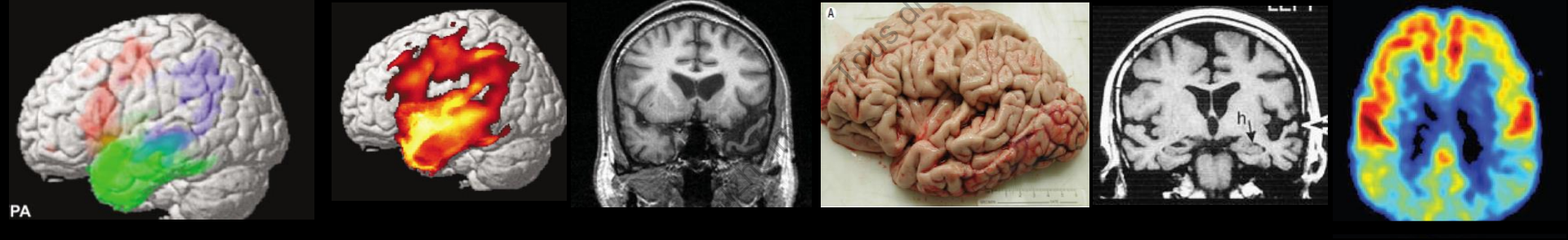


Langage et maladies neuro-évolutives :

