

Le model TBM appliqué au clinical staging model pour le traitement des CHR-P

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Plan

- ✓ Introduction: La trajectoire psychotique et l'entrée dans la psychose.
- ✓ De la détection à l'intervention précoce
- ✓ La mentalisation chez les FEP/CHR
- ✓ La TBM comme possible modèle thérapeutique chez les CHR-P

Introduction: La trajectoire psychotique et l'entrée dans la
psychose.

Epidémiologie des TSS

- ✓ Prévalence → 0.5% -3%. (Bhugra D. 2005 *PLoS Med*)
- ✓ M:F → 1.5:1 (symptomatologie négative et long durée plus fréquente chez les M, bref durée et présence de symptômes affectifs M=F)
- ✓ 75% des psychoses ont un début avant l'âge de 25 ans et le 25% avant l'âge de 18 ans. (Armando et al. 2015 *Current Opinion in Psychiatry*; Madaan et al. 2008 *Expert Opin Pharmacother*)
- Early Onset Psychosis (13-17 ans) (Madaan 2008; Vyas 2011; Hassan 2011)
- ✓ Prévalence 1-2/1000 adolescents
- Very Early Onset Psychosis (8-12 ans) (McClennan 2005; Addington 2007; David 2011)
- ✓ Prévalence 1/10.000 enfants

Epidémiologie des TSS

- Les troubles ont une prévalence de 23,6 millions de cas antérieurs dans le monde en 2013 (OMS, Lancet 2015).
- Une personne sur deux vivant avec la schizophrénie ne reçoit pas de soins pour cette affection (OMS, Lancet 2015).
- Le taux de récupération est de un sur sept (Jaaskelainen, Schiz Bull 2013).
- Handicap associé pertinent (11ème cause de handicap dans le monde en 2013) (OMS, Lancet 2015).
- Le risque de mortalité: deux fois plus élevé que dans la population générale (Walker et al, JAMA psy 2015).
- Les coûts nationaux annuels: 94 -102 milliards de \$ à l'échelle mondiale (Chong et al, Neuropsychiatr Dis Treat 2015).

Epidémiologie des TSS

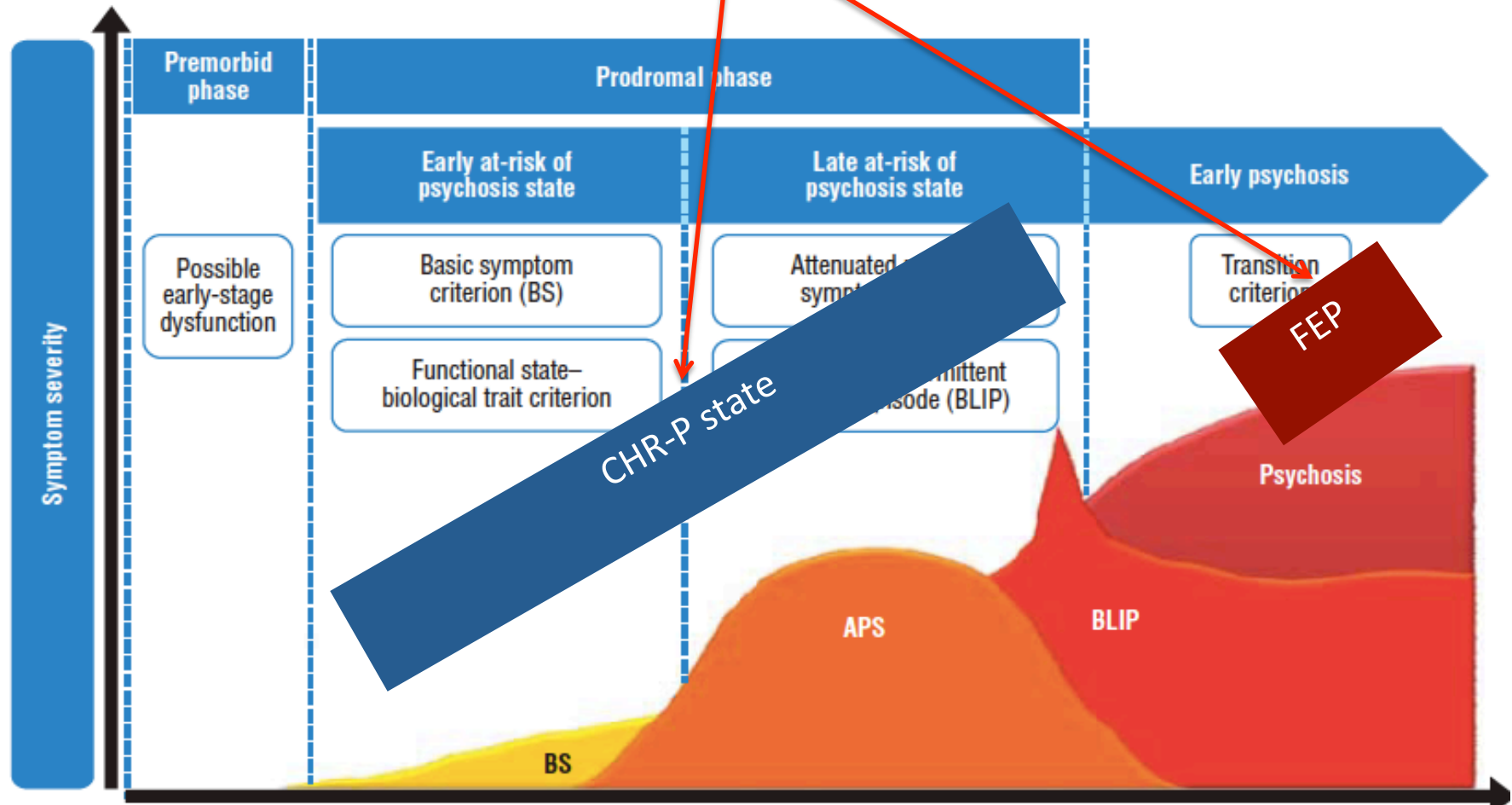
Males			Females		Total	
Cause	Total DALYs (100 000s) (%)		Cause	Total DALYs (100 000s) (%)	Cause	Total DALYs (100 000s) (%)
10-24 years						
1 Road traffic accidents	93 (7.8%)		Unipolar depressive disorders	115 (9.8%)	Unipolar depressive disorders	193 (8.2%)
2 Unipolar depressive disorders	78 (6.6%)		Schizophrenia	46 (4.0%)	Road traffic accidents	127 (5.4%)
3 Violence	69 (5.8%)		Bipolar disorder	44 (3.7%)	Schizophrenia	96 (4.1%)
4 Alcohol use	62 (5.3%)		Abortion	43 (3.7%)	Bipolar disorder	88 (3.8%)
5 Schizophrenia	50 (4.2%)		HIV/AIDS	38 (3.2%)	Violence	81 (3.5%)
6 Bipolar disorder	45 (3.8%)		Road traffic accidents	34 (2.9%)	Alcohol use	71 (3.0%)

