

**10° Convegno Nazionale sui Centri Diurni Alzheimer**  
*1-2 marzo 2019*

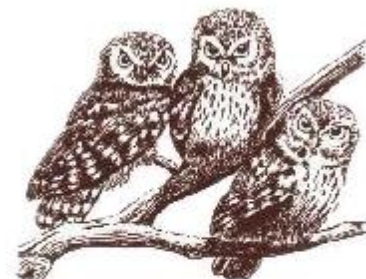


**Il ruolo del consulente medico e della  
terapia psicofarmacologica in Centro  
Diurno Alzheimer**

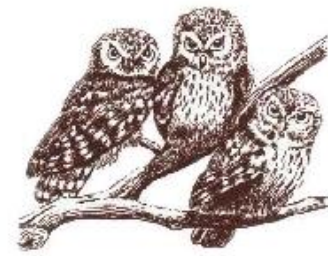
**Dr. Maristella Piccininni**  
**Responsabile Percorso demenze Firenze**  
**U.O. Neurologia**

# Tipologia del paziente che accede al CDA

- Cluster agitato/aggressivo
  - durante tutta la giornata
  - in particolari situazioni che implicano il contatto con il proprio corpo (toilette, bagno, igiene)
- Cluster apatico
- Cluster psicotico
- Tentativi di fuga



