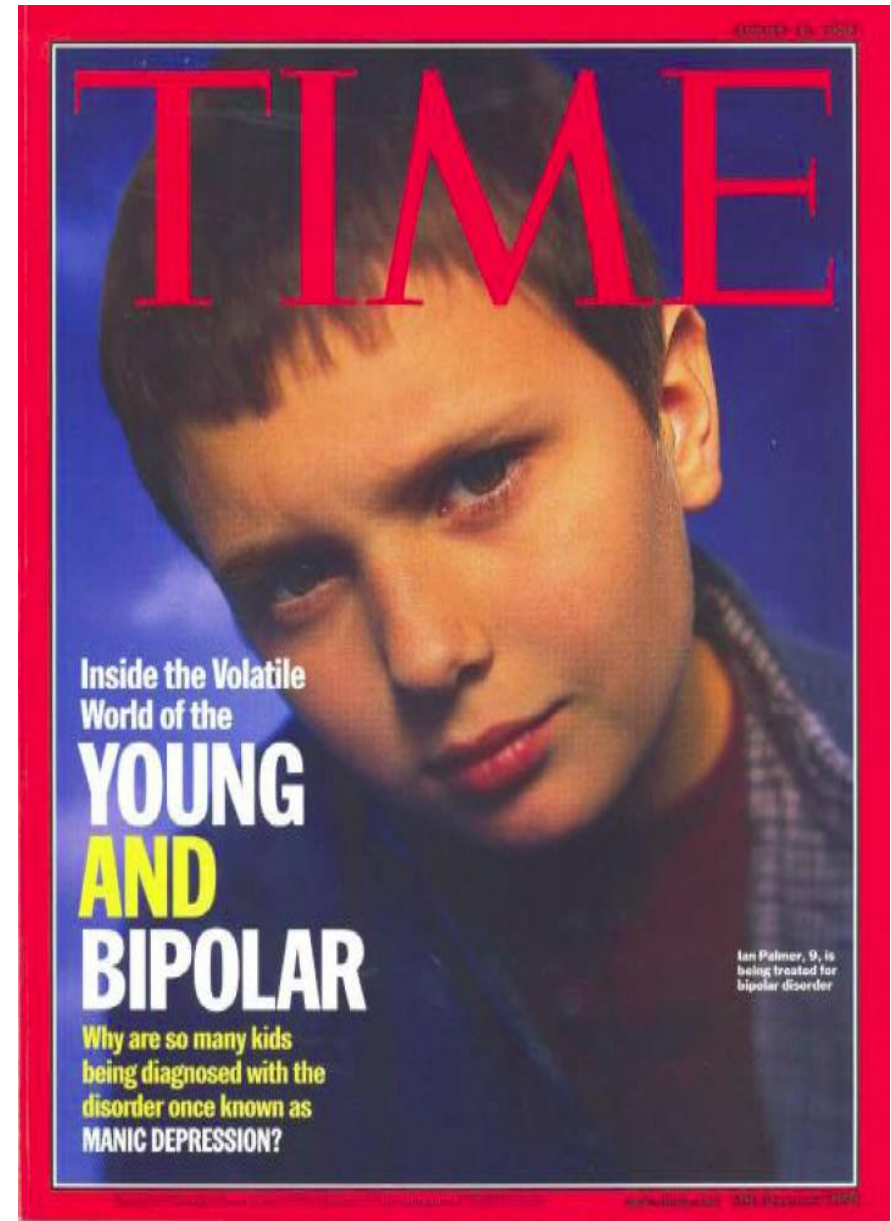


Gibt es tatsächlich eine kindliche Bipolare Erkrankung? – Eine Transatlantische Perspektive



„Pädiatrische bipolare Erkrankung“



„CBCL-positive Bipolar Disorder Epidemic“

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Abstract

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J Am Acad Child Adolesc Psychiatry. 1995 Apr;34(4):464-71.

CBCL clinical scales discriminate prepubertal children with structured interview-derived diagnosis of mania from those with ADHD.

Biederman J¹, Wozniak J, Kiely K, Ablon S, Faraone S, Mick E, Mundy E, Kraus I.

Author information

Abstract

OBJECTIVE: To evaluate the discriminative ability of the Child Behavior Checklist (CBCL) to identify children with structured interview-derived diagnosis of bipolar disorder.

METHOD: We evaluated the convergence of CBCL scales with the diagnosis of mania in 31 children with mania, 120 children with attention-deficit hyperactivity disorder, and 77 prepubertal normal control children aged 12 years or younger. We evaluated the strength of association between each CBCL scale and structured interview-derived diagnoses with total predictive value and the odds ratio.

RESULTS: Excellent convergence was found between the CBCL scales of Delinquent Behavior, Aggressive Behavior, Somatic Complaints, Anxious/Depressed, and Thought Problems and the diagnosis of mania.

CONCLUSIONS: These findings indicate that the CBCL could serve as a rapid and useful screening instrument to identify manic children in clinical settings.

PMID: 7751260 [PubMed - indexed for MEDLINE]



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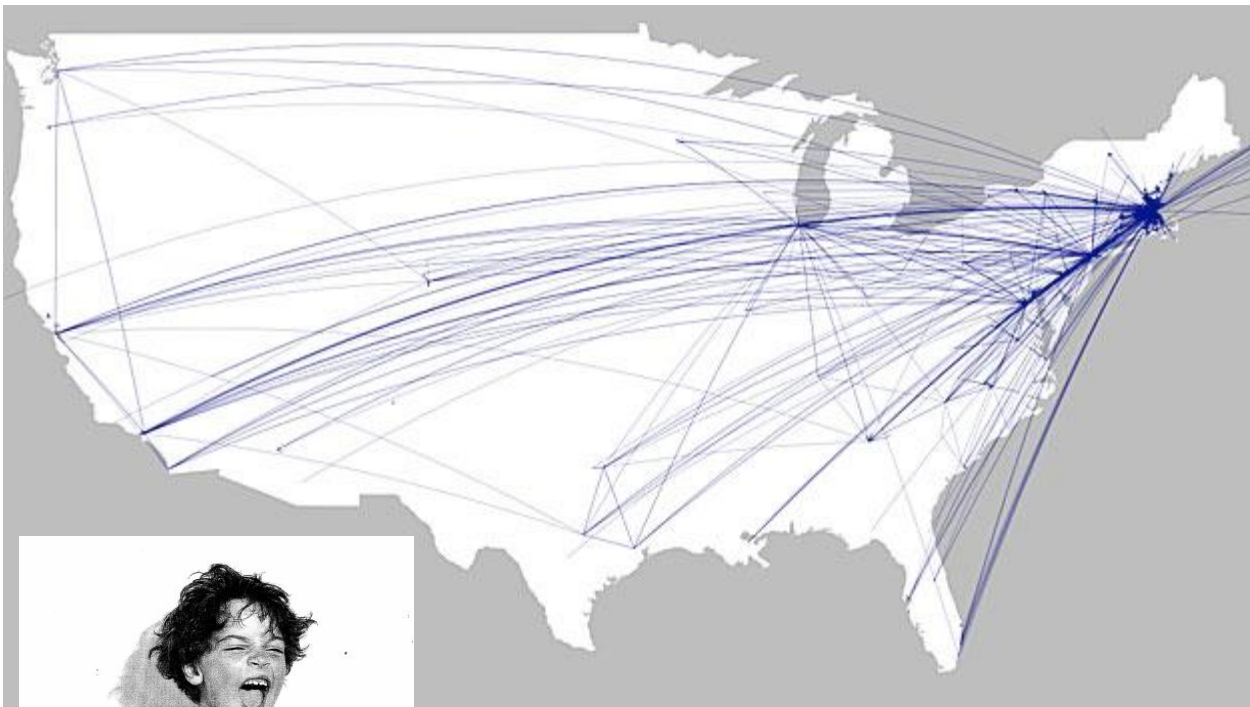
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„CBCL-positive Bipolar Disorder Epidemic“



MOMMY,
AM I
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Bi Polar?

HUNDREDS OF THOUSANDS OF CHILDREN IN THE U.S. HAVE BEEN WRONGLY DIAGNOSED WITH THE TRENDY DISORDER, ARGUES A NOTED PSYCHIATRIST. AND THE RESULTS CAN BE TRAGIC.

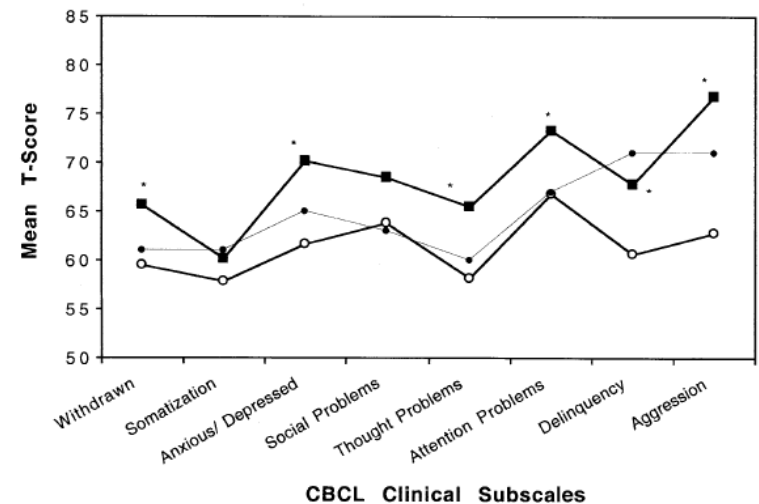
**BY STUART L. KAPLAN, M.D.
PHOTOGRAPHS BY FREDRIK BRODÉN**

CBCL Profile sind bei PBD erhöht (?)

Table 1. Demographics and Method of Diagnoses of Samples Studied

| Citation | N | Age (years) | Gender (% Male) | Setting | Interview Schedule | Time Referent | Diagnostic Criterion | Interviewer |
|--------------------------|----|-------------|-----------------|-----------------------|--------------------|---------------|----------------------|-------------------------|
| Biederman et al (1995) | 31 | 8.1 ± 2.8 | 84% | Outpatient | KSADS-E | Lifetime | DSM-IIIIR | Trained lay interviewer |
| Biederman et al (1996) | 14 | 10.7 ± 2.9 | 100% | Outpatient | KSADS-E | Lifetime | DSM-IIIIR | Trained lay interviewer |
| Geller et al (1998) | 39 | 6–11 | 69% | Outpatient | WASH-U KSADS | Current | DSM-IV | Research Nurse |
| Geller et al (1998) | 27 | 6–11 | 100% | Outpatient | WASH-U KSADS | Current | DSM-IV | Research Nurse |
| Geller et al (1998) | 12 | 6–11 | 0% | Outpatient | WASH-U KSADS | Current | DSM-IV | Research Nurse |
| Carlson and Kelly (1998) | 60 | 8.8 ± 2.1 | – | Inpatient | CSI-R | Current | DSM-IIIIR | Psychiatrist |
| Carlson et al (1998) | 23 | 8.2 | 100% | Outpatient | DICA-R | Current | DSM-IIIIR | Clinician |
| Hazell et al (1999) | 25 | 9–13 | 100% | Outpatient | DICA-R | Lifetime | DSM-IIIIR | Trained lay interviewer |
| Dienes et al (2002) | 16 | 10.9 ± 2.9 | 75% | Offspring of patients | WASH-U KSADS | Not reported | DSM-IV | Psychiatrist |

KSADS-E, Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version; DICA-R, Diagnostic Interview Schedule for Children-Revised; CSI-R, Child Symptom Inventory-Revised



...also prädiziert CBCL pädiatrische BPD?

