COGNITIONS ET TROUBLES DE L'HUMEUR

Ferrepsy 2023

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LIEN D'INTÉRÊT

- Aucun avec la présentation
- Workshop, congrès, symposium:
  - Jansenn,
  - Lundbeck,
  - Jazz

PLAN

- Cognitions
- Quelles atteintes?
  - Trouble dépressif
  - Trouble bipolaire

COGNITIONS

COGNITIONS?

- Cognitions dites chaudes vs Cognitions dites froides
- Cognitions « chaudes »:
  - Processus cognitif en lien avec les émotions et les stimuli sociaux
  - Interaction émotions-cognitions
- Cognitions « froides »:
  - Traitement de l'information en absence d'influence de l' motion
  - Attention, fonctions exécutives, mémoire de travail, mémoire autobiographique etc…

COGNITIONS DITES FROIDES

- **Attention**: vitesse de traitement de l'information, attention sélective, attention soutenue et traitement automatique
- **Fonctions exécutives**
- **Mémoires** (antérograde, rétrogrades (dont autobiographique): sémantique et épisodique, procédurale, perceptive)

COGNITION SOCIALE: THÉORIE DE L'ESPRIT

- Capacité:
  - à attribuer des états mentaux pour soi et les autres
  - À comprendre et prédire leurs comportements, leurs intentions et leurs souhaits
- Deux composantes:
  - Décoder l'état mental des autres
  - Capacités à raisonner sur l'état mentale des autres
- +/- TOM froide: cognitive et TOM chaude: affective

Unoka et al., 2015; Zabizadeh et al. 2017; Nazarov et al., 2014; Baron-Cohen et al.1995

QUELLES ATTEINTES

TROUBLE DÉPRESSIF

PLAINTES COGNITIVES

- Présent dans 85 à 94% des troubles dépressifs
- Présent chez 71% des patients qui répondent au TTT
- Présent également à rémission (env. 40%)

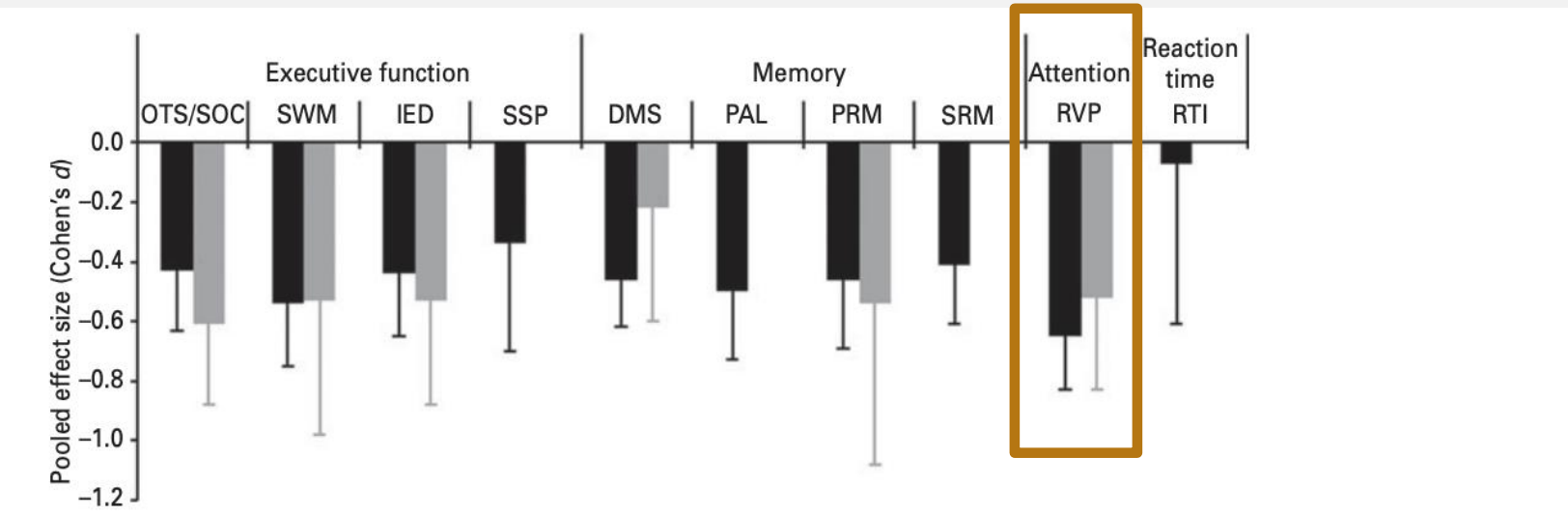
Conradi et al. 2011, McClintock et al. 2011, Zimmerman et al. 2012

COGNITIONS DITES CHAUDES

- 2 biais:
  - ⬆ mémoire et attention pour les stimuli négatifs
  - ⬆ « self-focus »:
    - Rumination
    - Auto-dépreciation

COGNITIONS DITES FROIDES: ATTENTION

Attention soutenue: Rapid Visual Information Processing: https://youtu.be/gxF9hSdrmnw



Méta-analyse 24 études

Rock et al. 2014

COGNITIONS DITES FROIDES: ATTENTION

- Altération de l'attention d'autant **+ importante qu'un effort soutenue est demandé:**
  - Phase aigue
  - Rémission : même si naif de tout traitement

Weiland-Fiedler et al. 2004;Hammar et al. 2014, Polosan et al. 2016

COGNITIONS DITES FROIDES: FONCTIONS EXÉCUTIVES

- **Les fonctions exécutives** = des processus de haut niveau cognitif qui contrôlent et régulent des processus de plus bas niveau (perception, réponse motrice…) => guider, avec un certain coût (effort), le comportement vers un but précis
- **Les fonctions exécutives**=> réponse flexible à l'environnement, en évitant de s'appuyer sur des habitudes, =>:
  - prendre des décisions
  - évaluer les risques,
  - planifier l'avenir,
  - anticiper,
  - séquencer les actions et
  - s'adapter aux situations nouvelles.

Polosan et al. 2011

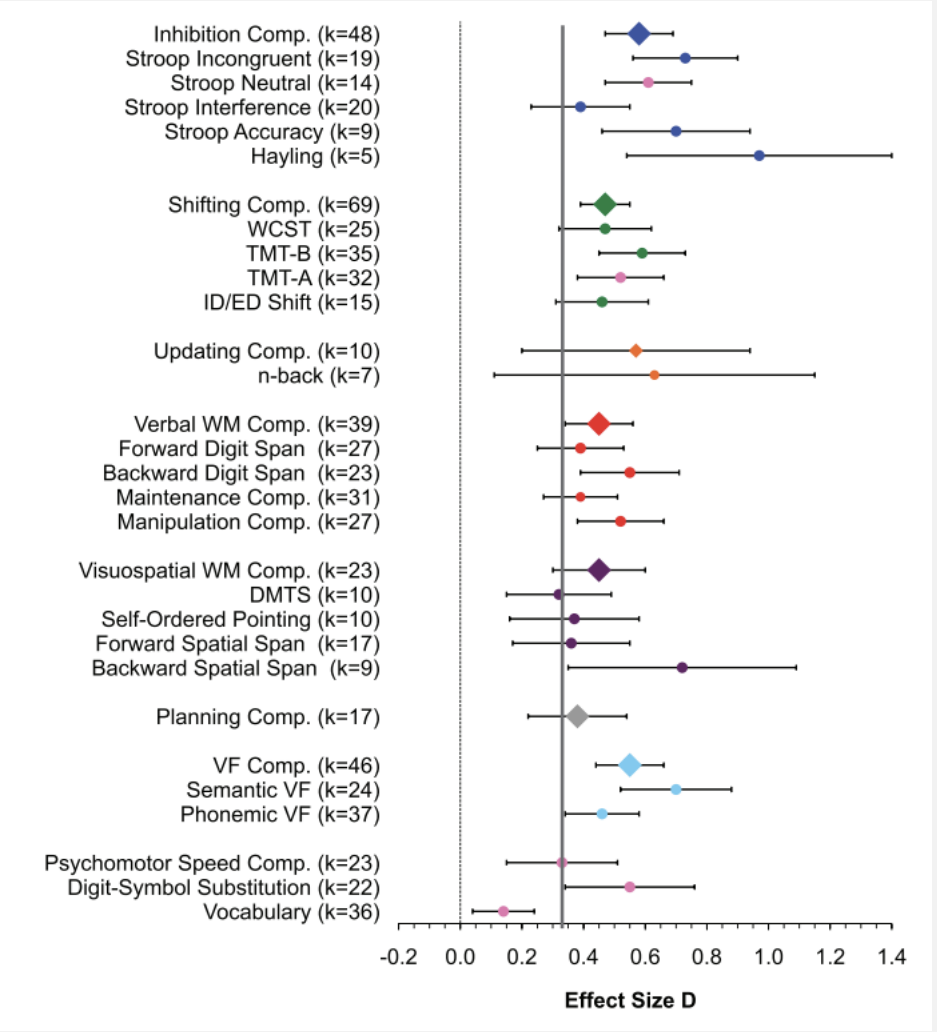
COGNITIONS DITES FROIDES: FONCTIONS EXÉCUTIVES

- Réactualisation
- Flexibilité
- Inhibitions de réponse
- Mémoire de travail
- Planification

COGNITIONS DITES FROIDES: FONCTIONS EXÉCUTIVES

Fonctions exécutives = 0,32-0,97

- Inhibition (interférence Stroop) = 0,39
- Inhibition (Hayling) = 0,97
- Flexibilité – Wisconsin test = 0,47
- Flexibilité – ID/ED Shiftc = 0,46
- Trail Making Task B = 0,59
- Réactualisation (n-back) = 0,63
- Mémoire de travail verbale = 0,45
- Mémoire de travail visuo-spatiale = 0,45
- Planification = 0,38
- Fluence verbale sémantique = 0,70
- Fluence verbale phonémique = 0,46



Snyder et al.2013

COGNITIONS DITES FROIDES: MÉMOIRE ANTÉROGRADE

- Atteintes mnésiques=
  - Rappel Libre >> Rappel Indicée
  - Rappel Libre >> Reconnaissance
- Impact du type de matériel: atteintes mnésiques:
  - Visuel << Verbal

Burt et al. 1995; Kindermann et al. 1997

COGNITIONS DITES FROIDES: MÉMOIRE AUTOBIOGRAPHIQUE

RAPPELS SPÉCIFIQUES

Table 2
Effect sizes (DELTA) of comparisons, Confidence Intervals (CI) and homogeneity (Q) between clinical subjects and healthy controls in studies on *specific* autobiographical memory scores

Variables	*N* comparisons	Effect size-DELTA	*p*	95% CI	Homogeneity *Q*
Positive specific memories	14	−0.96	0.00000	−0.75/−1.18	21.74
Negative specific memories	14	−0.70	0.00001	−0.38/−1.02	30.93*
Latency recall to positive cues	6	0.56	0.01219	0.07/1.04	13.19*
Latency recall to negative cues	6	0.36	0.22901	0.11/0.61	3.35
Age of subjects	14	−0.10	0.00000	−0.41/0.19	39.27**
Self-report depression score	14	1.65	0.00000	1.02/2.27	100.01**

* $p<0.05$.
** $p<0.001$.

RAPPELS GÉNÉRAUX

Table 3
Effect sizes (DELTA) of comparisons, Confidence Intervals (CI) and homogeneity (Q) between clinical subjects and healthy controls in studies on *overgeneral* autobiographical memory scores

Variables	*N* comparisons	Effect size-DELTA	*p*	95% CI	Homogeneity *Q*
Positive overgeneral memories	10	0.53	0.00000	0.34/0.72	10.21
Negative overgeneral memories	10	0.58	0.00138	0.20/0.96	24.52*
Latency recall to positive cues	5	1.03	0.08023	−0.41/2.46	42.93**
Latency recall to negative cues	5	0.40	0.11769	−0.20/0.78	14.67*
Age of subjects	5	−0.07	0.27637	−0.33/0.18	0.32
Self-report depression score	10	3.28	0.00000	2.29/4.27	78.02**

* $p<0.05$.
** $p<0.001$.

Van Vreeswijk et al. 2004

COGNITIONS DITES FROIDES: MÉMOIRE AUTOBIOGRAPHIQUE

	Correlation dataset		Standardised regression coefficient dataset	
Variable	Overgeneral/categorical	Specific	Overgeneral/categorical	Specific
Number of studies	18	15	12	12
Weighted effect size	0.13 ($p < 0.001$)	−0.04 ($p = 0.219$)	0.09 ($p = 0.003$)	−0.16 ($p = 0.001$)
95% CI	0.08, 0.17	−0.11, 0.02	0.03, 0.15	−0.25, −0.06
Heterogeneity (Q)	25.0 ($p = 0.093$)	43.8 ($p < 0.001$)	15.0 ($p = 0.180$)	21.9 ($p = 0.025$)
I^2 index	32%	68%	26%	50%

La surgénéralisation est associée à un moins bon pronostic

Hallford et al. 2021

PATIENTS EUTHYMIQUES

Psychological Medicine, Page 1 of 10. © Cambridge University Press 2012
doi:10.1017/S0033291712002085

REVIEW ARTICLE

Cognitive impairment in euthymic major depressive disorder: a meta-analysis

E. Bora[1]*, B. J. Harrison[1], M. Yücel[1,2] and C. Pantelis[1]

[1] *Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne and Melbourne Health, VIC, Australia*
[2] *Orygen Youth Health Research Centre, The University of Melbourne, VIC, Australia*

LOD= atteinte importante
EOD= atteinte de inhibition de la réponse (faible)

THÉORIE DE L'ESPRIT

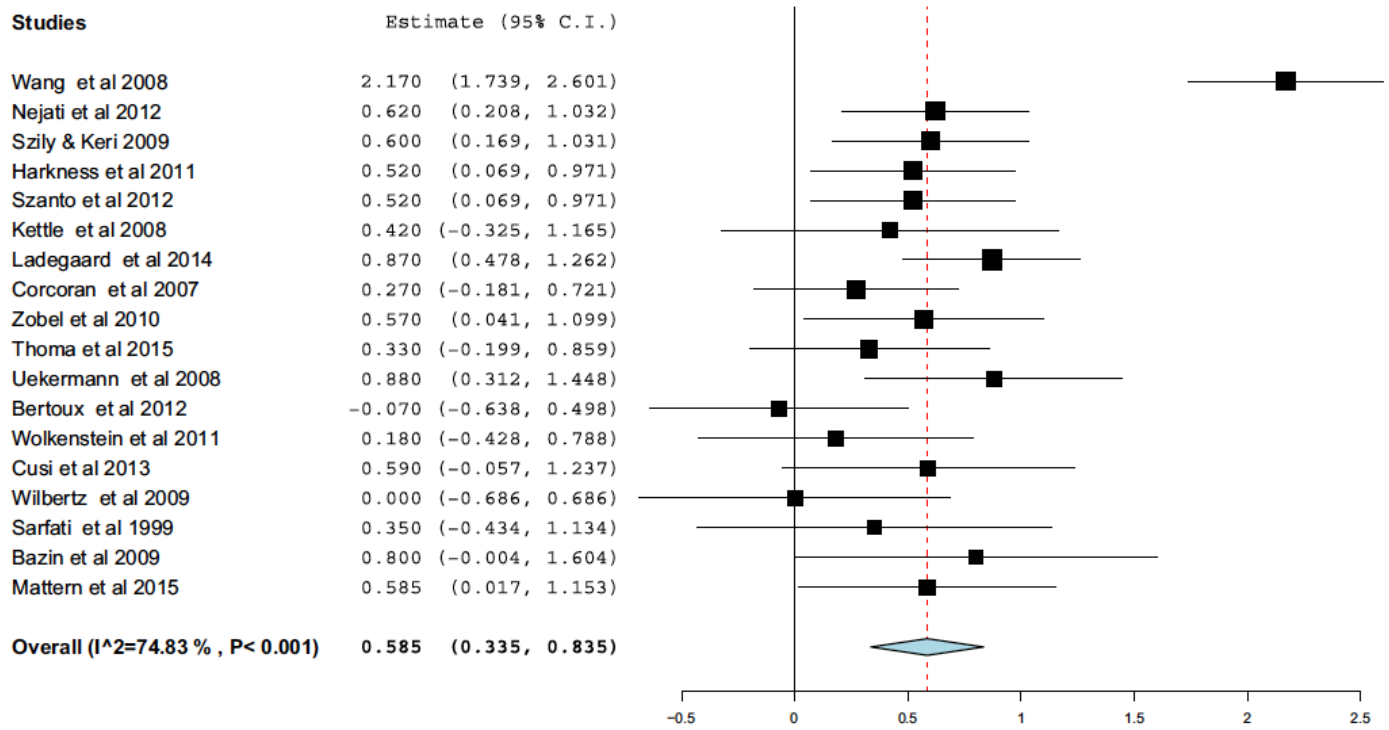


Fig. 1. Forest plot for emotion recognition differences between MDD and healthy controls (approximately here).

