# Differential diagnosis of jerky movement disorders.

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# What are jerky movements?

Medline plus

Jerky movement is a condition in which a person makes fast movements that they cannot control and that have no purpose. These movements interrupt the person's normal movement or posture.

So anything hyperkinetic!

# Why does Tourette's Syndrome (TS) represent the borderland between neurology and psychiatry?

1. the tics of TS are psychogenic in origin
2. the tics of TS have some "voluntary" but unwanted aspects
3. TS is accompanied by psychiatric co-morbidities
4. the tics in TS can not be discerned from functional or psychogenic movement disorders
5. all of the above answers are correct
6. b,c,d,e are correct
7. a, b,and c are correct
8. b and c are correct

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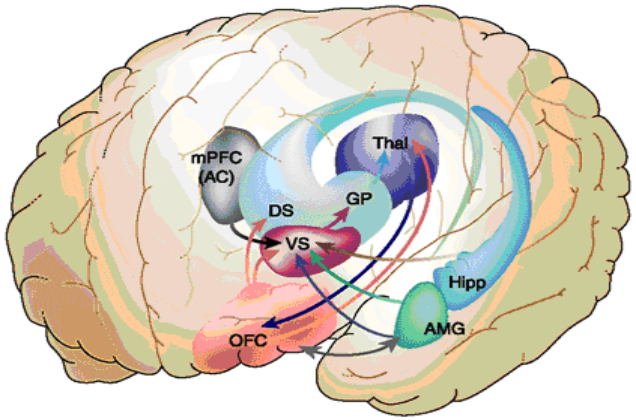
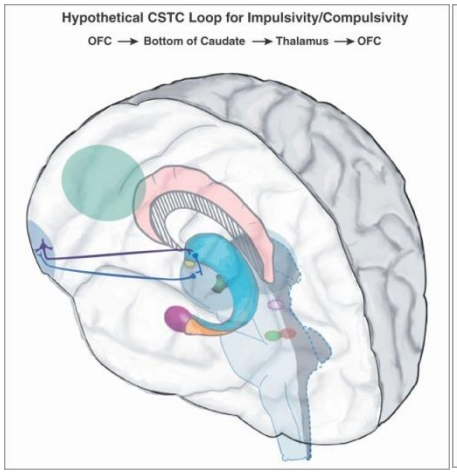
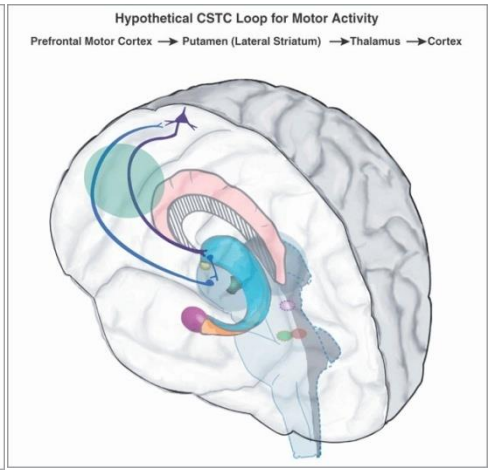
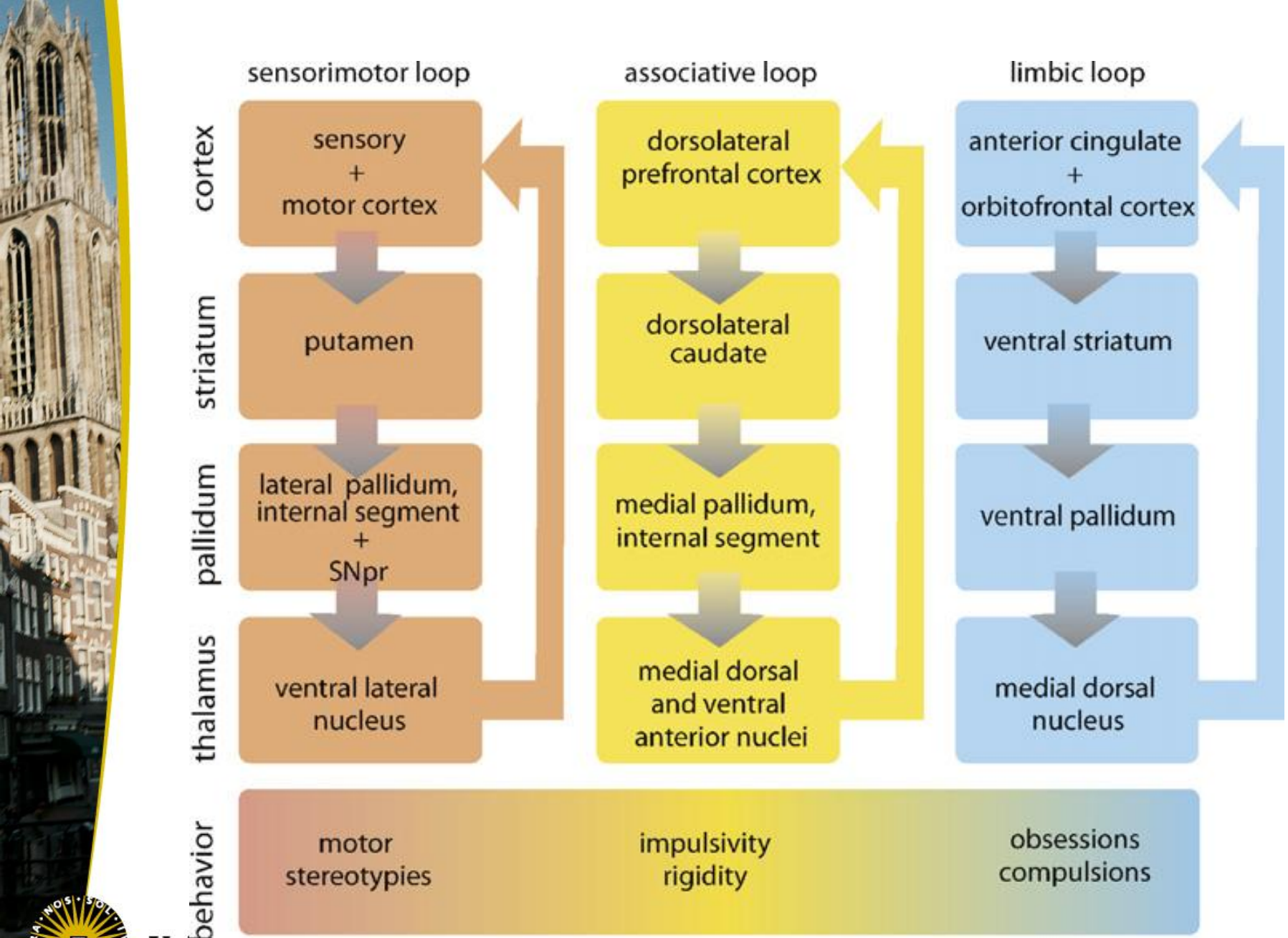
# Movement disorders as motion disorders
# Intrinsic relationship between motor-limbic emotional CSTC brain systems








