

Hypo- and Hyperkinetic, Dyscoordinative and Otherwise Inappropriate Motor and Behavioral Movement Disorders

Behavior is considered the response to internal and external stimuli. Both the basal ganglia as well as the cerebellum process internal (homeostatic) and external (environmental) cortical information in order to orchestrate adequately adapted behavior and send this processed information via the thalamus back to the cortex for final execution through motor neurons and neuromuscular structures. The basal ganglia arrange for the appropriate selection of behavioral fragments (response selection) out of the available pool of learned standard behaviors, and define their magnitude, while the cerebellum together with the sensory, visual, and vestibular organs deal with their coordination, that is, the exact timing of muscle actions so that the body can move smoothly. The final execution of these movements is enabled by upper/lower motor neurons and neuromuscular structures.

The basal ganglia have long been associated with sensorimotor functions only. In the last few decades, though, it has become generally accepted that, reflected by their functional-anatomical organization, their function not only comprises the tailored orchestration of sensorimotor behavior (through the sensorimotor circuit), but also cognitive-executive and emotional-motivational behaviors (via the associative cognitive and limbic circuits). This allows the basal ganglia to produce the most appropriate, tailored behavior to internal and external stimuli, and to suppress inadequate behavior. Any impairment in the production and realization of this behavior in the presence of clear consciousness, whether by inadequate selection of behavioral fragments or their final execution, might result in movement disorders, characterized by involuntary or uncontrolled movements interfering with our normal behavior. Generally speaking, movement disorders comprise hypokinetic (parkinsonism) and/or hyperkinetic (tremor, chorea, dystonia, myoclonus, tics and stereotypies, although these last conditions have an element of voluntary control) movement disorders, as well as dyscoordinative and otherwise dysexecutive and/or substantive deviant, behavioral, and/or emotional movement disorders.

Persistent or episodic involuntary motor behavior may manifest with both a scarcity (hypokinetic movement disorders) or an excess (hyperkinetic movement disorders) of spontaneous movements. As a rule, hypokinesia are caused by a primary dysfunction of the basal ganglia circuits, namely typical (presynaptic dopaminergic) and atypical (pre-/post-/synaptical dopaminergic) parkinsonisms, whereas hyperkinesia such as tremor, tics, chorea, myoclonus, ballism, and dystonia, on the other

hand, may be driven by basal ganglia dysfunction as well, but also from malfunction of other central or even peripheral regions of the nervous system. Both hypo- and hyperkinetic movement disorders often produce multiple cognitive (e.g. dysexecutive, mnemonic) and neuropsychiatric (e.g. mood, psychotic, motivational) symptoms. Such pathologic behaviors not only reflect abnormalities in associate and limbic basal ganglia circuits, but often also more generalized underlying neuropathology involving cortical and other brain areas.

In contrast to hypo- and hyperkinetic movement disorders, dyscoordinative and otherwise dysexecutive movement disorders do not manifest with hypo- or hyperkinesia, but with movements that lack proper coordination or proper central/peripheral execution. They arise from a lack of sensory or cerebellar input, or of other forms of feedbacks which are crucial for adequate movement execution. Thus, such movement disorders are the result of various cortical, cerebellar, sensory/visual/vestibular, and upper and lower motor neurons or musculoskeletal abnormalities. The most important entities in this group are ataxias and gait disorders.

This last category comprises also various movement disorders that cannot be classified as continuous hypokinetic, hyperkinetic, dyscoordinative and otherwise dysexecutive movement disorders. These inappropriate movement disorders arise from a variety of causes and conditions, and comprise episodic-paroxysmal movement disorders, sleep-related, drug-induced, psychiatric (stereotypies and the obsessive-compulsive disorder spectrum inclusive), and/or psychological (functional) movement disorders.

These various motor and behavioral movement disorders will be discussed after a basic introduction, in two different sections dealing with hypokinetic respectively hyperkinetic disorders, followed by a third section comprising the discussion of dyscoordinative and otherwise deviant, inappropriate movement disorders.

Generally accepted definitions are essential, not only for recognition and categorization, but also for selecting the appropriate therapeutic strategies and developing clinical pharmacologic research. This textbook aims to provide you with the proper tools to better understand and apply the terminology used. To complete this introduction, a short definition will be given of the most important hypokinetic, hyperkinetic, dyscoordinative, and otherwise dysexecutive movement disorders, as well as their phenomenologic classification (see Figure 1).

