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Neuroimaging characteristics of patients with focal hand dystonia.

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Abstract

Advances in structural and functional imaging have provided both scientists and clinicians with information about the neural mechanisms underlying focal hand dystonia (FHD), a motor disorder associated with aberrant posturing and patterns muscle contraction specific to movements of the hand. Consistent with the hypothesis that focal hand dystonia is the result of reorganization in cortical fields, studies in neuroimaging have confirmed alterations in the topography and response properties of somatosensory and motor areas of the brain. Non-invasive stimulation of these regions also demonstrates that focal hand dystonia may be due to reductions in inhibition between competing sensory and motor representations. Compromises in neuroanatomical structure, such as white-matter density and gray matter volume, have also been identified through neuroimaging methods. These advances in neuroimaging have provided clinicians with an expanded understanding of the changes in the brain that contribute to focal hand dystonia. These findings should provide a foundation for the development of retraining paradigms focused on reversing overlapping sensory representations and interactions between brain regions in patients with hand dystonia. Continued collaborations between health professionals that treat focal dystonia and research scientists that examine the brain using neuroimaging tools are imperative for answering difficult questions about patients with specific movement disorders.

Keywords

fMRI; MEG; focal hand dystonia; writer's cramp; neuroplasticity

Focal hand dystonia (FHD) is an idiopathic movement disorder characterized by abnormal, involuntary co-contractions of agonist and antagonist muscles in the affected limb. Patients with dystonia find it difficult to inhibit antagonist contractions. Thus excessive muscle activation leads to end range postures. Task specific focal hand dystonia is often referred to as occupational hand cramps, commonly associated with the performance of common tasks

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such as writing, typing, or playing a musical instrument. When performing the target task, abnormal posturing and twisting can not only be observed in the fingers and the wrist, but also in the entire upper limb and sometimes the neck. In some cases the condition can be bilateral, affecting both the left and right hands, and abnormal muscle contractions can also occur during other tasks involving the affected hand (1, 2, 3). The purpose of this manuscript is to review how neuroimaging techniques have been employed to examine the neural substrates of focal hand dystonia and how the same methods can be used to track changes in the brain that occur as the result of therapeutic intervention.

Characteristics of Focal Hand Dystonia, Clinical Management and the Role of Neuroimaging

While the critical problem is decreased motor control, focal hand dystonia may also be associated with decreased range of motion or hyperflexibility, decreased strength or excessive strength and muscle hypertrophy and/or impaired sensory processing. It is primarily the impairment of motor control that leads to an inability to perform the associated task and, in some cases, other activities of daily living, such as brushing one's teeth, shaving, cutting nails or buttoning a shirt. Current conservative interventions for focal hand dystonia include psychological counseling, physical rehabilitation and retraining (including constraint-induced movement therapy, biofeedback and sensorimotor retraining techniques such as Braille reading) and pharmaceutical agents, the most common and effective of which being the injection of botulinum toxin to weaken the muscles of the hand and forearm (4, 5, 6, 7). In extreme cases, when the condition begins to affect tasks required for activities of daily living and self care, surgical treatment (including the implantation of deep brain stimulators) is considered.

Most researchers and clinicians agree focal hand dystonia is a multifactorial disorder, the result of an interaction between genetic, neurobiological and environmental factors including as personal stress, musculoskeletal limitations, illness and trauma to the upper extremity. Although a combination of botulinum toxin and rehabilitative training may help manage the involuntary movements to enable individuals to continue to perform their tasks, no treatment is considered entirely successful in restoring normal motor control. While there are testimonials from musicians who claim they have been cured by using conservative treatment and self-training, the critical elements to ensure successful retraining are still elusive. The dispute over the effectiveness of conservative management may be due in part to the fact the pathophysiology of focal hand dystonia remains unknown.

Advances in non-invasive neuroimaging techniques have provided the means necessary to identify multiple levels of change in the brain likely to contribute to the motor deficits present in focal dystonia. For example, structural magnetic resonance imaging (MRI) allows us to examine the detailed anatomy of the brain as well as deviations in the volume, density and morphology of cortical and sub-cortical structures in patients with focal dystonia. A more recent application of MRI, diffusion tensor imaging (DTI), measures water diffusion across myelinated structures in the central nervous system, and is currently used to reconstruct the white-matter tracts that connect different areas of the brain. Other imaging

