I cosiddetti disturbi dell'umore

Gabriele MASI

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UOC di Psichiatria e Psicofarmacologia dello Sviluppo

Disturbi dell'umore nel DSM

Depressivi

- Disturbo depressivo maggiore (singolo, ricorrente)
- Disturbo depressivo persistente (distimia), per 2 anni (1 in bambini/adolescenti)
- Disruptive Mood Dysregulation Disorder (DMDD)

Bipolari

-Disturbo bipolare I (Episodio maniacale, ipomaniacale, depressivo), Bipolare II (episodio ipomaniacale, depressivo), ciclotimico (ansioso),

indotto da sostanze o da farmaci, da condizioni mediche generali, NAS

Disturbo misto: Specificatore di depressione e mania

Call for Papers

Utilizing Dimensional Approaches to Advance Science and Clinical Practice in Childhood-Onset Neurodevelopmental and Neuropsychiatric Disorders

Proposal Deadline: November 15, 2024

The *Journal of the American Academy of Child & Adolescent Psychiatry* and *JAACAP Open* will publish a special series of review and empirical articles devoted to examining the utility of dimensional alternatives to categorical diagnostic approaches for improving research insights and clinical practice in the field of child and adolescent neurodevelopmental and neuropsychiatric conditions.

The focus includes but is not limited to:

- autism spectrum disorder (ASD)
- attention-deficit/hyperactivity disorder (ADHD)
- obsessive-compulsive disorders
- mood disorders
- neurogenetic disorders

The particular emphasis will be on the Hierarchical Taxonomy of Psychopathology (HiTOP) and the Research Domains Criteria (RDoC) as two complementary approaches that have garnered the most empirical attention and offer promising ways to circumvent inherent limitations of categorial approaches, including symptom overlap between diagnostic categories, heterogeneity, instability, unreliability, and a limited capacity to quantify individual variations.

Cuthbert and Insel *BMC Medicine* 2013, **11**:126
http://www.biomedcentral.com/1741-7015/11/126

BMC Medicine

DEBATE Open Access

Toward the future of psychiatric diagnosis: the seven pillars of RDoC

Bruce N Cuthbert[1,3*] and Thomas R Insel[2,3]

Abstract

Background: Current diagnostic systems for mental disorders rely upon presenting signs and symptoms, with the result that current definitions do not adequately reflect relevant neurobiological and behavioral systems - impeding not only research on etiology and pathophysiology but also the development of new treatments.

Discussion: The National Institute of Mental Health began the Research Domain Criteria (RDoC) project in 2009 to develop a research classification system for mental disorders based upon dimensions of neurobiology and observable behavior. RDoC supports research to explicate fundamental biobehavioral dimensions that cut across current heterogeneous disorder categories. We summarize the rationale, status and long-term goals of RDoC, outline challenges in developing a research classification system (such as construct validity and a suitable process for updating the framework) and discuss seven distinct differences in conception and emphasis from current psychiatric nosologies.

Summary: Future diagnostic systems cannot reflect ongoing advances in genetics, neuroscience and cognitive science until a literature organized around these disciplines is available to inform the revision efforts. The goal of the RDoC project is to provide a framework for research to transform the approach to the nosology of mental disorders.

Am J Psychiatry. 2010 Jul;167(7):748-51. doi: 10.1176/appi.ajp.2010.09091379.

Research domain criteria (RDoC): toward a new classification framework for research on mental disorders

Thomas Insel [1], Bruce Cuthbert, Marjorie Garvey, Robert Heinssen, Daniel S Pine, Kevin Quinn, Charles Sanislow, Philip Wang

Am J Psychiatry. 2014 Apr;171(4):395-7. doi: 10.1176/appi.ajp.2014.14020138.

The NIMH Research Domain Criteria (RDoC) Project: precision medicine for psychiatry

Thomas R Insel

Biol Psychiatry. 2014 Sep 1;76(5):350-3. doi: 10.1016/j.biopsych.2014.01.006.

A neurodevelopmental perspective on the research domain criteria (RDoC) framework

B J Casey [1], Mary Ellen Oliveri [2], Thomas Insel [2]

The National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) project is developing a research classification system for psychopathology based upon dimensions of neurobiology and observable behavior (1). This commentary highlights the compatibility of the dimensional approach with extant research on brain and behavioral development and demonstrates how the application of a neurodevelopmental perspective can extend and enrich RDoC.

NEUROSVILUPPO E PSICOPATOLOGIA

Approccio clinico ispirato al neurosviluppo:

Storia naturale dei disturbi mentali lifetime

Cambiamento dei disturbi mentali nella storia naturale

Incrocio e sovrapposizione di diverse psicopatologie

Fattori che possono influenzare tali percorsi

Definizione delle traiettorie evolutive.

La prospettiva del neurosviluppo

Valutazione della psicopatologia in termini di **percorsi evolutivi ("traiettorie")**, nelle diverse fasi della vita.

Diverse diagnosi (es. ADHD-DOP-DC-DB-SUD-D.Bord), ma **un unico disturbo** che si declina nel tempo ("diagnosi di traiettoria").

Diagnosi di traiettoria anterograda-retrograda: opportunità di previsione e di prevenzione ("psichiatria di transizione")

COME SALVAGUARDARE LE CATEGORIE?

Difficile eliminare le diagnosi categoriali

Le categorie diagnostiche possono essere scomposte secondo una **prospettiva di sviluppo** («traiettorie evolutive» che portano al disturbo) e **dimensioni psicopatologiche transdiagnostiche,** comuni a pazienti con diverse diagnosi («dissezione dimensionale delle categorie»).

Call for Papers

Utilizing Dimensional Approaches to Advance Science and Clinical Practice in Childhood-Onset Neurodevelopmental and Neuropsychiatric Disorders

Proposal Deadline: November 15, 2024

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- obsessive-compulsive disorders
- mood disorders
- neurogenetic disorders

TIPOLOGIA DI IPPOCRATE (460-377 a.C).

- Temperamento malinconico — Bile nera-terra fredda e secca
- Temperamento sanguigno — Sangue-aria umida e calda
- Temperamento collerico — Bile gialla-fuoco caldo e secco
- Temperamento flemmatico — Linfa-acqua umida e fredda

Areteo di Cappadocia (Alessandria, I sec a.C.): connessione tra Melancolia e Mania, prima descrizione del dist.bipolare

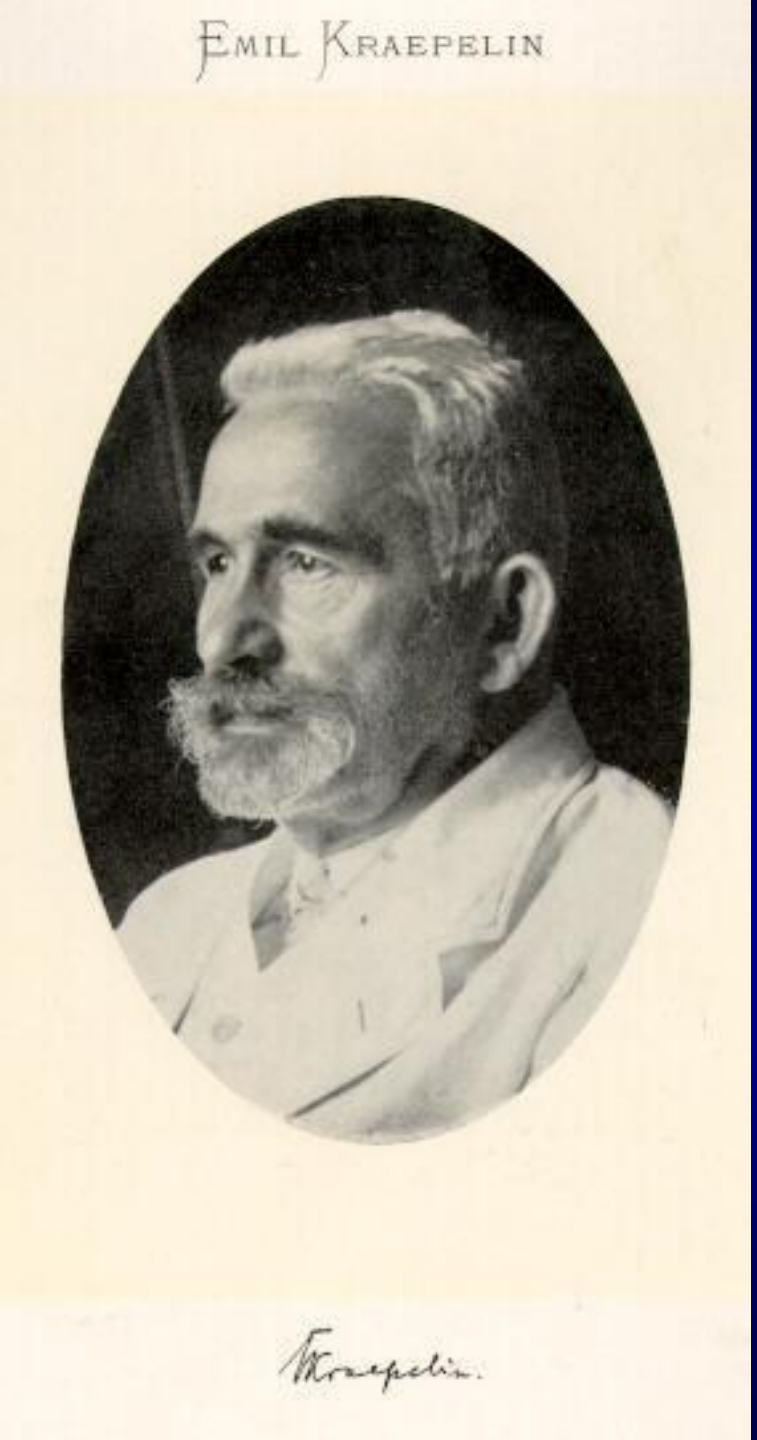
Main features of Mood Disorders

Mood Disorders are characterized by a dysregulation (excitation and/or inhibition) of

- **MOOD**
- **THINKING**
- **ACTIVITY**

These aspects may move in the same direction (depression, mania, hypomania), or in opposite directions (mixed states)

(Kraepelin, 1913)



"..I believe we can understand these states better, if we assume that they proceed from a mixture of different kinds of fundamental states…"

E. Kraepelin

KRAEPELIN´S SCHEME

Psychiatry, 8th Edition, 1913

1. Pure mania
2. Depressive mania
3. Agitated depression
4. Mania with poverty of thoughts
5. Pure depression
6. Manic stupor
7. Depression with flight of ideas
8. Inhibited mania

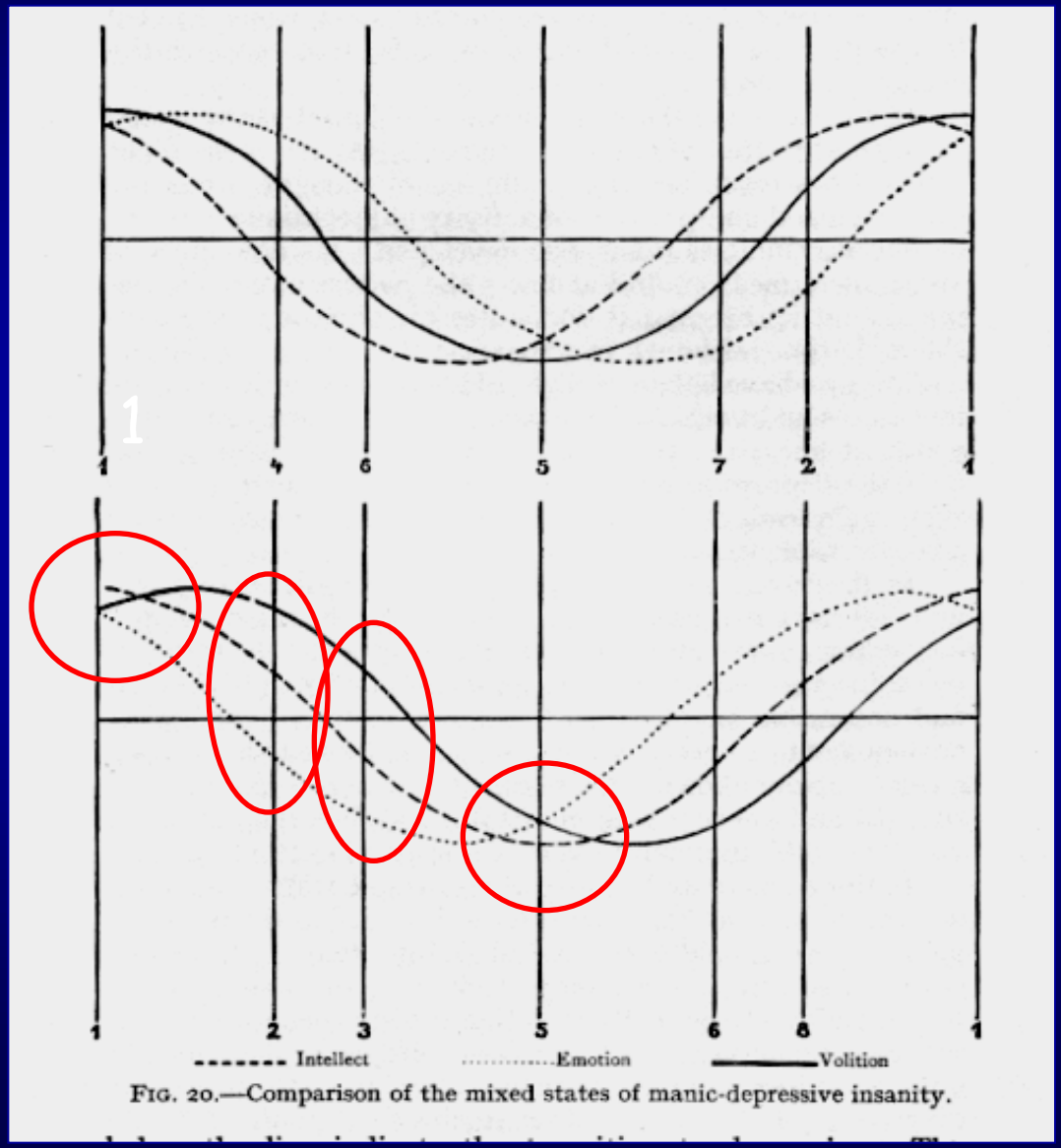
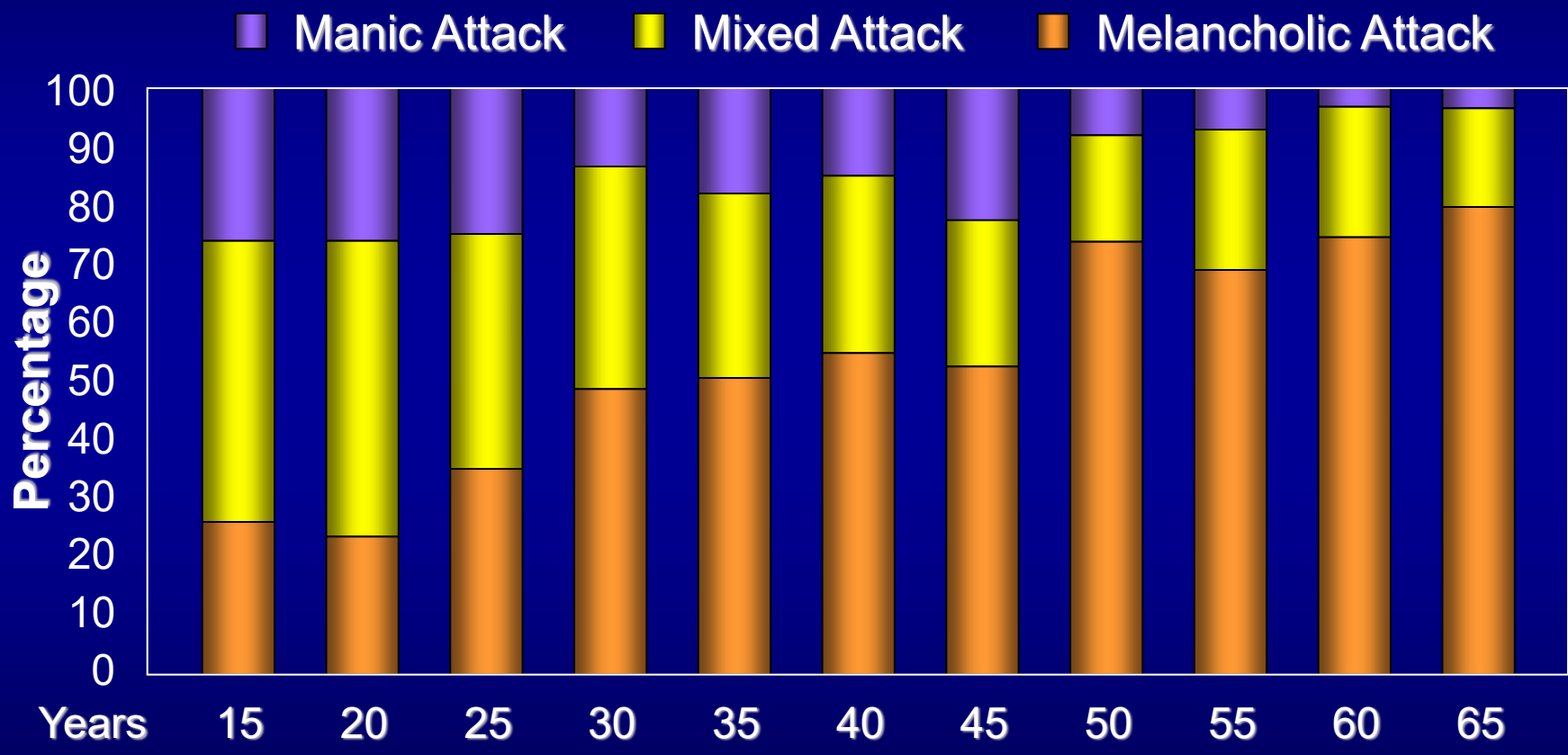