Movement disorders ADHD/ autism OCD

# Jan

# Jan

# A cursing brain:
# The histories of Tourette's syndrome

## Howard Kushner, 2000
## La maladie des tics

"convulsive" tics:

- Hereditary
- Developed in childhood
- Progressive in course
- Degenerative
- Chronic

Jean Itard, 1825
Archives generales de Medicine, case report

Georges Gilles de la Tourette 1885

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# 1885: Maladie des tics convulsives
# Description of 9 case reports including the Marquise de Dampierre

délire de toucher
délire de l'ordre
folie du pourquoi,
folie du doûte
onomatomania;
arhythmomania

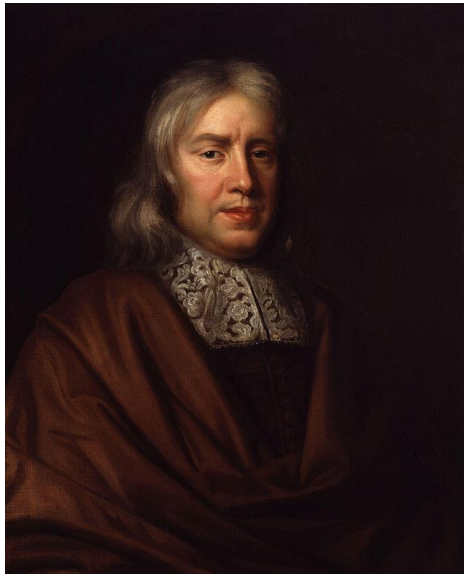
1. M, 24 yrs, CMT
2. M, 20 yrs, jumping when brushed, no vocal tics
3. M, 20 yrs, TS & coprolalia, jumping, remittent course
4. M, 11 yrs, CMT
5. M, 14 yrs, CMT+ self-inury due to tics
6. M, 15 yrs
7. M, 11 yrs, TS
8. M, 15, TS+coprolalia
9. **F, 84 yrs, The Marquise de D.,TS**

# Differential diagnosis Tourette's disorder

Hysteria
Psychogenic/ functional movement disorders

Myoclonus/ dystonias

Choreas / rheumatic causes



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# Differential diagnosis: symptom characteristics PM: all influenced by stress, fatigue!

| | Tic | Myoclonic Dystonic movement | Sydenhams Chorea movement | Psychogenic movement |
|---|---|---|---|---|
| Characteristic | Brief, sudden | rapid jerky, alone or in combination with sustained contractions / postures | Jerky, brief | Tremor, tic, dystonia, myoclonus, gait disorder |
| Voluntariliness | Unwanted, ***not*** in- voluntary | involuntary | involuntary | Variable; Sometimes not involuntary |
| Rhythm | Non-rhythmical | Rhythmical/ sustained | Non rhythmical | Often rhythmical |
| Localisation | Face, shoulder, follows homunculus | Central/ upper body parts body | Distal limbs | A-symmetric, localized |
| Suppressibility/ intentionality | Yes | No | No | No |
| Pre-monitory sensations | Yes | No | No | no |
| Natural course | Decrease with adolescence | Stable | Transitory | Unfavourable (40% worse) |
| Complexity, intensity | Variation | Variation | Variation | Variation |

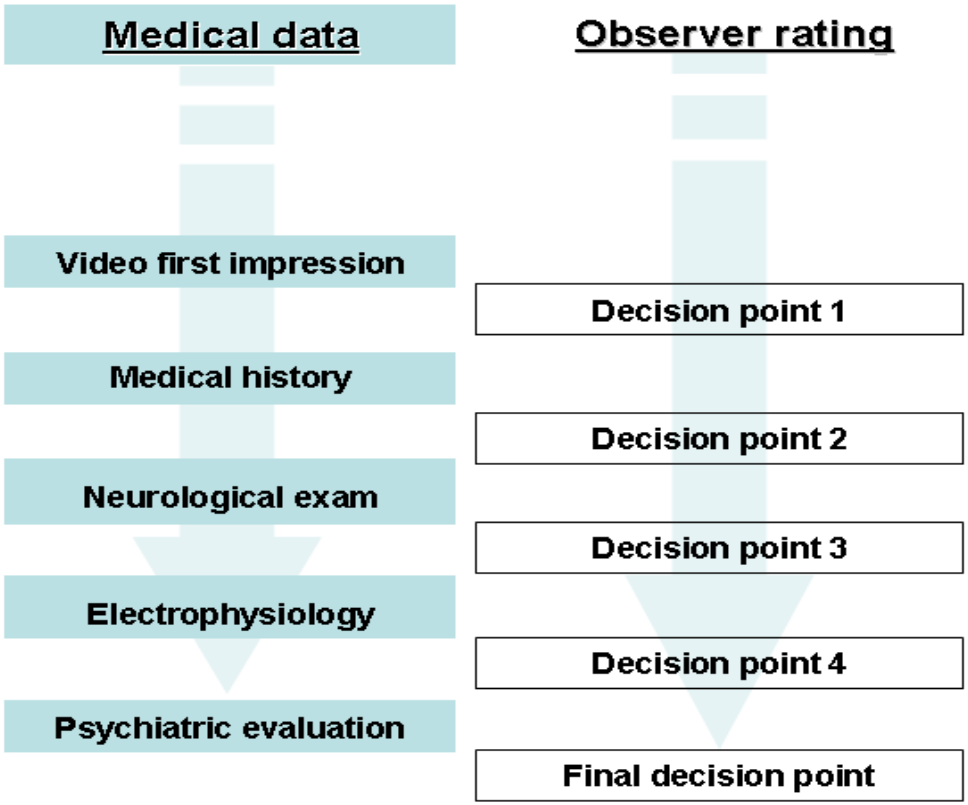
# Differential diagnosis: epidemiology

| | Tic | Myoclonic Dystonic movement | Sydenham Chorea movement | Psychogenic movement |
|---|---|---|---|---|
| Age at onset | 4-6 years | Variable; 7-20 years | 5-15 years*** | Mostly adulthood |
| Male: female | 2.5:1 | Dystonia: depends on type of dystonia**, mostly 1: 1.9 | Males < females | Males < females |
| Prevalence | 1% TS lifetime<br>9% tics in children | 2-50 cases per 1 milj.* | ? Rare | ? Frequent up to 3% |
| Course | 75% < tic intensity after age 18 | No epidemiol. Studies available | Benign, remission in 2-4 months | Unfavorable; 40% deteriorative |
| Familiality | Yes, one third of patients | Autosomal dominant, maternal imprinting in DYT 11 mutation carriers | 1 family studiy; familial involvement | ? |
| Heritability | 30%-45% | Genetically heterogeneous; DYT genes 100% | Yes, some**** | ? |
| Auto-immunity | Yes; but not unequivocal | no | Yes, clearly | No |
| Neuro-imaging findings | Yes;<br><asymmetry putamen volumes<br>CSTC circuit dysbalance | Cerebellar hyperactivation,<br>VL thalamus activation | Anti-basal ganglia antibodies CSF<br>Basal ganglia, putamen neuronal loss | Motor system inhibition |
| Psychiatric co- | Yes; OCD, ADHD! | Yes, especially in SCGE | Yes, OCD! | Association with |