techniques allow us to evaluate changes in the functionality of brain structures. Positron emission tomography (PET) and functional MRI (fMRI) indirectly measure neural activity through the consumption of oxygen in highly active brain regions, highlighting areas that are active during specific behaviors. Advanced applications of MR, such as spectroscopy, are used to identify certain biochemical markers, such as the neurotransmitters GABA and glutamate, as they are used by neural structures. Functional imaging methods such as electroencephalography (EEG) and magnetoencephalography (MEG) record brain activity through changes in electrical current (as in EEG) or changes in the magnetic fields (as in MEG) across the scalp induced by neural activity. Based on EEG and MEG findings, it is possible to reconstruct changes in brain activity on the order of milliseconds. Collectively, these studies provide researchers and clinicians with a clearer picture about the underlying neural mechanisms of focal hand dystonia, and how those mechanisms are modifiable as a result of behavioral intervention. However, it is challenging to determine if the changes in physiology and anatomy defined in imaging are the result of, or conversely contribute to, the motor deficits present in this population. Integration of this data with information from work done in genetics, computational modeling, comparative neuroscience and cortical excitation studies (using transcranial magnetic stimulation, or TMS) is imperative to our understanding of what contributes to and is affected by the disorder.

Sensorimotor Learning Hypothesis: Evidence for Neuroplasticity in Focal Dystonia

Even though focal hand dystonia is considered multifactorial, one prevailing hypothesis for the development of focal hand dystonia is based on aberrant sensorimotor learning. This hypothesis suggests highly repetitive, rapid, attenuated movements associated with the onset of focal hand dystonia result in maladaptive changes in the representation of the digits within the somatosensory and motor cortices of the brain (8, 9). Degradation of normal somatotopy occurs as a result of an inability of the brain to distinguish between near simultaneous sensory inputs to the cortex, disrupting sensory feedback to the motor system and consequently fine motor movements.

The sensorimotor learning hypothesis is supported by an animal model of focal hand dystonia developed by Byl and colleagues in which New World owl monkeys with no previous history of repetitive stress injury or repetitive motion injury were trained in a behavioral task that involved attending to a repetitive, rapid grasping movement in order to receive a liquid reward (8, 9). All animals continued training until their ability to perform the task began to degrade and they exhibited symptoms paralleling focal hand dystonia in humans. Following the development of the dysfunction, electrophysiological mapping of the representation of the hand in primary somatosensory cortex (S1) revealed robust dedifferentiation within the subdivisions of S1 that receive inputs from the cutaneous mechanoreceptors in the skin (10). Receptive fields for neurons in a subregion of S1, area 3a, that represent the hand were greatly increased, and the receptive fields of many of these neurons overlapped the representations of two or more neighboring digits (Figure 1). In addition, the representation of surfaces that remain generally separated in S1 (hairy and glabrous skin) became combined in animals that developed this condition (8, 9).

Consistent with the sensorimotor learning hypothesis, dedifferentiation of primary somatosensory cortex has been reported in several neuroimaging studies in human patients with focal hand dystonia. In one such study of patients with writer's cramp, vibrotactile stimulation delivered to digits two and five of the affected hand were stimulated during fMRI scan sessions in order to assess the somatotopic representation of these structures in S1. In area 1 of somatosensory cortex, not only was the separation of the digit representations reduced in patients with writer's cramp (with activation clusters in closer proximity than in the control subjects), but reordered in higher-order somatosensory fields such as S2 and posterior parietal cortex (11). Similar findings have been reported using MEG, with diminished separation in the digit representations of S1 when those structures are stimulated electrically (12) or pneumatically (13; Figure 2).

The disorganization of primary somatosensory cortex as identified using MEG has been shown to be related to the severity of the movement disorder (13). Imaging techniques have confirmed that this dedifferentiation of the primary somatosensory cortex is present both contralateral and ipsilateral to the affected hand indicating a bilateral sensory abnormality. Interestingly, the identification of altered cortical structure in the unaffected hemisphere suggests that sensitivity in this part of the brain may increase the likelihood of developing focal dystonia. The timing and amplitude of a cortical response in S1 is also affected in focal hand dystonia. In MEG, cutaneous stimuli delivered to the digits produce somatosensory evoked fields (SEFs) with decreased amplitude and longer duration in the hemisphere contralateral to the affected hand in these patients for both the early (~70msec) and late (~100ms) responses. These reduced and sustained SEFs in dystonia are correlated with clinical performance measures with the affected body structure (13). Converging evidence from both human and non-human primate studies suggests that the deficits observed in focal hand dystonia are the result of aberrant cortical reorganization in primary somatosensory fields as a result of extensive training and excessive neural plasticity.

