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#### 1. Introduction

Tics are the most frequent movement disorders during childhood; their highest prevalence occurs at scholar and adolescence-ages. Most tics are transient but some of them become chronic having educational, familial and social negative implications.

Moreover, some tics are related to disorders with significant impact, like attention-deficit hyperactivity disorder (ADHD), obsessive-compulsive (OCD) and affective disorders. Epidemiological studies are the initial approach to diagnose them and properly begin treatment.

In this chapter, we explained the clinical bases of tics, review the more representative epidemiological studies that assess the prevalence of tics and make a critical standpoint of these studies about epidemiology applicable to clinical practice.

#### 2. Content

## 2.1 Definition of tics and their practical ways to characterize them since clinical view

As we described elsewhere, tics are defined as "sudden, rapid, recurrent, nonrhythmic, stereotyped motor movements or vocalizations" and have clinical concerns¹. Tics are likely to differ in terms of the body location, number, frequency, complexity, intensity or forcefulness, noticeable and resulting social consequences². Intervals between tics can range from seconds, hours or even days. The forcefulness with which a tic is performed can range from slight and barely noticeable to intense and obvious. Over time, the frequency and intensity of tics may wax and wane and maybe influenced by a variety of internal and external stimuli including private events, contextual variables and social reinforcement contingencies³.

Tics can also vary considerably in their complexity. Tics that involve the contraction of a single muscle group are typically referred as simple tics and those that involve the contraction of multiple muscle groups are typically considered complex. Simple tics are typically of very short duration (*i.e.* 1 second) and include such behaviors as eye blinking; jerking of the face, head, torso, or limbs; coughing; sniffing; throat clearing and making singles syllable sounds. Complex tics are often sustained for longer durations or occur in paroxysms and can include virtually any orchestrated pattern of behavior otherwise

meeting the definition of a tic. Common examples include picking, tapping, gesturing, mimicking the gestures of others (echopraxia), repeating one's own speech (palilalia), mimicking the speech of others (echolalia) and the production of inappropriate words or sentences.

Tics comprise a group of movement disorders. Thus, transient tics, the most common form of the disorder, consists of single or multiple motor and/or vocal tics that occur for at last four weeks but no longer than 12 months. GTS has onset before 18 years of age, characterized by motor and vocal tics over more than a year, there is never a tic-free period of more than 3 consecutive months, not produced by Huntington disease neither viral encephalitis and produces a negative personal impact. The disorder is called chronic motor tics if the criteria of GTS are present but vocal tics are absent. By contrast, if there are vocal tics but no motor tics the disorder is called chronic vocal tics<sup>4</sup>.

#### 2.1.1 Differential diagnosis

Simple motor tics may need to be differentiated from myoclonic jerks, which are not typically repetitive in the same body part like tics. Tics are commonly associated with premonitory sensations and suppressibility. Complex motor tics need to be distinguished from stereotypies that are longer lasting, more stereotyped movements (eg, body rocking, head nodding, and hand/wrist flapping) or sounds (eg, moaning, yelling) that occur over and over again in a more continuous, less paroxysmal fashion. Stereotypies are typically seen in patients with autism, mental retardation, Down syndrome, Rett syndrome, psychosis, or congenital blindness and deafness.

Some tics are slow or twisting in character resembling dystonia and are termed "dystonic tics". Contrary to dystonic tics, dystonia *per se* tends to beslower and leads to more sustained disturbances in posture of a limb, the neck, or trunk. Compulsions frequently occur in association with tics, can sometimes be difficult to distinguish from complex motor tics but typically differ by being done in response to an obsession, being performed to avoid future problems or being done according to ritualistic rules<sup>5</sup> <sup>6</sup> With very high comorbidity rates of both ADHD and OCD, GTS may represent a multifaceted developmental neuropsychiatric brain disorder<sup>7</sup>.

## 2.1.2 Secondary tic disorders

A secondary cause for tics should be considered if it is accompanied by other movement disorders or neurologic abnormalities. Tics often indicate the presence of a global brain developmental disorder in conditions like mental retardation, autism and pervasive developmental disorder. Similarly, a variety of genetic and neurodegenerative conditions can cause tics, including Wilson disease, neuroacanthocytosis<sup>8</sup>, neurodegeneration with brain iron accumulation<sup>10</sup> <sup>11</sup>and Huntington disease<sup>12</sup>.Other potential causes of tics include lesions involving frontal-subcortical circuits like trauma<sup>13</sup>, carbon monoxide poisoning<sup>14</sup>, hypoxic-ischemic encephalopathy and stroke<sup>15</sup>; central nervous system (CNS) infections (neuroborreliosis<sup>16</sup>, viral encephalitis<sup>17</sup>) and central nervous system immune disorders (like antiphospholipid antibody syndrome<sup>18</sup>, Sydenham'schorea<sup>19</sup>). Tics can be a manifestation of neuroleptic drug-related tardive dyskinesia<sup>20</sup> or withdrawal emergent syndrome<sup>21</sup>. Induction or exacerbation of tics has been reported with antiepileptic drugs<sup>22</sup> <sup>23</sup>, cocaine<sup>24</sup>, caffeine<sup>25</sup>and stimulants<sup>26</sup>.

## 3. Biological frame to understand the base of tics and related comorbidities

## 3.1 Mechanism and pathways of tics and comorbidities

Figure 1 is a practical schema explaining the mechanism and pathways of tics and related disorders based in experimental models resulting of neuroanatomy and neurobiology grounds.

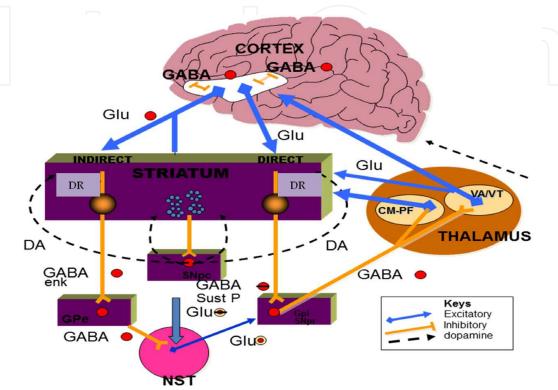


Fig. 1. Cerebral cortex giving glutamatergic excitatory projections to striatum. Abbreviations: Glu: glutamate, DR: dopamine receptors, DA: dopamine, GABA: gamma aminobutiric acid, enk: encephaline K, SNpc: substantia nigra pars compacta, SNpr: substantia nigra pars reticulata, Sust P: susbstantia P, GPe: external globus pallidus, GPi: internal globus pallidus, NST: nucleus subthalamic, VA: ventral anterior, VT: ventral nuclei, CM-PF: centromedian -parafascicular nuclear complex.

The cerebral cortex provides excitatory glutamatergic projections to striatum. The striatum has a topographic distribution as follows: somatosensorial dorsolateral, intermediate / associative and a centromedial / limbic.

