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DEUTSCHE FACHGESELLSCHAFT
PSYCHOSE UND SUCHT E. V.
HERBSTTAGUNG 2016

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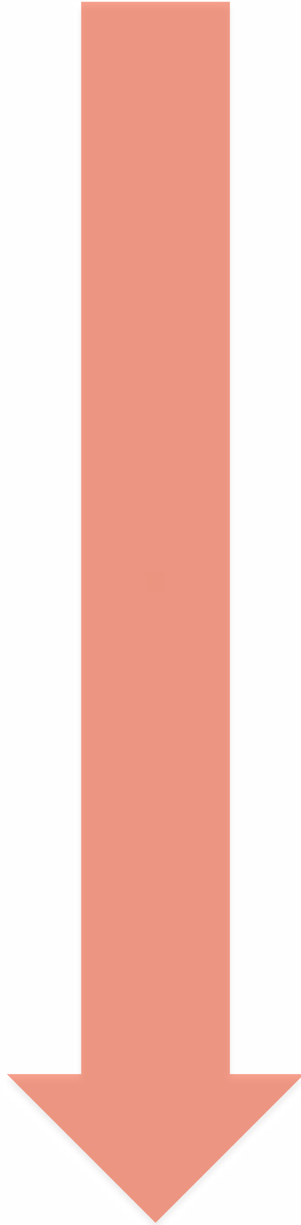
Was sind Minussymptome ?

Wie stelle ich sie fest ?

Spielt Sucht eine Rolle ?

Gibt es eine medikamentöse Behandlung ?

Gibt es noch andere Therapien ?



Was sind Minussymptome ?

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http://thinking-feeling-living.blogspot.de

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„Einschränkungen des normalen Lebens“

Begriff	Definition
Alogie	Verarmung der Sprache: z.B. ständige Verwendung der gleichen Wörter oder geringe Sprachproduktion
Affektverarmung	Reduzierte Spannbreite der Emotionalität: Gefühl der inneren Leere; wenig Möglichkeit, Emotionen zu erfahren
Asozialität / sozialer Rückzug	Reduzierte soziale Einbindung: Verminderte Geselligkeit; reduziertes sexuelles Interesse, wenig Freude am Kontakt
Anhedonie	Verminderte Fähigkeit, Freude zu empfinden: kein Vergnügen an Hobbies, keine Genussfähigkeit
Avolition	Verminderter Antrieb/Motivation. Reduzierte Aktivität in Alltag, Hygiene,...

Buchanan. Schiz Bull 2007
Kaiser et al. Psychopathology 2011

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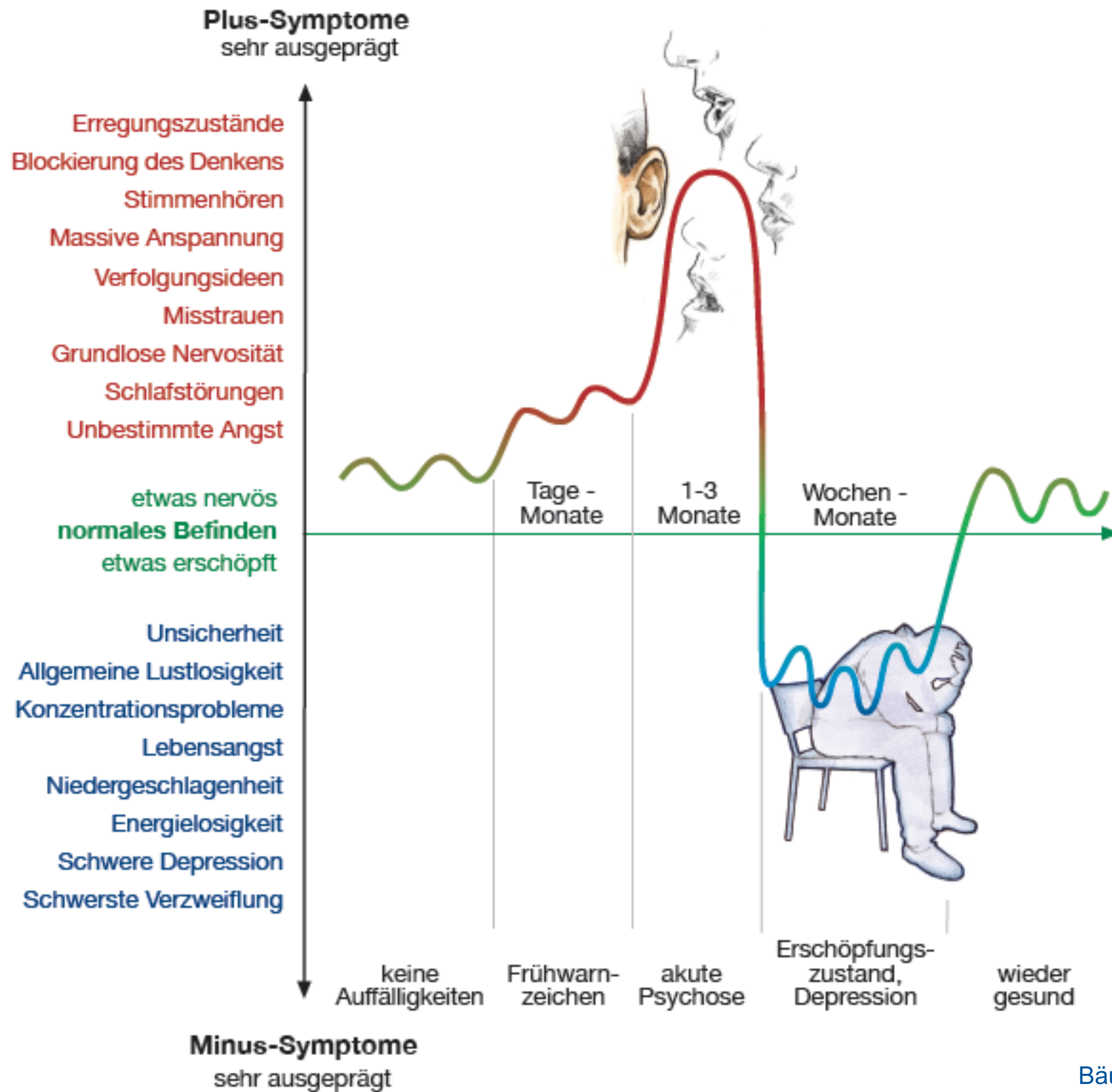
Psychoseverlauf



