

# DISTURBI PERCETTIVI NELLA DEMENZA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER

Un ostacolo o un aiuto nella diagnosi differenziale?

Sara Baldinelli

Clinica Neurologica

Dipartimento di Medicina Sperimentale e Clinica

Università Politecnica delle Marche

AOU — Ospedali Riuniti di Ancona



**Sin**  
SOCIETÀ ITALIANA DI NEUROLOGIA

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# DEMENTIA A CORPI DI LEWY & MALATTIA DI ALZHEIMER



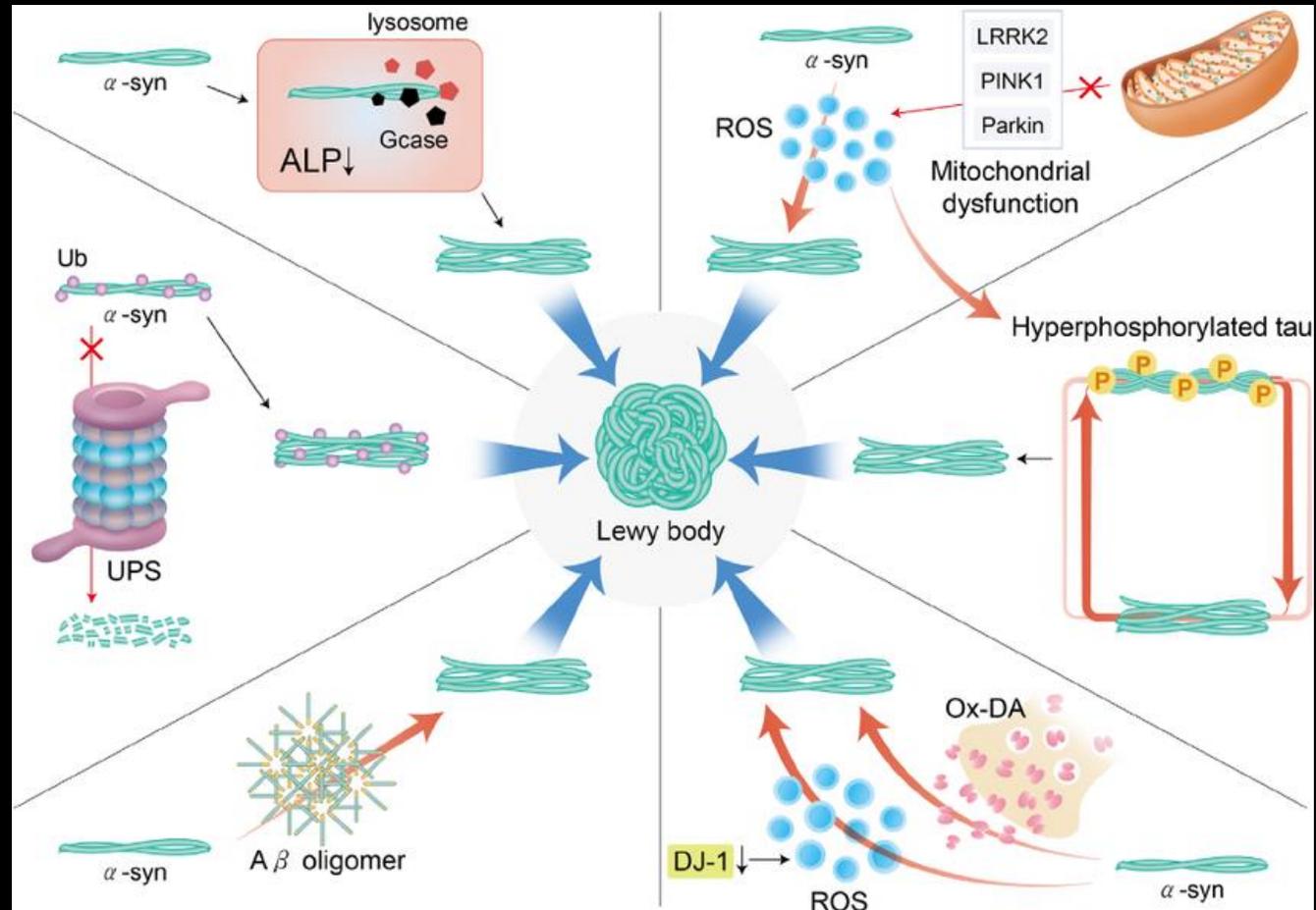
Uguali ma diverse ....



... o diverse ma uguali?

DISTURBI PERCETTIVI NELLA DEMENTIA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?

# OVERLAPPING NEUROPATHOLOGICO



DISTURBI PERCETTIVI NELLA DEMENZA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?

# OVERLAPPING GENETICO

Parkinsonism and Related Disorders 43 (2017) 1–8



ELSEVIER

Contents lists available at ScienceDirect

## Parkinsonism and Related Disorders

journal homepage: [www.elsevier.com/locate/parkreldis](http://www.elsevier.com/locate/parkreldis)



Review article

### An update on the genetics of dementia with Lewy bodies



Leonie J.M. Vergouw<sup>a,\*</sup>, Inger van Steenoven<sup>b,1</sup>, Wilma D.J. van de Berg<sup>c,1</sup>,  
Charlotte E. Teunissen<sup>d,1</sup>, John C. van Swieten<sup>a,2</sup>, Vincenzo Bonifati<sup>e,2</sup>,  
Afina W. Lemstra<sup>b,1</sup>, Frank Jan de Jong<sup>a,2</sup>

Rare disease-associated genetic variants in familial DLB.

Genetic characteristics			Clinical diagnosis	Family history			Number of affected family members	Pathological characteristics			References	
Gene	Protein	Chromosome location		Protein change	DLB	PD/PDD		AD or unspecified dementia	Autopsy performed	Cortical Lewy pathology		AD pathology
SNCA	$\alpha$ -synuclein	4q22.1	E46K	DLB**	no	yes	no	12	yes	yes	no	[14]
			A53T	DLB**	no	yes	no	3	yes	yes	no	[15]
				DLB	no	yes	no	4	no	NA	NA	[16]
			duplication	DLB	no	yes	no	1	no	NA	NA	[17]
LRRK2	leucine-rich kinase 2	12q12	G2019S	DLB	no	yes	no	4	yes	yes	yes	[18]
PSEN1	presenilin 1	14q24.2	T440 deletion*	DLB**	no	yes	no	2	no	NA	NA	[22,23]
			A79V	DLB	no	no	yes	1	no	NA	NA	[24]
PSEN2	presenilin 2	1q42.13	A85V	DLB	yes	no	yes	5	yes	yes	yes	[25]
			R71W	DLB	no	no	yes	1	no	NA	NA	[24]
			D439A	DLB	no	yes	no	1	yes	yes	yes	[13]
APP	amyloid precursor protein	21q21.3	V717I	DLB/AD	UN	UN	UN	>1	yes	yes	yes	[11]
			duplication	DLB	no	no	yes	2	yes	yes	yes	[26]
SNCB	$\beta$ -synuclein	5q35.2	P123H	DLB	yes	no	yes	7	yes	yes	yes	[32,34]

\*Confirmed in a son with PD and dementia. \*\*Based on the clinical criteria by McKeith et al., 2005, however no definite diagnosis was mentioned in article. DLB: Dementia with Lewy bodies, PD: Parkinson's Disease, PDD: Parkinson's Disease Dementia, AD: Alzheimer's Disease, UN: Unknown, NA: Not available.