Five parallel circuits connecting the cortex to the striatum<sup>27</sup> <sup>28</sup>:

- 1. Motor circuit: gives origin to motor tics and arises in the supplementary motor area.
- 2. Oculomotor circuits: is the potential source for ocular tics and connects the frontal eye field with the caudate nucleus.
- 3. Dorsolateral prefrontal circuit: related to difficulties in executive functions, motor planning, cognition and attention. It is connected to Brodmann areas 9 and 10 and caudate head.
- 4. Lateral orbitofrontal circuit: It is associated with OCD, irritability and mania. It originates from the inferolateral prefrontal cortex and projects to ventromedial caudate.

5. Anterior cingulate circuit: is part of limbic system and is associated to silence, apathy and tics. This circuit is originated in anterior cingulate gyrus and connects with ventral striatum, which is formed by olfactory tubercle, nucleus accumbens, caudate and putamen. Moreover, the striatum receives additional inputs of hippocampus, amygdala and entorhinal cortex.

Although the hypothesis of neural circuit was developed for tics and movement disorders, it is possible that this fundamental principle works for limbic and cognitive aspects. Gangliobasal outputs to frontal lobe via thalamus provide an anatomical substrate for the production of simple and complex tics and compulsions. Thus, abnormal activation of the motor cortex via thalamocortical circuit can cause motor and vocal tics. Abnormal activation of the supplementary area and gyrus cinguli can cause complex tics. Abnormal activation of orbitofrontal cortex can cause compulsions.

#### 3.1.1 Stratium

Striatum has three anatomical divisions: caudate, putamen and ventral striatum or limbic<sup>29</sup>. It has bony neurons with the inhibitory neurotransmitter GABA and another subgroup which uses substance P and dynorphin. Striatum projects to globus pallidus and substantia nigra pars reticulata<sup>30</sup>. By the way, neurons with encephalin projects to external globus pallidus and subthalamic nucleus.

Boneless interneurons are divided into five subgroups: cholinergic and GABAergic neurons expressing parvualbumin; those expressing somatostatin; neuropeptide Y; nicotinamide adenine dinucleotide phosphatase and nitric oxide<sup>31</sup>.

#### 3.1.2 Striatotalamhic and thalamocortical tracts

There are two different striatal pathways: one is direct and projects to the internal pallidus globus and substantia nigra pars reticulata; and the indirect going to the external globus pallidus. Both are inhibitory and mediated by GABA and neuroactive peptide. Integration of pathways inhibitory direct and indirect excitatory takes place at the internal globus pallidus and substantia nigra pars reticulata. Internal globus pallidus projects to thalamus through inhibitors GABA fibers.

The effects of facilitation played by the direct route or suppression maintained by the indirect on the outputs of the thalamus to the cortex influences movement and cognitive processing. Deinhibition of thalamic neurons results in hyperexcitability of the projections from the thalamus to the motor cortex leading to tics.

## 4. Initial treatment considerations

The critical first step in making treatment decisions in patients with tics or GTS is select the most appropriate target symptoms, the ones causing the most problemsin a patient's daily functioning. In one patient it maybe the tics themselves, in another it may be comorbid ADHD or OCD and in another it may be a combination of targets. Because psychosocial stresses can worsen symptoms, it is important to probe for these and consider interventions such as individual or family counseling. For patients with mild symptoms, educational and psychological interventions may be sufficient to bringing down symptoms to a tolerable

level. Clinicians should remember that tics characteristically wax and wane in severity, so sometimes just waiting for some period of time can result in a lessening of tics and avoid medication use or increases.

Tics that interfere with school or other daily activities or are disabling because of social embarrassment, physical discomfort or self-injury must be treated. Tic-suppressing medications should be dosage titrated to identify the lowest one that will produce resolution of disability.

#### 4.1 Tic-suppressing drugs

Usual medication treatment for tics centers in alpha agonists and antipsychotics. However, other types of drugs may be of benefit for patients having an inadequate response or problems with tolerability. Clonazepam has had reported modest ticsuppressing effects in published case series<sup>32</sup>. This drug may be particularly useful in patients with an associated anxiety disorder. The dopamine-depleting drug tetrabenazine has possible efficacy. The drug is marketed with restriction in some countries. In an openlabel study the drug showed sustained moderate to marked reduction in tics over an average of 2 years' follow-up<sup>33</sup>. However, only 22% of subjects were free of side effects. The most common side effects are sedation, depression, insomnia, and parkinsonism. Children may tolerate higher doses of tetrabenazine than adults<sup>34</sup>. Tetrabenazine does not cause tardive phenomena but dopamine-depleting agents can cause neuroleptic malignant syndrome even after years of use<sup>35</sup>.

Local injections of botulinum toxin can be considered when one or a few dystonic tics are present in patient's repertoire, such as holding of a sustained neck posture or sustained eye closure<sup>36</sup>, cervical tics associated with myelopathy<sup>37</sup> and laryngeal injections for severe vocal tics, including copralalia<sup>38</sup>.

#### 4.2 Deep brain stimulation surgery

Deep brain stimulation surgery (DBS) is an approach used to treat other movement disorders including tremor and may be effective for selected patients with severe, disabling and medication-refractory tics. Have been open-label reports of tic reduction following transcranial magnetic stimulation (TMS) of the supplementary motor area<sup>39</sup> <sup>40</sup>. To date, most reported cases involve bilateral targeting of the centro-median parafascicular and ventralis oralis complex or central nuclei of the thalamus<sup>41</sup>, the globus pallidus internus<sup>42</sup> and nucleus accumbens/anterior limb of the internal capsule<sup>43</sup>.

Although sustained benefit has been reported to at least 17 months and most patients continue to require some medication for tics<sup>44</sup>, more careful investigation of their efficacy, safety, and tolerability of DBS for the treatment of tics is needed.

## 4.3 Treatment of tics associated with streptococcal infection

The "Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS)" hypothesis suggested that chronic, recurrent tics and OCD can arise as an autoimmune sequel of infection with group A beta-hemolytic streptococcus<sup>45</sup>. Actually, there is insufficient evidence to conclude that streptococcal infection has a true

etiological role in causing tics. Children with documented streptococcal infections be treated with an appropriate course of antibiotics, but that treatment with chronic antibiotics or immune-modifying therapies like plasma exchange or intravenous immuneglobulin are not justified based on existing evidence.

#### 4.4 Treatment of secondary tic disorders

Tic disorders secondary to CNS lesions or infection may improve with antipsychotic drug therapy. Tics are not commonly a disabling feature of neurodegenerative diseases such as Huntington's disease and antipsychotics have the potential to worsen overall motor function. In tardive phenomena patients including tics, discontinuation of the offending agent is suggested as first-line treatment and improvement can be attained with use of clonazepam, clozapine, an alpha-2-agonist<sup>46</sup> or reintroduction of an antipsychotic<sup>47</sup>.