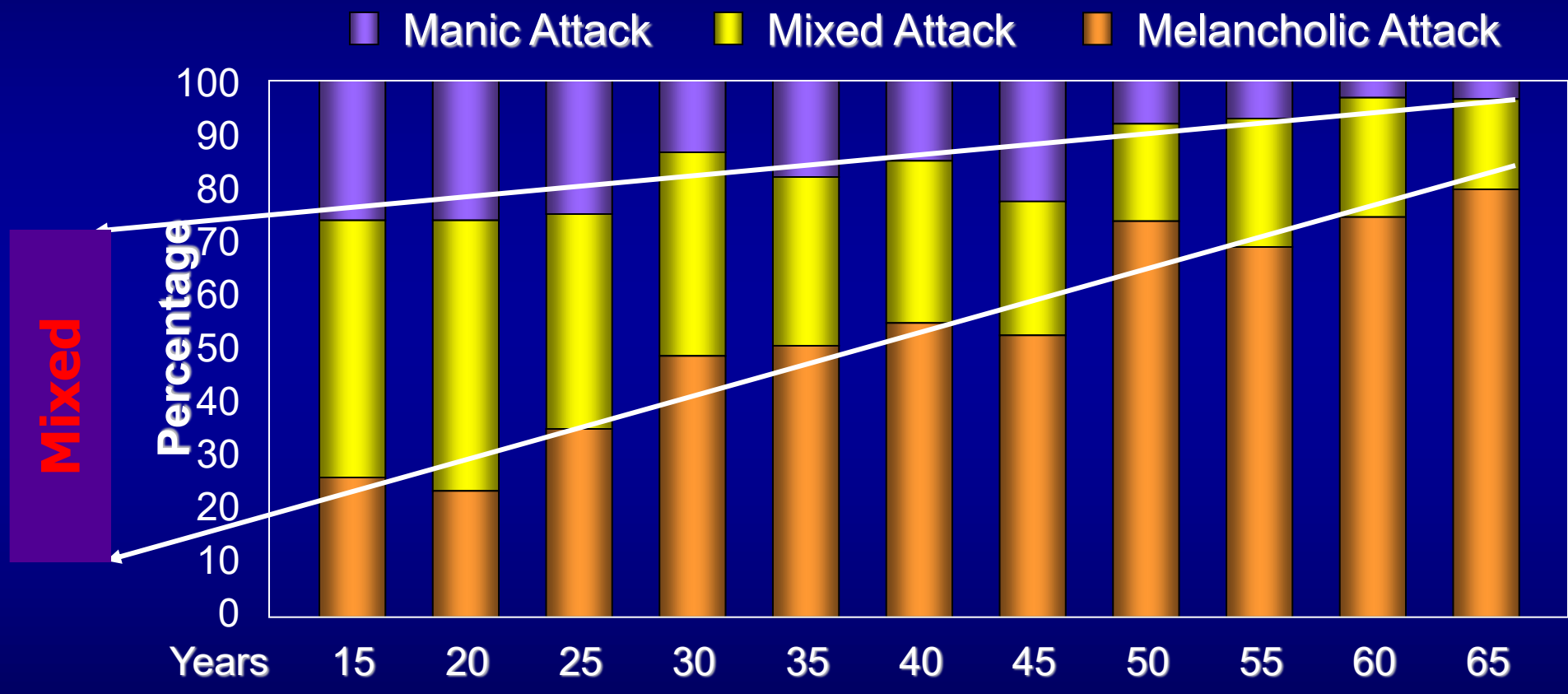
FIG. 20.—Comparison of the mixed states of manic-depressive insanity.

Attack Types at Different Ages



Kraepelin. Manic Depressive Insanity and Paranoia.
Edinburgh: E&S Livingstone; 1921:169.

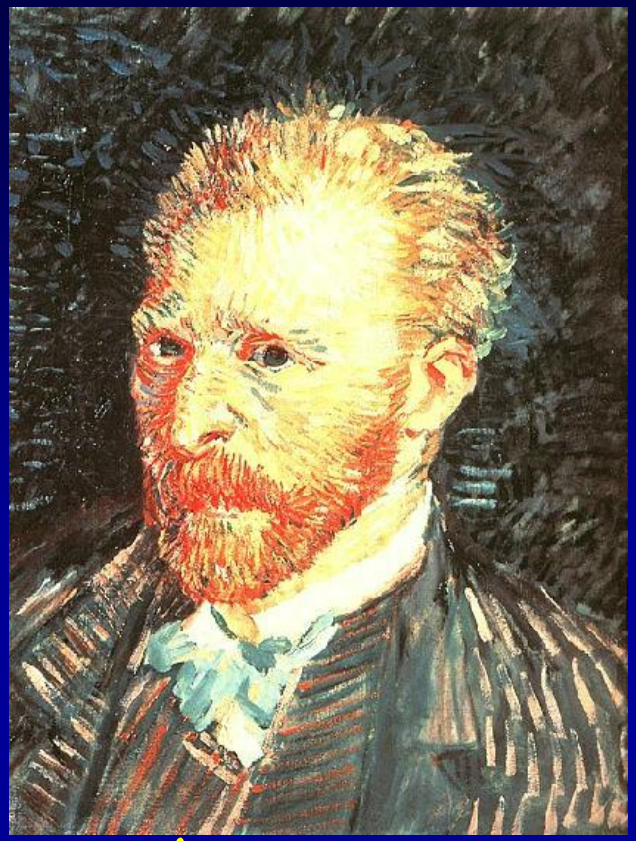
Attack Types at Different Ages



Kraepelin. Manic Depressive Insanity and Paranoia. Edinburgh: E&S Livingstone; 1921:169.

Paris, 1885

Unipolar Depression



Arles, 1888

Mood Switching (looks like a flight into health!)

Auvers sur Oise, 1890

Stage of Complications

Campo di grano con volo di corvi, V. van Gogh

Stati misti

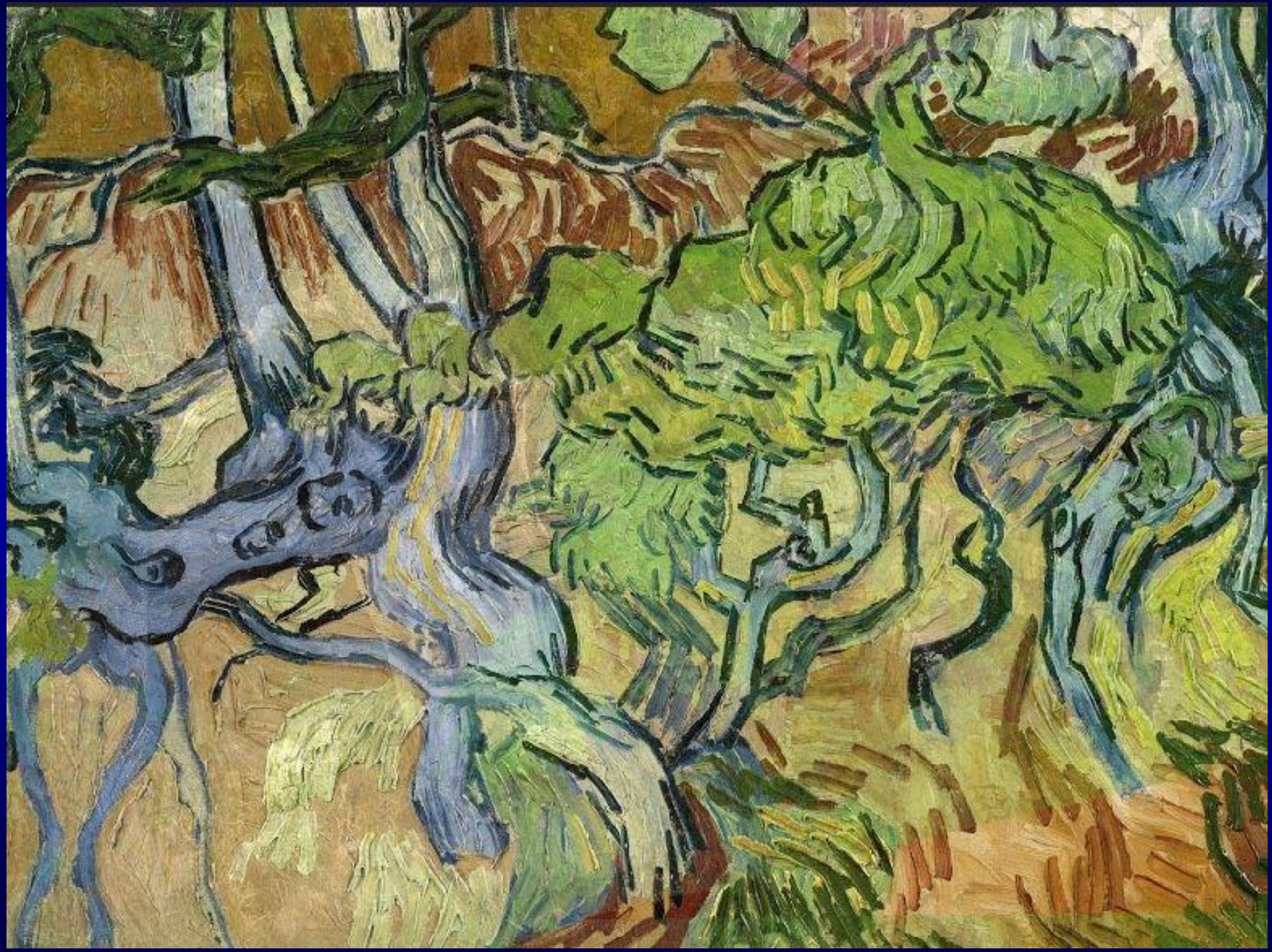
- **Negli ultimi 70 giorni di vita van Gogh dipinse 80 quadri, al termine dei quali si suicidò.**

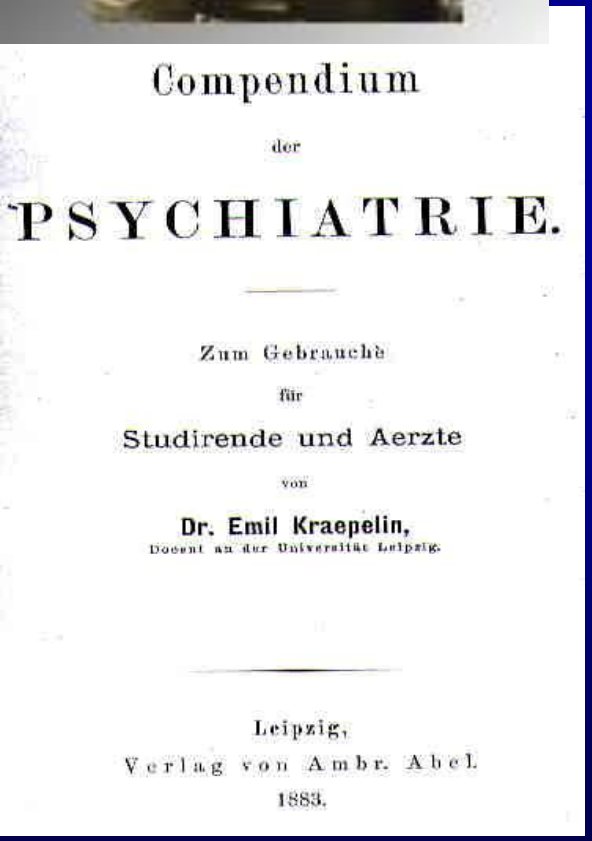
- Il quadro dei corvi neri **non** è il suo ultimo dipinto (completato 17 giorni prima del suicidio)

- L'ultimo dipinto è "Radici e tronchi d'albero", non si vede il fusto, solo radici che entrano nel terreno.

- Lo dipinse la mattina, il pomeriggio uscì per andare nei campi, dopo le 19 si sparò, poi tornò a casa, morì dopo due giorni

Radici e tronchi d’albero, V. van Gogh




Compendium

der

PSYCHIATRIE.

Zum Gebrauche

für

Studirende und Aerzte

von

Dr. Emil Kraepelin,

Docent an der Universität Leipzig.

Leipzig,

Verlag von Ambr. Abel.

1883.

Cyclothymic constitution variants :

Depressive

Hypomanic

Irritable

Emotionally instable

(Kraepelin, 1921)

Affective temperaments
Hagop S Akiskal , 1979

TEMPS-I
TEMPS-A

Hyperthymic
Depressive
Cyclothymic
Irritable ?
Anxious ?

Vulnerability (Bipolar spectrum)

Pathoplastic Effect

Compliance & treatment response

TEMPERAMENTO DEPRESSIVO

1. Triste, pessimista, privo di humor o incapace di gioire
2. Tranquillo, passivo o indeciso, chiuso od introverso
3. Scettico, ipercritico o lamentoso
4. Tendenza a preoccuparsi e a rimuginare
5. Coscienzioso o autodisciplinato
6. Autocritico, con tendenza all'autorimprovero e svalutazione
7. Preoccupato per la propria inadeguatezza, fallimento ed eventi negativi

TEMPERAMENTO IPERTIMICO

1. Esuberante, ottimista, allegro
2. Superficiale, presuntuoso, vanaglorioso, ampolloso, sicuro di sè
3. Energico, pieno di progetti, imprudente, impulsivo
4. Loquace
5. Sintonico, cordiale, in cerca di compagnia o estroverso
6. Entrante, indiscreto, prepotente
7. Disinibito, in cerca di emozioni, con tendenza alla promiscuità

TEMPERAMENTO CICLOTIMICO (I)

1. Bifasicità: bruschi passaggi da una fase all'altra, brevi cicli alterni con rara eutimia

2. Apatia alternata ad euforia

3. Pessimismo e tendenza a rimuginare alternati ad ottimismo e spensieratezza

4. Sensazione di testa confusa alternata con ideazione creativa e perspicace

5. Autostima variabile tra scarsa e spropositata fiducia in sé stessi

TEMPERAMENTO CICLOTIMICO (II)

