

Aggressive Symptoms in Adults with Tourette Syndrome

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Definition of Aggression

Overt behavior involving:

- the intent to deliver noxious stimulation to another organism, or
- the intent to act destructively toward inanimate objects

Types of Aggression in Humans

1. Verbal aggression
2. Physical aggression against other living things such as people or animals
3. Physical aggression against inanimate objects

Causes of Aggressive Symptoms

- Delirium
- Seizure disorders
- Head trauma
- Brain tumor
- Stroke
- Toxins

Causes of Aggressive Symptoms

- Alcohol/Substance Abuse
- Physical/Sexual Abuse
- Pain
- Sleep disorders
- Pre-existing psychopathology
- Medication side effects

Causes of Aggressive Symptoms in Adults

Pre-existing psychopathology:

- Antisocial Personality Disorder
- Borderline Personality Disorder
- Major Depression
- Bipolar Disorder
- Schizophrenia
- Attention Deficit Disorder
- Intermittent Explosive Disorder

Causes of Aggressive Symptoms in Adults

Psychotropic Medications:

- Alcohol
- Benzodiazepines
- Steroids
- Psychostimulants
- Guanfacine
- Neuroleptics
- SSRIs

Medication-related Aggression

- Medication-induced activation
- Disinhibition
- Paradoxical reactions
- Behavioral toxicity

Sx: Irritability, anger/rage, excitability
hyperactivity, agitation, lability

Neurobiology of Aggression

- DA, opioids, androgens, ACTH facilitate sexual behavior & aggression
- Serotonin (5HT) and NE modulate inhibitory responses
 - Disturbances of central 5HT linked with aggression and impulsivity
 - Low central 5HT associated with violence
 - Lesions of PFC or OFC linked with aggression

Extreme Irritability in Other Movement Disorders

- Parkinson's Disease: 20% Major depression
20% Dysthymia
10% Mania
- Huntington's Disease: 40% Mood disorder
30% unipolar depression
10% bipolar disorder (mostly Type II)
30% severe irritability
- Wilson's Disease: 30% Depression
45% Irritability

Aggressive Symptoms in TS

- Common in clinical settings
- Cause severe morbidity
- Complex etiology
- Treatment often non-specific

International TS Database

3,500 TS cases in 22 countries

(Freeman et al.1999)

- 37% anger control problems ever
- 26% anger control problems now
- <10% anger control problems TS only

Types of Aggressive Symptoms in Tourette Syndrome

- Proactive/non-impulsive
(bullying, predatory behavior)
- Reactive/impulsive
("rage attacks", affective storms)

Distinguishing Rage From Predatory Aggression

Predatory Aggression

versus

Rage Attacks

cruel indifference to
feelings of others

capable of empathy for
others

outburst accompanied by
decreased autonomic
activation

outburst accompanied by
increased autonomic
activation

Temper Tantrums

- Occurs < 1/3 children ages 3-12 years
- Most common: ages 3-5 years (75%)
- Least common: ages 9-23 (4%)
- More common: boys > girls (3:1)
- Hx: trauma, seizure, tics, hyperactivity, bedwetting, head banging, sleep problems

Common Comorbidities: Tourette Syndrome

- Obsessive Compulsive Disorder: 25-50%
- Non-OCD Anxiety Disorders: 30-40%
- Attention Deficit Hyperactivity Disorder: 50-60%
- Mood Disorders: 30-40%
- Learning Disabilities: 20-30%

Bipolar Affective Disorder and Tourette Syndrome

- **Comings & Comings 1987:** depression & manic- depressive symptoms common in TS
- **Kerbeshian et al. 1995:** 15/205 patients with TS + BPD
- **Berthier et al. 1998:** full spectrum BPD found in TS
- **Coffey et al. 2000:** comorbid Depression and BPD strongly predictive of illness severity in TS

DSM-IV-TR Diagnostic Criteria for Intermittent Explosive Disorder

- Discrete episodes of failure to resist aggressive impulses resulting in serious assaultive acts of destruction of property (Criterion A)
- Degree of aggression grossly out of proportion to provocation or stressor (Criterion B)
- Aggressive episodes not due to direct effects of a substance, other mental disorder, or general medical condition (Criterion C)

Prevalence & Correlates of DSM-IV Intermittent Explosive Disorder in the National Comorbidity Survey Replication

9282 people ages 18 and older
face-to-face household survey

- Lifetime prevalence: 5.4% - 7.3%
- 12-month prevalence: 2.7% - 3.9%
- Widely distributed in the population
- Usually begins in childhood or adolescence
- Significantly comorbid with mood, anxiety, and substance disorders
- Only 28.8% ever received treatment for their anger

(Kessler et al.2006)

Definition of Explosive Outbursts in TS

- Abrupt, unpredictable episodes of severe physical and/or verbal aggression
- Grossly out of proportion to any provocation
- Experienced as uncontrollable & distressing
- Accompanied by physiological activation

A Comparison of TS Adults ages 18 years and Older with and without Explosive Outbursts

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(unpublished data, 2006)

Objectives

1. To perform a cross-sectional analysis of TS adults who consecutively presented for consultation at a specialty TS program
2. To compare TS adults with and without explosive outbursts on a number of clinical and demographic variables

Subjects

- 68 Adults with TS (DSM-IV-TR) ages 18-60 yrs
- Experimental subjects also met criteria (DMS-IV) for Intermittent Explosive Disorder (IED) omitting Criterion C, experienced ≥ 3 rage episodes/week
- Known causes of explosive outbursts excluded
- No change in medication 1 month prior to evaluation