# ATTIVITA' DEL CENTRO

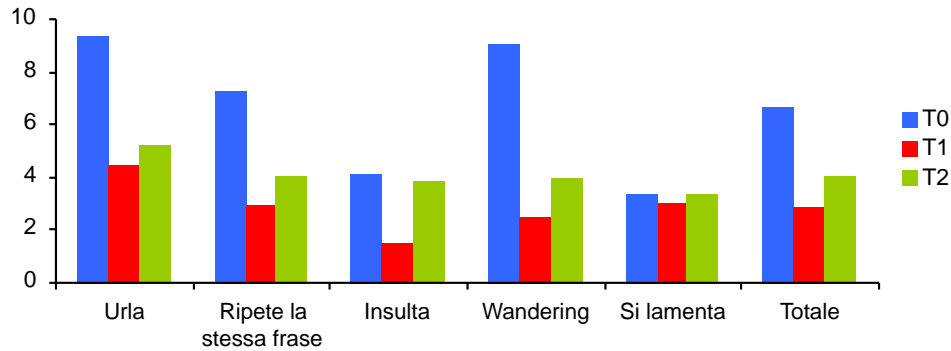


Centro Diurno Alzheimer  
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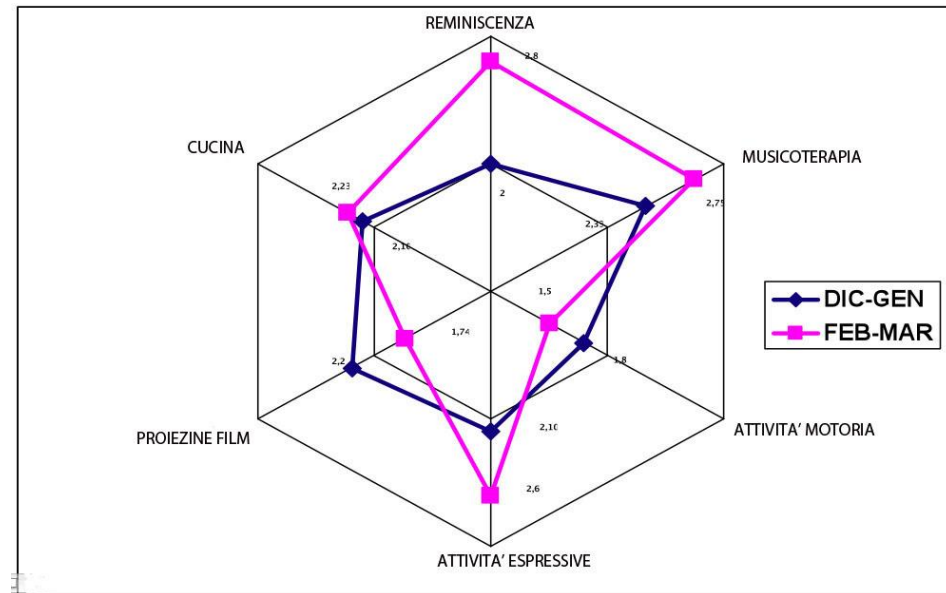
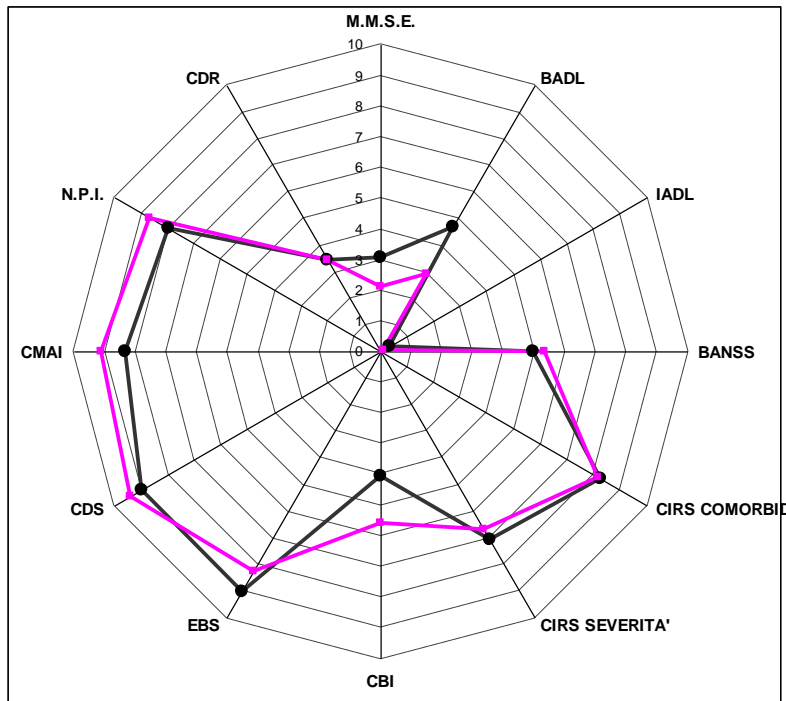
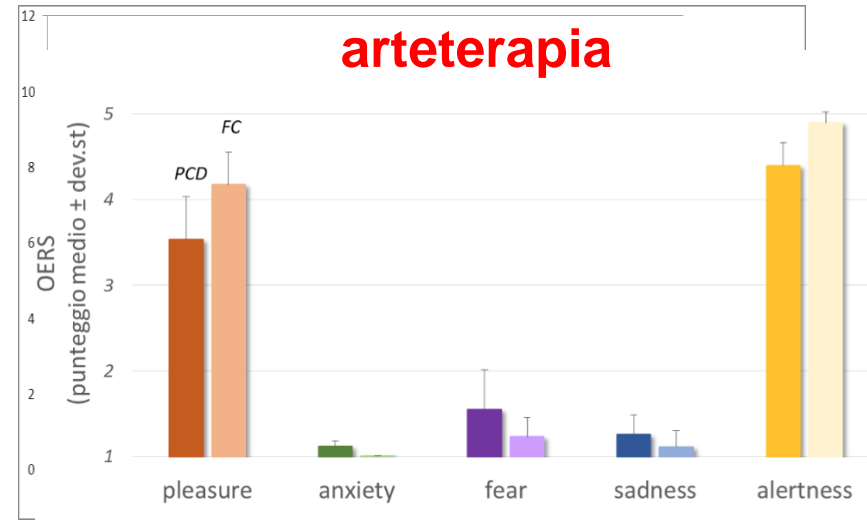
- ✓ Attività domestiche / giardinaggio / cucina
  - ✓ Musicoterapia (individuale e di gruppo)
  - ✓ Arteterapia – attività espressive
  - ✓ Attività di Reminiscenza
  - ✓ Doll therapy
  - ✓ Snoezelen
  - ✓ Fisioterapia e attività motoria
  - ✓ Proiezione film, documentari e opera
- Approccio Validante e Personalizzato

# Esperienza del CDA LE CIVETTE

## Snoezelen



## arteterapia



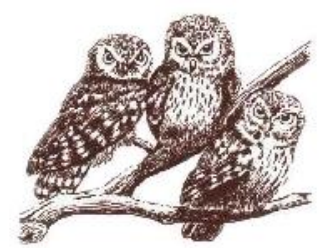
# IL PIANO ASSISTENZIALE INDIVIDUALE (PAI).



Interventi psico-sociali



Interventi farmacologici



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# Ruolo del medico

- Rimodulare la terapia con psicofarmaci in base all'efficacia degli interventi psico-sociali
- Individuare fattori scatenanti sia dall'osservazione diretta che tramite colloquio con gli operatori
- Identificare fattori che favoriscono l'accettazione dell'evento da parte del paziente
- Utilizzo di farmaci per consentire un migliore approccio a determinate situazioni (igiene personale) o in particolari circostanze (trasporto in macchina o pulmino)
- Utilizzo di farmaci per favorire partecipazione agli interventi psico-sociali del paziente apatico

