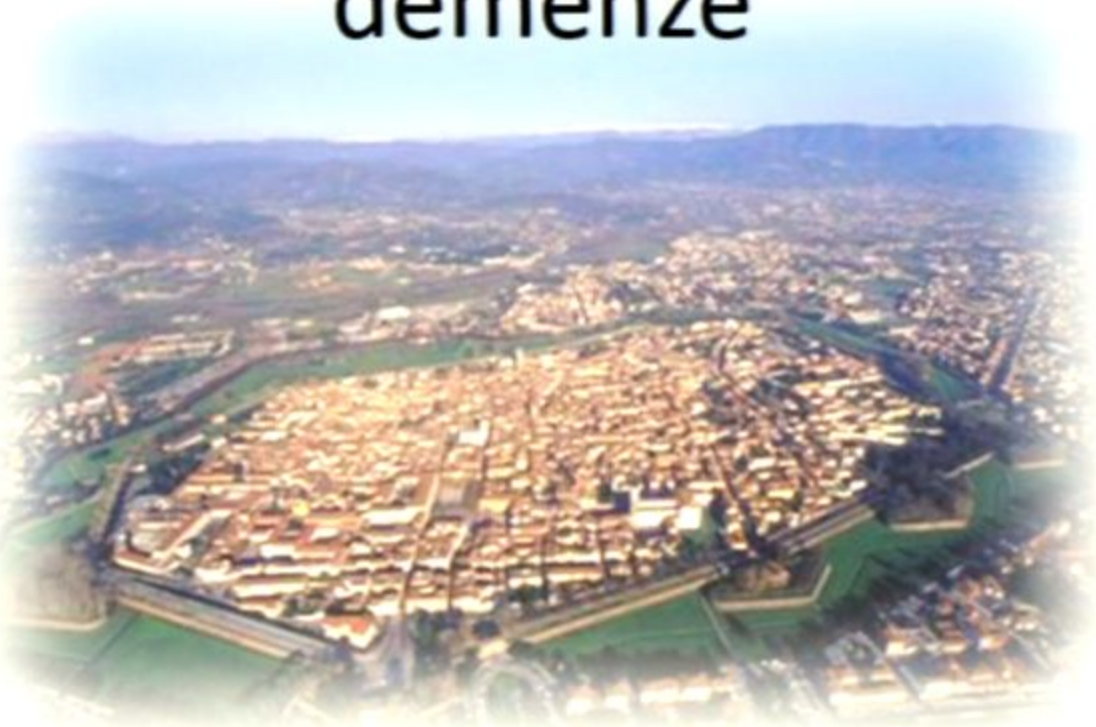
Le parole e la memoria: la dissoluzione del linguaggio nelle demenze



Dott. Marco Vista
S.C. Neurologia Lucca

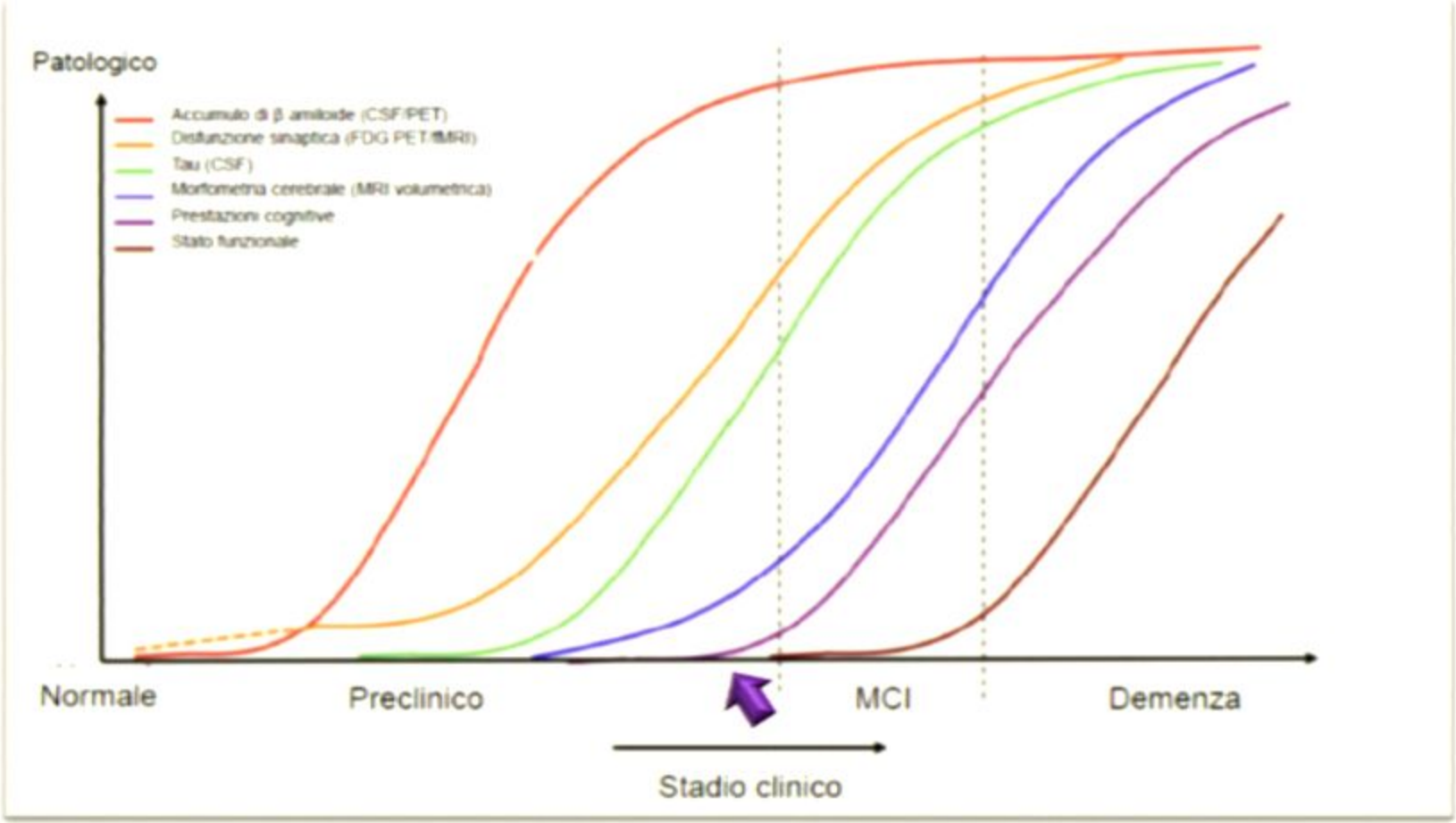
Azienda USL Toscana nord ovest
Servizio Sanitario della Toscana

Disturbi del linguaggio

- Malattia di Alzheimer
- Afasie Primarie Progressive

	Alzheimer's disease
DSM-5	Causative AD genetic mutation or all of the following: – Memory and learning decline plus one other cognitive domain – Steady gradual cognitive decline – No evidence of mixed aetiology (absence of other neurodegenerative or cerebrovascular disease or other condition contributing to cognitive decline)
IWG-2	Episodic memory impairment and one of the following: – Decreased $A\beta_{42}$ plus increased P-tau or T-tau in CSF – Increased tracer retention on amyloid PET – Autosomal dominant mutation Exclusions include cerebrovascular disease and signs and symptoms of DLB

Evoluzione temporale dei markers di malattia nella M. di Alzheimer



Lancet Neurol 2014; 13: 614–29

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

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 amnestic 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