Hypokinetic Disorders

Overview on Motor and Behavioral Movement Disorders

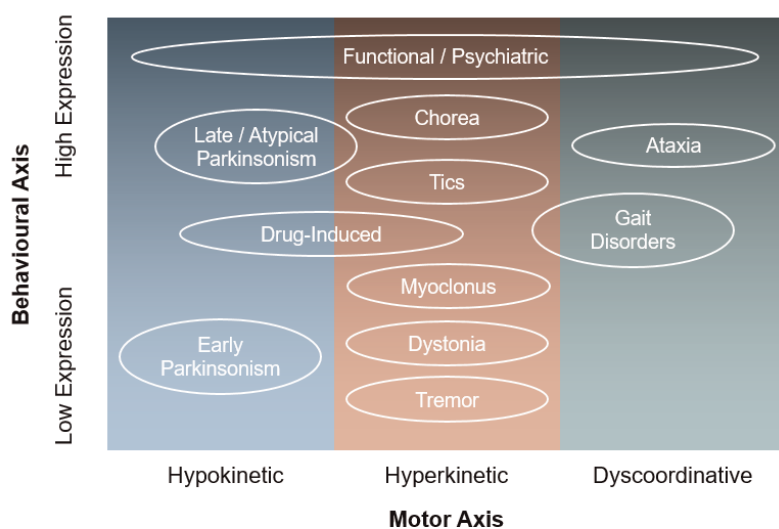


Figure 1 Overview on motor and behavioral movement disorders, schemed in a two-dimensional space reflecting the category of motor disorder against the expression of abnormal behaviors.

Hypokinetic Disorders

Parkinsonism

Signs and symptoms of parkinsonism comprise both appendicular (hypokinesia, bradykinesia, rigidity, and tremor) and axial (gait impairment, postural changes, and postural instability) motor impairments. Parkinsonism might be seen in typical and atypical, sporadic and genetic Parkinson syndromes. Typical sporadic (Parkinson's disease, also referred to as idiopathic Parkinson's disease) and familial/genetic presynaptic Parkinson syndromes are characterized by the presence of dopamine-responsive motor parkinsonism: bradykinesia and at least one of rest tremor and rigidity. In many if not all cases, motor parkinsonism is preceded or might be accompanied by a multitude of non-motor symptoms with substantial variability among patients. It must be noted that individual pathologic courses may vary significantly between patients. However, motor parkinsonism, although a characteristic clinical hallmark in these typical Parkinson syndromes, is also seen in various iatrogenic/toxic/genetic atypical Parkinson syndromes, involving striatal malfunction of presynaptic, synaptic, or postsynaptic nigral dopaminergic neurons, among others in multiple system atrophy, progressive supranuclear palsy, and corticobasal degeneration. Only presynaptic-induced parkinsonism is levodopa-responsive, however. As a rule, motor parkinsonism in disorders that also feature other non-parkinsonian symptoms and/or another clinical course than commonly observed in Parkinson's disease are considered atypical parkinsonism. Most patients with typical parkinsonism suffer from Parkinson's disease, which is the second most common neurodegenerative disease after Alzheimer's disease. About 15 percent of these patients suffer familiar, genetic parkinsonism.

Hyperkinetic Disorders

Tremor

A tremor is a rhythmic, involuntary, sinusoidal, oscillatory, alternating movement of one or more body parts, particularly

the limbs, but also including the head, chin, and soft palate, with a relatively fixed frequency and amplitude that occurs over an extended period of time. Tremors can be classified on the basis of clinical characteristics (resting tremor, postural tremor, kinetic or action tremor, intentional tremor, frequency, stability, amplitude), origin (cerebellar, extrapyramidal), or pathophysiologic mechanism (physiologic, essential, iatrogenic).

Tics

Tics are repetitive, not rhythmical, spasmodic or twitching, simple or complex movements (jerks), mainly occurring at irregular intervals and inconsistent in space. They primarily affect muscles (or groups of muscles) in the face and neck, although they may spread all over the body. They normally can be voluntarily suppressed, yet only temporarily. Patients typically report premonitory sensations (an urge to perform the movement), which are relieved by tic production.

Chorea

Chorea is a state of excessive, spontaneous movements (jerks), irregularly timed, non-repetitive, randomly distributed, with random expression, and abrupt in character, which might primarily occur in some genetic disorders and secondary to various (para)infectious, autoimmune, and structural conditions and some toxic, iatrogenic, and metabolic encephalopathies. These movements may vary in severity from restlessness with mild, intermittent exaggeration of gestures and expression, fidgeting movements of the hands, unstable dance-like gait to a continuous flow of disabling, violent movements.

Myoclonus

Myoclonus is a sudden, brief, involuntary jerk of a muscle or a group of muscles, consistent in time and space, which

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might be caused by muscle contraction (positive myoclonus) or by interruptions of tonic muscle activity (negative myoclonus). These movements can be focal or multifocal, although they are mostly restricted to one area of the body (eye, hand, palate), sometimes persisting for some time (for instance in action myoclonus), making it difficult to distinguish them from tremor. Myoclonus is classified based on its anatomic origin, i.e. cortex, subcortical areas (basal ganglia, brainstem), spinal cord, peripheral nerves, or based on clinical presentation (distribution, relation to motor activity, temporal pattern).