Bora et al.2016

FACTEURS DE RISQUE

- **Age de début**: En rémission: atteintes cognitives: LOD>>EOD= facteurs vasculaires?
- **Sévérité**:+++: attention et RPM
- **Co-morbidités** anxieuses
- **Durée de l'épisode**: fonctions exécutives
- **Récurrence**:
  - augmentation des temps de réponse
  - Atteinte des fonctions exécutives
  - Mémoire antérograde
- **Trauma précoces**= via HPA

Cléry-Mélin & Gorwood 2016, Bora et al. 2013, Rapp et al. 2005, Grant et al.2001, Beats et al.1996, Bhardwaj et al. 2010, Salvat-Pujol et al. 2021

TROUBLE BIPOLAIRE

SÉMIOLOGIE COGNITIVE

- Dépression: identique EDC
- Manie/hypomanie: distractibilité
- Euthymie:+++

COGNITIONS ET TROUBLES BIPOLAIRES

- Critères diagnostiques des épisodes:
  - Dépressifs:
    - Capacité à penser et à se concentrer diminuée ou indecision
    - Cognitions chaudes et froides
  - Maniaques: distractibilité
- Touchent la plupart des fonctions cognitives, dès le 1er épisode, tant pour les épisodes dépressifs (Ahern et al.2017) que maniaques (Kurtz et al.2009) avec des tailles d'effet modérées à importantes

COGNITIONS ET TROUBLES BIPOLAIRES

- 10 à 60% patients en rémission=> plaintes cognitives (Martinez-Aran et al. 2005):
  - Difficultés à apprendre des Nouvelles informations, oublis= **Troubles mnésiques**
  - Difficultés à maintenir la concentration sur le long terme, à diviser à l'attention = **troubles attentionnels**
  - Difficultés à organiser et à planifier des activités= **troubles des fonctions exécutives**

COGNITIONS ET TROUBLES BIPOLAIRES

- Cognitions:
  - 5.3–57.7% fonctions exécutives;
  - 9.6– 51.9% Attentions et mémoire de travail;
  - 23.3–44.2% traitement de l'information
  - 8.2–42.1% mémoire verbale;
  - 11.5–32.9% mémoire visuelle

=> Fréquent+++ mais Grande hétérogénéité++++

COGNITIONS ET TROUBLES BIPOLAIRES

Psychological Medicine (2008), 38, 771–785. © 2007 Cambridge University Press
doi:10.1017/S0033291707001675 Printed in the United Kingdom

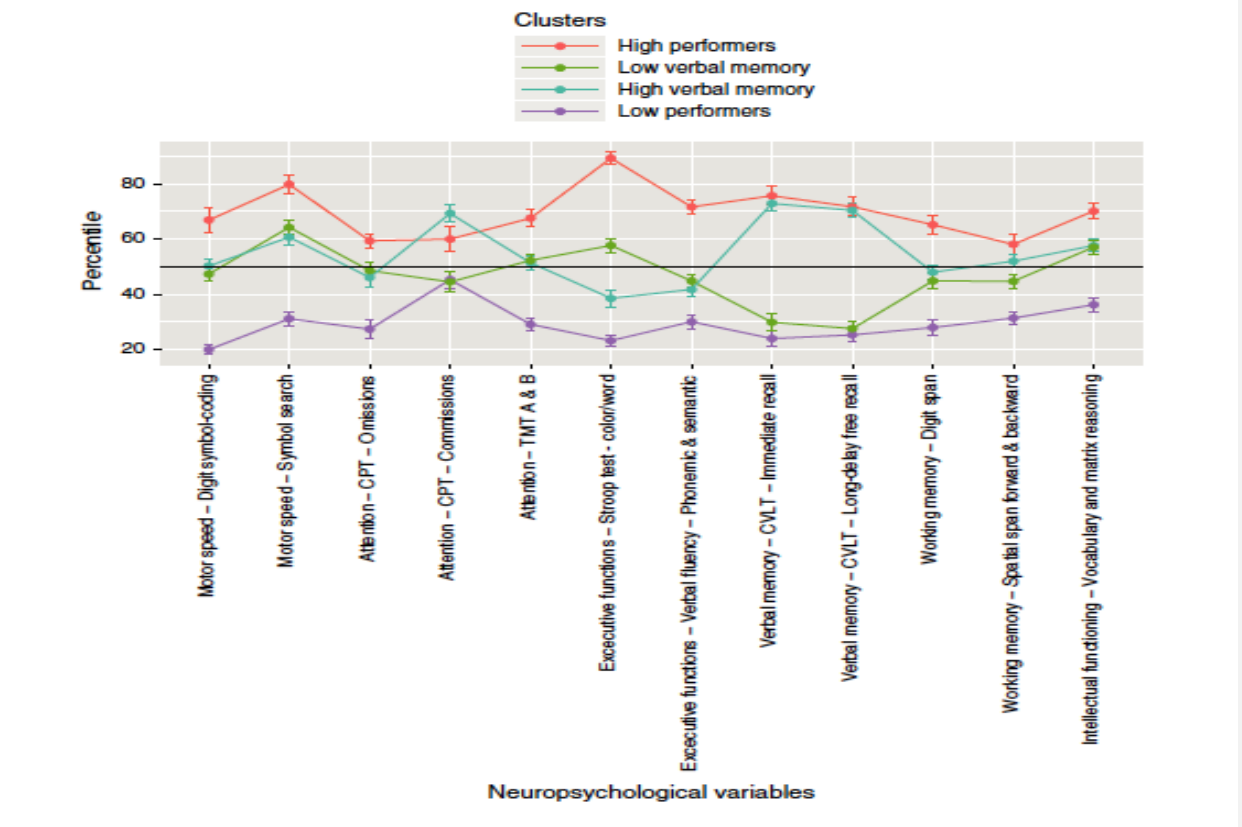
REVIEW ARTICLE

Meta-analyses of cognitive functioning in euthymic bipolar patients and their first-degree relatives

B. Arts[1*], N. Jabben[1], L. Krabbendam[1] and J. van Os[1,2]

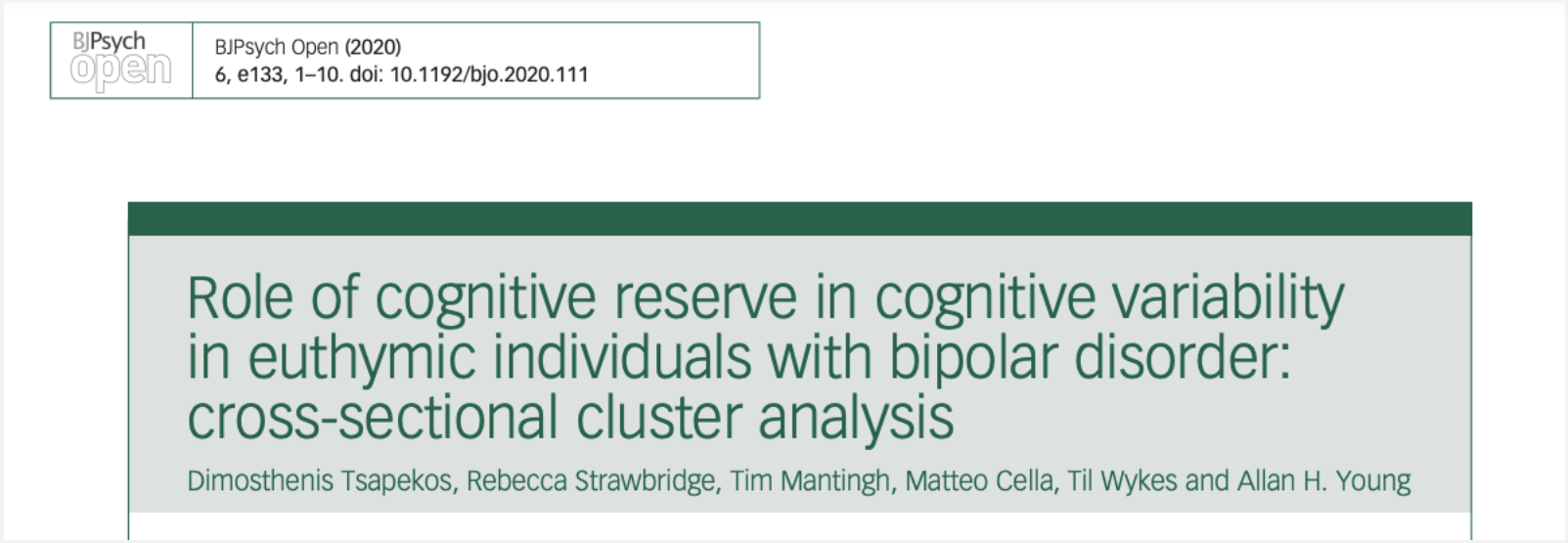
+++mémoire verbale et fonction exécutif (Mémoire travail, control exécutif, fluence verbale) (Taille effet++ d>0.8)
Les apparentés du 1er degrés: Fonction exécutif et mémoire verbale (taille d'effet faible) => endophénotypes
(Arts et al.2008, Bora et al. 2008)

COGNITIONS ET TROUBLES BIPOLAIRES



Roux et al. 2016

COGNITIONS ET TROUBLES BIPOLAIRES



BJPsych Open (2020)
6, e133, 1–10. doi: 10.1192/bjo.2020.111

Role of cognitive reserve in cognitive variability in euthymic individuals with bipolar disorder: cross-sectional cluster analysis

Dimosthenis Tsapekos, Rebecca Strawbridge, Tim Mantingh, Matteo Cella, Til Wykes and Allan H. Young

THÉORIE DE L'ESPRIT

BP I

BP2

Figure 3. Summary of results and forest plots of meta-analyses comparing Theory of Mind (ToM) between individuals with type I bipolar disorders (BD I) and healthy controls (HC).

Author, year	ToM task	BD I	HC	Hedges' g (95% CI)	p
Bora et al., 2005	Hinting Task	43	30	-0,673 (-1,147 to -0,199)	0,005
Bora et al., 2005	RMET	43	30	-0,655 (-1,128 to -0,182)	0,007
Mahli et al., 2008	ToM Appropriateness	20	20	-1,538 (-2,233 to -0,844)	0,000
Mahli et al., 2008	ToM Intentionality	20	20	-1,774 (-2,495 to -1,053)	0,000
Lahera et al., 2008	Happé Stories Task	33	48	-0,496 (-0,942 to -0,050)	0,029
Lahera et al., 2008	Happé Stories Task	42	48	-0,591 (-1,010 to -0,171)	0,006
Shamay-Tsoory et al., 2009	Faux Pas Cognitive	19	20	1,110 (0,447 to 1,772	0,001
Shamay-Tsoory et al., 2009	Faux Pas Emotion	19	20	0,427 (-0,195 to 1,050)	0,179
Montag et al., 2010	MASC	29	29	-0,831 (-1,361 to -0,301)	0,002
Wolf et al., 2010	ToM Cartoon	11	29	-2,299 (-3,146 to -1,453)	0,000
Martino et al., 2011	Faux Pas	45	34	-5,672 (-6,661 to -4,684)	0,000
Martino et al., 2011	RMET	45	34	-0,158 (-0,600 to 0,284)	0,484
Lee et al., 2013	TASIT lie	46	31	0,091 (-0,360 to 0,542)	0,692
Lee et al., 2013	TASIT sarcasm	46	31	-0,456 (-0,912 to 0,001)	0,050
Bora et al., 2016	Hinting Task	43	27	-0,641 (-1,128 to -0,153)	0,010
Bora et al., 2016	RMET	43	27	-0,793 (-1,287 to -0,299)	0,002
Espinós et al., 2018	RMET	65	112	-1,263 (-1,595 to -0,932)	0,000
Santos et al., 2017	Absence of mentalizing 4	31	31	0,955 (0,436 to 1,475)	0,000
Santos et al., 2017	FB1	31	31	-0,454 (-0,952 to 0,044)	0,074
Santos et al., 2017	FB2	31	31	0,691 (-1,198 to -0,185)	0,007
Santos et al., 2017	Hinting Task	31	31	-0,431 (-0,929 to 0,066	0,089
Santos et al., 2017	Inframentalization errors	31	31	0,567 (0,066 to 1,069)	0,027
Santos et al., 2017	MASC Total hit score	31	31	-1,194 (-1,728 to -0,659)	0,000
Santos et al., 2017	Overmentalization errors	31	31	0,476 (-0,023 to 0,975)	0,061
Azemat et al., 2015	RMET	30	30	-1,140 (-1,679 to -0,600)	0,000
Azemat et al., 2015	ToM Story Task	30	30	-1,376 (-1,933 to -0,819)	0,000
Budak, 2019	Faux Pas	52	60	-0,221 (-0,590 to 0,1490	0,243
Budak, 2019	FB1	52	60	0,527 (0,152 to 0,902)	0,006
Budak, 2019	FB2	52	60	-1,102 (-1,498 to -0,706)	0,000
Budak, 2019	RMET	52	60	-1,045 (-1,438 to -0,652)	0,000
Caponigro, 2007	FB1	19	15	-0,784 (-1,471 to -0,097)	0,025
Caponigro, 2007	FB2	19	15	-0,467 (-1,137 to 0,203)	0,172
TOTAL		**1135**	**1137**	**-0,663 (-0,954 to -0,372)**	**0.000**

Heterogeneity: Q=339.0, I^2=90.9%, p<0.000

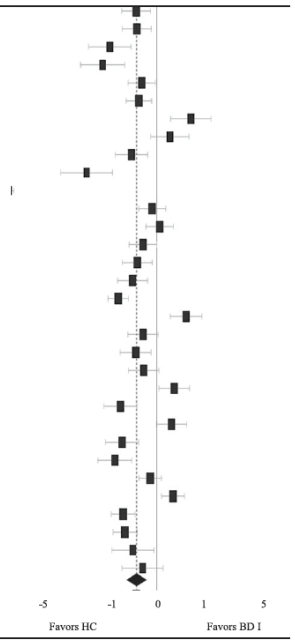
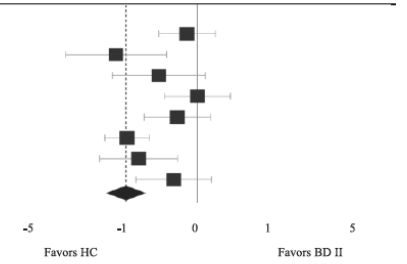


Figure 4. Summary of results and forest plots of meta-analyses comparing Theory of Mind (ToM) between individuals with type II bipolar disorders (BD II) and healthy controls (HC).

Author, year	ToM task	BD II	HC	Hedges' g (95% CI)	p
Martino et al., 2011	Faux Pas	36	34	-6,531 (-7,709 to -5,354)	0,000
Martino et al., 2011	RMET	36	34	-0,164 (-0,628 to 0,301)	0,490
Ibanez et al., 2012	Faux Pas	13	13	-1,327 (-2,154 to -0,499)	0,002
Ibanez et al., 2012	RMET	13	13	-0,624 (-1,387 to 0,140)	0,109
Lee et al., 2013	TASIT lie	22	31	0,011 (-0,527 to 0,549)	0,968
Lee et al., 2013	TASIT sarcasm	22	31	-0,322 (-0,864 to 0,220)	0,244
Espinós et al., 2018	RMET	47	112	-1,150 (-1,512 to -0,788)	0,000
Ibanez et al., 2014	Faux Pas	13	41	-0,958 (-1,598 to -0,317)	0,003
Ibanez et al., 2014	RMET	13	41	-0,381 (-1,000 to 0,238)	0,228
TOTAL		**215**	**350**	**-1,165 (-1,915 to -0,415)**	**0,002**

Heterogeneity: Q=117.3, I^2=92.2%, p<0.000



Siqueira Rotenberg et al.2020

COGNITIONS ET TROUBLES BIPOLAIRES DE LA PERSONNE ÂGÉE

- LOBD vs EOBD= > atteintes des fonctions psychomotrices, des fluences verbales et de la flexibilité mentale (ajustées sur l'âge, le niveau d'education et les facteurs de risque neuro-vasculaire)

- LOBD vs EOBD= > Hyper intensité lobe parietal et ganglions de la base

Cognitive Impairment in Early and Late Bipolar Disorder

TABLE 2. Neuropsychological Performance in Patients With Early- and Late-Onset Bipolar Disorder and Comparison Group: Mean (SD) and Mixed Group Analysis of Variance of Neuropsychological Functioning

Measure	Comparison Group (N = 78)	Early Onset (N = 59)	Late Onset (N = 60)	Patients Versus Comparison Group			Early Versus Late			Between Group Contrast
				F	p	η	*F*	p	η	
Psychomotor performance										
Trailmaking Test Part A, seconds	46.97 (19.6)	63.03 (34.3)	89.78 (68.3)	13.55	<0.01	0.30	7.2	0.01	0.06	CG>EO>LO
Mental effort										
ASTM 1 t/m 10	29.00 (1.0)	28.03 (1.6)	26.77 (5.6)	4.41	<0.01	0.12	2.79	0.09	0.02	CG>EO, LO
Attention and executive function										
Digits forward	5.73 (0.9)	5.32 (0.9)	5.08 (0.9)	7.74	<0.01	0.19	1.74	0.19	0.01	CG>EO, LO
Digits backward	4.71 (1.1)	3.93 (0.9)	3.88 (1.0)	11.27	<0.01	0.26	0.07	0.79	<0.01	CG>EO, LO
Trailmaking Test Part B, seconds	109.68 (58.7)	175.41 (118.6)	218.10 (129.4)	14.87	<0.01	0.32	3.54	0.06	<0.01	CG>EO, LO
Stroop Color Word test,[a] seconds	45.31 (12.8)	61.51 (29.4)	71.40 (33.5)	13.21	<0.01	0.29	2.91	0.09	0.02	CG>EO, LO
D-A-T	35.75 (10.7)	25.66 (11.0)	21.93 (11.5)	23.06	<0.01	0.42	3.22	0.07	0.02	CG>EO, LO
Animal naming	25.23 (6.6)	18.76 (5.4)	17.83 (5.6)	75.11	<0.01	0.54	0.87	0.35	<0.01	CG>EO, LO
Occupation naming	17.41 (4.9)	15.39 (5.4)	12.35 (4.8)	11.43	<0.01	0.26	10.32	<0.00	0.08	CG>EO>LO
Mazes, seconds	121.41 (95.32)	156.64 (108.8)	211.38 (140.4)	14.26	<0.01	0.31	5.63	0.02	0.05	CG>EO>LO
Rule Shift Cards BADS	1.06 (1.6)	1.53 (2.2)	2.70 (2.8)	9.37	<0.01	0.22	6.42	0.01	0.05	CG>EO>LO
Declarative memory										
10 Words Test										
Learning (Trials 1–5)	37.35 (5.7)	30.23 (6.5)	27.73 (7.3)	25.91	<0.01	0.45	3.84	0.05	0.03	CG>EO, LO
Retention	6.74 (1.9)	4.58 (1.9)	4.45 (2.3)	46.89	<0.01	0.54	0.47	0.75	<0.01	CG>EO, LO
Recognition[b]	19.26 (0.9)	18.61 (1.3)	18.00 (2.6)							CG>EO, LO
Visuoconstruction										
Copying ADS6[b]	12.37 (1.6)	12.27 (1.9)	12.33 (0.8)							
Clock drawing[b]	1.41 (0.8)	1.42 (0.8)	1.67 (1.1)							

Notes: ASTM: Amsterdam Short-Term Memory Test; BADS: Behavorial Assessment of the Dysexecutive Syndrome; ADS6: Amsterdam Dementia Screening test; EO: Early onset; LO: Late onset; CG: comparison group.

[a]This is a short form consisting of reading the first 4 lines.

[b]Kruskal-Wallis test patients versus comparison group: for 10 Words Test recognition errors, $\chi^2 = 34.14$, $p < 0.01$; for Figure-copying, $\chi^2 = 14.79$, $p = 0.13$; for Clock drawing, $\chi^2 = 7.76$ $p = 0.65$; Mann-Whitney U test early versus late: for 10 Word Test recognition errors, $Z = 0.87$, $p = 0.38$; for Figure copying, $Z = -1.08$, $p = 0.28$; for Clock drawing, $Z = -1.17$, $p = 0.24$.

Schouws et al. 2009, Tamashiro et al. 2008

COGNITIONS ET TROUBLES BIPOLAIRES DE LA PERSONNE ÂGÉE

- 30% (4-67%) des PA avec un TBP= troubles cognitifs (Tsai et al.2007, Roux et al. 2019)
- Troubles cognitifs chez les TBP PA euthymiques= Taille effet modéré à grande= Identique TBP jeune (Samamé et al. 2013). Mais exclusion LOBD
- PA avec TBP= atteintes cognitives >> sujets sans TBP du même âge (Schouws et al. 2009)
- Mais absence de degradation des fonctions cognitives à 5 ans (Schouws et al. 2009)

CONCLUSION

- Très fréquent +++
- Persistance en euthymie
- Impact des Late-Onset
- Pourquoi?
- Quels impacts?
- Que faire?

ATELIER

PLAN

- Physiopathologie
- impact
- Que faire?

PHYSIOPATHOLOGIE

TROUBLE DÉPRESSIF

INFLAMMATION

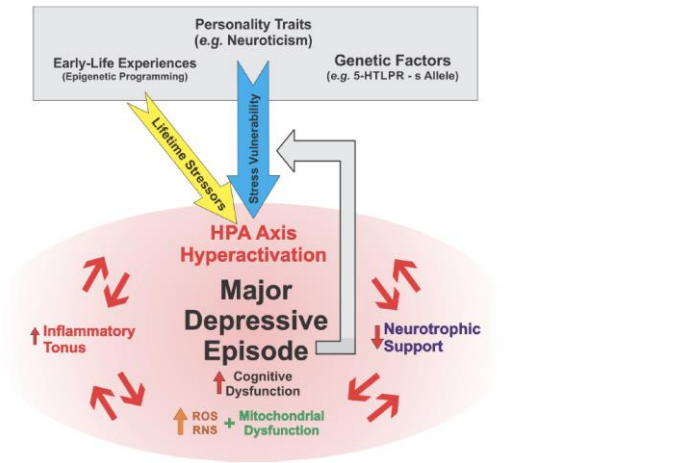
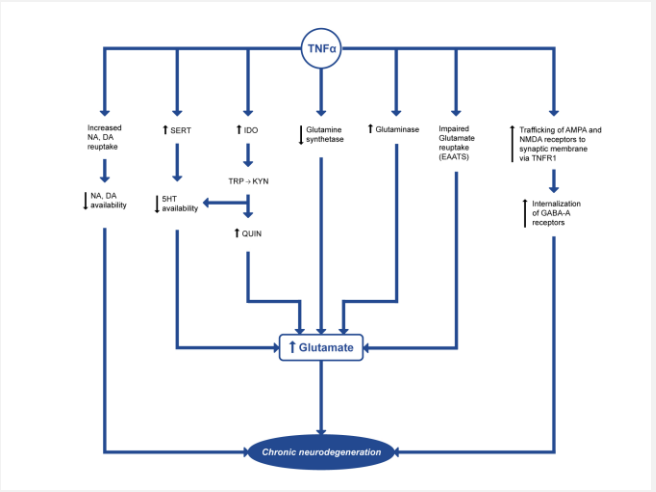


Fig. (1). Personality traits, early-life experiences, environmental risks (poor diet, smoking, physical inactivity, vitamin D insufficiency etc.) and genetic factors confer vulnerability to stress in part through epigenetic alterations in the glucocorticoid receptor (GR). The activation of the hypothalamic-pituitary-adrenal axis (HPA) leads to reciprocal interactions with immune-inflammatory pathways (e.g., increased production of pro-inflammatory cytokines), mitochondrial dysfunction, oxidative and nitrosative stress, and a decrease in production of neurotrophins (e.g., BDNF). These biological events characterize a major depressive episode. Each depressive episode increase vulnerability to a subsequent episode and contributes to cognitive decline. ROS: reactive oxygen species; RNS: reactive nitrogen species.

