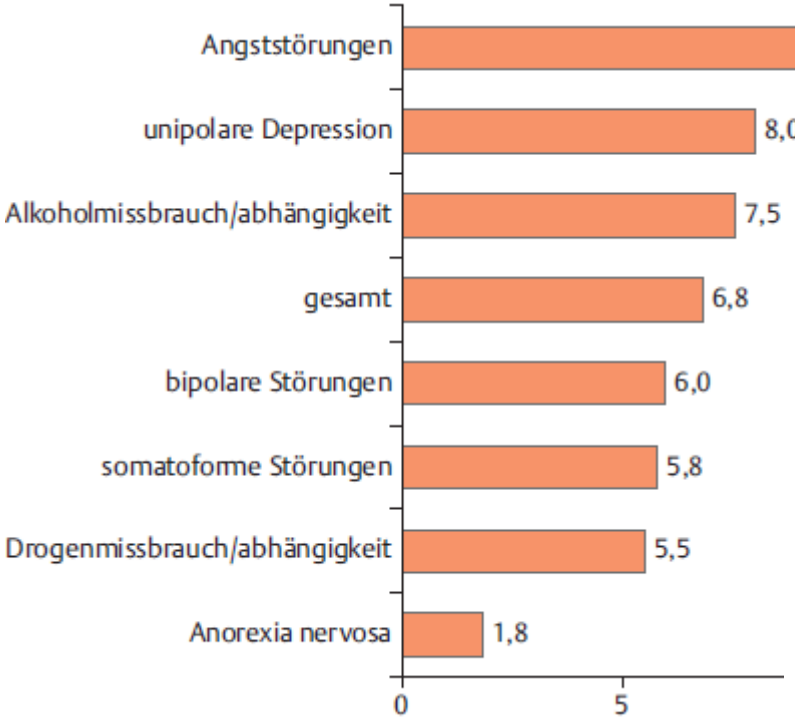
Universitätsklinikum Carl Gustav Carus
DIE DRESDNER.

Früherkennung bipolarer Störungen – Was wir bisher wissen...

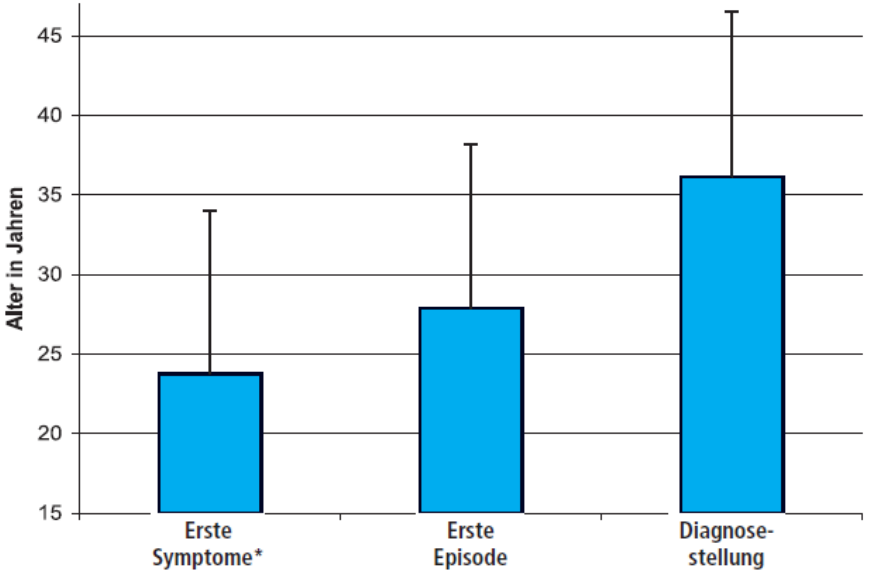
Andrea Pfennig

Wir erkennen und behandeln zu spät!

Behandlungsverzögerung
in Jahren
Lambert et al., Fortschritte Neurol Psychiat 2013



Zeit von ersten Symptomen
bis Diagnosestellung
Pfennig et al., Nervenheilkunde 2011



Konsequenzen

- Früher Beginn und lange Dauer bis zum Beginn einer adäquaten Behandlung assoziiert mit
  - schwererem Krankheitsverlauf[1]
  - erhöhtem Risiko für Arbeitsunfähigkeit und Jobverlust[2]

Frühzeitige Erkennung und Behandlung erscheinen dringend indiziert!

[1]Post RM et al., 2010; [2]McCraw et al., 2014

Früherkennungszentren in Deutschland

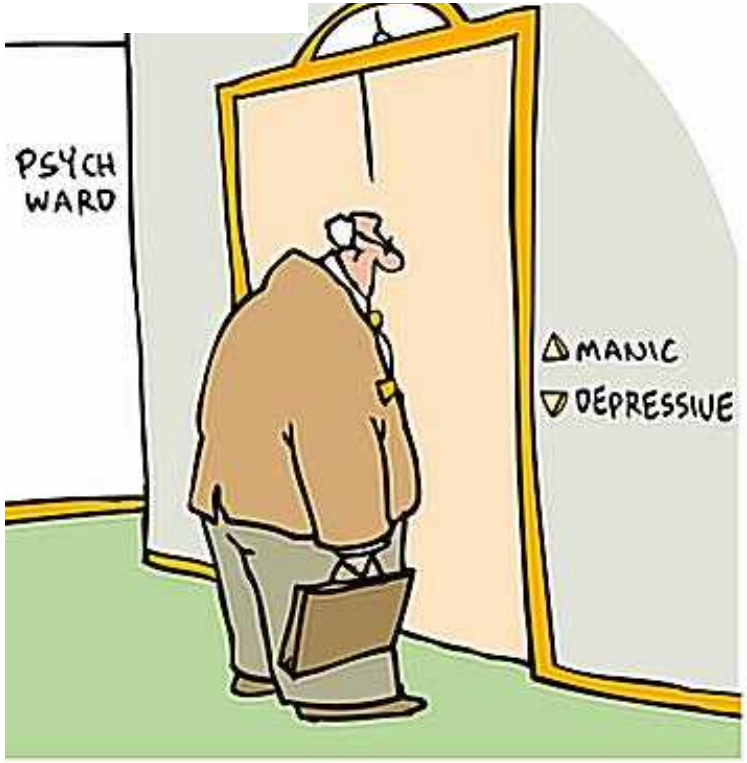
Für Psychosen:

- 1997 Uniklinikum Köln (**F**rüh**E**rkennungs- und **T**herapie**Z**entrum für beginnende Psychosen)
- 2000 Bonn, Düsseldorf und München
- 2003 Berlin Charité
- 2006 Bochum
- Weitere Zentren

Fokuserweiterung auf Spektrum der affektiven Störungen:

- 2008 Dresden, Bochum
- 2010 weitere Zentren (Hamburg, Berlin, Köln, Frankfurt)

Welche Faktoren sprechen für ein erhöhtes Risiko für bipolare Störungen?



