Dr. Carlo Serrati

Direttore DAI Neuroscienze e Organi di Senso e U.O. Neurologia

Dr. Cinzia Finocchi

Coordinatore DMT Malattie Cerebrovascolari

Dr. Matteo Pardini

Ricercatore UO Clinica Neurologica

Dr. Davide Sassos

U.O. Neurologia e Centro Ictus

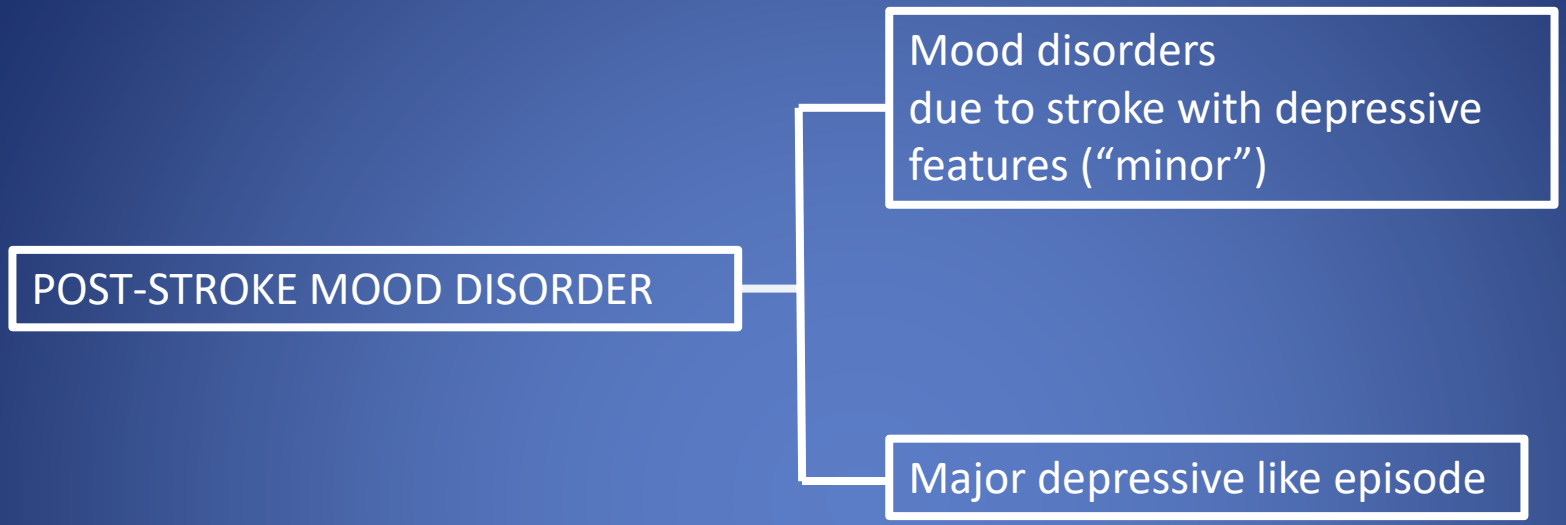
Ospedale Policlinico San Martino - Genova

LA DEPRESSIONE NEI PAZIENTI CON STROKE

DALLA DIAGNOSI AL TRATTAMENTO

TORINO 8 novembre 2019

Come si può classificare la depressione correlata alla malattia cerebrovascolare?



VASCULAR DEPRESSION

Am J Psychiatry 173:3, March 2016

La depressione post-stroke: aspetti epidemiologici e criticità

Disability and Rehabilitation, 2011; 33(7): 539–556

Depression in acute stroke: prevalence, dominant symptoms and associated factors. A systematic literature review

SIREN E. KOUWENHOVEN[1], MARIT KIRKEVOLD[2], KNUT ENGEDAL[3] & HESOOK S. KIM[1]

Table I. Studies of post-stroke depression within 1 month – depression diagnosed according to standardised criteria.

Study	*n*	Mean age (year)	Female %	Diagn criteria	Prof*	Time after	Prevalence %	Dominant symptoms	Factors associated
Aben et al., 2002 [16]	190	68.6	46.8	DSM IV	MD, trained to use the instruments	1 month	21.6		High neuroticism score
Aben et al., 2003 [15]									Level of handicap
Aben et al., 2006 [13]	189	68.5	47.1	DSM IV	Not described	1 month	Not given		
Agrell and Dehlin, 1993 [50]	93	76	41.9	DSM III	Not described	2–5 weeks	46		
				Major depression			19		
				Minor depression			27		
Berg et al., 2001 [33]	100	55.2	32	DSM-III-R	Neurologist	2 weeks	5.6		Severity of neurological impairment.
Berg et al., 2002 [18]				Major depression					
Caeiro et al., 2006 [43]	178	31% ≥ 65		DSM-IV					
House et al., 1990 [10]	128	71.2	54.7	DSM III†	Trained interviewer	1 month	11		Frontal pole lesion
House et al., 2001 [44]	448	70.7	46.2	ICD-10	Trained research interviewer	1 month	22.3		Low pre-stroke BI-score
				Severe					Female sex Low MMSE score Incontinence
Jiménez et al., 2009 [27]	134	70.4	32.8	DSM IV	Trained psychologist	1 week			High serum leptin levels (stat sign)
				Depression			40.3		
				Major depression			18.7		
				Depression		1 month	48.1		
				Major depression			22.1		
Kellermann et al., 1999 [46]	82	65.8	41	DSM IV	MD, Trained in administering depression scales for patients with acute stroke.	7 days	27		High BI-scores Severity of stroke Unable to walk
Leentjens et al. 2006 [12]	165	68.1	46	DSM IV	Not described	1 month	Not given		Aphasia (stat sign) Female sex Prior personal history of depression Disability (stat sign) Family history of depression Somatic comorbidity other than stroke
Nagaraja et al. 1997 [51]	40	42.2	27.5	DSM III-R	Not described	Within 3 weeks	42.5		
Nannetti et al., 2005 [35]	117			DSM IV	Not described	Within 30 days (average 2 weeks after stroke)	Not given		

La depressione post-stroke: aspetti epidemiologici e criticità

Table V. Longitudinal studies of post-stroke depressive symptoms – depressive symptoms screened according to various instruments.

Study	Instrument cut-off	Time after	Incidence %	Persistence	Factors associated	Recovery	Death
Alemida et al., 2006 [25]	HADS-D 7+	Within 2 weeks 26 weeks				No significant differences in the incidence of depressive symptoms during 24 weeks of Sertraline *vs.* placebo.	
Andersen et al., 1995 [48]	HDRS 13+ 18+	2–3 months 6 months 12 months		Of those who were depressed at 12 months, 79% depressed within 1 month			
Berg et al., 2001 [33]	BDI 10+	2 weeks 2 months 6 months	27	46% of those who were depressed during the first 2 months were also depressed at 12 and/or 18 months.	Male sex associated with more negative change in depressive symptoms during follow-up.		
Berg et al., 2002 [18]		12 months 18 months Major depressed at least once during follow-up	 26				
Fuentes et al., 2008 [28]	HDRS 8+	Within 10 days 3 months	9.9 28.6		Melancholy index upon admission associated with depression at follow-up		
Gillen et al., 2001 [38]	GDS 15+	Average 15 days Average 29 days	13		Prior depression	Depression => Length of stay at rehabilitation unit, efficiently use of rehabilitation service, lower outcome effect.	
House et al., 1990 [10]	BDI	1 month 10+	 32	Of those initially depressed, 43 % continued to be depressed at 6 months.			
House et al., 1991 [9]		13+ 17+ 6 months Depressive symptoms Major depressive disorder 12 months Depressive symptoms Major depressive disorder	20 8 15 9 8 5				

Linee Guida Spread VIII Edizione

La "depressione post-stroke" è un evento frequente a 2 mesi

Un terzo dei sopravvissuti ne soffre.

(sintesi 15.1)

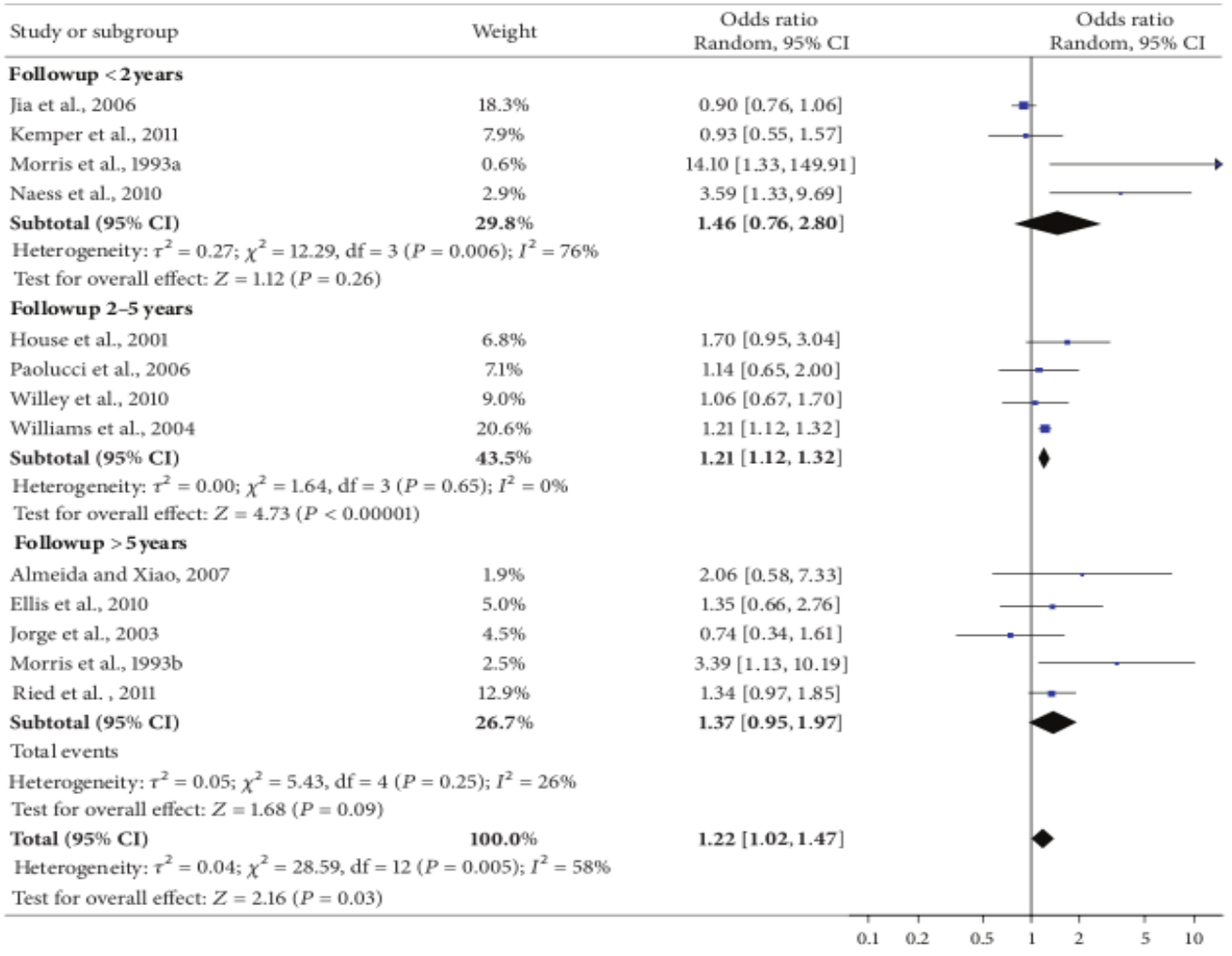
Perchè la depressione post-stroke è importante?