✓ Troisième cause de handicap fonctionnel en termes d'années vécues (DALYs) chez les jeunes de 10 à 24 ans. (Gore et al. 2011 *The Lancet*)

✓ Un début précoce est associé avec une augmentation de DALYs

Le model CHR-P

EARLY DETECTION AND INTERVENTION



Le model CHR-P

Critères de recherche pour le syndrome de psychose atténuée selon le DSM-5

A - Au moins l'un des symptômes suivants est présent sous une forme atténuée, sans altération importante de la capacité à discerner la réalité. Mais leur intensité ou leur fréquence est suffisante pour justifier une prise en compte clinique :

- Délire(s)
- Hallucination(s)
- Désorganisation du discours

B - Le(s) symptômes(s) a(ont) duré(s) au moins 1 semaine durant le mois passé.

C - Le(s) symptômes(s) a(ont) débuté(s) ou s'est(se sont) aggravé(s) l'année précédente.

D - Le(s) symptômes(s) est(sont) suffisamment stressant(s) ou handicapant(s) pour l'individu pour justifier une prise en compte clinique.

E - Le(s) symptômes(s) n'est(ne sont) pas mieux expliqué(s) par un autre trouble mental, incluant un trouble dépressif ou bipolaire avec caractéristiques psychotiques, et n'est pas attribuable à l'effet d'une substance ou d'une autre condition médicale.

F - Les critères pour un trouble psychotique n'ont jamais été remplis.