# The eye of the beholder: Inter-rater agreement between experts on various movement disorders

**S.M.A. van der Salm [1], R.J. de Haan [2], D.C. Cath[3], A.F. van Rootselaar[1], and M.A.J. Tijssen[1]**

**60 cases on video, rating in four steps by 39 experts (neurologists)**



# The eye of the beholder: Inter-rater agreement between experts on PMD, tics and dystonia

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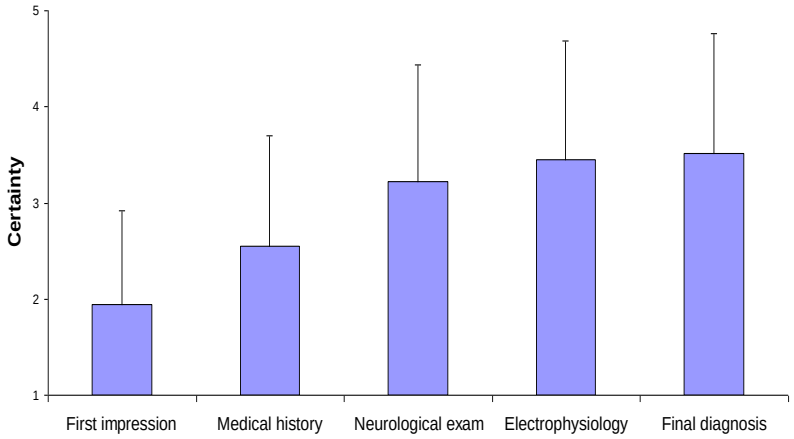


Absolute agreement on final diagnosis: 20% of cases.

- Moderate agreement (>75%): 2/3 of cases.
- Interrater agreement after step 1: moderate (κ =0.56)

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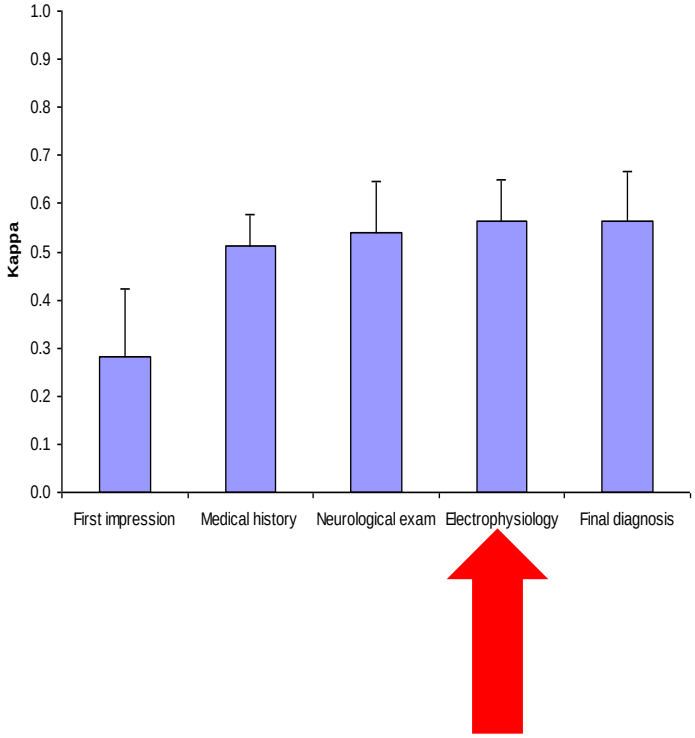
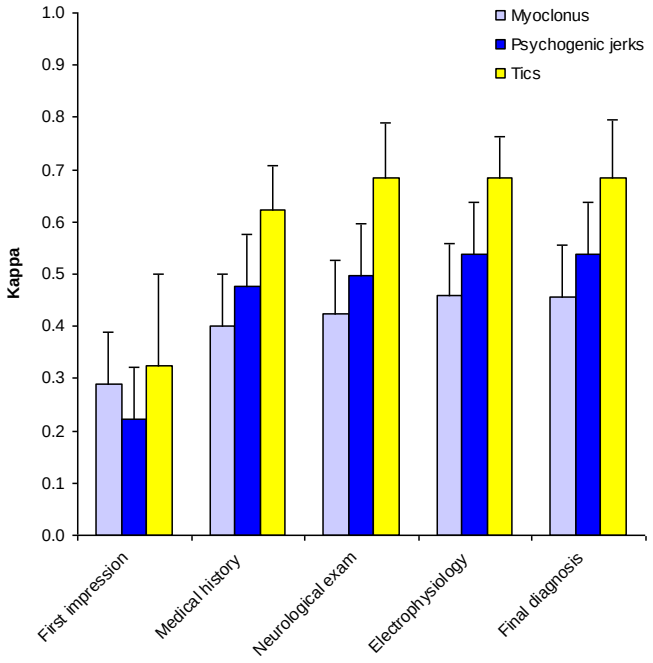
# Inter-rater agreement between experts on tics, myoclonus and psychogenic movement disorders

S.M.A. van der Salm [1], R.J. de Haan [2], D.C. Cath[3], A.F. van Rootselaar[1], and M.A.J. Tijssen[1]




Readiness potential

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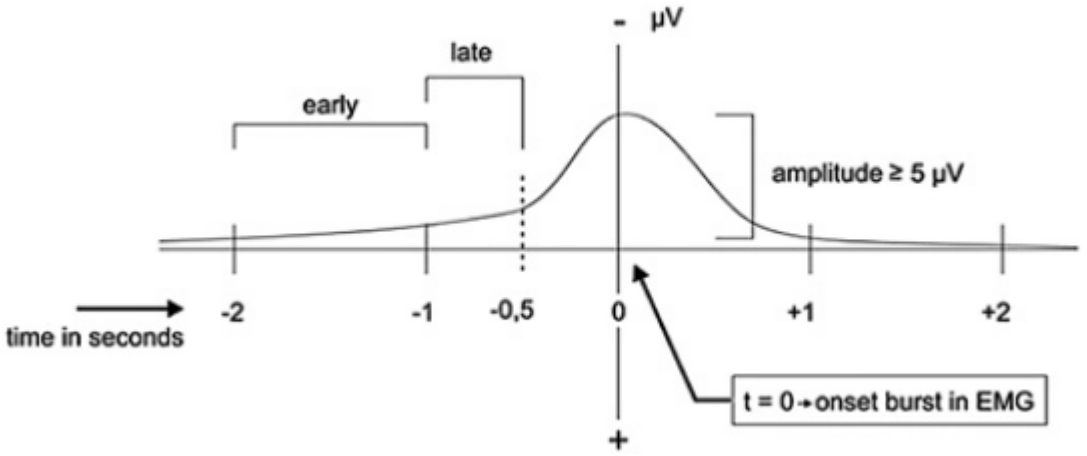
# Comparison of Bereitschafts potential between dystonia, TS and psychogenic movement disorders