Methods

20 TS Adults (+) Explosive Outbursts
compared with

36 TS Adults (-) Explosive Outbursts:

- General demographic characteristics
- Current psychotropic medications
- Tic type and severity
- Current psychiatric comorbidities

Methods

Assessment of Explosive Outbursts

- ≥ 3 episodes/week of sudden, uncontrollable rage characterized by all of the following:
- Failure to resist aggressive impulses resulting in verbal and/or physical attacks to self or others
- Behavior is grossly out of proportion to any provocation or frustration
- Atypical of baseline personality

Methods

Comorbidity Experimental Screens & Measures

- Semi-structured interview/DSM-IV-TR
- Wender-Utah Rating Scale (WURS)
- Adult Attention Deficit Disorder Rating Scale (ADHD-RS)
- Yale-Brown Obsessive Compulsive Scale (Y-BOCS)
- The Mood Disorder Questionnaire (MDQ)

Methods

Other Experimental Measures

- Yale Global Tic Severity Scale (YGTSS)
- Rage Screen and Questionnaire
- Global Assessment of Function (GAF)
- Hollingshead Scale socioeconomic status
- Psychotropic medication status

Statistical Analysis

- Retrospective, cross-sectional analysis, divided all TS adult cases into two groups: (+) rage and (-) rage
- Analyzed variables between these two groups, similarly to a case-controlled design
- Used Fisher's Exact Test to compare prevalence rates of categorical variables between experimental and control groups, as well as within the overall group with two-sided P
- Used Wilcoxon Rank Sum Test to examine continuous variables between experimental and control groups, as well as within the overall group with two-sided $P > [Z]$

Demographic Features: TS Adults

Mean age:	31 years \pm 11.1 (range: 18-60 years)
Mean age onset tics:	7.4 years \pm 2.8
Sex (ratio 5:1):	82% male 18% female
Handedness	84% R 16% L
Mean SES:	2.8 \pm 0.7 (range: Classes 2-4)
Race:	100% Caucasian

Demographic Features: TS Adults

Marital Status: 50% married, 48% single, 2% divorced

Living Status: 68% independent, 32% living at home

Medication Status: 59% un-medicated at time of initial consultation

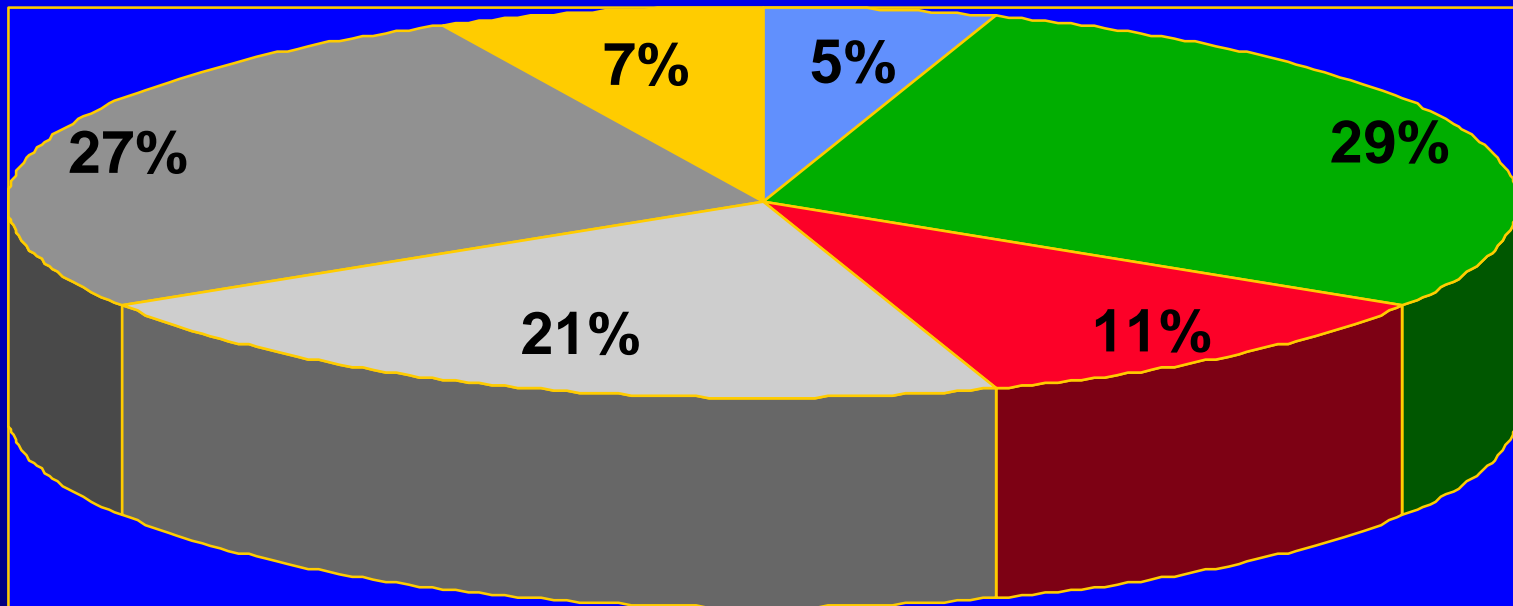
18% receiving neuroleptic

15% receiving SSRI

Demographic Features: TS Adults

Educational Status:	5% dropped out of high school
	29% completed high school
	11% dropped out of college
	27% completed college
	7% completed graduate school
	21% still in college