# Gestione non farmacologica durante il bagno

- ✓ Almeno 1 h prima parlare dell'argomento( tra poco ci laviamo...così poi ti potrai mettere...)
- ✓ Rispetto del giorno e del modo (bagno/doccia) secondo le sue abitudini
- ✓ Rispetto fattori di sicurezza: stuoino, maniglie, sedile.....
- ✓ Evento presentato come giocoso e tranquillo, approccio non direttivo, occhio a temperatura ambiente, acqua, occhio a illuminazione, caregiver sempre di fronte a portata di vista onde evitare paura alle spalle
- ✓ Se totalmente rifiutato: 1)bagno a letto, senza uso di sapone da risciacquare, ma con panni umidi di acqua tiepida 2) bagno a pezzi, lunedì gambe, martedì torace...
- ✓ Se nudità crea imbarazzo: si mantiene calze e biancheria intima che molto spesso quando bagnate il paziente acconsente a toglierle

# Sequential drug treatment algorithm for agitation and aggression in Alzheimer's and mixed dementia



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Benoit H Mulsant<sup>1,2,3</sup> and Tarek K Rajji<sup>1,2,3</sup>**

3) For the Following Drugs .... BENZODIAZEPINES, ZOPICLONE (and other Z-DRUGS)

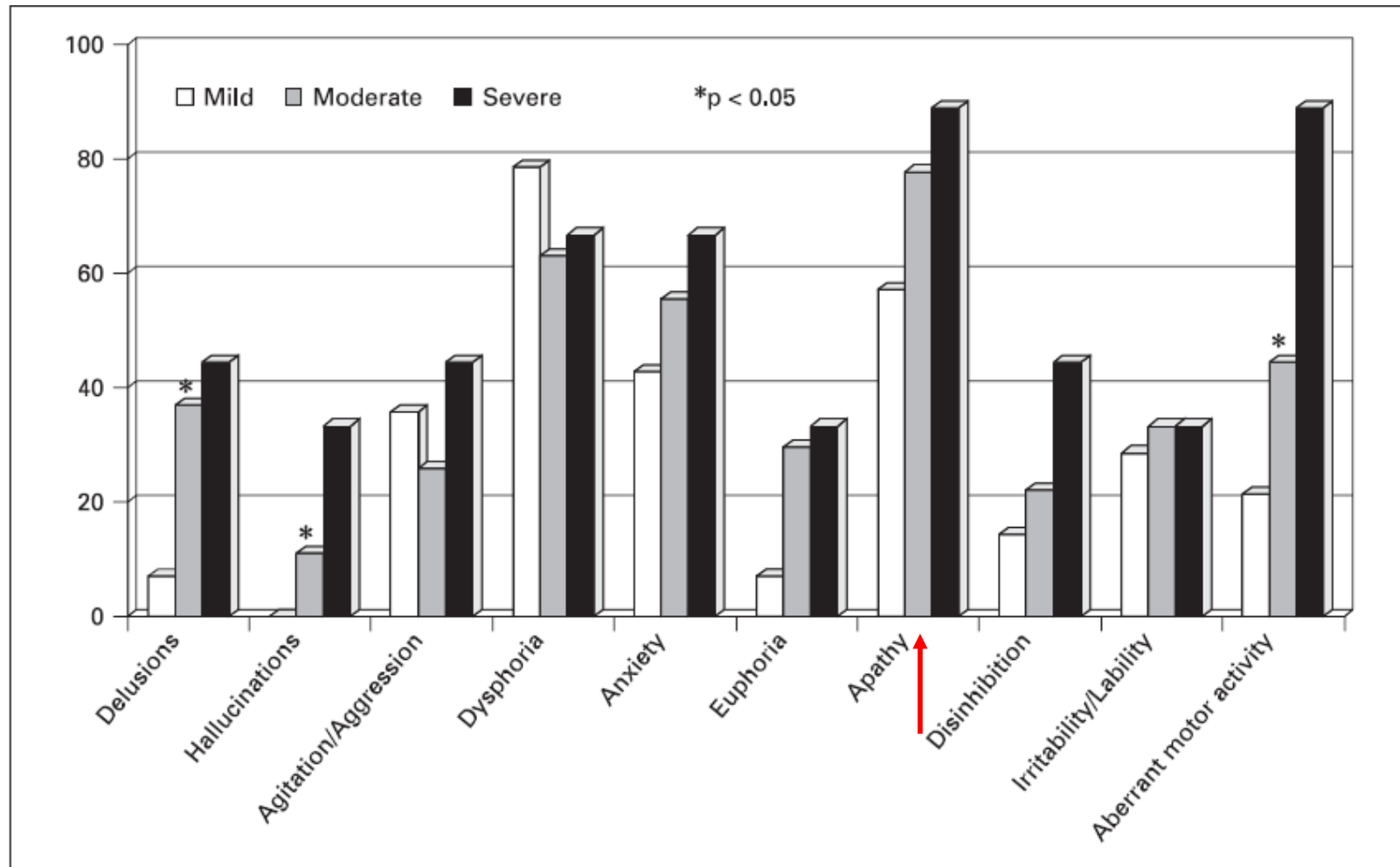
- DISCONTINUE UNLESS CLEAR RECENT EVIDENCE OF INSURMOUNTABLE DIFFICULTY IN STOPPING
- WHERE DISCONTINUATION INDICATED, IT SHOULD BE UNDERTAKEN AS SLOWLY AS NEEDED FOR SAFETY (therefore may continue down-titration process beyond 10 days).

