A Focus On Focal Dystonia – All In The Mind?

From psychology to physiology to plasticity: a search for therapy

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‘Every person complaining of cramp for which there is no organic cause should be considered as a psychiatric patient and treated accordingly.’


Abstract

The dystonias are a set of conditions which affect the lives of thousands across the world. Focal dystonia, in particular, can devastate livelihoods and quality of life, yet its pathogenesis is poorly understood. Medical and surgical treatments are limited and associated with complications and side-effects. In this essay, I propose that a third treatment option, that of sensory re-education through physical therapy, deserves more attention from clinicians. I examine the development of this theory: from the original view of focal dystonia as a learned or psychosomatic disorder (with attempts to psychoanalyse or re-educate sufferers), to its gradual re-classification as a physiological condition, and the development of associated medical and surgical treatments. Finally, I argue that we have in some ways come full circle, though with a more sophisticated understanding, to the disordered learning hypothesis. Imaging and recording studies in humans and animals have shown that disordered plasticity may lie at the heart of focal dystonia pathology. Constant sensory re-education may re-order this plasticity to regain function. After the application of so many pharmaceutical and ablative therapies, could the solution to focal dystonia truly lie all in the mind?

1. Introduction

‘I have had cervical dystonia/torticolis [sic] for forty seven years. When it started most American doctors had no idea what was wrong with me so they implied that I was crazy and that I should be seeing a pschycologist [sic]. Finally in 1972…an army doctor diagnosed my condition as cervical dystonia. For those intervening eleven years I could not turn my head off of my left shoulder.’

Anonymous poster, Symposium for families affected by dystonia

Connie Han
Dystonia is a ‘movement disorder characterised by patterned, directional, and often sustained muscle contractions that produce abnormal postures or repetitive movements.’ It may be classified according to body parts affected (e.g. focal, segmental, generalised), age of onset (early or late), putative causes (idiopathic or secondary to neurological insult), and response to treatment (e.g. dopa-responsive dystonia). See Panel 1.

Panel 1: Classification of dystonia

**Distribution**
- **Focal**
  - For example, cervical dystonia, blepharospasm, spasmodic dysphonia, oromandibular dystonia, brachial dystonia
- **Segmental**
  - For example, Meige syndrome, cranio cervical dystonia, bibrachial dystonia
- **Multifocal**
- **Hemidystonia**
- **Generalised**

**Age of onset**
- Early-onset (<26 years)
- Late-onset (>26 years)

**Cause**
- Primary (idiopathic) dystonia
- Secondary dystonia
  - Associated with inherited neurological disorders
  - Dystonia-plus syndromes
  - Degenerative diseases
  - Symptomatic of an exogenous or environmental cause
  - Associated with Parkinson’s disease and other parkinsonian disorders
  - Dystonic phenomenology in another movement disorder

Focal dystonia (FD) is defined as dystonia affecting only one body part. This set of dystonias includes writers’ cramp, musicians’ cramp, torticollis, and blepharospasm amongst others. Cervical dystonia is the most common and is associated with pain in 75% of cases.

Occupational dystonias, on the other hand, may destroy livelihoods. As they are aggravated by certain movements, they lead to an almost ironic task-specific debilitation, barring sufferers from their occupations but sparing other motor functions.

Sadly, the experience reported by the anonymous poster above is not uncommon. Sufferers of FD often report years of misdiagnosis and stigma before receiving therapy, their condition mistakenly labelled ‘non-organic’ or ‘functional disorder’ and being relegated to psychotherapy.

This association of FD with perceived neurosis is not a new one. It may be found in the first descriptions of dystonia in medical literature. In this essay, I trace the conceptual evolution of FD from a psychological to a physiological disorder; our treatments from psychotherapy to pharmacology. I also explore the rise of the plasticity theory of FD: and argue that to truly successfully treat it – not just manage its symptoms – we need to harness the brain’s plasticity through sensory re-education. Finally I

Connie Han
propose that we have in some ways come full circle – though not in quite the way the early researchers imagined. FD is once more viewed as a cerebral disturbance: not disturbances of *mentality*, but disturbances of *plasticity*. Could this new paradigm be the key to unlock new therapies to banish dystonia forever?

2. ‘All in the mind’

‘[Writers’ Cramp] is primarily psychogenic...[and]... resembles the disorders of function which occurs in hysterical paralysis.’

Brain W.R. ‘The Neuroses’

From its first descriptions in medical journals, debate has raged over whether FDs – and in particular, occupational dystonias – were psychogenic in origin or a true physical disorder. As late as 1976, it was accepted that occupational dystonias were psychogenic due to their perceived association with emotional disturbances such as anxiety, depression and obsessive-compulsive disorder.

