VIEWPOINT

Tics and Tourette Syndrome — Surplus of Actions Rather Than Disorder?

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Clinical Phenomenology

Gilles de la Tourette syndrome (GTS) is a multifaceted neuropsychiatric disorder with tics as the cardinal feature. For many years, GTS was perceived as a rare oddity. This view has changed. It has become clear that (1) tics are very common in childhood,[1] (2) a considerable proportion of children (and adults) with tics do fulfill diagnostic criteria for GTS,[1] and (3) most patients with GTS have mild symptoms. GTS can be associated with considerable morbidity, secondary problems including low self-esteem, depression, and reduced quality of life if not managed adequately.[2] Also, importantly, about 90% of GTS patients have comorbidities including attention deficit hyperactivity disorder and obsessive-compulsive disorder (41%).[3] Other characteristic features are echo- and coprophenomena[4] and increased impulsivity.[5]

The first motor tics appear around the age of 6.[6] The majority of GTS patients experience a prepubertal increase in tic severity, followed by a subsequent reduction or even complete remission toward the end of the second decade.[6] In about 20% of patients, however, symptoms continue or can become even more severe, often affecting social life.[2]

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Single tics are indistinguishable from single spontaneous movements in healthy controls,[7] but are repetitive, patterned, and misplaced in context and time. Tics can be simple, involving few muscles, and may then appear as a purposeless jerk (eg, rolling of the eyes, head jerk) or sound (eg, throat clearing), or they can be complex, coordinated, and seemingly goal-directed movements or sounds but lack an obvious purpose. Tics fluctuate considerably in severity, frequency, and distribution, leading to tic undulations and migration.[3] Importantly, there are periods when patients tic less or do not tic at all, particularly during concentration on other tasks and when engaging in voluntary activity, suggesting that tics are not completely involuntary. Echophenomena (echolalia and echopraxia) are subsets of delayed automatic imitation, occurring without particular awareness.[4] They are automatically released action fragments that appear misplaced in the context of intended goal-directed behavior.

Taken together, GTS can be complex and severe, leading to profound consequences. On the other hand, there are many children with uncomplicated motor and phonic tics qualifying for a diagnosis of GTS according to the Diagnostic and Statistical Manual 5th Edition solely because they have a few tics lasting for more than a year. Although inadequate, the term "Tourette" has the flavor of a catastrophe to many. In contrast, the term "tic" and the phenomenon tic per se are often not perceived as a problem. The severity spectrum of tics from near normal to disabling raises the questions of whether the pathophysiology of the different types of tics is the same and whether tics necessarily need to be considered a (movement) disorder.

Tics — Signs of Deficient Inhibitory Control?

GTS is currently considered a movement disorder characterized by a lack of inhibitory control. However, this is a contentious issue, with some studies

showing deficient inhibition of actions,[8] others showing normal or superior inhibitory control.[9] There is good evidence that GTS patients have abnormalities in the basal ganglia and frontostriatal circuits.[10,11] However, functional and structural imaging findings are heterogeneous and sometimes conflicting, often leaving researchers puzzled and leading to different interpretations.[10] Within frontostriatal circuits, changes in the dopaminergic system are considered crucial with the general notion of dopaminergic hyperactivity in GTS,[12] probably because of abnormalities in dopamine receptor binding and increased density of dopamine receptors in the prefrontal cortex[13] and the striatum.[14] It is assumed that dopaminergic changes are predominantly related to altered dopamine D2 receptors and their binding properties and density.[14] Consequently, dopamine D2 receptor antagonists are the mainstay of pharmacological treatment. Some studies have also documented abnormalities in other neurotransmitter systems including the GABAergic system.[15] Taken together, the different pieces of evidence do not fit together, and the overall picture of GTS is blurred.

Tics — Collateral Signs of Volitional Processes

There is no generally accepted model of tics or GTS. Although this is partly explained by empirical problems related to patient characteristics and methodological aspects, the main problem appears to be the lack of a coherent theoretical model for tics and other associated phenomena in GTS. We think the grouping of tics and GTS under the umbrella of "movement disorders" is questionable. GTS and tics may more appropriately be viewed as a disorder of purposeful action selection and execution for the following reasons.

Tics Are Associated With Premonitory Sensations

Tics are often associated with unpleasant sensations, typically an urge to move.[16] Urges typically precede tics and subside following their execution.[17] Sensory phenomena can occur in other movement disorders including parkinsonism and dystonia, but the often overwhelming intensity of urges in patients with tics considerably interfering with their quality of life,[18] sometimes more profoundly than tics per se, and also their relation to other physiological urge-like bodily sensations in the context of yawning, micturition, and swallowing[19] set tics apart from other movement disorders. Tics might be considered as purposeful behavior, as a reaction to certain bodily perceptions. However, whether there is a causal relationship between the perception of urges and the occurrence of tics is unclear. This notwithstanding, the presence of urges and also hypersensitivity to certain sensory stimuli, for example, increased distractibility and distress by tactile stimuli, suggest that sensory processing is altered in GTS.[20] The integration of sensory information with motor planning and execution seems to be impaired. This may be related to structural abnormalities including thinning of the somatosensory cortex in adolescent GTS[21] and white matter abnormalities underneath the primary somatosensory cortex (BA 3a) in adult GTS patients.[22] Moreover, fMRI-based functional connectivity analyses show reduced connectivity in long-range frontoparietal networks pointing in the same direction.[23]