Bäuml & Lambert (2009)
Psychosen erkennen, verstehen & behandeln

Schilderung von Betroffenen

Antriebslosigkeit / Anhedonie

„Ich habe zu nichts mehr eine Motivation“

„Ich habe kaum noch irgendwelche Gefühle“

Affektverflachung / Alogie

„Ich kann mich über nichts mehr freuen“

„Wenn Freunde kommen, habe ich keine Lust mehr mich zu unterhalten“

Bäuml & Lambert (2009)
Psychosen erkennen, verstehen & behandeln

Bedeutung von Negativsymptomatik

- schlechtere Prognose und reduzierte Lebensqualität [1,2]
- länger andauernd und schwieriger zu behandeln als Positivsymptome [3,4]
- beeinträchtigen Selbständigkeit im Alltag (Beruf, Soziales)
- höhere Belastung von Angehörigen / Bezugspersonen [5]

1. Milev et al. Am J Psychiatry 2005
2. Kurtz. Exp Rev Neurother 2005
3. Kirkpatrick und Fischer. Schizophr Bull 2006
4. Alphs. Schizophr Bull 2006
5. Provencher und Mueser. Schizophr Res 1997

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Konsequenzen

Negativsymptome: selten Inanspruchnahme des Hilfesystems

wenig spezialisierte Früherkennung

fehlendes Screening (stationär, ambulant)

lange unbehandelte Negativsymptome (>2.5x als positive)

Funktionsniveau & Lebensqualität sinken

Entwicklung PNS / DS vor Erstbehandlung

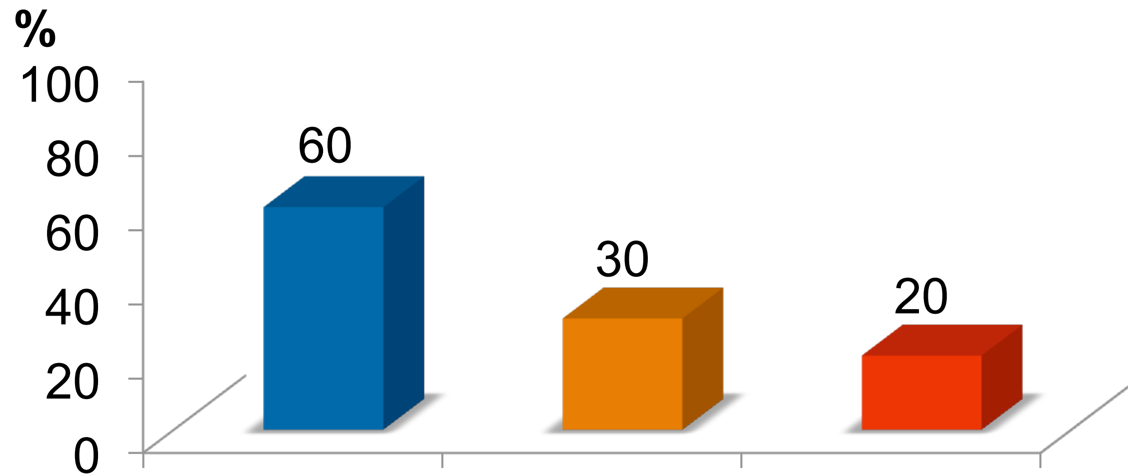
frühe Manifestation Schizophrenie

schlechtes Ansprechen auf Therapie & Gesundheitsverhalten

schwere psychische Erkrankung
& dauerhaft reduziertes Funktionsniveau

Lambert & Naber. Current schizophrenia 2014

Definition & Abgrenzung



Mind. 1 neg. Symptom

Primär / sekundär negative Symptome

Persistierende Negativsymptome

- PANSS negativ > 20 Punkte
- Negativ > Positiv Score
- Mind. 6 Monate
- EPMS & Depression gering

Defizitsyndrom

- Mind. 2 primär neg. Symptome
- Mind. mittlere Ausprägung
- Mind. 12 Monate
- Persistieren in psychotisch stabiler Phase

Bobes et al. J Clin Psychiatry 2011
Buchanan. Schiz Bull 2007
Kaiser et al. Psychopathology 2011

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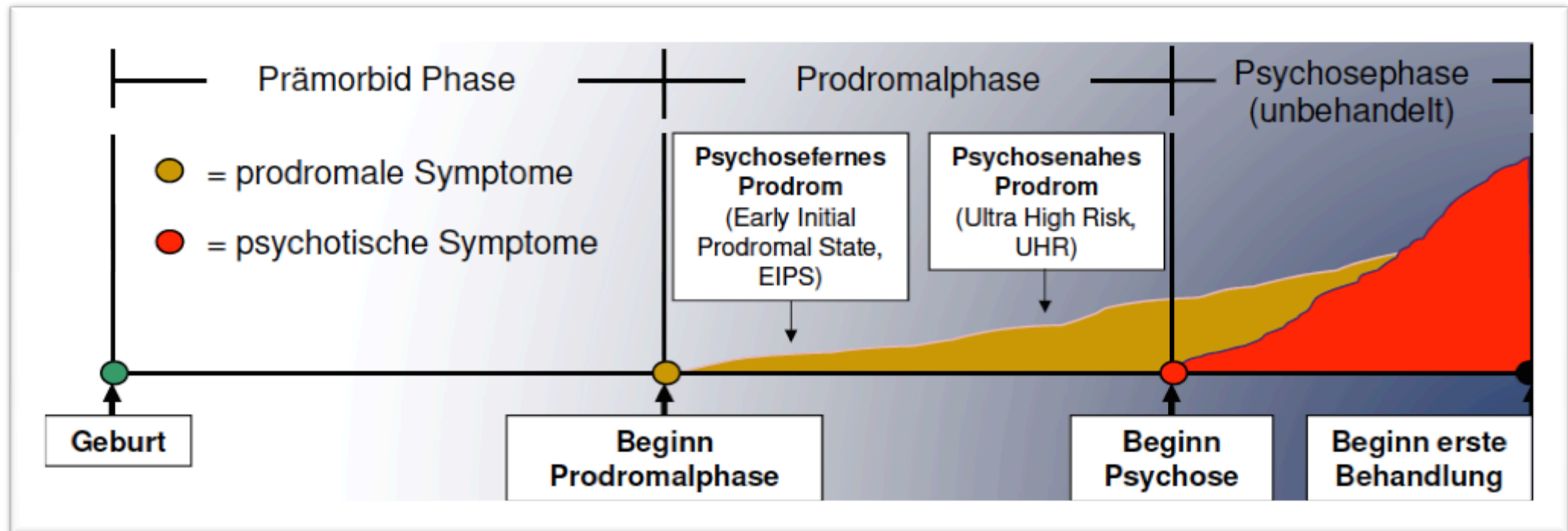
Risikofaktoren

