CURSO EVOLUTIVO Y SUBTIPOS EN EL TRASTORNO OBSESIVO-COMPULSIVO

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Fundación Ramón Areces
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ORIGINAL ARTICLE

A 40-Year Follow-up of Patients With Obsessive-compulsive Disorder

Gunnar Skoog, MD, PhD; Ingmar Skoog, MD, PhD

Arch Gen Psychiatry. 1999;56:121-127

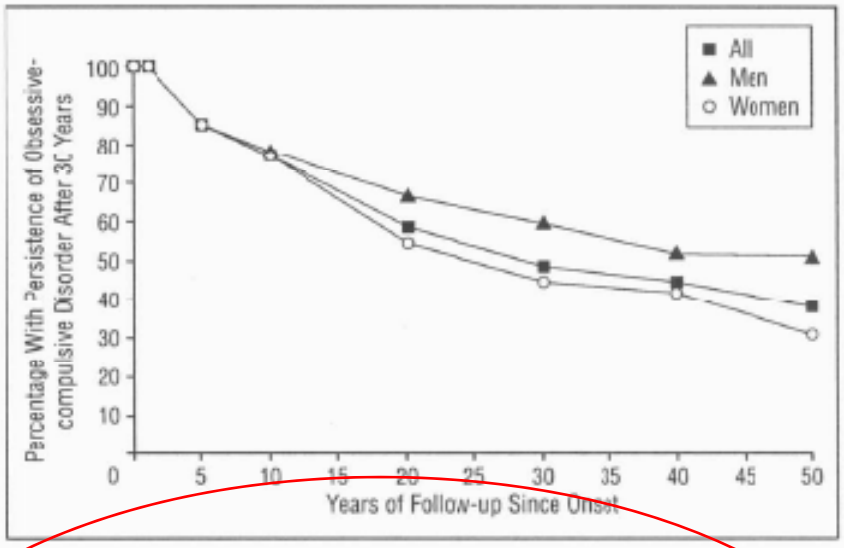


Table 3. Age at Onset in Relation to Prognosis*

Age at Onset, y	Status at the Examination in 1989-1993, No. (%)		
	Recovery	Improved With Clinical Symptoms	Unchanged/ Deteriorated
All patients			
<20 (n = 41)	15 (37)	12 (29)	14 (34)
20-29 (n = 57)	29 (51)	21 (37)	7 (12)
30-39 (n = 40)	22 (55)	16 (40)	2 (5)
≥40 (n = 6)	3 (50)	2 (33)	1 (17)
Men			
<20 (n = 18)	5 (28)	5 (28)	8 (44)
20-29 (n = 13)	5 (38)	6 (43)	2 (15)
30-39 (n = 8)	7 (88)	1 (13)	0 (0)
≥40 (n = 2)	2 (100)	0 (0)	0 (0)
Women			
<20 (n = 23)	10 (44)	7 (30)	6 (26)
20-29 (n = 44)	24 (55)	15 (34)	5 (11)
30-39 (n = 32)	15 (47)	15 (47)	2 (6)
≥40 (n = 4)	1 (25)	2 (50)	1 (25)

251 PACIENTES

47 AÑOS DE SEGUIMIENTO

✓83% MEJORÍA

✓20 % REMISIÓN COMPLETA

✓25% REMISIÓN CON SÍNTOMAS SUBCLÍNICOS

Table 2. Frequency of Some Obsessive-compulsive Symptoms From Onset to the First Examination in 1954-1956 in Relation to Recovery in 1989-1993

Symptoms From Onset Until 1954-1956 (n = 144)*	No. (%) Recovered From Obsessive-compulsive Disorder 1989-1993 (n = 69)	P†
Obsessions		
Rumination (n = 85)	40 (47)	.94
Impulsions (n = 69)	30 (44)	.39
Doubt (n = 64)	27 (42)	.29
Aggressiveness (n = 60)	25 (42)	.27
Aichmophobic (n = 55)	21 (38)	.10
Hypochondric (n = 29)	13 (45)	.87
Brooding on meaningless questions (n = 34)	13 (38)	.27
Guilt (n = 14)	3 (21)	.07
Magical (n = 22)	5 (23)	.02
Compulsions		
Checking (n = 43)	21 (49)	.97
Perfectionism (n = 29)	12 (41)	.56
Cleaning (n = 21)	7 (33)	.22
Repetitions (n = 20)	6 (30)	.14
Counting (n = 19)	9 (48)	.84
Rituals (n = 15)	3 (20)	.04
Washing (n = 14)	4 (29)	.21

Table 4. GAF Scores in 1954-1956 in Relation to GAF Scores and Recovery in 1989-1993*

GAF Scores at the Examination in 1954-1956		GAF Scores at the Examination in 1989-1993, No. of Patients						Recovery in 1989-1993, No. (%)
Score	No. of Patients	≥75	65-74	55-64	45-54	≤44	Undetermined	
≥75	28	27	0	0	1	0	0	18 (64)
65-74	39	15	16	8	0	0	0	19 (48)
55-64	66	25	7	21	12		1	30 (45)
45-54	11	2	1	3	2	3	0	2 (18)
Total	**144**	**69**	**24**	**32**	**15**	**3**	**1**	**69 (48)**

A 2-Year Prospective Follow-Up Study of the Course of Obsessive-Compulsive Disorder

Jane L. Eisen, MD; Anthony Pinto, PhD; Maria C. Mancebo, PhD; Ingrid R. Dyck, MPH; Maria E. Orlando, PhD; and Steven A. Rasmussen, MD

J Clin Psychiatry 2010;71(8):1033–1039

214 PACIENTES

22% REMISIÓN PARCIAL O COMPLETA

✓88% ISRS

✓49% CBT

Table 2. Probability of Full or Partial Remission From Obsessive-Compulsive Disorder Over 2 Years (N = 214)

	Full Remission		Full or Partial Remission	
Week	n	Probability	n	Probability
26	5	0.02	22	0.10
52	7	0.03	36	0.17
78	10	0.05	42	0.21
104	12	0.06	48	0.24

Table 3. Proportional Hazard Regression Testing Clinical Predictors of Full or Partial Remission From Obsessive-Compulsive Disorder Over 2 Years (N = 214)[a]

Predictor	β (SE)	χ^2	P^b	Hazard Ratio	95% CI
Age at OCD onset, y	.06 (.02)	13.62	**<.001**	1.06	1.03–1.09
OCD severity, YBOCS total score	−.12 (.03)	16.26	**<.001**	0.88	0.83–0.94
Insight, BABS total score	.02 (.04)	0.26	.607	1.02	0.95–1.09
Age at intake, y	−.05 (.01)	9.91	**.002**	0.96	0.93–0.98
Male sex	−.89 (.31)	8.08	**.005**	0.41	0.22–0.76
Axis I comorbidity[c]	−.13 (.16)	0.67	.413	0.88	0.64–1.20
Weekly SRI usage[d,e]	.27 (.38)	0.50	.478	1.31	0.63–2.72
Number of CBT sessions[f]	−.44 (.23)	3.78	.052	0.64	0.41–1.00

[a]Predictors entered simultaneously (df = 8, Wald χ^2 = 38.18, P < .001)

Table 4. Rate of Full or Partial Remission From Obsessive-Compulsive Disorder Over 2 Years by Principal Obsession Category (N = 212)[a]

Principal Obsession Category[b]	Rate of Full or Partial Remission, %
Overresponsibility for harm (n = 34)	41.8
Somatic (n = 18)	27.8
Miscellaneous (n = 21)	23.8
Sexual (n = 13)	23.1
Religious (n = 14)	21.4
Contamination (n = 42)	19.1
Symmetry (n = 27)	18.5
Aggressive (n = 24)	16.7
Hoarding (n = 19)	5.3

[a]Data for 2 subjects are missing.
[b]Refers to the Yale-Brown Obsessive Compulsive Symptom Checklist category of the single obsession subject "would most like to get rid of" (mutually exclusive categories).

Five-Year Course of Obsessive-Compulsive Disorder: Predictors of Remission and Relapse

Jane L. Eisen, MD; Nicholas J. Sibrava, PhD; Christina L. Boisseau, PhD; Maria C. Mancebo, PhD; Robert L. Stout, PhD; Anthony Pinto, PhD; and Steven A. Rasmussen, MD

J Clin Psychiatry 2013;74(3):233–239

213 PACIENTES

✓22,1% REMISIÓN PARCIAL

✓16,9% REMISIÓN COMPLETA

✓49% RECAÍDAS

TRATAMIENTO:

- **90% ISRS**
- **51% CBT**

Figure 1. Survival Curves for Remission of Obsessive-Compulsive Disorder Over Follow-Up According to Primary Obsessive Symptom

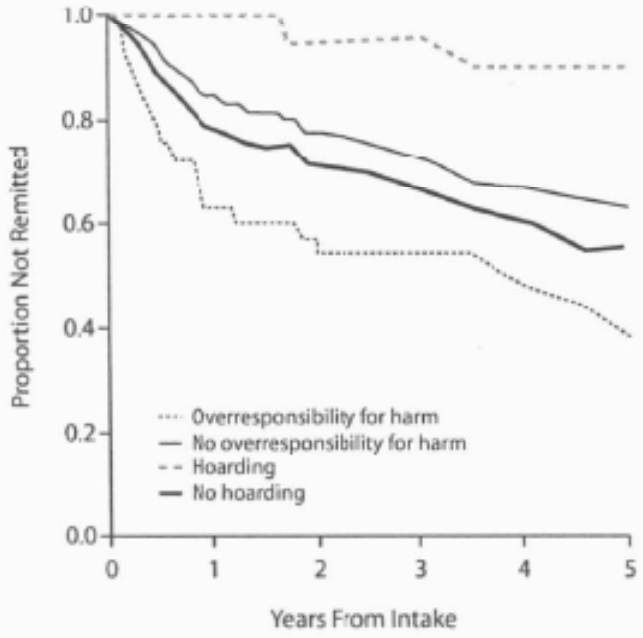
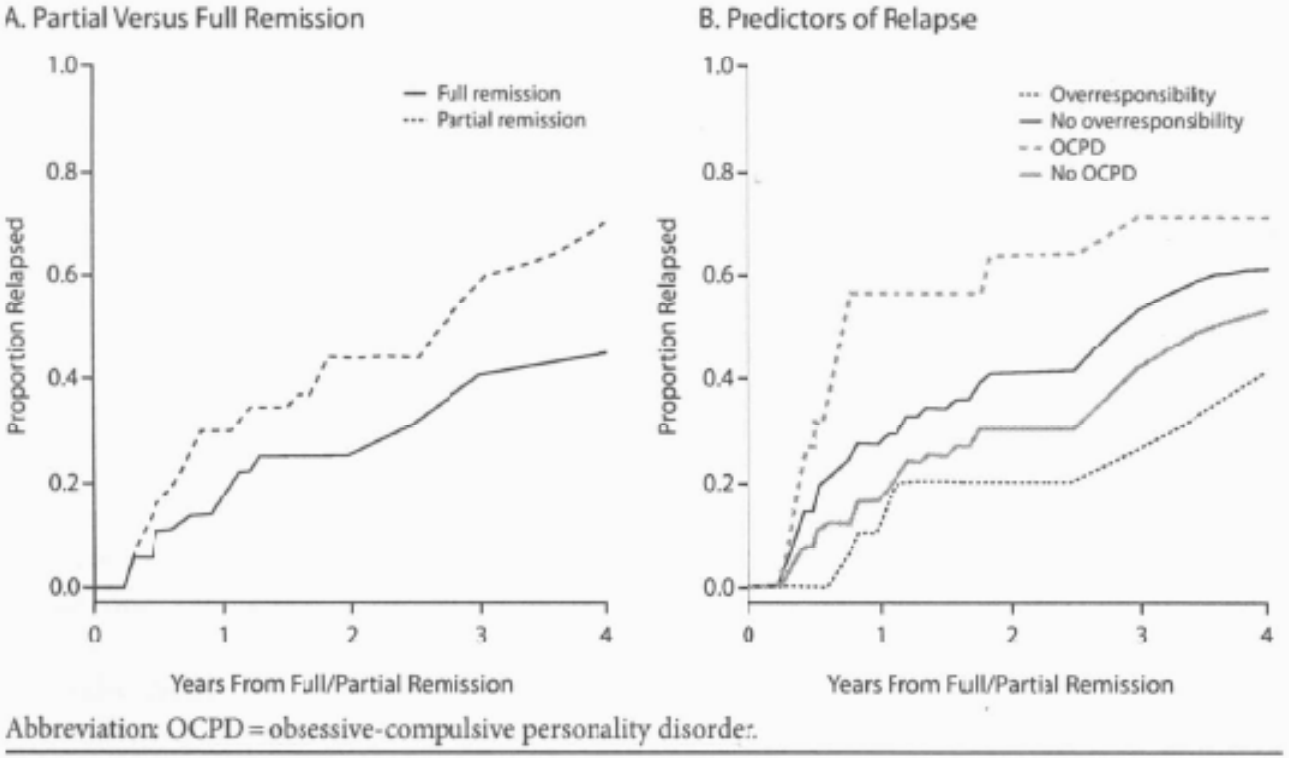


Table 2. Proportional Hazard Regression Testing Clinical Predictors of Remission and Relapse From Obsessive-Compulsive Disorder (OCD) Over 5 Years (N = 213)

	B (SE)	χ^2	*P*[a]	Hazard Ratio	95% CI
Remission predictors[b]					
Duration of OCD (years)	−0.06 (0.02)	26.14	**<.0001**	0.95	0.92–0.97
OCD severity (YBOCS total score)	−0.12 (0.02)	30.56	**<.0001**	0.88	0.85–0.92
Insight (BABS total score)	0.04 (0.03)	2.72	.10	1.04	0.99–1.10
Overresponsibility for harm	0.64 (0.27)	5.41	**.02**	1.89	1.11–3.22
Gender	−0.34 (0.23)	2.29	.13	0.71	0.45–1.11
Hoarding	−0.75 (0.73)	1.05	.31	0.47	0.11–1.98
OCPD	−0.48 (0.30)	2.62	.11	0.62	0.34–1.11
Axis I comorbidity[c]	0.06 (0.10)	0.33	.57	1.06	0.87–1.29
Relapse predictors[d]					
Duration of OCD (years)	−0.01 (0.01)	0.81	.37	0.99	0.97–1.01
OCD severity (YBOCS total score)	0.02 (0.02)	0.42	.52	1.02	0.97–1.07
Insight (BABS total score)	−0.71 (0.03)	4.42	.04[e]	0.93	0.87–1.00
Overresponsibility for harm	−0.73 (0.37)	3.81	.05[f]	0.48	0.23–1.00
Gender	0.18 (0.29)	0.40	.53	1.20	0.68–2.11
Hoarding[g]	…	…	…	…	…
OCPD	0.94 (0.34)	7.76	<.005	2.56	1.32–4.96
Axis I comorbidity[b]	0.19 (0.14)	1.89	.17	1.21	0.92–1.58

Figure 2. Survival Curves for Relapse of Obsessive-Compulsive Disorder Over Follow-Up



Abbreviation: OCPD = obsessive-compulsive personality disorder.

ORIGINAL RESEARCH

J Clin Psychiatry 2013;74(5):464–469

Six-Month Follow-Up of a Randomized Controlled Trial Augmenting Serotonin Reuptake Inhibitor Treatment With Exposure and Ritual Prevention for Obsessive-Compulsive Disorder

Edna B. Foa, PhD; Helen Blair Simpson, MD, PhD; Michael R. Liebowitz, MD; Mark B. Powers, PhD; David Rosenfield, PhD; Shawn P. Cahill, PhD; Raphael Campeas, MD; Martin Franklin, PhD; Chang-Gyu Hahn, MD, PhD; Elizabeth A. Hembree, PhD; Jonathan D. Huppert, PhD; Andrew B. Schmidt, PhD; Donna Vermes, MS, NPP; and Monnica T. Williams, PhD

Figure 1. Patient Flow Diagram (CONSORT) for a Trial of EX/RP or SMT Augmenting SRI Treatment in Obsessive-Compulsive Disorder

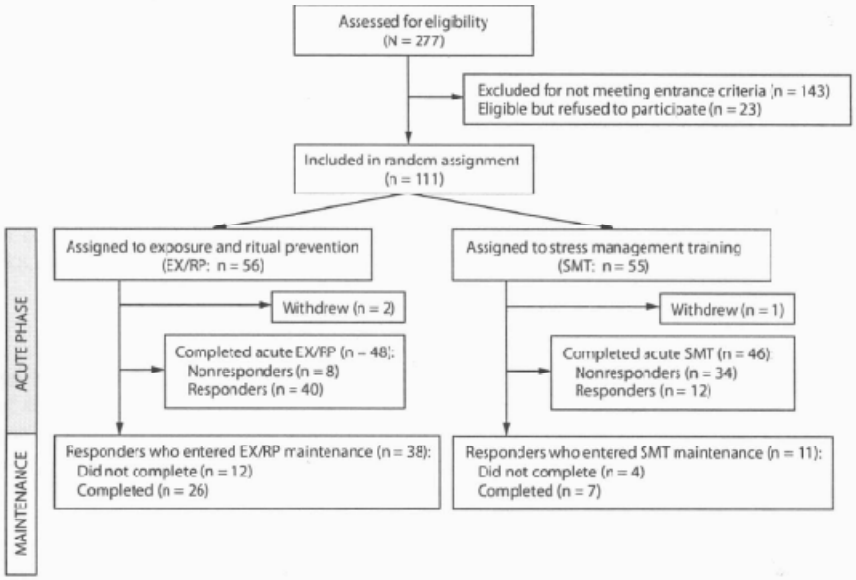
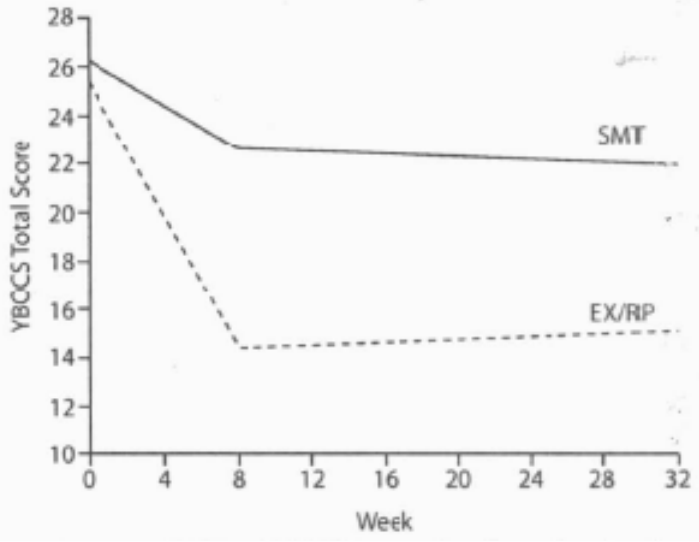


