Profili cognitivi e psicocomportamentali delle demenze

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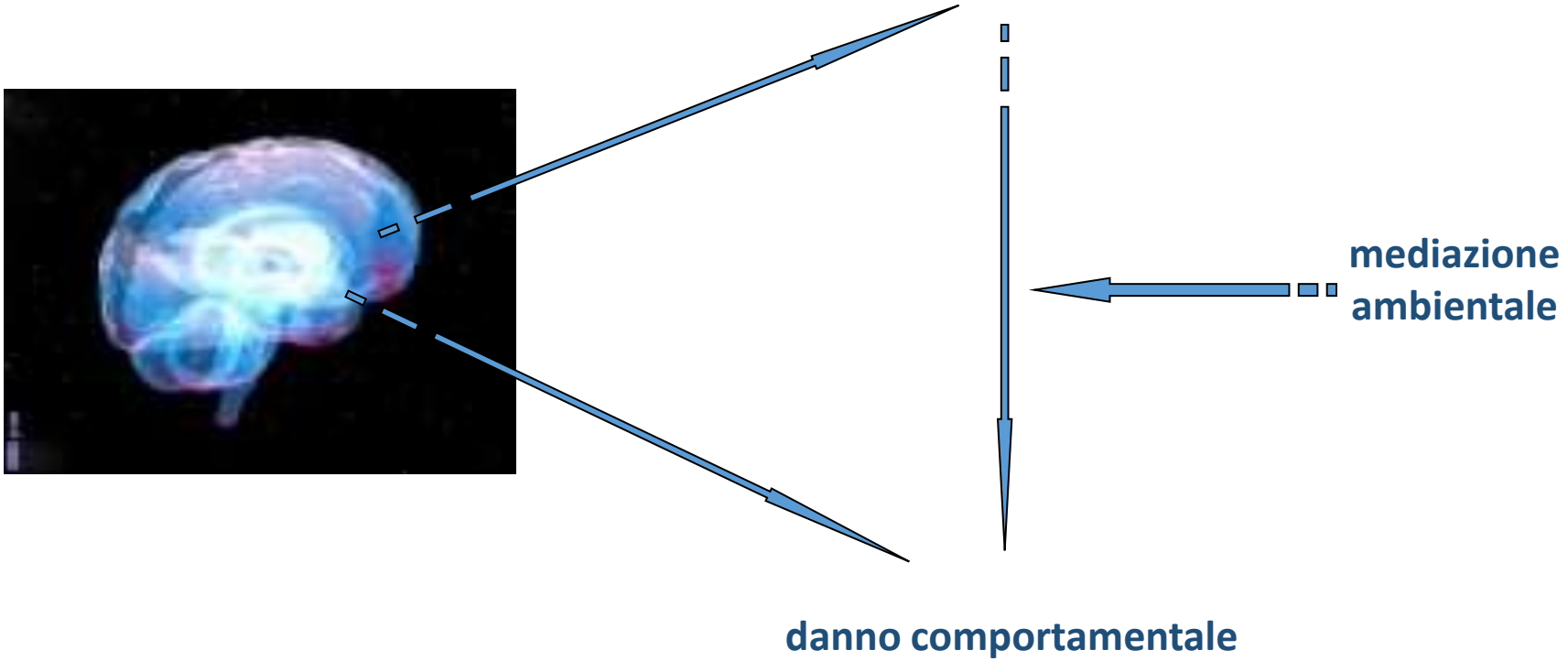
I disturbi cognitivi e psicocomportamentali nella demenza possono essere considerati espressioni cliniche diverse di uno stesso danno neurale?

(es: nella malattia da corpi di Lewy: rapporto tra allucinazione visiva e disturbo viosuospaziale) (Tiraboschi et al., 2006)


danno cognitivo
mediazione ambientale
danno comportamentale

I **disturbi cognitivi** identificano in maniera più specifica un particolare tipo di demenza

I **disturbi psicocomportamentali** sono meno specifici

(nella variante frontale/comportamentale della DFT sono tuttavia caratteristici e costituiscono il nucleo della sintomatologia)

Mancanza di chiari modelli neurobiologici del disturbo psicocomportamentale (rapporto tra substrato neurofunzionale e manifestazione clinica)

Alcune ipotesi

✓**sulla localizzazione del danno**

•***Depressione, apatia:*** *regioni parietali, temporali, giro cingolato anteriore, prefrontali, substantia nigra*

•***Sintomi psicotici:*** *regioni frontali*

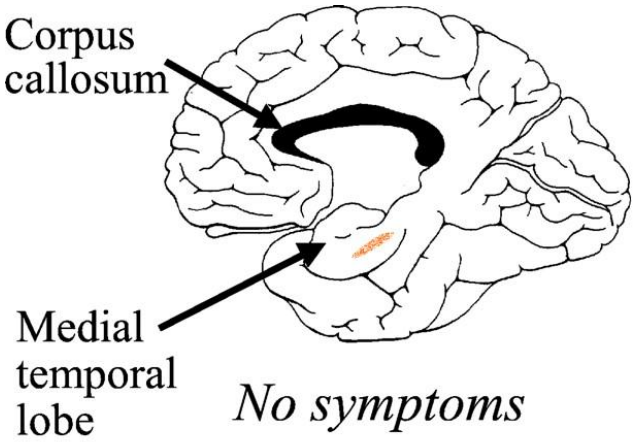
✓ **sull'alterazione dei sistemi recettoriali**

•***Serotonina vs. attività noradrenergica (comportamento aggressivo)***

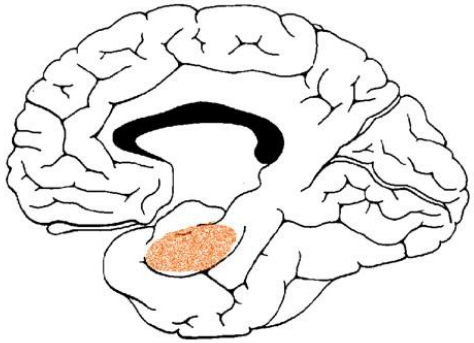
•***Sistema colinergico vs. monoaminergico (disordini affettivi)***

