IV Convegno Sezione Regionale Emilia Romagna

16 Novembre 2017 – Reggio Emilia

Neuropsicologia Comportamentale delle Demenze

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Neuropsychiatric Disorders

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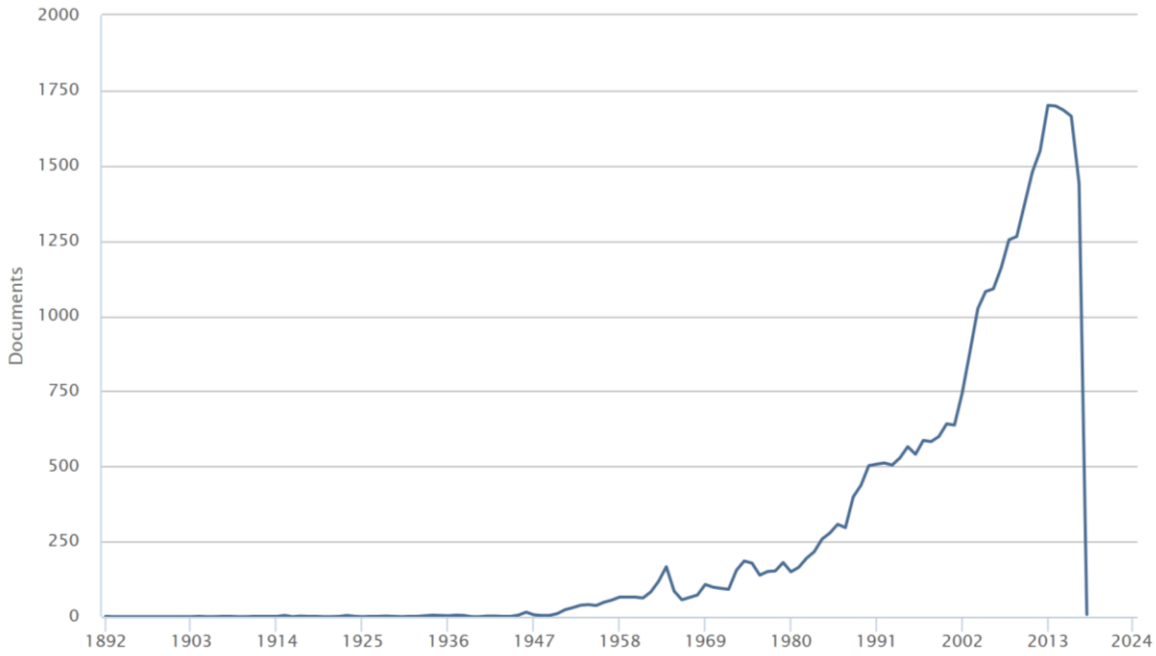

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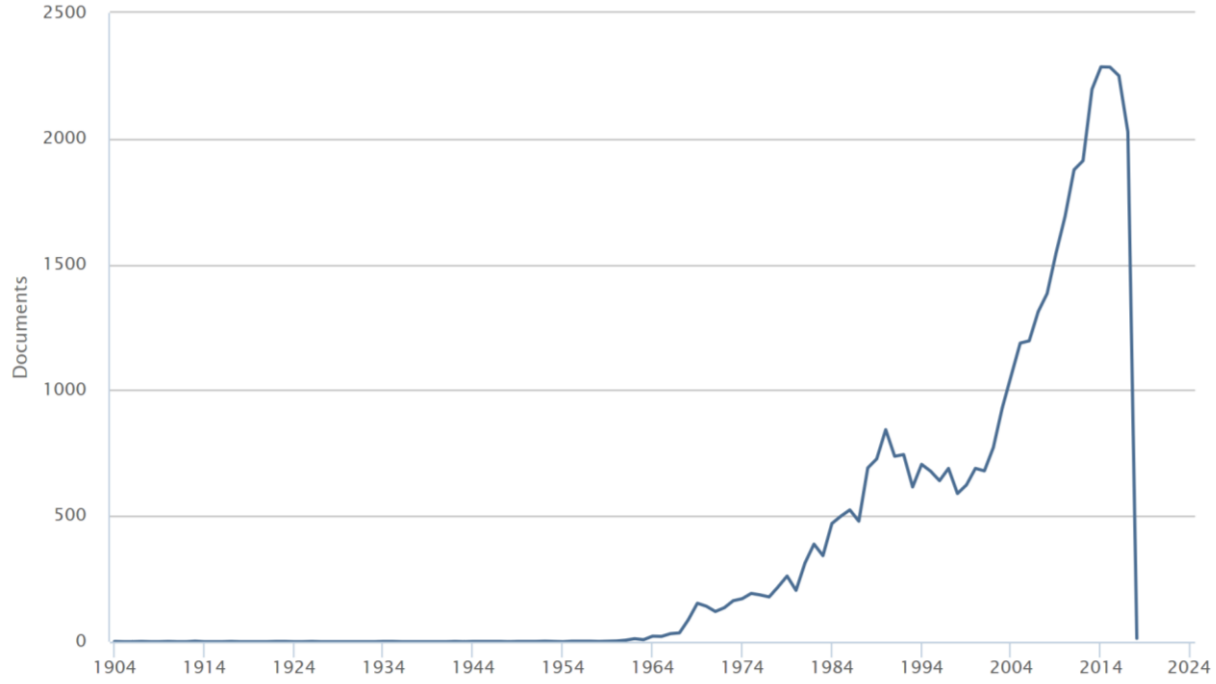

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Assessment and management of behavioral and psychological symptoms of dementia

Helen C Kales,[1 2 3] Laura N Gitlin,[4 5 6] Constantine G Lyketsos[7]

Cite this as: *BMJ* 2015;350:h369
doi: 10.1136/bmj.h369

Introduction

Behavioral and psychological symptoms of dementia are defined as signs and symptoms of disturbed perception, thought content, mood, or behavior.[1] They include agitation, depression, apathy, repetitive questioning, psychosis, aggression, sleep problems, wandering, and a variety of socially inappropriate behaviors.[2] One or more symptoms will affect nearly all people with dementia over the course of their illness.[2] These symptoms are among the most complex, stressful, and costly aspects of care, and they lead to a myriad of poor patient health outcomes, including excess morbidity, mortality, hospital stays, and early placement in a nursing home.[3-5] Most people with dementia are cared for in the home by family care givers, and these symptoms are strongly associated with stress and depression in carers, as well as reduced income from employment and lower quality of life.[6-8]

Types of behavioral and psychological symptoms of dementia*

- Delusions (distressing beliefs)
- Hallucinations
- Agitation:
  - Easily upset
  - Repeating questions
  - Arguing or complaining
  - Hoarding
  - Pacing
  - Inappropriate screaming, crying out, disruptive sounds
  - Rejection of care (for example, bathing, dressing, grooming)
  - Leaving home
- Aggression (physical or verbal)
- Depression or dysphoria
- Anxiety:
  - Worrying
  - Shadowing (following care giver)
- Apathy or indifference
- Disinhibition:
  - Socially inappropriate behavior
  - Sexually inappropriate behavior
- Irritability or lability
- Motor disturbance (repetitive activities without purpose):
  - Wandering
  - Rummaging
- Night-time behaviors (waking and getting up at night)

*Based on modified neuropsychiatric inventory-Q categories. Some behaviors under agitation need more research to determine whether they are part of agitation or their own entity (for example, rejection of care).

Assessment and management of behavioral and psychological symptoms of dementia

Helen C Kales,[1 2 3] Laura N Gitlin,[4 5 6] Constantine G Lyketsos[7]

Cite this as: *BMJ* 2015;350:h369
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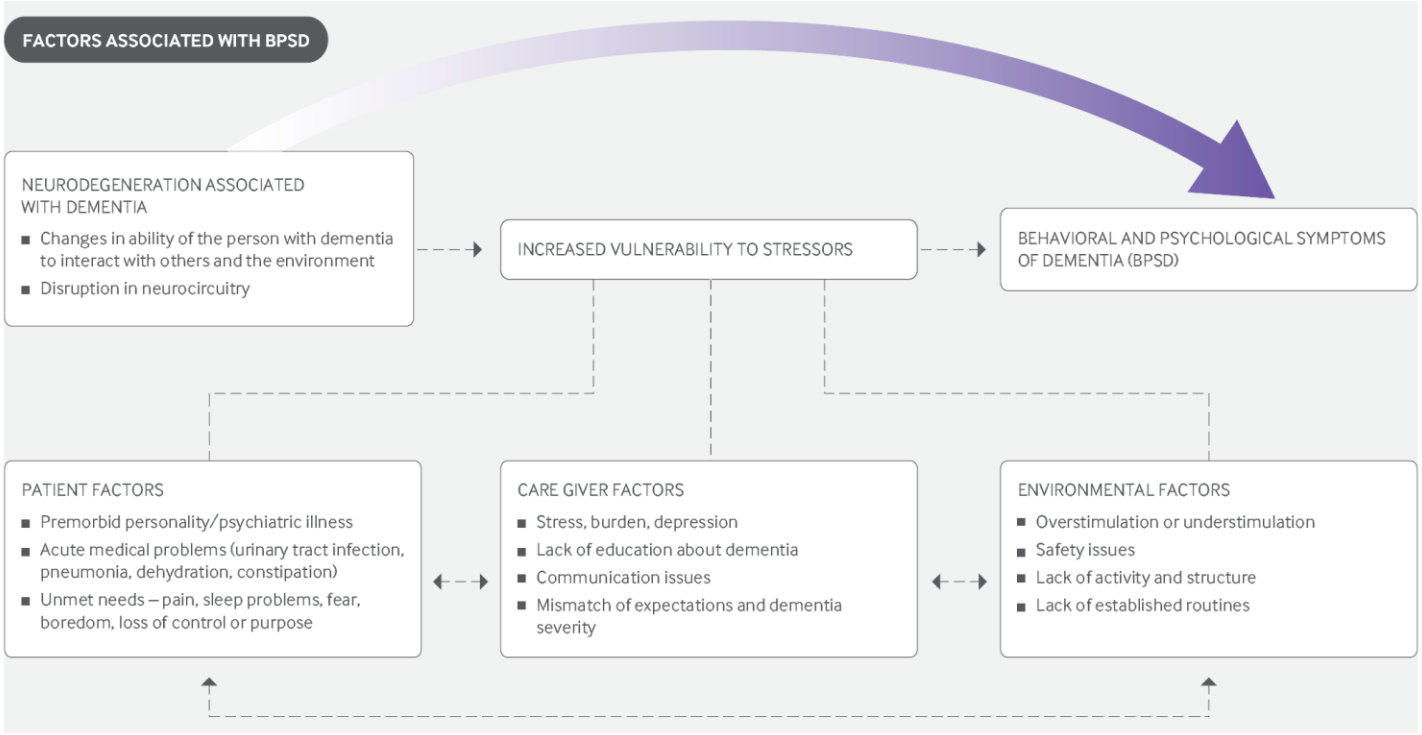