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# OVERLAPPING CLINICO

Parkinsonism and Related Disorders 18S1 (2012) S41-S44

Contents lists available at ScienceDirect

 Parkinsonism and Related Disorders 

journal homepage: [www.elsevier.com/locate/parkreldis](http://www.elsevier.com/locate/parkreldis)

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Mild cognitive impairment associated with underlying Alzheimer's disease versus Lewy body disease

Bradley F. Boeve\*

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Typical profile of neuropsychological impairment in early/mild Alzheimer's disease, dementia with Lewy bodies, and Parkinson's disease with dementia

Cognitive Domain	Alzheimer's disease	Dementia with Lewy bodies	Parkinson's disease with dementia
Memory	++ to +++	0 to ++	0 to ++
Attention/Executive	+ to ++	++ to +++	++ to +++
Language	+ to ++	0 to +	0 to +
Visuospatial	+ to ++	+ to +++	+ to ++

0 = no impairment, + = mild impairment, ++ = moderate impairment, +++ = marked impairment.

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# OVERLAPPING CLINICO

IEWS & REVIEWS

## Diagnosis and management of dementia with Lewy bodies

Fourth consensus report of the DLB Consortium

**Table 1** Revised<sup>1,2</sup> criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

**Essential** for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. 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 visuo-perceptual ability may be especially prominent and occur early.

**Core clinical features** (*The first 3 typically occur early and may persist throughout the course.*)

Fluctuating cognition with pronounced variations in attention and alertness.  
Recurrent visual hallucinations that are typically well formed and detailed.  
REM sleep behavior disorder, which may precede cognitive decline.  
One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.

### Supportive clinical features

Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.

### Indicative biomarkers

Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET.  
Abnormal (low uptake) <sup>123</sup>Iodine-MIBG myocardial scintigraphy.  
Polysomnographic confirmation of REM sleep without atonia.

### Supportive biomarkers

Relative preservation of medial temporal lobe structures on CT/MRI scan.  
Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity ± the cingulate island sign on FDG-PET imaging.  
Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

Neurology, 2017; 89 (4).

## Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria

Bruno Dubois, Howard H Feldman, Claudia Jacova, Harald Hampel, José Luis Molinuevo, Kaj Blennow, Steven T DeKosky, Serge Gauthier, Dennis Selkoe, Randall Bateman, Stefano Cappa, Sebastian Crutch, Sebastiaan Engelborghs, Giovanni B Frisoni, Nick C Fox, Douglas Galasko, Marie-Odile Habert, Gregory A Jicha, Agneta Nordberg, Florence Pasquier, Gil Rabinovici, Philippe Robert, Christopher Rowe, Stephen Salloway, Marie Sarazin, Stéphane Epelbaum, Leonardo C de Souza, Bruno Vellas, Pieter J Visser, Lon Schneider, Yaakov Stern, Philip Scheltens, Jeffrey L Cummings

### Panel 1: IWG-2 criteria for typical AD (A plus B at any stage)

#### A Specific clinical phenotype

- Presence of an early and significant episodic memory impairment (isolated or associated with other cognitive or behavioural changes that are suggestive of a mild cognitive impairment or of a dementia syndrome) that includes the following features:
  - Gradual and progressive change in memory function reported by patient or informant over more than 6 months
  - Objective evidence of an amnesic syndrome of the hippocampal type,\* based on significantly impaired performance on an episodic memory test with established specificity for AD, such as cued recall with control of encoding test

#### B In-vivo evidence of Alzheimer's pathology (one of the following)

- Decreased Aβ<sub>42</sub> together with increased T-tau or P-tau in CSF
- Increased tracer retention on amyloid PET
- AD autosomal dominant mutation present (in PSEN1, PSEN2, or APP)

#### Exclusion criteria† for typical AD

##### History

- Sudden onset
- Early occurrence of the following symptoms: gait disturbances, seizures, major and prevalent behavioural changes

##### Clinical features

- Focal neurological features
- Early extrapyramidal signs
- Early hallucinations
- Cognitive fluctuations

#### Other medical conditions severe enough to account for memory and related symptoms

- Non-AD dementia
- Major depression
- Cerebrovascular disease
- Toxic, inflammatory, and metabolic disorders, all of which may require specific investigations
- MRI FLAIR or T2 signal changes in the medial temporal lobe that are consistent with infectious or vascular insults

AD=Alzheimer's disease. \*Hippocampal amnesic syndrome might be difficult to identify in the moderately severe to severe dementia stages of the disease, in which in-vivo evidence of Alzheimer's pathology might be sufficient in the presence of a well characterised dementia syndrome. †Additional investigations, such as blood tests and brain MRI, are needed to exclude other causes of cognitive disorders or dementia, or concomitant pathologies (vascular lesions).

### Panel 2: IWG-2 criteria for atypical AD (A plus B at any stage)

#### A Specific clinical phenotype (one of the following)

- Posterior variant of AD (including)
  - An occipitotemporal variant defined by the presence of an early, predominant, and progressive impairment of visuo-perceptive functions or of visual identification of objects, symbols, words, or faces
  - A biparietal variant defined by the presence of early, predominant, and progressive difficulty with visuospatial function, features of Gerstmann syndrome, of Balint syndrome, limb apraxia, or neglect
- Logopenic variant of AD defined by the presence of an early, predominant, and progressive impairment of single word retrieval and in repetition of sentences, in the context of spared semantic, syntactic, and motor speech abilities
- Frontal variant of AD defined by the presence of early, predominant, and progressive behavioural changes including association of primary apathy or behavioural disinhibition, or predominant executive dysfunction on cognitive testing
- Down's syndrome variant of AD defined by the occurrence of a dementia characterised by early behavioural changes and executive dysfunction in people with Down's syndrome

#### B In-vivo evidence of Alzheimer's pathology (one of the following)

- Decreased Aβ<sub>42</sub> together with increased T-tau or P-tau in CSF
- Increased tracer retention on amyloid PET
- Alzheimer's disease autosomal dominant mutation present (in PSEN1, PSEN2, or APP)