- Sévérité des symptômes

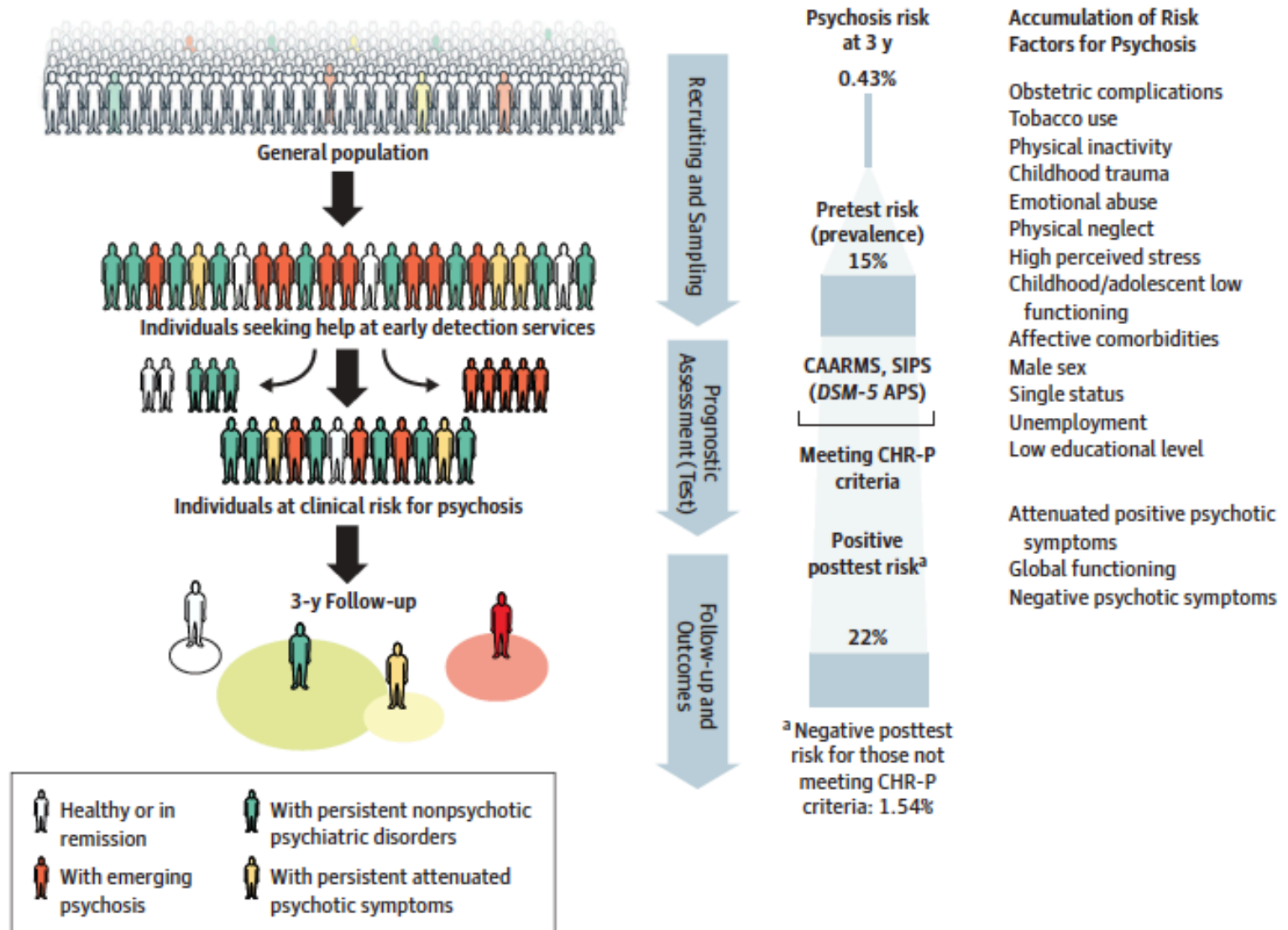
+

- Fréquence des symptômes

- Début des symptômes

- Handicap provoqué

Taux de transition et outcome



Taux de transition chez les adolescents

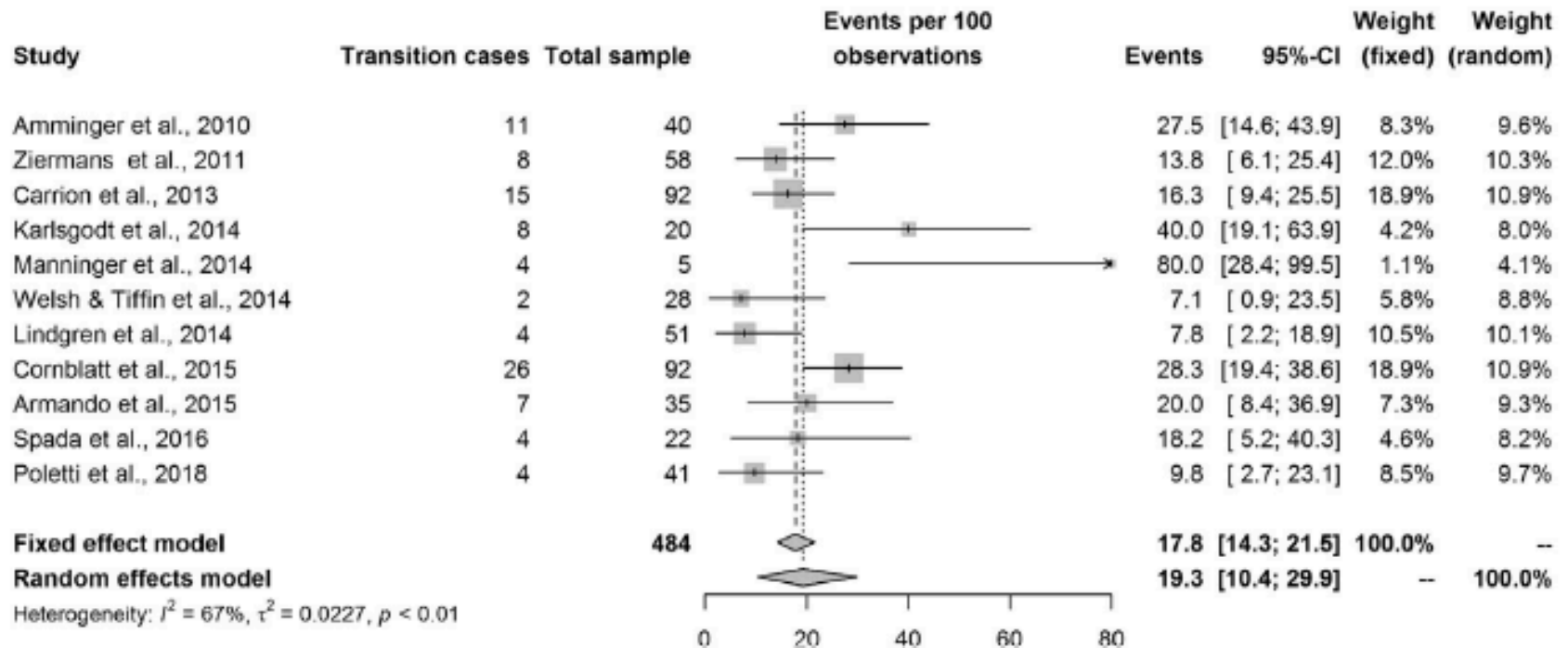
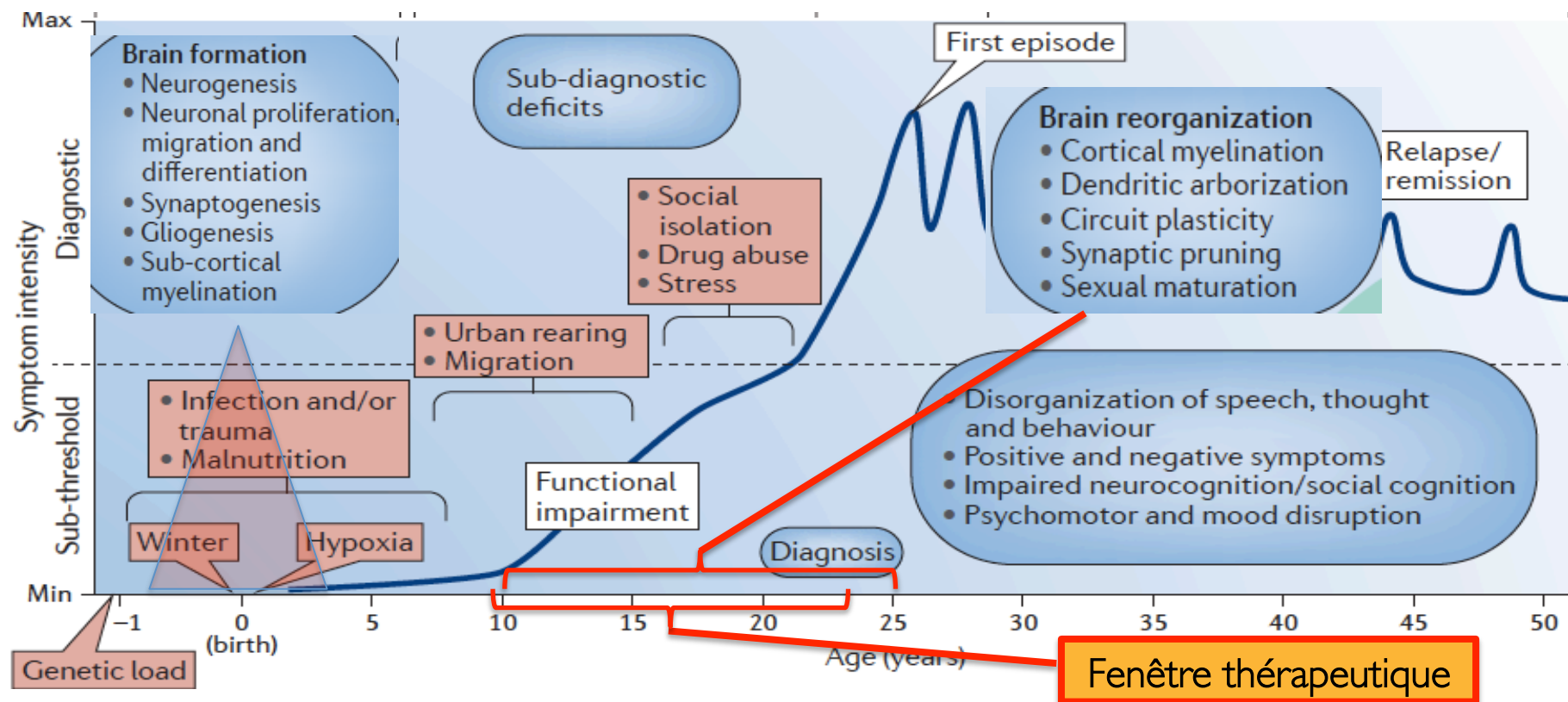


Fig. 3. Summary of pooled results: Conversion prevalence on the basis of the cumulative sample retained at follow up.