The Neuropsychiatric Inventory:

Assessing psychopathology in dementia patients

Jeffrey L. Cummings, MD

NEUROLOGY 1997;48(Suppl 6):S10–S16

Table 2 *Features of the Neuropsychiatric Inventory*

Caregiver-based, does not require patient cooperation, and can be used in very disturbed or advanced-disease patients
Screening-question strategy minimizes administration time
Assesses both frequency and severity of neuropsychiatric disorders
Assesses caregiver distress associated with individual neuropsychiatric abnormalities
Provides a profile of behavioral changes that helps to distinguish Alzheimer's disease from other types of dementia
Assesses conventional types of psychopathology that are readily recognized by clinicians and commonly require treatment
Well-established psychometric properties
Sensitive to drug-induced behavioral changes
Comprehensive
Available in several languages, used in transnational studies
Instructional module describing administration and scoring techniques
Videotape available demonstrating its application

UCLA Neuropsychiatric Inventory (NPI) (*)

	N.A.	Frequenza (a)	Gravità (b)	a x b	Distress Caregiver
Deliri	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Allucinazioni	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Agitaz./aggressività	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Depressione/ disforia	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Ansia	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Euforia/ esaltazione	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Apatia/ indifferenza	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Disinibizione	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Irritabilità/ Labilità	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Attività motoria aberrante	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Sonno	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]
Disturbi appetito e alimentazione	[ ]	[0] [1] [2] [3] [4]	[1] [2] [3]	_____	[0] [1] [2] [3] [4] [5]

Frequenza
0=mai
1=raramente (meno di 1 volta alla settimana)
2=talvolta (almeno 1 volta alla settimana)
3=frequentemente (parecchie volte ma meno di 1 volta al giorno)
4=quasi costantemente (1 o più volte al giorno)

Gravità
1=lieve (non producono disturbo al paziente).
2=moderata (comportano disturbo per il paziente).
3=severa (richiedono la somministrazione di farmaci; sono molto disturbanti per il paziente).

Stress emotivo o psicologico del caregiver
0= Nessuno
1= Minimo
2= Lieve
3= Moderato
4= Severo
5= Grave

Prevalence of Neuropsychiatric Symptoms in Dementia and Mild Cognitive Impairment Results From the Cardiovascular Health Study

JAMA. 2002;288(12):1475-1483. doi:10.1001/jama.288.12.1475

- **75% of people with dementia** (62% were clinically significant)
- **43% MCI participants** (29% rated as clinically significant)

Table 2. Prevalence of Any NPI Disturbance and of NPI Symptoms Compared With Prevalence Estimates in the Population Without Dementia From the Cache County Study*

	No. (%)			Comparison of MCI and Dementia	
	General Population (Cache County Study) (n = 653)†	MCI (n = 320)	Dementia (n = 362)	χ^2_2 Test	*P* Value
Delusions					
Any symptom (NPI >0)	16 (2.4)	10 (3.1)	65 (18.0)	40.5	<.001
Disturbance score of ≥4	NA	2 (0.6)	38 (10.5)		
Hallucinations					
Any symptom (NPI >0)	4 (0.6)	4 (1.3)	38 (10.5)	26.5	<.001
Disturbance score of ≥4	NA	4 (1.3)	18 (5)		
Agitation/aggression					
Any symptom (NPI >0)	19 (2.9)	36 (11.3)	110 (30.3)	37.3	<.001
Disturbance score of ≥4	NA	15 (4.7)	53 (14.6)		
Depression					
Any symptom (NPI >0)	47 (7.2)	64 (20.1)	117 (32.3)	18.4	<.001
Disturbance score of ≥4	NA	20 (6.3)	58 (16)		
Anxiety					
Any symptom (NPI >0)	38 (5.8)	30 (9.9)	78 (21.5)	19.3	<.001
Disturbance score of ≥4	NA	16 (5)	35 (9.7)		
Euphoria					
Any symptom (NPI >0)	2 (0.3)	2 (0.6)	11 (3.1)	6.06	.05
Disturbance score of ≥4	NA	0	5 (1.4)		

Prevalence of Neuropsychiatric Symptoms in Dementia and Mild Cognitive Impairment Results From the Cardiovascular Health Study

JAMA. 2002;288(12):1475-1483. doi:10.1001/jama.288.12.1475

Table 2. Prevalence of Any NPI Disturbance and of NPI Symptoms Compared With Prevalence Estimates in the Population Without Dementia From the Cache County Study*

	No. (%)			Comparison of MCI and Dementia	
	General Population (Cache County Study) (n = 653)†	MCI (n = 320)	Dementia (n = 362)	χ^2_2 Test	*P* Value
Apathy					
Any symptom (NPI >0)	21 (3.2)	47 (14.7)	130 (35.9)	52.2	<.001
Disturbance score of ≥4	NA	20 (6.3)	97 (26.8)		
Disinhibition					
Any symptom (NPI >0)	6 (0.9)	10 (3.1)	46 (12.7)	24.5	<.001
Disturbance score of ≥4	NA	1 (0.3)	25 (6.9)		
Irritability					
Any symptom (NPI >0)	30 (4.6)	47 (14.7)	98 (27)	15.2	<.001
Disturbance score of ≥4	NA	24 (7.5)	45 (12.4)		
Aberrant motor behavior					
Any symptom (NPI >0)	3 (0.4)	12 (3.8)	58 (16)	28.4	<.001
Disturbance score of ≥4	NA	7 (2.2)	43 (11.9)		
Sleep					
Any symptom (NPI >0)	NA	44 (13.8)	99 (27.4)	20.0	<.001
Disturbance score of ≥4	NA	28 (8.8)	72 (19.9)		
Eating					
Any symptom (NPI >0)	NA	33 (10.4)	71 (19.6)	15.3	<.001
Disturbance score of ≥4	NA	20 (6.3)	57 (15.7)		
Total NPI					
Any symptom (NPI >0)	106 (16.2)	138 (43.1)	270 (74.6)	81.8	<.001
NPI score of ≥4	NA	92 (28.7)	223 (61.6)		

*NPI indicates Neuropsychiatric Inventory; MCI, mild cognitive impairment; and NA, not available. Total NPI is not a sum of the columns because many people had more than 1 symptom.
†Data from Lyketsos et al.[20]

- **Depression (20%), apathy (15%)** and **irritability (15%)** are the most common symptoms in both MCI and demented patients
- In dementia, the most frequent disturbances were **apathy (36%), depression (32%)** and **agitation/aggression (30%)**

Prevalence of Neuropsychiatric Symptoms in Dementia and Mild Cognitive Impairment Results From the Cardiovascular Health Study

JAMA. 2002;288(12):1475-1483. doi:10.1001/jama.288.12.1475

Table 4. Prevalence of Individual NPI Symptoms in the Past Month in Participants With Alzheimer-Type Dementia Compared With Other Types of Dementia*

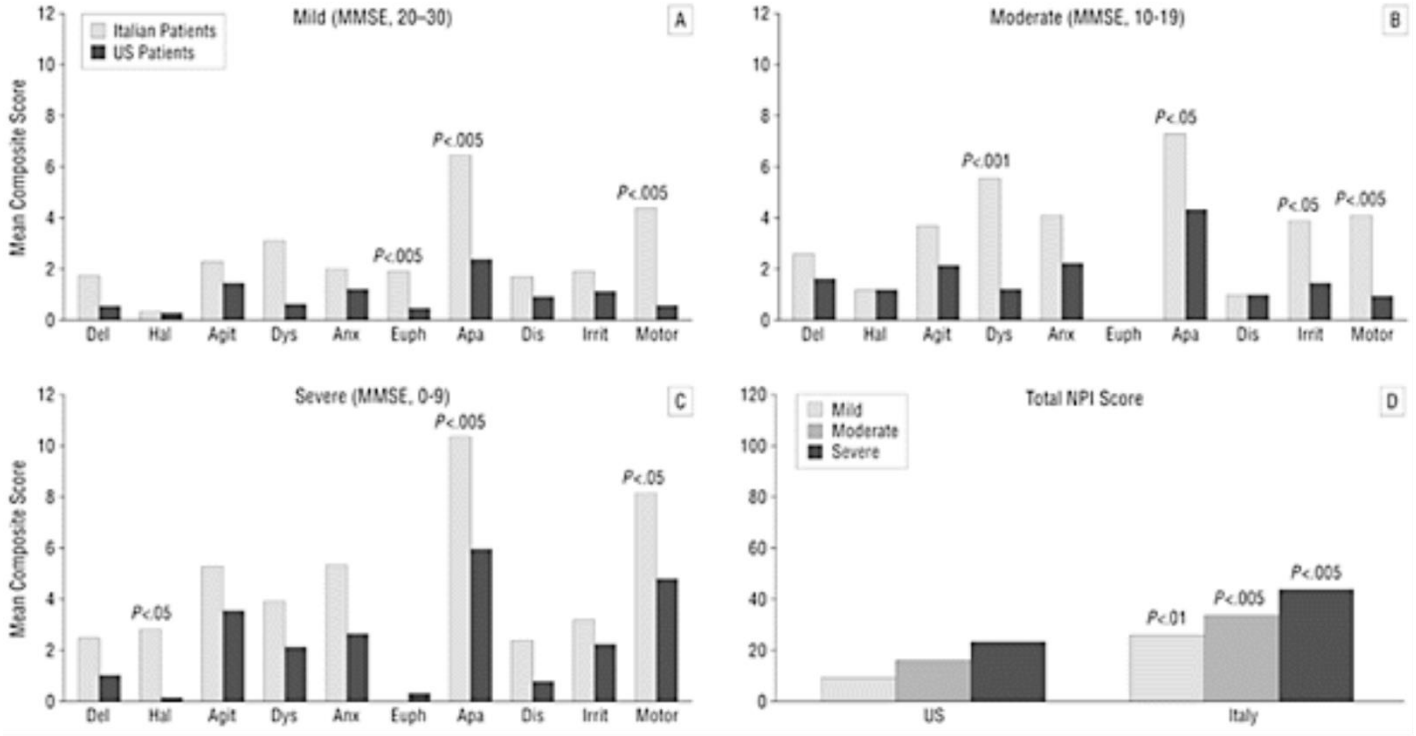
	No. (%)		Comparison of Alzheimer-Type Dementia and Other Dementia	
	Alzheimer-Type Dementia (n = 258)	Other Dementia (n = 104)	χ^2_2 Test	*P* Value
Delusions				
Mild disturbance (0-3)	19 (7.4)	8 (7.7)	2.205	.33
Disturbance score ≥4	31 (12.0)	7 (6.7)		
Hallucinations				
Mild disturbance (0-3)	13 (5)	7 (6.7)	1.67	.43
Disturbance score ≥4	15 (5.8)	3 (2.9)		
Agitation/aggression				
Mild disturbance (0-3)	43 (16.7)	14 (13.5)	2.05	.36
Disturbance score ≥4	41 (15.9)	12 (11.5)		
Depression				
Mild disturbance (0-3)	41 (15.9)	18 (17.3)	0.355	.84
Disturbance score ≥4	40 (15.5)	18 (17.3)		
Anxiety				
Mild disturbance (0-3)	29 (11.2)	14 (13.5)	0.352	.84
Disturbance score ≥4	25 (9.7)	10 (9.6)		
Euphoria				
Mild disturbance (0-3)	5 (1.9)	1 (1)	0.631	.73
Disturbance score ≥4	4 (1.6)	1 (1)		
Apathy				
Mild disturbance (0-3)	21 (8.1)	12 (11.5)	1.35	.51
Disturbance score ≥4	72 (27.9)	25 (24)		
Disinhibition				
Mild disturbance (0-3)	16 (6.2)	5 (4.8)	3.215	.20
Disturbance score ≥4	14 (5.4)	11 (10.6)		
Irritability				
Mild disturbance (0-3)	38 (14.7)	15 (14.4)	1.18	.56
Disturbance score ≥4	29 (11.2)	16 (15.4)		
Aberrant motor behavior				
Mild disturbance (0-3)	14 (5.4)	1 (1)	8.02	.02
Disturbance score ≥4	26 (14.0)	7 (6.7)		
Sleep				
Mild disturbance (0-3)	19 (7.4)	8 (7.7)	1.65	.44
Disturbance score ≥4	47 (18.2)	25 (24.0)		
Eating				
Mild disturbance (0-3)	9 (3.5)	5 (4.8)	1.82	.40
Disturbance score ≥4	37 (14.3)	20 (19.2)		
Total NPI				
Mild disturbance (0-3)	36 (14)	11 (10.6)	0.75	.69
NPI score ≥4	157 (60.9)	66 (63.5)		

