatest technical demand as it demarcates the notes on the finger board.

The requirement for precision or the need to perform while avoiding errors is another risk factor. Classical musicians are at greater risk of dystonia than jazz or rock musicians, which has been explained by the need in classical music performance to play without deviation from, at times, impossibly fixed musical constraints.

Parameters of task reproduction
Any shift of the motor task ‘parameters’ also seems to endow risk. For example, in the 19th century, a change to steel nibs in clerks increased the force required for writing and led to a relative epidemic of writing dystonia. Similarly, we have seen dystonia precipitated by the need to switch to performing on an electronic keyboard with higher force thresholds than the piano. Changes in spatial parameters of the task may also be important; we have observed dystonia precipitated in a policeman who was required to document incidents within the small lines of his notebook, and in a musician who was asked to play the banjo (smaller) at the same time as the classical guitar. In a similar vein, musicians may develop dystonia shortly after trying to change a well-learned technique, for example, the manner in which the bow is held or the angle at which the instrument is held.

Another risk modifier is a ‘time factor’. The task affected by dystonia needs to be performed for a significant duration of time per day (or at least per week) as evidenced by the occurrence of dystonia in tasks concerned with occupation. Within this ‘workload’ requirement not only do the number of hours seem to be important but whether there are any breaks in activity. Dystonia typically appears after the task has been performed for many years. What this signifies is uncertain. Perhaps certain risk factors have to be accrued over time, and only after a combination of ‘hits’ will dystonia start to develop. Alternatively, the age of presentation might reflect a time when the motor system needs to start to compensate for any age-related decline in function. Interestingly, musicians who start practising after the age of 10 years are at much higher risk of developing dystonia.

Table 1 Subtypes of motor impairments in musicians

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Description</th>
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<tbody>
<tr>
<td>Motor fatigue</td>
<td>Mental or bodily fatigue impairs movement coordination causing poor regularity of notes or a loss of sound quality. Short term and disappears after overnight rest.</td>
</tr>
<tr>
<td>Overuse injury</td>
<td>Should only be diagnosed when pain is the dominating feature, and a history of either prolonged or unaccustomed practice exists. Usually subsides a few weeks after onset.</td>
</tr>
<tr>
<td>Choking under pressure</td>
<td>Describes acute performance failure when individual perceives a subjectively unmanageable situation accompanied by fear of failure, anxiety and increased arousal leading to reduced motor control and worse performance outcome.</td>
</tr>
<tr>
<td>Dynamic stereotype</td>
<td>Used when motor incoordination persists for more than 4 weeks. More modifiable and fluctuating than musicians dystonia.</td>
</tr>
<tr>
<td>Dystonia</td>
<td>Persistent muscular incoordination, or loss of voluntary motor control.</td>
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</tbody>
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Movement disorders

order to reach professional levels of skill performance, it may be a pre-requisite that training is initiated when the motor system is most adaptable during early childhood.

Non-task-related factors

Injury is a risk factor for the development of both writing dystonia and musicians’ dystonia. For example, injury to the face can precipitate dystonia affecting the embouchure in wind and brass players. In some, this injury comes about through excessive practice/performance, but a task-unrelated injury can increase risk of development of task-specific dystonia. Workload of the affected body part in different tasks can also confer risk. For example, writing workload has been shown to be associated with the development of musicians’ dystonia.

The influence of personality and psychological factors is poorly understood. Perhaps one reason for this is that there has been a reluctance to consider such factors in the face of the history of task-specific dystonia (and indeed dystonia in general) as conditions that were considered as primary psychiatric disorders until relatively recent times. However, it has, in our view, led to a neglect of psychological factors which are clearly present. In questionnaire studies, anxiety and extreme perfectionism are elevated in musicians with dystonia and these characteristics appear to be present before the onset of dystonia.

Furthermore, there is a clear presence in some patients of performance-related stress in the run up to development of task-specific dystonia. These factors are well known to be associated with ‘self-focused’ attention and such an attentive form of movement control itself can have deleterious effects to motor performance.

PATHOPHYSIOLOGY

So how do these genetic and environmental factors interact to cause the motor phenotype of dystonia? There are two dominant themes: impaired inhibition and abnormal plasticity regulation. We will briefly evaluate each of these pathophysiological theories in turn.

Loss of inhibition

On the hypothesis of reduced inhibition, the evidence originates mainly from neurophysiological studies in humans. Early studies suggested that reciprocal inhibition (the inhibitory circuit that tunes the agonist-antagonist balance at the level of spinal cord) was abnormal in patients with task-specific dystonia. Recently, reduced inhibition has been reported in multiple intracortical and cortico-cortical networks. Reduced short intracortical inhibition (SICI) has been observed in multiple studies yet there are some issues with reproducibility (possibly due to the insensitivity of methods traditionally used to assess SICI). Long intracortical inhibition and silent period, which appear to be mediated by γ-aminobutyric acid (GABA) B inhibitory networks, may also be abnormal in patients with writing dystonia.

