Tics and Gilles de la Tourette syndrome: an introduction

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Athens, 23/11/2024

ESSTS
European Society for the Study of Tourette Syndrome

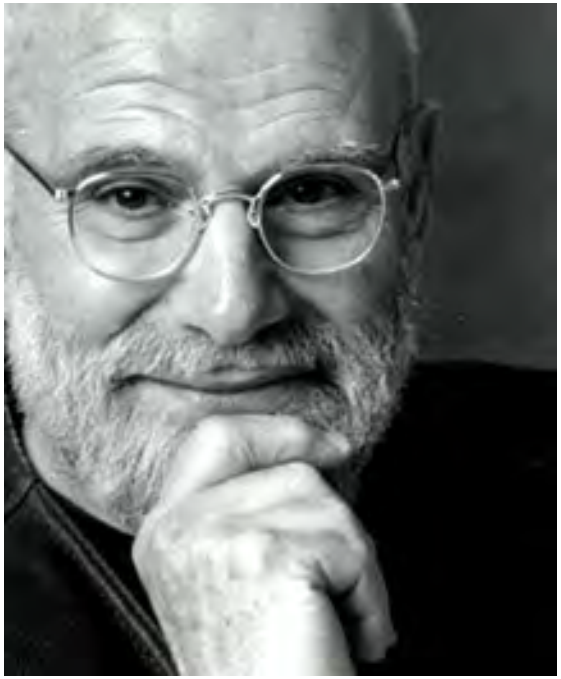
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Athens

"This is truly of tremendous importance. Any understanding of such a syndrome must vastly broaden our understanding of human nature in general ...

I know of no other syndrome of comparable interest."

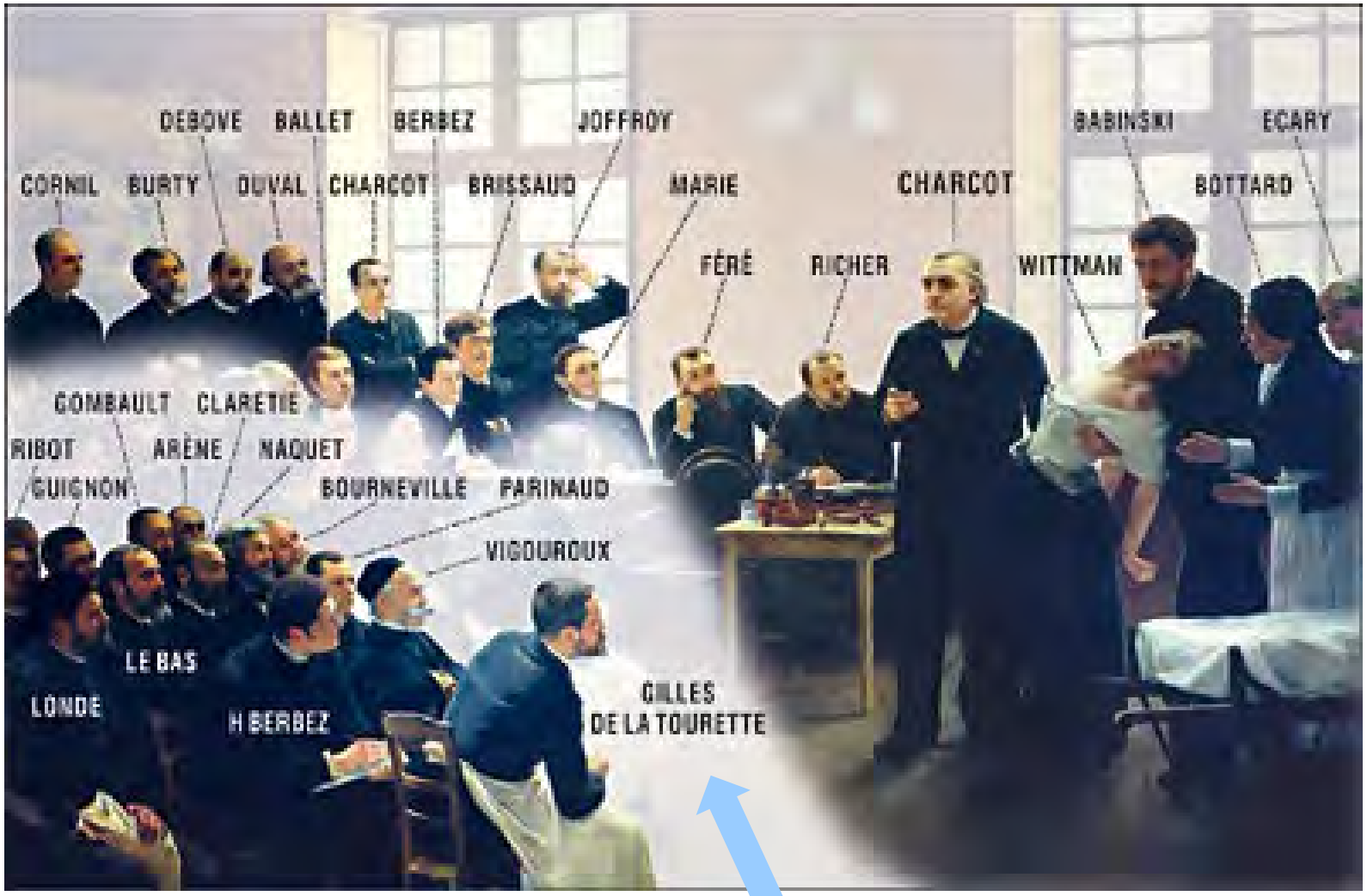
A.R. Louriia – O. Sacks (1977)



1857-1904

Itard (1825), Gilles de la Tourette (1885) et la Marquise de D….

La ‘maladie des tics’



L. Brouillet, *Une Leçon Clinique à la Salpêtrière* (1887)

The history of TS

PRIMER

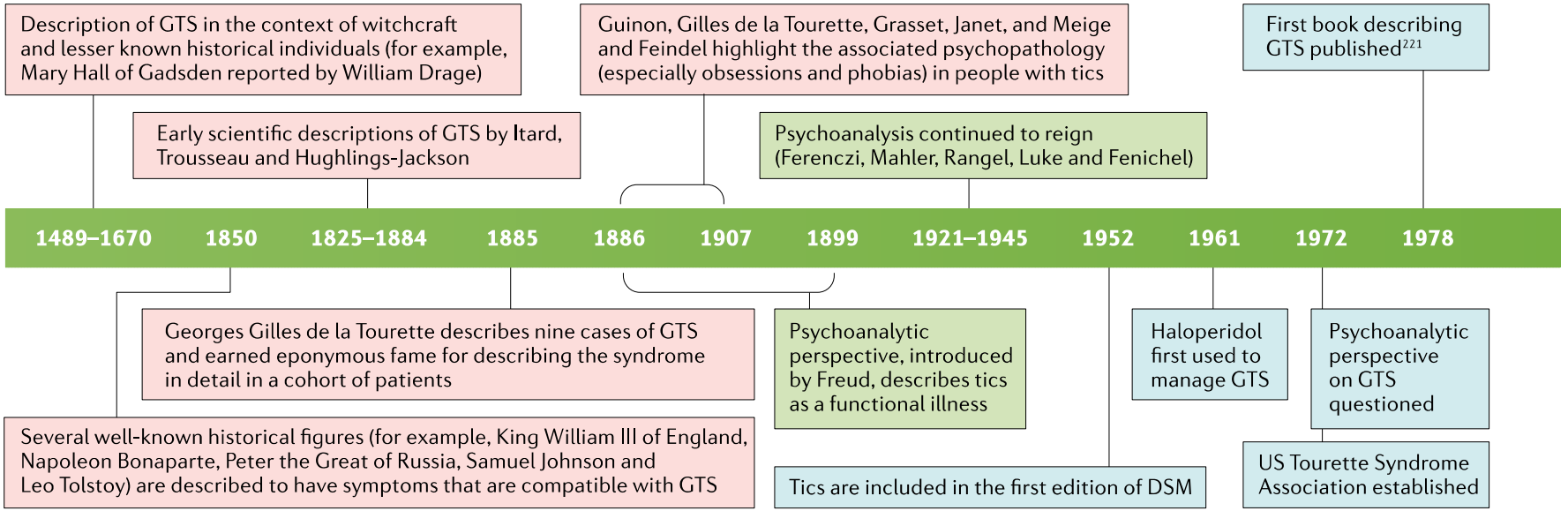


Figure 1 | **Key events in the history of Gilles de la Tourette syndrome.** Timeline depicting the key events in the history of Gilles de la Tourette syndrome (GTS), including events in the early description era, psychoanalytic era, early diagnostic era, and advanced diagnostic and research era. DSM, Diagnostic and Statistical Manual of Mental Disorders; PANDAS, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections; QOL, quality of life; YGTSS, Yale Global Tic Severity Scale.

Robertson et al. 2017

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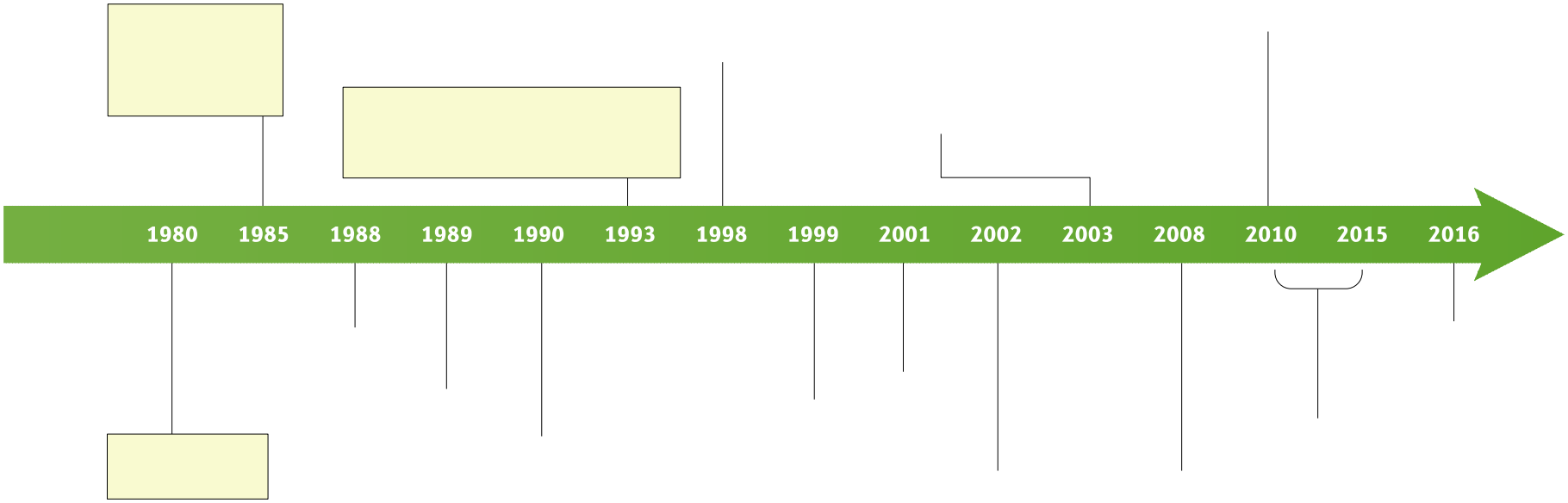
The history of TS



Robertson et al. 2017

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The French National Reference Centre for TS

Sara BAHADORI

Virginie CHARRIERE

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Marie BAHOUT

Virginie CZERNECKI

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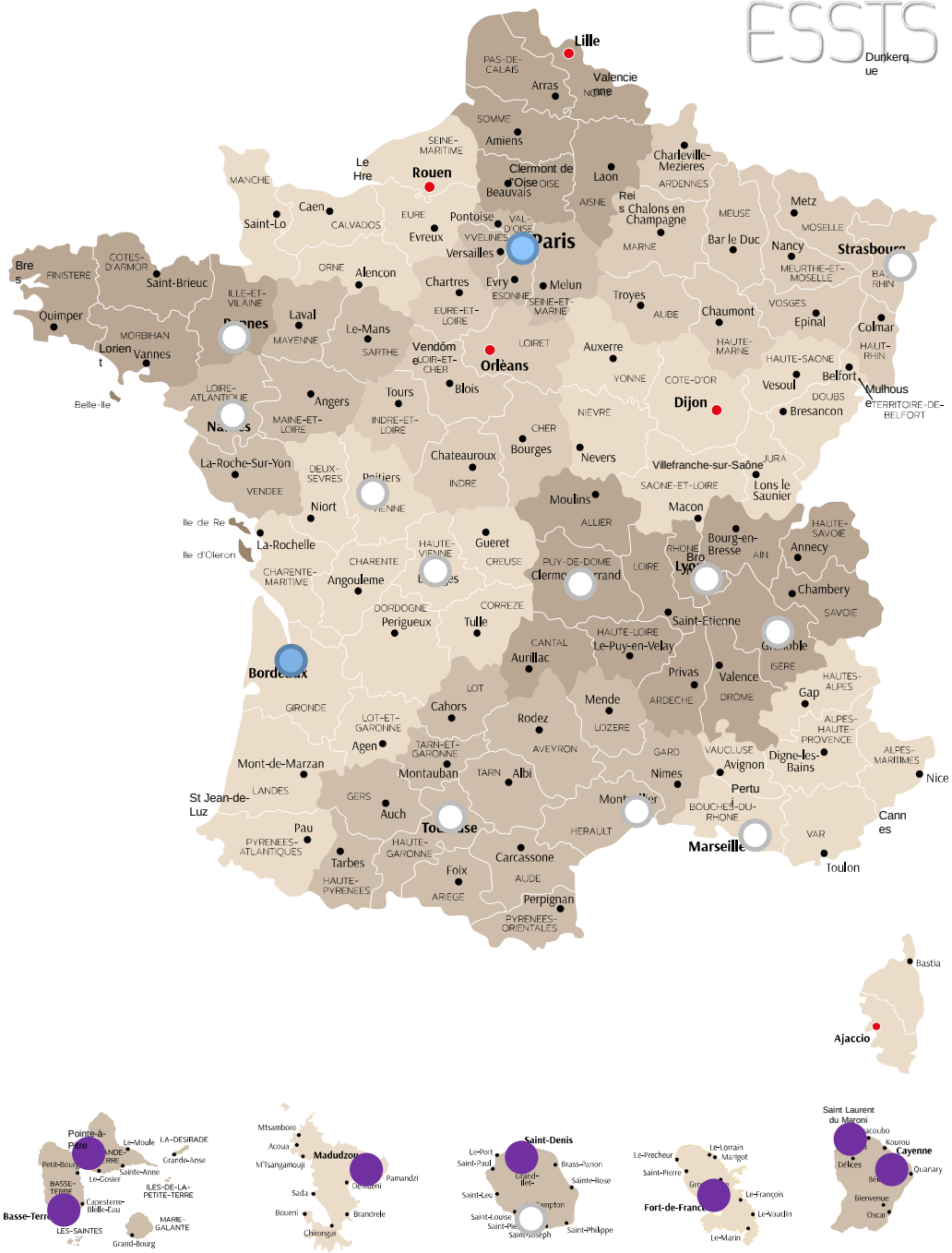