## Van der Salm et al., 2012

BP measurements prior to spontaneous jerks and voluntary wrist extension

**Table 1** Overview of clinical characteristics

| | # | Age | Gender M:F | Disease duration |
|---|---|---|---|---|
| Psychogenic | 29 | 52 (25–74)* | 19:10 | 5 (0.5–40) |
| Tourette | 14 | 34 (21–65) | 12:2 | 22 (5–58) |
| Myoclonus | 5 | 38 (24–59) | 1:4* | 18 (1–53) |
| Control subjects | 25 | 46 (21–76) | 16:9 | – |

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# Comparison of Bereitschafts potential between dystonia, TS and psychogenic movement disorders

## Van der Salm et al., 2012

BP measurements prior to spontaneous jerks and voluntary wrist extension

**Table 2** Overview of BP findings

| | | Spontaneous jerky movements | | | | Intended wrist extension |
|---|---|---|---|---|---|---|
| | Total included | BP (%) | Onset BP | Early BP (%) | Late BP (%) | BP (%) |
| Psychogenic | 29 | 25 (86)* | 1195 * (700–2410) | 22 (76)* | 3 (10) | 12 (41)* |
| Tourette | 14 | 6 (43) | 915 * (510–1700) | 4 (29) | 2 (14) | 13 (93) |
| Myoclonus | 5 | 0 (0) | * | 0 (0) | 0 (0) | 5 (100) |
| Control subjects | 25 | – | – | – | – | 25 (100)* |

The total number of participants and BPs is reported per condition (spontaneous jerks or intended wrist extension task) with the percentage between brackets. Median is reported (range) for onset of BP (msec).
*Indicates significant differences.
BP, bereitschaftspotential.

Bereitschaftspotential absence prior to intended movements: 0.59 sensitivity, 0.98 specificity in Psych movement diagnosis

| | Tic | Myoclonic Dystonic movement | Sydenham Chorea movement | Psychogenic movement |
|---|---|---|---|---|
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| Male: female | 2.5:1 | Dystonia: depends on type of dystonia**, mostly 1: 1.9 | Males < females | Males < females |
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| Course | 75% < tic intensity after age 18 | No epidemiol. Studies available | Benign, remission in 2-4 months | Unfavorable; 40% deteriorative |
| Familiality | Yes, one third of patients | Autosomal dominant, maternal imprinting in DYT 11 mutation carriers | No family studies available | ? |
| Heritability | 30%-45% | Genetically heterogeneous; DYT genes 100% | Yes, some**** | ? |
| Auto-immunity | Yes; but not unequivocal | no | Yes, clearly | No |
| Neuro-imaging findings | Yes;<br><asymmetry putamen volumes<br>CSTC circuit dysbalance | Cerebellar hyperactivation,<br>VL thalamus activation | Anti-basal ganglia antibodies CSF<br>Basal ganglia, putamen neuronal loss | Motor system inhibition |
| Psychiatric co-morbidity | Yes; OCD, ADHD! | Yes, especially in SCGE mutation carriers : anxiety, depression, alcohol, OCS?? | Yes, with OCD! | Yes, of all sorts; depression, trauma! |

# Weissbach et al., 2013
# Review: Psychiatric comorbidity in Myoclonic dystonia

**Table 2**
Frequency of psychiatric symptoms in level 1 study, general population and own study.

| Psychiatric disorder | MC | NMC | All | *p*-value | General population |
|---|---|---|---|---|---|
| OCD | 13% | 2% | 10% | 0.026 | 2–3% |
| AD | 40% | 6% | 30% | <0.001 | 15%–25% |
| MAD | 39% | 23% | 34% | 0.043 | 15%–18% |
| Alcohol abuse | 21% | 19% | 21% | 0.724 | 9% |
| 4 symptoms | 2% | 0% | 1% | 0.001 | – |
| 3 symptoms | 2% | 0% | 1% | | – |
| 2 symptoms | 27% | 8% | 21% | | – |
| 1 symptom | 37% | 35% | 36% | | – |
| Any symptom | 71% | 42% | 62% | | – |

AD = anxiety disorders, MAD = major affective disorders, MC = manifesting mutation carriers; NMC = non-manifesting carrier; *p*-value for manifesting mutation carriers vs. non-manifesting mutation carriers of level 1 data.

# Psychiatric comorbidity in Persistent and remitted Sydenham (n=50)

*J. Moreira et al. / Parkinsonism and Related Disorders 20 (2014) 233–236*

| | Total | Persistent SC | Remitted SC | p values |
|---|---|---|---|---|
| No Current Psychiatric Diagnosis | 23 (46%) | 7 (46.7%) | 16 (45.7%) | 0.63 |
| Any Current Psychiatric Disorder | 27 (54%) | 8 (53.3%) | 19 (54.3%) | 0.63 |
| Depressive Disorders | 9 (18%) | 5 (33.3%) | 4 (11.4%) | 0.03* |
| Major depression | 7 (14%) | 4 (26.7%) | 3 (8.6%) | 0.18 |
| Dysthymia | 2 (4%) | 1 (6.7%) | 1 (2.9%) | 0.51 |
| Bipolar Disorder | 1 (2%) | 1 (6.7%) | 0 | 0.30 |
| Any Anxiety Disorder | 20 (40%) | 5 (33.3%) | 15 (42.9%) | 0.53 |
| Social phobia | 12 (24%) | 4 (26.7%) | 8 (22.9%) | 0.77 |
| Simple phobia | 6 (12%) | 1 (6.7%) | 5 (14.3%) | 0.65 |
| GAD | 8 (16%) | 3 (20%) | 5 (14.3%) | 0.68 |
| Panic disorder | 3 (6%) | 1 (6.7%) | 2 (5.7%) | 1.00 |
| OCD | 12 (24%) | 4 (26.7%) | 8 (22.9%) | 0.77 |
| BDD | 2 (4%) | 1 (6.7%) | 1 (2.9%) | 0.51 |
| Trichotillomania | 1 (2%) | 0 | 1 (2.9%) | 1.0 |
| Adjustment disorder | 1 (2%) | 0 | 1 (2.9%) | 1.0 |
| Psychosis | 1 (2%) | 1 (6.7%) | 0 | 0.30 |
| ADHD | 4 (8%) | 2 (13.3%) | 2 (5.7%) | 0.50 |
| Alcoholism | 2 (4%) | 1 (6.7%) | 1 (2.9%) | 0.51 |
| Nicotine dependence | 6 (12%) | 3 (20%) | 3 (8.6%) | 0.35 |
| Ilicit drug dependence | 2 (4%) | 2 (13.3%) | 0 | 0.09 |

# Psychiatric comorbidities in tics

Cath et al., 2011

| Reference | Co-morbid disorder | % |
|---|---|---|
| **Freeman et al., 2007; CDC, 2009** | ADHD | 56% |
| **Freeman et al., 2007** | OCD/OCB | 22%/33% |
| **Freeman et al.,2007** | Anger control problems | 28% |
| **Freeman et al., 2007** | Sleep disorder | 18% |
| **Abwender et al., 1996; Erenberg et al. 1986** | Learning problems (math, spelling, reading) | 22% |
| **Freeman et al., 2007** | Mood disorder | 17% |
| **Freeman et al., 2007** | Anxiety disorder | 17% |
| **Mathews et al., 2004; Freeman et al., 2007** | Self injurious behavior | 15%-60% |
| **Burd et al., 2009; Cath et al., 2013** | Autism spectrum disorder | 5%- 12% |

## So what does this relationship represent? Cause, consequence or pleiotropy?

Movement disorder → Anxiety/ OCD

Anxiety/OCD → Movement disorder

Shared underlying etiology → Anxiety/OCD, Movement disorder

Family/ twin studies
Longitudinal studies: what comes first?

