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PREVALENZA E INCIDENZA DEL MILD COGNITIVE IMPAIRMENT-PARKINSON DISEASE E PROGRESSIONE A PARKINSON DISEASE-DEMENZA IN UN CAMPIONE DI 5632 ANZIANI: ITALIAN LONGITUDINAL STUDY ON AGING

Giannini M., Solfrizzi V., Valerio R., Gaetani M., Campobasso A., Cavallo M.L., Resta F., Sabbà C. (Bari)

La malattia di Parkinson

La Malattia di Parkinson è una malattia degenerativa del Sistema Nervoso, indotta da un deficit dei sistemi dopaminergici localizzati nei nuclei della base dell'encefalo.

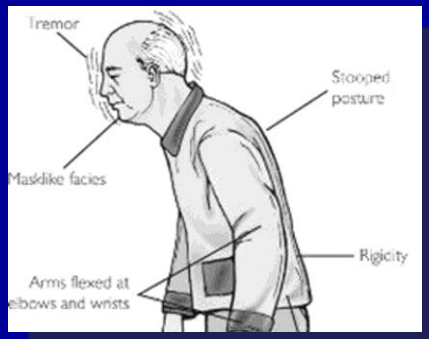
Manifestazioni cliniche

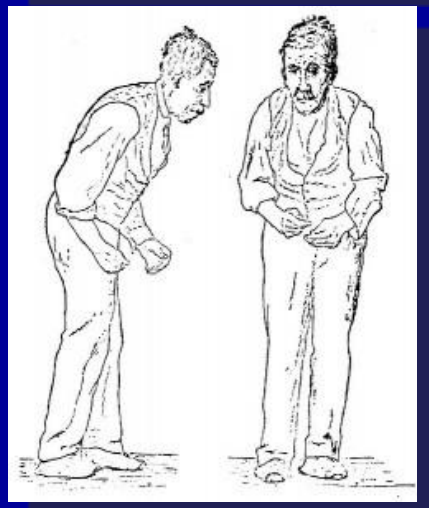
Sintomi Motori

- **Tremore**
- **Rigidità**
- **Bradicinesia**
- **Instabilità posturale**

Sintomi Non Motori

- **Sintomi sensoriali**
  (Dolori, distesie)
- **Sintomi disautonomici**
  (Disturbi urinari, gastroenterologici, ipotensione ortostatica)
- **Sintomi psichici e cognitivi**
  (Depressione, Ansia, Disturbi del Sonno, Psicosi, Disturbi Cognitivi)





Parkinson Demenza

Malattia di Parkinson

Demenza

La demenza insorge in un contesto di M. di Parkinson consolidata

TABLE 1. *Features of dementia associated with Parkinson's disease*

I. Core features

1. Diagnosis of Parkinson's disease according to Queen Square Brain Bank criteria
2. A dementia syndrome with insidious onset and slow progression, developing within the context of established Parkinson's disease and diagnosed by history, clinical, and mental examination, defined as:
   - Impairment in more than one cognitive domain
   - Representing a decline from premorbid level
   - Deficits severe enough to impair daily life (social, occupational, or personal care), independent of the impairment ascribable to motor or autonomic symptoms

II. Associated clinical features

1. Cognitive features:
   - Attention: Impaired. Impairment in spontaneous and focused attention, poor performance in attentional tasks; performance may fluctuate during the day and from day to day
   - Executive functions: Impaired. Impairment in tasks requiring initiation, planning, concept formation, rule finding, set shifting or set maintenance; impaired mental speed (bradyphrenia)
   - Visuo-spatial functions: Impaired. Impairment in tasks requiring visual-spatial orientation, perception, or construction
   - Memory: Impaired. Impairment in free recall of recent events or in tasks requiring learning new material, memory usually improves with cueing, recognition is usually better than free recall
   - Language: Core functions largely preserved. Word finding difficulties and impaired comprehension of complex sentences may be present
2. Behavioral features:
   - Apathy: decreased spontaneity; loss of motivation, interest, and effortful behavior
   - Changes in personality and mood including depressive features and anxiety
   - Hallucinations: mostly visual, usually complex, formed visions of people, animals or objects
   - Delusions: usually paranoid, such as infidelity, or phantom boarder (unwelcome guests living in the home) delusions
   - Excessive daytime sleepiness