Nom du CRMR : Syndrome Gilles de la Tourette (SGT)

Filière : BRAIN-TEAM

- Coordonnateur
- Constitutif
- Compétences

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European Child & Adolescent Psychiatry
https://doi.org/10.1007/s00787-021-01842-2

REVIEW

European clinical guidelines for Tourette syndrome and other tic disorders—version 2.0. Part I: assessment

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Tics

- Spontaneous, repetitive, involuntary movements
- Misplaced in time / context / frequency
- Motor or vocal*
- Simple or complex*

Tics

- Preceded by a sensation or urge to execute the tic
- Accompanied by transient relief after performing the tic
- Transiently suppressible

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Motor

Simple

- Eye blinking
- Eye movements
- Facial grimacing
- Nose twitching
- Head jerks
- Shoulder schrugging
- Leg jerks

Complex

- Gripping of the nose
- Jumping
- Bending
- Writing tics
- Copropraxia
- Tic-like compulsive behaviors
- Echopraxia
- Palipraxia
- Self-injurious behaviors

Vocal

Simple

- Throat clearing
- Sniffing
- Coughing
- Tongue clicking
- Popping
- Grunting
- Humming

Complex

- Repetition of syllables
- Repetition of words
- Stuttering
- Coprolalia
- Echolalia
- Palilalia

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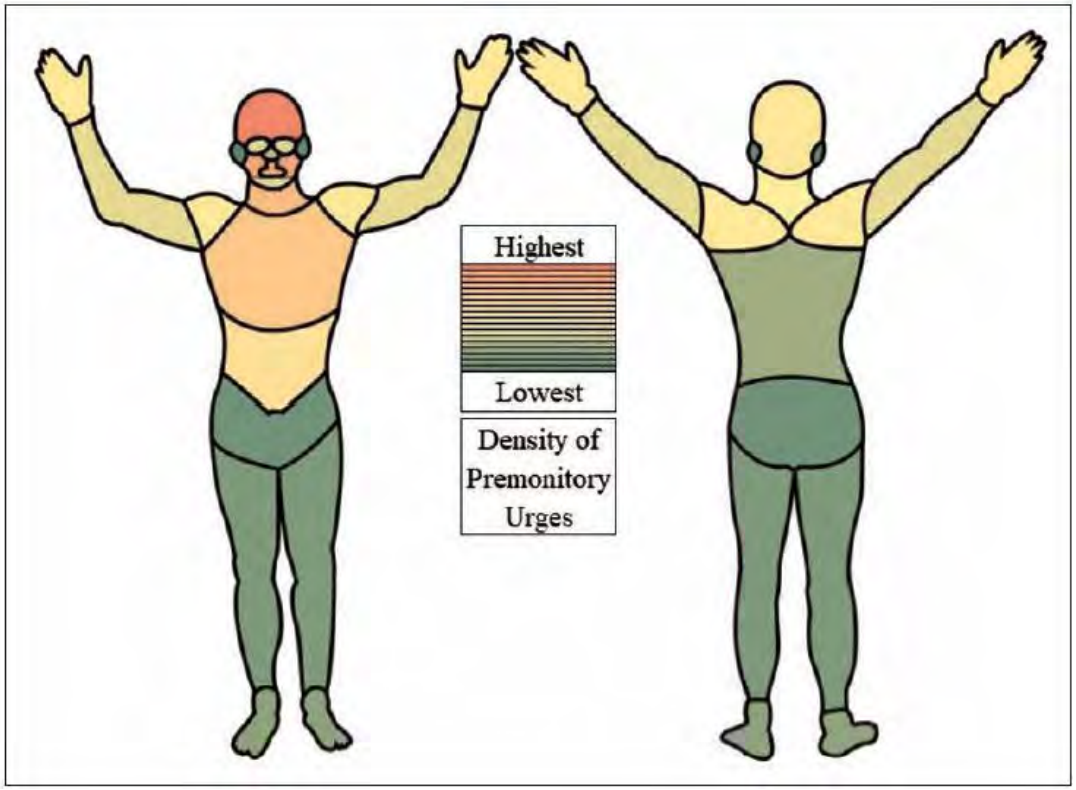
Type of tic	Typical features
Motor	Arise in the voluntary musculature and involve discrete muscles or muscle groups
Vocal	Consist of any noise produced by movement of air through the nose, mouth or pharynx
Stimulus-bound	Occur in response to internal or external stimuli (visual, phonic, tactile or mental)
Blocking	Motor or vocal tics that interrupt the voluntary action without alteration of consciousness (dysfluency of speech or gait)
Simple	Are restricted to one muscle or a single muscle group (e.g. eye blinking, nose twitching, tongue protrusion), simple, meaningless sounds (e.g. grunting, throat clearing, coughing, sniffling and barking)
Complex	Involvement of more muscle groups (e.g. repetitive touching of objects or people, repetitive obscene movements (copropraxia), mimicking others (echopraxia) complex vocal tics are words or phrases, expressing obscenities (coprolalia), repeating others (echolalia) or repeating oneself (palilalia))
Clonic	Last less than 100 ms
Dystonic	Last more than 300 ms Repetitively abnormal posture of a kind that one may see in dystonia
Tonic	Last more than 300 ms Relatively long duration of the contraction (in e.g. back muscles) without exhibiting abnormal postures

Typical features of tics

- Premonitory urge
- Distractibility
- Suggestibility
- Suppresibility
- Influenced by external factors
- Rostrocaudal distribution
- Waxing and waning course
- Onset (age, type)
- Family history
- Profile of comorbidities



Essing et al. 2022

Tourette syndrome

Tourette's Disorder 307.23 (F95.2)

A. Both **multiple motor** and **one or more vocal tics** have been present at some time during the illness, although not necessarily concurrently.

B. The tics may wax and wane in frequency but have persisted for **more than 1 year** since first tic onset.

C. Onset is **before age 18 years**.

D. The disturbance is **not** attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).

Persistent (Chronic) Motor or Vocal Tic Disorder 307.22 (F95.1)

A. Single or multiple motor or vocal tics have been present during the illness, but not both motor and vocal.

B. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset.

C. Onset is before age 18 years.

D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).

E. Criteria have never been met for Tourette's disorder.

Specify if:

With motor tics only

With vocal tics only

Provisional Tic Disorder 307.21 (F95.0)

A. Single or multiple motor and/or vocal tics.

B. The tics have been present for less than 1 year since first tic onset.

C. Onset is before age 18 years.

D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).

E. Criteria have never been met for Tourette's disorder or persistent (chronic) motor or vocal tic disorder.

Specifiers:

The "motor tics only" or "vocal tics only" specifier is only required for persistent (chronic) motor or vocal tic disorder.

Temporal occurrence of tics

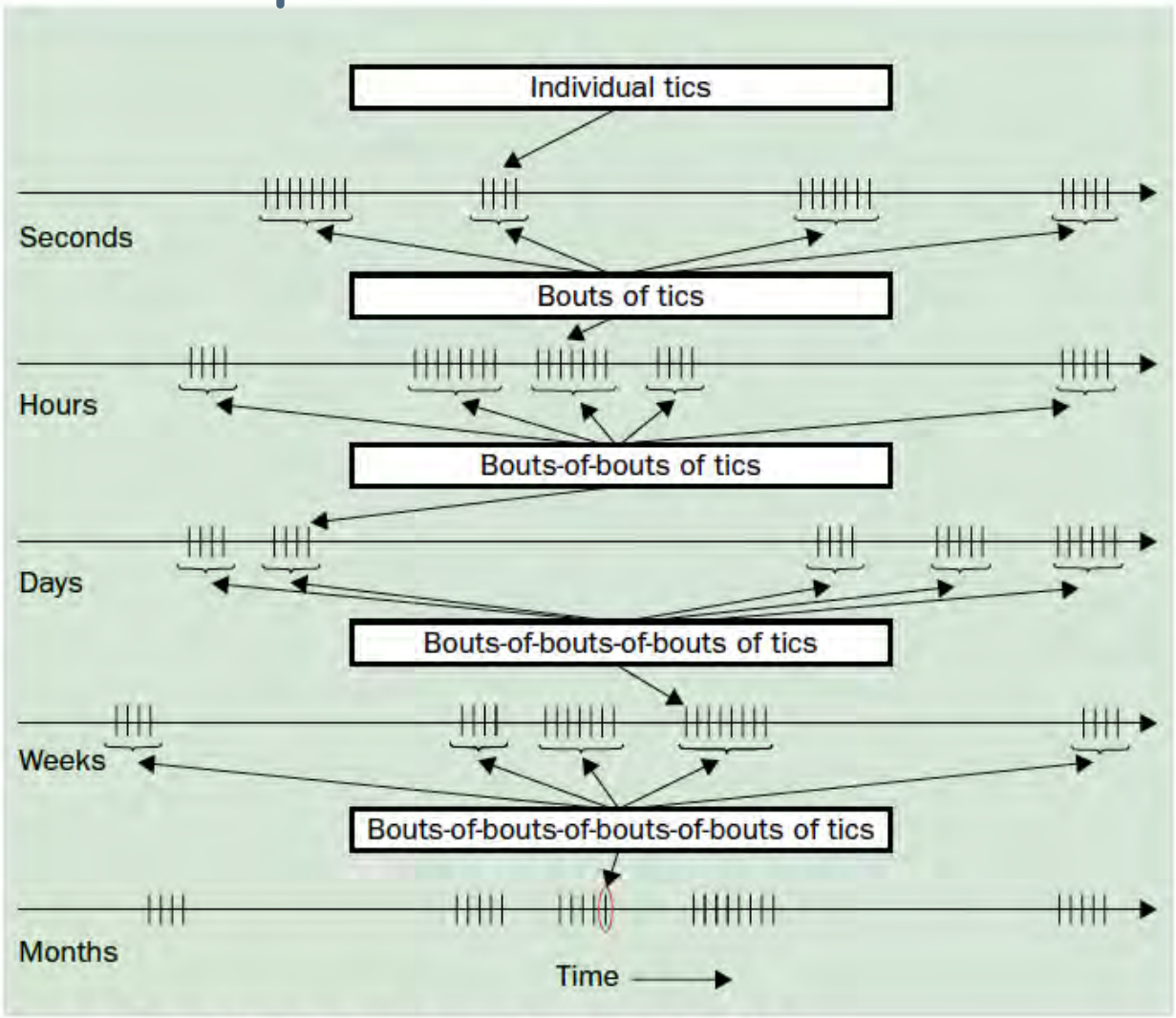


Figure 1: **Fractal character of temporal occurrence of tics**
Progressively longer time scales (seconds to months) are depicted.

Seminar

Tourette's syndrome

James F Leckman

Lancet 2002; **360:** 1577–86

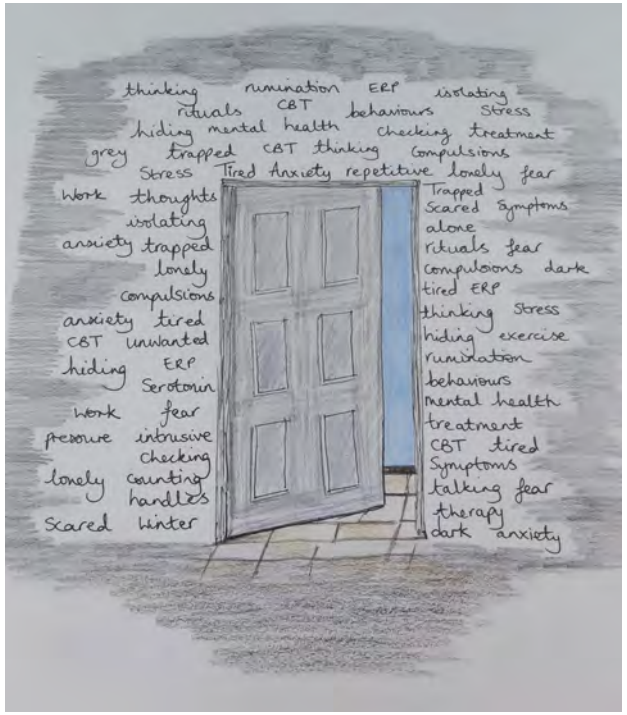
Differential diagnosis

- Myoclonus
- Dystonia
- Chorea
- Hemifacial spasm
- Stereotypies
- Compulsions
- Akathisia
- Restless legs syndrome
- Seizures
- Functional “tics”

Somatic conditions

- Ophthalmological (conjunctivitis or dry eye syndrome)
- Otolaryngological (allergy)
- Gastroesophageal reflux
- Stuttering

Compulsions



Repetitive and intrusive behaviours

Tics	Compulsions
Sudden, short	Ritualized, can be lengthy
Fragmented movements	Goal-directed behavior
Premonitory urges	Obsessions
Less related to anxiety	Mostly related to anxiety
Onset in primary school	Onset after primary school
Waxing and waning	More stable over time

Lewin et al. Psychiatry Res. 2010 Jul 30; 178(2): 317–322.

Tic-related compulsive behaviours (Tourettic OCD)

- Can be close phenomenologically with compulsions
- E.g. touching, tapping, grooming, evening-up
- More common in patients with co- existing tics and OCD.

Stereotypies

Common repetitive complex motor behaviors, during the neurodevelopmental period +

- usually start earlier than tics (3-4 yo)
- Patterned, seemingly purposeless
- Predictable amplitude and location
- Long periods of time, multiple times a day, at the expense of other movements.
- Cease any other activity.
- Last from seconds to minutes[2]
- Comfort and enjoyment
- Unaware, limited contact with the surrounding environment.

