TERAPIE INTEGRATE

Associazione di interventi farmacologici e non farmacologici nel trattamento dei disturbi mentali gravi

Interventi farmacologici e non farmacologici per giovani pazienti a rischio di sviluppare disturbi dello spettro psicotico

Marta Francesconi– Sapienza, University of Rome
19/06/2017

High Risk State

Definition

The Psychosis High-Risk State:

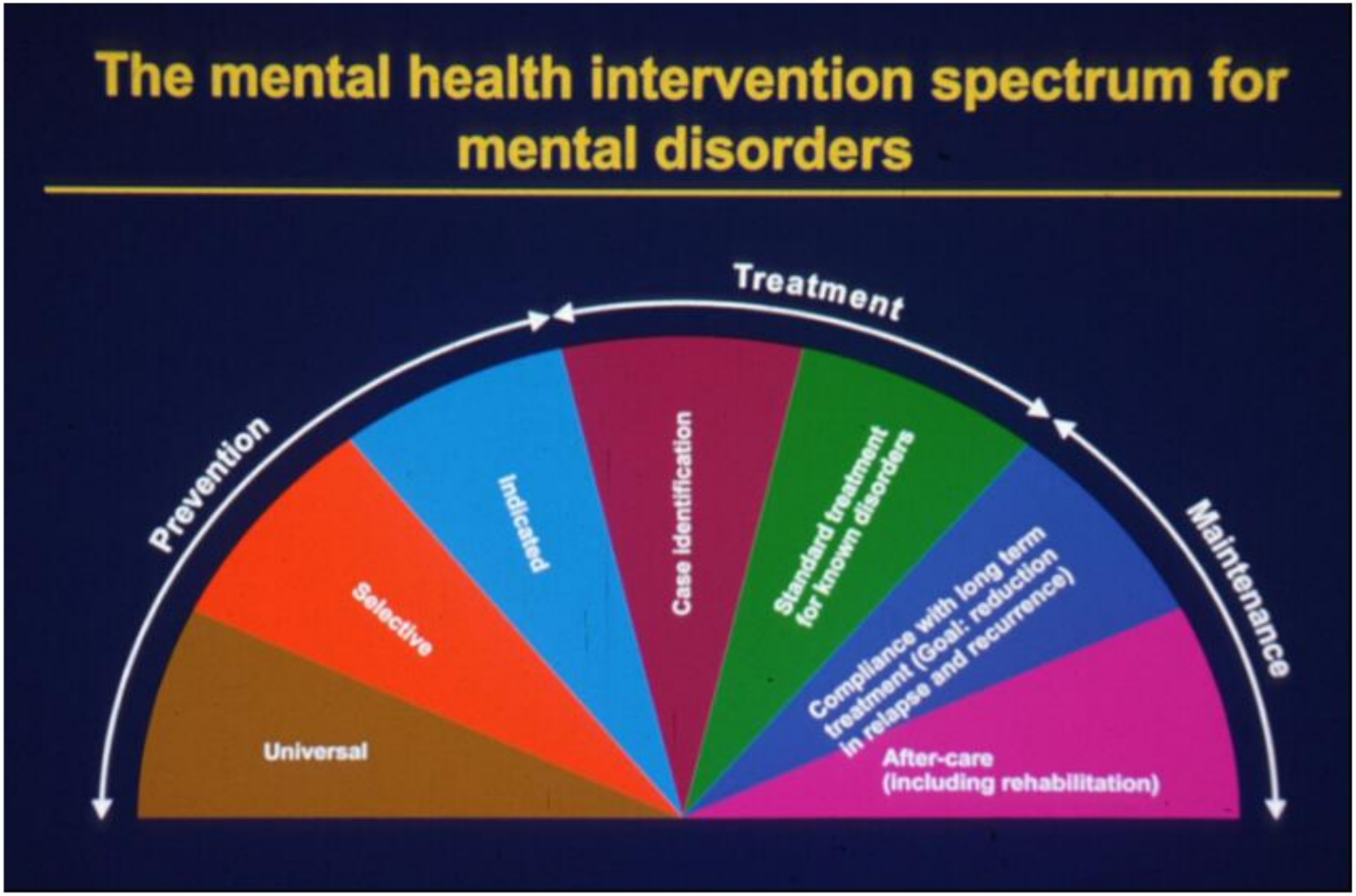
A Comprehensive State-of-the-Art Review

Dr Paolo Fusar-Poli, MD, PhD,
Department of Psychosis Studies, King's College London, London, United Kingdom; OASIS team for prodromal psychosis, NHSSLAM Foundation Trust, London

- During the last 2 decades significant improvements have been done regarding detection of early sings of psychosis, the most significant one being the development and validation of standardized instruments to define the prodromal phase of psychotic disorders
- However, these instruments showed a great ability to rule out, but not to rule in psychosis in help seeking individuals. There is an increasing need to better define the characteristics of those people that will develop frank psychosis, adding to risk algorithm other relevant domains of interest, such as socio-demographic, familiar risk, neurocognitive, neuroimaging risk factors.

Treatments?

(three largest trials - Omega 3 Mc Gorry; Family-aided assertive community treatment Mc Farlan ; Morrison CBT)



Mrazek P & Haggerty R, ed (1994) Washington D.C.: National Academy Press

Indicated prevention

"Targeted to high risk individuals with minimal but detectable signs or symptoms foreshadowing mental disorders…but who do not meet diagnostic level at the current time"

Mrazek and Haggerty -1994

Indicated prevention

Targets:

1) Psychosis onset
2) Functional decline

Indicated prevention

1) Psychosis onset

- Psychotherapy
- Antipsychotics