Figure 2. Discontinuous Growth Curve for Patients Receiving Either SMT or EX/RP (n = 54 per treatment condition) Added to SRI Treatment for Obsessive-Compulsive Disorder



Original Investigation

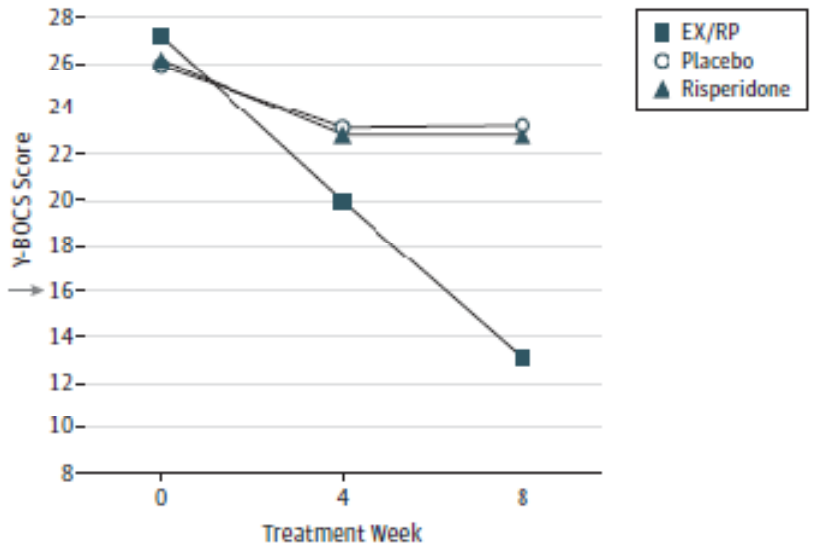
Cognitive-Behavioral Therapy vs Risperidone for Augmenting Serotonin Reuptake Inhibitors in Obsessive-Compulsive Disorder

A Randomized Clinical Trial

Helen Blair Simpson, MD, PhD; Edna B. Foa, PhD; Michael R. Liebowitz, MD; Jonathan D. Huppert, PhD; Shawn Cahill, PhD; Michael J. Maher, PhD; Carmen P. McLean, PhD; James Bender Jr, PsyD; Sue M. Marcus, PhD; Monnica T. Williams, PhD; Jamie Weaver, MPH; Donna Vermes, PMHNP; Page E. Van Meter, PhD; Carolyn I. Rodriguez, MD, PhD; Mark Powers, PhD; Anthony Pinto, PhD; Patricia Imms, RN; Chang-Gyu Hahn, MD, PhD; Raphael Campeas, MD

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2013.1932
Published online September 11, 2013.

Figure 2. Change in Symptom Severity During Augmentation



Long-Term Follow-Up Study of Patients With Serotonin Reuptake Inhibitor–Nonresponsive Obsessive-Compulsive Disorder

Y.C. Janardhan Reddy, DPM, ML
Thennarasu Kand

Journal of Clinical Psychopharmacology • Volume 30, Number 3, June 2010

TABLE 3. Course and Outcome of SRI Nonresponders With OCD (n = 36)

Variable	n (%)
Outcome	
Full remission	4 (11)
Partial remission	10 (28)
In episode	22 (61)
Course	
No OCD	4 (11)
Subclinical OCD	10 (28)
Episodic OCD	3 (8)
Chronic OCD	19 (53)
Improvement based on CGI-I	17 (47)

TABLE 5. Regression Analysis of Predictors of Poor Outcome

Variable	*B*	SE	Wald	*P*	OR	95% CI
Duration of follow-up	−0.134	0.052	6.553	0.010	0.875	0.789–0.969
Age at onset of OCD	0.279	0.141	3.893	0.048	1.321	1.002–1.743
Quality of life	−0.122	0.059	4.236	0.040	0.885	0.787–0.994
CBT treatment	−2.191	1.102	3.951	0.047	0.112	0.013–0.970

ARTICLE IN PRESS

Journal of Affective Disorders ■ (■■■■) ■■■–■■■

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/jad

Research report

A 5-year prospective follow-up study of patients with obsessive–compulsive disorder treated with serotonin reuptake inhibitors

Anish V. Cherian, Suresh Bada Math, Thennarasu Kandavel, Y.C. Janardhan Reddy *

National Institute of Mental Health & Neurosciences (NIMHANS), Bangalore, India

FULL REMISSION: 53%

PARTIAL REMISSION: 28%

TIEMPO EN TRATAMIENTO !!

Time (months)	Partial remission	Full remission
12	70%	53%
24	84%	62%
36	88%	63%
48	93%	65%
60	93%	65%

Table 3
Cox proportional hazard regression (forward stepwise, Wald) testing predictors of remission and relapse in obsessive–compulsive disorder patients over 5 years (n=106).

Variable	B (SE)	Wald	Significance	Hazard ratio	95% CI
Time to full remission					
Percentage of time on treatment	0.013 (0.004)	8.140	0.004	1.013	1.004–1.022
Time to at least partial remission					
Percentage of time on treatment	0.015 (0.004)	15.947	< 0.001	1.015	1.008–1.023
Treatment-naive at intake	0.411 (0.210)	3.846	0.05	1.509	1.000–2.277
Time to relapse after remission					
Doubts and checking dimension	−0.385 (0.167)	5.327	0.021	0.680	0.491–0.944
Full remission	−1.015 (0.369)	7.569	0.006	0.363	0.176–0.747

Longitudinal course of pharmacotherapy in obsessive–compulsive disorder

Jon E. Grant[a], Maria C. Mancebo[b], Eric Weinhandl[c], Brian L. Odlaug[a,d], Jane L. Eisen[b] and Steven A. Rasmussen[b]

International Clinical Psychopharmacology 2013, 28:200–205

43,7% ABANDONOS DE LA MEDICACIÓN

Table 3 Predictors of serotonin reuptake inhibitor discontinuation

		95% confidence interval		
	Odds ratio	Lower bound	Upper bound	*P*-value
Age at baseline (per 5-year increment)	0.91	0.84	0.98	0.01
CBT ≥ 11 sessions vs. <11 sessions in lifetime	0.68	0.47	0.98	0.04
OCD response to SRI use (at baseline)				
Improvement with treatment vs. no improvement with treatment	0.52	0.32	0.83	<0.01
Time since initiation of current SRI trial (per 12-week increment)	0.96	0.93	0.99	0.02
Current SRI treatment				
Citalopram: yes vs. no	1.61	1.02	2.52	0.04
Fluvoxamine: yes vs. no	0.31	0.14	0.68	<0.01
Current SRI dose				
Low vs. moderate	1.77	1.19	2.64	<0.01
High vs. moderate	1.09	0.62	1.94	0.76

Table 4 Predictors of worsening of obsessive–compulsive disorder after serotonin reuptake inhibitor discontinuation

		95% confidence interval		
	Hazards ratio	Lower bound	Upper bound	*P*-value
Age at baseline (per 5-year increment)	0.80	0.67	0.95	0.01
OCD onset nature				
Sudden vs. not sudden	2.13	0.92	4.94	0.08
Obsession at baseline				
Aggressive: yes vs. no	0.33	0.14	0.78	0.01
PSR score at conclusion of most recent SRI trial (per 1-point increment)	0.62	0.47	0.80	<0.01

DEPRESSION AND ANXIETY 30:763–772 (2013)

Research Article

CLINICAL PREDICTORS OF LONG-TERM OUTCOME IN OBSESSIVE-COMPULSIVE DISORDER

Ewgeni Jakubovski,[1*] Juliana B. Diniz, M.D., Ph.D.,[2] Carolina Valerio,[2] Victor Fossaluza, M.Sc.,[3] Cristina Belotto-Silva, M.Sc., Ph.D.,[2] Clarice Gorenstein, Ph.D.,[4,5] Eurípedes Miguel, M.D., Ph.D.,[2] and Roseli G. Shavitt, M.D., Ph.D.[2]

196 PACIENTES

TRATAMIENTO: TERAPIA DE CONDUCTA + FLUOXETINA

DURACIÓN: 21 MESES

✓50% RESPONDEDORES (REDUCCIÓN Y-BOCS > 35%)

✓21,3% REMISIÓN COMPLETA (Y-BOCS < 8)

PREDICTORES DE PEOR EVOLUCIÓN:

•EDAD INICIO PRECOZ

•DEPRESIÓN COMÓRBIDA

•DURACIÓN DEL TOC ANTES DEL TRATAMIENTO

Long-Term Follow-Up and Predictors of Clinical Outcome in Obsessive-Compulsive Patients Treated With Serotonin Reuptake Inhibitors and Behavioral Therapy

Pino Alonso, M.D.; Jose M. Menchon, M.D., Ph.D.; Josep Pifarre, M.D.; David Mataix-Cols, M.D., Ph.D.; Llanos Torres, M.D.; Purificación Salgado, M.D.; and Julio Vallejo, M.D., Ph.D.

J Clin Psychiatry 2001, 62 (7): 535-540

12 SEMANAS:

✓ REDUCCIÓN Y-BOCS: 29,9% (SD: 24,4%)

✓ RESPONDEDORES: 38,3% (n= 23)

1-5 AÑOS:

✓ REDUCCIÓN Y-BOCS: 43,8% (SD: 28,9)

✓ RESPONDEDORES: 63,3% (n= 38)

ANÁLISIS REGRESIÓN LOGÍSTICA:

SEXUAL/RELIGIOSO →

NO RESPONDEDORES

(R^2= 0,17, ß= -0,41; P= 0,001)

Table 3. Sociodemographic and Clinical Characteristics of 60 Patients With OCD[a]

Characteristic	Long-Term Assessment of OCD Severity: Responders[b] (N = 38)	Long-Term Assessment of OCD Severity: Nonresponders[c] (N = 22)	Statistical Comparison
Age, y, mean ± SD	29.3 ± 10.6	32.1 ± 10.0	NS (p = .3)
Male/female	26/12	14/8	NS (p = .7)
Never married, N (%)	27 (71.7)	15 (68.2)	NS (p = .4)
Age at onset of OCD, y, mean ± SD	17.9 ± 8.4	16.8 ± 5.6	NS (p = .6)
Duration of illness, y, mean ± SD	10.4 ± 9.0	15.3 ± 11.7	NS (p = .09)
Personality disorders, N (%)	16 (42.1)	10 (45.5)	NS (p = .8)
Familial psychiatric background, N (%)	22 (57.9)	12 (54.5)	NS (p = .8)
Previous OCD treatment, N (%)	25 (65.8)	18 (81.8)	NS (p = .09)
Baseline global Y-BOCS score, mean ± SD	23.5 ± 7.1	26.5 ± 5.4	NS (p = .09)
Baseline Y-BOCS obsessions score, mean ± SD	12.5 ± 3.7	14.5 ± 2.9	NS (p = .06)
Baseline Y-BOCS compulsions score, mean ± SD	11.2 ± 4.9	12.0 ± 4.6	NS (p = .5)
Reduction in Y-BOCS score after 12 wk of pharmacologic treatment, %, mean ± SD	34.4 ± 23.4	22.6 ± 24.8	NS (p = .08)

[a]Abbreviations: NS = not significant, OCD = obsessive-compulsive disorder, Y-BOCS = Yale-Brown Obsessive Compulsive Scale.
[b]Minimum Y-BOCS score reduction of 35% or final Y-BOCS score < 16.
[c]Y-BOCS score reduction < 35% and final Y-BOCS score ≥ 16.

Available online at www.sciencedirect.com
SciVerse ScienceDirect
Comprehensive Psychiatry 52 (2011) 670–677
Comprehensive PSYCHIATRY
www.elsevier.com/locate/comppsych

Longitudinal course of obsessive-compulsive disorder in patients with anxiety disorders: a 15-year prospective follow-up study

Brook A. Marcks[a,*], Risa B. Weisberg[b,c], Ingrid Dyck[b], Martin B. Keller[b]

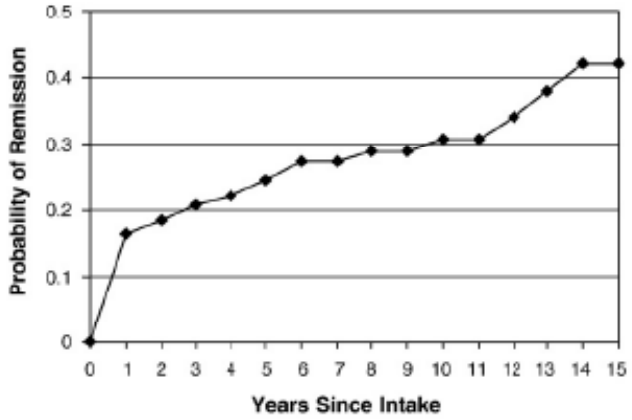


Fig. 1. Cumulative probability of full remission from O

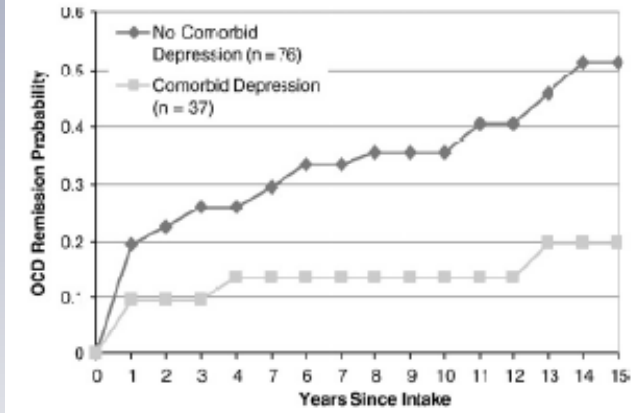


Fig. 3. Cumulative probability of full OCD remission by comorbid MDD.

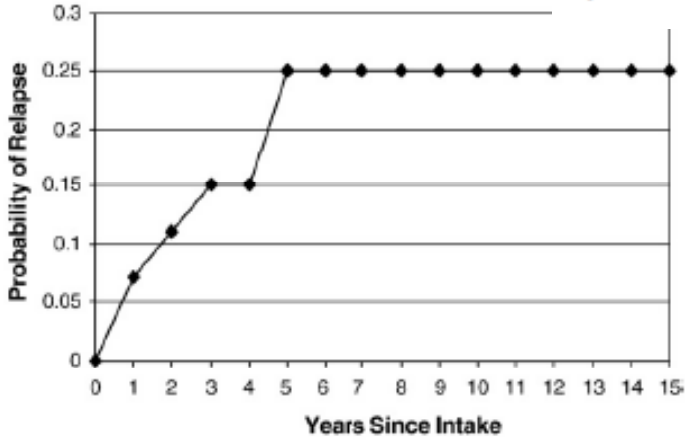


Fig. 2. Cumulative probability of relapse after remission from OCD among a subset of 113 patients.

Long-term outcomes of obsessive–compulsive disorder: follow-up of 142 children and adolescents

N. Micali, I. Heyman, M. Perez, K. Hilton, E. Nakatani, C. Turner and D. Mataix-Cols

BJPsych | The British Journal of Psychiatry (2010) 197, 128–134. doi: 10.1192/bjp.bp.109.075317

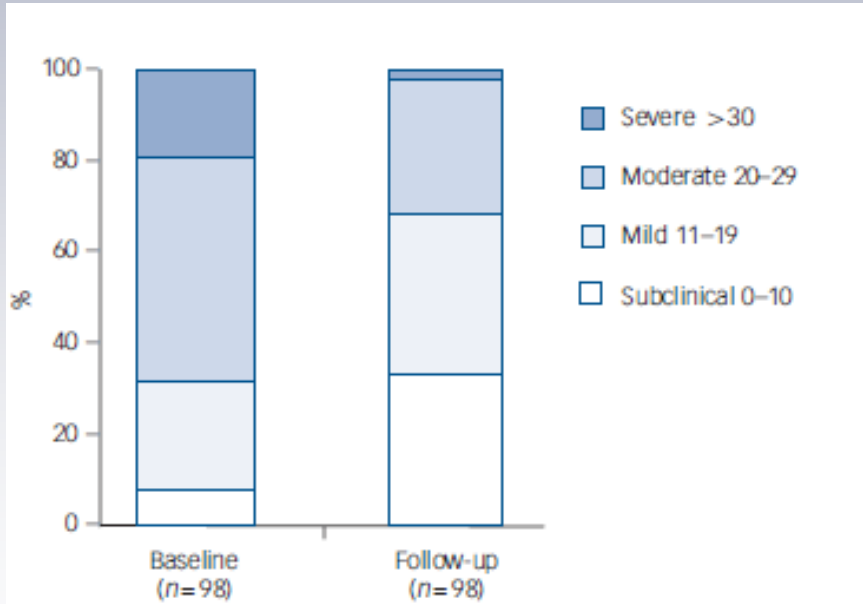


Fig. 2 Children's Yale–Brown Obsessive Compulsive Scale scores at baseline and follow-up.

Table 5 Predictors for persistence of obsessive–compulsive disorder (OCD) and other psychiatric disorders at follow-up: logistic regression, odds ratios (OR) and 95% CI

Predictors	OCD at follow-up OR (95%CI)	*P*	Any ICD–10 disorder at follow-up, OR (95%CI)	*P*
Gender, male	0.7 (0.4–1.5)	NS	0.5 (0.2–1.3)	NS
Age at onset	1.0 (0.9–1.1)	NS	1.0 (0.9–1.2)	NS
Duration of OCD	1.2 (1.0–1.3)	<0.05	1.0 (0.9–1.2)	NS
Family history of OCD	0.5 (0.1–2.3)	NS	0.9 (0.1–4.9)	NS
CY–BOCS score at baseline	1.0 (1.0–1.1)	NS	1.0 (1.0–1.1)	NS
Any tics at baseline	0.2 (0.1–0.6)	<0.01	0.6 (0.3–1.4)	NS
Strengths and difficulties questionnaire				
Parent total score at baseline[a]	1.0 (1.0–1.1)	0.1	1.1 (1.0–1.1)	<0.05
Parent emotional score at baseline[a]	1.1 (0.9–1.3)	NS	1.2 (1.0–1.4)	0.08
Parent conduct score at baseline[a]	1.0 (0.8–1.2)	NS	1.1 (0.9–1.4)	NS
Young person total score at baseline[b]	1.1 (1.0–1.1)	0.1	1.1 (1.0–1.2)	<0.05
Young person emotional score at baseline[b]	1.2 (1.0–1.5)	0.1	1.3 (1.0–1.6)	<0.05
Young person conduct score at baseline[b]	1.0 (0.7–1.2)	NS	1.1 (0.8–1.4)	NS

NS, not significant; CY–BOCS, Children's Yale–Brown Obsessive Compulsive Scale.
a. Available for 116 participants.
b. Available on 74 participants.