Lancet Neurol 2014; 13: 614–29

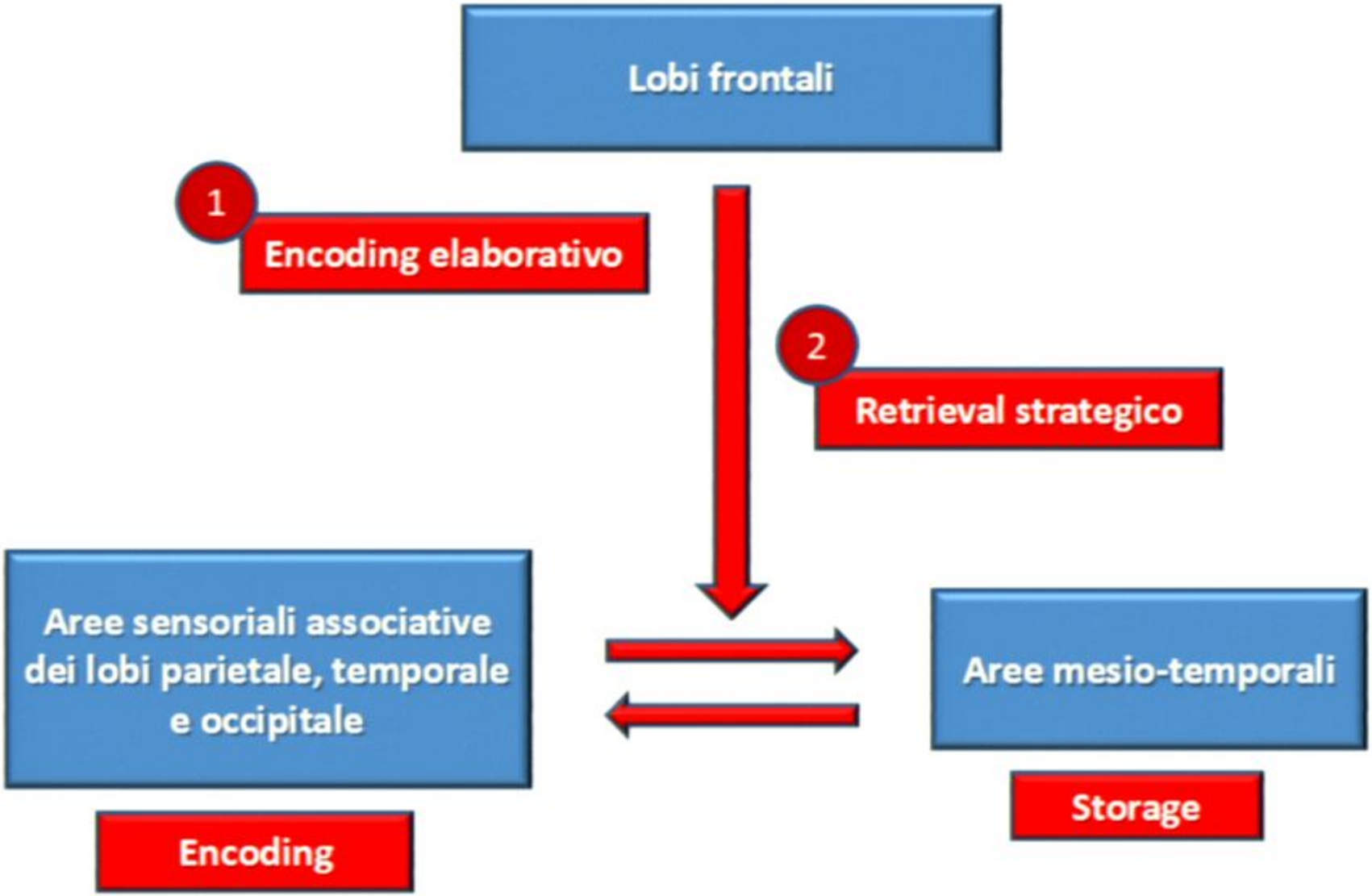
Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria

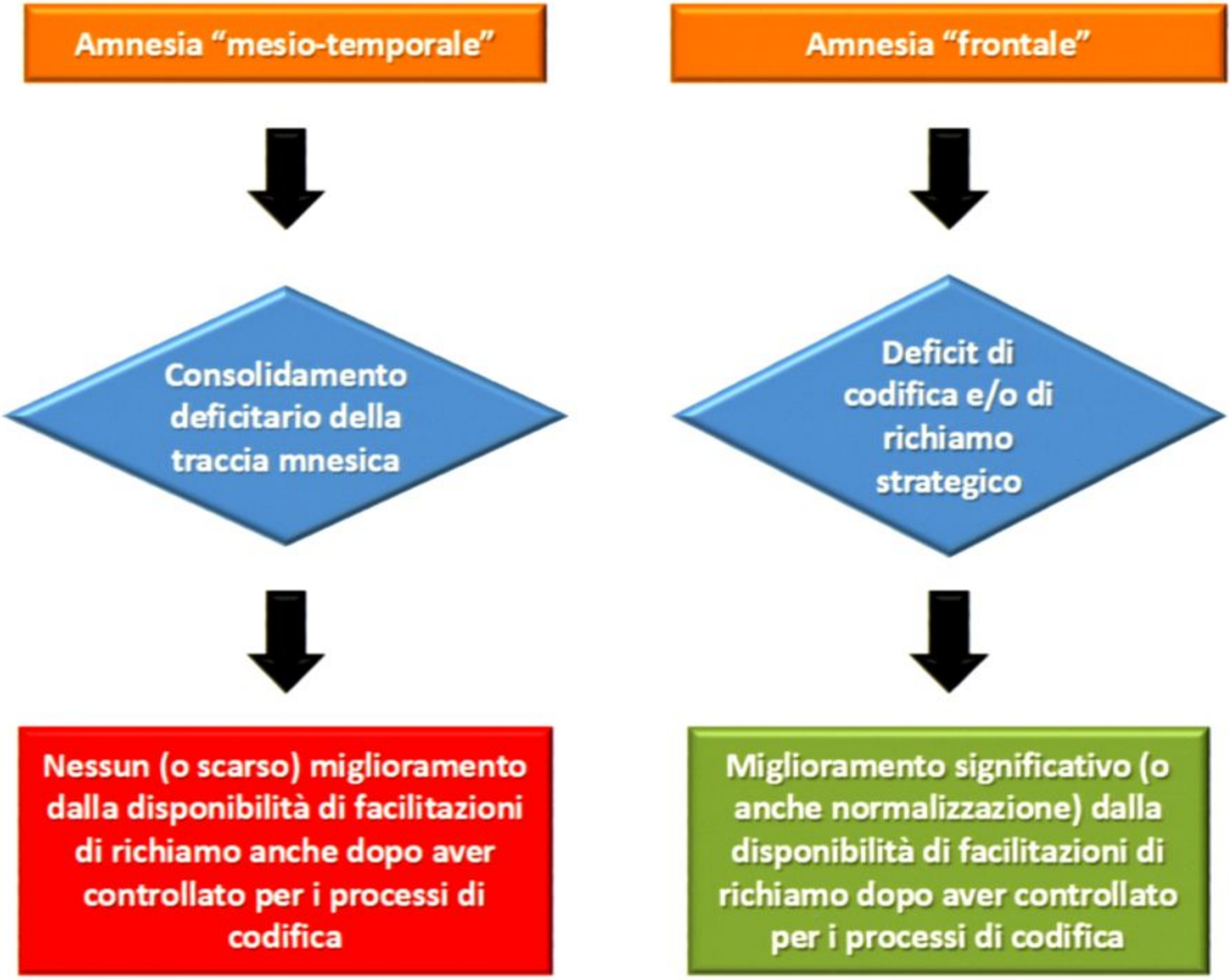
Bruno Dubois, Howard H Feldman, Claudia Jacova, Harald Hampel, José Luis Molinuevo, Kaj Blennow, Steven T DeKosky, Serge Gauthier, Dennis Selkoe, Randall Bateman, Stefano Cappa, Sebastian Crutch, Sebastiaan Engelborghs, Giovanni B Frisoni, Nick C Fox, Douglas Galasko, Marie-Odile Habert, Gregory A Jicha, 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

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 amnestic 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

Aree corticali coinvolte nel funzionamento della memoria a lungo termine dichiarativa




Amnesia "mesio-temporale"
Amnesia "frontale"
Consolidamento deficitario della traccia mnesica
Deficit di codifica e/o di richiamo strategico
Nessun (o scarso) miglioramento dalla disponibilità di facilitazioni di richiamo anche dopo aver controllato per i processi di codifica
Miglioramento significativo (o anche normalizzazione) dalla disponibilità di facilitazioni di richiamo dopo aver controllato per i processi di codifica

Neurol Sci
DOI 10.1007/s10072-011-0607-3

ORIGINAL ARTICLE

Free and cued selective reminding test: an Italian normative study

P. Frasson · R. Ghiretti · E. Catricalà · S. Pomati · A. Marcone · L. Parisi · P. M. Rossini · S. F. Cappa · C. Mariani · N. Vanacore · F. Clerici

Received: 12 January 2011 / Accepted: 23 April 2011

Cold Spring Harb Perspect Med 2012;2:a006171

The Neuropsychological Profile of Alzheimer Disease

Sandra Weintraub[1], Alissa H. Wicklund[1], and David P. Salmon[2]

[1]Cognitive Neurology and Alzheimer's Disease Center (CNADC), Northwestern University Feinberg School of Medicine, Chicago, Illinois 60611

