Neuroscience and Biobehavioral Reviews 37 (2013) 1050–1062

Contents lists available at SciVerse ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review

The functional anatomy of Gilles de la Tourette syndrome

Christos Ganos[a,*], Veit Roessner[b], Alexander Münchau[a]

[a] Department of Neurology, University Medical Centre Hamburg-Eppendorf (UKE), Hamburg 20246, Germany
[b] Department of Child and Adolescent Psychiatry, University of Dresden Medical School, Fetscherstrasse 74, 01307 Dresden, Germany

ARTICLE INFO

Article history:
Received 6 July 2012
Received in revised form 23 October 2012
Accepted 5 November 2012

Keywords:
Gilles de la Tourette syndrome
fMRI
Transcranial magnetic stimulation
Functional anatomy

ABSTRACT

Gilles de la Tourette syndrome (GTS) holds a prime position as a disorder transgressing the brittle boundaries of neurology and psychiatry with an entangling web of motor and behavioral problems. With tics as the disorder's hallmark and myriads of related signs such as echo-, pali- and coprophenomena, paralleled by a broad neuropsychiatric spectrum of comorbidities encompassing attention deficit hyperactivity disorder, obsessive–compulsive disorder and self-injurious behavior and depression, GTS pathophysiology remains enigmatic. In this review, in the light of GTS phenomenology, we will focus on current theories of tic-emergence related to aberrant activity in the basal ganglia and abnormal basal ganglia–cortex interplay through cortico-striato-thalamocortical loops from an anatomical, neurophysiological and functional-neuroimaging perspective. We will attempt a holistic view to the countless major and minor drawbacks of the GTS brain and comment on future directions of neuroscientific research to elucidate this common and complex neuropsychiatric syndrome, which merits scientific understanding and social acceptance.

Contents

Abbreviations: GTS, Gilles de la Tourette syndrome; ADHD, attention deficit hyperactivity disorder; OCD, obsessive–compulsive disorder; BG, basal ganglia; SPC, striato-pallidal complexes; dSPC, dorsal striato-pallidal complex; vSPC, ventral striato-pallidal complex; CSTC, cortico-striato-thalamo-cortical; MSN, medium spiny neurons; STN, subthalamic nucleus; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata; GPi, internal segment of the globus pallidus; SMA, supplementary motor area; M1, primary motor cortex; TMS, transcranial magnetic stimulation; rTMS, repetitive transcranial magnetic stimulation; MEG, magnetoencephalography; PUTS, Premonitory Urge for Tics Scale.

* Corresponding author at: Movement Disorders Group, Department of Neurology, University Medical Center Hamburg-Eppendorf, Martinistraße 52, 20246 Hamburg, Germany. Tel.: +49 40 7410 50134.
E-mail addresses: cganos@uke.de, cganos@gmail.com (C. Ganos).

0149-7634/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.neubiorev.2012.11.004

1. Introduction

Gilles de la Tourette syndrome (GTS) is a multifaceted neuropsychiatric disorder with the hallmarks of motor and phonic tics. It is commonly associated with attention deficit hyperactivity disorder (ADHD) and obsessive–compulsive disorder (OCD). Since its first clinical description by Jean-Marc Itard (Itard, 1825) and the paramount work of Georges Edouard Albert Brutus Gilles de la Tourette (Tourette, 1885), defining GTS as a distinct hyperkinetic disorder characterized by tics, copro- and echophenomena, the perception and interpretation of this disorder has changed considerably over time.

Following Gilles de la Tourette's original publications (Lajonchere et al., 1996; Tourette, 1885), popular explanatory approaches viewed tics at the time as "forms of hysteria", "weak self-control and lack of will-power", "stereotypic manifestations of onanism" or "a psychosomatic condition" (Kushner, 1999). It took more than half a century until following several conclusive reports on the successful treatment of tics with neuroleptics GTS started to be viewed primarily as a neuropsychiatric disorder. This paradigmatic change of view was soon followed by systematic work on the clinical facets of GTS and related disorders accompanied by tics (Robertson et al., 1988; Shapiro and Shapiro, 1982) and formulation of theories related to its *organicity* (Obeso et al., 1982). It also became clear that GTS is common, that tics were but one aspect of a more complex medical condition with numerous symptoms and signs, e.g. echo- or paliphenomena, and that GTS is often associated with ADHS and OCD (Robertson et al., 1988; Trimble, 1989), with the latter, particularly ADHD, typically being more troublesome than tics (Roessner et al., 2007).

With more than 30 years of systematic epidemiologic, clinical and neuroscientific research, there is substantial evidence to label GTS as a complex neuropsychiatric developmental disorder of erroneous inhibition.

In this review, we will set out by analyzing the clinical phenomenology of GTS. We will then turn to research data on its pathophysiology including structural and functional imaging, neurophysiology and theories of faulty habit formation. Finally, we will attempt to identify the core problem and address current and future scientific, clinical and societal challenges.