III. Features which do not exclude PD-D, but make the diagnosis uncertain

- Co-existence of any other abnormality which may by itself cause cognitive impairment, but judged not to be the cause of dementia, e.g. presence of relevant vascular disease in imaging
- Time interval between the development of motor and cognitive symptoms not known

IV. Features suggesting other conditions or diseases as cause of mental impairment, which, when present make it impossible to reliably diagnose PD-D

- Cognitive and behavioral symptoms appearing solely in the context of other conditions such as:

  Acute confusion due to
  a. Systemic diseases or abnormalities
  b. Drug intoxication

  Major Depression according to DSM IV
- Features compatible with "Probable Vascular dementia" criteria according to NINDS-AIREN (dementia in the context of cerebrovascular disease as indicated by focal signs in neurological exam such as hemiparesis, sensory deficits, and evidence of relevant cerebrovascular disease by brain imaging AND a relationship between the two as indicated by the presence of one or more of the following: onset of dementia within 3 months after a recognized stroke, abrupt deterioration in cognitive functions, and fluctuating, stepwise progression of cognitive deficits)

TABLE 2. *Criteria for the diagnosis of probable and possible PD-D*

Probable PD-D

A. Core features: Both must be present
B. Associated clinical features:
   - Typical profile of cognitive deficits including impairment in at least two of the four core cognitive domains (impaired attention which may fluctuate, impaired executive functions, impairment in visuo-spatial functions, and impaired free recall memory which usually improves with cueing)
   - The presence of at least one behavioral symptom (apathy, depressed or anxious mood, hallucinations, delusions, excessive daytime sleepiness) supports the diagnosis of Probable PD-D, lack of behavioral symptoms, however, does not exclude the diagnosis

C. None of the group III features present
D. None of the group IV features present

Possible PD-D

A. Core features: Both must be present
B. Associated clinical features:
   - Atypical profile of cognitive impairment in one or more domains, such as prominent or receptive-type (fluent) aphasia, or pure storage-failure type amnesia (memory does not improve with cueing or in recognition tasks) with preserved attention
   - Behavioral symptoms may or may not be present

OR

C. One or more of the group III features present
D. None of the group IV features present

Movement Disorders, Vol.22, No. 12, 2007

Clinical Review

A Systematic Review of Prevalence Studies of Dementia in Parkinson's Disease

Dag Aarsland, MD,[1,2*] Julia Zaccai, MSc,[3] and Carol Brayne, MD[3]

[1]*Section of Geriatric Psychiatry, Stavanger University Hospital, Stavanger, Norway*
[2]*University of Bergen, Bergen, Norway*
[3]*Department of Public Health and Primary Care, University of Cambridge, Cambridge, United Kingdom*

Abstract: Substantial variation in the prevalence of dementia in Parkinson's disease (PDD) has been reported. The aim of this study was to review systematically and critically previous studies of the prevalence of PDD using PubMed to search the literature. Studies focusing on PD and PDD, as well as those examining on the epidemiology of dementia subtypes, were included. Predefined inclusion and exclusion criteria were used and the quality of the studies included was rated. Articles were included if: (1) the proportion of PDD among patients with either PD or dementia was reported in an original study; (2) patients had been subjected to prospective clinical examination; and (3) strategies to include all subjects with either PD or dementia within the community or hospital clinics within a geographical area were employed. Twelve studies of the prevalence of PD or PDD (1,767 patients included) and 24 prevalence studies of dementia subtypes (4,711 patients included) met the inclusion criteria. In the PD/PDD studies, the proportion (mean and 95% confidence interval) with PDD in PD was 24.5% (17.4–31.5). There were significant methodological variations between studies and in the four studies that matched the quality criteria most closely, the rate of PDD was 31.1% (20.1–42.1). The prevalence of PDD was estimated as 0.5% in subjects 65 years or older. The percentage of PDD among those with dementia was 3.6% (3.1–4.1), with an estimated prevalence of PDD of 0.2% in subjects aged 65 years or older. Despite methodological variation, this systematic review suggests that 24 to 31% of PD patients have dementia, and that 3 to 4% of the dementia in the population would be due to PDD. The estimated prevalence of PDD in the general population aged 65 years and over is 0.2 to 0.5%. © 2005 Movement Disorder Society

