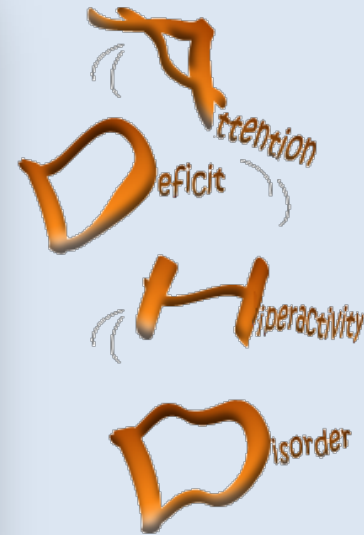


La comorbidità nell'ADHD



LA MULTIDIMENSIONALITÀ
DELLA COMORBILITÀ
NEI DISTURBI PSICHIATRICI
DELL'ETÀ EVOLUTIVA

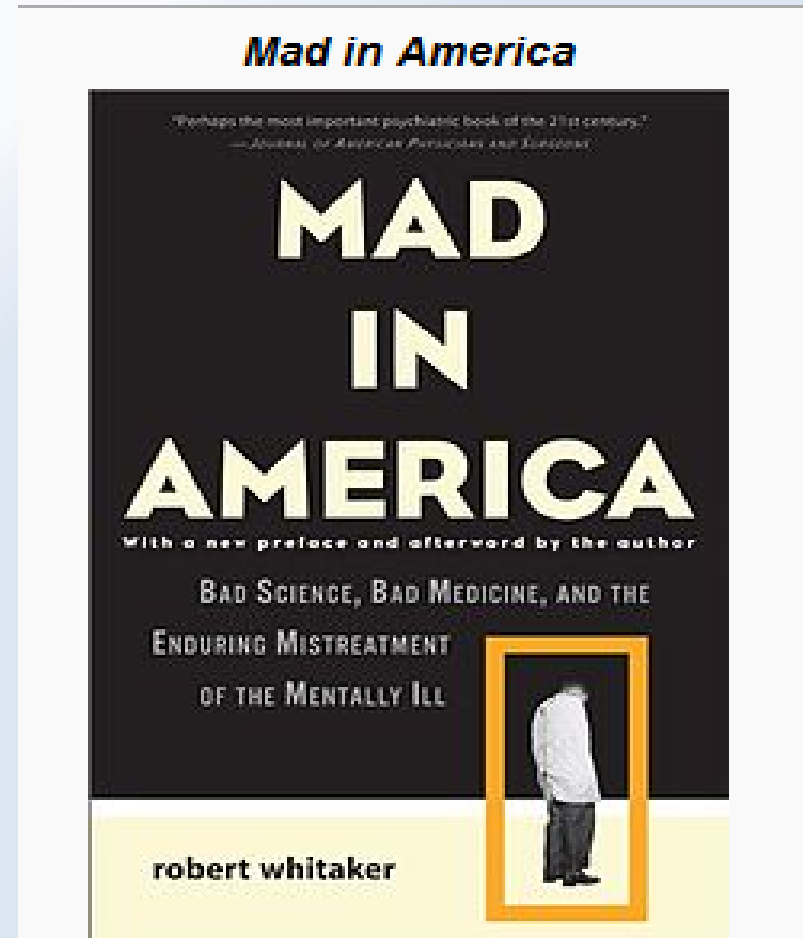




Da dove eravamo partiti?



ADHD: per una condivisione dei percorsi
diagnostico-terapeutici
Milano, 28 maggio 2013



Dove siamo arrivati

A Regional ADHD Center-Based Network Project for the Diagnosis and Treatment of Children and Adolescents With ADHD

**Maurizio Bonati¹, Laura Reale¹, Michele Zanetti¹, Massimo Cartabia¹,
Filomena Fortinguerra¹, Giuseppe Capovilla², Matteo Chiappedi³,
Antonella Costantino⁴, Paola Effedri⁵, Chiara Luoni⁶, Ottaviano Martinelli⁷,
Massimo Molteni⁸, Alberto Ottolini⁹, and Monica Saccani¹⁰, for the Lombardy
ADHD Group**

The impact of a model-based clinical regional registry for attention-deficit hyperactivity disorder

**Michele Zanetti, Massimo Cartabia, Anna Didoni,
Filomena Fortinguerra, Laura Reale,
Matteo Mondini and Maurizio Bonati**

IRCCS – Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

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Health Informatics Journal
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DOI: 10.1177/1460458216635835
jhi.sagepub.com


E adesso? Comorbidity??