Ballism

Ballism is characterized by involuntary, forceful, flinging, high-amplitude “throwing” movements. Ballism is often accompanied by choreatic movements, the latter being more distal, while ballism describes predominantly proximal movements. With time, the proximal ballistic movements may become less pronounced and the distal choreatic movements predominate. Ballism typically increases with action and is absent during sleep. It occurs usually only on one side of the body, and is in most cases caused by stroke or other lesions to basal ganglia/midbrain structures.

Dystonia

Dystonia is a neurologic condition that produces sustained or intermittent muscle contractions, affecting one or more muscles (focal, segmental, or generalized), and causing abnormal, often repetitive (dystonic tremor), or persistent (dystonic posturing) movements. It can manifest as a disorder of its own or manifest as a symptom of another disease. Dystonias are classified based on etiology (primary dystonias including a growing variety of genetic forms, and secondary dystonias), age of onset, and body regions involved.

Dyscoordinative and Otherwise Dysexecutive Movement Disorders

Ataxia

Ataxia is a continuous or episodic dysmetric motor behavior caused by defect coordination of the muscles during movements in time, direction, and force while the task concepts remain correct. Ataxia manifests with impaired balance and lack of coordination due to problems of stance and gait (wide base, imbalance), limb movements, speech (cerebellar dysarthria), and eye movements (saccadic smooth pursuit, dysmetric saccades, and downbeat nystagmus). It can be caused by dysfunction of the cerebellum (cerebellar ataxia), but also by the loss of proprioception (sensory ataxia) or by vestibular system dysfunction (vestibular ataxia).

Gait–Balance Disorders

Apart from ataxias, dyscoordinative gait–balance disorders may be caused by upper and lower motor neurons or

musculoskeletal disorders such as hemiplegia, spastic diplegia, neuropathies, and myopathies. Observation of such induced gait disorders are an important aspect of diagnosis that may provide information about the specific musculoskeletal and neurologic conditions.

Episodic Executive Dyskinesia

Episodic dyskinesias are movement disorders characterized by the appearance of symptoms in discrete, often brief, periods or episodes. These disorders comprise a heterogeneous group of rare conditions. Paroxysmal dyskinesias constitute the core of this group and usually exhibit normal interepisodic neurologic findings. Contrariwise, episodic dyskinesias occur as a particular feature of complex chronic neurologic disorders. Conjunction of accurate phenotyping with up-to-date methods of molecular genetics recently provided remarkable new insights concerning the genetic causes of episodic dyskinesia.

Stereotypies

Stereotypies are repetitive or ritualistic, non-functional dyskinesias such as body rocking or head banging, posture or utterance, which last more than 4 weeks, interfere strongly with normal activity, might cause bodily injury, and are not necessarily induced by a medical condition or substances. Stereotypies are disorders within the obsessive-compulsive spectrum or are the result of abnormal operant conditioning, include mannerisms, echopraxia, *mitgehen*, automatic obedience, and negativism. Mannerisms (such as rocking, head banging, whistling, humming, and/or grimacing or repeatedly running one’s hand through one’s hair) suggest social significance and include goal-directed activities, but are out of context or odd in appearance. Echopraxia is the imitation of another person’s movements. *Mitgehen* is moving a limb in response to light pressure despite being told not to do so, automatic obedience is carrying out commands in a robot-like fashion, and negativism is refusing to cooperate with simple requests for no reason. When someone persistently and repetitively engages in a behavior that serves no apparent function, the behavior is called a stereotypy. When the stereotypic behavior becomes emancipated from the environment, a diagnosis of compulsive disorder (CD) should be made.

Obsessive–Compulsive Disorders

The obsessive-compulsive spectrum is an important concept referring to where a number of dyskinetic disorders drawn from various psychiatric, neurologic, and/or medical conditions are described as existing on a spectrum of conditions from obsessions to compulsions behavior. This concept suggests that many conditions overlap with obsessive-compulsive disorders (OCD) in symptomatic profile, demographics, family history, neurobiology, comorbidity, clinical course, and response to various pharmacotherapies. An obsession might be defined as a recurring thought, image, or urge,

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characterized by harm avoidance, that cannot be controlled by the patient, whereas a compulsion can be described as a risk-seeking ritualistic impulsive behavior that the person feels compelled to perform. Based on the grouped clinical manifestations, this continuum can be split into the autism spectrum, bodily dysmorphic disorders, impulse control disorders such as pathologic gambling and sexual compulsivity, and obsessive-compulsive disorders.