6. Ipersonnia alternata a ridotta necessità di sonno

7. Periodi di introversione alternati a disinibita ricerca di compagnia

8. Periodi di aumentata loquacità alternati a periodi di ridotta attività verbale

9. Tendenza al pianto immotivato alternata con eccessiva scherzosità e tendenza al gioco di parole

10. Marcata incostanza quantitativa e qualitativa della produttività, con inusuali orari di lavoro

Disregolazione emotiva

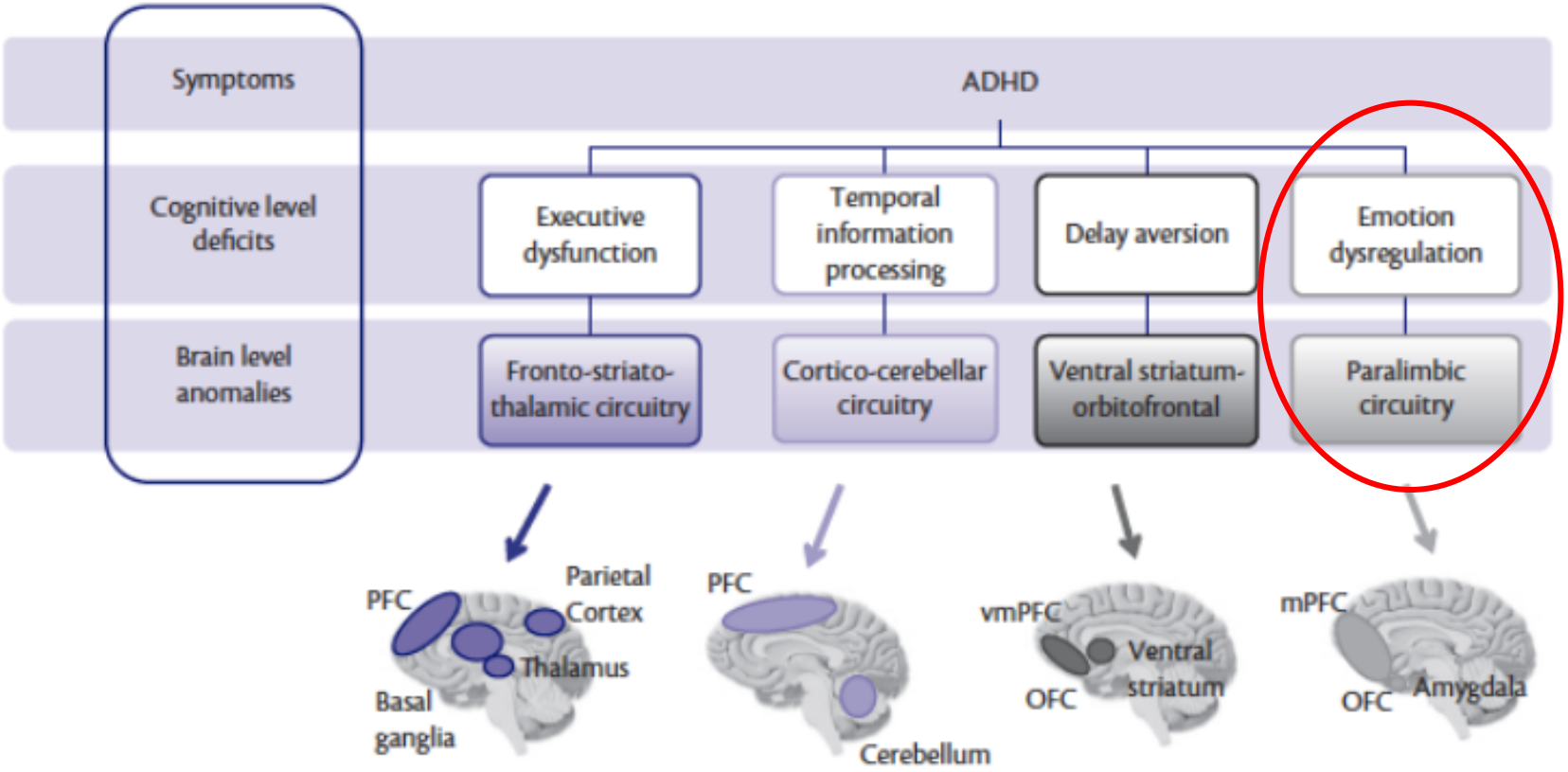
Scarsa abilità di modulare una risposta emotiva in modo adattivo al contesto

Esordio precoce **(neurosviluppo)**
Iper-reattività (bassa soglia)
Rapido incremento, intensità eccessiva, lenta normalizzazione
Cambiamenti di umore, ansia, energia, sensibilità agli stimoli

Fattore di vulnerabilità transnosografico
. aspetti comuni nelle varie categorie diagnostiche,
. persistente dall'età evolutiva alla adulta,
influenza decorso/prognosi a lungo termine

Il 30-40% dei pazienti ADHD **(> adolescenti/adulti)** ha sintomi di DE

Neuropsychological models of ADHD



Shaw & Szekely in: in: *Banaschewski, Coghill & Zuddas OT-ADHD, 2018*

Emotion dysregulation as cross-disorder trait in child psychiatry predicting quality of life and required treatment duration

Margreet Bierens[1]*, Catharina A. Hartman[2], Helen Klip[1], Stijn Deckers[3], Jan Buitelaar[1,4] and Nanda Rommelse[1,5]

Frontiers in Psychiatry

TYPE Original Research
PUBLISHED 20 July 2023
DOI 10.3389/fpsyt.2023.1101226

Methods: Information on clinical diagnosis (Attention Deficit/Hyperactivity Disorder ADHD, Autism Spectrum Disorder, Oppositional Defiant Disorder/Conduct Disorder, Anxiety and Mood Disorders), ED (measured by the CBCL-Emotion Dysregulation Index), Quality of Life (QoL, measured by the Kidscreen-27), and treatment duration (measured by Electronic Health Records) was retrieved from two large samples of toddlers (1.5–5 year old; $N = 1,544$) and school aged children (6–18 year old; $N = 7,259$). Frequency scores and logistic regression were used to study symptom profiles of ED, as measured with CBCL-EDI, across all disorders. Linear regression was used to determine the predictive value of ED (CBCL-EDI total score) regarding QoL and treatment duration in addition to—and in interaction with—clinical diagnosis.

Results: Across disorders, equal levels of total ED were found, which predicted lower QoL and a longer treatment duration in addition to clinical diagnosis. The majority of items (11/15 and 16/18) were of equal relevance to the disorders; items that were not, largely reflected disorder specific DSM definitions (i.e., externalizing symptoms in ODD/CD and internalizing symptoms in Anxiety and Mood disorders).

Conclusion: ED is a clinically useful cross-disorder trait to predict severity of impairment as well as required treatment duration. In addition, ED is largely composed of shared features across disorders, with certain disorder specific colored elements.

Journal of Affective Disorders 257 (2019) 207–213

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research paper

Sympathetic arousal in children with oppositional defiant disorder and its relation to emotional dysregulation

Alessandro Tonacci[a], Lucia Billeci[a,*], Sara Calderoni[b,c], Valentina Levantini[d], Gabriele Masi[d], Annarita Milone[d], Simone Pisano[e], Pietro Muratori[d]

Background: Emotional dysregulation (ED) is a trans-nosographical condition characterized by mood instability, severe irritability, aggression, temper outburst, and hyper-arousal. Pathophysiology of emotional dysregulation and its potential biomarkers are an emerging field of interest. A Child Behaviour Checklist (CBCL) profile, defined as Dysregulation Profile (DP), has been correlated to ED in youth. We examined the association between the CBCL-DP and indices of sympathetic arousal in children with Oppositional Defiant Disorder (ODD) and healthy controls.

Method: The current study sought to compare the arousal level measured via electrodermal activity in response to emotional stimuli in three non-overlapping groups of children: (1) ODD + CBCL-DP ($n = 28$), (2) ODD without CBCL-DP ($n = 35$), and (3) typically developing controls ($n = 25$).

Results: Analyses revealed a distinct electrodermal activity profile in the three groups. Specifically, children with ODD + CBCL-DP presented higher levels of sympathetic arousal for anger and sadness stimuli compared to the other two groups.

Limitations: The relatively small sample and the lack of assessing causality limit the generalizability of this study which results need to be replicated in larger, different samples.

Conclusion: The CBCL-DP was associated to higher levels of arousal for negative emotions, consistently with previous reports in individuals with depression and anxiety. Further work may identify potential longitudinal relationships between this profile and clinical outcomes.

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WWW.AACAP.ORG

META-ANALYSIS EMOTION DYSREGULATION

Check for updates

Systematic Review and Meta-Analysis: Altered Autonomic Functioning in Youths With Emotional Dysregulation

Alessio Bellato, PhD, Gianluca Sesso, MD, Annarita Milone, MD, Gabriele Masi, MD, Samuele Cortese, MD, PhD

Drs. Bellato and Sesso shared first authorship of this work. Drs. Masi and Cortese shared senior authorship of this work.

Objective: To systematically investigate if there is a significant association between markers of autonomic functioning and emotional dysregulation (ED) in children and adolescents.

Method: Based on a preregistered protocol (PROSPERO: CRD42021239635), PubMed, Web of Knowledge/Science, Ovid MEDLINE, Embase, and APA PsycInfo databases were searched until April 21, 2021, to identify empirical studies reporting indices of autonomic nervous system (ANS) functioning in youths meeting *DSM* (version III, IV, IV-TR, 5 or 5-TR) or *International Classification of Diseases* (*ICD*) (version 9 or 10) criteria for any psychopathological/neurodevelopmental condition and assessed for ED with a validated scale. Eligible outcomes included correlation coefficients between ED and ANS measures or differences in ANS measures between youths with and without ED. Study quality was assessed with the Appraisal tool for Cross-Sectional Studies (AXIS) and the Newcastle-Ottawa Scale (NOS) for cohort studies. Random-effects meta-analyses were used for data synthesis.

Results: There were 12 studies (1,016 participants) included in the descriptive review and 9 studies (567 participants) included in the meta-analyses. No evidence of a significant association between ED and altered cardiac or electrodermal functioning was found. However, exploratory meta-regressions suggested a possible association between reduced resting-state cardiac vagal control and increased ED.

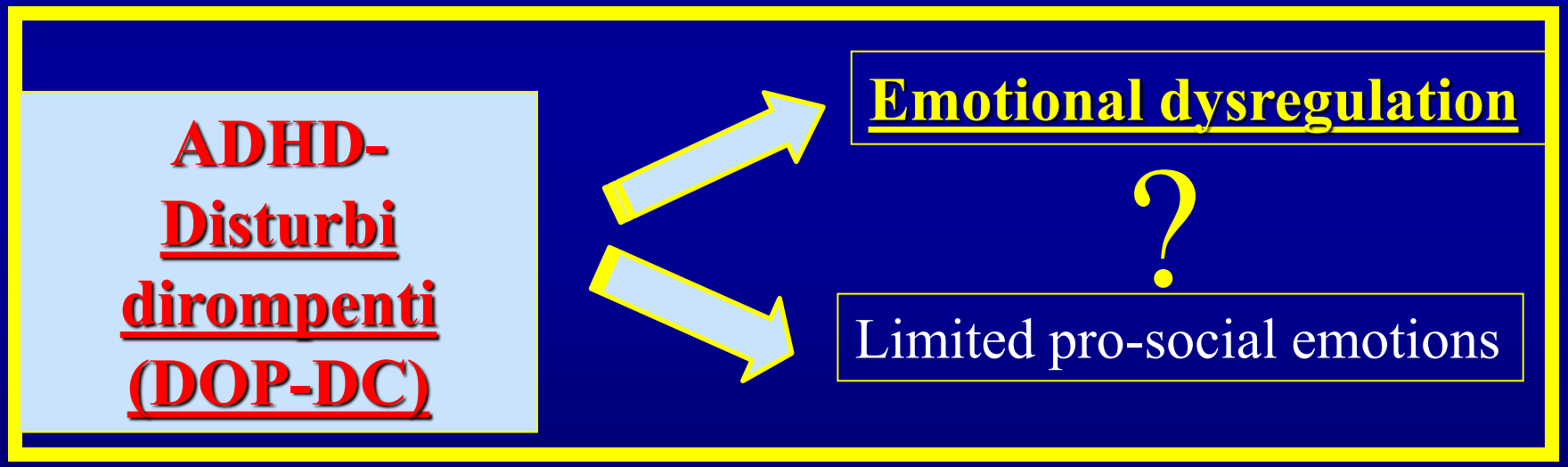
Conclusion: This study did not find evidence of an association between ED and autonomic dysfunction. However, preliminary evidence that reduced vagal control at rest might be a transdiagnostic marker of ED in young people was found. Additional studies comparing autonomic measures in youths with and without ED are needed and should also assess the effects of interventions for ED on ANS functioning.

Study preregistration information: Systematic Review and Meta-Analysis: Is Autonomic Nervous System Functioning Atypical in Children and Adolescents With Emotional Dysregulation? https://www.crd.york.ac.uk/prospero/; CRD42021239635.

Key words: autonomic nervous system; EDA; emotional dysregulation; HRV; RSA

J Am Acad Child Adolesc Psychiatry 2024;63(2):216-230.

Percorsi evolutivi e snodi cruciali



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Research report

Child behavior checklist dysregulation profile in children with disruptive behavior disorders: A longitudinal study

Gabriele Masi [a,*], Simone Pisano [b], Annarita Milone [a], Pietro Muratori [a]

[a] IRCCS Stella Maris, Scientific Institute of Child Neurology and Psychiatry, Calambrone, Pisa, Italy
[b] Department of Mental and Physical Health and Preventive Medicine, Child and Adolescent Psychiatry Division, Second University of Naples, Italy

ABSTRACT

Background: A Child Behavior Checklist (CBCL) profile defined as Dysregulation Profile (DP) (scores 2 standard deviations or more in anxiety/depression, aggression, attention subscales) has been correlated to poor emotional and behavioral self-regulation. The clinical meaning and the prognostic implications of CBCL-DP are still debated, although it seems associated with severe psychopathology and poor adjustment.

Method: In the present study, we used the CBCL-DP score to examine the adolescent outcomes (psychiatric diagnosis, substance use, psychiatric hospitalization) in 80 referred children with disruptive behavior disorders –DBD- (Oppositional Defiant Disorder or conduct disorder), aged 8–9 years, 72 males (90%) and 8 females (10%), followed-up until the age of 14–15 years.

Results: Children with higher score on the CBCL-DP profile were at increased risk for presenting ADHD and mood disorders in adolescence. While ADHD in adolescence was predicted also by an ADHD diagnosis during childhood, CBCL-DP score was the only significant predictor of a mood disorder at 14–15 years. On the contrary, CBCL-DP score was not associated with a higher risk of conduct disorder, substance use and hospitalizations in adolescence. A cost-effective and reliable diagnostic measure such as the CBCL may be a part of the diagnostic procedure aimed to capture these at-risk children, to monitor their natural history up to adolescence, and to prevent the risk of a full-blown mood disorder.

Limitations: The small sample size and a selection bias of severe patients with DBD limit the generalization of the findings.

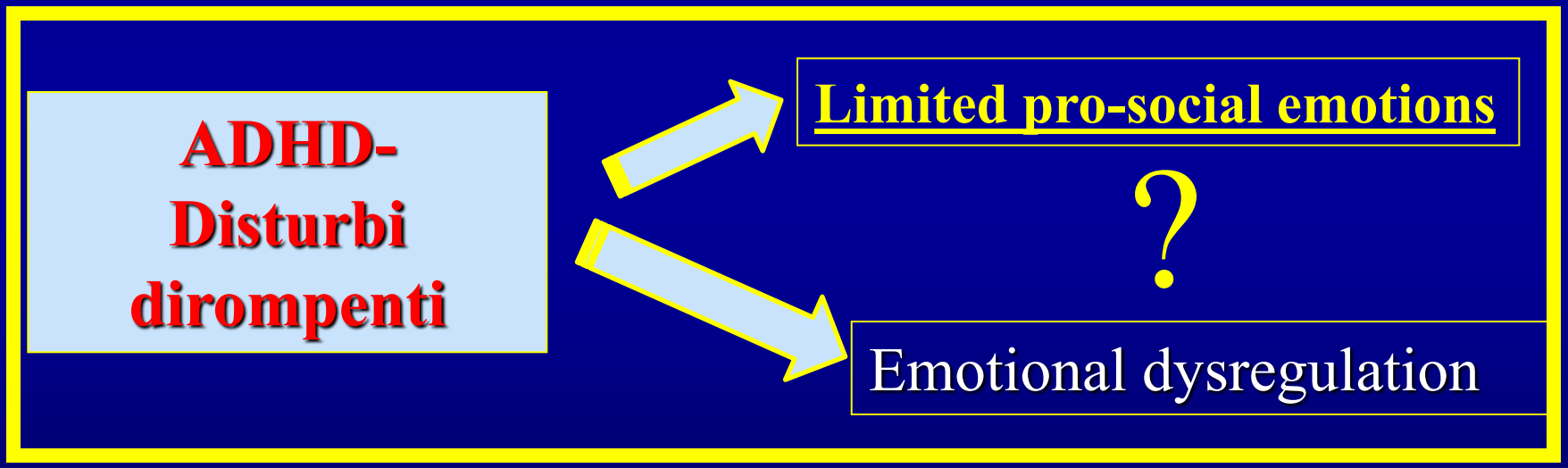
ODD e traiettorie evolutive

Irritabile/ emozionalità negativa

Dannoso/ aggressivo premeditato

Ostinato/ impulsivo

Percorsi evolutivi e snodi cruciali



Psychiatry Research 236 (2016) 35–41

Contents lists available at ScienceDirect

Psychiatry Research

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

Callous unemotional traits in children with disruptive behavior disorder: Predictors of developmental trajectories and adolescent outcomes

Pietro Muratori [a,*], John E. Lochman [b], Azzurra Manfredi [a], Annarita Milone [a], Annalaura Nocentini [c], Simone Pisano [d], Gabriele Masi [a]

The present study investigated trajectories of Callous Unemotional (CU) traits in youth with Disruptive Behavior Disorder diagnosis followed-up from childhood to adolescence, to explore possible predictors of these trajectories, and to individuate adolescent clinical outcomes. A sample of 59 Italian referred children with Disruptive Behavior Disorder (53 boys and 6 girls, 21 with Conduct Disorder) was followed up from childhood to adolescence. CU traits were assessed with CU-scale of the Antisocial Process Screening Device-parent report. Latent growth curve models showed that CU traits are likely to decrease linearly from 9 to 15 years old, with a deceleration in adolescence (from 12 to 15). There was substantial individual variability in the rate of change of CU traits over time: patients with a minor decrease of CU symptoms during childhood were at increased risk for severe behavioral problems and substance use into adolescence. Although lower level of socio-economic status and lower level of parenting involvement were associated to elevated levels of CU traits at baseline evaluation, none of the considered clinical and environmental factors predicted the levels of CU traits. The current longitudinal research suggests that adolescent outcomes of Disruptive Behavior Disorder be influenced by CU traits trajectories during childhood.