•***Ridotto tono serotoninergico***

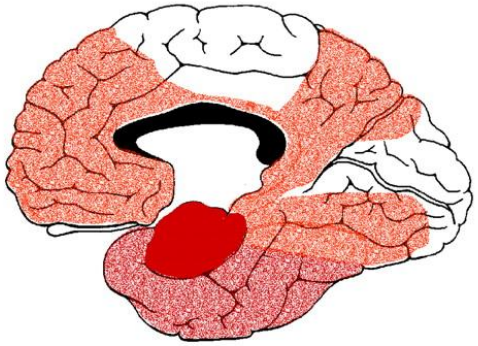
Malattia di Alzheimer



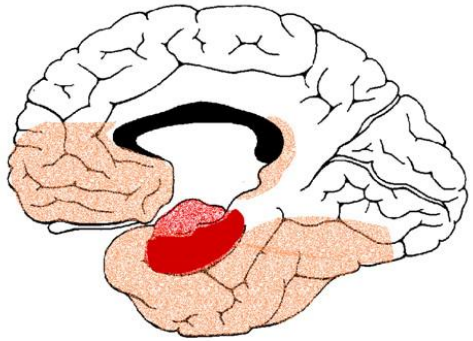
No symptoms



No obvious symptoms

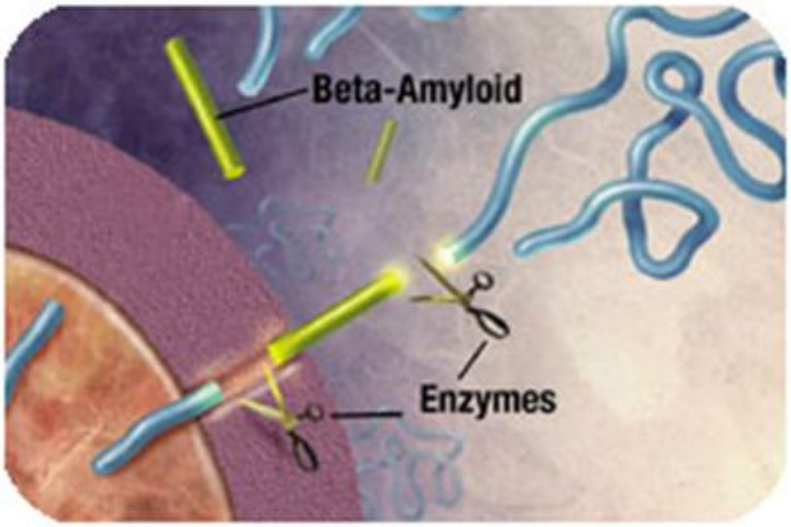


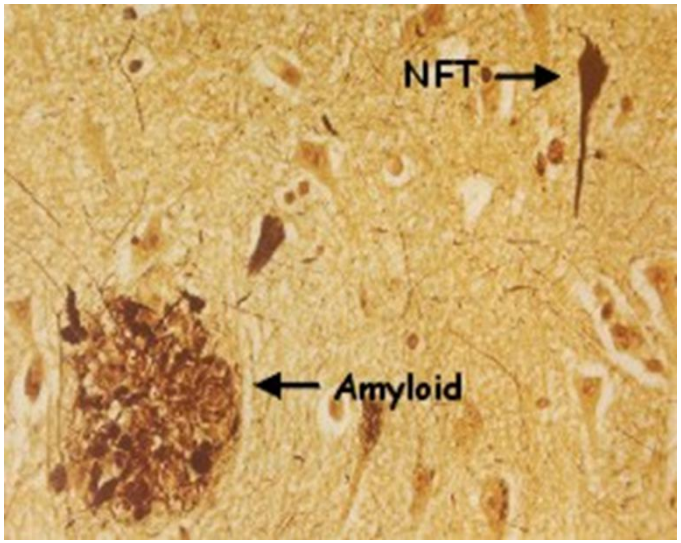
Dementia

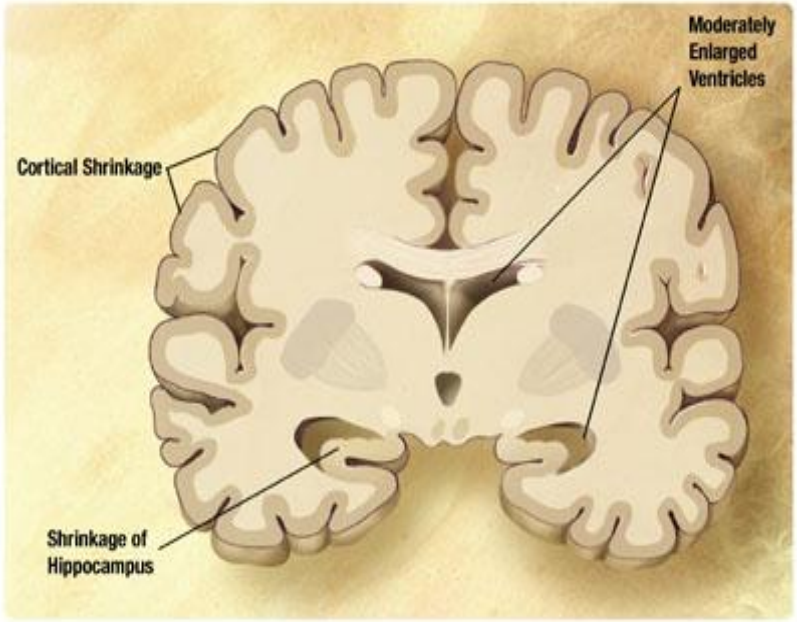


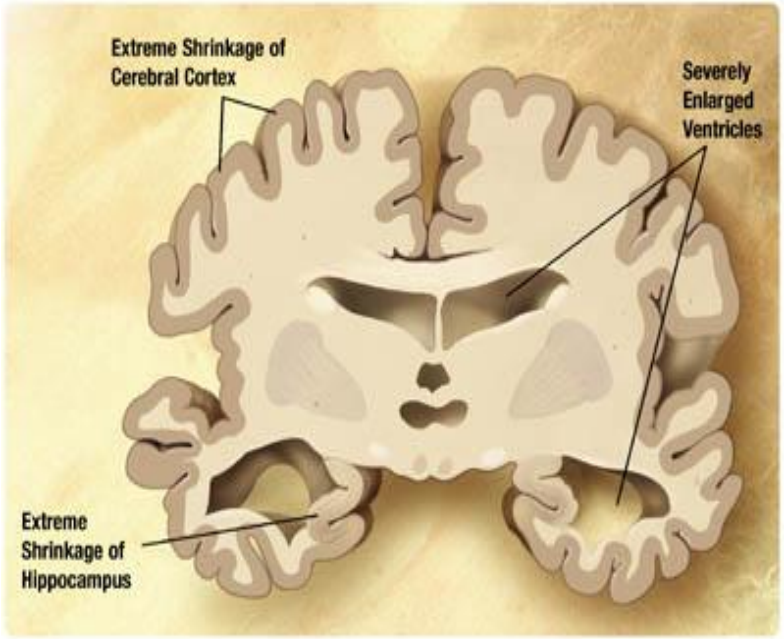
Mild cognitive impairment

Smith, A. David (2002) Proc. Natl. Acad. Sci. USA 99, 4135-4137

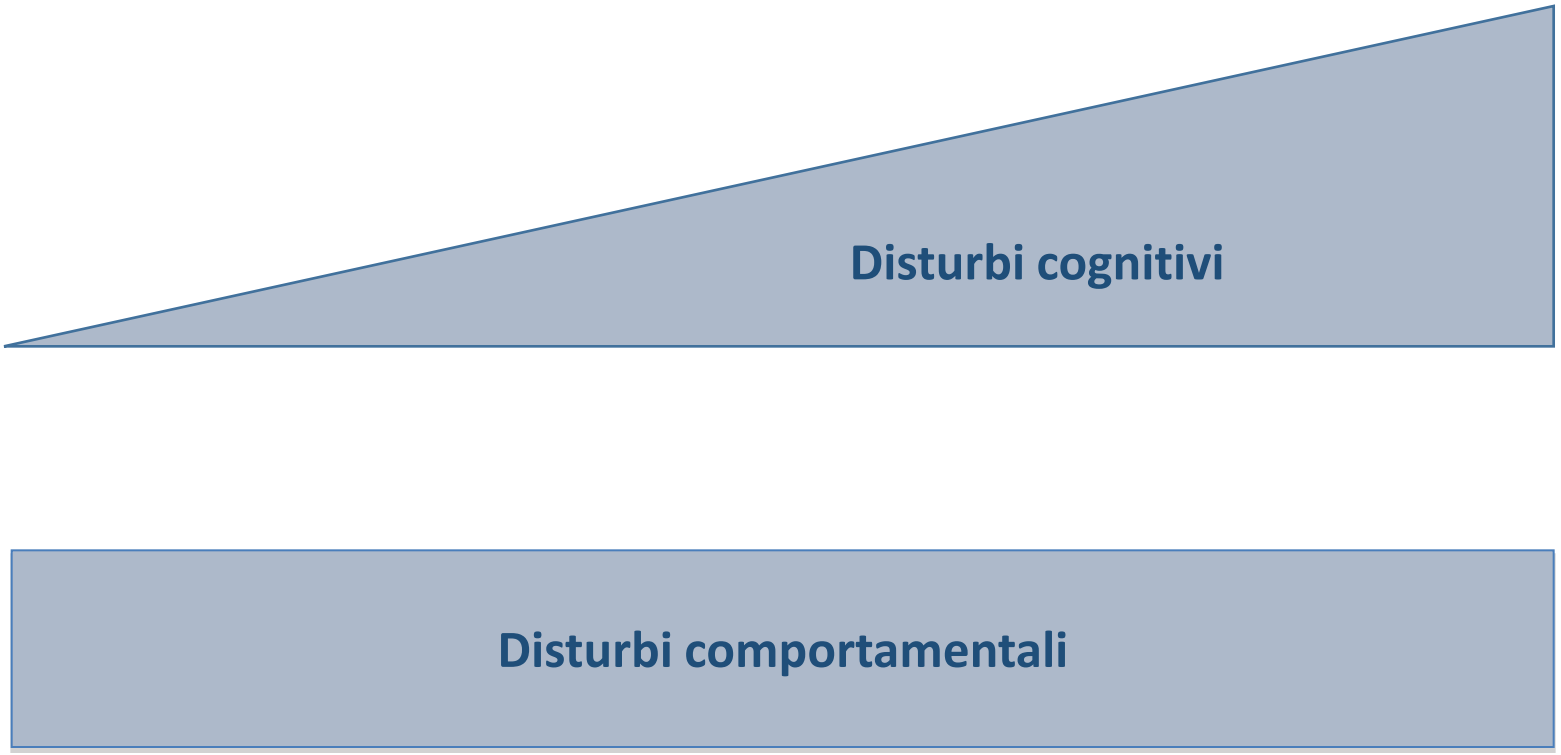

Beta-Amyloid
Enzymes


NFT
Amyloid


Moderately
Enlarged
Ventricles
Cortical Shrinkage
Shrinkage of
Hippocampus


Extreme Shrinkage of
Cerebral Cortex
Severely
Enlarged
Ventricles
Extreme
Shrinkage of
Hippocampus

demenza di Alzheimer
storia naturale della malattia



EVOLUZIONE DEL DEFICIT COGNITIVO NELLA MALATTIA DI ALZHEINER

Progressione della malattia

MEMORIA

deficit dell'
"ongoing memory"
e della memoria
prospèttica

deficit di memoria episodica
e semantica

coinvolgimento
della memoria di
breve termine e della
memoria
procedurale

amnesia globale

FUNZIONI DI CONTROLLO/ WORKING MEMORY

riduzione della risorsa
attenzionale disponibile

compiti automatici
facilitati rispetto a
compiti intenzionali

deficit del pensiero
logico-deduttivo

compiti intenzionali
attuabili con incremento
del carico attenzionale

risposte riflesse

FUNZIONI STRUMENTALI

anomia

eloquio ridotto
e poco informativo

disturbi percettivi

aprassie

disorientamento
topografico

linguaggio
parafasico

**sindrome
afasico-agnosico- aprassica**