Given the motor system receives somatosensory feedback during movement, disorganization in the topography of S1 may contribute to aberrant patterns of muscular co-contraction present in focal hand dystonia. A computational model based on the sensorimotor learning hypothesis that reconciles inputs from the somatosensory system with ongoing motor plans is shown in Figure 3 (14). According to this model, expanded, overlapping representation of the digits in S1 in dystonia can lead to excessive gain in the sensorimotor loop as the mapping between S1 and motor cortex becomes incongruent. As a result, activity in the corticospinal neurons of M1 becomes saturated, leading to unusual motor behaviors, such as sustained paralysis of the affected hand (14).

Somatosensory Processing

While no definitive clinical test exists to diagnose focal hand dystonia, impairments in tactile processing (likely as a result of reorganization in S1) are evident in this population when these individuals are tested for simple sensory function. Specifically, patients with focal hand dystonia exhibit deficits in fine spatial and temporal somatosensory processing. Spatial discrimination thresholds are increased in dystonia patients, for both affected and unaffected hands (15, 16).

Even in clinical measures of spatial discrimination where no deficit in ability is evident in patients with dystonia, deviations in neural activity can still be observed during spatial discrimination tasks in these individuals. For example, Peller et al., (17) report that while patients with writer's cramp are able to perform a simple spatial discrimination task of gratings in either vertical or horizontal orientation as well as control subjects, an increase in the amplitude of the BOLD signal in fMRI was greater in the basal ganglia and thalamus for patients with writer's cramp (when compared to changes in BOLD signal in healthy control subjects). This observation is consistent with the sensorimotor learning hypothesis, as expanded tactile receptive fields have been identified in sub-cortical structures (such as the thalamus) in animal models of focal dystonia (8).

In addition to deficits in tactile spatial processing, there is much evidence to suggest that there are abnormalities in temporal discrimination of somatosensory stimuli in focal hand dystonia. These impairments in temporal discrimination become evident during assessments of somatosensory processing such as kinesthesia, graphesthesia, and stereognosis (18). Patients with focal hand dystonia have difficulty discriminating between two closely timed tactile stimuli (19). Impairments in temporal discrimination in focal dystonia may be due to inefficient processing in somatosensory cortex.

Somatosensory evoked potentials (SEPs) recorded in MEG are enhanced (greater amplitude with respect to controls) in patients performing a temporal discrimination task, which may reflect an inability to discriminate between two rapidly presented tactile stimuli (19). Evoked responses in somatosensory cortex will adapt when the stimulus presentation is coupled with a motor activity. Typically, performing a behavior with the hand (such as writing or making circles with a toothbrush) will increase the distance between the finger representations in S1 localizations from MEG recordings (20). This mechanism seems to be preserved in focal hand dystonia. Although the distance between topographic representations in S1 are reduced in dystonia in response to passive tactile stimulation, this distance increases (and the representations stabilize) when the patient concurrently executes a movement (21). This suggests that sensory gating mechanisms may be spared in these individuals.

Motor Processing

While some aspects of sensorimotor integration (such as sensory gating) may remain uncompromised in patients with focal dystonia, it is well established that aberrant patterns of activity exist in the motor system of these patients, and this activity also contributes to the condition. Motor processing is complex and involves the preparation, initiation, and execution of movement followed by sensory feedback. During movement preparation, regions of the frontal lobe including pre-motor cortex (PMC) and the supplementary motor area (SMA) are active prior to execution of the behavior. In human fMRI studies, areas of pre-motor cortex are active when an external signal (such as a visual stimulus) is used to drive a motor response while activity in the SMA is associated with motor imagery and internally driven movements (22, 23). Higher-order motor areas such as PMC and SMA project directly to primary motor cortex (M1), where movement commands are issued through the corticospinal tract. Following movement onset, somatosensory feedback is

provided by processing in higher-order parietal fields (such as S2/PV and PPC) in order to guide the action itself.