The CBCL-Pediatric Bipolar Disorder Profile Predicts a Subsequent Diagnosis of Bipolar Disorder and Associated Impairments in ADHD Youth Growing Up: A Longitudinal Analysis

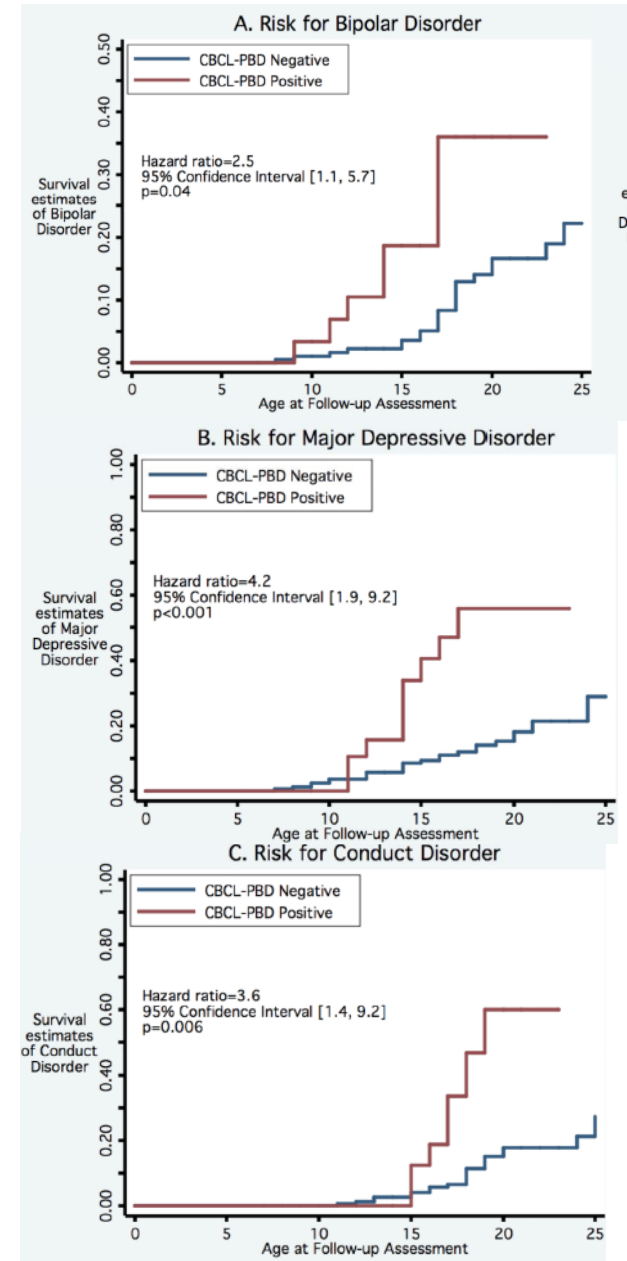
Joseph Biederman, M.D., Carter Petty, M.A., Michael C. Monuteaux, Sc.D., Margaret Evans, B.A., Tiffany Parcell, B.S., Stephen V. Faraone, Ph.D., and Janet Wozniak, M.D.
Clinical and Research Program in Pediatric Psychopharmacology (Drs. Biederman, Monuteaux, Wozniak, Mr. Petty, Ms. Evans, and Ms. Parcell); Department of Psychiatry, Massachusetts General Hospital, Department of Psychiatry, Harvard Medical School, Boston, MA (Drs. Biederman, Mick, Monuteaux, and Wozniak); and Departments of Psychiatry and Neuroscience and Physiology, SUNY Upstate Medical University, Syracuse, NY (Dr. Faraone).

Abstract

Objective—To examine the predictive utility of the Child Behavior Checklist Pediatric Bipolar Disorder (CBCL-PBD) profile to help identify children at risk for bipolar disorder.

Methods—Subjects were ascertained from two identically designed longitudinal case-control family studies of boys and girls with ADHD. Based on data from the baseline assessment, ADHD subjects without a lifetime diagnosis of bipolar disorder were stratified by the presence (CBCL-PBD Positive; N=28) or absence (CBCL-PBD Negative N=176) of a CBCL-Pediatric Bipolar Disorder (PBD) score ≥ 210 (total of Attention, Aggression, and Anxious/Depressed subscales). Subjects were comprehensively assessed at follow-up with structured psychiatric interviews.

Results—Over an average follow up period of 7.4 years, a positive CBCL-PBD score predicted subsequent diagnoses of bipolar disorder, major depression and conduct disorder, as well as impaired psychosocial functioning and higher risk for psychiatric hospitalization.



Was der „PBD-CBCL“ wirklich prädiziert

Young-adult diagnostic outcomes and childhood CBCL status

| Young-adult diagnoses | CBCL-PBD (<i>n</i> = 16) | No CBCL-PBD (<i>n</i> = 81) | Odds ratio ^a (95% CI) |
|---------------------------------------------|---------------------------|------------------------------|----------------------------------|
| Anxiety disorder | 44% (<i>n</i> = 7) | 17% (<i>n</i> = 14) | 3.72 (1.19–11.67)* |
| Drug abuse/dependence | 44% (<i>n</i> = 7) | 22% (<i>n</i> = 18) | 2.72 (0.96–7.75) ⊥ |
| Cluster B personality disorder ^b | 43% (<i>n</i> = 6) | 8% (<i>n</i> = 6) | 9.13 (2.21–37.62)** |
| ADHD ^c | 40% (<i>n</i> = 6) | 7% (<i>n</i> = 6) | 8.33 (1.91–36.27)** |
| Alcohol abuse/dependence | 38% (<i>n</i> = 6) | 20% (<i>n</i> = 16) | 2.44 (0.83–7.14) |
| Major depression | 38% (<i>n</i> = 6) | 20% (<i>n</i> = 16) | 2.44 (0.71–8.41) |
| Bipolar I or II disorder | 31% (<i>n</i> = 5) | 5% (<i>n</i> = 4) | 8.75 (1.89–40.58)** |
| PBD-adult comorbidity | 69% (<i>n</i> = 11) | 14% (<i>n</i> = 11) | 14.0 (4.08–48.06)** |
| Any psychiatric disorder | 75% (<i>n</i> = 12) | 53% (<i>n</i> = 43) | 2.64 (0.79–8.92) |
| Suicidal ideation | 25% (<i>n</i> = 4) | 10% (<i>n</i> = 8) | 3.04 (0.87–10.59) ⊥ |
| Suicide attempt | 19% (<i>n</i> = 3) | 6% (<i>n</i> = 5) | 3.51 (0.76–16.19) |

Relationship between childhood CBCL-PBD and young-adult diagnosis

| | Bipolar | | ADHD | | Cluster B | | PBD-adult comorbidity | |
|---------------------------|---------|-----------|-------|-----------|-----------|-----------|-----------------------|-----------|
| | Value | CI | Value | CI | Value | CI | Value | CI |
| Sensitivity | 0.56 | 0.23–0.85 | 0.50 | 0.22–0.78 | 0.50 | 0.22–0.78 | 0.50 | 0.41–0.87 |
| Specificity | 0.88 | 0.78–0.93 | 0.89 | 0.80–0.95 | 0.90 | 0.88–0.95 | 0.93 | 0.77–0.93 |
| Positive predictive value | 0.31 | | 0.40 | | 0.43 | | 0.69 | |
| Negative predictive value | 0.95 | | 0.93 | | 0.92 | | 0.86 | |

Was der „PBD-CBCL“ wirklich prädiziert (II)

Table 2
Summary statistics from logistic regressions examining Axis I Psychiatric Outcomes in ADHD youth with and without the “CBCL-JBD phenotype”.

| | CBCL-JBD positive N = 28 | | CBCL-JBD negative N = 62 | | p | Wald | Odds ratio | 95% CI |
|-----------------------------------------|--------------------------|----|--------------------------|----|------|------|------------|-----------|
| | % | # | % | # | | | | |
| ADHD | 42.9 | 12 | 44.3 | 27 | 0.90 | 0.02 | 1.06 | 0.43–2.61 |
| CD/ASPD | 35.7 | 10 | 35.5 | 22 | 0.98 | 0.00 | 1.01 | 0.40–2.57 |
| Mood disorder | 25.0 | 7 | 14.5 | 9 | 0.23 | 1.42 | 1.96 | 0.65–5.95 |
| Anxiety disorder | 32.1 | 9 | 22.6 | 14 | 0.34 | 0.92 | 1.62 | 0.60–4.39 |
| Substance abuse/dependence ^a | 42.9 | 12 | 50.8 | 31 | 0.90 | 0.02 | 0.73 | 0.30–1.79 |

^a Substance abuse data unavailable for one participant.

Table 3
Summary statistics from logistic regressions examining Axis II Personality Disorder (PD) Outcomes in ADHD youth with and without the “CBCL-JBD phenotype”.

| | CBCL-JBD positive N = 28 | | CBCL-JBD negative N = 62 | | p | Wald/ χ^2 | Odds ratio | 95% CI |
|---------------|--------------------------|----|--------------------------|----|-------|----------------|------------|------------|
| | % | # | % | # | | | | |
| Any cluster A | 25.0 | 7 | 12.9 | 8 | 0.161 | 1.97 | 2.25 | 0.73–6.98 |
| Any cluster B | 42.9 | 12 | 24.2 | 15 | 0.077 | 3.12 | 2.35 | 0.91–6.06 |
| Any cluster C | 35.7 | 10 | 8.1 | 5 | 0.003 | 9.13 | 6.33 | 1.91–20.97 |
| Any PD | 67.9 | 19 | 35.5 | 22 | 0.005 | 7.73 | 3.84 | 1.49–9.91 |

Aggression, and Anxiety/Depression subscales.

Results: The CBCL-JBD phenotype was found in 31% of those followed but only 4.9% of the sample continued to meet the phenotype criteria at follow-up. Only two of the sample developed Bipolar Disorder by late adolescence and only one of those had the CBCL-JBD profile in childhood. The proxy did not predict any Axis I disorders. However, the CBCL-JBD proxy was highly predictive of later personality disorders.