Functional Movement Disorders

Functional movement disorders (FMDs) are abnormalities of movement that are altered by distraction or non-physiologic maneuvers, and are clinically incompatible with movement disorders associated with neurologic disease. FMD is characterized by sudden symptom onset and inconsistent or incongruent movements.

Section 1

Basic Introduction

Chapter

1

Behavior

Basic Principles and Behavioral Movement Disorders

Mark Hallett

Introduction

To paraphrase the Wikipedia definition, *behavior* is the range of actions made by organisms; it is the “response of the organism to various stimuli or inputs, whether internal or external, conscious or subconscious, overt or covert, and voluntary or involuntary.” This is certainly a topic that should interest movement disorder specialists. However, there is another subspecialty field of neurology called behavioral neurology, which deals mainly with cognitive function such as memory and language. Movement disorders are situated in between neuromuscular and behavioral neurology. The field of movement disorders began with a focus on disorders stemming from the basal ganglia, not muscle or cortex, but as the field has matured it has expanded on both ends, including added interest now in behavior as we try to understand more aspects of our complex patients.

Basic Principles

Movement Generation

Movement occurs as a result of muscle contraction, and muscle is controlled by the alpha motoneurons in the spinal cord. Alpha motoneurons are influenced by both segmental and suprasegmental input, with the most important suprasegmental signals coming via the corticospinal and reticulospinal tracts. It is likely that the corticospinal tract conveys the most important information, with the reticulospinal system generally playing a supportive role. The corticospinal tract originates most importantly from the primary motor cortex (M1), but has contributions from some premotor areas as well. Input to the corticospinal tract from sensory cortex may largely modulate sensory input. M1 itself receives input from cortical and subcortical structures. Subcortically, the two major systems are the basal ganglia and the cerebellum. Both derive much of their input from the cortex and send processed information back to the cortex via the thalamus. Although these two systems had been thought to be largely separate, newer evidence has shown clear connections between them [1]. In general, the basal ganglia system supports features of movement concerning which movements to make and the magnitude of contraction, while the cerebellar system supports features of movement dealing with the detailed timing and coordination of the different body parts (see also Chapters 2 and 3) [2].

M1 also receives much cortico-cortical input coming from the entire cortical mantle (Figure 1.1). In general terms, the

posterior part of the brain is the sensory portion receiving visual, somatosensory, and auditory information. This information is integrated in multisensory regions in the parietal lobe and is the source of external triggering of movement. The parietal to premotor pathways have been the object of intense study in recent decades, and highly specific connections have been identified to which specific functions can be attached [3]. For example, the reach and grasp components of a reach-to-grasp movement have separate parietal premotor pathways. Again, in general, the front part of the brain receives and integrates information about the body and is considered the source of internal triggering [4]. Internal input includes homeostatic drive from regions such as the hypothalamus and includes factors such as hunger and thirst. Other internal input is limbic and includes factors such as vigilance, fear, anxiety, and sex. Another critical internal input is reward, seeking of pleasure, and this appears largely mediated by mesolimbic dopaminergic function. If a past behavior produced reward, the brain wants to do it again. Facilitation of behavior by repeated reward is called *operant conditioning*.

Both the external and internal inputs are integrated in mesial frontal areas such as the cingulate and

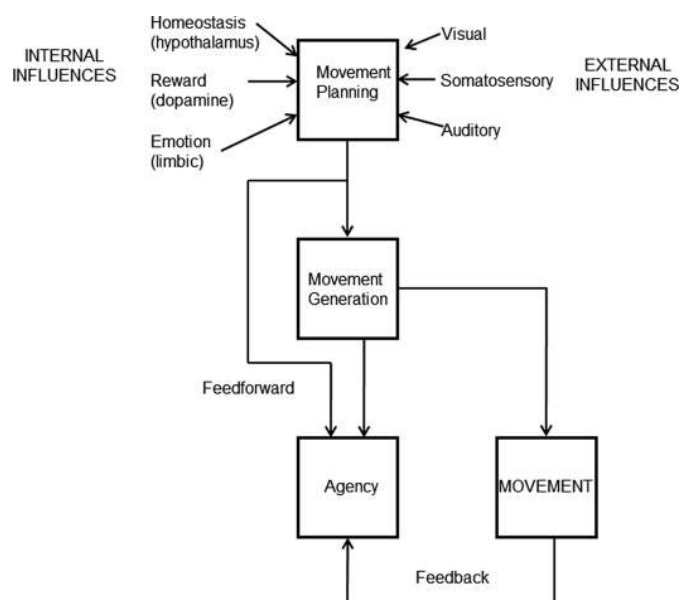


Figure 1.1 Scheme for the generation of behavior. Behavior is planned under internal and external influences and then generated. Normally, people think they control behavior (“self-agency”). Self-agency requires a sense of “willing” (feedforward signal) and of “registration” (feedback signal). If “willing” precedes the behavior, the *qualie* of agency can be generated. See more detail in the text. From [37] (with permission of author and publisher).