Functional neuroimaging techniques have been used to identify alterations in the subcortical and cortical motor system of patients with focal dystonia. In the basal ganglia, fMRI activity (BOLD signal amplitude) is greater for focal hand dystonia patients during a motor task when compared with normal individuals (24, 25). This increase in the fMRI signal (when compared to a subject-specific baseline resting period) is sustained in specific structures of the basal ganglia (namely the putamen and globus pallidus) following completion of the motor task, a pattern not identifiable in the control population (25; Figure 4). In the basal ganglia of these patients, an increase in the fMRI signal above what is normally seen during motor behavior is not specific to the affected task, and is present even when the patient performs a simple grasping movement (26). Although it is difficult to discern if abnormal overactivity in the basal ganglia contributes to or is the result of the motor impairments present in these patients, elevated activity in this sub-cortical structure seems to be a primary component of the disorder. Demonstrable differences in cortical activity between focal dystonia patients and healthy individuals have also been identified using functional neuroimaging techniques. Like the basal ganglia, the amplitude of the BOLD signal in primary motor cortex (M1) is greater in these patients when compared to control subjects during a motor task with the affected body structure (27). In contrast, percent signal change in regions such as pre-motor cortex and the SMA is significantly reduced in these patients when they perform a manual task with the affected hand (28). Although this pattern of hyperactivity in M1 and hypoactivity in PMC/SMA is in agreement with computational models of focal dystonia, other studies have reported greater activity in M1 during movement for control subjects when compared to FHD patients (28, 29). A lack of agreement between these findings may be due to the fact that baseline brain activity in M1 (in the absence of a motor task, or following the movement itself) of these patients are likely to be impaired, in a fashion seen in other brain regions such as the basal ganglia (25). Interpretation across studies is also confounded by how these areas are defined and subdivided by imaging researchers, particularly with how the same areas are identified across groups, as activity in one region may be influenced by “spreading” activity in altered neighboring cortical fields.

One emerging explanation for cortical overactivity (in M1) and underactivity (in PMC, SMA) is that muscular co-contraction in dystonia is the result of a break-down in mechanisms that inhibit unwanted movement plans generated in motor cortex (30, 31). Evidence to support this hypothesis has been generated through studies that observe the effects of direct stimulation of motor cortical areas, such as TMS. Generally, high-intensity stimulation of motor cortex through TMS will evoke movements that, when monitored through EMG, are of a larger amplitude (motor evoked potentials; MEPs) in dystonia patients when compared to controls (32). Rapid (<5ms) delivery of a second TMS pulse to motor cortex (paired-pulse stimulation) is known to result in decreased MEPs that reflect intracortical inhibition (ICI), a process mediated by neurotransmitters (such as GABA-A) that is designed to focus and select appropriate responses and inhibit unwanted movements (33). MEPs evoked under multiple paired-pulse TMS stimulation paradigms remained unattenuated in focal dystonia patients further supporting the posit that this process of motor

cortex (ICI) is deficient in this population (34, 35, 36, 37). When a TMS pulse is triggered by the flexion of one finger, MEPs recorded from a neighboring (stationary, and thus normally inhibited) digit are suppressed in control subjects and enhanced in dystonia patients (38; Figure 5). Studies utilizing TMS have complemented data from functional neuroimaging research that have previously identified increased activity in M1 by suggesting that this overactivity in dystonia is the result of reduced ICI in primary motor cortex.

Some evidence suggests that motor visualization and imagery is also impaired in focal dystonia. Behaviorally, patients with writer's cramp are slower to respond to mental rotation tasks of the hands but not the feet, while accuracy is relatively preserved, possibly due to an alteration of the representations of manual structures in primary somatosensory cortex (39). Additionally it may be a result of dysfunction in the basal ganglia or motor cortices. When TMS is delivered to M1 in these patients, enhanced MEP amplitudes persist even when the movement is imagined and not real (40). Visual processing areas may also play a more prominent role in motor imagery in this population. In simple somatosensory spatial discrimination tasks, overactivation in fMRI (greater amplitude of the BOLD signal versus controls) of visual cortical fields was present suggesting a reliance on visual imagery for tactile discrimination (17).

Effects of training

Knowledge about the underlying neural pathophysiology of focal hand dystonia obtained through animal models and neuroimaging techniques have allowed clinicians to develop successful behavioral treatment regimens. Some of these therapeutic interventions, such as Constraint-Induced movement therapy (41) and learning based sensorimotor retraining (13, 42) have been successfully applied with the ultimate goal of improving the sensory representations of the affected limbs in the brain. Completion of these physical therapy programs can produce demonstrable changes in cortical structure concurrent with the reduction of dystonic symptoms. For example, subjective reports of improvement following retraining with the hand coincide with changes in topographic organization that occur during the course of treatment (5). Imaging techniques with superior temporal resolution, such as EEG and MEG, are ideal for examining training-induced neuroplasticity. These methods have been used to identify changes in neural processing during the course of perceptual learning in healthy individuals. For example, activity in primary auditory cortex increases following auditory temporal interval discrimination training (43, 44). Transformations in primary sensory areas as a result of training can occur quite rapidly, with identifiable changes within the response properties of auditory cortex over the course of a few days (45) and can generalize across spatial location as well as sensory modality (46). Changes that occur in the brain as a result of treatment should extend outside of primary somatosensory cortex as well. In many clinical conditions, including low-grade gliomas and stroke, changes in cortical function occur bilaterally (47, 48). Further, recovery of fine motor function in the affected hand is associated with changes in the ipsilateral hemisphere (49). Whole-brain coverage provided by the majority of functional imaging techniques allows imaging experts to examine these changes as well.