- Familienanamnese Schizophrenie 1. Grades
- frühe Entwicklungsstörungen (kognitiv, motorisch, emotional)
- lange unbehandelte Negativsymptomatik
- lange unbehandelte Positivsymptomatik
- negative Kerndömänen:

  avolition & diminished expression Messinger et al. Clin Psychol Rev 2011
- schwere Negativsymptome
- ausgeprägte kognitive Symptome

Cohen et al. Schizophr Res 2010

Exkurs: Prodrom & DUP



Negativsymptome im schizophrenen Prodrom

•bei jedem 2. Patienten

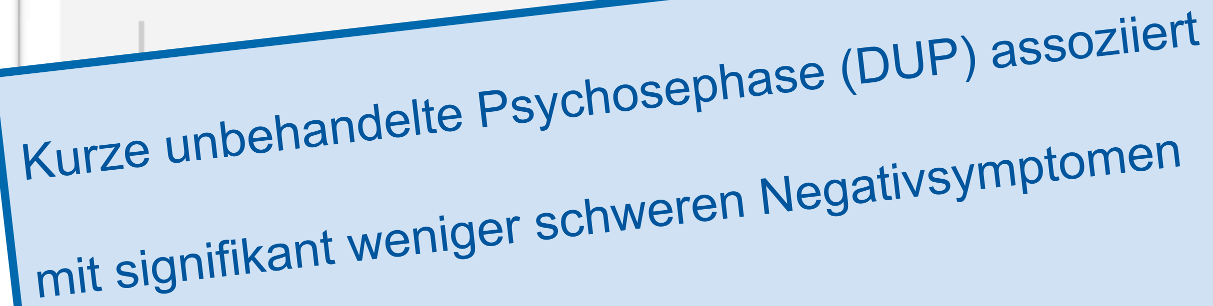
•beeinträchtigen subjektive Lebensqualität & Funktionsniveau

•Prädiktor für erhöhte Psychosewahrscheinlichkeit

•Ausmaß gibt Hinweis auf Ausmaß & Schwere kognitiver Symptome bei Erstmanifestation

Lyne et al., 2014; Dominguez-Martinez et al., 2014; Kim et al., 2013; Nelson et al., 2013; Cuesta et al., 2012

Exkurs: Prodrom & DUP



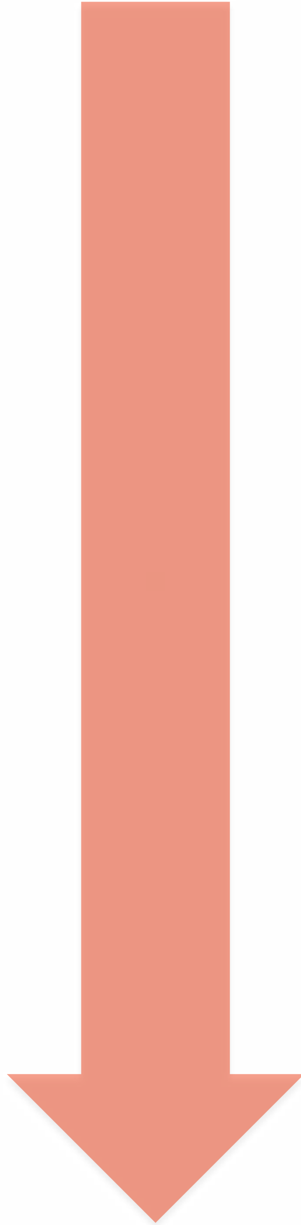
Kurze unbehandelte Psychosephase (DUP) assoziiert mit signifikant weniger schweren Negativsymptomen

- bei Aufnahme
- nach 1-2 Jahren
- nach 6-8 Jahren

16 Studien, N=3339, durchschnittliche DUP 61,4 Wochen Boonstra et al. Schizophr Res 2012.

… & Schwere kognitiver Symptome bei Erstmanifestation

Lyne et al., 2014; Dominguez-Martinez et al., 2014; Kim et al., 2013; Nelson et al., 2013; Cuesta et al., 2012



Wie stelle ich sie fest ?