Positive Familien-Anamnese

Table 2 Cumulative incidence (CI) of lifetime DSM-IV diagnoses

	High-risk offspring CI (%)	Control offspring CI (%)		HR	*P*
Bipolar disorder spectrum	22.21	0	→	20.885[d]*	0.039[d]*
Bipolar disorder type I	3.41	0		3.766[d]	0.421[d]
Bipolar disorder type II	6.24	0		8.315[d]	0.184[d]
Bipolar disorder NOS	7.29	0		6.220[d]	0.254[d]
Schizoaffective disorder	4.79	0		2.974[d]	0.556[d]
Cyclothymia	0.47	0		1.250[d,e]	0.923[d,e]
Depressive spectrum	61.11	45.57		1.632	0.073
Major depressive disorder	31.69	3.28	→	17.157*	0.004*
Depression NOS	7.77	1.56		3.443[e]	0.235[e]
Dysthymia	1.21	0		1.648[d]	0.811[d]
Adjustment disorder	20.44	40.72		0.624	0.137
Non-mood disorder					
Anxiety disorder	23.27	11.90	→	2.199*	0.028*
Sleep disorder	20.81	0	→	28.209[d]*	0.022[d]*
Behavioural disordera	2.28	0		3.477[d]	0.449[d]
Neurodevelopmental disorder[b]	11.10	5.81		1.802	0.264
Substance use disorder	30.36	15.70	→	2.596	0.053
Psychotic disorder[c]	12.68	0		3.657[d]	0.420[d]

HR, hazard ratio; LiR, offspring of lithium responder parent; LiNR, offspring of lithium non-responder parent; NOS, not otherwise specified.
a. Behavioural disorders include oppositional defiant disorder and conduct disorder.
b. Neurodevelopmental disorders include attention-deficit hyperactivity disorder, learning disorder and Cluster A traits.
c. Psychotic disorders include schizophrenia, psychosis NOS, schizoid and schizotypal disorder.
d. Firth's method with Breslow's method for handling ties.
e. Not adjusted for socioeconomic status.
*$P < 0.05$.

Duffy et al., BJP 2014

Entwicklung bei positiver Familienanamnese

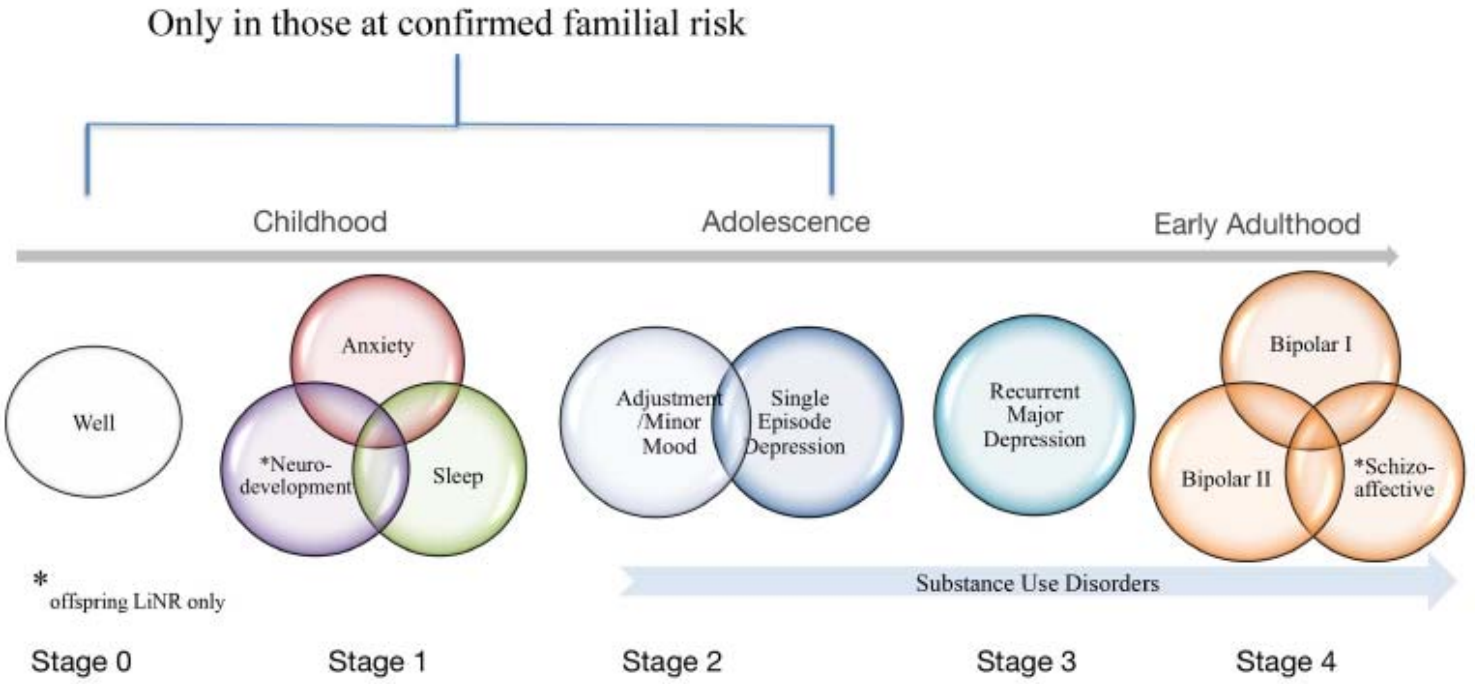


Figure 1 Development clinical staging model of bipolar disorder.