Impact TNF alpha, IL1 beta et IL6 => cognition



Carvalho et al. 2014, Misiak et al. 2018, Bortolato et al. 2015

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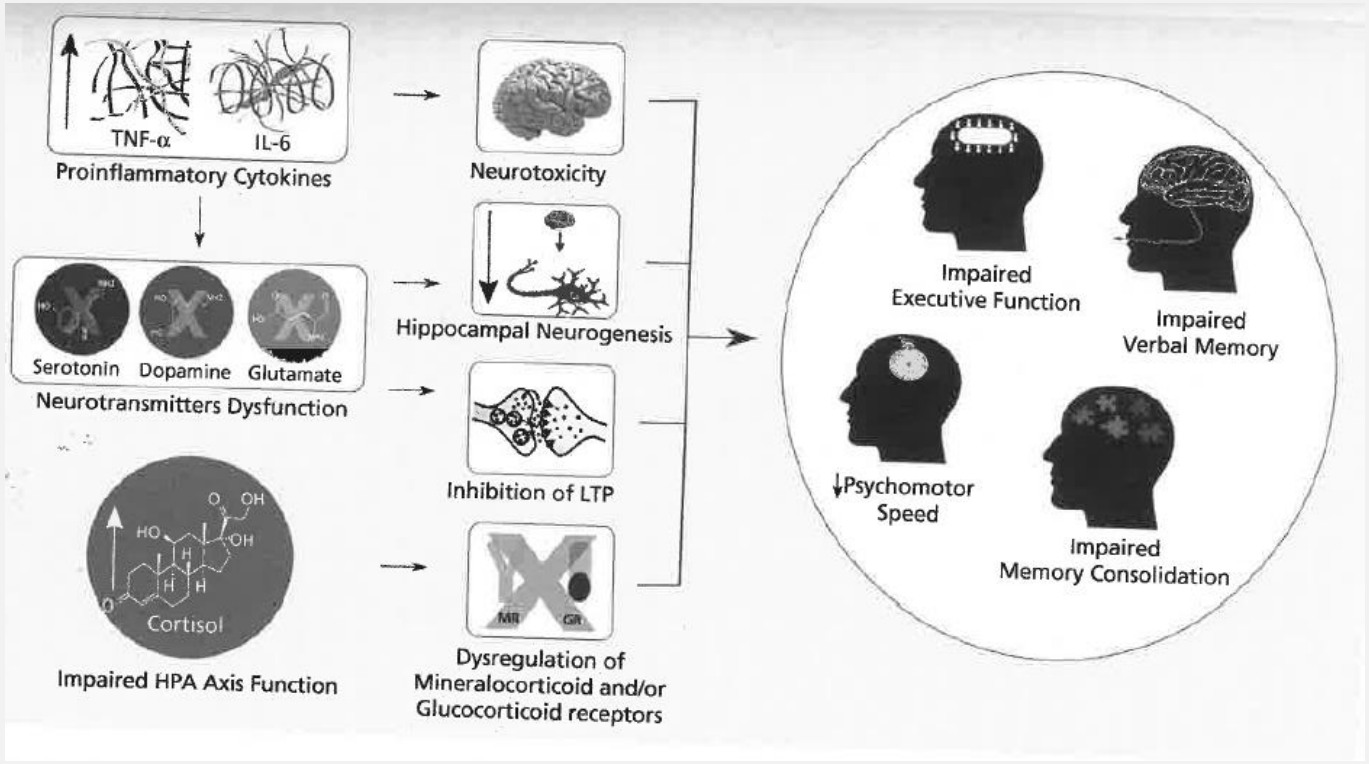

Mills & Baune 2019

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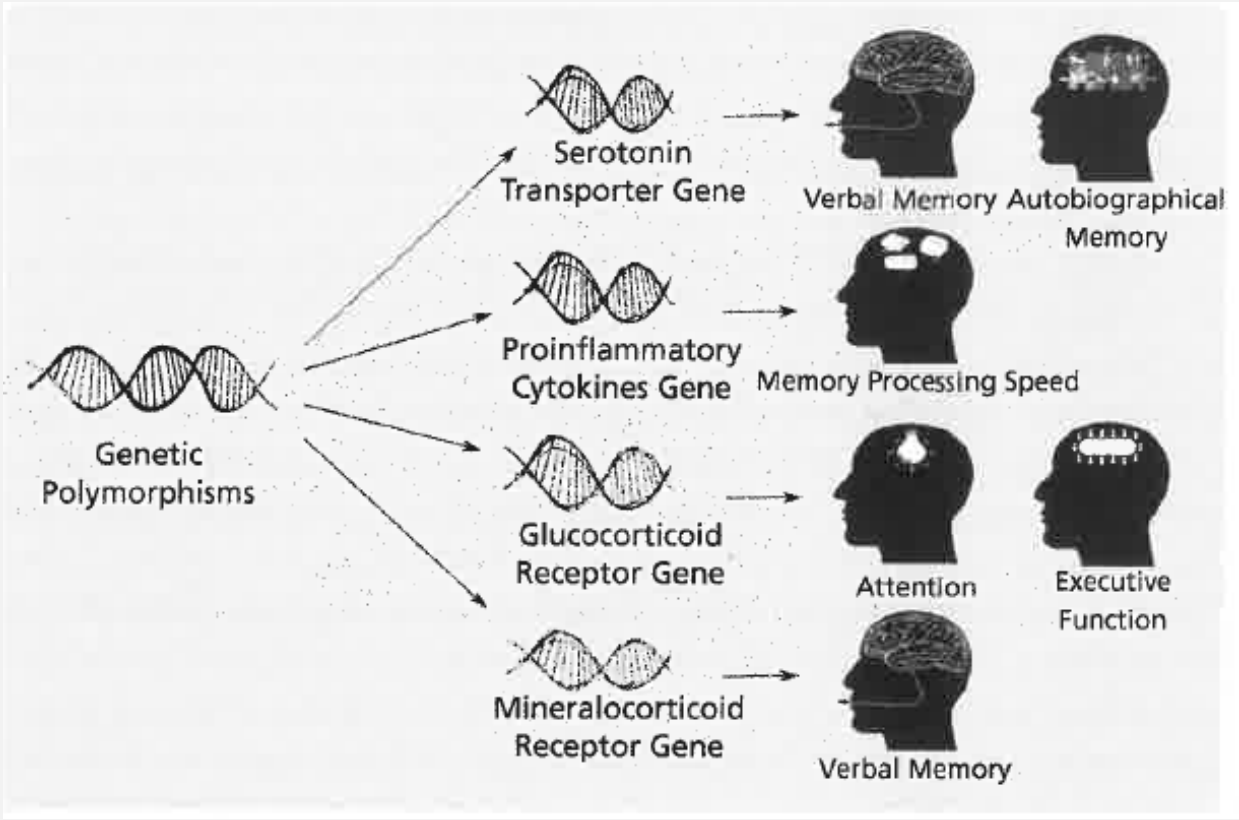


Mills & Baune 2019

INSULINO RÉSISTANCE

Incident Major Depressive Disorder Predicted by Three Measures of Insulin Resistance: A Dutch Cohort Study

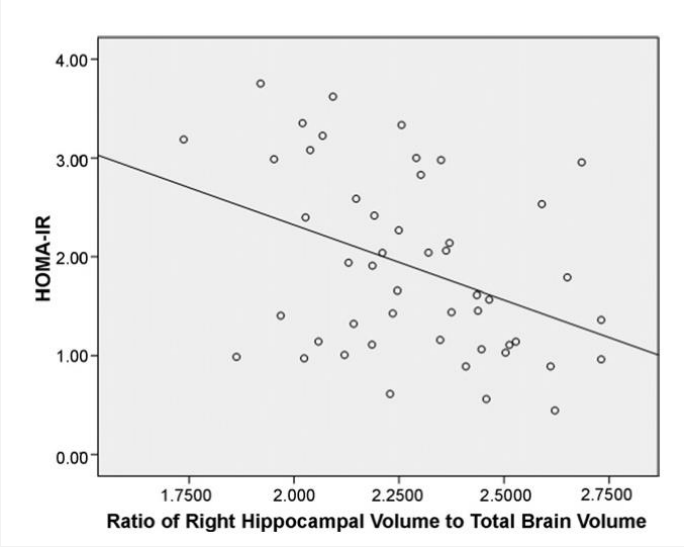
Kathleen T. Watson, Ph.D., Julia F. Simard, Sc.D., Victor W. Henderson, M.S., M.D., Lexi Nutkiewicz, B.A., Femke Lamers, Ph.D., Carla Nasca, Ph.D., Natalie Rasgon, M.D., Ph.D., Brenda W.J.H. Penninx, M.D., Ph.D.

Insulino-resistance prédit la survenue d'un EDC dans les 9 ans
Avec un RR= 2.6 dans les 2 ans

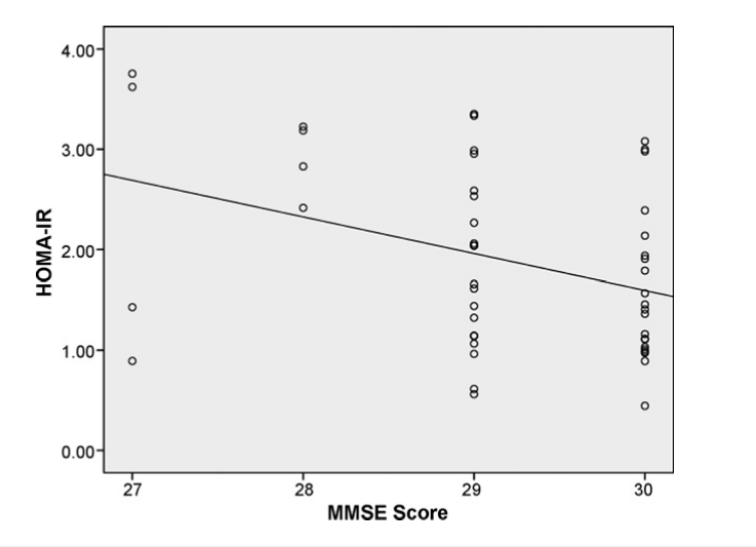
Watson et al. 2021_AJP

INSULINO-RESISTANCE

HIPPOCAMPES

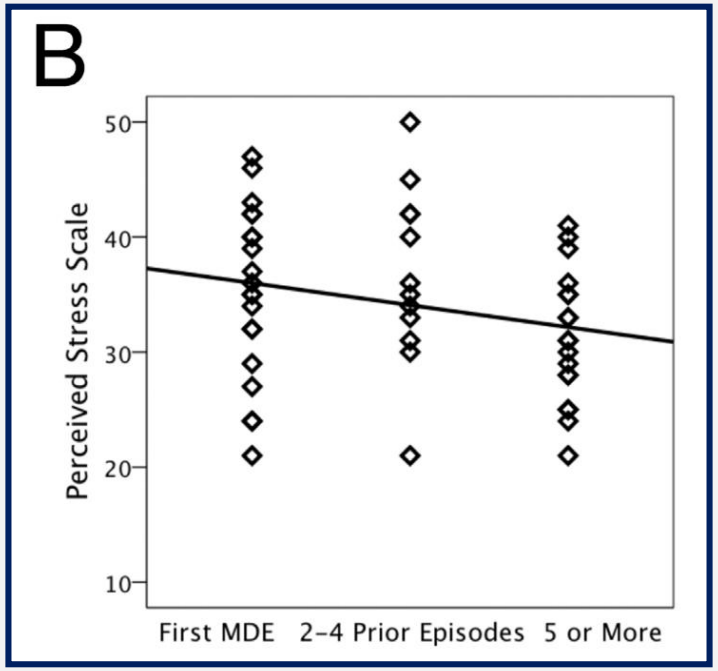


MMSE

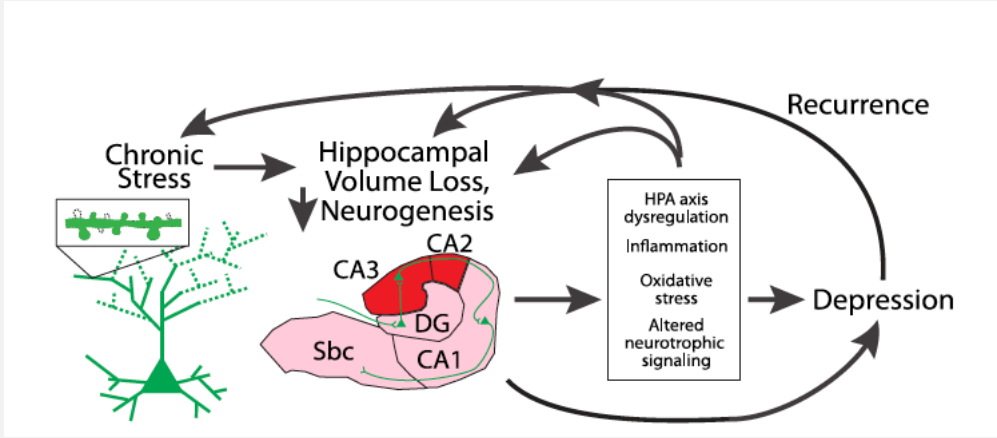


Ragson et al.2011

ETIOPATHOGÉNIE: NEURO-PROGRESSION??

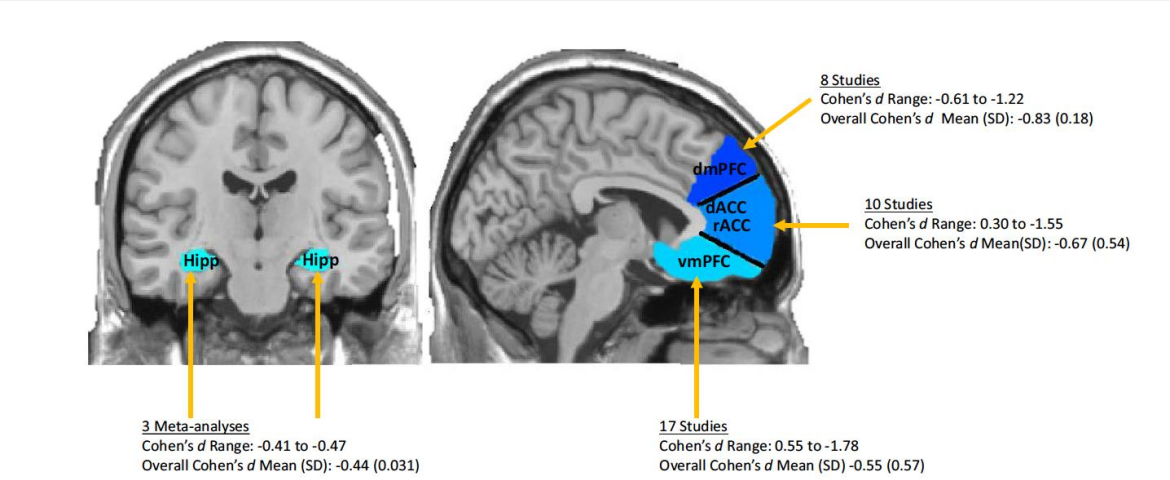


Treadway et al. 2015

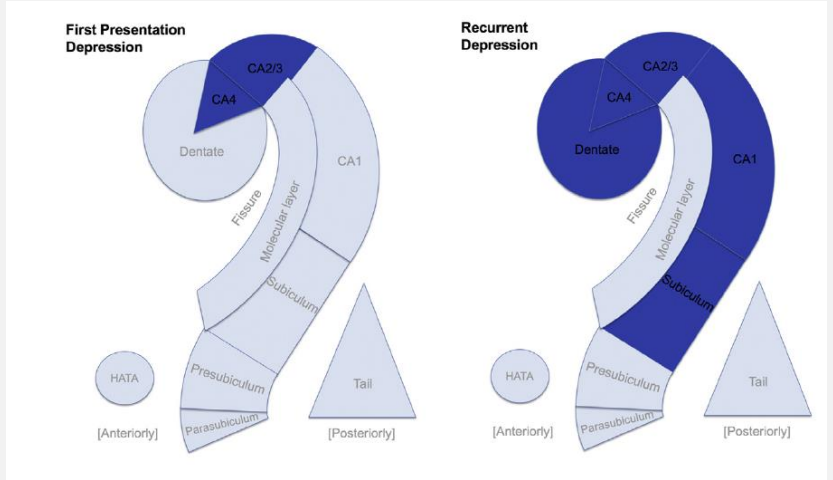


Sheline et al.2019

ETIOPATHOGÉNIE: NEURO-PROGRESSION??

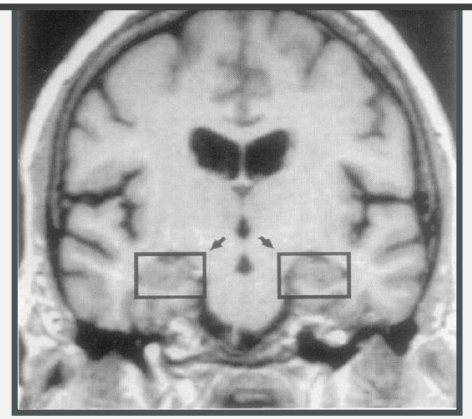


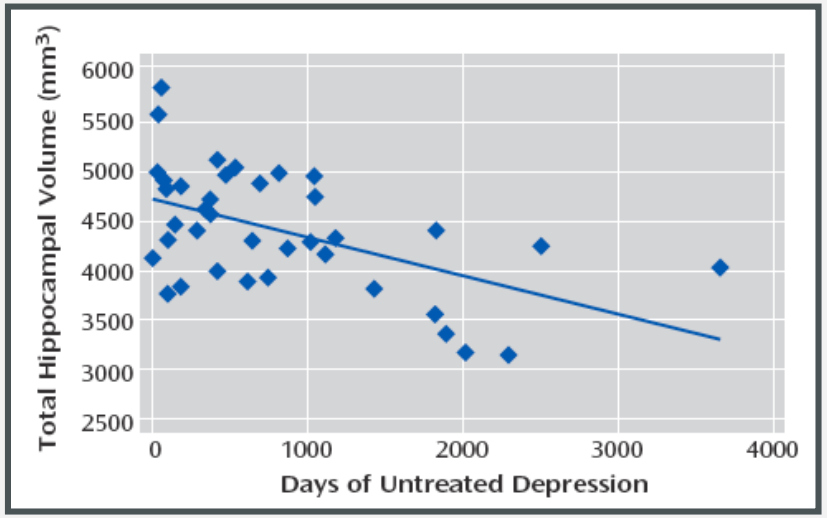
Belleau et al.2019



Roddy et al. 2019

ETIOPATHOGÉNIE: NEURO-PROGRESSION??