- Integrated therapy
- Experimental therapeutics

RCTs: Psychotherapy

Author & year	Treatment description	Control description	p-value (transition)
Morrison, 2004	Cognitive therapy	monitoring	p= 0.028
Addington, 2011	CBT	supportive therapy	p= 0.059
Morrison, 2012	Cognitive therapy + monitoring	monitoring	p=0.452
Bechdolf, 2012	Integrated Psychological interventions (CBT, group skills training, cognitive remediation, multifamily psychoeducation)	supportive counselling	p=0.008
Van der Gaag, 2012 (Ising, 2016)	CBT-uhr (CBT specifically targeted at cognitive biases combined with TAU)	TAU	p=0.032
Miklowitz, 2014	family-focused treatment (psychoeducation, problem-solving, stress control and better communication)	enhanced care, psychoeducation for symptom prevention	n.s
Stain, 2016	CBT	non-directive reflective listening	n.s.
McGorry, 2013 (Yung, 2010)	Cognitive therapy + placebo	supportive therapy + placebo	n.s.
McFarlane, 2015 [*Not an RCT]	Family-aided Assertive Community Treatment (FACT: case management, supportive counselling, psychoed in multi-family groups, supported employment/ed., medication management)	monitoring	n.s

RCTs: antipsychotics

Author	Treatment	Control	Duration of treatment	Total N	RR (95%CI) p-value [transition]
McGlashan, 2006	Olanzapine (5-15mg/day)	Placebo	12m	50	0.43 (0.17- 1.08) p=0.07
Yung et al, 2010	Cognitive therapy + Risperidone (0.5-2 mg/day)	Cognitive therapy + placebo	6m	87	0.51 (0.1- 2.65) p=0.42
McGorry, 2013 [FU Yung, 2010]	Cognitive therapy + Risperidone (0.5-2 mg/day)	Cognitive therapy + placebo	12m	87	1.02 (0.38- 2.67) p=0.96
Ruhrmann, 2007	Needs-focused intervention + Amisulpride (50-800mg/day)	Needs-focused intervention	3m treatment, FU=24m.	124	- Both groups: improved BAPPSS (Basic and Positive Symptoms) scores. - Lower PANSS-pos in treatment vs control (p<.001) by endpoint.