Malattia di Alzheimer
disturbi psicologici e comportamentali

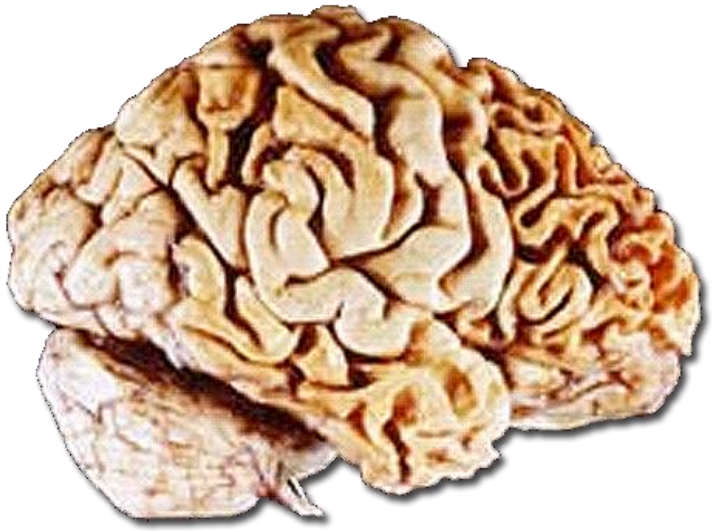
Possibile cause dei disturbi psicocomportamentali

incapacità ad inibire risposte inappropriate

interpretazione anomala di stimoli ambientali (visivi ed acustici)

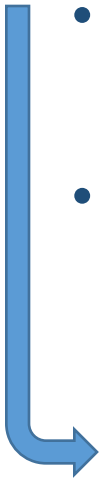
incapacità ad esprimere necessità, a verbalizzare malessere o sintomatologia dolorosa

DEMENZA FRONTOTEMPORALE



Demenze frontotemporali

- La Sindrome Disesecutiva o Variante Frontale
- L' Afasia Primaria Progressiva
- La Demenza Semantica (variante temporale)



le afasie primarie non sono tutte demenze FT

variante logopenica = demenza di Alzheimer

VARIANTE FRONTALE/DISESECUTIVA/COMPORTAMENTALE

Entità clinico patologica dominata da deterioramento della personalità e delle abilità intellettive prodotta da una atrofia che interessa prevalentemente le strutture frontali dell'encefalo

SINDROME COGNITIVA /DISESECUTIVA

ridotta capacità di processare informazione rilevante per pianificare strategie adattive

SINDROME COMPORTAMENTALE/ALTERAZIONE DELLE CONDOTTE SOCIALI

- ✓ **apatia**
- ✓ **disturbi dell'alimentazione**
- ✓ **ritiro sociale**
- ✓ **disinibizione**
- ✓ **condotte sociali inappropriate**

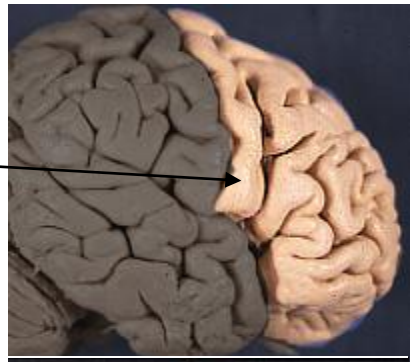
anatomia funzionale delle aree prefrontali

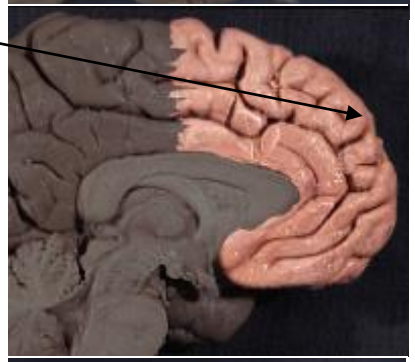
- 3 circuiti
  - Dorso laterale
  - Dorso mediale
  - Orbitale

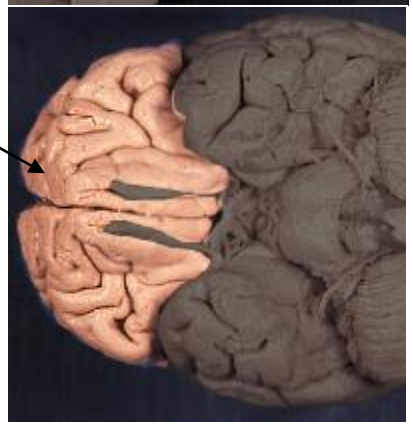
sindrome disesecutiva (cognitiva)