#### Exclusion criteria\* for atypical AD

##### History

- Sudden onset
- Early and prevalent episodic memory disorders

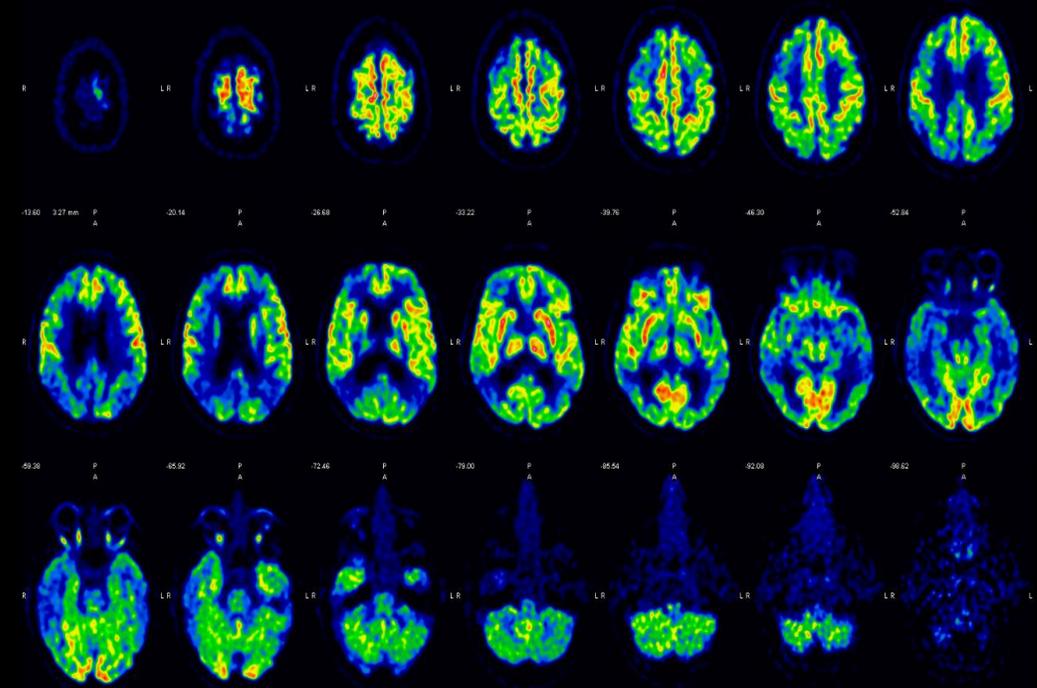
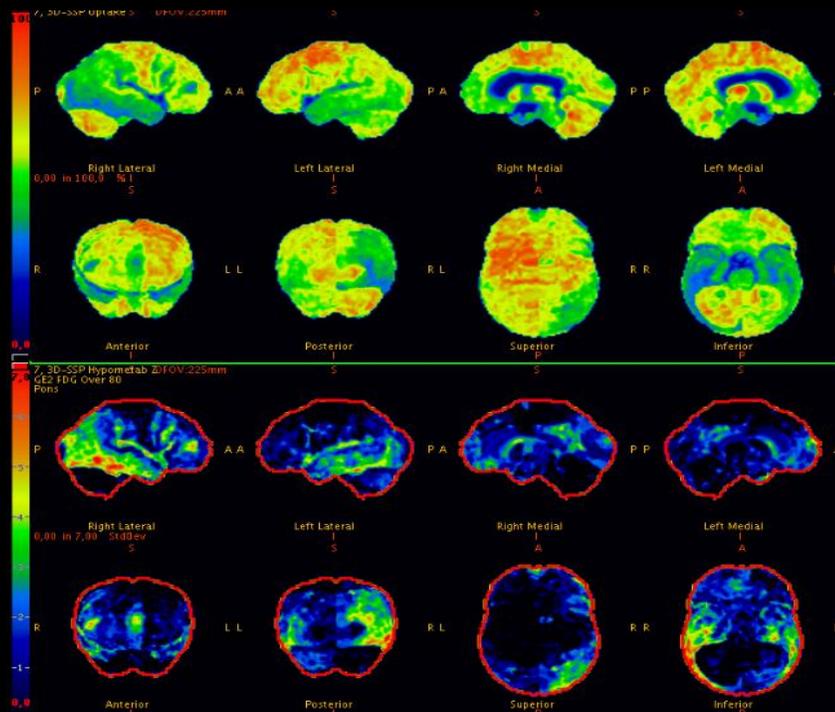
#### Other medical conditions severe enough to account for related symptoms

- Major depression
- Cerebrovascular disease
- Toxic, inflammatory, or metabolic disorders

AD=Alzheimer's disease. \*Additional investigations, such as blood tests and brain MRI, are needed to exclude other causes of cognitive disorders or dementia, or concomitant pathologies (vascular lesions).

Lancet Neurol, 2014; 13 (614-629)

# OVERLAPPING NEUROIMAGING



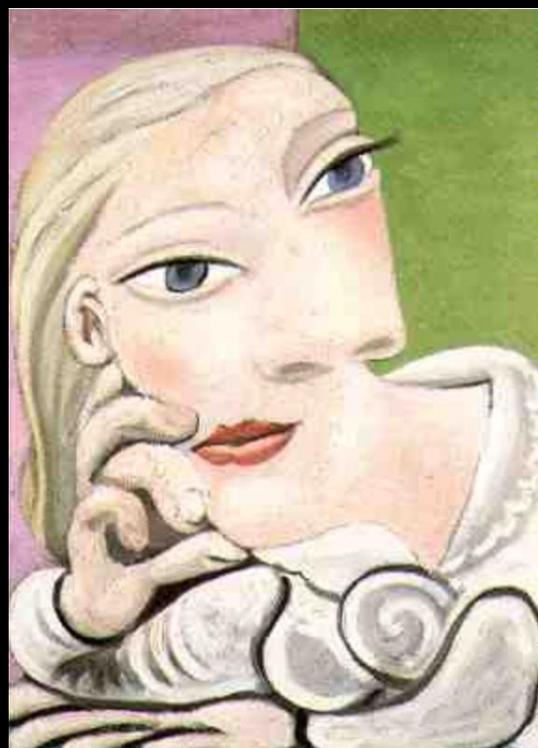
DEMENTIA CON CORPI DI LEWY ...

... MALATTIA DI ALZHEIMER

DISTURBI PERCETTIVI NELLA DEMENTIA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?