*NPI indicates Neuropsychiatric Inventory.

- **No differences between AD and non-AD dementias** with the exception of aberrant motor behavior, which was more frequent in AD

Behavioral Disorders in Alzheimer Disease: A Transcultural Perspective

Arch Neurol. 1998;55(4):539-544. doi:10.1001/archneur.55.4.539



The relationship of specific items on the Neuropsychiatric Inventory to caregiver burden in dementia: a systematic review

Int J Geriatr Psychiatry 2017; **32**: 703–717

Toril Marie Terum[1,2,3,4], John Roger Andersen[1,4], Arvid Rongve[3,5], Dag Aarsland[2,6], Ellen J. Svendsboe[2,7,8] and Ingelin Testad[2,6]

Table 3 Studies investigating the association between individual neuropsychiatric symptoms, assessed using the Neuropsychiatric Inventory, and caregiver burden sum scores

Studies	Delusion	Hallucination	Agitation/ aggression	Dysphoria/ depression	Anxiety	Apathy/ indifference	Irritability/ lability	Euphoria/ elation	Disinhibition	Aberrant motor behavior	Sleep and nighttime behavior disorder	Appetite and eating disorder
Allegri *et al.* (2006)[a]	6*	10*	7*	1	12*	2	4	3	5*	9*	11*	8*
Balieiro *et al.* (2010)[a]	10*	11*	na	8*	6*	7*	12*	na	na	9*	na	5*
Dauphinot *et al.* (2015)[b]	na	na	11*	na	na	12*	8*	na	na	9*	na	10*
Slachevsky *et al.* (2013)[b]	7	4	12*	1	11*	10	8	5	2	6	9	3
Hall *et al.* (2014)[c]	10*	12*	8*	7*	5*	4*	6*	1	9*	2	3*	11*
Lou *et al.* (2015)[a]	6*	4*	5*	7*	8*	12*	11*	3*	1*	10*	9*	2*
Wang *et al.* (2015)[a]	12*	8*	2*	3*	6*	1	11*	4	10	7*	9*	5*
Sousa *et al.* (2016)[b] Spanish sample	na	na	11*	9	8	12*	10*	na	na	na	na	na
Sousa *et al.* (2016)[b] Brazillian sample	na	na	10	12*	11*	8	9	na	na	na	na	na
Oh *et al.* (2015)[a]	12*	7*	9*	3	10*	1	11*	2	8*	6*	5*	4*
Lau *et al.* (2015)[b] A	12*	na	na	na	na	10*	11*	na	na	na	na	na
Lau *et al.* (2015)[b] B	na	na	na	10*	na	na	11*	na	12*	na	na	na
Number of studies ranked ≥9	5	3	5	3	4	5	8	—	3	4	4	2

Coefficients were only provided for the individual NPSs that were retained in the models.
na, data not available.
[a]Correlation analysis (e.g. Spearman's rank test or Pearson correlation analysis).
[b]Multiple regression (e.g. linear regression, stepwise multivariate linear regression, multiple linear regression or multiple linear regression analyses with backward stepping).

The relationship of specific items on the Neuropsychiatric Inventory to caregiver burden in dementia: a systematic review

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Table 2 Studies investigating the association between individual neuropsychiatric symptoms and Neuropsychiatric Inventory-distress subscores assessed using the Neuropsychiatric Inventory

Study	Delusion	Hallucination	Agitation/ aggression	Dysphoria/ depression	Anxiety	Apathy/ indifference	Irritability/ lability	Euphoria/ elation	Disinhibition	Aberrant motor behavior	Sleep and nighttime behavior disorder	Appetite and eating disorder
Godinho *et al.* (2008)[a]	8*	9*	2*	5*	6*	4*	12*	1*	10*	3*	11*	7*
Huang *et al.* (2012)[a]	7*	2	5*	3*	11*	8*	6*	12	4*	10*	9*	1
Khoo *et al.* (2013)[b]	7*	5*	12*	11*	9*	1*	10*	2*	8*	4*	6*	3*
Mean	7.3	5.3	6.3	6.3	8.7	4.3	9.3	5	7.3	5.7	8.7	3.7

[a]Correlation analysis (e.g. Spearman's rank test or Pearson correlation analysis).
[b]Multiple regression (e.g. linear regression, stepwise multivariate linear regression, multiple linear regression or multiple linear regression analyses with backward stepping).
*Correlation is significant ($p < 0.05$).

Key points

- Findings suggest that irritability, agitation, sleep disturbances, anxiety, apathy, and delusion seem to impact caregiver burden the most.
- Heterogeneity in the methodology makes it difficult to draw firm conclusions.

Journal of Alzheimer's Disease 48 (2015) 627–636
DOI 10.3233/JAD-150391
IOS Press

Longitudinal Neuropsychiatric Predictors of Death in Alzheimer's Disease

Gianfranco Spalletta[a,b,*], Jeffrey D. Long[c,d], Robert G. Robinson[c], Alberto Trequattrini[e], Sonia Pizzoli[a], Carlo Caltagirone[a,f] and Maria D. Orfei[a]

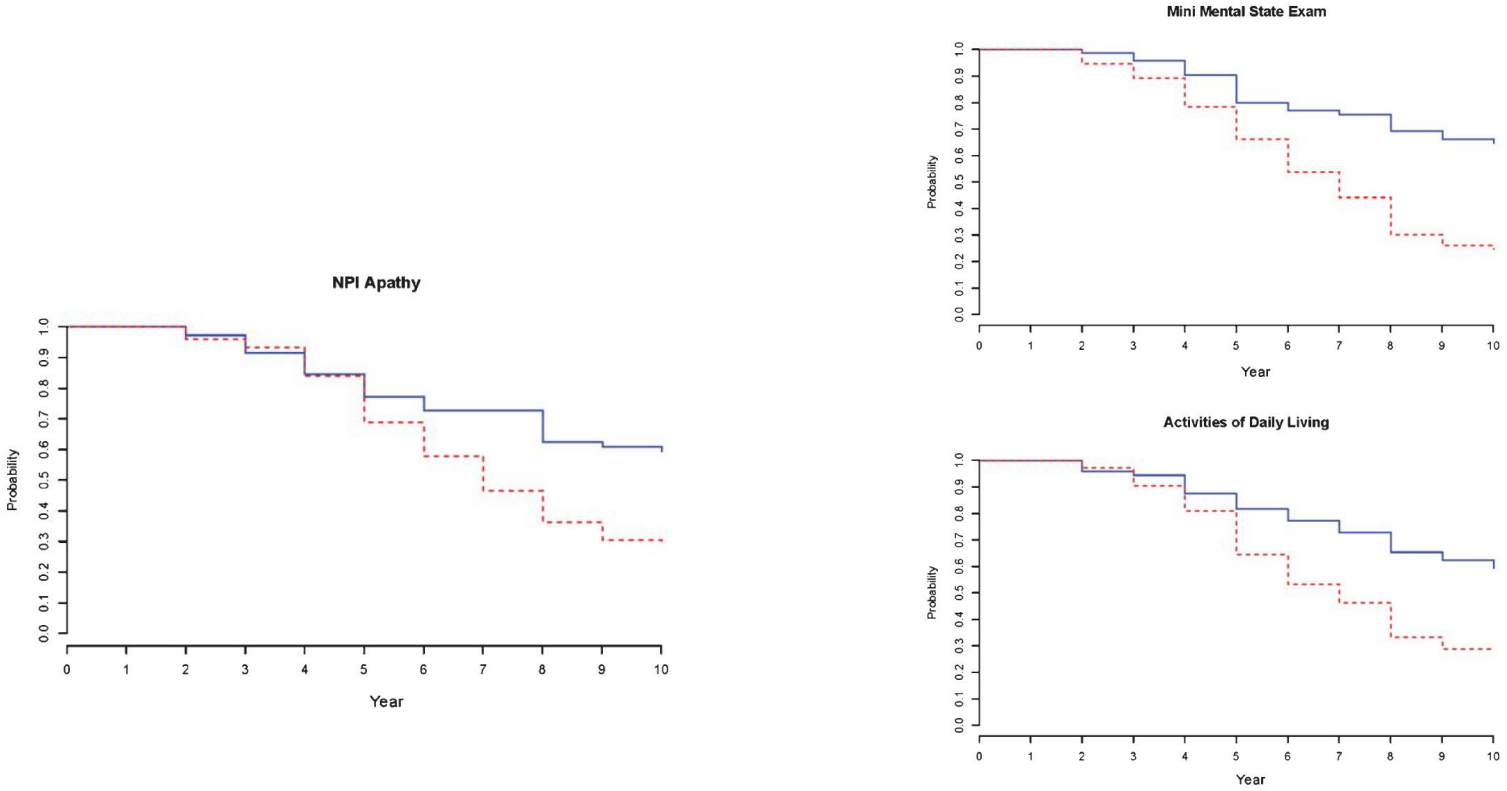


Fig. 1. Kaplan-Meier survival probabilities as a function of year in study and progression group based on a median split of the slopes of the longitudinal variable (slower = blue solid line, faster = dashed red line).