Limitations: Only a subgroup of the original childhood sample was followed. Given this sample

Was der „PBD-CBCL“ wirklich prädiziert (III)

Table 3 Predicting young adults' diagnostic outcomes from CBCL-DP score, controlling for parental education and per capita income¹

| Outcome at age 19 years | CBCL-DP | | Low parental education | | Per capita income (DM per month/100) | |
|-----------------------------------|-------------------|-----------------|------------------------|------------|--------------------------------------|----------|
| | <i>B (SE)</i> | <i>p</i> | <i>B (SE)</i> | <i>p</i> | <i>B (SE)</i> | <i>p</i> |
| Anxiety disorders | -.01 (.02) | .48 | .22 (.60) | .72 | -.01 (.03) | .99 |
| Mood disorders | .03 (.01) | <.01 | .38 (.57) | .51 | .01 (.02) | .53 |
| Conduct disorder | .01 (.02) | .45 | -.01 (.87) | .99 | -.08 (.07) | .28 |
| ADHD | .05 (.02) | <.01 | -.60 (1.15) | .60 | .04 (.03) | .25 |
| Alcohol abuse/dependence | .05 (.01) | <.01 | -.47 (.83) | .57 | .01 (.04) | .86 |
| Cannabis abuse/dependence | .03 (.01) | <.01 | .48 (.50) | .34 | .01 (.03) | .85 |
| Somatoform disorders ² | -.02 (.04) | .15 | .47 (n.a.) | 1 | .02 (.03) | .29 |
| Eating disorders ² | -.05 (.05) | .26 | .28 (n.a.) | 1 | .01 (.04) | .70 |
| Suicidal ideation | .03 (.01) | <.01 | -.51 (.57) | .37 | .01 (.02) | .56 |
| Suicidal attempt | .03 (.01) | .04 | .55 (.66) | .40 | -.04 (.06) | .48 |
| FTND score: <i>M (SD)</i> | .02 (.01) | <.001 | .52 (.29) | .07 | -.02 (.01) | .18 |
| GAF scale: <i>M (SD)</i> | -.26 (.04) | <.001 | -2.91 (1.62) | .07 | .09 (.07) | .24 |

FTND = Fagerström Test for Nicotine Dependence, GAF = Global Assessment of Functioning.

¹Values adjusted for gender.

²Median unbiased estimates from exact logistic regression.

Table 4 Predicting young adults' comorbidity from CBCL-DP score, controlling for parental education and per capita income.^{1, 2}

| Comorbidity of | CBCL-DP | | Low parental education | | Per capita income (DM per month/100) | |
|----------------------------------------------------------|------------------|----------------|------------------------|----------|--------------------------------------|----------|
| | <i>B (SE)</i> | <i>p</i> | <i>B (SE)</i> | <i>p</i> | <i>B (SE)</i> | <i>p</i> |
| Any psychiatric disorder | -.02 (.01) | .146 | -.02 (.66) | .98 | -.00 (.04) | .96 |
| Substance use disorders with anxiety or mood disorder | -.01 (.02) | .99 | 1.36 (.83) | .10 | -.04 (.08) | .59 |
| Cannabis and alcohol use disorders | .04 (.02) | <.05 | -1.02 (1.05) | .33 | -.07 (.07) | .27 |

„PBD-CBCL“ und PBD

Table 1. Prevalence of the Child Behavior Checklist-pediatric bipolar disorder (CBCL-PBD) phenotype across different ages

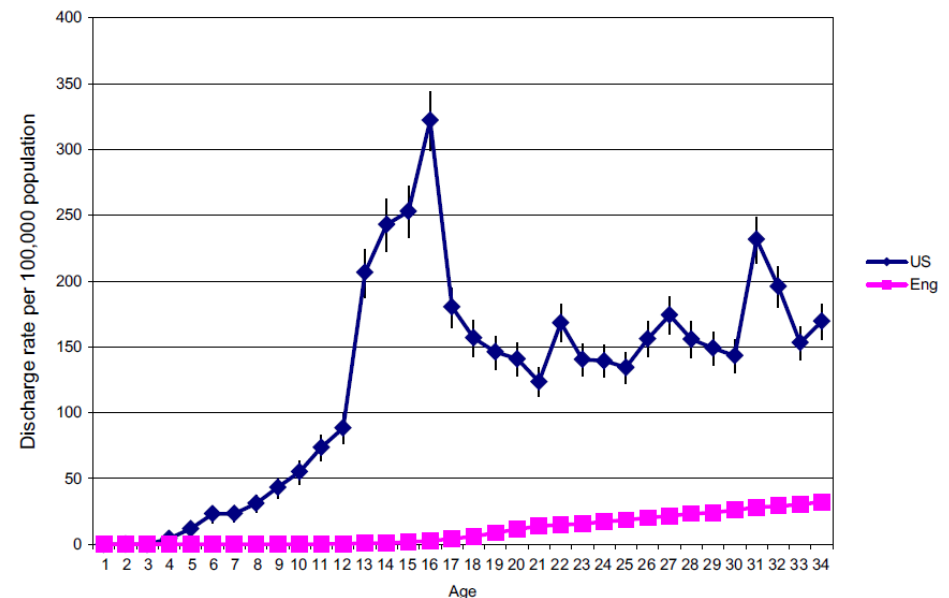
| Age (years) | Total sample | CBCL-PBD | | |
|-------------|--------------|-----------------|----------|------------|
| | | n (% of sample) | Male (%) | Female (%) |
| 4-7 | 670 | 6 (0.9) | 3 (50.0) | 3 (50.0) |
| 8-11 | 681 | 4 (0.6) | 1 (25.0) | 3 (75.0) |
| 12-15 | 800 | 8 (1.0) | 1 (12.5) | 7 (87.5) |
| 16-18 | 705 | 3 (0.4) | 0 (0.0) | 3 (100.0) |
| All (4-18) | 2,856 | 21 (0.7) | 5 (23.8) | 16 (76.2) |

Entlassungsdiagnose PBD in USA 72mal häufiger als in UK

→ PDB-CBCL in Deutschland gleich häufig wie z.B. in USA

→ CBCL Phänotyp ist universell, wird aber nur in den USA PBD genannt trotz unzulänglicher longitudinaler Daten!

FIGURE 1 Bipolar disorder (BD) (ICD-9-CM codes 296.40-296.89; ICD-10 code F31) discharge rates per 100,000 population in patients aged 1 to 34 years in the United States versus England, 2000 to 2010. Note: ICD-9-CM = International Classification of Diseases Version 9, Clinical Modification; ICD-10 = International Classification of Diseases Version 10.



Open-Label, 8-Week Trial of Olanzapine and Risperidone for the Treatment of Bipolar Disorder in Preschool-Age Children

Joseph Biederman, Eric Mick, Paul Hammerness, Theresa Harpold, Megan Aleardi, Meghan Dougherty, and Janet Wozniak

Background: *To evaluate short-term safety and efficacy of atypical antipsychotics in a single-site, prospective, open-label, 8-week study of risperidone and olanzapine monotherapy in preschoolers with bipolar disorder (BPD).*

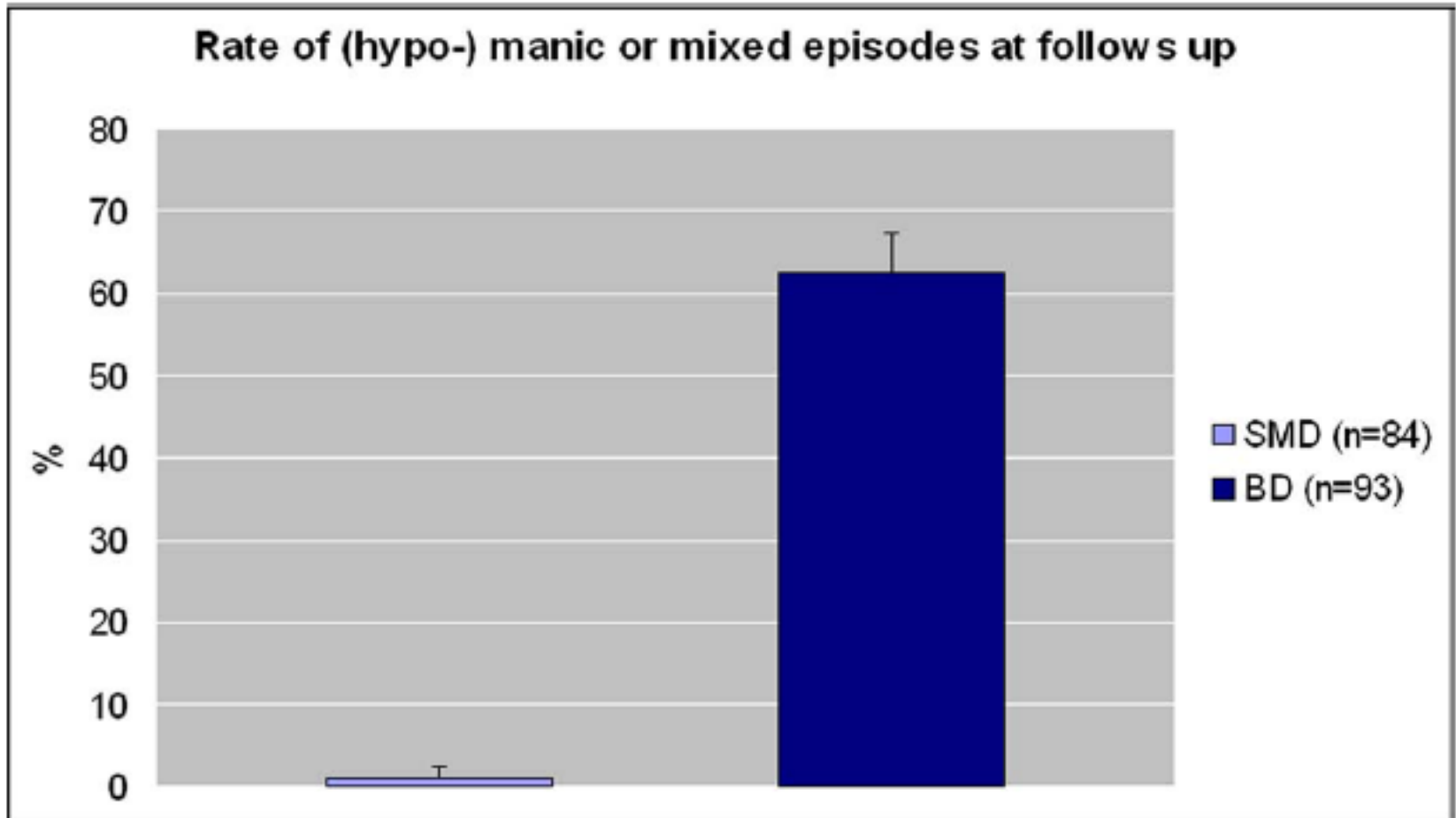
Methods: *Risperidone was initiated at an open-label dose of .25 mg/day, increased weekly according to response and tolerability to a maximum dose of 2.0 mg/day. Olanzapine was initiated at 1.25 mg/day and increased to no more than 10 mg/day.*

Results: *Thirty-one children aged 4–6 years were treated with olanzapine ($n = 15$, 6.3 ± 2.3 mg/day) or risperidone ($n = 16$, $1.4 \pm .5$ mg/day). At study end point (week 8 or last observation carried forward), there was a 18.3 ± 11.9 point ($t = -5.6$, $p < .001$) reduction in risperidone-treated subjects and a 12.1 ± 10.4 point ($t = -4.4$, $p < .001$) reduction in Young Mania Rating Scale (YMRS) scores in olanzapine-treated subjects that did not differ between groups ($t = 1.4$, $p = .2$). Response criteria (Clinical Global Impression improvement of “Much” or “Very Much” improved or a YMRS change of $\geq 30\%$ or more) indicated no difference in rate of response with risperidone and olanzapine (69% vs. 53%, $\chi^2_{(1)} = .8$, $p = .4$).*

Conclusions: *This prospective open study suggests that treatment with risperidone or olanzapine may result in a rapid reduction of symptoms of mania in preschool children with BPD. Because of substantial residual symptomatology and adverse effects, however, a pressing need exists to identify additional safe and effective treatments for the management of BPD in this high-risk population.*

Risiko für Manie bei „severe mood dysregulation“

FIGURE 2 Bars with standard errors show the percentage of patients with either severe mood dysregulation (SMD) or bipolar disorder (BD) who developed a (hypo-)manic or mixed episode during the follow-up period.