➤ ICD 10

F92 – Disturbi Misti della Condotta
e della sfera emozionale

F83 – Disturbi evolutivi specifici misti

➤ APPROCCIO QUANTITATIVO DIMENSIONALE

Analisi fattoriale lungo un continuum di sviluppo:
nessuna comorbidity.

Comorbidity

Adrian Angold, E. Jane Costello, and Alaattin Erkanli



Da studi di meta-analisi.....

«...La comorbidity è una caratteristica reale e ineliminabile dei comuni disturbi psichici dell'infanzia e dell'adolescenza....»

- **Disorder vs disease comorbidity**
- **Homotypic vs Heterotypic comorbidity**
- **Familial comorbidity**
- **Concurrent vs successive comorbidity**

Comorbidity

Adrian Angold, E. Jane Costello, and Alaattin Erkanli

Da studi di meta-analisi.....

«...La comorbidity è una caratteristica reale e ineliminabile dei comuni disturbi psichici dell'infanzia e dell'adolescenza....»

➤ Non è un artefatto metodologico

- informanti multipli,
- medesimo comportamento classificato in diverse categorie

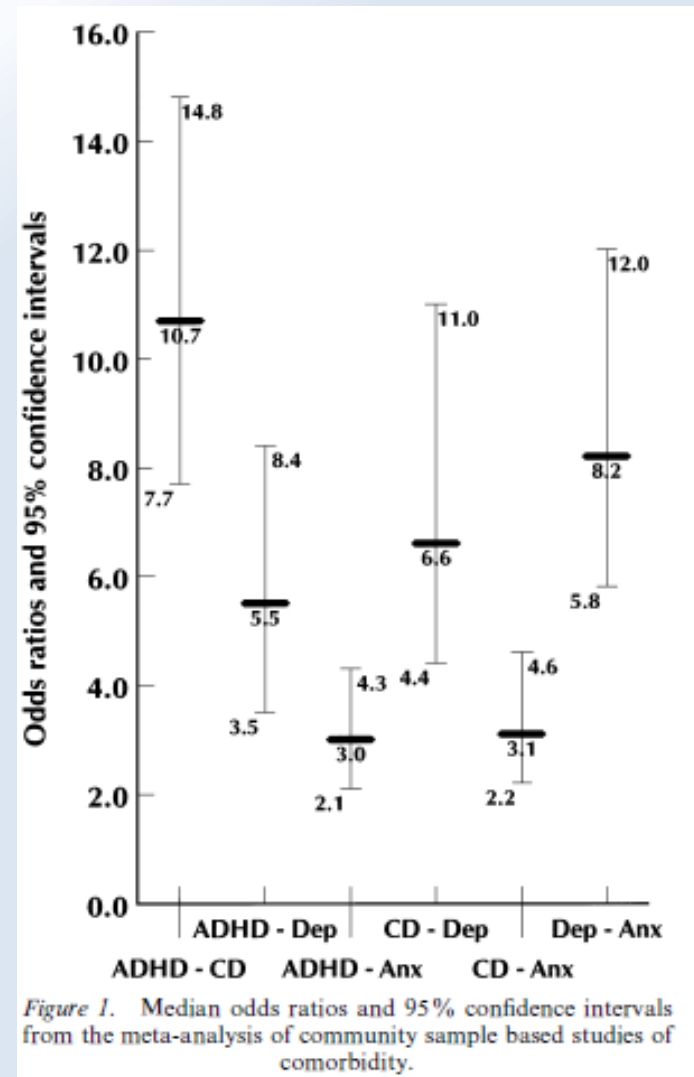
➤ Non è un artefatto dei sistemi diagnostici

(es.eliminando i sintomi che si sovrappongono si conferma la presenza di comorbidity; i sintomi non specifici non sono la causa di comorbidity eterotipica)

Comorbidity

Adrian Angold, E. Jane Costello, and Alaattin Erkanli

- **Comorbidity omotipica o continuità omotipica??**
 - I diversi tipi di ansia
 - Depressione e distimia
- **Comorbidity eterotipica**
 - marker di severità di un unico disturbo? (es adhd + odd)
 - Sottotipo di un unico disturbo? (Disturbo ipercinetico della condotta?)