#### 4.5 Behavioral treatment

Behavioral therapies have not been particularly beneficial for patients with disabling tics. Behavioral approaches have included operant conditioning models, rewarding tic suppression and discouraging disruptive tics and massed practice, repeated, voluntarily performance of a tic until fatigue occurs. Habit reversal therapy (HRT) can be considered if a single tic or small subset of tics is unduly disruptive or causing self-injury or pain. HRT trains patients to recognize their tics and to perform a volitional movement different from the tic each time a problem tic occurs. Open-label assessments have identified sustained benefit from HRT for up to 10months<sup>48</sup>. However, current trials will include raters blinded to treatment assignment lacking in previous trials.

In the school setting, approaches often include preferential classroom seating, extra time for tests, an opportunity to take tests in a separate quiet room and assistance with organizing schoolwork. An alpha-2-agonist, such as guanfacine, is a good first choice medication for patients experiencing problematic tics and ADHD because this type of drug can improve both conditions.

## 4.6 Treatment of ADHD

For patients with tics and ADHD without response to behavioral therapies, options of treatment including the use of the norepinephrine reuptake inhibitor atomoxetine. This drug has documented efficacy for ADHD and has been associated with either no change or a slight reduction in tics<sup>49</sup>. Stimulants remain the most potent and most predictably effective medications for treating ADHD in children with tics and they are well tolerated by the majority of patients. It does seem that upon initiation of therapy stimulants can worsen tics in some patients but this effect is temporary and tic severity usually returns to baseline or even declines from baseline within a few weeks<sup>50</sup>. The efficacy and good tolerability of the stimulant methylphenidate in children with tics and ADHD has been well documented in placebo-controlled trials<sup>51</sup>. Methylphenidate may be less likely to exacerbate tics than some other stimulant preparations, such as mixed amphetamine salts and dextroamphetamine<sup>52</sup>. Newer extended release preparations of methylphenidate tend to provide good coverage of ADHD during the school day and have been very well tolerated by patients with tics. Supplemental use of short-acting methylphenidate formulations can be useful, particularly for college students who have unpredictable study hours.

#### 4.7 Treatment of OCD

Associated OCD can be more disabling than the tics themselves and may create a state of tension and anxiety that heightens tic severity. Cognitive behavioral therapy performed by a well-trained and experienced therapist can be a very effective non-pharmacological treatment for OCD. Selective serotonin reuptake inhibitors (SSRIs) are considered the first-line medications for OCD. Combination with an atypical antipsychotic may be helpful for cases resistant to an SSRI alone. DBS involving the internal capsule/nucleus accumbens is under investigation as a therapy more severe and medication-refractory cases of OCD.

The Tourette Syndrome Association (TSA) is an informative reference guide to patients, parents, and teachers, because it clearly outlines many home and school psychoeducational modifications and interventions that may be effective for children with ADHD and tics. There are local support groups in many cities that can provide information, guidance, and support.

The optimum management of patients with tics involves a comprehensive approach that focuses not only on the tics themselves, but also on neuropsychiatric comorbidities (particularly ADHD and OCD) and existing psychosocial stressors. For young patients, major goals of treatment include helping the child to develop self-confidence, personal resilience, and positive psychosocial skills. A critical goal is to reduce obstacles to successful learning and socialization. The ultimate management usually requires a spectrum of interventions that may include education, cognitive-behavioral therapies, counseling, and medications. DBS might prove to be a useful therapy for patients with severe, disabling tics, or OCD.

#### 4.8 Educating the patient, family and school

Education of parents, teachers and peers is a critical initial intervention. Patients and their parents should be informed that it is appropriate explain to others that they have tics, that they cannot control certain movements or sounds, provide patients and parents with current information about the causes of tics such as genetic factors, brain neurochemical imbalances, emphasize that they are not signs of psychological or emotional illness, a common misperception, explain how tics change in type over time and that they naturally fluctuate in severity.

A majority of GTS patients experience improvement of tics in late adolescence or early adulthood. So the prognosis of TS could be quite good.

Education is often needed for school personnel because there are many misperceptions of tics as being voluntary, attention-seeking or purposely disruptive behaviors. It is recommended that special accommodations be considered in the school setting, like excusing the child, at his or her request, to the nurse's office to release tics or providing additional time in a separate room when taking school tests. Such provisions should be mandated in the countries under laws protecting individuals with disabilities.

#### 5. Studies about tics

As expected in behavior-analytic research, direct observation has been the preferred method for quantifying tic severity. However, researchers in psychiatry, neurology, and even the

broader field of behavior therapy have preferred indirect measures, such as clinical impression, self-report inventories and clinician-rated scales. The most commonly cited reasons for not using direct observation include concerns about generalization of observations made in clinic or research settings to other relevant settings, such as home or school<sup>53</sup> and disagreement about the best methods for collecting and scoring direct observation data<sup>54</sup>. Although the empirical basis for these concerns is not firmly established, acquisition of data supporting the use of direct observation methods may encourage those outside behavior analysis to use direct observation as a primary assessment method rather than relying on potentially biased verbal self-reports.

Studies in tics may be divided into three groups: 1) Studies made in clinical grounds, 2) Large-scale screenings and 3) Studies involving selectively school population.

Studies of in-hospital population comprise patients with most severe symptoms, in different age groups and different methods of final diagnosis confirmation are used. Procedures used in large-scale screening studies make possible the elimination of potential selection bias. Large populations are studied using transparent and repetitive confirmation of diagnoses. Their validity is additionally checked in parallel validity studies. The highest prevalence of tics is obtained in studies involving schoolchildren. Data are gathered from multiple sources: from parents, teachers, and children, as well as videos, from classroom observation and diagnoses made by experienced clinicians. Epidemiological surveys of school-age children have shown tic rates ranging from 4% to 50%55. This instability in reported rates is perplexing and is probably more artifact than truth. For example, prevalence of tics increases if transient tics are taken into account56, if studies were made just in public awards and when children attending special education schools were studied57. Inversely, prevalence of tics lowers after direct observation extends for a wide time58.

#### 5.1 Indirect observations

Majority of the studies regarding prevalence of tics based in indirect measures employs questionnaires for parents, teacher and patient; instruments self-administered for detect and draw characteristics of tics, as follows in Table 1.

## Tics are abnormal movements with the following characteristics:

They are sudden, brief, and rapid

They are repetitive

They can be controlled voluntarily during short periods of time

They can change and affect other body parts periodically

They improve and worsen from time to time

The most common tics are eye blinking, elevating the eyebrows, twitching the nose and the mouth and shoulder shrugging, shaking the head, twitching the neck, touching objects, other people, or body parts (hair, nose, etc.), kicking the legs, throat clearing, sniffing, barking, and verbalizations.

## According to these characteristics:

Do you believe that your son/daughter has had tics? (yes or no)

Do you believe that your son/daughter (or pupil) has tics? (yes or no)

Table 1. General structure used in questionnaires for tics detection.

The indirect measures of tic severity could seem inadequate and, as such, research that has relied exclusively on instruments designed for collection of indirect measures should be interpreted with caution.