REVIEW

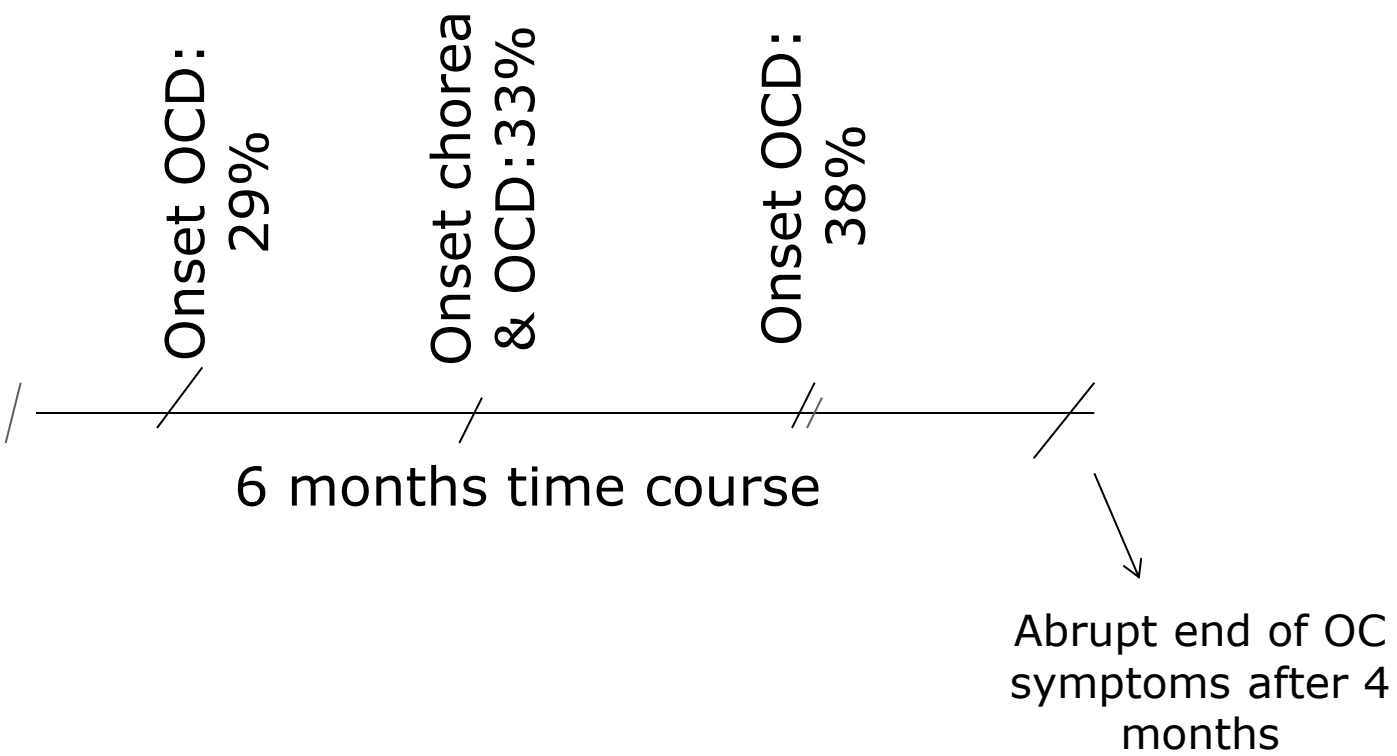
# Relationship between movement disorders and obsessive—compulsive disorder: beyond the obsessive—compulsive—tic phenotype. A systematic review

Lieneke A Fibbe,[1] Danielle C Cath,[2] Odile A van den Heuvel,[1,3] Dick J Veltman,[1] Marina A J Tijssen,[4] Anton J L M van Balkom[1]

*J Neurol Neurosurg Psychiatry* 2012;**83**:646—654. doi:10.1136/jnnp-2011-301752

Case control studies
Family studies
Prospective studies

# Asbahr 1998:N=50
# Sydenham chorea



# Obsessive-Compulsive Spectrum Disorders and Rheumatic Fever: A Family Study

Ana Gabriela Hounie, David L. Pauls, Maria Conceição do Rosario-Campos, Marcos Tomanik Mercadante, Juliana Belo Diniz, Maria Alice De Mathis, Maria Eugênia De Mathis, Priscila Chacon, Roseli Gedanke Shavitt, Mariana Curi, Luiza Guilherme, and Eurípedes Constantino Miguel

Biological Psychiatry 2007

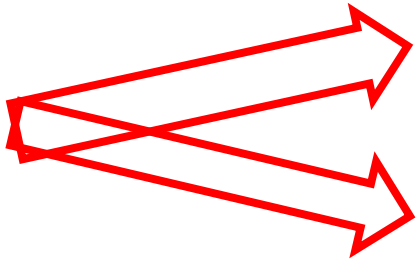
**Table 6.** Morbid Risks for Individual Obsessive-Compulsive Spectrum Disorders in Relatives of RF and Control Probands According to the Presence of an Obsessive-Compulsive Spectrum Disorder in the Proband

| | FDR of RF+OCSD ($n$=44) | % | FDR of RF−OCSD ($n$=207) | % | Controls −OCSD ($n$=130) | % | $p$ |
|---|---|---|---|---|---|---|---|
| OCD | 0 | 0% | 6 | 2.9% | 0 | 0% | .10 (F) |
| Subclinical OCD | 2 | 4.5% | 9 | 4.3% | 6 | 4.6% | .99 ($\chi^2$)[a] |
| OCD+subcOCD | 2 | 4.5% | 15 | 7.2% | 6 | 4.6% | .55 ($\chi^2$)[b] |
| TS | 1 | 2.3% | 1 | .5% | 1 | .8% | .35 (F) |
| CTD | 2 | 4.5% | 8 | 3.9% | 1 | .8% | .14 (F)[c] |
| TTD | 2 | 4.5% | 2 | 1% | 1 | .8% | .15 (F) |
| TS+CTD | 3 | 6.8% | 9 | 4.3% | 2 | 1.5% | .16 |
| TS+TCD+TTD | 5 a | 11.4% | 11 | 5.3% | 3 b | 2.3% | .055 ($\chi^2$)[d] |
| BDD | 4/32 a | 12.5% | 5/156 b | 3.2% | 1/92 c | 1.1% | .019 (F)[e] |

OCSD, obsessive-compulsive spectrum disorder (includes OCD, tic disorders and BDD); FDR, first-degree relatives; RF, rheumatic fever; OCD, obsessive-compulsive disorder; TS, Tourette syndrome; CTD, Chronic tic disorder; TTD, transient tic disorder; BDD, body dysmorphic disorder; $\chi^2$, chi-square test; F, Fisher test.