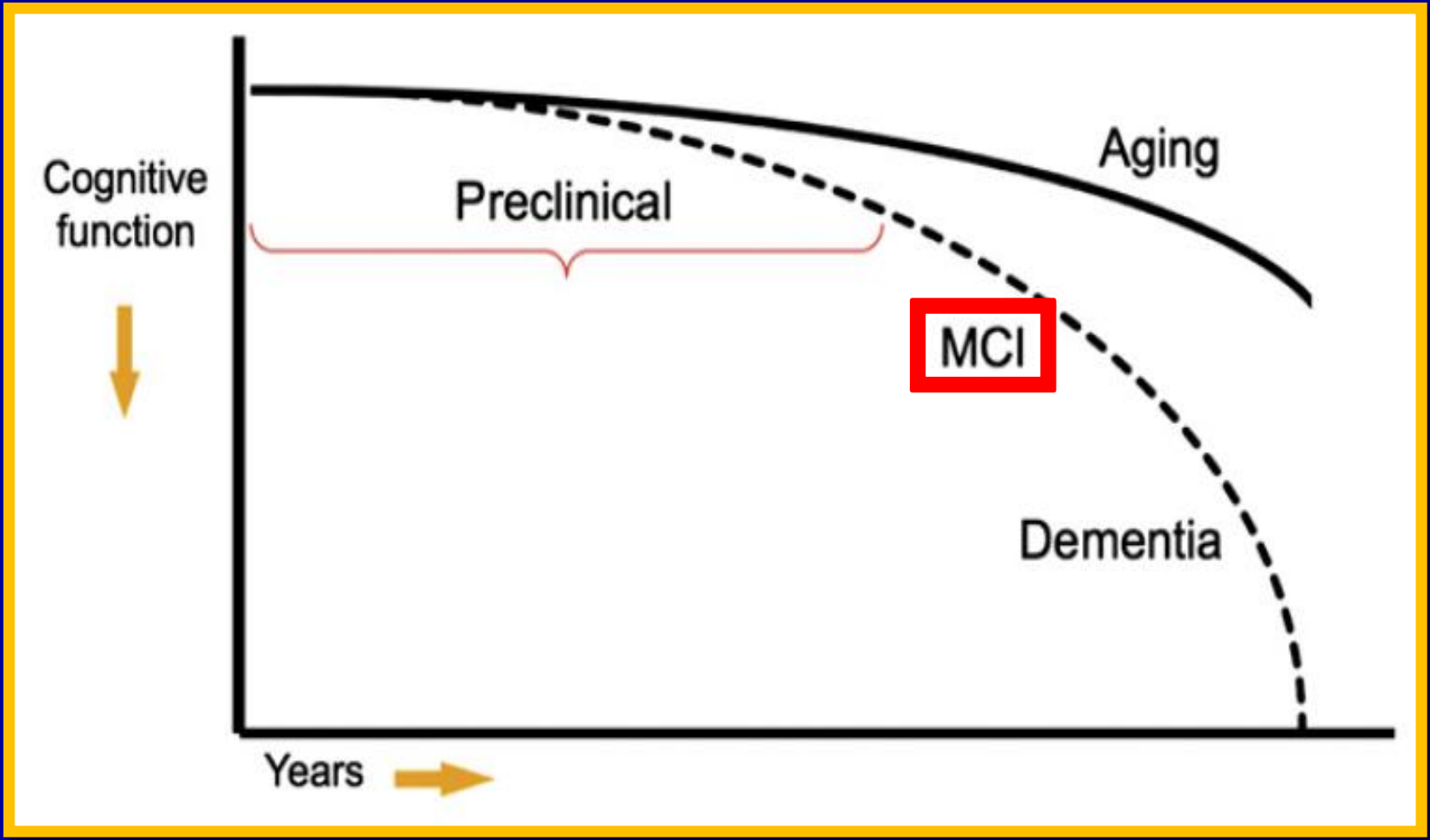
Key words: Parkinson's disease; dementia; prevalence; cognition; systematic review