#### 5.2 Direct observation

One of the hallmarks of behavior analysis is the use of direct observation to quantify behavior. This preference is based on the premise that direct observation is more objective than indirect methods such as self-report or clinician ratings of tic severity. Several studies, published in behavior-analytic outlets, demonstrate the value of using direct observation to quantify changes in tic frequency when evaluating behavioral treatments for tics<sup>59</sup>. Still, many researchers outside behavior analysis have largely preferred indirect measures over direct observation<sup>60</sup>. Among the foremost concerns raised by these researchers is that observations conducted within a clinical or research context may not generalize to other settings such as school or home. Generalization between settings is an important issue in both research and clinical practice. Indeed, it is not uncommon for parents to report that a child's tics are more or less severe while at the clinic compared to when the child is at home<sup>61</sup> Such reactivity to setting has been attributed to several factors including natural fluctuation, reinforcement contingencies, children's ability to volitionally suppress or temporarily withhold tics, reactivity to observation and internal states such as anxiety<sup>62</sup>.

Regardless of the reason for contextual variation in tics, such fluctuations have important implications for the measurement of tics. If the scientific and clinical community is to have confidence in the results of behavior-analytic work utilizing direct observation methodology, observations conducted within a research setting must be generalizable to other settings. Clinic- and homebased observations are highly related, suggesting that, in general, clinic observations correspond well with home observations<sup>63</sup>. However, examination of individual data shows that generalization should not necessarily be assumed; many children exhibited differential tic frequencies across the two settings, suggesting that, whenever possible, observations should be conducted in multiple settings. Lack of consensus regarding the most reliable, valid and feasible methods for collecting and coding direct observation data has also been cited as a reason for the preference of indirect measures over direct observation<sup>64</sup>. Practitioners and researchers in disciplines outside behavior analysis may be more likely to use direct observation methods if the effort associated with their use can be reduced, without any sacrifice of their validity and capacity to generate representative samples of target behaviors.

Direct observation to longer samples and event-frequency coding to a less arduous time-sampling method (*i.e.* partial-interval coding) have been used to evaluate outcomes in tic research<sup>65</sup>, although partial-interval coding is more user-friendly because it does not require the observer to record each occurrence of the tic; thus, it might be preferred over the event frequency method. However, partial-interval coding cannot be recommended as an alternative if it does not yield a reliable measure of the behavior. Because simulation studies have suggested that partial-interval coding may underestimate the frequency of high-rate short duration responses, especially if they occur in rapid succession or as bouts, as is the case with many tics<sup>66</sup>.

## 5.3 Yale global tic severity scale

Yale global tic severity scale (YGTSS) is a clinician-completed rating scale used to rate tic severity along several dimensions based on parent and child reports and clinician observations during the interview<sup>64</sup>. Each dimension is represented by a subscale designed to quantify the number, frequency, duration, intensity and complexity of both motor and vocal tics. Each subscale includes several descriptions to help the clinician make his or her ratings. Guided by these descriptions, each subscale is issued a rating between 0 and 5, with higher scores indicating greater severity. Examples of descriptions included on the number subscale are single tic, multiple discrete tics and multiple discrete tics plus several orchestrated paroxysms of multiple simultaneous or sequential tics where it is difficult to distinguish discrete tics. Examples of items on the frequency subscale are "rarely-specific tic behaviors have been present during the previous week; these behaviors occur infrequently, often not on a daily basis; if bouts of tics occur, they are brief and uncommon and "always – specific tic behaviors are present virtually all the time". Examples of items on the intensity subscale include "minimal intensity – tics not visible or audible (based solely on patient's private experience) or tics are less forceful than comparable voluntary actions and are typically not noticed because of their intensity" and "severe intensity - tics are extremely forceful and exaggerated in expression; these tics call attention to the individual and may result in risk of physical injury because of their forceful expression". Examples on the complexity subscale include "borderline – some tics are not clearly 'simple in character" and "severe - some tics involve lengthy bouts of orchestrated behavior or speech that would be impossible to camouflage or successfully rationalize as normal because of their duration or extremely unusual, inappropriate, bizarre or obscene character". Examples of interference items include "minimal-when tics are present, they do not interrupt the flow of behavior of speech" and "severe-when tics are present, they frequently disrupt intended action or communication". Finally, examples of items on the impairment subscale include "minimal-tics associated with subtle difficulties in self-esteem, family life, social acceptance or school or job functioning" and "severe—tics associated with extreme difficulties in self-esteem, family life, social acceptance or school or job functioning". The five subscales are rated separately for motor and vocal tics. The motor subscales are then summed to produce an overall motor tic severity rating and the vocal tic subscales are summed to provide an overall vocal tic severity rating; each ranges from 0 to 25. The motor and vocal tic severity ratings are then summed to produce an overall tic severity score that ranges from 0 to 50. Studies have shown the YGTSS total tic score to have acceptable internal consistency, good inter-rater reliability and acceptable convergent and divergent validity in samples of adults and children.

## 5.4 Gross-site procedural training

Prior to the beginning of the study, a face-to-face meeting between personnel for tic assessment must held to review the standardized observation protocol and to conduct training on YGTSS administration and scoring. Sample tapes of children with tics may be used to conduct cross site YGTSS training and direct observation coding. Tapes included an interview and YGTSS administration conducted by the primary investigators with a child and his or her parents, along with a while direct observation segment of the child (at least 10 minutes). YGTSS training has to continue until the clinicians obtained agreement of at least 90% on the training. Disagreements during training have to be resolved by discussion

between the primary investigators and coders and recoding of videotapes until agreement criterion is reached.

#### 5.5 Not clinical studies of tics

A key factor in understanding these divergent results of epidemiological studies concerns the sample size, randomization, stratification, steps in epidemiological assessment and clinical aspects to warrant quality of databases<sup>67</sup>. Most relevant studies about prevalence are showed in Table 2, including their methodological aspect.

