IL CERVELLO CHE CAMBIA 7

Sabato 11 novembre 2017

Genova, Aula Magna Clinica Neurologica

La neuropsicologia

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Kemp et al. Alzheimer's Research & Therapy (2017) 9:19
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Alzheimer's
Research & Therapy

RESEARCH Open Access

Cognitive profile in prodromal dementia with Lewy bodies

Jennifer Kemp[1,2,3,4*], Nathalie Philippi[1,2,3,4], Clélie Phillipps[1,2,3], Catherine Demuynck[1,2,3], Timothée Albasser[1,2,3], Catherine Martin-Hunyadi[1,2,3], Catherine Schmidt-Mutter[5], Benjamin Cretin[1,2,3,4] and Frédéric Blanc[1,2,3,4,5]

- La demenza a corpi di Lewy (DLB) è la seconda più comune forma di demenza neurodegenerativa
- Vi è sempre un maggiore interesse nello studio di questa patologia
- Pochi studi hanno indagato accuratamente il profilo cognitivo nelle fasi prodromiche della malattia
- Nel 2017 sono stati pubblicati i nuovi criteri diagnostici

Principali caratteristiche della DLB:

- Riduzione funzionamento cognitivo
  - Attenzione, funzioni esecutive, visuopercettive
- Fluttuazioni attentive
- Allucinazioni visive
- REM sleep behavior disorder
- Parkinsonismo (bradicinesia, tremore, rigidità)

Scopo del lavoro:

caratterizzazione del profilo cognitivo nella fase prodromica della DLB attraverso una estesa batteria neuropsicologica valutante:

Memoria

Funzioni esecutive

Funzioni strumentali (linguaggio, prassia, abilità visuospaziali)

Cognizione sociale

Comparazione dei risultati ai test dei pazienti con i dati normativi e un gruppo di controlli sani

Criteri di inclusione:

- MCI (Petersen 2004)
- Probable DLB – 2 core symptoms (McKeith 2005)
  - fluctuating attention and concentration,
  - recurrent well-formed visual hallucinations
  - spontaneous parkinsonian motor signs.

Principali criteri di esclusione (pazienti):

- 2 o più IADL perse
- abuso alcol o sostanze
- altre patologie neurologiche o psichiatriche
- DLB + 2 tra i seguenti criteri
  - deficit mnesico (storage)
  - atrofia ippocampale (Sheltens > 2)
  - CSF alterato in 2 parametri

Table 1 Demographic and clinical characteristics of patients and healthy control subjects

Characteristic	Patients with DLB	HCs	*p* Value
n	37	29	
Age, years[a]	67.19 (8.64)	68.79 (7.94)	NS
Education, years[a]	11.97 (4.14)	13.18 (3.08)	NS
Sex, M/F	18/19	15/14	NS
Handedness, R/L	35/2	27/2	NS
IADL score[a,b]	3.75 (0.50)	4 (0)	0.02
ADL score[a,c]	5.89 (0.39)	6 (0)	NS
MCI single/multiple domains			
Amnestic	0/18	–	–
Non-amnestic	10/9	–	–
Parkinsonism, *n* (%)[d]			
Rigidity	28/37 (76)	0/23	<0.001
Akinesia	22/37 (59)	1/24	<0.001
Tremor at rest	10/37 (27)	1/24	0.02
Hallucinations, *n* (%)[d]	24/37 (65)	1/24	<0.001
Fluctuations, *n* (%)[d,e]	28/37 (76)	0/24	<0.001
CSF[f,g]			
$A\beta_{42}$	902.6 (265.1, 2)	–	–
p-Tau	43.4 (12.2, 2)	–	–
Tau	306.1 (264.1, 1)	–	–
Hippocampal atrophy, 0/1/2/3/4[h]			
Left hippocampus	17/8/9/2/0	14/8/2/0/0	NS
Right hippocampus	15/10/11/0/0	11/11/2/0/0	NS

Abbreviations: $A\beta_{42}$ Amyloid-β 42, *ADL* Activities of daily living, *CSF* Cerebrospinal fluid, *DLB* Dementia with Lewy bodies, *HC* Healthy control subjects, *IADL* Instrumental activities of daily living, *MCI* Mild cognitive impairment, *NS* Not significant, *p-Tau* Phosphorylated tau