# DEMENZA A CORPI DI LEWY & MALATTIA DI ALZHEIMER.

## Come distinguerle?



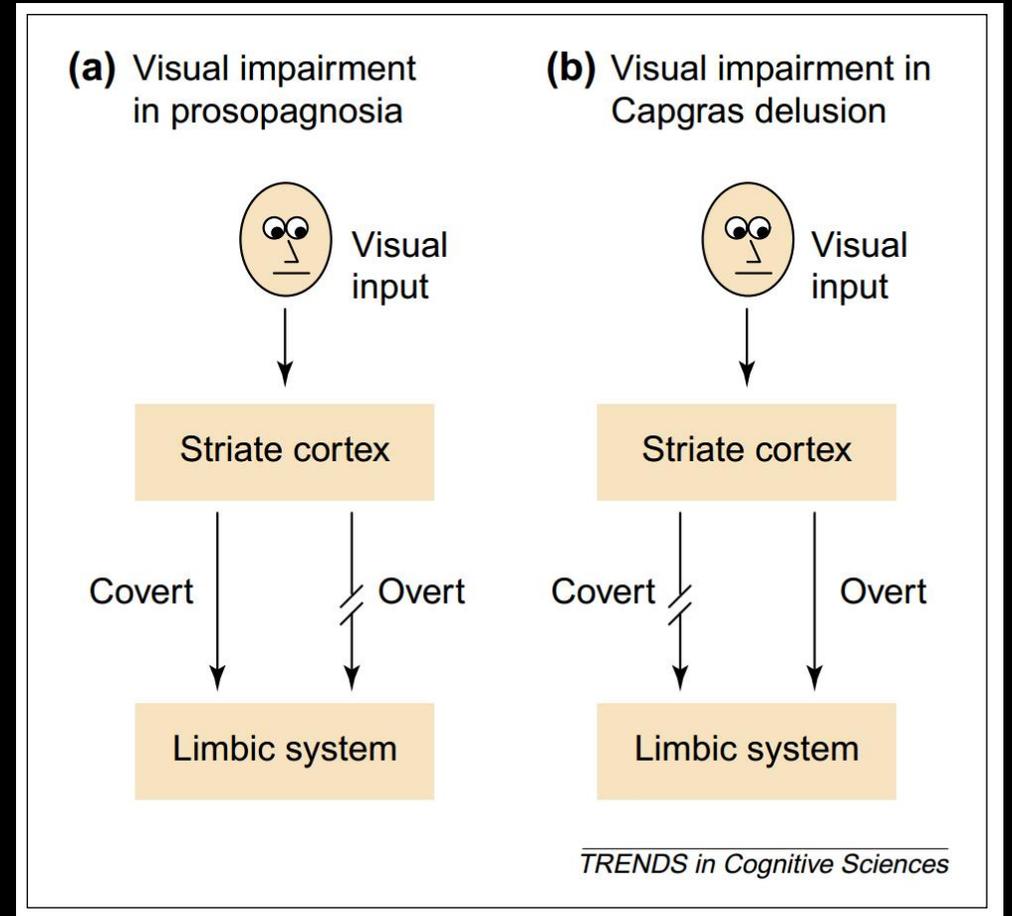
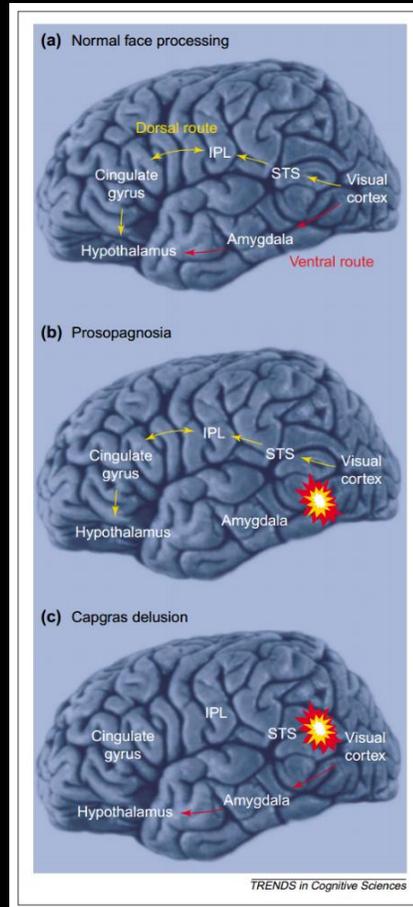
Elaborazione dei volti ....



... e copia di un disegno.

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# ELABORAZIONE DEI VOLTI

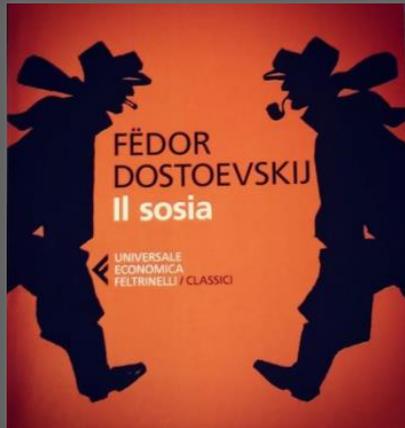


TRENDS in Cognitive Sciences Vol.5 No. 4 April 2001

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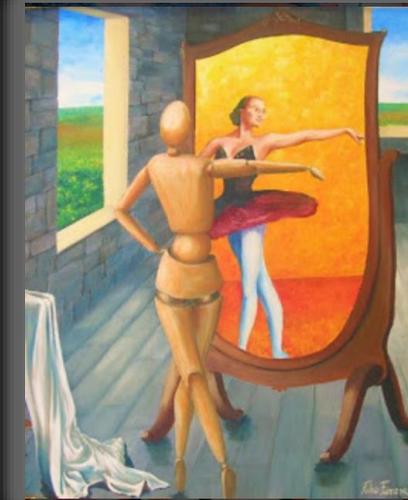
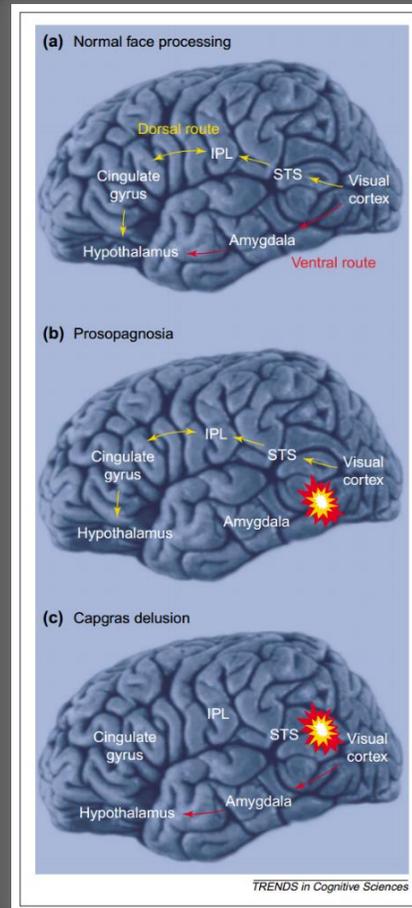
## DEMENZA CON CORPI DI LEWY Alterata percezione della familiarità

Risoluzione conflitto conosciuto-non familiare



## ELABORAZIONE DEI VOLTI

## MALATTIA DI ALZHEIMER Disturbo percettivo



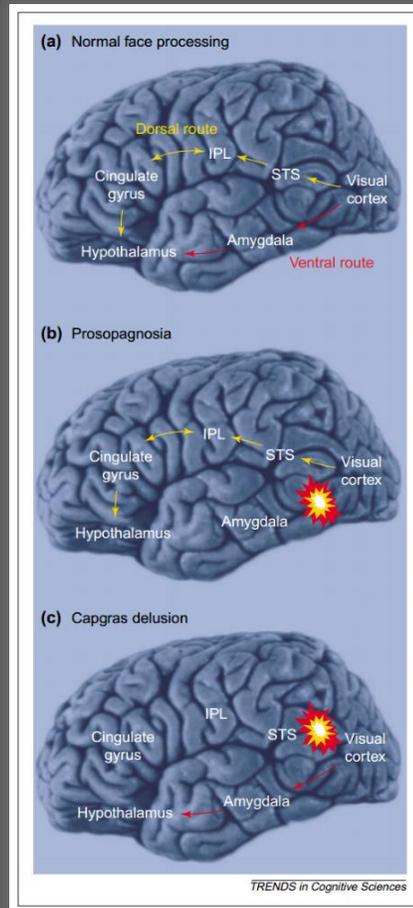
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# ELABORAZIONE DEI VOLTI

## DEMENTIA CON CORPI DI LEWY

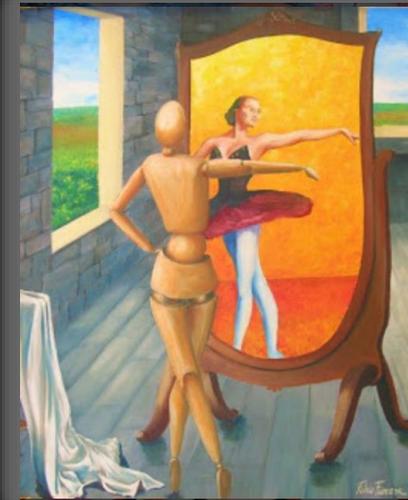
Alterata percezione della familiarità

Risoluzione conflitto conosciuto-non familiare



## MALATTIA DI ALZHEIMER

Disturbo percettivo

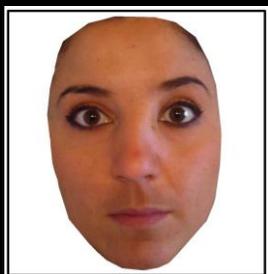


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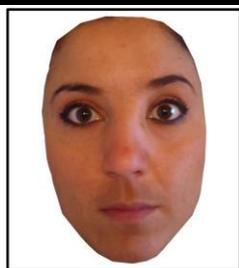
# ELABORAZIONE DEI VOLTI