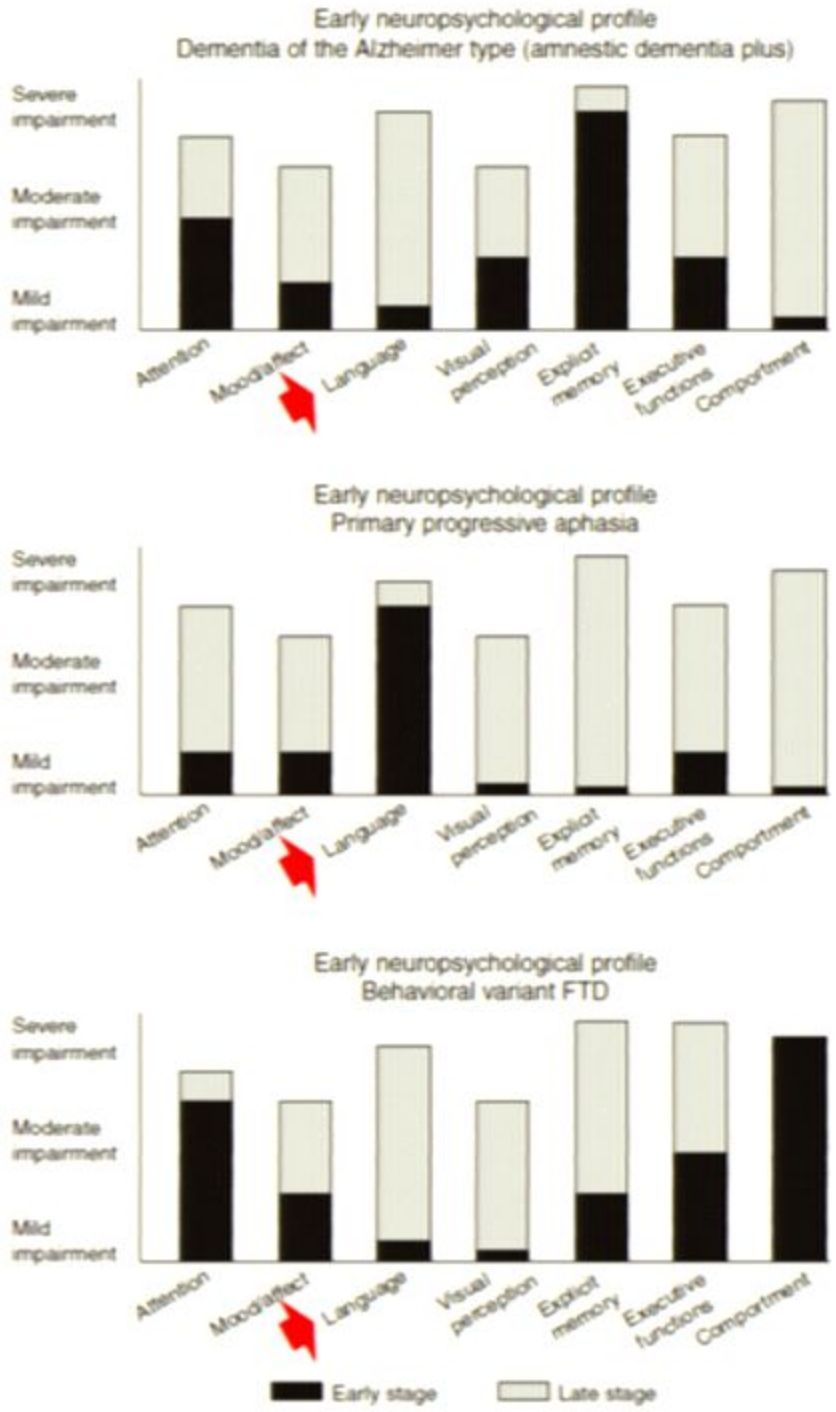
[2]Department of Neurosciences, University of California San Diego, La Jolla, California 92093-0662

Correspondence: sweintraub@northwestern.edu

Editors: Dennis J. Selkoe, Eckhard Mandelkow, and David M. Holtzman

Additional Perspectives on The Biology of Alzheimer Disease available at www.perspectivesinmedicine.org

Cite this article as Cold Spring Harb Perspect Med 2012;2:a006171



frontiers in Aging Neuroscience

Speaking in Alzheimer's disease, is that an early sign? Importance of changes in language abilities in Alzheimer's disease

Greta Szatloczki[1]*, Ildiko Hoffmann[2,3], Veronika Vincze[4], Janos Kalman[1] and Magdolna Pakaski[1]

[1] Research Institute for Linguistics, Hungarian Academy of Sciences, Szeged, Hungary, [2] Research Institute for Linguistics, Hungarian Academy of Sciences, Budapest, Hungary, [3] Department of Linguistics, University of Szeged, Szeged, Hungary, [4] MTA-SZTE Research Group on Artificial Intelligence, University of Szeged, Szeged, Hungary

Examination methods	Examination results	Sensitivity measures	Reference
Phonetics and phonology			
Temporal analysis of spontaneous speech	Mild AD and CTRL differ in speech tempo and hesitation ratio	No data	Hoffmann et al. (2010)
Temporal analysis of speech, oral reading task	Distinguishes moderate AD and CTRL. Best two parameters: speech tempo and articulation tempo	80%	Martinez-Sánchez et al. (2013)
Spoken task; speech-based detection	Might be a good method for detecting early AD	CTRL and MCI: 80% MCI and AD: 87%	Satt et al. (2014)
Automatic spontaneous speech analysis	Distinguishes between AD and CTRL	No data	López-de-Ipiña et al. (2013)

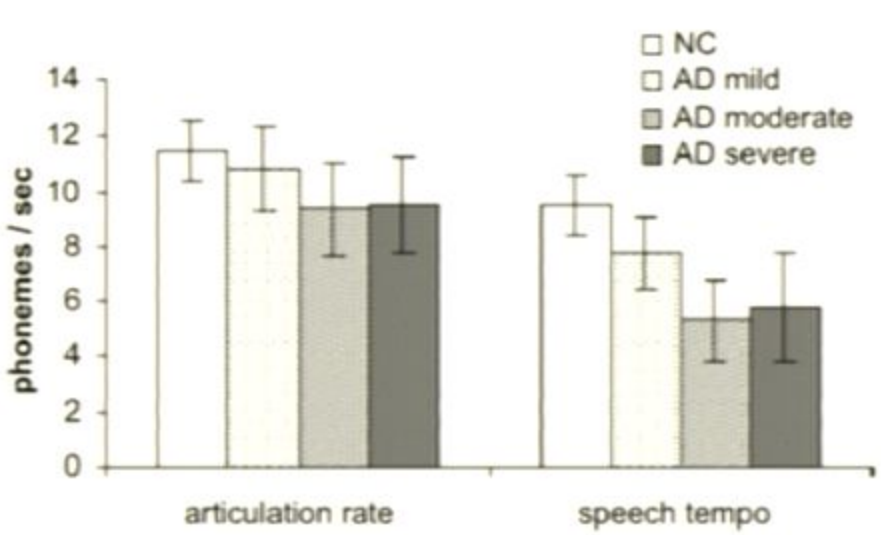
International Journal of Speech-Language Pathology, 2010; 12(1): 29–34

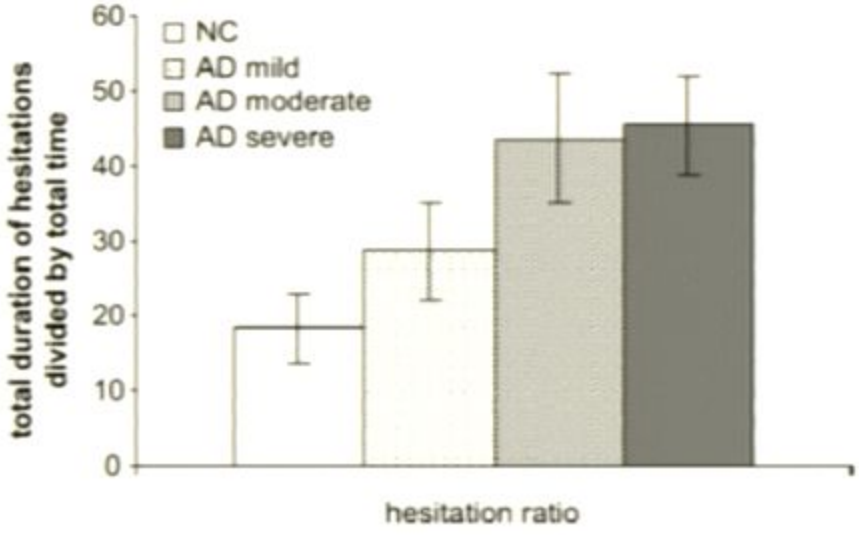
informa
healthcare

Temporal parameters of spontaneous speech in Alzheimer's disease

ILDIKO HOFFMANN[1], DEZSO NEMETH[1,2], CRISTINA D. DYE[2], MAGDOLNA PAKASKI[1], TAMAS IRINYI[1], & JANOS KALMAN[1]*

[1]University of Szeged, Szeged, Hungary, and [2]Georgetown University, USA





frontiers in Aging Neuroscience

Speaking in Alzheimer's disease, is that an early sign? Importance of changes in language abilities in Alzheimer's disease

