



# Disparities in patients with tic disorders

**Presented By:**

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# OVERVIEW OF THE TALK

1. Overview of cultural disparities in GTS
2. Overview of previous studies reporting about diverse ethnical groups
3. Racial and non-racial disparities analysis in All of Us Cohort
4. Sex differences in tic disorders

# Cultural/ethnic disparities

- an overrepresentation of GTS literature from European and North American perspectives
- the heterogenous nature of GTS
- the influence of race, culture and environmental factors on symptom expression

# Gilles de la Tourette Syndrome: Cross-Cultural Perspectives With a Focus on the Asia-Pacific Region

- GTS is seen less frequently in some cultures?
- Not diagnosed?
- Other diagnostic criteria (China)
- Lack of awareness?
- In all cultures the tic phenomenology is similar (biological underpinnings)
- There may be some variations in the occurrence of co-morbidities

Clinical Characteristics of Tourette syndrome patients in different samples

	UK	UAE	Bruun [65]
Male-female ratio	2.9:1	2.5:1	3:1
Mean age at onset (years)	6	6.4	7.2
Initial tic—eye and face (%)	51.4	57.1	NA
Facial tics (%)	100	100	91
Limb tics (%)	88	72	78
Complex motor tics (%)	14.3	8.6	68
Coprolalia (%)	25.7	8.6	10–30
Copropaxia (%)	11.4	2.9	2–21
Echolalia (%)	42.9	37.1	20–45
Self-injurious behavior (%)	28.6	17.1	NA
Aggression (%)	20	2.9	NA
Obsessive compulsive behaviors (%)	42.9	37.1	28–50
Attention deficit hyperactivity disorder symptoms (%)	60	68.6	35–65
Oppositional defiant disorder (%)	54.5	11.4	NA
Conduct disorder (%)	20	5.7	NA

Adapted from Eapen and Robertson [61].



Eapen et al. Editorial: Gilles de la Tourette Syndrome: Cross-Cultural Perspectives With a Focus on the Asia-Pacific Region. *Front Psychiatry*. 2021; 12: 678089.

Eapen and Robertson. Clinical Correlates of Tourette's Disorder Across Cultures: A Comparative Study Between the United Arab Emirates and the United Kingdom. *Prim Care Companion J Clin Psychiatry*. 2008; 10(2): 103–107. doi: 10.4088/pcc.v10n0203

Robertson et al. The international prevalence, epidemiology, and clinical phenomenology of Tourette syndrome: A cross-cultural perspective. *J Psychosom Res*. 2009 Dec;67(6):475-83. doi: 10.1016/j.jpsychores.2009.07.010.

# Prevalence of diagnosed Tourette syndrome in persons aged 6-17 years - United States

Prevalence of ever receiving a diagnosis of Tourette syndrome among persons aged 6--17 years, by selected characteristics* --- National Survey of Children's Health, United States, 2007						
Characteristic	No. in sample (unweighted)†	No. with reported diagnosis (unweighted)	Weighted prevalence per 1,000	(95% CI§)	Prevalence ratio	(95% CI)
<b>Total surveyed</b>	<b>64,034</b>	<b>225</b>	<b>3.0</b>	<b>(2.3--4.0)</b>	---	---
<b>Age (yrs)</b>						
6--11	27,776	61	1.9	(1.2--2.9)	Referent	Referent
12--17	36,258	164	4.0	(2.8--5.9)	2.1	(1.2--3.8)
<b>Sex</b>						
Male	33,264	179	4.4	(3.2--6.1)	2.9	(1.4--6.0)
Female	30,680	46	1.5	(0.8--2.9)	Referent	Referent
<b>Ethnicity/Race</b>						
Hispanic	7,347	26	1.6	(0.9--2.8)	0.4	(0.2--0.8)
Non-Hispanic white	43,766	164	3.9	(2.7--5.6)	Referent	Referent
Non-Hispanic black	6,445	18	1.5	(0.9--2.7)	0.4	(0.2--0.8)
<b>Highest level of education achieved by parent in household</b>						
High school diploma or less	14,902	58	3.5	(2.0--6.0)	1.3	(0.7--2.4)
At least some college or technical school	48,376	165	2.7	(2.0--3.8)	Referent	Referent
<b>Household income</b>						
≤200% of federal poverty level (FPL¶)	17,646	65	3.1	(1.8--5.2)	1.1	(0.4--3.2)
>200% to ≤400% above FPL	21,875	80	3.0	(1.8--5.1)	1.0	(0.3--3.2)
>400% above FPL	24,512	80	2.9	(1.9--4.4)	Referent	Referent

# Hispanic and Latino

- The clinical characteristics of TS were similar to that found elsewhere.
- The perceived impact of TS was different.
- Many subjects denied that their TS caused impairment or distress, even when objective evidence of impairment was available.

**TABLE 2**  
Demographic and Clinical Characteristics of the Tourette Syndrome Sample in Costa Rica

	Total Study Sample (N = 85)	Subjects Referred by Health Care Providers (n = 43)	Subjects Referred From Other Sources (n = 42)	Worldwide (Bruun, 1988) <sup>a</sup>
Male-female ratio	4.6:1	3.8:1	7.2:1	3:1
Mean age onset (yr)	6.1	5.8	6.3	7.2
SD	2.3	2.0	2.6	
Range	2–12	3–10	2–12	
Mean age at diagnosis (yr)	10.8	9.6	11.9	NA
SD	4.0	3.1	4.6	
Range	5–28	5–20	6–28	
Mean age at interview (yr)	11.4	10.8	12.0	NA
SD	4.3	4.1	4.5	
Range	5–28	5–25	6–28	
Simple facial tics (%)	100	100	100	91
Simple limb tics (%)	88	93	83	78
Complex motor tics (%)	88	98	80	68
Copropaxia (%)	9	12	7	2–21
Throat clearing/simple vocal tics (%)	85	84	85	65
Complex vocal tics (%)	8	7	10	NA
Echo- or palilalia (%)	27	35	20	20–45
Coprolalia	20	21	17	10–30
Self-injury (%)	15	28	2	Up to 30 <sup>b</sup>