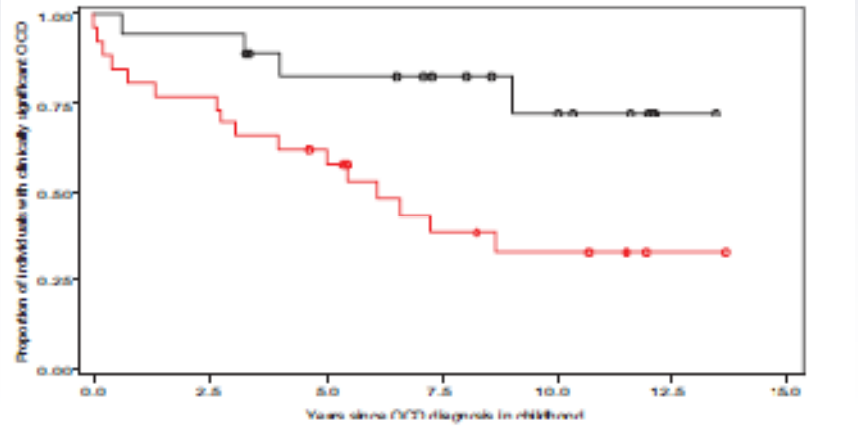
Predictors of Early Adult Outcomes in Pediatric-Onset Obsessive-Compulsive Disorder

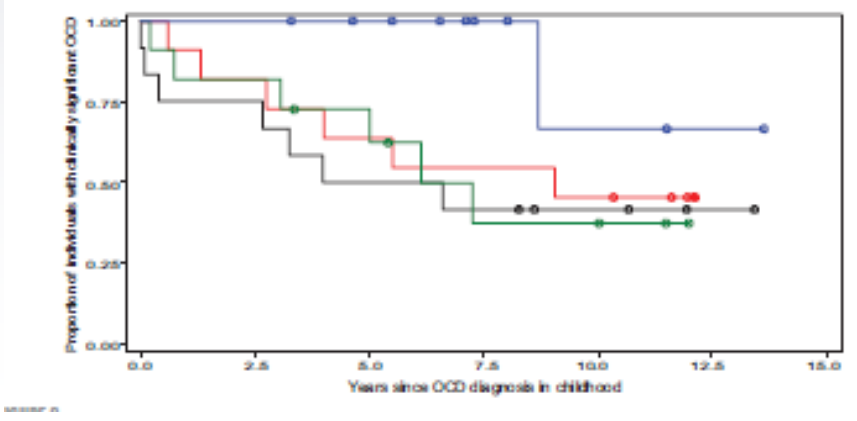
Michael H. Bloch, Brittany G. Craiglow, Angeli Landeros-Weisenberger, Philip A. Dombrowski, Kaitlyn E. Panza, Bradley S. Peterson and James F. Leckman
Pediatrics 2009;124;1085-1093; originally published online Sep 28, 2009;
DOI: 10.1542/peds.2009-0015

TABLE 3 Cox Proportional-Hazard Model of Time to Remission of Pediatric-Onset OC Symptoms

Parameter	Hazard Ratio (95% Confidence Interval)	*P*
Gender	0.06 (0.02–0.15)	.002
Childhood Children's Y-BOCS score	0.89 (0.85–0.94)	.018
Age at baseline assessment	2.00 (1.64–2.43)	<.001
CTD	4.50 (2.15–9.42)	.042
ODD	0.17 (0.08–0.35)	.014
Age of OCD onset	0.77 (0.70–0.84)	.004
Primary hoarding symptoms	0.09 (0.03–0.25)	.023

A lower hazard ratio indicates an increased time to remission of OC symptoms. Female gender, more-severe initial OC symptoms, younger age at initial assessment, later age of onset, comorbid ODD, absence of comorbid tic symptoms, and primary hoarding symptoms were associated with increased time to remission. Overall model fit statistics were as follows: likelihood ratio: $\chi^2_7 = 38.0$; $P < .0001$ ($N = 45$).





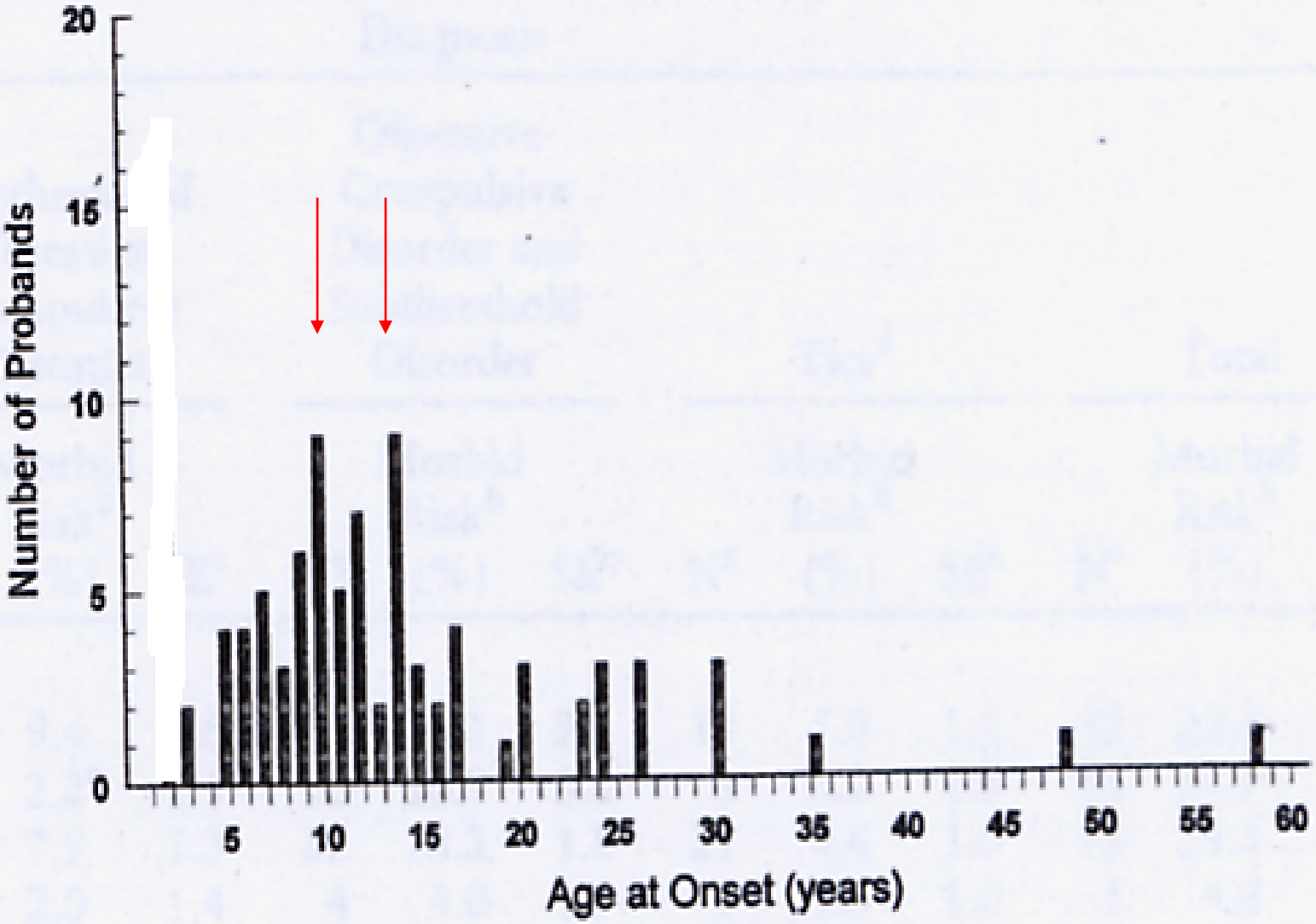
Heterogeneidad clínica del TOC.

Subtipos de TOC o fenotipos

Mediados por diferentes mecanismos psicobiológicos: sustrato genético y/o neurobiológico específico.

- ✓Edad de inicio (Geller et al., 1998)
- ✓Género (Lensi et al., 1996)
- ✓Comorbilidad (Leckman et al., 1997)
- ✓Insight (Aigner et al., 2005)
- ✓Dimensiones sintomáticas (Mataix-Cols et al., 2005)
- ✓Respuesta a tratamiento (Jenike et al., 1997)

FIGURE 1. Distribution of Ages at Onset for 100 Probands With Obsessive-Compulsive Disorder



FENOTIPOS DE TOC EN FUNCIÓN DE LA EDAD DE INCIO

- ✓ Ausencia de criterio standard para fijar la edad de corte: 10, 15, 17 o 18 años.
- ✓ Posible sesgo relacionado con la influencia del tiempo de evolución de la enfermedad (Ravizza et al., 1997; 1995).
- ✓ Comparación TOC pediátrico/TOC en adultos (edad de inicio?).
- ✓ Estudios en adultos EOCD/LOCD:
  - obtención retrospectiva de la edad de inicio.
  - primeros síntomas (sub-clínicos) vs síntomas acompañados de interferencia significativa ?

TOC PEDIÁTRICO

- Predominio de varones (Geller et al. 1998, Bellodi et al., 1992; Rasmussen y Eisen, 1990; Zohar, 1999). NO (Hemmings et al., 2004)

- Comorbilidad:
  - Tics, trastorno de Tourette
  - Conductas disruptivas
  - Trastornos del desarrollo

  (Geller et al., 1996; Miguel et al., 2001; Swedo et al., 1989).

TOC PEDIÁTRICO

- Mayor carga familiar de TOC (Pauls et al., 1995; Nestadt et al., 2000)
- Pobre insight (Geller et al. 1998).
- Neuropsicología: resultados controvertidos:
  - Behar et al., 1984 --- déficits en funciones ejecutivas
  - Beers et al., 1999 --- sin diferencias

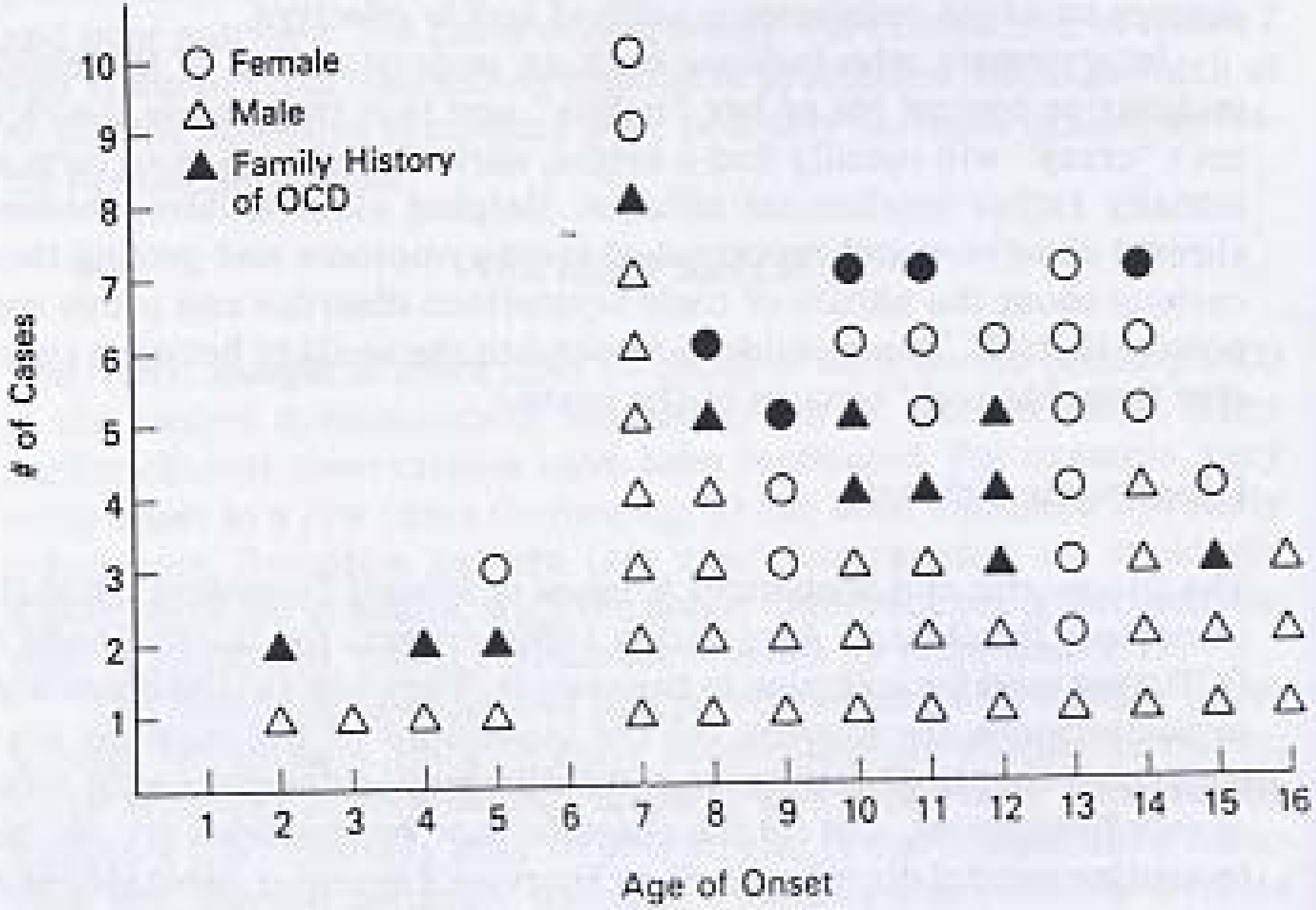


Figure 1. Sex, age of onset, and family history of OCD in NIMH childhood/adolescent OCD sample ($N = 70$).

TOC de inicio precoz

Rosario-Campos et al., Am J Psychiatry 2001; 158:1899-1903

- N= 42 TOC: EOCD < 10 años versus LOCD > 17 años
- Edad de inicio de los primeros síntomas, no afectación clínica completa.
- EOCD:
  - Mayor frecuencia de compulsiones "*tic-like*": *necesidad de tocar o gestualizar.*
  - Fenómenos sensoriales mentales y corporales.
  - Trastorno por tics comórbido
  - Mayor severidad basal del TOC
  - Mas compulsiones sin obsesiones (inicio previo compulsiones)(Geller et al., 1998, Rapoport, 1989)
  - Compulsiones de acumulación y repetición
  - Peor respuesta a corto plazo a ISRS (31% vs 81%)
  - Sin diferencias de género.

TOC de inicio precoz

Fontenelle et al., J Psych Research 2003; 37:127-133

- N= 66 TOC (33 sujetos inicio < 17 años)
- Predominio de varones
- EOCD:
  - Mayor número de obsesiones y compulsiones.
  - Mayor frecuencia de rituales de repetición
    - Cavallini et al. 2002:genotipo homozigoto para el alelo L de la región promotora del gen del trasportador de serotonina
  - Mayor severidad basal del TOC
  - Mayor número requerido de ensayos terapeúticos a largo plazo
  - SIN diferencias en la respuesta a largo plazo al tratamiento farmacológico y CBT.

Edad de inicio y predicción de respuesta a largo plazo

- ✓ RESULTADOS CONTROVERTIDOS:
  - NO valor predictivo:
    - Ackerman et al., 1998
    - Alonso et al., 2001
  - INICIO PRECOZ – PEOR EVOLUCIÓN:
    - Ackerman et al., 1994
    - Ravizza et al., 1995
    - Rosario-Campos et al., 2001

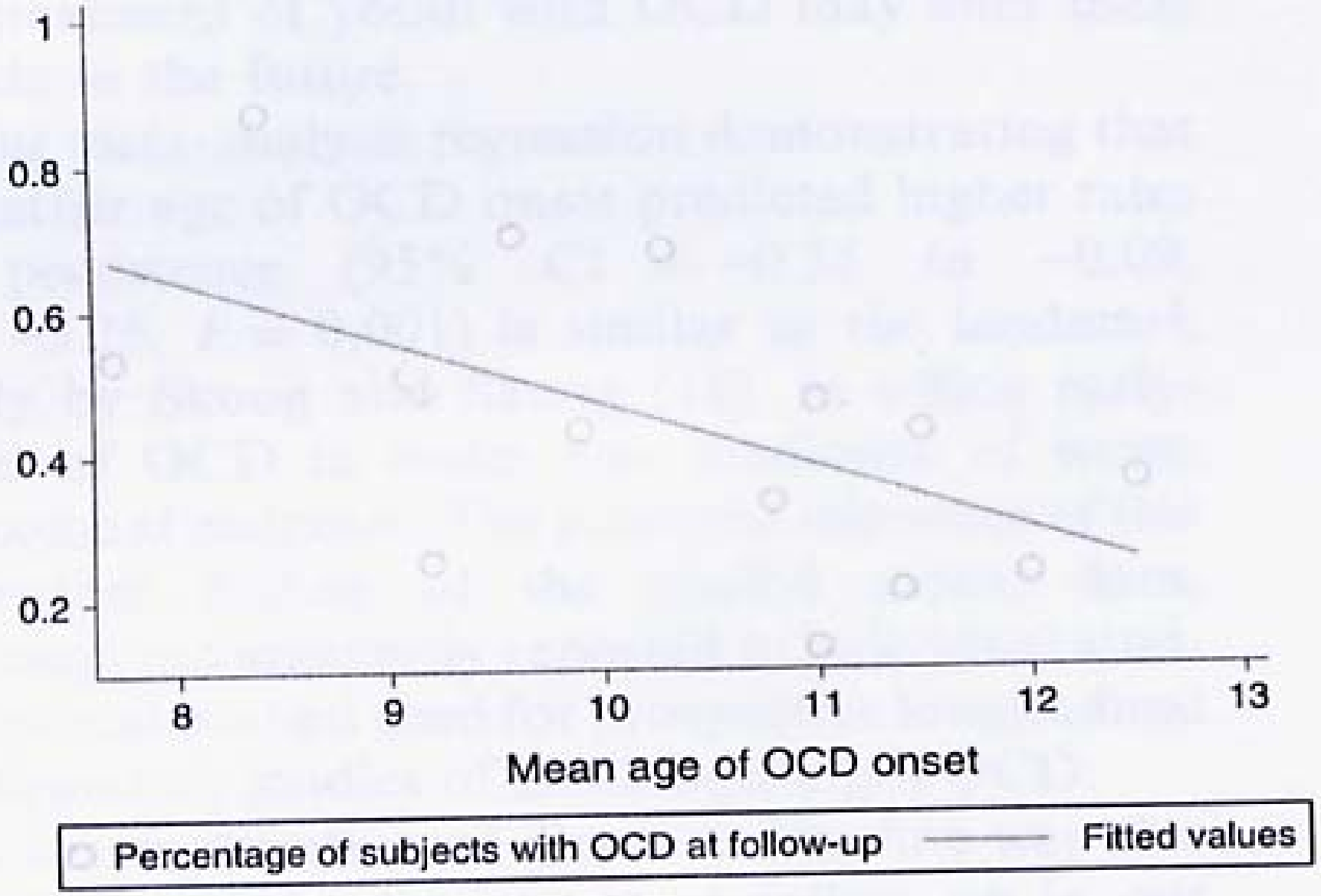


Fig. 1. Age of obsessive–compulsive disorder (OCD) onset vs. OCD persistence at long-term follow-up.