Additional open-label studies conducted but not reported here…

RCTs: combined psychotherapy/APD

Author	Treatment	Control	Duration of treatment	FU period reported	Total N	RR (95%CI) p-value [transition]
Yung et al, 2010	Cognitive therapy + Risperidone (0.5-2 mg/day)	Supportive therapy + placebo	12m	6m	71	0.65 (0.10– 4.36) p=0.66
McGorry, 2013 [FU Yung, 2010]	Cognitive therapy + Risperidone (0.5-2 mg/day)	Supportive therapy + placebo	12m	12m	71	0.76 (0.28-2.03) p=0.58
McGorry, 2002	(Specific Preventive Intervention, SPI): Risperidone (1-2mg/day) + CBT	Needs based intervention (NBI)	Both interventions 6m, then NBI offered 6m	6m	59	0.27 (0.08-0.89) p=0.03
McGorry, 2002	(SPI) Risperidone (1-2mg/day) + CBT	Needs based intervention (NBI)	Both interventions 6m, then NBI offered 6m	12m	59	0.54 (0.23- 1.30) p=0.17
Phillips, 2007 [FU McGorry]	(Specific Preventive Intervention, SPI): Risperidone (1-2mg/day) + CBT	Needs based intervention (NBI)	Both interventions 6m, then NBI offered 6m	36-48m	59	0.75 (0.39-1.46) p=0.40

RCTs: experimental therapeutics

Author	Treatment	Control	Duration of treatment	FU period reported	Total N	RR (95%CI) p-value [transition]
Amminger, 2010	Omega-3 PUFAs (1200mg/day)	Placebo	12 weeks	6m	81	0.10 (0.01-0.72) p=0.02
Amminger, 2010	Omega-3 PUFAs (1200mg/day)	Placebo	12 weeks	12m	81	0.20 (0.05-0.83) p=0.03
McGorry, 2017	Omega-3 PUFAs (1.4g/day) + cognitive-behavioural case management (CBCM)	Placebo + CBCM	6m	6m, 12m	304	*Kaplan-Maier (12m) 11.2% vs 11.5%,* ***NS****.*
Woods, 2013 [PILOT RCT]	Glycine (0.8g/kd/day)	Placebo	12 weeks, then 12 weeks open	12w, 24w	**8**	-Reduced symptoms (MDRS, p<.05) -Possibly improved cognition

BMJ 2013;346:f185 doi: 10.1136/bmj.f185 (Published 18 January 2013)

RESEARCH

Early interventions to prevent psychosis: systematic review and meta-analysis

Megan R Stafford *systematic reviewer*[1], Hannah Jackson *research assistant*[1], Evan Mayo-Wilson *senior research associate*[2], Anthony P Morrison *professor of clinical psychology*[3], Tim Kendall *codirector National Collaborating Centre for Mental Health*[4]

- Moderate quality evidence for CBT (RR 0.54)
- Very low quality evidence for omega-3 FA
- Low to very low quality evidence for integrated psychotherapy