Bipolare Störung bei Kindern bei „korrekter“ Diagnose

Table 2. Key characteristics of non-clinical observational studies that were eligible for inclusion in this review of rates of bipolar disorder in pre-pubertal children

| Study | Location | Age, years (screened sample) | Assessed sample, n | N for age ≤12 years ^a | Assessment schedule | Diagnostic criteria | Bipolar disorder cases age ≤12 years, n |
|---------------------------|----------|--------------------------------|--------------------|-------------------------------------------------------------------------|---------------------|---------------------|-----------------------------------------|
| Costello et al. 1996 (26) | USA | 9–13(n = 4,500) | 1,015 ^b | 9 or 11 years = 721 ^b (observations = 2,691) ^b | CAPA | DSM-III-R | 0 |
| Angold et al. 2002 (27) | USA | 9–17 (mean = 12.6) (n = 4,500) | 920 | 9–12 years = 645 | CAPA | DSM-IV | 0 |
| Clements et al. 2008 (34) | UK | 8–19(n = 7,329) | 5,325 | 8–12 years = 2,326 | DAWBA | ICD-10 | 1 |
| Lynch et al. 2006 (35) | Ireland | 12–15(n = 723) | 195 | 12 years = NR | K-SADS | DSM-IV | 0 |
| Roberts et al. 2007 (36) | USA | 11–17(n = 4,175) | 4,175 | 11–12 years = 1,127 | DISC-IV | DSM-IV | 11–12 years = NR 11–17 years = 13 |

CAPA = Child and Adolescent Psychiatric Assessment; DAWBA = Development and Well-Being Assessment; DISC-IV = Diagnostic Interview Schedule for Children-Version IV; K-SADS = Kiddie-Schedule for Affective Disorders and Schizophrenia; NR = not reported.

^aFor some studies, this is estimated from percentages or other information.

^bMulti-wave study design, involving re-assessments of original sample (n = 1,015; 70% were aged 9 or 11 years at Wave 1). Total observations (for all waves of study): n = 6,674, of which 2,691 involved children aged ≤12 years.

Bipolare Störung und Kognition

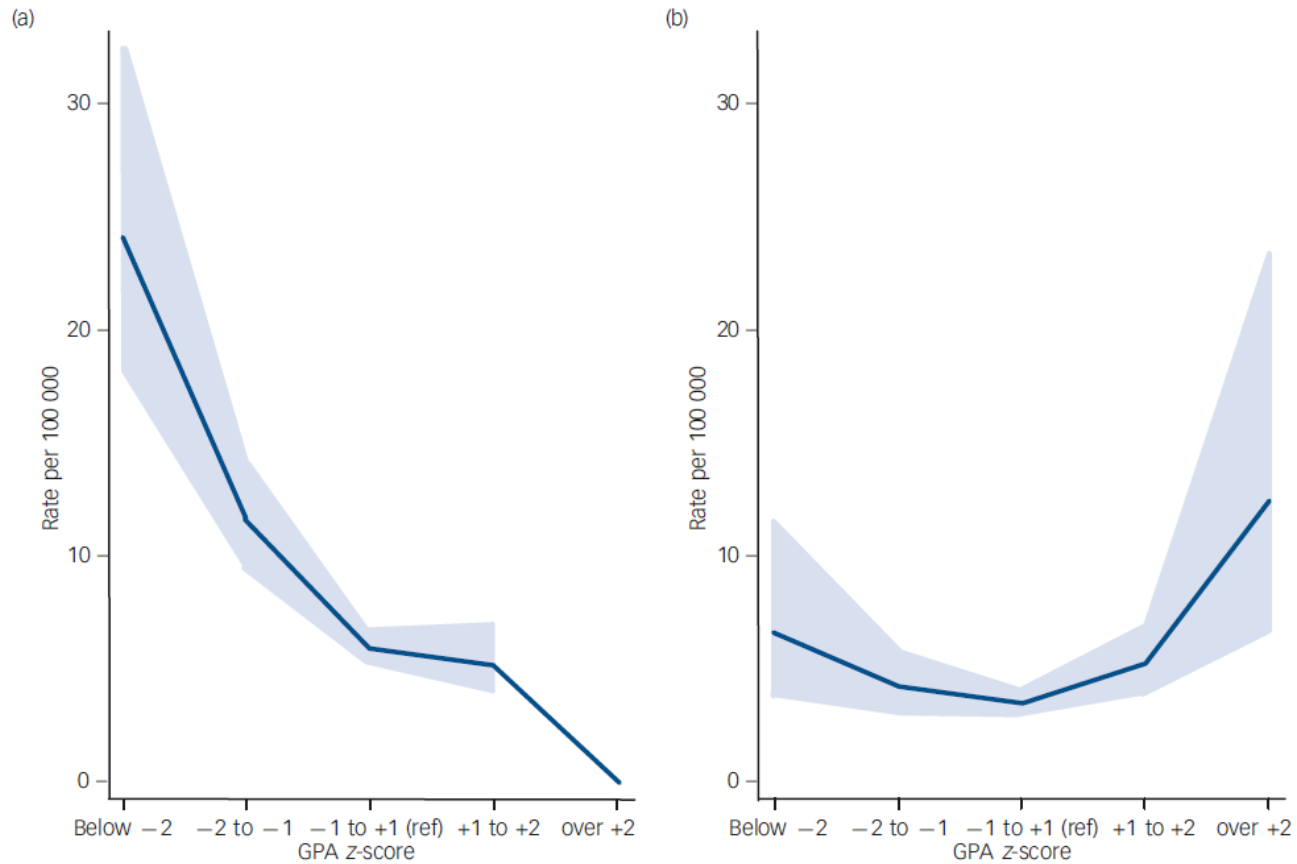


Fig. 1 Incidence rate of (a) schizophrenia and (b) bipolar disorder by grade-point average. The 95% confidence intervals are indicated by the shaded areas.

(Hypo)mane Episoden bei Jugendlichen

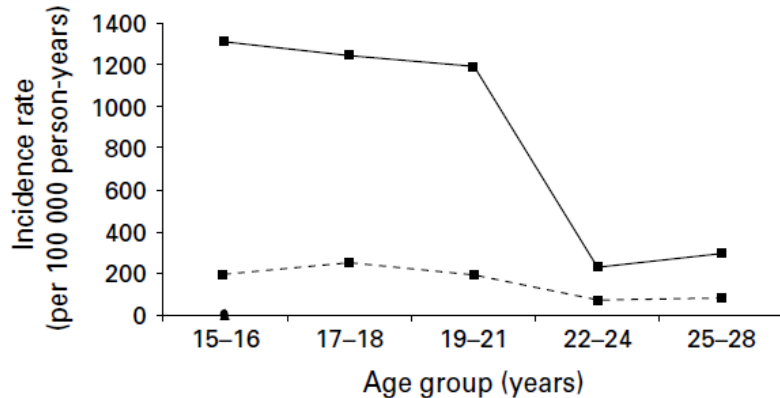


Fig. 1. Incidence of (hypo)manic disorder, stratified by age and care. —■—, (Hypo)manic episode^{a,b}; - -■- -, (hypo)manic episode^{a,b}, MHC+. MHC+, episodes in combination with mental health care. ^a (Hypo)manic episode: either hypomanic or manic episode. ^b Independent of having lifetime depressive episodes.

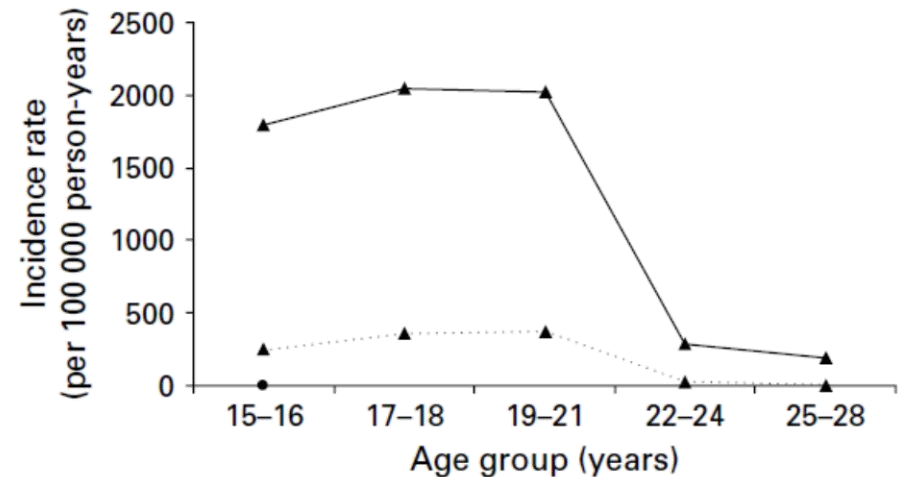
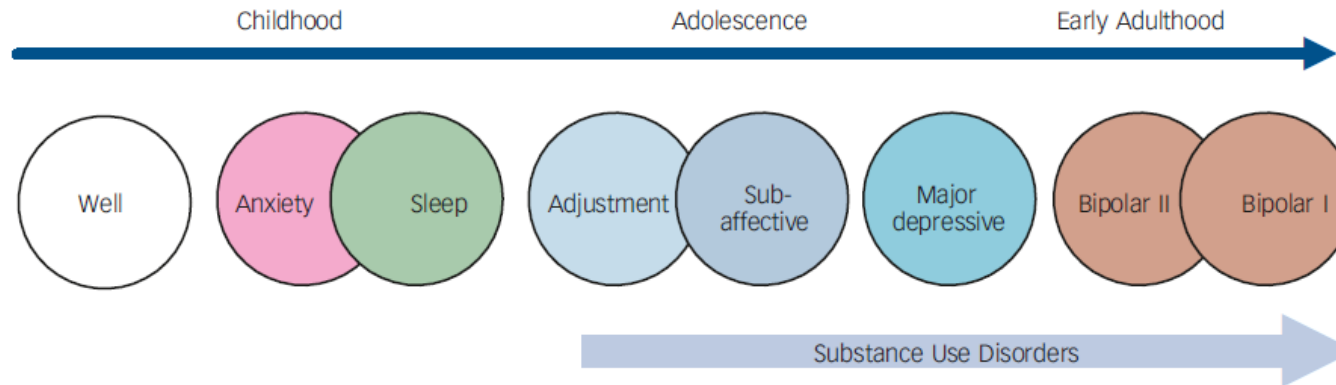


Fig. 3. Incidence of experienced distress in participants with ≥ 4 (hypo)manic symptoms, stratified by age and care. —▲—, Some distress; ···▲···, some distress, MHC+. MHC+, distress in combination with mental health care.