[a] Values are mean (SD)
[b] According to [32, 33]
[c] According to [34]
[d] Data partially missing for six HCs
[e] According to the Mayo Fluctuations Questionnaire [69]
[f] Data missing for ten patients
[g] Values are mean (SD, patients with abnormal values)
[h] According to [35]; one patient with DLB and five HCs did not have magnetic resonance imaging scans

Batteria test neuropsicologici:

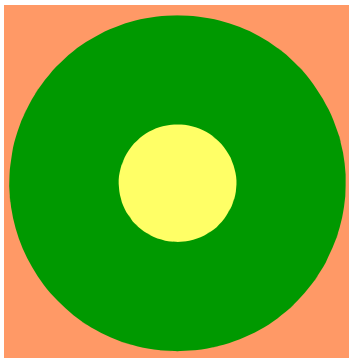
Memoria

FCSRT

DMS-48 (Test di riconoscimento visivo forzato immediato e differito)

Digit Span

A



B

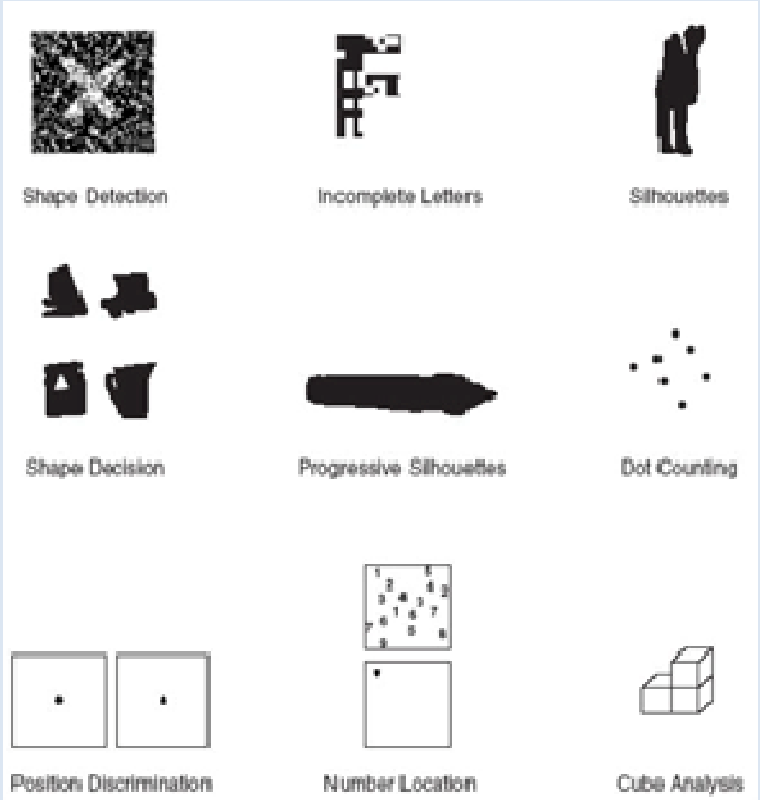
Batteria test neuropsicologici:

Funzioni esecutive
FAB
TMT
Fluenza fonemica

Velocità di elaborazione
Digit Symbol

Funzioni strumentali
Denominazione di oggetti
Fluenza semantica
Figura di Rey
Visual Object and Space Perception battery (VOSP)
Prassie

Cognizione sociale
Mini Social Cognition & Emotional Assessment
Reading the Mind in the Eyes test



Analisi dei dati: variabili cliniche e demografiche

Eventuali differenze tra le variabili e cliniche demografiche sono state calcolate tramite:

Test parametrici: ANOVA, t-test

Test non parametrici: Kruskal-Wallis, Mann-Whitney

Per variabili categoriali:

Chi-quadro

Analisi dei dati: test cognitivi

Dove possibile è stato calcolato lo **z-score** dei punteggi ai test derivato dai dati normativi della letteratura francese

Punteggi z inferiori o uguali a – 1,65 sono stati considerati patologici

L'analisi dei punteggi z è stata effettuata tramite l'ANOVA per gruppi indipendenti

L'analisi dei punteggi grezzi è stata calcolata tramite il test non parametrico di Kruskal-Wallis

Il livello di significatività è stato posto < 0.05

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Risultati:

I pazienti ed i controlli non differiscono per età, scolarità, sesso, lateralizzazione

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Risultati:

- funzioni cognitive, test patologici

Table 2 Neuropsychological test raw scores and z-scores of patients and healthy control subjects