Structural Correlates of Apathy in Alzheimer's Disease

Liana G. Apostolova[a, b] Gohar G. Akopyan[a] Negar Partiali[a] Calen A. Steiner[a]
Rebecca A. Dutton[b] Kiralee M. Hayashi[b] Ivo D. Dinov[b, c] Arthur W. Toga[a, b]
Jeffrey L. Cummings[a, d] Paul M. Thompson[a, b]

Dement Geriatr Cogn Disord 2007;24:91–97
DOI: 10.1159/000103914

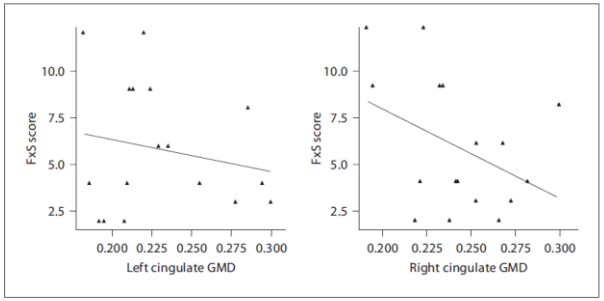


Fig. 2. Regression plots showing the inverse association between apathy (FxS score) and GM atrophy.

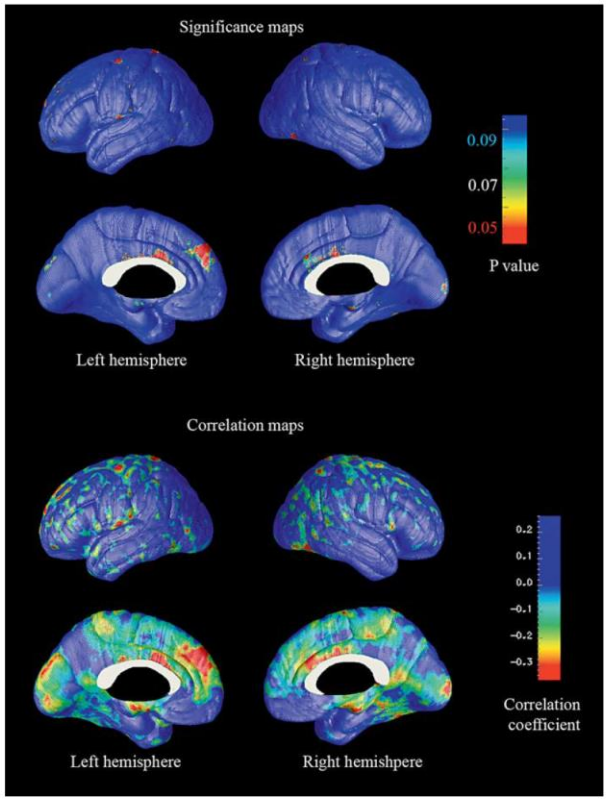


Fig. 1. Statistical (top) and correlation maps (bottom) showing the strength of the association between apathy severity and GMD among 17 probable AD patients with and 18 probable AD patients without apathy. As predicted, apathy severity correlated with bilateral anterior cingulate atrophy, as well as atrophy of the left supplementary motor area.

Table 2. Location, ICBM coordinates and statistical significance of the regions showing the strongest associations of apathy and GM atrophy

Region	BA	Coordinates, mm			r value	p value
		X	Y	Z		
Cingulate	left BA 24	−1	5.4	31.4	−0.42	<0.01
	right BA 24	3	4.4	31.9	−0.39	0.01
Supplementary motor area	left BA 9	−4	47.1	33.1	−0.40	<0.02

Apathy: a neurocircuitry model based on frontotemporal dementia

Ducharme S, *et al*. *J Neurol Neurosurg Psychiatry* 2017;**0**:1–8. doi:10.1136/jnnp-2017-316277

Simon Ducharme,[1,2] Bruce H Price,[3] Bradford C Dickerson[4]

Box 1 Clinical diagnostic criteria for behavioural frontotemporal dementia[1]

1. Three of the following behavioural/cognitive symptoms (A–F) must be present to meet criteria:
2. Shows progressive deterioration of behaviour and/or cognition by observation or history (as provided by a knowledgeable informant).
   - A. Early[1] behavioural disinhibition
   - B. Early apathy or inertia
   - C. Early loss of sympathy or empathy
   - D. Early perseverative, stereotyped or compulsive/ritualistic behaviour
   - E. Hyperorality and dietary changes
   - F. Neuropsychological profile: executive/generation deficits with relative sparing of memory and visuospatial functions.

From Rascovsky *et al*.[1]

Box 3 Recommended modifications to bvFTD diagnostic criteria B

B. Early apathy (one of the following symptoms (B.1–B.2) must be present):
   - B.1. Loss of motivation.
   - B.2. Diminished initiation and/or performance to completion of goal-directed behaviour.

Apathy: a neurocircuitry model based on frontotemporal dementia

Simon Ducharme,[1,2] Bruce H Price,[3] Bradford C Dickerson[4]

Ducharme S, *et al*. *J Neurol Neurosurg Psychiatry* 2017;**0**:1–8. doi:10.1136/jnnp-2017-316277

Cognitive (planning) Component
Deficits: task setting, set-shifting, abstraction
Test: Trail Making B

Initiation Component
Deficits: Energization
Test: F-A-S Fluency

Emotional/Affective (motivation) Component
Deficits: Social Cognition
Tests: Theory of Mind, Iowa Gambling Test

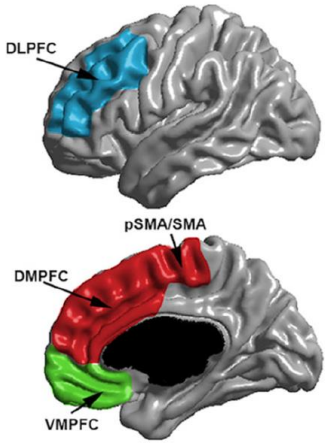


Table 1 Structural neuroimaging studies of apathy in FTD

Authors	Year	Sample	Apathy scale	Method	Main findings
Rosen *et al*[47]	2005	n=148 (AD, bvFTD, PNFA and SD)	NPI (continuous variable)	MRI–VBM	(1) Apathy in FTD/SD specifically associated with atrophy of right ventromedial superior frontal gyrus (2) Apathy and other neuropsychiatric symptoms associated with atrophy of right-sided frontotemporal areas, including the lateral OFC, MCC, vmSFG (mPFC), caudate head and ventral striatum
Zamboni *et al*[22]	2008	n=62 (bvFTD and PPA)	FrSBe (continuous variable)	MRI–VBM	(1) Apathy associated with increased atrophy in right DLPFC (2) Trends of association with left DLPFC, right ACC, right LOFC, right temporoparietal junction, right putamen
Massimo *et al*[44]	2009	n=40 (bvFTD=26, PPA=14)	NPI (continuous variable)	MRI–VBM	Apathy correlated with atrophy in bilateral mPFC, OFC, IFC, DLPFC, right middle temporal and right caudate
Links *et al*[45]	2009	n=21 (FTD)	Group contrast based on NPI	MRI–Semiautomated volume extraction	No association with basal ganglia
Eslinger *et al*[23]	2012	n=26 (bvFTD, SD, PNFA)	AES (continuous variable)	MRI–VBM	Apathy associated with higher atrophy in right caudate (ventral striatum), right temporoparietal junction, right posteroinferior and middle temporal gyri and the left anterior insula
Powers *et al*[46]	2014	n=11 (bvFTD)	NPI (continuous variable)	DTI-FA	Apathy severity associated with reduced FA in the temporal portion of the left uncinate faciculus
Massimo *et al*[42]	2015	n=18 (bvFTD)	Philadelphia Apathy Computerised Test	MRI-VBM DTI-FA	(1) Initiation deficits associated with decreased GM density in the ACC and reduced FA in the cingulum, inferior longitudinal fasciculus, unicinate fasciculus, corpus callosum (2) Planning deficits associated with decreased GM density in the DLPFC and decreased FA in the superior longitudinal fasciculus (3) Motivation deficits associated with decreased GM in the OFC and ACC and reduced FA in the uncinated fasciculus

AD, Alzheimer's disease; ACC, anterior cingulate cortex; AES, Apathy Evaluation Scale; bvFTD, behavioural variant frontotemporal dementia; DTI, diffusion tensor imaging; DLPFC, dorsolateral prefrontal cortex; FA, fractional anisotropy; FrSBe, Frontal Systems Behaviour Scale; FTD, frontotemporal dementia; GM, grey matter; IFC, inferior frontal cortex; LOFC, lateral orbitofrontal cortex; mPFC, medial prefrontal cortex; MCC, middle cingulate cortex; NPI, Neuropsychiatric Inventory; OFC, orbitofrontal cortex; PPA, primary progressive aphasia; PNFA, primary non-fluent aphasia; SD, semantic dementia; vmSFG, ventromedial superior frontal gyrus; VBM, voxel-based morphometry.

Apathy: a neurocircuitry model based on frontotemporal dementia

Simon Ducharme,[1,2] Bruce H Price,[3] Bradford C Dickerson[4]

Ducharme S, *et al*. *J Neurol Neurosurg Psychiatry* 2017;**0**:1–8. doi:10.1136/jnnp-2017-316277

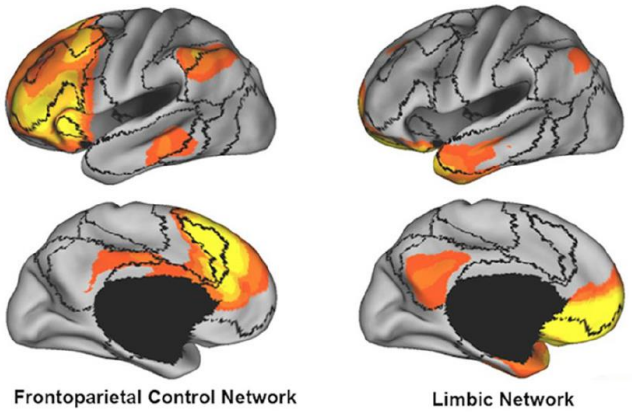


Table 2 Functional neuroimaging studies of apathy in FTD

Authors	Year	Sample	Apathy scale	Method	Main Findings
Franceschi *et al*[51]	2005	n=18 (bvFTD)	Group contrast based on NPI	FDG-PET	(1) Apathy associated with hypometabolism of bilateral DLPFC, mPFC (MCC, SMA), frontal pole/anterior OFC, insula (2) Apathy and disinhibition associated with hypometabolism of bilateral insula and thalamus
Peters *et al*[50]	2006	n=41 (bvFTD)	NPI (continuous variable and group contrast)	FDG-PET	(1) No association with NPI apathy as a continuous variable (2) Subjects with predominant apathy (n=13) had hypometabolism in posterior mOFC (gyrus rectus) compared with controls
Le Ber *et al*[49]	2006	n=17 (bvFTD) vs 28 age-matched controls	Group contrast based on clinical assessment	SPECT	Apathy associated with predominant hypoperfusion in vmSFG, ACC, MCC, pre-SMA/SMA and DLPFC
McMurtray *et al*[48]	2006	n=74 (bvFTD)	Single item 5-point Likert scale (continuous variable)	SPECT	Apathy associated with frontal hypoperfusion
Schroeter *et al*[52]	2011	n=54 (AD, FTD, MCI, SCI, others)	NPI (continuous variable)	FDG-PET	(1) Apathy specifically associated to hypometabolism of VTA and left inferior and middle temporal gyri (2) Apathy, disinhibition and eating disorders associated with mPFC/ACC/MCC (BA 9, 10, 24, 32, 33) and left anterior SFG (BA 9, 10)
Farb *et al*[53]	2012	n=16 (bvFTD, SD) vs 16 age-matched controls	FBI	fMRI intrinsic connectivity	(1) Apathy associated with PFC hyperconnectivity (2) Apathy associated with increased angular gyrus connectivity in bvFTD only
Day *et al*[54]	2013	n=15 (bvFTD, SD)	FBI	fMRI	(1) No correlation between severity of apathy and resting state activity (2) Left insula integrity could predict short-term worsening of apathy