Movement Disorders 2005; 20, 1255–63

Study	PD (n)	PDD (n)	PDD/PD %	PDD/PD 95% CI
Pollock[13]	84	7	8.3	4.1–16.3
Snow[14]	55	11	20	11.6–32.4
Okada[15]	66	7[a]	17.1	8.5–31.0
Sutcliffe[16]	353	145	41.1	36.1–46.3
Mutch[17]	249	93	37.3	31.6–43.5
Martilla[18]	421	122	29.0	24.9–33.5
Wang[19]	6	1	16.7	3.0–56.4
Melcon[20]	51	8	15.7	8.2–28.0
Wang[21]	23	3	13	4.5–32.1
Aarsland[24]	245	67	27.3	22.1–33.2
Mayeux[22]	179	74	41.3	34.4–48.7
Tison[23]	60	16	27.6[b]	17.0–39.0
All studies	1,767	554	31.3	29.2–33.6
Mean	147.3	46.2	24.5	17.4–31.5
95% CI	58.6–235.9	13.3–79.1		

Movement Disorders 2005; 20, 1255–63

The continuum of dementia



R.A. Sperling et al. / Alzheimer's & Dementia (2011) 1–13

MCI nella Malattia di Parkinson

Diagnostic Criteria for Mild Cognitive Impairment in Parkinson's Disease: *Movement* Disorder Society Task Force Guidelines

Irene Litvan, MD,[1*] Jennifer G. Goldman, MD, MS,[2] Alexander I. Tröster, PhD,[3] Ben A. Schmand, PhD,[4] Daniel Weintraub, MD,[5] Ronald C. Petersen, MD, PhD,[6] Brit Mollenhauer, MD,[7] Charles H. Adler, MD, PhD,[8] Karen Marder, MD,[9] Caroline H. Williams-Gray, MRCP, PhD,[10] Dag Aarsland, MD, PhD,[11] Jaime Kulisevsky, MD, PhD,[12] Maria C. Rodriguez-Oroz, MD, PhD,[13] David J. Burn, MD, FRCP,[14] Roger A. Barker, BSc, MBBS, MRCP, PhD,[10] and Murat Emre, MD[15]

III. Specific guidelines for PD-MCI level I and level II categories

A. Level I (abbreviated assessment)

- Impairment on a scale of global cognitive abilities validated for use in PD[a] *or*
- Impairment on at least two tests, when a limited battery of neuropsychological tests is performed (i.e., the battery includes less than two tests within each of the five cognitive domains, or less than five cognitive domains are assessed)

B. Level II (comprehensive assessment)

- Neuropsychological testing that includes two tests within each of the five cognitive domains (i.e., attention and working memory, executive, language, memory, and visuospatial)[b]
- Impairment on at least two neuropsychological tests, represented by either two impaired tests in one cognitive domain or one impaired test in two different cognitive domains
- Impairment on neuropsychological tests may be demonstrated by:
  - o Performance approximately 1 to 2 SDs below appropriate norms *or*
  - o Significant decline demonstrated on serial cognitive testing *or*
  - o Significant decline from estimated premorbid levels

Movement Disorders (2012)

Prevalenza MCI nella Malattia di Parkinson

Table 1 Recent studies of the frequency of MCI in PD

Study	*N*	MCI (%)	Definition of MCI	Cohort
Foltynie et al. [9]	146	30.1	1 SD[a] on one of two tests	Community/incident
Muslimovic et al. [10]	115	23.5	2 SD[a] on 3 of 28 tests	Clinic/early PD
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Mamikonyan et al. [55]	106	29.2	1.5 SD in one domain[a]	Clinic/convenience
Aarsland et al. [14]	1.346	25.8	One domain (1.5 SD)[a]	Multicenter pooled analysis
Sollinger et al. [56]	72	52.8	Impairment on at least two tests in at least one domain + subjective impairment	Retrospective analysis of consecutive referrals to a tertiary movement disorders clinic

[a] Minimum level below the normative data or control group

MCI mild cognitive impairment; *PD* Parkinson's disease; *SD* standard deviation

Aarsland D et al Curr Neurol Neurosci Rep (2011) 11:371–378

Obiettivi dello studio
Study Population ILSA

Valutare la prevalenza e l'incidenza del aMild Cognitive Impairment nei soggetti parkinsoniani anziani (aMCI-PD) e pregressione dell'aMCI-PD a Parkinson Demenza (PDD) arruolati in uno studio di popolazione italiano (ILSA)