		Patients with DLB ($n = 37$)		HCs ($n = 29$)		p Value
		Raw score[a]	z-Score[a]	Raw score[a]	z-Score[a]	
Memory						
DMS-48	Set 1	**44.05 (5.35)**	**−2.72 (5.71, 32.4)**	46.93 (1.28)	0.21 (0.97)	0.021
	Set 2	**44.23 (4.73)**	**−2.14 (4.05, 48.6)**	47.10 (0.94)	0.14 (0.72)	0.008
Executive function						
FAB		**15.49 (2.67)**	**−2.81 (4.61, 32.4)**	17.29 (1.15)	−0.02 (1.44)	0.014
TMT A		**64.89 (34.11)**	**3.00 (4.32, 51.4)**	40.62 (11.00)	0.09 (0.90)	0.011
TMT B		**139.13 (79.20)**	**3.06 (6.45, 45.9)**	90.34 (31.56)	0.12 (1.00)	0.049
Instrumental function						
Visuoconstruction	ROCF	**31.44 (5.25)**	**−1.95 (3.41, 32.4)**	34.37 (1.82)	0.13 (0.68)	NS

Funzioni cognitive

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		Raw score[a]	z-Score[a]	Raw score[a]	z-Score[a]	
Memory						
FCSRT	FR1	7.31 (2.36)	−0.66 (1.00)	8.79 (2.09)	0.02 (0.78)	0.006
	FR2	8.28 (2.91)	−0.55 (1.18)	10.62 (2.43)	0.40 (0.91)	0.001
	FR3	9.89 (2.67)	−0.51 (1.01)	11.38 (2.50)	0.08 (0.91)	0.035
	DFR	9.97 (3.82)	−0.50 (1.69)	12.45 (1.66)	0.53 (0.68)	0.003
Digit span (number of digits)		5.25 (1.13)		5.92 (1.02)		0.042
Executive function						
Digit span backward (number of digits)		3.61 (0.90)		4.42 (0.83)		0.002
Formal lexical evocation		17.28 (7.42)	−0.45 (1.09)	23.55 (7.11)	0.38 (1.09)	0.007
Instrumental function						
Praxis	Pantomime of tool use (score/10)	9.22 (1.03)		9.83 (0.38)		0.002
Language	DO80	77.61 (2.78)	0.39 (1.04)	79.62 (0.62)	0.95 (0.27)	0.022
	Formal semantic evocation	25.00 (7.72)	−0.88 (1.36)	37.38 (7.05)	0.69 (0.94)	<0.001
Visuoperception (VOSP)	Number location (score/10)	8.47 (1.78)		9.46 (0.81)		0.047
Social cognition						
Mini-SEA	FPRT	11.40 (2.39)	−1.20 (1.59)	12.73 (2.39)	−0.32 (1.11)	0.026
RME test		21.19 (4.95)	−0.19 (1.23)	23.19 (3.61)	0.35 (0.88)	0.046

In sintesi:

Il profilo cognitivo dei pazienti con prodromol DLB risulta caratterizzato da deficit:

Funzioni visuo-costruttive
Funzioni esecutive (FAB, visual search, attenzione divisa)
Memoria visiva

Punteggi siginificativamente più bassi rispetto ai controlli nei test di:

Memoria verbale (apprendimento, memoria immediata)
Funzioni esecutive (memoria di lavoro, fluenza verbale)
Funzioni strumentali (prassia, denominazione, abilità visuospaziali)
Social cognition (mind reading)

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Mov Disord. 2014 April 15; 29(5): 608–621. doi:10.1002/mds.25866.

The spectrum of cognitive impairment in Lewy body diseases

Jennifer G. Goldman, MD, MS[1], Caroline Williams-Gray, BMBCh, MRCP, PhD[2], Roger A. Barker, BSc, MBBS, MRCP, PhD[2], John E. Duda, MD[3], and **James E. Galvin, MD, MPH[4]**

Cognitive Features

Point—Both PDD and DLB have prominent executive and visuospatial dysfunction, in contrast to AD. Compared to AD patients, DLB patients generally show milder deficits on

Early neuropsychological discriminants for Lewy body disease: an autopsy series

Hiroshi Yoshizawa,[1] Jean Paul G Vonsattel,[1,2] Lawrence S Honig[1,3,4]

J Neurol Neurosurg Psychiatry 2013;**84**:1326–1330.