ADHD-DOP e traiettorie evolutive

Irritabile/
emozionalità
negativa

**Dannoso/
aggressivo
premeditato**

**Ostinato/
impulsivo**

Table 2 Rating scales developed to measure emotional symptoms

Scale	Reporter[a]	Children, adults, or both	Trials	Norms	Availability
Affective Lability Scale – Short Form (ALS-18) (Weibel et al., 2017)	A	Adults	Yes	Yes	Free
Affective Reactivity Index (ARI) (Stringaris et al., 2012)	Y, P	Children	Yes	Not found	Free
Barkley Deficits in Executive Functioning Scale — Children and Adolescents (BDEFS-CA) (Barkley, 2012)	Y, P	Children	None found	Yes	$
Behavior Rating Inventory of Executive Function (BRIEF or emotion control subscale) (Mahone et al., 2002)	Y, A, P, T	Both	Yes	Yes	$
Brown ADD Rating Scales for Children, Adolescents and Adults (BADDS) (Brown, 1996)	Y, A	Both	Yes	Yes	$
Conners Global Index (CGI) Emotional Lability Scale (Conners, 1997)	Y, A	Children	Yes	Yes	$
Child Behavior Checklist – Dysregulation Profile (CBCL-DP) (Geeraerts et al., 2015)	Y, A	Children	No	Yes	$
Difficulties in Emotion Regulation Scale (DERS) (Gratz & Roemer, 2004)	Y, A	Both	Yes	Not found	Free
Difficulties in Emotion Regulation Scale – Brief Version (DERS-16) (Kaufman et al., 2016]	Y, A	Both	None found	Not found	Free
Emotion Dysregulation Scale, short version (EDS-short) (Powers, Stevens, Fani, & Bradley, 2015)	Y, A	Both	None found	Not found	Free
Emotion Regulation Checklist (ERC) (Shields & Cicchetti,1997)	P	Children	Yes	Not found	Free
Emotion Regulation Index for Adults and Children (ERICA) (MacDermott, Gullone, Allen, King, & Tonge, 2010)	Y, A	Both	Yes	Not found	Free
Emotion Regulation Questionnaire (ERQ) (Gross & John, 2003)	Y, A	Both	Yes	Yes	Free
Emotional Lability *T*-scores on Conners Rating Scales – Revised (CRS-R) (Conners, 2001)	Y, A, P, T	Children	Yes	Yes	Free
Expression and Emotion Scale for Children (EESC) (Penza-Clyve & Zeman, 2001)	Y, A, P, T	Children	Yes	Yes	Free
State Difficulties in Emotion Regulation Scale (S-DERS) (Lavender, Tull, DiLillo, Messman-4 Moore, & Gratz, 2017)	Y, A	Both	None found	Not found	Free
Strengths and Difficulties Questionnaire – Dysregulation Profile (SDQ-DP) (Holtmann, Becker, Banaschewski, Rothenberger, & Roessner, 2011)	P	Children	Yes	Yes	Free
Wender-Reimherr Adult Attention Deficit Disorder Scale (Marchant et al., 2013)	C	Adults	Yes	Yes	Free
Distress Tolerance Scale (Simons & Gaher, 2005)	A	Adults	None found	Not found	Free
Frustration Discomfort Scale (Harrington, 2005)	A	Adults	None found	Not found	Free

[a]Y, youth self-report; P, parent; T, teacher; A, adult self-report; C, clinician.

Appendix A. Cyclothymic-hypersensitive temperament questionnaire [child and adolescent version]. F.H. Kochman, E.G. Hantouche, H.S. Akiskal

Please respond to the following questions with either a "YES" or "NO". What are the essential elements of your basic daily temperament?

		YES	NO
1	I often react intensely to minor upsets	☐	☐
2	I alternate between feeling low and high according to what is going on around me	☐	☐
3	When I get upset, it's very hard for me to calm down	☐	☐
4	I have periods of irritation during which I can lose control	☐	☐
5	I often experience intense emotions which I can feel all over my body (flushing, sweating, pounding heart)	☐	☐
6	I experience all negative or positive emotions (both of sadness or joy) more intensely than others	☐	☐
7	When watching a film, I often get overemotional (I can't help crying, being scared, or laughing)	☐	☐
8	I have been in love numerous times in my life	☐	☐
9	My mood often changes without me knowing why	☐	☐
10	Compared to my peers, when I get excited during the class recess, it is much harder for me to settle down upon return to the classroom	☐	☐
11	I am very excited during a video game, and it's very hard for me to calm down afterwards	☐	☐
12	I experience rapid shifts in mood and energy	☐	☐
13	At times I have a strong urge for risky or outrageous behavior	☐	☐
14	When I'm irritated, I can do stupid things I wouldn't have done otherwise	☐	☐
15	I can feel depressed for a few days and then be in a good mood again	☐	☐
16	After a big stressful situation it can take several days for me to recover my composure	☐	☐
17	I often explode at others, then feel guilty	☐	☐
18	I often need to attract the attention of others to me	☐	☐
19	I am sometimes bubbling with energy, and at other times sluggish	☐	☐
20	I know I have a tendency to get worked up, or to lose my temper too quickly when I'm frustrated	☐	☐
21	I often experience severe, sudden emotions	☐	☐
22	I can become strongly fond of a person I've just met	☐	☐
23	Often I crave certain foods, cigarettes, alcohol or upper drugs	☐	☐
24	I often daydream about things people consider unrealizable	☐	☐
25	I alternate between feeling overly confident and feeling unsure and self-critical	☐	☐

Journal of Affective Disorders 271 (2020) 272–278

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research paper

Cyclothymic-hypersensitive temperament in youths: Refining the structure, the way of assessment and the clinical significance in the youth population

Simone Pisano[a,b,*,**], Vincenzo Paolo Senese[c,**], Carmela Bravaccio[b], Pia Santangelo[a], Annarita Milone[d], Gabriele Masi[d], Gennaro Catone[e]

Background: Although a better understanding of the prodromes of affective disorders in youth has important clinical and research implications, empirical data are still unconclusive. Cyclothymic-hypersensitive temperament (CHT) has been linked to both depression and bipolarity, as well as to suicidality. Its conceptualization is still debated, as well as a comprehensive, psychometrically sound way of assessment.

Methods: factor structure, reliability, measurement invariance, convergent and divergent validity of the previously published CHT questionnaire (a youth version derived from Temperament Evaluation in Memphis Pisa and San Diego (TEMPS) was assessed in a school-based sample of 2959 students aged from 10 to 14 years (mean age = 11.8 ± 0.97 years). Furthermore, accuracy, sensitivity and specificity were calculated for a new cut-off score related to the presence of general psychopathology symptoms.

Results: CHT is better conceptualized in a two-correlated factors model, a moodiness/hypersensitiveness factor, more associated with internalizing symptoms, and an impulsiveness/emotional dysregulation factor, more associated with externalizing symptoms. The revised 22-items version of the CHT questionnaire with a cut-off score of 15 for females and 17 for males results accurate, sensitive and specific enough for the recognition of cyclothymic adolescents with clinical symptoms.

Limitation: the cross sectional design and the self-report nature of the measures limit the findings.

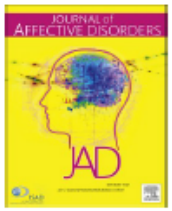
Discussion: Cyclothymic-hypersensitive temperament is a relevant concept in the realm of affective disorder and can be reliably assessed in youths. It may describe youths with the coexistence of both internalizing and externalizing symptoms that can be difficult to diagnose with a DSM perspective.

Journal of Affective Disorders 298 (2022) 322–328

Contents lists available at ScienceDirect

Journal of Affective Disorders

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



Research paper

The assessment of cyclothymic-hypersensitive temperament in youth with mood disorders and attention deficit hyperactivity disorder

Simone Pisano [a,*], Gianluca Sesso [b,c], Vincenzo Paolo Senese [d], Gennaro Catone [e], Annarita Milone [c], Gabriele Masi [c]

Background: Cyclothymic-hypersensitive temperament (CHT) has been related to both depression and bipolarity, as well as to suicidality. Recently, a psychometrically sound way of assessment has been validated in youth (Cyclothymic-Hypersensitive Temperament Questionnaire, CHTQ), but data on clinical populations are still scant. Aim of our study is to further explore the structure and other psychometric properties of the revised version of CHTQ and its clinical implications in clinical samples.

Methods: The study is based on a dataset of patients with unipolar depression, bipolar disorder and attention deficit and hyperactivity disorder (ADHD) (243 patients, 135 males, mean age 14.22 ± 2.16 years, age range 9–18 years), compared to a community sample of adolescents (398 subjects, 95 boys, mean age 15.47 ± 1.96 years, age range 10–18 years)

Results: The two-correlated factor structure of CHT has been confirmed, with a moodiness/hypersensitiveness factor, correlated with internalizing symptoms, and an impulsiveness/emotional dysregulation factor, correlated with externalizing symptoms. All CHTQ scores correlate with global functioning. CHTQ total scores discriminate patients from healthy controls. Only CHTQ impulsiveness/emotional dysregulation subscale score is higher in bipolar patients, compared to unipolar depression and ADHD, whereas neither CHTQ moodiness/hypersensitiveness subscale score nor CHTQ total score discriminate between clinical groups.

Limitation: Data on current mood states are unavailable. Patients were recruited in a third level clinic. The unipolar depression group is relatively small.

Conclusion: CHT may be a rapid and reliable screening and diagnostic tool in the clinical practice with youth, exploring the cyclothymic dimension in different psychiatric disorders.

Journal of Affective Disorders 291 (2021) 359–367

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

A novel multidimensional questionnaire for the assessment of emotional dysregulation in adolescents: Reactivity, Intensity, Polarity and Stability questionnaire–youth version (RIPoSt–Y)

Gianluca Sesso [a,b], Annarita Milone [b,*], Flavia Drago [c], Valentina Viglione [b], Stefano Berloffa [b], Silvia Boldrini [a,b], Nina Loriaux [d], Elena Valente [b], Agnese Molesti [b], Francesca Placini [b], Anna Rita Montesanto [b], Simone Pisano [d], Gabriele Masi [b]

[a] Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
[b] Department of Developmental Neuroscience, IRCCS Stella Maris Foundation, Pisa, Italy
[c] Department of Health Promotion, Maternal-Infant, Internal and Specialised Medicine of Excellence G. D'Alessandro, University of Palermo, Italy
[d] Department of Translational Medical Sciences, University of Naples Federico II, Italy

Background: The failure to regulate emotions, namely emotional dysregulation (ED), is a relevant construct in adolescent psychiatry, in terms of prognostic and developmental implications. We developed and validated a novel self-report questionnaire for the assessment of ED, the RIPoSt-Y, both in clinical and non-clinical samples.

Methods: Items selection and subscales construction were conducted on healthy controls (n=374), while test-retest reliability was evaluated in a subsample (n=72); internal consistency was examined both in the control group and in two clinical samples, respectively including patients with Bipolar Spectrum Disorders (BSD; n=44) and ADHD (n=34). Construct, concurrent and convergent validity were also assessed.

Results: Thirty-one items were finally retained, and three subscales were identified (Affective Instability, Emotional Reactivity, Interpersonal Sensitivity). Test-retest was significant for each subscale with moderate-to-good correlations, and internal consistency showed good-to-excellent coefficients. Construct validity was supported by significant differences between patients and controls and gender-related differences. Concurrent validity was confirmed through significant associations with two subscales of the CHT-Q, while convergent validity proved to be significant with the CBCL/YSR dysregulation-profile. Cut-offs were also computed to discriminate clinically significant scores of ED.

Limitations: The use of a school-based survey to recruit controls could have biased our results; gender distributions between clinical and non-clinical samples were significantly different.

Conclusions: Our novel questionnaire proved to be a valid and reliable tool able to assess the presence of ED in youths and to characterize this fundamental construct in its multidimensional facets.

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 14 April 2021
doi: 10.3389/fpsyt.2021.619037

An Exploratory Study of Emotional Dysregulation Dimensions in Youth With Attention Deficit Hyperactivity Disorder and/or Bipolar Spectrum Disorders

Gabriele Masi[1*], *Gianluca Sesso*[1,2], *Chiara Pfanner*[1], *Elena Valente*[1], *Agnese Molesti*[1], *Francesca Placini*[1], *Silvia Boldrini*[1,2], *Nina Loriaux*[1], *Flavia Drago*[1], *Anna Rita Montesanto*[1], *Simone Pisano*[3,4] and *Annarita Milone*[1]

administered to both groups. Our results indicate that affective instability and negative emotionality subscales, as well as negative emotional dysregulation, are higher in BSD, both pure and comorbid with ADHD, while emotional impulsivity is higher in the comorbid condition and similar in the ADHD and BSD alone group; all clinical groups scored higher than HC. Conversely, positive emotionality is similar among ED. Hence, the five subscales of the RIPoSt can be reliably used as an effective tool to study the emotional dysregulation in different clinical conditions, to help disentangle the complex relationship between ADHD and juvenile BSD and to provide clinicians with crucial evidence for better diagnostic characterization and therapeutic indications.

IPERSENSITIVITA'

Percezione traumatica di esperienze vitali "normali" in termini di disinteresse, rifiuto, abbandono, separazione, critiche, ecc.

Voracità affettiva, possessività esclusiva, gelosia, sospettosità; o altruismo patologico.

Eccessiva reazione ad eventi positivi (eccessivo entusiasmo), ma soprattutto **negativi** (disperazione, condotte autolesive, suicidalità anche dimostrativa, sostanze, ecc).

Sensibilità al "trauma" percepito" ("PTSD")

Spettro Ciclotimico («comorbidità»)

Umore

Episodi depressivi maggiori o minori

Disturbo bipolare II («dark»)

Ipomania indotta da sostanze

Ansia- Ipersensitività

Disturbo ossessivo-compulsivo

Ansia di separazione/Panico

Ansia sociale

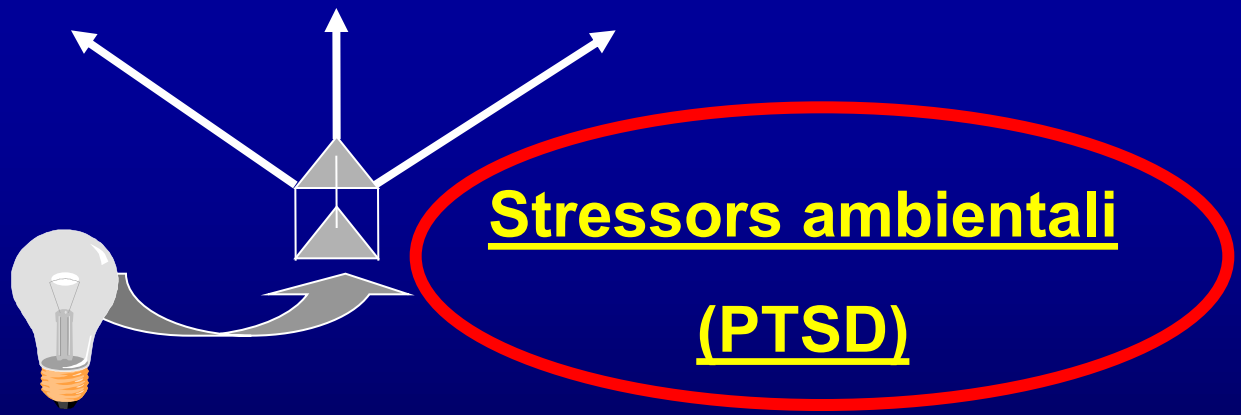
Condotte impulsive-additive

ADHD-DOP

Abuso di sostanze o alcool

Dipendenze comportamentali

Bulimia, Binge Eating Disorder



Temperamento ciclotimico-ansioso- ipersensitivo

Spettro Ciclotimico («comorbidità»)

Umore

Episodi depressivi maggiori o minori

Disturbo bipolare II («dark»)

Ipomania indotta da sostanze

Ansia- Ipersensitività

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Ansia sociale

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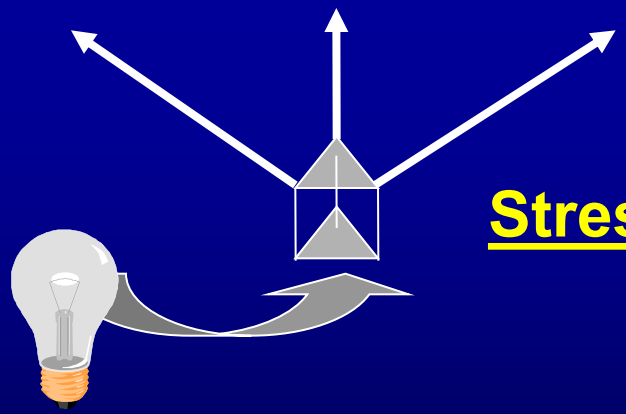
Abuso di sostanze o alcool