In order to evaluate the extent to which neuroplasticity contributed to this recovery, Byl and colleagues (50) applied the techniques of MEG to map the distribution, amplitude, and latency of somatosensory evoked responses both prior to and following learning based sensorimotor retraining. After treatment, significant functional changes in somatosensory cortex were present (Figure 6). Sensorimotor retraining expanded representations of manual structures that were previously intermixed in somatosensory cortex (Figure 6A). Digit reordering in S1, generally distinct in normal individuals, became normalized and more like the ordering in control subjects following treatment (Figure 6B). Lastly, temporal properties of the somatosensory evoked response such as amplitude and latency became stabilized in patients that had completed the program, reducing the strength of the magnetic dipole and tightening the duration of the SEF to a level comparable to healthy controls (Figure 6C).

The role of neuroimaging in the diagnosis of focal hand dystonia

While the behavioral manifestations of focal hand dystonia are evident to the clinician, limited testing is available to confirm such a diagnosis. A diagnosis of focal hand dystonia is typically generated through behavioral testing by the clinician, however, neuroimaging tools can and do play a powerful role in verification of the disorder (3). Although some genetic mutations, specifically those of the DYT1 and DYT7 genes, are associated with the development of a focal dystonia (51, 52, 53) many carriers of these genes do not develop the condition. Given the lack of a definitive genetic marker for focal dystonia, imaging methods such as MRI and MEG have the potential to become an important tool for clinicians for the assessment and monitoring treatment of focal dystonia. This is especially important as many other forms of adult-onset primary dystonia share common genetic mechanisms (30). While MRI is commonly employed by clinicians to clear patients of other neurological conditions (such as tumor and stroke), it is also a powerful tool for assessment. The most common application of these imaging methods is to identify and track changes in the cortical representation of the affected body structure, generally done using fMRI or MEG. Studies using structural MRIs have also isolated specific anatomical changes in the cortical volume of FHD, such as the expansion of gray matter volume in the putamen of patients with focal hand dystonia (54). This is consistent with SPECT studies that have identified reduced dopamine D2 receptor binding in structures of the basal ganglia (55). Some of these changes in anatomy, such as increased gray matter volume around sensorimotor cortex, have been found to be specific to focal dystonia and absent in other forms of adult-onset dystonia (56, 57, 58).

It is likely that neuroimaging will soon be used to identify individuals who are at-risk for developing focal dystonia. Many of the changes of functional brain activity identified in focal hand dystonia are also present in some individuals that carry certain genes, such as DYT1. In a study done by Ghilardi and colleagues (2003), individuals that carry the DYT1 gene yet do not express any clinical symptoms were impaired in the acquisition of a motor sequence, and furthermore showed aberrant patterns of activity in higher-order motor areas (pre-motor cortex, SMA) as well as the cerebellum during the training phase of the task (59, 60). Also, in DYT1 carriers, the integrity of the fiber tracts (as measured by DTI) connecting sensorimotor cortex with other cortical and sub-cortical brain structures is reduced, suggesting that even in the absence of motor impairment, aberrations in neuroanatomical

structure still exist (61). Changes in white matter integrity, specifically in fiber tracts that connect the basal ganglia, can be identified in the patient prior to treatment and can also be tracked following a therapeutic intervention (62). Although it is difficult to determine if changes in the behavior, neuroanatomy and physiological functioning of the brain in both clinical patients and gene carriers are the cause of or are a result of focal hand dystonia, a greater understanding of these characteristics through applied neuroimaging will allow us to understand endophenotypic traits inherent to the condition (30, 31).