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pre-supplementary motor area, as well as the premotor areas directly [5]. Strong inputs come from the mesial frontal areas to the premotor and motor cortex. What the motor cortex will produce, as behavior, at any one time, is the consequence of the integration of all these factors. In essence, behavior is constantly influenced by all environmental (external) stimuli and multiple forces from frontal (internal) drives. The more information available about all these factors, the more behavior can be probabilistically predicted. It is ordinarily a difficult calculation, which is also influenced by neural noise. However, in some circumstances individual factors are so strong that prediction would be almost certain. If someone is hungry and is presented with a pizza, it is very likely that they would eat it. If someone had immense pleasure from cocaine and was offered it again, they might take it again even though cognitively they know that this will only make the situation worse in the long run.

Consciousness and Voluntariness

From all we know about the brain, it is constantly in action, and it appears that many different things are being processed simultaneously. For example, as was already pointed out, there are multiple, continuous, external and internal inputs. Additionally, many different thought processes can be going on simultaneously. If you are asked a question, such as someone's name, and cannot immediately think of it, you can go on and think about something else, and, often, sooner or later, the name will "pop into your head." This is likely the product of ongoing searching. If given a difficult decision, you might say, "I will think about it and let you know later." Even if you do not devote considerable time thinking about it at a conscious level, you will be able to come to a decision. Much of this brain activity is unconscious. Only one thing at a time, or rarely two things, will bubble up into consciousness. And the stream of consciousness does not always flow smoothly; the topic may change quickly and not always logically from one to the next.

What is in consciousness must be in some way what is important at the time and is a result of the process called attention. Attention can be bottom up or top down. A strong external stimulus will usually bottom up into consciousness regardless of what else is going on. However, if a soldier is paying top-down attention to fighting with an enemy, he might not notice that he has been shot in the leg.

The individual elements of consciousness are called *qualia*, and one quale, relevant for movement disorders and other reasons, is voluntariness [6]. Much of the time, it would be fair to say that persons are not thinking about whether a movement is voluntary. Things happen. For most movement, people generally think that they are the "agent" of the movement; that is, they willed the movement and it occurred. This is the sense of agency or, specifically, *self-agency*. Self-agency presumably requires both a sense of willing, a feedforward signal, and the sense that the willed movement occurred, a feedback signal. If willing precedes the specific action that was willed, then the quale of agency can be created (see Figure 1.1).

The sense of agency utilizes a brain network with a prominent role for the temporoparietal junction (TPJ) [7]. Presumably this feedforward–feedback process is happening all the time but does not create a quale because it is so routine. However, if the process does not work correctly – for example, a movement occurs for which there is no feedforward signal – that might bubble up to consciousness as a surprise, generating the quale of an involuntary movement. Whether movements are voluntary or involuntary is often a concern to the patient and to the movement disorder neurologist.

Behavioral Movement Disorders

Many of the patients seen by movement disorder neurologists have some behavioral aspects and some are even "primarily" behavioral. Several features are easier to explain than others, and some examples will be given here to illuminate general as well as specific issues. These disorders overlap to some extent to the "*disorders of volition*" (see Table 1.1) [6, 8].

Behavioral Abnormalities due to Parietal-Premotor Disorders (Apraxia and Task-Specific Disorders)

There are many types of apraxia; the one most commonly recognized is *ideomotor apraxia* in which there appears to be the loss of a motor memory for a skilled movement [9, 10]. The patient seems to understand what movement is to be made, there is no responsible deficit of language, and the motor machinery is in good enough shape to make the movement, but the proper sequence of actions is not generated. Bedside testing is generally done with external movements, either asking someone to make a particular movement (such as "show me how you would use a hammer") or to mimic the examiner making a novel movement. However, such patients often cannot make the complex movement even in the natural context and might be impaired in activities of daily living. Such an apraxia, for example, is characteristic in patients with corticobasal syndrome (see Chapter 32).

Table 1.1 Some disorders of volition [37] (with permission of author and publisher)

Disorder	Clinical features
Tic	Movements are often considered voluntary, but the patients cannot not do them, and often say that they let the movements happen
Functional movement disorder	Movements look like normal movements and share much of the normal voluntary movement physiology, but the patients believe them to be involuntary
Huntington's chorea	Early in the disease, patients believe that the movements are voluntary
Anosognosia	Patients may believe that they have moved when they have not
Alien hand	Unwanted movements/postures arise without the sense that they are willed
Schizophrenia	In patients with passivity phenomena, the movements may look normal and even goal-directed, but the patient feels as if he is being externally controlled