TOC de inicio precoz

Diniz et al., J Clin Psychiatry 2004; 65:22-27

- ✓ N= 161 TOC adultos
- ✓ Edad precoz inicio se asocia:
  - trastorno por tics 39%
  - T. Bipolar 9%
  - T. alimentacion 11%
  - cleptomania 4%
  - tricotilomania 10%.
- ✓ Período prolongado de enfermedad se asocia a trastornos depresivos (71%)
- ✓ Fobia social se asocia a ambos por igual (39%).

Figure 1. Odds Ratio for Lifetime Tic Disorders by Age at Onset of Obsessive-Compulsive Symptoms (binary logistic regression)

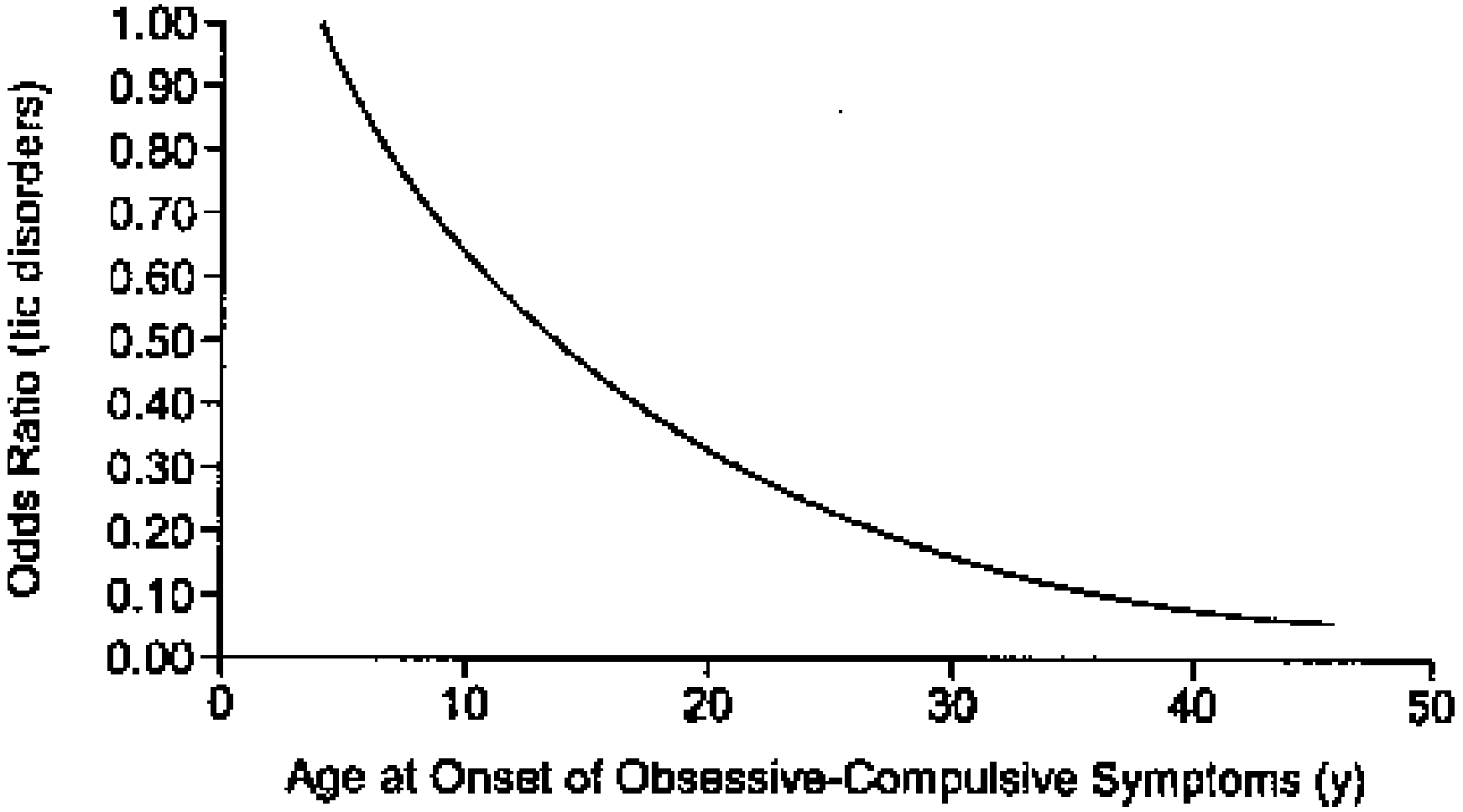
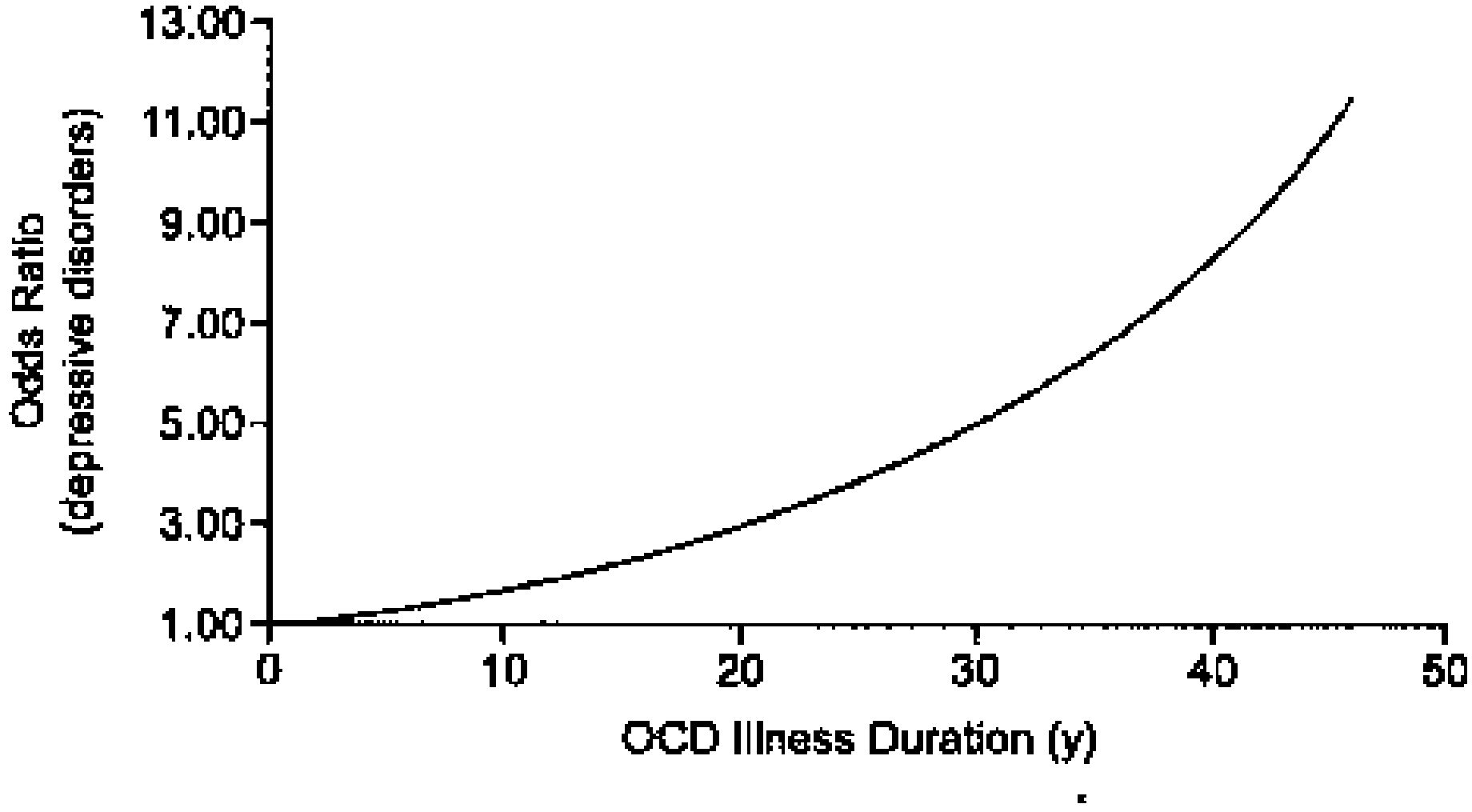


Figure 2. Odds Ratio for Lifetime Depressive Disorder by Duration of Obsessive-Compulsive Disorder (OCD) Illness (binary logistic regression)



Edad de inicio del TOC y factores genéticos.

Bellodi et al., Psychiatry Research 1992; 42: 11-120

- N= 92 pacientes TOC adultos
- TOC inicio precoz (n= 21) > antecedentes familiares de TOC que en sujetos con inicio tardío (8,8% vs 3,4%)

Edad de inicio del TOC y factores genéticos.

Hemmings et al., Psychiatry Research 2004; 128: 175-182

- N = 252 TOC (133 sujetos con inicio < 15 años).
- Polimorfismo DRD4 VNTR: menor frecuencia del alelo a7 en la muestra global de TOC respecto a controles sanos.
- Menor frecuencia en TOC de inicio precoz (11,5% vs 20%; p=0,028)
- Edad precoz de inicio se asocia a: tics, Sd. Tourette, tricotilomania, TP esquizotípico y límite.

Edad de inicio del TOC y factores genéticos.

Cavallini et al., 2002

- Estudio de la anticipación en la edad de inicio del TOC (DNA inestable; repetición de trinucleótidos)
- N= 40 TOC con familiares de primer orden afectados

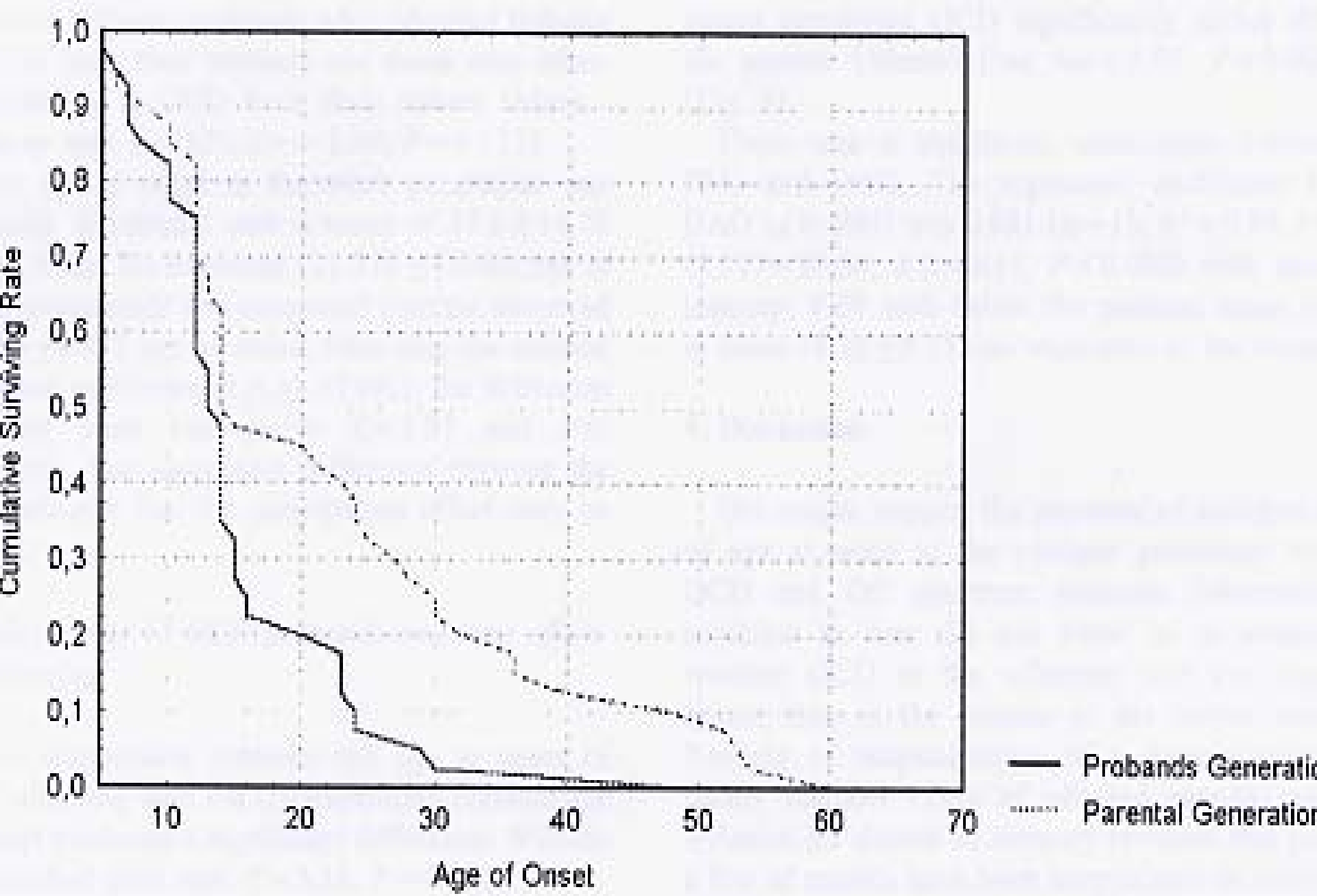


Fig. 2. Comparison of age at onset between parental and offspring generation.

Neuroimagen funcional y edad de inicio del TOC

Bussato et al., J Am Acad Child Adolesc Psychiatry 2001; 40:347-354

- EOCD: menor flujo sanguíneo cerebral regional que LOCD en el tálamo derecho, cortex cingulado anterior izquierdo y córtex prefrontal bilateral inferior.
- Las alteraciones del tálamo explicarían la mayor resistencia a los tratamientos.

Brain Imaging Behav. 2010 March ; 4(1): 35–45. doi:10.1007/s11682-009-9083-2.

Correia et al.

Basal Ganglia MR Relaxometry in Obsessive-Compulsive Disorder: T2 Depends Upon Age of Symptom Onset

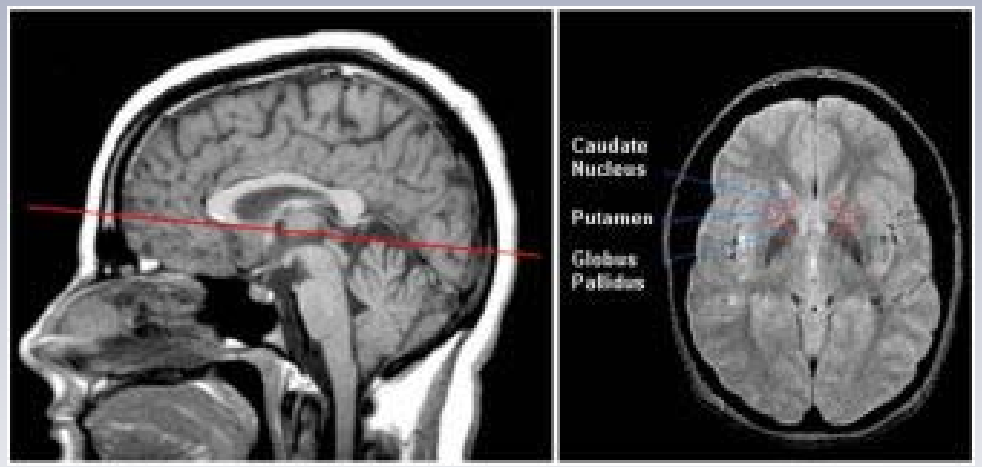


Table 3

Pairwise comparisons of globus pallidi T2 values

Region	Group A Mean (SD)	Group B Mean (SD)	Mean difference (A–B)	Standard error	*p*
T2 right globus pallidus	Controls 54.01 (3.96)	Early onset 52.85 (2.92)	1.16	1.15	.574
		Late onset 50.67 (4.47)	3.34	1.20	.019*
	Early onset	Late onset	2.18	1.36	.253
T2 left globus pallidus	Controls 53.43 (4.34)	Early onset 53.14 (2.65)	0.29	1.13	.964
		Late onset 49.85 (3.47)	3.58	1.18	.009*
	Early onset	Late onset	3.29	1.34	.044*