## Sydenhams chorea: pleiotropy most likely

Shared underlying etiology



Anxiety/OCD

Sydenhams chorea

Family/ twin studies
Longitudinal studies: what comes first?

# Psychiatric comorbidity in Myoclonic dystonia

Weissbach et al., 2013; Foncke et al., 2008

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| Any symptom | 71% | 42% | 62% | | – |

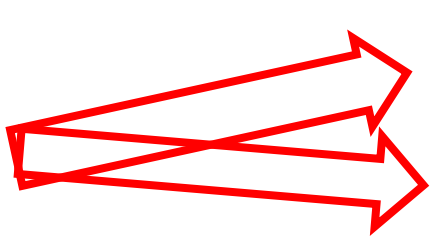
AD = anxiety disorders, MAD = major affective disorders, MC = manifesting mutation carriers; NMC = non-manifesting carrier; *p*-value for manifesting mutation carriers vs. non-manifesting mutation carriers of level 1 data.

In M-D, OC & anxiety symptoms perfectly co-segregate with manifesting symptoms

# Myoclonus dystonia: Cause, consequence or pleiotropy?

M-D → Anxiety/ OCD

Shared underlying etiology cannot be ruled out due to Maternal imprinting: multigenerational family study needed



# The complex relationship between tics and OCD

- GTS/ tics:
  - 1:1000/ 5%
  - Male:female = 2:1
  - 20-60% OCD
  - Up to 25% GTS,CT, OCD in first degree relatives
  - Age at onset: 5-7 yrs

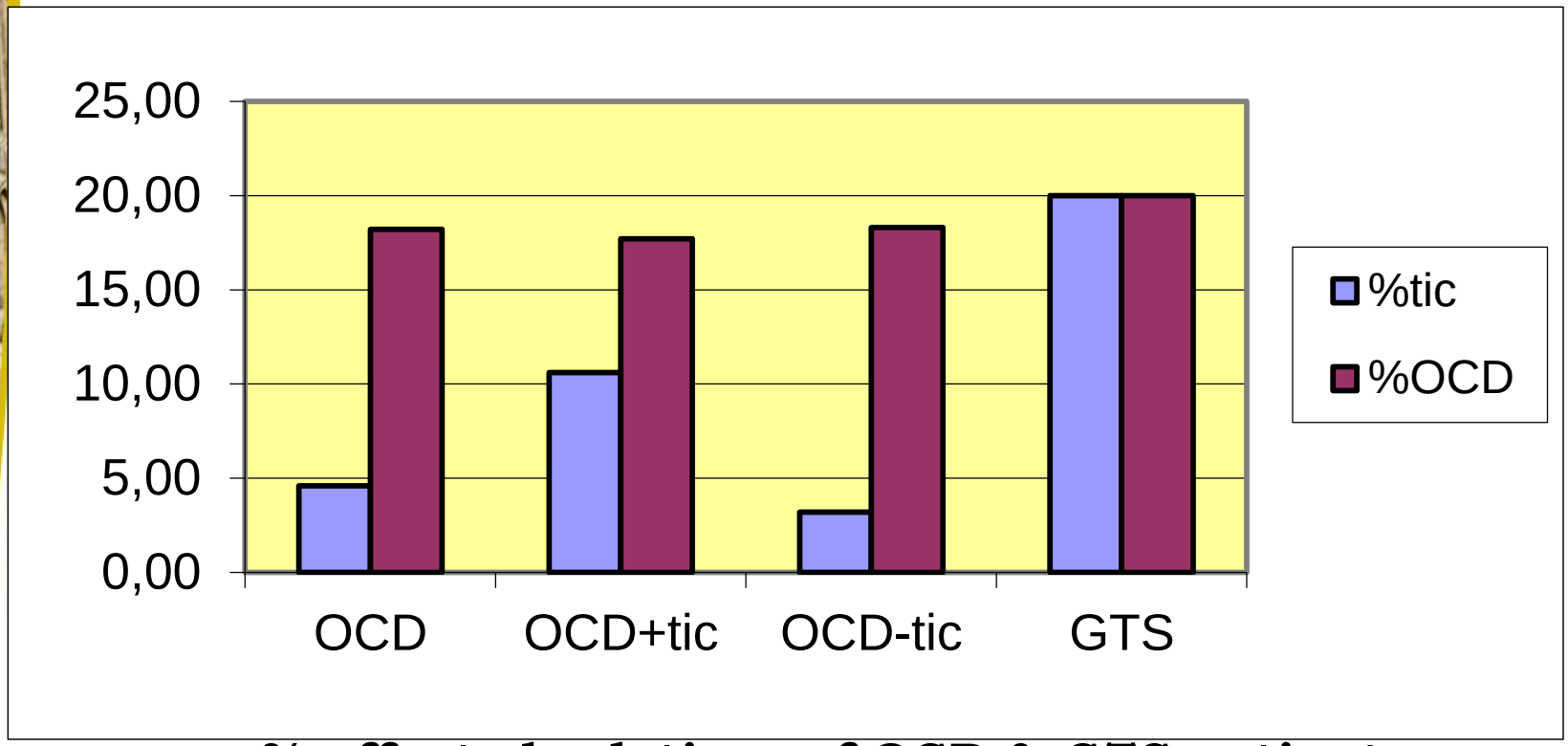
- OCD
  - 2-3%
  - Male: female= 1: 1.5
  - 15-25% tics
  - Up to 10% tics in first degree relatives; OR= 5
  - age at onset: bimodal (age 7-8 and age 14)

# Family studies:
# Risk of tics, OCD or ADHD in relatives of GTS patients

**Pauls et al. 1993; Stewart et al. 2006, O'Rourke 2009**

| Diagnosis GTS proband | Relatives: Men | Relatives Women | Total |
|---|---|---|---|
| **GTS** | 15% | 3.4% | 8.7% |
| CT | 21.5% | 13.8% | 17.3% |
| **OCD** | 7.2% | 15.2 % | 11.5% |
| Total | 43.0% | 31.8% | ±37.5% |

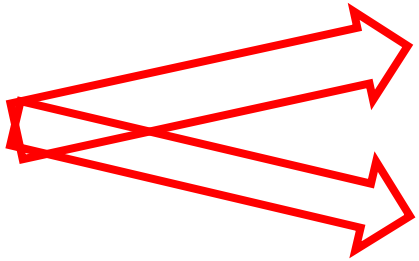
# Genetic relationship between GTS & OCD: family studies
## Tic-free versus tic-related OCD/ GTS
## Pauls et al., 1995
## n=100 probands, 466 relatives, 33 controls & 150 relatives