Greta Szatloczki[1]*, Ildiko Hoffmann[2,3], Veronika Vincze[4], Janos Kalman[1] and Magdolna Pakaski[1]

[1]Research Institute for Linguistics, Hungarian Academy of Sciences, Szeged, Hungary, [2]Research Institute for Linguistics, Hungarian Academy of Sciences, Budapest, Hungary, [3]Department of Linguistics, University of Szeged, Szeged, Hungary, [4]MTA-SZTE Research Group on Artificial Intelligence, University of Szeged, Szeged, Hungary

Examination methods	Examination results	Sensitivity measures	Reference
Phonetics and phonology			
Temporal analysis of spontaneous speech	Mild AD and CTRL differ in speech tempo and hesitation ratio	No data	Hoffmann et al. (2010)
Temporal analysis of speech, oral reading task	Distinguishes moderate AD and CTRL. Best two parameters: speech tempo and articulation tempo	80%	Martinez-Sánchez et al. (2013)
Spoken task; speech-based detection	Might be a good method for detecting early AD	CTRL and MCI: 80% MCI and AD: 87%	Satt et al. (2014)
Automatic spontaneous speech analysis	Distinguishes between AD and CTRL	No data	López-de-Ipiña et al. (2013)

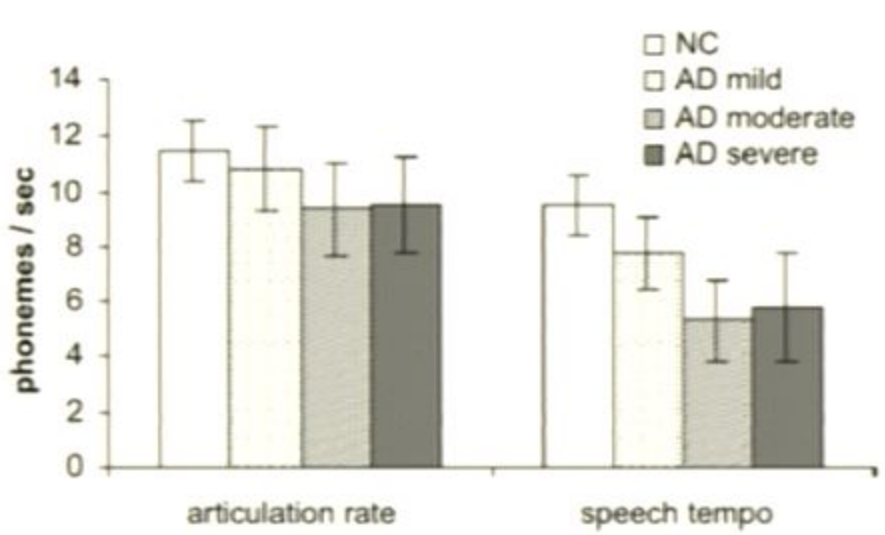
International Journal of Speech-Language Pathology, 2010; 12(1): 29–34

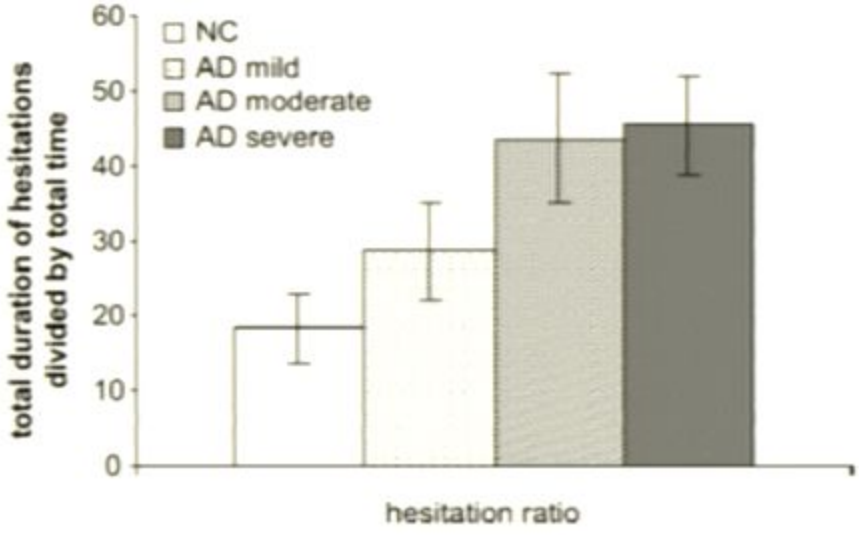
informa
healthcare

Temporal parameters of spontaneous speech in Alzheimer's disease

ILDIKÓ HOFFMANN[1], DEZSO NEMETH[1,2], CRISTINA D. DYE[2], MAGDOLNA PAKASKI[1], TAMAS IRINYI[1], & JANOS KALMAN[1]*

[1]University of Szeged, Szeged, Hungary, and [2]Georgetown University, USA



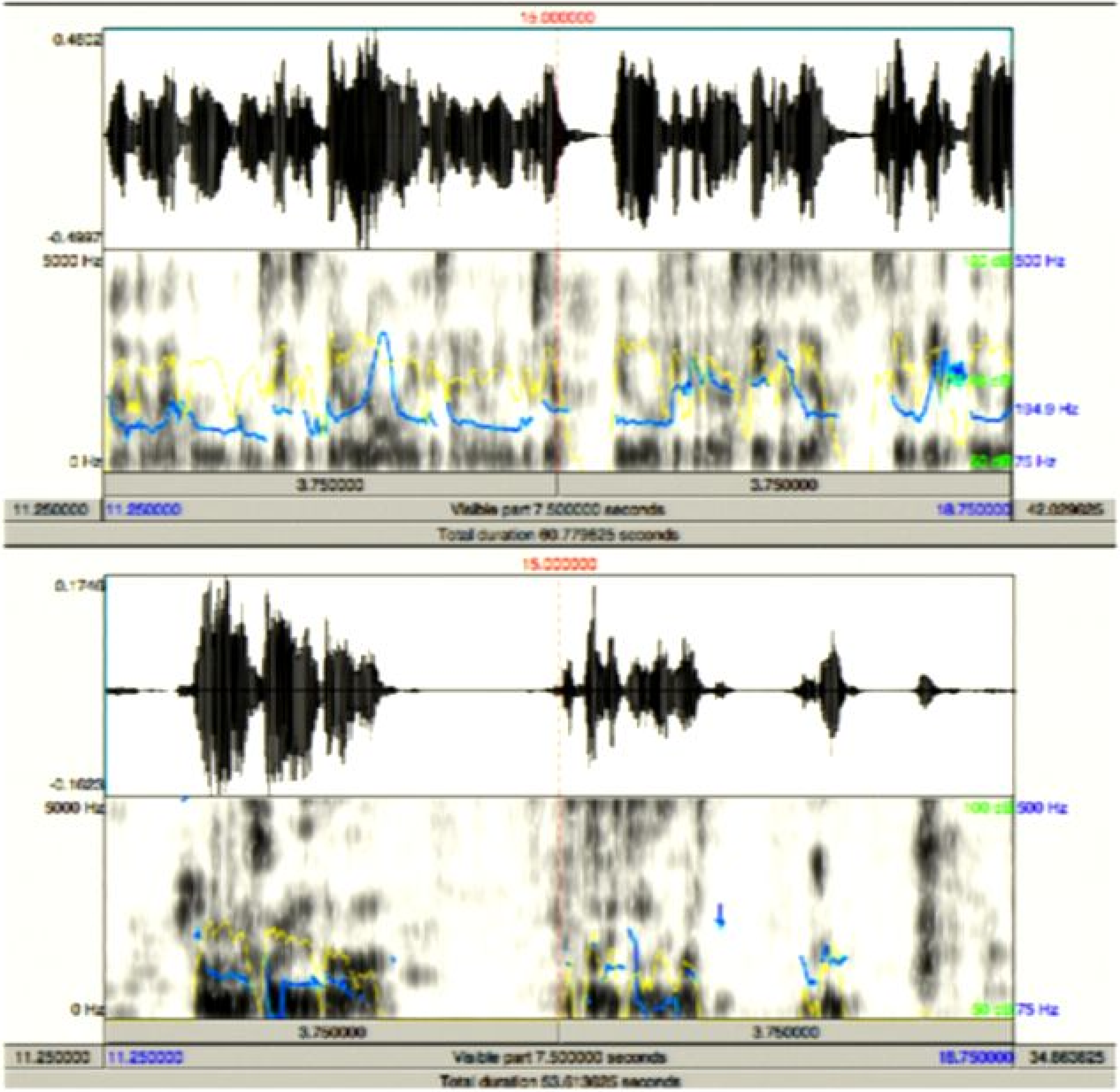



sensors
ISSN 1424-8220

On the Selection of Non-Invasive Methods Based on Speech Analysis Oriented to Automatic Alzheimer Disease Diagnosis