Indicated prevention

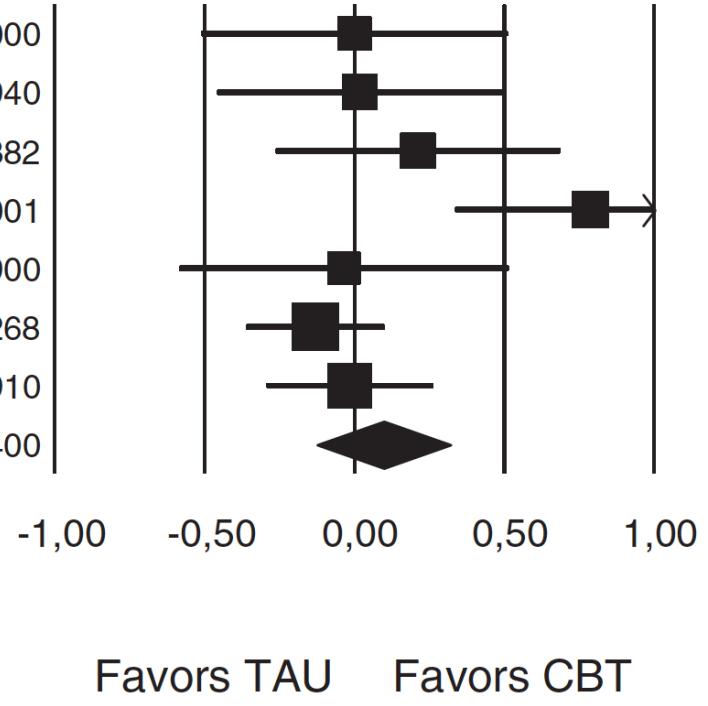
2) Functional Decline

Social Functioning (GAF and SOFAS): CBT vs TAU, 12m FU

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McGorry, 2002	0,000	0,261	0,068	-0,511	0,511	0,000	1,000
McGorry, 2013	0,018	0,243	0,059	-0,458	0,494	0,075	0,940
McGorry, 2013b	0,212	0,242	0,059	-0,263	0,687	0,874	0,382
Amminger, 2001	0,788	0,231	0,053	0,335	1,240	3,414	0,001
Adington, 2011	-0,035	0,281	0,079	-0,585	0,515	-0,125	0,900
Morrison, 2012	-0,131	0,118	0,014	-0,362	0,101	-1,107	0,268
vander Gaag, 2012	-0,016	0,141	0,020	-0,292	0,261	-0,113	0,910
	0,096	0,114	0,013	-0,127	0,319	0,841	0,400

Statistics for each study

Std diff in means and 95% CI



van der Gaag et al. (2013) Schizophrenia Research

Need for:

1)Redefinition of the At Risk Mental State

1)More targeted interventions

1. Redefinition of the At Risk Mental State

Schizophrenia Bulletin vol. 43 no. 1 pp. 44–47, 2017
doi:10.1093/schbul/sbw158

The Clinical High-Risk State for Psychosis (CHR-P), Version II

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Clinical Stage	Definition	Definition in the Clinical Staging Model	Possible Interventions
0	Asymptomatic genetic risk	Premorbid	Improved mental health literacy, family psychoeducation
1a	Negative and cognitive symptoms	CHR-P	As for 0 plus active reduction of substance misuse
1b	Attenuated Psychotic Symptoms (APS)	CHR-P	As for 1a plus individual psychological therapies
1c	Short-lived remitting psychotic episodes (BLIPS/BIPS)[a]	CHR-P	As for 1c plus close-in monitoring and prevention of psychosis recurrence
2	Full-threshold first-episode psychosis (FEP)	FEP	As for 1c plus antipsychotics and vocational rehabilitation

2. More targeted interventions

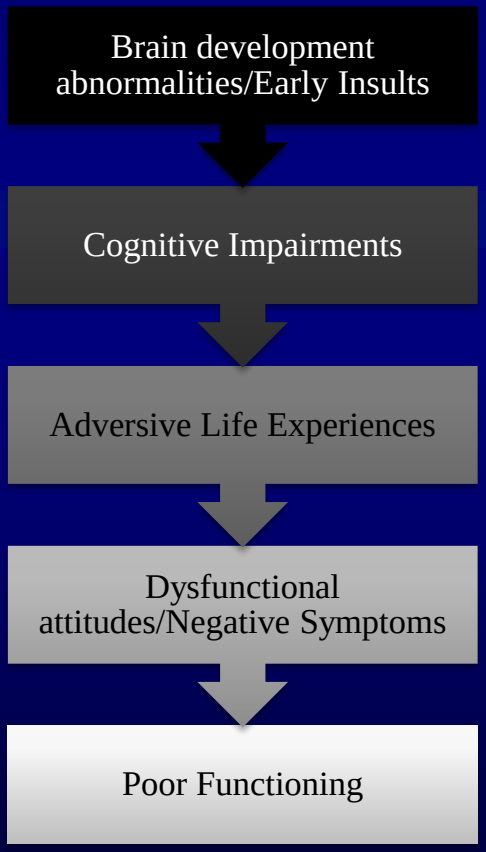
- Identification and intervention on key determinants:

  -Neurocognition
  -Theory of Mind
  -Experiential Negative Symptoms

- Transdiagnostic approach

Functional decline

NIMH – Functioning working group



M. Green et al. 2012

A. T. Beck et al. 2006

B. Cornblatt et al. 2013

2) Functional decline

Psychological Medicine, Page 1 of 12. © Cambridge University Press 2017
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ORIGINAL ARTICLE

From neurological soft signs to functional outcome in young individuals in treatment with secondary services for non-psychotic disorders: a path analysis

A. Minichino[1,2]*†, M. Francesconi[1,2]†, R. E. Carrión[3], R. Delle Chiaie[1], A. Bevilacqua[4,5], M. Parisi[6], S. Rullo[7], F. S. Bersani[1], M. Biondi[1] and K. Cadenhead[2]

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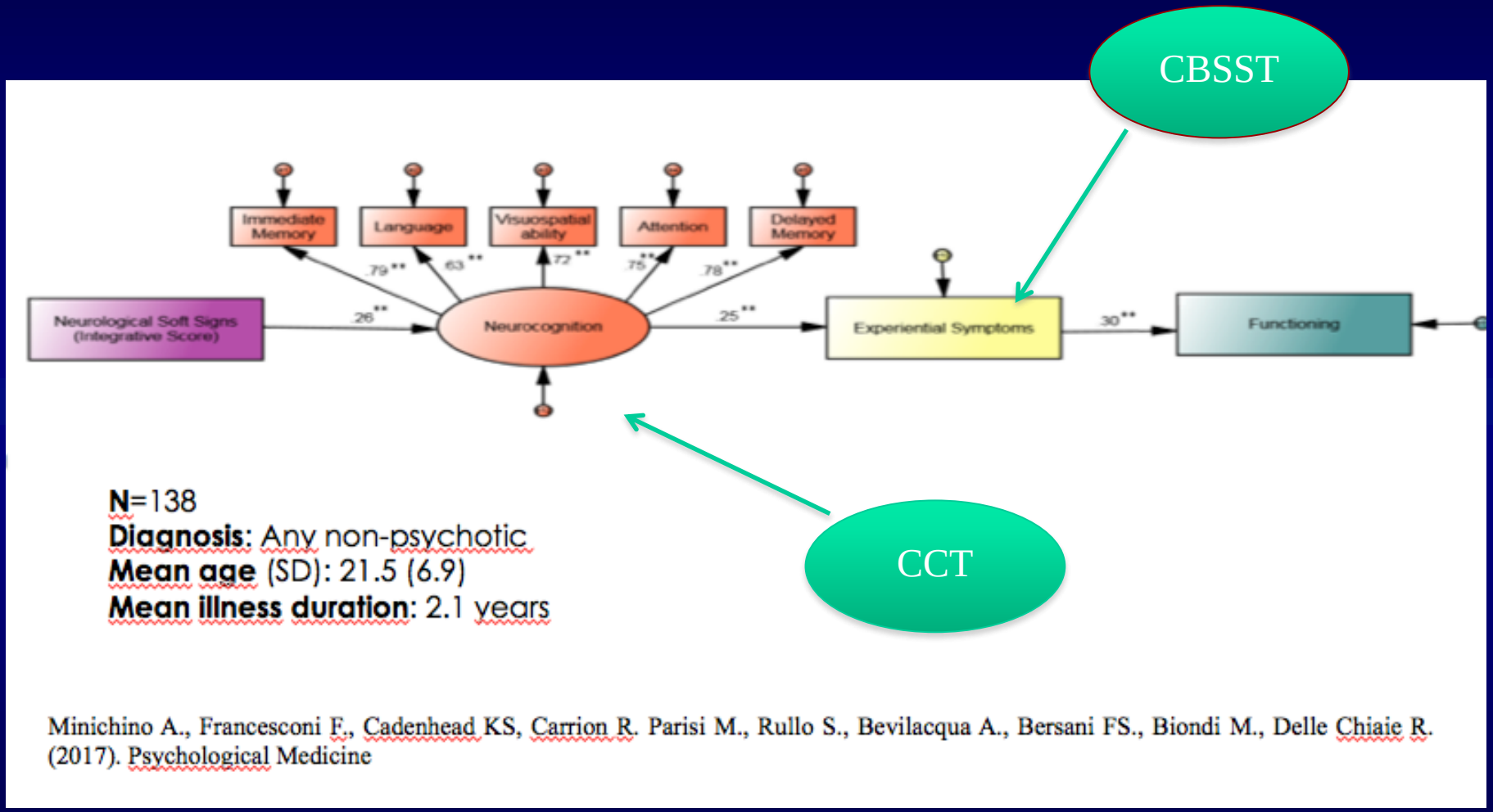
Theory of Mind as a mediator variable between neurocognition and functioning in young individuals in treatment with secondary services for non-psychotic disorders