The repertoire of stereotypies may vary considerably.

- thumb sucking
- tapping one's feet
- arm and hand movements (flapping, shaking, waving…)
- pacing.

Tics and stereotypies

	Repetitiveness	Goal-directed	Volitional control	Sensory antecedent	Emotional antecedent	Cognitive-ideational antecedent
Tics	++ (occur in discrete bouts)	−	++	+++	+	−
Stereotypies	+++ (occur unchanged for long periods of time)	−	+	− Rewarding sensations may occur after the motor behavior	−	−

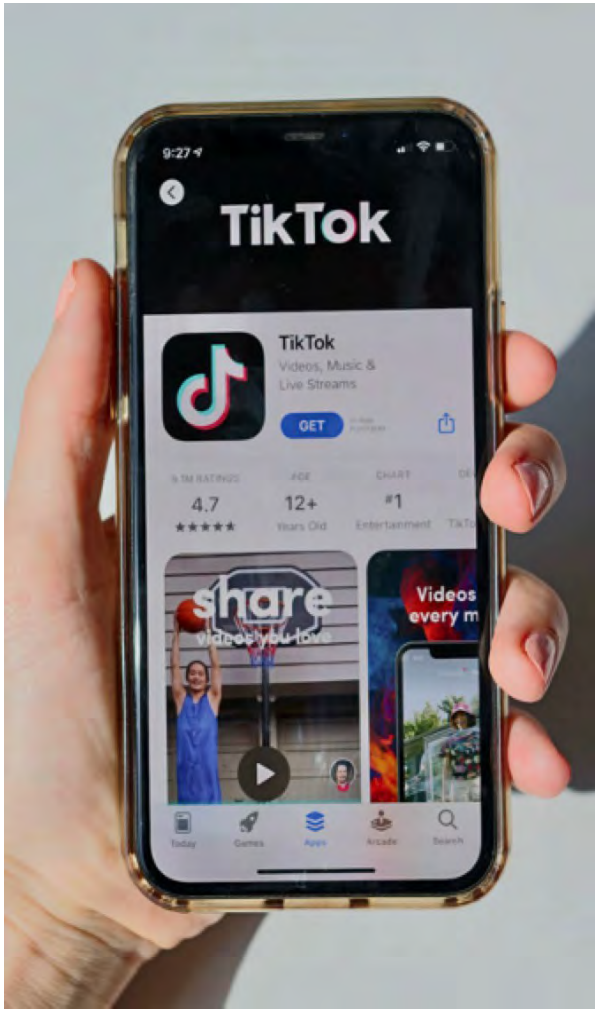
Source: Adapted from Martino D, Espay A, Fasano A, Morgante F. Disorders of Movement: A Guide to Diagnosis and Treatment. Springer; 2015.

Functional tic-like behaviours (FTLB)

Movements or vocalizations that resemble tics.

Unlike Tourette syndrome:

- Late and rapid onset
- Large-amplitude arm movements, self-injurious behaviour, coprophenomena, bizarre words and phrases.
- Complex tics >simple tics
- May be influenced by popular references (TikTok).



Pringsheim et al., 2021; Müller-Vahl et al., 2021

Functional tic-like behaviours (FTLB)

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european journal of neurology
the official journal of the european academy of neurology

ORIGINAL ARTICLE

European Society for the Study of Tourette Syndrome 2022 criteria for clinical diagnosis of functional tic-like behaviours: International consensus from experts in tic disorders

Tamara Pringsheim[1] | Christos Ganos[2] | Christelle Nilles[1] | Andrea E. Cavanna[3,4,5] | Donald L. Gilbert[6,7] | Erica Greenberg[8] | Andreas Hartmann[9] | Tammy Hedderly[10] | Isobel Heyman[11] | Holan Liang[11] | Irene Malaty[12] | Osman Malik[13] | Nanette Mol Debes[14,15] | Kirsten Muller Vahl[16] | Alexander Munchau[17] | Tara Murphy[11] | Peter Nagy[18] | Tamsin Owen[10] | Renata Rizzo[19] | Liselotte Skov[20] | Jeremy Stern[21] | Natalia Szejko[22] | Yulia Worbe[23] | Davide Martino[1]

How to diagnose FTLB

Pringsheim et al, 2022

Clinically definite diagnosis : 3 major criteria

Clinically probable diagnosis : 2 major criteria +1 minor criterion

Major criteria	Age onset ≥12 yr
	Rapid onset and evolution of symptoms
	Phenomenology :4/9
Minor criteria	Comorbid depression or anxiety disorder
	Other functional neurological symptoms/ somatoform disorders

Complex >simple tic-like behaviours
Variable reproduction
Complex tic-like behaviours: banging chest/head, tapping, hitting others, sign language, throwing objects, offensive gestures, drop attacks, context dependent, self- injury or injury to others
Do not to follow the typical rostrocaudal progression
Coprolalia, context-dependant words, statements
Popular culture references
Large variation in symptom frequency and intensity in a day
Tic-like behaviours change rapidly
More tic-like behaviours during the examination

Secondary tics

If you suspect secondary tics - order brain MRI!

- Exposure to drugs (neuroleptics) and toxic substances (cocaine)
- Neurodegenerative illnesses (Huntington, neuroacanthocytosis, NBIA)
- Acute brain lesions (vascular, trauma)
- Infectious causes (VZV, HSV) & immune-mediated conditions (postviral encephalitis)

Clues :

- A late age of onset of tics without a prior/family history of tics
- An abrupt onset
- An association with other neurological manifestations.

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NULL HYPOTHESIS | February 10, 2021 |

Check for updates

Association of Group A *Streptococcus* Exposure and Exacerbations of Chronic Tic Disorders

A Multinational Prospective Cohort Study

VIEW EDITORIAL

Davide Martino, MD, PhD, Anette Schrag, MD, PhD, Zacharias Anastasiou, PhD, Alan Apter, MD, Noa Benaroya-Milstein, MD, PhD, Maura Buttiglione, PhD, Francesco Cardona, MD, Roberta Creti, PhD, Androulla Efstratiou, PhD, Tammy Hedderly, MD, Isobel Heyman, MBBS, PhD, FRCPsych, Chaim Huyser, MD, PhD, Marcos Madruga, MD, Pablo Mir, MD, PhD, Astrid Morer, MD, PhD, Nanette Mol Debes, MD, PhD, Natalie Moll, MSc, Norbert Müller, MD, Kirsten Müller-Vahl, MD, Alexander Munchau, MD, Peter Nagy, MD, Kerstin Jessica Plessen, MD, PhD, Cesare Porcelli, MD, Renata Rizzo, MD, PhD, Veit Roessner, MD, PhD, Jaana Schnell, MSc, Markus Schwarz, MD, PhD, Liselotte Skov, MD, Tamar Steinberg, MD, Zsanett Tarnok, PhD, Susanne Walitza, MD, MSc, Andrea Dietrich, PhD, Pieter J. Hoekstra, MD, PhD, and on behalf of the EMTICS Collaborative Group SHOW FEWER AUTHORS INFO & AFFILIATIONS

March 23, 2021 issue • 96 (12) e1680-e1693 • https://doi.org/10.1212/WNL.0000000000011610

The clinical interview

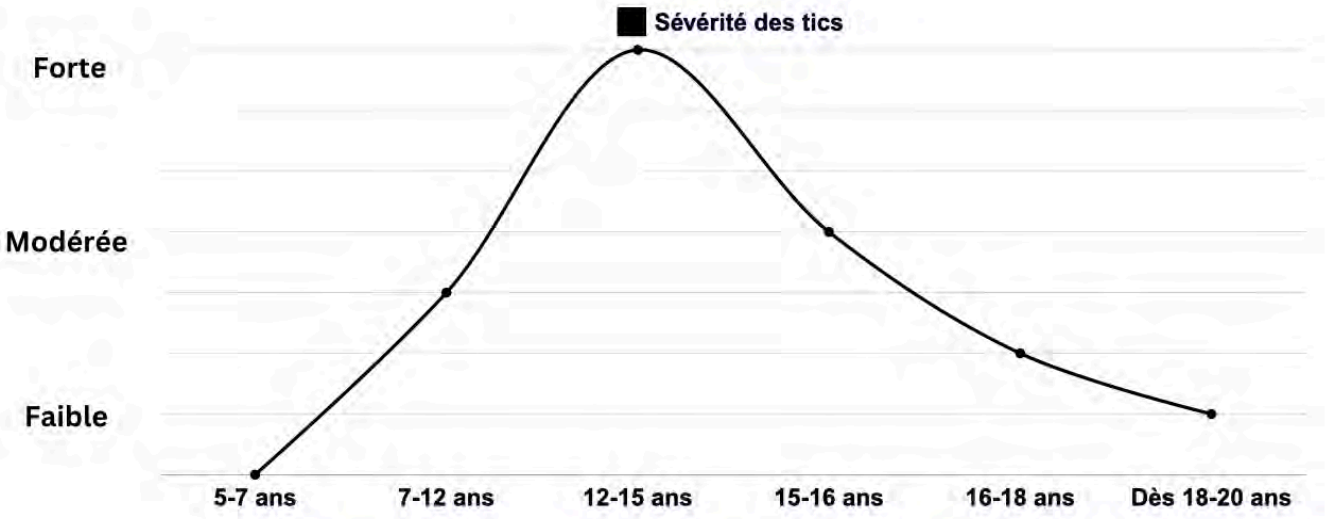
- What was the primary reason for referral? (tics, comorbidities?)
- History of pregnancy and birth
- Developmental milestones
- Past medical history
- Family history
- Overview of the medication
- Social history

The clinical interview

- When was the onset?
- What was the first/were the first tics? Course?
- What are the current tics? (YGTSS)
- Other typical features for tics (PU, suppressibility, distractibility, suggestibility)
- Factors influencing tics
- Medication for tics, behavioral therapy
- History of comorbidities (ADHD, OCD, depression, anxiety, rage attacks, sleeping problems)

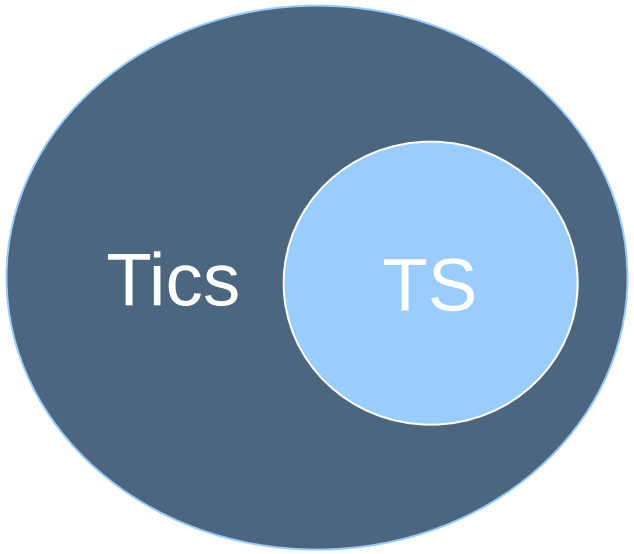
Natural history of TS

- Begins in childhood
- Severity peak during adolescence
- Significant reduction/arrest at adult age in 75% of cases



Epidemiology

- 0.3-0.8% of school age children
- Transient motor tics during childhood: 15-25%
- M:F ratio – 4:1



TS Genetics

- Global risk in first degree relatives ~ 10-15% *(Pauls 2003)*
- Autosomal-dominant transmission with variable expression/penetrance ?
- Polygenic transmission ?

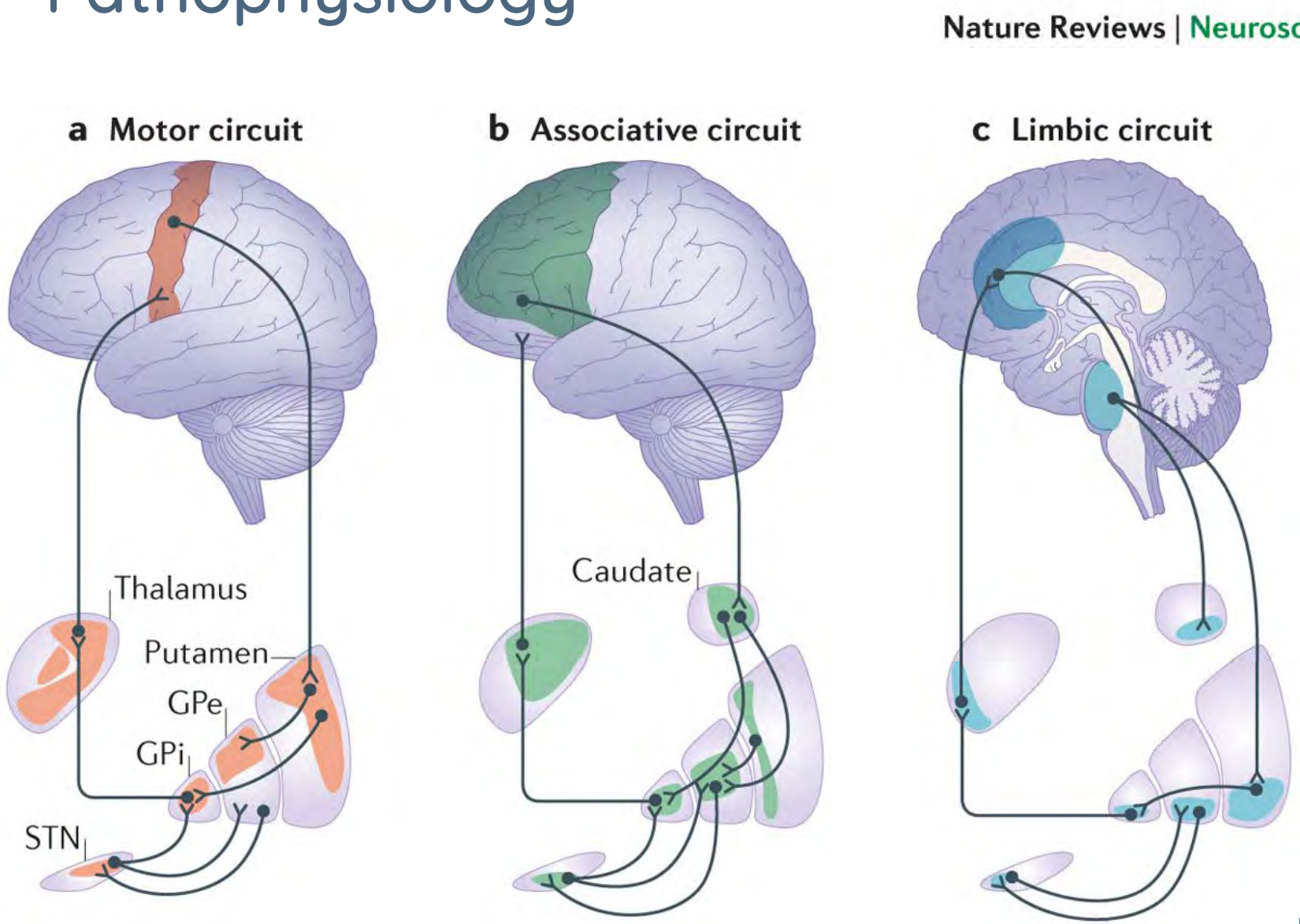
TS Genetics

- Genes involved in TS are difficult to identify !