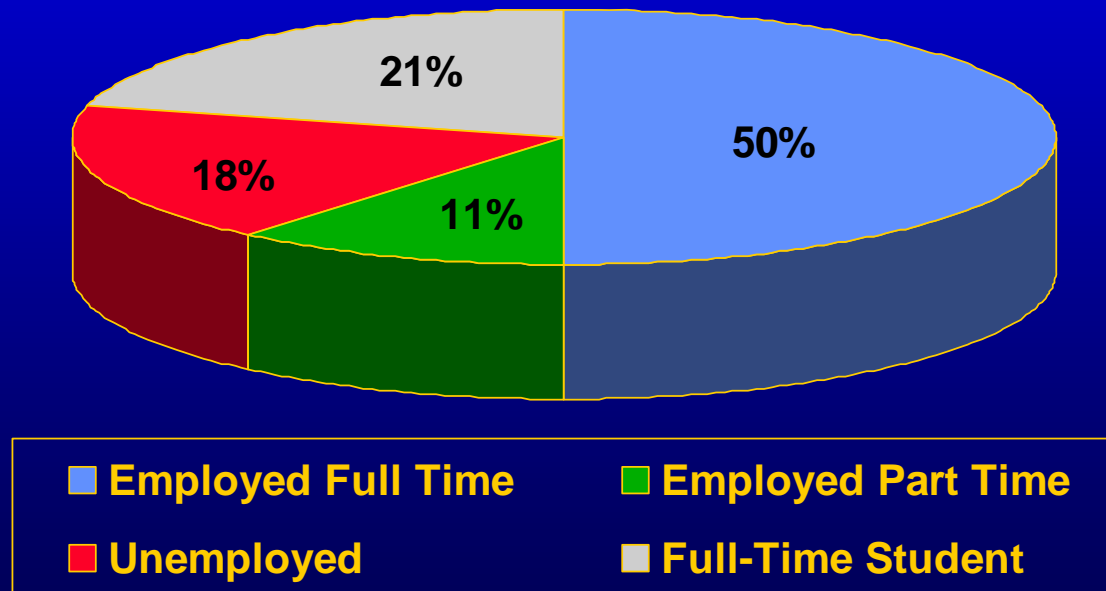
Educational Status: TS Adults



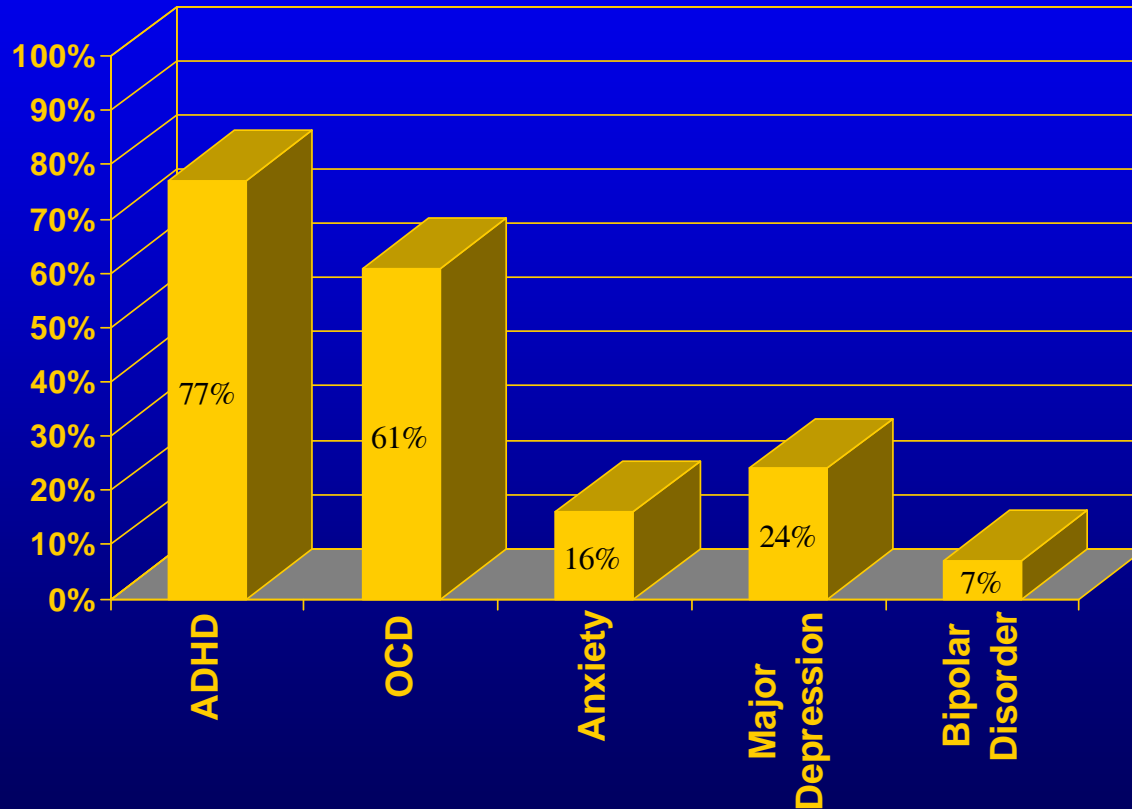
Employment Status: TS Adults

Employment Status:

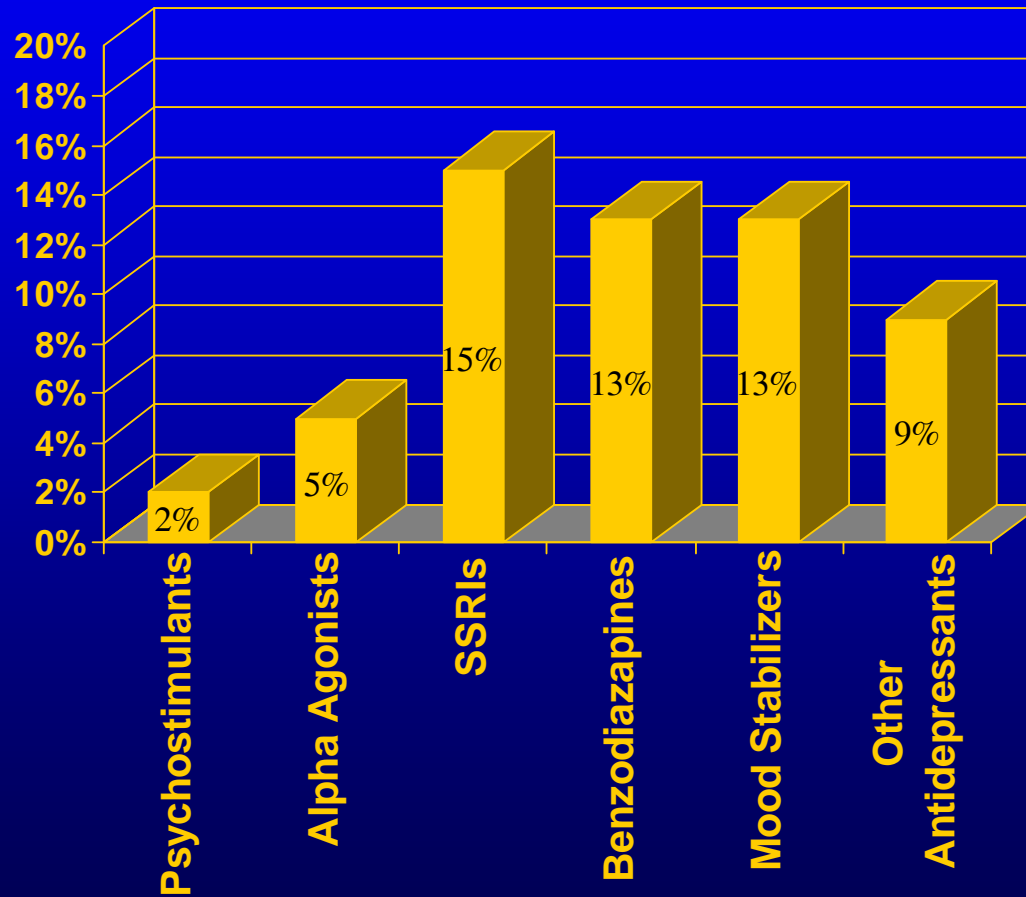
- 50% employed full-time
- 11% employed part-time
- 18% unemployed
- 21% full-time student



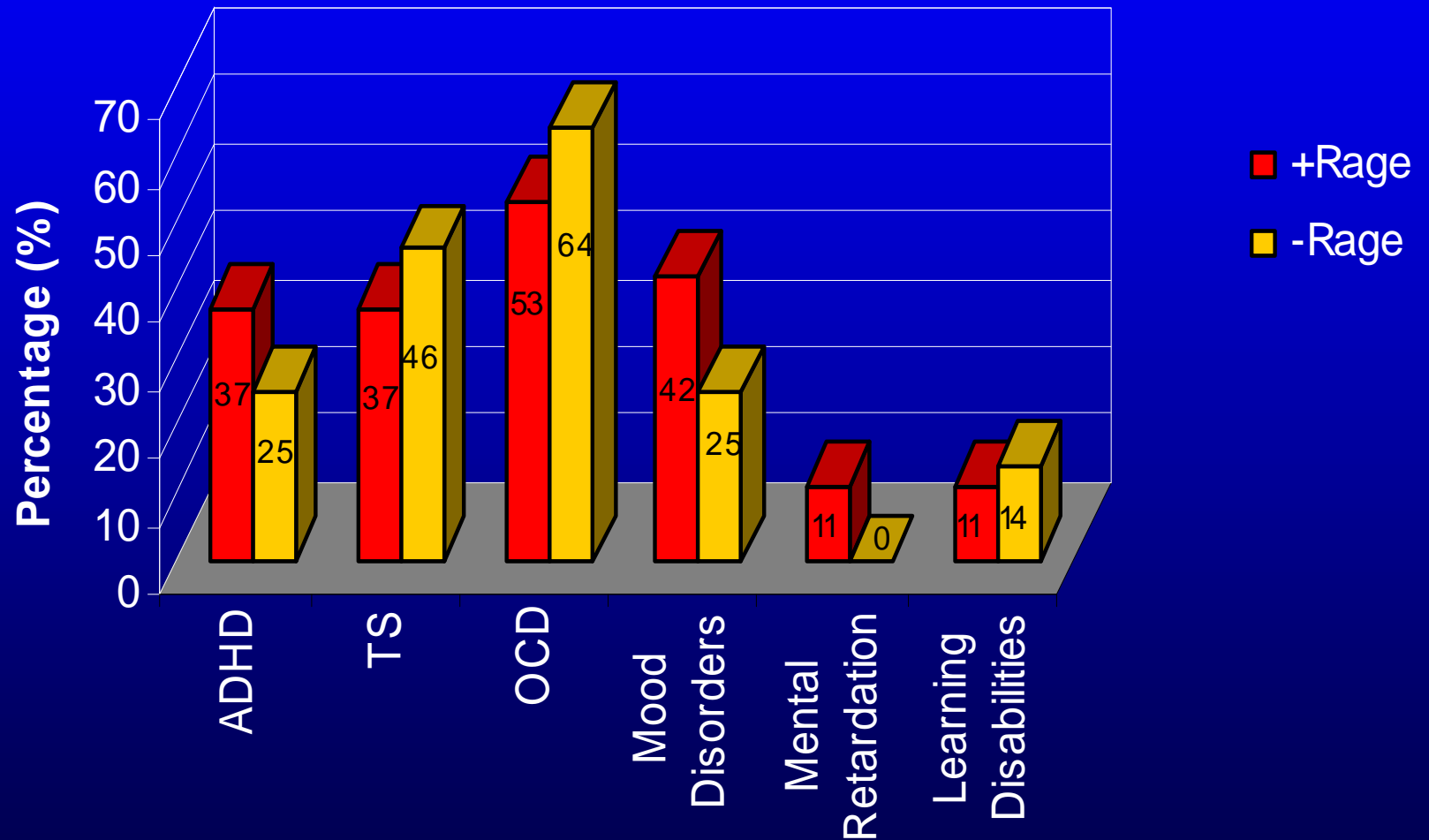
Current Psychiatric Comorbidities: TS Adults