Echantillon: 553 patients
 Age moyen ($\pm$ SD): 15.8 ans ($\pm$ 0.8)
 Taux de transition: 19.3 (10.4-29.9)

De la détection à l'intervention précoce



Pre-adolescence et adolescence

1. Période clé pour le développement de diverses compétences cognitives et sociales. (Debbané et al. *Frontiers in Hum Neur* 2016; Velthorst et al. *Devel and Psychopath* 2017)
2. Phase de maturation progressive du cerveau (jusqu'à 25 ans). (Araín et al. *Neuoprsy Dis Treat* 2013; Galvan *Neuron* 2016)

Clinical staging model – CHR-P

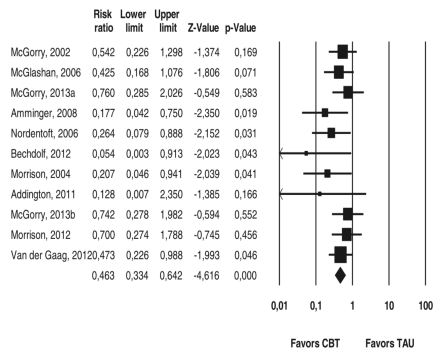
Clinical stage	Definition	Definition in clinical staging model	Intervention
0	Asymptomatic genetic risk	Premorbid	<i>Selective primary prevention</i> Improved mental health literacy Family psychoeducation
1a	Negative and cognitive symptoms	CHR-P	<i>Indicated primary prevention</i> Formal mental health literacy Family psychoeducation
1b	Attenuated psychotic symptoms	CHR-P	Active reduction of substance misuse <i>Indicated primary prevention</i> Family and individual psychoeducation Active reduction of substance misuse Vocational support Psychological therapies
1c	Short-lived remitting psychotic episodes	CHR-P	<i>Indicated primary prevention</i> As for 1b
2	Full-threshold FEP	Early full recovery	Close-in monitoring <i>Early intervention and secondary prevention</i> Family and individual psychoeducation Psychological therapies Active reduction of substance misuse Atypical antipsychotics and other medications Vocational rehabilitation

Efficacy of prevention in CHR-P

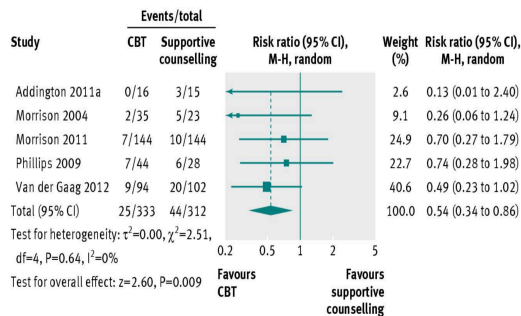
12m transition to psychosis

Previously suggested

Overall risk reduction at 12m = 50% (NNT = 9)



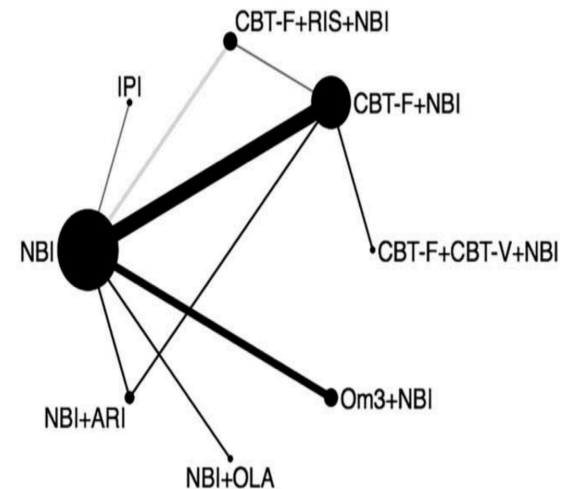
Antipsychotics
Omega-3
CBT
van der Gaag et al.
Schizophr Res 2013



CBT
Stafford et al.
BMJ 2013

But lack of evidence to support specific interventions

Network meta-analysis including 16 RCT, 2035 CHR-P



Davies et al. World Psychiatry 2018

La mentalisation chez les FEP/CHR

“Theory of Mind” in Schizophrenia: A Review of the Literature

Martin Brüne

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The term *theory of mind* (ToM) refers to the capacity to infer one's own and other persons' mental states. A substantial body of research has highlighted the evolution of ToM in nonhuman primates, its emergence during human ontogeny, and impaired ToM in a variety of neuropsychiatric disorders, including schizophrenia. There is good empirical evidence that ToM is specifically impaired in schizophrenia and that many psychotic symptoms—for instance, delusions of alien control and persecution, the presence of thought and language disorganization, and other behavioral symptoms—may best be understood in light of a disturbed capacity in patients to relate their own intentions to executing behavior, and to monitor others' intentions. However, it is still under debate how an impaired ToM in schizophrenia is associated with other aspects of cognition, how the impairment fluctuates with acuity or chronicity of the schizophrenic disorder, and how this affects the patients' use of language and social behavior. In addition to these potential research areas, future studies may also address whether patients could benefit from cognitive training in this domain.

Keywords: Theory of mind/brain evolution/
schizophrenia/linguistics/behavior/social competence

There may, however, be costs to having a highly developed ToM (Brüne 2001). In humans, for instance, ToM is apparently permanently “online,” such that other persons and sometimes even nonliving objects are continuously “screened” for their putative intentions. Thus, human ToM is inherently linked to the risk of making false conjectures about other people's intentions, for instance, by inferring “too much” or simply by overrating one's personal affectedness in a given social interaction. It is therefore crucial that every person who imputes mental states to others be able to crosscheck his or her inference against reality—that is, to interpret signals from the social environment supporting or refuting his or her assumption. Extract the *relevant* meaning from speech depends upon an intact ToM. To effectively use and interpret language, one usually has to go beyond the literal meaning of words and utterances on the basis of contextual information (Sperber and Wilson 1986, 2002). However, functional or structural disruption of the neural mechanisms underlying ToM may give rise to various types of psychopathology, including schizophrenia (Frith 1992; Brüne 2001).

In fact, impaired ToM has been described in a variety of neuropsychiatric disorders. The most extensive ToM studies have been carried out in autistic spectrum disorders (e.g., Baron-Cohen et al. 1985; Baron-Cohen 1995), in adult patients with frontal lobe damage (e.g., Rowe et al. 2001; Stuss et al. 2001), and in schizophrenia (overviews in Corcoran 2000; Brüne 2003a). Only recently has ToM research been extended to patients with frontotemporal dementia, Alzheimer's dementia or other dementias (Brüne et al. 2001; Brüne 2003b).