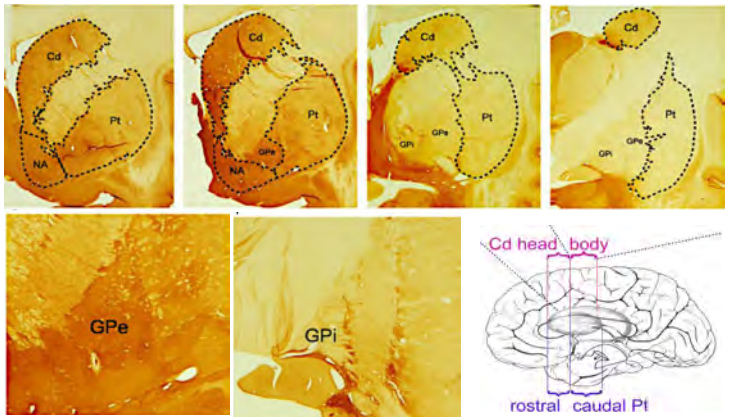
- Possible reasons:
  - Genetic heterogenetity
  - Several disorders
  - Several modes of inheritance
  - Interactions with environmental factors
  - Genetic factors contributing to TS missed by current methods
- Candidate genes identified point toward possible dysfunctions in synaptic or other neuronal processes
- No explanation for the excess of males in TS

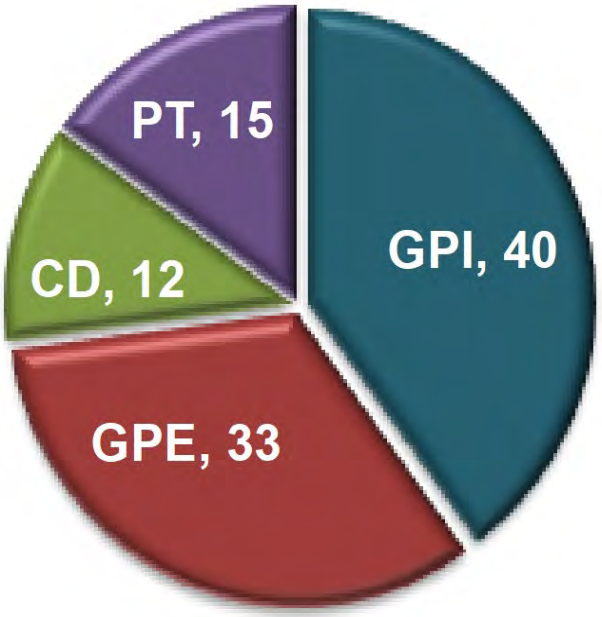
- Overlap between factors involved in TS and other ‘psychiatric’ disorders including ASD, ADHD, OCD, MDD, migraine…

Pathophysiology

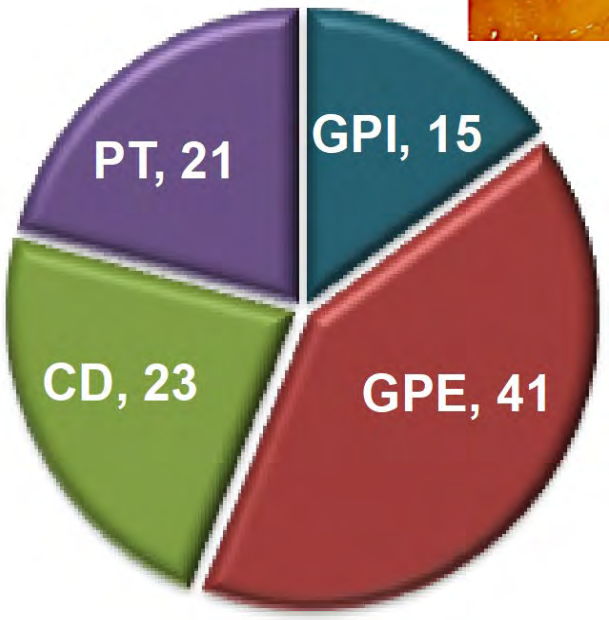


Neuropathology : neuronal migration





Patient



Controls

Kalanithi et al., PNAS 2005; Kataoka et al., J of Com Neurol 2010

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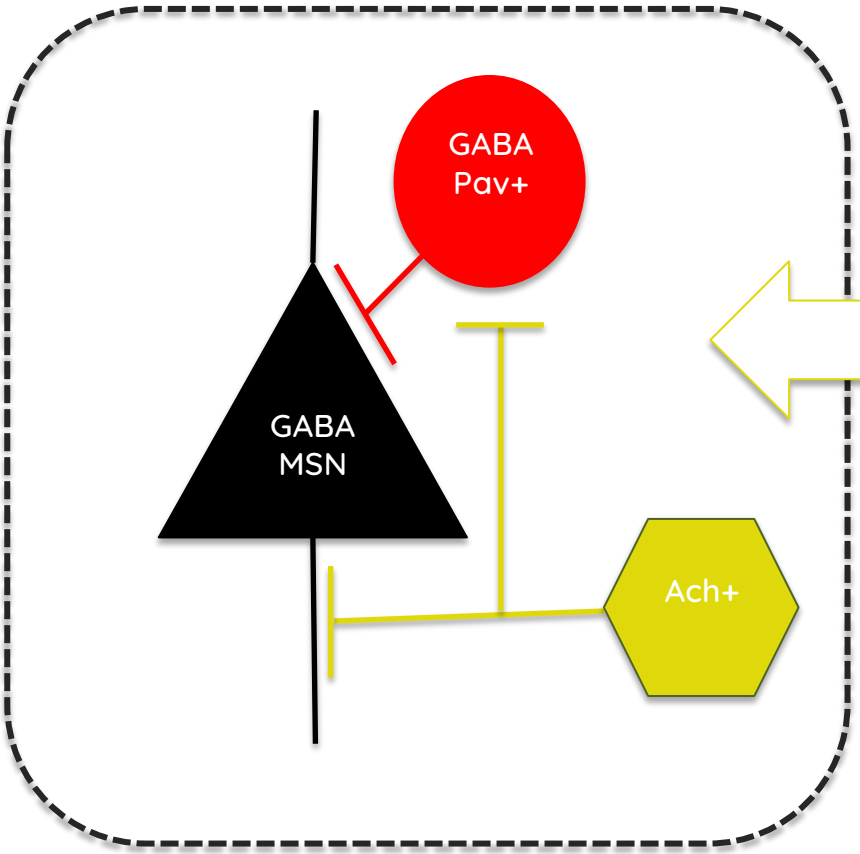
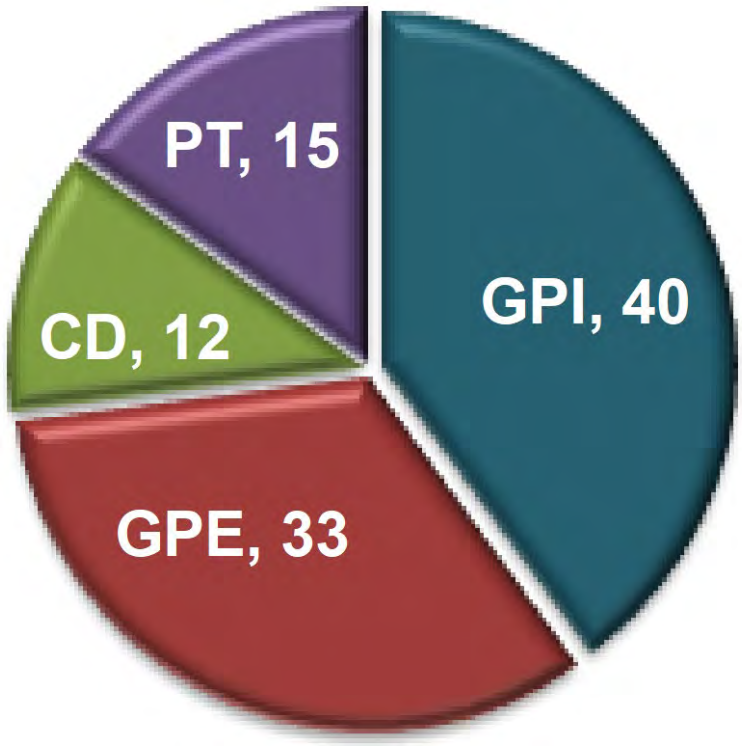
Neuropathology : basal ganglia inhibition