Control n=33; Early-Onset n=17; Late-Onset n=15

*p<.05

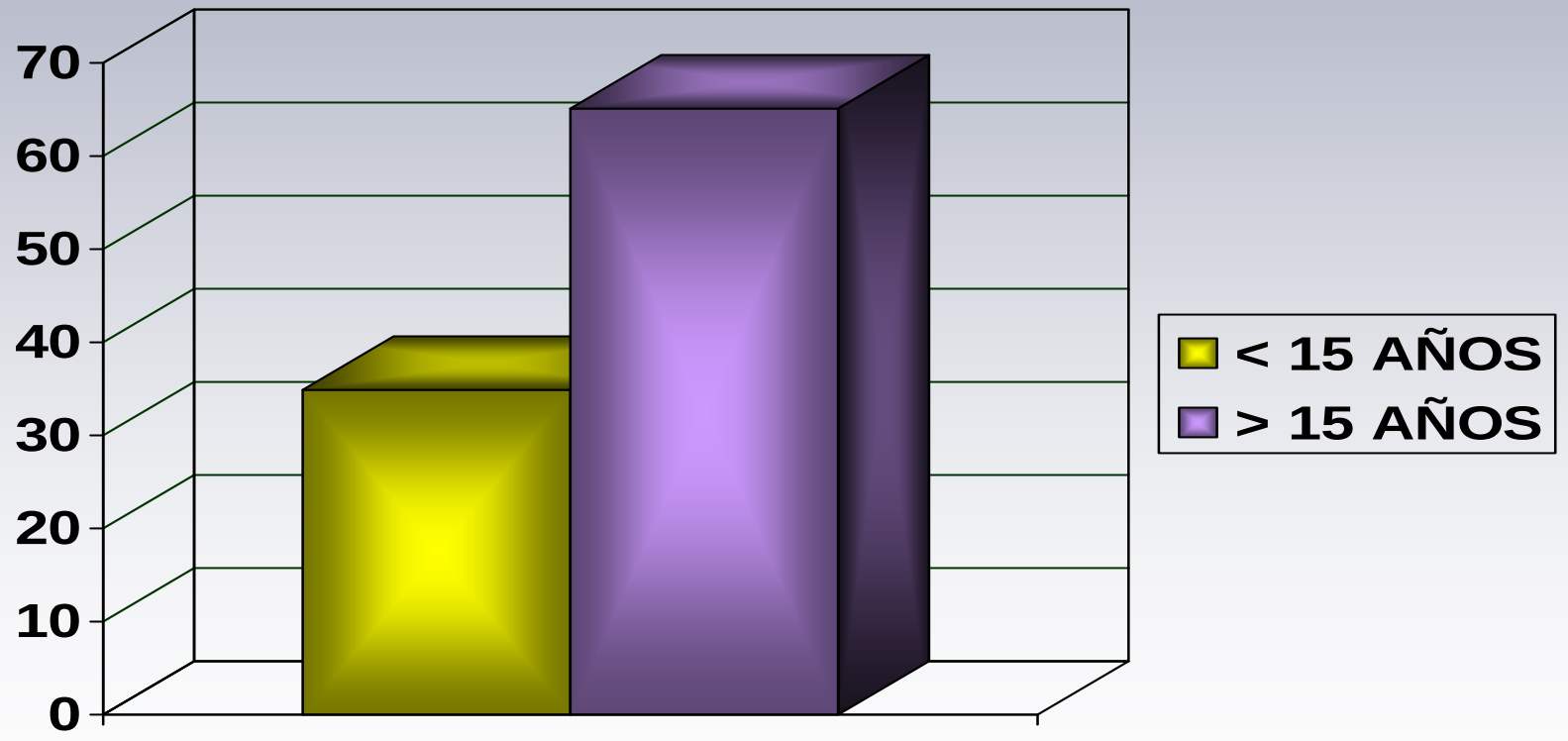
UNIDAD DE TRASTORNOS OBSESIVO-COMPULSIVOS
HOSPITAL DE BELLVITGE

475 TOC Adultos (1994-2013)

- 237 varones (49,8 %)/238 mujeres (51,2%)
- Edad actual: 31,7 años (SD: 11,57) (18-65)
- Edad inicio TOC: 19,2 años (SD: 7.6) (5-52)
- Tiempo evolución TOC: 12,4 años (10,7) (1-50)
- HDRS: 13,6 (SD:5,7)
- Y-BOCS: 25,8 (SD:6,7)
- Y-BOCS Obsesiones: 12,5 (SD:4,5)
- Y-BOCS Compulsiones: 13,2 (SD:3,5)

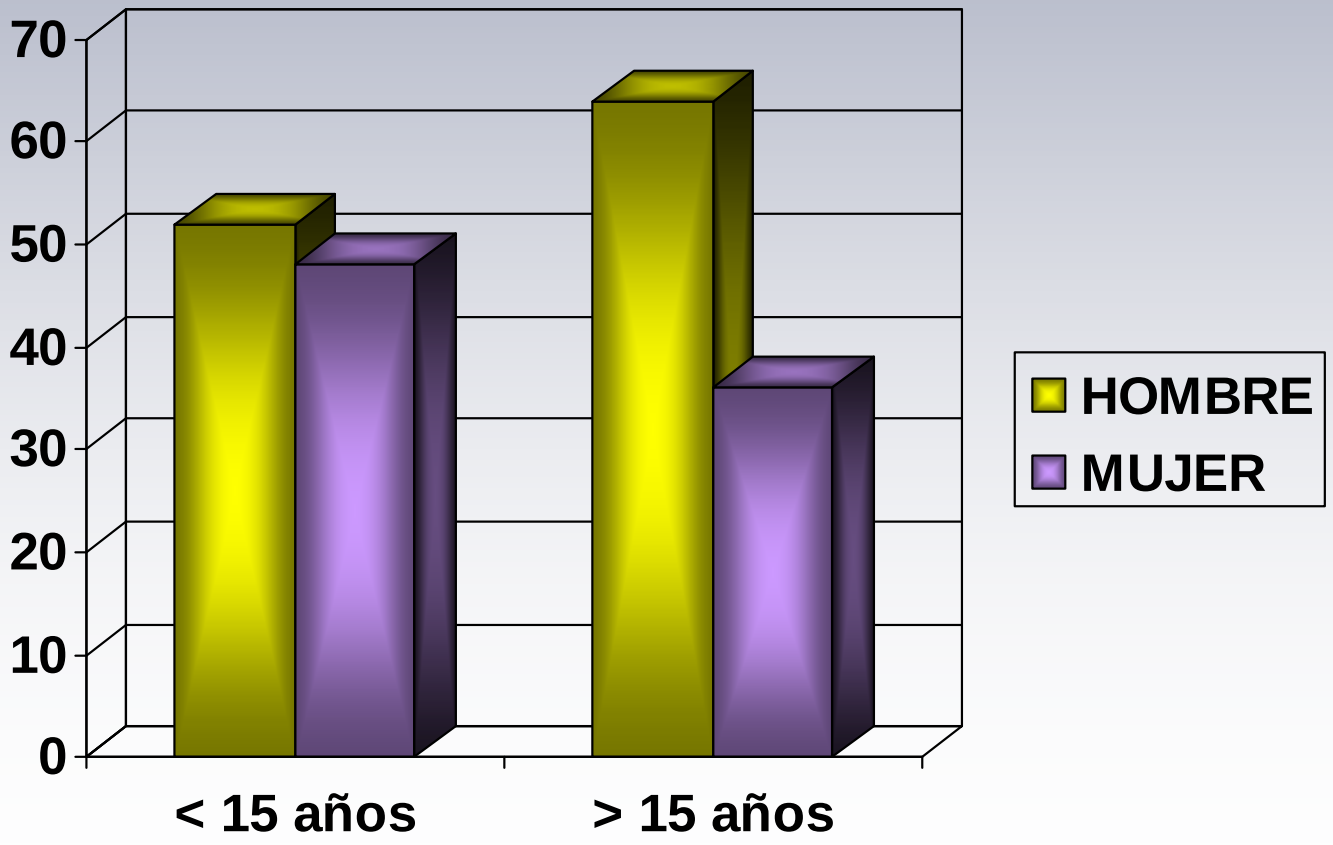
TOC Y EDAD DE INICIO

- ✓ PUNTO DE CORTE: 15 años



TOC Y EDAD DE INICIO

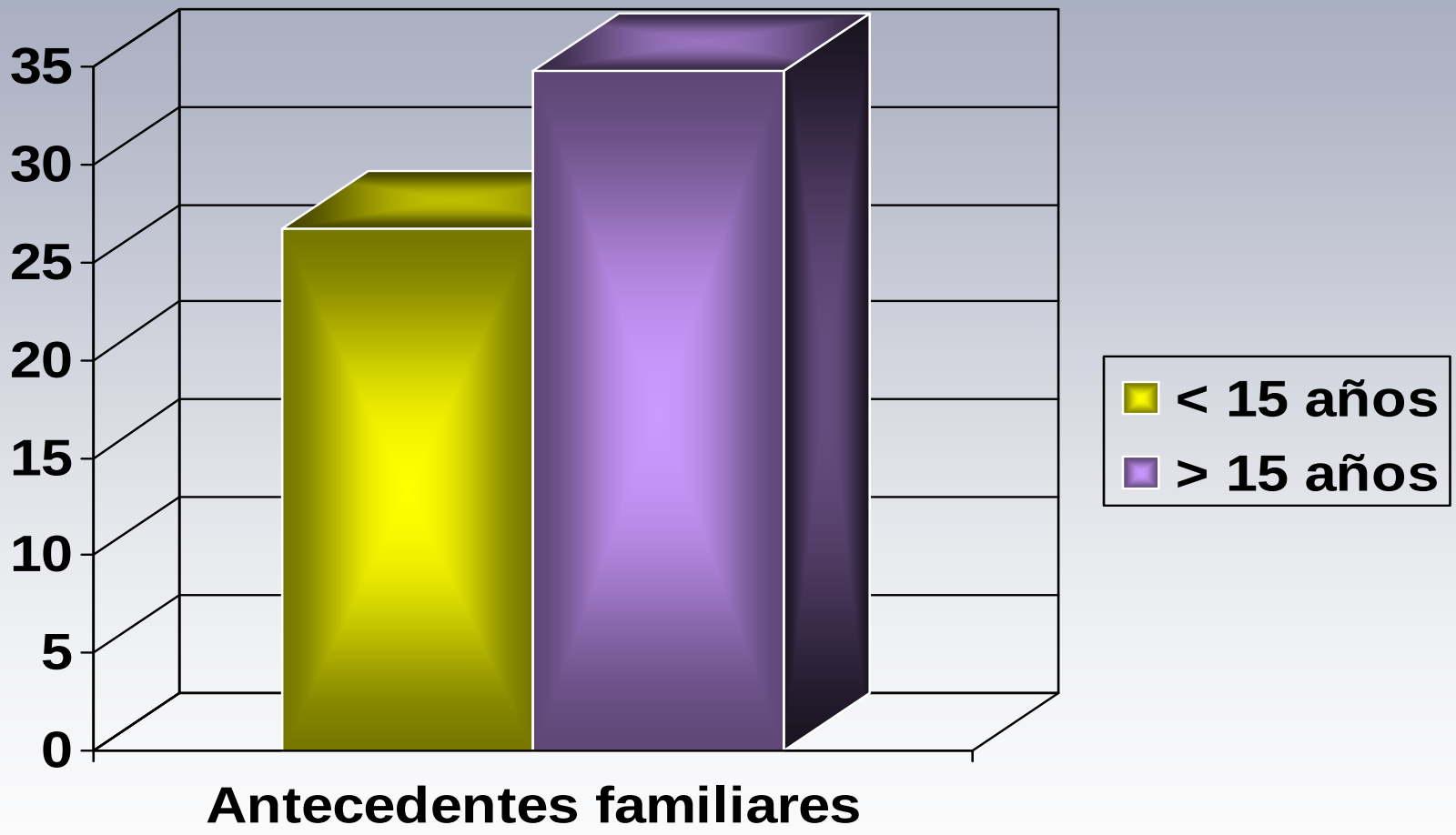
- ✓ SIN DIFERENCIAS SIGNIFICATIVAS EN LA DISTRIBUCIÓN POR GÉNERO



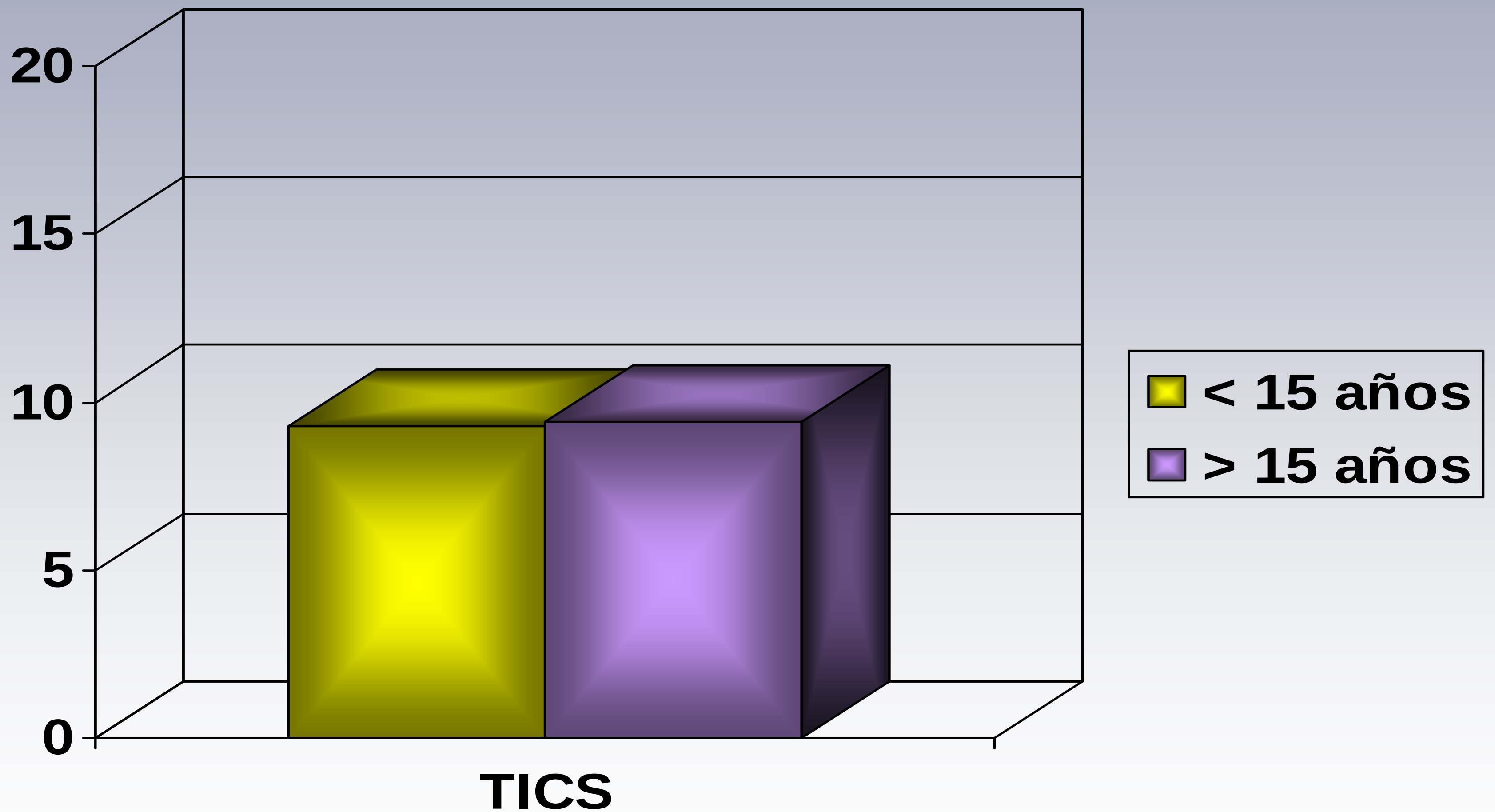
TOC Y EDAD DE INICIO: Características clínicas

	< 15 años	> 15 años	
Edad actual	30,0 años	32,0 años	
Edad de inicio	12,2 años	22,9 años	*
1ª Consulta	8,7 años	4 años	*
HDRS	14,2	13,5	
Y-BOCS basal	27,1	25,3	
Y-BOCS obs	13,9	12,8	*
Y-BOCS comp	13,2	12,4	
HDRS 12 sem	9,7	9,3	
Y-BOCS 12 sem	19,7	18,4	
Y-BOCS obs	10,2	9,4	
Y-BOCS comp	9,5	9,0	
Reduc 12 sem	29,08 %	30,08 %	