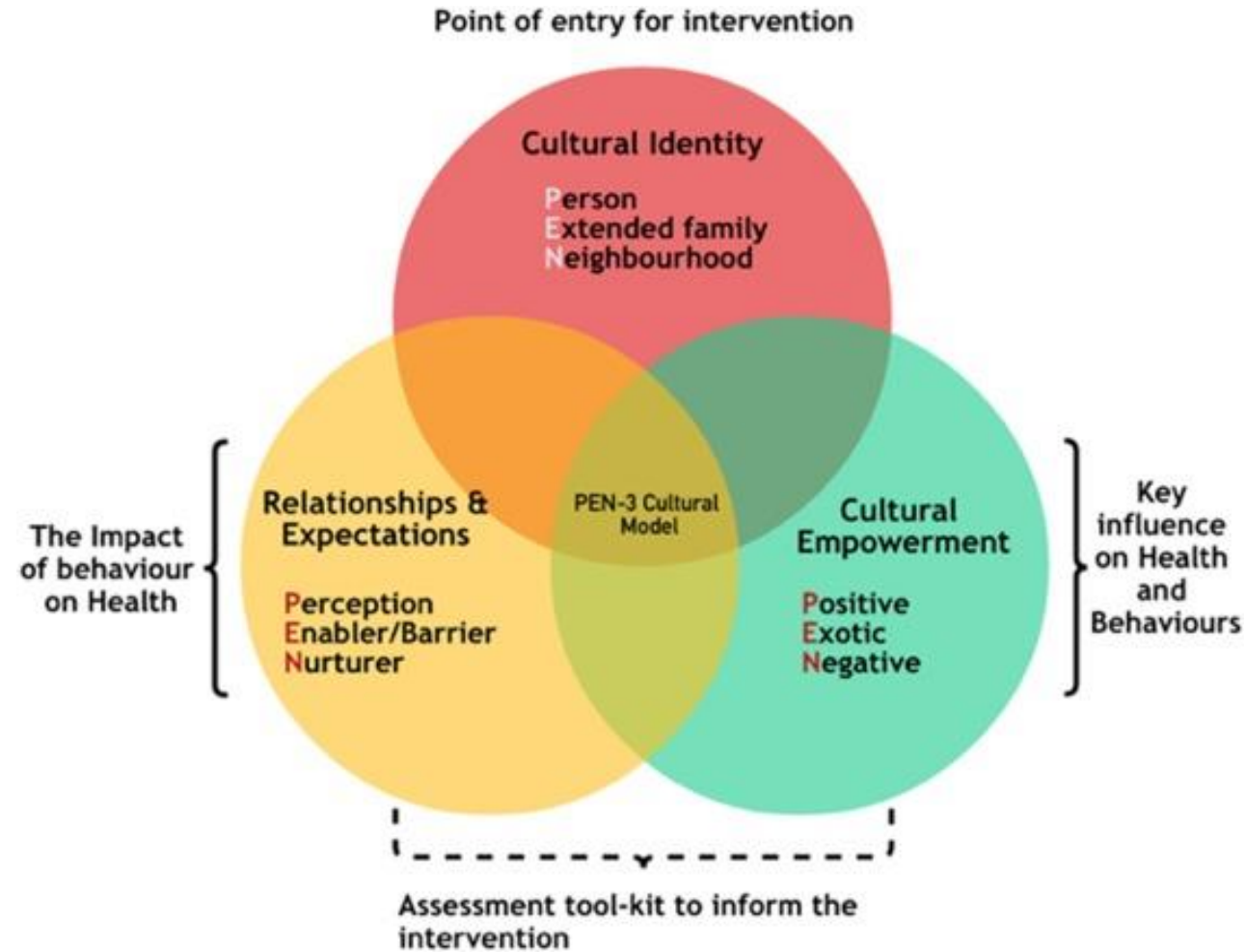
*Note:* NA = not available.

<sup>a</sup> Data represent averages and ranges compiled from multiple epidemiological studies of Tourette syndrome.

<sup>b</sup> Robertson (1992).



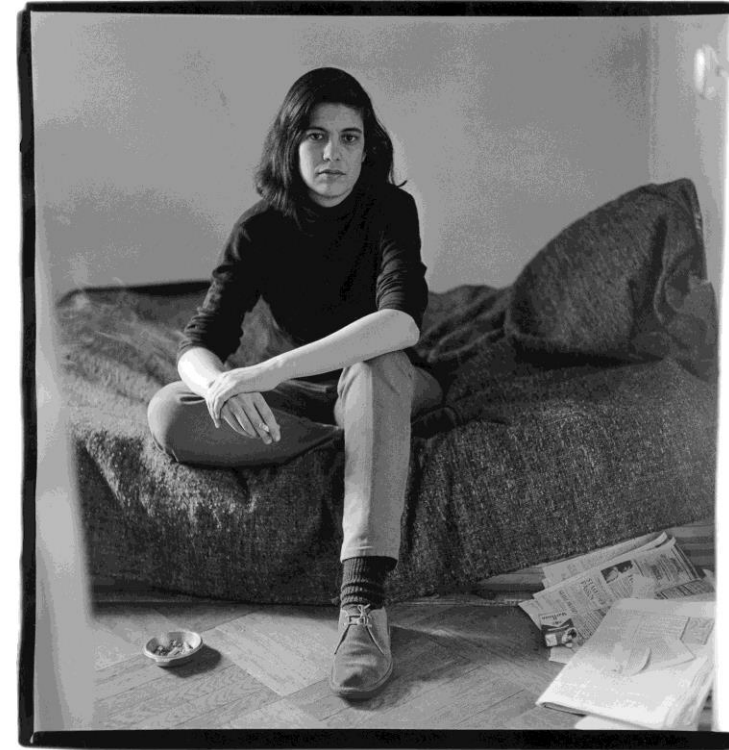
# Culture and disease perception







SUSAN SONTAG  
*Illness as Metaphor*



Two diseases have been spectacularly, and similarly, encumbered by the trappings of metaphor: tuberculosis and cancer.