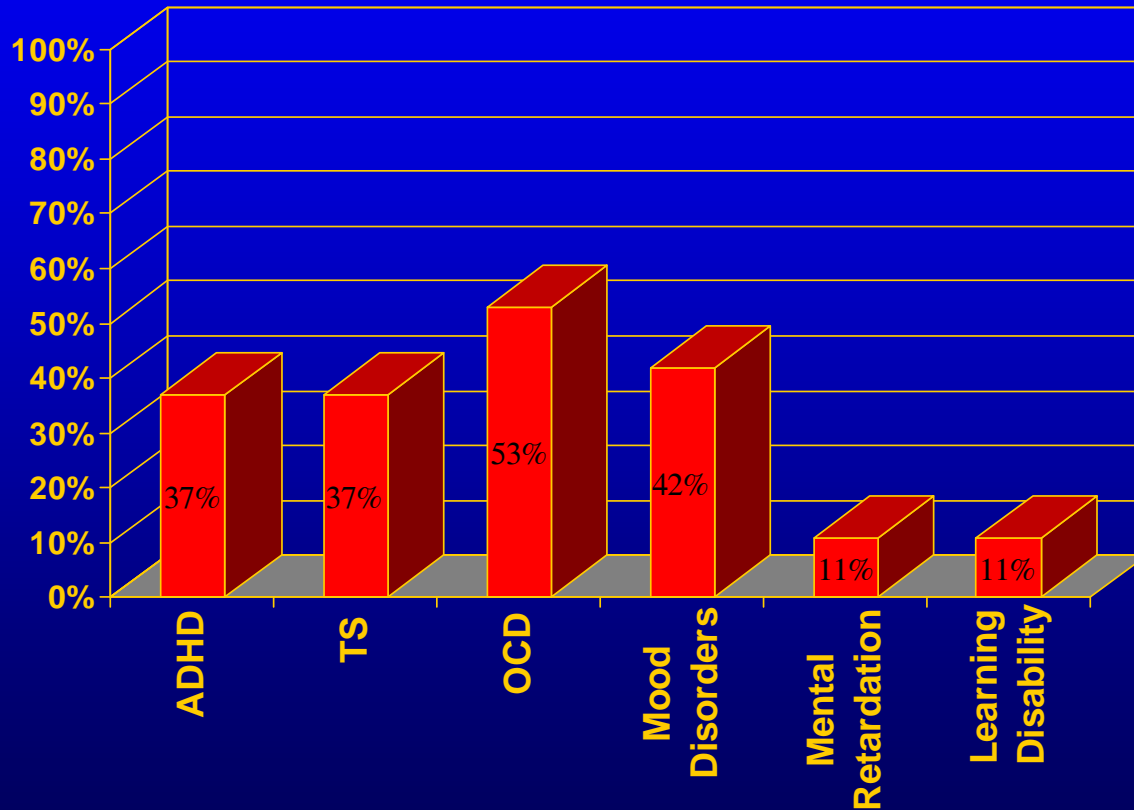
Current Psychotropic Medications: TS Adults