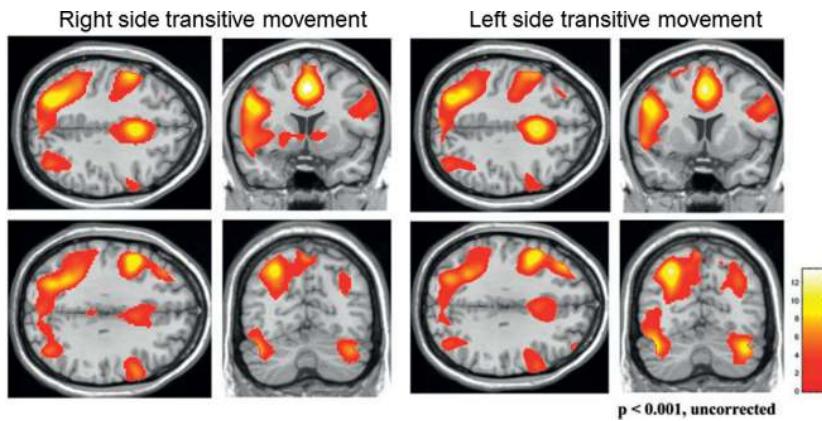


Figure 1.2 Functional magnetic resonance imaging (fMRI) from normal subjects making transitive movements (mimicked movements that employ a tool) with right and left hands. Axial and coronal sections are shown. There are prominent activations in parietal, premotor, and supplementary motor cortex, more on the left side even with left sided movement. Modified from Bohlhalter et al. [11] with permission.

Patients with focal hand dystonia commonly begin with a derangement of just a single task, such as only writing or only playing the piano. Other tasks are done normally. When attempting the task, the motor coordination falls apart and a dystonic spasm intervenes. This is referred to as *task specificity*. It is similar to ideomotor apraxia in that there is a failure of a learned motor program.

There is good evidence that skilled movements are stored in the brain in the parietal area or, perhaps more accurately, in parietal-premotor networks, mainly in the left hemisphere, for both right or left hand movements [11]. Basic observations as to how movements are learned in human studies show that activity in parietal-premotor pathways increases as movements are learned. As the movements are learned to the point of automaticity, the activity declines but the connectivity in the network becomes stronger [12]. In praxis movements, such as handwriting [13], the activation of left-sided parietal-premotor pathways can be identified with both neuroimaging and electroencephalography (EEG) studies (see Figure 1.2).

So, in apraxia there appears to be a general failure of the parietal-premotor pathway. Lesions of the parietal area are common causes of the disorder, but premotor lesions can also be responsible as well as “pure disconnections” between the two areas. In writer’s cramp, we identified that the specific writing parietal-premotor connection is hypoactive [14], but why this is accompanied by dystonic spasm is not understood.

Behavioral Abnormalities due to Paralimbic Disorders (Tics)

Tics are on the border between voluntary and involuntary movements. If pressed, most adults who have tics say that they are voluntary movements made to reduce an inner psychic tension or a sensory feeling. When the movement is made, the person feels temporarily better, but then the tension or sensation begins rising again. However, the movements are done so automatically that ordinarily there is no sense of willing or even recognition that the tic occurred. Children with tics have a more difficult time explaining the nature of their movements but will generally say that they are involuntary. When a movement leads to a good feeling, it can be considered rewarding, and it is possible that tics are perpetuated in part

due to operant conditioning. Thus, a tic could be thought of as an undesirable habit [15].

The sensory feeling that provokes the tic is called a sensory tic, and little work has been done to understand it. Patients feel that they are particularly sensitive to sensory stimuli; they become very annoyed, for example, with tags on shirts. However, the psychophysics of their sensory perception, including thresholds, is normal, suggesting a possible failure of habituation [16].

The urge to tic is similar to normal urges such as the urge to scratch an itch or the urge to blink when trying to keep the eyelids open. fMRI studies of the urge to blink show that the anterior insula is particularly active [17]. Using an event-related design with fMRI, it has been demonstrated that the anterior insula and the anterior cingulate are active prior to tics (see Figure 1.3) [18]. Additionally, comparing the resting brain activity while awake, when tics are occurring, and asleep, when tics are rare, there is also increased activity of the anterior insula and cingulate [19]. Hence, the urge to tic may well arise in these structures.

There is an EEG signature called the *Bereitschaftspotential* or BP that can be identified in the 1.5 s or so prior to a voluntary movement [20, 21]. It is a slowly rising negativity that begins fairly symmetrically around the vertex, and as the movement approaches the negativity rises a bit faster and, at least for right-sided dominant hand movements, the potential peaks more over the left sensorimotor cortex. The early part of the potential, BP1, arises from the supplementary motor area (SMA) and the lateral premotor cortex, both parts of area 6. The later part of the potential, BP2, emphasizes more the premotor cortex and the primary motor cortex (M1). With tics, there is either no BP at all or just a BP2 [22]. This suggests that tics originate with only minimal involvement of area 6. Perhaps the anterior insula and anterior cingulate access the motor cortex directly.