Future Directions for Neuroimaging and Focal Hand Dystonia

While many advances in the treatment of focal hand dystonia have been made through insights provided by neuroimaging, a considerable amount of work remains to be done in linking these motor impairments to underlying anatomical and physiological mechanisms. It is challenging to evaluate the extent to which changes in brain anatomy and function are the result of primary versus secondary effects of the disorder, and this becomes critical to understand in the development of behavioral treatment regimens targeted to reverse neurobiological changes. One of the stronger supports for impaired neural mechanisms as the source of focal hand dystonia comes from demonstrations of deviant brain activity in non-manifesting genetic carriers (59, 60, 61). Here, changes in brain function can be observed in the absence of any dystonic symptoms in the nonmanifesting carriers, suggesting that these alterations in neurophysiology contribute to, and are not the result of, the condition. However, given that the genetic contributions to FHD are some of the most complex and poorly understood of all dystonias, focal or otherwise (30, 31), more work needs to be done in this area. Conflicting reports in the literature—such as why in some studies an increase in activity in primary motor cortex is seen (63) and in some studies a decrease is seen in the same region (29, 64)—necessitate further studies. Although this lack of parsimony may be due to inherent differences in experimental paradigms, it is equally likely due to the fact that none of these brain regions act in isolation, and that further work in this area will need to focus on how interaction between these areas may contribute to the disorder. Alterations in these motor networks may become disentangled through MEG and fMRI studies of functional connectivity combined with MRI and DTI studies of anatomical connectivity (65, 66). A greater understanding of the neural architecture that is affected in focal dystonia can provide clinicians and scientists with information needed to develop accurate surgical interventions (such as the placement of deep brain stimulators) in addition to the opportunity to track recovery and guide retraining paradigms tailored for each individual patient.

Conclusion

Therapists, neuroscientists, neuroradiologists, neurosurgeons and neurologists have an exciting opportunity to work together to discover more about the risk factors, etiology and effective intervention paradigms to facilitate recovery of normal motor control in patients with focal hand dystonia. Although today, the application of functional neuroimaging is most commonly used for research purposes, neuroimaging may begin to play a more important role in objectively documenting and guiding appropriate intervention strategies for patients with focal dystonia.

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Figure 1.

Electrophysiological recording map of digit representations in somatosensory area 3a from two owl monkeys following extensive training on a repetitive movement task. Topographic representations of the structures of the affected hand in 3a of owl monkeys that develop symptoms similar to dystonia were overlapping, with receptive fields that included multiple digits (hatched) as well as receptive fields with overlapping palmar and digit representations (cross-hatched). Reproduced, with permission, from 9.

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Figure 2.

Neuromagnetic dipole localizations of digit representations in primary somatosensory cortex of patients with focal hand dystonia. A) In the hemisphere contralateral to the non-affected hand, digit representation is ordered, independent, and well separated. B) Consistent with the sensorimotor learning hypothesis, sources localized in S1 in the hemisphere contralateral to the affected hand show little distance between each other, with a digit topography that does not conform to the traditional ordering of these structures in primary somatosensory cortex. Reprinted, with permission, from 12.

Figure 3.

Diagram of the computational model of sensory feedback in focal dystonia developed by Sanger and Merzenich (2000). Here, disorganized representations in somatosensory cortex (S) contribute to excessive gain in a mapping from sensory to motor cortex (C), leading to saturation in motor cortical activity (m) when combined with normal inputs from feed back through the basal ganglia-corticostriatal circuit (B) and the initial motor command (u). Reprinted, with permission, from 14.

Figure 4.

fMRI time-series data from two regions of the basal ganglia, the putamen (4A) and globus pallidus (4B) and two cortical areas, primary motor cortex (4C) and primary somatosensory cortex (4D) during a simple finger tapping task (4E). While activity increased all regions during the task, in patients with focal hand dystonia (in red) this activity was increased in amplitude, persistent and sustained following movement, a pattern not seen in control subjects (in blue). Reproduced, with permission, from 25.

Figure 5.

Percentage change in compound movement amplitude potential (%CMAP) in the little finger evoked by TMS during both a resting condition and a self-triggered movement of the second digit of the right hand. When TMS is applied over motor cortex during self-paced movement, MEPs of the little finger in patients with focal hand dystonia (in white) are increased compared to when control subjects (in gray) perform the same movement (* = $p < 0.05$). This data indicates that cortical mechanisms that normally inhibit unwanted movements are compromised in patients with focal dystonia. Reproduced, with permission, from 38.

Figure 6.

Changes in the response properties of primary somatosensory cortex recorded in MEG following sensory discrimination training. Following a comprehensive rehabilitation paradigm, observable changes in the volume of activity (6A), digit order representation (6B) and amplitude and latency of the S1 response (6C) are stabilized in focal dystonia patients in conjunction with alleviation of symptoms. Reproduced, with permission, from 50.