• La littérature et les résultats des études sur l'altération de la mentalisation chez les pz avec TSS

- ✓ De nombreuses recherches ont montré que les patients atteints de schizophrénie ont des difficultés spécifiques à déduire ce que les autres veulent dire, pensent ou font semblant.
- ✓ Cette altération affecte la façon dont les patients schizophrènes utilisent le langage et interprètent la parole.



Metacognition within narratives of schizophrenia: Associations with multiple domains of neurocognition

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BRIEF REPORT

Associations of Metacognition With Symptoms, Insight, and Neurocognition in Clinically Stable Outpatients With Schizophrenia

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Michele Procacci, MD,*† Jay Hamm, MA,§ Kelly D. Buck, CNS,|| Enrico Pompili, MD,‡ Ivana Buccione, PhD,*
Brunella Lagrotteria, PhD,* and Paul H. Lysaker, PhD||¶

- Des études menées sur des patients schizophrènes ont montré qu'une altération de la mentalisation est associée :

- ✓ les symptômes positifs et négatifs
- ✓ faible efficacité thérapeutique
- ✓ faible insight
- ✓ de mauvaises performances sociales et professionnelles

(Lysaker et al., 2007, 2010, 2011 ;
Nicolò et al., 2012)



Contents lists available at ScienceDirect

Psychiatry Research

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

Metacognition in first-episode psychosis and its association with positive and negative symptom profiles[☆]

Anne Marie Trauelsen^{a,b,c,*}, Andrew Gumley^d, Jens Einar Jansen^{b,c},
Marlene Buch Pedersen^c, Hanne-Grethe Lyse Nielsen^c, Christopher Høier Trier^e,
Ulrik H. Haahr^{c,f}, Erik Simonsen^{b,f}

Comparison of baseline characteristics between groups based on positive and negative symptoms (N=83).

	Standardized discriminant function coefficients	1 Low negative/low positive (n=34) Mean (SD)	2 Low negative/high positive (n=14) Mean (SD)	3 High negative/low positive (n=12) Mean (SD)	4 High negative/high positive (n=23) Mean (SD)	F(15, 231)	P=	η^2	Post hoc comparisons p < 0.05
ANOVA^a									
MAS-A total	0.96	16.03 (3.19)	14.57 (3.33)	11.71 (3.80)	13.35 (2.99)	6.40	< 0.001	0.20	1 > 3, 4; 2 > 3
DUP ^b	0.54	119.09 (177.06)	179.21 (214.17)	129.92 (248.68)	192.26 (225.54)	2.57	0.06	0.09	3 < 2, 4
Number of adversities ^c	−0.40	2.88 (1.97)	2.50 (1.61)	2.92 (1.98)	3.04 (1.97)	0.24	0.87	0.01	
Premorbid academic	0.31	2.36 (1.15)	1.61 (1.37)	2.25 (0.98)	2.93 (1.53)	1.38	0.26	0.05	
Premorbid social ^b	−0.44	1.90 (1.28)	2.83 (1.23)	1.78 (1.62)	2.38 (1.45)	1.15	0.35	0.04	

Le FEP et la cognition sociale

- Patients atteints de PEF montrent des capacités de mentalisation significativement plus faibles que l'échantillon de contrôle.
- En particulier, les déficits de mentalisation sont associés à une symptomatologie négative

(MacBeth et al, 2014, 2015 ;
McLeod et al, 2014 ;
Trauelsen et al, 2016)

Cognition sociale et risque psychotique

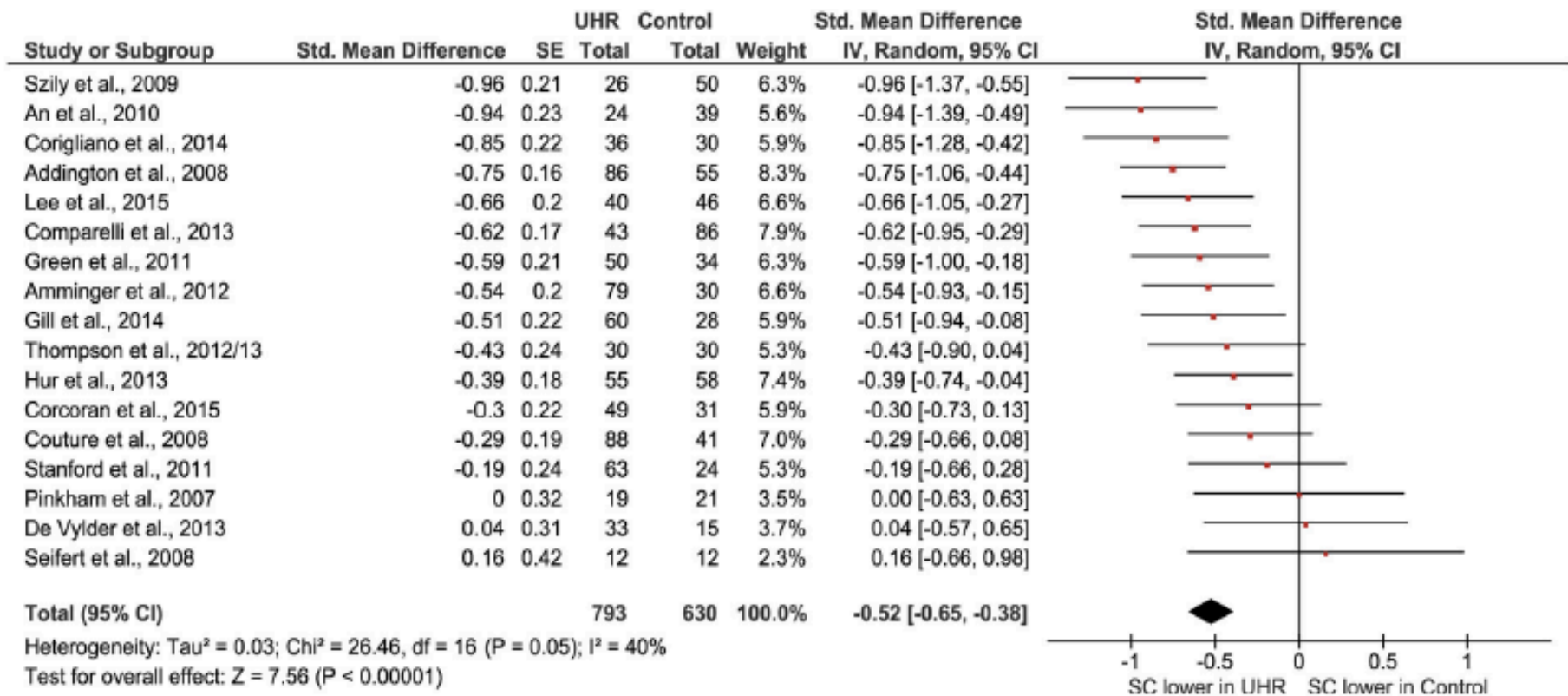


Fig 2. Forest plot of social cognition in UHR versus healthy controls.