2. The clinical phenomenology

2.1. Tics

A single tic is indistinguishable from a single spontaneous movement (Finis et al., 2012). However, tics are repetitive, stereotypic movements misplaced in context and time. Nearly every possible human movement can occur as a tic. Thus, amongst hyperkinesias, tics have the greatest intra- and interpersonal phenomenological variability. When a tic involves one muscle or single muscle group and appears as a purposeless jerk (e.g. rolling of the eyes, head jerk) or sound (e.g. grunting, throat clearing), then it is defined as simple. Complex tics, on the other hand, are more coordinated and often seemingly goal-directed movements (or sounds) but lack an obvious purpose and appear repetitively with an inappropriate intensity and frequency (Jankovic, 1997). The majority of tics are brief and fast (e.g. eye blinking). They can also be slow, e.g. contractions of the platysma or abdominal muscles and writhing, e.g. turning and twisting of neck muscles (Jankovic, 1997). Tics may cause a brief disruption (blocking tics) (Jankovic, 1997) or interference with communication or activities. Some tics are difficult to distinguish from other repetitive behaviors such as compulsions (e.g. repetitive touching, writing a letter in a specific way and repeating it *n*-times) or hyperactive movements in ADHD.

Tics in GTS, defined by the fluctuating occurrence of multiple motor tics and at least one phonic tic for more than a year with onset before the age of 18 (American Psychiatric Association. Task Force on DSM-IV., 1994) have been studied extensively. Typically, the first motor tics appear around the age of 5–7 followed by phonic tics several months to a few years later (Robertson, 2011). The majority of tics affect the eyes, head, neck and shoulder (Jankovic, 1997). Most tics are preceded by premonitory sensations (e.g. urge to move, impulse to tic, increased tension, unpleasant bodily sensation), which are usually relieved by the tic (Kwak et al., 2003). The sequence of events, i.e. when premonitory sensations develop; before, at the same time of or after the manifestation of tics, is not entirely clear. There is some evidence that they develop during the first years of the manifested disorder (Banaschewski et al., 2003). Tics can typically be suppressed for variable periods of time (from seconds to hours), which appears to depend on the strength of premonitory sensations that have to be "released" sooner or later. This feature sets tics apart from other hyperkinesias, particularly myoclonus and chorea, both non-suppressible phenomena. The relation between preceding urges and the capacity to suppress tics, though, is not clear. For instance, in a recent study we could show that there is no correlation between the perceived strength of premonitory sensations and patients' ability to inhibit tics (Ganos et al., 2012a).

Tics in GTS appear in bouts. They fluctuate in frequency, intensity and distribution which leads to tic undulations and migration throughout the disease course (Jankovic, 1997).

Further motor behaviors in GTS encompass echo- and coprophenomena, both often categorized as complex tics. Echophenomena (echolalia and echopraxia) are subsets of automatic imitation, occurring without particular awareness, and commonly involve vocal reverberations (echolalia), or – less frequently – motor acts (echopraxia) (Ganos et al., 2012b). Whereas their appearance in the first years of life is a normal characteristic of human development, their persistence or re-emergence in adolescence points to pathology (Ganos et al., 2012b). Echophenomena are present in the majority of patients (Finis et al., 2012) and are intimately related to GTS rather than comorbidities (Section 2.2) (Ganos et al., 2012b).

Coprophenomena represent obscene, offensive, or other socially inappropriate behaviors (verbal–coprolalia, gestures–copropraxia), depleted of intent. If they appear they usually do so within 5 years after tic onset (Freeman et al., 2009) and often remit spontaneously after some time. They correlate with tic-severity, the number of tic-suppressing medications, repetitive behaviors as well as with the rate of comorbidities (including self-injurious, obsessive–compulsive and sexually inappropriate behaviors, and ADHD) (Freeman et al., 2009). The lifetime prevalence of coprophenomena in GTS is roughly 20%, with coprolalia being more common (18.5%) than copropraxia (5.7%) (Freeman et al., 2009).

2.2. Comorbidities, natural course and quality of life

GTS is more than a complex tic disorder. In fact, approximately 90% of GTS patients have psychiatric comorbidities, the most common of which are ADHD and OCD (Robertson, 2011). Additional comorbidities include depression, impulsivity (reported as anger control problems and sexually inappropriate behaviors), personality disorders, self-injurious behavior and sleep problems and mostly affect GTS-plus (ADHD or OCD or both), rather than GTS-only patients (Cavanna et al., 2009; Freeman et al., 2000; Muller-Vahl et al., 2010; Robertson, 2011; Roessner et al., 2005, 2007; Wanderer et al., 2012). Thus, given the number of comorbidities and the complexity of the phenomenology of tics and tic -related behaviors (Lewis and Kim, 2009; Worbe et al., 2010b) GTS is a prototype of a complex neuropsychiatric spectrum