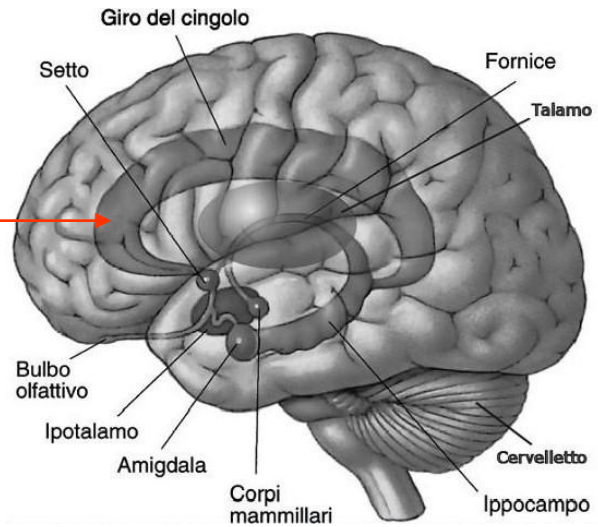
sindrome comportamentale

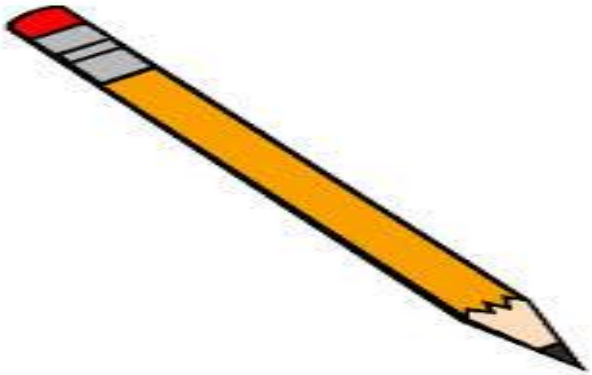
alterazione delle condotte sociali



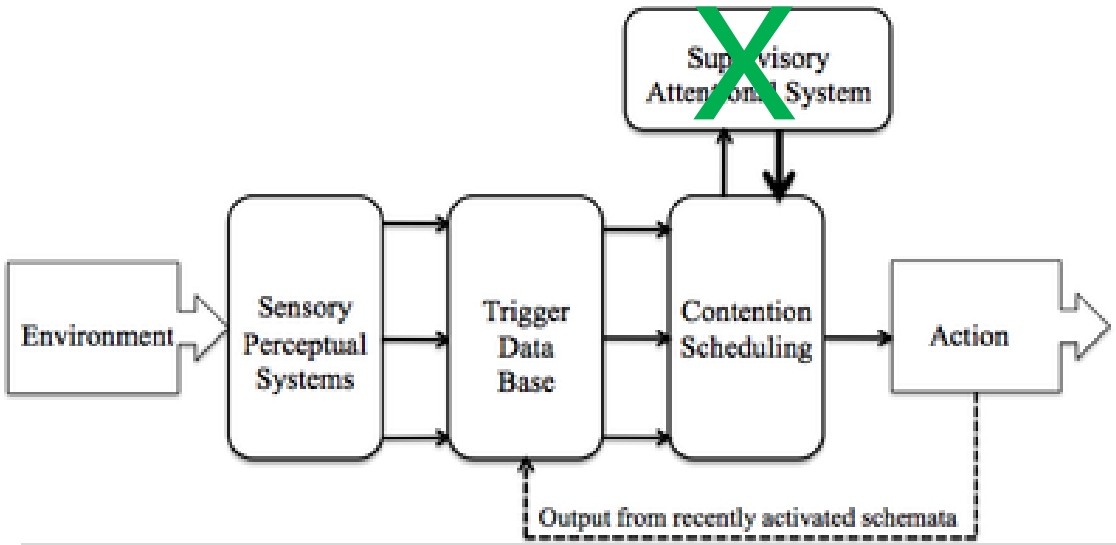








Shallice & Burgess, 1996



sindrome disesecutiva
danno del «Central Executive», corrispettivo del SAS nel modello di Baddeley (1986)

ridotta capacità di processare informazione rilevante per pianificare strategie adattive

- **Stimuli enter the perceptual processing system and activate "schema" (knowledge structures in long-term memory)**
- **The activated schema captures control of actions without any control by voluntary attention (automatic system)**
- **The Supervisor Attention System (SAS) allows the schema relevant to our intended goal take control of action (inappropriate schema are suppressed)**

Norman & Shallice, 1986;1989

Contention scheduling= selezione competitiva

Demenze frontotemporali

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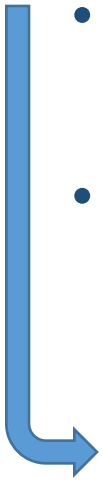

le afasie primarie non sono tutte demenze FT

variante logopenica = demenza di Alzheimer

Table 2 Diagnostic features for the nonfluent/agrammatic variant PPA

I. Clinical diagnosis of nonfluent/agrammatic variant PPA
At least one of the following core features must be present:
1. Agrammatism in language production
2. Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)
At least 2 of 3 of the following other features must be present:
1. Impaired comprehension of syntactically complex sentences
2. Spared single-word comprehension
3. Spared object knowledge
II. Imaging-supported nonfluent/agrammatic variant diagnosis
Both of the following criteria must be present:
1. Clinical diagnosis of nonfluent/agrammatic variant PPA
2. Imaging must show one or more of the following results:
a. Predominant left posterior fronto-insular atrophy on MRI or
b. Predominant left posterior fronto-insular hypoperfusion or hypometabolism on SPECT or PET
III. Nonfluent/agrammatic variant PPA with definite pathology
Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
1. Clinical diagnosis of nonfluent/agrammatic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLD-tau, FTLD-TDP, AD, other)
3. Presence of a known pathogenic mutation

Abbreviations: AD = Alzheimer disease; FTLD = frontotemporal lobar degeneration; PPA = primary progressive aphasia.

Table 3 Diagnostic criteria for the semantic variant PPA

I. Clinical diagnosis of semantic variant PPA
Both of the following core features must be present:
1. Impaired confrontation naming
2. Impaired single-word comprehension
At least 3 of the following other diagnostic features must be present:
1. Impaired object knowledge, particularly for low-frequency or low-familiarity items
2. Surface dyslexia or dysgraphia
3. Spared repetition
4. Spared speech production (grammar and motor speech)
II. Imaging-supported semantic variant PPA diagnosis
Both of the following criteria must be present:
1. Clinical diagnosis of semantic variant PPA
2. Imaging must show one or more of the following results:
a. Predominant anterior temporal lobe atrophy
b. Predominant anterior temporal hypoperfusion or hypometabolism on SPECT or PET
III. Semantic variant PPA with definite pathology
Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
1. Clinical diagnosis of semantic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLD-tau, FTLD-TDP, AD, other)
3. Presence of a known pathogenic mutation

Abbreviations: AD = Alzheimer disease; FTLD = frontotemporal lobar degeneration; PPA = primary progressive aphasia.

Table 4 Diagnostic criteria for logopenic variant PPA

I. Clinical diagnosis of logopenic variant PPA
Both of the following core features must be present:
1. Impaired single-word retrieval in spontaneous speech and naming
2. Impaired repetition of sentences and phrases
At least 3 of the following other features must be present:
1. Speech (phonologic) errors in spontaneous speech and naming
2. Spared single-word comprehension and object knowledge
3. Spared motor speech
4. Absence of frank agrammatism
II. Imaging-supported logopenic variant diagnosis
Both criteria must be present:
1. Clinical diagnosis of logopenic variant PPA
2. Imaging must show at least one of the following results:
a. Predominant left posterior perisylvian or parietal atrophy on MRI
b. Predominant left posterior perisylvian or parietal hypoperfusion or hypometabolism on SPECT or PET
III. Logopenic variant PPA with definite pathology
Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
1. Clinical diagnosis of logopenic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g. AD, FTLD-tau, FTLD-TDP, other)
3. Presence of a known pathogenic mutation

Abbreviations: AD = Alzheimer disease; FTLD = frontotemporal lobar degeneration; PPA = primary progressive aphasia.