Duffy et al., Int J Neuropsychopharmacol. 2015

Verlauf der Erstmanifestation der Manie

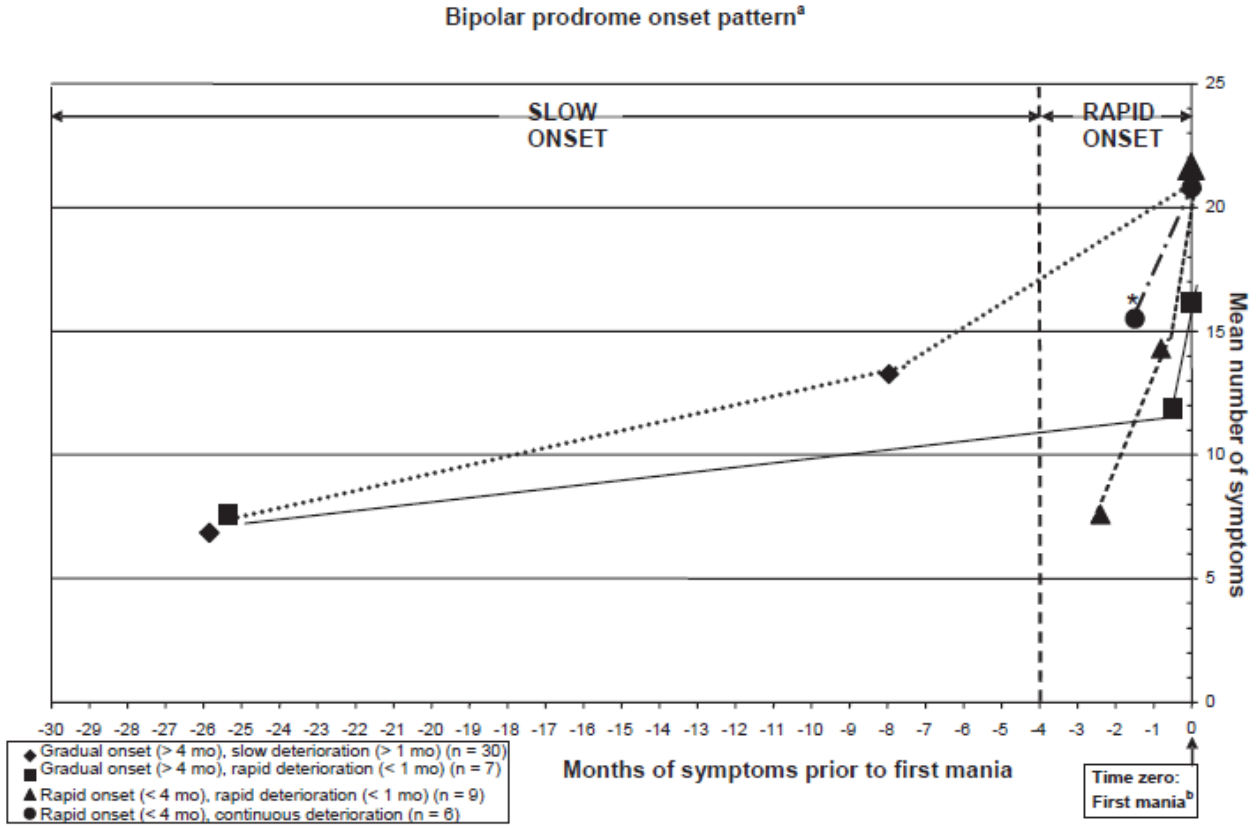
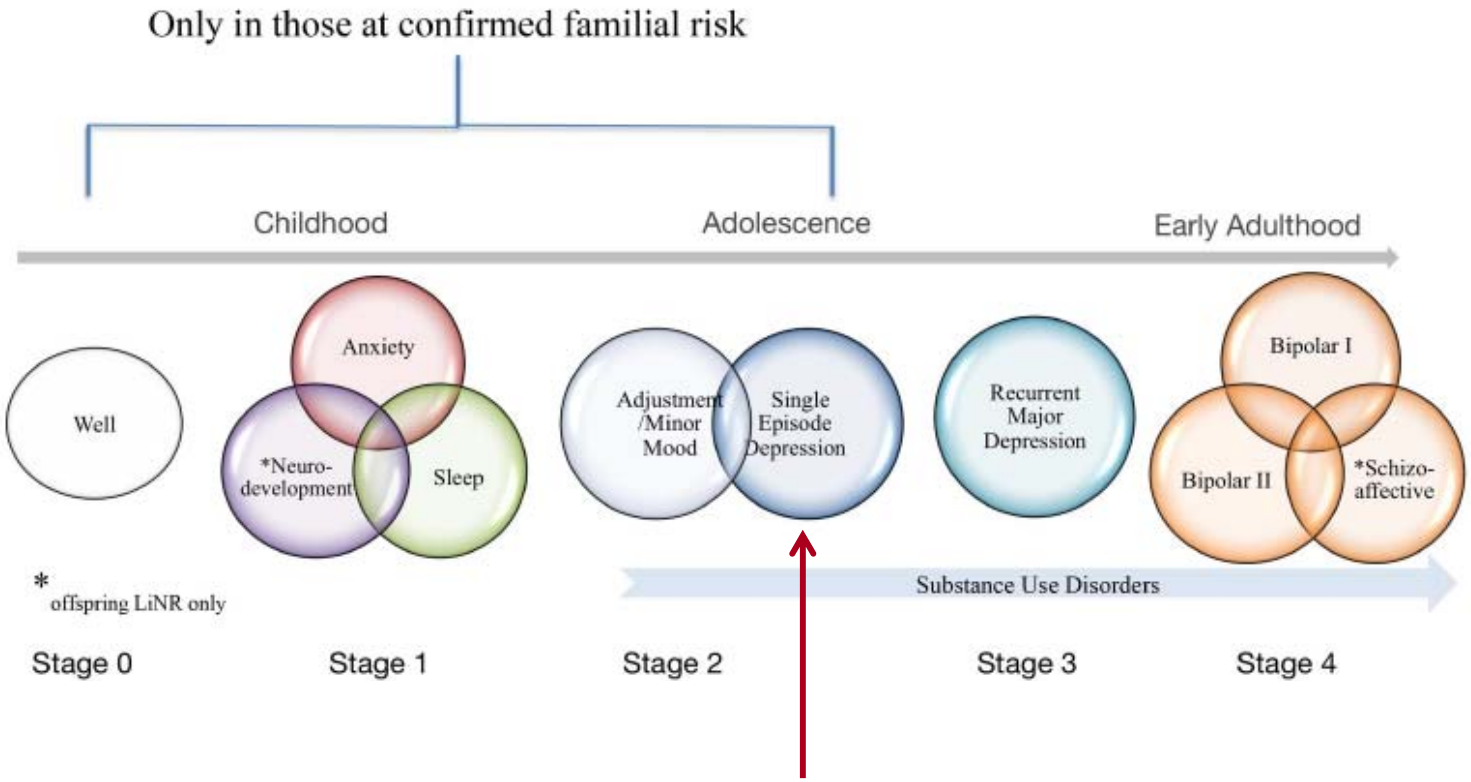