Italian Longitudinal Study On Aging - ILSA

1° Survey (1992-1993)
2° Survey (1995-1996)

Population – based sample of 5632 subjects (65-84 yrs)

Eight Italian municipalities (each centre : 704 subjects)

Dati CNR-PF Invecchiamento

Dati nazionali ILSA sulla prevalenza età-specifica e sesso-specifica della Malattia di Parkinson

Parkinson's disease and parkinsonism in a longitudinal study

Two-fold higher incidence in men

M. Baldereschi, MD; A. Di Carlo, MD; W.A. Rocca, MD, MPH; P. Vanni, MD; S. Maggi, MD; E. Perissinotto, ScD; F. Grigoletto, ScD; L. Amaducci, MD†; and D. Inzitari, MD, for the ILSA Working Group*

	Maschi	Femmine
65-69 anni	0.5%	0.9%
	(5.2%)	(9.1%)
70-74 anni	1.0%	2.2%
	(10.3%)	(21.8%)
75-79 anni	3.7%	3%
	(36.2%)	(29.1%)
80-84 anni	5.1%	4.1%
	(48.3%)	(40%)

Baldereschi M et al NEUROLOGY 2000;55:1358–1363

METODI

Criteri adottati per la diagnosi di aMCI

Assenza di demenza

Normale assetto cognitivo valutato al MMSE

(*cut off* calcolato sottraendo 1,5 DS dal punteggio del MMSE)

corretto per età e scolarità

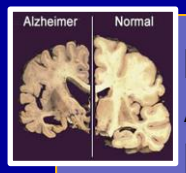
Evidenza obiettiva di declino mnesico valutato con il Test di Babcock corretto per età media e scolarità

Indipendenza nelle attività del vivere quotidiano

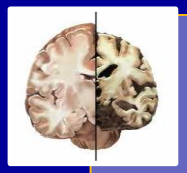
ADL=6; ADL debolmente compromesse ma con nessuna compromissione nelle IADL; presenza di disabilità visive, uditive, muscolo-scheletriche che compromettono le ADL ma non i campi cognitivi; compromissione delle ADL dipendente dalla presenza di patologie concomitanti

METODI

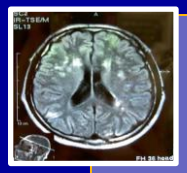
Diagnosi di esclusione
con la Demenza associata a Malattia di Parkinson