Conclusions Visuospatial function was more affected in pure DLB than in AD while memory retrieval deficit was more affected in AD than in pure DLB, in the early stages of dementia. However, DLB+AD did not show significant neuropsychological difference from pure AD.

A REVIEW OF COGNITIVE IMPAIRMENTS IN DEMENTIA WITH LEWY BODIES RELATIVE TO ALZHEIMER'S DISEASE AND PARKINSON'S DISEASE WITH DEMENTIA

Claudia Metzler-Baddeley

Cortex, (2007) 43, 583-600

Cognitive Impairments in Dementia with Lewy Bodies

Most studies that have investigated cognitive impairments in DLB have primarily used standard neuropsychological tests to outline DLB patients' cognitive profile. The overall pattern emerging indicates that DLB patients tend to develop earlier and more severe visuoperceptual, attentional and frontal-executive impairments than AD patients, whereas AD patients tend to be earlier and more impaired in memory tasks (Collerton et al., 2003; Dalrymple-Alford, 2001; Noe et al., 2004). Patients with DLB and PDD tend to show a similar neuropsychological pattern (Aarsland et al., 2003; Noe et al., 2004).

Lewy body dementias

Zuzana Walker, Katherine L Possin, Bradley F Boeve, Dag Aarsland

www.thelancet.com **Vol 386 October 24, 2015**

pertinent to Lewy body dementias. Characteristically, visuospatial and executive deficits with fluctuations in cognition and arousal are present in Lewy body dementias. Visuospatial or constructional impairment is

Punti critici:

Manca confronto con AD prodromal e/o con MCI-PD

Nella selezione del campione non è stato fatto il DATscan

Non viene discussa la definizione di prodromal DLB

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The clinical characteristics of dementia with Lewy bodies and a consideration of prodromal diagnosis

Donaghy and McKeith *Alzheimer's Research & Therapy* 2014, 6:46

Paul C Donaghy* and Ian G McKeith

change when new information or treatments become available. At present, diagnosis of DLB in the early stages of dementia would seem more timely and appropriate than an earlier diagnosis of prodromal LB disease of uncertain prognosis. That said, knowledge of the prodromal

Lewy body dementias

Lancet 2015; 386: 1683–97

Zuzana Walker, Katherine L Possin, Bradley F Boeve, Dag Aarsland

Prodromal and early Lewy body dementias

There is no consensus on how pre-dementia dementia with Lewy bodies should be defined. Given the complex clinical phenotype, the prodromal phase is probably heterogeneous.[49] Figure 1 shows a hypothetical model for

Journal of Geriatric Psychiatry and Neurology
2016, Vol. 29(5) 249-253

Revisiting DLB Diagnosis: A Consideration of Prodromal DLB and of the Diagnostic Overlap With Alzheimer Disease

Ian McKeith, F Med Sci[1], John-Paul Taylor, PhD[1], Alan Thomas, PhD[1], Paul Donaghy, PhD[1], and Joseph Kane, MRC Psych[1]

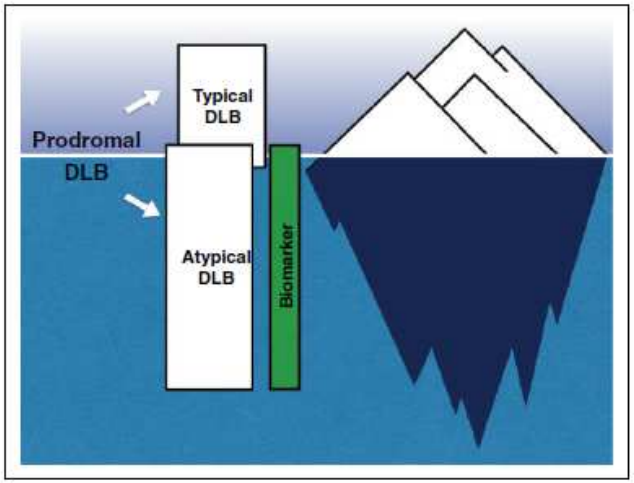

Figure 1. Schematic of the relationships between the prodromal and dementia stages of DLB.

approximately equally likely events. This poses some difficulties for the validation of a prodromal DLB diagnosis, since progression to a more typical state over time is the usual standard. Given that this is the case, it is apparent that there

Grazie per l'attenzione!