TOC Y EDAD DE INICIO: Características clínicas

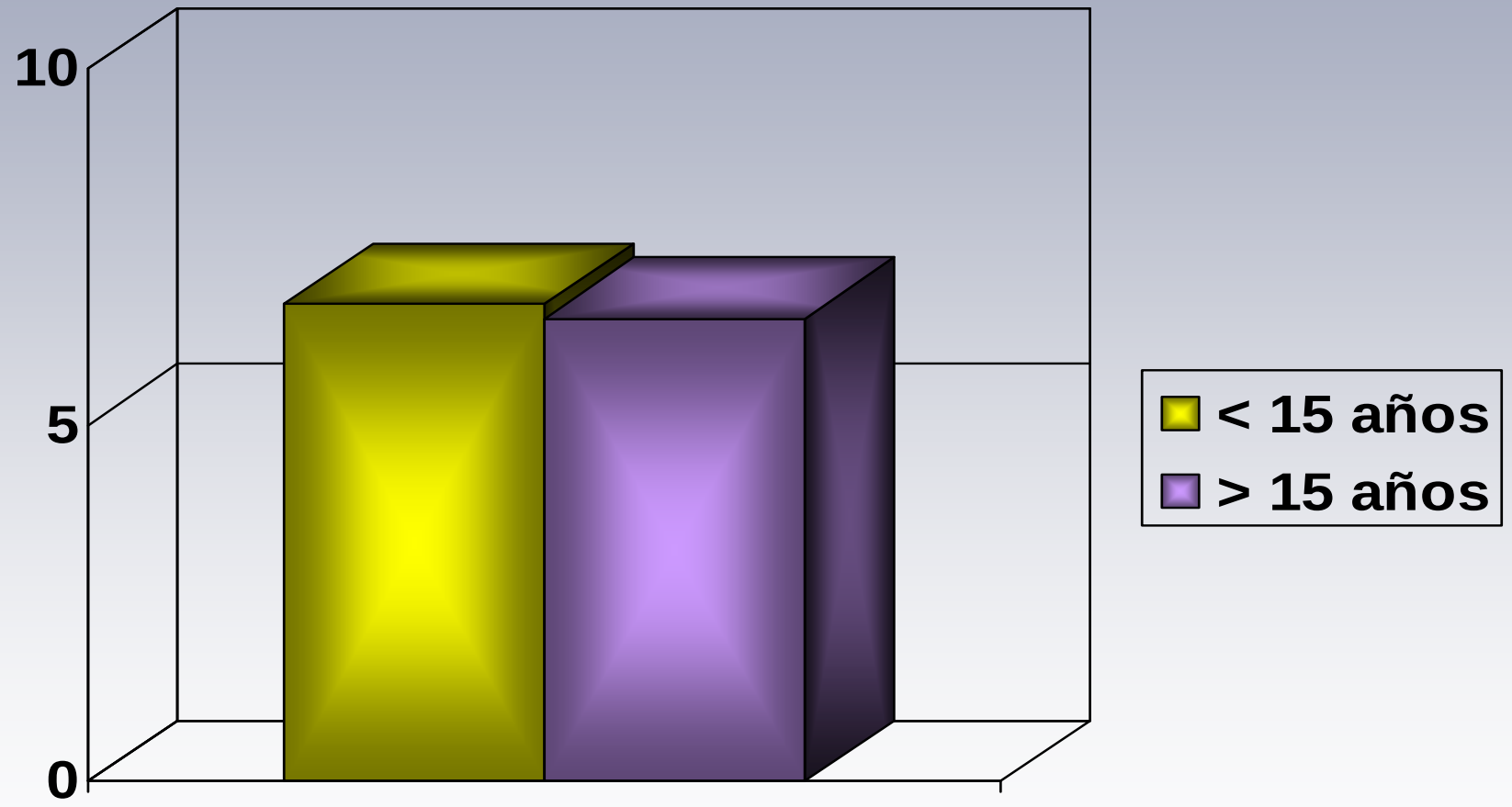


TOC Y EDAD DE INICIO: Características clínicas



9,3% 9,4%

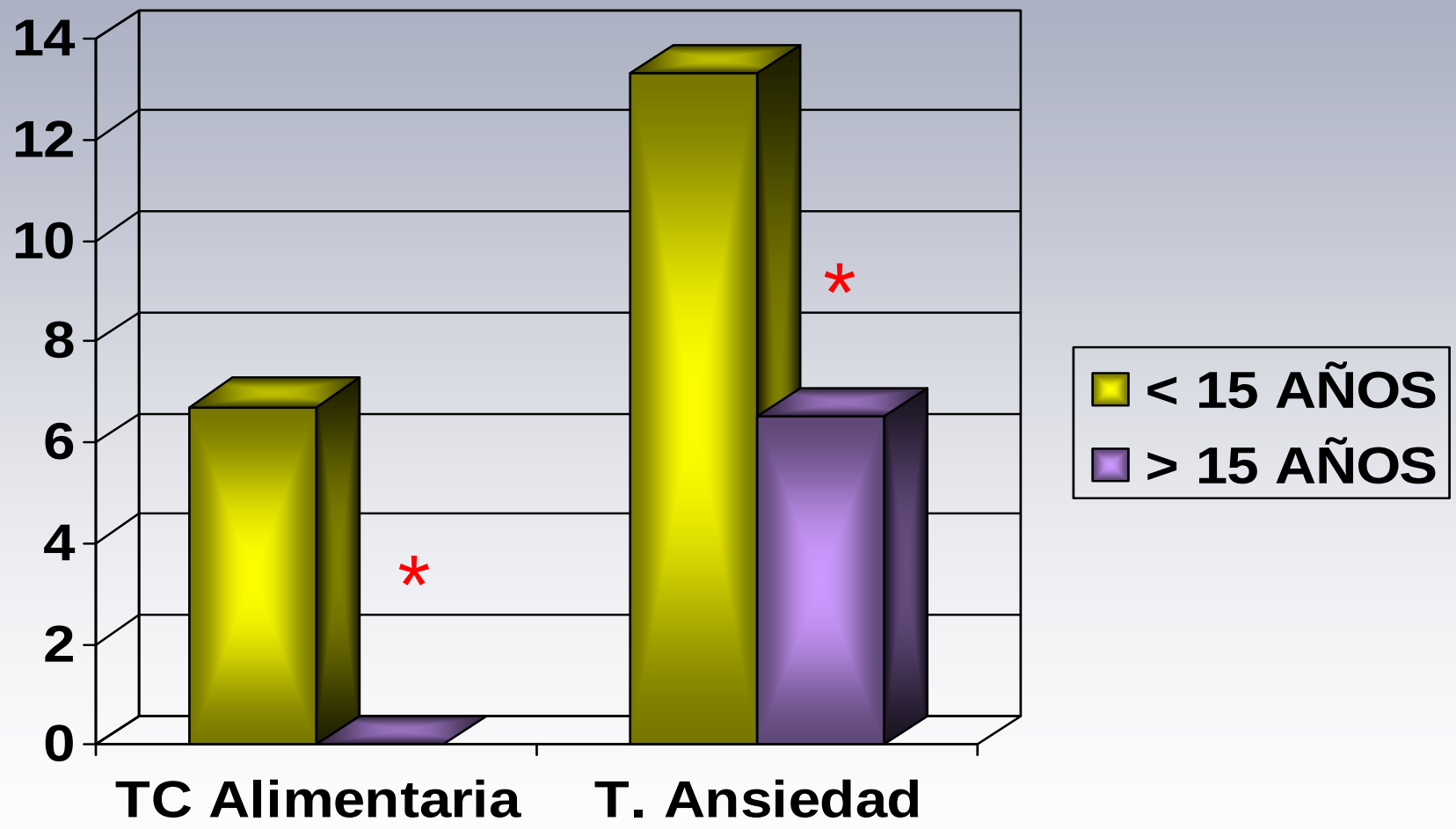
TOC Y EDAD DE INICIO: Características clínicas



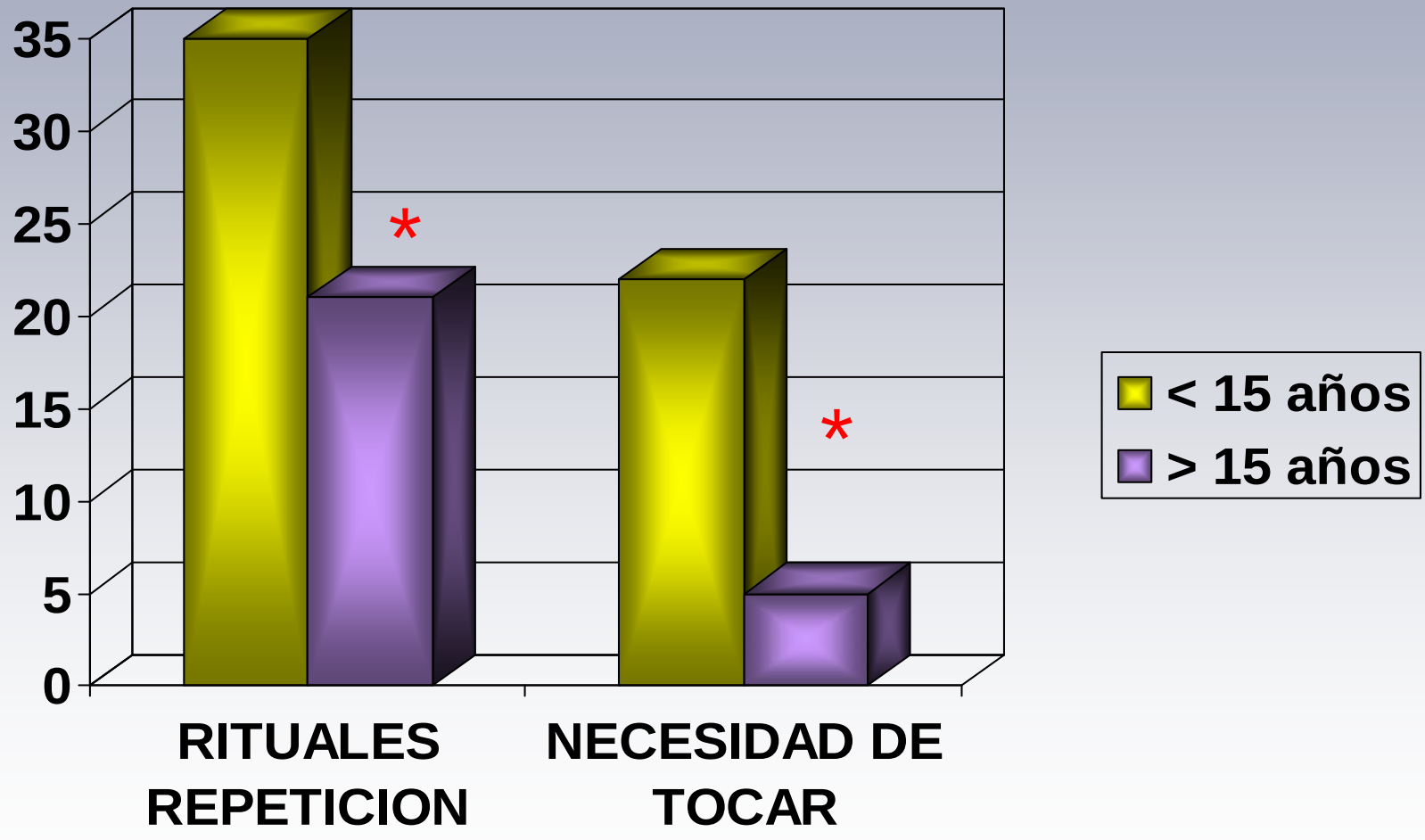
26,7% 26,5%

HISTORIA DE DEPRESIÓN

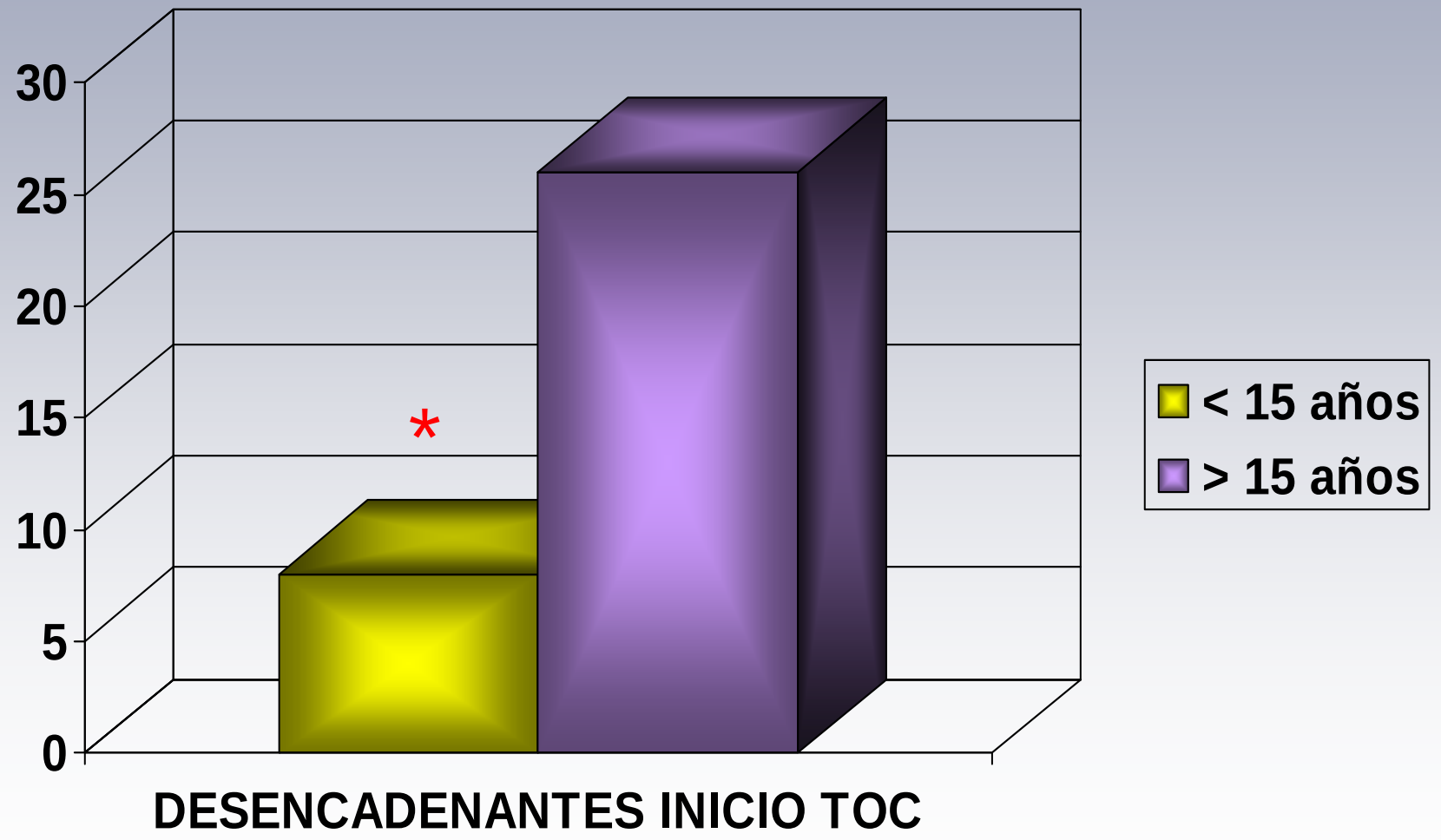
TOC Y EDAD DE INICIO: Características clínicas



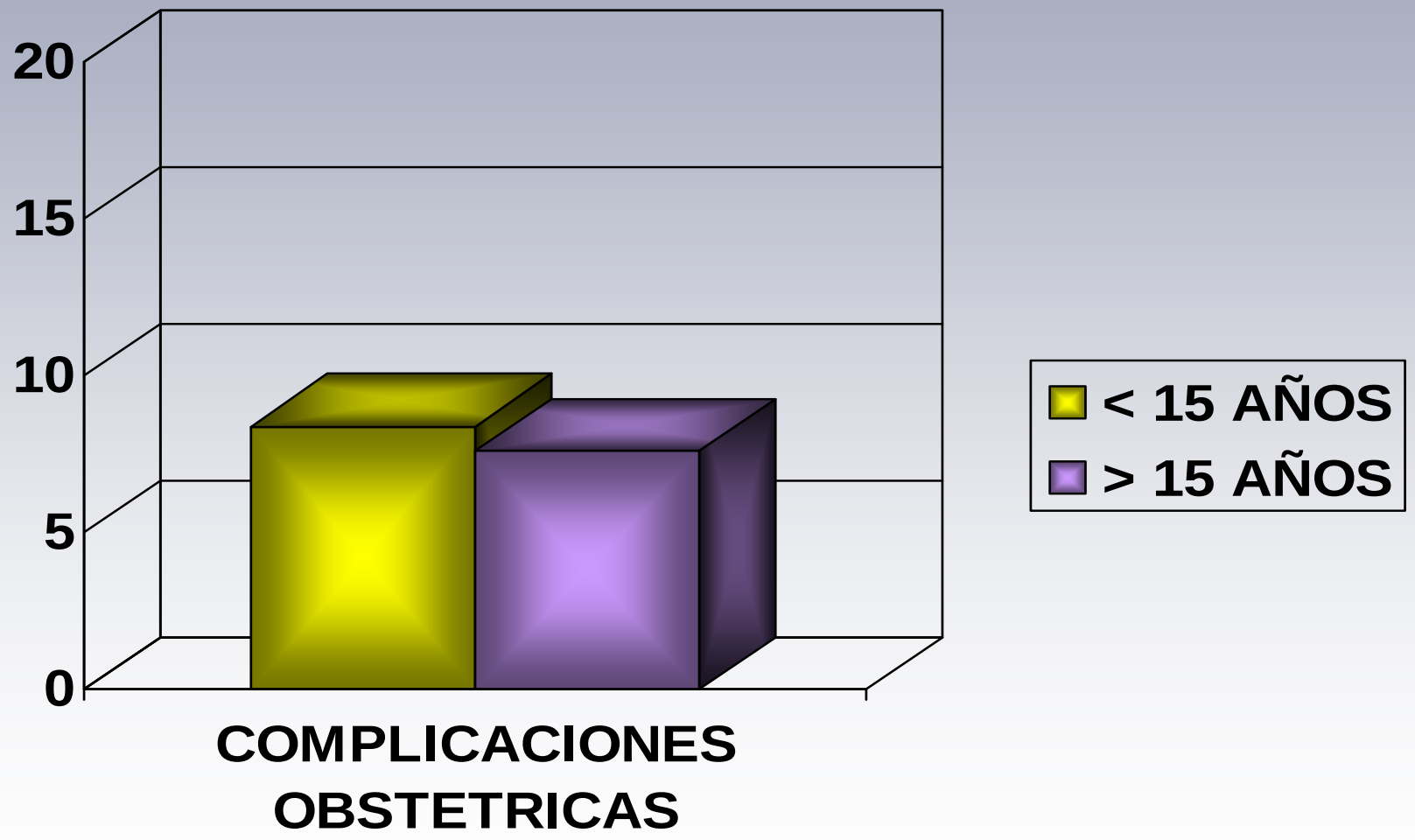
TOC Y EDAD DE INICIO: Características clínicas