Gorno Tempini et al., 2011

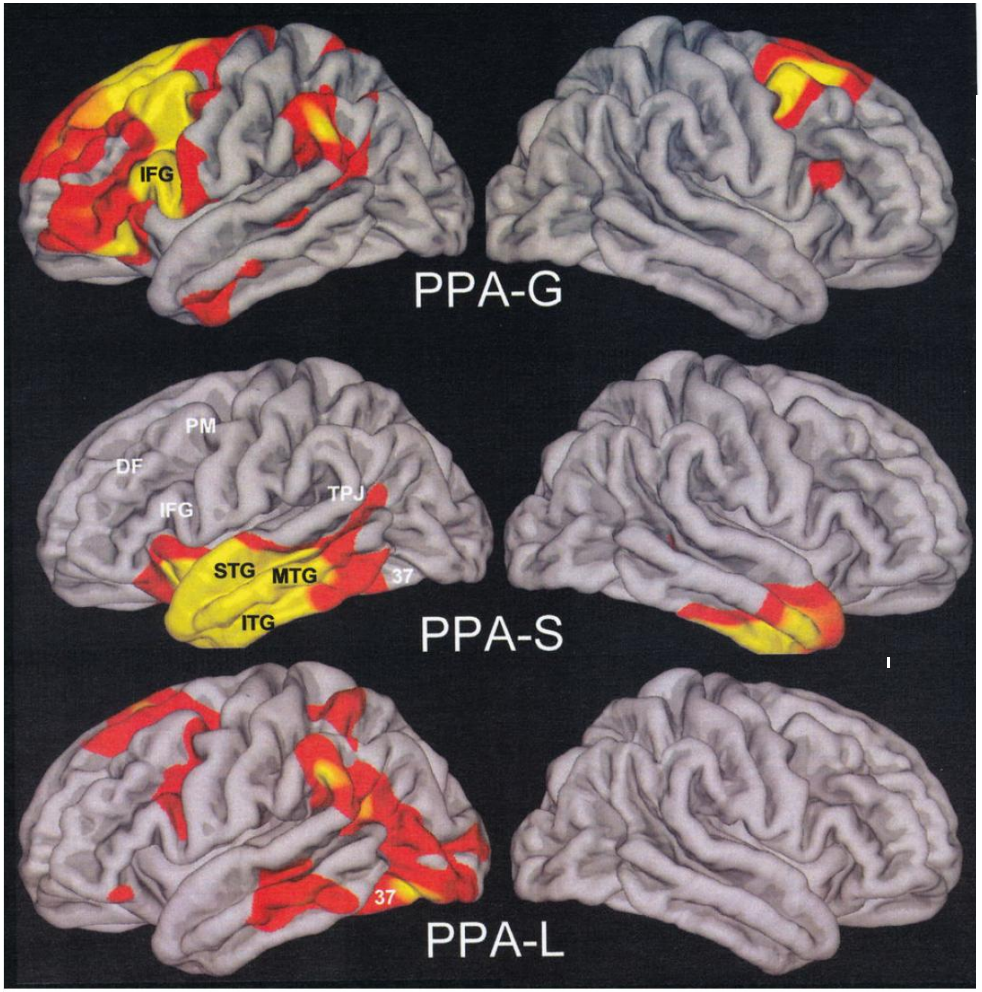

Figure 5.
Distribution of cortical thinning. Red shading indicates a significance level of $p<0.01$, and the yellow $p<0.001$. Abbreviations: DF, Dorsolateral prefrontal cortex; IFG, Inferior frontal gyrus; ITG, Inferior temporal gyrus; MTG, Middle temporal gyrus; PM, Premotor cortex; STG, Superior temporal gyrus; TPJ, Temporoparietal junction; 37, Area 37 of Broadmann;

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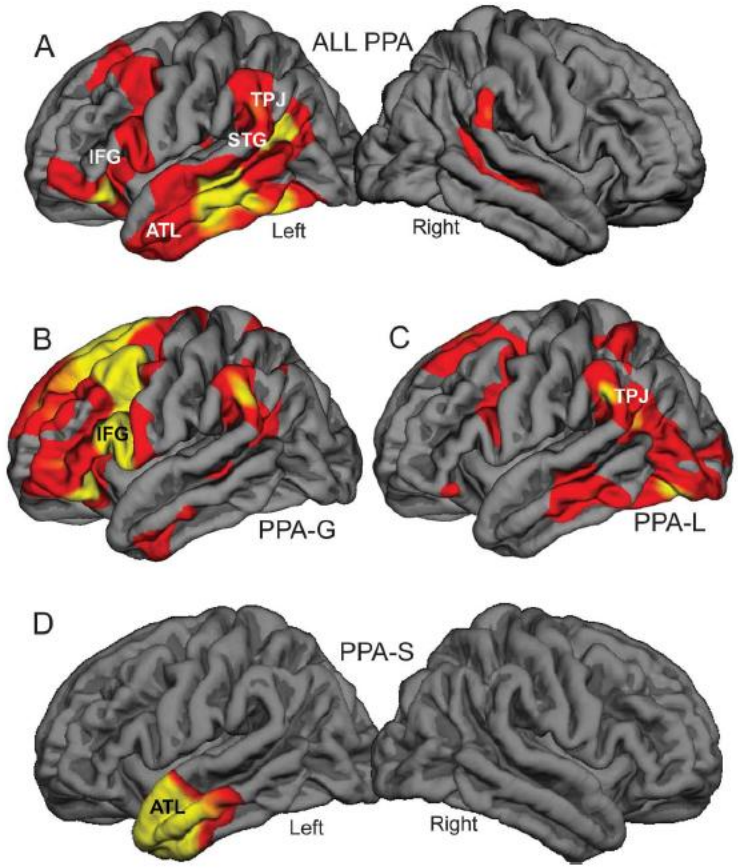
QUANTITATIVE TEMPLATE FOR SUBTYPING PRIMARY PROGRESSIVE APHASIA

Marsel Mesulam, MD, **Christina Wieneke, BA**, **Emily Rogalski, PhD**, **Derin Cobia, PhD**, **Cynthia Thompson, PhD**, and **Sandra Weintraub, PhD**

Figure 1 Quantitative map of peak atrophy sites in primary progressive aphasia



SPECIAL ARTICLE

Primary progressive aphasia and the language network

The 2013 H. Houston Merritt Lecture

M.-Marsel Mesulam, MD

ABSTRACT

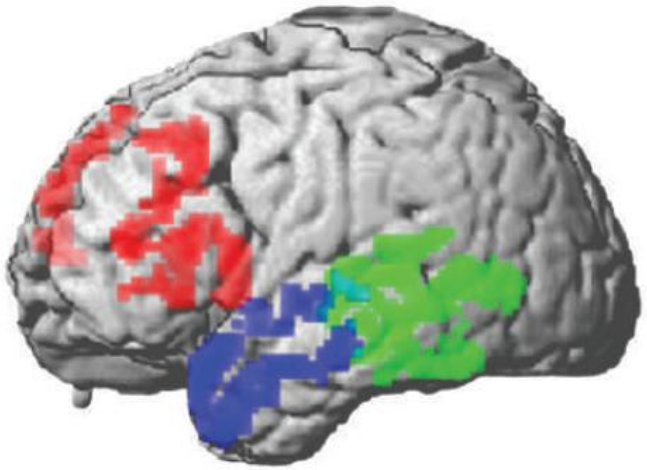


Figure 5 | Distribution of cortical atrophy in three primary progressive aphasia syndromes. This image is based on a quantitative cortical thickness analysis of high-resolution 3T MRI studies[129] in patients with primary progressive aphasia. Statistically significant cortical thinning is observed in inferior, dorsolateral prefrontal and insular regions of the left frontal lobe in progressive nonfluent aphasia (red, $n = 12$ patients), in the left lateral temporal and inferior parietal regions in logopenic progressive aphasia (green, $n = 9$ patients), and in the left anterior temporal lobe in semantic dementia (blue, $n = 11$ patients) relative to age-matched healthy adults.