Karmele Lopez de Ipiña, Jesus Bernardino Alonso, Carlos Manuel Travieso, Jordi Solé-Casals, Harkaitz Egiraun, Marcos Faundez-Zanuy, Aitzol Ezeiza, Nora Barroso, Miriam Ecay-Torres, Pablo Martinez-Lage and Unai Martinez de Lizardui

Figure 1. Signal and spectrogram of a control subject (**Top**) and an AD subject (**Bottom**) during spontaneous speech (pitch in blue, intensity in yellow).



Neurologia. 2013;28(6):325–331

NEUROLOGÍA

www.elsevier.es/neurologia

ORIGINAL ARTICLE

Oral reading fluency analysis in patients with Alzheimer disease and asymptomatic control subjects☆

F. Martinez-Sánchez[a,*], J.J.G. Meilán[b], J. Garcia-Sevilla[a], J. Carro[b], J.M. Arana[b]

[a] Departamento de Psicología Básica y Metodología, Facultad de Psicología, Universidad de Murcia, Murcia, Spain
[b] Departamento de Psicología Básica, Psicobiología y Metodología, Universidad de Salamanca, Salamanca, Spain

Measurement	Description
Duration	Total duration of reading task including pauses (seconds)
Number of pauses	Number of intersyllabic pauses >250 ms (*n*)
Pause proportion	Pause time compared to total reading time (%)
Phonation time	Intra- and intersyllabic nuclei times without pauses (seconds)
Phonation proportion	Phonation time compared to total reading time (%)
Speech rate	Number of syllables/total reading time without pauses (syllables/second)
Articulation rate	Number of syllables/phonation time without pauses (syllables/second)

Table 1 Demographic information, descriptive statistics, and comparison of means of study variables between both groups.

Dependent variables	Group		*t*	*P*
	Alzheimer (TD)	Control (TD)		
Age	80.17 (7.43)	76.31 (12.25)	1.69	.096
Years of education	7.37 (4.78)	9.42 (4.65)	−1.64	.105
MMSE	16.29 (7.42)	26.21 (3.80)	6.78	.000
Reading fluency				
Duration	76.61 (48.96)	46.02 (21.08)	−3.39	.001
Number of pauses	33.26 (24.49)	16.51 (12.01)	−3.60	.001
Pause proportion	51.80 (14.99)	34.40 (14.65)	−5.22	.000
Phonation time	43.54 (18.96)	34.36 (12.21)	−2.40	.019
Phonation time	48.19 (14.99)	66.37 (14.08)	5.22	.000
Speech rate	2.63 (0.75)	3.48 (0.73)	4.80	.000
Speech rate	4.16 (±0.49)	4.41 (±0.44)	2.24	.028

Speech-Based Automatic and Robust Detection of Very Early Dementia

Aharon Satt [1], *Ron Hoory* [1], *Alexandra König* [2,4], *Pauline Aalten* [4], *Philippe H Robert* [3]

[1] IBM Research – Haifa, Israel
[2] University of Nice Sophia Antipolis, France
[3] Centre Mémoire de Ressources et de Recherche, CHU de Nice, Nice, France
[4] Maastricht University Medical Center, Maastricht, Netherlands

Conference Paper · May 2014

Task	Description
1. Countdown	Count backwards from 305 down to 285
2. Picture description	Look at a picture and describe it as detailed as you can in one minute
3. Sentence repeating	Repeat ten short sentences after the clinician (one at a time)
4. Semantic fluency (animals)	Name as many animals as you can think of as quickly as possible, in one minute

frontiers in Aging Neuroscience

Speaking in Alzheimer's disease, is that an early sign? Importance of changes in language abilities in Alzheimer's disease

Greta Szatloczki[1]*, Ildiko Hoffmann[1,2], Veronika Vincze[3], Janos Kalman[1] and Magdolna Pakaski[1]

[1]Research Institute for Linguistics, Hungarian Academy of Sciences, Szeged, Hungary, [2]Research Institute for Linguistics, Hungarian Academy of Sciences, Budapest, Hungary, [3]Department of Linguistics, University of Szeged, Szeged, Hungary, [4]MTA-SZTE Research Group on Artificial Intelligence, University of Szeged, Szeged, Hungary

Examination methods	Examination results	Sensitivity measures	Reference
Lexicon, semantics and pragmatics			
Semantic association test	AD performs significantly worse than CTRL	No data	Visch-Brink et al. (2004)
Semantic verbal fluency and phonological verbal fluency	Good tool for diagnosis of early AD	No data	Laws et al. (2010)
Picture naming, semantic probes, lexical decision and priming, Stroop-picture naming	AD group was impaired in semantic tasks	No data	Duong et al. (2006)
Verbal task	AD group produces shorter texts, less relevant information and multiple error types than CTRL	No data	Taler and Phillips (2008)

frontiers in Aging Neuroscience

Speaking in Alzheimer's disease, is that an early sign? Importance of changes in language abilities in Alzheimer's disease

Greta Szatloczki[1]*, Ildiko Hoffmann[1]*, Veronika Vincze[2], Janos Kalman[1] and Magdolna Pakaski[1]

Language characteristic changes		MCI	Mild AD	Moderate AD	Severe AD
Phonetics-phonology					
Temporal changes in spontaneous speech (increasing hesitation number and time)		+	+	++	+++
Phonemic paraphasia		+	+	++	+++
Lexical-semantics					
Word-finding and word retrieval difficulties		+	+	++	+++
Verbal fluency difficulties	Phonemic (letter)	+	+	++	+++
	Semantic	+	+	++	+++
Semantic paraphasia		?	+	++	+++
SYNTAX					
Reduced syntactic complexity		−	−	+	+++
Agrammatisms		−	−	−	+++
DISCOURSE-PRAGMATICS					
Reduction in productive and receptive discourse-level processing		−/+	+	++	+++

Disturbi del linguaggio

- Malattia di Alzheimer
- Afasie Primarie Progressive

Classification of primary progressive aphasia and its variants

M.L. Gorno-Tempini, MD, PhD
A.E. Hillis, MD
S. Weintraub, PhD
A. Kertesz, MD
M. Mendez, MD
S.F. Cappa, MD
J.M. Ogar, MS
J.D. Rohrer, MD
S. Black, MD
B.F. Boeve, MD
F. Manes, MD
N.F. Dronkers, PhD
R. Vandenberghe, MD, PhD
K. Rascovsky, PhD
K. Patterson, PhD
B.L. Miller, MD
D.S. Knopman
J.R. Hodges, MD*
M.M. Mesulam, MD*
M. Grossman, MD*

ABSTRACT

This article provides a classification of primary progressive aphasia (PPA) and its 3 main variants to improve the uniformity of case reporting and the reliability of research results. Criteria for the 3 variants of PPA—nonfluent/agrammatic, semantic, and logopenic—were developed by an international group of PPA investigators who convened on 3 occasions to operationalize earlier published clinical descriptions for PPA subtypes. Patients are first diagnosed with PPA and are then divided into clinical variants based on specific speech and language features characteristic of each subtype. Classification can then be further specified as "imaging-supported" if the expected pattern of atrophy is found and "with definite pathology" if pathologic or genetic data are available. The working recommendations are presented in lists of features, and suggested assessment tasks are also provided. These recommendations have been widely agreed upon by a large group of experts and should be used to ensure consistency of PPA classification in future studies. Future collaborations will collect prospective data to identify relationships between each of these syndromes and specific biomarkers for a more detailed understanding of clinicopathologic correlations. *Neurology*® 2011;76:1006-1014