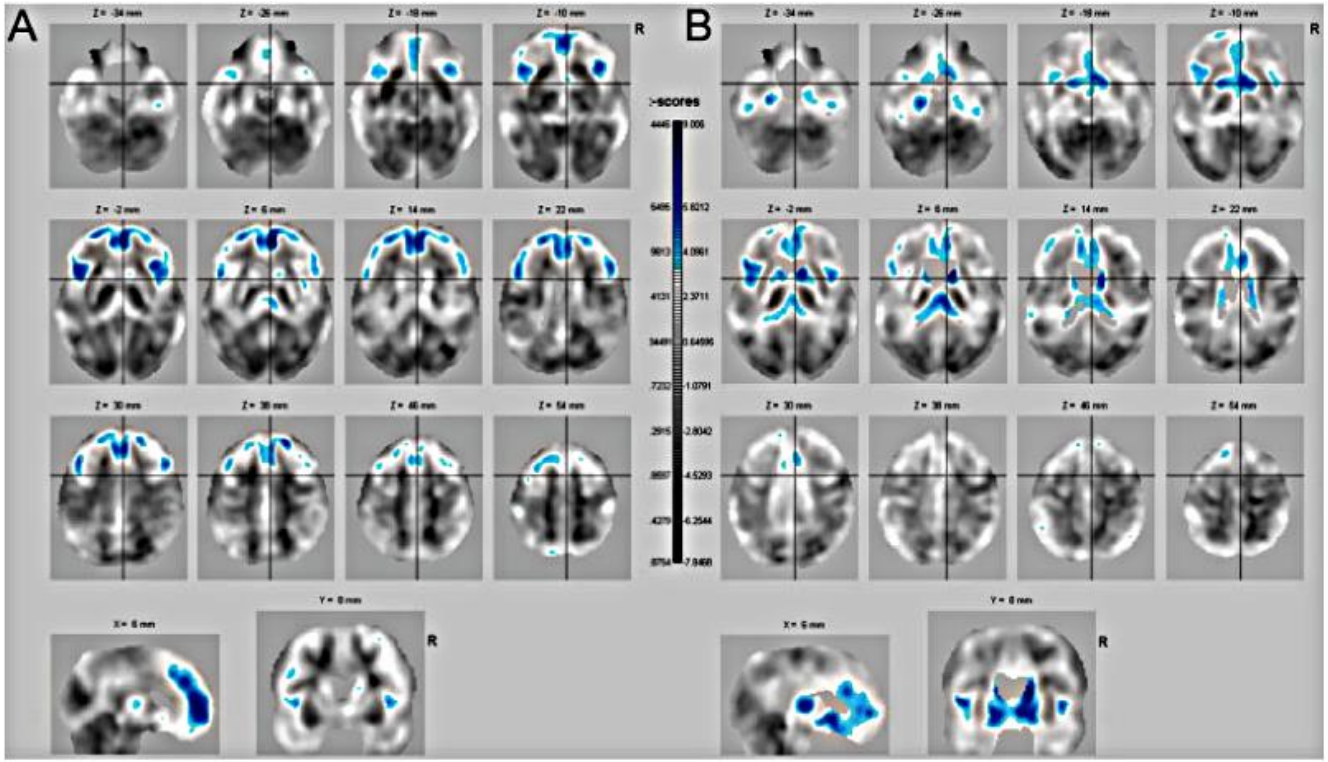
AD, Alzheimer's disease; ACC, anterior cingulate cortex; bvFTD, behavioural variant frontotemporal dementia; BA, Brodmann area; DLPFC, dorsolateral prefrontal cortex; FDG-PET, fluorodeoxy glucose positron emission tomography; FBI, Frontal Behaviour Inventory; FTD, frontotemporal dementia; fMRI, functional MRI; mPFC, medial prefrontal cortex; MCC, middle cingulate cortex; MCI, mild cognitive impairment; NPI, Neuropsychiatric Inventory; OFC, orbitofrontal cortex; PFC, prefrontal cortex; SD, semantic dementia; SPECT, single-photon emission CT; SCI, subjective cognitive impairment; SMA, supplementary motor area; vmSFG, ventromedial superior frontal gyrus; VTA, ventral tegmental area.

Glucose Metabolism and Serotonin Receptors in the Frontotemporal Lobe Degeneration

Massimo Franceschi, MD,[1] Davide Anchisi, MD, PhD,[2] Oriana Pelati, MS,[2] Marta Zuffi, MD,[1] Mario Matarrese, MS,[3] Rosa Maria Moresco, MS,[3,4] Ferruccio Fazio, MD,[2–4] and Daniela Perani, MD[5]

Ann Neurol 2005;57:216–225

Apathetic behaviour **Disinhibited behaviour**



A. Fronto-medial and dorsolateral prefrontal cortices FDG-PET hypometabolism

***B. FDG-PET hypometabolism in the interconnected limbic structures** (cingulate cortex, hippocampus, amygdala, accumbens nucleus)*

Neurol Sci (2007) 28:80–86
DOI 10.1007/s10072-007-0791-3

ORIGINAL

A. Alberici • C. Geroldi • M. Cotelli • A. Adorni • M. Calabria • G. Rossi • B. Borroni • A. Padovani
O. Zanetti • A. Kertesz

The Frontal Behavioural Inventory (Italian version) differentiates frontotemporal lobar degeneration variants from Alzheimer's disease

FRONTAL BEHAVIORAL INVENTORY

Spiega al caregiver che vuoi capire se c'è stato un cambiamento nel comportamento o nella personalità del paziente. Fai le domande al carer in assenza del paziente. Per ogni domanda, chiedigli di "quantificare" il cambiamento di comportamento. Attribuisci un punteggio secondo i seguenti criteri: 0 – nessuno; 1 – lieve, occasionale; 2 – moderato; 3 – grave, per la maggior parte del tempo.

1. **Apatia**
   Il/la paziente ha perso interesse per gli amici o per le attività quotidiane? ☐
2. **Spontaneità /Iniziativa**
   Il/la paziente inizia le cose di sua iniziativa o gli/le deve essere chiesto? ☐
3. **Indifferenza, appiattimento emotivo**
   Il/la paziente reagisce alle situazioni di gioia o tristezza come prima o ha notato una ridotta risposta emotiva? ☐
4. **Inflessibilità**
   Il/la paziente è capace di cambiare idea ragionevolmente o si dimostra testardo/a e rigido/a ultimamente? ☐
5. **Concretezza/Capacità di astrazione**
   Il/la paziente interpreta correttamente il significato delle cose dette o non sembra capace di coglierne il significato astratto? ☐
6. **Igiene personale**
   Il/la paziente ha sufficiente cura della propria igiene personale ed appare come di solito? ☐
7. **Disorganizzazione**
   Il/la paziente riesce a pianificare / organizzare attività complesse o si distrae facilmente non riesce a completare un lavoro? ☐
8. **Disattenzione**
   Il/la paziente presta attenzione all'ambiente circostante o perde il filo, o non segue del tutto? ☐
9. **Perdita di consapevolezza**
   Il/la paziente è o meno consapevole di problemi e cambiamenti o li nega quando se ne discute? ☐

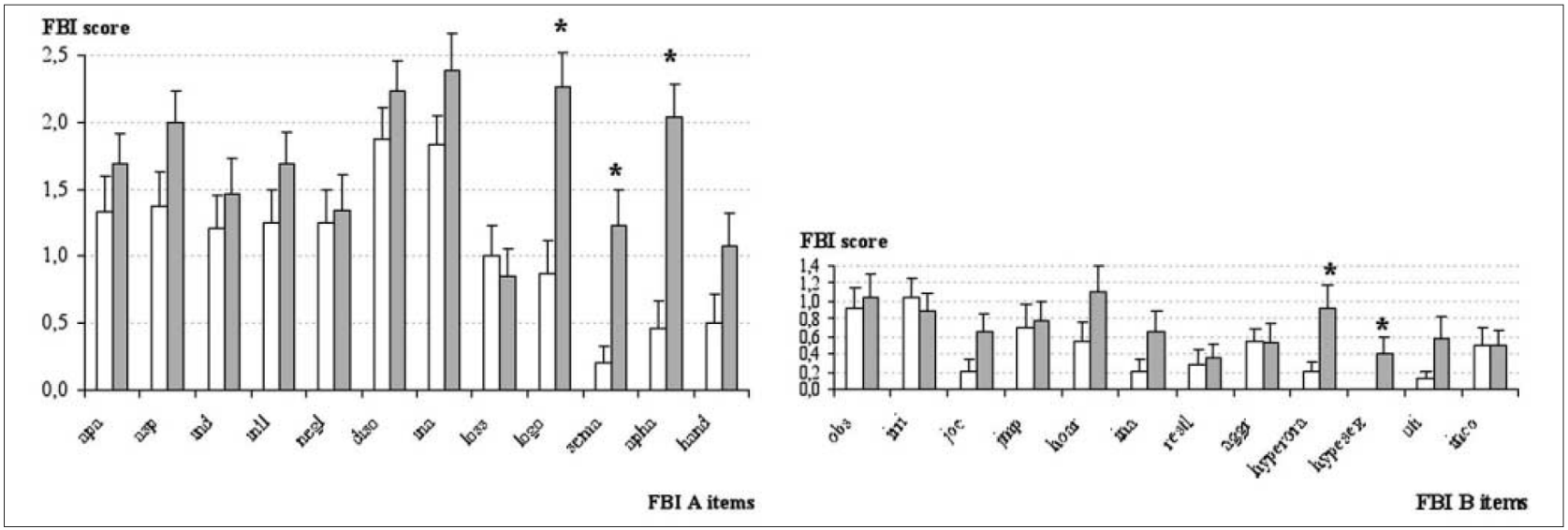


Fig. 1 Items significantly different between FTLD and AD patients are marked as follows. $p<0.05$. *FBI A*, FBI subscale for negative symptoms: *apa*, apathy; *asp*, aspontaneity; *ind*, indifference; *negl*, personal neglect; *diso*, disorganisation; *ina*, inattention; *loss*, loss of insight; *logo*, logopenia; *sema*, semantic dementia; *apha*, aphasia and verbal apraxia; *hand*, alien hand. *FBI B*, FBI subscale for positive symptoms: *obs*, obsessions; *irri*, irritability; *joc*, excessive jocularity; *imp*, impulsivity; *hoar*, hoarding; *ina*, inappropriateness; *restl*, restlessness; *aggr*, aggression; *hyperora*, hyperorality; *hypersex*, hypersexuality; *uti*, utilisation behaviour; *inco*, incontinence