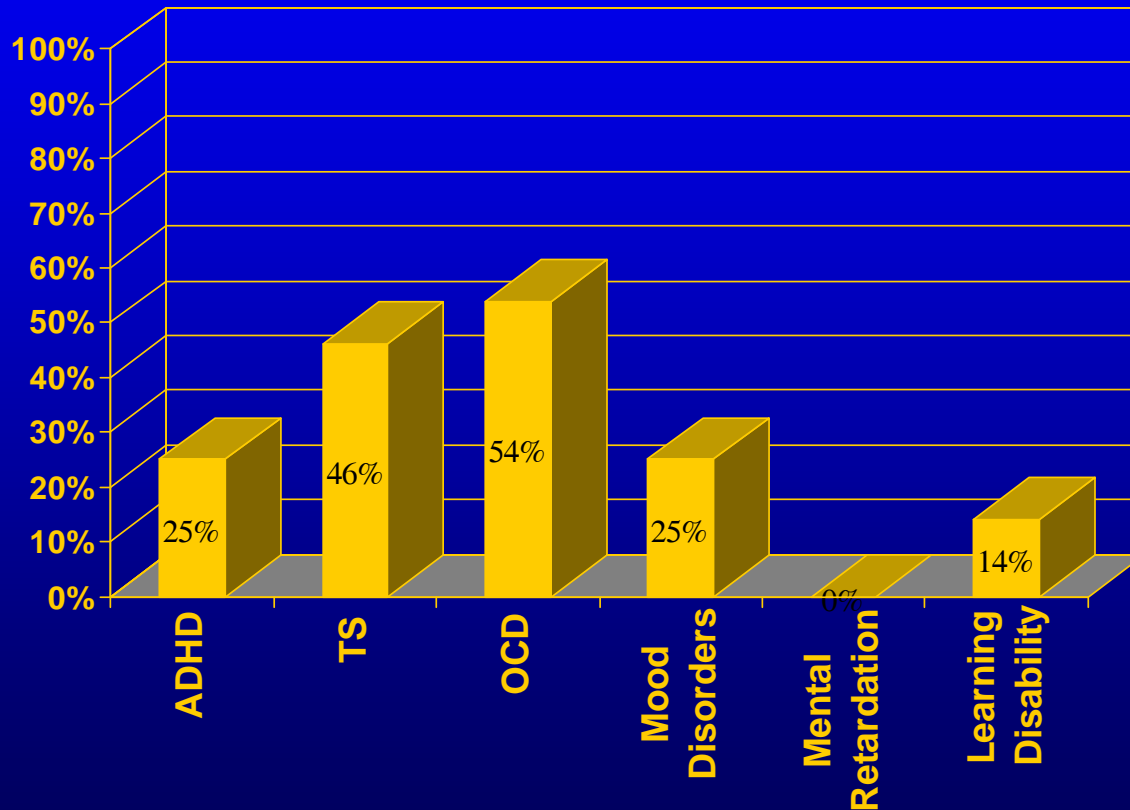
Family Psychiatric History



Family Psychiatric History: TS Adults with Rage



Family Psychiatric History: TS Adults without Rage



Distribution of Mean YGTSS, CY-BOCS, and Adult TS Rage Status

	Experimental	Control	p
Mean (SD)			
YGTSS	51.1 (19.3)	46.3 (13.4)	NS
Motor Tics	11.9 (4.6)	12.6 (4.2)	NS
Vocal Tics	8.3 (5.1)	6.6 (6.2)	NS
Total Tics	20.2 (8.4)	19.2 (8.9)	NS
Y-BOCS	12.9 (7.9)	15.7 (9.3)	NS
Obsessions	6.3 (3.8)	8.0 (4.7)	NS
Compulsions	6.7 (4.2)	7.9(4.7)	NS

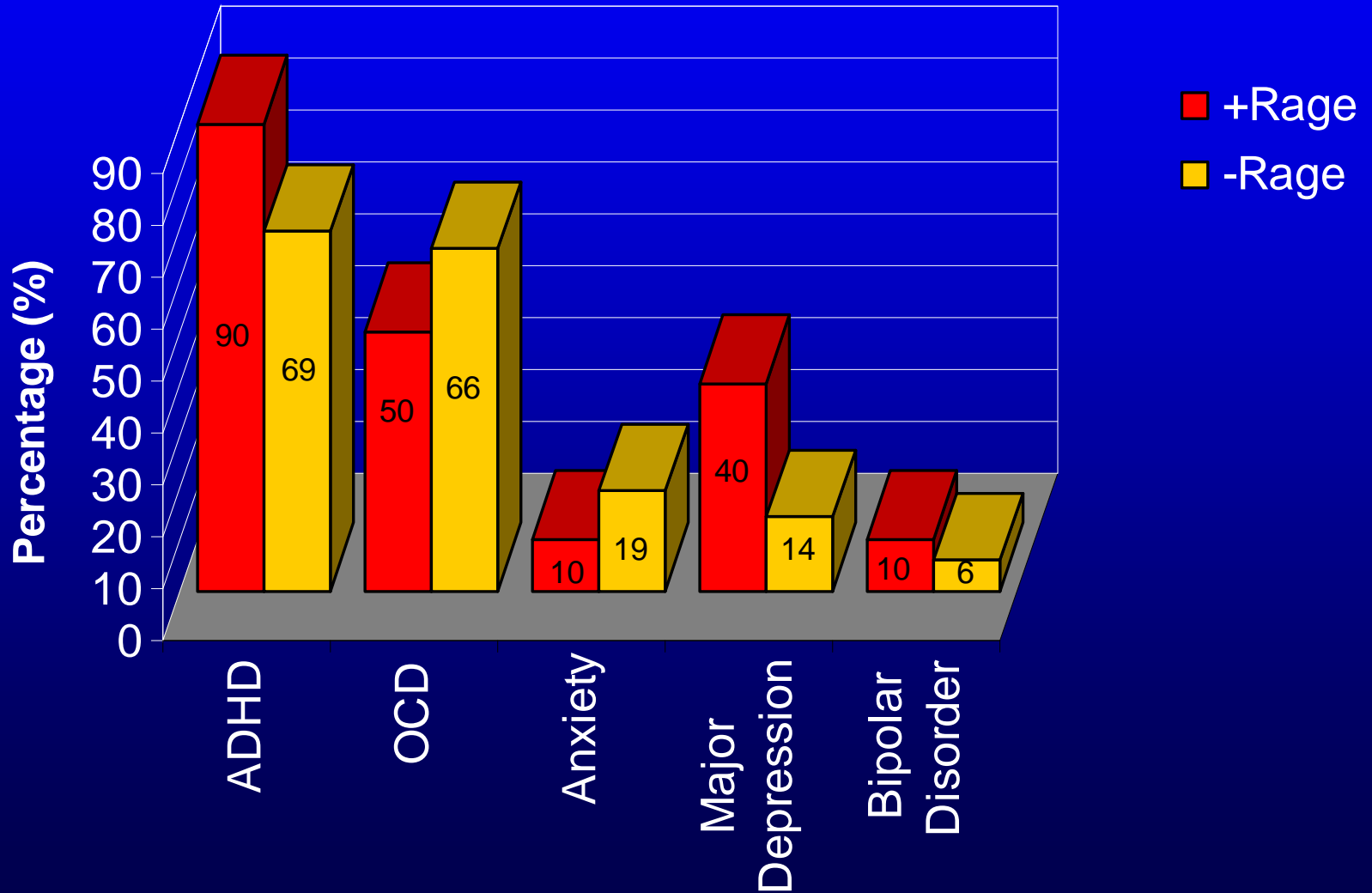
Distribution of Mean WURS, ADHD-RS, and Group Status