Fig. 1. Mean duration and number of prodromal symptoms during the mania prodrome onset and deterioration phase. mo = months. [a]Definition of onset pattern based on pragmatically *a priori*-defined duration threshold of four months for gradual versus rapid onset and of four weeks for slow versus rapid deterioration. The deterioration phase consists of a newly emerging symptom cluster after prodrome onset but before full mania criteria were met. [b]Time zero = mean number of symptoms during the first manic episode. *$F(3,48) = 7.19$, $p = 0.0004$ for number of symptoms during the onset phase.

Correll et al., Bipolar Disorders 2014



Unterscheiden sich die **ersten depressiven Episoden** bei jungen Menschen, die später eine bipolare Störung entwickeln und denen, die unipolar-depressiv bleiben?

Table 3. Comparison of the symptomatic profile, early bipolar vs. unipolar depression

	Non-converted $N = 659$		Converted to bipolar $N = 35$		OR adjusted for age, sex, age of onset and parental affective disorder			
Symptoms	*N*	%w	*N*	%w	OR	95% CI		*P*-value
Major depressive episode criteria symptoms								
Depressed mood	604	92.0	35	100.0	–			
Markedly diminished interest or pleasure	355	53.7	16	52.6	0.94	0.44	2.01	0.869
Significant weight loss/gain, or decrease/increase in appetite	312	47.1	17	55.6	1.49	0.65	3.45	0.347
Insomnia or hypersomnia	439	65.4	23	69.3	1.25	0.56	2.79	0.594
Psychomotor agitation or retardation	116	18.3	8	24.9	1.49	0.59	3.79	0.403
Fatigue or loss of energy	316	48.7	17	56.6	1.51	0.72	3.15	0.253
→ Feelings of worthlessness or excessive or inappropriate guilt	369	56.2	27	80.1	2.52	1.07	5.91	0.034
Diminished ability to think or concentrate, or indecisiveness	485	74.3	24	73.6	1.37	0.58	3.24	0.480
→ Recurrent thoughts of death, recurrent suicidal ideation, or a suicide attempt or a specific plan for committing suicide	340	50.0	24	73.7	2.31	1.04	5.12	0.039
Severity indicators								
Melancholic features								
Complete loss of interest	230	34.1	16	47.8	1.64	0.74	3.67	0.224
→ Complete loss of pleasure	203	31.4	18	56.2	2.53	1.23	5.22	0.012
→ Worse mood in the morning	369	56.6	28	85.4	4.30	1.73	10.65	0.002
At least 2 h early morning awakening	48	7.6	4	10.9	1.34	0.35	5.10	0.666
Decreased motor activity observed by others	62	9.0	4	9.2	1.07	0.32	3.63	0.908
Increased motor activity	99	15.7	9	30.4	1.85	0.79	4.32	0.157
Significant weight loss	148	23.9	6	22.1	0.87	0.28	2.67	0.804
Feeling guilty	156	22.9	12	28.3	1.17	0.52	2.62	0.709
Atypical features								
Affective reagibility	456	68.6	17	43.9	0.40	0.19	0.81	0.012
Significant weight gain due to overeating	35	5.2	4	17.4	2.12	0.48	9.46	0.324
Increased appetite	144	21.1	10	27.4	0.88	0.34	2.24	0.782
Increased sleep	198	30.9	9	27.4	0.75	0.30	1.87	0.538
Other severe symptoms								
Complete loss of appetite	104	17.3	6	24.6	1.49	0.58	3.81	0.404
Complete loss of sexual interest	95	15.8	4	11.3	0.58	0.17	2.04	0.396
Suicidal thoughts	188	27.7	12	43.4	1.28	0.55	2.96	0.566
Suicidal plans	82	11.5	7	25.8	1.01	0.37	2.78	0.978
Suicidal attempts	38	5.2	6	17.9	2.61	0.84	8.12	0.099

N, number; %w, percentage weighted; OR, odds ratio.

Pfennig et al., Acta Psychiatr Scand 2016

Angst / Angststörung

Table 1 Overview of the prevalence of anxiety disorders in recent longitudinal studies of offspring at high risk for bipolar disorder

Study (author, year)	Age (mean)	OR (95 % CI)[a]	Prevalence of anxiety disorders (*N*)	
			High-risk offspring	Control offspring
Birmaher, 2009 [31]	11.9	2.3 (1.3–4.0)	25.8 % (100/388)	10.8 % (27/251)
Nurnberger, 2011 [40]	16.7	2.1 (1.0–4.7)	26.2 % (37/141)	14.3 % (13/91)
Vandeleur, 2012 [41]	11.8	2.1 (1.2–3.8)	42.5 % (59/139)	22.8 % (29/127)
Duffy, 2013 [42•]	22.6	2.6 (1.2–6.4)	23.4 % (53/229)	10.42 % (9/86)
Mesman, 2013 [43]	16.5		25 % (27/108)	

[a] Odds ratios were obtained directly from the cited paper or calculated unadjusted from the raw numbers