Dipendenze comportamentali

Bulimia, Binge Eating Disorder



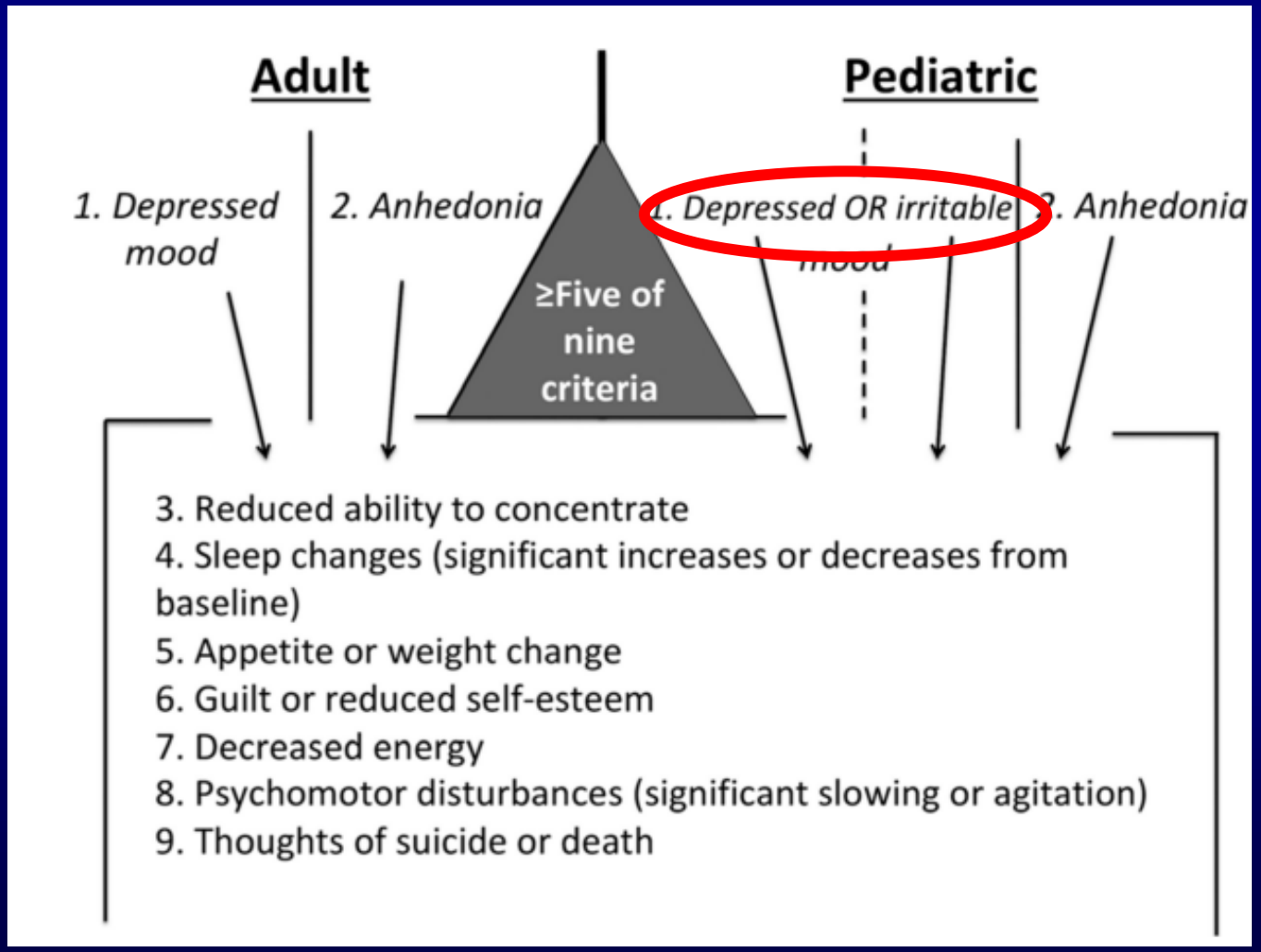
Stressors ambientali (PTSD)

Temperamento ciclotimico-ansioso- ipersensitivo

Psychology and Psychiatry
Journal of Child Psychology and Psychiatry 61:3 (2020), pp 312–332 doi:10.1111/jcpp.13202

Annual Research Review: Defining and treating pediatric treatment-resistant depression

Jennifer B. Dwyer,[1,2] Argyris Stringaris,[3] David A. Brent,[4,5] and Michael H. Bloch[1,6]
[1]Yale Child Study Center, Yale University School of Medicine, New Haven, CT, USA; [2]Yale Department of Radiology and Biomedical Imaging, Yale University School of Medicine, New Haven, CT, USA; [3]Mood Brain and Development Unit, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, USA; [4]Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA; [5]University of Pittsburgh Medical Center Western Psychiatric Hospital, Pittsburgh, PA, USA; [6]Yale Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA



Disturbi depressivi nel DSM 5

- Disruptive Mood Dysregulation Disorder (DMDD)
- Disturbo depressivo maggiore (singolo, ricorrente)
- Disturbo depressivo persistente (2 aa, 1 bambini/adolescenti)

What are the signs and symptoms of DMDD?

Children or adolescents with DMDD experience:

- Severe temper outbursts (verbal or behavioral), on average, 3 or more times per week
- Outbursts and tantrums that have been happening regularly for at least 12 months
- Chronically irritable or angry mood most of the day, nearly every day
- Trouble functioning due to irritability in more than one place, such as at home, at school, or with peers

Youth with DMDD are diagnosed between the ages of 6 and 10. To be diagnosed with DMDD, a child must have experienced symptoms steadily for 12 or more months.

FREQUENZA DEL DISTURBO BIPOLARE 10 ANNI DOPO DEPRESSIONE **PREPUBERALE**

	Depressione prepuberale (n = 72)	Controlli normali (n = 28)	*P* Value
Bipolare I o II	**48.6%**	7.1%	.0001
Bipolare I	33.3%	0	.001
Bipolare II	15.3%	7.1%	.34

- Mania in un genitore o in un nonno è un fattore predittivo di evoluzione bipolare (*P*=0.02)

Geller et al. *Am J Psychiatry*. 2001;158:125-7.

Depressione bipolare (sottovalutazione)

- ✓ sopravvalutazione della «depressione»
- ✓ sopravvalutazione del criterio "euforia"
- ✓ negazione della eccitazione non euforica,

(Impulsività, agitazione, irritabilità, stati di eccitazione transitori, comportamenti a rischio, tensione interna, eccessiva reattività emotiva e comportamentale, ipersensitività, ….)

- Almeno il 30% dei disturbi depressivi è un DB II?

Depressione con caratteristiche miste

Depressione+(Ipo)mania **non euforica**:

-Irritabilità

-Iperattività mentale

(ruminazione mentale, affollamento e sovrapposizione dei contenuti, fuga di idee, passaggio da un pensiero all'altro, la testa che mi scoppia)

-Iperattività comportamentale

(agitazione psicomotoria, impulsività, logorrea).

-Familiarità per disturbo bipolare

-Rischio suicidio (monoterapia con antidepressivi?)

Depressione atipica ed Ipersensitività

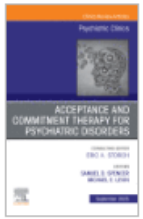
L'esagerata reattività emotiva in situazioni di stress e nelle relazioni interpersonali può favorire una distorta percezione di esperienze "traumatiche", storie personali caratterizzate da frequenti "abusi emotivi", traumi ripetuti in diversi contesti (scuola, famiglia, vita sociale, relazioni affettive).

La attribuzione psicotraumatica della depressione può essere fuorviante rispetto alla valutazione della fragilità emotiva.

ELSEVIER

Psychiatric Clinics of North America

Volume 22, Issue 3, 1 September 1999, Pages 517-534



THE EVOLVING BIPOLAR SPECTRUM: Prototypes I, II, III, and IV

Hagop S. Akiskal MD *, Olavo Pinto MD *

Bipolar ½	Schizobipolar
Bipolar I	Mania with or without depression
Bipolar I½	Protracted hypomania with depression
Bipolar II	Depression with hypomania
Bipolar II½	Depression with cyclothymia
Bipolar III	Depression with hypomania associated with antidepressants
Bipolar IV	Depression with hyperthymic temperament, or trait hypomania

Indicatori di bipolarità nascosta ("hidden bipolarity") nella depressione adolescenziale

- Familiarità per disturbo di spettro bipolare (alcolismo, suicidio)
- **Esordio precoce di depressione**
- Episodica irritabilità ed aggressività, elevata energia
- Depressione ricorrente, psicotica, atipica
- Alterazioni combinate di disturbi di umore - anergia
- Destabilizzazione da antidepressivi

Psychiatry Research 249 (2017) 244–251

Contents lists available at ScienceDirect

Psychiatry Research

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

What do childhood attention deficit/hyperactivity symptoms in depressed adults tell us about the bipolar spectrum?

D. Purper-Ouakil[a,*], MC Porfirio[b], Y. Le Strat[c,e], B. Falissard[d], P. Gorwood[e,f], G. Masi[g]

- 3963 unselected adult depressed patients, 1124 (28.4%) with ADHD

- Depressed with childhood ADHD symptoms were:
- . prevalently males,
- . earlier onset of the first depressive episode
- . more severe (number of symptoms, functioning)
- . higher rates of anxiety
- . higher number of previous depressive episodes,
- . greater number of (hypo)manic symptoms
- . frequent familiarity for bipolar I or II disorder
- . more frequent psychotic symptoms

Multicenter Study > J Affect Disord. 2019 Mar 1:246:346-354. doi: 10.1016/j.jad.2018.12.089. Epub 2018 Dec 25.

The relationship between attention deficit hyperactivity disorder, bipolarity and mixed features in major depressive patients: Evidence from the BRIDGE-II-Mix Study

G Vannucchi [1], P Medda [2], A Pallucchini [2], M Bertelli [3], J Angst [4], J-M Azorin [5], C Bowden [6], E Vieta [7], A H Young [8], S Mosolov [9], G Perugi [10]; BRIDGE-II-Mix Study Group

Objective: This study primarily focused on the relationship between comorbid attention deficit-hyperactivity disorder (ADHD), mixed features and bipolarity in major depressive patients.

Methods: The sample comprised 2777 patients with Major Depressive Episode (MDE) enrolled in a multicentre, multinational study originally designed to assess different definitions of mixed depression. Socio-demographic, familial and clinical characteristics were compared in patients with (ADHD +) and without (ADHD-) comorbid ADHD.

Results: Sixty-one patients (2.2%) met criteria for ADHD. ADHD was associated with a higher number of (hypo)manic symptoms during depression. Mixed depression was more represented in ADHD + patients than in ADHD- using both DSM-5 and experimental criteria. Differences were maintained after removing overlapping symptoms between (hypo)mania and ADHD. ADHD in MDE was also associated with a variety of clinical and course features such as onset before the age of 20, first-degree family history of (hypo)mania, past history of antidepressant-induced (hypo)manic switches, higher number of depressive and affective episodes, atypical depressive features, higher rates of bipolarity specifier, psychiatric comorbidities with eating, anxiety and borderline personality disorders.

Limitations: The study was primarily designed to address mixed features in ADHD, with slightly reduced sensitivity to the diagnosis of ADHD. Other possible diagnostic biases due to heterogeneity of participating clinicians.

Arch Gen Psychiatry. 2010 October ; 67(10): 1044–1051. doi:10.1001/archgenpsychiatry.2010.127.

Very Early Predictors of Adolescent Depression and Suicide Attempts in Children With Attention-Deficit/Hyperactivity Disorder

Andrea Chronis-Tuscano, PhD, **Brooke S. G. Molina, PhD**, **William E. Pelham, PhD**, **Brooks Applegate, PhD**, **Allison Dahlke, BA**, **Meghan Overmyer, AM**, and **Benjamin B. Lahey, PhD**

J Clin Psychol. 2013 Sep;69(9):980-93. doi: 10.1002/jclp.21994. Epub 2013 Jun 17.

Symptoms of attention-deficit/hyperactivity disorder (ADHD) moderate suicidal behaviors in college students with depressed mood

Connor H G Patros [1], Kristen L Hudec, R Matt Alderson, Lisa J Kasper, Collin Davidson, LaRicka R Wingate

Association between suicidal spectrum behaviors and Attention-Deficit/ Hyperactivity Disorder: A systematic review and meta-analysis

Mathilde Septier[a,b,1], Coline Stordeur[a,1], Junhua Zhang[c], Richard Delorme[a,d], Samuele Cortese[e,f,g,h,i,*]

90,805 participants with ADHD and 239,778 without ADHD

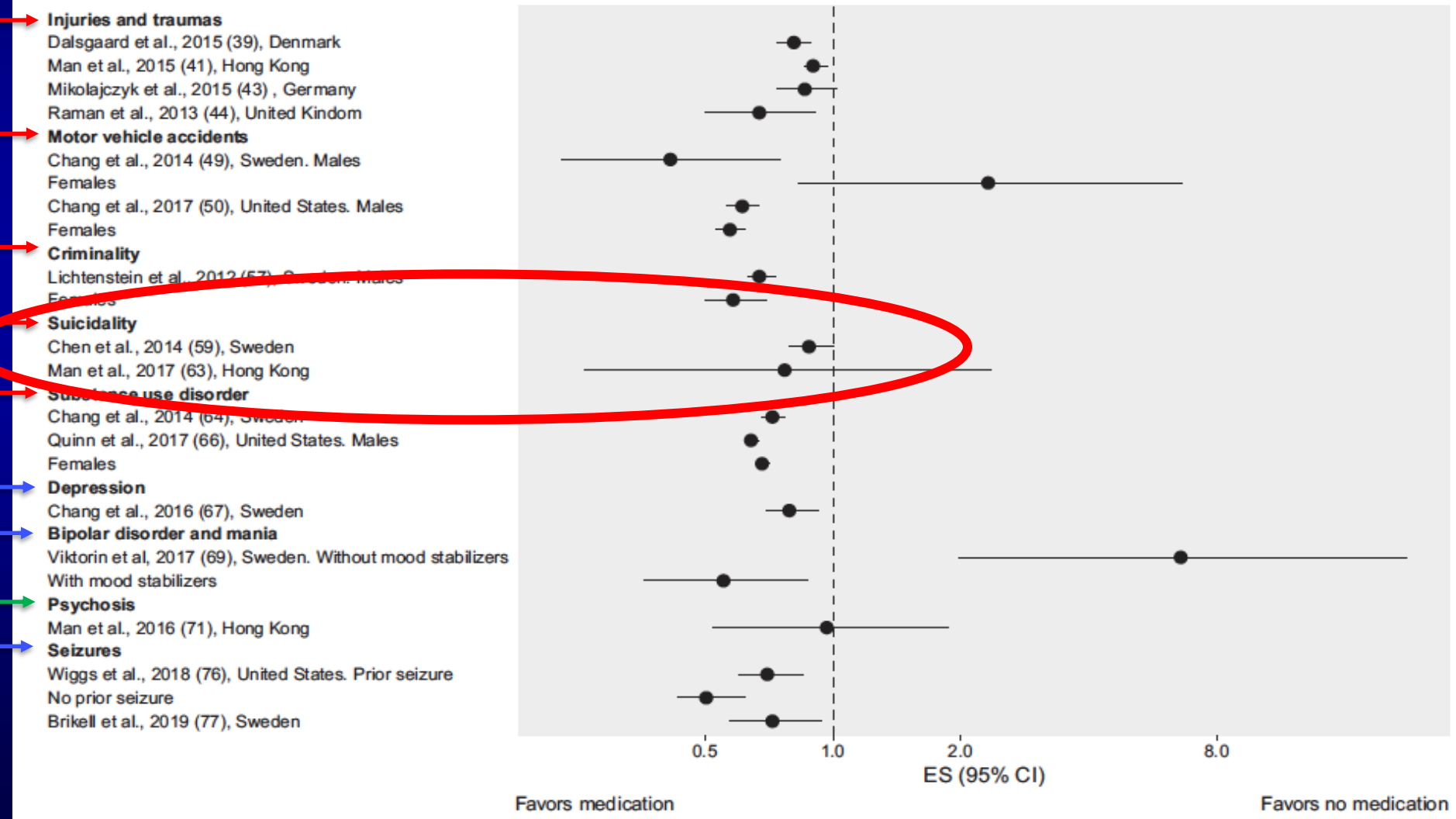
201

Type of analysis	N Datasets	N Participants	OR (95% CI)	p	Heterogeneity						Egger's Test publication Bias	
					Q	df	p	I^2	LL_I^2	UL_I^2	t	*p
Suicidal attempts												
Unadjusted ORs	44	228,420	2.37 (1.64,3.43)	< 0.0001	2408.14	43	0.000	98.21	97.96	98.43	2.24	0.030
Adjusted ORs	6	65,204	2.08 (1.27,3.47)	0.005	78.79	5	0.000	93.65	88.83	96.40	1.80	0.145
Suicidal ideation												
Unadjusted ORs	23	73,344	3.53 (2.94,4.25)	< 0.0001	83.76	22	0.000	73.73	60.41	82.58	0.11	0.911
Adjusted ORs	3	9,584	4.48 (1.72,11.63)	< 0.0001	9.82	2	0.007	79.62	35.34	93.59	7.88	0.080
Suicide												
Unadjusted ORs	4	398359	6.69 (3.24,17.39)	< 0.0001	24.06	3	0.000	87.53	70.30	94.77	0.41	0.715
Unspecified Suicidal behaviors												
Unadjusted ORs	8	2478	1.05 (0.43,2.55)	0.916	81.89	7	0.000	91.45	85.56	94.94	0.83	0.434
Suicidal Plans												
Unadjusted ORs	2	6483	4.54 (2.46,8.37)	< 0.0001	0.14	1	0.711	0.00	0.00	0.00	N/A	N/A