Classification of primary progressive aphasia and its variants

M.L. Gorno-Tempini, MD, PhD
A.E. Hillis, MD
S. Weintraub, PhD
A. Kertesz, MD
M. Mendez, MD
S.F. Cappa, MD
J.M. Ogar, MS
J.D. Rohrer, MD
S. Black, MD
B.F. Boeve, MD
F. Manes, MD
N.F. Dronkers, PhD
R. Vandenberghe, MD, PhD
K. Rascovsky, PhD
K. Patterson, PhD
B.L. Miller, MD
D.S. Knopman
J.R. Hodges, MD*
M.M. Mesulam, MD*
M. Grossman, MD*

ABSTRA
This artic
to improv
variants
tional gr
lished cli
divided i
each sub
pattern c
able. The
ment tas
large gr
future st
between
of clinic

Table 1 Inclusion and exclusion criteria for the diagnosis of PPA: Based on criteria by Mesulam[32]

Inclusion: criteria 1–3 must be answered positively
1. Most prominent clinical feature is difficulty with language
2. These deficits are the principal cause of impaired daily living activities
3. Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease
Exclusion: criteria 1–4 must be answered negatively for a PPA diagnosis
1. Pattern of deficits is better accounted for by other nondegenerative nervous system or medical disorders
2. Cognitive disturbance is better accounted for by a psychiatric diagnosis
3. Prominent initial episodic memory, visual memory, and visuoperceptual impairments
4. Prominent, initial behavioral disturbance

Abbreviation: PPA = primary progressive aphasia.

in variants
a for the 3
an interna-
arlier pub-
d are then
teristic of
expected
are avail-
d assess-
upon by a
fication in
ationships
rstanding

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 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.

Table 5 Tasks that may be used to assess speech and language functions in PPA

Speech/language function	Task	Behavioral measures	Variant in which impaired
Speech production			
Grammar	Picture description task; story retelling (e.g., picture aided); constrained-syntax sentence production task	Grammatical structure; mean length of utterance; speech rate; accuracy of content; melody; prosody; specific error types in word selection; articulation	Nonfluent/agrammatic variant
Motor speech	Motor speech evaluation, including multiple repetitions of multisyllabic words; diadochokinesis of speech articulators; spontaneous speech	Effortfulness; hesitations; presence of apraxia of speech or dysarthria; specific types of speech sound errors; factors that affect articulation (e.g., word length in syllables)	Nonfluent/agrammatic variant
Confrontation naming	Single-word retrieval in response to pictures, sounds, foods, and odors	Error rate; delay in naming; factors that affect naming accuracy (e.g., familiar vs unfamiliar items, nouns vs verbs, semantic category); error types (e.g., semantic errors, phonemic errors)	Severe deficit in semantic variant with semantic errors; moderate impairment in logopenic variant with phonemic errors
Repetition	Oral repetition of words, pseudowords, phrases, and sentences	Factors that affect repetition accuracy (e.g., predictability of the phrase, sentence length, grammatical complexity); error types	Logopenic variant with phonological errors
Sentence comprehension	Matching orally presented sentences to pictures; answering yes/no questions; following directions	Factors that affect comprehension (e.g., grammatical complexity; reversibility of the sentence, e.g., The boy was kicked by the girl vs The ball was kicked by the girl)	Nonfluent/agrammatic variant, effect of grammatical complexity; logopenic variant, length and frequency effect
Single-word comprehension	Word-to-picture matching; Word-to-definition matching; Synonym matching	Factors that affect comprehension (e.g., familiarity; frequency; grammatical word class)	Semantic variant
Object/people knowledge	Picture-picture matching; odd-one-out; semantic associations; gesture-object matching; sound-picture matching	Factors that affect object knowledge (e.g., familiarity, semantic category)	Semantic variant
Reading/spelling	Lists including regular and irregular word lists, from various word classes, matched for other factors; pseudowords matched to words in length	Factors that affect reading/spelling accuracy (e.g., regularity, frequency, word class); error types (e.g., regularization, phonologically plausible errors; articulatory distortions)	Semantic variant with "regularization" errors; logopenic variant phonologic errors

Neurol Sci
DOI 10.1007/s10072-012-1181-z

ORIGINAL ARTICLE

An Italian battery for the assessment of semantic memory disorders

Eleonora Catricalà · Pasquale A. Della Rosa · Valeria Ginex · Zoe Mussetti · Valentina Plebani · Stefano F. Cappa

Received: 6 June 2012 / Accepted: 22 August 2012

1. Denominazione su descrizione verbale
2. Denominazione figure a colori
3. Associazione parola-figura
4. Sorting di figure a vari livelli
   i. Superordinata
   ii. Ordinata
   iii. Categoria
   iv. Sottocategoria
5. Generazione e verifica di caratteristiche

Algoritmo per le afasie progressive

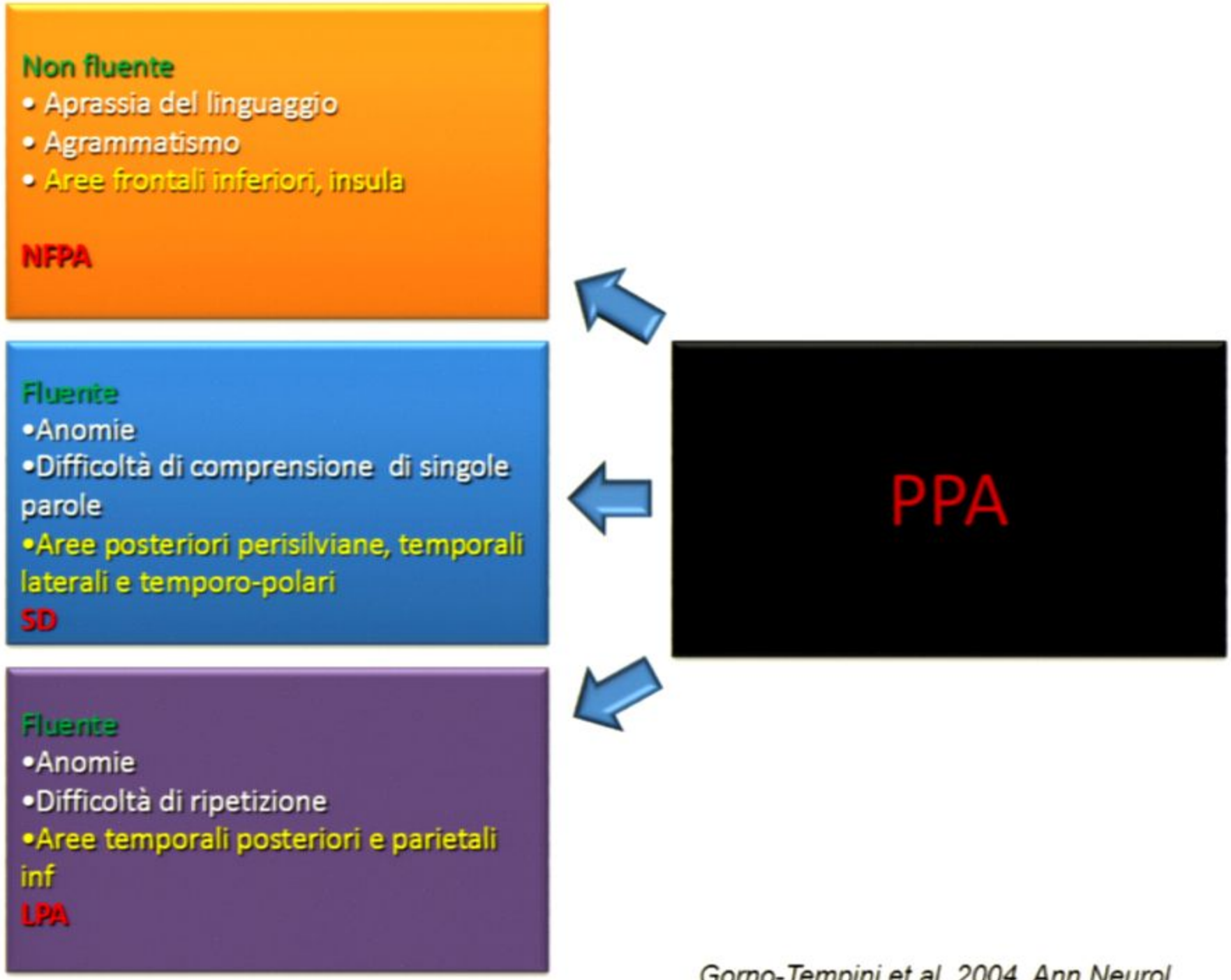
1. Produzione
   a) Errori motori: aprassici e disartrici
   b) Pause anomiche ed errori fonologici/semantici
   c) Sintassi semplificata ed errori morfologici
2. Denominazione e comprensione parole isolate
3. Ripetizione parole e frasi
4. Comprensione di frasi a crescente complessità sintattica