In Stendhal's *Armance* (1827), the hero's mother refuses to say 'tuberculosis,' for fear that pronouncing the word will hasten the course of her son's malady



# Asian

- No studies from multicultural/multiethnic countries, such as USA and Canada
- Growing literature from China, Taiwan and Japan



[Front Psychiatry](#). 2020; 11: 774.

Published online 2020 Aug 13. doi: [10.3389/fpsy.2020.00774](https://doi.org/10.3389/fpsy.2020.00774)

PMCID: PMC7438753

PMID: [32903695](https://pubmed.ncbi.nlm.nih.gov/32903695/)

## Current Status, Diagnosis, and Treatment Recommendation for Tic Disorders in China

[Zhi-Sheng Liu](#),<sup>1,\*</sup> [Yong-Hua Cui](#),<sup>2</sup> [Dan Sun](#),<sup>1</sup> [Qing Lu](#),<sup>1</sup> [Yu-Wu Jiang](#),<sup>3</sup> [Li Jiang](#),<sup>4</sup> [Jia-Qin Wang](#),<sup>5</sup> [Rong Luo](#),<sup>6</sup> [Fang Fang](#),<sup>2</sup> [Shui-Zhen Zhou](#),<sup>7</sup> [Yi Wang](#),<sup>7</sup> [Fang-Cheng Cai](#),<sup>4</sup> [Qing Lin](#),<sup>3</sup> [Lan Xiong](#),<sup>8,\*</sup> [Yi Zheng](#),<sup>9,\*</sup> and [Jiong Qin](#)<sup>10,\*</sup>,  
Chinese Child Neurology Society Tic Disorders Consortium †

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# Differences with other populations

- fewer OCS and behavioral problems have been observed in Korea
- greater male preponderance has been noted in Japanese population and Eastern and Asiatic samples

Nomura and Segawa. Gilles de la tourette syndrome in oriental children. *Brain Dev.* 1979;1(2):103-11. doi: 10.1016/s0387-7604(79)80018-2.

Min SK, Lee H. A clinical study of Gilles de la Tourette's syndrome in Korea. *Br J Psychiatry.* 1986 Nov;149:644-7. doi: 10.1192/bjp.149.5.644.

Nomura and Segawa. Social adaptation of Tourette syndrome families in Japan. *Adv Neurol.* 1992;58:323-32.



# African Americans

## Why don't children in Uganda have tics? A mixed-methods study of beliefs, knowledge, and attitudes of health professionals

**Table 3.** Barriers in diagnosing tic disorders and service development

Challenges	Total
Lack of knowledge about tic disorder	115 (75.6%)
Families not seeing tics as a clinical concern	91 (59.9%)
The complexity of the symptoms	65 (42.8%)
Families being too guilty to disclose tics to professionals	42 (27.6%)

# African Americans

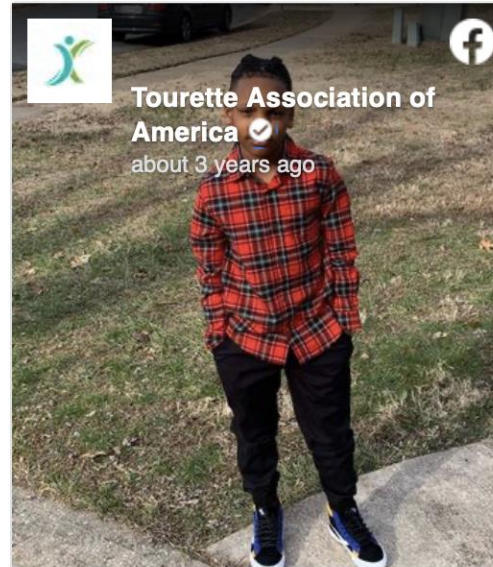
- Other medical priorities and less propensity to seek health care
- Ethnic and epigenetic differences,
- Genetic and allelic differences in different races
- Presence of an admixture of races

Roberston (2008) The prevalence and epidemiology of Gilles de la Tourette syndrome: Part 2: Tentative explanations for differing prevalence figures in GTS, including the possible effects of psychopathology, aetiology, cultural differences, and differing phenotypes

## Voices from the Community:



"My name is Carter Jackson, and I was diagnosed with [#TouretteSyndrome](#) around 12 years old. I'm currently 21 and a working, part-time student. As a black, transgender man with [#Tourette](#), it has been difficult at times to navigate



"My son was diagnosed with [#Tourette](#) in February of last year. We didn't know what it was or what to do. Teachers and peers taunted him, and he didn't understand why he was different suddenly. But at 9, he kept pushing forward and continued to play football and basketball. Each day he is learning to live with Tourette and I am honored to be his mom.

In the beginning, Jaiden was nervous but he did educate his coaches which wasn't too hard because one is his dad. But for flag f... [See more](#)



"My daughter, Jamariah, was diagnosed with [#TouretteSyndrome](#) last year! It's been a struggle and we're starting to finally adjust. We've had to learn how to overcome people staring in public places, and kids saying things or laughing at her because of her jerking and grunting. I've explained to many kids in the classroom setting and in our hometown about her tics. I've shown videos so others could understand what tics were and why they occur.

# Genetic studies

- Most (GWAS) have been carried out in populations of European descent
- Few results from other populations showed population-specific results

Chromosome	Position <sup>a</sup>	Gene	Protein	Allele <sup>b</sup>	PolyPhen-2/SIFT	Family member (available DNA sample)		Transmission
						Affected ( <i>n</i> = 3)	Unaffected ( <i>n</i> = 4)	
3	1.84E+08	<i>CLCN2</i>	G161S	C/T	Damaging	3	0	Father
11	1.19E+08	<i>C2CD2L</i>	R497W	C/T	Damaging	2	2	Mother
1	76,288,239	<i>MSH4</i>	E379K	G/A	Damaging	1	1	/
6	1.59E+08	<i>TULP4</i>	S1451I	G/T	Damaging	1	1	/
16	69,201,044	<i>UTP4</i>	R634W	C/T	Damaging	2	1	/

WES, whole-exome sequencing; GTS, Gilles de la Tourette syndrome; SIFT, Sorting Intolerant from Tolerant.