le modèle des APP

Jérémie Pariente

Unité de Neuropsychologie, Service de Neurologie,
INSERM TONIC

CHU Purpan

UNIVERSITÉ TOULOUSE III PAUL SABATIER Université de Toulouse

Inserm
Institut national
de la santé et de la recherche médicale

Hôpitaux de Toulouse

2 façons d’aborder la question à la consultation

1. Le trouble du langage est la plainte principale du patient

2. Le trouble du langage n’est pas au centre de la plainte du patient

1. Le trouble du langage est la plainte principale du patient

2. Le trouble du langage n’est pas au centre de la plainte du patient

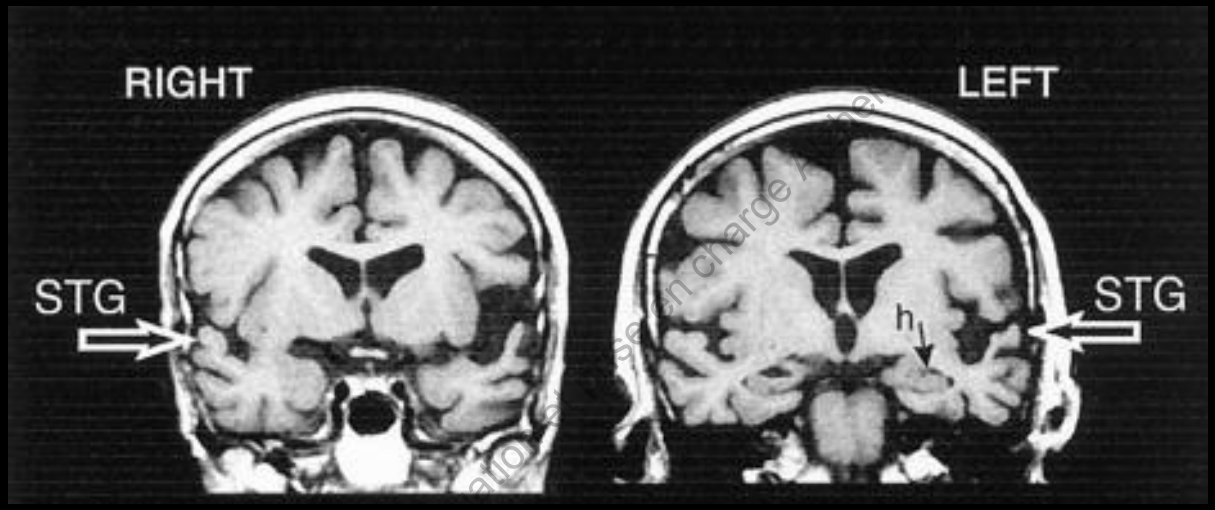
NEUROLOGICAL PROGRESS

Primary Progressive Aphasia

M.-Marsel Mesulam, MD

Primary progressive aphasia (PPA) is a focal dementia characterized by an isolated and gradual dissolution of language function. The disease starts with word-finding disturbances (anomia) and frequently proceeds to impair the grammatical structure (syntax) and comprehension (semantics) of language. The speech output in PPA can be fluent or nonfluent. Memory, visual processing, and personality remain relatively well-preserved until the advanced stages and help to distiguish PPA from frontal lobe dementia and the typical forms of Alzheimer's disease. The term "semantic dementia" was originally introduced to designate a different group of patients with a combination of verbal and visual processing deficits. In practice, however, this diagnosis is also being used in a variant sense to denote a subtype of PPA with fluent speech and impaired comprehension, even in the absence of visual processing deficits. Insofar as the diagnosis of semantic dementia can have these two different meanings, it is important to specify whether it is being used in the original sense or to denote a subtype of PPA. Structural and physiological neuroimaging confirms the selective predilection of PPA for the left hemisphere, especially for its language-related cortices. A few patients with PPA display the neuropathological markers of Alzheimer's disease, but in an unusual distribution. The majority of the autopsies in PPA have shown either Pick's disease or lobar atrophy without distinctive histopathology. The suggestion has been made that PPA and frontal lobe dementia constitute phenotypical variations of a unitary disease process within the "Pick-lobar atrophy" spectrum. Recent advances in chromosome 17-linked dementias justify a rigorous search for tau polymorphisms and tauopathy in sporadic PPA. An informed approach to this syndrome will increase the effectiveness with which clinicians can address the unique challenges associated with the diagnosis and care of PPA.

Ann Neurol 2001;49:425–432


RIGHT
LEFT
STG
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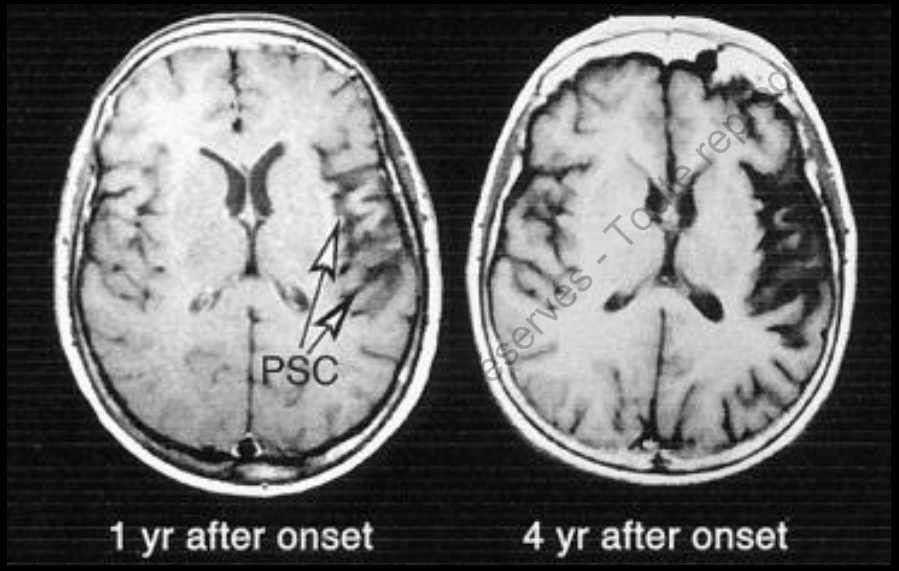