Coexistence of positive and negative behavioural symptoms *yet in the early disease phase*

	BV-FTD	SV-PPA	NFV-PPA
Social symptoms			
Disinhibition, inappropriate or offensive behaviour, excessive jocularity, exaggerated emotional display, impulsivity, inappropriate sexual remarks, lack of embarrassment	73–98%	59%	18%
Loss of empathy, lack of emotional insight, social coldness	49–78%	28–49%	18%
Selfishness, disregard for others' feelings	83–89%	91%	No
Aggression	25–61%	28–64%	12%
Personal neglect, neglect of hygiene	83–92%	64%	No
Strange manner of dressing	Yes	Right-sided cases	No
Personality changes	Sometimes	Sometimes	Rarely
Emotional symptoms			
Apathy, low motivation, aspontaneity, decreased initiation of behaviour	64–96%	18–47%	41%
Depression, emotional detachment	Common	44%	Sometimes depression
Irritability	33%	50%	47%
Anxiety, social avoidance	No	Not usually	Yes
Exaggerated emotional display	33–39%	55%	Rarely
Eating and oral behaviours			
Overeating, gluttony	61–83%	36%	Rarely
Reduced selectivity, indiscriminate eating	41–55%	9%	Rarely
Increased selectivity, food fads	8–22%	55%	Rarely
Preference for sweet foods	25–56%	36%	Rarely
Preference for savoury foods	0%	9%	Rarely
Hyperorality	0–22%	18%	Rarely
Repetitive or compulsive behaviours			
Behavioural stereotypies	95%	72%	24%
Compulsive behaviours	5–15%	60–80%	Rarely
Word obsessions, repetitious use of verbal expressions	Sometimes	Often	Rarely

Table 2: **Clinical symptoms characteristic of FTD**

Bang, Spina & Miller, Lancet 2015

Psychotic symptoms are relatively rare in bvFTD

	BV-FTD	SV-PPA	NFV-PPA
(Continued from previous page)			
Neuropsychiatric symptoms			
Delusions	14%	9%	6%
Hallucinations	20%	6%	6%
Other symptoms			
Sleep disorders	Sometimes	Rarely	Rarely
Restlessness	Sometimes	Sometimes	Rarely
Prosopagnosia	3%	47%	0%
Decreased libido	Sometimes	Sometimes	Rarely
Episodic memory deficits	Rarely	Rarely	Rarely

BV-FTD=behavioural-variant frontotemporal dementia. SV=semantic variant. NFV= non-fluent variant. PPA=primary progressive aphasia.

Table 2: **Clinical symptoms characteristic of FTD**

Bang, Spina & Miller, Lancet 2015

	VAD (n = 85)	AD/VAD (n = 92)	AD (n = 2,474)	AD/DLB (n = 87)	DLB (n = 151)	PDD (n = 74)
Agitation						
Occurrence (0/1)	52% [a]	37% [a]	47% [a]	48% [a]	47% [a]	51% [a]
Mean Severity (0–3)	0.86 (0.10) [a]	0.61 (0.10) [a]	0.73 (0.02) [a]	0.70 (0.10) [a]	0.72 (0.07) [a]	0.62 (0.11) [a]
Observed Severity (1–3)	1.66 (0.10) [a]	1.65 (0.12) [a]	1.56 (0.02) [a]	1.45 (0.11) [b]	1.52 (0.08) [b]	1.21 (0.11) [b]
Hallucinations						
Occurrence (0/1)	14% [a]	12% [a]	13% [a]	39% [b]	55% [c]	46% [b]
Mean Severity (0–3)	0.24 (0.07) [a]	0.15 (0.06) [a]	0.19 (0.01) [a]	0.62 (0.07) [b]	0.99 (0.05) [b]	0.60 (0.07) [c]
Observed Severity (1–3)	1.67 (0.20) [a]	1.27 (0.21) [a]	1.50 (0.04) [a]	1.59 (0.12) [a]	1.80 (0.08) [b]	1.29 (0.12) [a]
Delusions						
Occurrence (0/1)	27% [a]	22% [a]	28% [b]	41% [c]	40% [c]	32% [b]
Mean Severity (0–3)	0.44 (0.09) [a]	0.29 (0.08) [a]	0.43 (0.02) [a]	0.75 (0.09) [b]	0.68 (0.07) [b]	0.50 (0.09) [a]

Johnson et al., ADAD 2011

REVIEW

CNS Neuroscience & Therapeutics

Hallucinations in Neurodegenerative Diseases

Lothar Burghaus,[1] Carsten Eggers,[1] Lars Timmermann,[1] Gereon R. Fink[1,2] & Nico J. Diederich[3]

CNS Neuroscience & Therapeutics **18** (2012) 149–159

VH should suggest a synucleopathy

Table 5 Special features and treatment strategies for hallucinations in common neurodegenerative disease

	Synucleinopathies		Tauopathies	
	PD	DLB	AD	FTD MSA PSP CBD
Most common clinical presentation	Visual hallucinations and visual delusions in later course of disease under dopaminergic treatment	Visual hallucinations in early stages of disease Detailed and scenic hallucinations	Visual, paranoid delusions, and hallucinations	Overall rare, symptoms in less than 10% of patients Visual hallucinations and delusions
Treatment	Reduction of dopaminergic drugs clozapine id: 6.25–12.5 mg/d md: 75–100 mg/d quetiapine id: 12.5–25 mg/d md: 100–125 mg/d coping strategies (Table 3)	Cholinesterase-inhibitors rivastigmine id: 2 × 1.5 mg/d md: 6–12 mg/d donepezil id: 5 mg/d md: 10 mg/d Cave: hypersensitivity to neuroleptic drugs second-generation antipsychotics in lowest dosage quetiapine id 12.5 mg, clozapine id 6.25 mg	second-generation antipsychotics (risperidone, olanzapine, quetiapine, aripripazol)	second-generation antipsychotics?

PD, Parkinson's disease; DLB, Dementia with Lewy Bodies; AD, Alzheimer's disease; FTD, Frontotemporal Dementia; MSA, Multiple system atrophy; PSP, Progressive supranuclear palsy; CBD, Corticobasal degeneration; id, initial dose, md, maximum dose.

Diagnosis and management of dementia with Lewy bodies

Third report of the DLB consortium

Mc Keith et al., Neurology 2005

Table 1 *Revised criteria for the clinical diagnosis of dementia with Lewy bodies (DLB)*

1. *Central feature* (essential for a diagnosis of possible or probable DLB)
   - Dementia defined as progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuospatial ability may be especially prominent.
2. *Core* features (two core features are sufficient for a diagnosis of probable DLB, one for possible DLB)
   - Fluctuating cognition with pronounced variations in attention and alertness
   - Recurrent visual hallucinations that are typically well formed and detailed
   - Spontaneous features of parkinsonism
3. *Suggestive features* (If one or more of these is present in the presence of one or more core features, a diagnosis of probable DLB can be made. In the absence of any core features, one or more suggestive features is sufficient for possible DLB. Probable DLB should not be diagnosed on the basis of suggestive features alone.)
   - REM sleep behavior disorder
   - Severe neuroleptic sensitivity
   - Low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET imaging
4. *Supportive features* (commonly present but not proven to have diagnostic specificity)
   - Repeated falls and syncope
   - Transient, unexplained loss of consciousness
   - Severe autonomic dysfunction, e.g., orthostatic hypotension, urinary incontinence
   - Hallucinations in other modalities
   - Systematized delusions
   - Depression
   - Relative preservation of medial temporal lobe structures on CT/MRI scan
   - Generalized low uptake on SPECT/PET perfusion scan with reduced occipital activity
   - Abnormal (low uptake) MIBG myocardial scintigraphy
   - Prominent slow wave activity on EEG with temporal lobe transient sharp waves
5. A diagnosis of DLB is *less likely*
   - In the presence of cerebrovascular disease evident as focal neurologic signs or on brain imaging
   - In the presence of any other physical illness or brain disorder sufficient to account in part or in total for the clinical picture
   - If parkinsonism only appears for the first time at a stage of severe dementia
6. *Temporal sequence* of symptoms

Neuropsychiatric Symptoms and Syndromes in a Large Cohort of Newly Diagnosed, Untreated Patients With Alzheimer Disease

American J Geriatr Psych 2010

Gianfranco Spalletta, M.D., Ph.D., Massimo Musicco, M.D., Alesandro Padovani, M.D., Ph.D., Luca Rozzini, M.D., Roberta Perri, M.D., Ph.D., Lucia Fadda, Psy.D., Vincenzo Canonico, M.D., Alberto Trequattrini, M.D., Carla Pettenati, M.D., Carlo Caltagirone, M.D., Katie Palmer, Ph.D.

TABLE 4. Occurrence and Association Between Clinically Significant Syndromes and AD Severity

	No/Mild Syndrome n (%)	Clinically Significant Syndrome n (%)	Odds of Having a Clinically Significant Syndrome		
			OR (95% CI)	Wald	*df*
Psychotic					
Mild AD	576 (94.4)	34 (5.6)	1.0 (reference)		
Moderate AD	281 (87.0)	42 (13.0)	1.9 (1.1–3.2)	5.459	1
Severe AD	69 (84.1)	13 (15.9)	2.6 (1.4–4.8)	8.793	1
Affective					
Mild AD	433 (71.0)	177 (29.0)	1.0 (reference)		
Moderate AD	228 (70.6)	177 (29.0)	0.9 (0.7–1.2)	0.721	1
Severe AD	57 (69.5)	25 (30.5)	0.8 (0.5–1.2)	1.408	1
Manic					
Mild AD	592 (97.0)	18 (3.0)	1.0 (reference)		
Moderate AD	298 (92.3)	25 (7.7)	2.1 (1.0–4.4)	3.666	1
Severe AD	74 (90.2)	8 (9.8)	3.9 (1.8–8.8)	11.204	1
Psychomotor					
Mild AD	563 (92.3)	47 (7.7)	1.0 (reference)		
Moderate AD	276 (85.4)	47 (14.6)	2.0 (1.2–3.3)	7.059	1
Severe AD	60 (73.2)	22 (26.8)	4.2 (2.4–7.2)	26.620	1
Apathetic					
Mild AD	396 (64.9)	214 (35.1)	1.0 (reference)		
Moderate AD	197 (61.0)	126 (39.0)	1.2 (0.9–1.6)	1.367	1
Severe AD	34 (41.5)	48 (58.5)	1.7 (1.2–2.5)	8.596	1

Syndrome severity: no syndrome, score = 0 on at least one of the symptoms in the syndrome; mild syndrome: NPI score 1–3 on every symptom in the syndrome; clinically significant syndrome: NPI score ≥1 on all symptoms in the syndrome with at least one symptom score ≥4.