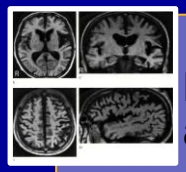
Malattia di Alzheimer probabile



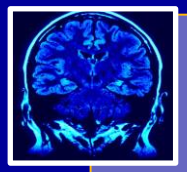
Malattia di Alzheimer possibile



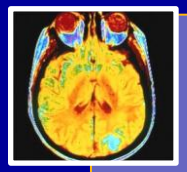
Demenza vascolare



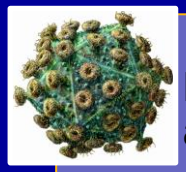
Demenza associata alla Malattia di Pick



Demenza associata alla Malattia di Creutzfeldt-Jakob



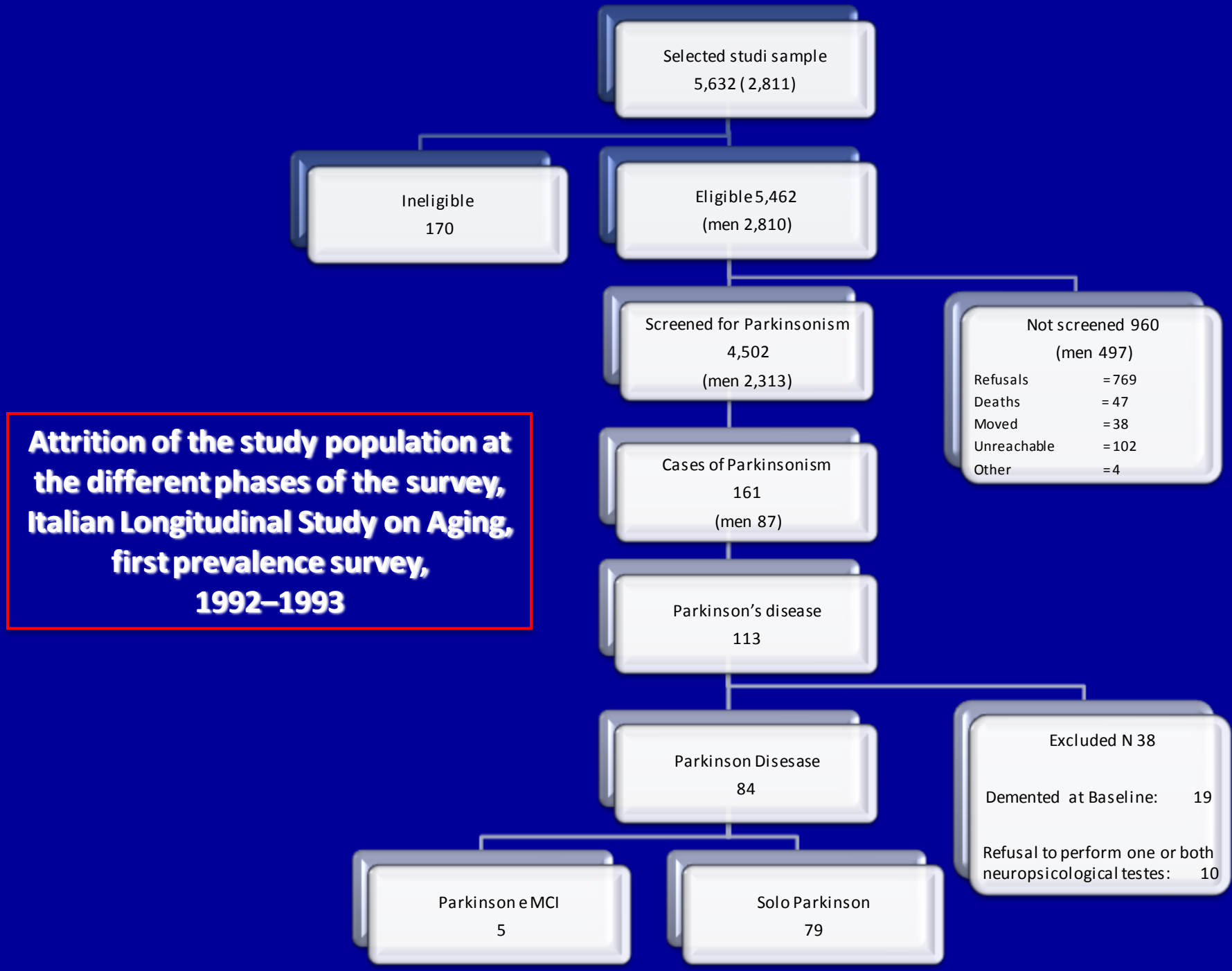
Demenza associata alla malattia di Huntington



Demenza associata ad infezione da HIV

Demenza associata ad altre malattie

Demenza non specificabile


Attrition of the study population at the different phases of the survey, Italian Longitudinal Study on Aging, first prevalence survey, 1992–1993
Selected studi sample
5,632 (2,811)
Ineligible
170
Eligible 5,462
(men 2,810)
Screened for Parkinsonism
4,502
(men 2,313)
Not screened 960
(men 497)
Refusals = 769
Deaths = 47
Moved = 38
Unreachable = 102
Other = 4
Cases of Parkinsonism
161
(men 87)
Parkinson's disease
113
Parkinson Disesase
84
Excluded N 38
Demented at Baseline: 19
Refusal to perform one or both neuropsicological testes: 10
Parkinson e MCI
5
Solo Parkinson
79

EPIDEMIOLOGY OF MCI IN ITALY

ILSA - ITALIAN LONGITUDINAL STUDY ON AGING

aMCI PREVALENCE

3.2%

Solfrizzi V et al Neurology. 2004 23;63(10):1882-91

aMCI INCIDENCE

21.5

(1,000 person-year)