Cappa S., SIN-DEM, 2010

Afasie Primarie Progressive

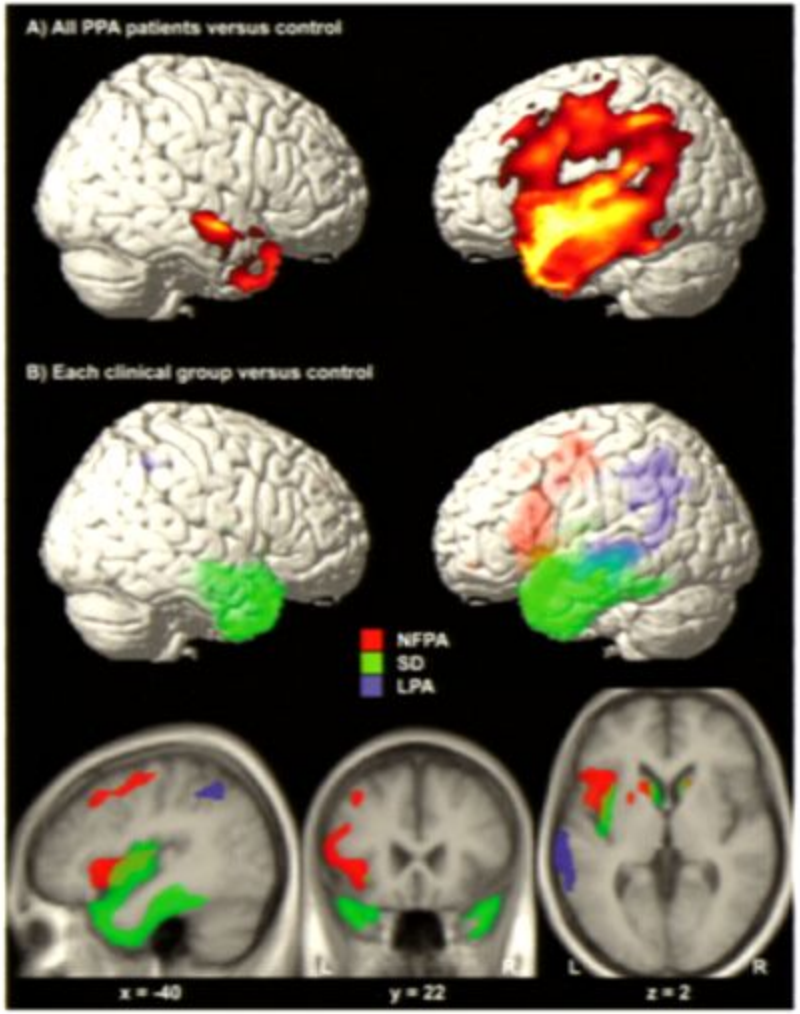
Fenotipo	Articolazione	Denominazione	Comprensione di parole	Ripetizione	Comprensione di frasi
NFPA	Alterata	Alterata [PF]	Normale	Alterata	Alterata
SD	Normale	Gravemente alterata [PS]	Alterata	Normale	Relativa-mente normale
LPA	Normale (lenta-esitante)	Alterata [PF]	Normale	Alterata	Alterata

Cappa S., SIN-DEM, 2010



Gorno-Tempini et al, 2004, Ann Neurol

Aree di atrofia nelle Afasie Primarie Progressive



Gorno-Tempini et al., Ann Neurol. 2004 ; 55: 335–346

Progression of language decline and cortical atrophy in subtypes of primary progressive aphasia

M. Rogalski, PhD
S. Cobia, PhD
E. M. Thomas, BS
J. Wicklund, BA
J. Weintraub, PhD
M. M. Mesulam, MD

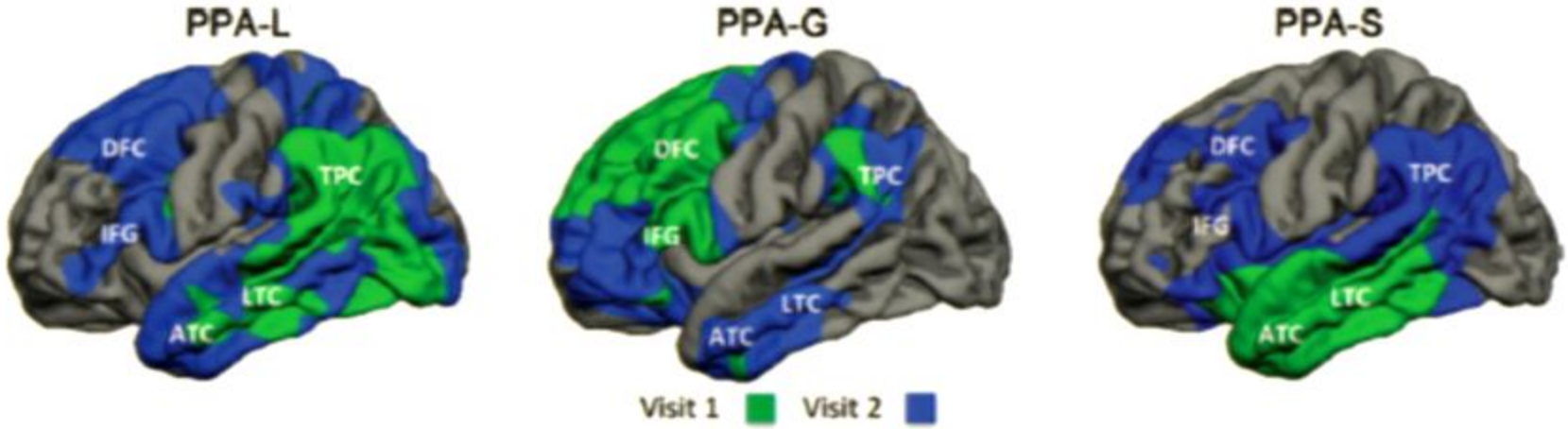
Objectives: To examine the longitudinal course of primary progressive aphasia (PPA) over a 2-year period and to offer quantitative ranges of expected change that could be used to guide the design and evaluation of therapeutic intervention trials.

Methods: Regional changes in cortical thickness and whole-brain cortical volume loss as well as neuropsychological language performance were assessed at baseline and 2 years later in 11 right-handed, clinically characterized patients who fulfilled research criteria for logopenic, agrammatic, and semantic PPA subtypes (L-PPA-L, L-PPA-G, and L-PPA-S).

Results: There was substantial progression of clinical deficits and cortical atrophy over 2 years. Neuroanatomical findings in language-performance subtypes over the study demonstrate that differentiated one PPA variant from another. Nonetheless, the subtype-specific differential impairment of word comprehension vs grammatical processing was largely maintained. Peak atrophy sites spread beyond the initial distinctive locations that characterized each of the 3 subtypes and displayed a more cortical-wide distribution encompassing all 3 major components of the language network: the inferior frontal gyrus, the temporoparietal junction, and lateral temporal cortex. Despite the progression, overall peak atrophy remained lateralized to the left hemisphere.

Conclusions: The results suggest that the unique features which sharply differentiate the PPA variants at the early to middle stages may lose their distinctiveness as the degeneration becomes more severe. Given the substantial atrophy over 2 years, PPA clinical trials may require fewer patients and shorter study durations than Alzheimer disease trials to detect significant therapeutic effects.