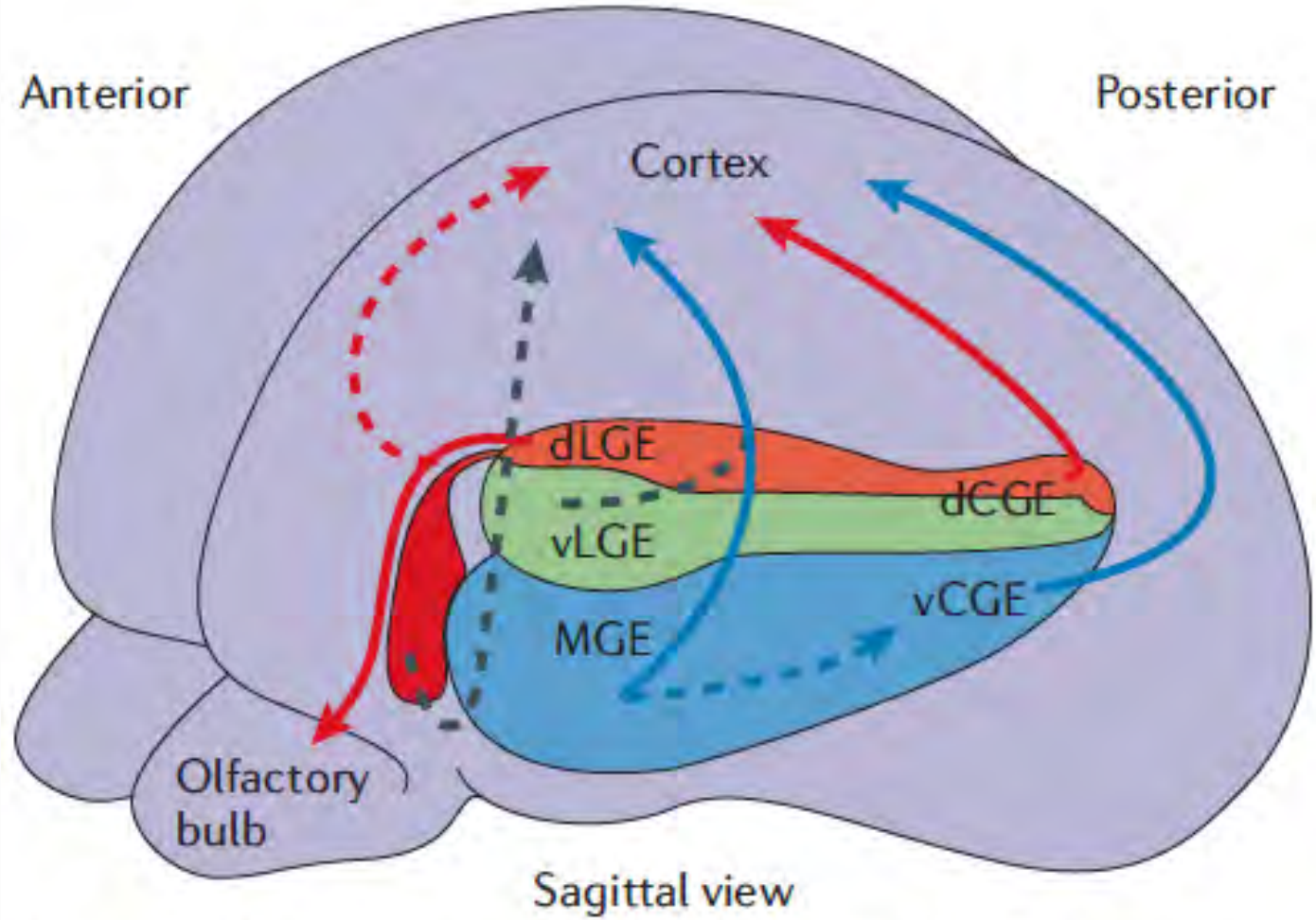
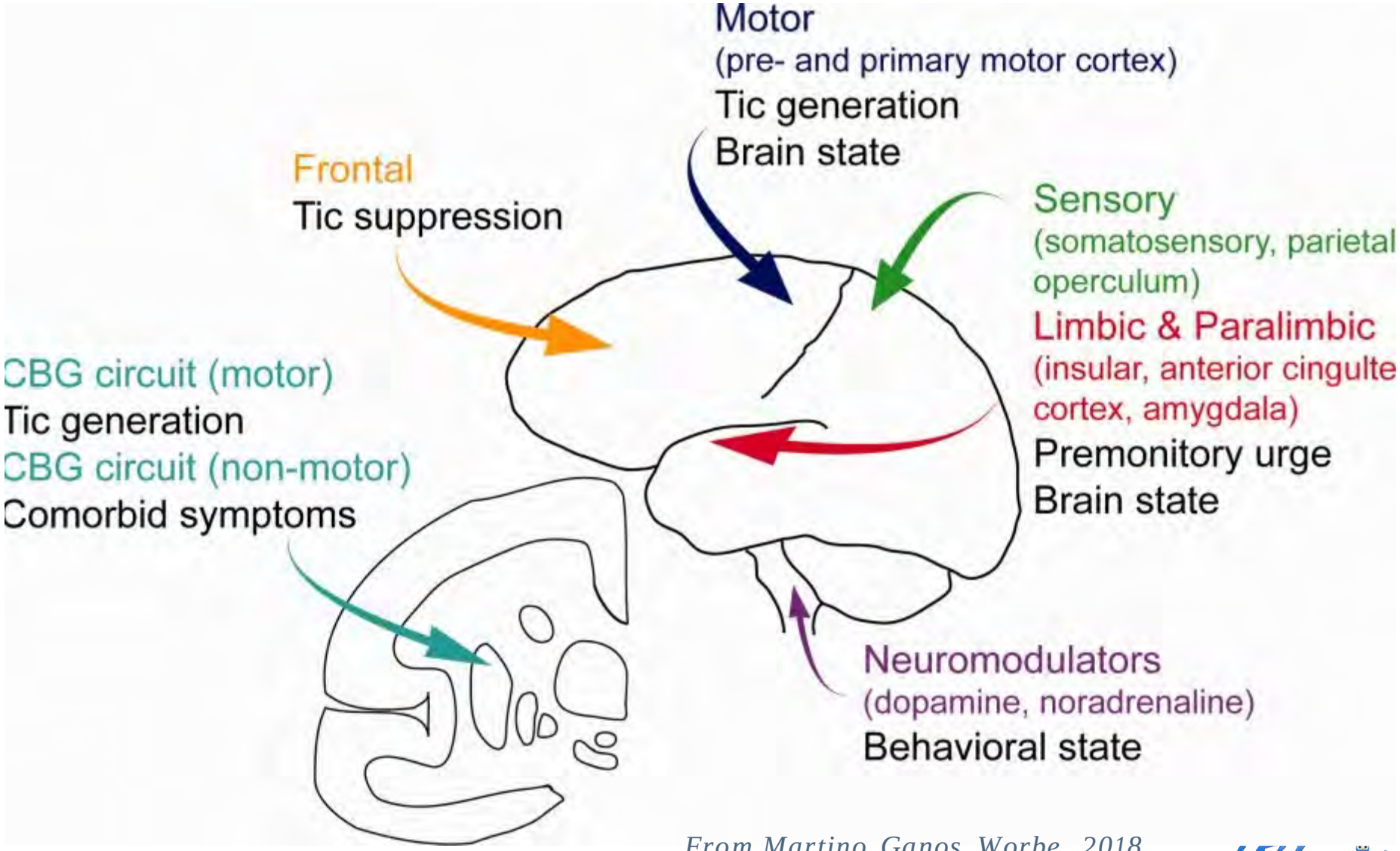
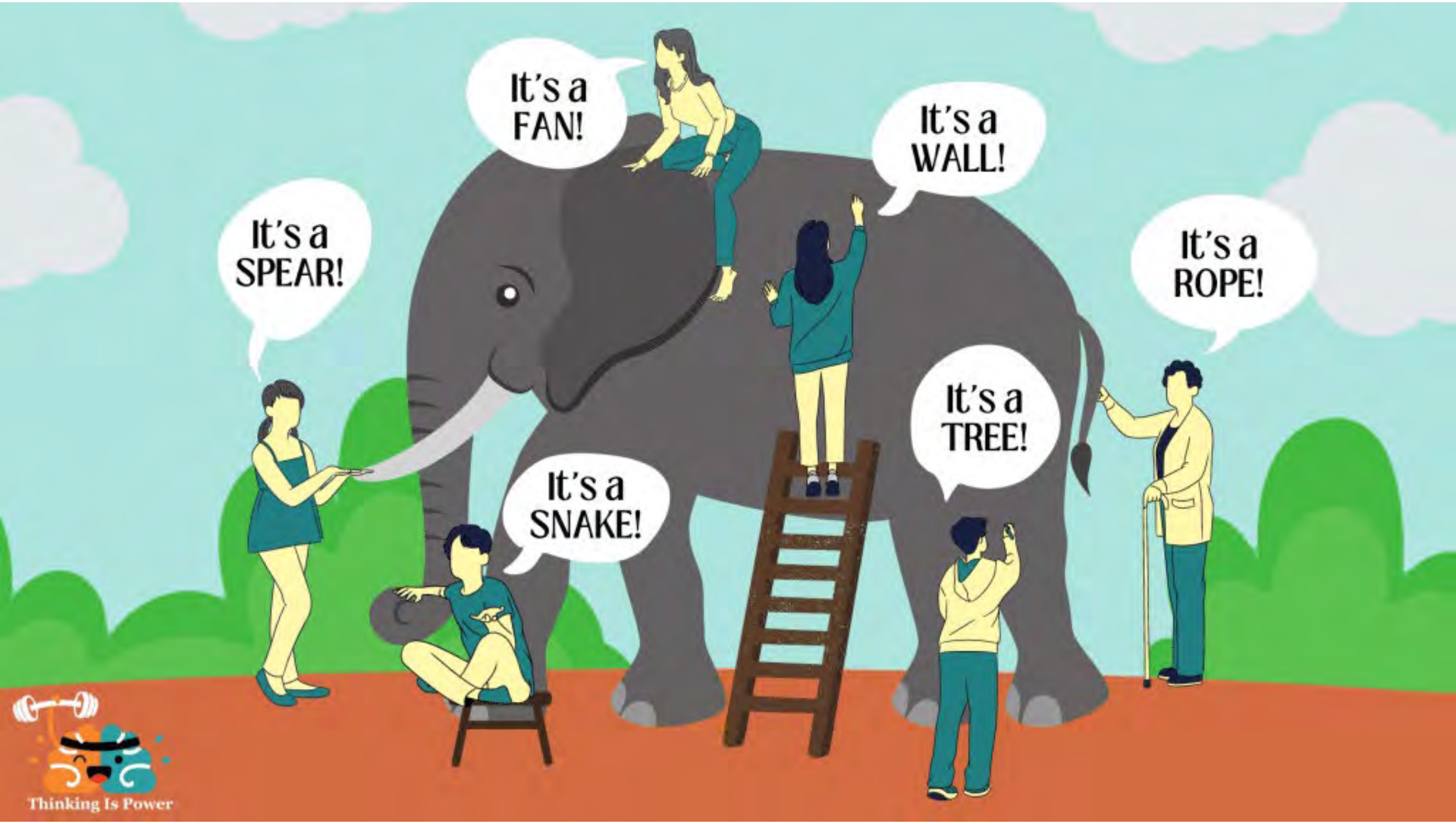


Figure 1 | **Migration pathways of cortical interneuron subgroups from the ventral telencephalon.** Schematic

Pathophysiology : Résumé



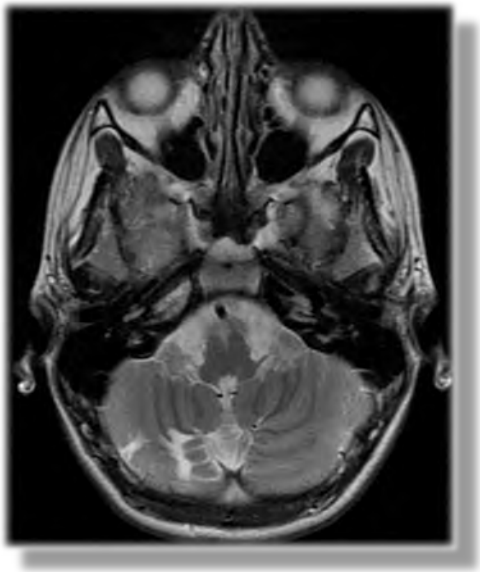
From Martino, Ganos, Worbe , 2018


It's a FAN!
It's a WALL!
It's a SPEAR!
It's a ROPE!
It's a TREE!
It's a SNAKE!
Thinking Is Power

Therapy

- Psychoeducation
- Control tics, if *troublesome*
- Non-pharmacologic vs. pharmacologic approaches
- Treatment of comorbidities
- Treatment of behavioral abnormalities
- Prioritize problems (tics, LD, ADHD, ASD, OCD)

When to treat



- Tics cause sustained social problems for the patient (e.g., social isolation or bullying)
- Tics cause social and emotional problems for the patient (e.g., reactive depressive symptoms)
- Tics cause functional interference (attention)
- Tics cause subjective discomfort (e.g. pain or injury)

Treatment types

- Non-pharmacologic
  - Behavioral therapies (BT)
- Pharmacologic
  - Drugs
  - Botulinum toxin
- Surgical
  - Deep brain stimulation

European Child & Adolescent Psychiatry
https://doi.org/10.1007/s00787-021-01845-z

REVIEW

European clinical guidelines for Tourette syndrome and other tic disorders—version 2.0. Part II: psychological interventions

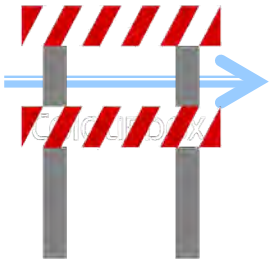
Per Andrén[1] · Ewgeni Jakubovski[2] · Tara L. Murphy[3] · Katrin Woitecki[4] · Zsanett Tarnok[5] · Sharon Zimmerman-Brenner[6] · Jolande van de Griendt[7] · Nanette Mol Debes[8] · Paula Viefhaus[4] · Sally Robinson[9] · Veit Roessner[10] · Christos Ganos[11] · Natalia Szejko[12,13,14] · Kirsten R. Müller-Vahl[2] · Danielle Cath[15] · Andreas Hartmann[16] · Cara Verdellen[17]

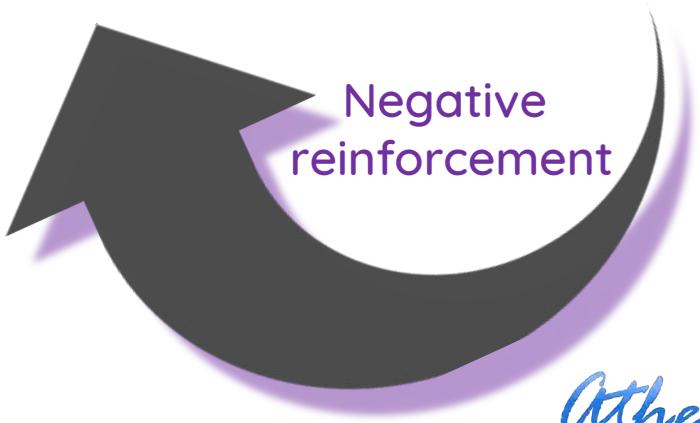
Received: 9 March 2021 / Accepted: 7 July 2021

BT: theoretic principle

Stimulus  Response  Consequence

Tic blockage

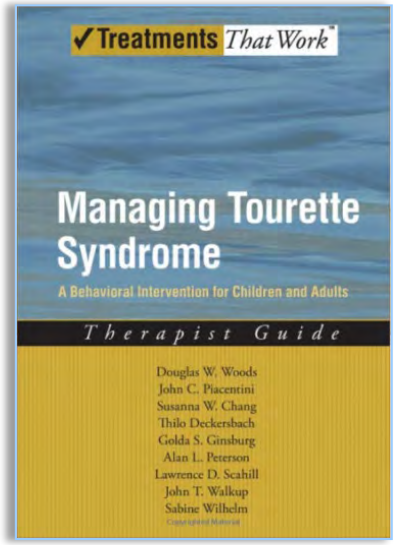
Premonitory sensation  TIC  Relief



BT for tics: two methods

Habit reversal training (HRT):

- Treat tics one by one
- Awareness training and competing response training
- Change environmental factors



Exposure and response prevention (ERP):

- Targets all tics at once
- Resisting tics for a long period of time
- Exposure to premonitory urges

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STUDY	N	Mean AGE M(SD)	Condition	YGTSS Pre	YGTSS Post	% improvement	Effect Size
Wilhelm et al, 2003 HRT – ST	32	36.2 (12.7)	HRT ST	30.5 26.6	19.8 26.9	35.1% -1.1%	1.50 -0.03
Verdellen et al, 2004 HRT – ERP	43	20.6 (12.1)	HRT ERP	24.1 26.2	19.7 17.6	18.3% 32.8%	1.06 1.42
Deckersbach et al, 2006 HRT – ST	30	35.1 (12.2)	HRT ST	29.3 27.7	18.3 26.8	37.5% 3.2%	
Piacentini et al, 2010 HRT- ST	126	11.7 (2.3)	HRT PE	24.7 24.6	17.1 21.1	30.8% 14.2%	0.68
Wilhelm et al, 2012 HRT - ST	122	31.5 (13.7)	HRT ST	24.0 21.8	17.8 19.3	25.8% 11.5%	0.57
Yates et al, 2016 Group HRT -PE	32	12.06 (1.38)	G HRT PE	29.0 30.5	25.6 27.2	18% 11%	0.39

Athens

BT for tics: the future

- Group therapy

(Yates et al. 2016; Nissen et al. 2018; Dabrowski et al. 2018)

- Videoconference therapy

(Himle et al. 2018)

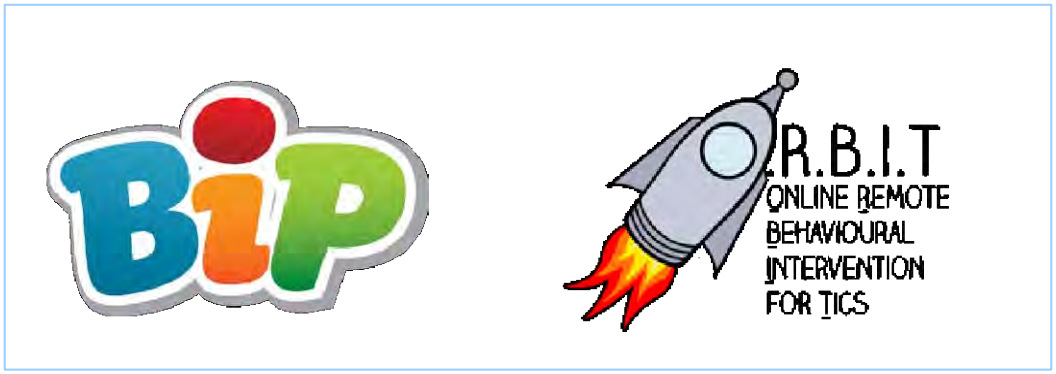
- Online therapy

(www.tichelper.com; ONLINE-TICS: Jakubovski et al. 2016)