Goes, Curr Psychiatry Rep 2015

Veränderungen Schlaf und zirkadiane Rhythmik

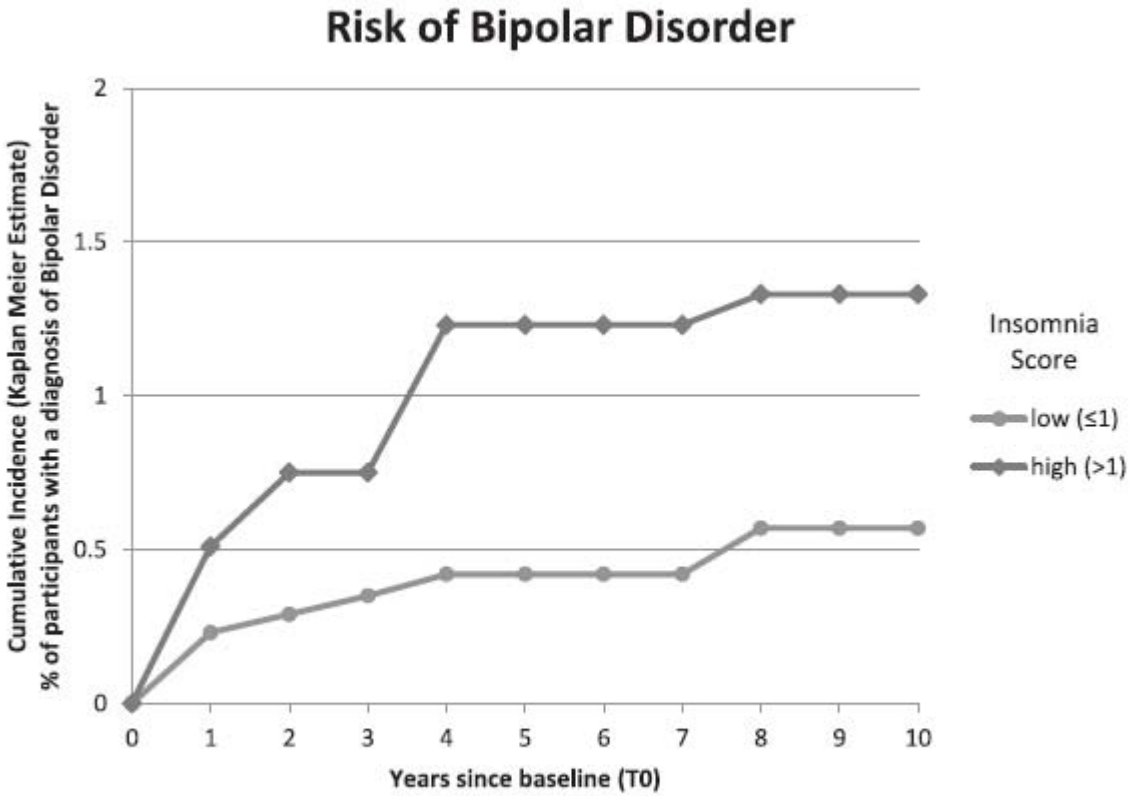


Fig. 1. Cumulative incidence of bipolar disorder for participants with a low (≤1) and high (>1) insomnia-score.

OR: 1.75

Besonders:
Schwierigkeiten, einzuschlafen;
Früherwachen

Ritter et al., J Psychiat Res 2015

Veränderungen Schlaf und zirkadiane Rhythmik

Fig. 1 *BIPS-Q results* Recurrent short hypersomnia (**a**) and recurrent short insomnia (**b**). The number of episodes is shown on the *y*-axis with 9 denoting >8 times. Post hoc pairwise comparison, $**p < 0.01$ versus control

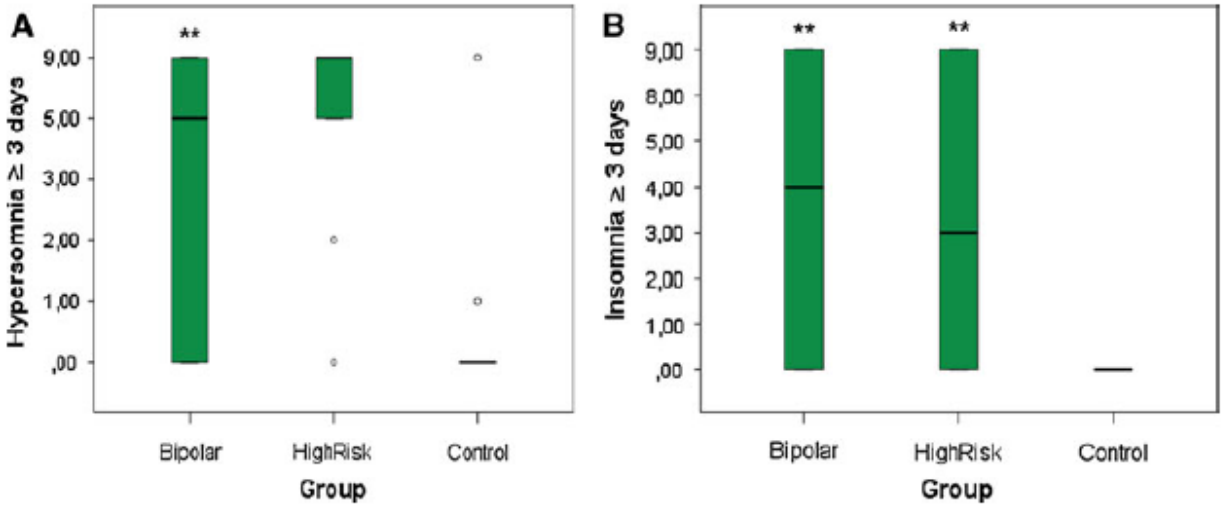
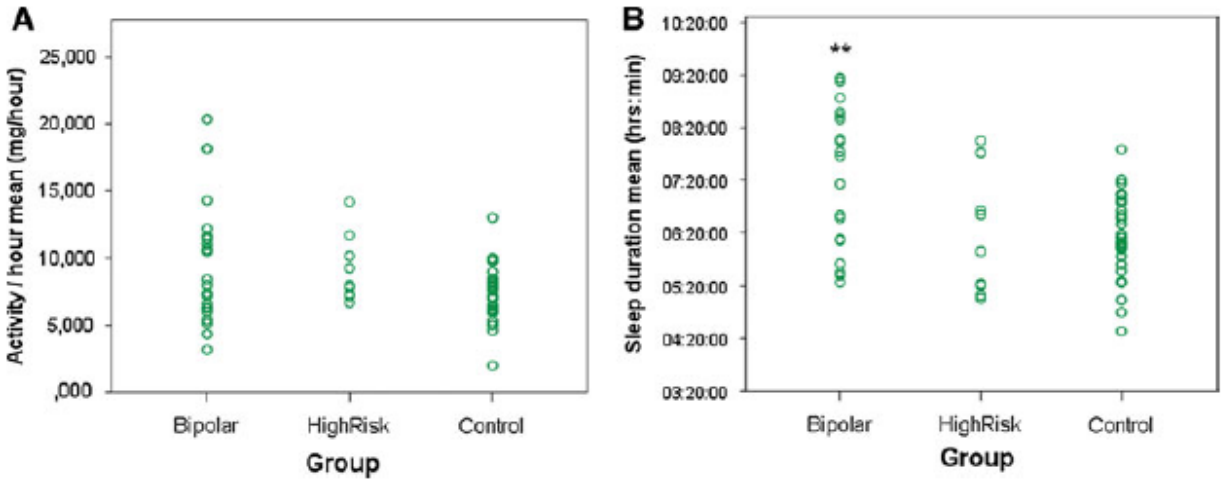


