Neuroscience and Biobehavioral Reviews xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Neuroscience and Biobehavioral Reviews

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

Review

Theoretical and practical considerations behind the use of laboratory animals for the study of Tourette syndrome

Simone Macrì, Martina Proietti Onori, Giovanni Laviola*

Section of Behavioural Neuroscience, Dep. Cell Biology & Neuroscience, Istituto Superiore di Sanità, Rome, Italy

ARTICLE INFO

Article history:
Received 5 November 2012
Received in revised form 19 March 2013
Accepted 23 March 2013

Keywords:
Animal models
Risk factors
Tics
Stereotypies
Abnormal repetitive behaviors
Basal Ganglia

ABSTRACT

In the present manuscript we review a substantial body of literature describing several pre-clinical animal models designed and developed with the purpose of investigating the biological determinants of Tourette syndrome (TS). In order to map the animal models onto the theoretical background upon which they have been devised, we first define phenomenological and etiological aspects of TS and then match this information to the available pre-clinical models. Thus, we first describe the characteristic symptoms exhibited by TS patients and then a series of hypotheses attempting to identify the multifactorial causes of TS. With respect to the former, we detail the phenomenology of abnormal repetitive behaviors (tics and stereotypies), obsessive-compulsive behaviors and aberrant sensory-motor gating. With respect to the latter, we describe both potential candidate vulnerability genes and environmental factors (difficult pregnancies, psychosocial stressors and infections). We then discuss how this evidence has been translated in pre-clinical research with respect to both dependent (symptoms) and independent (etiological factors) variables. Thus, while, on the one hand, we detail the methodologies adopted to measure abnormal repetitive and obsessive-compulsive behaviors, and sensory-motor gating, on the other hand, we describe genetic engineering studies and environmental modulations aimed at reproducing the proposed biological determinants in laboratory rodents. A special emphasis is placed upon "programming" events, occurring during critical stages of early development and exerting organizational delayed consequences. In the final section, we outline a heuristic model with the purpose of integrating clinical and pre-clinical evidence in the study of TS.

© 2013 Elsevier Ltd. All rights reserved.

Contents

1. Introduction 00
   1.1. Tourette syndrome: clinical phenomenology 00
   1.2. Comorbidity: OCD, ADHD 00
2. Neurobiological substrates of tourette 00
   2.1. The basal ganglia 00
      2.1.1. Neurotransmitters of the BG 00
   2.2. Basal ganglia circuit impairments in TS 00
3. Etiology 00
   3.1. Genetic factors 00
   3.2. Environmental risk factors 00

Abbreviations: 5-HT, serotonin; ADHD, attention deficit hyperactivity disorder; ARB, abnormal repetitive behavior; BDNF, brain-derived neurotrophic factor; BG, basal ganglia; CNTNAP2, contactin-associated protein-like 2; CRF, corticotrophin releasing factor; CSTC, cortico – striatal – thalamocortical; DA, dopamine; DAT, dopamine transporter; GABA, gamma-aminobutyric acid; GABHS, group A β-hemolytic streptococcus; GAS, group A streptococcus; GPe, globus pallidus externa; GPi, globus pallidus interna; HDC, L-histidine Decarboxylase; HPA, hypothalamic-pituitary-adrenal; IL-12, interleukin 12; IMMP2L, inner mitochondrial membrane peptidase 2 like; NA, norepinephrine; NLGN4X, neuroligin–4, X–linked; OCD, obsessive – compulsive disorder; PANDAS, pediatric autoimmune neuropsychiatric disorders associated with streptococcal; PPI, prepulse inhibition; SERT, serotonin transporter; SLITRK1, SLIT and NTRK-like 1; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata; STN, subthalamic nucleus; TNF-α, tumor necrosis factor alpha; TS, Tourette syndrome.

* Corresponding author at: Sect. Behavioural Neuroscience, Dept. Cell Biology & Neuroscience, Istituto Superiore di Sanità, Viale Regina Elena, 299, I-00161 Roma, EU, Italy. Tel.: +39 06 4990 2105; fax: +39 06 495 7821.
E-mail address: giovanni.laviola@iss.it (G. Laviola).

0149-7634/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.neubiorev.2013.03.014

Please cite this article in press as: Macrì, S., et al., Theoretical and practical considerations behind the use of laboratory animals for the study of Tourette syndrome. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.03.014

4. Animal models 00
4.1. Experimental paradigms for the analysis of TS and comorbid symptoms (dependent variables) 00
4.1.1. Abnormal repetitive behaviors: tics and spontaneous stereotypies 00
4.1.2. Impulsivity and compulsivity 00
4.1.3. Sensorimotor gating 00
4.2. Experimental models for the induction of TS and comorbid symptoms (independent variables) 00
4.2.1. Pharmacological models 00
4.2.2. Genetic models 00
4.2.3. Environmental models and early risk factors 00
4.2.4. Immune-mediated models 00
4.3. Concluding considerations regarding the use of rodent models of TS 00
5. A unifying perspective bridging clinical and pre-clinical evidence in TS 00
Acknowledgements 00
References 00