This perception led to the development of various psychoanalytic theories and therapies. In 1965, Crisp and Moldofsky published a grand hypothesis of FD pathogenesis, hypothesising that as the upper limbs develop first with ‘grasping, clinging, rejecting, incorporating and supporting’ and with the ‘expression of emotional states’, so the hand becomes ‘a major organ of the expression of anger at the non-verbal musculo-skeletal level.’ Simultaneous agonist and antagonist muscle action in writing, they suggested, is triggered by emotional upsets disturbing muscle tension. A study of 7 subjects concluded dystonic patients were ‘particularly tense, strong, sensitive, conscientious, precise, emotionally over-controlled people...this personality type has been said to be generally characteristic of patients suffering with various psychosomatic diseases.’ In short, Crisp and Moldofsky concluded, *difficulty in expressing anger caused focal dystonias.*
Crisp and Moldofsky, amongst others, relied on psychotherapy and relaxation techniques. These provided temporary relief, limited to the clinic. Crisp and Moldofsky explained these limitations by proposing that when patients encountered stressful situations outside clinic, they relapsed due to psychological weakness. Personally I prefer an explanation combining the placebo effect and regression to the mean.

This view of dystonia, however, was not without its challengers. In 1982, Sheehy and Marsden published a key paper refuting the association between mental illness and focal dystonia. They examined 29 people with writers’ cramp. They reported that subjects’ focal dystonia was reproducible and movement specific, with distinct similarities to basal ganglia (BG) related movement disorders. Finally, they administered a psychiatric interview – the Present State Examination (PSE), which consisted of 140 items scored by a computer – and found no significant difference between the dystonic and control group. Though they too noted the association with stress, Sheehy and Marsden wrote, ‘we do not feel that an association with emotional stress implies a psychological aetiology. Many physical illnesses, and not just other basal ganglia diseases, can be exacerbated or improved by the presence or resolution of emotional conflict.’

3. From psychology to physiology

‘Although we can give no cure for their disorder, at least we can agree that it is not caused by a psychiatric illness.’

Sheehy and Marsden, 1982

If focal dystonia is not all in the mind, what is the organic origin? As early as 1922, it was proposed that ‘...the combination of [symptoms in FD] points to the…basal ganglia as the site of the breakdown

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* It is well known there is a substantial placebo effect in treatment of focal dystonias, and the disease can show spontaneous temporary remission. As an aside, there is no doubt that stress can worsen dystonias - however, stress worsens many organic disorders and this association is obviously no argument for a purely psychogenic version of dystonia.

Connie Han
in function 7. It was well known that BG disturbances led to movement disorders similar to generalised idiopathic dystonia – chorea and hemiballismus – and that BG diseases such as Parkinsonism were associated with some dystonias. Indeed, pallidectomies, thallidectomies and deep brain stimulation can relieve patients with severe generalised dystonia, and are recommended by NICE 8.

Unfortunately, these BG targeted therapies are not curative, nor are they effective for focal dystonias. Medical management of focal dystonias relied on symptom relief, mainly muscle relaxants such as benzodiazepines, muscle paralysis via botulinum toxin, or in extreme cases surgical denervation (Fig. 2, 3).

These pharmacological solutions are associated with unpleasant side-effects. Anti-cholinergics are associated
with drowsiness, memory difficulties, confusion and hallucinations. Benzodiazepines may be addictive and are associated with personality changes, psychiatric symptoms, and short term memory loss. Botulinum toxin can cause autonomic disturbances, including constipation and decreases in blood pressure, heart rate, and saliva production. Immunoresistance may also occur, although this is rare.  

In addition, medical treatments are not curative. A patient must remain on medication or injections for the rest of their life. Many patients may also fail to respond or tolerate treatment. Costs – time spent, expenses, expert time, decreased quality of life and disruption of function – add up. For many FD sufferers, drugs are not the answer.

If drugs and surgery are not the answer, what is? In a recent Lancet review on dystonia treatment options, a small section suggested physical therapy as an adjunct to medical treatment. In recent years, this option has gained attention as another theory of FD grew: the plasticity theory.

4. The plasticity theory

Numerous theories have been proposed for FD pathogenesis. While we are beginning to elucidate the pathogenesis of idiopathic generalised dystonia (DYT gene studies), and various secondary dystonias (e.g. in Wilson’s disease), FD remains relatively mysterious. What we do know is that a huge number of factors are involved, from genetics to age-of-onset to muscles involved, encompassing a variety of environmental triggers – from trauma to type of activity and number of repetitions. Combining these separate influences into one pathogenic mechanism has been elusive. In my opinion, however, the plasticity theory may provide the beginning of an amalgamated theory.