Results. Incidence rates (IRs) of both (hypo)manic episodes and (hypo)manic symptoms (at least one DSM-IV core symptom) were far higher (714/10⁵ person-years and 1720/10⁵ person-years respectively) than traditional estimates. In addition, the risk of developing (hypo)manic episodes was very low after the age of 21 years [hazard ratio (HR) 0.031, 95% confidence interval (CI) 0.0050–0.19], independent of childhood disorders such as attention deficit hyperactivity disorder (ADHD). Most individuals with hypomanic and manic episodes were never in care (87% and 62% respectively) and not presenting co-morbid depressive episodes (69% and 60% respectively). The probability of mental health care increased linearly with the number of symptoms on the mania symptom scale. The incidence of the bipolar categories, in particular at the level of clinical morbidity, was strongly associated with previous childhood disorders and male sex.

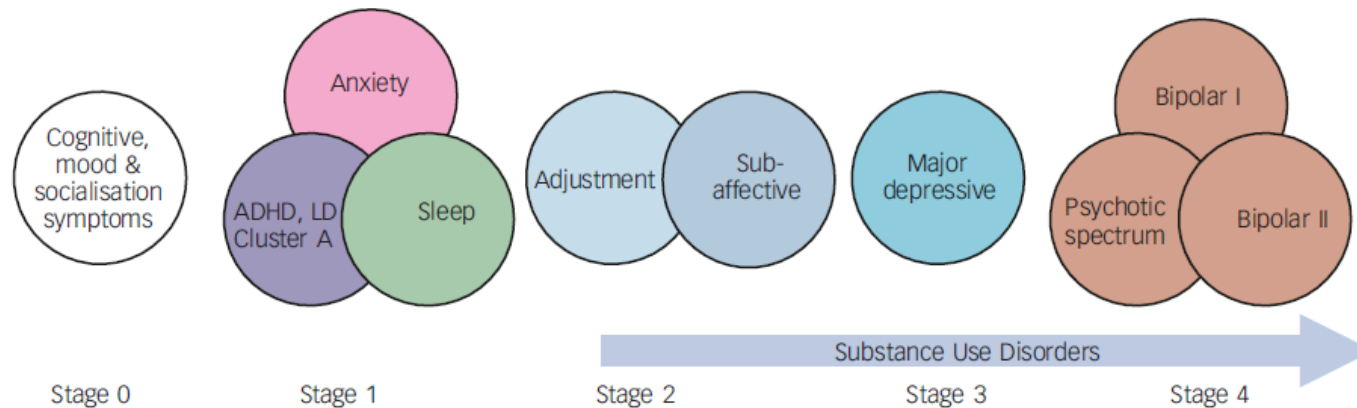
ADHD & BPD – Entwicklungsperspektive

Staging for offspring of Lithium Responsive Parents



Lithium Non-Responder sind die „Problemgruppe“
Alda-Score!

Staging for offspring of Lithium Non-Responsive Parents



ADHD & BPD – Entwicklungsperspektive

Article

Psychiatric Disorders in Preschool Offspring of Parents With Bipolar Disorder: The Pittsburgh Bipolar Offspring Study (BIOS)

Boris Birmaher, M.D.

David Axelson, M.D.

Benjamin Goldstein, M.D.

Kelly Monk, R.N.

Catherine Kalas, R.N.

Mihaela Obreja, M.S.

Mary Beth Hickey, B.A.

Satish Iyengar, Ph.D.

David Brent, M.D.

Wael Shamseddeen, M.D.

Rasim Diler, M.D.

David Kupfer, M.D.

Objective: The authors evaluated lifetime prevalence and specificity of DSM-IV psychiatric disorders and severity of depressive and manic symptoms at intake in preschool offspring of parents with bipolar I and II disorders.

Method: A total of 121 offspring ages 2–5 years from 83 parents with bipolar disorder and 102 offspring of 65 demographically matched comparison parents (29 with non-bipolar psychiatric disorders and 36 without any lifetime psychopathology) were recruited for the study. Parents with bipolar disorder were recruited through advertisements and adult outpatient clinics, and comparison parents were ascertained at random from the community. Participants were evaluated with standardized instruments. All staff were blind to parental diagnoses.

Results: After adjustment for within-family correlations and both biological parents' non-bipolar psychopathology, offspring of parents with bipolar disorder,

particularly those older than age 4, showed an eightfold greater lifetime prevalence of attention deficit hyperactivity disorder (ADHD) and significantly higher rates of having two or more psychiatric disorders compared to the offspring of the comparison parents. While only three offspring of parents with bipolar disorder had mood disorders, offspring of parents with bipolar disorder, especially those with ADHD and oppositional defiant disorder, had significantly more severe current manic and depressive symptoms than comparison offspring.

Conclusions: Preschool offspring of parents with bipolar disorder have an elevated risk for ADHD and have greater levels of subthreshold manic and depressive symptoms than children of comparison parents. Longitudinal follow-up is warranted to evaluate whether these children are at high risk for developing mood and other psychiatric disorders.

Epidemiologie BPD / adultes ADHD Co-morbidität

Primäres Sample **bipolar**

| Autor/Jahr | n (BPD) | Rate | Dx Bip | Dx ADHD | Sonstiges |
|-----------------|---------|------|------------------------|-----------------|----------------------|
| Nierenberg 2005 | 919 | 9.5% | MINI | MINI | STEP-BD, akute Ph. |
| Kessler 2006 | Pop. | 21% | CIDI | Semistr. | NCSR |
| Tammam 2006 | 44 | 16% | SCID-I | DSM-Crit., WURS | Remittiert Bipolar-I |
| McIntyre 2010 | 175 | 18% | MINI+, MDQ, ASRS, WURS | | Akute Phase |
| Bernardi 2010 | 100 | 10% | SCID-I | DSM, WURS | Euthymie |
| Reif in prep. | 43 | 20% | OPCRIT | DSM, WURS... | Euthymie |

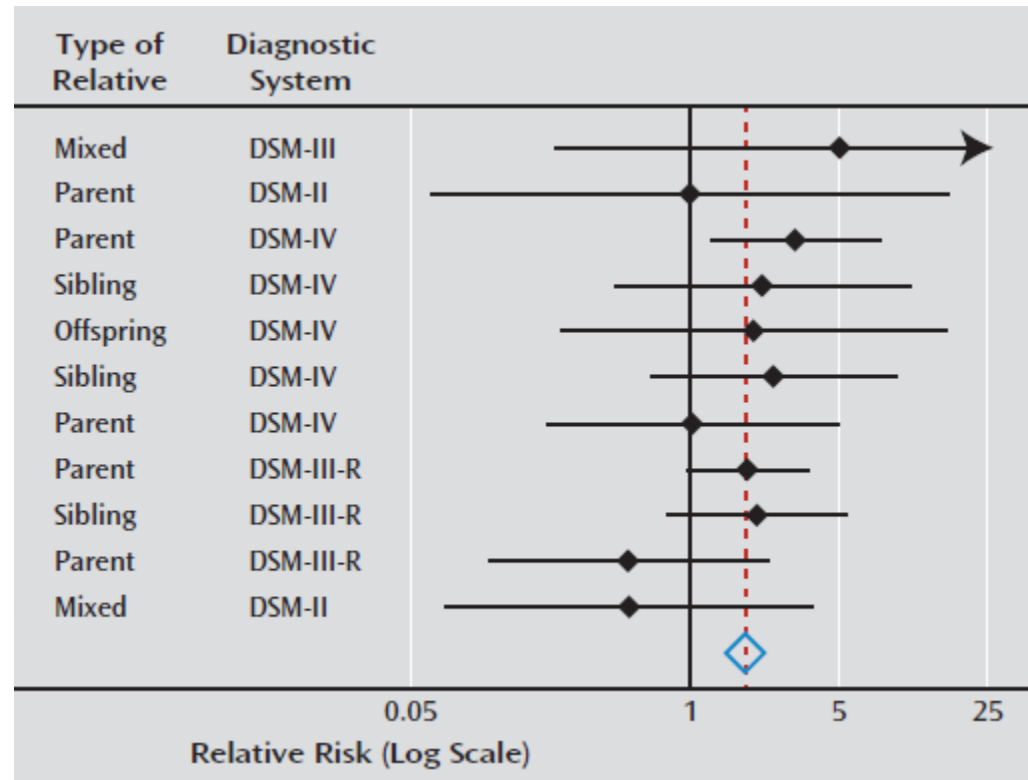
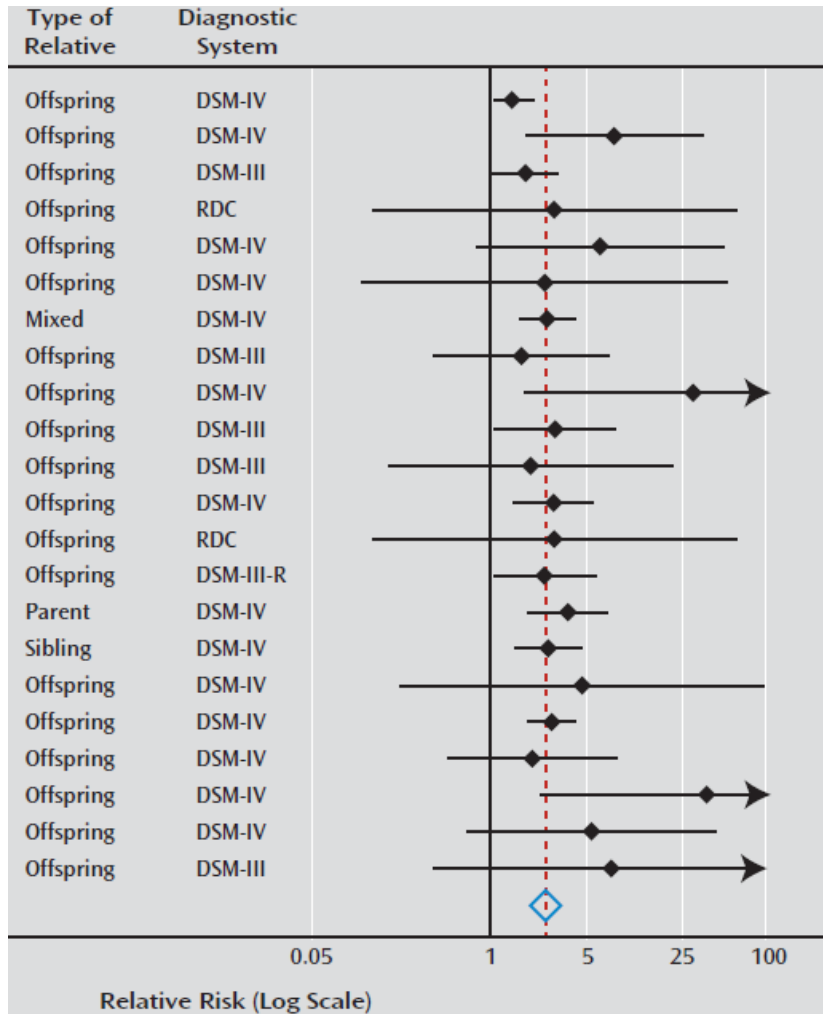
Primäres sample **adultes ADHD**

| Autor/Jahr | n (ADHD) | Rate | Dx Bip | Dx ADHD | Sonstiges |
|-----------------|------------|--------|---------------------|------------------|-------------------|
| Wilens 2003 | 51 | 47% | SCID | SCID / DSM-Crit. | |
| McGough 2005 | 79 | 5.1% | SADS | DSM-Crit. | Selected sample |
| Kessler 2006 | Pop. | 19% | CIDI | Semistr. | NCSR |
| Faraone 2005 | 127 | 18% | SCID | SCID / DSM-Crit. | |
| Halmoy 2009 | 510 | 51/32% | MDQ | ICD-10 RC, ASRS | Screening/Interv. |
| Park 2010 | 69 (pop.) | 9% | CIDI | ASRS | Laien-Interview |
| Friedrichs 2010 | 227 (pop.) | OR=8 | -- self report acc. | DSM-IV - | |

Meta-Analyse Familien-basierter Studien

Primäres Sample **bipolar**

Primäres Sample **adultes ADHD**



Meta-Analyse familienbasierter Studien (Anwesenheit der heterotypen Erkrankung in Angehörigen) legt eine gemeinsame genetische Basis für BPD und ADHD nahe (Sub-Gruppe?)