Fig. 2 *Actimetry* Activity per hour in mg (**a**) and Sleep duration (**b**). Post hoc pairwise comparison, $**p < 0.01$ versus control



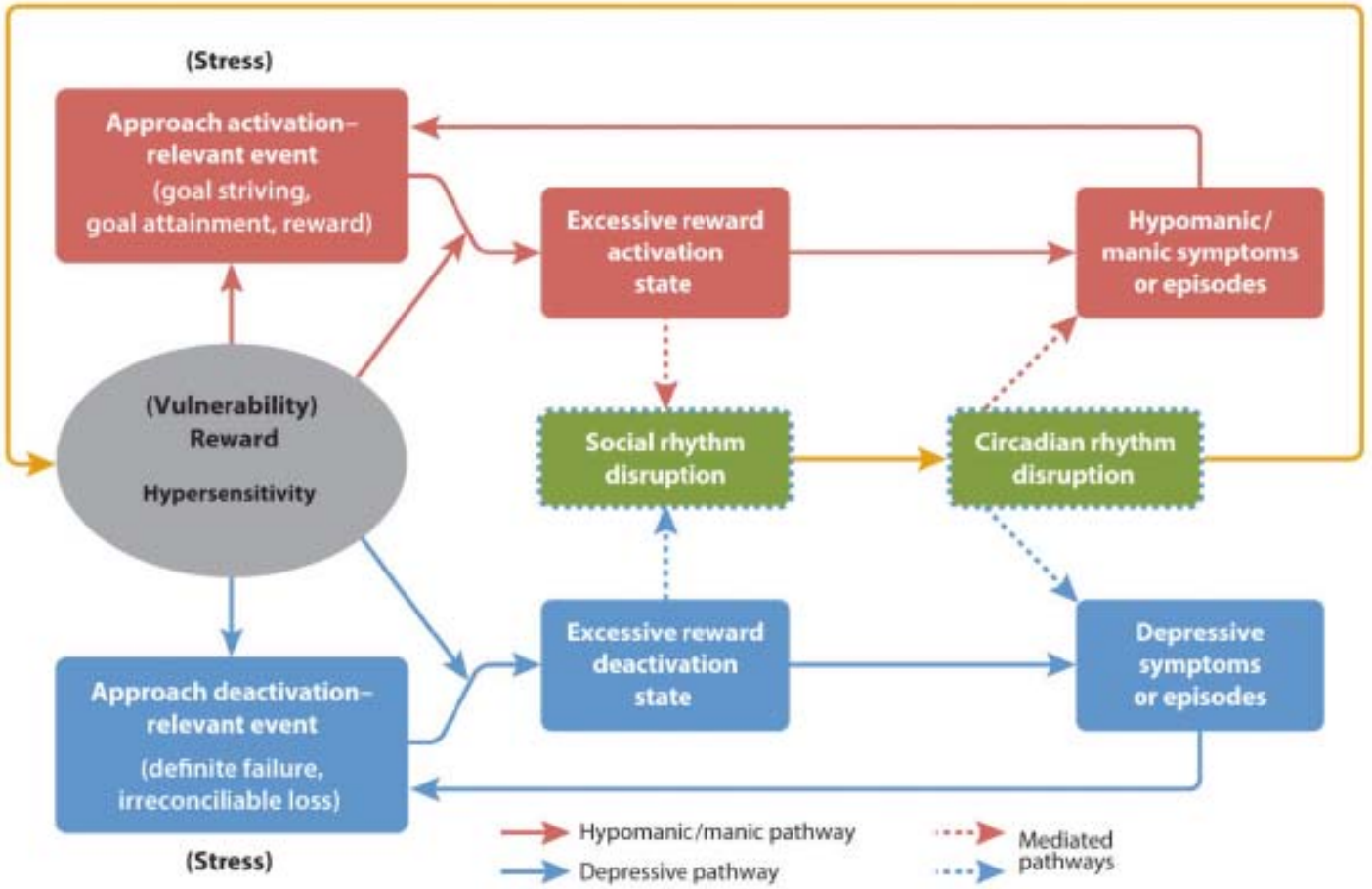
Ritter et al., Neural Transm 2012

Persönlichkeit, Temperament und Charakter

- Hohe prämorbide Extraversion ⇒ ↑ BD[1]
- Novelty seeking ⇒ ↑ manische Episode[2]
- Hohe Belohnungssensitivität ⇒ ↑ BD spectrum[3]

[1]Lönnqvist et al., J Abnorm Psychol 2009, [2]Tjissen et al., Acta Psychiatr Scand 2010, [3]Alloy et al., J Abnorm Psychol 2012

Persönlichkeit und sozialer Rhythmus



Alloy et al. Annu Rev Clin Psychol 2015

Kognitive Defizite bereits vor Erkrankungsbeginn?