Neuroimaging and direct recordings have shown that our sensory cortices contain maps of body surfaces. Our hands are represented in order, with modality segregation, sequential organisation of
digits, and equal digital distributions\textsuperscript{10}. This order is, however, \textit{plastic}: it is easily disrupted by altered sensory input. Sensory disturbances affect patterns of neuronal firing by altering neural thresholds, changing receptive fields, and shaping neural network connections via long-term potentiation (LTP), long-term depression (LDP), and ‘LTP-and-LDP-like’ mechanisms\textsuperscript{11}. Animal experiments have shown that repeated, attended sensory input results in proportionately increased cortical representation, and vice versa\textsuperscript{12,13}. It is also well known that changes in sensory input and cortical representation affect motor output and learning\textsuperscript{14}.

Based on these findings, authors have speculated that sensory over-stimulation from repetitive fine motions associated with occupational dystonia may result in disordered plasticity\textsuperscript{15}. In support of this theory, a variety of cortical changes have been found in sufferers and in animal models of dystonia. Monkeys who developed signs of dystonia subsequent to training on repetitive tasks de-differentiated selective neural responses, becoming responsive to both dorsal and palmar surface stimulation simultaneously – echoing the simultaneous contraction of agonist and antagonist muscles in FD\textsuperscript{16}. Magnetic Encephalography (MEG) has revealed increases in sensory cortex excitability\textsuperscript{17}, loss of inhibition\textsuperscript{18}, and disruptions to sensorimotor integration\textsuperscript{19}, as well as abnormal firing in the BG (globus pallidus and thalamus)\textsuperscript{20} in dystonic patients. Spatial discrimination is often impaired in patients with FD\textsuperscript{b}, with higher sensory thresholds required for spatial orientation in \textit{both} hands\textsuperscript{21}.

So dystonia is associated with disordered sensory input and representation – but is this responsible for disordered motor output? In one experiment, Rosenkranz et al used proprioceptive inputs to change motor cortex hand representation in patients with writers’ and musicians’ cramp, and healthy controls. They vibrated either the abductor pollicis brevis or to index finger skin. In healthy volunteers, vibration of one muscle increased short interval intracortical inhibition (SICI) of other muscles and decreased

\textsuperscript{b} Though intriguingly not in generalised idiopathic dystonia – however a discussion of this is outside the scope of this essay

\textsuperscript{8} Connie Han
SICI to the vibrated muscle. There was a much weaker or no response in dystonic patients\textsuperscript{22}, showing that they had impaired translation of sensory signals to motor output.

In another experiment, Byl et al trained monkeys to actively close and open their hand on a piece of moulded metal. They were compared against a control group whose hands were moved passively. This was repeated 2 hours a day, 5 days a week, rewarded with food, and continued for at least 5 weeks, and up to 12 months. Neural activity was directly mapped in area 3b of the somatosensory cortex.

Two out of three animals in the active task and one out of two in the passive task developed changes in area 3b (see Fig. 4). The monkeys also developed dystonic hand movements. Byl concluded that the increase in sensory representation of the used digits – by as much as 10 times in some cases – led to a decrease in the ability of cortical neurones to accurately signal specific digital inputs – and that this sensory confusion led to dystonia development\textsuperscript{23}.

This evidence, along with clinical findings that sensory tricks can relieve dystonic postures, while tonic vibration of a muscle can induce attacks\textsuperscript{24}, supports the idea that dystonia may be influenced by
sensory input, and could be induced through repetitive movements. However, it does not explain why only some people get dystonia. Skilled performers – musicians, for instance – have increased sensory representations of the digits used in their occupation when compared with laymen\textsuperscript{25,26}. So why do they not all develop dystonia? Schicatano et al addressed this issue. They found that weakening the orbicularis oculi muscle in rats induced adaptive gain in blinking to ensure eyelid closure but did not result in blepherospasm. When they modified an underlying dopaminergic circuit in the basal ganglia (that by itself had no effect on eye-blinking), weakening the orbicularis oculi led to a much greater adaptive response, which progressed into blepherospasm. This led Schicatano et al to suggest that FD was caused by underlying differences in plasticity which predisposed the patient to disease after exposure to trauma or to repeated sensory inputs\textsuperscript{27}.

Quartarone et al suggested that these differences were due to lowered specificity of plasticity, leading to problems maintaining normal cortical organisation. They measured the mean electric potential (MEP) of the median-nerve-innervated abductor pollicis brevis (APB) and the ulnar-nerve-innervated first dorsal interosseus (FDI) responding to transcranial magnetic stimulation (TMS) alone. They then paired APB stimulation with TMS of the associated motor neurone. Finally they measured the APB and FDI MEP associated with TMS alone again. In healthy controls, Quartarone et al found that paired TMS with stimulation of APB led to a slight increase in APB MEP response to TMS, but no increase in FDI response to TMS. However, in dystonic patients, they found a huge increase in both APB and FDI response to TMS stimulation, suggesting that adaptive plasticity was less specific in patients with dystonia (Fig. 5).
Quartarone et al also found impaired *homeostatic* plasticity in dystonic patients. 1Hz repeated TMS (rTMS) inhibits cortical activation. Cortical preconditioning in healthy controls with excitatory transcranial direct current stimulation (anodal or aTCDS) potentiates the inhibitory effect of 1Hz rTMS, whereas a depressive stimulus (cathodal or cTCDS) reverses the effect. However, in dystonic patients, this potentiating effect is lost (Fig. 6).