Reduced dorsal and ventral premotor-motor inhibition has additionally been found. Paradigms which test inhibition of the motor cortex after peripheral nerve stimulation results have generated uncertain results so far. Similarly, preliminary data which suggested impaired cerebellar inhibitory input to the motor cortex has not, to date, been replicated. Surround inhibition (SI) is proposed as a cortically driven mechanism whereby muscles surrounding an active muscle are actively inhibited to prevent overflow of muscle activation. This has obvious links with the semiology of dystonia, but the evidence that SI is impaired in task-specific dystonia comes from small studies with large variability.

The main problem with the inhibitory theory is that it is not a specific in finding task-specific dystonia and ‘reduced inhibition’ is seen in many other diseases. Furthermore, it is difficult to know if inhibitory changes drive dystonia, or whether they represent epiphenomenon collateral to the disease process.

Abnormal plasticity regulation

A complementary hypothesis (reduced inhibition would interact with plasticity mechanisms) is that task-specific dystonia is a disorder of plasticity regulation within the brain. It has been proposed that individuals with dystonia have plasticity responses that are excessive in magnitude and unspecific topographically (‘abnormal spread’). Following the observation in healthy controls that there is a large amount of variability of plasticity responses within individuals (when tested in separate sessions) and between individuals, we critically re-evaluated how well a classic, non-invasive, plasticity paradigm defined a clinically pure group of patients with writing dystonia. We revealed that similar to healthy controls, when a group of patients with writing dystonia are examined, that there is significant variability. In individuals, both facilitatory and inhibitory responses are seen, and little net plasticity response is observed across the group in the target muscle of the paradigm (figure 3). We also did not find evidence of abnormal spread of plasticity responses to muscles not targeted by the plasticity paradigm. By analytically reviewing the literature in task-specific dystonia, it can be convincingly argued that many previous studies may have been underpowered. The range of results seen across studies probably reflects such physiological variability and mean plasticity response in task-specific dystonia has not been reproducibly shown to be systematically different to the healthy population.

Another important question is to consider what non-invasive plasticity responses signify at the neuronal or synaptic level as it cannot be assumed that paired associative stimulation responses have a simple correlation with levels of synaptic plasticity. Clarity and further research on this topic is important, as clinical brain stimulation studies claiming therapeutic effect based only on neurophysiological markers may not be founded on a solid theoretical basis.

One possible consequence of abnormal plasticity regulation is that this could lead to a ‘merged’ sensory homunculus of the dystonic body part, such that, focal hand dystonia represents a condition in which the spatial distances between individual digits are diminished leading to coactivation of digits when only single digit action is desired. This idea was first substantiated using a primate model for repetitive strain injury and dystonia in which neuronal recordings in the primary sensory cortex demonstrated receptive fields that were 10–20 times larger than healthy monkeys. Subsequently, studies in patients with task-specific dystonia using both magnetic source and functional magnetic imaging techniques also suggested that finger representations in the primary somatosensory cortex were ‘closer to each other’ than in healthy subjects. However, it is now appreciated that the representations of individual digits in the motor and somatosensory cortex, in health, are highly overlapping. As such analysis of group data with traditional distance measures which calculate Euclidian distances between the points of highest activation for individual fingers, or a centre of gravity measures for individual finger may be ill equipped to explore the true organisational principles of cortical representations for individual fingers.
Therefore, there is a growing evidence base to suggest that task-specific dystonia may not share core pathophysiological features which, traditionally, define other syndromes of dystonia. Furthermore, one would not predict that a disorder affecting a defined task would be caused by general changes in inhibition or plasticity. The clear influence of environmental risk factors and psychological factors suggest that a broader pathophysiological model may be relevant.

NEW PERSPECTIVE ON TASK-SPECIFIC DYSTONIA

A different approach would be to consider the pathophysiology of task-specific dystonia from the perspective of motor-skill learning, an area of neuroscience that has a significant theoretical and experimental foundation. This viewpoint allows us to propose that the whole range of motor dysfunction that occurs in a highly task-specific manner in those who intensely practice a particular skill may share at least some aspects of the same underlying pathophysiology.

The fundamental feature of motor skill learning in health is that performance of a specific task improves with practice, to a point of relative stability of performance. Once this point has been reached, task performance is relatively resistant to decline, and performance of the task becomes largely automatic. The challenge in understanding the pathophysiology of task-specific dystonia is how a stable and highly practiced motor skill (and typically just a small part of it) can become degraded.

A key trigger for dystonic symptoms is change. For example, we have been very struck in musicians by the number reporting an attempted alteration in technique prior to the onset of symptoms in order to meet the technical demands of a particular piece. This has echoes in historical and current reports of dystonia aforementioned, where symptom onset has been apparently triggered by modifications of the spatial and mechanical demands of the task. Furthermore, many report an injury prior to symptom onset. Thus, it seems that this change or perturbation can either be intrinsic to the individual (injury, fatigue) or extrinsic (a change in technique, spatial/mechanical demands). Importantly, this perturbation necessitates a revision to the motor skill such as a ‘scaling’ in strength to an increase in drive to fatigued muscles, or a scaling correction to write smaller. Attempting to change a stable motor skill may reactivate a neural state similar to that observed in early skill learning taking the network supporting the motor skill into a state which is more vulnerable to disruption (or the initiation of a dystonic skill representation) despite so many years of prior consolidation. It is of interest that the task affected is often the one of most complexity. Perhaps the network associated with such tasks is at the very limits of complexity that can be kept stable in the brain with limited ability to generalise to shifts in task demands. Attempting to alter an overpractised automatic motor skill also implies the use of explicit strategies for movement control. Here, attention focuses on the mechanics of movement production rather than the goal of movement, which can cause a deterioration in performance.