4) During Clean up period, may use PRN PSYCHOTROPIC DRUGS AS FOLLOWS

- a) TRAZODONE : can be used 25 mg every hour as needed, initial maximum set at 150mg/24hours, may be increased at prescriber discretion to 300mg in 24 hours in non-FRAIL patients. NOTES: helpful as inducer of sleep but could cause paradoxical agitation in some patients due to anxiogenic metabolite, watch for falls, hypotension and excessive sedation
- b) BENZODIAZEPINES (use lorazepam 0.5 mg every 4 hours as needed, max 2 mg/24 hours).
  - While a PRN benzodiazepine drug can be helpful to allow procedures such as imaging and activities such as dental visits to take place, it may cause agitation and disinhibition, in particular in those with frontal deficits, therefore patients should be assessed for risks of falls and excessive sedation.



# Frequency of each behavioral disturbance at the various levels of mental impairment in AD patients



# Apatia nella Demenza di Alzheimer

Presenza di perdita di motivazione e iniziativa in ognuno dei seguenti ambiti:

- a) diminuzione di comportamenti diretti a uno scopo
- b) diminuzione di attività cognitive dirette a uno scopo (diminuzione dell'interesse nell'apprendere nuove cose o nuove esperienze, riduzione dell'interesse per i propri problemi)
- c) diminuzione di aspetti correlati al comportamento diretto a uno scopo (riduzione della risposta emotiva a eventi positivi e negativi)

# APATIA E DEPRESSIONE

## SINTOMI DELL'APATIA

Risposta emotiva offuscata  
Indifferenza  
Scarso coinvolgimento  
Scarsa intraprendenza  
Incostanza