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Notwendige Untersuchungen

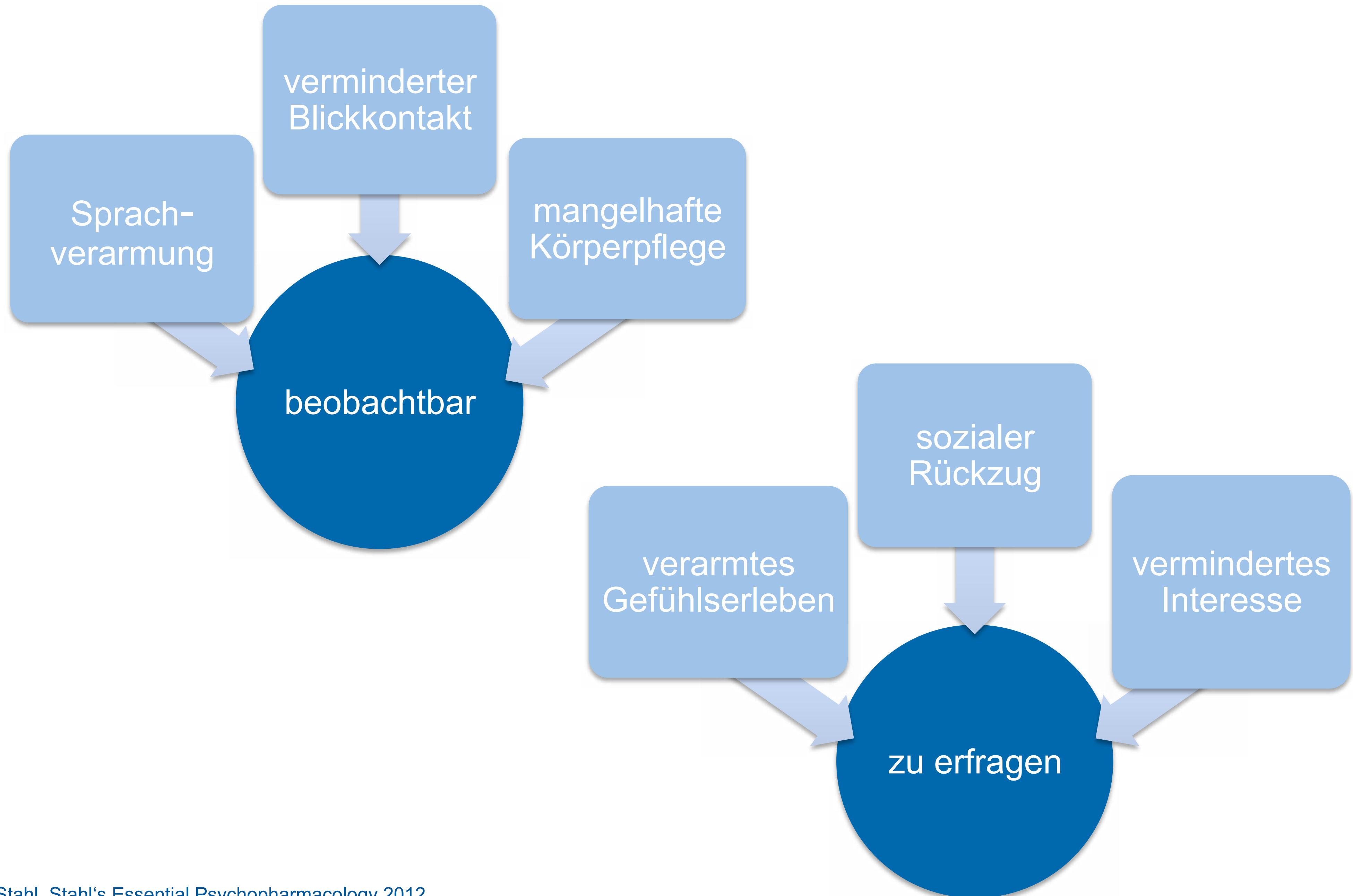
- Beobachten & Erfragen von Symptomen
- Dauer der unbehandelten Symptomatik
- Diagnostik von Sekundärsymptomen:

  Depression, EPMS, amotivationales Syndrom, komorbide Störung
- Testpsychologie:

  Art und Schwere der Negativsymptome, Positivsymptome, kognitive Symptome
- körperliche Untersuchung

Lambert & Naber. Current schizophrenia 2014

Identifikation von Negativsymptomen



Stahl. Stahl's Essential Psychopharmacology 2012.

Primär vs. Sekundär

PRIMÄR

Ursächlich: Pathophysiologie der Schizophrenie

vor Ersterkrankung,
in stabilen Phasen,
Zunahme im Verlauf

SEKUNDÄR

Positivsymptomatik

Nebenwirkungen

Depression

Suchtmittelkonsum

Lambert & Naber. Current schizophrenia 2014

Diagnostische Instrumente

Selbstbewertung negativer Symptome (SNS) Dollfus et al., 2015

Selbstbewertung Motivation and Pleasure Scale-Self-Report (MAP-SR) Llerena et al., 2013; Engel und Lincoln, 2016

Fremdbewertung Scale of Assessment of Negative Symptoms (SANS) Andreasen, 1982

Fremdbewertung Calgary Depression Scale for Schizophrenia Addington und Addington, 1993

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Self-evaluation of Negative Symptoms
(SNS, S. Dollfus and C. Mach, V1_2014)

For each statement, put a cross in the box which best corresponds to your current feelings (based on the previous week).

	Strongly agree	Somewhat agree	Strongly disagree
1. I prefer to be alone in my corner			
2. I'm better off alone, because I feel uncomfortable when anyone is near me			
3. I'm not interested in going out with friends or family			
4. I don't particularly try to contact and meet friends (letters, telephone, text messaging, etc.)			
5. People say I'm not sad or happy and that I'm not often angry			
6. There are many happy or sad things in life but I don't feel concerned by them			
7. Watching a sad or happy film, reading or listening to a sad or happy story does not especially make me want to cry or laugh			
8. It is difficult for people to know how I feel			
9. I don't have as much to talk about as most people			
10. I find it 10 times harder to talk than most people do			
11. People often say that I don't talk much			
12. With friends and family, I want to talk about things but it doesn't come out			
13. I find it difficult to meet the objectives I set myself			
14. It's hard to stick to doing things on an everyday regular basis			
15. There are many things I don't do through lack of motivation or because I don't feel like it			
16. I know there are things I must do (get up or wash myself for example) but I have no energy			
17. I don't take any great pleasure in talking to people			
18. I find it hard to take pleasure even when doing things I have chosen to do			
19. When I imagine doing one thing or another, I don't feel any particular pleasure in the idea			
20. I am not interested in having sex			

SNS

5 Bereiche – 20 Aussagen

sozialer Rückzug
reduzierte emotionale Bandbreite
Freudlosigkeit
Antriebsarmut
Sprachverarmung

letzte Woche
0 (stimme gar nicht zu) – 2 (sehr zu)

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The Motivation and Pleasure Scale–Self-Report (MAP-SR) items.

Item
Social pleasure
1. In the past week, what is the *most* pleasure you experienced from being with other people?
2. In the past week, *how often* have you experienced pleasure from being with other people?
3. Looking ahead to being with other people *in the next few weeks*, how much pleasure do you expect you will experience from being with others?
Recreational or work pleasure
4. In the past week, what is the *most* pleasure you experienced from hobbies, recreation, or from work?
5. In the past week, *how often* have you experienced pleasure from hobbies, recreation, or from work?
6. Looking ahead to the *next few weeks*, how much pleasure do you expect you will experience from your hobbies, recreation, or work?
Feelings and motivations about close, caring relationships
7. When it comes to close relationships with your *family members*, how important have these relationships been to you over the past week?
8. In the past week, I have chosen not to spend time with my *family* and would just as soon be alone.[a]
9. When it comes to having a close relationship with a *romantic partner*, how important has this type of relationship been to you over the past week?
10. In the past week, I have chosen not to spend time with a *romantic partner* (or find a partner) and would just as soon be alone.[a]
11. When it comes to close relationships with your *friends*, how important have these relationships been to you over the past week?
12. In the past week, I have chosen not to spend time with my *friends* (or make friends) and would just as soon be alone.[a]
Motivation and effort to engage in activities
13. In the past week how *motivated have you been to be* around other people and do things with them?
14. In the past week how much *effort* have you made to actually do things with other people?
15. In the past week how *motivated* have you been to go to work or school or look for a job or class to take?
16. In the past week how much *effort* have you made to do things at work or school? (If you are not working or going to school, how much effort have you made to look for a job or go to school.)
17. In the past week how *motivated* have you been to do hobbies or other recreational activities?
18. In the past week how much *effort* have you made to actually do any hobbies or recreational activities?