| Author                | Year | Population    | Mothodology                         | Prevalence       | Stronghto                        | Limitations                          |
|-----------------------|------|---------------|-------------------------------------|------------------|----------------------------------|--------------------------------------|
|                       | 2002 | -             | <b>Methodology</b><br>1596 children |                  | Strenghts                        | Data obtained                        |
| Kurlan R,<br>Como PG, | 2002 | Community-    | assessed using                      | 21.2 % Had tics. | Community sample should minimize | from the Child                       |
| Miller B,             |      | school        | interviews to                       |                  | problems with                    | Behavior                             |
| Palumbo D,            |      | children 12.5 | determine the                       |                  | ascertainment bias,              | Checklist                            |
| Deeley C,             |      | to 15.7 years | prevalence of tics                  |                  | controlled study.                | (CBCL) can be                        |
| Andresen              |      | old.          | and                                 |                  | controlled study.                | influenced by                        |
| EM, et al5.           |      | oid.          | psychopathological                  |                  |                                  | which parent or                      |
| Eivi, et alo.         |      |               | disorders.                          |                  |                                  | teacher                              |
|                       |      |               | disorders.                          |                  |                                  | completed the                        |
|                       |      |               |                                     |                  |                                  | scale, tic severity                  |
|                       |      |               |                                     |                  |                                  | and                                  |
|                       |      |               |                                     |                  |                                  | psychotropic                         |
|                       |      |               |                                     |                  |                                  | medication,                          |
|                       |      |               |                                     |                  |                                  | factors that were                    |
|                       |      |               |                                     |                  |                                  | not included in                      |
|                       |      |               |                                     |                  |                                  | analyses.                            |
| Khalifa N,            | 2003 | 4479 Swedish  | Total population                    | 6.63% were       | Investigators used the           | As a result of a                     |
| Knorring              |      | school        | and their parents                   | found to have    | DSM-IV instead DSM-              | decision from                        |
| ALV <sup>68</sup> .   |      | children aged | were asked to fill in               | tics, 4.24%      | III-R criteria. The first        | the ethics                           |
|                       |      | 7 to 15 years | a questionnaire                     | were male and    | one requires that the            | committee,                           |
|                       |      | -             | covering both                       | 2.43% female.    | tics cause a marked              | investigators                        |
|                       |      |               | motor and vocal                     | Further, 4.8%    | disturbance or                   | were not                             |
|                       |      |               | tics. A three-stage                 | of the children  | significant functional           | allowed to ask                       |
|                       |      |               | procedure was                       | had transient    | impairment. Inclusion            | the teachers                         |
|                       |      |               | used: screening,                    | tics. All        | criteria were that tics          | about their                          |
|                       |      |               | interview and                       | together, 6.6%   | had occurred sometime            | pupils' tics in the                  |
|                       |      |               | clinical                            | of 7 to 15 year  | during the last 12               | main study and                       |
|                       |      |               | investigation. SGT                  | old children     | months. Same physician           |                                      |
|                       |      |               | were diagnosed                      | currently had    | performed both the               | have been                            |
|                       |      |               | according to DSM-                   | or had           | telephone interview              | missed. Some                         |
|                       |      |               | IV criteria.                        | experienced      | and the clinical                 | parents were no                      |
|                       |      |               |                                     | some kind of     | assessment.                      | Swedish and the                      |
|                       |      |               |                                     | tic disorder     |                                  | screening                            |
|                       |      |               |                                     | during the last  |                                  | questionnaire                        |
|                       |      |               |                                     | year.            |                                  | could be not                         |
|                       |      |               |                                     |                  |                                  | easy to complete                     |
|                       |      |               |                                     |                  |                                  | in its language.                     |
|                       |      |               |                                     |                  |                                  | However, in                          |
|                       |      |               |                                     |                  |                                  | these cases a                        |
|                       |      |               |                                     |                  |                                  | professional                         |
|                       |      |               |                                     |                  |                                  | translator helped                    |
|                       |      |               |                                     |                  |                                  | the parents. If<br>the child refused |
|                       |      |               |                                     |                  |                                  | further                              |
|                       |      |               |                                     |                  |                                  | participation, the                   |
|                       |      |               |                                     |                  |                                  | telephone                            |
|                       |      |               |                                     |                  |                                  | terepriorie                          |

Lanzi G, Zambrino CA, Termine C, Palestra M, Ferrari O, Orcesi S, et al<sup>69</sup>.

2004

The study population comprised 2347 primary school children from the city of Pavia, Northern Italy, 5-12 years from 15 primary schools.

Using trained school teachers as the source of cases, all children with motor or vocal tics occurring intermittently and unpredictably out of a background of normal motor activity were accepted. The type, frequency, and circumstances of tic was 4.4% in disorders were noted. School performance was correlated to the presence of tics. Diagnostic criteria for a tic disorder were those of the Tourette Syndrome significant Classification Study Group.

A total of 68 children (56 boys, 12 girls) aged 6-11 years were tic disorders. The period prevalence was 2.9% (95% CI 2.3 to 3.7). The prevalence boys and 1.1% in girls, with no detectable trends at age 6-11. Situation related tics were noted in 37 cases. A correlation was found between the presence of tic disorders and impaired school performance.

The purposes of the study, the definition and characteristics of the tic disorders were illustrated by authors to identified with all the school teachers, with the support of videotaped interviews. Investigators used stringent and different diagnostic criteria; data sources and movement disorders were excluded. Different sources have been used to identify subjects with tic disorders, including direct observations at school, parents' interview/questionnair e, teachers interview/quiestionnair e and clinical examination. A pilot study was conducted on 232 children from one school, evenly distributed across school years (two classes for each school year). This sample served to test the validity and reliability of the school teachers as a source for the

> ascertainment of patients with tics. In each class, one investigator with experience in the field of movement disorders

interview was expanded to make a correct diagnosis. Thus it is plausible that misdiagnoses were minimized. The study has not focused on the severity of the disorders, functional impairment as well as comorbid disorders, school problems and learning disabilities. Case ascertainment was no attempt to verify the teachers' observations through direct examination of all the affected children.

| Linazasoro G,<br>Blercom NV,<br>Ortiz C <sup>58</sup> .  | 2006 | 867 Children of two schools, 4 to 16 years.  | successive steps: information to   | direct observation in the classroom,   | spent four morning hours observing the students and noted any symptoms resembling tics. High participation rate and collaboration offered by parents and teachers data highly reliable. Investigators chose one private and one public school to | Investigators decided not to interview directly parents and children, but some children could be   |
|--|------|--|--|--|--|--|
|  |      |  | videotapes; anonymous fulfilling of specified questionnaire by teachers and parents and identification of children as possible tic disorder according to questionnaire; and confirmation of presence of tics by 20 minutes direct observation of children at school. | was 6.5%. The vast majority of tics were mild in severity and duration. Most of identified cases were                                      | exclude possible<br>selection bias related to<br>the socioeconomic<br>status. Blind<br>observation phase of  | identified during direct observation phase. Diagnosis of tics was not confirmed. Investigators emphasize the convenience of including a later step in the methodology to confirm the diagnosis. Length of direct observation in the classroom was 20 min, which could be quite limited. To observe children during their routine school activity requires a considerable degree of mental concentration. |
| Stefanoff P,<br>Wolanczyk T,<br>Gawrys A,<br>Swirszcz K,<br>Stefanoff E,<br>Kaminska A,<br>et al <sup>70</sup> . | 2008 | 12-15 year old<br>Warsaw<br>schoolchildren<br>attending 24<br>randomly<br>selected<br>schools. | screened by  | 9.9% (95%CI<br>7.1–12.6%) and<br>a point<br>prevalence of<br>6.7% (4.3–<br>9.1%). Lifetime<br>prevalence of<br>ICD-10 tic<br>disorders was | The schools were chosen randomly and should not differ systematically from other mainstream schools.   | Reference group differed significantly from the total study population in terms of gender distribution. The number of subjects with tics found in this group could be even higher, leading to lower positive predictive value. Teachers interviewed in the study protocol knew their students for  |

3-4 years and

high sensitivity (92%) and low positive predictive value (18%). International Classification of Diseases-10 (ICD-10) criteria were used for tic disorders.