Neurology® 2011;76:1804–1810

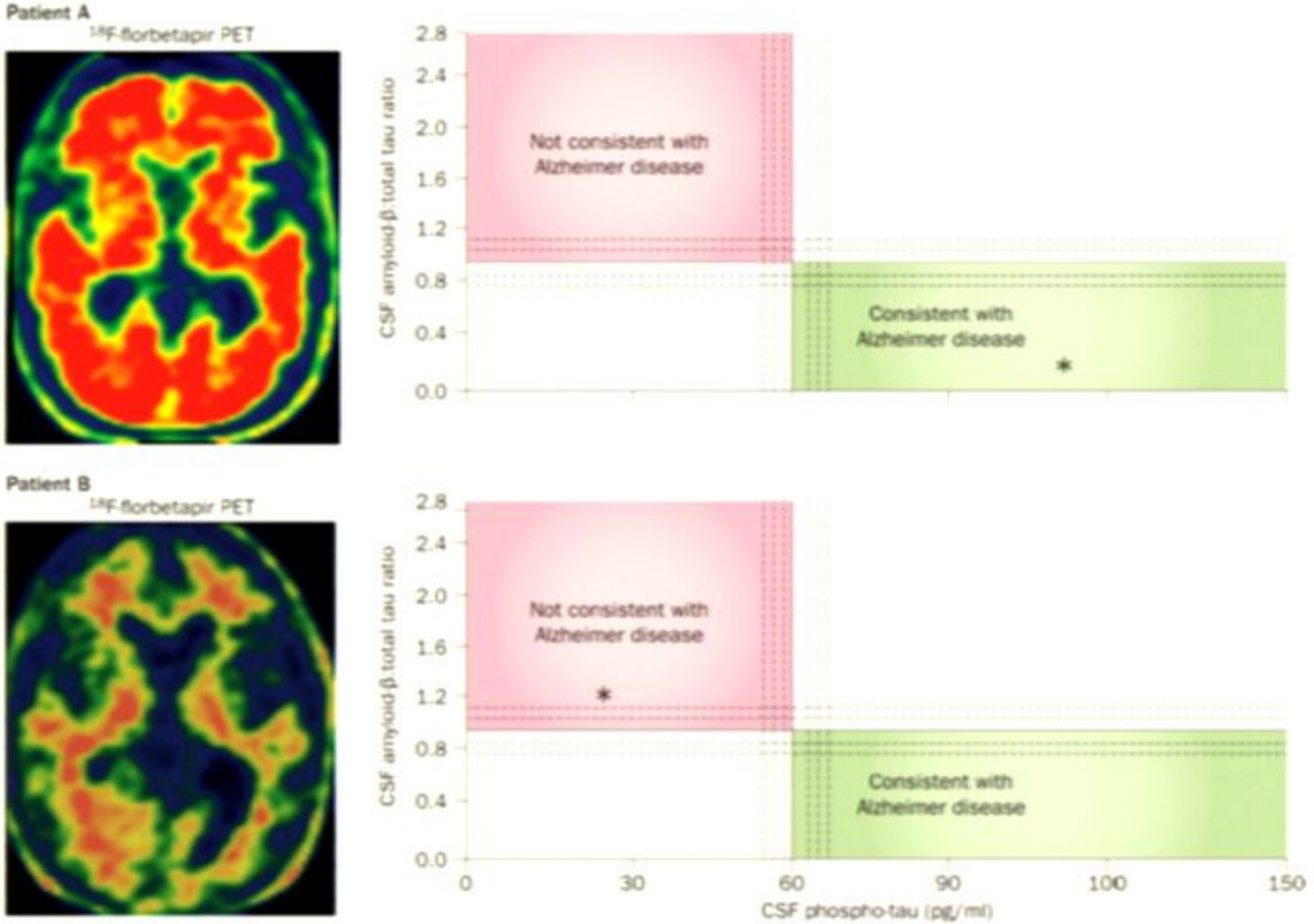


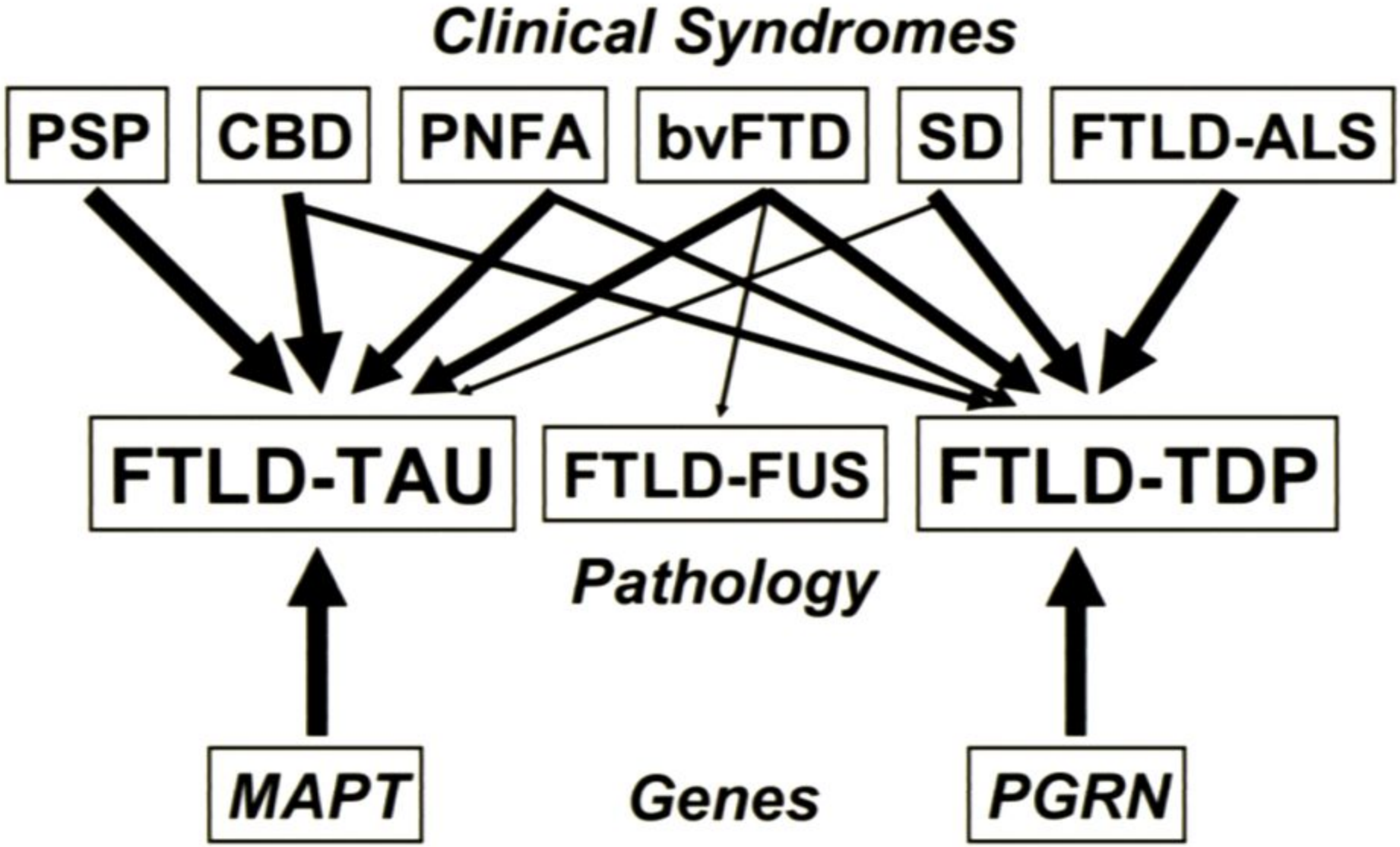
Areas of significant cortical thinning in the left hemisphere at baseline (green) and 2 years later (blue) for each of the primary progressive aphasia variants. ATC = anterior temporal cortex; DFC = dorsal frontal cortex; IFG = inferior frontal gyrus; LTC = lateral temporal cortex; PPA-G = agrammatic primary progressive aphasia subtype; PPA-L = logopenic primary progressive aphasia subtype; PPA-S = semantic primary progressive aphasia subtype; TPC = temporoparietal cortex.

Nat Rev Neurol. 2014 October ; 10(10): 554–569. doi:10.1038/nrneurol.2014.159

Primary progressive aphasia and the evolving neurology of the language network

M.-Marsel Mesulam, **Emily J. Rogalski**, **Christina Wieneke**, **Robert S. Hurley**, **Changiz Geula**, **Eileen H. Bigio**, **Cynthia K. Thompson**, and **Sandra Weintraub**
Cognitive Neurology and Alzheimer's Disease Centre, 320 East Superior Street, Searle Building, 11-450, Northwestern University, Chicago, IL 60611, USA (**M.-M.M.**, **E.J.R.**, **C.W.**, **R.S.H.**, **C.G.**, **S.W.**). Department of Neuropathology, Northwestern University Feinberg School of Medicine, 710 North Fairbanks Court, Chicago, IL 60611, USA (**E.H.B.**). Department of Communication Sciences and Disorders, Northwestern University, 633 Clark Street, Evanston, IL 60208, USA (**C.K.T.**)





Rabinovici e Miller, CNS Drugs; 2010; 24: 375-398

Correlazione probabilistica

- **Fenotipo clinico PPA**
  - NFPA
  - SD
  - LPA
- **Localizzazione atrofia con neuroimmagini**
  - RM encefalo con VBM
  - PET cerebrale con FDG
- **Istopatologia**
  - Amiloidopatie
  - Taupatie
  - TDP-43patie
  - Altre (FUS,...)
- **Genetica**
  - APP, PS1, PS2
  - MAPT, C9ORF72
  - PGRN