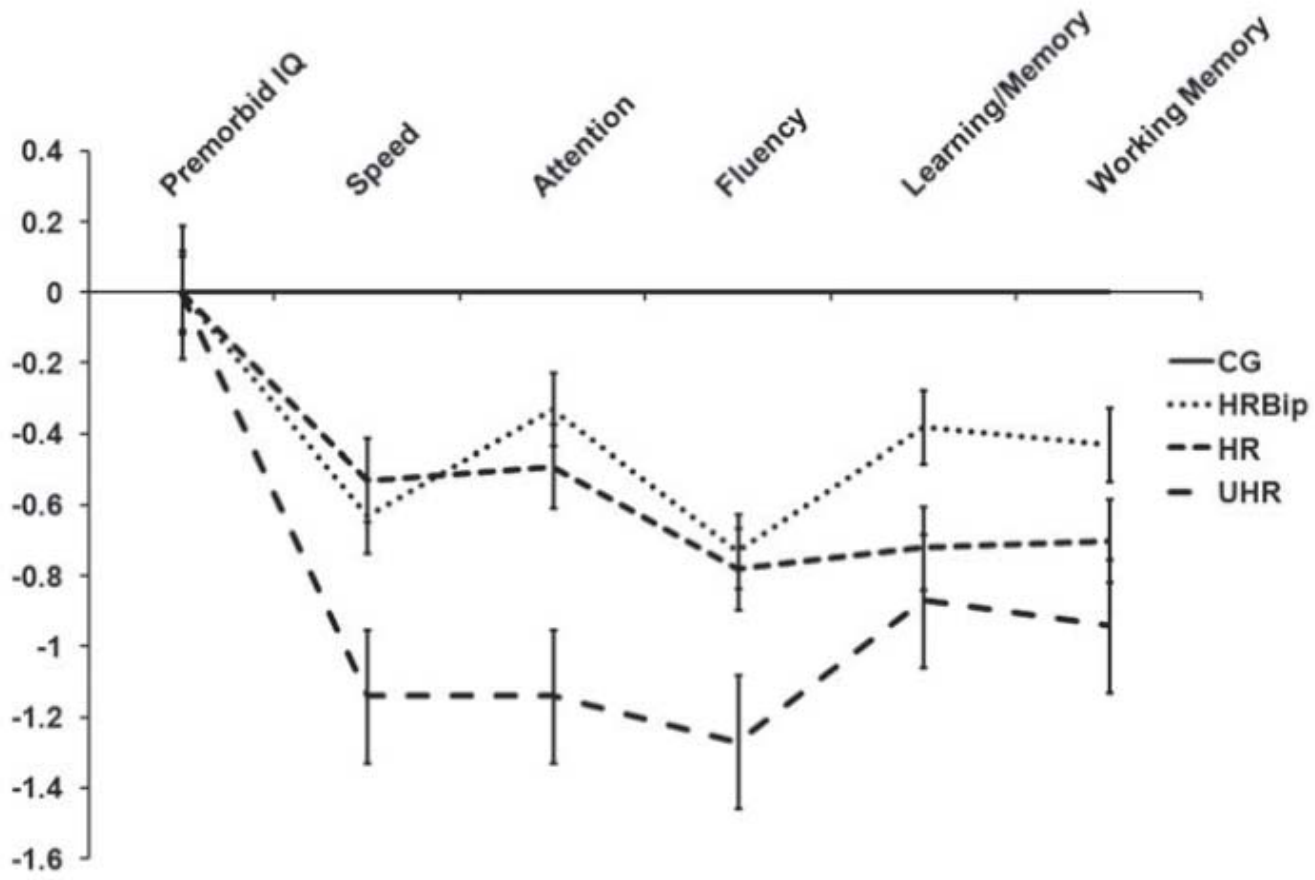


Fig. 1. Mean scores in cognitive domains for the three at-risk groups [high risk (HR) or ultra-high risk (UHR) for schizophrenic and affective psychoses and high risk for bipolar disorder (HRBip)], presented as *z*-score deficits relative to the healthy control group (CG).