These results led Quartarone et al to suggest that it is a failure of synaptic homeostasis and hyperplasticity that leads to dystonia. There is now speculation that these failures may be due to endophenotypic traits\(^{28}\). However, though such patients seem fated to become dystonic in the combination of environmental triggers, Quartarone et al suggest that they are not fated to remain so. By understanding the mechanisms which created pathology, we may be able to manipulate plasticity to regain normal function. If aberrant sensory inputs had got us here, then why can’t controlled sensory inputs get us back?\(^{29}\)
5. Back to Square One?

Unfortunately, while the theories are sound, physical therapy is often unsatisfactory. For example, one case-series involving 4 weeks of physiotherapy (involving muscle stretching exercises) in 6 patients with torticollis found that at 6-months follow-up, 3 patients reported less pain, while all 6 reported some improvement in posture and lowered movement energy requirements. However, none of these changes were significant, suggesting they could have been due to the placebo effect or to spontaneous temporary remission

Why does physical therapy so often fail? In my opinion, physiotherapy and occupational therapy have not been successful because sensory re-education cannot be achieved by relaxing muscles or learning to alter your grip; it lies in deliberate, planned, attended and rewarded sensory stimulation over the affected area to re-map the affected cortices.

Indeed, there is evidence that targeted physical therapy can be effective. Removing sensory input may help reassert normal cortical organisation – seen in peripheral deafferentation and hand-splinting. Novel, attended sensory inputs also help. Teaching dystonia patients to read Braille improved cramping. Byl et al found that sensorimotor re-training in 3 patients led to improvements on their affected side of 86.6% on somatosensory hand representation, 117% on target-specific performance, 23.9% on fine motor skills, 22.7% on sensory discrimination, 31.9% on musculoskeletal skills, and 32.3% on independence, though some were non-significant. No change was seen in healthy controls (Fig. 7, 8).
Fig. 7 – Changes in sensory discrimination between healthy controls and dystonic patients: A. 2-point discrimination B. Localization C. Stereognosis accuracy D. Stereognosis speed E. Kinesthesia F. Graphesthesia

Fig. 8 – Changes in musculoskeletal performance between healthy controls and dystonic patients: A. Finger spread (abduction) B. Shoulder external rotation C. Supination and pronation D. Lumbricals; extensor digitorum ratio E. Posture F. Neural Tension
In another study, Candia et al assessed 101 musicians with FD who had responded poorly to pharmaceutical treatment. They were treated with splinting for 1.5-2.5 hours a day to alter sensory input from instrument playing (Fig. 9). String players especially experienced significant and visible relief, lasting for up to 25 months in some cases (Fig. 10). MEG measurements showed that, after treatment, sensory representation of the dystonic hand had increased organisation and decreased representation (Fig. 11) 37.

Fig. 9 – The splint

Fig. 10 – Left: pre-splinting finger posture, Right: post-splinting finger posture

Fig. 11 – Mean size of hand representations in sensory cortex pre and post splinting

Connie Han
In my opinion, there is evidence for a significant role for physical therapy in the treatment of focal dystonias. It is clear that more research is needed to exploit this potential. We still do not have any standardised programme for sensory stimulation, and few models for how such a programme may improve symptoms\textsuperscript{38}, nor do we fully understand the effects of placebo and spontaneous remission. Double-blinded, placebo-controlled, large studies with long follow-up times are needed. However, I believe physical therapy offers the best hope for a long-term solution to focal dystonia. The plasticity theory then, has led us back to the concept of sensory re-education – an old concept updated for a modern age.

**Conclusion**

Focal dystonia is a devastating disease and treatment options are limited. At first, it was treated unsuccessfully as a psychiatric disorder. Now, it is treated somewhat successfully using drugs. I believe in the future it will be treated much more successfully with physical therapies based on manipulating the aberrant plasticity underlying its pathology. There is a substantial body of evidence based on animal and human studies to support this view, but more research is urgently needed on this much neglected therapy in this much neglected disease. The plasticity theory will, I hope, inspire new therapies, so that eventually treatment will be focussed on the underlying cause of FD – ‘all in the mind’ – instead of merely palliating symptoms with muscle relaxants and chemodenervation.

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Connie Han
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Connie Han
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