<sup>a</sup>Position according to GRCh 37.

<sup>b</sup>Referenced/mutation allele.



# Racial and non-racial disparities in tic disorders in the United States: analysis of All of Us Study

## OBJECTIVES

- determine whether the prevalence of tic disorders varies depending on race, ethnicity and gender
- Cross-sectional analysis of **All of Us research program**
- National Institutes of Health database that is designed to provide health and genetic data on over 1 million Americans, focusing on groups that have generally been underrepresented in research



# Racial and non-racial disparities in tic disorders in the United States: analysis of All of Us Study

## METHODS

- Tic disorders cases were identified in Electronic Health Record data using **ICD-9-CM, ICD-10-CM and SNOMED codes**
- We calculated the prevalence of diverse tic disorders among participants across self-identified racial and ethnic groups



# Results

- **369,297** All of Us participants with available data (average age 56 years, SD 19; 59 % female)
- **3134** patients with diverse tic disorders with an average age of 54 years (SD 12) and female predominance (n=1685, 54%)
- No difference in tic prevalence in males and females (**0.8 vs 0.7%**)
- When comparing tic prevalence among diverse racial groups, the highest prevalence was among **Whites** (n=2060, 1%), following by Asians (n=94, 0.7%) and Blacks and African Americans (n=461, 0.6%)
- Similarly, tic prevalence was statistically significantly higher in ethnical group of not Hispanic or Latino (n=2604, 0.9%) vs 0.4% in Hispanic or Latino group (n=276)

# Conclusions

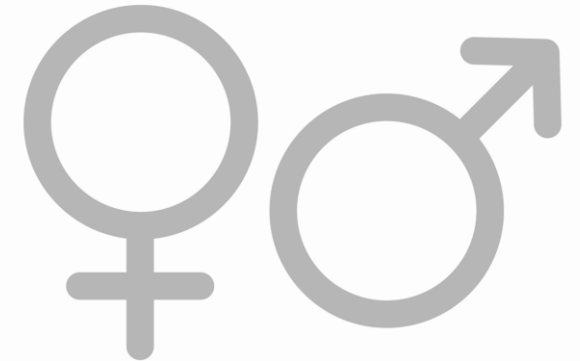
- In the All of Us study, the prevalence of tic disorders among US adults was **0.8 %**
- The highest prevalence was detected in **Whites** and the ethnical group of **not Hispanic or Latino**

# OVERVIEW OF THE TALK

1. Overview of cultural disparities in GTS
2. Overview of previous studies reporting about diverse ethnical groups
3. Racial and non-racial disparities analysis in All of Us Cohort
4. **Sex differences in tic disorders**

# TOURETTE SYNDROME: a male bias

- **Like in other neurodevelopmental disorders** (ASD, ADHD), there is a male predominance in Tourette syndrome (TS).
- **Attenuation with age:**
  - Childhood: Sex ratio 3-4 males : 1 female.<sup>1</sup>
  - Adulthood: Sex ratio 2 males : 1 female.<sup>2,3</sup>



*Are there sex-specific phenotypes and prognoses for TS?*



# Exploration of sex differences in tic disorders in childhood

## Influence of sex on tic severity and psychiatric comorbidity profile in patients with pediatric tic disorder

JOSEPH GIRGIS<sup>1</sup> | DAVIDE MARTINO<sup>2</sup> | TAMARA PRINGSHEIM<sup>2,3</sup> 