Journal of Alzheimer's Disease 24 (2011) 35–45
DOI 10.3233/JAD-2010-101836
IOS Press

Predicting Disease Progression in Alzheimer's Disease: The Role of Neuropsychiatric Syndromes on Functional and Cognitive Decline

Katie Palmer[a,*], Federica Lupo[a], Roberta Perri[a,b], Giovanna Salamone[a], Lucia Fadda[a,b], Carlo Caltagirone[a,b], Massimo Musicco[a,c] and Luca Cravello[a]

Table 2
Risk of functional decline over two-year follow-up in AD patients with baseline neuropsychiatric syndromes

		ADL decline		Crude risk of ADL decline		Adjusted for baseline ADL		Adjusted for comorbidity		Fully adjusted model[3]	
		n	%	HR[1]	(95% CI)	HR[1]	(95% CI)	HR[1]	(95% CI)	HR[1]	(95% CI)
Apathy syndrome	No[2]	15	34.1	1.0		1.0		1.0		1.0	
	Yes	44	41.1	1.0	(0.5–1.7)	0.9	(0.5–1.7)	1.0	(0.5–2.1)	0.9	(0.4–1.8)
Affective syndrome	No[2]	29	33.0	1.0		1.0		1.0		1.0	
	Yes	30	47.6	1.8	(1.1–3.0)	1.7	(1.0–2.9)[a]	1.8	(1.0–3.2)[b]	2.0	(1.1–3.6)
Psychomotor syndrome	No[2]	50	36.8	1.0		1.0		1.0		1.0	
	Yes	9	60.0	1.0	(0.4–2.6)	0.9	(0.3–2.4)	1.6	(0.5–4.9)	1.6	(0.5–5.1)
Manic syndrome	No[2]	51	36.7	1.0		1.0		1.0		1.0	
	Yes	8	66.7	2.3	(1.0–5.6)[c]	2.3	(0.9–5.8)	2.1	(0.7–6.1)	2.3	(0.8–6.9)
Psychotic syndrome	No[2]	53	37.3	1.0		1.0		1.0		1.0	
	Yes	6	66.7	2.5	(0.9–6.9)	2.4	(0.8–6.8)	2.4	(0.7–8.4)	1.4	(0.3–5.8)

[1] Hazard ratios calculated with Gompertz regression, with 95% confidence intervals.
[2] Reference category includes patients with any other syndrome and patients with no syndromes.
[3] Adjusted for age, gender, education, baseline ADL, baseline MMSE, and comorbidity (CIRS).
[a] $p = 0.046$; [b] $p = 0.042$; [c] $p = 0.062$.

Journal of Alzheimer's Disease 24 (2011) 35–45
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IOS Press

Predicting Disease Progression in Alzheimer's Disease: The Role of Neuropsychiatric Syndromes on Functional and Cognitive Decline

Katie Palmer[a,*], Federica Lupo[a], Roberta Perri[a,b], Giovanna Salamone[a], Lucia Fadda[a,b], Carlo Caltagirone[a,b], Massimo Musicco[a,c] and Luca Cravello[a]

Table 3
Risk of cognitive decline over two-year follow-up in AD patients with baseline neuropsychiatric syndromes

		MMSE decline		Crude risk of MMSE decline		Adjusted for baseline MMSE		Adjusted for comorbidity		Fully adjusted model[3]	
		n	%	HR[1]	(95% CI)	HR[1]	(95% CI)	HR[1]	(95% CI)	HR[1]	(95% CI)
Apathy syndrome	No[2]	51	79.7	1.0		1.0		1.0		1.0	
	Yes	72	63.7	0.6	(0.4–0.9)	0.6	(0.4–0.9)	0.6	(0.4–1.0)[a]	0.6	(0.4–1.0)[b]
Affective syndrome	No[2]	79	71.2	1.0		1.0		1.0		1.0	
	Yes	44	66.7	0.9	(0.6–1.4)	0.9	(0.6–1.4)	0.8	(0.5–1.2)	0.7	(0.5–1.2)
Psychomotor syndrome	No[2]	110	67.9	1.0		1.0		1.0		1.0	
	Yes	13	86.7	2.4	(1.2–4.5)	2.6	(1.3–5.2)	3.5	(1.5–8.3)	2.3	(0.8–6.5)
Manic syndrome	No[2]	110	67.5	1.0		1.0		1.0		1.0	
	Yes	13	92.9	2.7	(1.4–5.2)	2.6	(1.3–5.0)	2.7	(1.2–5.8)	3.2	(1.3–7.5)
Psychotic syndrome	No[2]	116	69.5	1.0		1.0		1.0		1.0	
	Yes	7	70.0	0.6	(0.2–1.4)	0.6	(0.2–1.5)	0.3	(0.1–1.1)	1.0	(0.2–5.0)

[1] Hazard ratios calculated with Gompertz regression, with 95% confidence intervals.
[2] Reference category includes patients with any other syndrome and patients with no syndromes. All models are adjusted for the presence of other syndromes.
[3] Adjusted for age, gender, education, baseline ADL, baseline MMSE, and comorbidity (CIRS).
[a] $p = 0.030$; [b] $p = 0.049$.

Social Behavior disturbances

Structural anatomy of empathy in neurodegenerative disease

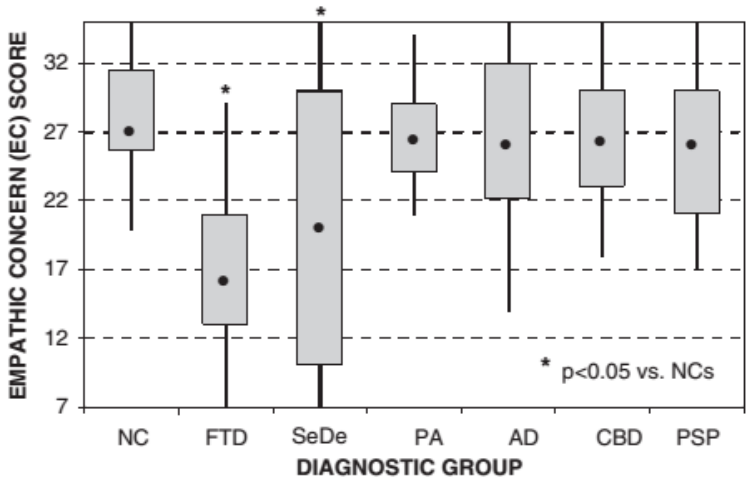
Brain 2006

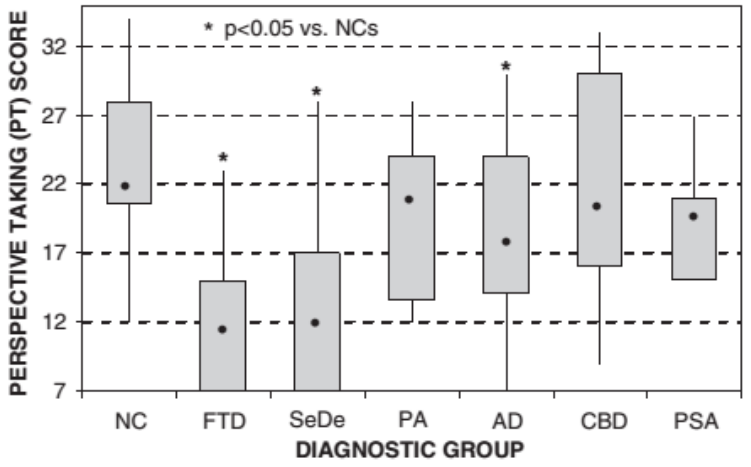
Katherine P. Rankin, Maria Luisa Gorno-Tempini, Stephen C. Allison, Christine M. Stanley, Shenly Glenn, Michael W. Weiner and Bruce L. Miller

INTERPERSONAL REACTIVITY INDEX (IRI)

Prendendo in considerazione il comportamento del/della paziente, decida quanto secondo lei le seguenti affermazioni descrivono il/la paziente. Segni la risposta mettendo una X nell'apposito spazio. Si prega di rispondere a tutte le domande.

Secondo lei il/la paziente…..	**Mai vera**	**Raramente vera**	**Qualche volta vera**	**Spesso vera**	**Sempre vera**
F1. Sogna ad occhi aperti e fantastica regolarmente sulle cose che potrebbero accadergli					
EC2. Prova spesso sentimenti di tenerezza e di preoccupazione per le persone meno fortunate					
PT3. A volte trova difficile vedere le cose dal punto di vista di un altro					
EC4. A volte NON si sente molto dispiaciuto/a per le persone che hanno dei problemi					
F5. Resta veramente coinvolto/a dagli stati d'animo dei protagonisti di un Racconto					
PD6. In situazioni d'emergenza, si sente in tensione e a disagio					
F7. Di solito riesce ad essere obiettivo/a quando guarda un film o una rappresentazione teatrale e raramente si lascia coinvolgere del tutto					
PT8. In caso di disaccordo, cerca di tenere conto del punto di vista dell'altro prima di prendere una decisione					
EC9. Quando vede qualcuno che viene sfruttato, prova sentimenti di protezione nei suoi confronti					





Structural anatomy of empathy in neurodegenerative disease

Brain 2006

Katherine P. Rankin, Maria Luisa Gorno-Tempini, Stephen C. Allison, Christine M. Stanley, Shenly Glenn, Michael W. Weiner and Bruce L. Miller