Depression-Related Variation in Brain Morphology Over 3 Years

Effects of Stress?

Thomas S. Frodl, MD; Nikolaos Koutsouleris, MD; Ronald Bottlender, MD; Christine Born, MD; Markus Jäger, MD; Isabel Scupin; Maximilian Reiser, MD; Hans-Jürgen Möller, MD; Eva M. Meisenzahl, MD

Context: Results of experimental studies suggest that neuroplastic changes may occur during depressive episodes. These effects have not been confirmed in patients with depression, to our knowledge.

Objective: To examine changes in the brains of patients with major depression vs those of healthy control subjects.

Design: Prospective longitudinal 3-year study.

Setting: Inpatients with major depression were recruited from the Department of Psychiatry and Psychotherapy, Ludwig Maximilians University of Munich, Munich, Germany, and controls were recruited from the local community.

Participants: The study included 38 patients with major depression and 30 healthy controls.

Main Outcome Measures: High-resolution magnetic resonance imaging was performed at baseline and 3 years later. Voxel-based morphometric measurements were estimated from magnetic resonance images, and psychopathologic findings were assessed at baseline, weekly during the inpatient phase, and then after 1, 2, and 3 years.

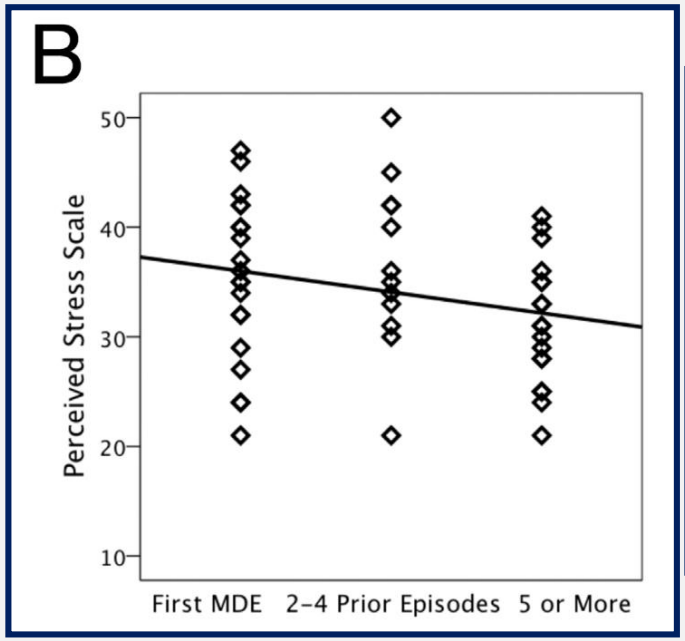
Results: Compared with controls, patients showed significantly more decline in gray matter density of the hippocampus, anterior cingulum, left amygdala, and right dorsomedial prefrontal cortex. Patients who remitted during the 3-year period had less volume decline than nonremitted patients in the left hippocampus, left anterior cingulum, left dorsomedial prefrontal cortex, and bilaterally in the dorsolateral prefrontal cortex.

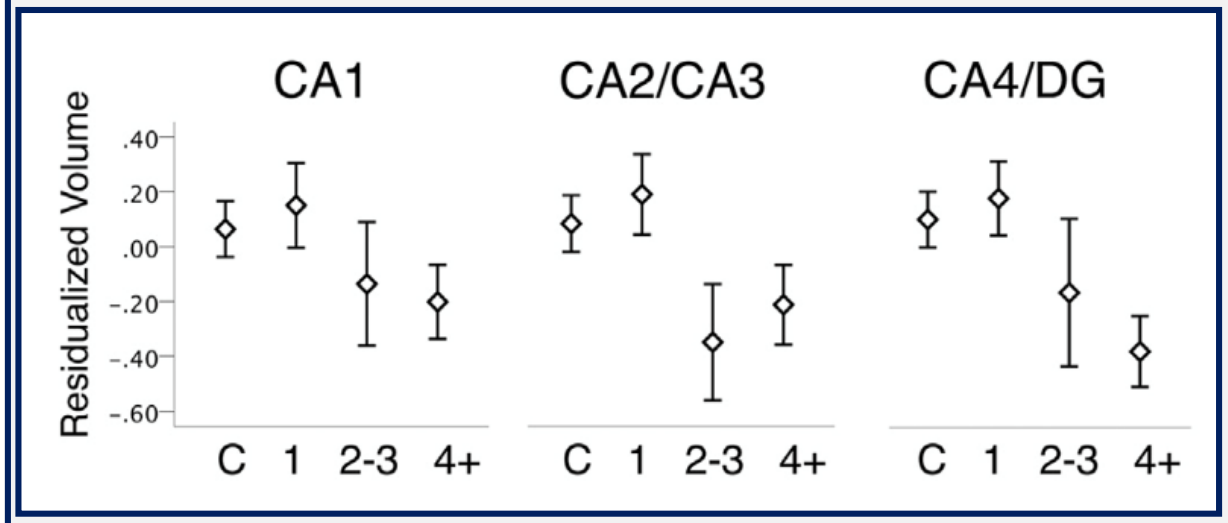
Conclusion: This study supports findings from animal studies of neuroplastic stress-related processes that occur in the hippocampus, amygdala, dorsomedial prefrontal cortex, dorsolateral prefrontal cortex, and anterior cingulum during depressive episodes.

Arch Gen Psychiatry. 2008;65(10):1156-1165

Sheline et al., 1997
Frodl et al., 2008

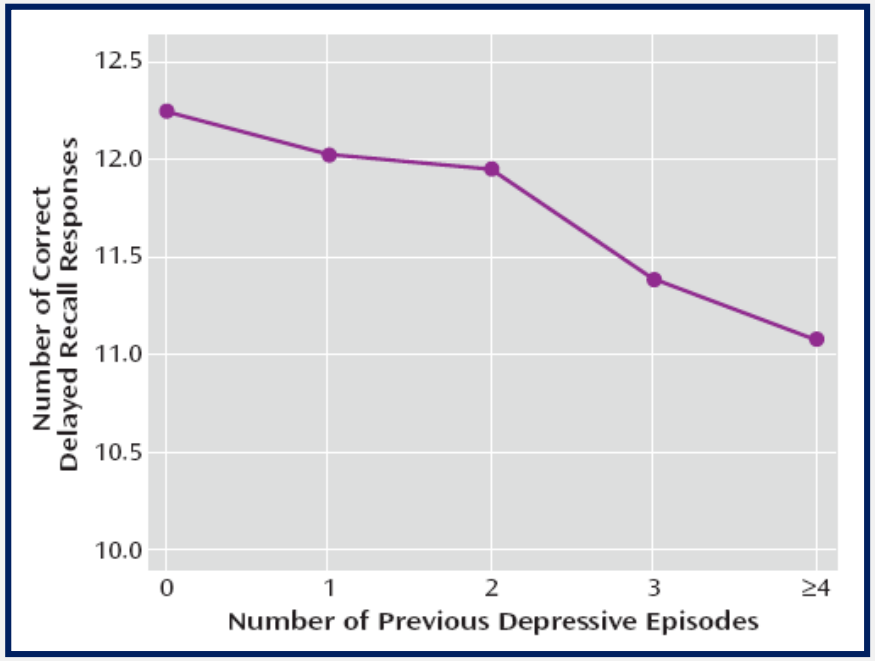
ETIOPATHOGÉNIE: NEURO-PROGRESSION??

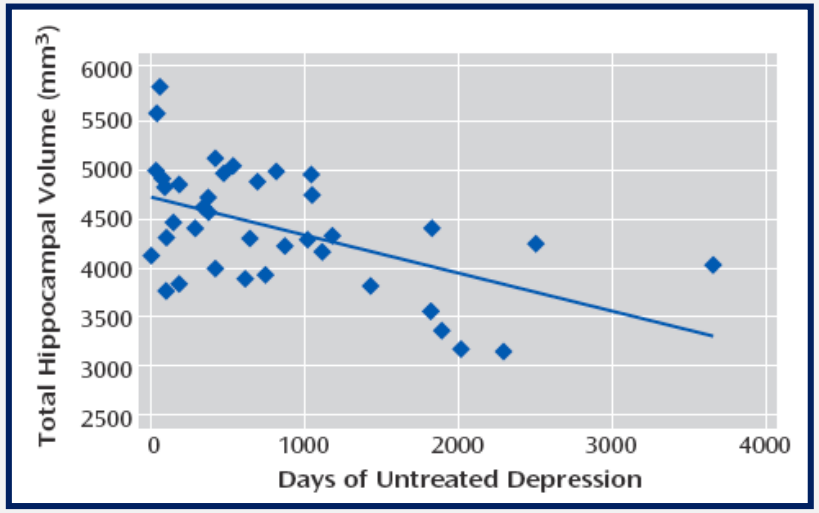




Treadway et al., 2015

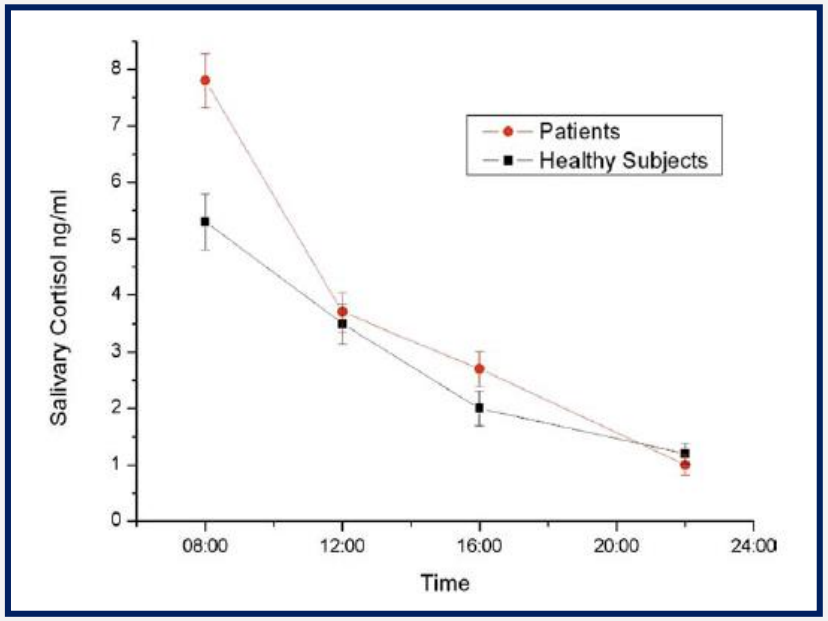
ETIOPATHOGÉNIE: NEURO-PROGRESSION??

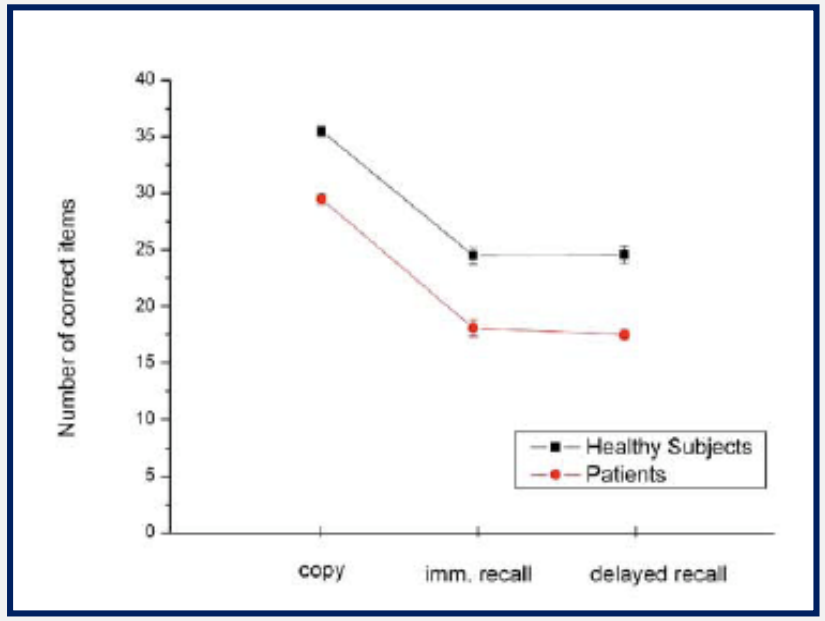




Sheline et al., 1997
Gorwood et al., 2008

ETIOPATHOGÉNIE: NEURO-PROGRESSION??





Hinkelman et al., 2009

ETIOPATHOGÉNIE: NEURO-PROGRESSION??

Table 2 Mean scores (SE) of cognitive variables for patients before and after treatment compared to healthy subjects.

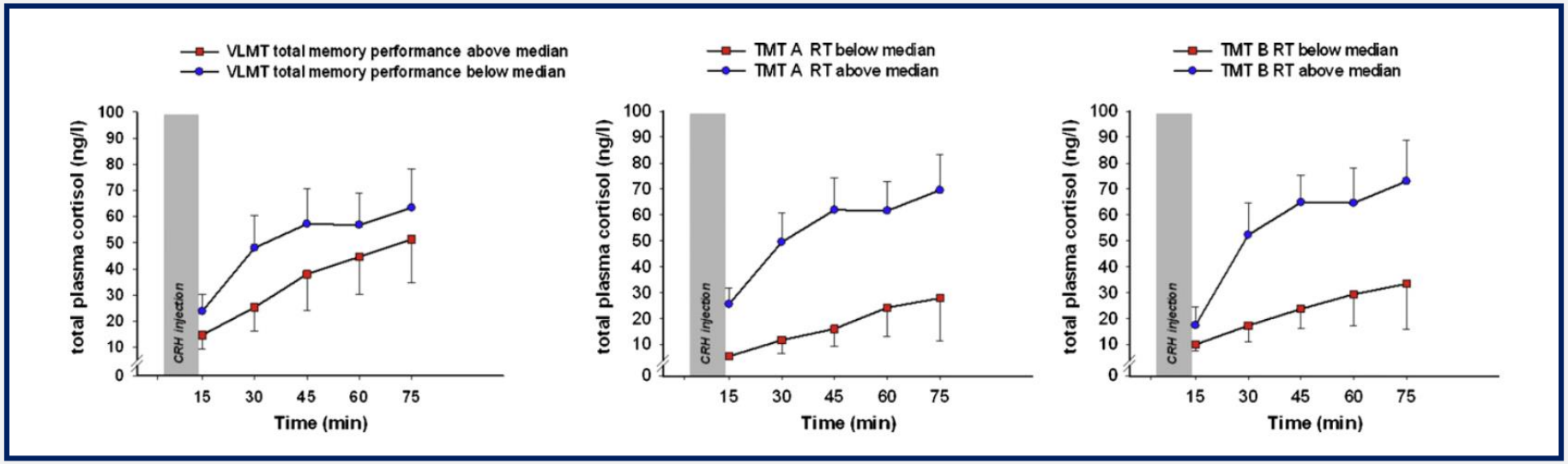
	Patients (n = 44)		Healthy subjects (n = 47)	
Cognitive domain (Test)	Day 0 Mean (SD)	Day 21 Mean (SD)	Day 0 Mean (SD)	Day 21 Mean (SD)
AVLT				
Total score	81.4 (15.6)	82.1 (16.0)	86.8 (12.2)	85.6 (11.4)
Delayed recall	11.8 (2.8)	12.0 (3.2)	13.2 (1.9)	12.5 (2.7)
TMT-A (time)	26.1 (7.8)	22.6 (7.1)	26.6 (9.8)	23.7 (8.3)
TMT-B (time)	70.8 (40.2)	57.2 (32.9)	61.3 (22.6)	54.5 (18.9)
TMT-diff (time)	44.7 (34.6)	34.6 (24.7)	34.7 (19.0)	30.8 (16.1)
Digit span forward	8.3 (2.5)	8.8 (2.7)	9.6 (2.1)	9.9 (2.5)
Digit span backward	7.2 (2.3)	7.3 (2.7)	7.4 (2.5)	7.6 (2.6)
Rey/Taylor copy	29.3 (4.2)	30.0 (4.0)	35.5 (1.1)	35.5 (1.2)
Rey/Taylor immediate recall	18.1 (7.9)	23.2 (6.9)	24.5 (5.4)	26.7 (4.6)
Rey/Taylor delayed recall	17.5 (7.7)	21.6 (5.8)	24.6 (5.6)	26.7 (4.4)
d2 Concentration score	158.3 (38.9)	185 (52.1)	190.7 (38.4)	215.4 (45.2)

Patients improved to a greater extent in verbal memory (repeated-measures ANCOVA group × time interaction, AVLT long term memory: $F(1;90) = 5.1$, $p = .02$) and non-verbal memory (repeated-measures ANCOVA group × time interaction, Rey/Taylor Figure: $F(1;90) = 8.8$, $p < .01$) compared to healthy controls.
AVLT: Auditory Verbal Learning Test, TMT A and B: Trail Making Test A and B.

under the curve (AUC) cortisol values. Repeated-measures ANCOVA revealed a significant time × group interaction ($p = .05$). Post hoc tests revealed a significant reduction of cortisol in patients (t-test, $t = 2.5$, df = 51, $p = 0.01$).

Hinkelman et al., 2011

ETIOPATHOGÉNIE: NEURO-PROGRESSION??



Bhenken et al., 2013

ETIOPATHOGÉNIE: NEURO-PROGRESSION??