Psychiatric Disorders in Children With Autism Spectrum Disorders: Prevalence, Comorbidity, and Associated Factors in a Population-Derived Sample

EMILY SIMONOFF, M.D.,
F.R.C.PSYCH., ANDREW PICKLES,
PH.D., TONY CHARMAN, PH.D.,
SUSIE CHANDLER, PH.D., TOM
LOUCAS, PH.D., AND GILLIAN BAIRD,
F.R.C.P.C.H.

Disorder	3-Mo Point Prevalence/100	95% CI
Any disorder	70.8	58.2–83.4
Any main disorder ^a	62.8	49.8–75.9
Any emotional disorder ^b	44.4	30.2–58.7
Any anxiety or phobic disorders ^c	41.9	26.8–57.0
Generalized anxiety disorder	13.4	0–27.4
Separation anxiety disorder	0.5	0–1.6
Panic disorder	10.1	0–24.8
Agoraphobia	7.9	3.0–12.9
Social anxiety disorder	29.2	13.2–45.1
Simple phobia	8.5	2.8–14.1
Obsessive-compulsive disorder	8.2	3.2–13.1
Any depressive disorder	1.4	0–3.0
Major depressive disorder	0.9	0–2.3
Dysthymic disorder	0.5	0–1.4
Oppositional or conduct disorder	30.0	14.9–45.0
Oppositional defiant disorder	28.1	13.9–42.2
Conduct disorder	3.2	0–7.1
Attention-deficit/hyperactivity disorder	28.2	13.3–43.0
Other disorders ^d	24.7	14.1–35.3
Enuresis	11.0	4.1–17.7
Encopresis	6.6	1.8–11.4
Tourette syndrome	4.8	0.1–9.5
Chronic tic disorder	9.0	3.3–14.6
Trichotillomania	3.9	0–10.3

Prevalence and Development of Psychiatric Disorders in Childhood and Adolescence

E. Jane Costello, PhD; Sarah Mustillo, PhD; Alaattin Erkanli, PhD; Gordon Keeler, MS; Adrian Angold, MRCPsych Arch Gen Psychiatry. 2003;60:837-844

Table 4. Concurrent Comorbidity*†

Diagnosis	Any Anxiety Disorder	Any Depressive Disorder	ADHD	Conduct Disorder	Oppositional Defiant Disorder	SUDs
Any anxiety disorder		25.1 (9.9-63.3)	6.6 (2.9-15.4)	2.5 (1.1-5.5)‡	3.3 (1.7-6.5)	0.6 (0.2-1.9)
		27.9 (8.9-87.8) 	3.4 (1.2-9.8)‡	1.6 (0.7-3.9)	0.8 (0.5-2.5)	0.2 (0.04-0.8)‡
Any depressive disorder	28.4 (14.3-55.0)		8.0 (3.4-16.5)	5.0 (2.3-11.2)	20.7 (8.8-48.8)	9.9 (3.1-31.5)
	28.9 (13.8-60.7) 		2.2 (0.6-8.2)	0.7 (0.2-2.4)	16.7 (5.9-47.8) 	10.4 (2.7-40.3)
ADHD	7.7 (2.7-22.2)	3.3 (0.7-15.1)		3.7 (1.8-7.6)	8.7 (4.6-16.4)	NC
	6.0 (1.3-28.1)‡	0.1 (0.002-1.6)		1.9 (1.0-3.5)	6.6 (3.6-12.2) 	0.1 (0.01-1.1)
Conduct disorder	3.5 (1.3-5.9)	21.3 (9.0-50.5)	41.3 (14.0-121.9)		9.6 (5.3-17.3)	7.2 (3.1-16.7)
	0.3 (0.06-1.2)	10.6 (2.0-54.7)§	3.9 (1.1-13.6)		8.0 (4.5-14.0) 	5.7 (2.3-13.9)
Oppositional defiant disorder	7.7 (3.8-15.7)	15.1 (7.4-30.6)	79.0 (32.1-191.5)	44.1 (15.7-124.1)		4.1 (1.7-10.2)§
	2.4 (0.8-6.7)	7.1 (2.2-22.6) 	56.3 (10.6-153.4) 	29.4 (6.9-126.0) 		1.9 (0.7-4.6)
SUDs	0.4 (0.9-1.9)	3.5 (1.1-11.1)‡	0.3 (0.04-2.4)	23.4 (9.1-60.3)	2.4 (1.1-5.2)‡	
	NC	2.9 (0.6-12.9)	NC	30.7 (12.7-73.8) 	0.4 (0.04-2.7)	

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; NC, model would not converge; SUDs, substance use disorders.