Staging-Modell bipolarer Störungen

Leitliniengerechte Diagnostik und Therapie, Langzeitbeobachtung

**Therapie bei Suizidalität,
Komorbidität, Therapieresistenz**

Einbindung von Selbsthilfe

Früherkennung und Frühintervention

Krankheitsverlauf

Erste
Symptome

Erste
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Erst-
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Erneute
Episoden

Chronifizierung

(Phasenübergreifende) Biomarker:

Auswahl aus: Schlaf/Rhythmik, Immunantwort, Kognition, Neurophysiologie, Emotionen/
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Öffentlichkeitsarbeit: altersadaptierte Aufklärungs- und Antistigmaarbeit

Staging-Modell bipolarer Störungen

Alter

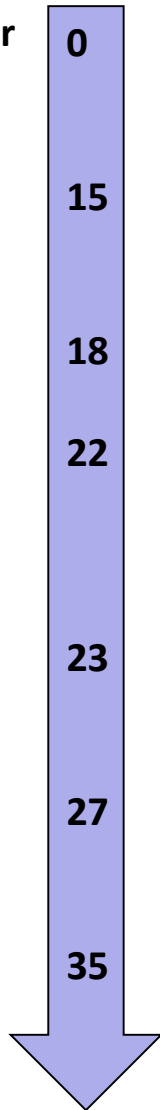


Table 1. Clinical presentation of the staging model of bipolar disorder, strategies for genetic analysis and neuroimaging findings

| Clinical stage | Clinical presentation | Strategies for genetic analysis | Neuroimaging findings |
|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 0 | Increased risk of bipolar disorder; no symptoms currently | Evaluate endophenotypes using GWAS confirmed SNPs; risk prediction studies | <i>Resilience markers:</i> abnormal prefrontal cortical activity increases during cognitive control of emotion and cognitive control tasks; abnormal volumetric increases in right-sided vIPFC and left-sided subcortical regions <i>Risk markers:</i> Abnormally increased amygdala activity; abnormal prefrontal WM |
| 1a | Mild or nonspecific symptoms | Evaluate putative endophenotypes using GWAS confirmed SNPs | <i>Resilience markers:</i> Abnormally increased prefrontal cortical activity during cognitive control of emotion and cognitive control tasks; abnormally increased prefrontal cortical volume <i>Risk markers:</i> Abnormally decreased prefrontal cortical volumes; left-sided subcortical volume increases; abnormally decreased WM volume |
| 1b | Ultra-high-risk: moderate but subthreshold symptoms, with neurocognitive changes and functional decline to caseness | Discovery of rare variants and <i>de novo</i> mutations | |
| 2 | First episode of bipolar disorder; full threshold disorder with moderate to severe symptoms, neurocognitive deficits and functional decline | Mapping endophenotypes, biomarker studies | <i>Theme 1:</i> Abnormally decreased prefrontal cortical activity (especially right-sided vIPFC activity) during cognitive control of emotion and cognitive control tasks; abnormally increased amygdala activity during these tasks; abnormally decreased prefrontal cortical volumes and decreased prefrontal WM; altered subcortical volumes <i>Theme 2:</i> Abnormally increased left-sided striatal and prefrontal cortical activity during reward processing |
| 3a | Incomplete remission from first episode (could be linked or fast-tracked to Stage 4) | Contribute to GWAS mega analyses | <i>Markers of disease progression:</i> A negative association between prefrontal cortical volumes (especially right vIPFC gray matter volume) and illness duration; reductions in amygdala, striatal and hippocampal volumes with illness progression |
| 3b | Recurrence or relapse of psychotic or mood disorder which stabilizes with treatment, residual symptoms or neurocognition below the best level achieved following remission from first episode | Pleiotropy analysis, examine longitudinal trajectories | |
| 4 | Severe, persistent illness as judged on symptoms, neurocognition and disability criteria | Pleiotropy analysis, examine longitudinal trajectories | |

Abbreviations: GWAS, genome-wide association studies; SNP, single-nucleotide polymorphism; vIPFC, ventrolateral prefrontal cortex; WM, white matter. Adapted from Scott *et al.*³.

Das bipolare Prodrom

Symptoms and signs of the initial prodrome of bipolar disorder A systematic review

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ABSTRACT

Background: Systematic studies addressing symptoms, signs and temporal aspects of initial bipolar prodrome are reviewed to identify potential clinical targets for early intervention.

Methods: The databases PsycINFO, PubMed, EMBASE and British Nursing Index were searched for original studies.

Results: Eight studies were identified. Irritability and aggressiveness, sleep disturbances, depression and mania symptoms/signs, hyperactivity, anxiety, and mood swings are clusters representing common symptoms and signs of the distal prodrome of bipolar disorder (BD). As time to full BD onset decreases, symptoms of mania and depression seem to increase gradually in strength and prevalence. The specificity of prodromal symptoms and signs appears to be low. Not every person who develops BD experiences a prolonged initial prodrome to the full illness. Current data on the mean duration of the prodrome are contradictory, ranging from 1.8 to 7.3 years. No qualitative studies were found.

Limitations: Because of the scarcity of data, studies that did not explicitly investigate bipolar prodrome were included when thematically relevant. The selected studies are methodologically diverse and the validity of some findings is questionable. Findings must be interpreted cautiously.

Conclusions: The initial prodrome of BD is characterized by dysregulation of mood and energy. Because of the apparently low specificity of prodromal symptoms and signs of BD, it is currently neither possible nor advisable to predict the development of BD based solely on early phenomenology. More well-designed in-depth studies, including qualitative ones, are needed to characterize the initial bipolar prodrome.

Zeit zur Konversion Unipolar > Bipolar

FIGURE 1. Kaplan-Meier Survival Curves for Time to Change in Diagnosis for Patients With Major Depressive Disorder (N=550)^a

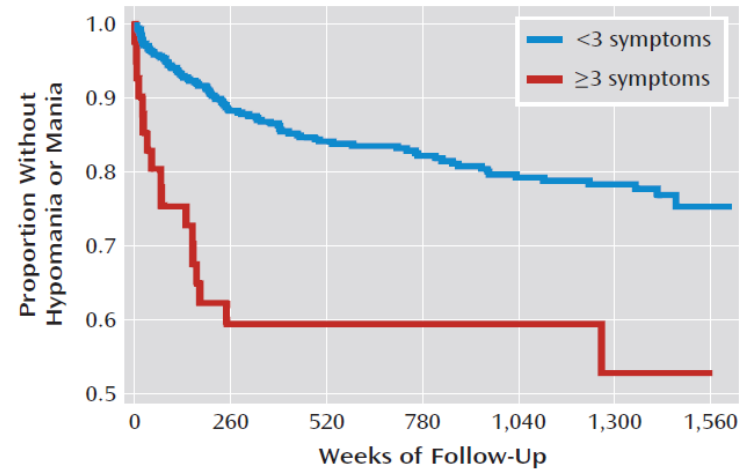
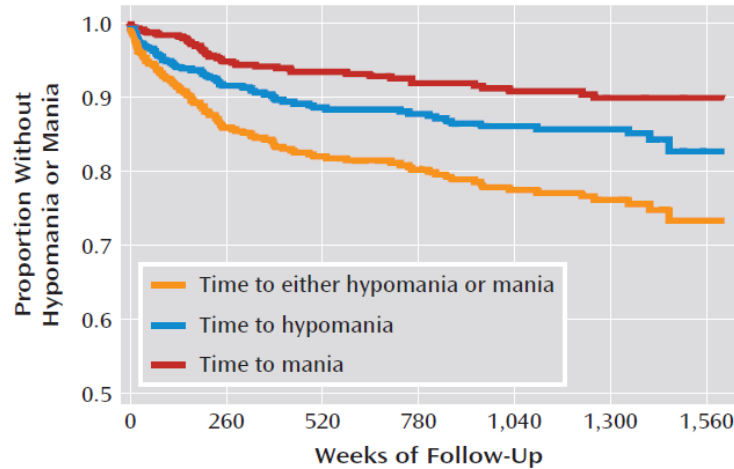


TABLE 3. Cox Proportional Hazards Ratio Estimates, With Covariates, for the Association of Number of Positive Mania Screen Items With Onset of Mania or Hypomania in Major Depression

| Variable | Hazard Ratio | 95% CI | p |
|---------------------------------------------------|--------------|-----------|--------|
| Model 1: Time to either hypomania or mania | | | |
| Number of positive manic screens | 1.24 | 1.09–1.41 | 0.001 |
| Age at onset | 0.97 | 0.95–1.00 | 0.02 |
| Family history of bipolar disorder | 1.91 | 1.18–3.08 | 0.008 |
| Psychosis | 1.97 | 1.25–3.10 | 0.004 |
| Age at intake | 1.00 | 0.98–1.03 | 0.67 |
| Model 2: Time to mania | | | |
| Number of positive manic screens | 1.40 | 1.16–1.68 | 0.0004 |
| Age at onset | 0.98 | 0.95–1.02 | 0.34 |
| Family history of bipolar disorder ³ | 1.93 | 0.88–4.21 | 0.10 |
| Psychosis | 3.54 | 1.85–6.77 | 0.0001 |
| Age at intake | 1.01 | 0.98–1.05 | 0.41 |

Staging-Modell bipolarer Störungen: what's next?