Insulin Resistance, Affective Disorders, and Alzheimer's Disease: Review and Hypothesis

Natalie Rasgon[1] and Lissy Jarvik[2,3]

Ragsobn et al. 2004

TROUBLE DÉPRESSIF ET PATHOLOGIES NEURO-DÉGÉNRATIVES

ARTICLE IN PRESS

Archival Report

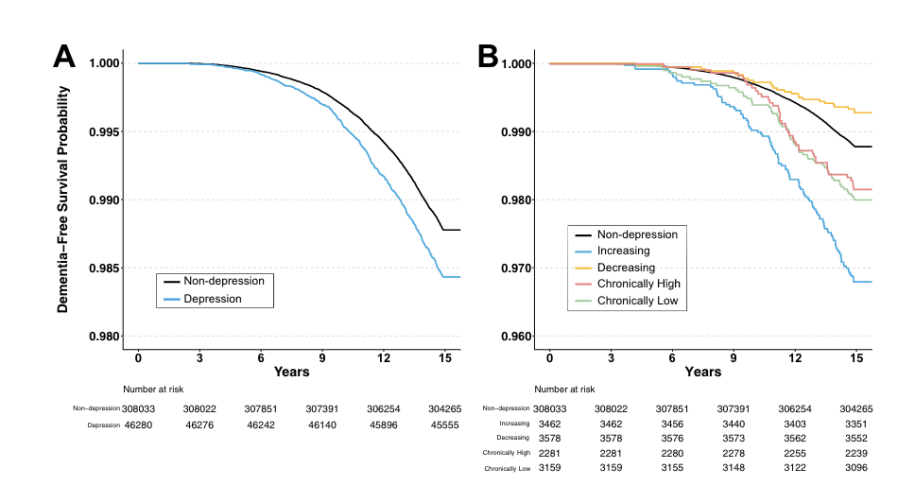
Biological Psychiatry

Depression, Depression Treatments, and Risk of Incident Dementia: A Prospective Cohort Study of 354,313 Participants

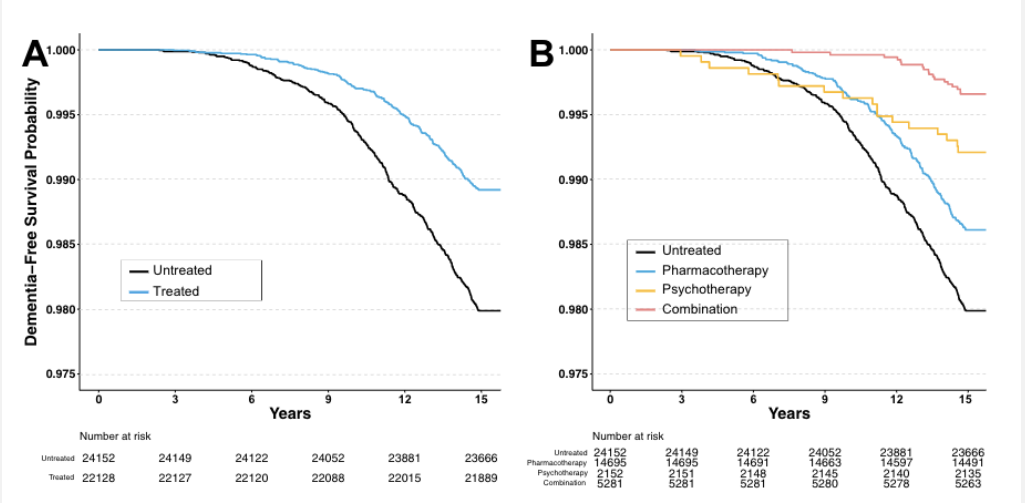
Liu Yang, Yue-Ting Deng, Yue Leng, Ya-Nan Ou, Yu-Zhu Li, Shi-Dong Chen, Xiao-Yu He, Bang-Sheng Wu, Shu-Yi Huang, Ya-Ru Zhang, Kevin Kuo, Wei Feng, Qiang Dong, Jian-Feng Feng, John Suckling, A. David Smith, Fei Li, Wei Cheng, and Jin-Tai Yu

TROUBLE DÉPRESSIF ET PATHOLOGIES NEURO-DÉGÉNRATIVES

LLD

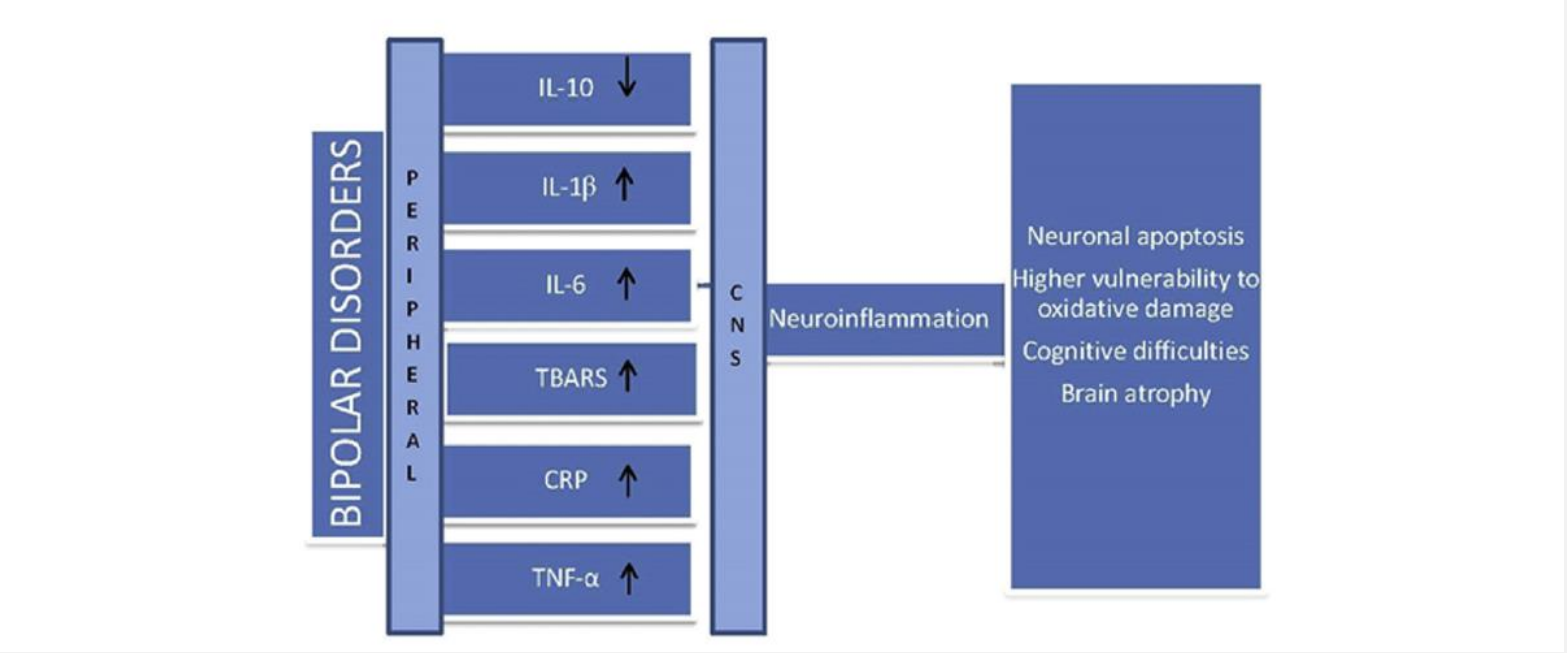


TREATMENT



TROUBLE BIPOLAIRE

ETIOPATHOGÉNIE: NEURO-DÉVELOPPEMENT ET/OU NEURO-PROGRESSION??



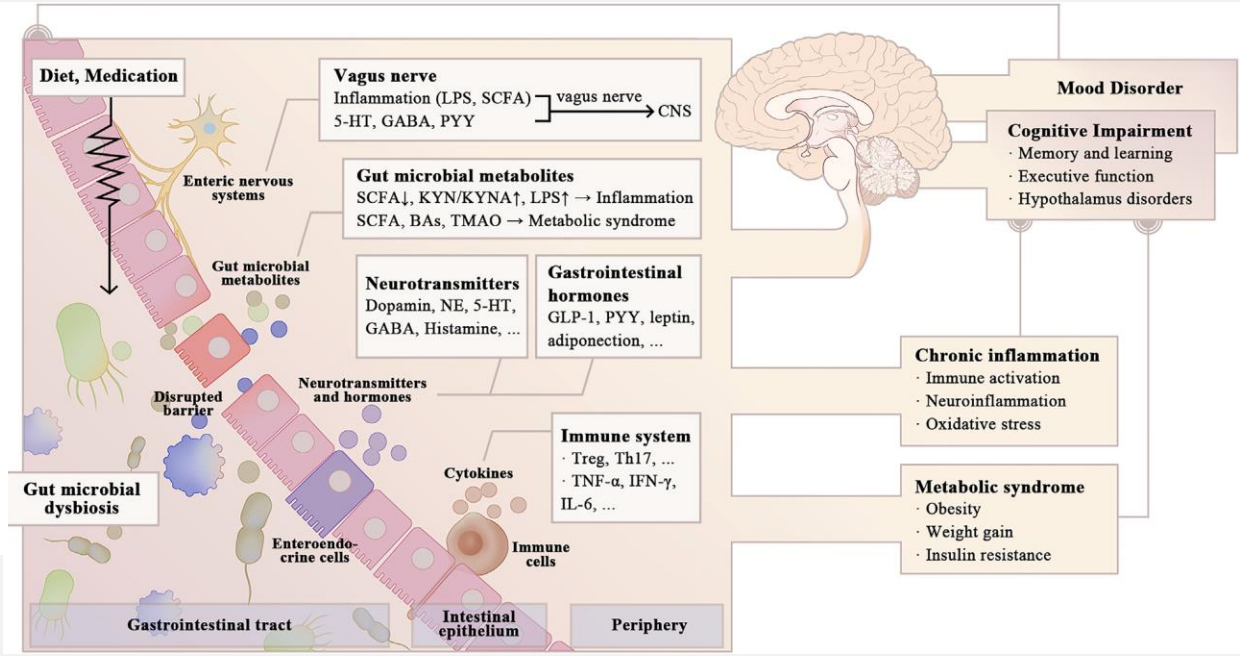
Bauer et al. 2014

ETIOPATHOGÉNIE: NEURO-DÉVELOPPEMENT ET/OU NEURO-PROGRESSION??

Gut Microbial Dysbiosis and Cognitive Impairment in Bipolar Disorder: Current Evidence

Wenyu Dai[1], Jieyu Liu[2], Yan Qiu[1], Ziwei Teng[1], Sujuan Li[1], Hui Yuan[2], Jing Huang[1], Hui Xiang[1], Hui Tang[1], Bolun Wang[3], Jindong Chen[1] and Haishan Wu[1]**

[1]National Clinical Research Center for Mental Disorders, Department of Psychiatry, China National Technology Institute on Mental Disorders, The Second Xiangya Hospital of Central South University, Changsha, China, [2]Department of Ultrasound Diagnostic, The Second Xiangya Hospital of Central South University, Changsha, China, [3]Department of Radiology, The Second Xiangya Hospital of Central South University, Changsha, China*



Dai et al.2022

NEURO DÉVELOPPEMENT VS NEURO PROGRESSION

DOI: 10.1111/bdi.12841

REVIEW ARTICLE

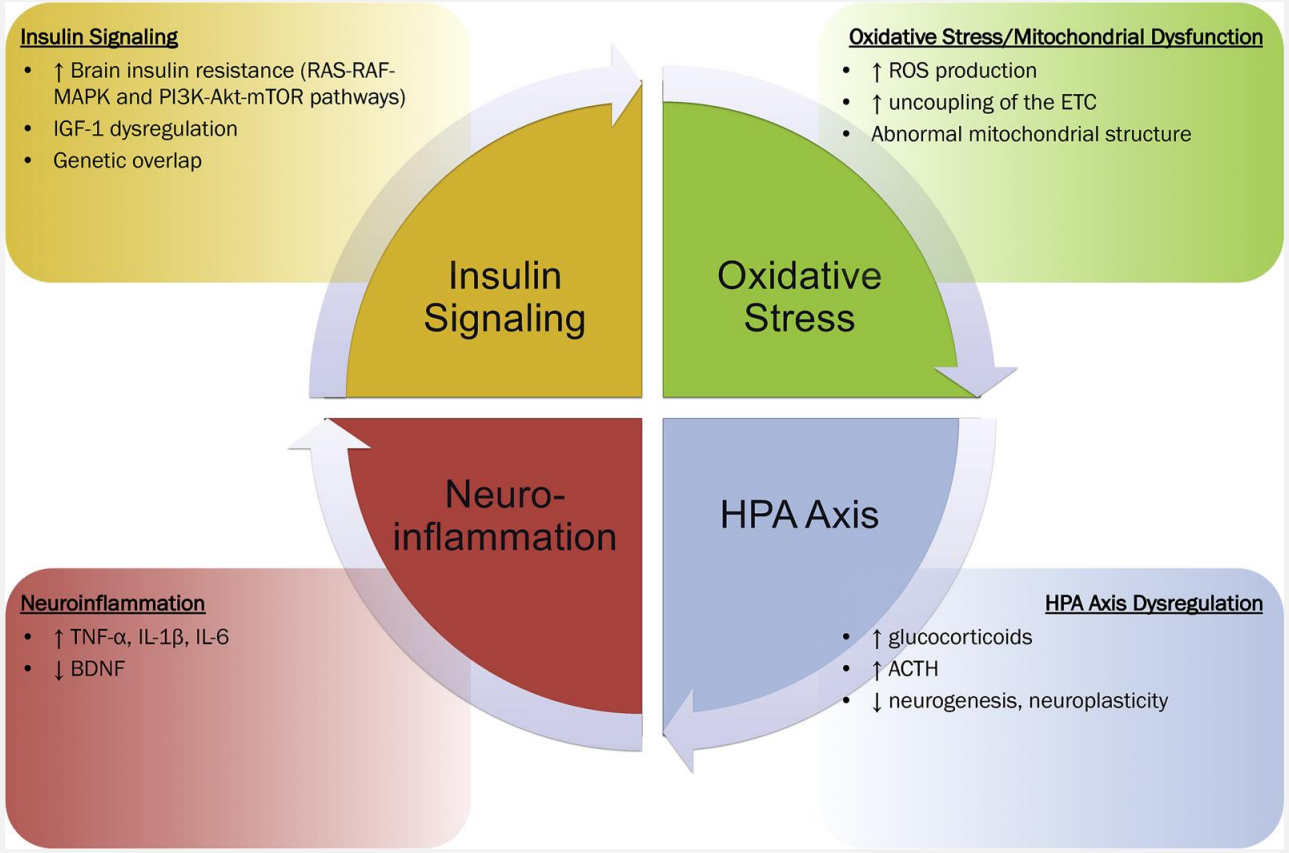
BIPOLAR DISORDERS WILEY

Longitudinal analysis of cognitive performances in recent-onset and late-life Bipolar Disorder: A systematic review and meta-analysis

Alejandro Szmulewicz[1,2,3] | Marina P. Valerio[2,4] | Diego J. Martino[4,5]

Facteurs neuro développementaux:
=> Rôle +++ dans les déficits cognitifs

ETIOPATHOGÉNIE: NEURO-DÉVELOPPEMENT ET/OU NEURO-PROGRESSION??



Cuperfain et al.2020

ETIOPATHOGÉNIE: NEURO-DÉVELOPPEMENT ET/OU NEURO-PROGRESSION??

Insulin Resistance, Affective Disorders, and Alzheimer's Disease: Review and Hypothesis

Natalie Rasgon[1] and Lissy Jarvik[2,3]

Ragsobn et al. 2004

TBP ET PATHOLOGIES NEURODÉGÉNÉRATIVES

- Une étude épidemiologique sur > 42000 patients avec TBP= Aug. risque de pathologie neuro dégénérative avec le nombre d'épisode maniaque et surtout dépressif (Aug de 6% à chaque nouveau episode)

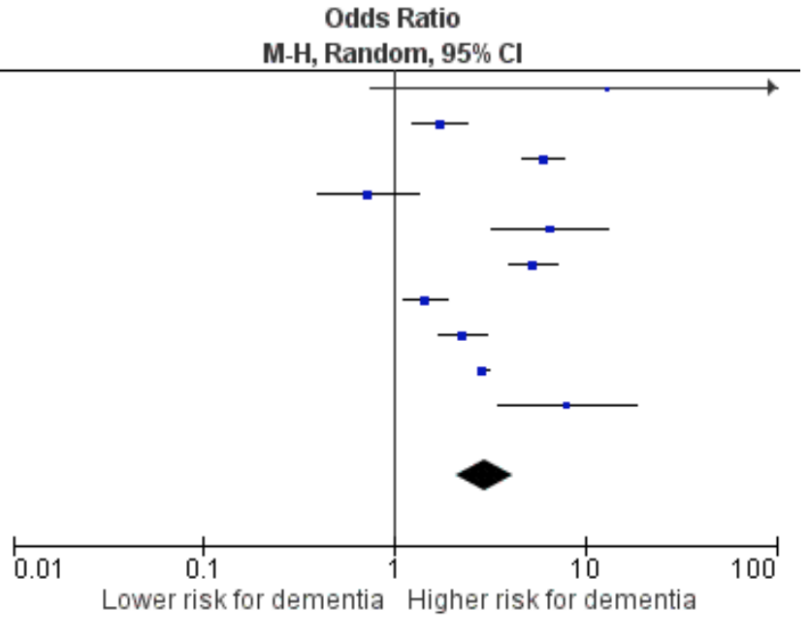
(Kessing et al. 2004)

TBP ET PATHOLOGIES NEURODÉGÉNÉRATIVES

Figure 2: Forest plot of the meta-analysis of BD as risk factor for dementia.

Study or Subgroup	Bipolar Disorder Events	Total	Controls Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Cooper et al, 1998	6	6	553	1112	1.3%	13.14 [0.74, 233.82]
Kessing et al., 2003*	38	2007	895	81380	11.8%	1.74 [1.25, 2.41]
Wu et al., 2013	114	229	9190	64575	12.2%	5.97 [4.61, 7.75]
Aprahamian et al, 2014	27	106	33	103	9.4%	0.72 [0.40, 1.32]
Zilkens et al., 2014	59	68	13509	27030	8.5%	6.56 [3.25, 13.24]
Chen et al, 2015	92	345	133	2063	12.0%	5.28 [3.92, 7.10]
Taipale et al., 2015	133	225	24833	49726	12.2%	1.45 [1.11, 1.89]
Almeida et al., 2016	65	256	4860	37512	12.1%	2.29 [1.72, 3.03]
Cheng et al., 2017	2074	3537	61274	186504	13.1%	2.90 [2.71, 3.10]
Almeida et al., 2018**	6	80	383	37923	7.4%	7.95 [3.44, 18.37]
Total (95% CI)		**6859**		**487928**	**100.0%**	**2.96 [2.09, 4.18]**
Total events	2614		115663			

Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 115.96$, df = 9 ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: $Z = 6.15$ ($P < 0.00001$)



* Kessing et al., 2003 - We considered as a control group the patients with osteoarthritis.
**Almeida et al., 2018 - We have only included in the meta-analysis data for patients aged 50 years or younger.

Velosa et al. 2020

TBP ET PATHOLOGIES NEURODÉGÉNÉRATIVES

- Patients avec une importante **reserve cognitive** (QI élevé, niveau d'étude, statut professionnel)= **moins de risque de pathologies neuro dégératives** (Stern et al. 2002, Sajatovic et al. 2015)
- Mais, le TBP peut diminuer la réserve cognitive ou agir en synergie avec d'autres mécanismes neuropathologiques (ex: pathologies vasculaires) pour accélérer le vieillissement cérébrale et la deterioration cognitive (Kessing et al. 2004, Cooper et al. 1998, Da Silva et al. 2013, Meng et al. 2012, Ng et al. 2008, Rizzo et al 2008, Wu et al. 2013)

TBP ET PATHOLOGIES NEURODÉGÉNÉRATIVES

- => les patients avec un trouble bipolaire non (mal) stabilisé sont plus à risque de développer un trouble neuro-dégénératif que la population Générale et que le trouble dépressif (Velosa et al. 2020)
- Le lithium semble diminuer le risque de survenue de pathologie neuro dégénérative (Velosa et al. 2020)

TBP ET PATHOLOGIES NEURODÉGÉNÉRATIVES

Anticonvulsivant

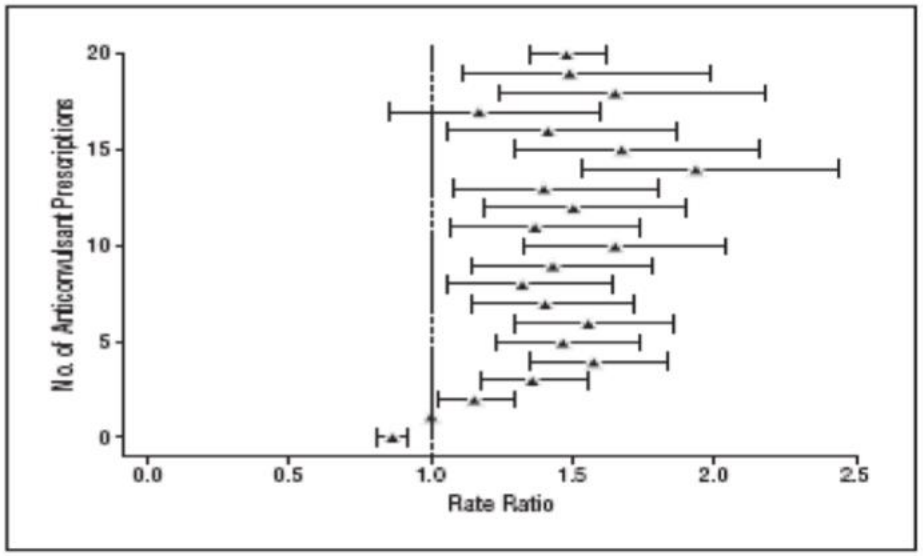


Figure 2. Rate ratios (bars represent 95% confidence intervals) of dementia according to the number of prescriptions for anticonvulsants (the period with 1 prescription is used as the reference). Findings are adjusted for the effect of age, sex, calendar period, and purchase of antidepressants or lithium.