*Data are given as odds ratio (95% confidence interval). Data for girls are presented below the diagonal row of empty cells; boys, above the diagonal.

†Values in regular type are simple bivariate estimates, and values in boldface type are corrected for other possible comorbidities involving the 2 diagnoses under consideration (eg, anxiety and depression) controlling for comorbidity of depression with oppositional defiant disorder.

Comorbidity più comuni

- **Sviluppo di ODD: rischio aumentato di 11 volte** (*Costello et al – 2001*)
- **Comorbidity con ODD e CD >30% < 50%** (*Yoshimasu K, et al - 2012*)
- **ADHD + ODD + aggressività > 7 < 10 anni: aumentato rischio per grave CD – criminalità e condotte da abuso** (*Nagin et al – 2005; Odgers, Moffitt et al- 2008; Pardini et al 2010*)
- **ADHD e ODD condividono fattori di rischio comuni (età di insorgenza analoga)** (*Costello et al – 2001*)
- **ADHD predispone a CD: possibile condivisione di fattori di rischio comuni** (*Biederman et al 2008 – 2009*)
- **Comorbidity con disturbi d'ansia: odd ratio 3.1** (*Jensen et al 2001; Tsang et al 2012*)
→ outcome è peggiore
- **ADHD conferisce un rischio per lo sviluppo di disturbi d'ansia** (*Drabick et al 2006 – 2009*)
- **ADHD e Depressione: odd ratio 5.5** (*Costello et al 2001 – Spencer et 2003*)
- **Bambini con ADHD: rischio aumentato per depressione in adolescenza e giovane età adulta** (*Biedermann et al 1998, Monuteaux et al 2007; Daviss et al 2008; Seymour et al 2010*)

Functional Impairments in Children With ADHD: Unique Effects of Age and Comorbid Status

Journal of Attention Disorders

16(3) 179–189

© 2012 SAGE Publications

**Genery D. Booster¹, George J. DuPaul¹, Ricardo Eiraldi²,
and Thomas J. Power²**

ADHD con comorbidità psicopatologiche

- **sintomi più severi,**
- **maggiore persistenza del disturbo**
- **prognosi più negative**
- **maggiore difficoltà nella integrazione sociale (specie quando sono presenti disturbi esternalizzanti)**
- **maggiori conseguenze negative sul funzionamento scolastico**

Relationships Between Learning Disability, Executive Function, and Psychopathology in Children With ADHD

Journal of Attention Disorders
16(2) 138–146
© 2012 SAGE Publications

Richard E. Mattison¹ and Susan Dickerson Mayes²

- La presenza di **Learning Disabilities** non aumenta la presenza di altre comorbidity psicopatologiche.
- Deficit nelle funzioni esecutive correlano con la presenza di learning disabilities ma non con un aumentato rischio di psicopatologia

Impact of executive function deficits and attention-deficit/hyperactivity disorder (ADHD) on academic outcomes in children.

Biederman J¹, Monuteaux MC, Doyle AE, Seidman LJ, Wilens TE, Ferrero F, Morgan CL, Faraone SV.