PSC
1 yr after onset
4 yr after onset

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

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

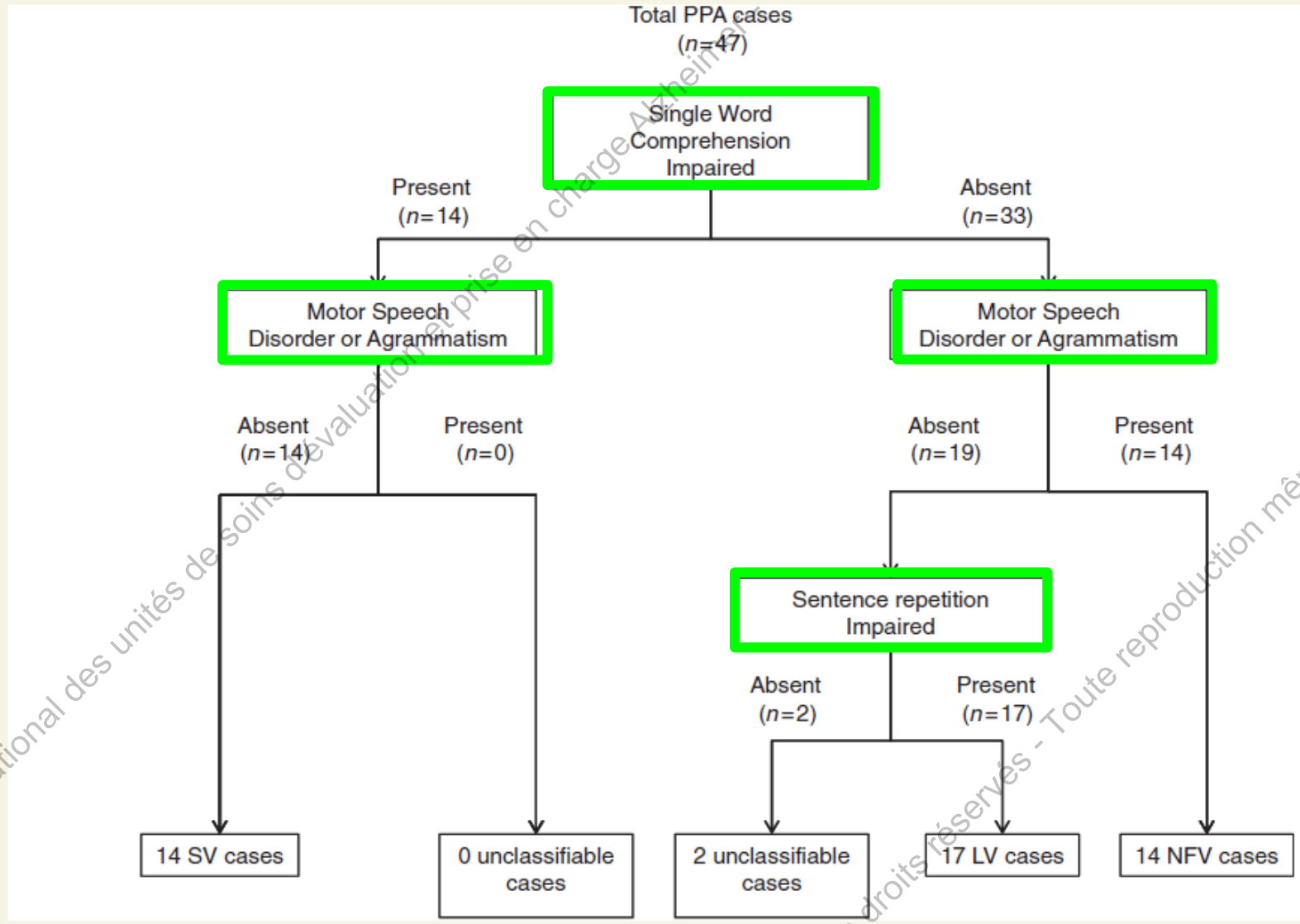


Figure 2 Algorithm for diagnosing PPA cases based on four key clinical features. 'Present' represents a rating of definite or severe on PALS. NFV = non-fluent variant; LV = logopenic variant; SV = semantic variant.