Lithium

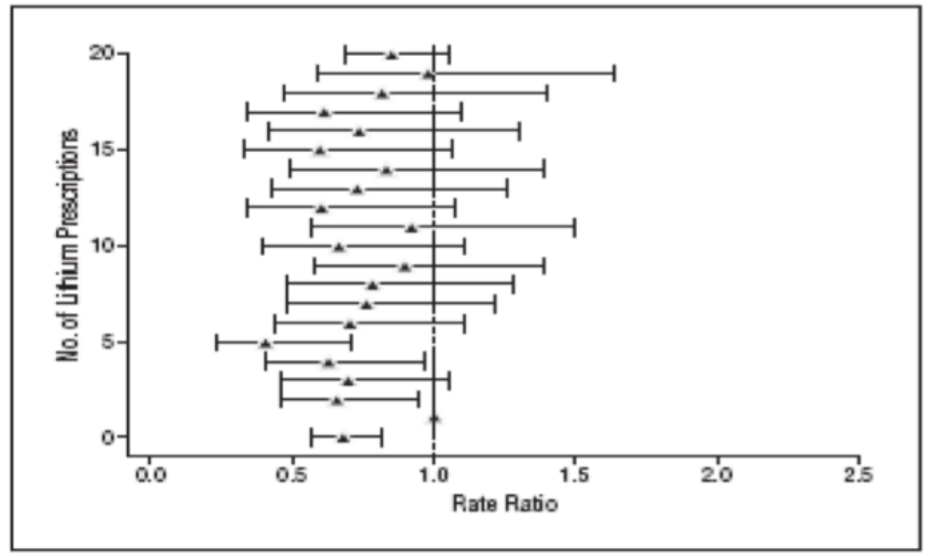


Figure 1. Rate ratios (bars represent 95% confidence intervals) of dementia according to the number of prescriptions for lithium (the period with 1 prescription is used as the reference). Findings are adjusted for the effect of age, sex, calendar period, and purchase of antidepressants or anticonvulsants.

Kessing et al. 2008

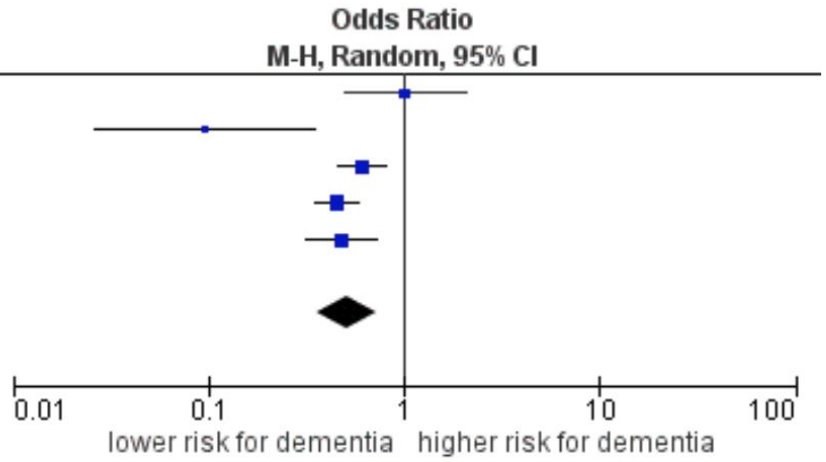
TBP ET PATHOLOGIES NEURODÉGÉNÉRATIVES

Figure 3: Forest plot of the meta-analysis of neuroprotective/neurotrophic effect of lithium.

	Lithium		Non-lithium			Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Angst et al., 2007	14	77	26	144	13.8%	1.01 [0.49, 2.07]
Nunes et al., 2007	3	66	16	48	5.8%	0.10 [0.03, 0.35]
Kessing et al., 2010	84	2449	132	2407	28.1%	0.61 [0.46, 0.81]
Gerhard et al., 2015	64	3766	1377	37485	29.1%	0.45 [0.35, 0.58]
Cheng et al., 2017	32	125	1431	3412	23.2%	0.48 [0.32, 0.72]
Total (95% CI)		**6483**		**43496**	**100.0%**	**0.51 [0.36, 0.72]**
Total events	197		2982			

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 12.47$, $df = 4$ ($P = 0.01$); $I^2 = 68\%$

Test for overall effect: $Z = 3.86$ ($P = 0.0001$)



Velosa et al. 2020

THYMORÉGULATEURS

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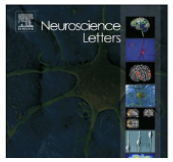

Mitochondrial dy
of lithium

Monique P. Singulani,

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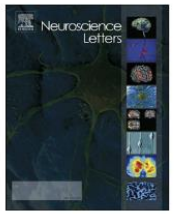


Short communication

Lithium: A therapeu
prodromal stages?

Robert Haussmann [a,*], Fel

Beneficial effects of low-dose lithium on cognitive ability and pathological alteration of Alzheimer's disease transgenic mice model

Meng Liu[a], Ting Qian[a], Wei Zhou[a], Xiaodong Tao[a], Shaoming Sang[a] and Lei Zhao[b]

COMMUNS

SOMMEIL?

Journal of Affective Disorders 327 (2023) 207–216

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Review Article

The relationship between sleep disturbance and cognitive impairment in mood disorders: A systematic review

Oliver Pearson [a,b,*], Nora Uglik-Marucha [a], Kamilla W. Miskowiak [c], Scott A. Cairney [d,e], Ivana Rosenzweig [f,g], Allan H. Young [b,h], Paul R.A. Stokes [b,h]

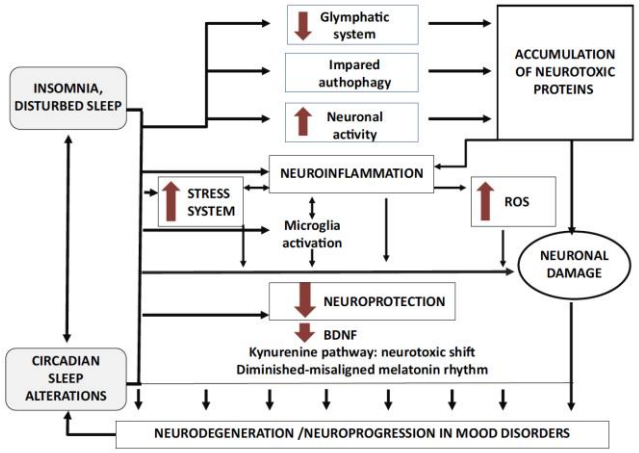


Figure 1. A proposed model: role of insomnia, sleep loss, and circadian sleep alterations in neurodegeneration and neuroprogression of mood disorders.

Palagini et al.2021

IMPACT

TROUBLE DÉPRESSIF

PLAINTE COGNITIVE

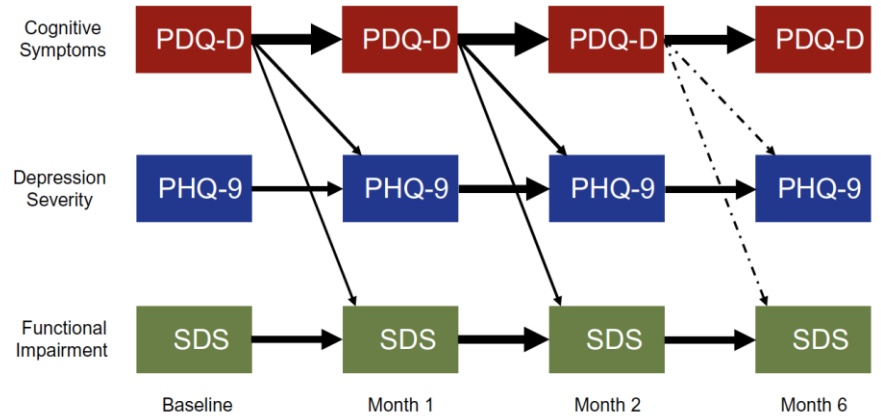


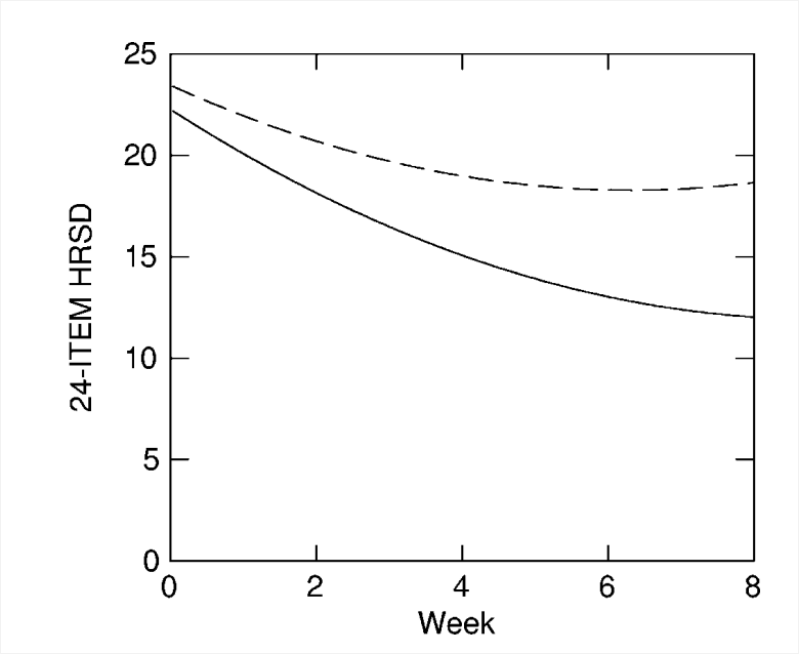
Figure 4 Temporal interdependencies among patient-reported measures of cognitive symptoms, patient-reported depressive symptoms, and functional impairment. Standardized regression coefficients based on the structural equation models (SEM) with *p*-values <0.05 (n=451). The thickness of arrows is proportional to the strength of association. A solid arrow indicates *p*-value <0.001; a dot-dashed arrow indicates *p*-value <0.05.
Abbreviations: PDQ-D, Perceived Deficits Questionnaire – Depression; PHQ-9, Patient Health Questionnaire-9; SDS, Sheehan Disability Scale.

Wang et al. 2019

FONCTIONS EXÉCUTIVES: LLD

Inhibition de la réponse (STROOP)

P=0.002



Sneed et al. 2007

Table 1. Baseline Demographic and Clinical Data in 112 Elderly Patients with Major Depression Treated with Citalopram for 8 Weeks: Comparisons Among Responders (50% Change in HAM-D from Baseline) and Nonresponders

	Responders (n = 68)		Nonresponders (n = 44)		Mann-Whitney Wilcoxon	
	Mean	SD	Mean	SD	z	p
Age (y)	71.56	6.25	75.66	6.15	3.51	.004
Education (ys)	15.26	3.49	14.36	3.10	−1.57	.11
Depressive Symptoms						
Total HAM-D	23.69	4.35	25.32	5.08	1.52	.13
Medical Burden						
CIRS total[2]	6.77	3.48	8.86	4.45	2.38	.018
Cognitive Impairment						
DRS total	136.33	6.29	134.31	6.81	−1.61	.11
DRS Attention	35.55	1.57	35.16	1.62	−1.29	.20
DRS Initiation/Perseveration	35.37	2.49	33.98	3.17	−2.72	.007
Response Inhibition						
Stroop Color–Word	30.87	10.74	26.15	7.63	−2.45	.014
Treatment						
Maximal citalopram dose (mg)	36.35	7.15	33.64	9.94	−1.20	.23

HAM-D, 24-item Hamilton Depression Rating Scale; CIRS, Cumulative Illness Rating Scale–Geriatric Version; DRS, Mattis Dementia Rating Scale; Stroop Color–Word, Stroop Response Inhibition Test.

Alexopoulos et al. 2005

FONCTIONS EXÉCUTIVES: LLD

TABLE 3. Baseline Neurocognitive Performance of High Response Versus Low Response

	High Response N = 66, Mean (SD)	Low Response N = 34, Mean (SD)
WMS-R LM delayed recall[a]	20.50 (8.56)	15.50 (8.74)
WMS-R LM percent retention[a,b]	0.79 (0.198)	0.72 (0.256)
CERAD word list recall[c]	6.21 (2.02)	6.00 (2.06)
Trail Making Test Part A	47.17 (36.25)	44.44 (21.13)
Trail Making Test Part B	123.20 (69.88)	141.21 (75.32)
Symbol Digit Modalities Test	38.94 (11.03)	35.62 (10.45)

Notes: WMS-R LMII: F (1, 97) = 15.124, p = 0.001, η^2 = 0.135; WMS-R LM Percent Retention: F (1, 97) = 9.56, p = 0.001, η^2 = 0.090; CERAD Word List Recall: F (1, 97) = 5.210, p = 0.025, η^2 = 0.051; Trails A: F (1, 98) = 0.783, p = 0.378, η^2 = 0.008; Trails B: F (1, 95) = 3.026, p = 0.085, η^2 = 0.031; SDMT: F (1, 93) = 5.951, p = 0.017, η^2 = 0.060.

[a]Subtest from the Wechsler Memory Scale–Revised.

[b]Multiply value by 100 for percentage score.

[c]Subtest from the Consortium to Establish a Registry for Alzheimer's Disease.

Réponse à 1 an

Story et al. 2008

FONCTIONS EXÉCUTIVES: LLD

Rémission à 3 mois

Table 2 Bivariate Analysis of Neuropsychological Measures by Remission Status

	Nonremitted, mean (SE) ($n = 87$)	Remitted, mean (SE) ($n = 23$)	*P*
Digit span—forward	8.27 (0.27)	9.64 (0.55)	0.046
Digit span—backward	6.73 (0.26)	7.14 (0.65)	NS
COWA—total correct	37.35 (1.19)	36.35 (1.94)	NS
Animal naming (AN)—total correct	15.01 (0.48)	15.48 (1.18)	NS
BVRT—perseverative errors	1.03 (0.15)	1.30 (0.26)	NS
COWA—perseverative errors	1.43 (0.18)	0.78 (0.23)	0.048
AN—perseverative errors	0.55 (0.12)	0.30 (0.12)	NS
Total perseverative errors (COWA+AN)	2.17 (0.25)	1.27 (0.32)	0.059
Confabulations	0.97 (0.15)	0.87 (0.30)	NS
Trail making A (sec)	56.62 (5.52)	61.61 (10.12)	NS
Trail making B (sec)	144.92 (9.11)	164.52 (22.00)	NS

NS = not significant.

Table 3 Odds Ratios and Confidence Intervals for Neuropsychological Measures

	Odds ratio	95% CI	*P*
Digit span—forward	1.31	0.99:1.72	0.056
Digit span—backward	1.11	0.83:1.47	NS
COWA—total correct	0.99	0.95:1.04	NS
Animal naming (AN)—total correct	1.06	0.93:1.19	NS
BVRT—perseverative errors	1.12	0.79:1.57	NS
COWA—perseverative errors	0.71	0.49:1.05	0.082
AN—perseverative errors	0.56	0.29:1.05	0.079
Total perseverative errors (COWA+AN)	0.74	0.55:0.99	0.045
Confabulations	0.95	0.67:1.35	NS
Trail Making A (sec)	1.00	0.99:1.01	NS
Trail Making B (sec)	1.00	0.99:1.01	NS

NS = not significant.

Potter et al. 2004

FONCTIONS EXÉCUTIVES: LLD

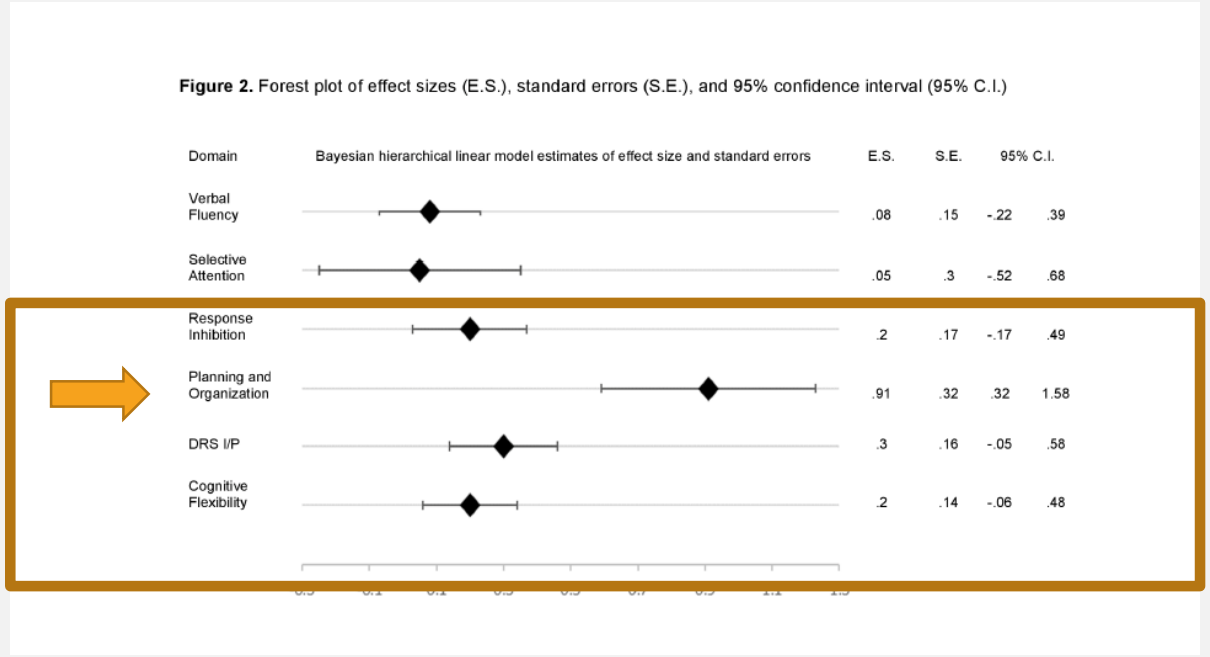
Méta-analyse

Table 3 Weighted Mean effect sizes for pre-treatment cognitive differences between antidepressant responders and non-responders—studies using standardised administration of SSRIs.