- Apps and learning devices

(BT coach – www.bt-tics.com/btcoach)

BT for tics: the best of both worlds



Therapist-supported online remote behavioural intervention for tics in children and adolescents in England (ORBIT): a multicentre, parallel group, single-blind, randomised controlled trial

Chris Hollis, Charlotte L Hall, Rebecca Jones, Louise Marston, Marie Le Novere, Rachael Hunter, Beverley J Brown, Charlotte Sanderson, Per Andrén, Sophie D Bennett, Liam R Chamberlain, E Bethan Davies, Amber Evans, Natalia Kouzoupi, Caitlin McKenzie, Isobel Heyman, Kareem Khan, Joseph Kilgariff, Cristine Glazebrook, David Mataix-Cols, Tara Murphy, Eva Serlachius, Elizabeth Murray

Advice to patients

Ancient (intuitive)

- Ignore tics
- Tics cannot be controlled
- Evacuate tics
- Behavioural approaches/therapies don't work
- Tic suppression increases tics
- Tic suppression increases premonitory sensation
- Tic suppression creates new/different tics

New (counter-intuitive)

- Becoming aware of tics
- Learn to conrol tics
- Reward tic control
- Use behavioura approaches/therapies
- Tic suppression does not increase tics
- Tic suppression does not increase premonitory sensation
- Tic suppression does not create new/different tics

European Child & Adolescent Psychiatry
https://doi.org/10.1007/s00787-021-01899-z

REVIEW

European clinical guidelines for Tourette syndrome and other tic disorders—version 2.0. Part III: pharmacological treatment

Veit Roessner[1] · Heike Eichele[2,3] · Jeremy S. Stern[4] · Liselotte Skov[5] · Renata Rizzo[6] · Nanette Mol Debes[5] · Péter Nagy[7] · Andrea E. Cavanna[8] · Cristiano Termine[9] · Christos Ganos[10] · Alexander Münchau[11] · Natalia Szejko[12,13,14] · Danielle Cath[15] · Kirsten R. Müller-Vahl[16] · Cara Verdellen[17,18] · Andreas Hartmann[19,20] · Aribert Rothenberger[21] · Pieter J. Hoekstra[22] · Kerstin J. Plessen[23,24]

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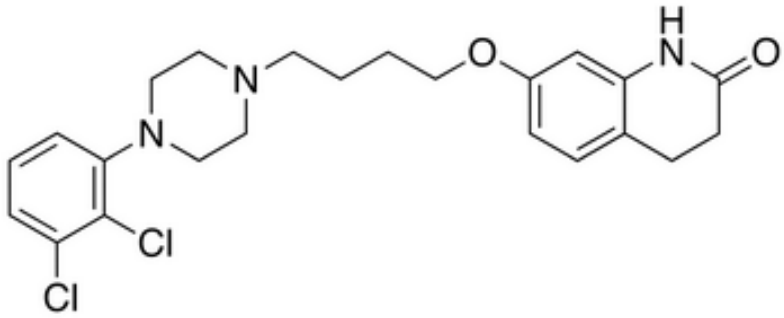
Pharmacologic treatments - principles

- Treatment is symptomatic, non-curative, long-term, with partial efficacy (30-80%)
- Wait at least 6-12 weeks to judge treatment efficacy (or lack thereof)
- Consider therapeutic windows

Pharmacologic treatments - types

- Antipsychotics
- Monoamine depletors
- Alpha2 adrenergic antagonists
- Benzodiazepines
- Anticonvulsants
- Cannabinioids
- Botulinum toxin (peripheral & vocal)

Aripiprazole



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Mary Ann Liebert, Inc.
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DOI: 10.1089/cap.2016.0026

Randomized, Double-Blind, Placebo-Controlled Trial Demonstrates the Efficacy and Safety of Oral Aripiprazole for the Treatment of Tourette's Disorder in Children and Adolescents

Floyd Sallee, MD,[1] Eva Kohegyi, MD,[2] Joan Zhao, PhD,[2] Robert McQuade, PhD,[2] Kevin Cox, MD,[2] Raymond Sanchez, MD,[2] Alet van Beek, BSc,[3,*] Margaretta Nyilas, MD,[2] William Carson, MD,[2] and Roger Kurlan, MD[4]

Athens

Aripiprazole

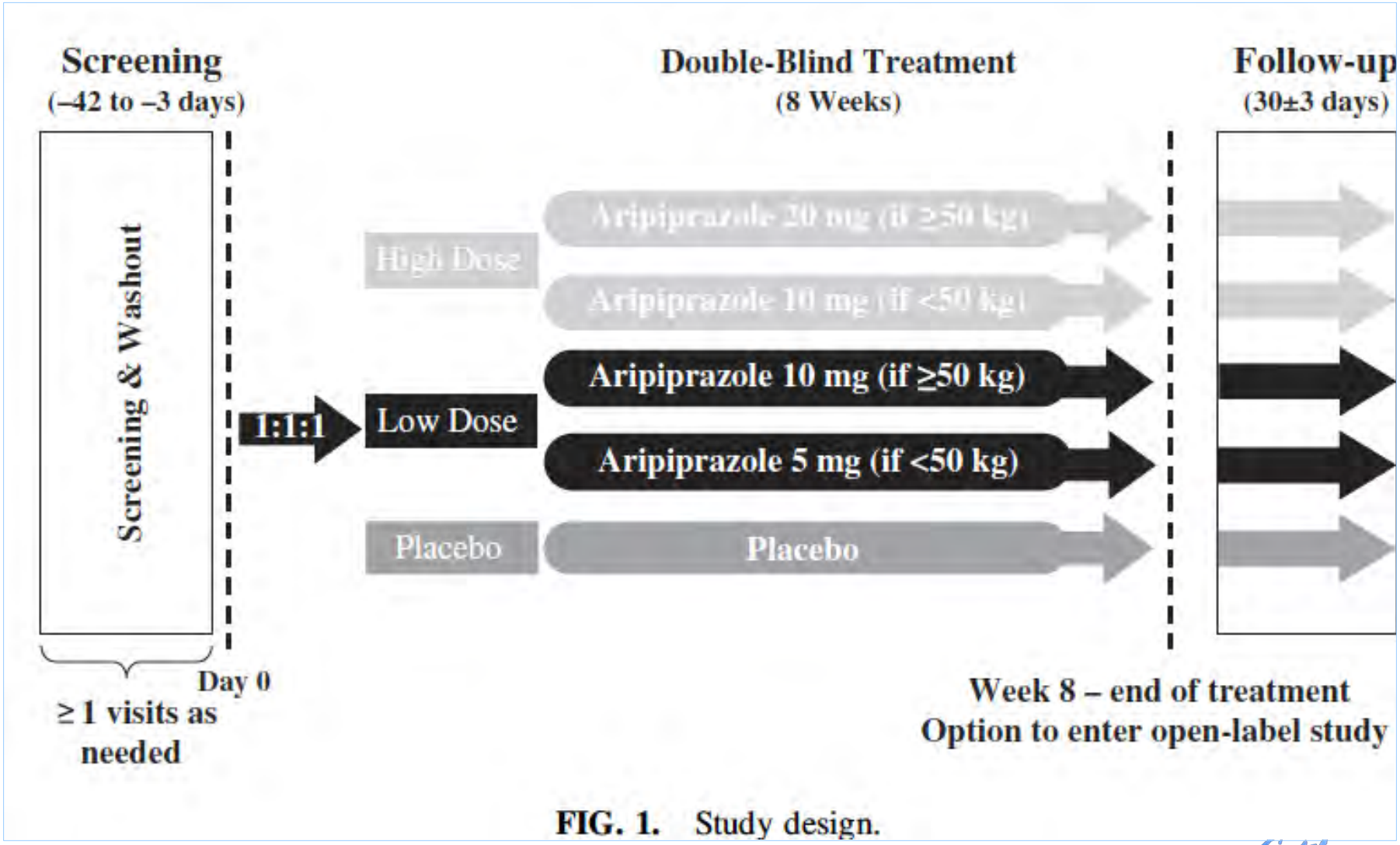
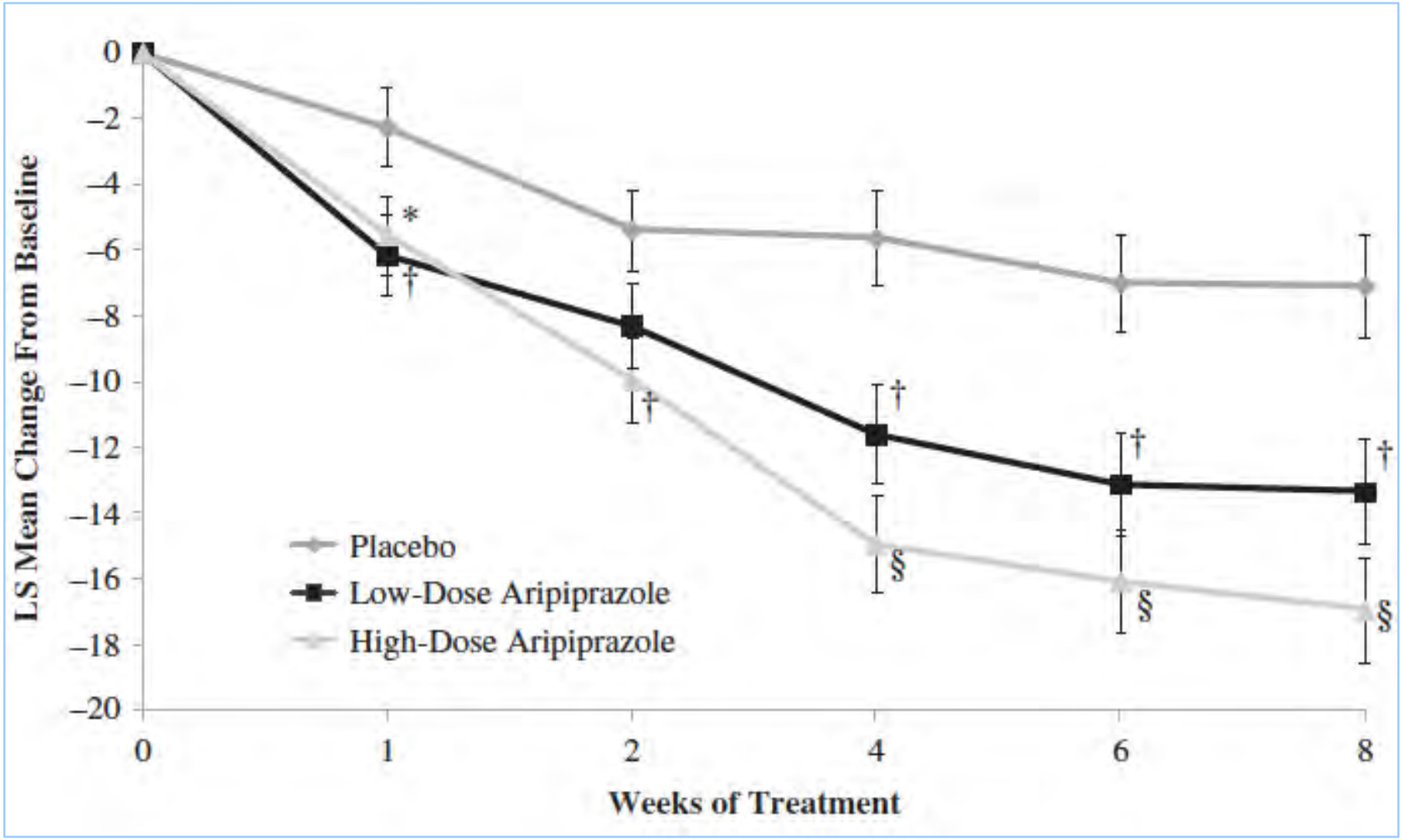


FIG. 1. Study design.

Aripiprazole



Low-dose Aripiprazole

Does TS prevent tardive dyskinesia ?

In Tourette syndrome (TS) neuroleptics (NLs) are the most effective drugs for the treatment of tics. However, because of concern about NL-induced tardive dyskinesia (TD), less effective drugs are often used. In a general psychiatric population, the annualized TD incidence is 3.9% for second-generation antipsychotics (SGAs) and 5.5% for first-generation antipsychotics (FGAs), respectively.[1] Surprisingly, in TS there are only 11 case studies available reporting about a total of 20 patients with suggested NL-induced TD

To investigate the annualized TD incidence in a large TS sample, we reviewed the records of 917 outpatients (male, 722 [78.7%]; female, 195 [21.3%]; mean age, 20.5 ± 12.7 years; range, 2–72 years). All patients were investigated by 1 of the authors (K.M.V.), including a detailed medical history

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Published online 28 September 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23894

Müller-Vahl KR, Krueger D. Mov Disord. 2011 Nov;26(13):2442-3.