Leyton et al, 2011

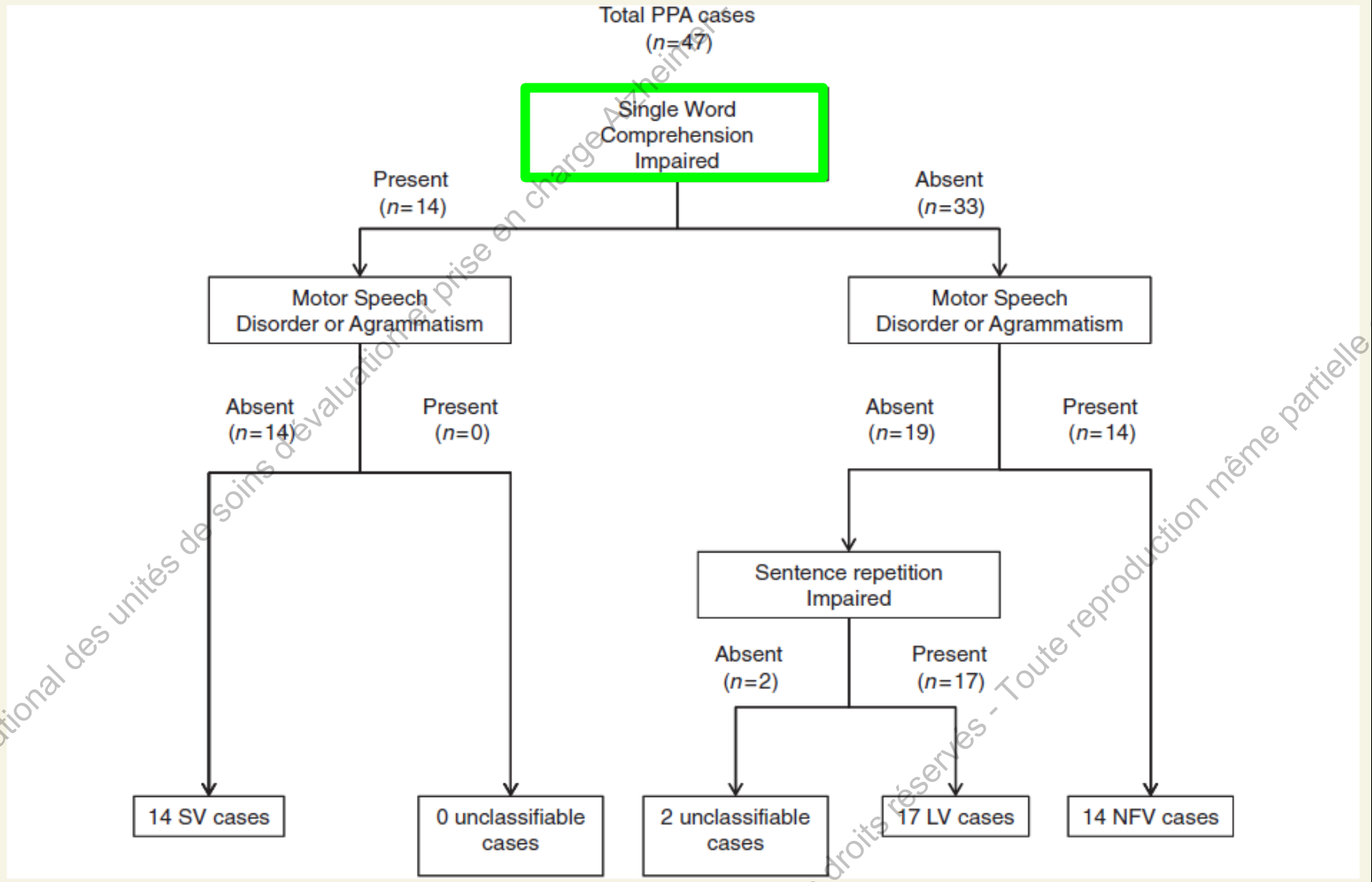


Figure 2 Algorithm for diagnosing PPA cases based on four key clinical features. 'Present' represents a rating of definite or severe on PALS. NFV = non-fluent variant; LV = logopenic variant; SV = semantic variant.