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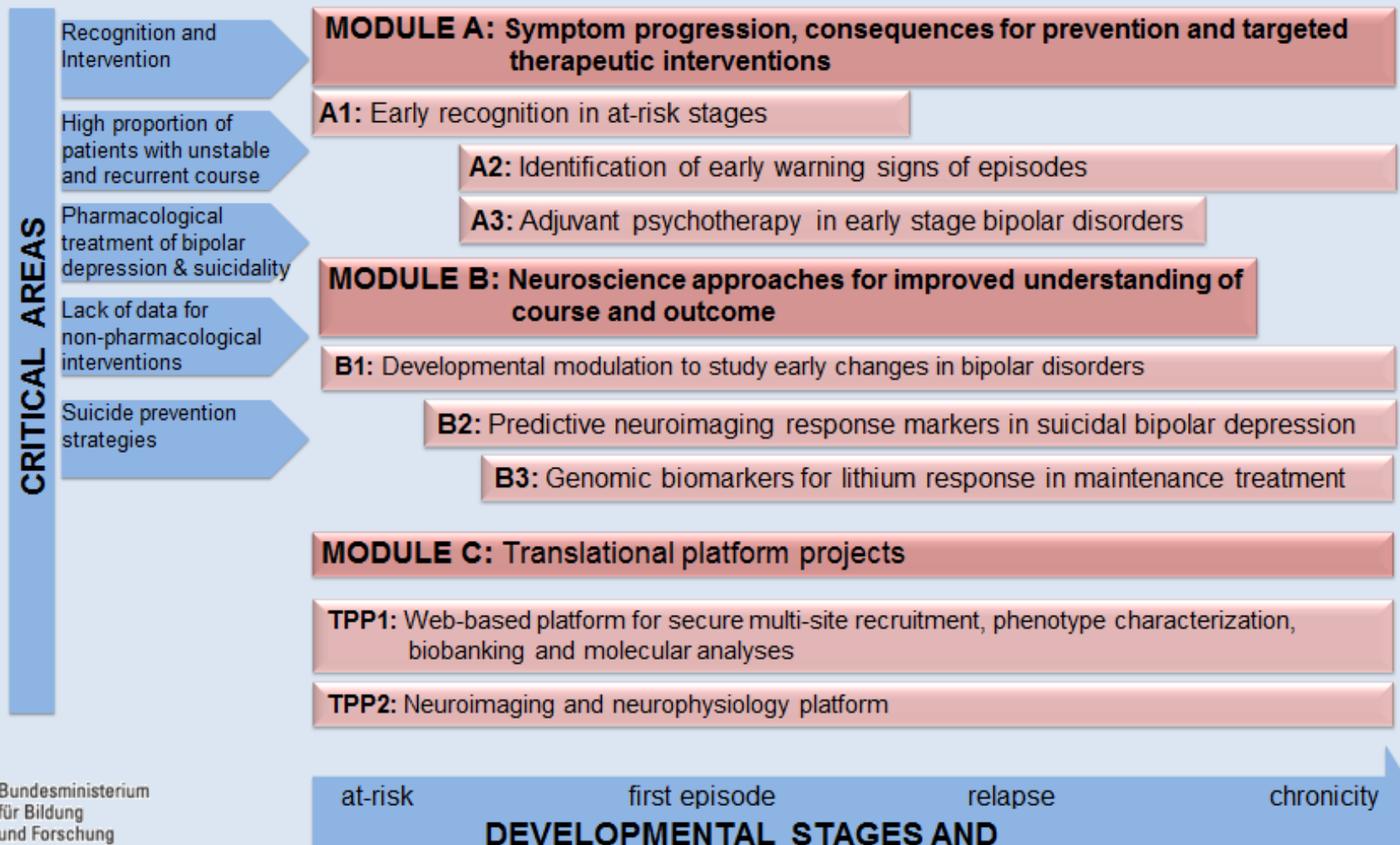
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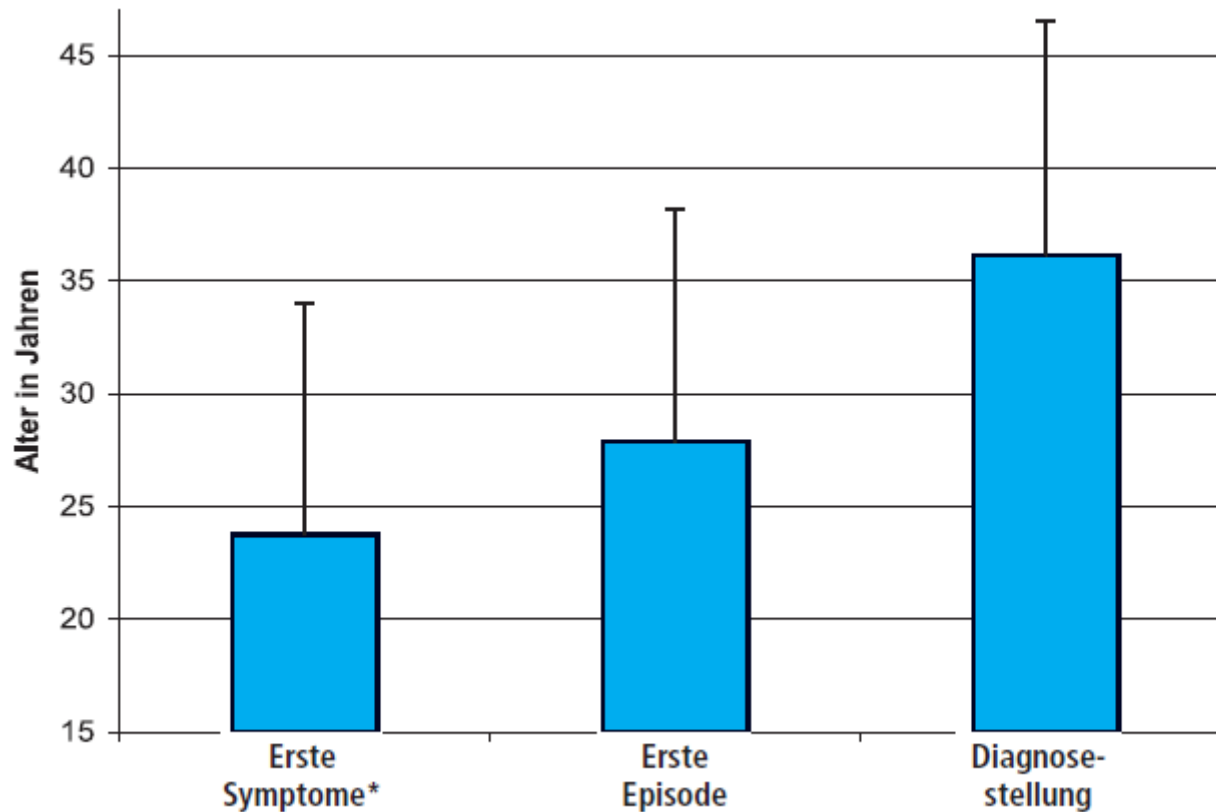
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BMBF BipoLife (Beginn 2015)

DRESDEN-TÜBINGEN-BERLIN-BOCHUM-MARBURG-HAMBURG-WÜRZBURG-GÖTTINGEN
International collaborations • German Association for Bipolar Disorders • Associate national partners



Dauer von Auftreten erster Symptome bis Diagnosestellung bei Bipolarer Störung



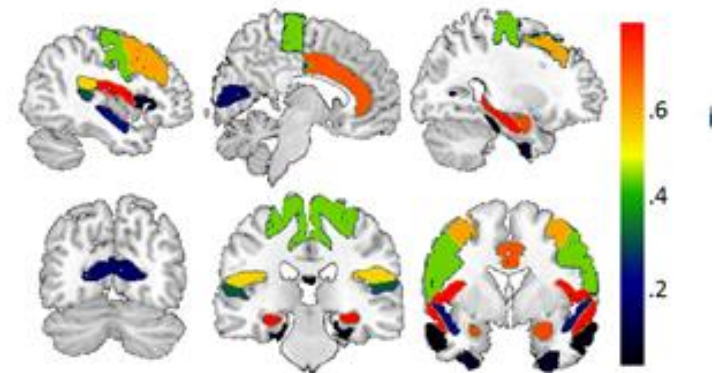
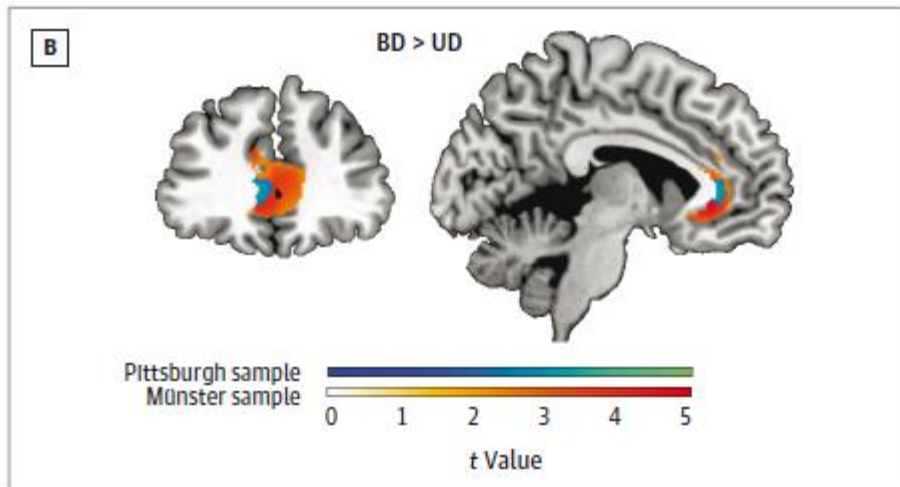
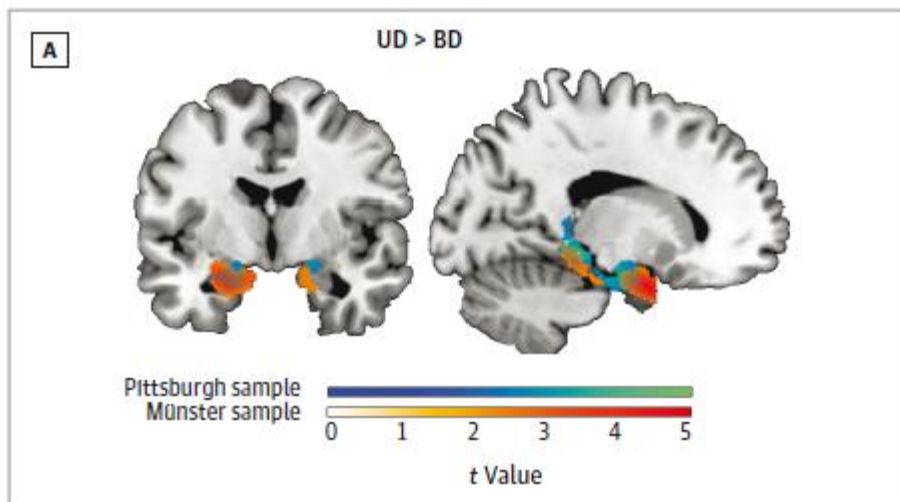


**Je länger eine Bipolare Störung unbehandelt bleibt,
desto ...**

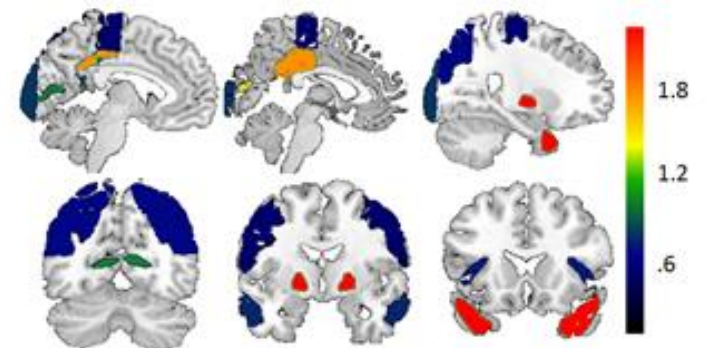
- **länger dauern die Krankheitsphasen**
- **schlimmer sind die Symptome**
- **mehr Episoden solcher Phasen treten auf**
- **weniger und kürzer sind die gesunden Phasen**

Notwendigkeit für frühprädiaktive Biomarker!!!