Marta Francesconi [a, b, 1], Amedeo Minichino [a, b, *, 1], Ricardo E. Carrión [c], Roberto Delle Chiaie [a], Arturo Bevilacqua [d, e], Maurizio Parisi [f], Santo Rullo [g], Francesco Saverio Bersani [a], Massimo Biondi [a], Kristin Cadenhead [b]

Functional decline

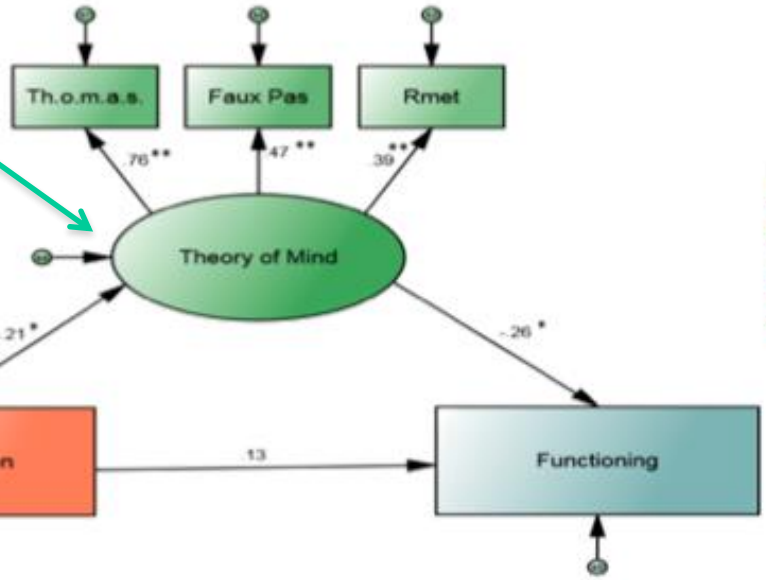


Minichino A., Francesconi F., Cadenhead KS, Carrion R. Parisi M., Rullo S., Bevilacqua A., Bersani FS., Biondi M., Delle Chiaie R. (2017). Psychological Medicine

Functional decline

CBSST

CCT



N=138
Diagnosis: Any non-psychotic
Mean age (SD): 21.5 (6.9)
Mean illness duration: 2.1 years

Mediation model. *p<0.05; **p< 0.01. The ellipse represents the unobserved latent variable ToM. Rectangles represent observed measured variables. Values are standardized path coefficients

Francesconi M., Minichino A., Cadenhead KS, Carrion R. Parisi M., Rullo S., Bevilacqua A., Bersani FS., Biondi M., Delle Chiaie R. (2016). Psychiatry Res. In press

Aim

Improving the outcomes