- ADHD con deficit funzioni esecutive
- → **aumentato rischio di fallimento scolastico** rispetto a
 - ADHD puro
 - Presenza o meno di learning disabilities
 - QI
- **NON AUMENTATO RISCHIO DI COMORBIDITA' PSICOPATOLOGICA**

A Developmental Psychopathology Perspective on ADHD and Comorbid Conditions: The Role of Emotion Regulation

Child Psychiatry Hum Dev (2015) 46:951–966

Elizabeth A. Steinberg · Deborah A. G. Drabick

Il profilo emozionale e il temperamento come fattori che predispongono all'insorgenza di comorbidità nei soggetti con ADHD, attraverso la «mediazione» con l'interazione parentale

Table 1 Potential temperament and emotion regulation profiles for comorbid conditions among children with ADHD

Comorbid condition	Temperament profile	Emotion regulation profile
ODD	Low effortful control, high negative emotionality, low agreeableness, high irritability/anger, high emotional lability	Under-regulation; high reactivity, low inhibition, high approach/aggression
CD—without callous-unemotional traits	Low effortful control, high negative emotionality, low agreeableness, high anger/irritability, high activity level, high fear	Under-regulation; high approach/reactive aggression, low inhibitory control, executive functioning deficits
CD—with callous-unemotional traits	Low fear and anxiety, low emotional distress, low anger/irritability, low neuroticism, low prosocial emotions, low agreeableness, low conscientiousness, high activity level	Age-appropriate regulation in general, but under-regulation with reward; high proactive aggression, high effortful control, low fearful inhibition, fewer executive functioning deficits, low arousal to punishment
Anxiety	Low effortful control, high social inhibition, high neuroticism, high fear, high positive emotionality	Over-regulation; high avoidance and withdrawal, high social inhibition, low attentional control, high attentional bias to threat, low regulation of threat-related affect and arousal
Depression	Low effortful control, high neuroticism, low positive emotionality, high need for affiliation	Over-regulation; high avoidance, overregulated emotional expression; low attentional control

Emotional dysregulation and Attention-Deficit/Hyperactivity Disorder


Philip Shaw, Argyris Stringaris, Joel Nigg, and Ellen Leibenluft

- La disregolazione emozionale è prevalente nella sindrome ADHD – lifespan – ed è la causa delle maggiori conseguenze
- La disregolazione emozionale è determinata da deficit neurocognitivi nell'orientare, riconoscere e porre attenzione agli stimoli emotivi
- Gli interventi migliorano la disregolazione emozionale, ma non incidono sui sintomi ADHD

Three models to explain the overlap between ADHD and emotional dysregulation are summarized with their predictions about clinical features, pathophysiology, and treatment.

	Phenomenology		Pathophysiology			Treatment
	Correlations between ADHD and emotion dysregulation	Clinical course	Psychological basis	Neural basis	Genetic	
Emotion dysregulation is integral to ADHD	Extremely high	Yoked clinical courses for symptoms of ADHD and emotion dysregulation	Deficits in behavioral inhibition and working memory mediate both core ADHD symptoms and emotion dysregulation	Anomalies confined to fronto-striatal-cerebellar circuits	Same genetic basis for ADHD + emotion dysregulation as ADHD	Treatments which improve ADHD will improve emotion dysregulation
Combined ADHD +emotion dysregulation defines a distinct entity	ADHD subgroup exists that is high on both symptom domains	Distinct clinical course in ADHD+emotion dysregulation from ADHD alone	Distinct cognitive deficits in ADHD+emotion dysregulation vs. ADHD alone.	Distinct neural basis for ADHD+emotion dysregulation vs. ADHD alone	Distinct genetic basis for ADHD+emotion dysregulation vs. ADHD alone	Existing treatments for ADHD may be less effective for ADHD+emotion dysregulation
Symptoms of ADHD and emotion dysregulation are correlated but distinct dimensions	Modest	Similar but dissociable clinical course for symptoms of ADHD and emotion dysregulation	Deficits in emotional processing mediate dysregulation and correlate with deficits mediating core ADHD symptoms	Anomalies extend beyond fronto-striato-cerebellar circuits to (para) limbic regions.	Some genes shared between ADHD alone and ADHD +emotion dysregulation	Treating 'core' ADHD benefits emotion dysregulation but separate treatment may also be needed

Latent classes of emotional and behavioural problems in epidemiological and referred samples and their relations to DSM-IV diagnoses

Valentina Bianchi^{1,2}  · Paolo Brambilla^{3,4} · Marco Garzitto⁵ · Paola Colombo¹ · Livia Fornasari⁵ · Monica Bellina¹ · Carolina Bonivento^{6,7} · Alessandra Tesei¹ · Sara Piccin⁵ · Stefania Conte^{8,9} · Giampaolo Perna¹⁰ · Alessandra Frigerio¹ · Isabella Castiglioni² · Franco Fabbro⁵ · Massimo Molteni¹ · Maria Nobile^{1,10}