Solfrizzi V et al Neurology 2004 23;63(10):1882-91

aMCI PREVALENCE

in Parkinson's Disease

4,65%

RISULTATI

Prevalenza (5/84)

Intero campione	4,65%

Età	
75-79 anni	6,67%
80-84 anni	11,1%

Sesso	
Uomo	2,63%
Donna	6,67%

Scolarità	
≤ 3 anni	6,86%
> 3 anni	3,38%

EPIDEMIOLOGY OF MCI IN ITALY

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aMCI PREVALENCE in Parkinson's Disease

4,65%

aMCI INCIDENCE in Parkinson's Disease

46,1

RISULTATI

Incidenza (3/18)

		IC 95%
Intero campione	**46.1**	**(14.9 –142)**
Età		
75-79 anni	115.6	(37.3 – 358)
80-84 anni	0	(0)
Sesso		
Uomo	59.8	(14.9-239)
Donna	31.6	(4.5 – 225)
Scolarità		
≤ 3 anni	188	(60,7-583)
> 3 anni	0	(0)

Prevalenza MCI nella Malattia di Parkinson

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Subtypes of Mild Cognitive Impairment in Parkinson's Disease: Progression to Dementia

Carmen Cristea Janvin, M Psych,[1] Jan Petter Larsen, MD, PhD,[2] Dag Aarsland, MD, PhD,[1]* and Kenneth Hugdahl, M Psych, PhD[3]

[1]*Stavanger University Hospital, Section of Geriatric Psychiatry, Stavanger, Norway*
[2]*Stavanger University Hospital, Department of Neurology, Stavanger, Norway*
[3]*University of Bergen, Department of Biological and Medical Psychology, Bergen, Norway*

RESULTS

Baseline Assessment

There were 11 patients who declined to participate, 58 (43.3%) of the remaining 134 patients with PD had dementia, and 76 (56.7%) were without dementia, but 4 of these did not perform all the neuropsychological tests. Thus, 72 nondemented PD patients comprised the at-risk population. The control group had similar demographic characteristics and MMSE scores as the nondemented PD patients (Table 1), but performed better on all the neuropsychological tests. Of the nondemented PD patients, 34 PD patients (47.2%) were cognitively intact, whereas 38 (52.8%) were diagnosed with MCI. Twenty-six (68%) cognitively impaired PD patients also reported memory complaint or other subjective cognitive impairment. The following MCI subtypes were identified: amnestic type (n = 6; 15.8%), single nonmemory domain type (n = 17, 44.7%), and multiple domains slightly impaired type (n = 15; 39.5%). The demographic and clinical characteristics of these subgroups are shown in Table 2.