Athens

An alternative/complement to antipsychotics

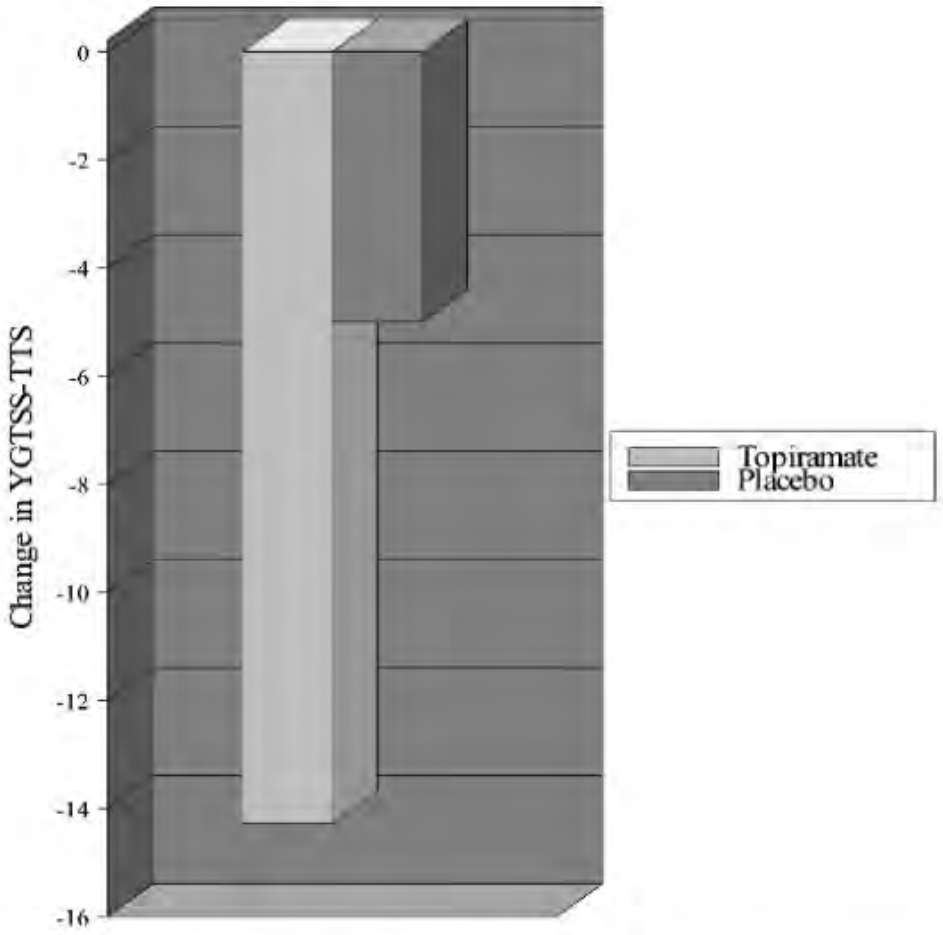

Figure 2 Change from baseline to visit 5 (day 70) in Total Tic Score component of Yale Global Tic Severity Scale (YGTSS-TTS) in response to topiramate.

A randomised, double-blind, placebo-controlled study of topiramate in the treatment of Tourette syndrome.

J Neurol Neurosurg Psychiatry 2010;**81**:70–73. doi:10.1136/jnnp.2009.185348

Jankovic J, Jimenez-Shahed J, Brown LW

European Child & Adolescent Psychiatry
https://doi.org/10.1007/s00787-021-01881-9

REVIEW

European clinical guidelines for Tourette syndrome and other tic disorders—version 2.0. Part IV: deep brain stimulation

Natalia Szejko[1,2,3] · Yulia Worbe[4,5] · Andreas Hartmann[14] · Veerle Visser-Vandewalle[6] · Linda Ackermans[7] · Christos Ganos[8] · Mauro Porta[9] · Albert F. G. Leentjens[10] · Jan-Hinnerk Mehrkens[11] · Daniel Huys[12] · Juan Carlos Baldermann[12] · Jens Kuhn[12,13] · Carine Karachi[5,14,15] · Cécile Delorme[14] · Thomas Foltynie[16] · Andrea E. Cavanna[17] · Danielle Cath[18,19] · Kirsten Müller-Vahl[20]

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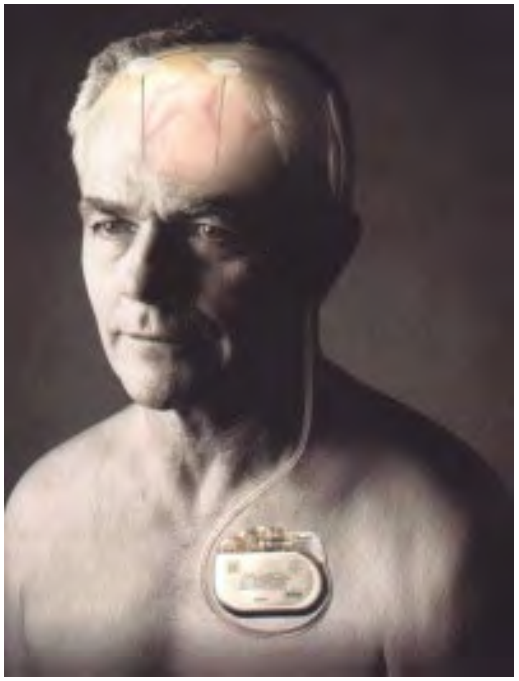
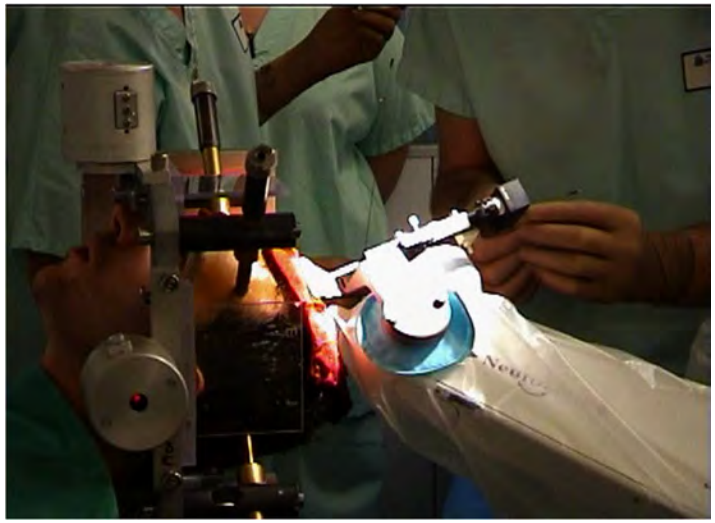
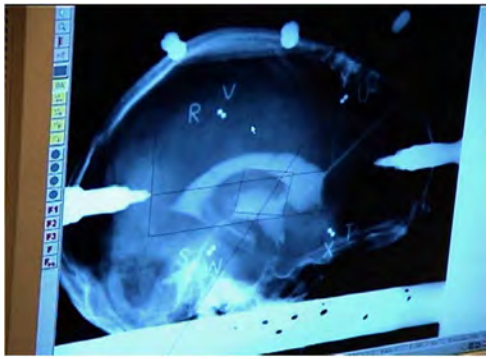
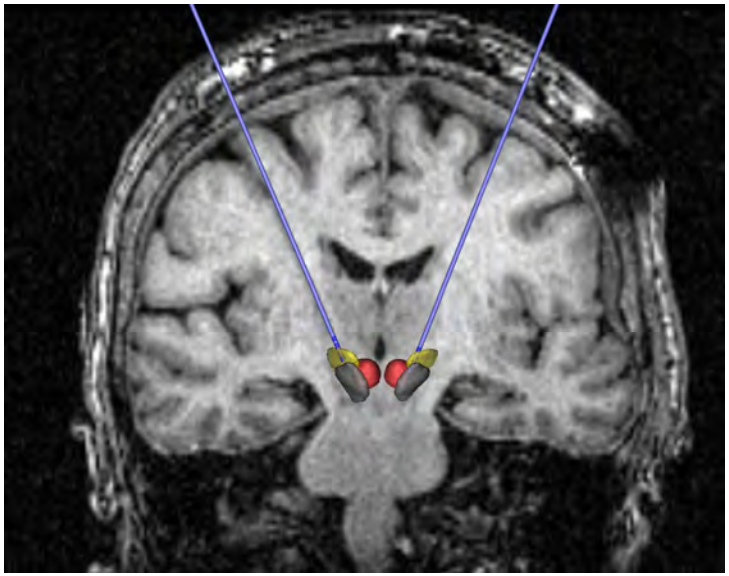
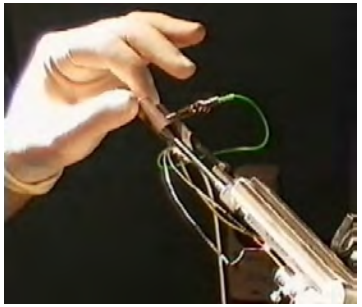
ESSTS

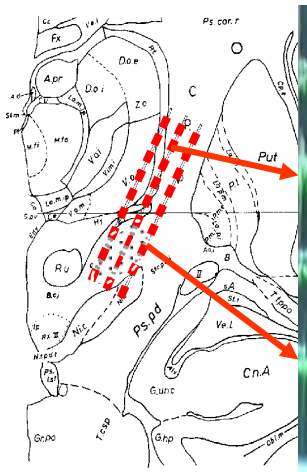








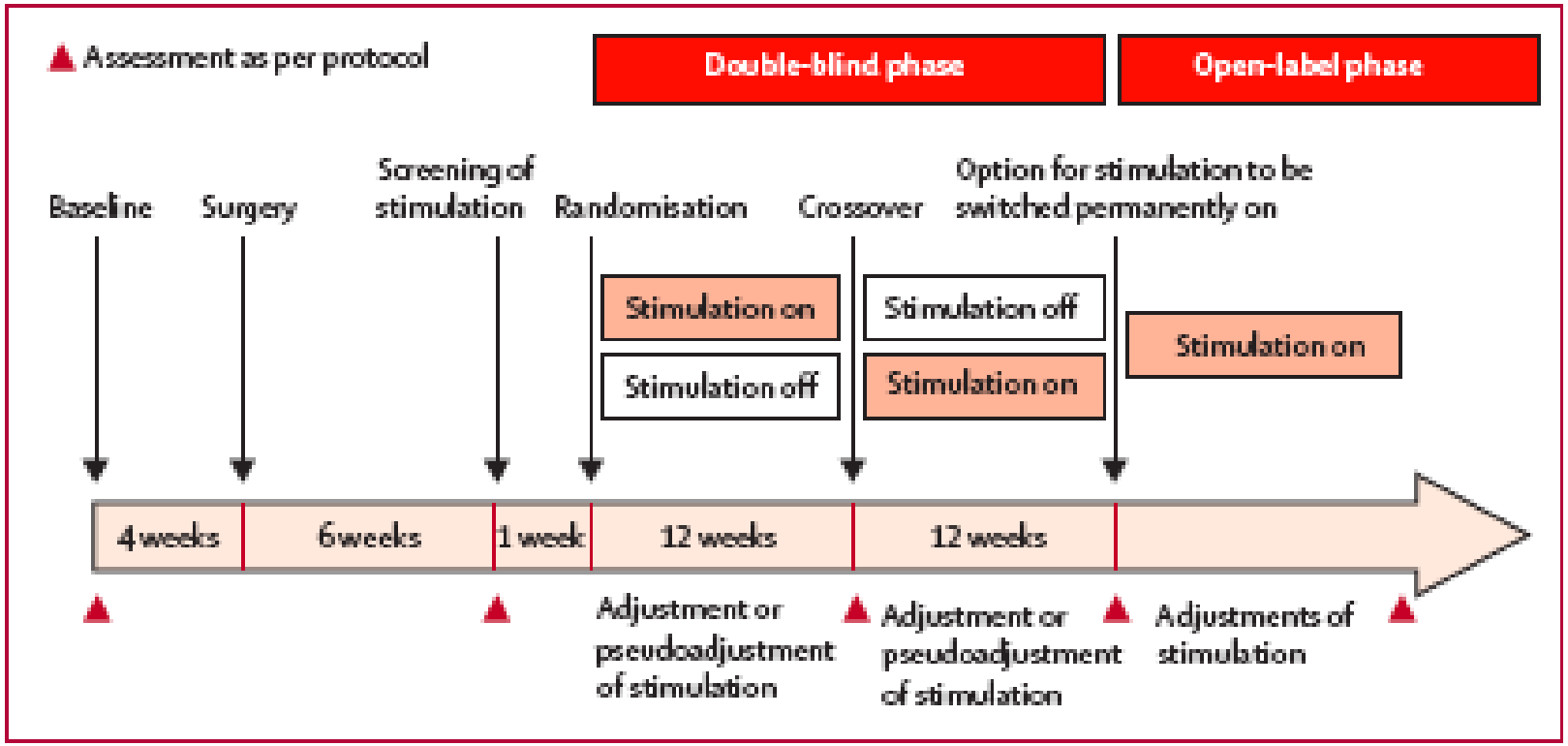




Bilateral globus pallidus stimulation for severe Tourette's syndrome: a double-blind, randomised crossover trial

Zinovia Kefalopoulou, Ludvic Zrinzo, Marjan Jahanshahi, Joseph Candelario, Catherine Milabo, Mazda Beigi, Harith Akram, Jonathan Hyam, Jennifer Clayton, Lewis Kass-Iliyya, Monty Silverdale, Julian Evans, Patricia Limousin, Marwan Hariz, Eileen Joyce, Thomas Foltynie

Lancet Neurol 2015; 14: 595–605



ESSTS

	YGTSS score						Difference in YGTSS scores	
	Baseline	6 weeks postoperative	Treatment group	Blinded off-stimulation	Blinded on-stimulation	Open-label on-stimulation	Blinded phase (off-stimulation period vs on-stimulation period)	Baseline vs open-label stimulation phase
Patient A	80	48	Off, on	68	39	33	29 (43%)	47 (59%)
Patient B	99	98	Off, on	99	78	42	21 (21%)	47 (58%)
Patient C	93	92	NA	NA	NA	4	..	89 (96%)
Patient D	87	74	Off, on	85	66	63	19 (22%)	24 (28%)
Patient E	81	81	Off, on	81	81	66	0	15 (19%)
Patient F	93	70	On, off	67	59	48	8 (12%)	45 (48%)
Patient G	74	75	On, off	75	77	74	−2 (−3%)	0
Patient H	93	79	Off, on	82	63	49	19 (23%)	44 (47%)
Patient I	82	83	On, off	NA	NA	47	..	35 (43%)
Patient J	80	55	On, off	67	62	62	5 (7%)	18 (23%)
Patient K	96	96	On, off	70	55	46	15 (21%)	50 (52%)
Patient L	71	59	Off, on	71	71	59	0	12 (17%)
Patient M	98	97	On, off	94	97	83	−3 (−3%)	15 (15%)
Patient N	99	100	Off, on	98	100	51	−2 (−2%)	48 (48%)
Patient O	92	40	On, off	92	40	46	52 (57%)	46 (50%)
Mean (SD)	87·9 (9·2)	76·5 (19·1)	..	80·7 (12·0)	68·3 (18·6)	51·5 (18·5)	12·4 (15·9)	36·3 (22·6)
95% CI for mean difference (p value)	..	..	..	..	..	..	0·1–24·7 (p=0·048)*	23·8–48·9 (p<0·0001)†
Proportional mean difference (95% CI)	..	..	..	..	..	..	15·3% (5·3–25·3)	40·1% (28·1–52·1)