## SINTOMI COMUNI

Riduzione interessi  
Lentezza psicomotoria  
Astenia  
Ipersonnia  
Anosognosia

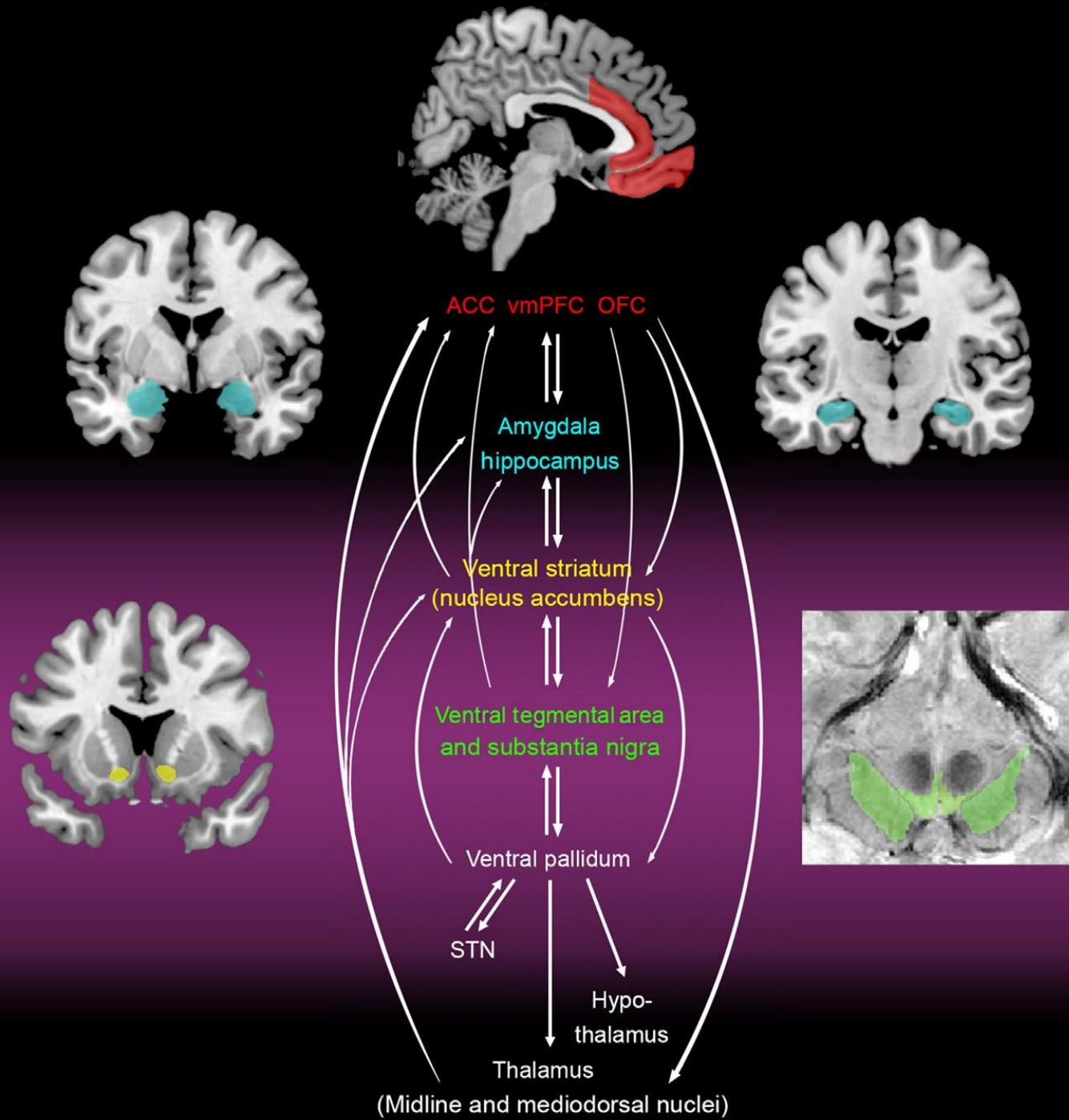
## SINTOMI DELLA DEPRESSIONE

Disforia  
Ideaioni suicidarie  
Sensi di colpa  
Eccessiva criticità  
Pessimismo  
Mancanza di speranza

# Prevalenza dell'apatia

Disorders	Prevalence
Mild Cognitive Impairment <sup>40,51,52</sup>	14.7% <sup>2</sup> –39.8% <sup>51</sup>
Parkinson's disease <sup>5,33,53–61</sup>	17.0% <sup>56</sup> –45.7% <sup>61</sup>
Progressive supranuclear palsy <sup>5,29,56,61,62</sup>	22% <sup>61</sup> –91% <sup>5,29</sup>
Huntington's disease <sup>5,62</sup>	59% <sup>5</sup> –82% <sup>62</sup>
Corticobasal degeneration <sup>61,63</sup>	40% <sup>61,63</sup>
Frontotemporal dementia <sup>5,37,64,65</sup>	89% <sup>5</sup> –100% <sup>65</sup>
Dementia with Lewy body	52% <sup>61</sup>
Multiple sclerosis <sup>66,67</sup>	20% <sup>66</sup> –31% <sup>67</sup>
Stroke <sup>12,15,68–70</sup>	15.2% <sup>12</sup> –42% <sup>70</sup>
Vascular dementia <sup>32,37,38,48,71</sup>	22.6% <sup>48</sup> –93.6% <sup>37</sup>
Traumatic brain injury <sup>72,73</sup>	20% <sup>72</sup> –70% <sup>73</sup>
Amyotrophic lateral sclerosis <sup>74</sup>	55.6% <sup>74</sup>
HIV <sup>9</sup>	12% <sup>9</sup>
Cardiovascular disease <sup>71</sup>	29% <sup>71</sup>

HIV, Human Immunodeficiency Virus.





# NIH Public Access

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## New Approaches to the Treatment of Frontotemporal Lobar Degeneration

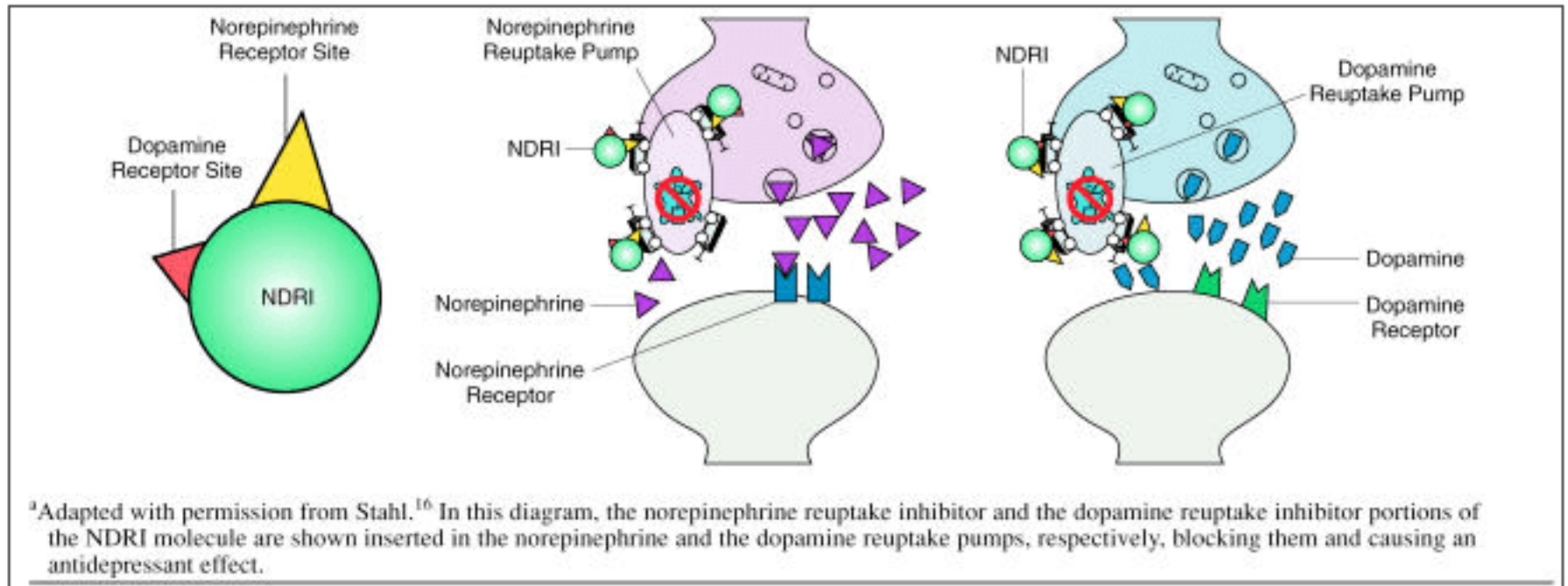
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### Apathy