EPIDEMIOLOGY OF MCI IN ITALY

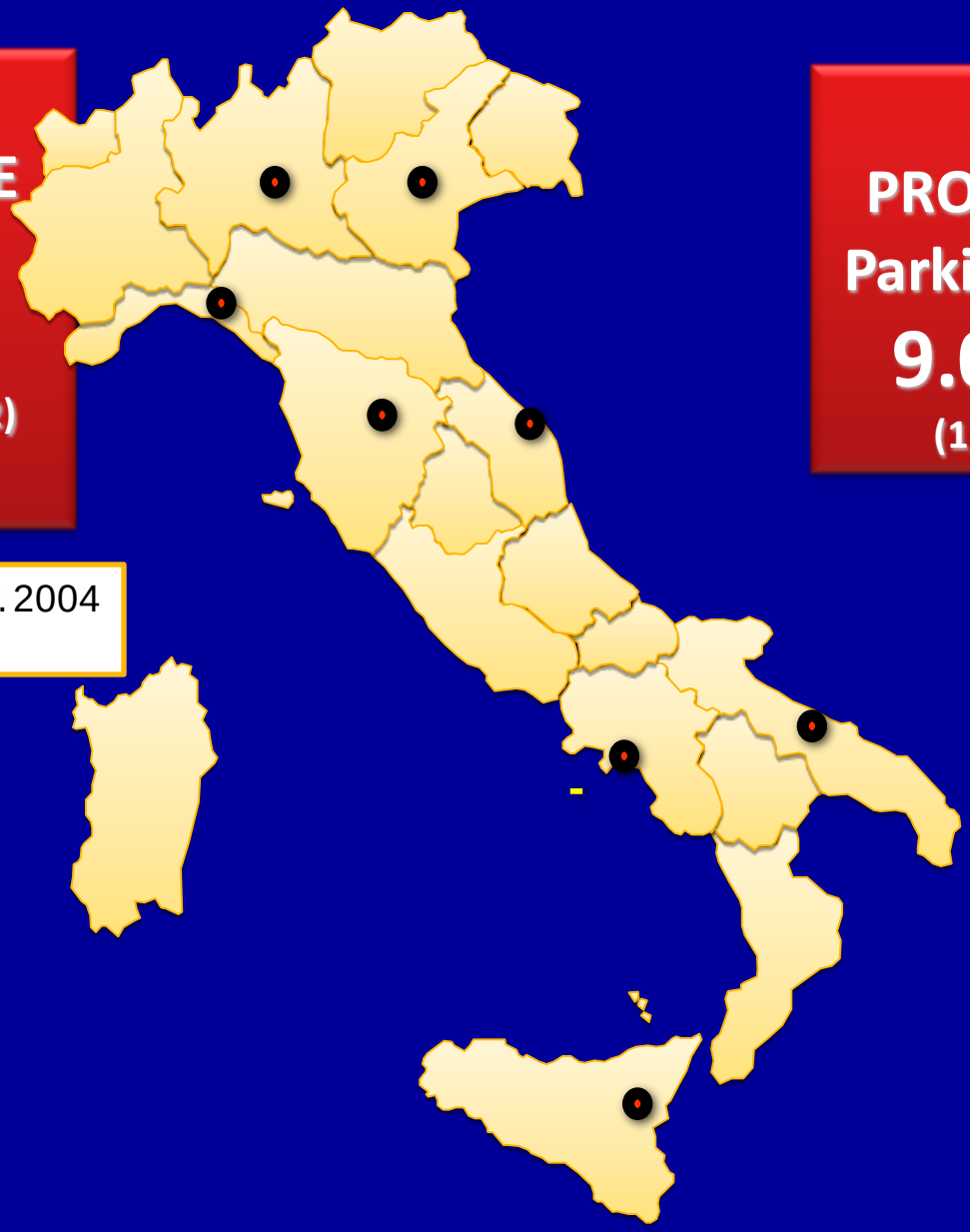
ILSA - ITALIAN LONGITUDINAL STUDY ON AGING

aMCI PROGRESSIONE in Demenze

3.8 (95% IC 2,3-6,2)

(1,000 person-year)

Solfrizzi V et al Neurology. 2004 23;63(10):1882-91



aMCI PROGRESSIONE in Parkinson's Disease

9.0 (95% IC 1,3-63,6)

(1,000 person-year)

Conclusioni 1

PREVALENZA

La prevalenza del aMCI in una popolazione di soggetti parkinsoniani è condizionata dalla tipologia dello studio e dai criteri adottati.

Il dato di prevalenza del aMCI in soggetti parkinsoniani nel nostro studio è maggiore di quello calcolato sulla popolazione generale.

Come verificato sulla popolazione generale, la prevalenza cresce con l'età, è lievemente superiore nelle donne rispetto agli uomini, è maggiore nei soggetti meno scolarizzati.

Conclusioni 2

INCIDENZA

Nel confronto tra l'incidenza del aMCI nei soggetti parkinsoniani rispetto al aMCI della popolazione generale, la stima globale risulta essere più del doppio (nei soggetti parkinsoniani) rispetto al MCI della popolazione generale.

Conclusioni 3

PROGRESSIONE

Nel confronto tra la progressione del aMCI nei soggetti parkinsoniani rispetto al aMCI della popolazione generale, il tasso di conversione risulta essere una volta e mezzo (nei soggetti parkinsoniani) rispetto a quello della popolazione generale.

Conclusioni 4

Il Mild Cognitive Impairment è una fase prodromica della demenza.

Molta attenzione dovrebbe essere posta in questa fase preclinica di malattia, perchè aumenterebbe l'accuratezza diagnostica e potrebbe modificare il decorso della storia clinica della demenza.

Grazie per l'Attenzione