**% affected relatives of OCD & GTS patients**

# Relationship GTS and OCD: pleiotropy most likely *within tic* families

Shared underlying etiology



OCD

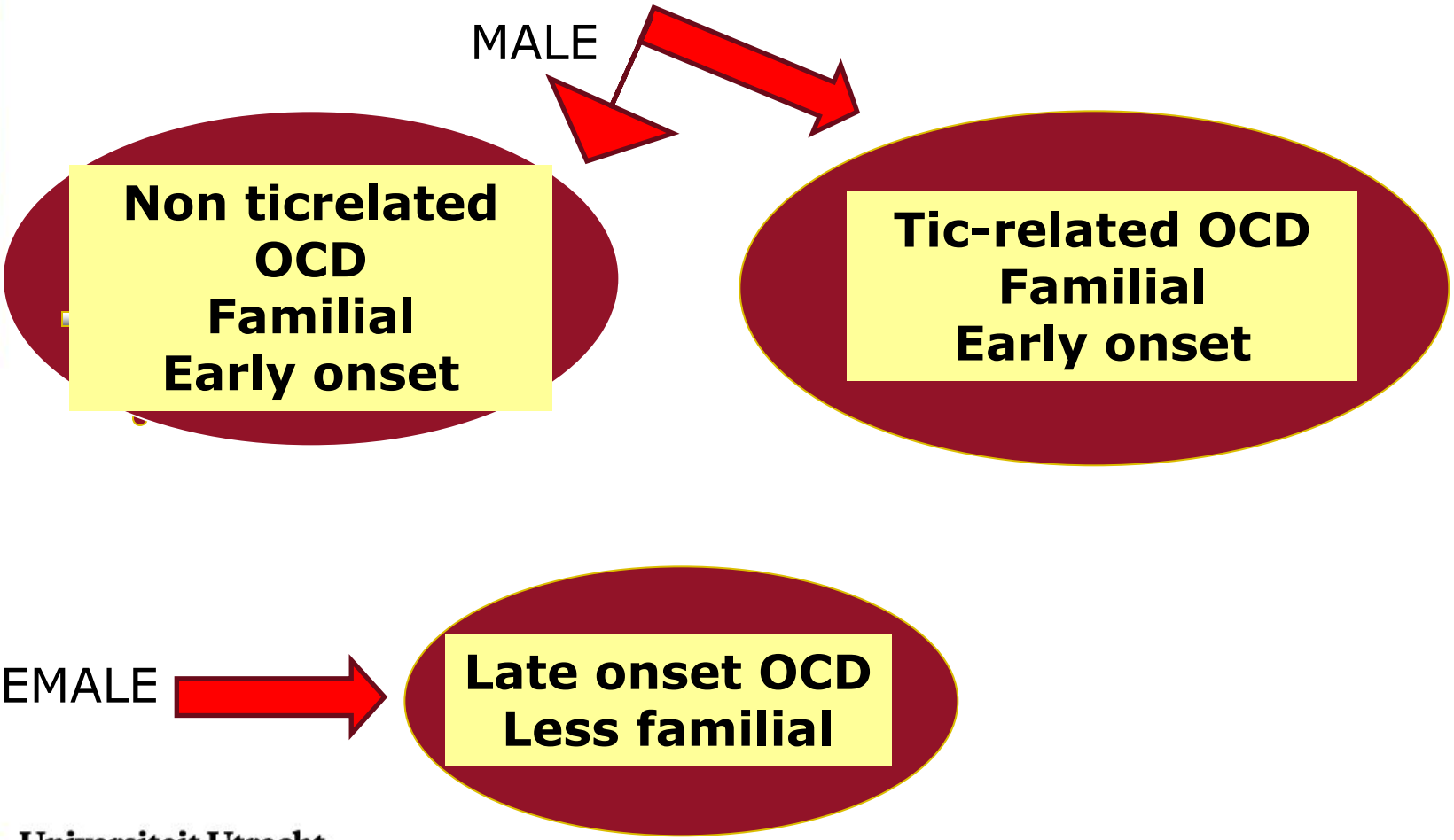
Tics

Family/ twin studies
Longitudinal studies: what comes first?

# Summary of OCD family studies

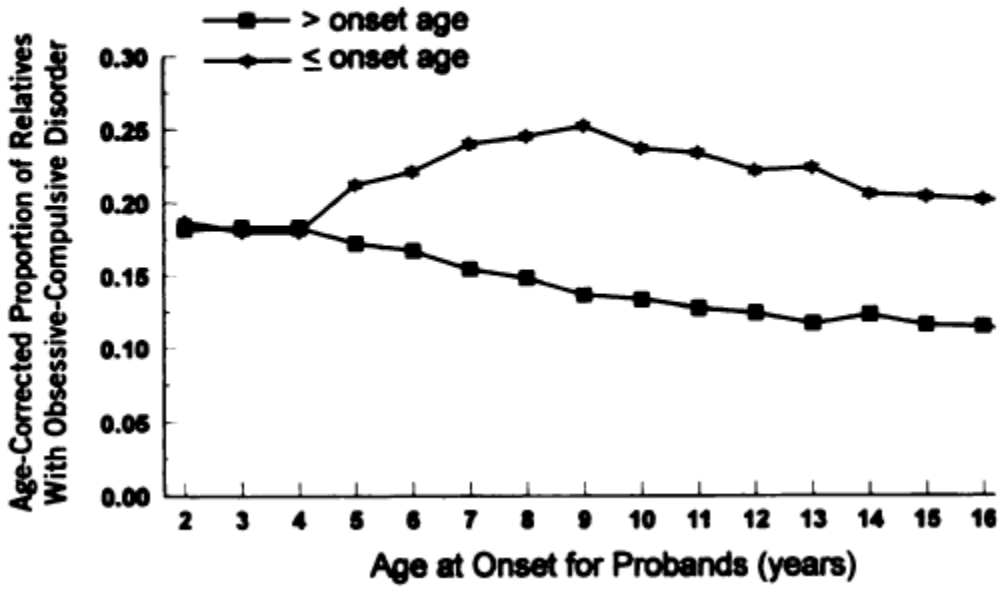
Pauls et al. 1995; Grados et al. 2001;