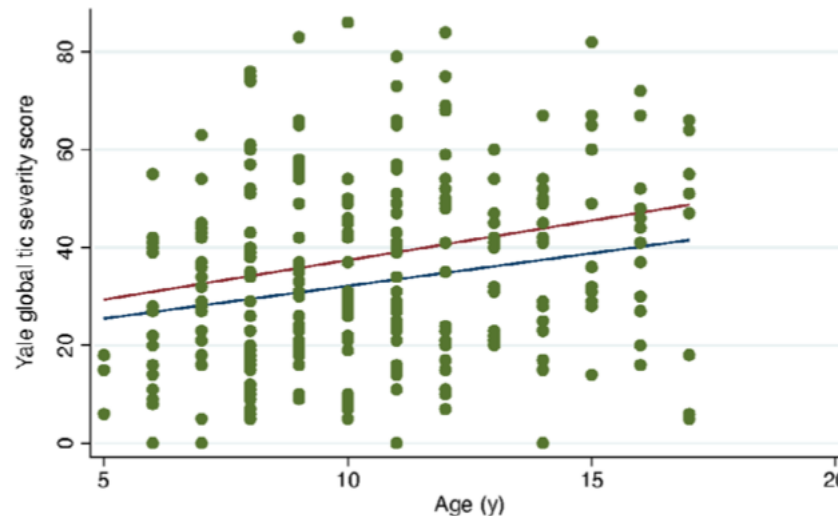
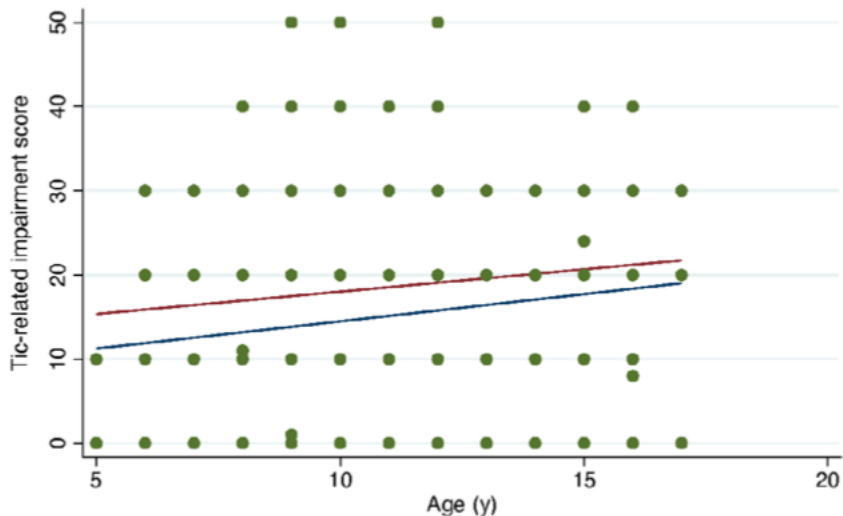
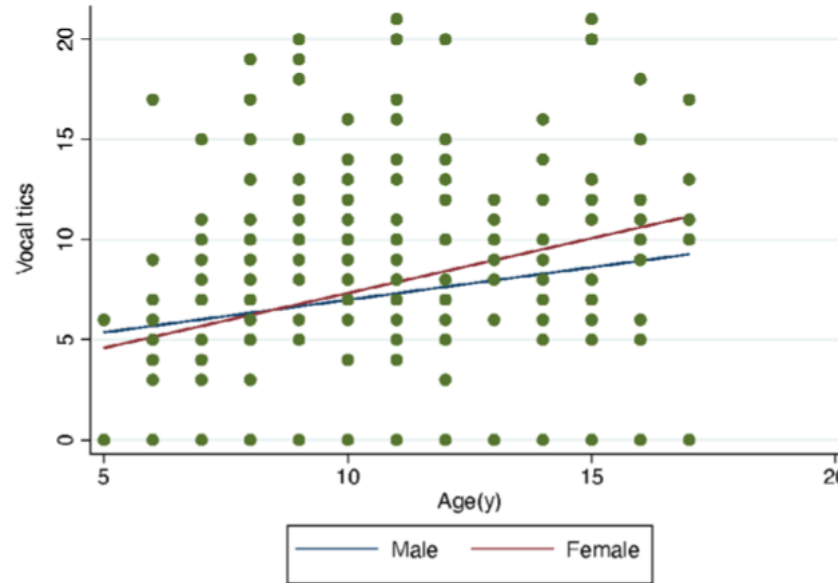
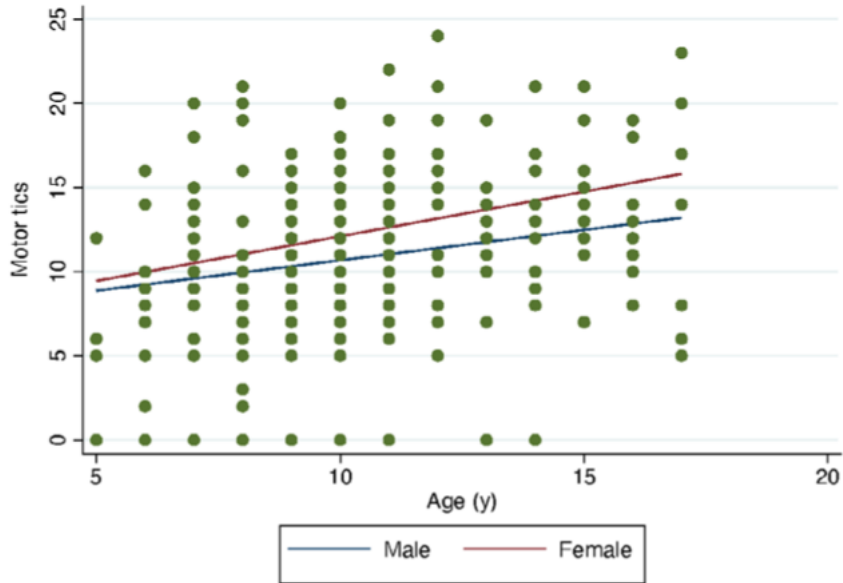
- Cross-sectional study in 270 children and adolescents (aged 5-17y, mean 10y 6mo), 212 males and 58 females
- **Objective:** to examine differences in tic severity and comorbidity profiles between the sexes

**Table 2:** Average age, age at onset, and scale scores

Scale	Males (n=212) Mean (SD)	Females (n=58) Mean (SD)	t-test p
Age at evaluation, y:mo	10:5 (2:10)	10:10 (3:7)	0.33
Age at tic onset, y:mo	6:6 (2:5)	6:4 (3:1)	0.78
<u>YGTSS – total motor</u>	10.81 (4.57)	12.55 (5.35)	<b>0.01</b>
YGTSS – total vocal	7.11 (5.50)	7.79 (5.29)	0.40
YGTSS – total tic (motor + vocal)	17.93 (8.36)	20.33 (9.10)	0.06
YGTSS – impairment rating	15 (12.60)	18.47 (13.06)	0.07
<u>YGTSS – global severity score</u>	32.66 (18.15)	38.79 (20.49)	<b>0.03</b>



# INCREASED SYMPTOM SEVERITY WITH AGE



- Increased symptom severity with increased age was **more pronounced in females** for all the measurements except for tic-related impairments.
- Motor tic severity ( $p=0.025$ ), tic-related impairments ( $p=0.051$ ), and global severity ( $p=0.045$ ) were **higher in females** at all ages.
- Vocal tics were more severe in males at a younger age ( $p=0.121$ ) but were **more severe in females at an older age** ( $p=0.077$ ).