La majorité des études menées sur la cognition sociale chez les patients de l'CHR-P montrent que celle-ci est déficitaire par rapport aux groupes de contrôle.

La mentalisation comme facteur de résilience face à la progression des symptômes psychotiques subcliniques

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ACTA PSYCHIATRICA SCANDINAVICA

Course of auditory vocal hallucinations in childhood: 11-year follow-up study

Les hallucinations chez les enfants et les adolescents sont moins souvent suivies d'un FEP chez les jeunes ayant de bonnes capacités de mentalisation.

(Bartels-Velthuis et al, 2011;2016)

La mentalisation comme facteur de résilience face à la progression des symptômes psychotiques subcliniques

Psychological Medicine, Page 1 of 15. © Cambridge University Press 2015
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ORIGINAL ARTICLE

Psychotic experiences and hyper-theory-of-mind in preadolescence – a birth cohort study

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OPEN ACCESS Freely available online

PLOS ONE

Hyper-Theory-of-Mind in Children with Psychotic Experiences

Lars Clemmensen^{1*}, Jim van Os², Anne Mette Skovgaard³, Mette Væver⁴, Els M. A. Blijd-Hoogewys⁵,
Agneta A. Bartels-Velthuis⁶, Pia Jeppesen¹

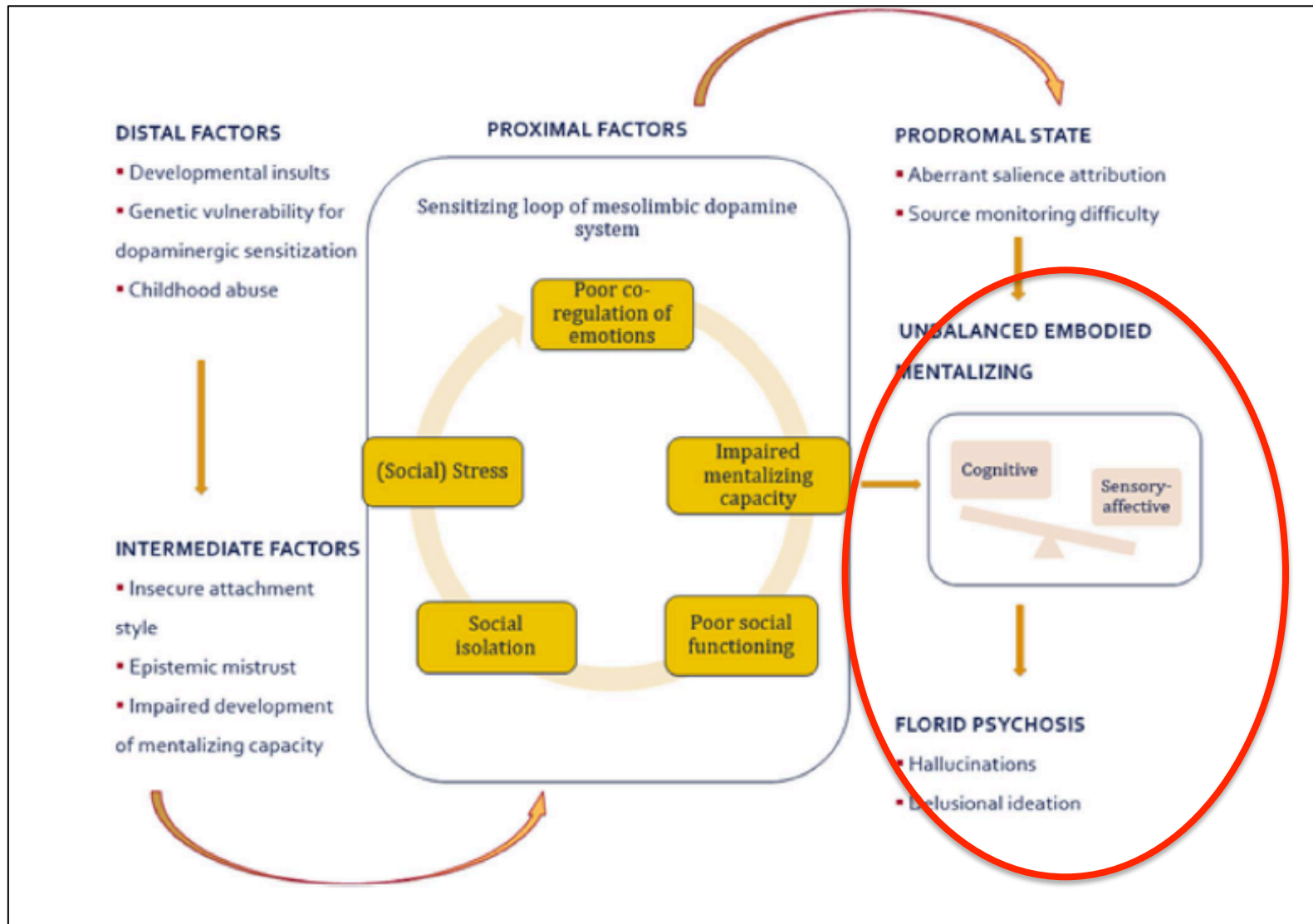
1 Child and Adolescent Mental Health Center, Mental Health Services, the Capital Region of Denmark, Copenhagen, Denmark, 2 Department of Psychiatry and Psychology, Maastricht University Medical Centre, Maastricht, The Netherlands, 3 Department of Public Health, University of Copenhagen, Copenhagen, Denmark, 4 Department of Psychology, University of Copenhagen, Copenhagen, Denmark, 5 INTER-PSY Groningen, Groningen, The Netherlands, 6 University of Groningen, University Medical Center Groningen, University Center for Psychiatry Groningen, Groningen Triadegebouw, The Netherlands