## Demenza con corpi di Lewy

*LBD con SdC versus controlli sani*



Riconoscimento di genere



Riconoscimento di età



Discriminazione percettiva



Riconoscimento familiari



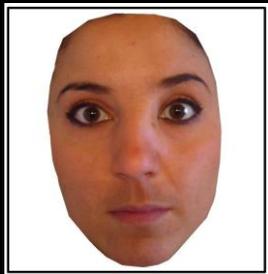
Associazione di emozioni

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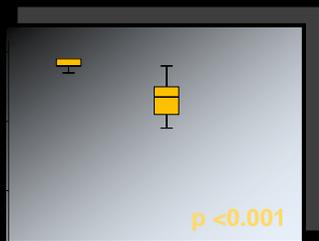
# ELABORAZIONE DEI VOLTI

## Demenza con corpi di Lewy

*LBD con SdC versus controlli sani*



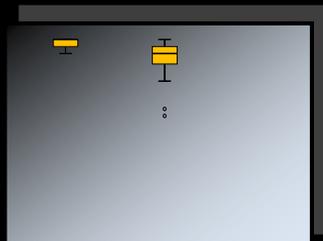
Riconoscimento di genere



NORMALI LBD



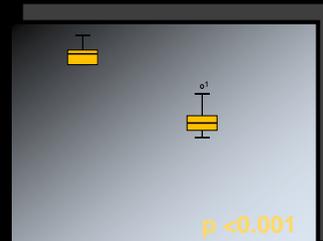
Riconoscimento di età



NORMALI LBD



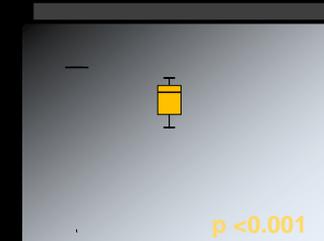
Discriminazione percettiva



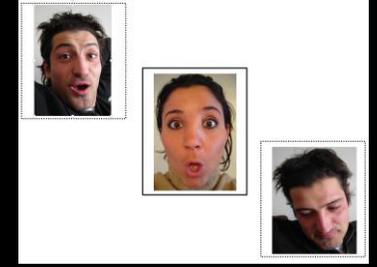
NORMALI LBD



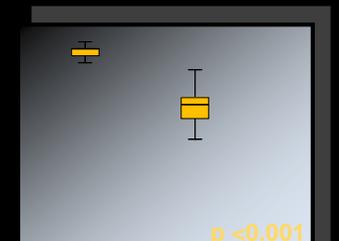
Riconoscimento familiari



NORMALI LBD



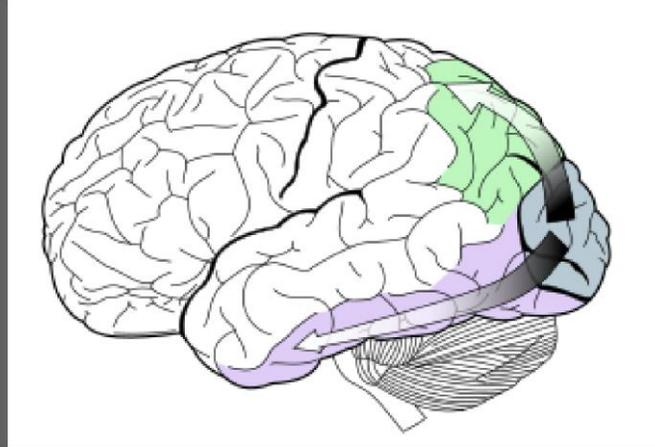
Associazione di emozioni



NORMALI LBD

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# RIPRODUZIONE SU COPIA



**SISTEMA DORSALE : «WHERE PAATHWAY»**

**CORTECCIA VISIVA I > CORTECCIA PARIETALE POSTERIORE**

- GESIONE DELLO SPAZIO
- RELAZIONI SPAZIALI
- LOCALIZZAZIONE NELLO SPAZIO
- MOVIMENTO NELLO SPAZIO

**SISTEMA VENTRALE : «WHAT PATHWAY»**

**CORTECCIA VISIVA I > CORTECCIA TEMPORALE INFERIORE**

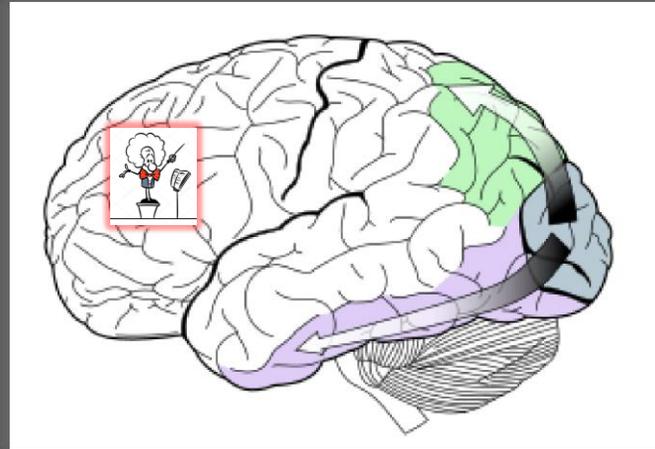
- RICONOSCIMENTO
- RAPPRESENTAZIONE MENTALE

**DISTURBI PERCETTIVI NELLA DEMENZA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?**

# RIPRODUZIONE SU COPIA

## AREE PREMOTORIE E PREFRONTALI

- PLANNING MOTORIO
- SELF MONITORING
- INIBIZIONE DI STIMOLI AUTOMATICI



## SISTEMA DORSALE : «WHERE PAATHWAY»

CORTECCIA VISIVA I > CORTECCIA PARIETALE POSTERIORE

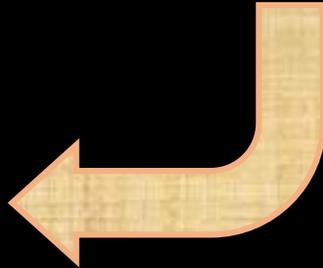
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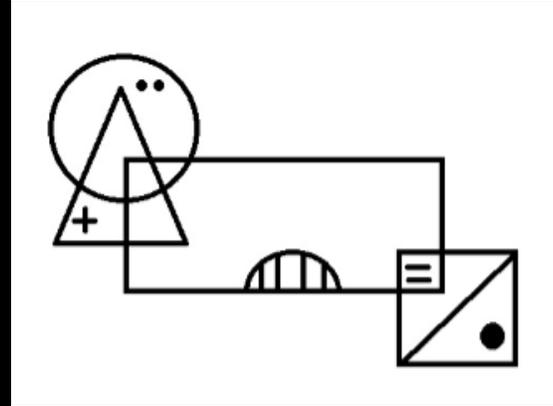
- RICONOSCIMENTO
- RAPPRESENTAZIONE MENTALE