Review Article

Stroke Research and Treatment
Volume 2013, Article ID 862978, 11 pages

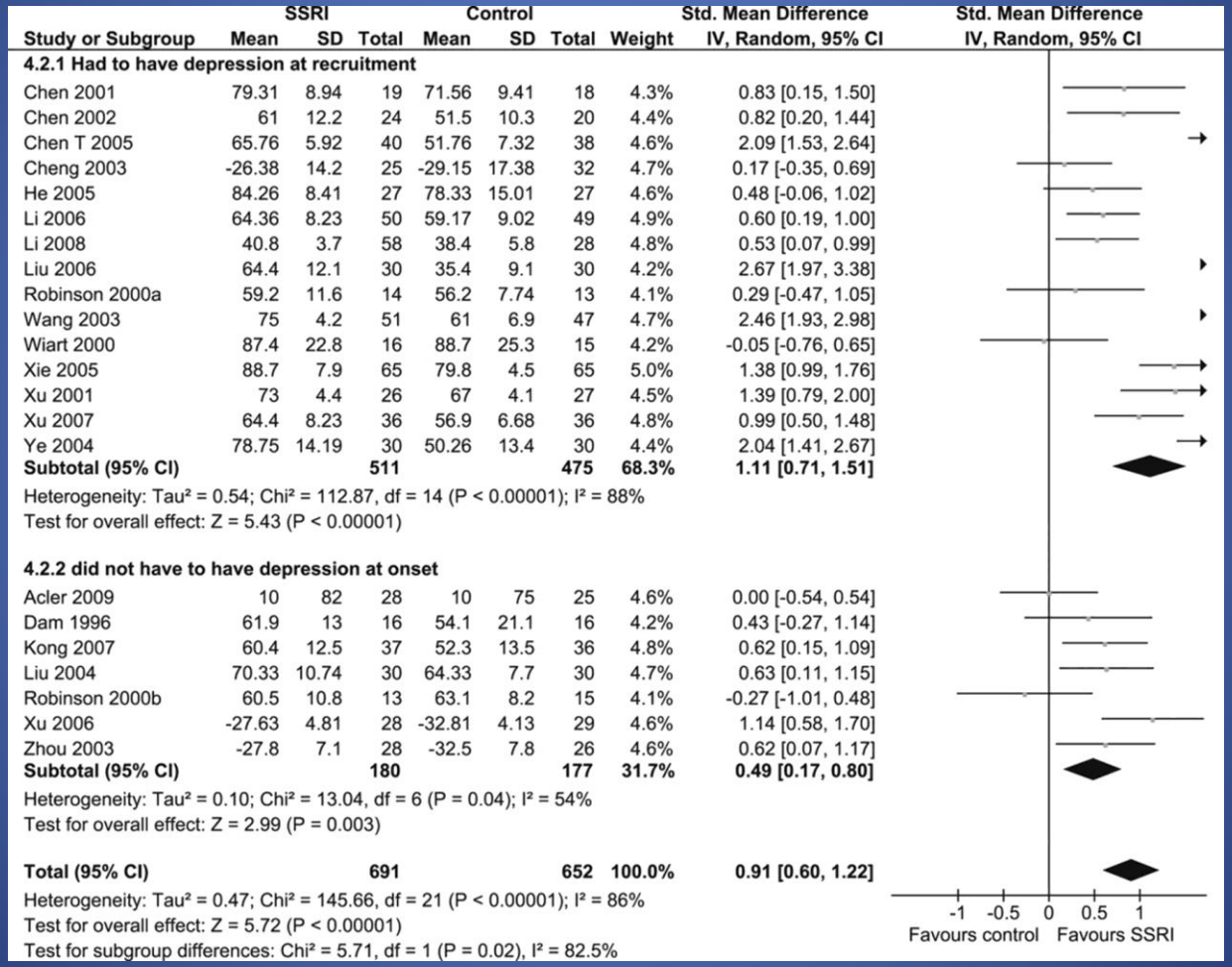
Depression after Stroke and Risk of Mortality: A Systematic Review and Meta-Analysis

Francesco Bartoli,[1] Nicoletta Lillia,[2] Annamaria Lax,[1] Cristina Crocamo,[3] Vittorio Mantero,[2] Giuseppe Carrà,[3,4] Elio Agostoni,[2] and Massimo Clerici[1,3]



Perchè la depressione post-stroke è importante?

Forest plot of disability at the end of treatment, according to whether depression was present at recruitment.



Study or Subgroup	SSRI Mean	SSRI SD	SSRI Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.2.1 Had to have depression at recruitment								
Chen 2001	79.31	8.94	19	71.56	9.41	18	4.3%	0.83 [0.15, 1.50]
Chen 2002	61	12.2	24	51.5	10.3	20	4.4%	0.82 [0.20, 1.44]
Chen T 2005	65.76	5.92	40	51.76	7.32	38	4.6%	2.09 [1.53, 2.64]
Cheng 2003	-26.38	14.2	25	-29.15	17.38	32	4.7%	0.17 [-0.35, 0.69]
He 2005	84.26	8.41	27	78.33	15.01	27	4.6%	0.48 [-0.06, 1.02]
Li 2006	64.36	8.23	50	59.17	9.02	49	4.9%	0.60 [0.19, 1.00]
Li 2008	40.8	3.7	58	38.4	5.8	28	4.8%	0.53 [0.07, 0.99]
Liu 2006	64.4	12.1	30	35.4	9.1	30	4.2%	2.67 [1.97, 3.38]
Robinson 2000a	59.2	11.6	14	56.2	7.74	13	4.1%	0.29 [-0.47, 1.05]
Wang 2003	75	4.2	51	61	6.9	47	4.7%	2.46 [1.93, 2.98]
Wiart 2000	87.4	22.8	16	88.7	25.3	15	4.2%	-0.05 [-0.76, 0.65]
Xie 2005	88.7	7.9	65	79.8	4.5	65	5.0%	1.38 [0.99, 1.76]
Xu 2001	73	4.4	26	67	4.1	27	4.5%	1.39 [0.79, 2.00]
Xu 2007	64.4	8.23	36	56.9	6.68	36	4.8%	0.99 [0.50, 1.48]
Ye 2004	78.75	14.19	30	50.26	13.4	30	4.4%	2.04 [1.41, 2.67]
Subtotal (95% CI)			**511**			**475**	**68.3%**	**1.11 [0.71, 1.51]**
Heterogeneity: Tau² = 0.54; Chi² = 112.87, df = 14 (P < 0.00001); I² = 88%								
Test for overall effect: Z = 5.43 (P < 0.00001)								
4.2.2 did not have to have depression at onset								
Acler 2009	10	82	28	10	75	25	4.6%	0.00 [-0.54, 0.54]
Dam 1996	61.9	13	16	54.1	21.1	16	4.2%	0.43 [-0.27, 1.14]
Kong 2007	60.4	12.5	37	52.3	13.5	36	4.8%	0.62 [0.15, 1.09]
Liu 2004	70.33	10.74	30	64.33	7.7	30	4.7%	0.63 [0.11, 1.15]
Robinson 2000b	60.5	10.8	13	63.1	8.2	15	4.1%	-0.27 [-1.01, 0.48]
Xu 2006	-27.63	4.81	28	-32.81	4.13	29	4.6%	1.14 [0.58, 1.70]
Zhou 2003	-27.8	7.1	28	-32.5	7.8	26	4.6%	0.62 [0.07, 1.17]
Subtotal (95% CI)			**180**			**177**	**31.7%**	**0.49 [0.17, 0.80]**
Heterogeneity: Tau² = 0.10; Chi² = 13.04, df = 6 (P = 0.04); I² = 54%								
Test for overall effect: Z = 2.99 (P = 0.003)								
Total (95% CI)			**691**			**652**	**100.0%**	**0.91 [0.60, 1.22]**
Heterogeneity: Tau² = 0.47; Chi² = 145.66, df = 21 (P < 0.00001); I² = 86%								
Test for overall effect: Z = 5.72 (P < 0.00001)								
Test for subgroup differences: Chi² = 5.71, df = 1 (P = 0.02), I² = 82.5%								

Mead G E et al. Stroke 2013;44:844-850

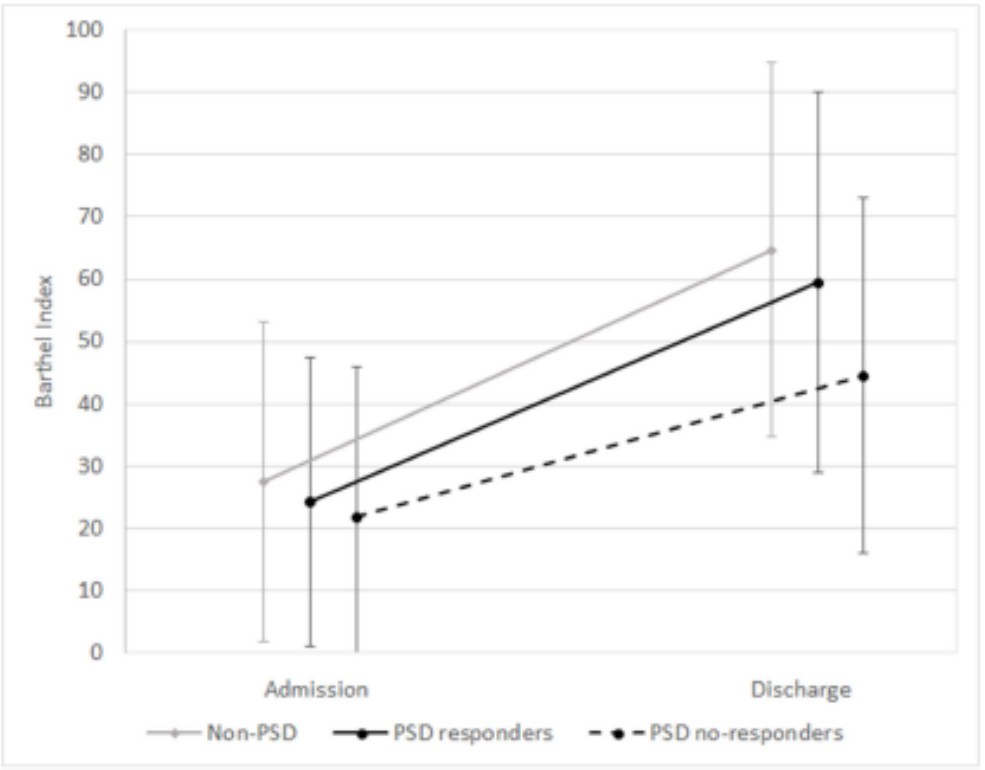
Perchè la depressione post-stroke è importante?

Post-stroke Depression Increases Disability More Than 15% in Ischemic Stroke Survivors: A Case-Control Study

Stefano Paolucci, Marco Iosa, Paola Coiro, Vincenzo Venturiero, Anna Savo, Domenico De Angelis and Giovanni Morone*

frontiers in Neurology

ORIGINAL RESEARCH
published: 27 August 2019
doi: 10.3389/fneur.2019.00926



Linee Guida Spread 2017

- La genesi è multifattoriale
- La probabilità cresce con l'aumento dei fattori di rischio

(sintesi 15.3)

Age, subjective stress, and depression after ischemic stroke

Michael J. McCarthy[1], **Heidi J. Sucharew**[2], **Kathleen Alwell**[3], **Charles J. Moomaw**[3], **Daniel Woo**[3], **Matthew L. Flaherty**[3], **Pooja Khatri**[3], **Simona Ferioli**[3], **Opeolu Adeoye**[4], **Dawn O. Kleindorfer**[3], and **Brett M. Kissela**[3]

[1]College of Allied Health Sciences, School of Social Work, University of Cincinnati, PO Box 210108, Cincinnati, OH 45221, USA

[2]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

[3]Department of Neurology and Rehabilitation Medicine, University of Cincinnati, Cincinnati, OH, USA

[4]Department of Emergency Medicine, University of Cincinnati, Cincinnati, OH, USA

[5]Department of Neurology, University of Cincinnati, Cincinnati, OH, USA

Abstract

The incidence of stroke among younger adults in the United States is increasing. Few studies have investigated the prevalence of depressive symptoms after stroke among different age groups or the extent to which subjective stress at the time of stroke interacts with age to contribute to post-stroke depression. The present study examined whether there exists an age gradient in survivors' level of depressive symptoms and explored the extent to which financial, family, and health-related stress may also impact on depression. Bivariate analyses ($N = 322$) indicated significant differences in depression and stress by age group, as well as differences in age and stress by 3-month depression status. Linear regression analyses indicated that survivors between the ages of 25–54 and 55–64 years old had, on average, significantly higher depressive symptom scores. Those with financial, family, and health-related stress at the time of stroke, irrespective of age, also had significantly higher scores.

Keywords

Depressione, stroke ed età: psicopatologia di un crocevia

Early-life risk factors for late-onset depression

Joel R. Sneed*, Stephanie Kasen and Patricia Cohen

Int J Geriatr Psychiatry 2007; **22**: 663–667.