Cognitive assessment tool	*N* studies	*N* subjects	d_w	SD	95% CI	% OL	N_{fs}	Study references
Executive Function								
Trail making test B: time	2	22	0.75	0.82	−0.14–1.64	53	6	(Dunkin *et al.*, 2000; Mayberg *et al.*, 2000)
WCST: % perseverative errors	2	26	0.71	0.66	−0.09–1.52	57	5	(Dunkin *et al.*, 2000; Alexopoulos *et al.*, 2007)
DRS initiation-perseveration subtest (raw)	**2**	**134**	**0.59**	**0.42**	**0.24–1.95**	**62**	**4**	(Kalayam and Alexopoulos, 1999; Kalayam and Alexopoulos, 2003)
Stroop interference	4	156	0.49	0.44	0.17–0.82	73	6	(Dunkin *et al.*, 2000; Mayberg *et al.*, 2000; Kalayam and Alexopoulos, 2003; Alexopoulos *et al.*, 2005)
COWAT	4	85	0.42	1.23	−0.05–0.89	73	4	(Dunkin *et al.*, 2000; Mayberg *et al.*, 2000; Devanand *et al.*, 2003; Taylor *et al.*, 2006)
WCST: perseverative errors	2	51	0.16	0.71	−0.42–0.75	85	0	(Dunkin *et al.*, 2000; Taylor *et al.*, 2006)
WCST: categories completed	2	51	0.10	0.80	−0.48–0.69	92	0	(Dunkin *et al.*, 2000; Taylor *et al.*, 2006)
Speed/Reaction time								
Trail making test A: time	2	157	0.78	0.03	−0.09–1.65	53	6	(Dunkin *et al.*, 2000; Mayberg *et al.*, 2000)
Stroop colour: number completed	**2**	**51**	**0.64**	**0.23**	**0.05–1.23**	**62**	**4**	(Dunkin *et al.*, 2000; Taylor *et al.*, 2006)
Stroop word: number completed	**2**	**51**	**0.63**	**0.06**	**0.04–1.22**	**62**	**4**	(Dunkin *et al.*, 2000; Taylor *et al.*, 2006)
WAIS digit symbol (scaled)	2	51	0.45	0.38	−0.14–1.03	67	2	(Dunkin *et al.*, 2000; Taylor *et al.*, 2006)
WAIS digit symbol (raw)	2	412	−0.02	0.17	−0.23–0.20	100	0	(Devanand *et al.*, 2003; Doraiswamy *et al.*, 2003)

McLennan et al. 2010

FONCTIONS EXÉCUTIVES: LLD



Pimontel et al. 2016

FONCTIONS EXÉCUTIVES: LLD

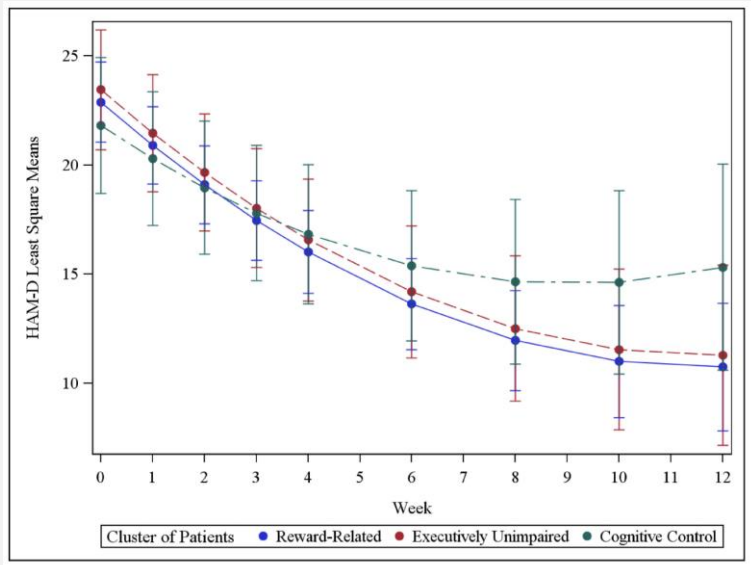


Figure 1.
Trajectory of 24-item Hamilton Depression Rating Scale (HAM-D) Scores in Three Clusters of Older Patients with Major Depression (N=53) Treated with Escitalopram

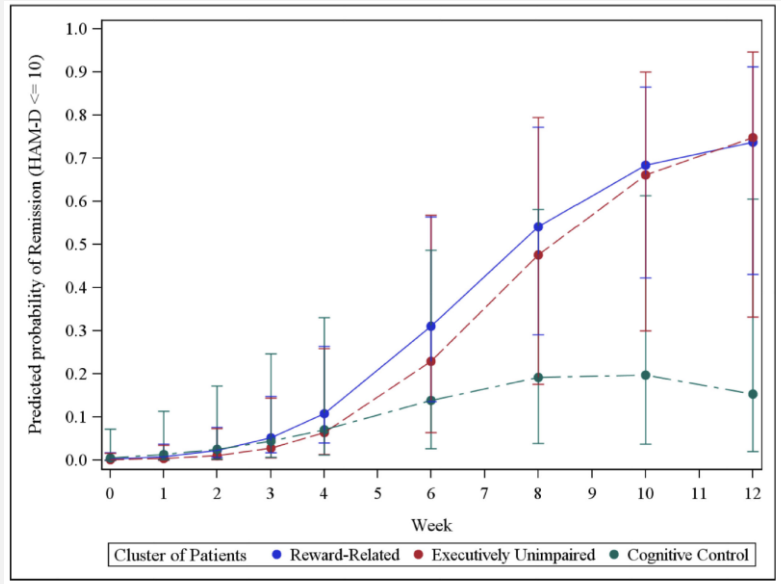


Figure 2.
Longitudinal Trajectory of the Probability of Remission (HAM-D≤10) in Three Clusters of Older Patients with Major Depression (N=53) Treated with Escitalopram

Cognitive Control Cluster= abnormal Stroop, Tower, and DRS-IP

Alexolpoulos et al. 2015

FONCTIONS EXÉCUTIVES: EOD

14 sujets

Table 4
Results of omnibus MANCOVAs (Hotelling's T): responders versus nonresponders, controlling for HAM-D

Domain	*F*	Sig of *F*
Basic Attention[a]	1.474	0.250
Processing Speed	0.30	0.869
Language[a]	3.33	0.095
Visuospatial Tasks	0.69	0.582
Verbal Memory	1.15	0.436
Nonverbal Memory	1.29	0.364
Executive Functioning	9.75	0.044

[a] These analyses used ANCOVA, since the domain was comprised of only one measure.

Dunkin et al. 2000

FONCTIONS EXÉCUTIVES: EOD

Table 2. *ANCOVA of neuropsychological test scores on admission depending on the course of treatment (response, non-response) until the fourth week*

Cognitive tests	Responder ($n=35$)	Non-responder ($n=38$)	$F(1, 62)$	p
Attention				
Intensity				
Trail-making (s)	93·6 (40·5)	111·6 (44·8)	4·4	0·038
Alertness (−wt) (ms)	295·2 (63·4)	334·4 (146·0)	1·3	N.S.
Alertness (+wt) (ms)	283·1 (60·6)	310·9 (95·1)	1·1	N.S.
Selectivity				
Letter cancellation	125·2 (48·3)	117·2 (39·9)	2·2	N.S.
CAB	110·5 (17·5)	100·2 (19·6)	4·2	0·046
Stroop (s)	93·7 (26·5)	92·2 (32·8)	0·1	N.S.
Divided attention (ms)	675·7 (67·5)	735·0 (100·3)	9·2	0·004
Memory				
Digit span forward	7·5 (2·0)	7·2 (2·2)	0·1	N.S.
Block span forward	7·6 (1·8)	7·2 (1·5)	1·1	N.S.
Digit span backward	5·8 (2·1)	5·8 (2·2)	0·1	N.S.
Block span backward	6·9 (1·8)	6·6 (1·6)	1·5	N.S.
Executive function				
WCST (TE)	46·9 (12·4)	47·8 (14·1)	1·3	N.S.

Table 3. *ANCOVA of neuropsychological test scores on admission depending on the course of treatment (remission, no remission) at discharge*

Cognitive tests	Remission ($n=39$)	No remission ($n=32$)	$F(1, 61)$	p
Attention				
Intensity				
Trail-making (s)	102·3 (46·9)	102·9 (40·3)	0·1	N.S.
Alertness (−wt) (ms)	297·7 (77·2)	329·4 (145·2)	0·1	N.S.
Alertness (+wt) (ms)	282·5 (62·9)	308·5 (93·3)	0·3	N.S.
Selectivity				
Letter cancellation	128·2 (46·6)	122·5 (41·9)	0·0	N.S.
CAB	109·5 (19·2)	99·9 (16·7)	1·6	N.S.
Stroop (s)	87·6 (34·0)	97·4 (34·6)	0·3	N.S.
Divided attention (ms)	677·9 (75·4)	742·4 (94·3)	4·5	0·038
Memory				
Digit span forward	7·6 (2·2)	7·0 (2·0)	0·4	N.S.
Block span forward	7·4 (1·7)	7·5 (1·4)	0·3	N.S.
Digit span backward	5·9 (2·1)	5·6 (2·1)	0·0	N.S.
Block span backward	6·6 (1·6)	6·8 (1·7)	0·1	N.S.
Executive function				
WCST (TE)	47·0 (11·9)	46·7 (15·5)	0·3	N.S.

Controlled for age, gender, years of education, severity of depression on admission (HDRS score), duration of illness, type of medication/additional medication on admission, duration of hospitalization.
(−wt), Without warning tone; (+wt), with warning tone.

Majer et al. 2004

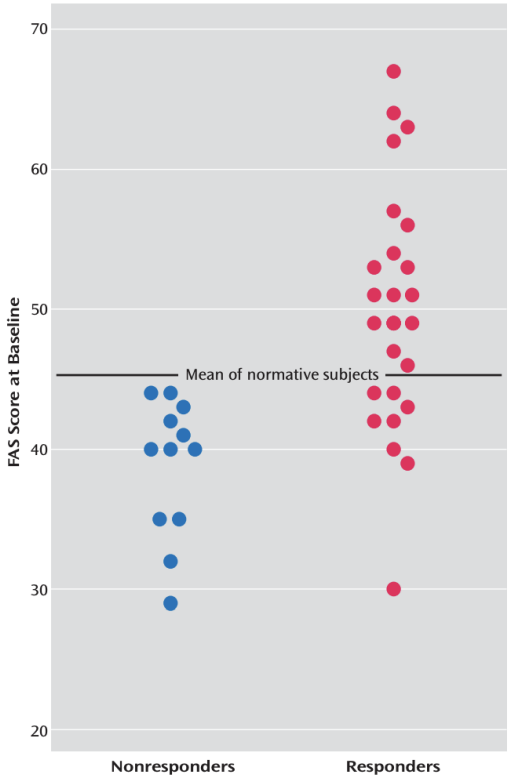
FONCTIONS EXÉCUTIVES: EOD

TABLE 2. Neuropsychological Performance of Responders and Nonresponders to 12 Weeks of Fluoxetine Treatment[a]

Measure	Score of Responders (N=25) Mean	SD	Score of Nonresponders (N=12) Mean	SD	Analysis t (df=35)	p	Effect Size
Controlled Oral Word Association Test FAS	49.84	8.70	38.75	4.88	–4.10	0.001	1.44
Stroop Color and Word Test							
Word reading	109.68	14.05	99.55	18.43	–1.86	<0.08	0.65
Color naming	75.64	10.72	67.09	13.25	–2.10	<0.05	0.74
Interference	–1.21	8.58	–1.55	5.48	–0.12	0.90	
Wisconsin Card Sorting Test							
Perseverative errors	12.25	10.21	11.08	9.31	–0.33	0.74	
Categories completed	5.17	1.70	5.50	1.24	0.60	0.55	
WAIS-III							
Digit symbol	11.12	2.93	9.25	3.33	–1.74	<0.10	0.61
Block design	11.33	3.92	9.75	2.49	–1.28	0.21	
Digit span	11.44	3.24	10.42	2.91	–0.93	0.36	
Vocabulary	13.48	2.45	12.91	3.00	–0.62	0.54	

[a] Significant difference between groups on measures of psychomotor speed (MANOVA: Wilks's lambda=0.639, F=4.51, df=4, 32, p=0.005).

FIGURE 1. Baseline Controlled Oral Word Association Test FAS Scores of Depressed Responders (N=25) and Nonresponders (N=12) to 12 Weeks of Fluoxetine Treatment



Taylor et al. 2006

FONCTIONS EXÉCUTIVES: EOD

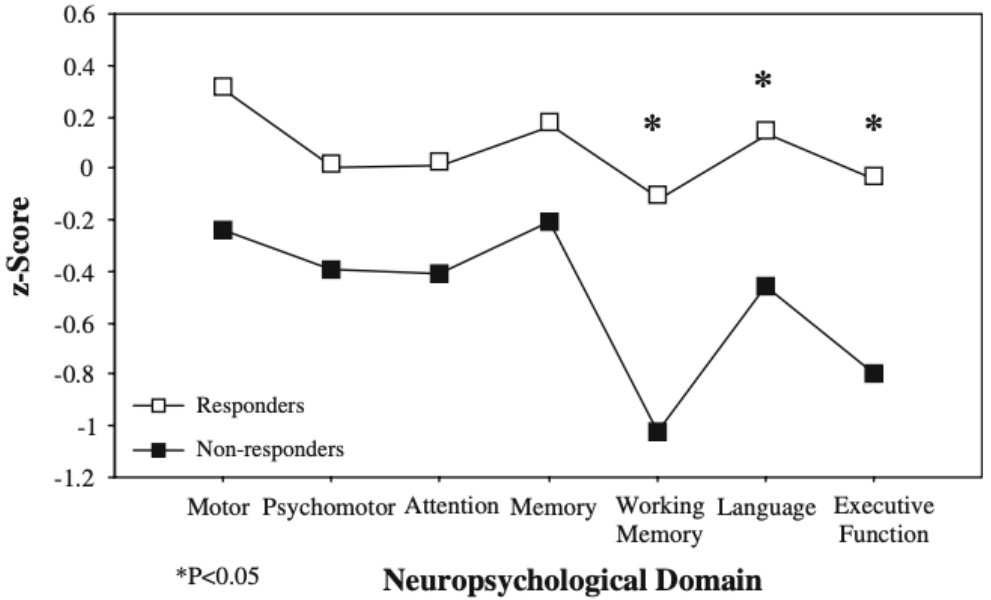


Fig. 1 Neuropsychological domain scores of responders and nonresponders

Gorlyn et al. 2008

FONCTIONS EXÉCUTIVES: EOD

SYMPTÔMES DÉPRESSIFS

Table 4. *Results of hierarchical regression analysis for HAMD score at follow-up (n = 48)*

Variable	*B*	S.E. *B*	*β*	Significance
Step 1				
HAMD	0.611	0.130	0.580	0.000***
Reaction time	0.008	0.010	0.097	0.438
Step 2				
HAMD	0.459	0.154	0.436	0.005**
Reaction time	−0.019	0.011	−0.241	0.105
PM categories	−0.918	0.618	−0.201	0.146
COWAT phonemic	0.013	0.070	0.027	0.855
S-WCST perseverative errors	0.674	0.233	0.390	0.006**
SET score	0.050	0.675	−0.009	0.942
CVLT long delay free recall	−0.821	0.413	−0.262	0.054

HAMD, Hamilton Depression Rating Scale; S.E., standard error; PM, prospective memory; COWAT, Controlled Oral Word Association Test; S-WCST, Shortened Wisconsin Card Sorting Test; SET, Six Elements Test; CVLT, California Verbal Learning Test.

IMPACT FONCTIONNEL

Table 5. *Results of hierarchical regression analysis for SOFAS score at follow-up (n = 48)*

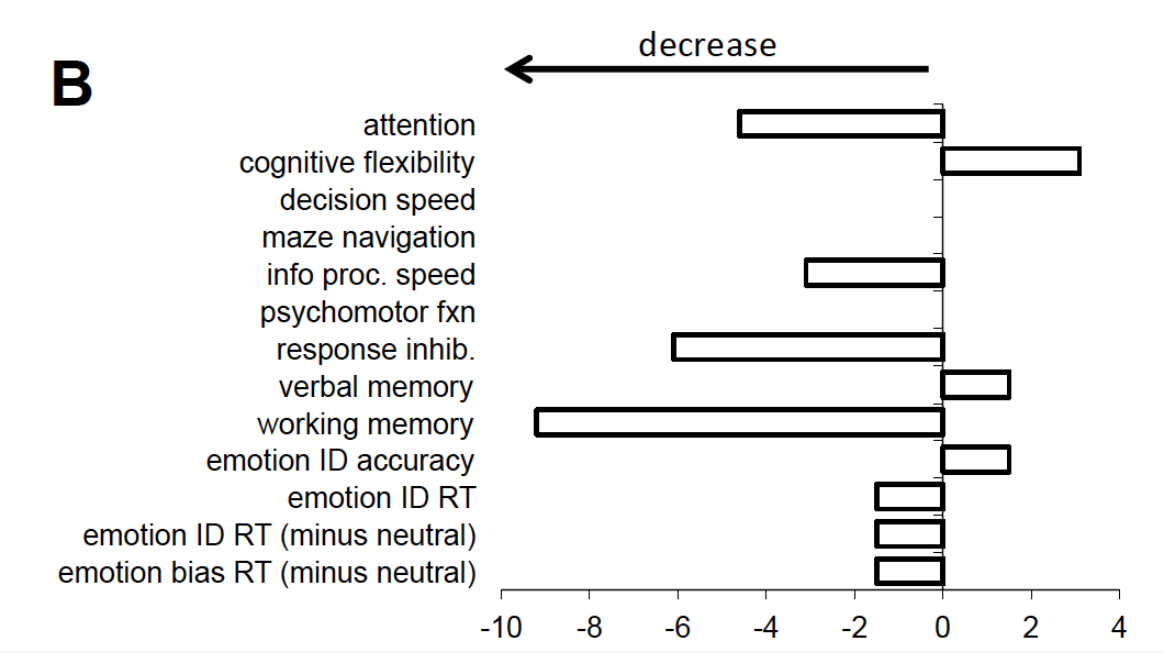
Variable	*B*	S.E. *B*	*β*	Significance
Step 1				
SOFAS	0.728	0.112	0.657	0.000***
Reaction time	−0.040	0.016	−0.254	0.016*
Step 2				
SOFAS	0.699	0.119	0.631	0.000***
Reaction time	0.006	0.018	0.040	0.730
PM categories	2.260	0.974	0.248	0.026*
COWAT phonemic	−0.136	0.115	−0.143	0.246
S-WCST perseverative errors	−1.036	0.363	−0.300	0.007**
SET score	1.796	1.028	0.157	0.088
CVLT long delay free recall	0.887	0.619	0.142	0.160

SOFAS, Social and Occupational Functioning Assessment Scale (DSM-IV); S.E., standard error; PM, prospective memory; COWAT, Controlled Oral Word Association Test; S-WCST, Shortened Wisconsin Card Sorting Test; SET, Six Elements Test; CVLT, California Verbal Learning Test.

Significance following Benjamini–Hochberg correction: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Whithall et al. 2008

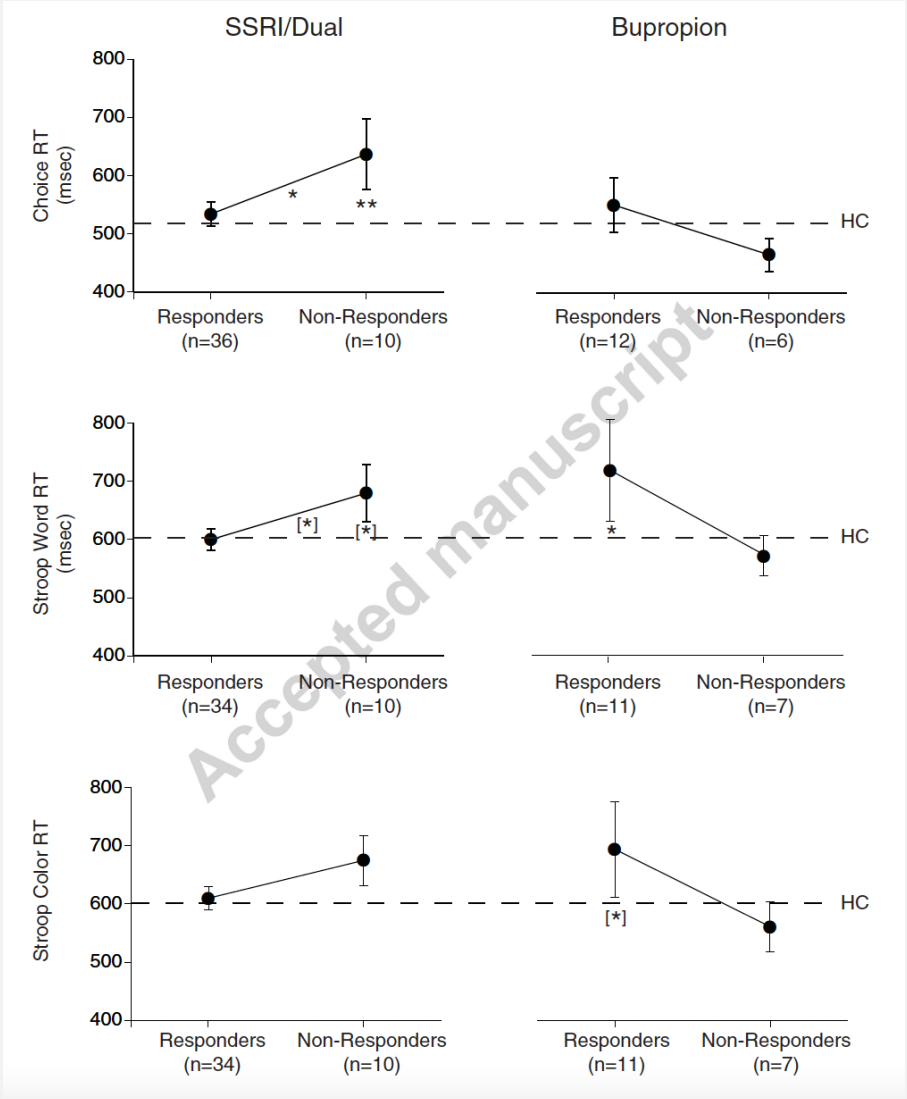
FONCTIONS EXÉCUTIVES: EOD



Etkin et al. 2014

FONCTIONS EXÉCUTIVES: EOD

Différence de réponse entre IRS/ association vs Bupropion



MÉMOIRES: LLD

TABLE 3. Baseline Neurocognitive Performance of High Response Versus Low Response

	High Response N = 66, Mean (SD)	Low Response N = 34, Mean (SD)
WMS-R LM delayed recall[a]	20.50 (8.56)	15.50 (8.74)
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[a]Subtest from the Wechsler Memory Scale–Revised.