Les enfants de 9 à 12 ans ayant vécu des expériences psychotiques (PLE) ont tendance à l'hypermentalisation

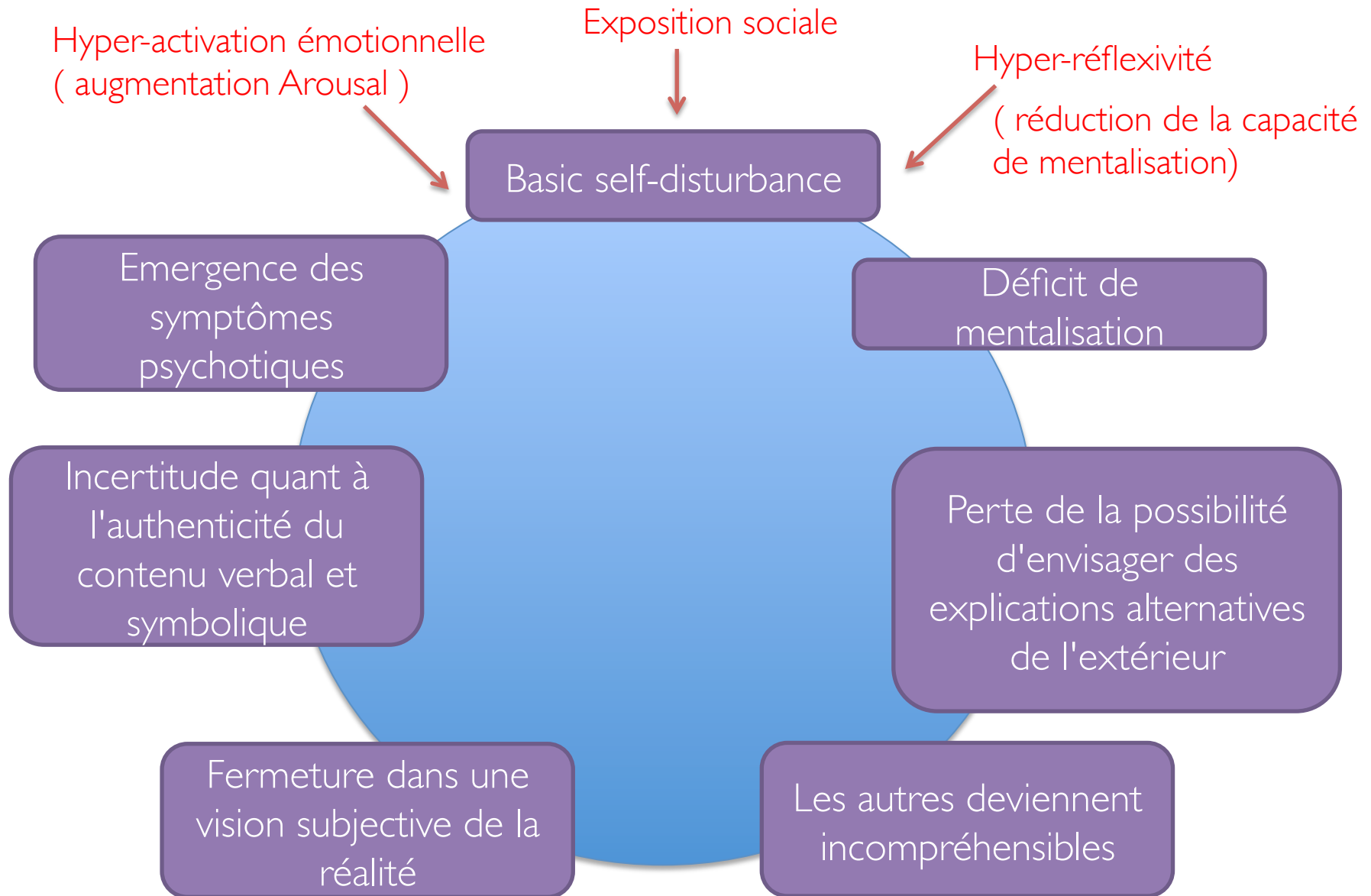
(Hyper Theory of Mind ; Clemmensen et al., 2014, 2015)

La TBM comme possible modèle thérapeutique chez les
CHR-P

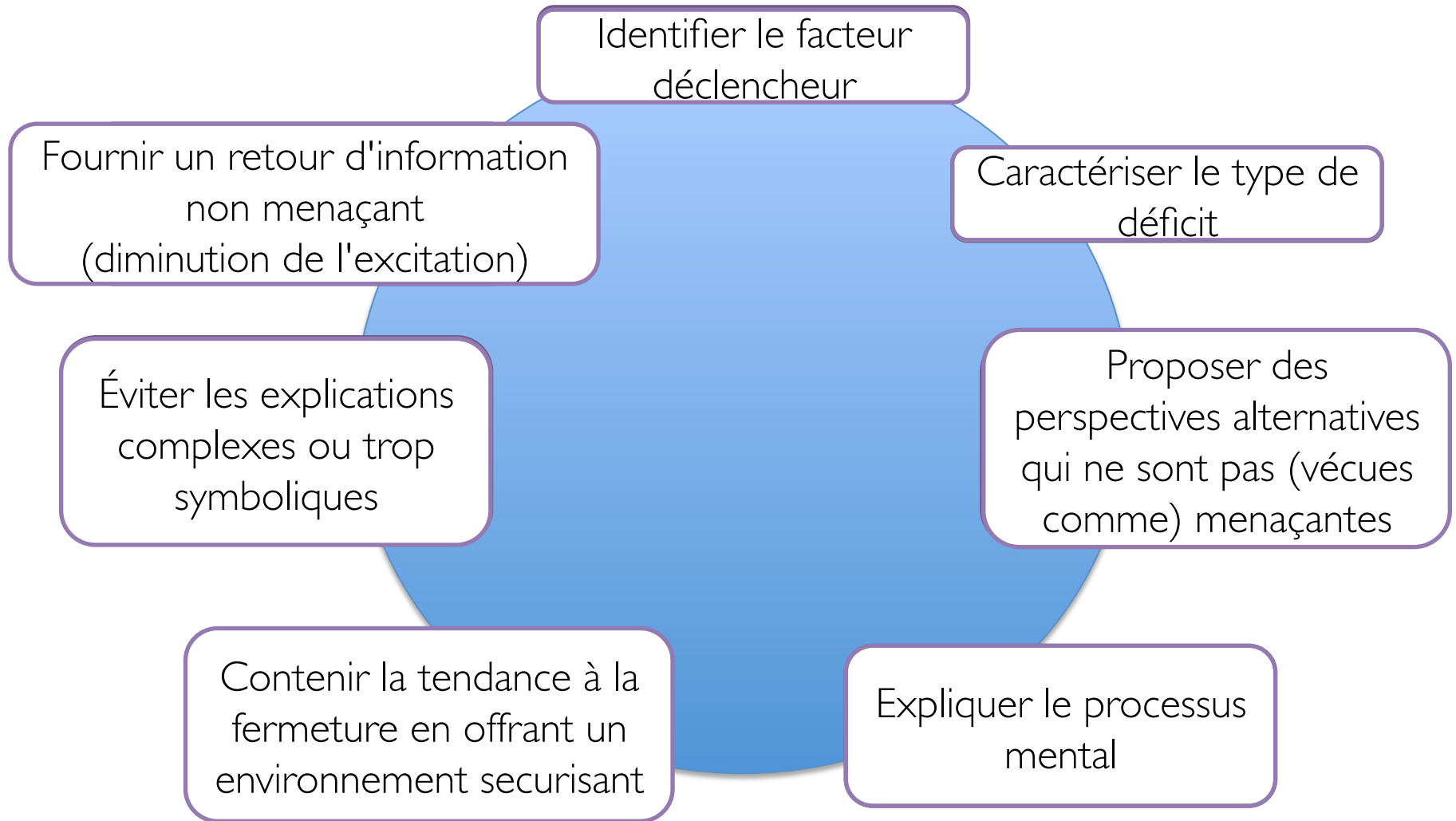
Le role de la mentalisation dans le processus psychotique