Table 2. Estimated marginal Means from ANCOVAs comparing No MDD, EOD, and LOD groups of social support, marital conflict, neuroticism, and overall health

Variable	No MDD	EOD	LOD	F
Social support	1.26	1.28	1.29	1.51 (2, 703)
Marital conflict	1.51	1.55	1.62	1.33 (2, 703)
Neuroticism	47.27^{b}	$54.45^{a,c}$	49.44^{b}	18.60** (2, 690)
Overall health	4.24^{c}	$4.086^{\dagger}$	3.80^{a}	6.50* (2, 674)

Depressione, stroke ed età: psicopatologia di un crocevia

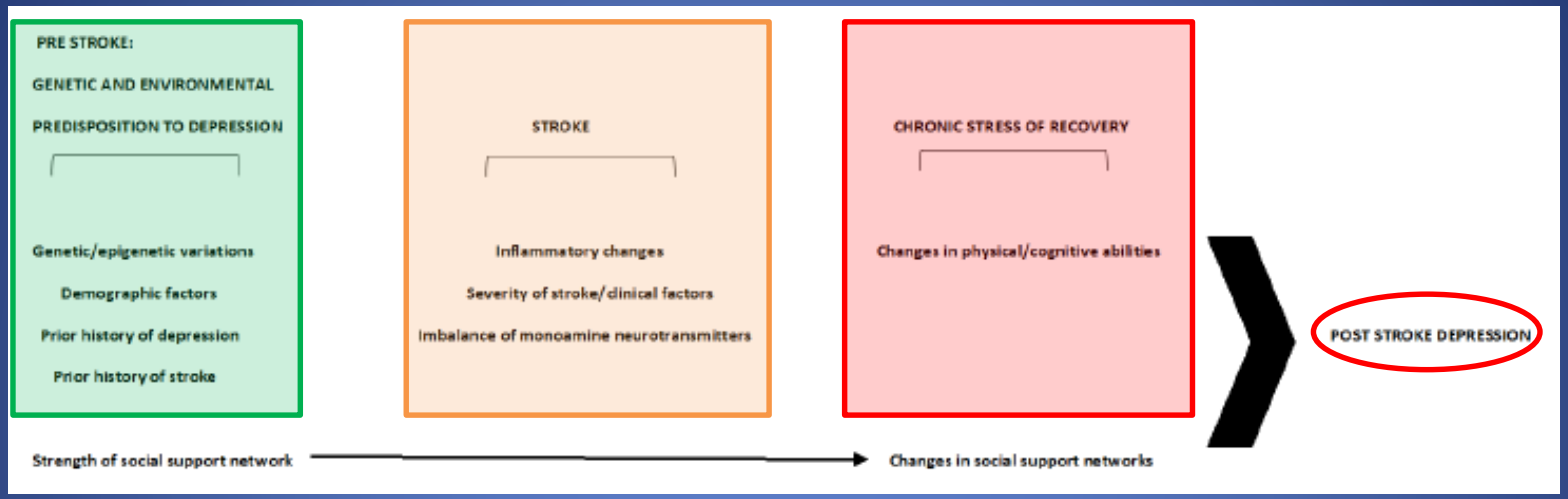
	OR (95% CI)	
	All patients ($n = 251$)	All except severely aphasic patients ($n = 235$)
Female gender	2.01 (1.06–3.82)[b]	2.07 (1.03–4.16)[b]
Age >60 y	0.73 (0.38–1.43)	0.99 (0.95–1.03)
Prior history of depression	2.97 (1.44–6.12)[c]	3.85 (1.67–8.85)[c]
Physical disability (mRS score >2 at discharge)	2.17 (1.05–4.48)[b]	3.08 (1.32–7.16)[c]
Pathologic crying	3.48 (1.22–9.98)[b]	3.42 (0.94–12.48)
Left caudate and/or lenticular nucleus lesion	2.40 (0.97–5.91)	4.04 (1.28–12.71)[b]
Prior history of stroke	2.23 (1.00–4.95)[b]	2.23 (0.98–5.12)
Concomitant psychological and/or physical chronic illness[a]		1.09 (0.43–2.78)
Stressful life event exposure in the month preceding stroke onset[a]		2.68 (1.18–6.07)[b]

[a]Only assessed in the population excluding severely aphasic patients.
[b]$P < 0.05$.
[c]$P < 0.01$.

Depression predictors within six months of ischemic stroke: The DEPRESS Study. *Guiraud et al. International Journal of Stroke. 2016, Vol. 11(5) 519–525*

Depressione, stroke ed età: psicopatologia di un crocevia

A review and conceptual model of dopaminergic contributions to post stroke depression



- Left basal ganglia strokes are highly likely to result in PSD (Robinson, 2003)
  - → *The basal ganglia is a major center for the production of dopamine, a monoamine neurotransmitter.*

- The association between left frontal lobe/left hemisphere strokes and PSD is compelling, although these associations could be mediated by prevalence differences between various stroke locations by sex (Alajbegovic et al., 2014).
  - → *These locations are also rich in monoamine projections.*

While the consensus is that location alone does not predict whether an individual will or will not develop PSD, disruption in monoamine pathways does seem to play some role.

J Neurosci Nurs. 2016 October

Stanfill et al.

Depressione, stroke ed età: psicopatologia di un crocevia

White matter changes in late-life depression: A diffusion tensor imaging study

Journal of Affective Disorders 135 (2011) 216–220

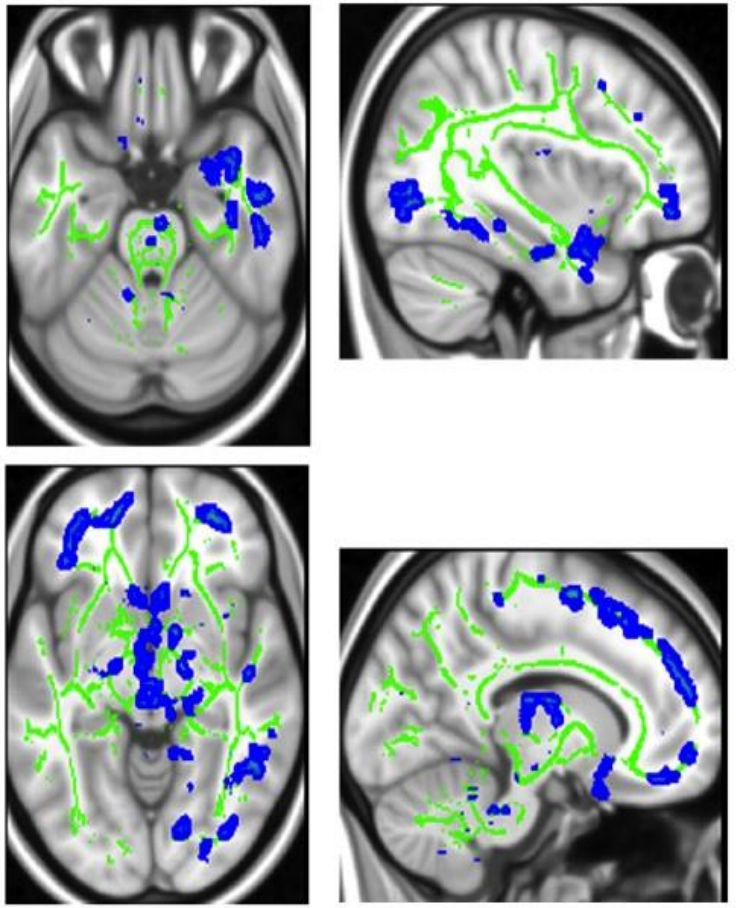
Sean J. Colloby *, Michael J. Firbank, Alan J. Thomas, Akshya Vasudev, Steve W. Parry, John T. O'Brien

Background: Numerous studies have revealed white matter abnormalities in late-life depression (LLD). The objective was to investigate the integrity of white matter tracts in subjects with LLD compared to similar aged healthy individuals using diffusion tensor imaging (DTI).

Methods: Sixty eight subjects (30 healthy individuals, 38 depressed) underwent DTI on a 3 T scanner following clinical and cognitive assessment. An automated tract-based spatial statistics (TBSS) method was used to derive estimates of fractional anisotropy (FA) and mean diffusivity (MD) for each subject. Group effects and correlations with clinical features on DTI parameters were examined.

Results: Compared to controls, uncorrected maps revealed patients with LLD exhibited lower FA in frontal, temporal and midbrain regions relative to older healthy subjects ($p<0.05$). However, using corrected maps no significant differences were observed in LLD patients in FA and MD parameters ($p<0.05$, family-wise error corrected for multiple comparisons). Regression analyses revealed no significant relationship between DTI parameters and current depressive symptoms in LLD ($p>0.05$, uncorrected and corrected).

Conclusions: Findings are suggestive of loss of integrity in white matter fibres within frontal, temporal and midbrain regions, increasing the evidence that implicates disruptions to the limbic–orbitofrontal networks in the pathogenesis of LLD. However, as results did not survive strict control for multiple comparisons, they should be considered tentative and replication in larger cohorts is needed.

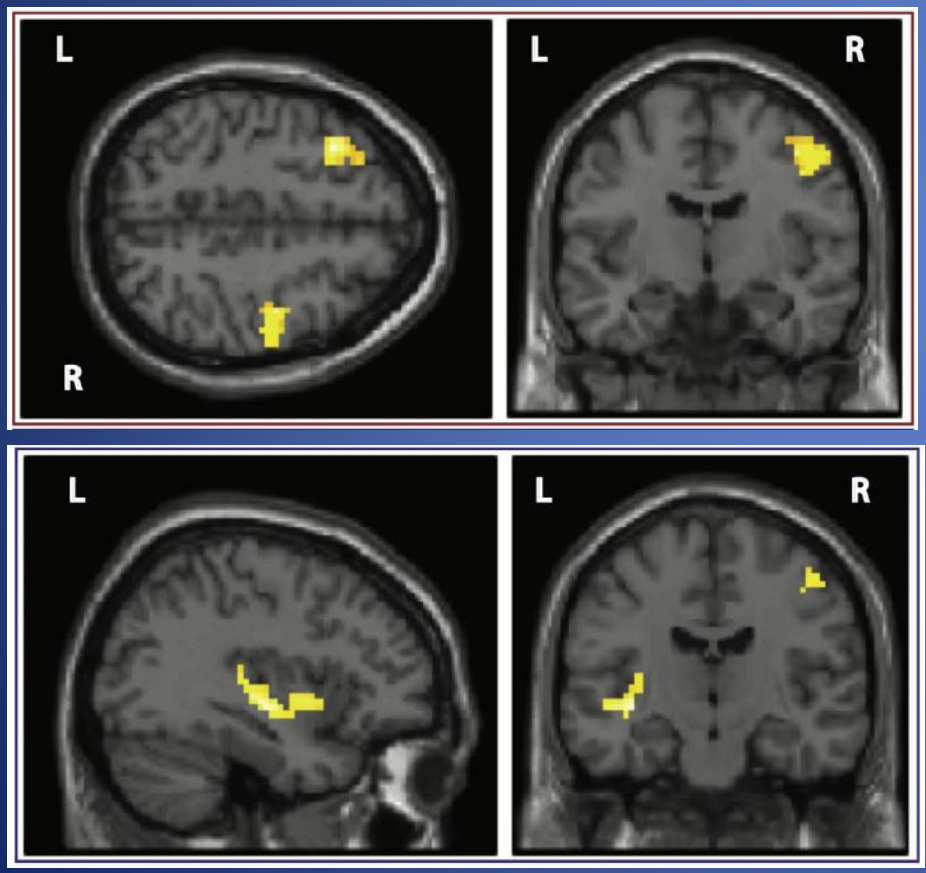


Depressione, stroke ed età: psicopatologia di un crocevia

Fractional amplitude of low-frequency fluctuations (fALFF) in post-stroke depression

N. Egorova et al.

- Lesion overlap maps for the depressed and non-depressed groups failed to reveal any consistent association between the lesion location and depression level.



fALFF in 0.01–0.08 Hz range

A direct comparison between depressed and non-depressed patients showed a significant group difference in the left dorsolateral prefrontal cortex and the right precentral gyrus.

A regression with the PHQ-9 scores in all patients showed a significant cluster in the posterior left insula/superior temporal gyrus.

NeuroImage: Clinical 16 (2017) 116–124

Vascular depression

- Esordio in età avanzata
- Presenza di lesioni sotto-corticali con iperintensità della sostanza bianca alla RM
- Assenza di precedenti personali di depressione
- Maggiore prevalenza di disturbi cognitivi e disfunzione funzioni esecutive
- Scarsa risposta agli antidepressivi

Linee Guida Spread VIII Edizione

- Afasia, Anosognosia, Emiinattenzione, Deterioramento cognitivo rendono la diagnosi difficile.

- Correlazione tra depressione, funzioni esecutive, working memory.

(sintesi 15,4)

Come e quando valutare la depressione post-stroke?

Major Depressive Disorder

Diagnostic Criteria

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Diagnosi differenziale difficile nello stroke

RESEARCH ARTICLE

Clinical Manifestation of Depression after Stroke: Is It Different from Depression in Other Patient Populations?

Janneke M. de Man-van Ginkel[1,2]*, Thóra B. Hafsteinsdóttir[1,2,3,4], Eline Lindeman[1,5], Mirjam I. Geerlings[6], Diederick E. Grobbee[6], Marieke J. Schuurmans[1,2,3]

1 Department of Rehabilitation, Nursing Science and Sports, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands, **2** Nursing Science, program in Clinical Health Sciences University Medical Center Utrecht, Utrecht, The Netherlands, **3** University of Professional Education Utrecht, Department of Healthcare, Utrecht, The Netherlands, **4** Faculty of Nursing, University of Iceland, Reykjavik, Iceland, **5** Centre of Excellence for Rehabilitation Medicine, Rehabilitation Center 'De Hoogstraat', The Netherlands, **6** Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

* J.M.deMan@umcutrecht.nl

Abstract

Background

Despite ample research on depression after stroke, the debate continues regarding whether symptoms such as sleep disturbances, loss of energy, changes in appetite and diminished concentration should be considered to be consequences of stroke or general symptoms of depression. By comparing symptoms in depressed and non-depressed stroke patients with patients in general practice and patients with symptomatic atherosclerotic diseases, we aim to further clarify similarities and distinctions of depression after stroke and depression in other patient populations. Based on this, it is possible to determine if somatic symptoms should be evaluated in stroke patients in diagnosing depression after stroke.

Methods

An observational multicenter study is conducted in three hospitals and seven general practices including 382 stroke patients admitted to hospital with a clinical diagnosis of intracerebral hemorrhage or ischemic infarction, 1160 patients in general practice (PREDICT-NL), and 530 patients with symptomatic atherosclerotic diseases (SMART-Medea).

RESEARCH ARTICLE

Clinical Manifestation of Depression after Stroke: Is It Different from Depression in Other Patient Populations?

