

REVIEW

The Phenomenon of Exquisite Motor Control in Tic Disorders and its Pathophysiological Implications

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ABSTRACT: The unifying characteristic of movement disorders is the phenotypic presentation of abnormal motor outputs, either as isolated phenomena or in association with further clinical, often neuropsychiatric, features. However, the possibility of a movement disorder also characterized by supranormal or enhanced volitional motor control has not received attention. Based on clinical observations and cases collected over a number of years, we here describe the intriguing clinical phenomenon that people with tic disorders are often able to control specific muscle contractions as part of their tic behaviors to a degree that most humans typically cannot. Examples are given in accompanying video documentation. We explore medical literature on this topic and draw analogies with early research of fine motor control physiology in healthy humans. By systematically analyzing the

probable sources of this unusual capacity, and focusing on neuroscientific accounts of voluntary motor control, sensory feedback, and the role of motor learning in tic disorders, we provide a novel pathophysiological account explaining both the presence of exquisite control over motor output and that of overall tic behaviors. We finally comment on key questions for future research on the topic and provide concluding remarks on the complex movement disorder of tic behaviors. © 2021 The Authors. *Movement Disorders* published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society

Key Words: tic disorders; Tourette syndrome; motor control; skilled movements; motor learning

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Neurological movement disorders are conditions with the predominant clinical feature of abnormal motor output.¹ They encompass disorders of excessively generated oscillatory muscle activity (eg, tremor), disorders associated with spontaneous muscle jerks (eg, myoclonus), disorders of abnormally executed motor programs (eg, dystonia or parkinsonism), and disorders where the movement has a clearly organized pattern, but its occurrence is inappropriate or abnormal (eg, tics or chorea). In many of these disorders the motor abnormality may be one of several clinical signs and indeed additional features, such as neuropsychiatric symptoms, are often present. Here, we aim to highlight a previously underreported phenomenon in neurological movement disorders, namely that of exquisite control over motor output in people with tic disorders.

We first describe the intriguing phenomenon, which we also illustrate with video-documented material based on a series of well-characterized cases. We discuss putative underlying mechanisms that may facilitate its manifestation based on previous literature and existing models of motor control, and generate a series of pathophysiological hypotheses with regard to people with tics. Finally, we comment on implications for future research, which may in turn inform treatments in patients where the occurrence of hyperkinetic movements and exquisite motor control may co-occur.

The Phenomenon of Exquisite Motor Control in People with Tics

Over a period of several years and through our clinics, we came across a number of patients with tic disorders including Tourette syndrome (TS), who as part of their tic repertoire demonstrated an exceptional ability to voluntarily control individual muscles, in a way most humans typically cannot (see Table 1 and Video SS1 for documented examples). That is, the isolated muscle movements that formed the tic could also be performed voluntarily: patients could execute these

behaviors on command. This capacity was not confined to a particular somatotopic area but was apparent for different muscles in different patients. Importantly, the exquisite voluntary control was found in the same muscles that expressed the tic, and the temporal profile of the voluntary contraction resembled that of the tic. Further, there was no clear preference for the left or right side of the body. People with tics were typically able to generate the movement equally well on either side of the body. Moreover, nearly all patients we examined did not view these exceptional movements as any different from their other motor behaviors, either voluntary or involuntary. They were in fact surprised to be informed that most humans cannot typically generate similar motor performance.

The literature on this phenomenon in people with tic disorders is sparse. Meige and Feindel in their exhaustive clinical description of tics first commented on this phenomenon.² They reported a pediatric patient of Oppenheim, who exhibited isolated tic movements of each side of the platysma and also had the ability to voluntarily contract either one of them.² They also provided clinical documentation of patients who showed characteristic tics of the scalp with to-and-fro movements (also see segment C of video supplement). Only

TABLE 1. Description of main clinical characteristics of the cases illustrated in this article, the types of exquisite movements, and the predominant muscles involved