	Experimental	Control	p
Mean (SD)			
WURS	73.5(31.0)	60.9(31.5)	NS
ADHD-RS	24.8(11.3)	22.9(11.4)	NS

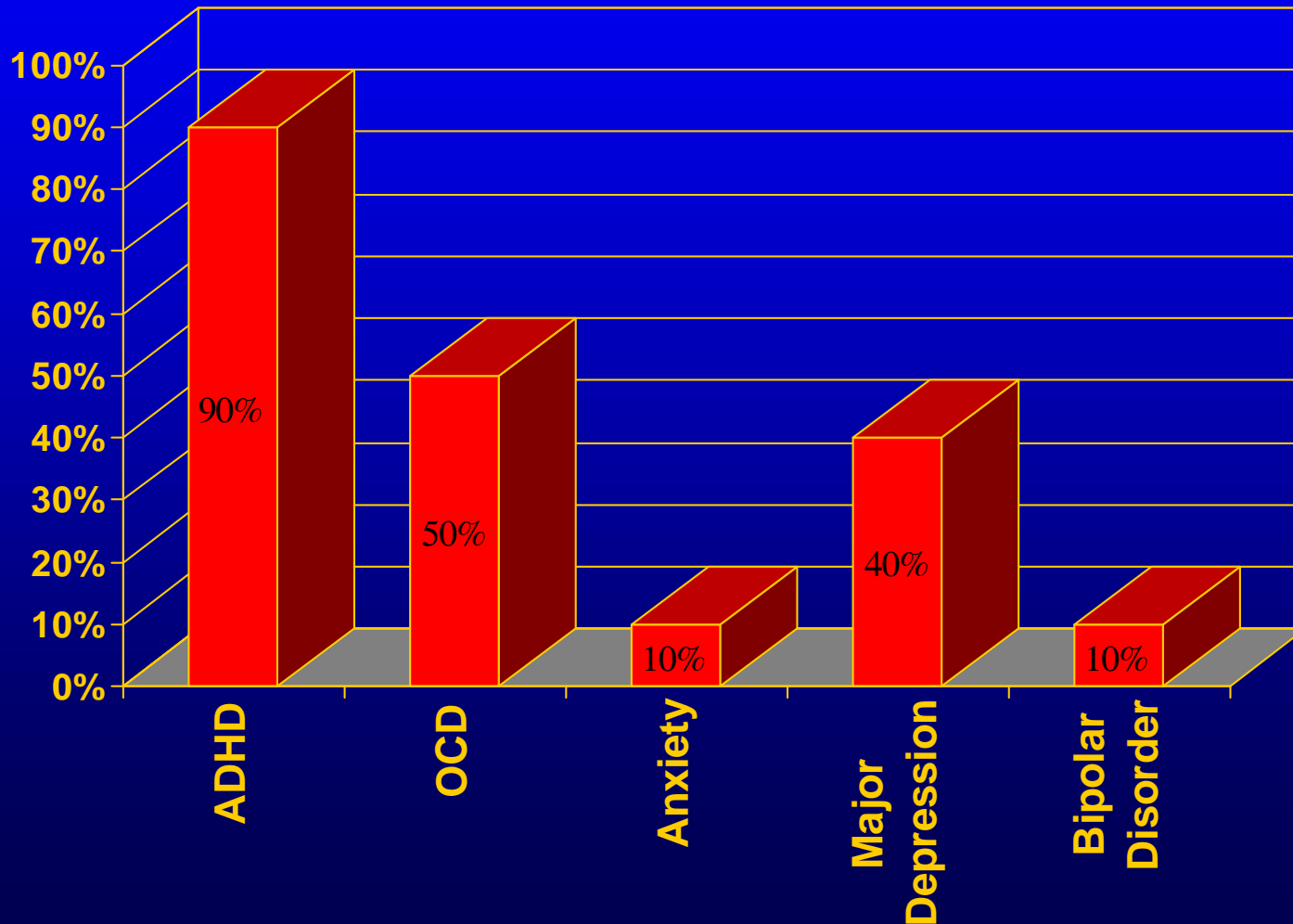
Current Comorbid Diagnoses: TS(+) Rage v. TS (-) Rage

Comorbidity %(n)	Total	Experimental	Control	p
ADHD	77 (43)	90 (18)	69 (25)	NS
OCD	61 (34)	50 (10)	66 (24)	NS
Anxiety	16 (9)	10 (2)	19 (7)	NS
Mood Dis	30 (17)	50 (10)	19 (7)	.05
Depression	23 (13)	40 (8)	14 (5)	.05
BIPNOS	7 (4)	10 (2)	6 (2)	NS