Apathy, characterized by paucity of spontaneous ideation and motivation, localizes to the medial frontal lobe [5,34], a region that is atrophied in all FTLN clinical syndromes, particularly bvFTD [5]. In general, apathy is recalcitrant to pharmacotherapy and can be a welcome relief for the caregivers in the severely disinhibited patient. In some cases, though we have tried bupropion. Bupropion has additional indirect dopaminergic agonist properties [35] and could be considered in a patient with Parkinsonism who is suspected of having low dopamine levels.

# Profilo recettoriale del bupropione



- ❑ Farmacocinetica: emivita 8-10
- ❑ Trasformato in 3 metaboliti attivi con T/2 di 24 h
- ❑ Metabolismo: epatico CYP 2B6
- ❑ Eliminazione: renale
- ❑ Effetti collaterali: eccitazione, insonnia, nausea

# Interventi non farmacologici per l'apatia nella malattia di Alzheimer

Trial	N (IG/C)	Intervention	Treatment Duration (Weeks)	Apathy Scale (Primary)	Outcome <sup>a</sup>	Comments
Amieva et al, 2016 <sup>107</sup>	653 (499/154), cognitive training (n = 170), reminiscence therapy (n = 172), individualized cognitive rehabilitation program (n = 157)	Individual cognitive therapies cognitive training (group sessions), reminiscence therapy (group sessions), individualized cognitive rehabilitation program (individual sessions) vs controls	104	NPI/Apathy Inventory (rate of survival at 2 years for patients without moderately severe to severe dementia)	Greater clinical improvement was seen with the individualized cognitive rehabilitation intervention (lower functional disability and delayed institutionalization)	Apathy secondary measure
Treusch et al, 2015 <sup>108</sup>	117 (67/50)	Biography-orientated mobilization	40	AES/NPI (AES/NPI)	Positive	
Ferrero-Arias et al, 2011 <sup>109</sup>	146 (73/71)	Music and art therapy and psychomotor activity or free activities in the day room	8	NPI/DAIR (NPI/DAIR)	Positive	Institutionalized or day care patients with dementia
Leone et al, 2013 <sup>110</sup>	230 (119/111)	Nursing home staff education program	16	NPI/AI (NPI/AI)	Positive	13 Nursing homes
Baker et al, 2001 <sup>111</sup>	33 (15/18)	MSS	4	Interact Short/BRS/BMD (Interact Short /BRS/BMD)	Positive	7 VaD and 10 mixed patients with dementia included Benefit declined following end of intervention
Baker et al, 2003 <sup>112</sup>	136 (65/71)	MSS	4	BRS/BMD/GIP/Interact Short (BRS/BMD/GIP/ INTERACT Short)	Negative	3 Country sites. Data used here include data used in the study by Baker et al <sup>111</sup>
Sánchez et al, 2016 <sup>113</sup>	32 (11/10), n = 11 for one-to-one activity session	MSSE vs one-to-one activity session vs control group.	16- and 8-weeks follow-up	NPI (NPI)	MSSE may have better effects on neuropsychiatric symptoms and dementia severity in comparison with one-to-one activity sessions	Improvements found during the intervention were lost in the follow-up period
Niu et al, 2010 <sup>114</sup>	32 (16/16)	Cognitive stimulation.	10	NPI (NPI)	Positive	
Maci et al, 2012 <sup>115</sup>	14 (7/7)	Cognitive stimulation, physical activity, and socialization	12	AES (AES)	Positive	
Politis et al, 2004 <sup>116</sup>	36 (18/18)	Kit-based activity intervention	4	NPI (NPI)	Positive	
Holmes et al, 2006 <sup>117</sup>	32	Live interactive music	Immediately	DCM (DCM)	Positive	Only immediate effects of a 30-minute intervention are reported
Raglio et al, 2010 <sup>118</sup>	60 (30/30)	Music therapy	24	NPI (NPI)	Positive	