Case/age	Diagnosis	Most common tics at time of presentation	Type of exquisite movement and predominant muscles involved
1/44	CMTD	Dystonic cervical tics, neck jerking and turning, shoulder shrugging, immediate echopraxia	Side-to-side contractions of trapezius muscle
2/26	TS	Eye blinks, eyebrow movements, grimacing, sideways lip pulling, mouth opening, neck jerking, shaking hands, leg movements, grunting, chuckling, snorting	Isolated contractions of each sternocleidomastoid muscle
3/35	CMTD	Eyebrow movements, neck jerking and turning, respiratory and abdominal tics, pelvic thrusts, quadriceps tensing, immediate echopraxia	Contractions of frontalis and occipitalis muscles leading to to-and-fro movements of scalp
4/15	TS	Eye blinks, oculogyric tics, facial grimacing, lip pouting, head and shoulder jerking, wrist turning, finger tics, "hm" sounds	Contractions of frontalis and occipitalis muscles leading to to-and-fro movements of scalp. Isolated contractions of lateral head of triceps brachii muscle
5/66	TS	Eye blinks, ear clicking, throat clearing, phonations such as humming sounds, whole body tensing	Isolated contractions of oblique abdominal muscles on each side. Targeted contractions of short head of biceps femoris muscle
6/45	CMTD	Opening eyes wide, mouth movements, arm jerking, leg jerking, isolated muscle contractions all over the body	Isolated contractions of brachioradial muscle, parts of the platysma and lateral head of triceps brachii muscle
7/36	TS	Ear clicks, throat clearing, sniffing, dystonic trunk movements, stretching tics, exerting pressure on muscles, self-injurious behavior (hitting abdomen or pelvic area), immediate echopraxia	Side-to-side movements of peroneal muscle tendons under the superior fibular retinaculum
8/22	TS	Eye blinks, oculogyric tics, ear movements, facial grimacing, tongue movements, side-to-side movements of neck, wrist turning, pressing air through nose, "hm" sounds, immediate echopraxia	Side-to-side movements of hand extensor muscle tendons under transverse fibers of extensor expansions at metacarpophalangeal joints
9/16	TS	Eye blinks, oculomotor tics, neck jerking, mouth opening and grimacing, movements of trunk, inward turning of feet, hissing sounds	Side-to-side movements of hand extensor muscle tendons under transverse fibers of extensor expansions at metacarpophalangeal joints

Abbreviations: CMTD, chronic motor tic disorder; TS, Tourette syndrome.

very few subsequent reports followed on this topic, focusing on a particular type of isolated movements – also referred to as vestigial movements – namely ear wiggling. In 1927 Wilder and Silberman reported the case of a patient with tic disorders and ear wiggling as part of their tic repertoire.³ Approximately 60 years later Keshavan published 10 cases of people with ear wiggling tics, as well as scalp movement tics in eight of them.⁴ Although not much clinical information was provided, some of the patients Keshavan presented had an adult onset of the reported tic movements. Moreover, in cases, which may be misdiagnosed with palatal tremor, tic disorders might often be an underlying etiology,⁵ and we have seen a number of patients with the capacity to voluntarily control some of their soft palate muscles, as part of their tic repertoire.

Taken together, these observations highlight that the ability to voluntarily control individual muscles in people with tics and TS is a pervasive and most likely commonly occurring feature. They also evoke key scientific questions with regard to the mechanisms underlying its emergence and the specific relation of exquisite motor control over voluntary output to the occurrence of tics.

The Physiology of Exquisite Motor Control

Here we highlight the exquisite capacity of motor control over isolated muscles in people with tic disorders. However, this phenomenon is also encountered, albeit less frequently, in patients diagnosed with functional movement disorders – though in these cases the movements are characteristically experienced as involuntary – and in people without movement disorders, including athletes. Medical literature contains some examples of functional movement disorders presenting with exquisite motor control, including functional belly dancer's dyskinesia,⁶ functional palatal tremor with ear clicks,⁵ and functional or possibly functional posttraumatic shoulder movements.⁷ In healthy individuals, exquisite motor control is often directly observed in body builders, where the success of intense, hypertrophy-oriented muscle training may be defined by the ability to produce specific muscle contractions at will in order to show observers.

Medical literature has provided few accounts beyond tic disorders, discussing the specific topic of exquisite motor control, including McDonald Critchley's succinct "Discussion on volitional movement" from 1954.⁸ Critchley commented on this "unusual human capacity", which he labeled as "skilled minimal movements" and contrasted it to practiced complex movements. Critchley defined "skilled minimal movements" as "unusual tricks of motility, whereby a single muscle, or a part of a single muscle, can be made voluntarily to contract".⁸ He

hypothesized that such movements were learned motor behaviors, akin to the increasing capacity of infants to control portions of their body, that is, during the critical period of shaping motor responses from the early "blossoming buzzing confusion"⁹ of the sensorimotor circuitry at birth. Although Critchley also commented on tic disorders in the same chapter, he failed to appreciate that the coexistence of both phenomena was in fact very common.