were coping with them on a daily basis as their formal  $tutors.\ A$ relatively high proportion of false negative subjects in the reference group is the result of poor knowledge of involuntary movements in the polish population and indicates a possible underestimation of prevalence estimates. classification of tic disorders based on the ICD-10 criteria could yield misdiagnosing of tic disorders. The ICD classification reflects the current concepts of tic disorders as a behavioral continuum, and two most severe syndromeschronic tic disorders and GTS-differ only in terms of duration of tic symptoms. The use of ICD criteria should not constitute a problem in terms of comparability with previous epidemiological studies, especially that most of them that utilized DSM-III-R criteria, very

similar toICD-10.

| Schlander M,   | 2009 | 2.2 million live  |  | Prevalence of  | Prevalence rates within  |   |
|--|------|---|--|--|--|---|
| Schwarz O,<br>Rothenberger<br>A, Roessner<br>V <sup>71</sup> .             |      | records during 2003 covered by Statutory Health Insurace (SHI) in Norbaden, Germany, 0 to 50 years old. | administrative prevalence rates as well as rates of co-occurrence of tics and ADHD based upon the number of diagnosed cases of tics disorders.   | and ADHD<br>were<br>diagnosed<br>most often in<br>the age group<br>7-12 years. Tic | this large sample established the remitting course of tics. The study confirms the co-ocurrence of tics and ADHD in children and adolescents, presenting both perspectives: the rate of ADHD in patients with tics as well the rate of tics in patients with ADHD.   | outpatients have no detailed information about the exact diagnostic procedures. Short time of follow-up. Diagnoses in children made more often by a medical specialist and by a primary care physician in adults. The study is difficult to compare with previous reports, which is related to different study design. The absolute administrative prevalence rates should be interpreted cautiously. Some people could not be assisted to SHI. |
| Ortiz B, David M, Sánchez Y, Mira J, Sierra JM, Cornejo JW <sup>72</sup> . | 2011 | 346 students of public basic school.  | Students were assessed by structured questionnaire, interview and 20 minutes of clinical examination. Comorbidity with ADHD was detected by DSM-IV criteria. Severity and interference produced by tics was determined by apply YGTSS. | chronic tic<br>disorder. 53.4%<br>of patients<br>with tics agree<br>with DSM-IV    | First study in South America establishing prevalence of tics in children. Wide clinical sample that includes training to teachers and parents, structured questionnaire, clinical assessment and direct observation in the classroom by experts in tics detection. Percentage of children with GTS was higher than other studies probably because evaluators considered milder cases and depicting that the disorder was not as rare as previously was believed. | Authors detected that hyperactivity was confused with tics by parents and teachers on parents and teachers questionnaires   |

Table 2. Not clinical studies of tics.

#### 5.6 Clinical studies of tics

Clinic-based studies are believed to underestimate the frequency of tics, as only a small fraction of children and adults with tics are brought to a health care provider for evaluation<sup>73</sup>. There is evidence of a reporting bias in community studies with 50% of the children with observed tics reported to have tics by their parents. Results of investigations also support the previously reported findings that tics wax and wane in severity and frequency over time, as individual shad fluctuating symptoms over the observation period<sup>74</sup>. Most relevant clinical studies about prevalence are showed in Table 3.

|                           |      |                |                     |                         | /   ( )   (          |                      |
|---------------------------|------|----------------|---------------------|-------------------------|----------------------|----------------------|
|                           | Year |                | Methodology         | Results                 | Strenghts            | Limitations          |
| Chouinard                 | 2000 |                | Patients' charts    | 5.35% presented for     | The study shows      | The study cannot     |
| S, Ford B <sup>75</sup> . |      | with tic       | were                | the first time with tic | that adult onset tic | estimate the         |
|                           |      |                | retrospectively     | disorders after the     | disorders represent  |                      |
|                           |      | presented      | reviewed for        | age of 21. 2.18% of     | an underrecognised   |                      |
|                           |      | between 1988   | demographic         | patients had a history  | condition that is    | in general           |
|                           |      | and 1998 to    | information, age of | of previous childhood   |                      |                      |
|                           |      |                | onset of tics, tic  | transient tic disorder, | generally            | Establishing that an |
|                           |      | disorders      | phenomenology,      | but in 3.16% of         | appreciated or       | adult patient with   |
|                           |      | clinic at      | distribution, the   | patients, the adult     | reported and         | apparent new onset   |
|                           |      | Columbia-      | presence of         | onset tic disorder      | clinical evidence    | tics did not have    |
|                           |      | Presbyterian   | premonitory         | was new. Among the      | suggesting that      | tics during          |
|                           |      | Medical        | sensory symptoms    | new onset cases,        | adult tic disorders  | childhood can        |
|                           |      | Center after   | and tic             | 1.45% of patients       | are part of a range  | rarely be done with  |
|                           |      | the age of 21. | suppressibility,    | developed tics in       | of illness that      | certainty because    |
|                           |      |                | family history and  | relation to an external |                      | some patients are    |
|                           |      |                | associated          | trigger, secondary      | onset tics and GTS.  | unaware of their     |
|                           |      |                | psychiatric         | tic disorders.          | Authors propose a    | tics and reliable    |
|                           |      |                | features. These     | The remaining           | new classification   | observers who        |
|                           |      |                | patients'           | patients had            | of tic disorders in  | knew the patient as  |
|                           |      |                | videotapes were     | idiopathic tic          | adult age category   | a child may not be   |
|                           |      |                | reviewed for        | disorders. The          | that is subdivided   | available. All       |
|                           |      |                | diagnostic          | categorical             | by disease course    | patients were self   |
|                           |      |                | confirmation and    | breakdown among 22      | into tic disorders   | referred for tics, a |
|                           |      |                | information was     | patients was:           | that persist from    | referral bias that   |
|                           |      |                | obtained about      | idiopathic new onset    | childhood, tic       | usually selects for  |
|                           |      |                | disability, course, | tics in seven (32%),    | disorders that       | more severely        |
|                           |      |                | and response to     | new onset secondary     | represent a          | affected people.     |
|                           |      |                | treatment in a      | tic                     | recurrence of        |                      |
|                           |      |                | structured follow   | disorder in six (27%)   | transient childhood  |                      |
|                           |      |                | up interview.       | and recurrent           | tics and genuine     |                      |
|                           |      |                |                     | childhood tic           | new onset adult tic  |                      |
|                           |      |                |                     | disorder in nine        | disorders.           |                      |
|                           |      |                |                     | (41%). The appearance   |                      | 71111                |
|                           | l l  |                |                     | of the tic disorder,    |                      |                      |
|                           |      |                |                     | the course and          |                      |                      |
|                           |      |                |                     | prognosis, the          |                      |                      |
|                           |      |                |                     | family history of tic   |                      |                      |
|                           |      |                |                     | disorder and the        |                      |                      |
|                           |      |                |                     | prevalence of           |                      |                      |
|                           |      |                |                     | obsessive-compulsive    |                      |                      |
|                           |      |                |                     | disorder were found     |                      |                      |
|                           |      |                |                     | to be similar in adult  |                      |                      |
|                           |      |                |                     | patients with           |                      |                      |
|                           |      |                |                     | recurrent childhood     |                      |                      |
|                           |      |                |                     | tics and those with     |                      |                      |
|                           |      |                |                     | new onset adult tics.   |                      |                      |
|                           |      |                |                     | Adults with new         |                      |                      |