Janneke M. de Man-van Ginkel[1,2]*, Thóra B. Hafsteinsdóttir[1,2,3,4], Eline Lindeman[1,5], Mirjam I. Geerlings[6], Diederick E. Grobbee[6], Marieke J. Schuurmans[1,2,3]

Results

The prevalence of major depressive disorder according to DSM-IV criteria was 14.1% (95% CI 11.0%-18.0%) in the stroke cohort, 5.4% (95% CI 3.8%-7.9%) in the symptomatic atherosclerotic diseases cohort and 12.9% (95% CI 11.1%-15.0%) in the general practice cohorts. Comparing depressed patients of the three cohorts demonstrated broadly similar symptom profiles, as well as comparable levels of individual symptom prevalence. However, the stroke patients suffered more severely from these symptoms than patients in the other populations.

Conclusions

The findings suggest that depression after stroke is not a different type of depression. This finding indicates that all depressive symptoms should be evaluated in stroke patients, including somatic symptoms.

Come e quando valutare la depressione post-stroke?

Depression Screening in Stroke

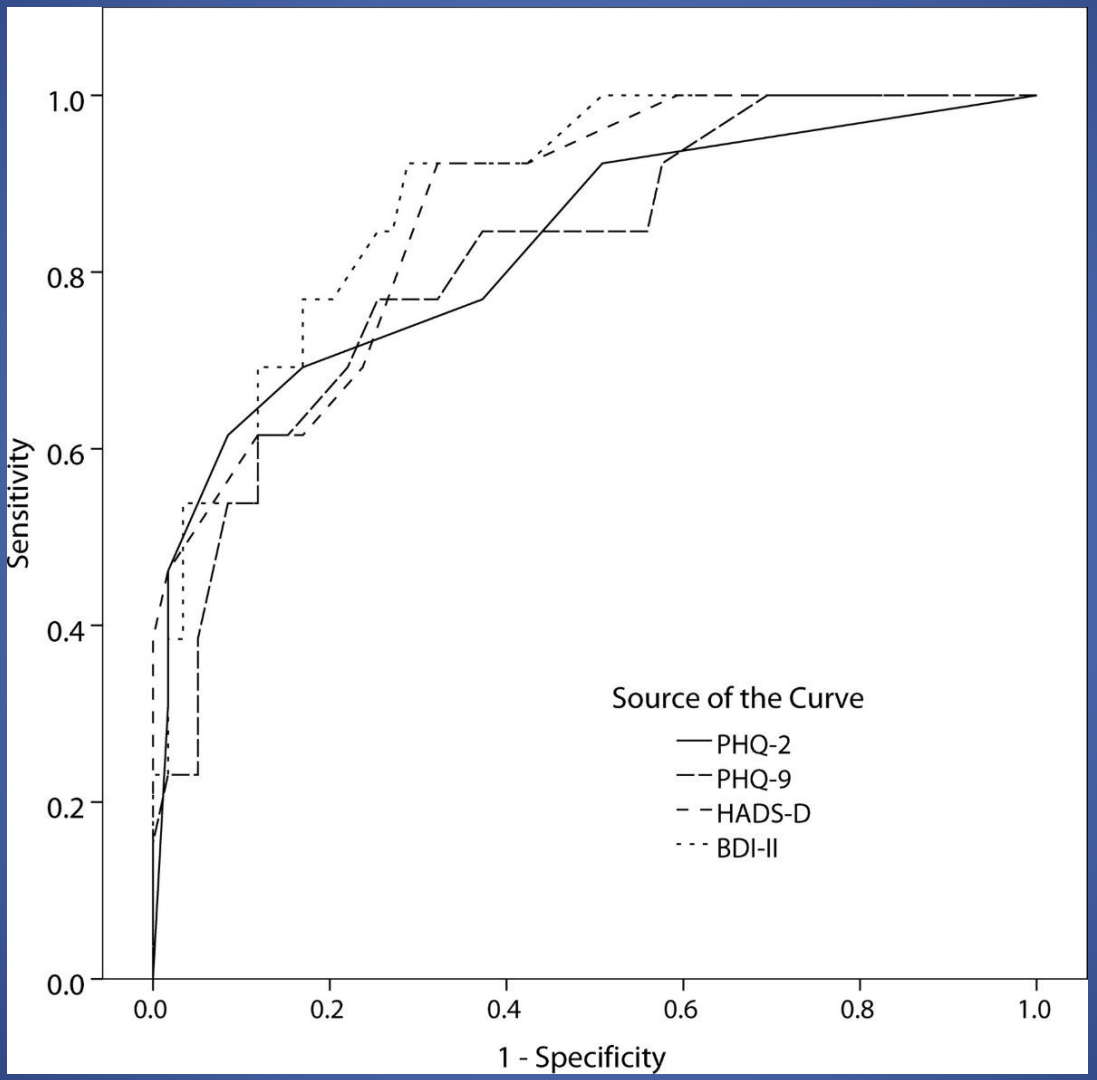
by Alyna Turner, John Hambridge, Jennifer White, Gregory Carter, Kerrie Clover, Louise Nelson, and Maree Hackett

Methods—Seventy-two participants ≥3 weeks poststroke underwent a diagnostic interview for major depressive episode and completed the Patient Health Questionnaire-2 and -9, Hospital Anxiety and Depression Scale, Beck Depression Inventory-II, Distress Thermometer, and Kessler-10. Internal consistency, sensitivity, specificity, likelihood ratios, and posttest probabilities were calculated. Each measure was validated against the gold standard using receiver operating characteristic curves with comparison of the area under the curve for all measures.

Stroke
Volume 43(4):1000-1005
March 26, 2012

American Heart Association
Learn and Live

ROC curves for depression measures versus SCID cases of MDE. Area under the curve (95% CI): PHQ-2=0.83 (0.72–0.91), z=4.76; PHQ-9=0.82 (0.71–0.90), z=4.93; HADS-D=0.87 (0.77–0.94), z=7.27; BDI-II=0.89 (0.79–0.95), z=8.48.



Turner A et al. Stroke 2012;43:1000-1005

Come e quando valutare la depressione post-stroke?

Conclusions—Apart from the Distress Thermometer, selected scales performed adequately in a stroke population with no significant difference between measures. The Patient Health Questionnaire-2 would be the most useful single screen given free availability and the shortest number of items. (***Stroke*. 2012;43:1000-1005.**)

The Patient Health Questionnaire-2 (PHQ-2)

Patient Name _____ Date of Visit _____

Over the past 2 weeks, how often have you been bothered by any of the following problems?	Not At all	Several Days	More Than Half the Days	Nearly Every Day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3

American Heart Association
Learn and Live

Come e quando valutare la depressione post-stroke?

The use of nurses' and carers' observations in the identification of poststroke depression

C. Elizabeth Lightbody, Malcolm Auton, Robert Baldwin, Bernard Gibbon, Samantha Hamer, Michael J. Leathley, Chris Sutton & Caroline L. Watkins

Table 1 Agreement between the nurse and the carer on the individual items of the Signs of Depression Scale (SODS)

SODS item	κ (95% CI)
Sometimes looks sad	0·10 (−0·23 to 0·42)
Cry or seem weepy	0·10 (0·00–0·41)
Agitated, restless or anxious	0·33 (0·01–0·67)
Lethargic/reluctant to mobilize	0·01 (−0·32 to 0·37)
Needs a lot of encouragement	0·31 (−0·07 to 0·63)
Seems withdrawn	−0·14 (−0·36 to 0·21)

Come aumentare la sensibilità nella diagnosi di depressione post-stroke?

Poststroke Depression Biomarkers: A Narrative Review

Oleg A. Levada and Alexandra S. Troyan* Frontiers in Neurology July 2018

(I)

NEUROIMAGING BIOMARKERS OF PSD

- PSD associata a infarti localizzati nella **regione corticale frontale sinistra**, nei **gangli della base sinistra** e nel **tronco cerebrale**. (Murakami T et al, 2013)
- Uno studio con RM funzionale resting-state ha identificato alterazioni della rete affettiva nei soggetti con PSD ed ha rivelato che l'ictus della **parte orbitale sinistra del giro frontale inferiore** era strettamente associato alla gravità della PSD. (Zhang P et al, 2014)
- Lesioni **talamiche** erano significativamente associate alla PSD nella fase acuta dell'ictus. (Omura T et al, 2017)
- Gli infarti **lenticolo-capsulari a sinistra** erano un predittore indipendente dei sintomi depressivi ad un mese dall'insorgenza dell'ictus. (Nishiyama Y et al, 2010)
- La presenza di **microbleeds pontini** nei pazienti con ictus ischemico acuto si associa ad un aumentato significativo del rischio di sviluppare PSD. (Tang WK et al, 2014)
- Grave **iperintensità della sostanza bianca**, indice di microvasculopatia cerebrale, rappresenta un fattore di rischio indipendente di PSD a 3 mesi dall'esordio dell'ictus. (Kim JT et al, 2011)

Come aumentare la sensibilità nella diagnosi di depressione post-stroke?

Poststroke Depression Biomarkers: A Narrative Review

Oleg A. Levada and Alexandra S. Troyan* Frontiers in Neurology July 2018

(II)

MOLECULAR BIOMARKERS OF PSD

- I pazienti con PSD presentano **concentrazioni liquorali di acido 5-idrossiindolacetico** (un metabolita 5-HT), significativamente **più basse** rispetto ai soggetti non depressi con lesioni ischemiche acute e rispetto ai pazienti non depressi senza lesioni ischemiche. (Bryer JB et al, 1992)

- L'espressione del fattore neurotrofico **BDNF** è coinvolta nei meccanismi fisiopatologici della depressione e della PSD. Significativa **diminuzione** delle concentrazioni sieriche di BDNF nel primo periodo dopo l'ictus predispongono allo sviluppo della depressione. (Li Y et al, 2015)

- La **disfunzione immunitaria** svolge un ruolo cruciale nella fisiopatologia della PSD. I meccanismi immunologici possono dare inizio alla morte cellulare legata all'infiammazione nelle aree cerebrali legate all'umore (Pascoe MC et al, 2011). Elevate concentrazioni sieriche di proteina C-reattiva ad alta sensibilità (**Hs-CRP**) nella fase acuta dell'ictus aumentano indipendentemente il rischio di PSD a 6 mesi dall'esordio. (Tang CZ et al, 2016)

Come aumentare la sensibilità nella diagnosi di depressione post-stroke?

Poststroke Depression Biomarkers: A Narrative Review

Oleg A. Levada and Alexandra S. Troyan* Frontiers in Neurology July 2018

(III)

Markers of Hypothalamic-Pituitary-Adrenal Axis (HPA)

- La **disregolazione** persistente dell'**asse ipotalamo-ipofisi-surrene** si verifica nel 40% dei pazienti con ictus. (Mitchell AJ et al, 1997)
- È stata evidenziata un'associazione avversa tra la risposta al risveglio del cortisolo e la gravità della depressione nel gruppo PSD. (Kwon OJ et al, 2015)

Markers of Oxidative Damage

- Correlazione positiva tra i livelli sierici di **malondialdeide** (biomarcatore di stress ossidativo) e gravità della PSD durante il follow-up di 1 mese dopo l'insorgenza dell'ictus. (Liu Z et al, 2017)

Come aumentare la sensibilità nella diagnosi di depressione post-stroke?

Poststroke Depression Biomarkers: A Narrative Review

Oleg A. Levada and Alexandra S. Troyan* Frontiers in Neurology July 2018

(IV)

Metabolites

- Il PSD score (in accordo con la Beck Depression Inventory) a 12 mesi dall'ictus presenta un'associazione positiva con la **glicemia** rilevata al momento del ricovero (Ormstad H et al, 2012).

Genetic Markers

- Diversi studi sono stati dedicati al **genotipo della regione polimorfica** legata al **gene della serotonina** (5-HTTLPR) nei soggetti PSD. La maggior parte degli studi ha dimostrato che il genotipo 5-HTTLPR di **alleli S/S (short allele)** era significativamente più frequente nei pazienti con PSD rispetto ai soggetti con ictus non depressi (Guo WY et al, 2016).

Come aumentare la sensibilità nella diagnosi di depressione post-stroke?

Poststroke Depression Biomarkers: A Narrative Review

Oleg A. Levada and Alexandra S. Troyan*

Frontiers in Neurology July 2018

(V)

NEUROPHYSIOLOGICAL MARKERS

EEG

- I pazienti con PSD e **ictus emisferico sinistro** hanno mostrato un aumento dell'attività **beta2** nelle aree **frontali e centrali**, mentre i pazienti PSD e **ictus emisferico destro** hanno mostrato un aumento dell'attività **theta e alfa** principalmente nelle **regioni occipitale e temporale**.

- Inoltre, per le lesioni dell'**emisfero sinistro**, l'attività **beta2** nelle regioni **parietali centrale e destra** ha presentato un elevato potere discriminativo tra i soggetti non depressi e quelli affetti da PSD, mentre per le lesioni dell'**emisfero destro**, l'attività **theta** era analogamente discriminante nella maggior parte delle regioni, specialmente nelle regioni temporali. (Wang C et al, 2017)

Quali elementi contribuiscono a rendere complessa la diagnosi di depressione del paziente con stroke?

Fattori confondenti

- Apatia
- Fatica
- Dolore
- Delirium

Diagnosi differenziale: apatia

Table 1
Diagnostic criteria for apathy (adapted from Marin (1991)).