Grossman, M. *Nat. Rev. Neurol.* 6, 88–97 (2010): doi:10.1038/nrneurol.2009.216

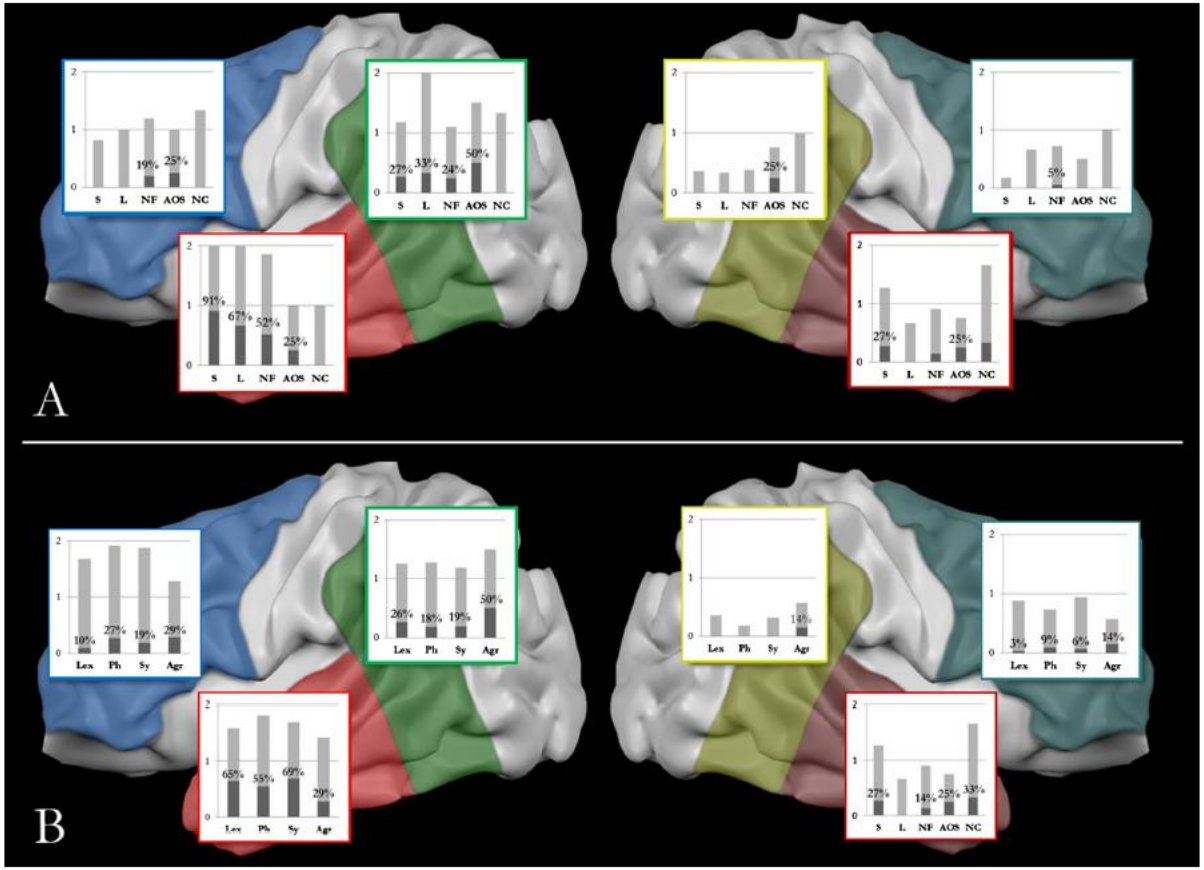
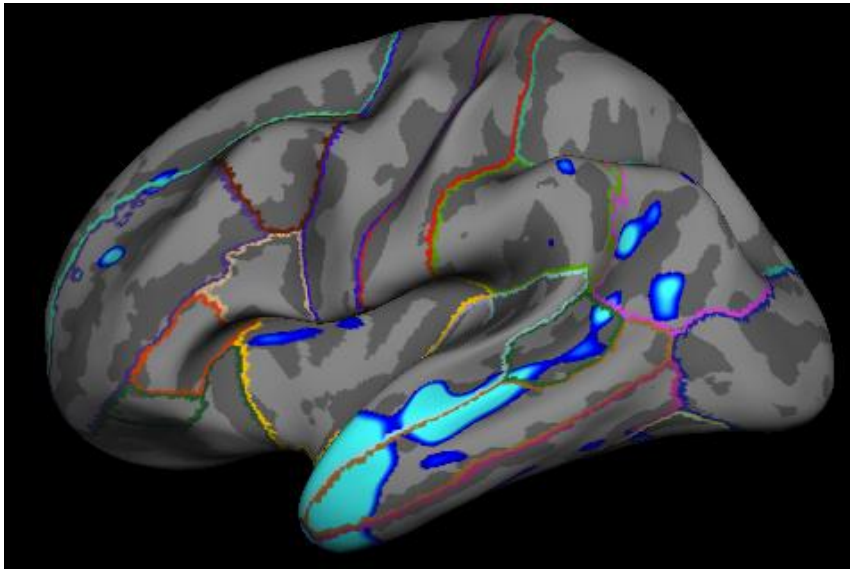
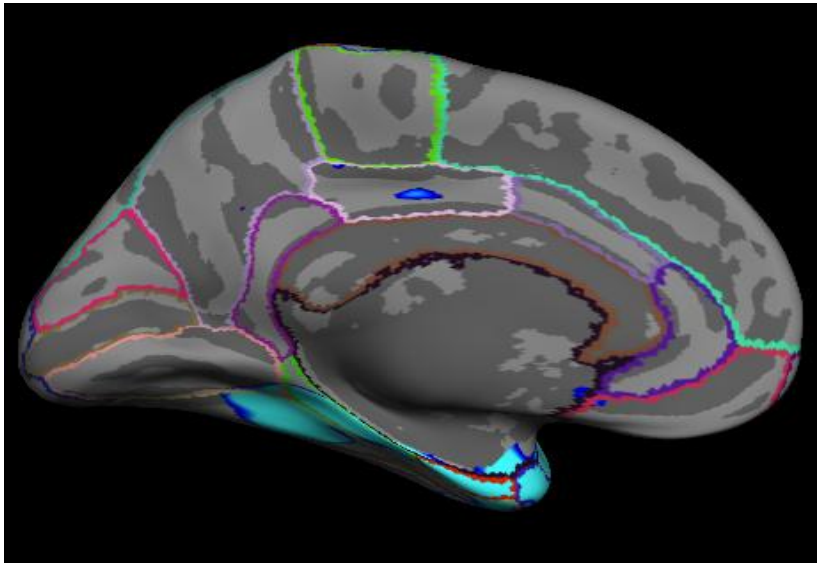