MAP-SR

3 Bereiche – 18 Fragen

erlebtes/erwartetes Vergnügen
sozial
in Freizeit/Beruf

Gefühle/Motivation
in engen Beziehungen

Motivation/ Bemühungen,
aktiv zu werden

letzte / kommende Woche(n)
0 (gar nicht) – 4 (sehr)

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Affektive Verflachung oder Abstumpfung	1. Starrer Gesichtsausdruck 2. Verminderte Spontanbewegungen 3. Fehlen expressiver Gesten 4. Unzureichender Blickkontakt 5. Fehlende Affektive Reaktionen 6. Mangel an Stimm-Modulation 7. Globalbeurteilung der Affektiven Verflachung
Alogie	8. Reduzierung des Sprachumfangs 9. Reduzierung des Sprachinhalts 10. Gedankensperre 11. Vergrößerte Antwortlatenz 12. Globalbeurteilung der Alogie
Willensschwäche – Apathie	13. Kleidung und Hygiene 14. Unbeständigkeit bei der Arbeit oder in der Schule 15. Fehlende Energie 16. Globalbeurteilung der Willensschwäche – Apathie
Anhedonie – Ungeselligkeit	17. Interesse an Freizeitaktivitäten 18. Sexuelle Aktivität 19. Fähigkeit, Intimität und Nähe zu erleben 20. Beziehungen zu Freunden und Alterskameraden 21. Globalbeurteilung der Anhedonie – Ungeselligkeit
Aufmerksamkeit	22. Fehlende Aufmerksamkeit in sozialen Situationen 23. Unaufmerksamkeit während der Prüfung des psychischen Status 24. Globalbeurteilung der Aufmerksamkeit

SANS

5 Bereiche – 24 Aussagen

affektive Verarmung
Sprachverarmung
Antriebsarmut
Freudlosigkeit
Aufmerksamkeit

letzte Woche / Monat
0 (gar nicht) – 5 (schwer)

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Interviewer: Ask the first question as written. Use follow up probes or qualifiers at your discretion. Time frame refers to last two weeks unless stipulated. **N.B.** The last item, #9, is based on observations of the entire interview.

1. Depression: How would you describe your mood over the last two weeks? Do you keep reasonably cheerful or have you been very depressed or low spirited recently? In the last two weeks how often have you (own words) every day? All day?

0. Absent
1. Mild — Expresses some sadness or discouragement on questioning.
2. Moderate — Distinct depressed mood persisting up to half the time over last 2 weeks: present daily.
3. Severe — Markedly depressed mood persisting daily over half the time interfering with normal motor and social functioning.

2. Hopelessness: How do you see the future for yourself? Can you see any future? - or has life seemed quite hopeless? Have you given up or does there still seem some reason for trying?

0. Absent
1. Mild — Has at times felt hopeless over the last two weeks but still has some degree of hope for the future.
2. Moderate — Persistent, moderate sense of hopelessness over last week. Can be persuaded to acknowledge possibility of things being better.
3. Severe — Persisting and distressing sense of hopelessness.

3. Self Depreciation: What is your opinion of your self compared to other people? Do you feel better, not as good, or about the same as others? Do you feel inferior or even worthless?

0. Absent
1. Mild — Some inferiority; not amounting to feeling of worthlessness.
2. Moderate — Subject feels worthless, but less than 50% of the time.
3. Severe — Subject feels worthless more than 50% of the time. May be challenged to acknowledge otherwise.

4. Guilty Ideas Of Reference: Do you have the feeling that you are being blamed for something or even wrongly accused? What about? (Do not include justifiable blame or accusation. Exclude delusions of guilt.)

0. Absent
1. Mild — Subject feels blamed but not accused less than 50% of the time.
2. Moderate — Persisting sense of being blamed, and/or occasional sense of being accused.
3. Severe — Persistent sense of being accused. When challenged, acknowledges that it is not so.

5. Pathological Guilt: Do you tend to blame yourself for little things you may have done in the past? Do you think that you deserve to be so concerned about this?

0. Absent
1. Mild — Subject sometimes feels over guilty about some minor peccadillo, but less than 50% of time.
2. Moderate — Subject usually (over 50% of time) feels guilty about past actions the significance of which he exaggerates.
3. Severe — Subject usually feels s/he is to blame for everything that has gone wrong, even when not his/her fault.

6. Morning Depression: When you have felt depressed over the last 2 weeks have you noticed the depression being worse at any particular time of day?

0. Absent — No depression.
1. Mild — Depression present but no diurnal variation.
2. Moderate — Depression spontaneously mentioned to be worse in a.m.
3. Severe — Depression markedly worse in a.m., with impaired functioning which improves in p.m.

7. Early Wakening: Do you wake earlier in the morning than is normal for you? How many times a week does this happen?

0. Absent — No early wakening.
1. Mild — Occasionally wakes (up to twice weekly) 1 hour or more before normal time to wake or alarm time.
2. Moderate — Often wakes early (up to 5 times weekly) 1 hour or more before normal time to wake or alarm.
3. Severe — Daily wakes 1 hour or more before normal time.

8. Suicide: Have you felt that life wasn't worth living? Did you ever feel like ending it all? What did you think you might do? Did you actually try?

0. Absent
1. Mild — Frequent thoughts of being better off dead, or occasional thoughts of suicide.
2. Moderate — Deliberately considered suicide with a plan, but made no attempt.
3. Severe — Suicidal attempt apparently designed to end in death (i.e.: accidental discovery or inefficient means).

9. Observed Depression: Based on interviewer's observations during the entire interview. The question "Do you feel like crying?" used at appropriate points in the interview, may elicit information useful to this observation.

0. Absent
1. Mild — Subject appears sad and mournful even during parts of the interview, involving affectively neutral discussion.
2. Moderate — Subject appears sad and mournful throughout the interview, with gloomy monotonous voice and is tearful or close to tears at times.
3. Severe — Subject chokes on distressing topics, frequently sighs deeply and cries openly, or is persistently in a state of frozen misery if examiner is sure that this is present.