A. Lack of motivation relative to the patient's previous level of functioning or the standards of his or her age and culture as indicated either by subjective account or observation by others.

B. Presence, while with lack of motivation, of at least 1 symptom belonging to each of the following three domains:

Diminished goal-directed behavior.

1. Lack of effort.
2. Dependency on others to structure activity.

Diminished goal-directed cognition

3. Lack of interest in learning new things, or in new experiences.
4. Lack of concern about one's personal problems.

Diminished concomitants of goal-directed behavior.

5. Unchanging affect.
6. Lack of emotional responsivity to positive or negative events.

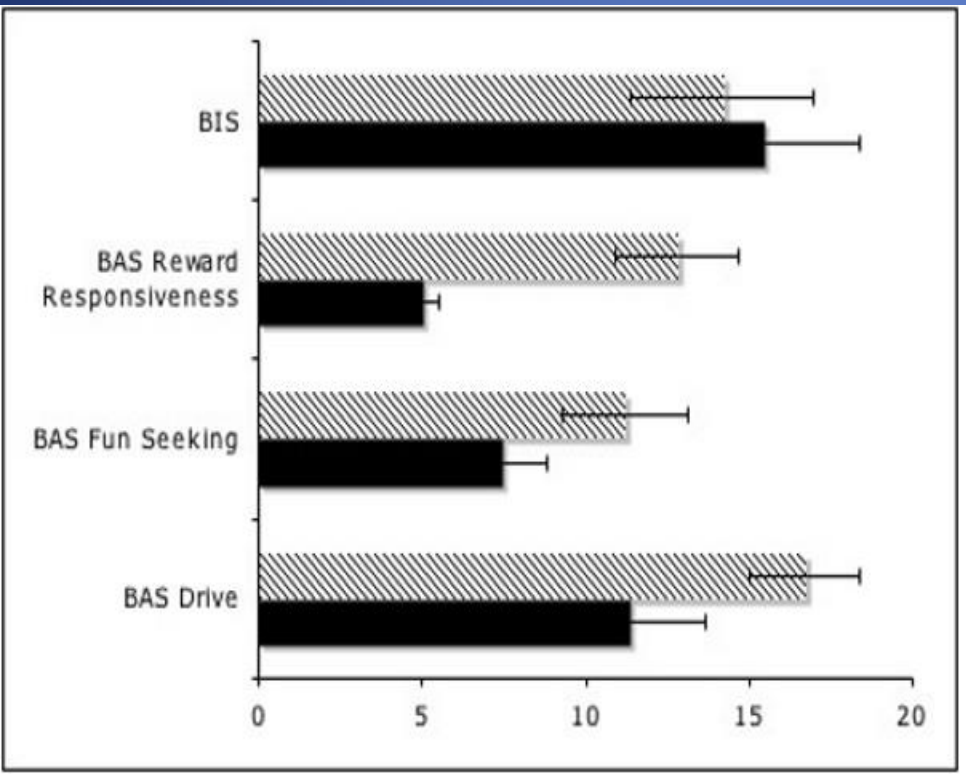
C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to diminished level of consciousness or the direct physiological effects of a substance (e.g., a drug of abuse, a medication).

Diagnosi differenziale: apatia

- Le abilità di decision making sottendono una sindrome comportamentale di rilevanza neuropsichiatrica, l'apatia isolata

- Nei soggetti non depressi, l'apatia è associata a una ridotta sensibilità al reward (barre nere nel grafico a sx) *(Pardini et al., 2015)*



Diagnosi differenziale: apatia

Poststroke Apathy

Stroke March 2013

Jan Willem van Dalen, MSc; Eric P. Moll van Charante, MD, PhD; Paul J. Nederkoorn, MD, PhD; Willem A. van Gool, MD, PhD; Edo Richard, MD, PhD

Table 8. Trials Regarding Treatment of Poststroke Apathy

Author	Year	Design	Main Outcome	Setting	Diagnosis	NI	ND	Intervention	Dose	Follow-up, wk	Outcome
Robinson[43]	2009	RCT	Depression	Outpatient PSD	Modified AS	26	69	Nefiracetam	600 mg	12	ITT ANOVA: 900 mg vs placebo: 4 point decrease in AS score (P=0·01), ARR 0.18 (95 CI, 0.02–0.34), more frequent remissions
						22			900 mg		
						22	…	Placebo	…		
Whyte[44]	2008	OT + RC	CI	Inpatient PSCI	AES	13	41	Donepezil	5–10 mg	12	PP ANOVA: Donepezil and decrease of apathy both independently associated with an increase in FIM-gain over time
						13		Galantamine	4–12 mg		
				PS non-CI	…	98	…	Control: none	…	20	

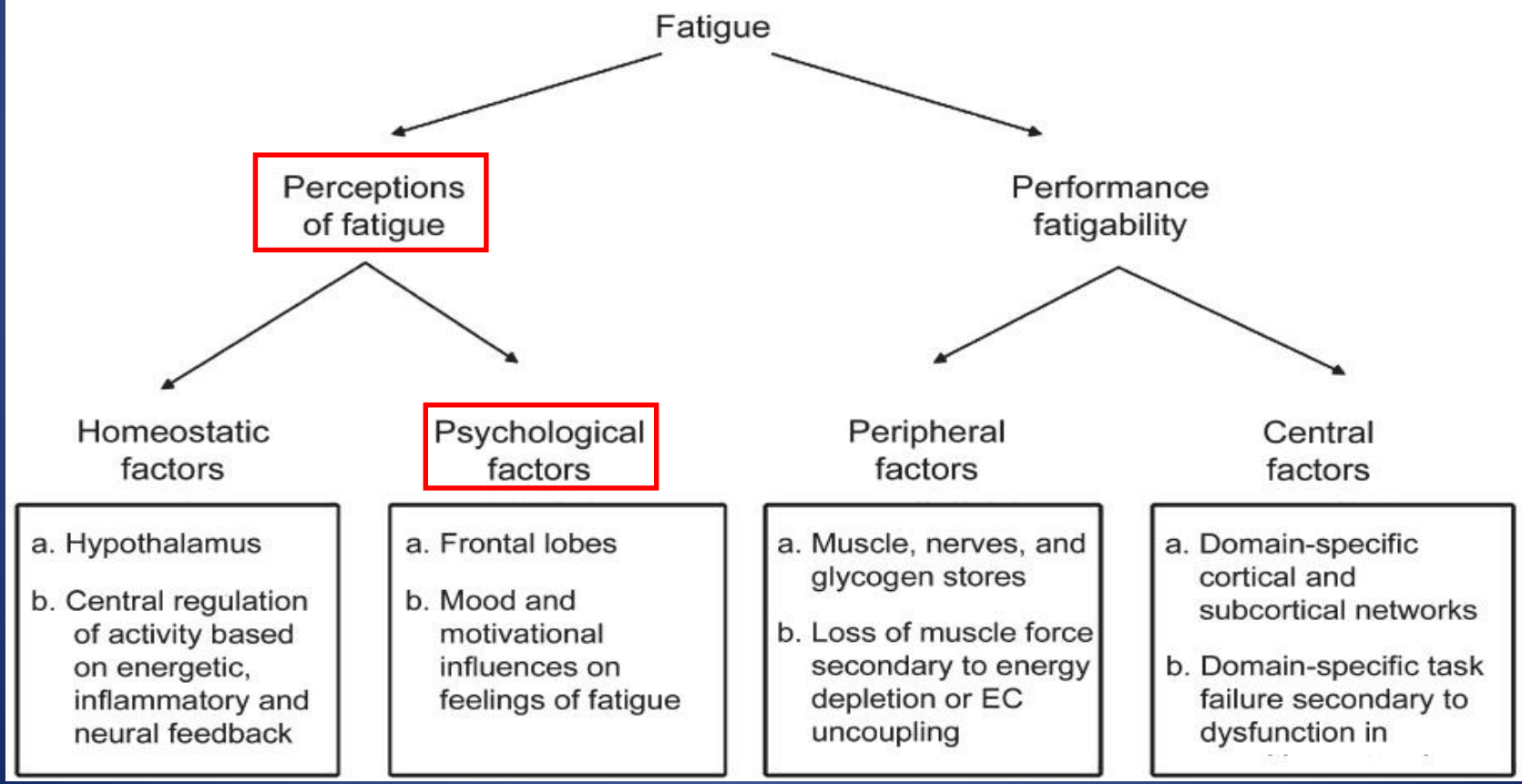
Diagnosi differenziale: fatica

Fatigue and fatigability in neurologic illnesses

Proposal for a unified taxonomy

Neurology 80 January 22, 2013

Benzi M. Kluger, MD, MS
Lauren B. Krupp, MD
Roger M. Enoka, PhD



Diagnosi differenziale: fatica

Fatigue Severity Scale (FSS, English version)*

	strongly disagree 1	2	3	4	5	6	*strongly agree* 7
1. My motivation is lower when I am fatigued.	0	0	0	0	0	0	0
2. Exercise brings on my fatigue.	0	0	0	0	0	0	0
3. I am easily fatigued.	0	0	0	0	0	0	0
4. Fatigue interferes with my physical functioning.	0	0	0	0	0	0	0
5. Fatigue causes frequent problems for me.	0	0	0	0	0	0	0
6. My fatigue prevents sustained physical functioning.	0	0	0	0	0	0	0
7. Fatigue interferes with carrying out certain duties and responsibilities.	0	0	0	0	0	0	0
8. Fatigue is among my three most disabling symptoms.	0	0	0	0	0	0	0
9. Fatigue interferes with my work, family, or social life.	0	0	0	0	0	0	0

**Patients are instructed to choose a number from 1 to 7 that indicates their degree of agreement with each statement where 1 indicates strongly disagree and 7, strongly agree.* [Krupp et al, Arch Neurol 1989]

Diagnosi differenziale: fatica

Author	Mean age (year)/% male	Tools used	Prevalence	Control subjects	Related factors
Leegaard (1983)	51/66	Simple questions	75%	Patients with myocardial infarction	
Ingeles (1999)	67/63	FIS	68%	Healthy persons	
Van der Werf (2001)	62/72	Checklist of Individual Strength (≥40)	50% (severe fatigue)	Healthy persons	Functional disability, depression
Glader (2002)	72/54	Simple questionnaire	10% (always tired) 29% (often tired)	None	Age, poor QOL, high mortality
Naess (2005)	48/57	FSS (≥4)	51%	Healthy persons	Depression, functional disability, basilar artery territory stroke
Choi-Kwon (2005)	60/73	VAS, FSS, FIS	57%	None	Prestroke fatigue, depression functional disability
Schepers (2006)	56/59	FSS (>4)	52%/64%/70%	None	Age, depression
Jaracz (2007)	55/66	FIS	34% (above theoretical median)	None	Emotion-oriented style of coping
Van de Port (2007)	57/60	FSS	68%/74%/58%	None	
Christensen (2008)	65/56	MFI-20	59%/44%/38%/40%	Healthy persons or those with diseases other than stroke	
Winward (2009)	74/58	Chalder fatigue scale	56%	TIA patients	Initial stroke severity
Park (2009)	60/65	FSS (≥4)	30%	None	Depression, sleep disturbance
Tang (2010)	64/65	FSS (≥4)	23%	None	Female, depression, basal ganglia lesion
Lerdal (2010)	68/59	FSS (≥4)	57%	None	Prestroke fatigue, depression, functional disability

(Choi-Kwon et al., 2015)

Diagnosi differenziale: il dolore

- Rilevare la presenza di dolore in soggetti con difficoltà comunicative (afasia), con deterioramento cognitivo o delirium è difficile

- La presenza di dolore può pesantemente interferire con la capacità di collaborare al piano riabilitativo, con il tono timico, con la prognosi finale

Scale di rilevazione del dolore

- Esistono molte scale validate che permettono la rilevazione «comportamentale» del dolore

- La applicazione sistematica può integrare le scale abitualmente utilizzate per la rilevazione del dolore nei soggetti cognitivamente competenti e permettere una rilevazione e trattamento precoci

Numeric Rating Scale

Scala Panaid
(Pain Assessment in Advanced Dementia)

Scala per la misurazione del **dolore** nei pazienti con **demenza** o **inabili** a comunicare

Indicatori	**0**	**1**	**2**
Respirazione	Normale	Respiro affannoso	Respiro rumoroso ed affannoso, alternanza di periodi di apnea e polipnea
Vocalizzazione	Nessun Problema	Pianti occasionali o brontoli	Ripetuti urli e lamenti
Espressioni del volto	Sorridente o inespressivo	Triste e/o ciglia aggrottate	Smorfie
Linguaggio del corpo	Rilassato	Teso	Rigido con i pugni chiusi o che tenta di colpire
Consolazione	Nessun bisogno di essere consolato	Confuso e che cerca rassicurazione	Incapacità di distrazione e/ o consolazione
0-1 Dolore Assente	2-4 Dolore Lieve	5-7 Dolore Moderato	8-10 Dolore Severo

Monacelli F. J Alzheimers Dis. 2017 56(2):519-527

Definizione di delirium (DSM-V)

Per ***delirium*** si intende una sindrome caratterizzata da:

- A: Disturbo dell'attenzione (i.e. ridotta capacità a dirigere, focalizzare, sostenere e shiftare l'attenzione) e consapevolezza (ridotto orientamento di sé nell'ambiente)
- B: Il disturbo si sviluppa in un periodo di tempo relativamente breve (da poche ore a pochi giorni), rappresenta un cambiamento dai livelli di attenzione e consapevolezza di base, e tende a fluttuare in gravità nel corso della giornata
- C: Presenza di un altro deficit cognitivo (es, memoria, disorientamento, linguaggio, abilità visuospaziali, o dispercezioni)
- D: I disturbi descritti nei criteri A e C non devono essere spiegabili esclusivamente sulla base di un preesistente disturbo neurocognitivo (stazionario o in evoluzione) e non devono verificarsi in un contesto di grave riduzione dei livelli di vigilanza (es. coma)
- E: vi è evidenza dalla storia clinica, dagli esami laboratoristici o dall'esame fisico che i disturbi sono una diretta/fisiopatologica conseguenza di una condizione medica generale, abuso o sospensione di sostanze, esposizione a tossine o a eziologie multiple
- La diagnosi viene posta se sono presenti tutti i 5 criteri (A-E)

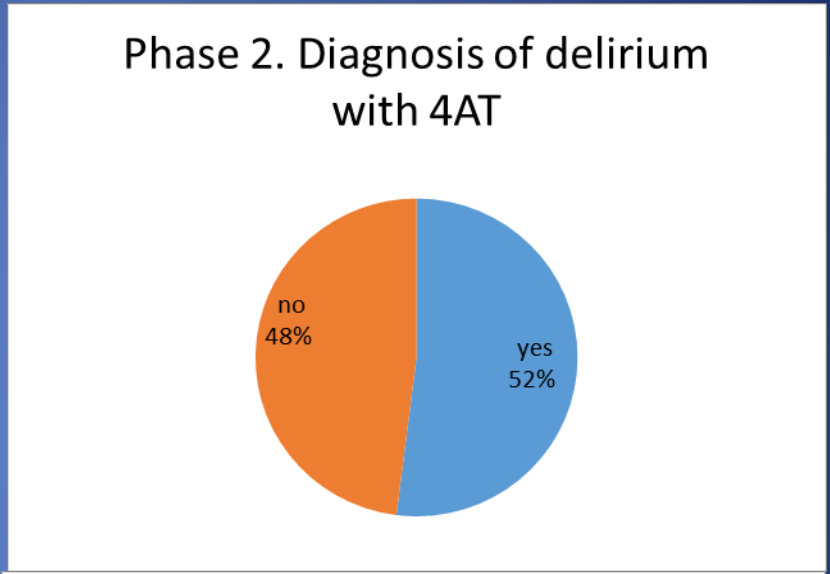
American Psychiatric Association. DSM V. May 18.2014 pag. 591-605

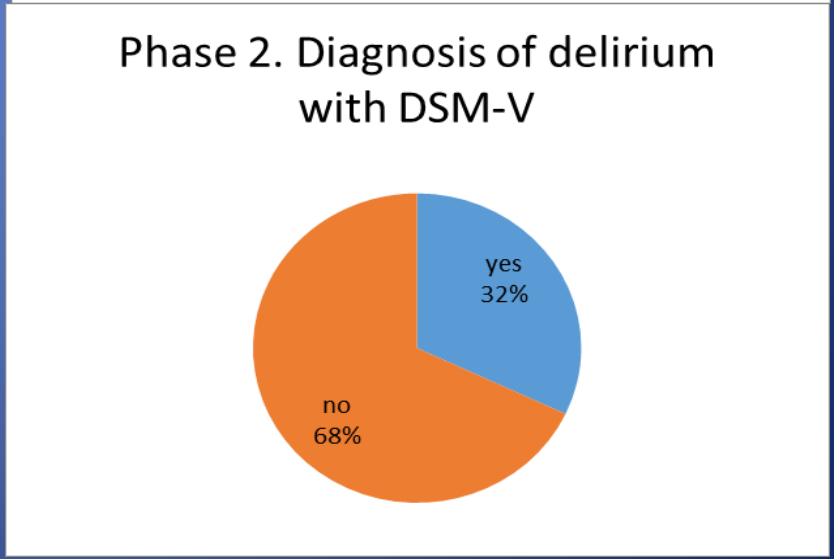
Studi recenti

- In un recente studio, è stata valutata l'incidenza del delirium post stroke rilevando una incidenza di delirium del 11,8% utilizzando la scala CAM (Confusion Assessment Method)
- Il questo studio il delirium è stato valutato durante la prima settimana di degenza in Stroke Unit

Studio Ospedale San Martino

- Valutati 100 pazienti consecutivi con diagnosi di ictus (ischemico o emorragico)
- Delirium post stroke valutato con scala 4AT all'ingresso in reparto e dopo 7 giorni di ricovero
- Esclusi pazienti afasici e già dementi
- Riscontro di delirium post stroke nel 32% dei casi applicando i criteri del DSM-V (dopo training adeguato) e nel 52% dei casi con scala 4AT





Delirium in the acute phase after stroke. Comparison between methods of detection

Infante MT, Pardini M, C. Serrati et al.. Neurological Sciences.

La depressione post-stroke e demenza

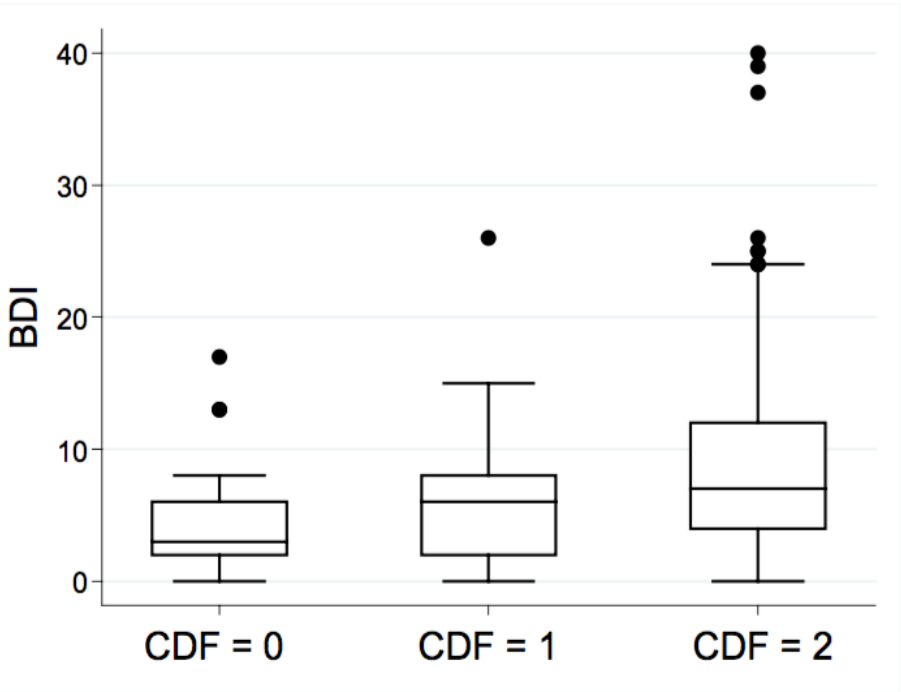
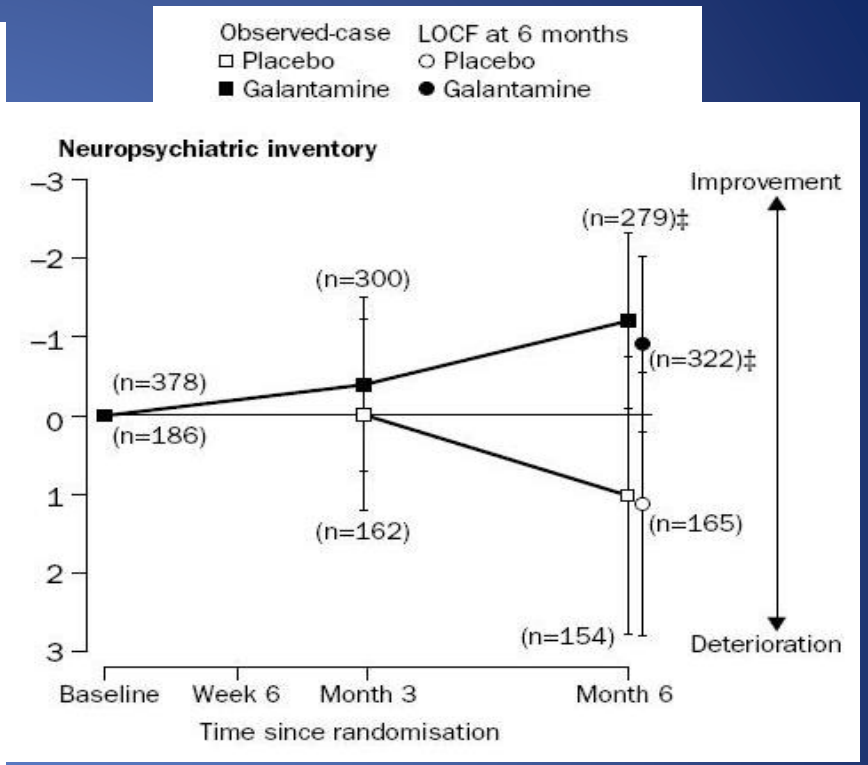
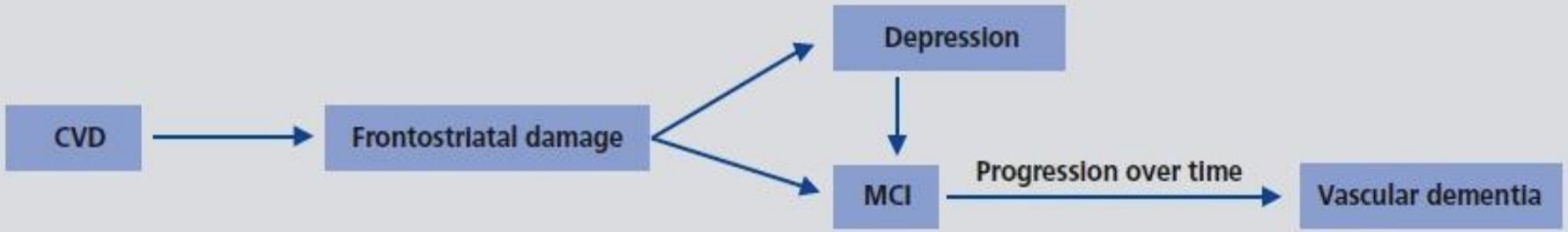


Fig. 1 Boxplot of Beck Depression Inventory (BDI) for levels of cognitive dysfunctioning (CDF).

(Hommel et al., 2015)



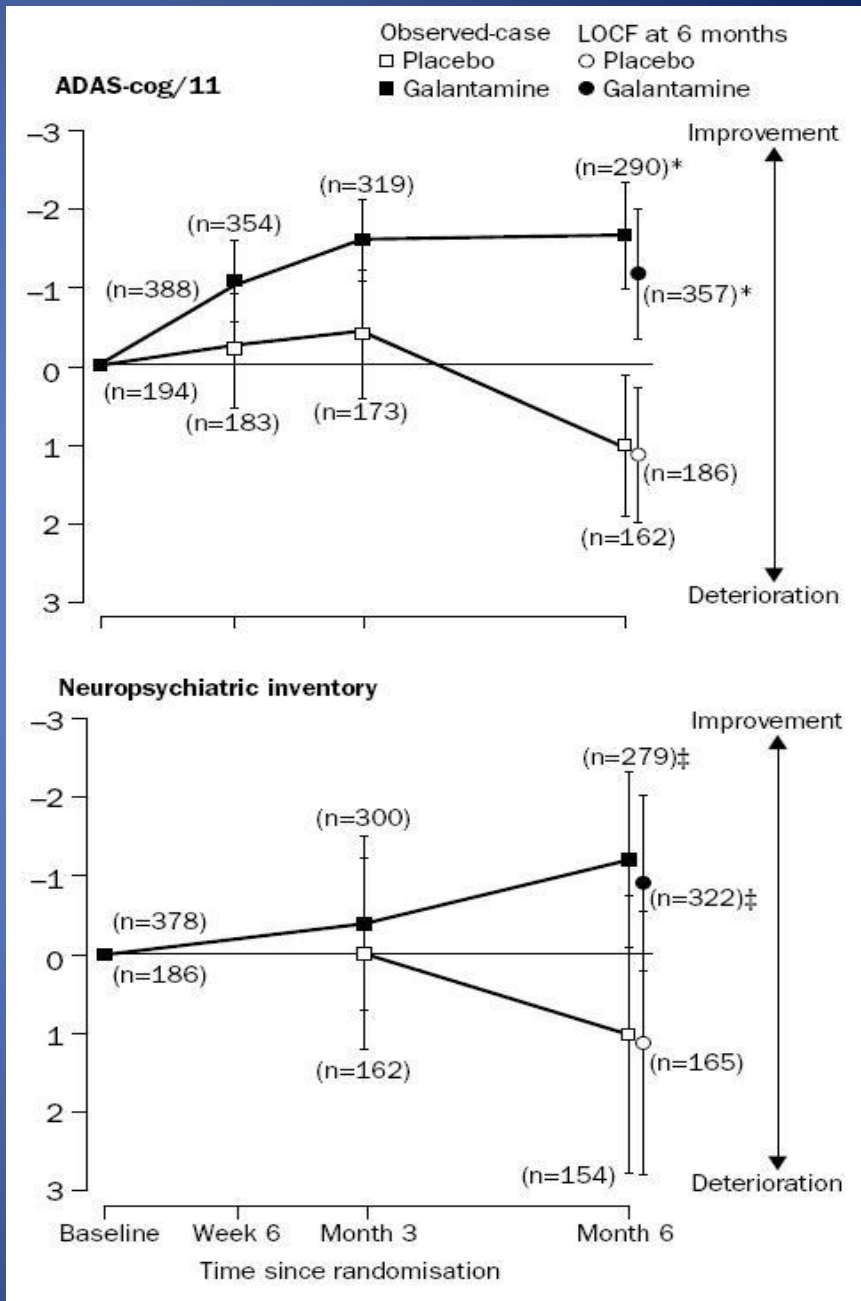
(Erkinjuntti et al, 2002)