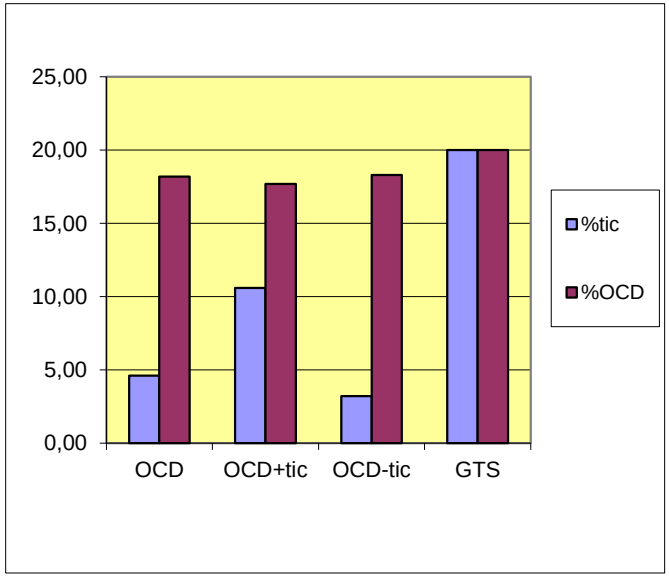
Lower age at onset OCD↓ > OCD relatives
> tic relatives



# More complex genetic relationship *within OCD families*

**FIGURE 2. Risk of Obsessive-Compulsive Disorder Among Relatives of 100 Probands With Obsessive-Compulsive Disorder at Ages Less Than or Equal to Probands' Ages at Onset and Ages Greater Than Probands' Ages at Onset**

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# In line with this notion: Lea Davis et al., 2013

OPEN ACCESS Freely available online

PLOS | GENETICS

## Partitioning the Heritability of Tourette Syndrome and Obsessive Compulsive Disorder Reveals Differences in Genetic Architecture

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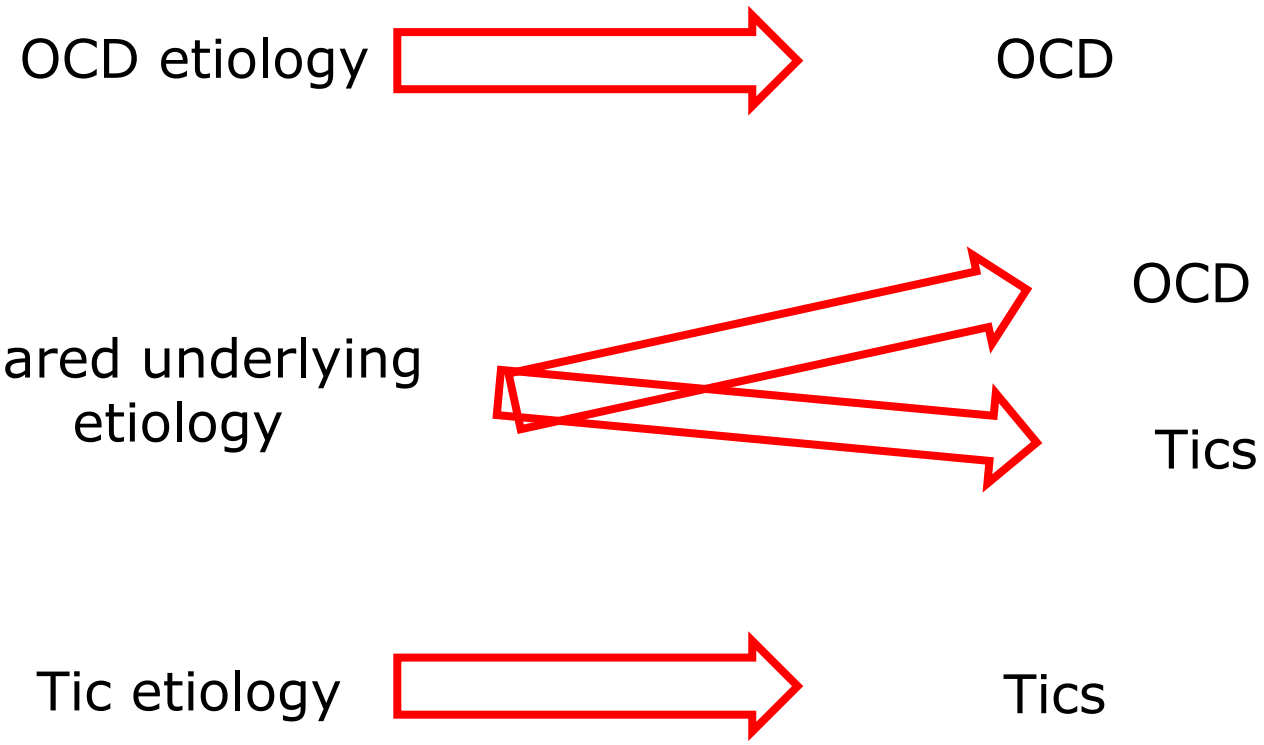
## OCD and tics: complex genetic relationship




Family/ twin studies
Longitudinal studies: what comes first?

# To conclude:

- Tics are easy to recognize, the hardship is in the co-morbidities
- Differential diagnosis with other hyperkinetic movement disorders AND with psychogenic tics (use BP?)
- All hyperkinetic movement disorders have some intrinsic relation with anxiety disorders and OCD
- Relationship with OCD is straight forward within TS families, Complex within OCD families

- Working in Hyperkinetic movement disorders means; working together between neurologists and psychiatrists!

# Tourette's Syndrome has first been described by:

1. George Gilles de la Tourette
2. Jean Martin Charcot
3. Jean Marc Gaspard Itard
4. Pierre Janet
5. Sigmund Freud

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# The most important characteristics of a tic are:

1. a-rhythmical character
2. Suppressability
3. Voluntaryliness
4. premonitory urges preceding the tic
5. onset in childhood
6. onset in head/ face, caudal spread
7. all of the aspects mentioned here-above

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# The most important co-morbidities of tics are:

1. ADHD and bipolar disorder
2. ADHD and Obsessive-compulsive disorder
3. Obsessive-compulsive disorder and depression
4. Sleep disorders
5. Dystonia

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# The proportion of variance in tics explained by genetic factors is:

1. Between 20%-30%
2. Between 30%-50%
3. Between 50%-70%
4. > 70 %

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# The most frequent natural course of childhood tics into adulthood is:

1. progression into severe tics
2. development of disabling psychiatric co-morbidities
3. Improvement of tic severity and decrease of tic impact on quality of life
4. development of disabling co-morbid other hyperkinetic movement disorders

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# The most robust (mostly replicated) neuro-imaging volumetric findings in TS are:

1. Decreased asymmetry of putamen volumes in TS versus controls

2. Decreased activity in secondary motor areas during finger tapping tasks

3. Cortical thinning and reduced grey matter volumes in limbic regions in adult TS, suggesting a failure in neural compensation to control tics

4. Increased caudate nuclei volumes in TS, with a positive correlation between tic severity and caudate volumes

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# Which of the following statements is best supported by evidence from RCTs?

1. Behaviour therapy has the best treatment effect at longer term follow-up
2. Pharmacotherapy with clonidine has the best treatment effect of tics with least side-effects
3. Antipsychotic drugs have the best treatment effect but pose challenges with respect to side-effects
4. Progressive relaxation strategies provide the most effective treatment of tics at longer term follow-up
5. Botulin toxin injections are currently the best treatment options for isolated tics in the area of the face and neck.

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