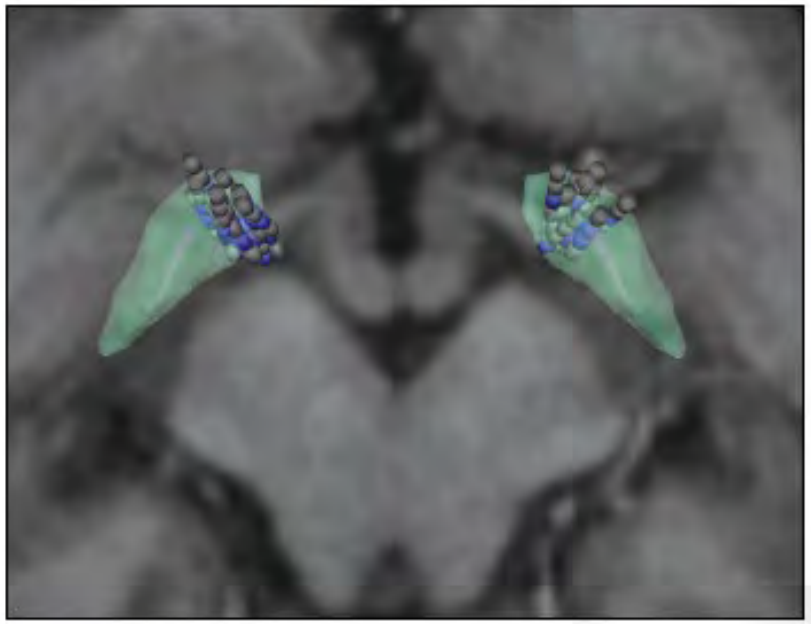
For purposes of maintaining confidentiality, the patient sequence presented in here (and in the appendix) does not correspond with the sequence presented in table 1. YGTSS total score on a scale of 0 to 100. This scale comprises a total tic severity subscore (providing an evaluation of the number, frequency, intensity, complexity, and interference of motor and vocal tics, ranging from 0 to 50) and an impairment subscore (taking into account difficulties in self-esteem, family life, social acceptance, or school or job functioning due to tics, ranges from 0 to 50), with higher scores suggesting greater severity. During trial recruitment, impairment subscore was transformed to a 0–5 analogue and added to the total tics severity subscore (ranging from 0 to 55). Positive difference means improvement. YGTSS=Yale Global Tic Severity Scale. NA=not available. *Primary endpoint analysis; pairwise comparisons of YGTSS total scores after Bonferroni correction. †Post-hoc analysis.

Table 2: Individual results for YGTSS total score in all patients

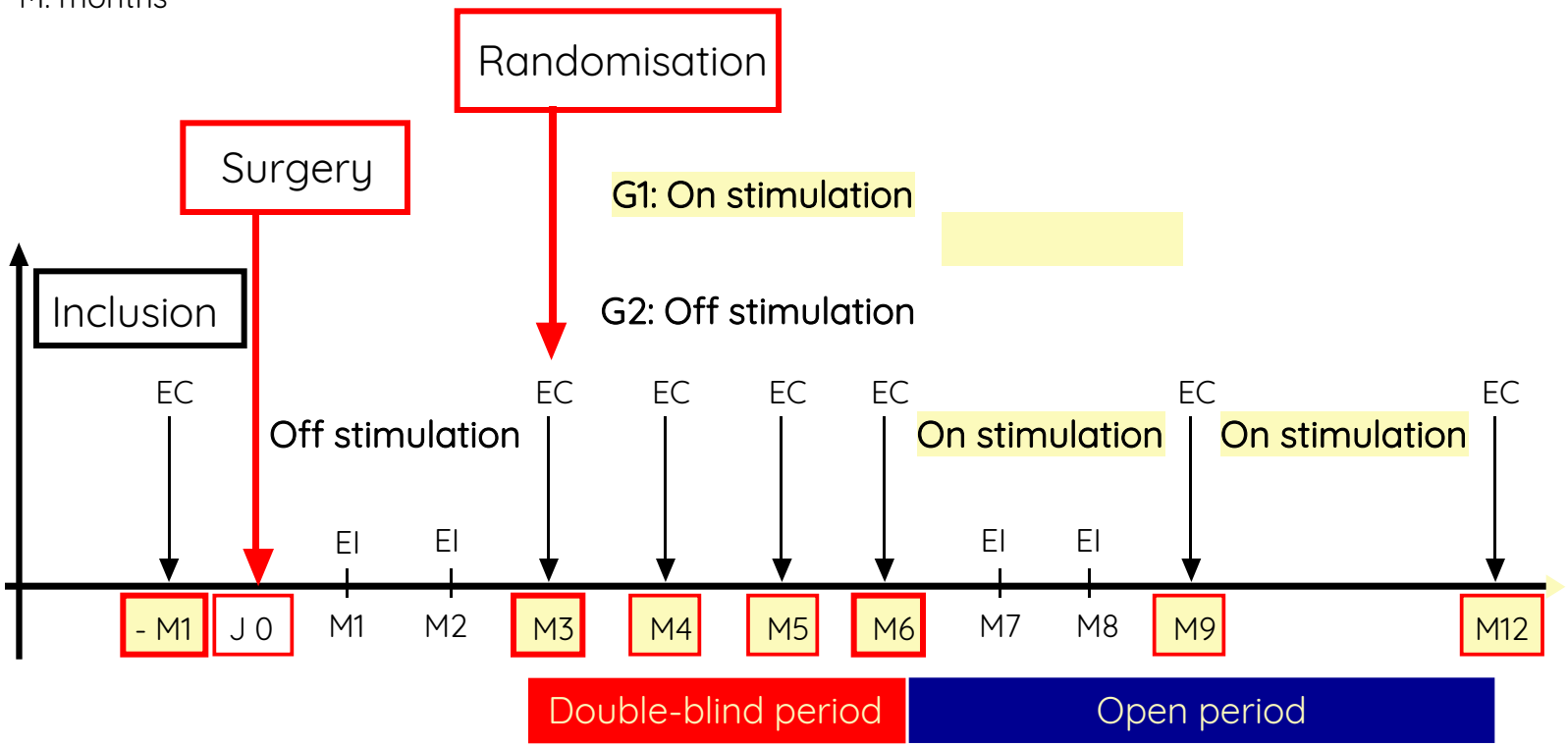
Anterior pallidal deep brain stimulation for Tourette's syndrome: a randomised, double-blind, controlled trial

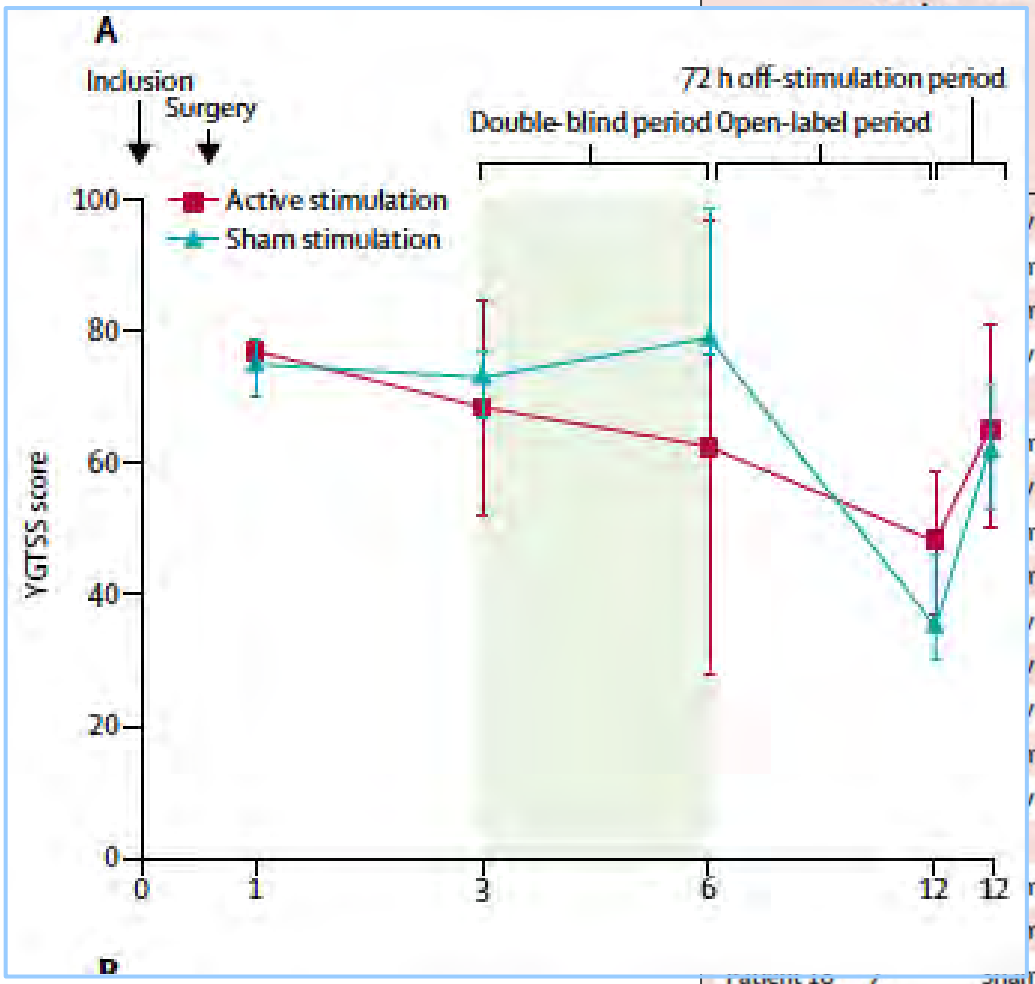
*Marie-Laure Welter, Jean-Luc Houeto, Stéphane Thobois, Benoit Bataille, Marc Guenot, Yulia Worbe, Andreas Hartmann, Virginie Czernecki, Eric Bardinet, Jerome Yelnik, Sophie Tezenas du Montcel, Yves Agid, Marie Vidailhet, Philippe Cornu, Audrey Tanguy, Solène Ansquer, Nematollah Jaafari, Emmanuel Poulet, Giulia Serra, Pierre Burbaud, Emmanuel Cuny, Bruno Aouizerate, Pierre Pollak, Stephan Chabardes, Mircea Polosan, Michel Borg, Denys Fontaine, Bruno Giordana, Sylvie Raoul, Tiphaine Rouaud, Anne Sauvaget, Isabelle Jalenques, Carine Karachi, Luc Mallet, for the STIC study group**

www.thelancet.com/neurology **Published online June 20, 2017** **http://dx.doi.org/10.1016/S1474-4422(17)30160-6**



7 EC: Complete assessment
5 EI: Partial assessment
M: months





	Centre	Stimulation	Sex	Age (years)	YGTSS score	Difference in YGTSS score	
					Inclusion	Double-blind phase (month 6 vs month 3)	Inclusion vs end of open-label active stimulation period (month 12)
			Male	57	77	14 (63%)	−48 (−62%)
			Male	22	76	0	−54 (−71%)
			Female	23	75	41 (108%)	−40 (−53%)
			Male	47	71	..	..
			Female	21	75	..	..
			Male	33	75	−32 (−43%)	−32(−43%)
			Male	31	82	−1 (−1%)	−11 (−13%)
			Female	19	67	1 (1%)	−40 (−60%)
			Female	22	79	−21 (−30%)	−55 (−70%)
			Male	22	63	−45 (−46%)	31 (49%)
			Male	37	83	1 (1%)	5 (6%)
			Male	40	58	25 (104%)	−22 (−37%)
			Male	28	97	−10 (−11%)	−17 (−18%)
			Male	28	81	8 (12%)	−33 (−41%)
			Male	27	78	..	..
			Male	21	95	3 (5%)	−71 (−75%)
			Female	57	68	−1 (−1%)	−28 (−41%)
			Male	21	71	6 (8%)	−34 (−48%)
Patient 19	9	Active	Male	30	59	−35 (	−36 (−61%)
Mean (SD)	..	..	..	30·8 (11·8)	75·3 (10·3)	−1·2 (22·6); (6·8% [48·2])	−30·3 (24·5); (−39·9% [32·6])

Data are the absolute mean change in YGTSS score, with percentage change in parentheses, unless otherwise indicated. A negative value indicates improvement. YGTSS=Yale Global Tic Severity Scale. *Withdrew before receiving stimulation in the double-blind period. †Withdrew before randomisation.

Table 1: **Changes in YGTSS score at baseline and after anterior internal globus pallidus deep brain stimulation**

Management: take home messages

- Treat tics if troublesome (*4 criteria*)
- The value of of *psychoeducation*
- Behavioral therapy *first*
- If medication: start with *very low-dose aripiprazole*
- Consider *topiramate* as *add-on/alternative*
- Don't forget botulinum toxin
- GPi DBS for severe cases of TS *works*

Case #1

- Elia, 12 yrs old
- First tics at age 5
- Multiple changing tics over the years
- Head tics - > recurrent headaches
- Bullied by his classmates because of coprolalia
- Comorbid ADHD, intensified by his attempts to control / hide his tics; might need to redouble his class
- Weekly rehab sessions for dyslexia and dysgraphia
- Occasional rage attacks / explosive outburst
- High anxiety levels with developing school phobia
- Depressive symptoms with sleep problems (ruminations, awakenings)

-> What to do, and why ?

Case #2

- Lucie, 10 yrs old
- First tics at age 6
- Initially simple motor and vocal tics, neither bothersome to Lucie or her classmates
- Complexifying over the past six months, disturbing the class, especially a vocal tic (throat clearing); some complaints made but no bullying or harassment
- Lucie is tired by her tics and has therefore trouble with her homework; until now, she was a good student, motivated, without ADHD or learning disabilities

-> What to do, and why ?

Case #3

- John, 20 yrs old
- First tics at age 5
- From the beginning complex tics and multiple comorbidities
- Over the years, several pharmacological treatments gave been tried but none has managed to reduce the tics sufficiently and, foremost, continuously
- CBT was tried but unsuccessful
- BTX injections into the vocal cords were helpful for coprolalia but John is bothered by the hypophonia
- More recently, mutilations have set in
- Gained + 30 kg of weight over the past decade

-> What to do, and why ?

Thank you for your attention and …

TOURETTE
GREECE