DEFORMAZIONI E ROTAZIONI  
DIFFICOLTÀ DI AUTOCORREZIONE  
PERSEVERAZIONI



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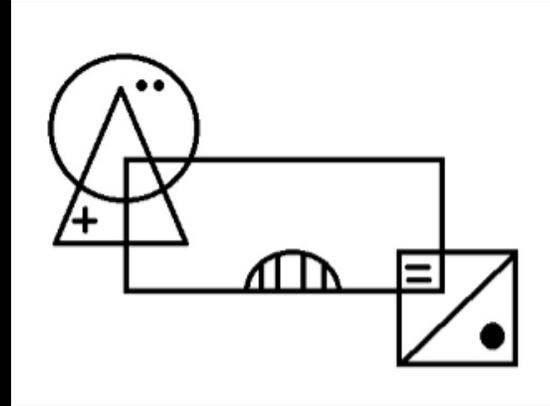
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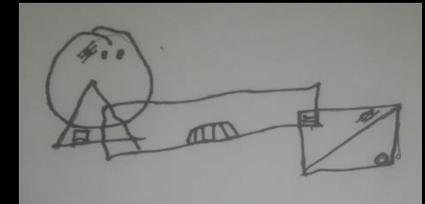
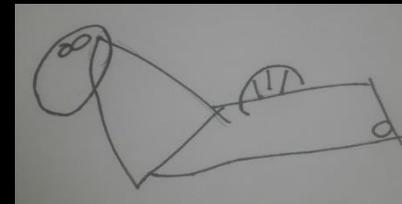
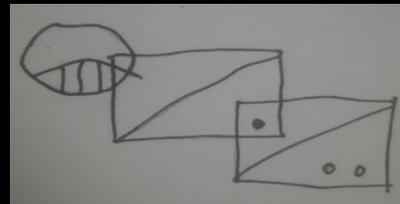
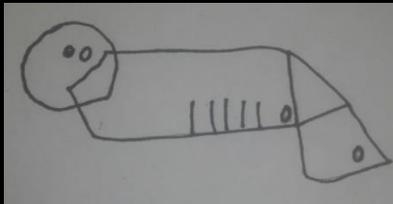
*DEMENTIA CON CORPI DI LEWY versus MALATTIA DI ALZHEIMER*

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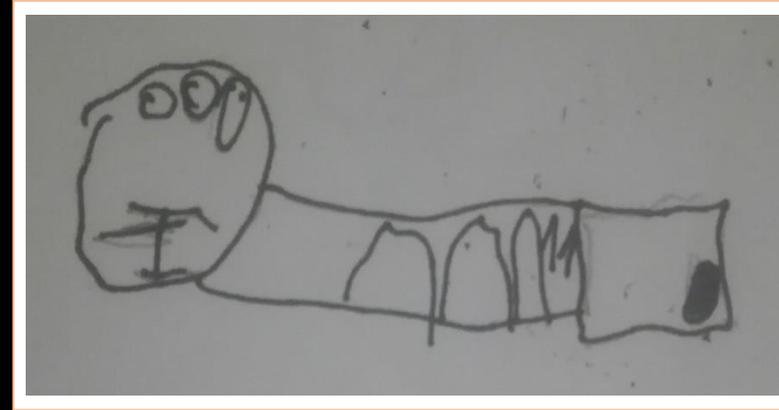
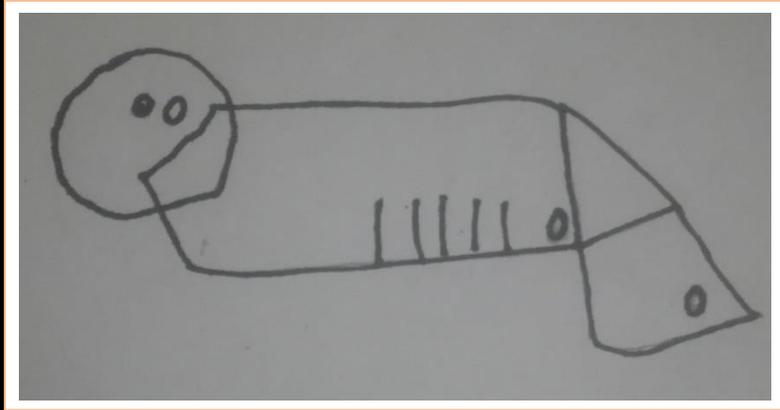


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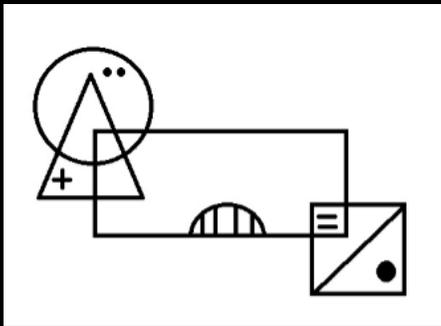


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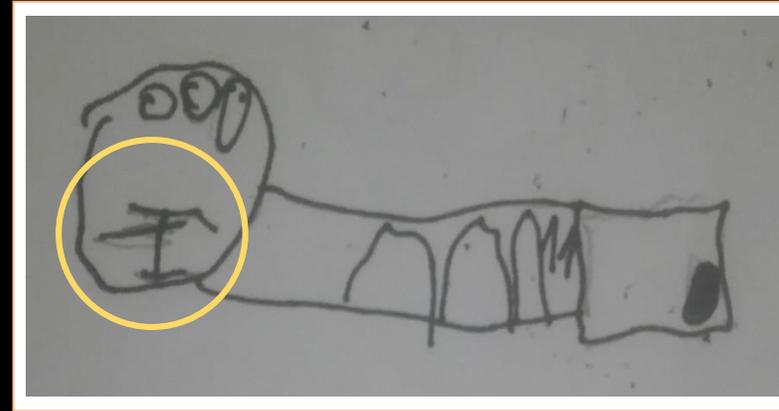
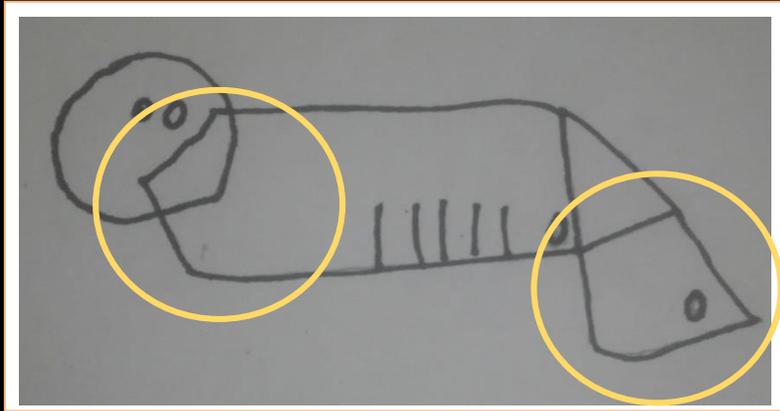