The end result is a degraded neural network supporting the motor skill. This degraded network could be consolidated by continued unsuccessful attempts at task performance in the setting of excessive attention towards task production, and often mounting anxiety and stress due to the impact of the motor impairment.

Although such a model of task-specific dystonia is predominantly theoretical, we believe it has utility for future research and management. Viewing the disorder through a motor learning lens may yield rehabilitative therapies which target the core drivers of the disorder, in contrast with existing medical management that is largely symptomatic.

MANAGEMENT OF TASK-SPECIFIC DYSTONIA

Overview

The presence of environmental risk factors suggests that some cases of task-specific dystonia could be prevented. Avoiding motor fatigue and avoiding ergonically clumsy devices in the workplace may well reduce the frequency of the condition. In athletes, dancers and musicians, there is also an encouraging increase in the awareness of looking after general health and promoting healthy practice routines in professional training.
Movement disorders

Early diagnosis is likely to be critical to optimise response to treatment. To facilitate this, increased education among physicians and within high-risk patient groups is needed, as time to diagnosis is lengthy in most studies.8

The management of task-specific dystonia should be coordinated within specialist movement disorder clinics whenever possible, as correct diagnosis and recovery necessitate a team that is well versed in the disorder, and is able to deliver the different facets of specialist therapy (many specialists are amateur artists themselves). There is an unfortunate scarcity of evidence to define an algorithm for treatment. This is, in part, due to the need to develop sensitive outcome scales/measures to enable the evaluation of different treatments. Currently, treatment is tailored to the individual depending on the expertise available. For example, within the National Health Service, rehabilitation expertise is very limited for this patient group, and thus, many physicians would advocate a single drug trial, and then electromyography-guided botulinum toxin injections for appropriate cases. Charitable trusts provide an important funding avenue for musicians to help musicians fund private therapy.

Task-specific dystonia can seem, at first sight, a rather irrelevant disorder in the context of human health more widely. However, it nearly always impacts on the livelihood of the individual, and in performing artists or athletes their skill is likely to be intricately linked to their sense of self-worth and their professional and personal relationships.64 As such, it carries a very significant disability and impact.

Medical

Oral medications rarely offer significant relief, often have dose-limiting side effects, and none have been fully assessed within a randomised controlled clinical trial. Anticholinergic medications, such as trihexyphenidyl, are the most commonly tried. Botulinum toxin injections aim to control excess activity in dystonic muscles, and the injection pattern is usually guided by electromyography. In writing dystonia and musicians’ dystonia a majority of patients report a positive initial response to therapy.64 66 However, a significant proportion discontinue therapy due to inadequate response,67 and this reflects our experience that the long-term utility of botulinum injections is often disappointing. This is particularly true in musicians, as the window between treatment efficacy and weakness that impairs function is particularly narrow. Stereotactic brain surgery and deep brain stimulation (thalamic) have been suggested for writing dystonia after claims of benefit in small non-randomised studies.68 69 These approaches should be considered highly experimental particularly while the pathophysiology is so poorly understood.

Rehabilitative

Many different rehabilitative approaches have been employed in studies attempting to treat task-specific dystonia. For example, some advocate ‘slow down exercise treatment’ so that the task causing the dystonia is repeated multiple times but at a speed at which does not elicit dystonic movements, with the hope that the dystonic task representation can eventually be overwritten.70 Other therapies have been developed in synergy with the idea that the sensory representation of the affected region is distorted in task-specific dystonia. Sensory-motor retuning uses splints to immobilise dystonic or compensatory movements during task performance to allow a different repertoire of movements during practice.71 72 Other techniques include attempting to improve sensory discrimination of the affected body by training subjects with tactile tasks such as identifying everyday household objects, or the values of dominos by touch alone, or even learning braille.73

We believe that there is a large potential for rehabilitative techniques to improve symptoms especially if the disorder is diagnosed early. However, the current state of the evidence is very poor, with no clear guidance on treatment selection, treatment intensity, outcome assessment and efficacy of current approaches. This makes it difficult to argue for expanded provision of such treatments for people with task-specific dystonia within public healthcare systems, even though some published data and our own experience is that such treatment can be highly beneficial in some patients. Learning from rehabilitation techniques in the sports sciences, as well as incorporating psychological approaches, will further equip rehabilitation strategies. This is a key area for research development.

CONCLUSIONS

Task-specific dystonia has unique features within the wider concept of dystonia. We have highlighted the central contribution of environmental risk factors and how these features may impact on the physiology of normal control of skilled movement. Viewing task-specific dystonia through this new lens should provoke new research and therapeutic avenues for this highly motivated group of patients.

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