# OUR EXPERIENCE (1)

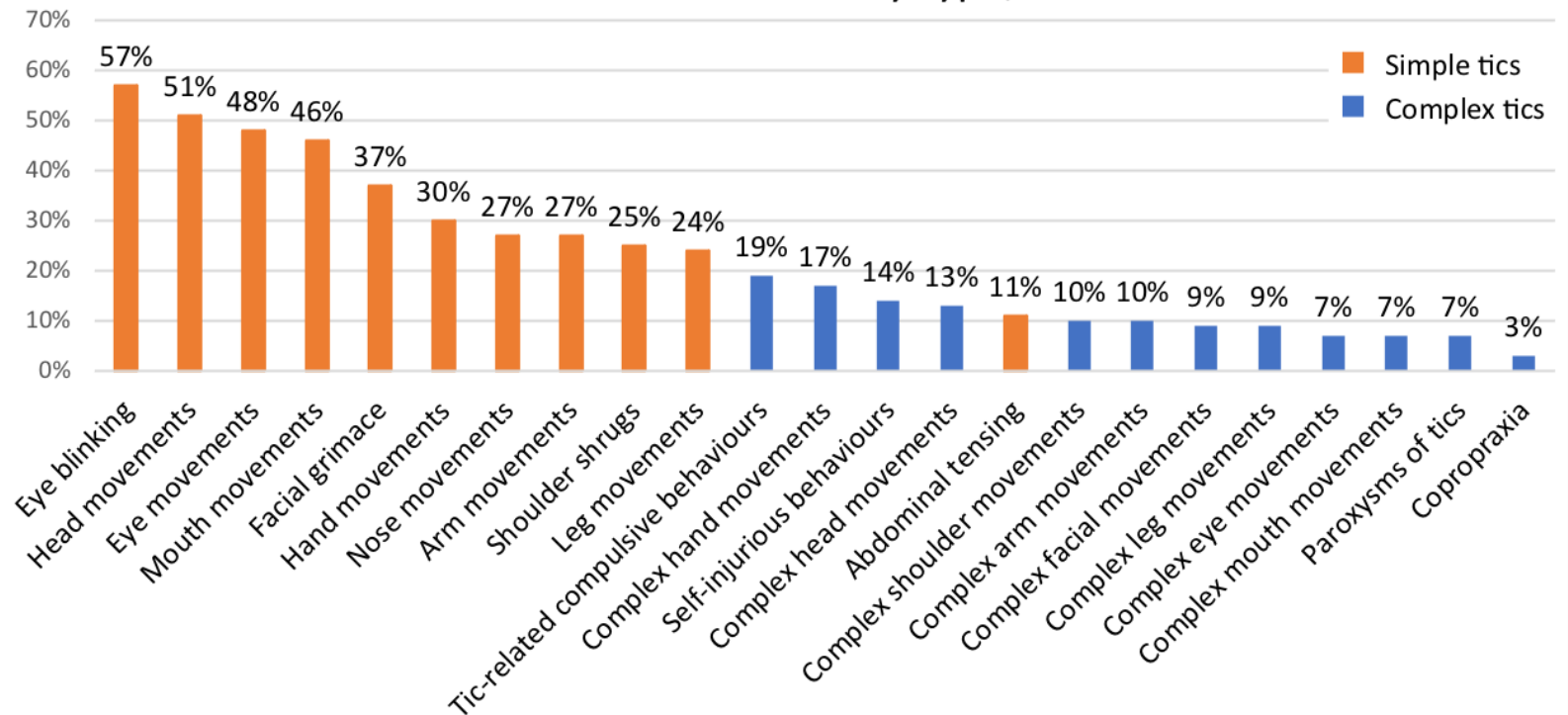
## Have We Forgotten What Tics Are? A Re-Exploration of Tic Phenomenology in Youth with Primary Tics

Christelle Nilles MD, Davide Martino MD, PhD, Julian Fletcher BA, Tamara Pringsheim MD ✉

First published: 21 February 2023 | <https://doi.org/10.1002/mdc3.13703>

- N=203 children and adolescents with primary tic disorders.
- 76.4% males.
- Mean age: 10.7y.

Prevalence of motor tics by type/location



# OUR EXPERIENCE (2)

In comparison with young males,<sup>1</sup> young females had:

**1) More simple tics:** nose movements (OR=2.87,  $p=0.003$ ), shoulder shrugs (OR=2.52,  $p=0.010$ ), simple leg/foot/toe movements (OR=2.11,  $p=0.040$ ), sniffing tics (OR=2.21,  $p=0.027$ ) and grunting tics (OR=4.10,  $p=0.016$ )

**2) Higher frequency** ( $p=0.032$ ) **and intensity** ( $p=0.006$ ) **of motor tics** and **greater tic-related impairment** ( $p=0.045$ ).

- *Differences in tic awareness and self-report of tics?*
- *Increased levels of stress and depression in females?*
- *Different phenotype and natural history of tics based on sex?*




# What about sex differences in adults with tics?



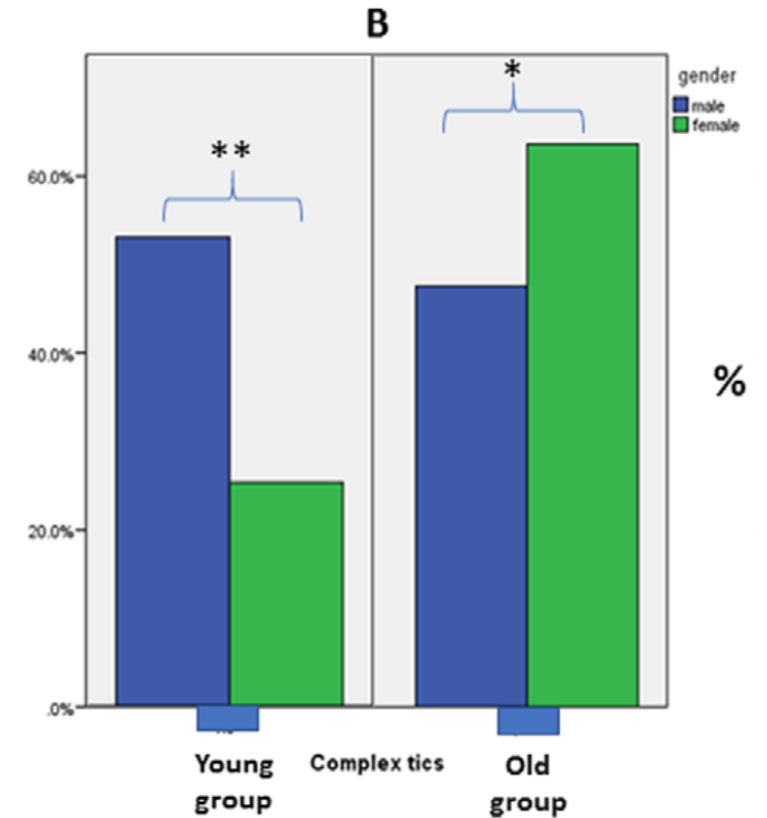
# A GROWING INTEREST IN SEX DIFFERENCES IN TIC DISORDERS

## Sex differences in patients with Tourette syndrome

José Fidel Baizabal-Carvallo<sup>1,2\*</sup>  and Joseph Jankovic<sup>1</sup>

<sup>1</sup>Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas, USA and <sup>2</sup>Department of Sciences and Engineering, University of Guanajuato, Guanajuato, México

- **N=201 individuals** (age 4-65 years) with tic disorders
- Males < 18 years had a greater complexity and severity of tics than females (p=0.049). These differences were not present in subjects > 18yr.
- **Only females had increased tic complexity and severity in adulthood** compared to childhood.