|  |  |   | onset tics were more   |  |  |
|--|--|---|--|--|--|
|  |  |   | likely to have a<br>symptomatic or<br>secondary tic<br>disorder, likely<br>caused by infection,<br>trauma, cocaine use,  |  |  |
|  |  |   | and neuroleptic exposure.  |  |  |
| Eapen V,<br>Lees A,<br>Lakke<br>JPWF,<br>Trimble<br>MR;<br>Robertson<br>MM <sup>76</sup> . |  | All the cases were evaluated using the National Hospital Interview Schedule for the assessment of GTS and related behaviors; this is a standardized, semistructured instrument that includes systematic assessment of personal and family history of GTS, ADHD and OCB. | trigger event,<br>such as drug<br>exposure, viral or<br>bacterial infection,<br>physical trauma,<br>cerebrovascular<br>disease or psychiatric<br>illness prior to the  | the patient well<br>enough to give<br>relevant details | the phenomenology  |
| Prior AC,<br>Tavares S,<br>Figueiroa<br>S, Temudo<br>T <sup>77</sup> .                     | 2006 78 Children<br>and teenagers<br>with tics<br>diagnosed<br>based by<br>DSM-IV<br>criterions. | Retrospective<br>analyses from<br>clinical archives of<br>child neurology<br>outpatients of<br>Hospital General<br>de Santo Antonio,<br>Spain.  | 84.6% were boys. Family history of tics, depression and OCD occurred in 30%. ADHD was the most frequent neuropsychologycal disorder (67.9%). In more than two thirds of the patients, tics were simple. Mean age for tics was 7 years old. 59.7% of tics were chronic and 45.7% of those were GTS. | Wide clinical sample.                                  | Boys were derived to the clinic because symptoms of ADHD instead of tics. Descriptions were extracted of patients untreated. Sex selection bias may take place (male:female ratio was 5.5:1) because ADHD was more frequent in boys. Neurobehavioral and family aspects may be overestimated by the type retrospective of study. |

Table 3. Clinical warding studies of tics.

## 5.7 Clinical characterization of tics

| Author   | Year | Population  | Methodology   | Motor (%) | Vocal | SGT<br>(%) |
|--|------|---|---|-----------|-------|------------|
| Khalifa N,<br>Knorring ALV <sup>78</sup> .   | 2003 | 4479 Swedish school children aged 7 to 15 years.  | Total population and their parents were asked to fill in a questionnaire covering both motor and vocal tics. A three- stage procedure was used: screening, interview and clinical investigation. SGT were diagnosed according to DMS-IV criteria.   | 0,8       | 0,5   | 0,6        |
| Himle, M. B., & Woods, D. W <sup>63</sup> .  | 2006 | 43 children, ages 8<br>to 17 years  | Patients recruited through print advertisement, physician referrals and Tic Disorder Clinics. The assessment consisted of a structured diagnostic interview, including intelligence quotient (IQ), videotape and patient, parent and clinics-reports. Monetary compensation was given to children.  | 15,4      | 10    | 95,3       |
| Prior AC,<br>Tavares S,<br>Figueiroa S,<br>Temudo T <sup>77</sup> .  | 2006 | 78 Children and<br>teenagers with tics<br>diagnosed based<br>by DSM-IV<br>criterions.       | Retrospective analyses from clinical archives of child neurology outpatients of Hospital General de Santo Antonio, Spain.   | NA        | NA    | 45,7       |
| Stefanoff P,<br>Wolanczyk T,<br>Gawrys A,<br>Swirszcz K,<br>Stefanoff E,<br>Kaminska A, et<br>al <sup>70</sup> . | 2008 | 12-15 year old<br>Warsaw<br>schoolchildren<br>attending 24<br>randomly selected<br>schools. | Students were screened by inquiring their parents and teachers. Children indicated as tic-positive by the screening procedure were investigated using semi-structured questionnaires and the Polish version of YGTSS scale. A validity study involved random selection and investigation of 130 non indicated subjects. Screening procedure had high sensitivity (92%) and low positive predictive value (18%). | NA        | NA    | 0,6        |
| Ortiz B, David<br>M, Sánchez Y,<br>Mira J, Sierra<br>JM, Cornejo<br>JW <sup>72</sup> .                           | 2011 | 346 students of public elementary school.   | Assessment by structured questionnaire, interview and 20 minutes of clinical examination.   | 63,8      | 12    | 19         |

Table 4. Clinical characteristics of tics.

## 6. Related problems in tic disorders along life

Oftenly, presence of tics are associated with messing conditions that impair the performance at work, familiar and social environments. Prevalence studies should consider these entities because detection is a first step to diagnose and treat them. We illustrate studies of tic disorders and related morbidities in Table 3.

## 6.1 Studies of comorbidity in tics

| Author   | Year | Methodology   | Results  | Strenghts  | Limitations  |
|--|------|---|--|--|--|
| Kurlan R,<br>Como PG,<br>Miller B,<br>Palumbo<br>D, Deeley<br>C,<br>Andresen<br>EM, Eapen<br>S, et al5.    |      |   | 1596 children interviewed,<br>21.2% had tics, 38.4% with<br>ADHD, 10.9% with OCD,<br>29.2% with social phobia,<br>9.4% with agoraphobia,<br>14.8% with separation<br>anxiety, 21.2% with anxiety<br>disorder, 1.2% with mania  | Community sample is intended to minimize problems with ascertainment bias, controlled study. | Data obtained from the CBCL can be influenced by which parent or teacher completed the scale, tic severity and psychotropic medication, factors that were not included in analyses.  |
| Snider LA,<br>Seligman<br>LD,<br>Ketchen<br>BR, Levitt<br>SJ, Bates<br>LR, Garvey<br>et al <sup>79</sup> . | 2002 | 553 children of<br>kindergarten through<br>sixth grade, observed<br>monthly from November<br>1999 to June 2000 by 3   | One quarter of all children exhibited problem behaviors. The monthly point prevalence was significantly higher during winter months compared with the spring months. Behavior comorbidity is associated with the more persistent tic symptoms versus all tic symptoms, as children with isolated tics lasting only 1 to 2 months did not have increased rates of problem behaviors, whereas those with a more persistent course did. | three independent  | Conclusions about seasonal prevalence are limited because the children were not observed from July through October. It's possible that clinic-based studies overestimate the frequency of comorbid behavior problems, in part because the behavior problems can be more troublesome than the tic symptoms and become the motivating factor for seeking treatment. It is also possible that clinic-based studies estimate accurately the prevalence of comorbid conditions and that the discrepancy came from the inappropriate generalization of clinic based data to community populations. |
| Prior AC,<br>Tavares S,<br>Figueiroa<br>S, Temudo<br>T <sup>77</sup> .                                     | 2006 | 78 Children and teenagers with tics diagnosed based by DSM-IV criterions. Retrospective analyses from clinical archives of child neurology outpatients of Hospital General de Santo Antonio, Spain. | ADHD was present in 67.9%, learning difficulties in 59%, sleep disorders in 23.1%, developmental delay in 21.8%, unspecified mental retardation in 16.7%, ODD in 10.3%, obsessive compulsive symptoms (OCS) in 7.7%, epilepsy in 6.4%, autism in 3.8%, migraine/headache in 3.8% and depression in 2.6%  | sample. DSM-IV criteria were used for tics, which allow comparison                           | Data was extracted from clinic archives and patients were selected by an unknown and not-validated questionnaire.  |

Table 5. Related disorders in tics.