Risks and Benefits of Attention-Deficit/ Hyperactivity Disorder Medication on Behavioral and Neuropsychiatric Outcomes: A Qualitative Review of Pharmacoepidemiology Studies Using Linked Prescription Databases

Zheng Chang, Laura Ghirardi, Patrick D. Quinn, Philip Asherson, Brian M. D'Onofrio, and Henrik Larsson

Biol Psychiatry 2019



Spettro Ciclotimico («comorbidità»)

Umore

Episodi depressivi maggiori o minori

Disturbo bipolare II («dark»)

Ipomania indotta da sostanze

Ansia- Ipersensitività

Disturbo ossessivo-compulsivo

Ansia di separazione/Panico

Ansia sociale

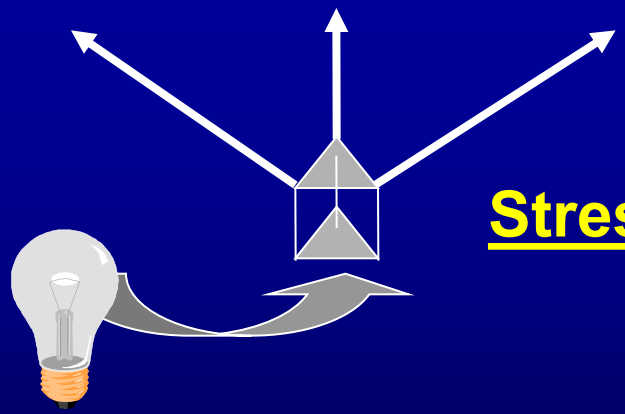
Condotte impulsive-additive

ADHD-DOP

Abuso di sostanze o alcool

Dipendenze comportamentali

Bulimia, Binge Eating Disorder



Stressors ambientali (PTSD)

Temperamento ciclotimico-ansioso- ipersensitivo

Journal of Affective Disorders 293 (2021) 186–196

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Review article

Development of bipolar disorder in patients with attention-deficit/hyperactivity disorder: A systematic review and meta-analysis of prospective studies

Giulio Emilio Brancati [a], Giulio Perugi [a,*], Annarita Milone [b], Gabriele Masi [b], Gianluca Sesso [a,b]

Background: Increasing attention has been recently paid to precursors of bipolar disorder (BD). Symptoms of attention-deficit/hyperactivity disorder (ADHD) have been reported among the most common prodromes of BD. The aim of this study was to estimate the risk of BD in youths affected by ADHD based on prospective studies.

Methods: A systematic review was conducted according to the PRISMA guidelines. A meta-analysis of single proportions was performed to compute the overall occurrence of BD in ADHD individuals. Binary outcome data were used to calculate risk estimates of BD occurrence in ADHD subjects *versus* Healthy Controls (HC).

Results: An overall proportion of BD occurrence of 10.01% (95%-confidence interval [CI]: 6.47%-15.19%; I^2 = 82.0%) was found among 1248 patients with ADHD over 10 prospective studies. A slightly higher proportion was found when excluding one study based on jack-knife sensitivity analysis (11.96%, 95%-CI: 9.15%-15.49%; I^2 = 54.1%) and in three offspring studies (12.87%, 95%-CI: 8.91%-18.23%). BD occurrence was not significantly associated with mean follow-up duration (p-value = 0.2118). A greater risk of BD occurrence in ADHD *versus* HC from six studies was found (risk ratio: 8.97, 95%-CI: 4.26-18.87, p-value < 0.0001).

Limitations: Few prospective studies have been retrieved in our search and most were not specifically aimed at assessing BD in followed-up ADHD patients.

Conclusions: Greater clinical attention should be paid to ADHD as an early precursor of BD since a substantial proportion of ADHD patients is expected to be diagnosed with BD during the developmental age.

Diagnosi di disturbo bipolare

Diverse caratteristiche cliniche in diverse età?

Clinical Course of Children and Adolescents With Bipolar Spectrum Disorders

Boris Birmaher, MD, David Axelson, MD, Michael Strober, PhD, Mary Kay Gill, MSN, Sylvia Valeri, PhD, Laurel Chiappetta, MS, Neal Ryan, MD, Henrietta Leonard, MD, Jeffrey Hunt, MD, Satish Iyengar, PhD, and Martin Keller, MD

Arch Gen Psychiatry. 2006 February ; 63(2): 175–183.

The Long-term Natural History of the Weekly Symptomatic Status of Bipolar I Disorder

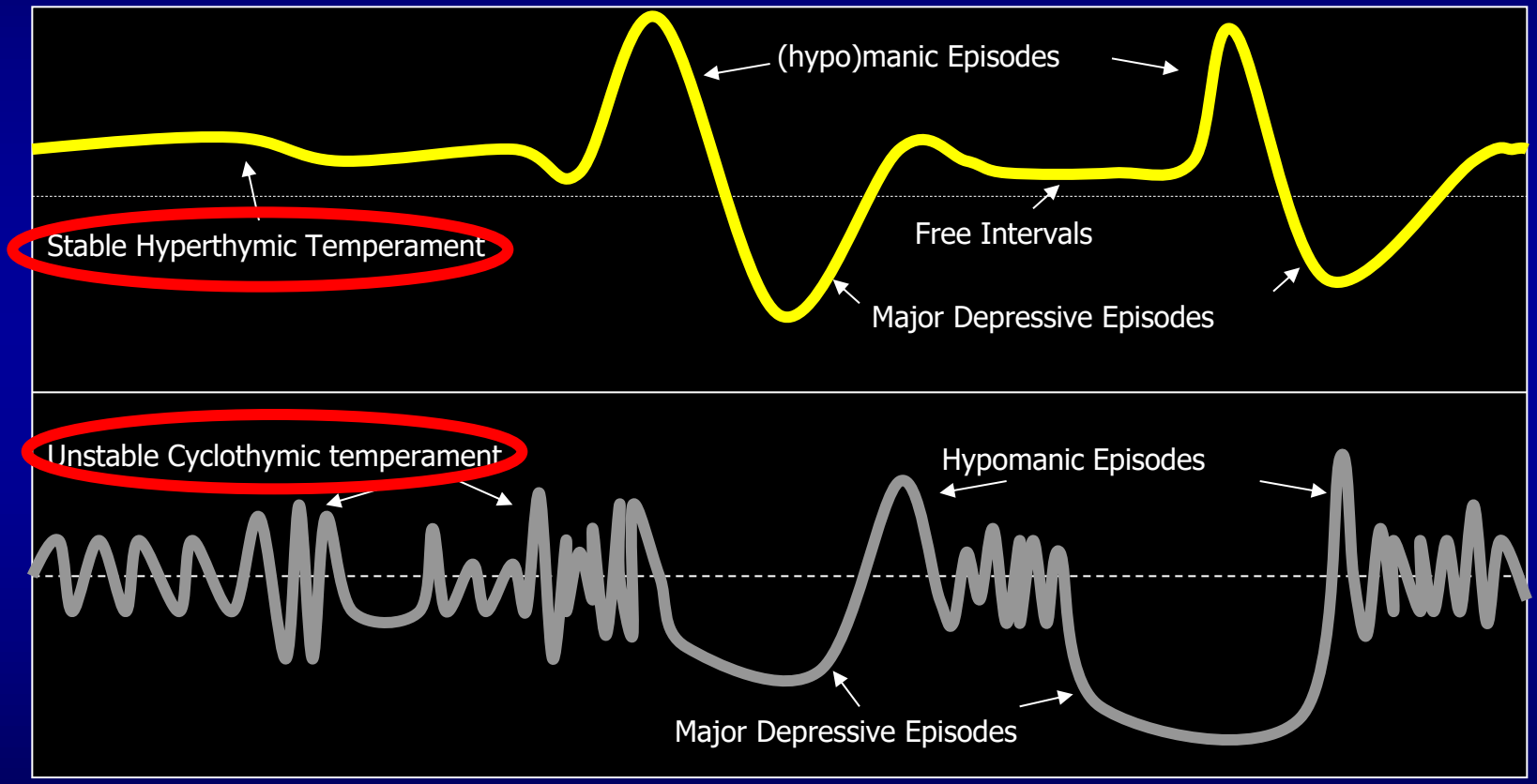
Lewis L. Judd, MD; Hagop S. Akiskal, MD; Pamela J. Schettler, PhD; et al

Arch Gen Psychiatry. 2002;59(6):530-537.

Negli adolescenti rispetto agli adulti:

- stati misti o rapida ciclicità (28.9% vs. 5.9%)
- cambi di polarità per anno (15.7±17.5 vs. 3.5± 7.4)

Intra-Bipolar Dichotomy



Variables: Age of Onset / Basic Temperament / Time Course of the illness

ELSEVIER

Journal of Affective Disorders 73 (2003) 49–57

JOURNAL OF AFFECTIVE DISORDERS

www.elsevier.com/locate/jad

Research report

Bipolar II with and without cyclothymic temperament: "dark" and "sunny" expressions of soft bipolarity

Hagop S. Akiskal[a,*], Elie G. Hantouche[b], Jean François Allilaire[b]

[a]*International Mood Center, UCSD Department of Psychiatry, 9500 Gilman Drive, La Jolla, San Diego, CA 92093-0603, USA*
[b]*Mood Center, Psychiatry Department, Pitié-Salpêtrière Hospital, Paris, France*

ELSEVIER

Journal of Affective Disorders

Volume 73, Issues 1–2, January 2003, Pages 39-47

Research report

Factor structure of hypomania: interrelationships with cyclothymia and the soft bipolar spectrum

Elie G. Hantouche [a], Jules Angst [b], Hagop S. Akiskal [c]

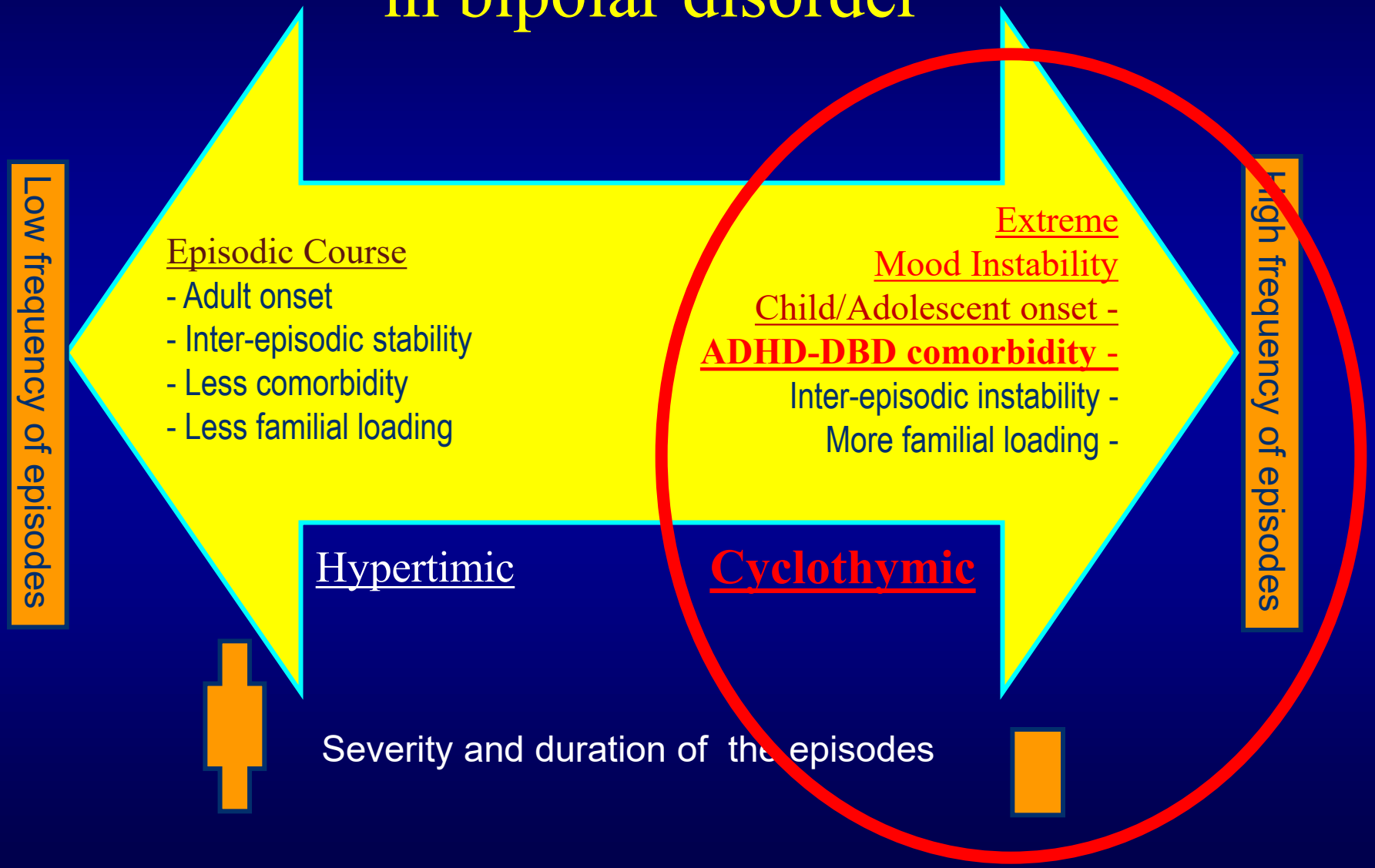
The Sunny Side" of Hypomania

- Sonno ridotto
- Maggiore energia
- Alta fiducia in sé stessi
- Alta motivazione nello studio o nel lavoro
- Maggiori relazioni sociali
- Maggiore attività fisica (anche nello studio/lavoro)
- Più progetti ed idee
- Minore timidezza ed inibizione
- Maggiore loquacità del solito
- Umore elevato, ottimismo, euforia
- Pensiero più rapido

The Dark Side of Hypomania

- Instabilità nella finalizzazione di desideri e progetti
- Relazioni interpersonali instabili
- Comportamenti impulsivi ed a rischio
- Irritabilità, impazienza
- Ipersessualità (promiscuità, condotte a rischio)
- Elevato consumo di sigarette, caffè
- Elevato consumo di alcool e sostanze di abuso
- Ipersensibilità a rifiuto/abbandono/separazione
- Voracità affettiva, gelosia, sospettosità
- **Suicidalità, condotte autolesive**

Spectrum of illness course in bipolar disorder



ELSEVIER

Journal of Affective Disorders 85 (2005) 181–189

JOURNAL OF AFFECTIVE DISORDERS

www.elsevier.com/locate/jad

Research report

Cyclothymic temperament as a prospective predictor of bipolarity and suicidality in children and adolescents with major depressive disorder

F.J. Kochman[a,b,*], E.G. Hantouche[c], P. Ferrari[b], S. Lancrenon[d], D. Bayart[a], H.S. Akiskal[e]

[a] *Department of Child and Adolescent Psychiatry, Unit 59I13, 304 Avenue Motte, 59100 Roubaix, France*
[b] *Laboratory of Child and Adolescent Psychopathology, Université of Kremlin-Bicêtre, Paris XI, France*
[c] *Hôpital Pitié-Salpétrière, University of Paris VI, Paris, France*
[d] *Sylia-Stat, Antony, France*

Journal of Affective Disorders 227 (2018) 477–482

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research paper

Non suicidal self-injury in referred adolescents with mood disorders and its association with cyclothymic-hypersensitive temperament

Gabriele Masi[a], Annarita Milone[a], Anna Rita Montesanto[a], Elena Valente[a], Simone Pisano[b,*]

[a] IRCCS Stella Maris, Scientific Institute of Child Neurology and Psychiatry, Calambrone, Pisa, Italy
[b] Clinic of Child and Adolescent Neuropsychiatry, Department of Medicine and Surgery, University of Salerno, Baronissi, Salerno, Italy

Background: Non suicidal self-injuries (NSSIs) are deliberate self-harm behaviors without suicidal intent, usually starting in adolescence, with increasing rates of occurrence both in epidemiological and clinical samples. Several studies associated cyclothymic-hypersensitive temperament (CHT) with self-harm behaviors and suicidal risk. Aim of this study is to explore the association between NSSIs and CHT in a clinical sample of adolescents. We hypothesized that CHT may differentiate NSSI from non-NSSI adolescents with mood disorders, when other psychopathological features are controlled for.

Methods: A consecutive sample of 89 adolescents with mood disorders were assessed for presence and phenomenology of NSSIs, CHT, demographics, comorbid categorical psychiatric diagnoses, dimensional psychopathology, impairment and previous suicide attempts.