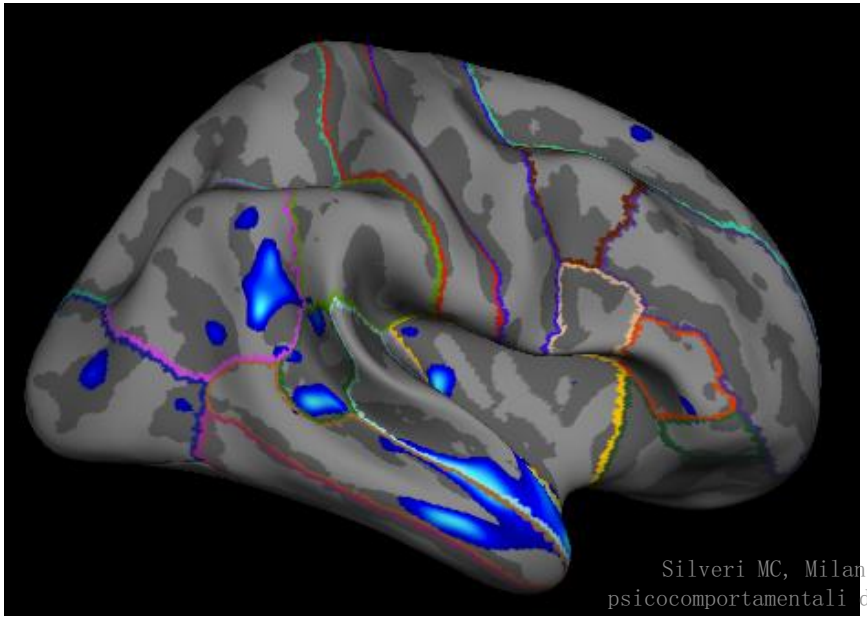
Fig. 1. (A and B) – Average and predominant regional atrophy patterns in patients stratified according to the criteria for clinical diagnosis of aphasia variants into the S, NF, L and AOS groups (A), and in Ph, Lex, Sy and Agr groups according to the presence of deficits in different dimensions of language (*See Methods Section*) (B). Non-categorized subjects in A are indicated as "NC". Only patients with moderate-to severe disorders were included in the classification in B. Since more than one linguistic deficit could be seen in a single subject, patients were assigned to different groups categories at the same time (Table 4), if appropriate. Regional atrophy was visually scored on individual MR examinations. For each group/category, light-gray bars in histograms indicate the average score of atrophy in a given region (range 0–2), while dark-gray bars indicate the percentages of cases with predominant atrophy ranks (i.e. beyond the 3rd quartile) in a given brain region: Blue box = Left Anterior Frontal lobe; Light Blue box = Right Anterior Frontal Lobe; Red box = Left Anterior Temporal Lobe; Dark Red box = Right Anterior Temporal Lobe; Green box = Left Temporo-Parietal/BA37 Region; Yellow box = Right Temporo-Parietal/BA37 Region. Each box is superimposed on the corresponding brain region for anatomical reference.

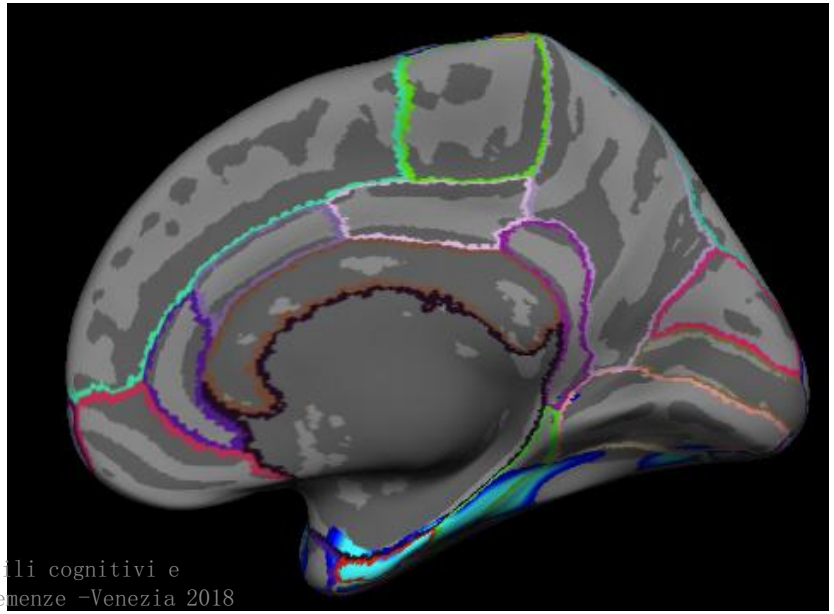
Left H





Right H





Malattia da corpi di Lewy diffusi

- ✓**Presenza di segni extrapiramidali**
- ✓**Declino cognitivo progressivo**
- ✓**Disturbi comportamentali (soprattutto allucinazioni visive strutturate)**
- ✓**Fluttuazione delle prestazioni cognitive**

altri elementi:

- ✓**Disturbi attenzionali e visuospaziali, sensibilità ai neurolettici, frequenti cadute, rapidità del declino cognitivo, alterazioni del sonno REM**

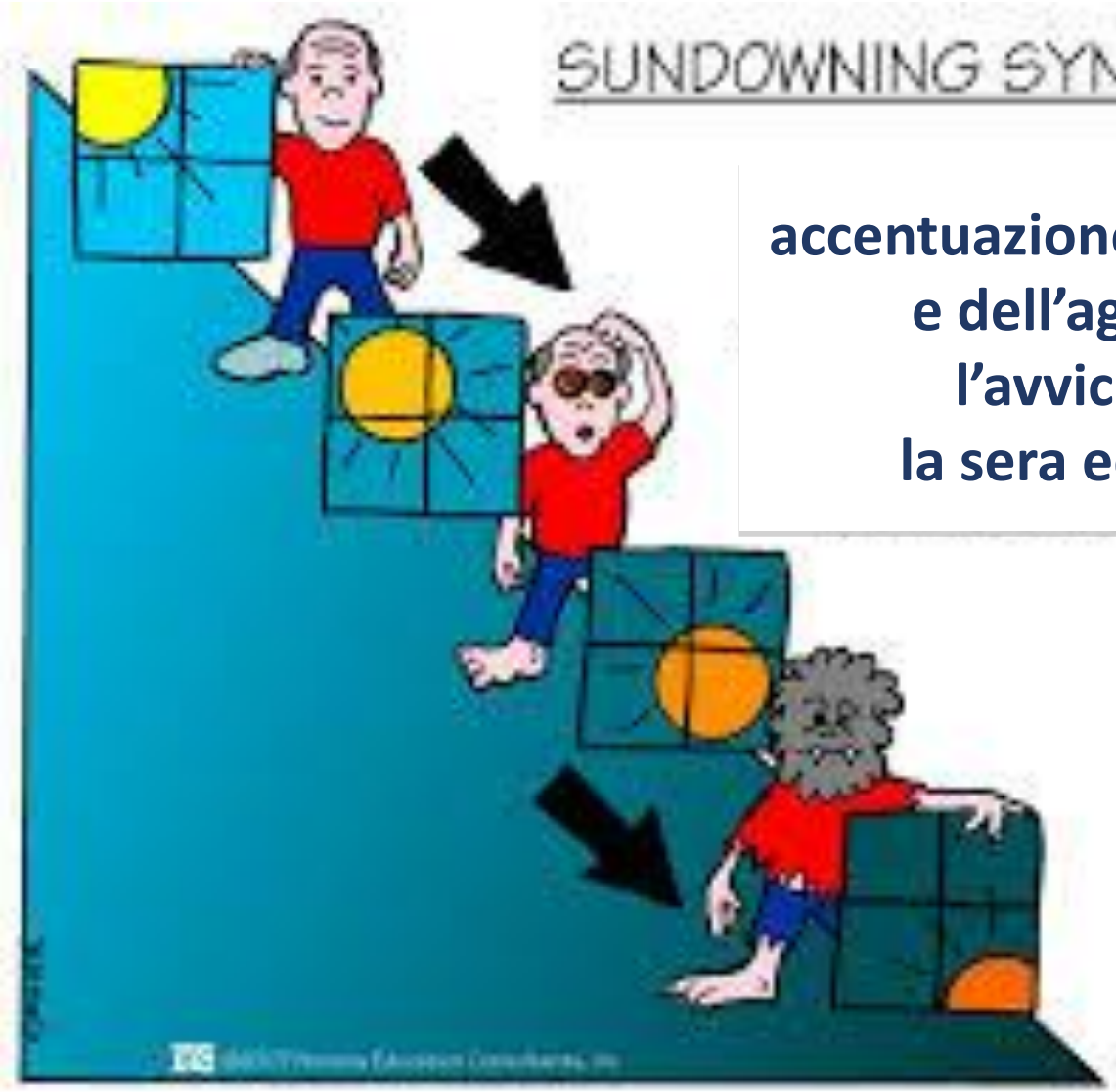
		Total	Alzheimer disease	Frontotemporal dementia	Vascular dementia	Mixed dementia	Dementia with Lewy Bodies	*p* value
Number of BPSD domains	0	1 (0.93)	1 (1.52)	0 (0)	0 (0)	0 (0)	0 (0)	0.415
	1	5 (4.67)	3 (4.55)	1 (5.26)	1 (9.09)	0 (0)	0 (0)	
	2	9 (8.41)	7 (10.61)	0 (0)	0 (0)	2 (28.57)	0 (0)	
	3	15 (14.02)	11 (16.7)	1 (5.26)	4 (36.36)	0 (0)	0 (0)	
	≥4	77 (71.96)	44 (66.7)	17 (89.47)	6 (54.55)	5 (71.43)	4 (100)	
NPI 12-item score		27.42±18.24	24.47±17.68	38.95±18.95	22±12.21	27.86±20.64	35.5±15.8	0.026
Delusions		1.93±3.39	1.92±3.28	1.68±3.9	1.27±2.87	2.14±3.76	4.5±3.87	0.334
Hallucinations		1.26±2.66	1.09±2.44	1.42±2.89	0.82±1.94	0.14±0.38	6.5±4.12	0.005
Agitation/aggression		4.07±3.77	3.55±3.49	6±4.24	2.45±3.27	5.14±3.8	6±4.24	0.062
Depression/dysphoria		2.55±2.71	2.52±2.66	2.37±2.89	3.09±3.18	2.86±3.02	2±1.63	0.954
Anxiety		2.28±2.79	2.27±2.82	1.74±2.26	2.91±3.24	2.86±3.63	2.25±2.63	0.883
Elation/euphoria		0.27±1.02	0.18±0.82	0.84±1.8	0±0	0±0	0.25±0.5	0.168
Apathy/indifference		4.60±3.80	4.23±3.76	6.32±3.94	4±3.35	4.71±4.86	4±1.41	0.256
Disinhibition		0.83±2.56	0.58±2.10	2.32±4.22	0±0	0.86±2.27	0.25±0.5	0.067
Irritability/lability		2.67±2.87	2.38±2.69	3.53±3.52	2.27±2.45	3.86±3.39	2.5±2.65	0.609
Aberrant motor behaviour		1.79±2.95	1.32±2.35	4.42±4.13	0.73±1.85	1.71±2.93	0±0	0.003
Sleep and nighttime behaviour disorders		2.87±3.31	2.39±3.06	4.74±4.33	2.18±2.71	2.43±2.7	4.5±1	0.083
Appetite and eating disorders		2.31±2.61	2.05±2.41	3.58±2.95	2.27±3.07	1.14±2.27	2.75±2.5	0.178