In the longitudinal European Multicenter Tics in Children Study<sup>1</sup> (16 different centres, n=709 children and adolescents with TS/persistent tic disorders): **greater tic severity in boys, but higher tic severity in girls with age.**

<sup>1</sup>the EMTICS collaborative group et al, 2021



# THE CALGARY AND PARIS TIC REGISTRY (1)



- N=164 adults with tic disorders; mean age: 32.9y in French participants, 31.7y in Canadian participants. 88% had TS.
- Sex ratio **1.9 males: 1 female**.



## In the Canadian subgroup

- Women had **more simple hand tics** than men (OR=2.96,  $p=0.03$ )
- Women had a **greater complexity of motor tics** ( $p=0.048$ ), a **greater motor tic score** ( $p=0.03$ ), and a **greater tic-related impairment** ( $p=0.003$ ) than men.

**A prospective  
Canadian-French study**



# EXAMINATION OF THE MORE EVEN SEX RATIO IN ADULTS WITH TICS

***In our study, sex ratio was 1.9 males:1 female.***

- Females have less resolution of symptoms with age?
- Women seek health-care more often in adulthood due to higher tic-related impairment?
- Underdiagnosis of TS in girls in childhood?

## TWO STUDIES

### ***Cross-sectional study in 185 females and 275 males with tic disorders, aged 18-79 years <sup>1</sup>***

- Women experienced greater tic-related interference in their social lives than men.
- 1/3 women first received treatment >18 years.

### ***Study in 75 adults with TS from a university-based clinic<sup>2</sup>***

- Women had higher YGTSS motor tic severity scores than men ( $p=0.036$ ) and greater TS-related impairment.
- Women were more likely than males to show expansion of the number of body regions affected by tics and to have a tic worsening as opposed to tic improvement in adulthood.

<sup>1</sup>Lewin et al, 2012; <sup>2</sup>Lichter et al, 2015



# THE CALGARY AND PARIS TIC REGISTRY (2)



- In the Canadian subgroup, **women had more anxiety disorders** than men (OR=3.18, p=0.01).
- In the French subgroup, **women had more OCD** than men (OR=4.84, p=0.02).



- 
- Females with TS are more likely than males to have depression and anxiety.<sup>1</sup>
  - **Tic severity correlates with comorbid depression** in children and adolescents <sup>2</sup> and in adults <sup>3</sup> and **with comorbid anxiety.** <sup>4</sup>

→ *The high prevalence of mood and anxiety disorders in women with TS **may play a role in the severity of their tics.***

**A prospective  
Canadian-French study**



<sup>1</sup>Hirschtritt et al, 2015; <sup>2</sup>Rizzo et al, 2017; <sup>3</sup>Lewin et al, 2012; <sup>4</sup>Johnco et al, 2016

# Substrates underlying sex differences in TS

# Sex and gender in neurodevelopmental conditions

Sven Bölte<sup>1,2,3</sup>✉, Janina Neufeld<sup>1,4</sup>, Peter B. Marschik<sup>1,5,6</sup>, Zachary J. Williams<sup>7,8,9</sup>, Louise Gallagher<sup>10,11</sup>  
& Meng-Chuan Lai<sup>11,12,13</sup>✉

*Explores the sex and gender-related factors (biological, behavioural) that influence neurodevelopmental conditions.*