#### 6.2 Adults with tics and comorbidities

Tics and vocalizations developing in later life in association with neuroacanthocytosis<sup>80</sup>, Sydenham's chorea and L-dopa-treated postencephalitic parkinsonian syndrome<sup>81</sup>. There are a few reports of isolated and spontaneous adult-onset tics disorders.

Chouinard and colleagues reported on 7 cases of idiopathic tic disorder that presented after the patients were 21 years of age<sup>75</sup>. Adult-onset tic disorder in the absence of any other primary neurological disorder has onset of tic symptoms from 23 to 52 years<sup>76</sup>.

Adult-onset cases need to be evaluated using a wide screening, like the National Hospital Interview Schedule for the assessment of GTS and related behavior<sup>82</sup>; this is a standardized, semistructured instrument that includes systematic assessment of personal and family history of GTS, ADHD, and obsessive compulsive behavior (OCB). The interview is conducted with the patient and a family member (usually a parent) who knows the patient well enough to give relevant details about childhood.

Several cases of secondary tourettism have been described in the literature. The causes have included postencephalic syndrome and carbon monoxide intoxication, and other causes have been degenerative or vascular<sup>75</sup>. Tourettism has also occurred secondary to trauma<sup>83</sup>, infection<sup>84</sup>, alcohol withdrawal<sup>85</sup>, or intake of certain drugs such as stimulants, anticholinergics, or antipsychotics<sup>86</sup> <sup>87</sup>. In almost all patients there was a potential trigger event, such as drug exposure, viral or bacterial infection, physical trauma, cerebrovascular disease, or psychiatric illness prior to the onset of tic symptomatology. These may have acted as a trigger to unmask the symptoms in a constitutionally predisposed individual. In this regard, it is interesting to note that in 50% of cases there is either a personal or family history of GTS-related behavior. However, it is also possible that these represented secondary tics. It is now recognized that GTS has a genetic cause, with some studies suggesting an autosomal dominant transmission and others a mixed model<sup>88</sup>.

Goetz and coworkers in a study of 58 adult GTS patients diagnosed during childhood observed that childhood tic severity had no predictive value and that coprolalia did not increase the risk for severe tics in adult life<sup>89</sup>. Features predictive of mild tics in adulthood were mild tics during the patients' worst preadulthood function and mild tics during adolescence. The phenomenology of tics encountered in later life may also be somewhat different from those in early-onset GTS. For example, it has been reported reduced response to treatment (31%), a high degree of social morbidity (89%) and a low frequency of spontaneous complete remission in adult-onset cases. It seems that adult-onset tic disorder, whether idiopathic, secondary or a recurrence of childhood tics, may be different from younger-onset GTS.

A majority of patients exhibit OCB in childhood and have a positive family history of tics or OCB. It may also be noted that childhood rheumatic chorea may resolve only to return in late adult life<sup>89</sup>. Linazasoro and colleagues described a patient who had presented with only OCD since childhood but developed GTS symptoms at the age of 72 years and suggested that the expression of the gene may be different in the same patient during the course of his life<sup>90</sup>.

#### 7. Conclusions

Data from tics research prompt significant variations in prevalence. Future research should, at minimum, supplement indirect measures with direct methods. Nolan demonstrated that

correspondence between direct observation scores and YGTSS ratings may be lower for low-frequency tics than for high-frequency tics<sup>91</sup>.

Whether tic frequency is the most important dimension of tic severity (e.g. best predicts psychosocial functioning) is an empirical issue that warrants investigation. Studies should evaluate methods capable of quantifying multiple dimensions of tics including overt physical dimensions (e.g. frequency, intensity, complexity), social dimensions (e.g. social reinforcement and punishment contingencies, functional interference) and the concomitant private dimensions commonly reported to accompany tics (e.g. sensory events). The research will likely require novel direct observation techniques used in combination with other measurement methods (e.g. functional assessment, self-report, clinician ratings, social acceptability ratings, physiological measures, neuroimaging techniques, etc.) and research strategies (e.g. functional analysis, group research designs, inferential statistical analyses).

The use of not traditional measurement techniques to complement direct observation is likely to increase in popularity within the broader field of clinical behavior analysis. Clinical researchers are increasingly concerning themselves with the study of behavior that is complex, highly variable and not easily accessible by traditional direct-observation techniques (e.g. the private behaviors of individuals who suffer from anxiety and mood disorders). If behavior analysts are to continue to be at the forefront for understanding and treating clinical problems (including tic disorders), they must systematically determine which dimensions of specific target behaviors are socially relevant and must be diligent not to restrict themselves by investigating only those aspects that are easily quantifiable with traditional direct observation methods<sup>92</sup>. This will require researchers both to refine their current measurement techniques and to incorporate techniques that have not traditionally been employed in behavior-analytic research (e.g. clinician ratings, self-report, physiological and neuroimaging techniques, etc). This is not to suggest that clinical behavior analysts abandon direct observation in favor of other measurement techniques. On the contrary, it is a call to behavior analysts to develop, investigate and incorporate new direct and indirect measurement techniques that will enhance scientific investigation of the environmentbehavior relations involved in clinical problems.

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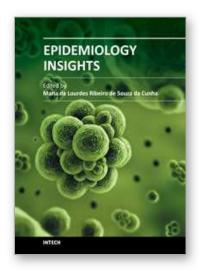
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#### **Epidemiology Insights**

Edited by Dr. Maria De Lourdes Ribeiro De Souza Da Cunha

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This book represents an overview on the diverse threads of epidemiological research, brings together the expertise and enthusiasm of an international panel of leading researchers to provide a state-of-the art overview of the field. Topics include the epidemiology of dermatomycoses and Candida spp. infections, the epidemiology molecular of methicillin-resistant Staphylococcus aureus (MRSA) isolated from humans and animals, the epidemiology of varied manifestations neuro-psychiatric, virology and epidemiology, epidemiology of wildlife tuberculosis, epidemiologic approaches to the study of microbial quality of milk and milk products, Cox proportional hazards model, epidemiology of lymphoid malignancy, epidemiology of primary immunodeficiency diseases and genetic epidemiology family-based. Written by experts from around the globe, this book is reading for clinicians, researchers and students, who intend to address these issues.

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