Bildgebung – Prädiktoren



Akquisition

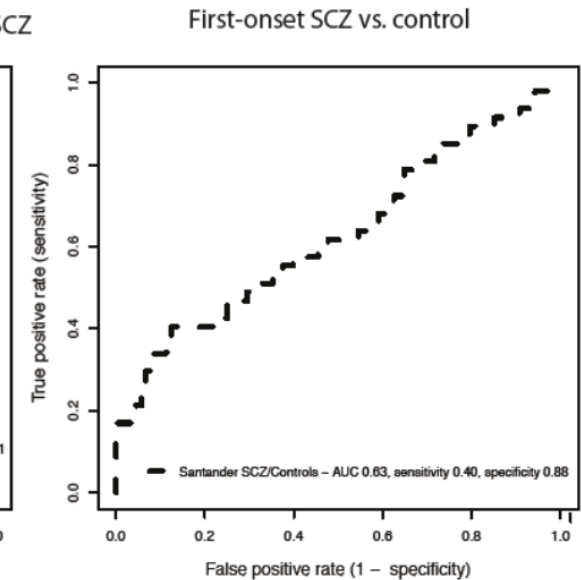
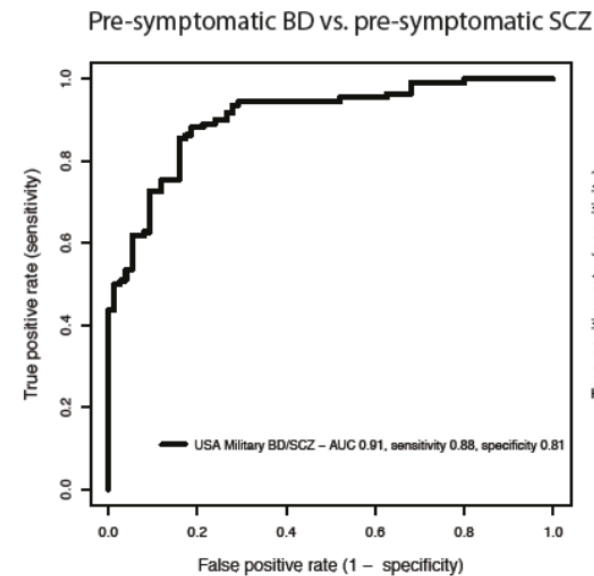
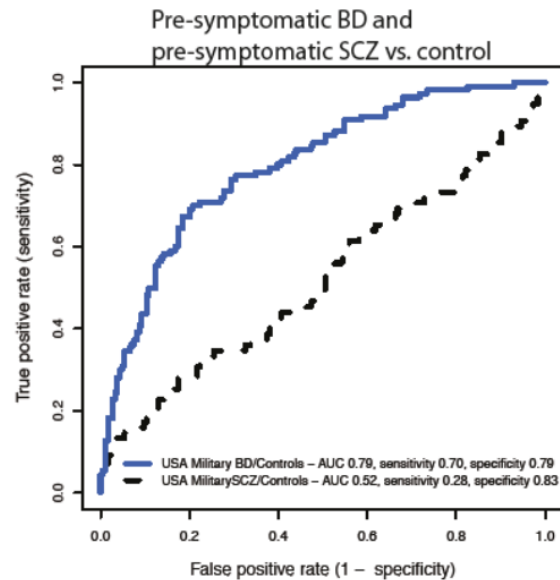
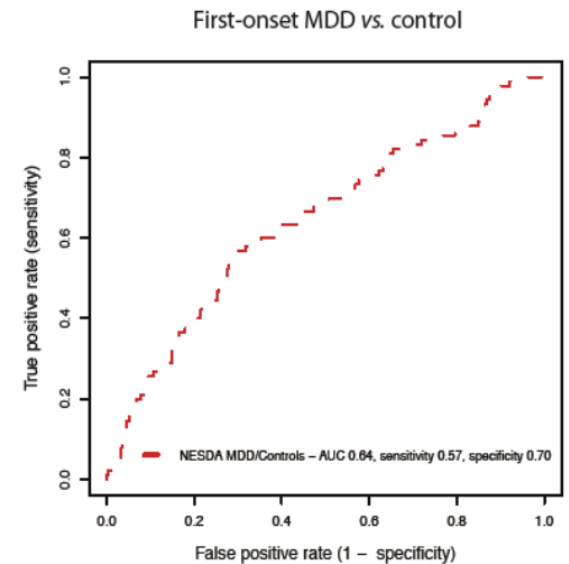
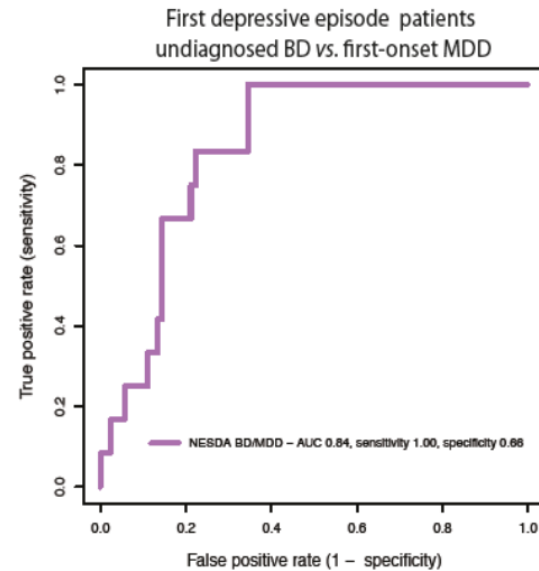
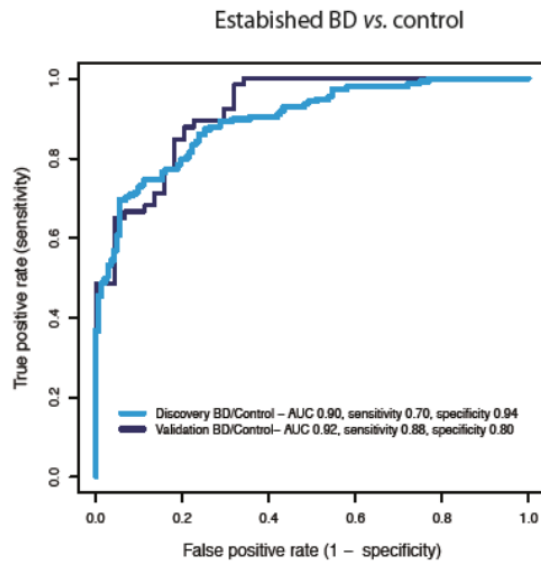


Extinktion

**Strukt. MRT: Differentialdiagnose
Depression vs. bipolare Störung**

**fRMT: Response auf CBT
bei der Panikstörung**

Proteomik – Prädiktoren



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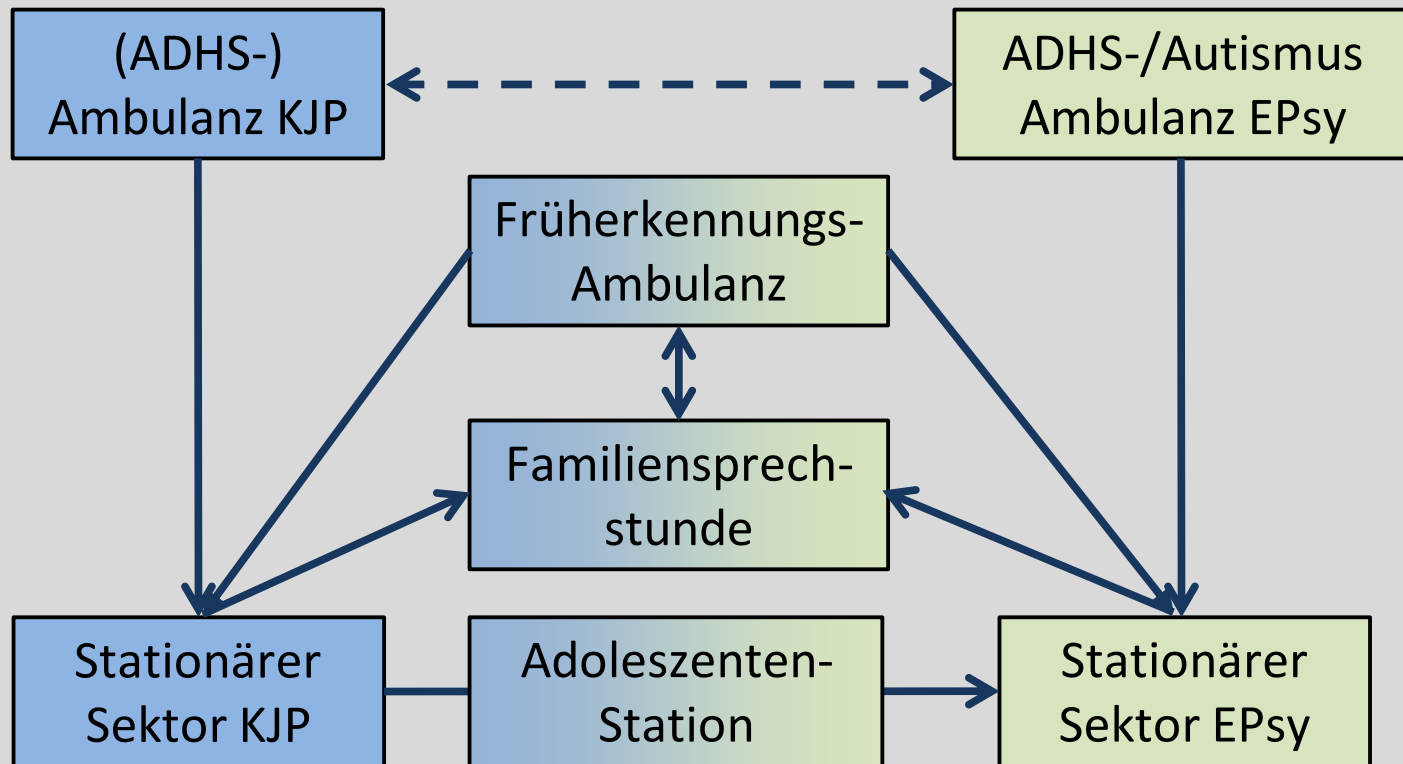
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Eröffnungssymposium D-ZEP: 21.09.2012, Haus 23

| | | |
|--------------------|---------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| 15:00-15:30 | Prof. Dr. Reif Prof. Dr. Freitag | Einführung |
| 15:30-16:00 | Prof. Dr. Barbara Franke | Molecular Psychiatry of neurodevelopmental disorders: from gene finding to understanding disease biology |
| 16:00-16:30 | Prof. Dr. Andreas Heinz | Entwicklung von Suchterkrankungen |
| 16:30-17:00 | Prof. Jan Buitelaar | Results from NeuroIMAGE: a prospective longitudinal DNAXMRI integrated study of childhood ADHD |
| 17:30-18:00 | Prof. Dr. Andreas Fallgatter | Neurophysiologische Grundlagen der ADHS |
| 18:00-18:30 | Prof. Dr. Johannes Hebebrand | Übergewicht und psychische Störungen |
| 18:30-19:00 | Prof. Dr. Martin Hautzinger | Kognitive Verhaltenstherapie bei Depressionen im höheren Lebensalter |
| 19:00 | Podiumsdiskussion | Wohin soll es gemeinsam gehen? |