Results: NSSIs were reported in 52% of the sample, with higher rates in females and in bipolar disorder. Regression analyses showed that CHT, but not age, gender, bipolar vs depression diagnosis, functional impairment, was associated with NSSIs.

Discussion: CHT may be in close association with NSSIs in adolescents with mood disorders. An assessment of CHT in adolescents referred for mood disorder may help to detect specific psychological features of NSSIs, which may improve diagnostic and treatment strategies.

Limitations: Given the cross-sectional design, a developmental relation between CHT and NSSIs cannot be determined. The small sample size and the selection bias of severely impaired patients limit the generalization of the results. More sophisticated measures of CHT may consent to explore other dimensions of the cyclothymic construct (i.e., emotional intensity, emotional reactivity, emotional stability, positive vs. negative emotions, interpersonal sensitivity, impulsivity).

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[b] Clinic of Child and Adolescent Neuropsychiatry, Department of Medicine and Surgery, University of Salerno, Baronissi, Salerno, Italy

Table 3
Bivariate correlations.

Variables	NSSI	Gender	Age	CGAS	Suicidal behav.	CHT	Bipolar
NSSI	1	− 0.27**	0.14	− 0.17	0.2	0.32**	0.21*
Gender	− 0.27**	1	0.09	− 0.8	− 0.09	− 0.28**	− 0.33**
Age	0.14	0.09	1	− 0.25*	0.27**	− 0.06	− 0.05
CGAS	− 0.17	− 0.08	− 0.25*	1	− 0.28**	− 0.29**	− 0.11
Suicidal behav.	0.2	− 0.09	0.27**	− 0.28**	1	0.21	0.00
CHT	0.32**	− 0.28**	− 0.67	− 0.29**	0.21*	1	0.07
Bipolar	0.21*	− 0.33**	− 0.56	− 0.11	0.00	0.79	1

Bivariate association between variables of interest. NSSI: Non-Suicidal Self-Injuries status. CGAS: Children Global Assessment Scale. CHT: Cyclothymic-Hypersensitive Temperament.
* $p < 0.05$, **$p < 0.01$.

Table 4
Association between Cyclothymic-Hypersensitive Temperament and NSSI status.

Variables	Beta	SE	Wald	Sig	Odds Ratios
CHT	1.276	0.581	4.825	0.028	3.584
CGAS	− 0.012	0.042	0.079	0.778	[illegible]
Bipolar diagnosis	0.848	0.613	1.915	0.166	2.335
Suicidal behav.	0.543	0.778	0.487	0.485	1.721
Gender	− 0.825	0.566	2.127	0.145	0.438
Age	0.021	0.015	2.006	0.1571.012	1.012

Logistic regression model in predicting group (NSSI+ or NSSI-) membership: Cyclothymic-hypersensitive temperament is significantly associated to NSSI+ above confounding variables. CGAS: Children Global Assessment Scale. CHT: Cyclothymic-Hypersensitive Temperament.

brain sciences

MDPI

Article

Persistent Non-Suicidal Self-Injury and Suicidality in Referred Adolescents: A Longitudinal Study Exploring the Role of Cyclothymic Temperament

Gabriele Masi [1,†], Simone Pisano [2,*,†], Gianluca Sesso [1,3], Cristina Mazzullo [1], Stefano Berloffa [1], Pamela Fantozzi [1], Antonio Narzisi [1], Francesca Placini [1], Elena Valente [1], Valentina Viglione [1] and Annarita Milone [1]

Brain Sci. **2023**, *13*, 755. https://doi.org/10.3390/brainsci13050755

Abstract: Non-suicidal self-injury (NSSI) is deliberate harm to the body surface without suicidal intent, though it may be a predictor of suicide attempts. Our aim was to test the hypothesis that persisting and recovering NSSI may have a different longitudinal risk for suicidal ideation and behavior and that the intensity of Cyclothymic Hypersensitive Temperament (CHT) may increase this risk. Fifty-five patients (mean age 14.64 ± 1.77 years) referred for mood disorders according to the DSM-5 were consecutively recruited and followed-up for a mean of 19.79 ± 11.67 months and grouped according to the presence/absence of NSSI at baseline and follow-up into three groups: without NSSI (non-NSSI; n = 22), with NSSI recovered at follow-up (past-NSSI; n = 19), and with persistent NSSI at follow-up (pers-NSSI; n = 14). At follow-up, both NSSI groups were more severely impaired and failed to improve internalizing problems and dysregulation symptoms. Both NSSI groups reported higher scores in suicidal ideation compared to non-NSSI, but only pers-NSSI presented higher scores in suicidal behavior. CHT was higher in pers-NSSI, followed by past-NSSI and then by non-NSSI. Our data support a continuity between NSSI and suicidality, and they suggest the prognostic validity of persistent NSSI, associated with highest CHT scores.

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Is emotional dysregulation a risk indicator for auto-aggression behaviors in adolescents with oppositional defiant disorder?

Pietro Muratori[a,*], Simone Pisano[b], Annarita Milone[a], Gabriele Masi[a]

[a] IRCCS Stella Maris, Scientific Institute of Child Neurology and Psychiatry, Calambrone, Pisa, Italy
[b] Department of Mental and Physical Health and Preventive Medicine, Child and Adolescent Psychiatry Division, Second University of Naples, Italy

….In 72 consecutively referred youths with Oppositional Defiant Disorder, greater Emotional Dysregulation scores were associated to higher levels of auto-aggression, even when controlled for the levels of aggression against others and other covariates (age,gender, severity, comorbidities)

Developmental Pathways for Different Subtypes of Early-Onset Bipolarity in Youths

Gabriele Masi, MD; Maria Mucci, MD; Chiara Pfanner, MD; Stefano Berloffa, MD; Angela Magazù, MD; and Giulio Perugi, MD

Conclusions: The presence of comorbid ADHD versus anxiety disorders is indicative of fundamental differences in the phenomenology of bipolar disorder in youth. While ADHD prior to bipolar disorder is associated with a specific bipolar phenotype, bipolar patients with multiple anxiety disorders are similar to "typical" bipolar patients.

J Clin Psychiatry 2012;73(10):1335–1341

Developmental Pathways for Different Subtypes of Early-Onset Bipolarity in Youths

Gabriele Masi, MD; Maria Mucci, MD; Chiara Pfanner, MD; Stefano Berloffa, MD; Angela Magazù, MD; and Giulio Perugi, MD

J Clin Psychiatry 73:10, October 2012

Table 1. Demographic and Clinical Features of Children and Adolescents With Bipolar Disorder With ADHD, With Bipolar Disorder With Multiple Anxiety Disorders, and With Bipolar Disorder Without ADHD or Multiple Anxiety Disorders

	Bipolar Disorder					
Feature	With ADHD (n = 49)	With Multiple Anxiety Disorders (n = 76)	Without ADHD or Multiple Anxiety Disorders (n = 52)	F/χ^2	*df*	*P*
Male sex, n (%)	40 (81.6	34 (44.7)	33 (63.5)	17.2	2	.0001***
Age, mean (SD), y	12.5 (2.9)	14.5 (2.6)	14.6 (2.6)	10.2	176	<.0001***[a]
Age at onset, mean (SD), y	8.4 (2.4)	11.1 (3.0)	11.3 (3.0)	17.0	176	<.0001***[a]
Prebubertal onset (< 12 ys), n (%)	45 (91.8)	43 (56.6)	32 (61.5)	18.3	2	<.0001***
Follow-up, mean (SD), mo	11.3 (1.8)	11.0 (2.0)	11.7 (1.6)	2.2	176	.109
CGI-S baseline score, mean (SD)	5.7 (0.7)	5.1 (1.0)	5.3 (0.7)	7.6	176	<.0001***[a]
CGI-I score, mean (SD)	2.8 (0.8)	2.1 (0.8)	2.4 (0.8)	11.4	176	.001***[a]
C-GAS baseline score, mean (SD)	38.2 (4.7)	41.8 (6.3)	41.5 (5.1)	10.6	173	<.0001***[a]
Responders, n (%)	18 (36.7)	57 (75.0)	29 (55.8)	18.3	2	<.0001***
Bipolar I disorder, n (%)	16 (32.7)	23 (30.3)	26 (50.0)	5.7	2	.059
Bipolar II disorder, n (%)	10 (20.4)	47 (61.8)	19 (36.5)	22.1	2	<.0001***
Bipolar disorder NOS, n (%)	23 (46.9)	6 (7.9)	7 (13.5)	30.2	2	<.0001***
Chronic course, n (%)	33 (67.3	19 (25.0)	17 (32.7)	23.7	2	<.0001***
Irritable mood, n (%)	32 (65.3)	22 (28.9)	22 (42.3)	16.1	2	<.0001***
Psychotic symptoms, n (%)	10 (20.4)	14 (18.4)	20 (38.5)	7.4	2	.025*
Index episode manic/mixed, n (%)	39 (79.6)	35 (46.1)	29 (55.8)	14.0	2	<.0001***

Developmental Pathways for Different Subtypes of Early-Onset Bipolarity in Youths

Gabriele Masi, MD; Maria Mucci, MD; Chiara Pfanner, MD; Stefano Berloffa, MD; Angela Magazù, MD; and Giulio Perugi, MD

J Clin Psychiatry 73:10, October 2012

Table 2. Current and Lifetime Comorbidities in Children and Adolescents With Bipolar Disorder With ADHD, With Bipolar Disorder With Multiple Anxiety Disorders, and With Bipolar Disorder Without ADHD or Multiple Anxiety Disorders

	Bipolar Disorder				
Comorbidity, n (%)	With ADHD (n = 49)	With Multiple Anxiety Disorders (n = 76)	Without ADHD or Multiple Anxiety Disorders (n = 52)	χ^2_2	*P*
Generalized anxiety disorder	0 (0.0)	55 (72.4)	0 (0.0)		
Separation anxiety disorder	0 (0.0)	39 (51.3)	0 (0.0)		
Panic disorder	0 (0.0)	43 (56.6)	0 (0.0)		
Social phobia	0 (0.0)	43 (56.6)	0 (0.0)		
Simple phobia	0 (0.0)	22 (28.9)	0 (0.0)		
Obsessive-compulsive disorder	12 (24.5)	37 (48.7)	18 (34.6)	7.7	.021*
ADHD	49 (100)	0 (0.0)	0 (0.0)		
Oppositional defiant disorder	18 (36.7)	10 (13.2)	10 (19.2)	10.0	.007*
Conduct disorder	23 (46.9)	2 (2.6)	11 (21.2)	36.1	<.0001***

Comorbidity of Conduct Disorder and Bipolar Disorder in Clinically Referred Children and Adolescents

Gabriele Masi, M.D., Annarita Milone, M.D., Azzurra Manfredi, M.D., Cinzia Pari, M.D., Antonella Paziente, M.D., and Stefania Millepiedi, M.D.

JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 18, Number 3, 2008

Pp. 271–279
DOI: 10.1089/cap.2008.0051

	CD w/out BD n = *106*	*BD w/out CD* n = *109*	*CD + BD* n = *92*	*F or t/χ^2 (df)*	p
Gender (males), *n* (%)	87 (82.1)	63 (57.8)	66 (71.7)	15.3 (2)	0.000*
Age, mean (sd)	13.1 (2.5)	14.3 (2.9)	13.2 (2.6)	6.5(304)	0.002*[a]
SES, mean (sd)	2.8 (.6)	3.2 (.9)	3.0 (.9)	6.6 (304)	0.002*[b]
Lifetime comorbidity, *n* (%)					
Generalized anxiety disorder	42 (39.6)	45 (41.3)	27 (29.3)	3.5 (2)	0.176
Separation anxiety disorder	24 (22.6)	30 (27.5)	16 (17.4)	2.9 (2)	0.233
Panic disorder	6 (5.7)	21 (19.3)	5 (5.4)	14.2 (2)	0.000*
Social phobia	28 (26.4)	32 (29.4)	18 (19.6)	2.6 (2)	0.271
Simple phobias	23 (21.7)	13 (11.9)	16 (17.4)	3.7 (2)	0.160
Depression	35 (33.0)	31 (28.4)	34 (37.0)	0.8 (2)	0.655
Obsessive compulsive disorder	16 (15.1)	54 (49.5)	27 (29.3)	29.8 (2)	0.000*
ADHD	61 (57.5)	27 (24.8)	61 (66.3)	39.7 (2)	0.000*
Substance abuse	34 (32.1)	18 (16.6)	43 (46.7)	21.4 (2)	0.000*

I soggetti con ADHD pre-bipolare sono

. prevalentemente maschi

. hanno un esordio precoce del disturbo

. umore disforico irritabile **(dark, mixed),**

. decorso più cronico che episodico

. più elevata comorbidità con DOP/DC

. maggiore compromissione funzionale

. maggiore resistenza ai trattamenti (litio).

(Masi et al., 2006, 2007)

Storia naturale ?

Clinical and Diagnostic Implications of Lifetime Attention-Deficit/Hyperactivity Disorder Comorbidity in Adults with Bipolar Disorder: Data from the First 1000 STEP-BD Participants

Andrew A. Nierenberg, Sachiko Miyahara, Tom Spencer, Stephen R. Wisniewski, Michael W. Otto, Naomi Simon, Mark H. Pollack, Michael J. Ostacher, Leslie Yan, Rebecca Siegel, and Gary S. Sachs, for the STEP-BD Investigators

Background: *Systematic studies of children and adolescents with a diagnosis of bipolar disorder show that rates of attention-deficit/hyperactivity disorder (ADHD) range from 60% to 90%, but the prevalence and implications of ADHD in adults with bipolar disorder are less clear.*

Methods: *The first consecutive 1000 adults with bipolar disorder enrolled in the National Institute of Mental Health's Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) were assessed for lifetime ADHD. The retrospective course of bipolar disorder, current mood state, and prevalence of other comorbid psychiatric diagnoses were compared for the groups with and without lifetime comorbid ADHD.*

Results: *The overa… 7.6%–11.4%); 14.7… disorder and ADH… ADHD comorbidity… comorbid with AD… with substantially…*

Conclusions: *Lifet… bipolar disorder an… of treating ADHD …*

- **Lifetime prevalence 9.5% (14.7% males, 5.8% Females**
- **Early onset of BD (5 years before)**
- **Comorbid anxiety, alcohol and substance use disorders**

Caratteristiche di ADHD-BD in età adulta

. Esordio più precoce (Sachs et al., 2000; Nierenberg et al. 2005; Masi et al., 2006; Tamam et al. 2008)

. Maggiore gravità (impulsività) (Wingo e Ghaemi, 2007; McIntyre et al. 2010; Masi et al. 2010)

. Maggiore compromissione funzionale (Nierenberg et al., 2005)

. No funzionamento ottimale interepisodico (Bernardi et al. 2010)

. Più spesso BD type I (Nierenberg et al., 2005)

. Primo episodio depressivo (71% vs 22%) (Nierenberg et al., 2005)

. Più frequenti episodi depressivi (Tamam et al., 2006; Rydén et al. 2009)

Caratteristiche di ADHD-BD in età adulta

. Comorbidità multiple (ansia, sostanze, DP antisociale) (Nierenberg et al. 2005; McIntyre et al.2010) .
Maggior numero di tentativi di suicidio
(Nierenberg et al. 2005; Rydén et al. 2009)
. Minore compliance al trattamento (Tamam et al., 2006)
. Minore risposta agli stabilizzanti (<< litio)
(Strober et al., State et al., 2004; Masi et al., 2004, 2011).
. Peggiore funzionamento sociale, occupazione, qualità della vita complessiva (Sentissi et al. 2008)

. Trattamenti per ADHD: basso rischio switch?
(Biederman et al., 1998; Sheffer et al., 2005)

ADHD e Disturbi della Personalità

	All Patients (N=174)[a]		Patients With an Autism Spectrum Disorder Only (N=47)		Patients With ADHD Only (N=81)	
Personality Disorder	N	%	N	%	N	%
Paranoid	37	21.2	12	25.5	18	22.2
Schizotype	18	10.3	11	23.4	4	4.9
Schizoid	33	19.0	15	31.9	10	12.3
Histrionic	0	0.0	0	0.0	0	0.0
Narcissistic	7	4.0	3	6.4	3	3.7
Borderline	41	23.6	5	10.6	30	37.0
Antisocial	30	17.2	0	0.0	25	30.9
Avoidant	39	22.4	16	34.0	18	22.2
Dependent	32	18.4	4	8.5	21	25.9
Obsessive-compulsive	41	23.6	20	42.6	11	13.6
Depressive	38	21.8	9	19.1	21	25.9
Passive-aggressive	15	8.6	4	8.5	7	8.6

Anckarsäter et al. Am J Psych, 2006

ADHD E DISTURBI DI PERSONALITA'

J Atten Disord. 2022 May 10;10870547221098174. doi: 10.1177/10870547221098174. Online ahead of print.

ADHD Symptoms, Peer Problems, and Emotion Dysregulation as Longitudinal and Concurrent Predictors of Adolescent Borderline Personality Features

Julia D McQuade [1]

Abstract

Objective: ADHD and borderline personality (BP) disorder are highly comorbid and characterized by emotion dysregulation and peer problems. However, limited research has examined social and emotional predictors of BP features in samples that include youth with ADHD.