[b]Multiply value by 100 for percentage score.

[c]Subtest from the Consortium to Establish a Registry for Alzheimer's Disease.

Réponse à 1 an

Story et al. 2008

MÉMOIRES: LLD

TABLE 4 | Multiple linear regression analysis of predictors of antidepressant efficacy in LLD.

Variable	B	Std. error	Beta	*t*-value	*p*-value
(Constant)	0.196	0.202		0.973	0.335
Picture naming	0.043	0.02	0.269	2.101	0.04
Figure copy	−0.025	0.008	−0.397	−2.98	0.004
Digit span	0.028	0.012	0.325	2.282	0.027

Pan et al. 2022

MÉMOIRES: LLD

Méta-analyse

Memory								
Word list recall: short delay	**2**	**26**	**0.86**	**0.09**	**0.05–1.66**	**48**	**7**	(Dunkin *et al*., 2000; Alexopoulos *et al*., 2007)
Word list learning: 5 trials	2	26	0.43	0.41	−0.36–1.21	73	2	(Dunkin *et al*., 2000; Alexopoulos *et al*., 2007)
DRS memory subtest (raw)	2	134	0.05	0.54	−0.30–0.40	92	0	(Kalayam and Alexopoulos, 2003; Alexopoulos *et al*., 2005)

McLennan et al. 2010

TROUBLE BIPOLAIRE

TABLE 3 Comparisons between clusters on demographic, clinical, functional, and pharmacological variables

	HiP		LoVM		HiVM		LoP		
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Test
Age (years)	38.7	12.2	42.2	11.2	42	11	39.9	11.9	Main effect: $F(3, 254)=1.2$, p [BC]>.1
Educational level (years)	14.5	2.2	14.8	2.7	14.4	2.9	14	2.8	Main effect: $F(3, 254)=1.2$, p[BC]>.1
Estimated IQ [mean=100, sd=15]	110.9	9.6	103.8	11	104.2	10.1	93.3	11.5	**Main effect: *F(3, 254)=26.1, p[BC]<.001*** ***HiP vs LoVM: F(1, 113)=10.8, p[BC]=.008*** ***HiP vs HiVM: F(1, 100)=10.2, p[BC]=.011*** ***HiP vs LoP: F(1, 109)=61.8, p[BC]<.001*** LoVM vs HiVM: ***F***(1,145)=0.1, ***p***[BC]>.1 ***LoVM vs LoP: F(1, 154)=34.1, p[BC]<.001*** ***HiVM vs LoP: F(1, 141)=35.8, p[BC]<.001***
Age at onset (years)	23.8	10.3	25.8	9.4	25.5	10.1	24.1	8	Main effect: $F(3 ,246)=0.7$, p[BC]>.1
Number of mixed episodes	0.1	0.3	0.2	1	0.1	0.4	0.3	0.7	Main effect: $F(3, 228)=1.1$, p[BC]>.1
Number of hypomanic episodes	1.4	1.9	3.8	6.5	2.4	3.9	2.8	5.6	Main effect: $F(3, 183)=1.4$, p[BC]>.1
Number of manic episodes	1.7	2.1	1.1	1.5	1.1	1.7	1.6	2.1	Main effect: $F(3, 245)=1.7$, p[BC]>.1
Number of major depressive episodes	4.9	4.8	5.2	5.4	5.3	5.4	5	5.1	Main effect: $F(3, 212)=0.1$, p[BC]>.1
MADRS [0–60]	3.7	3.2	4.2	3.5	3.9	3.2	4.3	3.4	Main effect: $F(3, 247)=0.3$, p[BC]>.1
YMRS [0–60]	1.6	2.5	1.1	1.9	1	2.1	1.1	2.1	Main effect: $F(3, 248)=0.7$, p[BC]>.1
FAST [0–72]	11.9	7.4	18.5	14.4	13.1	10.1	20.8	14.8	**Main effect: *F(3, 240)=6.1, p[BC]=.009*** HiP vs LoVM: $F(1, 108)=6.2$, p[BC]=.088 HiP vs HiVM: $F(1, 92)=0.4$, p[BC]>.1 ***HiP vs LoP: F(1, 104)=10.7, p[BC]=.009*** LoVM vs HiVM: $F(1, 136)=6.1$, p[BC]=.087 LoVM vs LoP: $F(1, 148)=1$, p[BC]>.1 ***HiVM vs LoP: F(1, 132)=12, p[BC]=.004***

COGNITIONS ET TROUBLES BIPOLAIRES

- Les symptomes cognitifs et les symptômes résiduels dépressifs= 2 sources d'atteinte du fonctionnement.
- Possibilité d'agir sur les 2 compostantes

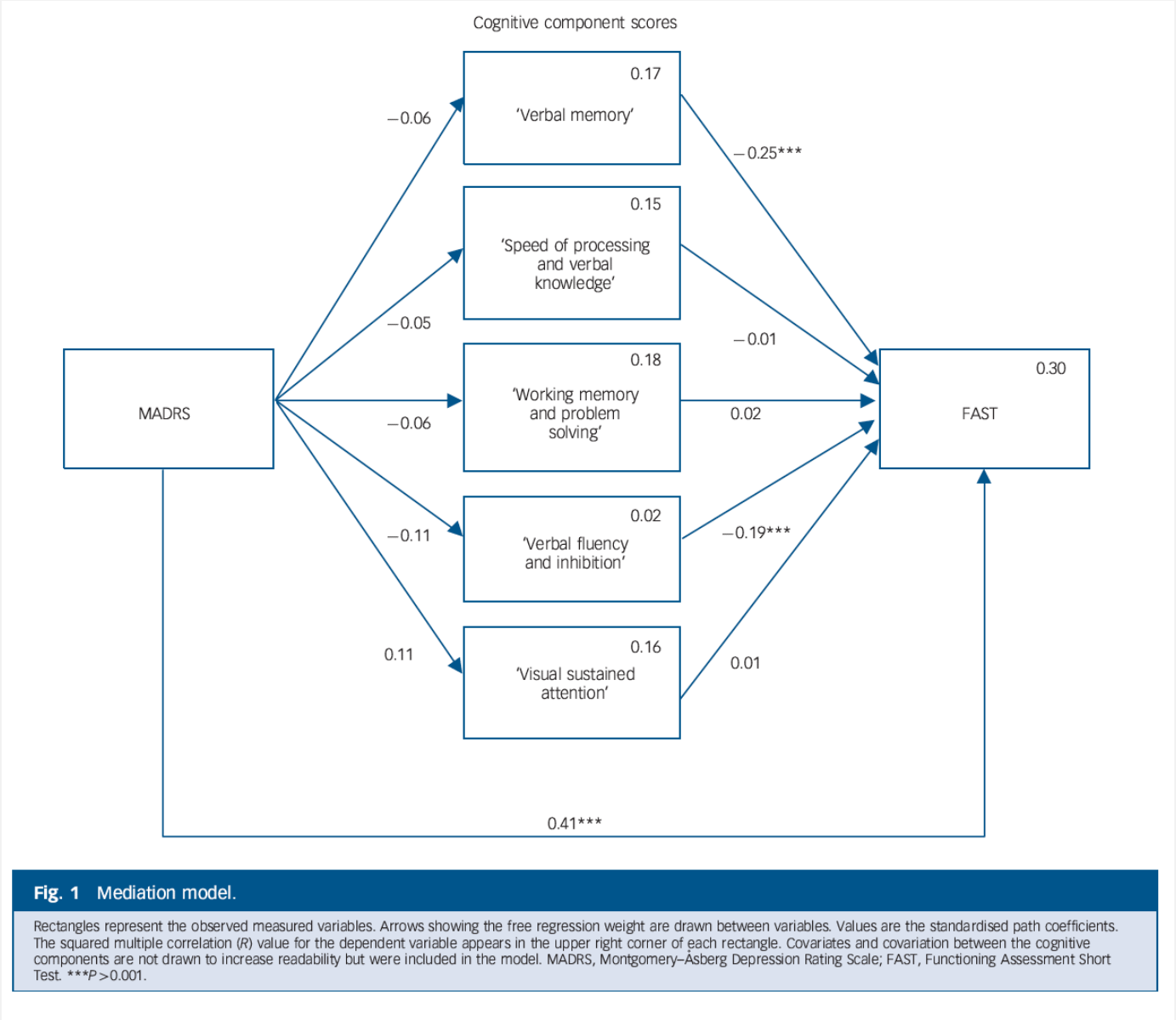

Fig. 1 Mediation model.

Rectangles represent the observed measured variables. Arrows showing the free regression weight are drawn between variables. Values are the standardised path coefficients. The squared multiple correlation (*R*) value for the dependent variable appears in the upper right corner of each rectangle. Covariates and covariation between the cognitive components are not drawn to increase readability but were included in the model. MADRS, Montgomery–Åsberg Depression Rating Scale; FAST, Functioning Assessment Short Test. ***$P > 0.001$.

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COGNITIONS ET TROUBLES BIPOLAIRES

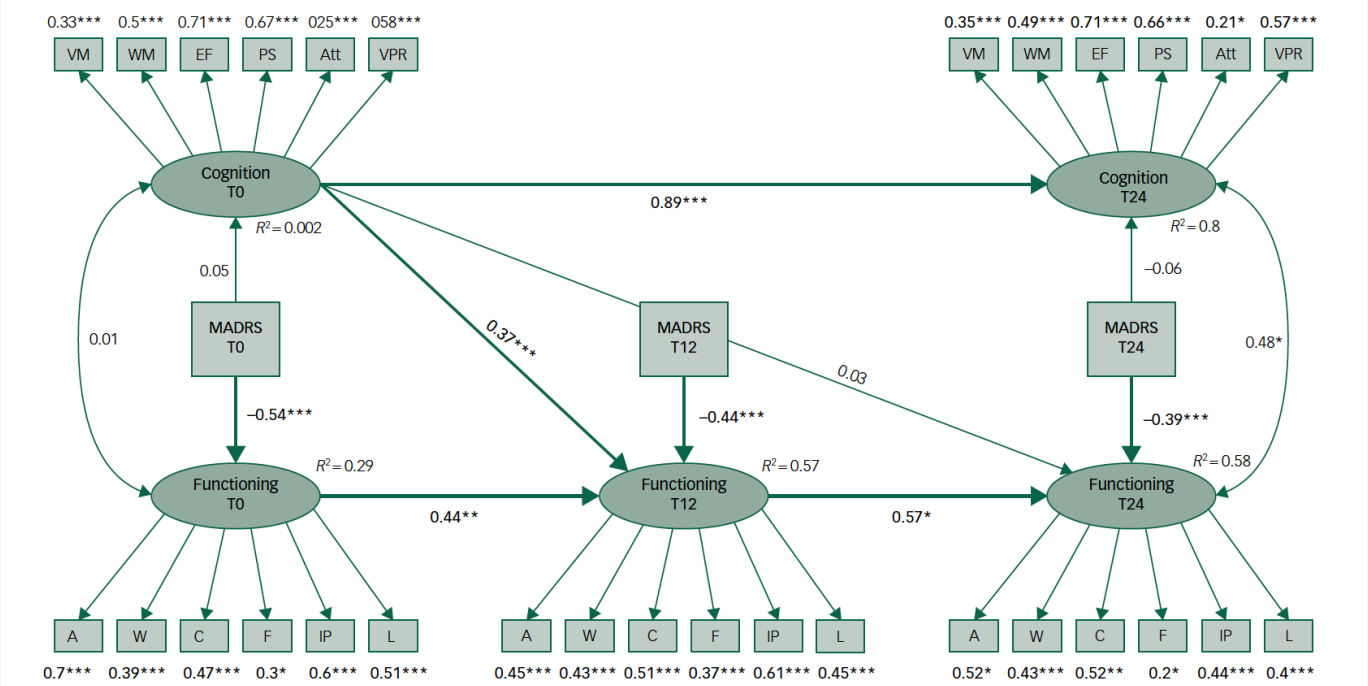

Fig. 1 Final structural equation model with standardised path coefficients.

For readability, the names of indicators are truncated. Rectangles indicate the observed variables, ovals the latent variables, single-headed arrows the regressions (freely estimated regression weight), double-headed arrows the correlations or covariances. For readability, the serial correlations between indicators in the latent variables were not reported in the Figure but were indeed estimated in the model. The squared multiple correlation R^2 value for the dependent variables is presented above them. Significance levels are as follows: *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$.
A, autonomy; Att, attention; C, cognition; EF, executive functions; F, finances; IP, interpersonal relationship; L, leisure; MADRS, Montgomery–Asberg Depression Rating Scale; PS, processing speed; T0, inclusion; T12, 12 months; T24, 24 months; VM, verbal memory; VPR, visual and perceptual reasoning; W, work; WM, working memory.

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COGNITIONS ET TROUBLES BIPOLAIRES

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ORIGINAL ARTICLE

WILEY BIPOLAR DISORDERS

Cognitive function, treatment response to lithium, and social functioning in Japanese patients with bipolar disorder

Satoshi Saito[1,2] | Kumiko Fujii[2] | Yuji Ozeki[2] | Kenichi Ohmori[3] | Gyo Honda[4] | Harunobu Mori[4] | Kazuko Kato[5] | Jinichi Kuroda[6] | Akiko Aoki[2] | Haruhiko Asahi[7] | Hayato Sato[8] | Kazutaka Shimoda[2] | Kazufumi Akiyama[1]

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Research paper

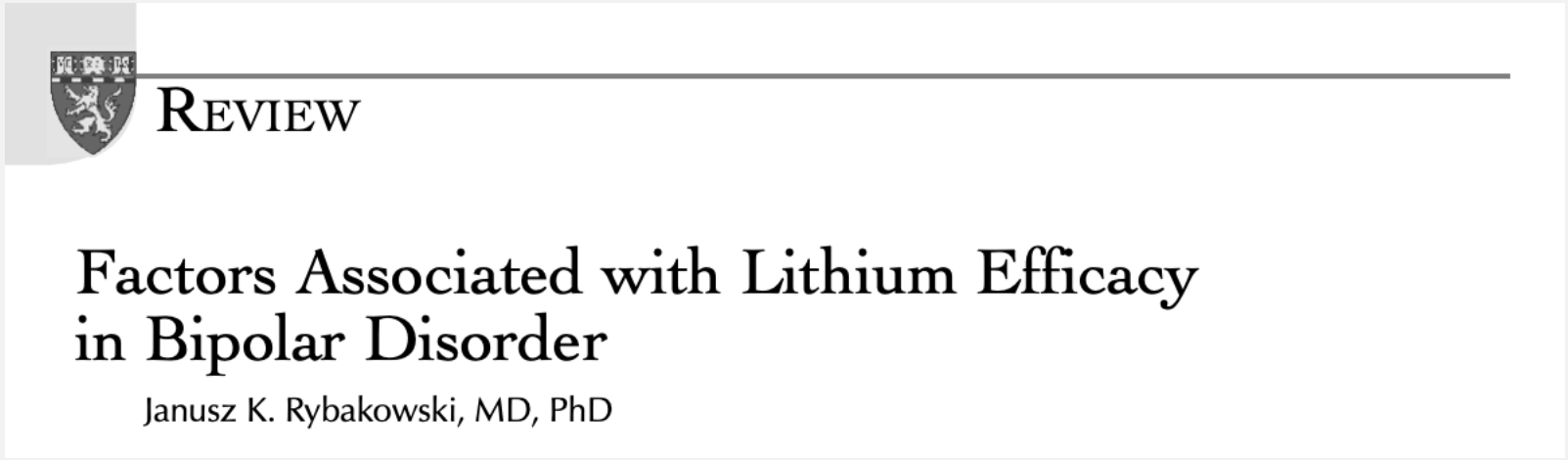
Memory performance predicts response to psychotherapy for depression in bipolar disorder: A pilot randomized controlled trial with exploratory functional magnetic resonance imaging

Thilo Deckersbach[a,b,*], Amy T. Peters[c], Conor Shea[d], Aishwarya Gosai[a], Jonathan P. Stange[c], Andrew D. Peckham[b,e], Kristen K. Ellard[a,b], Michael W. Otto[f], Scott L. Rauch[b,e], Darin D. Dougherty[a,b], Andrew A. Nierenberg[a,b]

32 patients BPI (EDC):=

- Mémoire verbale: associé amélioration syndrome dépressif= TCC ou thérapie de soutien

COGNITIONS ET TROUBLES BIPOLAIRES



REVIEW

Factors Associated with Lithium Efficacy in Bipolar Disorder

Janusz K. Rybakowski, MD, PhD

A lack of cognitive impairment predict the best results of lithium

COGNITIONS ET TROUBLES BIPOLAIRES

Treatment Nonadherence and Neurocognitive Impairment in Bipolar Disorder

Anabel Martinez-Aran, Ph.D.; Jan Scott, Ph.D.; Francesc Colom, Ph.D.;
Carla Torrent, Ph.D.; Rafael Tabares-Seisdedos, M.D., Ph.D.;
Claire Daban, Ph.D.; Marion Leboyer, M.D.; Chantal Henry, M.D.;
Guy M. Goodwin, F.Med.Sci., F.R.C.Psych.; Ana Gonzalez-Pinto, M.D., Ph.D.;
Nuria Cruz, M.D.; Jose Sanchez-Moreno, Psy.D.; and Eduard Vieta, M.D., Ph.D.

QUE FAIRE?

STRATÉGIES DE DÉPISTAGE: TROUBLE DÉPRESSIF

- Batterie neuropsychologique brève: screen for cognitive impairment in psychiatry: SCIP (Rojo et al. 2010) avec un cut-off à 70
- 5 mots
- Histoire du Lion Barbizet et Truscelli
- Empans
- Mémoire rétrograde: hier, Noel et été dernier

STRATÉGIES DE DÉPISTAGE: TROUBLE BIPOLAIRE

- BNP complet: non recommandé de manière systématique mais après dépistage
- Quand faire ce dépistage:
  - HDRS<14 et 2-3 mois après la fin de l'episode
  - Tous les 5 ans
- Comment faire ce dépistage: Combinaison évaluation objective réduite et plaintes cognitives subjectives:
  - Batterie neuropsychologique brève: screen for cognitive impairment in psychiatry: SCIP (Rojo et al. 2010) avec un cut-off à 70
  - Auto evaluation: complaints in BD Rating assessment: COBRA (Rosa et al. 2013) avec un cut off à 14
  - Montreal Cognitive Assessment: MOCA: <26/30 (Rej et al. 2017)

QUEL BNP?

PRISE EN CHARGE?

DISCUSSION