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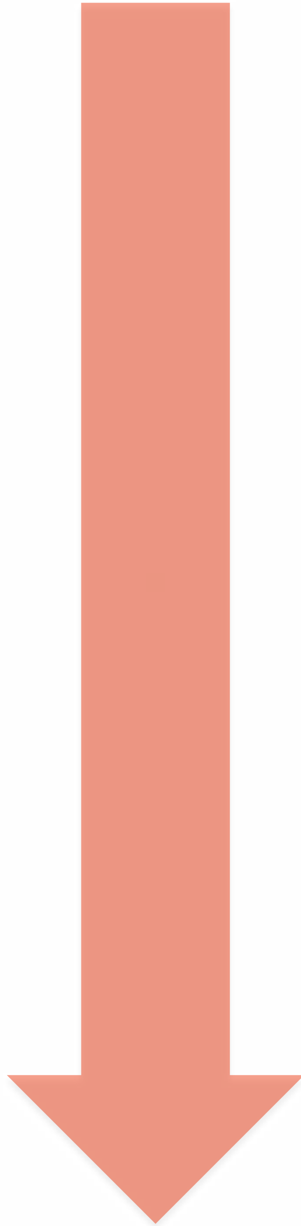
CDSS

8 depressive Symptome
1 Gesamteindruck

Gedrückte Stimmung
Hoffnungslosigkeit
Selbstabwertung
Schuldhafte Beziehungsideen
Pathologische Schuld
Morgentief
Frümorgendliches Erwachen
Suizidalität

Beobachtbare Depression

2
generell / letzte 14 Tage
0 (gar nicht) – 3 (schwer)



Spielt Sucht eine Rolle ?

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Substanzgebrauch bei Schizophrenie

- Risiko einer Suchterkrankung
  in psychiatrischen Patienten 4-5x> als Allgemeinbevölkerung

- Lebenszeit-Prävalenz für Doppeldiagnose: 50% Thoma & Daum, 2013

- Schizophrene Patienten konsumieren häufig Tabak, Alkohol und Cannabis
- Risiko kardiovaskulärer Erkrankungen steigt
- Nebenwirkungsprofil der Antipsychotika
  + kardiovaskuläre Erkrankungen
  + Lebensstil
  + Konsum
  ➔ höhere Morbidität
  ➔ vorzeitige Mortalität
- Hohe Konsumraten zu Beginn der Erkrankung / bei Ersterkrankung

Addy et al., 2012; Davidson et al., 2001; McCreadie, 2003; De Hert et al., 2001; Saha et al., 2007; Wahlbeck et al., 2001; Barnett et al., 2007

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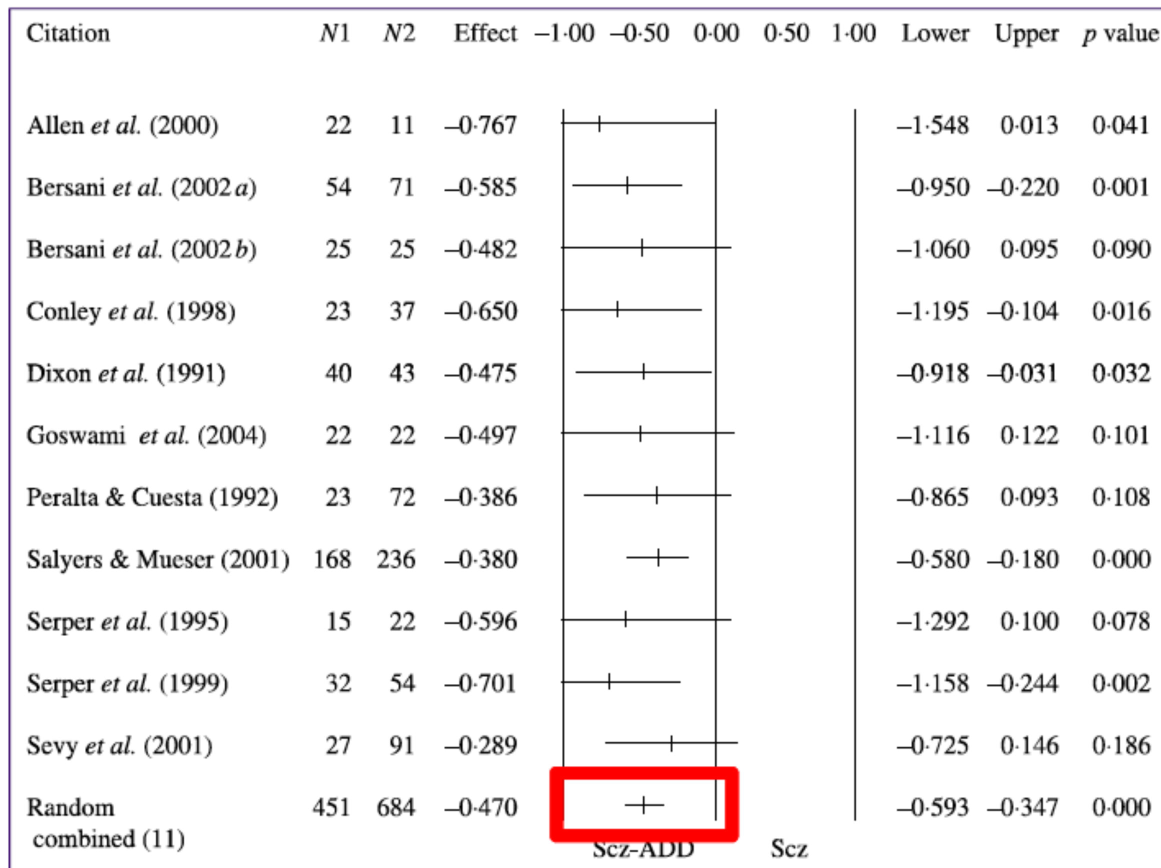
Substanzgebrauch bei Negativsymptomen