Metzler et al., Psychol Med 2014

Drogenkonsum

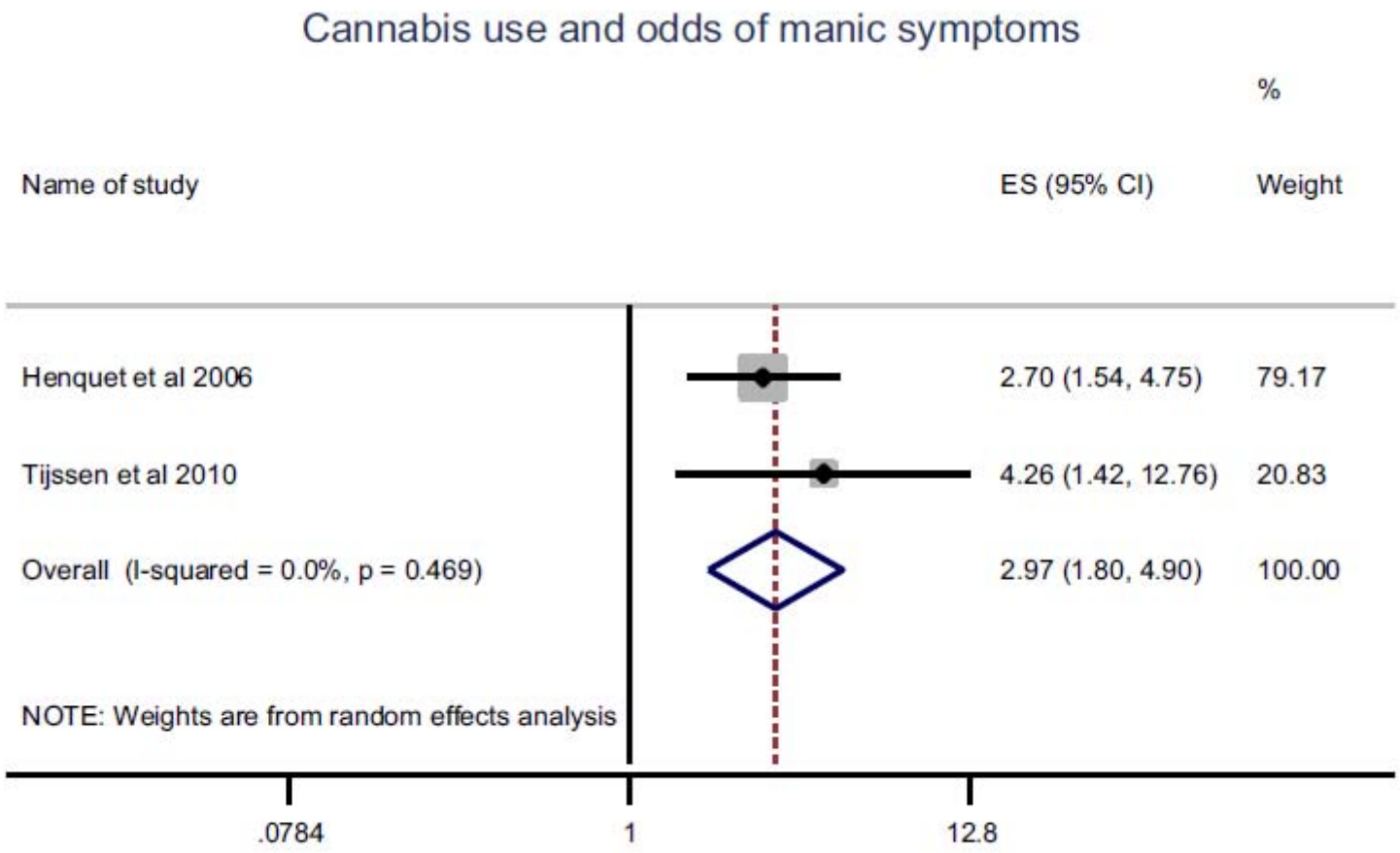
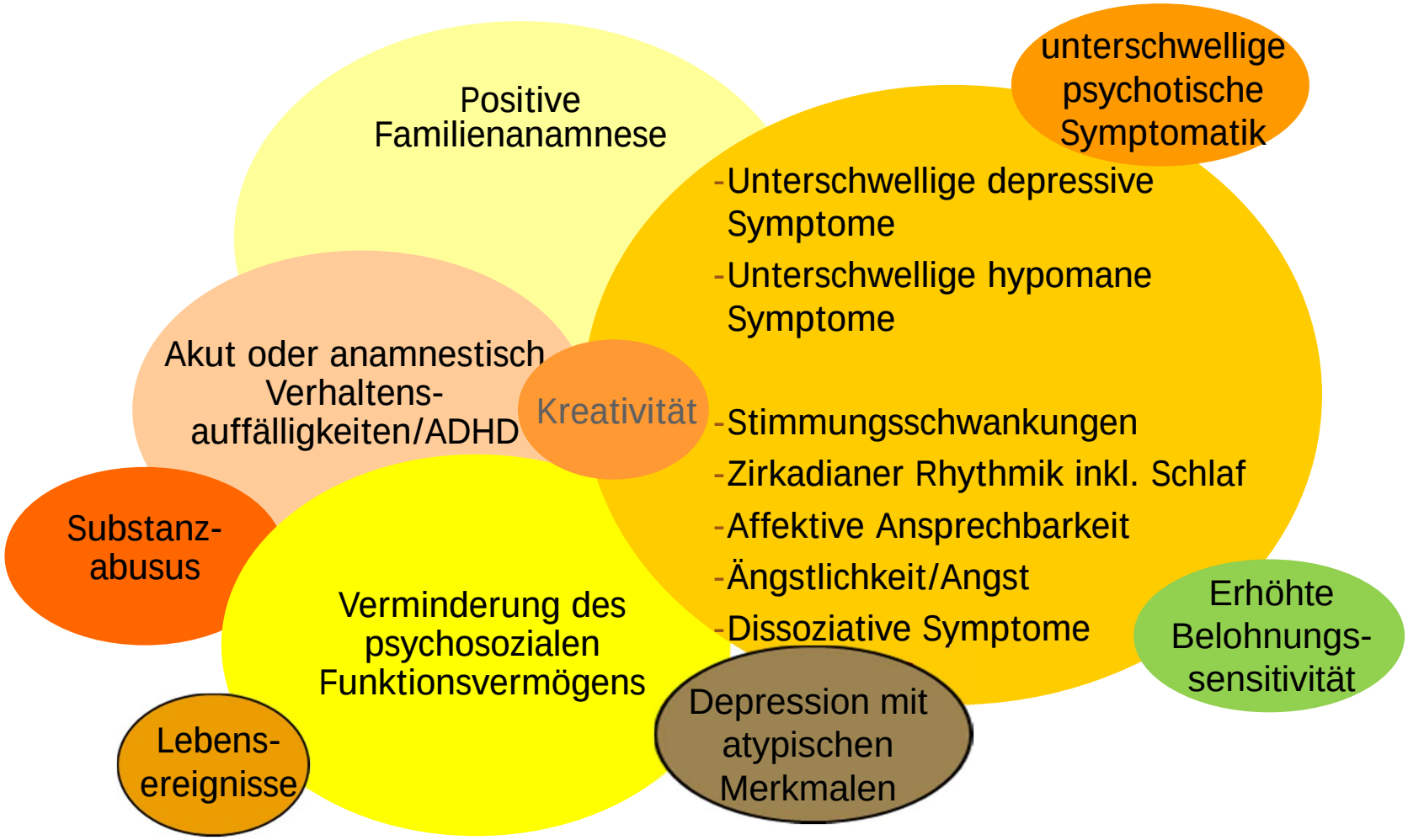


Fig. 2. Cannabis and manic symptoms.

Gibbs et al., J Aff Disord 2015

Risikokonstellation Bipolare Störung



Leopold et al. 2012, complemented with Skjelstad 2010, Conus 2010, Pfennig & Ritter 2015

Was bleibt zu tun?

- Prädiktive Werte der Risikofaktoren
- Integration in ein Instrument
- Resilienzfaktoren
- Weitere biologische Risikofaktoren (Hirnstruktur und –funktion, Genetik, Immunologie...)
- Adäquate frühe Therapien

Vielen Dank für Ihr Interesse.

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andrea.pfennig@uniklinikum-dresden.de