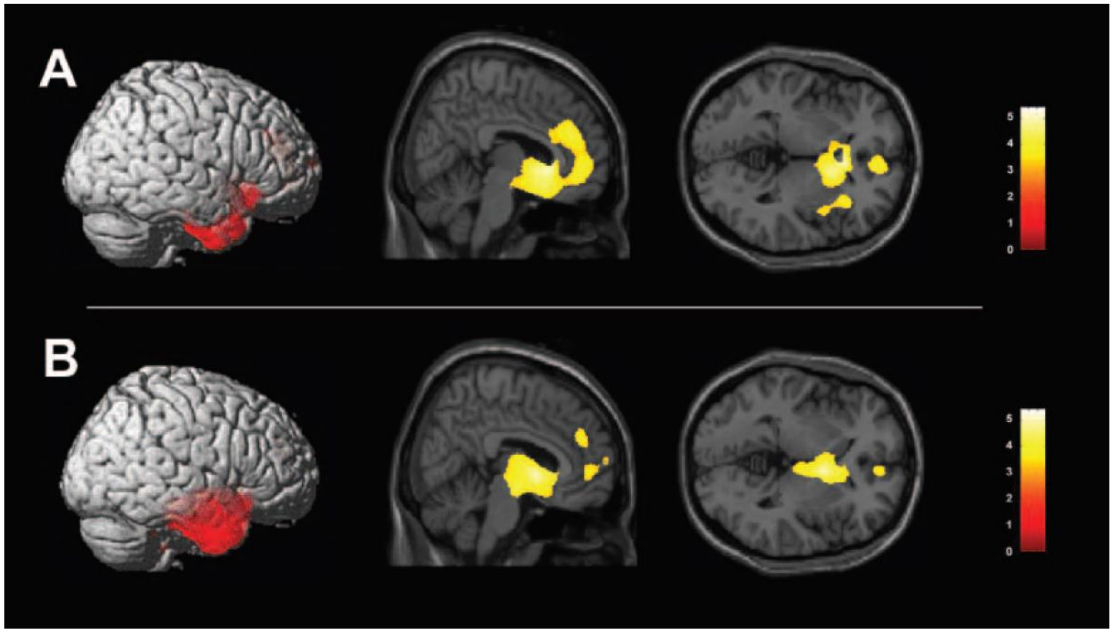


Fig. 5 (**A**) Main effect of EC score, showing rendered, sagittal ($x = 7$) and axial ($z = 0$) views of voxels significantly related to EC score at $P < 0.001$ uncorrected for multiple comparisons across the whole brain. Maps of significant correlation were superimposed on sections of a normal brain template image (SPM2: single_subj_T1.mnc). The design matrix for this analysis contained only EC score, with sex, age and TIV included as nuisance covariates, and a *t*-test was used. (**B**) Main effect of PT score, showing voxels significantly related to PT score at $P < 0.001$ uncorrected. The design matrix for this analysis contained only PT score, with sex, age and TIV included as nuisance covariates, and a *t*-test was used.

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2010, 32 (3), 289–298

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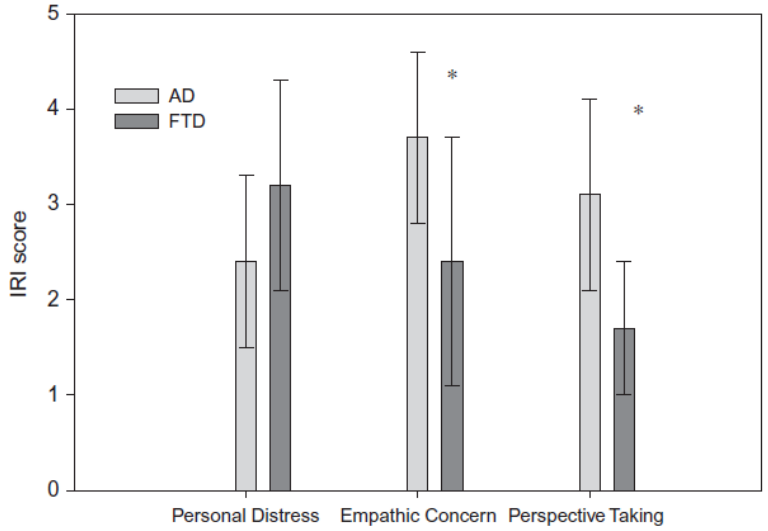
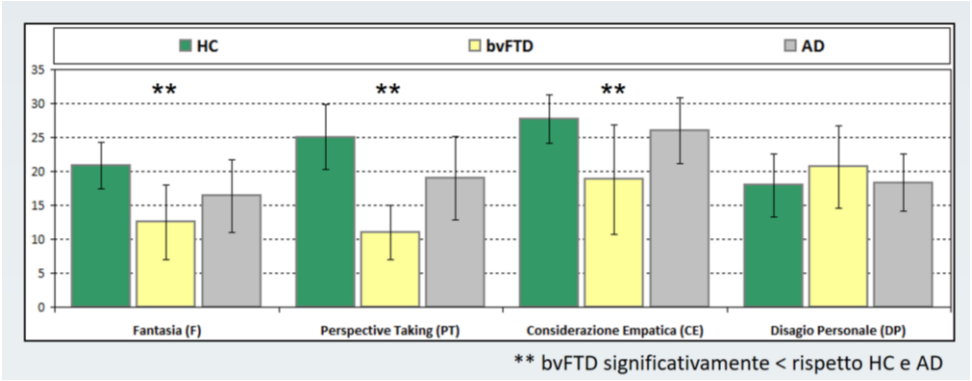
Empathy in frontotemporal dementia and Alzheimer's disease

Diego Fernandez-Duque,[1] Sara D. Hodges,[2] Jodie A. Baird,[3] and Sandra E. Black[4]





personal data

DAPHNE: A New Tool for the Assessment of the Behavioral Variant of Frontotemporal Dementia

Claire Boutoleau-Bretonnière[a, b, h] Christelle Evrard[a, b] Jean Benoît Hardouin[c, d] Laëtitia Rocher[a, b] Tiphaine Charriau[a, b] Frédérique Etcharry-Bouyx[i] Sophie Auriacombe[j] Aurélie Richard-Mornas[k] Florence Lebert[l] Florence Pasquier[l] Anne Sauvaget[e] Samuel Bulteau[e] Martine Vercelletto[a, b] Pascal Derkinderen[a, f] Cédric Bretonnière[g] Catherine Thomas-Antérion[h, m]

Dement Geriatr Cogn Disord Extra 2015;5:503–516

Table 1. DAPHNE scale

	Normal (0)	Very mild (1)	Mild (2)	Moderate (3)	Severe (4)
Hyperorality					
Eating disorders, new preference for sweets	no trouble	subject has a new preference for sweets	subject has new or bizarre food preferences but can listen to reason	subject eats or drinks excessively and cannot listen to reason (padlock on cupboard, etc.)	subject eats and drinks everything within reach, including in other people's plates or glasses, or eats inedible substances
Bulimia, gluttony	no trouble	subject eats much more, has put on weight	subject eats gluttonously, voraciously, without getting dirty	subject eats quickly and gets dirty, takes big pieces, risking choking	subject eats with hands, uncleanly, does not cut his food, keeps food in mouth; subject has put on a lot of weight
Neglect					
Personal neglect	no trouble	subject looks less neat	subject must be stimulated to wash or change clothes	subject can wash or change clothes only when threatened or tricked	subject has very poor hygiene (dirty fingernails, dirty hair, dirty clothes, etc.)
disinhibition		inappropriate sexual comments or jokes, but can stop if asked to	inappropriate and uncontrolled sexual comments or jokes, which he/she then acts on	priate and uncontrolled sexual comments or jokes, which he/she then acts on; subject is indecent (undresses in inappropriate places, etc.)	unwanted and inappropriate sexual behavior (public masturbation, sexual touching of a minor, sexual attraction to animals, etc.)

DAPHNE-6 (screening) is computed from the six synthetic binary domains. For a given domain, score 1 point if at least one symptom is present, regardless of the number of items present in the domain and irrespective of the severity. The maximum score is six.

DAPHNE-40 (diagnosis) is computed as the sum of the boxes of the ten items. The maximum score is 40.

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Table 4. Diagnostic accuracy of the revised criteria and behavioral scales to differentiate bvFTD

	Threshold	Sensitivity	Specificity	Positive likelihood ratio
Rascovsky's clinical criteria	≥3	100%	41%	1.7
DAPHNE-6	≥4	92%	57%	2.1
DAPHNE-40	≥15	56%	92%	**7.0**
DAPHNE 'combined'	–	92%	92%	**11.5**
FBS	≥3	97%	45%	1.7
FBI	≥27	67%	91%	**7.4**

The positive likelihood ratio is assumed to demonstrate the interest of a diagnostic tool when >5, and better >10. Thus, values >5 are written in bold.

TAKE-HOME MESSAGE

Need to Recalibrate Research Outcomes in Alzheimer's Disease: Focus on Neuropsychiatric Symptoms

Marco Canevelli, PhD, Matteo Cesari, PhD,*† Flaminia Lucchini, MD,* Martina Valletta, MD,* Michele Sabino, MD,* Eleonora Lacorte, MSci,§ Nicola Vanacore, PhD,§ and Giuseppe Bruno, PhD**

J Am Geriatr Soc, 2017

OBJECTIVES: To determine whether neuropsychiatric symptoms (NPSs) are adequately considered in clinical research on Alzheimer's disease (AD).

DESIGN: Systematic review.

SETTING: Randomized controlled trials (RCTs) recruiting individuals with AD and published during the last 10 years in 16 major general medicine, neurology, psychiatry, and geriatric psychiatry journals and RCTs registered on clinicaltrials.gov and currently enrolling individuals with AD.

PARTICIPANTS: Individuals with AD.

MEASUREMENTS: Outcome measures adopted by the included studies.

RESULTS: Only 21.4% of the included studies identified through the bibliographic searches had measures of NPSs as a primary outcome. Only 17.7% of the studies retrieved on clinicaltrials.gov made a specific effort to test the effect of pharmacological or nonpharmacological interventions on NPSs.

CONCLUSION: These findings show how rarely previous and current research on AD has considered NPSs as primary research targets. Although these symptoms are widely recognized as the most-stressful and -challenging manifestations of dementia, they are addressed much less often than other research targets. J Am Geriatr Soc 65:2071–2073, 2017.

This study has some limitations. In particular, the narrow focus on a limited body of evidence (only 16 scientific journals plus the clinicaltrials.gov registry) might have prevented the hypothesis from being thoroughly explored, although the main aim was to provide a brief, concise, clinically friendly message emerging from commonly adopted and referenced sources of evidence.

In conclusion, reducing the burden of NPSs should be more widely considered as a priority in research on AD and other dementias. Further exploration of the clinical and neurobiological determinants of NPSs is also needed. This also implies the need to develop specific tools allowing a more-accurate and ecological assessment of NPSs. Ad hoc RCTs targeting NPSs are also urgently needed.

SINdem4Juniors

6th Winter Seminar on Dementia and Neurodegenerative Disorders

January 17-19, 2018

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Dolomiti – Sud Tirol

Save the date!

January 17th - Contamination Session

January 18-19th - Scientific Session

Deadline for abstract submission and moderators call:
November 19th

Call for Abstracts

Call for Young Moderators

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