# Interventi non farmacologici per l'apatia nella malattia di Alzheimer

**Table 5.** (continued)

Trial	N (IG/C)	Intervention	Treatment Duration (Weeks)	Apathy Scale (Primary)	Outcome <sup>a</sup>	Comments
Gidin et al, 2008 <sup>122</sup>	60 (30/30)	Tailored activity program or wait-list control	16	Activity engagement measured using a 5-item, investigator-developed index of caregiver report of patient in the past 2 weeks	Positive	Apathy nonspecific outcome reported
Lam et al, 2010 <sup>123</sup>	74 (37/37)	Individualized daily activities (functional enhancement program)	16	NPI (NPI)	Positive	
Staal et al, 2007 <sup>124</sup>	24 (12/12)	Multisensory behavior therapy	Immediately	Assessment of negative symptoms in Alzheimer Disease Scale (assessment of negative symptoms in Alzheimer Disease Scale)	Positive	Effects after 6 sessions of a 25- to 30-minute intervention are reported
Chapman et al, 2004 <sup>125</sup>	54 (26/28)	Cognitive communication stimulation (Donepezil-plus) vs Donepezil-only)	48	NPI (NPI)	Negative	Differences in change scores were at $P = .0773$ for the apathy severity index, $P = .0556$ for a group factor, $P = .0618$ for a group $\times$ time factor Effect size was 0.45, in apathy severity index

Abbreviations: AES, Apathy Evaluation Scale; AI, Apathy Inventory; BMD, Behavior and Mood Disturbance Scale; BRS, Behavioral Rating Scale; DAIR, Dementia Apathy Interview and Rating; DCM, dementia care mapping; GIP, Gedragsobservatieschaal voor de Intramurale Psychogeriatric; IG/C, Intervention Group/Controls; MOSES, Multidimensional Observation Scale for elderly participants; MSS, multisensory stimulation; MSSE, multisensory stimulation environment; NPI, Neuropsychiatric Inventory; (Primary), Primary Outcome measure for the study; RCT, randomized controlled trial; VaD, vascular dementia.

<sup>a</sup>Table with RCTs after excluding the overlapping studies. Positive outcome for statistical significant results ( $P < .05$ ) favoring the specific treatment for apathy.

# Sindrome del tramonto



Definizione: comparsa improvvisa ed imprevedibile di stato confusionale, di iperattività motoria, comportamento agitato e deficit della vigilanza nelle ore pomeridiane e/o serotine con picco tra le 15.00 e le 17.00

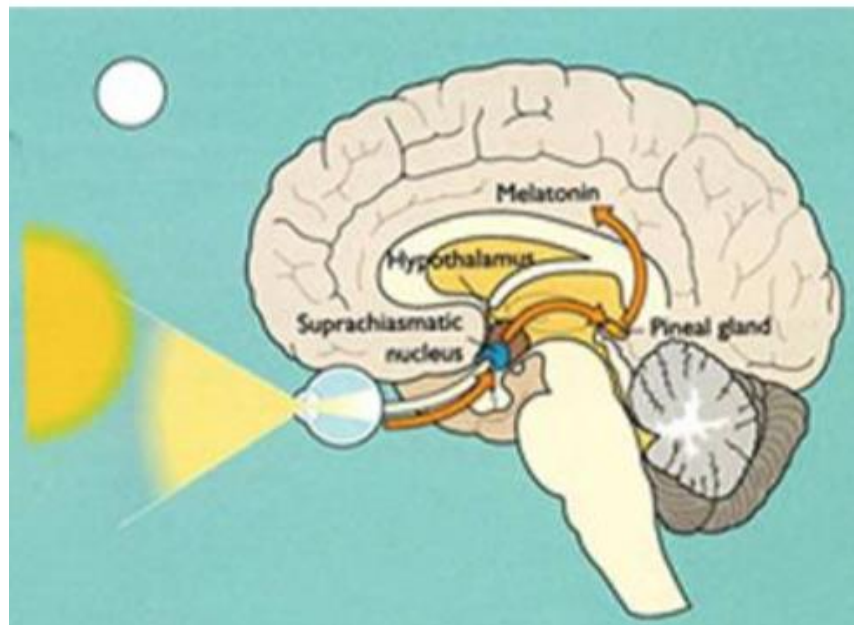
Colpisce il 10% anziani e 80% AD



# Sundowning in Dementia: Clinical Relevance, Pathophysiological Determinants, and Therapeutic Approaches

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Fabrizia D'Antonio, Leonardo Tariciotti, Carlo de Lena and Giuseppe B...