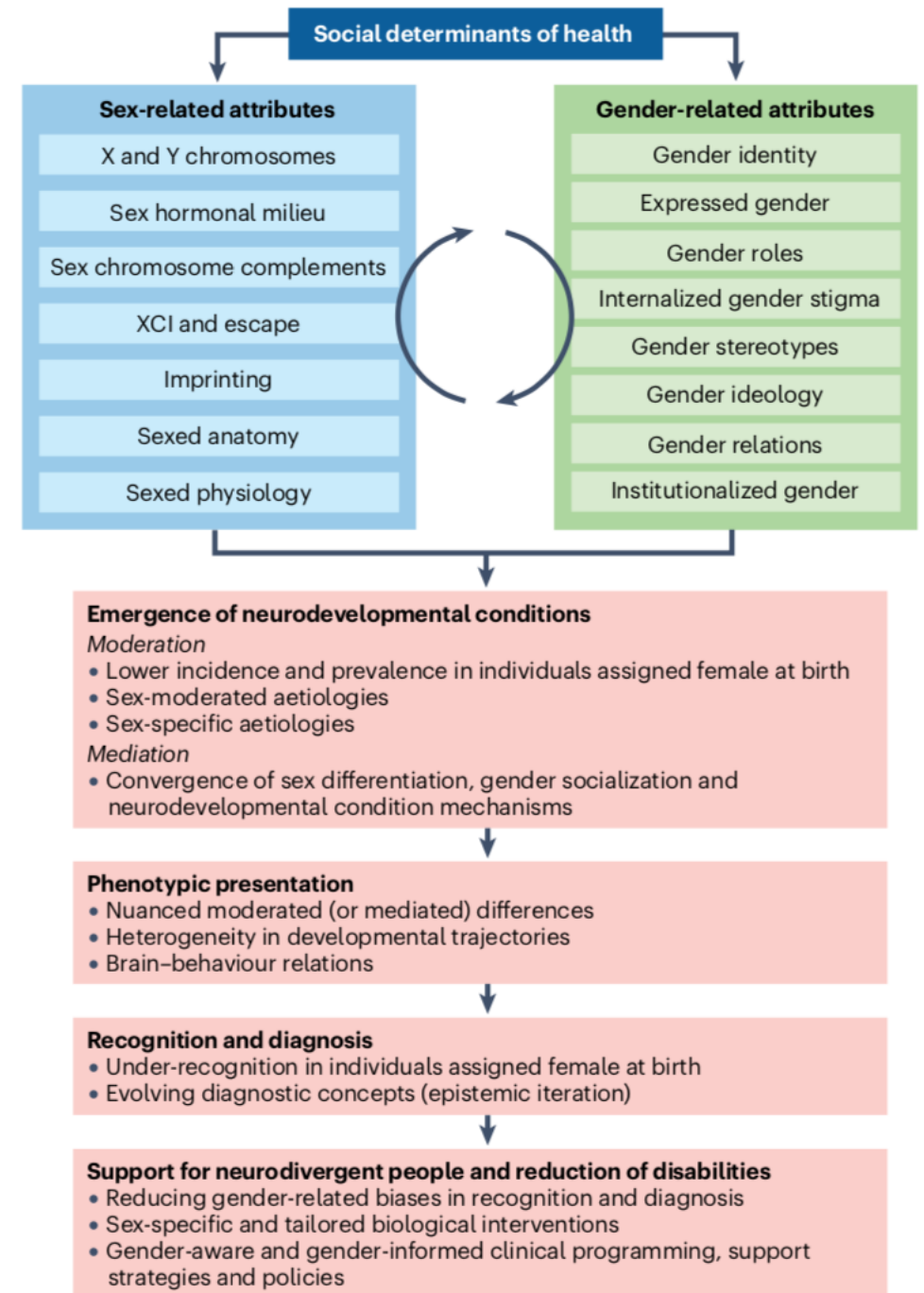


Fig. 1 | Why are sex and gender important for neurodevelopmental conditions?



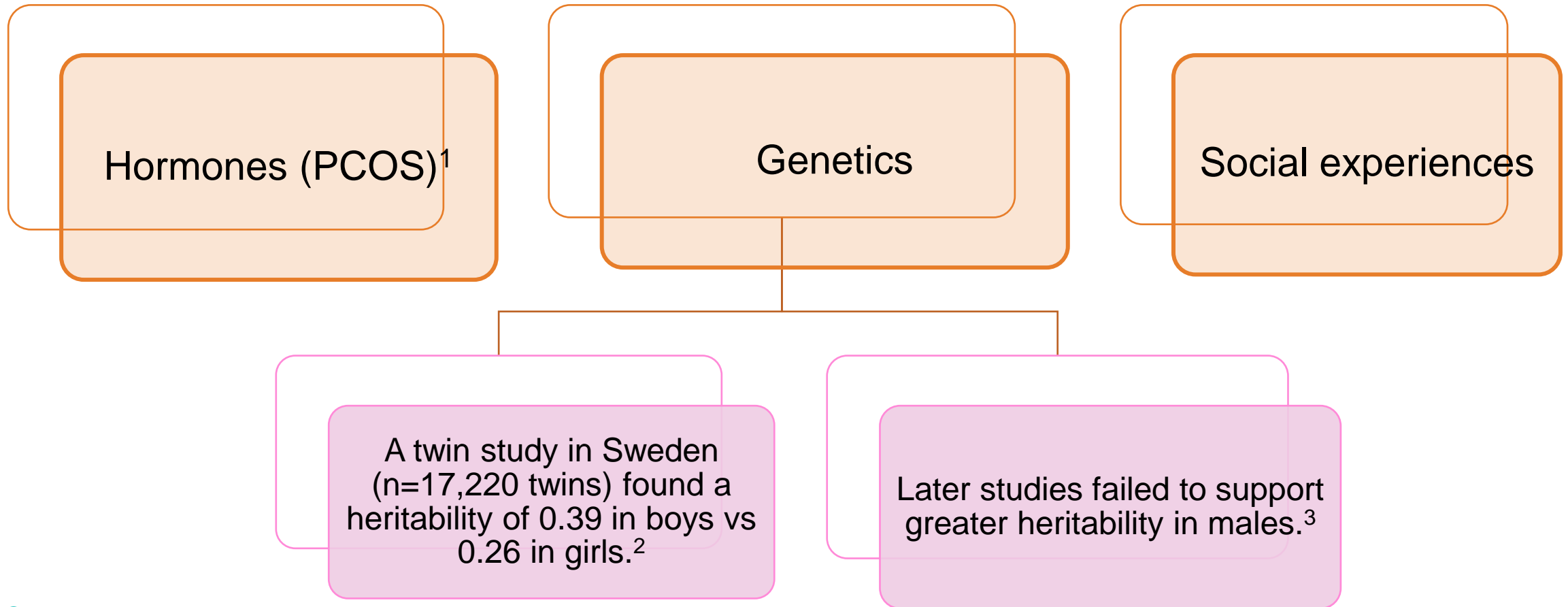
# A DIFFERENT BRAIN IN TS?



- Brain imaging studies have suggested that **males with TS might have more widespread brain alterations than females with TS** compared with typically developing peers.<sup>1</sup>
  - Altered cortical and callosal thickness and basal ganglia volume in childhood.<sup>2,3</sup>
  - ↓ cortical thickness in prefrontal, orbitofrontal and parietal regions.<sup>4</sup>

<sup>1</sup>Bölte et al, 2023; <sup>2</sup>Garris et al, 2021; <sup>3</sup>Pinares-Garcia et al, 2018; <sup>4</sup>Fahim et al, 2010

# OTHER SEX-RELATED FACTORS INFLUENCING TIC DISORDERS





# KEY MESSAGES & FUTURE RESEARCH



- Overall, although findings on sex differences before age 18 varied, there is accumulating evidence that **females may have slightly greater tic severity and tic-related impairment with age.**
- **Sex seems to contribute to the variability in TS** via genetics, endocrinological factors, brain structure, behaviours, comorbidities...
- **Future research:** exploring the female experience of tic disorders in childhood and adulthood; considering sex but also gender in studies; examination of the association between tic severity and tic-related impairment in women versus men; imaging studies.



# Thank you for your attention!



Dr Andreas  
Hartmann



Pr Emmanuel  
Flamand-Roze



Dr Yulia Worbe