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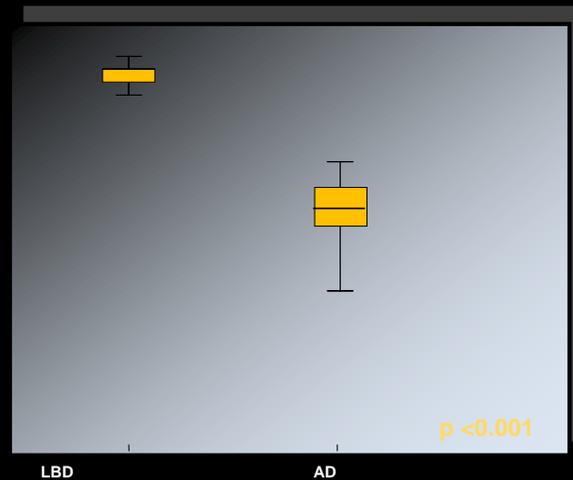
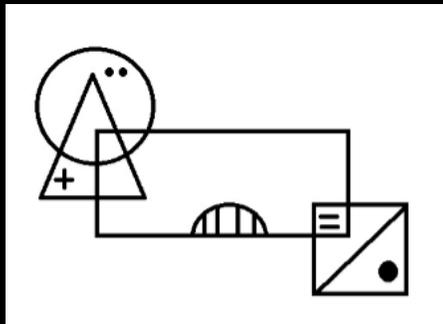


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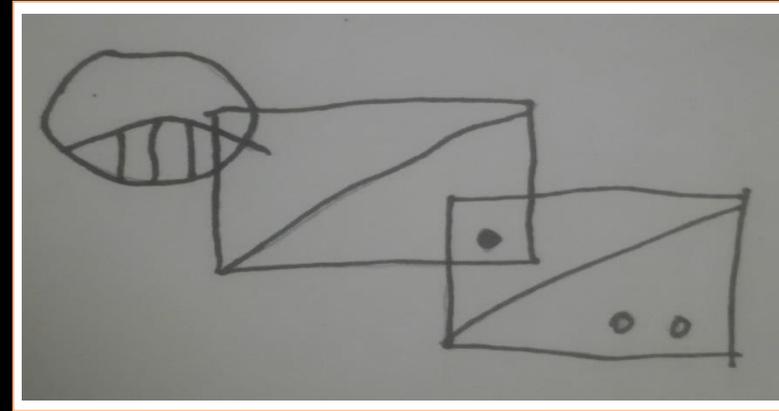
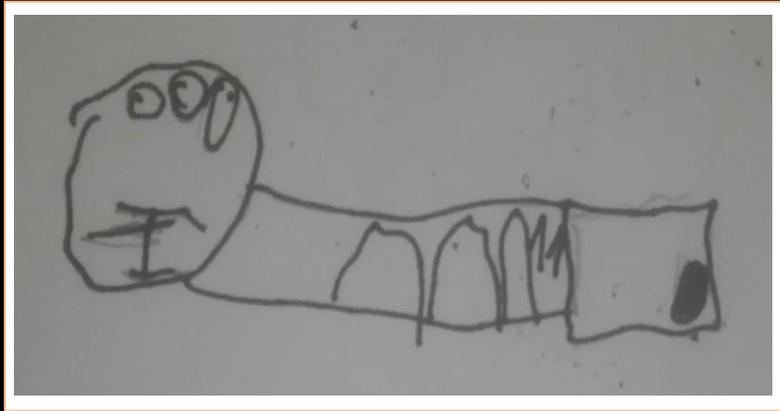
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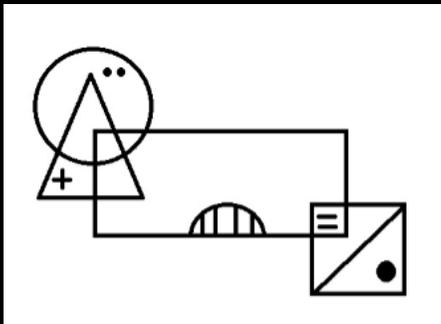
**DEFORMAZIONI**

**DISTURBI PERCETTIVI NELLA DEMENTIA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?**

# RIPRODUZIONE SU COPIA

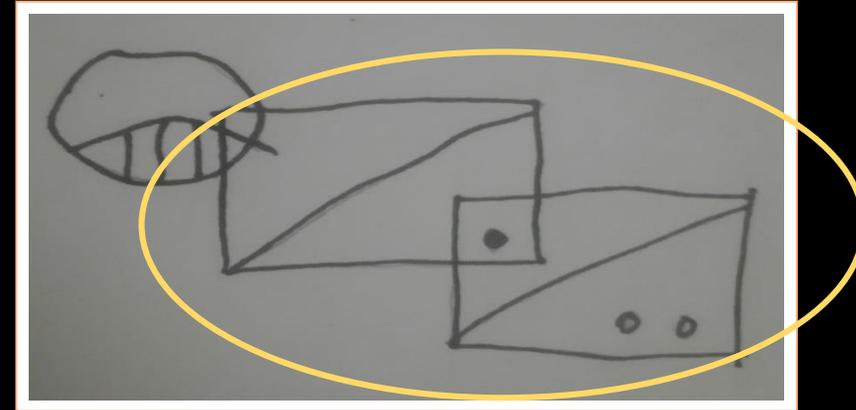
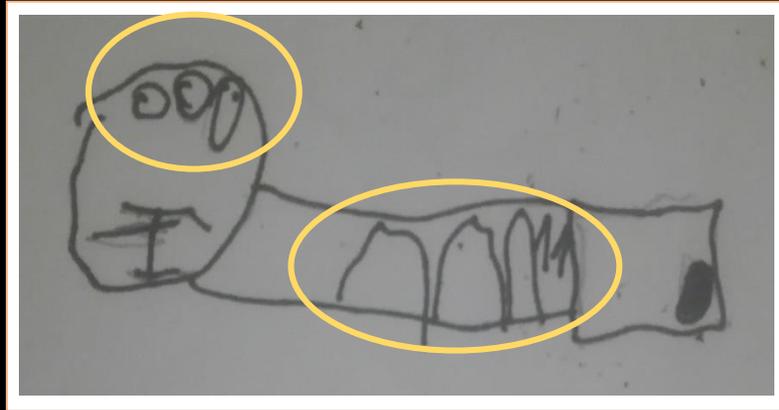


*DEMENTIA CON CORPI DI LEWY versus MALATTIA DI ALZHEIMER*

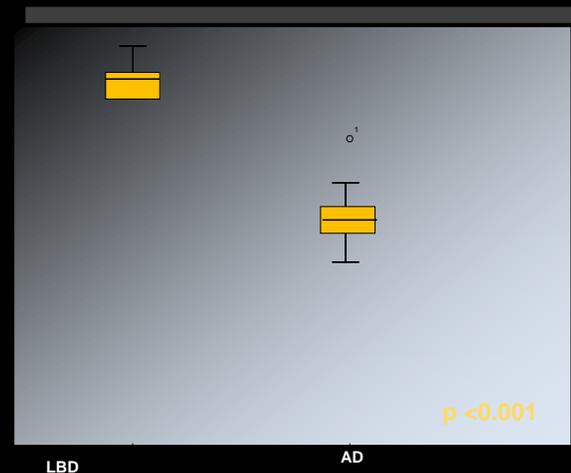
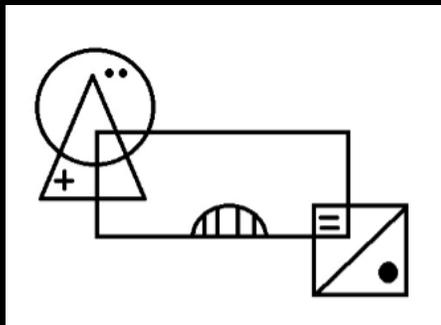


DISTURBI PERCETTIVI NELLA DEMENTIA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?