The notion that exquisite motor control over isolated muscles (or skilled minimal movements) is the result of learning is also supported by experimental data from pioneering neurophysiological research on motor unit control in healthy subjects.^{10,11}

One early study demonstrated that 85% of adult participants tested were able to *learn* how to activate single motor units of different muscles (eg, tibialis anterior or abductor pollicis brevis) and engage them on command.¹¹ According to the experimental setup, electromyographic activity from the selected muscles was presented both visually and audibly. Upon the identification of individual motor units, participants were then instructed to activate them in different frequencies and order according to task demands, guiding their behavior through the provided visual and audio feedback. Positive reinforcement was also provided for successful trials. The degree of voluntary control over isolated motor units differed between participants. Such differences involved not only the extent of control over one individual single motor unit (ie, temporal properties of activation), but also the overall number of different motor units which could be selectively recruited on command (ie, spatial properties of activation). This offers one example of the general principle of using 'biofeedback' signals to acquire voluntary control over signals that normally elude it.¹²

This and similar studies^{10,11,13} highlight several important principles relevant to the capacity to *learn* control over a highly selective subset of motor units. First, the control is strictly voluntary, meaning that the distinctive muscular activation occurs if the subject intends it, but not otherwise. Second, acquiring such exquisite voluntary targeting of motor performance could depend on having suitable sensory feedback about the movement, and being able to monitor such feedback to guide performance. Indeed, even though sensory feedback may not be necessary after having learned to perform the individual muscle contraction – that is, after the formation of specific motor commands¹⁴ – it is essential during the motor learning phase. Third, positive reinforcement may increase the control of subsequent movements. Voluntary control of movement appears absent at birth in humans, and precise voluntary control over some movements, notably dexterous finger movements, is achieved only after several years of neuroanatomical development, such as myelination, and neurophysiological plasticity, notably through practice. The exquisite voluntary

control of our patients may be viewed as an extreme manifestation of a normal neurodevelopmental process of acquiring capacity for voluntary action.¹⁵

These studies also provide a useful framework to interrogate the phenomenon of exquisite motor control in tic disorders. Indeed, the ability to exert voluntary control over isolated motor units as the result of motor learning may lay the foundation for developing the exquisite type of motor output we highlight here. However, studies with healthy humans generally focused on isolated motor unit control of intrinsic hand or calf muscles, and most likely involved the activation of very low threshold motor units. In contrast, in tic disorders there is a surprisingly large selection of involved muscles, voluntary control over which leads to rather unusual type of movements. Moreover, isolated control of motor units in healthy humans occurs as part of a highly artificial experimental exercise augmented by contingencies of reinforcement, and presentation of specific feedback signals: participants can only control the motor unit once they see or hear the consequences of activating it. In contrast, in tic disorders there is no obvious external reinforcer to drive the shaping of a novel sensorimotor behavior questioning the role of motor learning and reinforcement as key players in the formation and maintenance of the exquisite type of motor control we document here.

The Role of Learning and Reinforcement in Exquisite Voluntary Motor Control in People with Tic Disorders

Most clinical observations support a key role for learning in the formation of tic behaviors. For example, old tics may be replaced by new ones, some of which may be the result of behaviors observed in others. The efficacy of behavioral interventions for tics, such as habit-reversal training, further supports the role of conditioning and reinforcement in modulation of tic behaviors.¹⁶ However, given the difficulties of directly studying the learning processes underlying the formation of tics, most experimental studies in people with tic disorders have in fact focused on motor learning mechanisms for voluntary actions, including the role of external reinforcers in shaping sensorimotor behavior. This provides a fortuitous advantage for the investigation of exquisite voluntary motor control in this population.

Palminteri et al demonstrated that unmedicated adults with tics were more sensitive to the effects of reinforcement for newly acquired motor skills – that is, learning a specific motor sequence – compared to adults with tics who received antidopaminergic medication and to healthy controls.¹⁷ Moreover, it was shown that the reinforcement of learned behaviors in people with

tics may extend beyond goal-directed motor output. Delorme et al demonstrated an overreliance on newly learned sensorimotor sequences, irrespective of their actual behavioral salience in adults with TS.¹⁸ Participants who were more severely affected by tics also had a greater reliance on habitual motor control, providing a strong pathophysiological link between the expression of tics and motor habits. These studies underscore the relevance of abnormally enhanced reinforcement signals in the formation and maintenance of motor programs, and point towards the possibility that tic disorders are the result of an ill-calibrated motor learning system.