Eur Child Adolesc Psychiatry

DOI 10.1007/s00787-016-0918-2

CAMPIONE

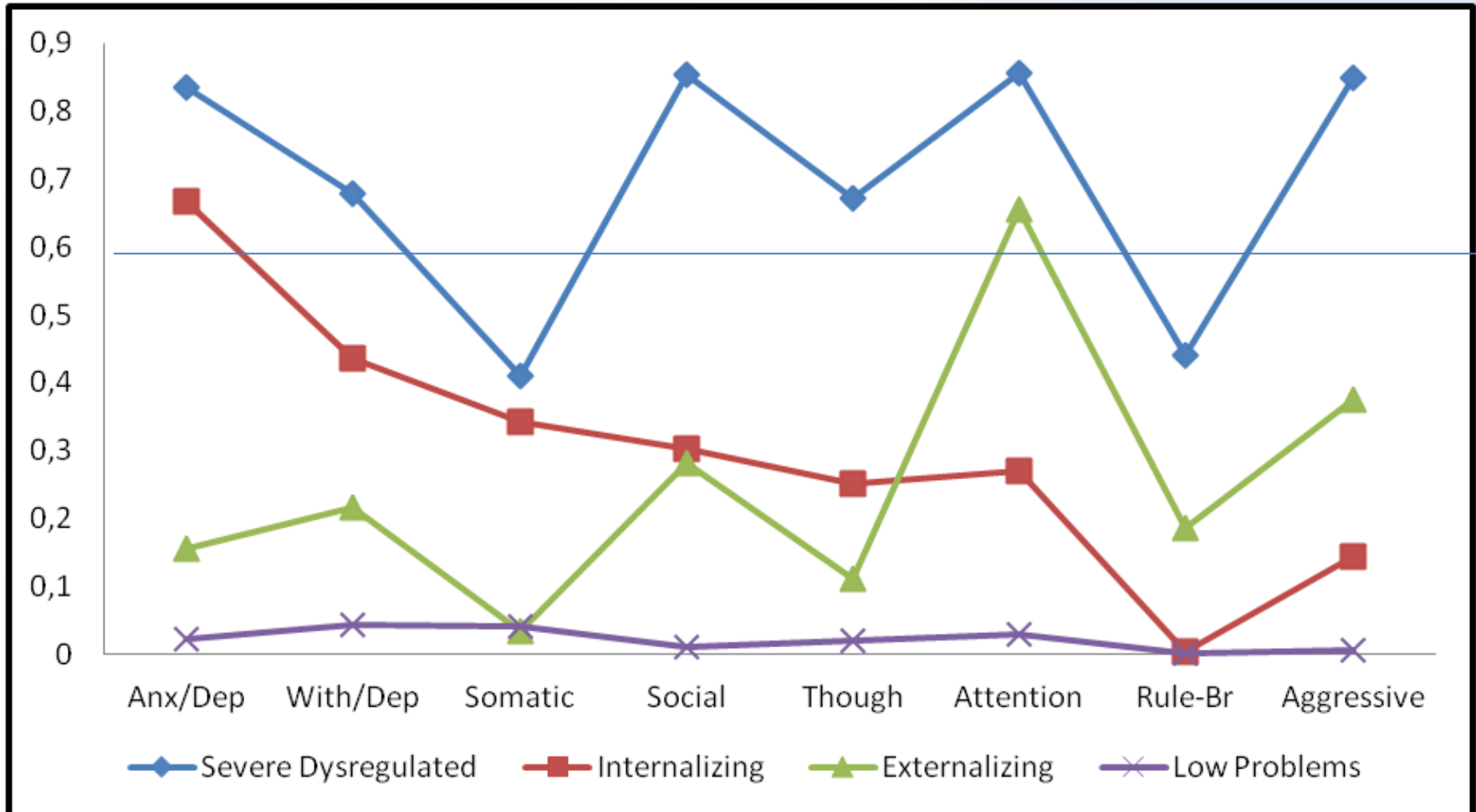
Campione di popolazione generale (PrISMA): 3418 soggetti

Campione clinico(GENESIS/CABALA): 1226 soggetti

TOTALE: 4644 soggetti con profilo CBCL/6-18

VALUTAZIONE DIAGNOSTICA: 1856 soggetti (631 da PrISMA + 1225 da GENESIS).