- weniger Symptome bei Substanzgebrauch Simon et al., 2015

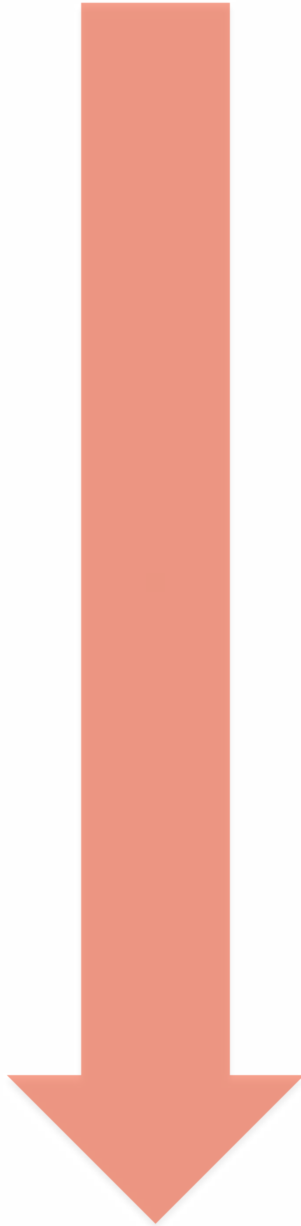
  evtl. verhindern ausgeprägte Negativsymptome das Beschaffen & den Konsum

  evtl. erleichtern manche Substanzen (Kokain) Symptome (Anhedonie, Alogia)



Citation	N1	N2	Effect	Lower	Upper	p value
Allen *et al.* (2000)	22	11	–0·767	–1·548	0·013	0·041
Bersani *et al.* (2002 *a*)	54	71	–0·585	–0·950	–0·220	0·001
Bersani *et al.* (2002 *b*)	25	25	–0·482	–1·060	0·095	0·090
Conley *et al.* (1998)	23	37	–0·650	–1·195	–0·104	0·016
Dixon *et al.* (1991)	40	43	–0·475	–0·918	–0·031	0·032
Goswami *et al.* (2004)	22	22	–0·497	–1·116	0·122	0·101
Peralta & Cuesta (1992)	23	72	–0·386	–0·865	0·093	0·108
Salyers & Mueser (2001)	168	236	–0·380	–0·580	–0·180	0·000
Serper *et al.* (1995)	15	22	–0·596	–1·292	0·100	0·078
Serper *et al.* (1999)	32	54	–0·701	–1·158	–0·244	0·002
Sevy *et al.* (2001)	27	91	–0·289	–0·725	0·146	0·186
Random combined (11)	451	684	–0·470	–0·593	–0·347	0·000

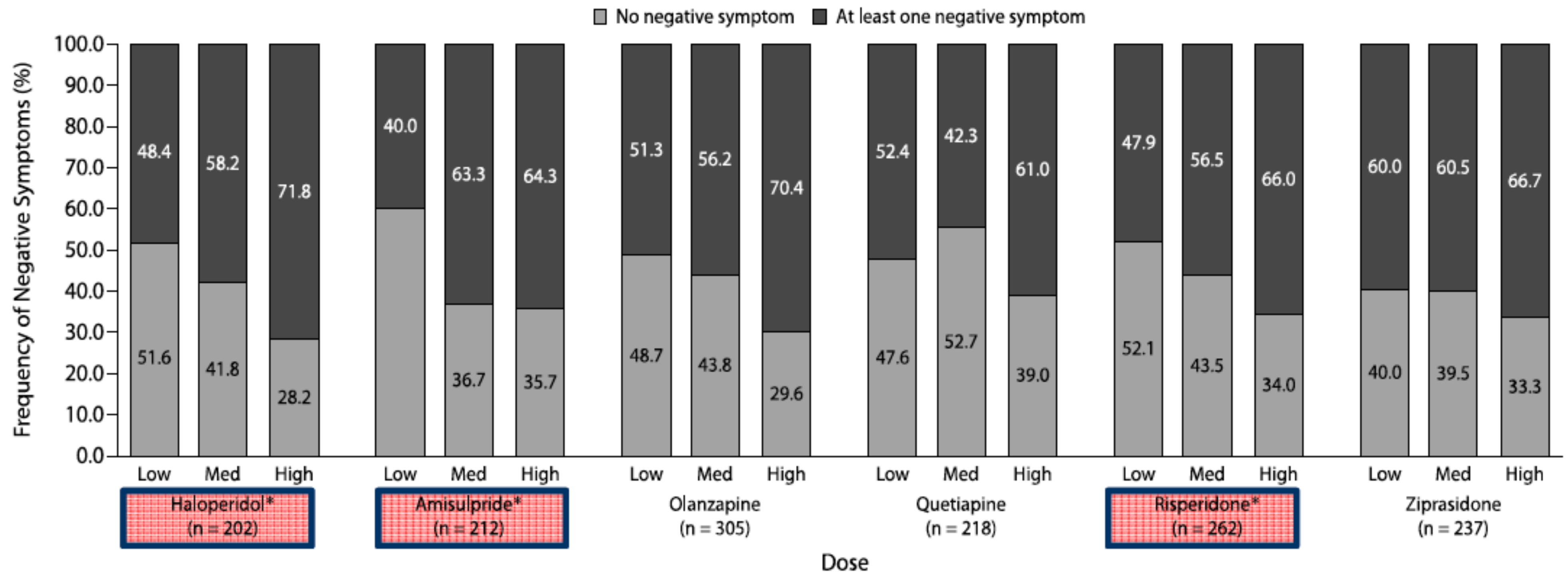
Potvin et al. Psych Med 2006



Gibt es eine medikamentöse Behandlung ?

Einfluss der Dosis von Antipsychotika

Prevalence of Negative Symptoms in Outpatients With Schizophrenia Spectrum Disorders Treated With Antipsychotics in Routine Clinical Practice: Findings From the CLAMORS Study Bobes et al. J Clin Psychiatry 2011



signifikanter Unterschied zwischen niedrigen, mittleren und hohen Dosen in Bezug auf die Häufigkeit von Negativsymptomen

Outcome unter Antipsychotika

Second-generation antipsychotic effect on cognition in patients with schizophrenia - a meta-analysis of randomized clinical trials Nielsen et al. Acta Psychiatr Scand 2015

- 37 Studien, N= 3526 Patienten, kongnitive Symptome
- 7 SGA vs. FGA vs. SGA untereinander
- kein Unterschied zwischen SGA & FGA
- marginale Unterschiede zwischen Einzelsubstanzen
- keine Substanz hat rein positives Profil bzgl. kognitiver Symptome

Medikation bei Negativsymptomatik

- orientiert an der Ursache

- sekundär zu Positivsymptomen:
  antipsychotische Medikation erhöhen/wechseln Buckley und Stahl, 2007

- sekundär zu EPMS:
- antipsychotische Medikation reduzieren /wechseln (Atypika) Velligan und Alphs, 2008

- keine grundsätzliche Überlegenheit der Atypika Catie-Studie: Lieberman et al., 2005