1. Introduction

"While Tourette's may be considered, like Parkinsonism, a movement disorder (albeit of an explosive rather than an obstructive kind), it is much more. It has a mind of its own. Tourette's is impulsive, productive. . ." (Sacks, 2008). So does Oliver Sacks encapsulate the essence of Tourette syndrome (TS). The explosive nature of the symptoms is highly debilitating from its origin, whereby children exhibiting TS-typical behavioral abnormalities easily attract "savage ridicule and bullying from [his] schoolmates". Thus, while becoming embodied in patients' habits and conduct, TS strongly interferes with individual daily life. Understanding its biological determinants constitutes a challenge to a number of scholars as it may disclose avenues to temper the difficulties encountered by multitudes of patients, and as it may inform as to the intersection between biology (fundamental mechanisms governing the onset/exacerbation of symptoms), psychology (mental processes occurring in TS patients) and social sciences (development of holistic therapeutic strategies involving patients, family members, care-takers and schoolmates). In this review, we outline some of the core aspects of TS, ranging from its clinical phenomenology, biological and environmental determinants, to the experimental models devised to facilitate its understanding.

1.1. Tourette syndrome: clinical phenomenology

TS is a neurodevelopmental disorder characterized by the presence of multiple motor tics and at least one phonic tic throughout a period of more than one year (chronic tics) (Grados and Mathews, 2009). Motor tics usually occur earlier than phonic tics (Leckman et al., 2006). According to the DSM-IV, tic is defined as a "sudden, rapid, recurrent, nonrhythmic, stereotyped motor movement or vocalization" (APA, 2000).

Tic phenomenology is characterized by the repetitive and stereotypic nature of the movements or vocalizations with different degrees of intensity and frequency, and variable durations. Despite their repetitive nature, tics should be kept clearly distinguished from stereotypies (Kurlan, 2010). Several characteristics may help to differentiate them. Compared to tics, stereotypies have an earlier age of onset, are more constant, fixed in their pattern and prolonged in duration. Additionally, tics are generally associated with the need of reducing an inner state of tension (see "premonitory urge") and with a voluntary control over the manifestation of the movement; these features are not present in stereotypies (Singer, 2009).

Early signs of Tourette's usually begin with transient bouts of simple motor tics that generally consist of the movement of the facial and oral musculature; the latter can translate into more complex, elaborate manifestations of the whole body that involve multiple muscle groups (Felling and Singer, 2011). The expression of tics can be preceded by a "premonitory urge", an inner state of discomfort, experienced as irresistible and annoying, often localized in a small area of the body where the tic is about to occur (Bliss, 1980; Bullen and Hemsley, 1983). The need to relieve the sense of distress associated with the urge contributes to give tics a partial characterization of a voluntary act (Leckman et al., 2006; Leckman et al., 1993). Premonitory urges have been proposed to relate to impaired capability of inhibiting responses to irrelevant or inappropriate information (Amitai et al., 2012). This cognitive domain has been studied in TS patients through negative visuospatial priming tasks. These tasks require the subject to respond to a target stimulus during a "probe" trial after a previous exposure to a "prime" trial. Subjects are requested to respond to the presentation of the target stimulus that can be presented in the same or in a different location compared to a previously presented non-target "priming" stimulus ("negative priming"). Normal subjects show a slower response to the target stimulus when this is presented in the same location of the non-target than when it is presented in a different location. TS subjects show a significant impairment in this response (Ozonoff et al., 1998). An additional correlate of premonitory urges that has been shown to be impaired in TS patients is pre-pulse inhibition (PPI), consisting of the inhibition of a startle response following the presentation of a weaker stimulus (Castellanos et al., 1996). Similar to negative priming, PPI entails an appropriate level of attention devoted to a priming stimulus. Experimental procedures for testing "negative priming" and PPI have been developed in humans (Amitai et al., 2012) and translated in rodents (Domeney and Feldon, 1998). Beside being dysfunctional in TS patients and related to premonitory urges, PPI possesses other features particularly relevant to the study of TS. Specifically, it is regulated by the same structures involved in TS pathophysiology (basal ganglia), it is inheritable through genetic mechanisms, and is sensitive to drugs that are frequently used in the treatment of TS, like antipsychotics (Swerdlow, in press). An additional domain, that seems to distinguish TS patients from the normal population is interval timing, i.e. the processing of temporal information (Vicario et al., 2010).

Symptoms have a typical prepubertal age of onset, between 5 and 7 years, with a waxing and waning course, and occur more frequently in males than females, at a ratio of approximately 4:1 (Leckman et al., 2010). Most patients show a gradual increase in tics severity until 8–12 years of age with a marked reduction by the end of adolescence (Lombroso and Scahill, 2008). Although epidemiological studies show that transient tics are quite common in childhood, with up to 20–30% of children exhibiting brief, repetitive, involuntary movements or sounds (Kurlan et al., 2001), the prevalence of TS is estimated to range between 0.4% and 1% in the general pediatric population (Singer, 2005). While particular conditions, such as anxiety, stress, immune reactions and emotional excitement can exacerbate tics, other factors, like those behaviors that involve focusing and attention, can reduce the severity of the symptoms (Leckman et al., 2006; Lin et al., 2007). Specifically, patients

Please cite this article in press as: Macrì, S., et al., Theoretical and practical considerations behind the use of laboratory animals for the study of Tourette syndrome. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.03.014

Download English Version:

https://daneshyari.com/en/article/10461796

Download Persian Version:

https://daneshyari.com/article/10461796

Daneshyari.com