RISULTATI – CAMPIONE TOTALE



	Class 1: DYS (339)	Class 2: INT (500)	Class 3: ADHD (416)	Class 4: LOW (601)	P value ^a
<i>DSM-IV diagnoses (n %)</i>					
Any Diagnosis	302 (89.1%)	296 (59.2%)	351 (84.4%)	213 (35.4%)	X ² = 377.667 P = .000 ^{a, c, d, e, f}
ADHD	<u>104 (30.7%)</u>	32 (6.4%)	<u>204 (49.0%)</u>	67 (11.1%)	X ² = 304.967 P = .000 ^{a, b, c, d, e, f}
Any Behaviour Disorder	64 (18.9%)	16 (3.2%)	66 (15.9%)	29 (4.8%)	X ² = 93.263 P = .000 ^{a, c, d, f}
Any Mood Disorder	<u>151 (44.5%)</u>	<u>132 (26.4%)</u>	66 (15.9%)	36 (6.0%)	X ² = 212.112 P = .000 ^{a, b, c, d, e, f}
Any Anxiety Disorder	<u>184 (54.3%)</u>	<u>214 (42.8%)</u>	99 (23.8%)	117 (19.5%)	X ² = 156.639 P = .000 ^{a, b, c, d, e}
Presence of comorbidity	<u>177 (52.2%)</u>	<u>144 (28.8%)</u>	<u>100 (24.0%)</u>	64 (10.6%)	X ² = 196.882 P = .000 ^{a, b, c, e, f}

a: class 1 vs. class 2 was significantly different ($P < .05$)

b: class 1 vs. class 3 was significantly different ($P < .05$)

c: class 1 vs. class 4 was significantly different ($P < .05$)

d: class 2 vs. class 3 was significantly different ($P < .05$)

e: class 2 vs. class 4 was significantly different ($P < .05$)

f: class 3 vs. class 4 was significantly different ($P < .05$)