(Butters et al., 2008)

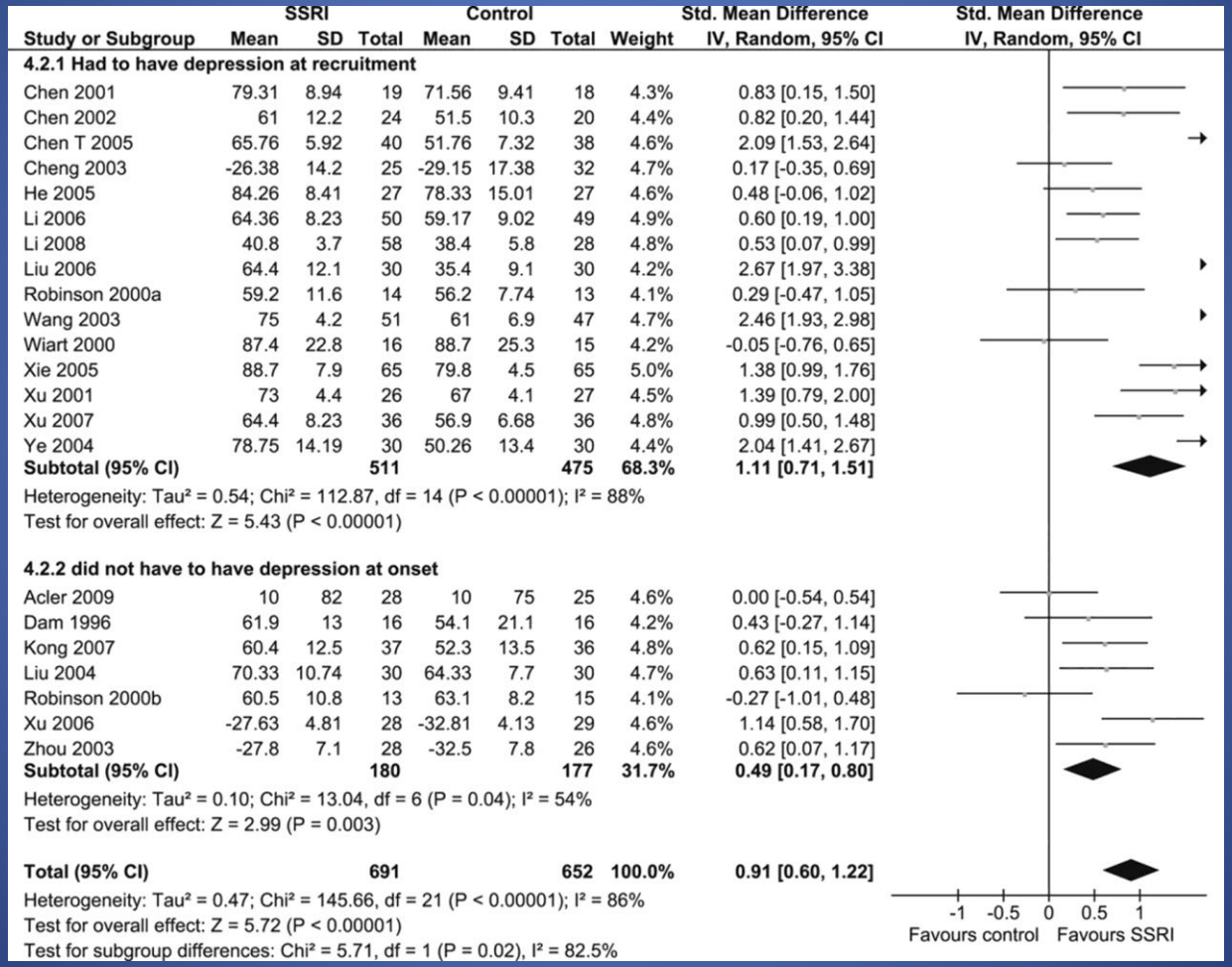
Trattare e prevenire la depressione post-stroke

- 592 soggetti affetti da demenza mista o demenza vascolare randomizzati tra galantamina 24 mg/die (n=396) o placebo (n=196). Studio randomizzato, controllato, multicentrico, della durata di sei mesi *(Erkinjuntti et al, 2002)*
- Effetto significativo sulle performance cognitive, **sintomi comportamentali tra cui la depressione** e qualità della vita
- Terapia ben tollerata
- Nell'analisi post-hoc, gli effetti sono rimasti significativi anche considerando separatamente i soggetti affetti da demenza mista o da demenza vascolare



Trattare e prevenire la depressione post-stroke

Forest plot of disability at the end of treatment, according to whether depression was present at recruitment.



Study or Subgroup	SSRI Mean	SSRI SD	SSRI Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.2.1 Had to have depression at recruitment								
Chen 2001	79.31	8.94	19	71.56	9.41	18	4.3%	0.83 [0.15, 1.50]
Chen 2002	61	12.2	24	51.5	10.3	20	4.4%	0.82 [0.20, 1.44]
Chen T 2005	65.76	5.92	40	51.76	7.32	38	4.6%	2.09 [1.53, 2.64]
Cheng 2003	-26.38	14.2	25	-29.15	17.38	32	4.7%	0.17 [-0.35, 0.69]
He 2005	84.26	8.41	27	78.33	15.01	27	4.6%	0.48 [-0.06, 1.02]
Li 2006	64.36	8.23	50	59.17	9.02	49	4.9%	0.60 [0.19, 1.00]
Li 2008	40.8	3.7	58	38.4	5.8	28	4.8%	0.53 [0.07, 0.99]
Liu 2006	64.4	12.1	30	35.4	9.1	30	4.2%	2.67 [1.97, 3.38]
Robinson 2000a	59.2	11.6	14	56.2	7.74	13	4.1%	0.29 [-0.47, 1.05]
Wang 2003	75	4.2	51	61	6.9	47	4.7%	2.46 [1.93, 2.98]
Wiart 2000	87.4	22.8	16	88.7	25.3	15	4.2%	-0.05 [-0.76, 0.65]
Xie 2005	88.7	7.9	65	79.8	4.5	65	5.0%	1.38 [0.99, 1.76]
Xu 2001	73	4.4	26	67	4.1	27	4.5%	1.39 [0.79, 2.00]
Xu 2007	64.4	8.23	36	56.9	6.68	36	4.8%	0.99 [0.50, 1.48]
Ye 2004	78.75	14.19	30	50.26	13.4	30	4.4%	2.04 [1.41, 2.67]
Subtotal (95% CI)			**511**			**475**	**68.3%**	**1.11 [0.71, 1.51]**
Heterogeneity: Tau² = 0.54; Chi² = 112.87, df = 14 (P < 0.00001); I² = 88%								
Test for overall effect: Z = 5.43 (P < 0.00001)								
4.2.2 did not have to have depression at onset								
Acler 2009	10	82	28	10	75	25	4.6%	0.00 [-0.54, 0.54]
Dam 1996	61.9	13	16	54.1	21.1	16	4.2%	0.43 [-0.27, 1.14]
Kong 2007	60.4	12.5	37	52.3	13.5	36	4.8%	0.62 [0.15, 1.09]
Liu 2004	70.33	10.74	30	64.33	7.7	30	4.7%	0.63 [0.11, 1.15]
Robinson 2000b	60.5	10.8	13	63.1	8.2	15	4.1%	-0.27 [-1.01, 0.48]
Xu 2006	-27.63	4.81	28	-32.81	4.13	29	4.6%	1.14 [0.58, 1.70]
Zhou 2003	-27.8	7.1	28	-32.5	7.8	26	4.6%	0.62 [0.07, 1.17]
Subtotal (95% CI)			**180**			**177**	**31.7%**	**0.49 [0.17, 0.80]**
Heterogeneity: Tau² = 0.10; Chi² = 13.04, df = 6 (P = 0.04); I² = 54%								
Test for overall effect: Z = 2.99 (P = 0.003)								
Total (95% CI)			**691**			**652**	**100.0%**	**0.91 [0.60, 1.22]**
Heterogeneity: Tau² = 0.47; Chi² = 145.66, df = 21 (P < 0.00001); I² = 86%								
Test for overall effect: Z = 5.72 (P < 0.00001)								
Test for subgroup differences: Chi² = 5.71, df = 1 (P = 0.02), I² = 82.5%								

Mead G E et al. Stroke 2013;44:844-850

Trattare e prevenire la depressione post-stroke

Depression and Antidepressant Use After Stroke and Transient Ischemic Attack

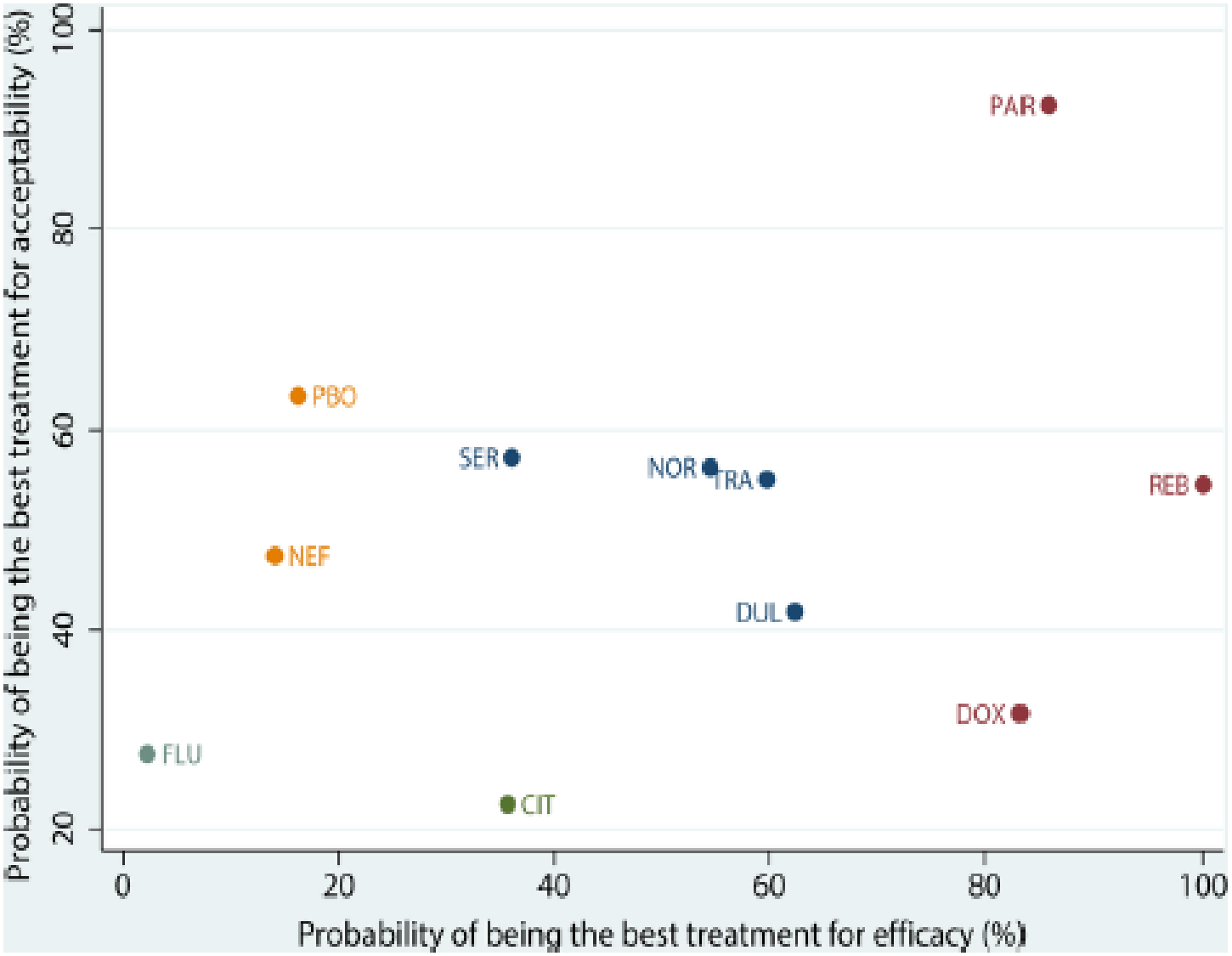
El Husseini et al

	Stroke (N=1450; Proportional Frequency; 95% CI)	TIA (N=397; Proportional Frequency; 95% CI)	Univariate OR, 95% CI	*P* Value	Multivariate OR,* 95% CI	*P* Value
PHQ-8 ≥10 at 3 mo	260	57	1.3	0.09	1.05	0.79
	17.9% (16.0–20.0)	14.4% (11.2–18.2)	(0.9–1.8)		(0.75–1.46)	
Antidepressant use at 3 mo	201	61	0.89	0.45	N/A	N/A
	13.9% (12.2–15.7)	15.4% (12.1–19.3)	(0.65–1.21)			
PHQ-8 ≥10 and/or use of antidepressant at 3 mo	406	104	1.09	0.47	0.94	0.67
	28.0% (25.8–30.4)	26.2% (22.1–30.7)	(0.85–1.41)		(0.72–1.23)	
PHQ-8 ≥10 at 12 mo	238	51	1.33	0.08	1.09	0.63
	16.4% (14.6–18.4)	12.8% (9.9–16.5)	(0.96–1.84)		(0.77–1.55)	
Antidepressant use at 12 mo	232	58	1.11	0.50	N/A	N/A
	16.0% (14.2–18.0)	14.6% (11.5–18.4)	(0.81–1.52)			
PHQ-8 ≥10 and/or use of antidepressant at 12 mo	404	96	1.21	0.14	1.08	0.58
	27.9% (25.6–30.2)	24.2% (20.2–28.6)	(0.94–1.56)		(0.82–1.42)	

1450 patients with ischemic stroke → **more than two thirds** of those with persistent depression (**67.9%**) were **not appropriately treated** with Ads.