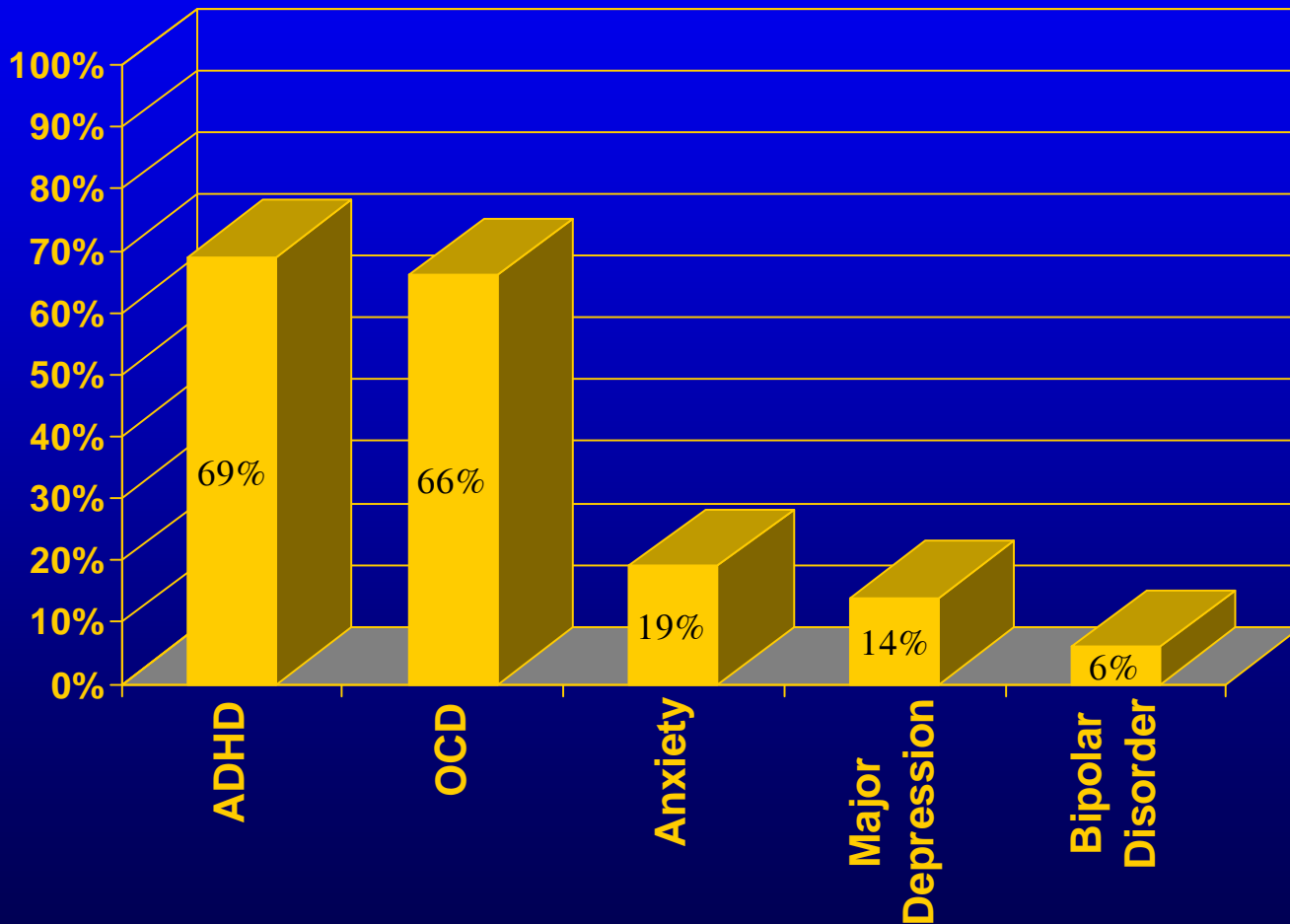
Current Psychiatric Comorbidity



Current Psychiatric Comorbidity: TS Adults with Rage



Current Psychiatric Comorbidity: TS Adults without Rage



Results

- 36% of TS Adults presenting to specialty clinic met diagnostic criteria for Explosive Outbursts/"Rage"
- TS Adults with Rage had statistically lower global functioning overall ($p < .02$) when compared with TS Adults without Rage
GAF at initial consultation: 65 (TS + Rage)
68 (TS – Rage)
- TS Adults with Rage did not differ from those without Rage on measures of tic type, tic severity or global severity on YGTSS

Results

- TS Adults With Rage are statistically ($p < .05$) more likely to meet current DSM-IV-TR diagnostic criteria for a mood disorder
- The majority of TS Adults With and Without Rage who presented to this specialty clinic had significant psychiatric comorbidity but less than half were taking any prescribed psychotropic medication at the time of initial evaluation.

Conclusion

- Explosive outbursts in TS Adults are associated with significant morbidity and require psychiatric evaluation and intervention
- Explosive outbursts in TS Adults should alert clinician to underlying comorbid disorders, especially mood disorders, ADHD, and OCD
- Etiology of rage in TS Adults is complex and includes both biological & environmental factors

**Treatment of Explosive Outbursts
in
Tourette Syndrome**

Treatment of Rage Symptoms in TS

Comprehensive Evaluation

- **Diagnosis:** medical, psychiatric, neuropsychological
psychosocial assessment
- **Medications:** side effects, drug interactions
- **Psychosocial function:** family, work, community

Treatment of Rage Symptoms in TS

- **Atypical antipsychotics:**
risperidone, aripiprazole, olanzapine, ziprasidone, quetiapine
- **SSRIs:**
fluoxetine, sertraline, fluvoxamine, citalopram, paroxetine
- **Anticonvulsants/Mood Stabilizers:**
Lithium, divalproex, lamotrigine, carbamazepine, topiramate
- **Other:**
psychostimulants, propranolol, clonidine, mecamylamine, EFAs

Treatment of Rage Symptoms in TS

- Psycho-education
- Family therapy/Marital Therapy
- Anger Management programs
- Dialectical behavioral therapy
- Relapse prevention therapy
- Medication therapy