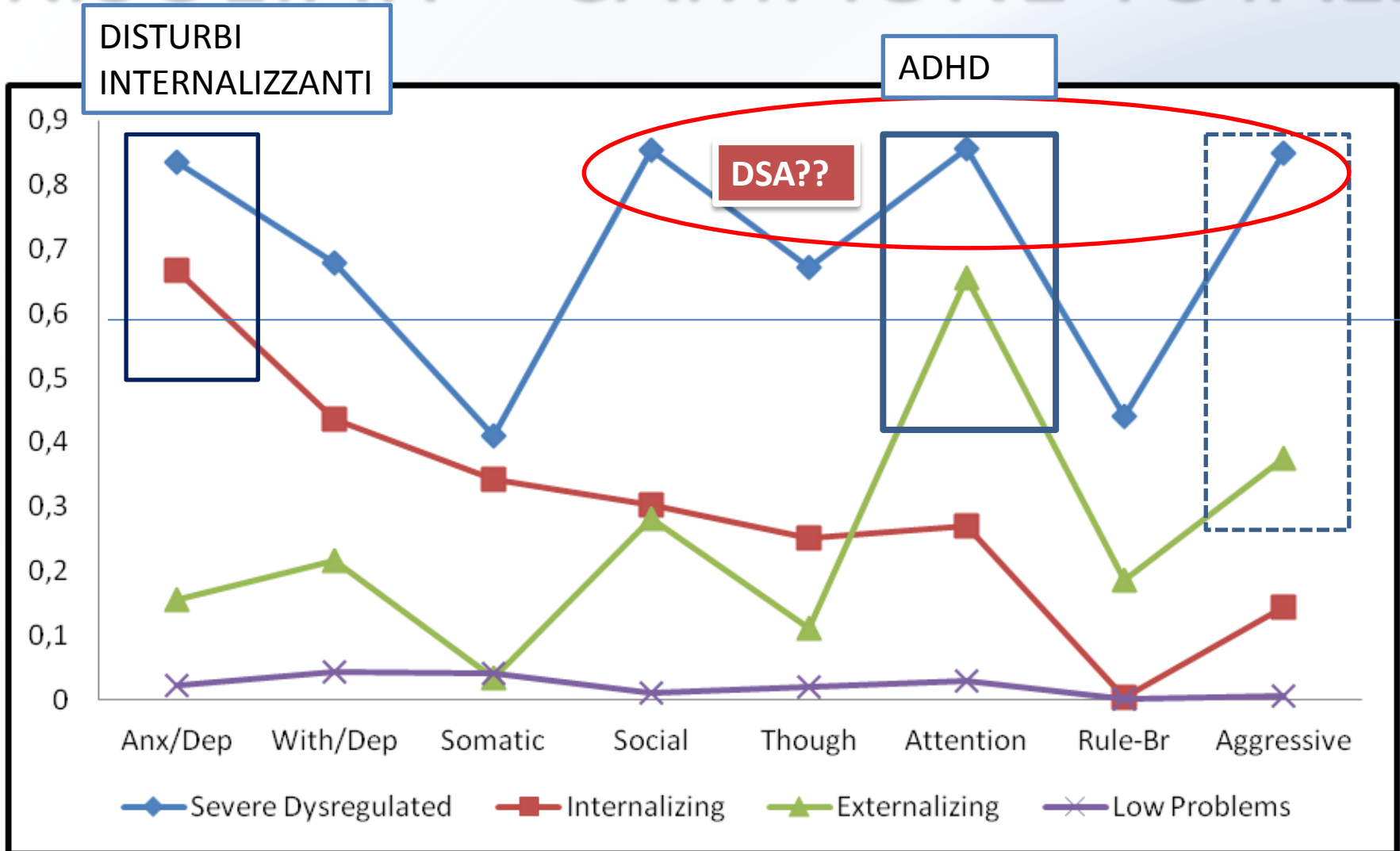
	Logistic Regression	Multinomial Regression (Absence of Diagnosis is the reference category)	
	Absence of diagnosis (N=694)	One diagnosis (N=677)	Comorbidity (N=486)
Severe Dysregulated Class	0.58** (0.36–0.94)	8.57*** (5.38–13.66)	27.69**** (16.78–45.70)
Internalizing Class	2.02** (1.40–2.98)	2.93** (2.08–4.12)	6.63*** (4.43–9.94)
Attention/Hyperactivity Class	-	8.51*** (5.74–12.60)	7.27*** (4.54–11.65)
Low Problems Class	8.17*** (5.61–11.91)	-	-
Age	1.55** (1.46–1.65)	0.66** (0.62–0.71)	0.62** (0.58–0.66)
Gender	1.77** (1.37–2.30)	1.79** (1.34–2.37)	1.76** (1.28–2.41)
Mother's Education	0.63** (0.47–0.83)	1.56** (1.16–2.11)	1.65** (1.18–2.29)
Father's Education	-	-	-
Nagelkerke pseudo-R ²	0.41	0.41	

In brackets 95% CI for significant OR ($p < 0.05$); * weak association; ** moderate association, *** strong association, ****very strong association.

I RISULTATI DI QUESTO STUDIO

- 1) approccio ***bottom-up*** scale CBCL: **identifica un profilo di disregolazione** che emerge spontaneamente e con caratteristiche simili sia all'interno della popolazione generale, sia in campioni clinici.
- 2) L'elevata frequenza di **Disturbi d'Ansia, dell'Umore e dell'Adhd** conferma **eterogeneità delle diagnosi** nei bambini con disregolazione emotiva e comportamentale.
- 3) Risultati compatibili con il modello che correla ADHD e Dysregulation Profile, mantenendo una parziale sovrapposizione.

RISULTATI – CAMPIONE TOTALE



**SCARSA
CAPACITA' DI
CONTROLLO**

**ELEVATA
REATTIVITA'
EMOZIONALE**



**ELEVATA
INATTENZIONE**

**SINTOMI IPERATTIVI
IMPULSIVI**



**COMPETENZE
LINGUISTICHE**

FUNZIONI ESECUTIVE



**ADHD
DISTURBI SPECIFICI**



**DOP
DISTURBI DELLA
CONDOTTA
DISTURBI ANSIOSI E
DEPRESSIVI**



ci sono più cose
in cielo e in terra
Orazio
di quante
possa comprenderne
la tua filosofia

SHAKESPEARE
"Antonia"