Stroke. 2012;43:1609-1616

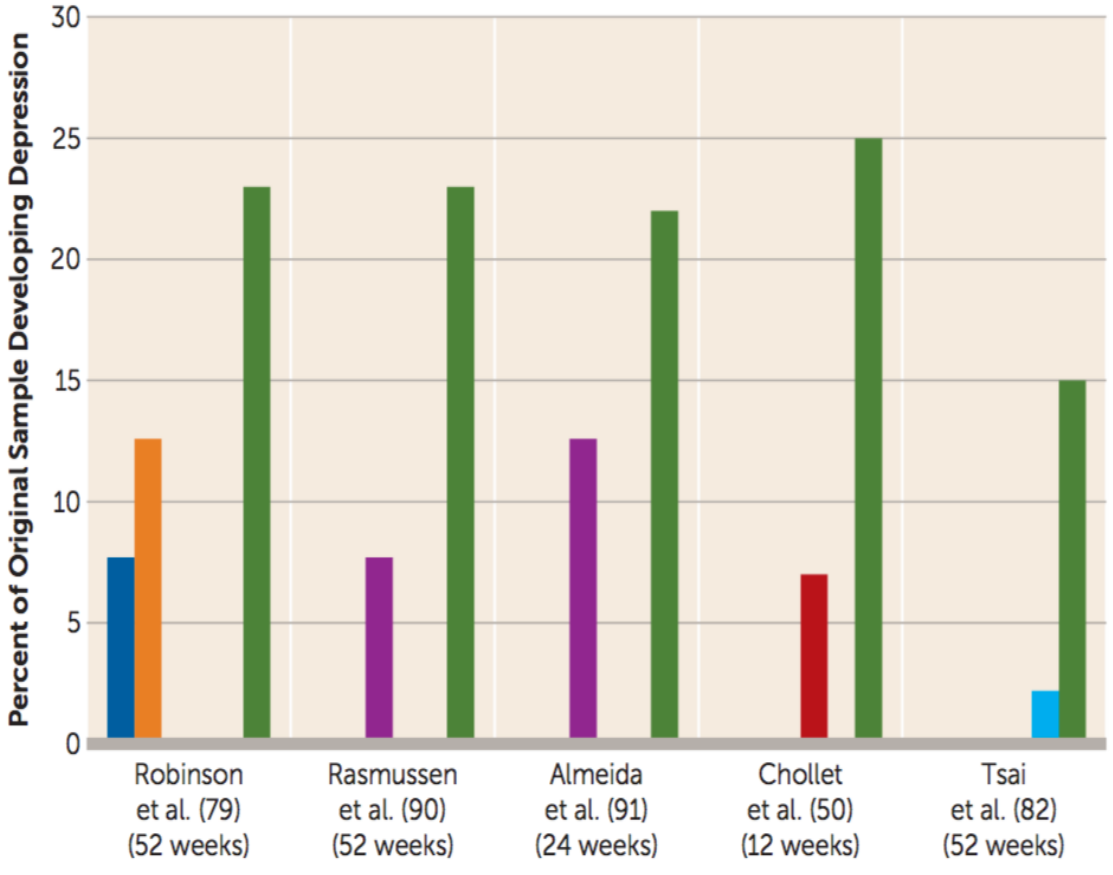
Stroke


Probability of being the best treatment for acceptability (%)
100
80
60
40
20
PAR
PBO
SER
NOR
TRA
REB
NEF
DUL
DOX
FLU
CIT
0
20
40
60
80
100
Probability of being the best treatment for efficacy (%)

June et al

Trattare e prevenire la depressione post-stroke

FIGURE 3. Randomized Controlled Trials for Evaluation of Preventative Treatments for Poststroke Depression[a]



	Robinson et al. (79) (52 weeks)	Rasmussen et al. (90) (52 weeks)	Almeida et al. (91) (24 weeks)	Chollet et al. (50) (12 weeks)	Tsai et al. (82) (52 weeks)
Completers	134	67	56	88	56
Randomized	176	137	92	113	111

(Robinson et al., 2016)

Quali sono le caratteristiche ideali di un antidepressivo da utilizzare nella depressione post-stroke

L’antidepressivo ideale dovrebbe soddisfare questi cinque punti:

1 efficacia terapeutica documentata

2 tollerabilità e sicurezza

3 assenza di interazioni farmacologiche

4 maneggevolezza d’impiego

5 sicurezza in overdose

Trattare e prevenire la depressione post-stroke

Cognitive behavioral therapy for post-stroke depression: A meta-analysis

S.-B. Wang et al.

CBT for post-stroke depression: effects on anxiety, neurological functional deficits, activities of daily living and cognitive function.

Variables		Endpoint symptomatic improvement				
		Subjects (arms)	SMDs or MDs[a] (95%CI)	I^2 (%)	P-value of overall effect	P-value of subgroup difference
Anxiety	Overall	403 (5)	−0.49 (−0.79, −0.19)	55	0.001	0.64
	No antidepressant	88 (1)	−0.49 (−0.92, −0.07)	NA	0.02	
	Use of antidepressants	254 (3)	−0.58 (−1.09, −0.06)	74	0.03	
	Some patients received antidepressants	61 (1)	−0.25 (−1.09, −0.06)	NA	0.34	
Neurological function deficit	Overall	382 (5)	−1.22 (−1.80, −0.64)	84	<0.001	0.07
	No antidepressant	160 (1)	−0.67 (−0.99, −0.35)	NA	<0.001	
	Use of antidepressants	222 (4)	−1.38 (−2.07, −0.69)	81	<0.001	
Activities of daily living	Overall	753 (7)	0.78 (0.15, 1.41)	94	0.01	0.15
	No antidepressant	551 (4)	0.68 (−0.14, 1.51)	95	0.10	
	Use of antidepressants	120 (2)	1.42 (−0.41, 3.24)	95	0.13	
	Some patients received antidepressants	82 (1)	0.00 (−0.43, 0.43)	NA	1.00	
Cognitive function	Overall	283 (2)	−2.67 (−7.04, 1.70)	95	0.28	<0.001
	No antidepressant	173 (1)	−0.40 (−1.98, 1.18)	NA	0.62	
	Use of antidepressants	110 (1)	−0.75 (−0.95, −0.55)	NA	<0.001	

- CBT showed positive effects on PSD compared to control groups and CBT with antidepressants significantly improved depressive symptoms in PSD.
- CBT had significantly higher remission (6 arms, RR=1.76, 95% CI: 1.37–2.25, P<0.00001) and response rates (6 arms, RR=1.41, 95% CI: 1.22–1.63, P<0.00001), with improvement in anxiety, neurological functional deficits and activities of daily living.

Journal of Affective Disorders 235 (2018) 589–596

Depressione post-stroke: sfide aperte

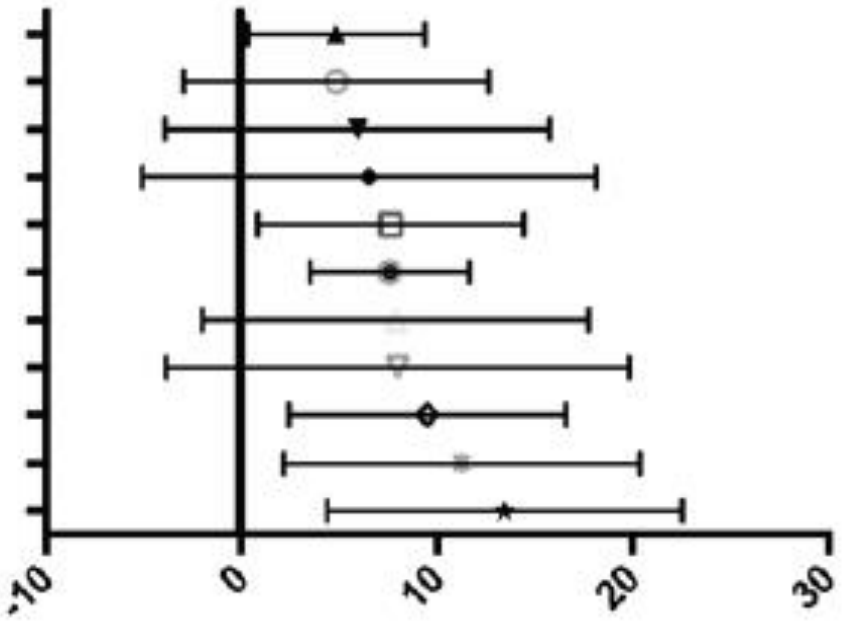
- Depressione come “modello” dei disturbi comportamentali post-stroke
- Le difficoltà nell'assessment, date dai sintomi motori, dalla possibile afasia, dal setting, impongono l'uso di strumenti validati e semplici per la valutazione della depressione post-stroke
- Rilevanza clinica
  - Impatto sulla mortalità e morbilità
  - Possibilità di prevenire la depressione
- Nonostante la rilevanza epidemiologica, i soggetti con malattia neurologica sono esclusi nei RCT per farmaci anti-depressivi
- Problemi per il trattamento:
  - Efficacia dei serotoninergici…ma... ci vorrebbe un farmaco con effetti anche su altri sistemi recettoriali come quello colinergico
  - Tollerabilità come primo obiettivo
  - Stretta relazione con cognitività

Efficacy and tolerability of pharmacotherapy for post-stroke depression: a network meta-analysis

Linghui Deng[1,*], Shi Qiu[2,*], Yan Yang[3,*], Lu Wang[1,*], Yuxiao Li[1], Jing Lin[1], Qiang Wei[2], Lu Yang[2], Deren Wang[1] and Ming Liu[1]

Oncotarget, 2018, Vol. 9, (No. 34), pp: 23718-23728

Treatment	MD (95% CrI)	SUCRA
Clomipramine	3.89 (-5.92, 13.15)	31%
venlafaxine	4.33 (-5.07, 13.77)	34%
TCM	5.47 (-2.33, 13.19)	40%
Fluoxetine	5.99 (1.48, 10.24)	44%
Citalopram	6.92 (0.18, 13.61)	49%
Sertraline	6.99 (-10.99, 12.58)	50%
Nortriptyline	6.98 (2.79, 10.56)	51%
Reboxetine	8.71 (2.13, 15.24)	62%
Imipramine	10.93 (2.04, 19.38)	73%
Paroxetine	12.12 (3.10, 20.10)	80%
Duloxetine	12.52 (1.42, 23.30)	81%



Conclusions: Paroxetine is probably the best option to consider for patients with PSD. To get a quicker relief of depression, duloxetine might be useful for its rapid onset of antidepressant action. The tolerability was comparable among all the antidepressants. But more high-quality RCTs are needed.

Trattare e prevenire la depressione post-stroke

Advances in antidepressants for treating post-stroke depression

Stefano Paolucci

- **TCAs**: Amitriptyline, nortriptyline, and clomipramine have an anticholinergic activity, scoring 3 at Anticholinergic Burden Scale, the maximum score for risk of occurrence of delirium → TCAs are not recommended as first-line choice for treatment of PSD.
- ADs are beneficial in improving depressive symptoms, but evidence for the choice of optimal drug and length of treatment are inconclusive → the choice of the drug must be based on guidelines and clinical factors.
- There is a wide debate of safety of ADs, in particular if a treatment with SSRIs is associated with high risk of mortality.
- Although some data are available about usefulness of ADs for preventing depression and for promoting functional recovery, further studies are necessary to elucidate their mechanisms and consolidate this evidence.
- Vortioxetine might become an important option for treatment PSD.