- assoziiert mit depressivem Affekt: antidepressive Therapie
- positiver Effekt von Antidepressiva auch auf Negativsymptome Cochrane-Review: Rummel et al., 2006

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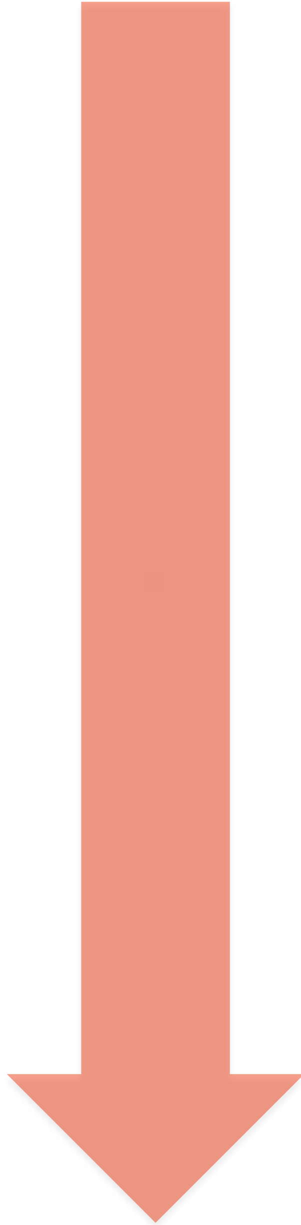
Medikation bei Negativsymptomatik

- Amisulprid: explizit zur Behandlung von Negativsymptomen Buchanan, 2007
- Clozapin-Augmentation:

antipsychotisch:	Aripiprazol Srisurapanont et al., 2015
	Sulpirid Wang et al., 2010
antidepressiv:	Citalopram Lan et al., 2006
antikonvulsiv:	Lamotrigin Zoccali et al., 2007
andere:	Memantine Lucena et al., 2009

- kein signifikanter Effekt:
  Risperidon, Amisulprid, Mirtazapin, Fluoxetin, Topiramat Sommer et al., 2011



Gibt es noch andere Therapien ?

Therapeutische Gruppenangebote

Psychoedukation Schizophrenie
Psychoedukation Sucht und Psychose

offene Gesprächsgruppe (VT)
Therapiegruppe Negativsymptomatik

Metakognitives Training Schizophrenie
Soziales Kompetenztraining

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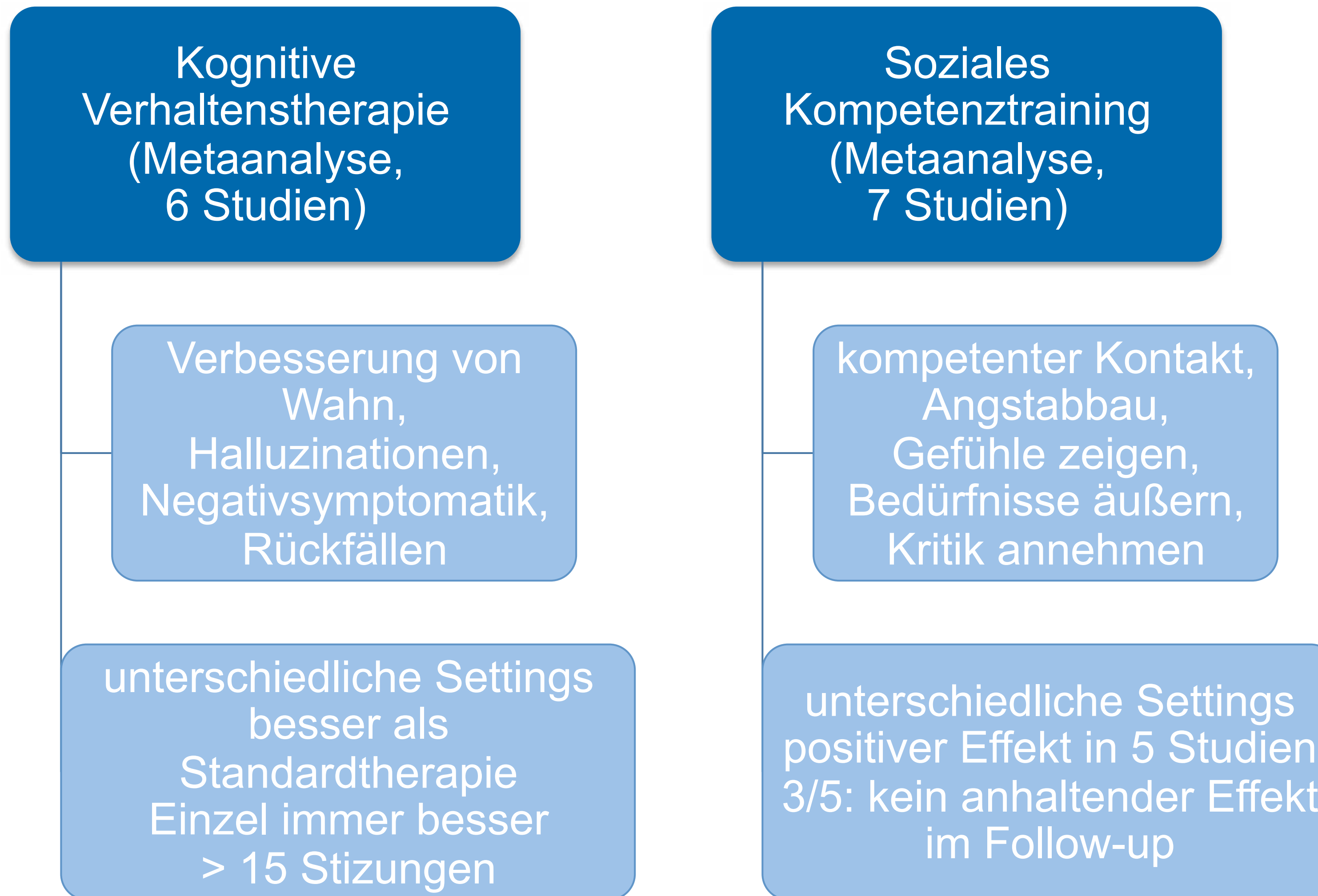
Nicht-medikamentöse Therapieverfahren



Elis et al. Clin Psych Review 2013
Jones et al. Cochrane Database Syst Rev. 2012

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Vielen Dank für Ihre Aufmerksamkeit!

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