TOC Y EDAD DE INICIO: Características clínicas



TOC Y EDAD DE INICIO: Características clínicas



BAER, 1994

- ✓ CONTAMINACIÓN + LIMPIEZA + COMPROB
- ✓ SIMETRÍA+ ORDEN + ACUMULACIÓN
- ✓ AGRESIVO/ SEXUAL/RELIGIOSO

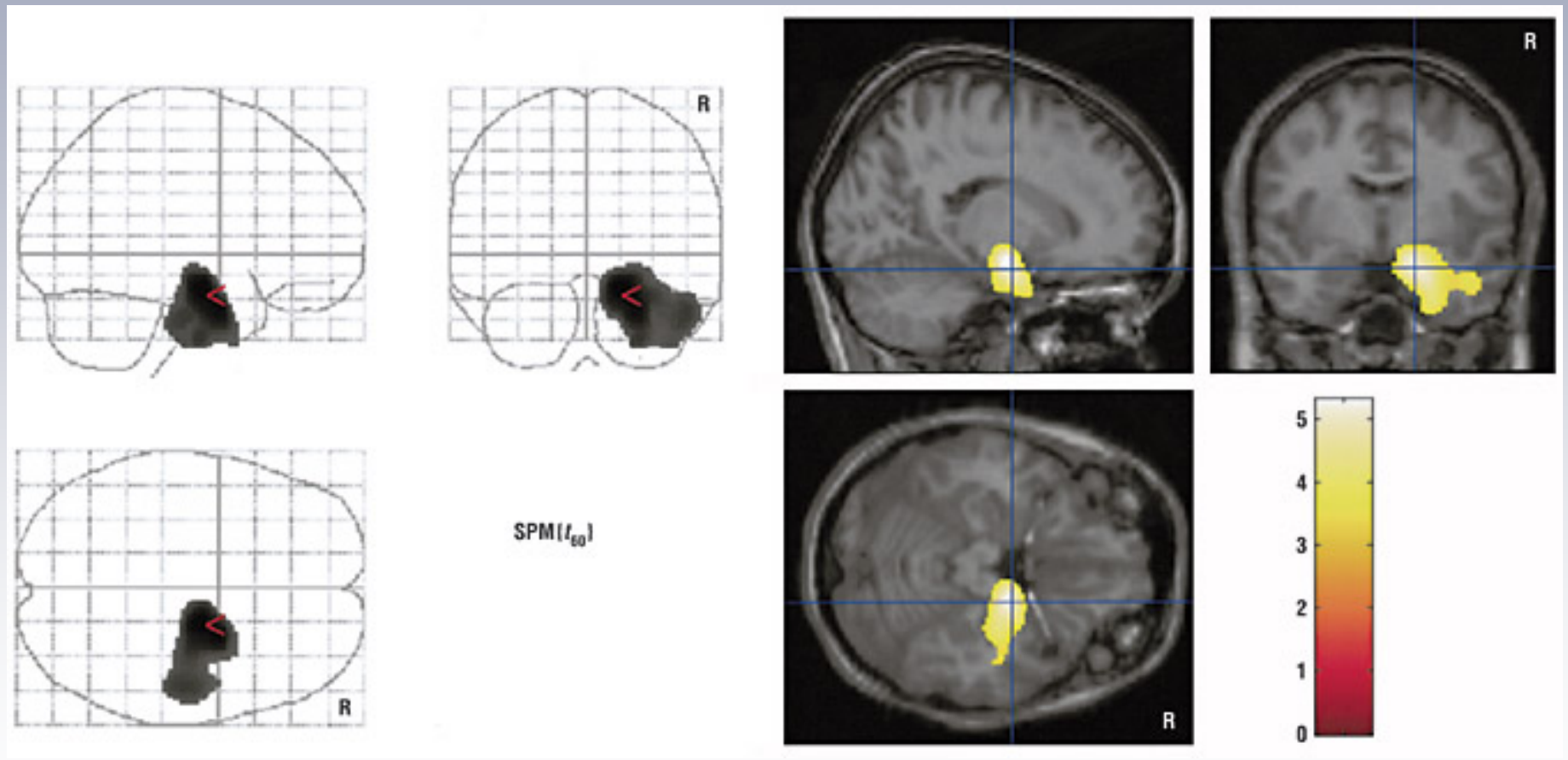
LECKMAN Y COLS., 1997

- ✓ CONTAMINACIÓN + LIMPIEZA
- ✓ SIMETRÍA+ORDEN
- ✓ ACUMULACIÓN
- ✓ AGRESIVAS/SEXUAL/RELIGIOSO + COMPROBACIÓN

MATAIX-COLS Y COLS, 1999; CALAMARI Y COLS, 1999

- ✓ CONTAMINACIÓN + LIMPIEZA
- ✓ SIMETRÍA + ORDEN
- ✓ ACUMULACIÓN
- ✓ AGRESIVAS + COMPROBACIÓN
- ✓ SEXUAL/RELIGIOSO

Relative gray matter volume reduction in patients with prominent aggressive obsessions and checking compulsions



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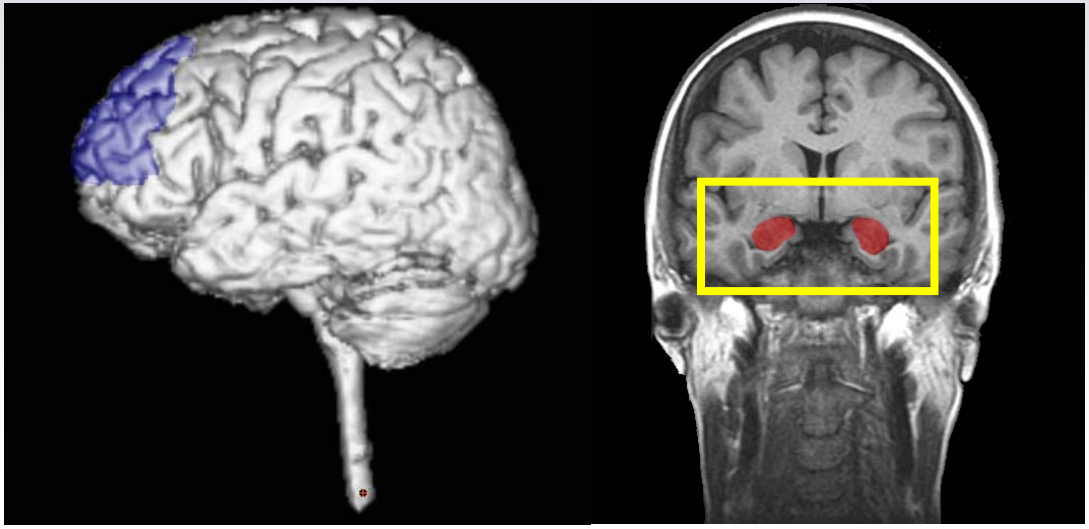
Estímulo

Amígdala:

Circuito del miedo

Respuesta

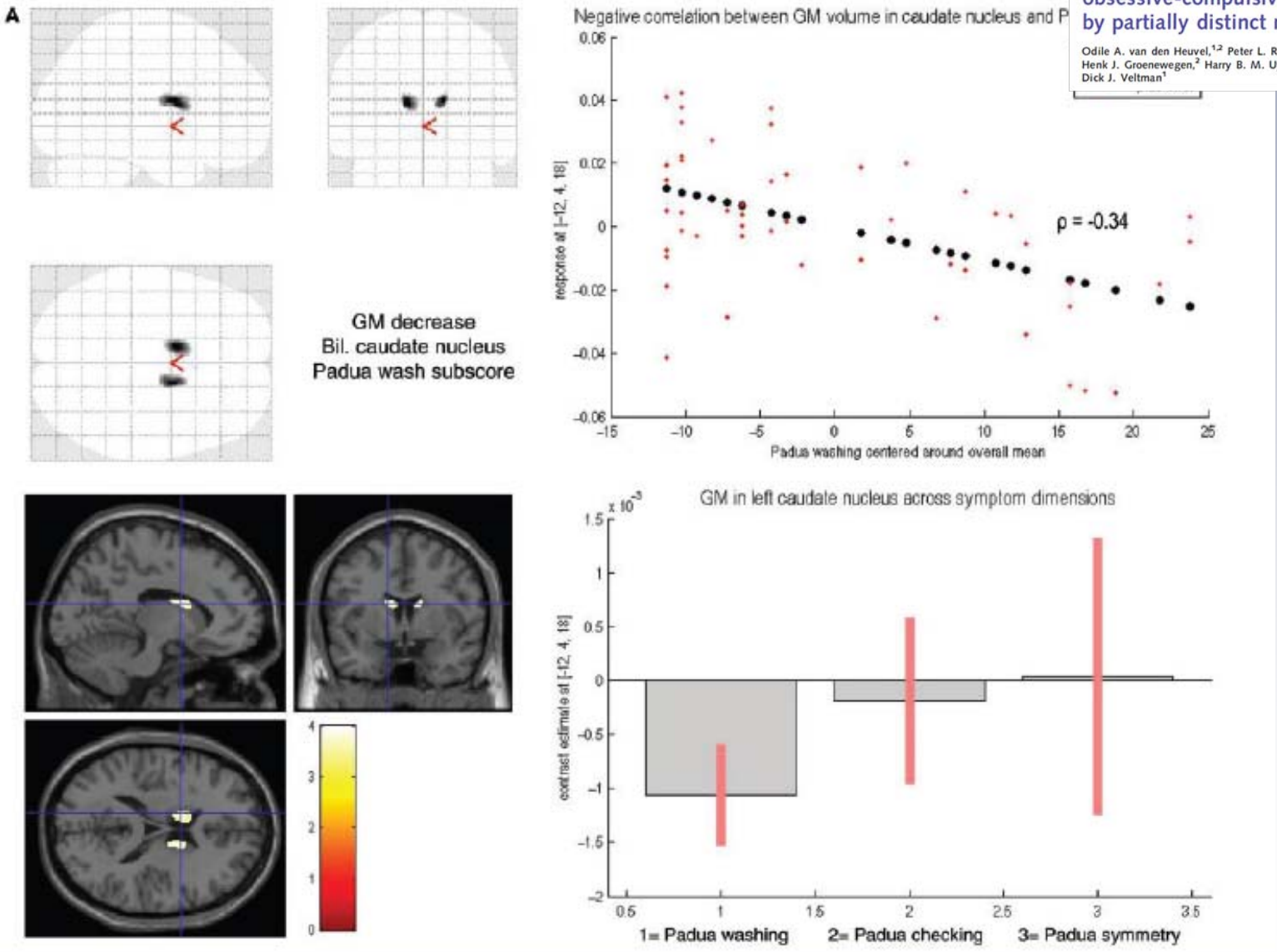


doi:10.1093/brain/awn267 Brain 2009: 132; 853–868 | 853

BRAIN
A JOURNAL OF NEUROLOGY

The major symptom dimensions of obsessive-compulsive disorder are mediated by partially distinct neural systems

Odile A. van den Heuvel,[1,2] Peter L. Remijnse,[1] David Mataix-Cols,[3] Hugo Vrenken,[4] Henk J. Groenewegen,[2] Harry B. M. Uylings,[2,5] Anton J. L. M. van Balkom[1] and Dick J. Veltman[1]



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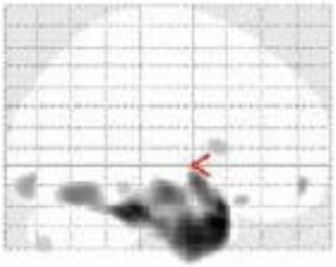
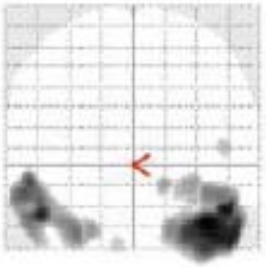
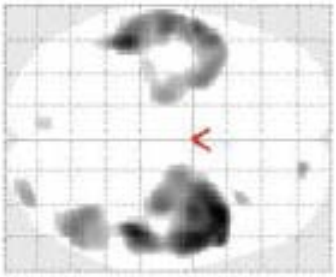
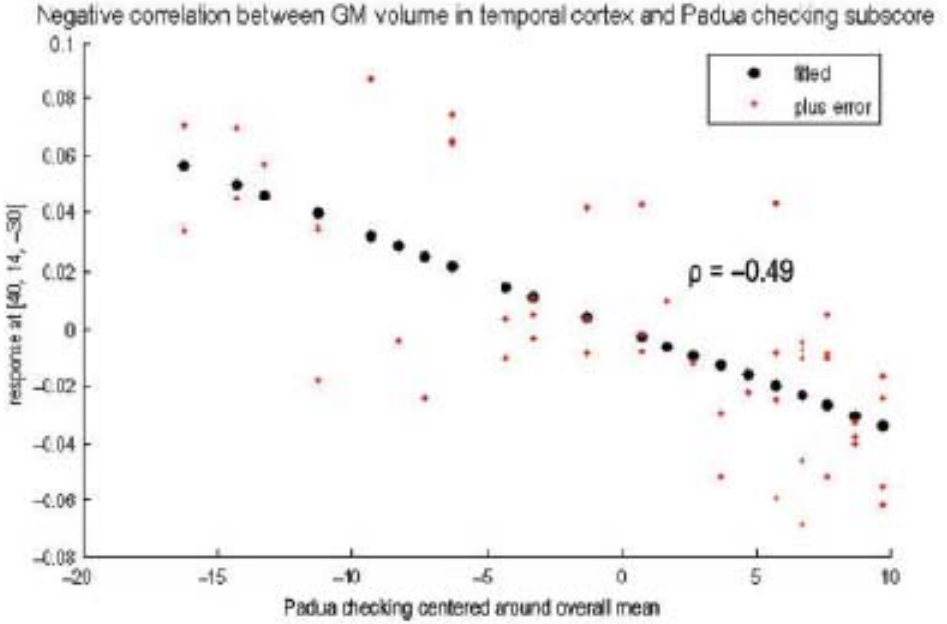
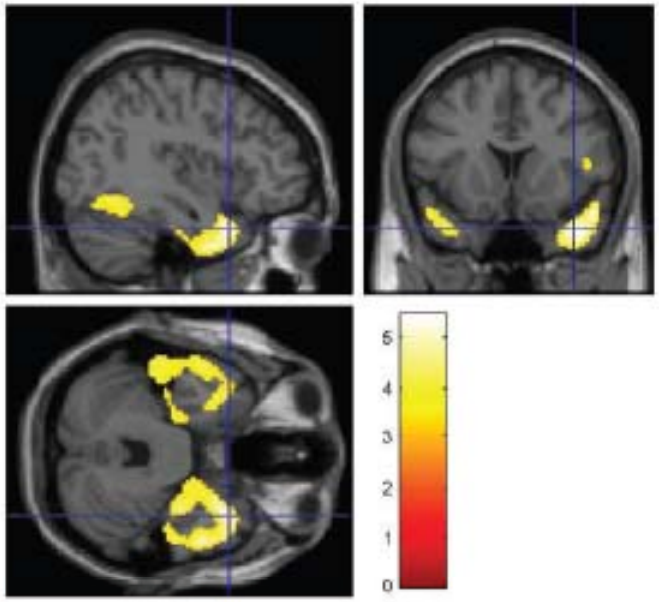