Tics Can Be Controlled

Focusing attention on tics significantly increases and diverting attention to other tasks decreases tic frequency,[24,25] which places tics close to processes important for voluntary action generation. Also, urges preceding tics are reported in about 25% of 8- to 10-year-old children with GTS but nearly 60% of 15- to 19-year-old adolescents with GTS,[26] that is, at an age when interoceptive awareness increases. This illustrates that not only tics but also urges depend on attention. In addition, tics are partially suppressible and can be postponed, sometimes for hours, for example, in schoolchildren, who tic little at school but much more when they come home and then "get off the brake." This also shows that tics are not clear-cut involuntary. In fact, GTS patients experience some of their tics as unwanted but voluntary, quasi-intentional movements that are executed to transiently relieve an uncontrollable and unpleasant urge to tic.[16] Of note, the onset of tics is preceded by activation of the supplementary motor area,[27] a region that is strongly associated with the generation of voluntary movements and cognitive control.

Tics May Be Related to Motor Learning and Habit Formation

In line with the assumption that tics share features with voluntary response selection, it has been shown that patients have great difficulties switching from ticcing to other actions until a tic or a cascade of tics is completed.[10] These difficulties reflect a central characteristic of processing capacity limitations during controlled, voluntary response selection[28] and thus suggest a relationship between tic generation and physiological response selection. Also, tics have been proposed to represent stimulus-driven sequential movements that change in time and are repetitive and patterned.[29] Therefore, they bear a resemblance to habits and hence may, in some aspects, represent intensive learning processes. In fact, there is evidence that tics resemble overlearned behavior.[30] In a similar vein, habit formation tendencies are increased in GTS patients, which is correlated with stronger connectivity

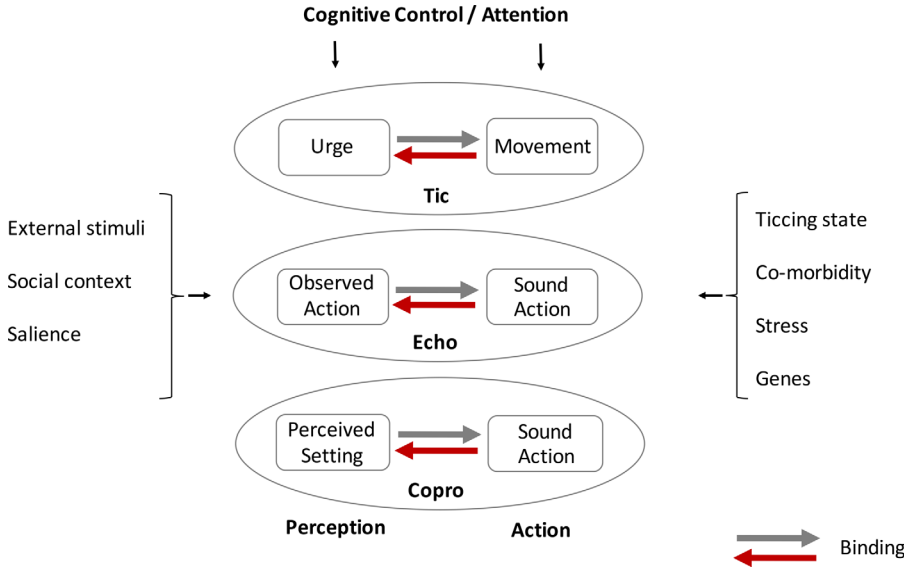

FIG. 1. Tics, echophenomena, and coprophenomena conceptualized within the framework of the theory of event coding (TEC). These clinical phenomena all have perceptual and action elements and might be conceived as events with common representational domains. The arrows indicate that perceiving (eg, an urge) presupposes and determines behavior (eg, a tic), and performing an action both relies on and produces perceptual information, that is, perception and action are bound. The occurrence of tics, echophenomena, and coprophenomena and presumably also their binding depends on cognitive control and attention, but is also influenced by predominantly external factors (eg, external stimuli, social context, salience) and internal states (eg, ticcing state, comorbidity, stress level, genetic factors). [Color figure can be viewed at wileyonlinelibrary.com]

between the basal ganglia and motor cortical regions.[31] Moreover, GTS patients who are not medically treated have increased reward learning compared with healthy controls and GTS patients under dopamine antagonist treatment.[32] It is thus possible that dopaminergic hyperactivity in GTS[12] augments learning and habit-formation processes, and that is why tics emerge — as a surplus phenomenon. This would be in keeping with recent data and neurocomputational modeling studies suggesting that the basal ganglia may be a fast, reward-based learning system supporting cortical wiring for motivation, cognition, and motor action as required for goal-directed behavior.[33] One might argue that when first occurring, a given tic does not represent a learned behavior per se. However, the onset of tics or occurrence of new tics may nonetheless represent the brain's propensity to form habits for which the "overproduction" of prewired bits of behavior, that is, tics,[29] may be one sign. Echo- and coprophenomena as well as increased impulsivity, the latter as a sign of readily triggered emotional actions, could likewise be considered surplus phenomena.