Behavioral Abnormalities due to the Loss of “Self-Agency” (Functional Movement Disorders)

Functional movement disorders come in many varieties, both positive and negative. Virtually any other movement disorder can be mimicked. The negative disorders of weakness and

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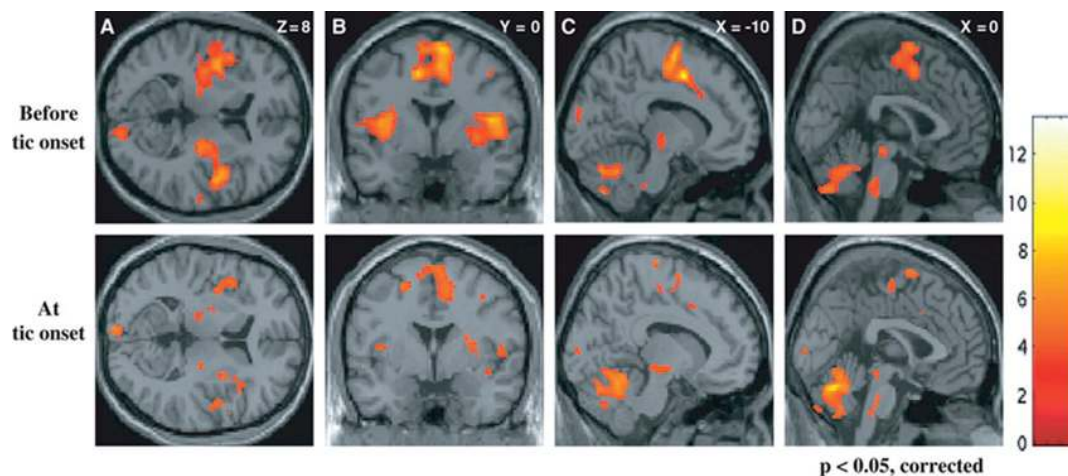


Figure 1.3 fMRI of axial (A), coronal (B), and sagittal (C and D) views in event-related design of spontaneous tics. The upper row shows significant activations ($P < 0.05$, corrected for multiple comparisons) of paralimbic areas (anterior cingulate cortex and insular region bilaterally) before tic onset; these activations were much less prominent at tic onset (lower row). From Bohlhalter et al. [18] with permission.

paralysis are common, but typically present to neurologists, for example, seeing strokes, neuromuscular disease, or multiple sclerosis. At the other extreme, paroxysmal hyperkinetic functional movements are often categorized as functional seizures (psychogenic non-epileptic seizures). The underlying etiology for such disorders is complex and multifactorial, and requires considering a biopsychosocial model, including genetic factors, stress responsivity, childhood trauma, and the current social structure [23–25].

The psychiatric etiology is most commonly considered to be conversion, where, in Freudian terms, a psychological symptom is converted to a somatic symptom. This is an unconscious process and the movement is not voluntary. Alternate etiologies are factitious and malingering, where the movement is voluntary, but the patient says that they are involuntary. At present, we have no clinical or laboratory way of separating these entities, except by secret surveillance. For the rest of this discussion, the etiology will be assumed to be conversion.

Functional movements appear to utilize brain mechanisms very close to those used by ordinarily voluntary movements [26, 27]. In functional paralysis, transcranial magnetic stimulation (TMS) of the motor cortex produces normal motor-evoked potentials (MEPs), indicating a normal motor cortex and pathway all the way to the muscle. When imagining movement of a body part, the MEPs should enhance, but in functional paralysis, the MEPs are reduced, suggesting an inhibitory influence on M1. When apparently trying to move the paretic limb in functional paralysis, fMRI shows activity changes in frontal lobe areas. Perhaps the inhibition comes from the frontal lobe.

In functional tremor, one important observation is that the tremor can be *entrained* by voluntary rhythmic movement of another body part. This suggests that the functional tremor generator is likely shared with the voluntary generator. Similarly, functional tremor is typically synchronous in different limbs, different from other tremors such as seen in Parkinson's disease (PD) and essential tremor.

Functional myoclonus has an electromyography (EMG) pattern similar to quick voluntary movements in terms of EMG burst length and antagonist muscle relationships. When stimulus-induced, it behaves like a normal reaction time movement in terms of mean latency and variability of latency, unlike cortical or brainstem myoclonus where the latency is very short with little variability. Importantly, there is often a typical BP preceding the functional myoclonus, indicating preparation for movement in area 6 (see Figure 1.4).