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**TABLE 1 | Factors that have been associated with the pathophysiology and clinical occurrence of sundowning among persons with dementia.**

Neurobiological factors	Degeneration of the suprachiasmatic nucleus Decreased melatonin production Disruption of circadian rhythms Impaired cholinergic neurotransmission Dysregulation of the HPA axis
Pharmacological factors	Antipsychotics Anticholinergics Antidepressants Hypnotics
Physiological factors	Fatigue Hunger Unmet physical or psychological needs Temporal changes in body temperature Circadian modifications of blood glucose levels Circadian changes in blood pressure
Medical factors	Sleep disorders Sensory deprivation Pain Mood disorders and fluctuations Cognitive deficits (e.g., agnosia)
Environmental factors	Exposure to inadequate amount of light Lower staff-patients ratio in residential facilities Lessened availability of home caregivers Caregiver fatigue Environmental overstimulation (noise and chaos)

# Sundowning in Dementia

**TABLE 2 | Experimental studies investigating the clinical effectiveness of pharmacological and non-pharmacological therapies for the management of sundowning in dementia.**

Reference	Study design	Study sample	Intervention	Assessment	Main outcomes
<b>Melatonin</b>					
Fainstein et al. (48) Brusco et al. (49)	Open-label	41 elderly subjects (10 with Alzheimer's disease (AD) and vascular dementia)	3 mg/day for 21 days	Daily logs of sleep and wake quality completed by caregivers	Significant decrease of sundown agitation in the 70% of demented patients. Decrease of the coefficient of variation of bed time between days 0–2 and days 19–21 of treatment ( $58.0 \pm 24.7$ vs $41.5 \pm 20.9$ ; $p = 0.03$ )
Brusco et al. (49)	Retrospective	14 outpatients with AD; mean MMSE score: $14.4 \pm 7.9$	9 mg/day for 22–35 months	Daily logs of sleep and wake quality completed by caregivers	Remission of sundowning 12 patients; attenuation in two cases. Significant improvement of sleep quality between baseline and end of treatment ( $p < 0.01$ )
Cohen-Mansfield et al. (50)	Open-label	11 older nursing home residents with dementia	3 mg/day for 21 days	Daily logs of sleep and wake quality completed by nurses, Cohen-Mansfield Agitation Inventory	Significant reduction of sundown agitation between week 1 and 4 (physically non-aggressive behavior: 1.92 vs 1.46; $p = 0.022$ . Verbally non-aggressive behavior: 2.30 vs 1.75; $p = 0.028$ )
Cardinali et al. (31)	Open-label	45 outpatients with AD	6–9 mg/day for 4 months	Daily logs of sleep and wake quality completed by caregivers	Suppression of sundowning (regardless of the concomitant medication employed to treat cognitive or behavioral signs of AD)
Mahlberg et al. (51)	Open-label	7 AD outpatients	3 mg/day for 3 weeks	Actigraphy	Remission of sundowning in four patients; attenuation in two cases
<b>Light therapy</b>					
Satin et al. (41)	Open-label	10 AD inpatients	2 h/day of exposure to bright light between 7:00 and 9:00 p.m. for 1 week	Clinical observation and actigraphy	Reduction of sundowning episodes

Only studies specifically targeting sundowning were included in the table.

# Interventi non farmacologici nella sundown syndrome

- ✓ Evitare di impegnare il paziente in attività o di formulare richieste pressanti e complicate
- ✓ proporgli delle situazioni tranquille in cui si possa rilassare come, per esempio, ascoltare musica
- ✓ Ridurre al minimo gli stimoli
- ✓ Aumentare l'illuminazione evitando eccessive zone d'ombra
- ✓ Proporre interventi di attività fisica
- ✓ Evitare riposi pomeridiani
- ✓ Proporre un bagno caldo e rilassante che possa predisporre al riposo notturno
- ✓ evitare, assunzione di alcool, thè e caffè
- ✓ Curare il tono della voce evitando noi stessi di essere troppo impositivi ed aggressivi
- ✓ Non avere fretta
- ✓ Utilizzare un linguaggio non verbale
- ✓ Garantire la sicurezza fisica ed ambientale

# Vantaggi della presenza di un medico del CDCD

- Rapidità di accesso nei casi urgenti
- Continuità terapeutica
- Possibilità di presa in carico dei caregivers
- Possibilità di prescrizione dei farmaci
- Accesso a pazienti con demenze più rare e/o giovanili



*Grazie per l'attenzione*