GTS — A Condition of Altered Perception Action Binding

Taken together, rather than viewed as a disorder, tics may be conceptualized as an excess of purposeful actions. Moreover, given increased habit formation tendencies and arguments in favor of tics representing overlearned behavior, tics might not exclusively be perceived as defective, but, at least in certain settings, could be advantageous. For mildly affected patients, the concept of tics as a "surplus," as a near-normal phenomenon, could be helpful and relieving.

The intricate relation between tics and urges, suggesting exaggerated internal monitoring[34] and evidence for an increased sense of agency,[35] calls for a concept encompassing both action and perception. GTS could be conceptualized in a cognitive framework integrating perceptual, cognitive, and motor aspects of action, that is, the theory of event coding (TEC).[36] TEC challenges the view that perception has a unidirectional effect on action.[37] Instead, it assumes that perceiving presupposes and determines behavior, and performing an action both relies on and produces perceptual information,[36] that is, the same coding underlies both perception and actions. Such codes are stored in a common representational domain, the so-called event file. Event files establish bindings between features that characterize a perceptual stimulus and features that specify an action.[37] Because event files represent a network of bindings between perceptual and action-related features, their activation follows a pattern-completion logic, that is, once a stimulus is reencountered, it activates the event file it has previously been integrated into.[37] With respect to GTS, single features of conditions/situations, for example, bodily sensations or settings, with which tics have previously formed events, can automatically activate a tic. Tics comprising urges and corresponding movements might represent event files with abnormally strong perception action binding[17] (Fig. 1). Similarly, echophenomena

could be viewed as event files consisting of observed actions and own actions and coprophenomena as event files in which certain perceived settings are bound to vocalizations or actions.

One might argue that many if not most young children and many adolescents or adults with GTS do not experience urges preceding tics, only report urges in relation to some tics, or are unaware of some tics, implying that these tics are not associated with unpleasant sensations. However, this does not imply that these tics that are not obviously or not consciously coupled with distinctive bodily sensations are not composed of both action and perception elements. Certain sensory or more generally perceptual processes that might trigger action elements (tics) through previously established perception action bindings might go unnoticed by those who tic. Even if there were (theoretically) a "pure" motor event without preceding perceptual elements, this could be conceptualized as an action file in the TEC framework. However, such an action file manifesting as a tic would then inevitably have sensory/perceptual repercussions, for example, through modulation of afferent input caused by that action.

In the TEC context, key assumptions related to tics can easily be reconciled with the established role of the basal ganglia and the dopaminergic system in the pathophysiology of GTS. This is because the basal ganglia and frontostriatal loops play an important role in action selection, which depends on the relative salience of competing actions and also in the integration of different sensory processes for action selection by phasic dopaminergic signals.[38] The striatum contains a vast number of neurons sensitive to sensory inputs.[39] Striatal processes are therefore likely to play an important role in perception action binding. This is underscored by event file binding being altered in Parkinson's disease and able to be modulated by dopaminergic medication.[40]

An influential concept of how tics may be generated is related to the model of motor pattern generators (MPGs).[11] It assumes that the basal ganglia serve as a "brake" on MPGs and that loosening of this brake will lead to the execution of a movement/action. With respect to GTS, it is hypothesized that braking mechanisms within the basal ganglia are defective so that aberrant, particularly unwanted activations of MPGs are not held at bay but manifest clinically as tics. This model of MPGs and their control and TEC are not mutually exclusive. The important difference between the MPG-based model and TEC is that the former focuses on motor phenomena and processes and does not account for antecedent processes leading to aberrant activation foci that become apparent as tics. TEC, in contrast, extends such a motor-centered perspective to include antecedent mechanisms that can lead to the formation of activity foci, that is, *how* these are established. The MPG model proposes that factors increasing corticostriatal synaptic strength, for example, dopamine, can increase the activity of the MPG. However, such modulations only provide the basis or prerequisite to establish or to maintain aberrant activity foci in the striatum. The formation of such foci requires input into the striatum. As pointed out above, it has been shown that different sensory inputs are integrated in the striatum for action/movement selection. This input and its effect on or integration with subsequent actions/motor responses are what is conceptualized in the TEC framework. Therefore, TEC complements and extends the MPG model.

Using TEC as a cognitive framework, the key assumption that increased perception action binding in GTS is associated with a propensity to generate a surplus of action could be tested in established behavioral experiments during fMRI and EEG. If confirmed, it would imply that tics do not categorically differ from other actions but rather with respect to the strength of perception action binding. This in turn would explain why there is such a large spectrum of tics from near normal to severe. This approach could also pave the way to new treatments, for example, those aiming at unbinding event files and thus "dissolving" tics. ■

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