Studies of reinforcement learning typically focus on well-formed functional actions. In contrast, the motor phenomena we present here are brief and fragmented movements. Despite these kinematic differences, dopamine is the best characterized neurotransmitter associated with neural reinforcement in the human brain. Several lines of evidence suggest that both tonic and phasic dopaminergic drive may contribute to the pathophysiology of tic disorders and may also be intrinsically related to the formation of motor behaviors we highlight here. First, molecular imaging approaches in drug-naïve patients have revealed increased binding of dopamine transporters, increased dopamine release, and higher synthesis in patients with TS.¹⁹ Second, the development of striatal dopaminergic innervation coincides in time with the prevalence of tic disorders in the periadolescent period. This supports the notion of a transient increase of susceptibility to dopaminergic hyperinnervation associated with increased likelihood of developing tics.¹⁹ Third, antidopaminergic therapies have long served as symptomatic treatments of tics. At the behavioral level, a phasic burst of dopamine is rewarding and pleasurable. If a motor tic relieves the psychic tension or sensory tic associated with urge, it is likely rewarded.²⁰

Interestingly, striatal dopaminergic modulation has also been associated with gain modulation and motor learning in movement disorders.²¹ Specifically, dopaminergic hyperinnervation could result in excessive reinforcement within the cortex–basal ganglia loop.²² Tic-related oscillatory activity has been observed in both thalamic and pallidal neural populations recorded invasively through deep brain stimulation electrodes in people with tic disorders.^{23,24} The basal ganglia receiving thalamic nuclei (the anterior portion of the ventrolateral nucleus) can modulate synaptic plasticity of frontal cortical pyramidal cells through synaptic connections to neocortical layer-I.²⁵ Plasticity in such connections has been demonstrated to be a crucial factor in skill learning.²⁶ Thus, a putative mechanism for the amplification of tic-related motor commands could be dopamine-related synaptic invigoration both through direct and basal ganglia-mediated modulation of cortex.²⁷ In some people with tics this may also enable the development of exquisite control of finely tuned motor

programs. That is, strong reinforcement through dopaminergic corticostriatal loops could strengthen the cortical ensembles that represent specific movements, thus making those representations more available for voluntary control, and also more likely to be recruited as habitual actions – that is, as tics.

These suggestions remain tentative, and it is currently unclear to what extent abnormalities of dopaminergic input and aberrant reinforcement signals alone can sufficiently explain this type of motor behavior. Other or additional factors may predispose both for exquisite motor control over minimal motor output and for the overall presence of tics. Hyperdopaminergic animal models of tic disorders have indeed demonstrated the induction of repetitive behaviors, such as grooming, sniffing, or biting.²⁸ Such behaviors, however, may best fall within the rubric of complex repetitive actions, as for example stereotypies, which clearly differ from the brief motor fragments that we highlight here.

GABAergic Disinhibition Could Provide the Building Blocks of Learning

Based on previous theories of striatal involvement in tic generation^{29,30} and neuropathological evidence,³¹ neurophysiological experiments demonstrated that pharmacologic administration of GABA_A receptor antagonists to the striatum can lead to the emergence of tic-like behaviors in animals (reviewed in³²). These behaviors are typified by brief fragments of motor output, which may phenomenologically fall within the spectrum of tics. The location of the induced striatal deficit dictated the somatotopy and type (motor vs phonic) of the elicited involuntary behavior, the timing of which relied on striatal afferents,³³ including corticostriatal input.^{33,34}

The GABAergic disinhibition animal model attributes the appearance of tics to a stochastic process of striatal inhibitory deficits. Experimental studies in healthy adults, such as the pioneering research of Harrisson,¹⁰ Basmajian,¹¹ and others, demonstrated the importance of audiovisual feedback in guiding the learning process of isolated motor unit control. This appears to be an instance of a general principle of biofeedback in particular and closed-loop control in general, namely that acquiring functional control of a system is improved by having a clear feedback signal. A good percept is a prerequisite of good control. The occurrence of involuntary brief fragments of motor output could provide this type of necessary sensory feedback, serving thereby as the fundamental building blocks for the development of the wide range of skilled minimal movements in people with tics.