Values are presented as mean ± SD or *n* (%). BPSD, behavioural and psychological symptoms of dementia; NPI, Neuropsychiatric Inventory.

Mukherjee et al., 2017

EXTRA Dementia and Geriatric Cognitive Disorders

alcuni sintomi e sindromi…..



accentuazione della confusione e dell'agitazione con l'avvicinarsi della la sera ed il tramonto

TABLE 1.

Sleep Disturbance Prevalence in Dementia Disorders

Disturbance	AD	PSP	PDD and DLB	FTD	VaD
Insomnia	46-53	~100	66-72	48-89	47-67
Daytime somnolence	5-48	See footnote b	57-100	11-64	16-58
SDB	40-70	55	50-76	68	74
Sleep fragmentation	18	57	See footnote c	See footnote c	See footnote c
REM[d] and NREM parasomnias	20-22	35-85	65-95	24-89	26-73
Leg restlessness[e]	4-24	57	50-83	8-78	5-11
Sleep architecture	Reduced REM and SWS, more arousals, degraded sleep features (spindles/ K-complex)	Decreased REM; increased sleep-onset latency; decreased efficiency	Decreased REM; decreased efficiency	Decreased REM; less N2; less NREM/ REM cycles	Disrupted sleep-wake cycles
Poor quality sleep	See footnote c	43	54-63	See footnote c	See footnote c

Note: Results are in percentage (%) points, whereas prevalence varies with disease stage.
Abbreviations: AD, Alzheimer's disease; DLB, dementia with Lewy bodies; FTD, frontotemporal dementia; NREM, nonrapid eye movement; PDD, Parkinson's disease dementia; PSP, progressive supranuclear palsy; REM, rapid eye movement; SDB, sleep-disordered breathing; SWS, slow wave sleep; VaD, vascular dementia.
[a]FTD is a diverse clinical syndrome in which sleep disturbances strongly depend on underlying affected networks, explaining the wide range in reported results.[101]
[b]Patients with PSP may report somnolence, but are actually hyperaroused during the day compared to cognitively nonimpaired controls.
[c]Studies specifically and clearly answering these questions are lacking.
[d]In REM parasomnias, REM without atonia is included.
[e]Leg restlessness and restless legs syndrome are combined, as strict criteria are not followed in most studies.
Adapted from El-Sayed,[72] McCurry et al.,[92] Pistacchi et al.,[93] Sixel-Doring et al.,[94] Aldrich et al.,[95] Boddy et al.,[96] Arnulf et al.,[97] Rose et al.,[98] Guarnieri et al.,[99] and Bonakis et al.[100]

Swallowing disturbance	Difficulty in swallowing food
	Difficulty in swallowing liquids
	Coughing or choking when swallowing
	Taking a long time to swallow
	Placing food in mouth but not chewing it
	Chewing food but not swallowing it
Appetite change	Loss of appetite
	Increase in appetite
	Seeking out food between meals
	Overeating at meal time
	Requesting more food
	Reporting hunger
	Reporting being overfull
	Other change about appetite
	Needs to limit food
Food preference	Preferring sweet foods more than before
	Drinking more soft or sweet drinks
	Drinking more tea/coffee or water
	"Taste" in food changed in some way
	Adding more seasoning to their food
	Developing other food fads
	Hoarding foods
	Drinking more alcohol
Eating habits	Wanting to cook or eat the same food every day
	Tending to eat foods in the same order
	Wanting to eat at the same time every day
	Decline in table manners
	Eating with hands
	Other change about food preference
	Taking a long time to eat
Other eating behaviors	Tending to overfill mouth
	Chewing or sucking without trying to eat
	Eating non-edible foodstuffs
	Tending to snatch or grasp any food items
	Becoming a heavier smoker or taking up smoking
	Episodes of vomiting naturally
	Episodes of vomiting by using their fingers

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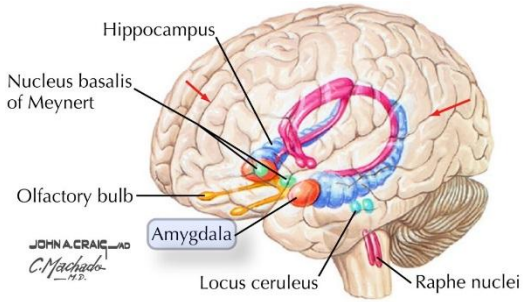
Symptoms of Kluver-Bucy Syndrome

Individuals with Kluver-Bucy syndrome display the following behavioural manifestations:

- Acts of licking and touching that are unacceptable for public display.
- Demonstrating excessive desire to engage in human sexual practices (hypersexuality).
- Engagement in binge-eating (excessive, uncontrollable over eating) with feelings of guilt and depression afterwards.
- People suffering from Kluver-Bucy syndrome tend to be subjected to memory disorders consisting of short-term memory loss and other serious presentations of memory-related ailments.
- Inability to recognize people.
- Lack of fear reaction.
- Patients of Kluver-Bucy syndrome may also exhibit presentations of flattened emotions (placidity) like rare and extreme feelings of calmness and undisturbed emotions.
- Having some extent of difficulty in distinguishing and identifying some objects.



Features Seen in Experimental Monkey

1. Visual agnosia
2. Increased oral tendency
3. Decreased emotional reaction
4. Hypersexuality
5. Hypermetamorphosis

Grazie