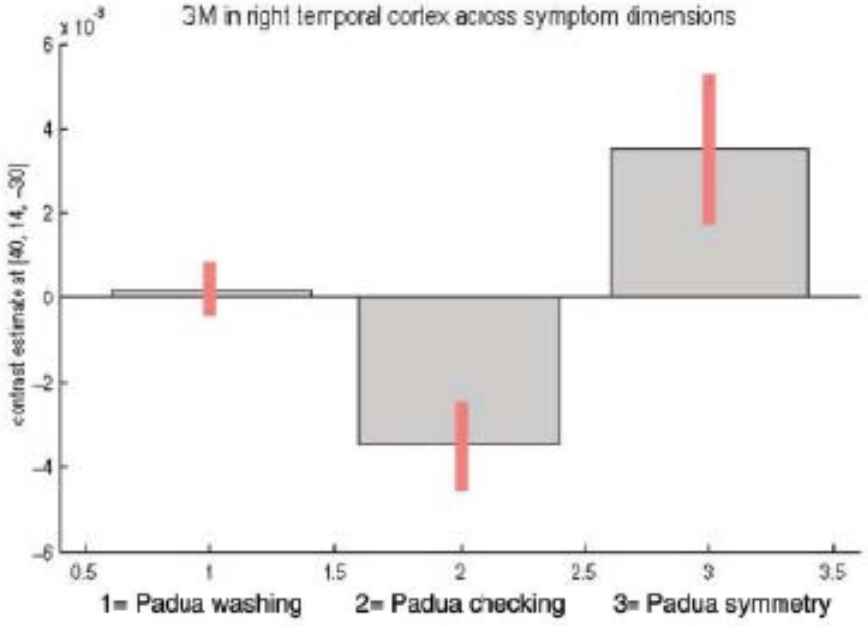




GM decrease
Bil. temporal cortex
Padua checking subscore







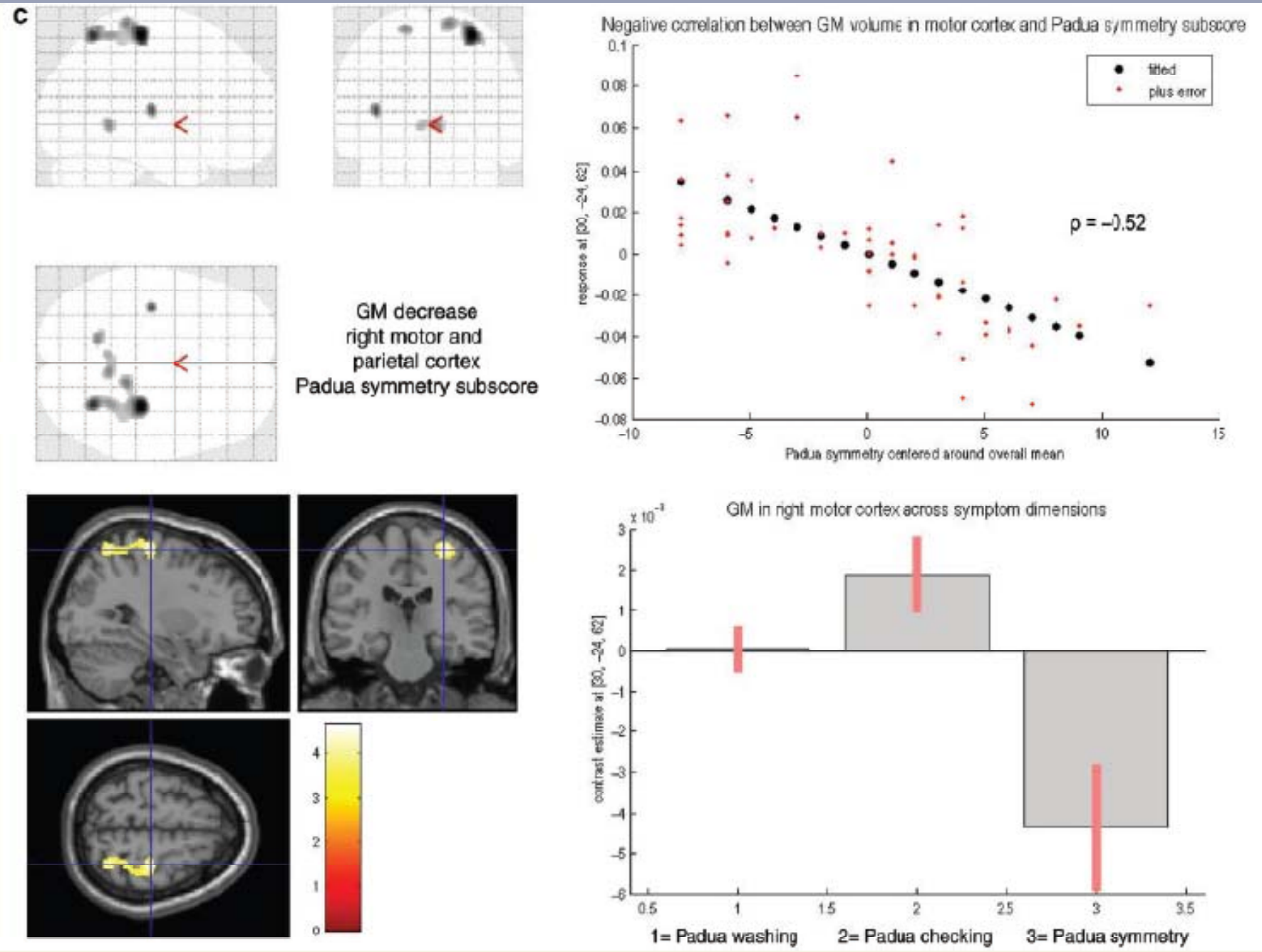


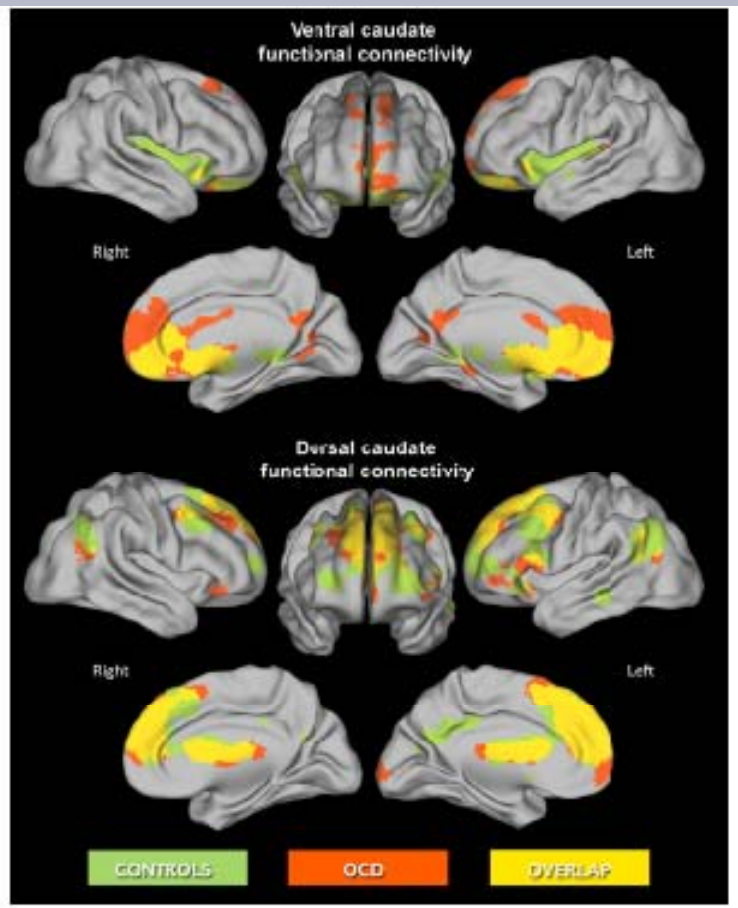
Figure 3 Continued.

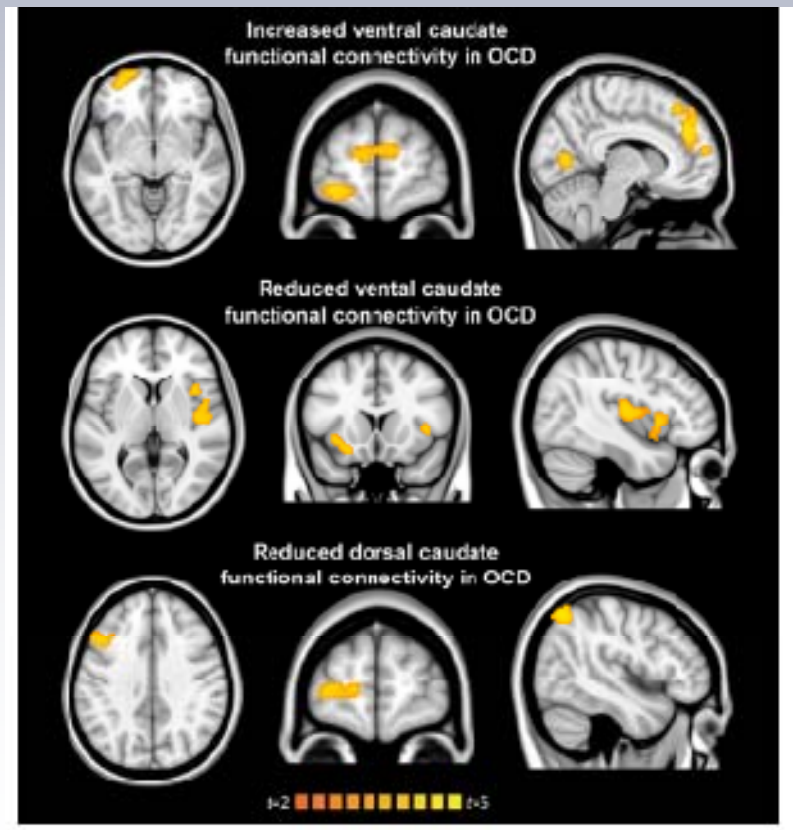
ARCHIVAL REPORT

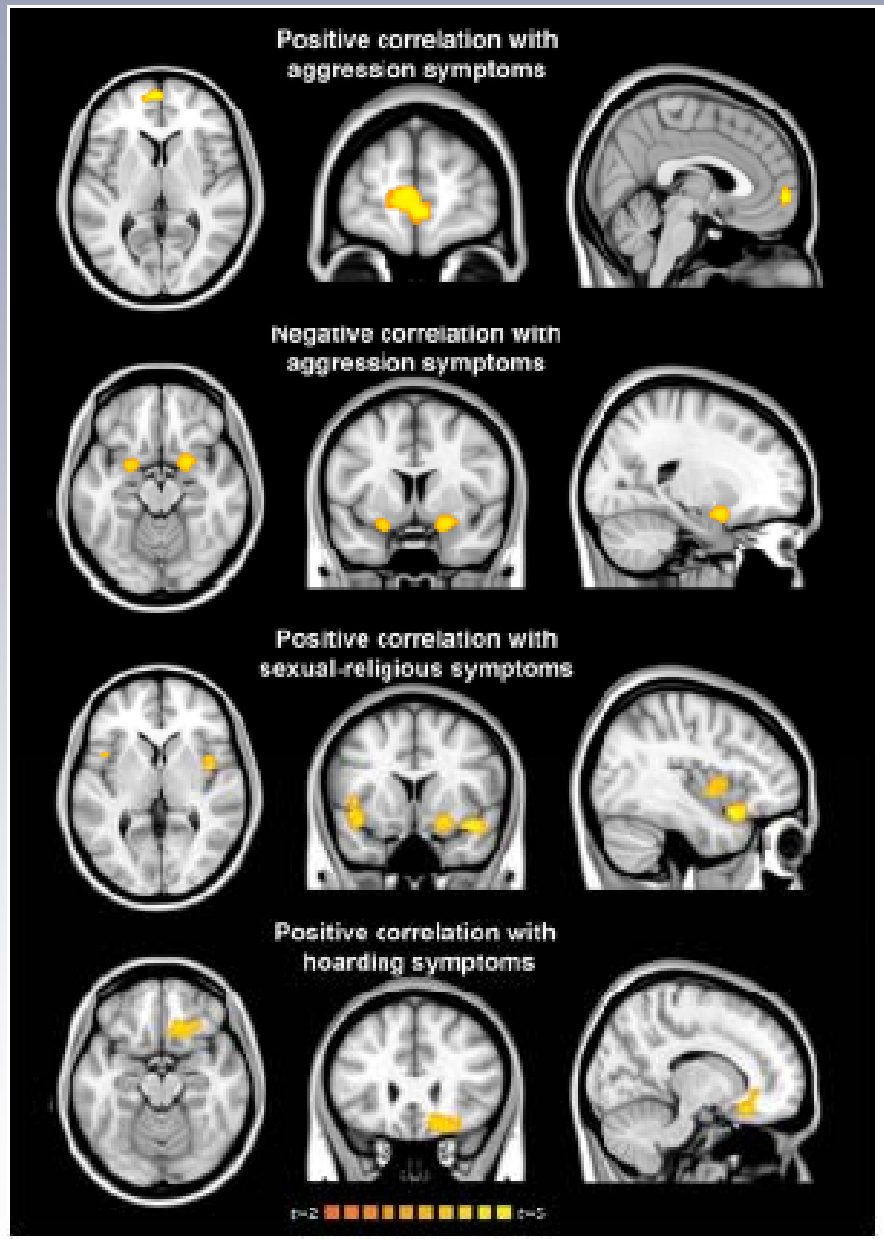
Brain Corticostriatal Systems and the Major Clinical Symptom Dimensions of Obsessive-Compulsive Disorder

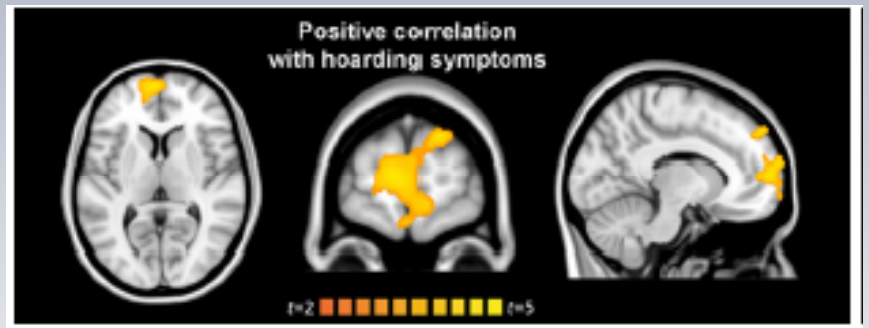
Ben J. Harrison, Jesus Pujol, Narcis Cardoner, Joan Deus, Pino Alonso, Marina López-Solà, Oren Contreras-Rodríguez, Eva Real, Cinto Segalàs, Laura Blanco-Hinojo, José M. Menchon, and Carles Soriano-Mas

BIOL PSYCHIATRY 2013;73:321–328






Positive correlation with aggression symptoms
Negative correlation with aggression symptoms
Positive correlation with sexual-religious symptoms
Positive correlation with hoarding symptoms
t=2
t=5

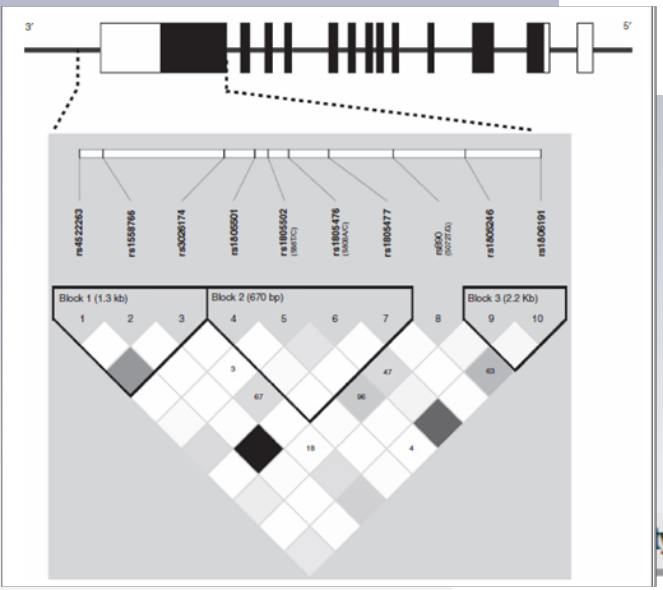

Positive correlation with hoarding symptoms
t=2
t=5

Research Paper

Association between the NMDA glutamate receptor *GRIN2B* gene and obsessive–compulsive disorder

Pino Alonso, PhD;* Mónica Gratacós, PhD;* Cinto Segalàs, PhD; Georgia Escaramís, PhD; Eva Real, MD; Mónica Bayés, PhD; Javier Labad, MD; Clara López-Solà, MD; Xavier Estivill, PhD; José M. Menchón, PhD

J Psychiatry Neurosci 2012;37(4)



ype distribution in patients with and without contamination/cleaning obsessions and compulsions

rs1805501	rs1805502	rs1805476	rs1805477	Group, haplotype frequency, %				*p* value	
				All patients	No contamination/ cleaning	Contamination/ cleaning	OR (95% CI)	Crude	Permuted
A	A	G	C	45.7	39.0	51.0	1.0	—	—
A	A	T	C	36.4	30.8	42.6	1.92 (1.22–3.01)	0.0047	0.023
A	G	G	C	16.2	16.7	15.7	1.23 (0.72–2.09	0.45	—

CI = confidence interval; OR = odds ratio.

Psychoneuroendocrinology (2011) 36, 473–483

available at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/psyneuen

Variants in estrogen receptor alpha gene are associated with phenotypical expression of obsessive-compulsive disorder

P. Alonso [a,b,c,1,*], M. Gratacòs [d,e,1], C. Segalàs [a], G. Escaramís [d,e], E. Real [a,f], M. Bayés [g], J. Labad [h], A. Pertusa [a], J. Vallejo [a,c], X. Estivill [d,e,f,i], J.M. Menchón [a,b,c]

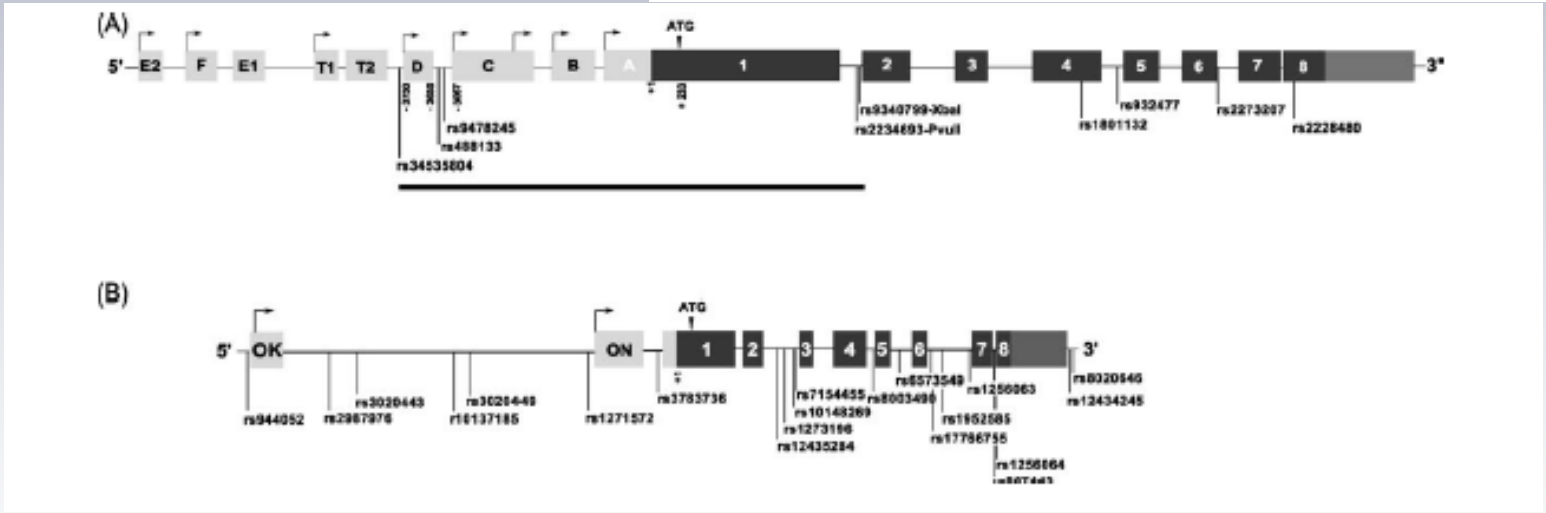

Table 2A Multinomial risk ratios of the effect of rs34535804 on contamination/cleaning symptoms, considering control individuals as a reference.

Genotype	Controls			No contamination/cleaning			Contamination/cleaning			
	N, Frequency (%)	Risk ratio	*p*-Value*	*N*, Frequency (%)	Risk ratio	*p*-Value*	*N*, Frequency (%)	Risk ratio	*p*-Value*	Trend *p*-value
GG	258 (92.47)	1.0	–	107 (87.7)	1.0	–	106 (99.1)	.01	–	–
AG	21 (7.52)	2.15 (1.03–4.49)	0.04	15 (12.2)	2.15 (1.03–4.5	0.04	1 (0.9)	0.06 (0.01–0.46)	0.007	0.0001

* Adjusted by sex and age.

CONCLUSIONES

- ✓ LOS PACIENTE CON TOC TRATADOS DE FORMA INTENSIVA PRESENTAN A LARGO PLAZO UNA BUENA EVOLUCIÓN:
  - 70-80 % MEJORAN
  - 40-50% REMITEN PARCIAL O TOTALMENTE
- ✓ TRATAMIENTO INTENSIVO:
  - ISRS DE FORMA PROLONGADA
  - **TERAPIA DE CONDUCTA, TERAPIA DE CONDUCTA, TERAPIA DE CONDUCTA**

- ES NECESARIO IDENTIFICAR FENOTIPOS HOMOGÉNEOS DE TOC QUE FACILITEN EL ESTUDIO DE LA ETIOPATOGENIA DE LA ENFERMEDAD:
  - EDAD DE INICIO
  - DIMENSIONES DE SÍNTOMAS
  - INTERACCIONES ENTRE DISTINTOS FENOTIPOS
- OBJETIVO FINAL: PERSONALIZAR EL TRATAMIENTO Y MEJORAR EL PRONÓSTICO A LARGO PLAZO DE NUESTROS PACIENTES

¡MUCHAS GRACIAS!

EN LA ANTERIOR SESIÓN ME DIJO QUE SUS PADRES ERAN AVA GARDNER Y ALBERT EINSTEIN Y HOY DICE QUE FUERON ZSA ZSA GABOR Y EL FARY ¿EN QUE QUEDAMOS?
EN QUE UD. ME COBRE A 7.000 LA HORA, PERO SE LAS VA A CURRAR