While the origin of functional movements is obscure, in several circumstances there is fMRI evidence of a hyperactive limbic system. The passive response of the right amygdala is increased to emotional faces, and several structures in the limbic system are hyperactive even with voluntary movements [28]. Another relevant fMRI observation is that the right TPJ is hypoactive with psychogenic tremor compared to voluntarily mimicked tremor [29]. As noted earlier, the TPJ is implicated in the sense of agency, and therefore, this hypoactivity might explain the loss of self-agency for the movements. It can be speculated that the lack of the normal feedforward signal from the aberrant movement intention may explain the abnormal TPJ activity.

If stress is one of the responsible factors in functional movements, abnormal signals from the limbic system can well be understood as the prime mover. A further question that typically arises is why different persons have different types of functional movement disorders. One possible explanation for this is that the brain often mimics what it knows. If a person knows someone with a stroke, they might have paralysis. If another person has a relative with PD, they might have a tremor. Some subjects even mimic themselves. This is common with functional seizures, where many of these patients also have organic seizures. Mimicry is a major function of the brain that aids in the process of motor learning and which also may be responsible for empathy [30]. I feel your pain. The mirror neurons, those motor neurons that show responses when seeing specific movements, as well as when

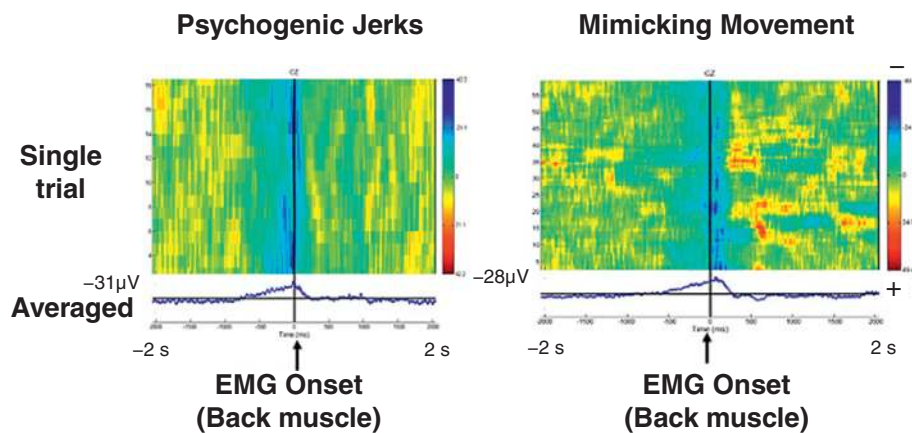


Figure 1.4 EEGs associated with functional jerks of trunk and self-initiated movements mimicking the jerks, arranged time-locked to the EMG discharge. Fifty traces of individual EEG records are shown on the top panel (single trial) and averaged waveforms are shown on the bottom (averaged). In single trials, blue and red colors indicate surface-negative and surface-positive, respectively. Note slowly rising surface-negative potential preceding both the functional jerks and the mimicking jerks. Data recorded by Dr. Zoltan Mari in the Human Motor Control Section, NINDS. From Shibasaki [20] with permission.

making those same movements, may be the underlying substrate for the mimicry [31].

Behavioral Abnormalities due to Reduced Internal Triggering (Akinesia, Hypokinesia, Bradykinesia)

Slowness of movement, or bradykinesia, is one of the major features of PD [32]. In general terms, the explanation fits well into the scheme of behavior put forward here. The basal ganglia support mainly the front half of the brain, and it is the front half where internal triggering of movement is generated. Hence, patients find it difficult to initiate movement (akinesia) and make slow (bradykinetic) and small (hypokinetic) movements. Patients must compensate for this difficulty by paying more attention to movements requiring more cortical resources. Externally triggered movements are much better because these appear to require less basal ganglia support. External triggering underlies the phenomenon of paradoxical kinesia [33].

Another feature of the slowness in PD is the *sequence effect*, where repetitive movements get gradually slower or smaller.

The sequence effect is easily seen with handwriting that gradually becomes more micrographic through the sentence. Additionally, the sequence effect commonly precedes a gait-freezing episode. This feature may be specific to PD; at least, it is not common in progressive supranuclear palsy (PSP) [34]. The pathophysiology of this behavior is not known. It is not responsive to dopamine [35] and hence can be a significant clinical problem even when the PD is generally responsive to oral therapy.

Behavioral Abnormalities due to Abnormal Operant Conditioning (Impulse Control Disorders)

PD patients may show a variety of abnormal behaviors, which are discussed in Chapter 13 in this book. Such behaviors include pathological gambling, pathological shopping, and punding [36]. These are all repetitive activities, which, similar to other forms of addiction, the patient continues to do even though recognizing that it might not be the best thing to do. These behaviors are related to abnormal dopamine functioning and operant conditioning creating undesirable habits.

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