# RIPRODUZIONE SU COPIA



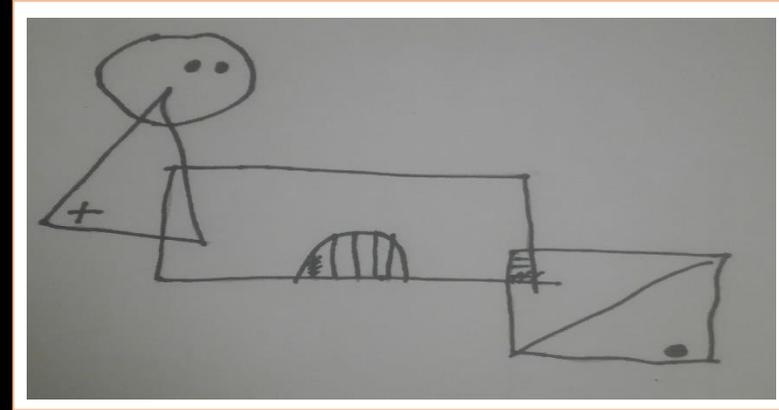
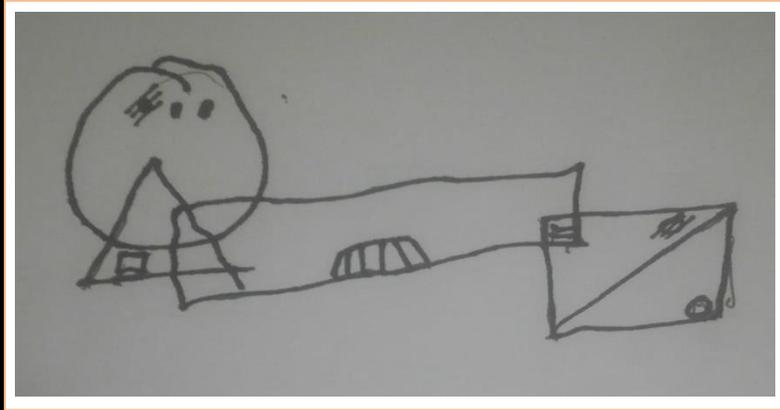
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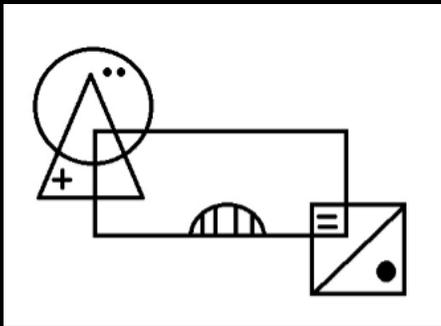
**PERSEVERAZIONI**

**DISTURBI PERCETTIVI NELLA DEMENTIA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?**

# RIPRODUZIONE SU COPIA

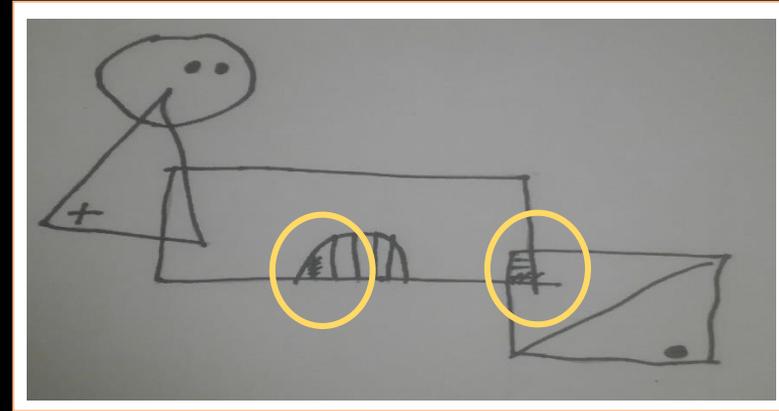
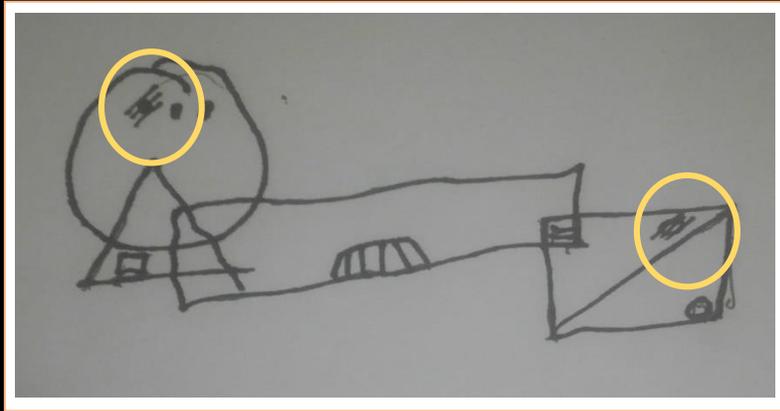


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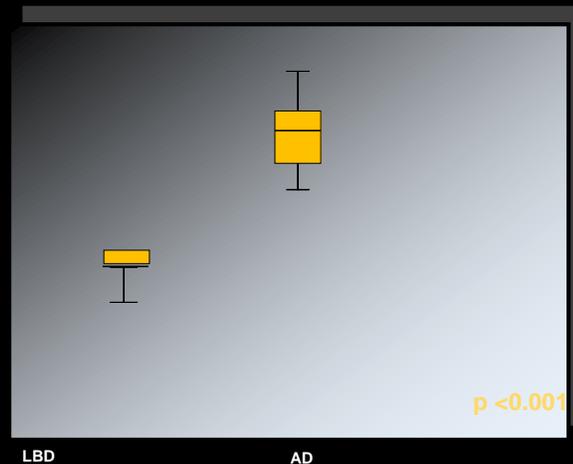
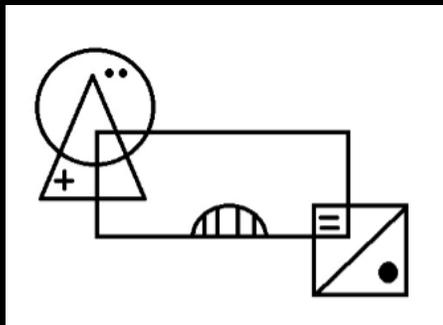


DISTURBI PERCETTIVI NELLA DEMENTIA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?

# RIPRODUZIONE SU COPIA



*DEMENTIA CON CORPI DI LEWY versus MALATTIA DI ALZHEIMER*



**AUTOCORREZIONI**

**DISTURBI PERCETTIVI NELLA DEMENTIA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?**

# DEMENZA A CORPI DI LEWY & MALATTIA DI ALZHEIMER.

## Come distinguerle?



Elaborazione dei volti ....

**COMPROMISSIONE**

**QUALITATIVAMENTE**

**DIFFERENTE**



... e copia di un disegno.

DISTURBI PERCETTIVI NELLA DEMENZA A CORPI DI LEWY E NELLA MALATTIA DI ALZHEIMER. Un ostacolo o un aiuto nella diagnosi differenziale?

*...grazie per l'attenzione.*