Given the strong interplay of GABAergic and dopaminergic neurons in the regulation and reinforcement of motor output, one could construe a two-step

pathophysiological model: first a lack of local inhibition within the striatum could lead to a high occurrence probability of multiple sensorimotor tic events; in a second step dopaminergic hyperinnervation could favor the repetition of these events through D1/D2 receptor signaling and consecutive downstream pallidothalamic disinhibition.³⁵ Crucially, increased occurrence rates of such sensorimotor events could explain both their emergence as tic movements, and their feedback-based further development as part of an individual's voluntary motor output (Fig. 1).

A consequential or additional mechanism further contributing to the honing of exquisite voluntary motor control may be use-dependent plasticity. This mechanism can explain why an already practiced motor behavior comes to dominate the motor repertoire.³⁶ It relies on the optimization of temporal and spatial properties of neuronal ensembles as a result of Hebbian associative learning, with evidence to support a role of the primary motor cortex, facilitated via both striatal and intracortical dopaminergic, as well as glutamatergic and GABAergic contributions.^{36,37}

Cortical processes of Hebbian associative learning (or associative plasticity) have been investigated using transcranial magnetic stimulation (TMS) in people with tic disorders (reviewed in³⁸). Unfortunately, the results of these studies remain inconclusive with some evidence for and some evidence against enhanced cortical

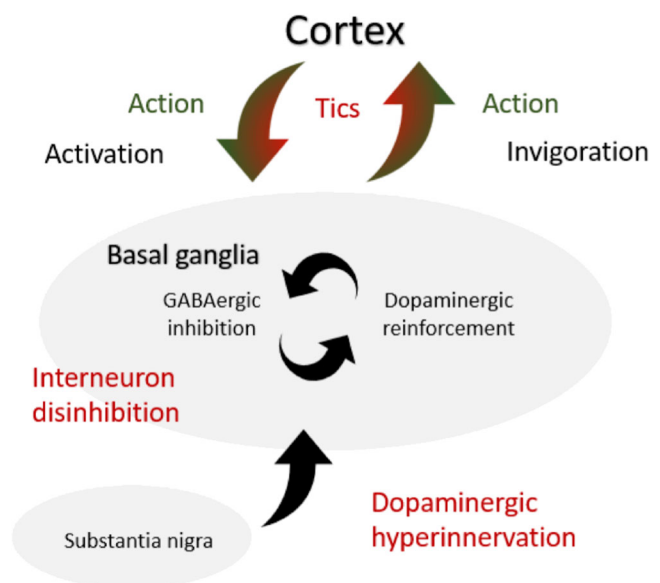


FIG. 1. Simplified model of how actions and tics arise. In health, dopamine-related striatal reinforcement of cortical input leads to synaptic invigoration of action-specific circuit activity. In people with tics, local disinhibition of striatal GABAergic interneuron populations could increase the likelihood of occurrence of discreet sensorimotor events, parallel to the occurrence of voluntary actions. Dopaminergic hyperinnervation and consecutive synaptic strengthening may leave an imprint of these discreet excess events as a tic precursor in the somatosensory circuit. [Color figure can be viewed at wileyonlinelibrary.com]

associative plasticity. For instance, two studies examined the effects of a paired associative plasticity protocol on M1 excitability in adults with TS and healthy controls.^{39,40} One of them provided evidence for *enhanced* facilitatory responses in patients,³⁹ whereas the other showed *reduced* facilitation in TS.⁴⁰ Consistent with this latter result, the application of a different facilitatory neuroplasticity protocol, namely intermittent theta burst stimulation over the M1, also failed to enhance M1 excitability in TS compared to healthy controls.^{41,42} Unfortunately, several methodological differences, including variability in clinical populations, tic severity, medication status, and most importantly lack of online control of tic condition (eg, free ticcing vs active voluntary tic inhibition⁴³) during TMS, complicate comparisons between these studies. In addition, no study, to our knowledge, has specifically examined use-dependent motor plasticity in people with tic disorders, and hence no firm conclusions can be drawn on its role in the formation of tics, including skilled minimal tic behaviors.

Resting-state functional connectivity provides an additional opportunity to assess use-dependent plastic changes in the brain.^{44,45} These changes are suggested to reflect the functional organization of the brain shaped through day-to-day behaviors.⁴⁶ Although several studies revealed extensive age-specific changes in resting-state functional connectivity patterns in people with primary tics compared to controls (reviewed in⁴⁷), none has specifically looked into the neuroplasticity of functional brain circuits during motor skill learning.