Activation du symptôme psychotique selon une approche de TBM



Exemple d'intervention TBM pour un sym psychotique atténué



Nous ne sommes que au debut....

A Mentalization-Based Approach to the Development of the Therapeutic Alliance in the Treatment of Schizophrenia

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The Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School*

This article presents a clinical illustration of a mentalization-based approach to the development of a therapeutic alliance in the treatment of schizophrenia. A clinically focused overview of the attachment-based understanding of mentalization central to the mentalization-based treatment model is first provided. This is followed by a brief summary of the theory and evidence supporting the possible link between attachment disturbances and deficits of mental state understanding in schizophrenia. A case presentation then illustrates the application of core mentalization-based principles and interventions to enhance the therapeutic alliance by addressing disruptions of mentalization and reducing paranoia in the treatment of a patient with early course schizophrenia. © 2014 Wiley Periodicals, Inc. *J. Clin. Psychol.: In Session* 71:146–156, 2015.

 **frontiers**
in Human Neuroscience

Attachment, Neurobiology, and Mentalizing along the Psychosis Continuum

Martin Debbané^{1,2,3,*†}, George Salaminios^{2†}, Patrick Luyten^{2,4}, Deborah Badoud¹,
Marco Armando³, Alessandra Solida Tozzi⁵, Peter Fonagy^{2,4} and Benjamin K. Brent⁶

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ORIGINAL PAPER

Mentalization-Based Treatment in Clinical High-Risk for Psychosis: A Rationale and Clinical Illustration

Martin Debbané^{1,2,3} · Jallal Benmiloud² · George Salaminios³ ·
Alessandra Solida-Tozzi⁵ · Marco Armando² · Peter Fonagy^{3,4} ·
Anthony Bateman^{3,4}

A Mentalization-Informed Staging Approach to Clinical High Risk for Psychosis

Marco Armando¹, Joost Hutsebaut² and Martin Debbané^{1,3,4*}

TABLE 2 | Possible mentalizing interventions according to the clinical stage.

Stage	Interventions	Timing/Setting	Targets/Goals
Stage 0	School and family-based prevention	'mental' or 'emotional' education in primary prevention large scale campaigns	Providing psychoeducation about mentalization, the linkage between arousal, anxiety, reduction of cognitive performance and mentalization.
Stage Ia	MBT-A; MBT-F psycho-education	Short intervention, including psycho-education, skills strenghtening in adolescent groups and/or family therapy	More focused psychoeducation about the linkage between arousal, loss of mentalization and the development of psychotic symptoms. Patients are told about the key aspects of MBT, including the meaning of mentalizing and its sensitivity to arousal
Stage Ib	As for 1a Medications targeted to treat comorbid disorders (eg. anxiety, depression) Take into account low doses of antipsychotics in accordance to severity of BLIPS	More intensive intervention including individual work, combined with intervention at multiple levels (school, family,...)	Starting from stage Ib the intervention is progressively focused on 1) the patient's state of mind as central to the rehabilitation of the capacity for social understanding; 2) the emphasis on the role of affect in disruptions of the ability to mentalize; and 3) the importance given to understanding the links between the quality of mentalization and specific Interpersonal/ attachment contexts. Five problem areas are developed and routinely reviewed with the patient, including: commitment to treatment, psychiatric symptoms, social interaction/relationships, destructive behavior, and community functioning
Stage II	As for Ib MBT-G for psychosis Antipsychotics	Long and intensive intervention	
Stage III	As for II AMBIT	Very long intervention with an explicit focus on case management and an outreaching approach	

Perspectives



Traitement basé sur la mentalisation chez 40 jeunes avec CHR-P: une étude pilote randomisée.

Objectif principal : étudier l'effet de la MBT-A sur les symptômes psychotiques et sur l'incidence de la FEP dans une cohorte de CHR-P.

Objectif secondaire : étudier l'effet de la MBT-A sur les capacités de mentalisation, la symptomatologie, la fonction cognitive, la qualité de vie.

Le programme MBT-A est un programme de psychothérapie manuelle d'une durée de six mois. Il comprend des séances individuelles hebdomadaires de MBT-A (soit 24 séances au minimum) et une thérapie de famille mensuelle basée sur la mentalisation (MBT-F, soit 6 séances au minimum).

Pour résumer...

- Les preuves scientifiques montrent que le déficit de mentalisation n'est pas simplement une conséquence de la psychose, mais plutôt un facteur (de risque, de vulnérabilité) déjà présent dans les premiers stades de la trajectoire psychotique.
- En même temps, une bonne capacité de mentalisation semble représenter un facteur de résilience (protecteur) par rapport à la progression vers la psychose.

D'où la justification possible de l'utilisation de techniques visant à mettre en œuvre cette compétence dans les premiers stades de la trajectoire vers un trouble psychotique.

Le model TBM appliqué au clinical staging model pour le traitement des CHR-P

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