Method: Using a sample of 124 youth with and without ADHD (52% female), ADHD symptoms, peer problems, and emotion dysregulation were assessed in childhood (8-13 years) and in adolescence, along with BP features (13-18 years).

Results: In addition to the significant effect of ADHD symptoms, teacher-rated child peer victimization and adolescent-reported peer victimization, poorer close friendships, and emotion dysregulation domains significantly predicted adolescent BP features. Greater parent-rated child and adolescent emotion dysregulation domains also significantly predicted adolescent BP features, with ADHD symptoms no longer significant.

Conclusion: Even for youth with ADHD, peer and emotional vulnerabilities in childhood and adolescence may serve as important markers of risk for adolescent BP features.

Personal Ment Health. 2017 Aug;11(3):195-205. doi: 10.1002/pmh.1389.

Identifying a borderline personality disorder prodrome: Implications for community screening

Stephanie D Stepp [1], Sophie A Lazarus [1]

Elucidating early signs and symptoms of borderline personality disorder (BPD) has important implications for screening and identifying youth appropriate for early intervention. The purpose of this study was to identify dimensions of child temperament and psychopathology symptom severity that predict conversion to a positive screen for BPD over a 14-year follow-up period in a large, urban community sample of girls (n = 2 450). Parent and teacher reports of child temperament and psychopathology symptom severity assessed when girls were ages 5-8 years were examined as predictors of new-onset BPD cases when girls were ages 14-22 years. In the final model, parent and teacher ratings of emotionality remained significant predictors of new-onset BPD. Additionally, parent ratings of hyperactivity/impulsivity and depression severity, as well as teacher ratings of inattention severity, were also predictive. Results also revealed that elevations in these dimensions pose a notable increase in risk for conversion to BPD over the follow-up period. Supplementary analyses revealed that with the exception of parent-reported depression severity, these same predictors were associated with increases in BPD symptom severity over the follow-up period. These findings suggest BPD onset in adolescence and early adulthood can be detected from parent and teacher reports of temperament and symptom severity dimensions assessed in childhood. The identification of this prodrome holds promise for advancing early detection of children at risk prior to the development of the full-blown disorder.

ADHD E DISTURBO BORDERLINE

Final personality diagnosis for all 47 subjects, ADHD alone, ADHD + ED, and ADHD + ED + ODD: Number and percentage of patients meeting DSM-IV criteria for each Axis II diagnosis

	Total[a]		ADHD only		ADHD + ED[b]		ADHD + ED + ODD[c]		
	n	%	n	%	n	%	n	%	*P* value
CLUSTER A									
Paranoid	4	9%	0	0%	2	11%	2	11%	
Schizoid	0	0%	0	0%	0	0%	0	0%	
Schizotypal	0	0%	0	0%	0	0%	0	0%	
Any cluster A diagnosis	4	9%	0	0%	2	11%	2	11%	$\chi^2 = .95$; $df = 2$; P = ns
CLUSTER B									
Antisocial	4	9%	0	0%	2	11%	2	11%	
Borderline	7	15%	0	0%	3	17%	4	21%	
Histrionic	1	2%	0	0%	1	6%	0	0%	
Narcissistic	1	2%	0	0%	0	0%	1	5%	
Any cluster B diagnosis	8	17%	0	0%	3	17%	5	26%	$\chi^2 = 2.69$; $df = 2$; $P = .30$

Reimherr et al. Ann Clin Psych, 2010

Acta Psychiatr Scand. 2023 Jun;147(6):603-613. doi: 10.1111/acps.13564. Epub 2023 Apr 24.

Association of pharmacological treatments and real-world outcomes in borderline personality disorder

Johannes Lieslehto [1 2], Jari Tiihonen [1 2 3], Markku Lähteenvuo [1], Ellenor Mittendorfer-Rutz [2], Antti Tanskanen [1 2 3], Heidi Taipale [1 2 3 4]

Results: We identified 17,532 patients with BPD (2649 men; mean [SD] age = 29.8 [9.9]). Treatment with benzodiazepines (HR = 1.38, 95% CI = 1.32-1.43), antipsychotics (HR = 1.19, 95% CI = 1.14-124), and antidepressants (HR = 1.18, 95% CI = 1.13-1.23) associated with increased risk of psychiatric rehospitalization. Similarly, treatment with benzodiazepines (HR = 1.37, 95% CI = 1.33-1.42), antipsychotics (HR = 1.21, 95% CI = 1.17-1.26), and antidepressants (HR = 1.17, 95% CI = 1.14-1.21) was associated with a higher risk of all-cause hospitalization or death. Treatment with mood stabilizers did not have statistically significant associations with the outcomes. Treatment with ADHD medication was associated with decreased risk of psychiatric hospitalization (HR = 0.88, 95% CI = 0.83-0.94) and decreased risk of all-cause hospitalization or death (HR = 0.86, 95% CI = 0.82-0.91). Of the specific pharmacotherapies, clozapine (HR = 0.54, 95% CI = 0.32-0.91), lisdexamphetamine (HR = 0.79, 95% CI = 0.69-0.91), bupropion (HR = 0.84, 95% CI = 0.74-0.96), and methylphenidate (HR = 0.90, 95% CI = 0.84-0.96) associated with decreased risk of psychiatric rehospitalization.

Conclusions: ADHD medications were associated with a reduced risk of psychiatric rehospitalization or hospitalization owing to any cause or death among individuals with BPD. No such associations were found for benzodiazepines, antidepressants, antipsychotics, or mood stabilizers.

Percorsi evolutivi come modello interpretativo dei disturbi della personalità?

I disturbi della personalità possono essere una modalità di adattamento (instabile) della personalità a dimensioni psicopatologiche e/o disturbi del neurosviluppo ad esordio precoce ed andamento cronico (ADHD, ASD, Disabilità intellettiva)?

“La diagnosi di traiettoria”

La traiettoria evolutive con ADHD, **ED**, DOP, DB, DC, DUS individua un fenotipo specifico per:

- storia naturale,
- caratteristiche cliniche,
- comorbidità (disturbo della condotta),
- complicazioni (autolesività, suicidalità)
- prognosi (sostanze)
- esigenze terapeutiche.

Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis

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Findings We deemed 34 trials eligible, including 5260 participants and 14 antidepressant treatments. The quality of evidence was rated as very low in most comparisons. For efficacy, only fluoxetine was statistically significantly more effective than placebo (standardised mean difference –0·51, 95% credible interval [CrI] –0·99 to –0·03). In terms of tolerability, fluoxetine was also better than duloxetine (odds ratio [OR] 0·31, 95% CrI 0·13 to 0·95) and imipramine (0·23, 0·04 to 0·78). Patients given imipramine, venlafaxine, and duloxetine had more discontinuations due to adverse events than did those given placebo (5·49, 1·96 to 20·86; 3·19, 1·01 to 18·70; and 2·80, 1·20 to 9·42, respectively). In terms of heterogeneity, the global I^2 values were 33·21% for efficacy and 0% for tolerability.

Interpretation When considering the risk–benefit profile of antidepressants in the acute treatment of major depressive disorder, these drugs do not seem to offer a clear advantage for children and adolescents. Fluoxetine is probably the best option to consider when a pharmacological treatment is indicated.

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New generation antidepressants for depression in children and adolescents: a network meta-analysis

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Main results: Twenty-six studies were included. There were no data for the two primary outcomes (depressive disorder established via clinical diagnostic interview and suicide), therefore, the results comprise only secondary outcomes. Most antidepressants may be associated with a "small and unimportant" reduction in depression symptoms on the CDRS-R scale (range 17 to 113) compared with placebo (high certainty evidence: paroxetine: MD -1.43, 95% CI -3.90, 1.04; vilazodone: MD -0.84, 95% CI -3.03, 1.35; desvenlafaxine MD -0.07, 95% CI -3.51, 3.36; moderate certainty evidence: sertraline: MD -3.51, 95% CI -6.99, -0.04; fluoxetine: MD -2.84, 95% CI -4.12, -1.56; escitalopram: MD -2.62, 95% CI -5.29, 0.04; low certainty evidence: duloxetine: MD -2.70, 95% CI -5.03, -0.37; vortioxetine: MD 0.60, 95% CI -2.52, 3.72; very low certainty evidence for comparisons between other antidepressants and placebo). There were "small and unimportant" differences between most antidepressants in reduction of depression symptoms (high- or moderate-certainty evidence). Results were similar across other outcomes of benefit. In most studies risk of self-harm or suicide was an exclusion criterion for the study. Proportions of suicide-related outcomes were low for most included studies and 95% confidence intervals were wide for all comparisons. The evidence is very uncertain about the effects of mirtazapine (OR 0.50, 95% CI 0.03, 8.04), duloxetine (OR 1.15, 95% CI 0.72, 1.82), vilazodone (OR 1.01, 95% CI 0.68, 1.48), desvenlafaxine (OR 0.94, 95% CI 0.59, 1.52), citalopram (OR 1.72, 95% CI 0.76, 3.87) or vortioxetine (OR 1.58, 95% CI 0.29, 8.60) on suicide-related outcomes compared with placebo. There is low certainty evidence that escitalopram may "at least slightly" reduce odds of suicide-related outcomes compared with placebo (OR 0.89, 95% CI 0.43, 1.84). There is low certainty evidence that fluoxetine (OR 1.27, 95% CI 0.87, 1.86), paroxetine (OR 1.81, 95% CI 0.85, 3.86), sertraline (OR 3.03, 95% CI 0.60, 15.22), and venlafaxine (OR 13.84, 95% CI 1.79, 106.90) may "at least slightly" increase odds of suicide-related outcomes compared with placebo. There is moderate certainty evidence that venlafaxine probably results in an "at least slightly" increased odds of suicide-related outcomes compared with desvenlafaxine (OR 0.07, 95% CI 0.01, 0.56) and escitalopram (OR 0.06, 95% CI 0.01, 0.56). There was very low certainty evidence regarding other comparisons between antidepressants.

TRATTAMENTO DELLA CICLOTIMIA

Motivo frequente di consultazione, fonte di sofferenza soggettiva: "depressione/vuoto" e/o "ansia" (interpretate come **reattive** a cause "ambientali".

Scarsa consapevolezza di eccessiva reattività, sensibilità ed instabilità emotive ed impulsività.

Richiesta (ed uso) di ansiolitici (BDZ) ed antidepressivi, minore efficacia, rischio di destabilizzazione

TRATTAMENTO DELLA CICLOTIMIA

Alta intensità affettiva, impulsività comportamentale, suicidalità: Sali di litio

Stato ansioso-misto – reattività di umore: Acido valproico (gabapentin).

Prevalente polarità depressiva: lamotrigina.

Combinazione di bassi dosaggi di litio (300–450 mg/d) e lamotrigina (25–100 mg/d)

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Extended-Release Lithium Sulfate in Adolescents with Bipolar Disorder: Results from a Longitudinal Prospective Cohort Study

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Abstract

Objectives: Bipolar disorder (BD) in adolescence often associates with risky conducts, nonsuicidal self-injury (NSSI), and suicidal ideation. Lithium salts represent the first-line choice for BD in youth to manage manic symptoms and prevent both manic and depressive relapses. Our study aimed to assess efficacy and tolerability of extended-release lithium sulfate (ERLS) in youths with BD.

Methods: A longitudinal perspective intervention study was thus conducted on a single cohort of 36 patients with BD aged 12–17 years treated with ERLS and followed up for 1 year. ERLS was titrated up to reach optimal plasma concentrations during the 3 months before baseline visit (T0). Then, patients underwent five follow-up visits after 1, 2, 3, 5, and 11 months and were administered with a battery of self- and parent-rated questionnaires and interviews to evaluate, at each timepoint, ERLS-related side effects, manic and depressive symptoms, emotional dysregulation (ED), NSSI and suicidality, and aggressiveness. Regular clinical assessments were also conducted, as well as blood tests, urinalysis, and EKG. Regression models were applied to examine the time course of outcome variables.

Results: Twenty-four patients completed the follow-up. Regressions showed a significant reduction of most dependent variables included in the models, including depressive symptoms (β = –0.0006; adj-p = 0.0007), aggressiveness (β = –0.0031; adj-p < 0.0001), ED (β = –0.0002; adj-p = 0.0497), and unstructured suicidal ideation (β = –0.0058; adj-p = 0.0340). Fine distal tremor, increased thirst, and diuresis were among the most frequently reported side effects.

Conclusions: Findings from the present study support the use of ERLS as an effective and well-tolerated agent for the management of BD in youth, with a beneficial effect on associated severe symptoms, including NSSI and suicidality.

brain sciences

MDPI

Review

Efficacy and Safety of Lithium for Suicide and Suicide-Related Behaviors in Youth: A Review of the Literature

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Abstract: Objectives: This systematic review evaluates the anti-suicidal properties of Lithium in children and adolescents with Bipolar Disorder (BD), addressing gaps in evidence regarding its efficacy and safety in reducing suicidality and self-harming behaviors. Methods: A comprehensive literature search was conducted across PubMed, Web of Science, and Scopus up to February 2024. Eligible studies were those focusing on patients aged 25 years or younger, examining Lithium therapy and its impact on suicidal ideation and behaviors. The review included randomized controlled trials, longitudinal prospective and retrospective studies, and cross-sectional studies, while excluding expert opinions and case reports. Results: Evidence generally supports the efficacy of Lithium in reducing suicidal ideation and self-harming behaviors in youth with BD, though results are mixed. Randomized controlled trials demonstrated its effectiveness in mitigating suicidal thoughts during acute manic episodes, with effects persisting post-treatment. Longitudinal studies suggested that Lithium might offer superior outcomes compared to other mood stabilizers, although its specific impact on suicidality remains inconclusive. Cross-sectional studies and retrospective analyses reveal associations between Lithium use and reduced self-harming behaviors, but causality remains uncertain. While mood-stabilizing effects of Lithium offer potential benefits for reducing suicidality in youth, evidence on its direct impact on emotional dysregulation (ED) and long-term efficacy is limited. Variability in individual responses and adherence issues underscore the need for further research. Future studies should include larger, diverse samples, focus on ED symptoms, and explore Lithium mechanisms in suicidality prevention. Conclusions: Lithium remains a promising treatment for mood stabilization and reduction in suicidality in youth with BD.

ANTIPSICOTICI NEL DISTURBO BIPOLARE

Pazienti bipolari ciclotimici più **sensibili** all'antagonismo D2 (depressione, appiattimento affettivo e motivazionale, sintomi EPS), più spesso ed a dosi inferiori che in altri disturbi.

La induzione di depressione può contribuire alla destabilizzazione del disturbo.

Antipsicotici meno depressogeni (quetiapina, lurasidone, aripiprazolo, olanzapina in acuzie), a basse dosi, per periodi possibilmente limitati

Dialectical Behavior Therapy for Adolescents With Repeated Suicidal and Self-harming Behavior: A Randomized Trial

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Table 4. Mehlum *et al.* 2014[120]; 2016[121].

Sample size (at randomization)	Sample characteristics	Recruitment setting	Inclusion criteria	Exclusion criteria	Major diagnoses
Total = 77; T = 39, C = 38	12–18 years old; 88% female; 85% Norwegian	Outpatient	Lifetime SH ≥2 episodes; ≥1 SH episode in past 16 weeks; ≥2 DSM-IV BPD criteria or 1 BPD criteria and 2 subthreshold-level criteria; fluent in Norwegian	BP; SZ; SCAD; psychotic disorder not otherwise specified; intellectual disability; Asperger syndrome	ANX (43%); other depressive disorder (38%); MDD (22%); BPD (21%); PTSD (17%); PD (9%); ED (8%); SUD (8%)
SH outcome measures	**Treatment condition**	**Control condition**	**Assessments**	**Treatment attrition and completion**	**Results**
SH (LPC); SI (SIQ-Jr)	DBT: individual sessions, multifamily skills training, family therapy, or telephone coaching as needed Dose: 19 weeks of weekly individual (1 hour) and multifamily skills training (1.5 hour)	EUC (any enhanced, non-DBT treatment plus suicide risk assessment, and therapist agrees to minimum dose) Dose: 19 weeks minimum of weekly individual sessions	Pretreatment (baseline), mid-treatment (9 and 15 weeks), post-treatment (19 weeks), and follow-up at 71 weeks (1 year post-treatment)	Treatment completion (≥50% of sessions): DBT: 74.4% EUC: 71% Attrition post-treatment: DBT: 0% EUC: 0% 71-week follow-up: DBT: 2.6% EUC: 2.6%	Significantly fewer SH episodes, significantly greater decrease in SI, significant decrease in depressive symptoms for DBT (compared to EUC) at post-treatment. Significantly fewer SH episodes from post-treatment to 71-week follow-up. NS between-group differences in SI, hopelessness, depressive symptoms, and BPD at 71-week follow-up.

”La mente umana deve prima costruire le forme, indipendentemente, per poi poterle ritrovare nelle cose.”

Albert Einstein, 1927