Finally, the manifestation of exquisite control likely requires inhibition of nearby muscles not activated. The focusing of the motor command can be accomplished by a process of surround inhibition⁴⁸ and practicing isolated movements does lead to an increase of short intracortical inhibition for muscles not desired to be moved.⁴⁹

In conclusion, sensorimotor feedback has been described as critical for learning of single motor unit control in healthy subjects. In people with tics, GABA-dependent striatal susceptibility for sensorimotor events in combination with aberrant dopamine-dependent reinforcement signals may constitute an altered state of reinforcement, which would lead to both tics on the one hand, and ability to produce exquisite minimal movements on the other. This view does not preclude the contribution of other striatal neurotransmitter systems. For example, deficits in striatal cholinergic interneurons of the dorsolateral striatum have also been suggested to lead to tic-like behaviors in rodents.⁵⁰

Key Predictions and Implications for Future Research

The exploration of exquisite motor control in the example of the wide range of skilled minimal

movements we present here provides an unusual window of opportunity to better examine the mechanisms underlying tic behaviors in people with tic disorders. It also highlights important knowledge gaps in our understanding of these behaviors. These reflections motivate a new research agenda for tic pathophysiology. For example, it seems important to establish whether skilled minimal movements in people with tics closely follow the somatotopic distribution of their ticcing, or not. Also, research should establish whether age, tic severity, and comorbidity (particularly obsessive–compulsive disorder [OCD]), are associated with skilled minimal movement capacity. Approximately two-thirds of people with tic disorders meet the criteria for the diagnosis of OCD behavior/disorder.⁵¹ Very often, as part of their symptom spectrum, these individuals will experience cognitive states, which, similar to somatic premonitory urges, further reinforce the repetition of certain motor programs. For example, people often report “the need to do” a certain tic or action and the “not just-right” experience.⁵² The latter describes the compulsive need to repeat a specific motor event, until it is perceived as “just-right”.⁵² Although the neurobiological underpinnings of these experiences remain speculative, it is clear that the sheer repetition of the motor behaviors that are triggered, along with the reduction in the aversive psychic tension of premonitory urge, could have two effects. First, it could reinforce tic behaviors in response to such urges. Second, it could facilitate the optimization of exquisite voluntary motor control as part of tic disorders. This view also predicts that people with tic disorders who also show enhanced self-monitoring, perhaps as a result of premonitory urges and/or obsessive–compulsive symptoms focused on their own bodily sensations and movements, will also have a higher likelihood of developing these types of behaviors.

Given that skilled minimal movements are performed voluntarily, and that cortical motor maps undergo plastic use-dependent changes,⁵³ it seems likely that the neural representation of body parts where tic behaviors and exquisite voluntary motor control coincide will be more extensive compared to body parts that just exhibit (less frequent) tics, or no tics at all. Behaviorally, the former, tic-susceptible body parts could also exhibit specific neurophysiological changes such as use-dependent plasticity for the corresponding muscles. Indeed, the role of body part specificity in tic behaviors with regard to motor learning as an intraindividual factor to explain performance has not been previously explored. Novel behavioral, neurophysiological, and possibly neuroimaging protocols, which will account for performance differences between the different body parts, are necessary to address these key predictions. These protocols may also allow probing the effects of pharmacological agents, including antidopaminergic

medications and GABA_A receptor inhibitors, on neurophysiological measures, such as, for example, use-dependent plasticity. This could in turn facilitate the translation of targeted neuropharmacological interventions to treat tics.

The pathophysiological assessment of tics often invites analogies with motor habits.^{54,55} Based on these analogies, some authors have even questioned whether tics are really a “movement disorder”.⁵⁶ The analysis of exquisite volitional motor control in people with tics sheds some light on these considerations. In particular, people with tic disorders are often able to exquisitely control isolated muscle movements. These movements may occur not only as part of their tic repertoire, but also voluntarily. Importantly, this capacity is not the result of overall superior motor control compared to people without tics, nor the result of effortful learning.^{17,57-59} This demonstrates that exquisite volitional motor control might, paradoxically, be driven by a reinforcement process over which people with tics in fact have little control. This absence of control over key factors that drive movement generation for selected motor outputs appears to lie at the heart of tic pathophysiology and constitutes the defining feature of tic movement disorders. ■

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Supporting Data

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