Leyton et al, 2011

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)

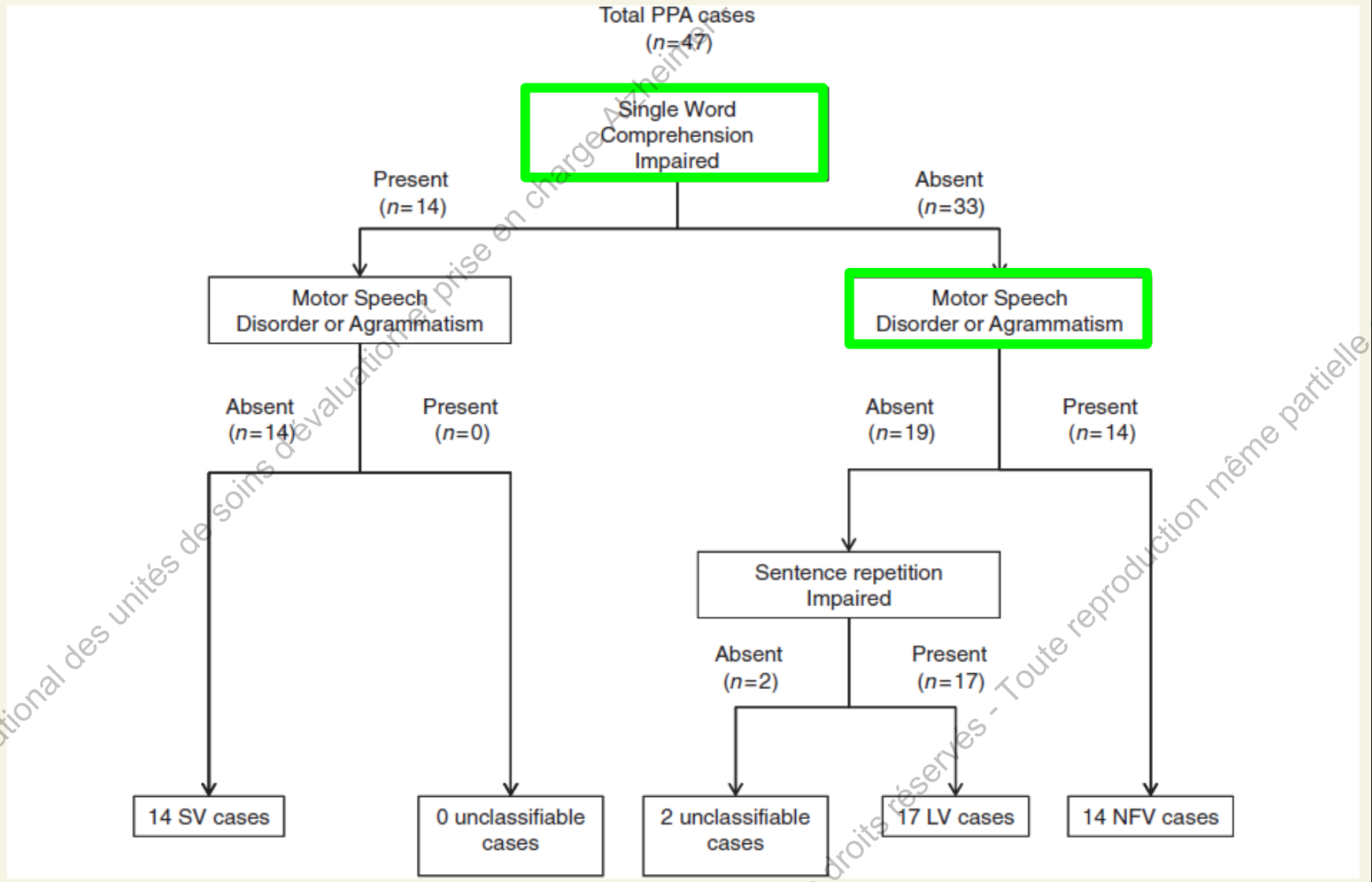


Figure 2 Algorithm for diagnosing PPA cases based on four key clinical features. 'Present' represents a rating of definite or severe on PALS. NFV = non-fluent variant; LV = logopenic variant; SV = semantic variant.

Leyton et al, 2011

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

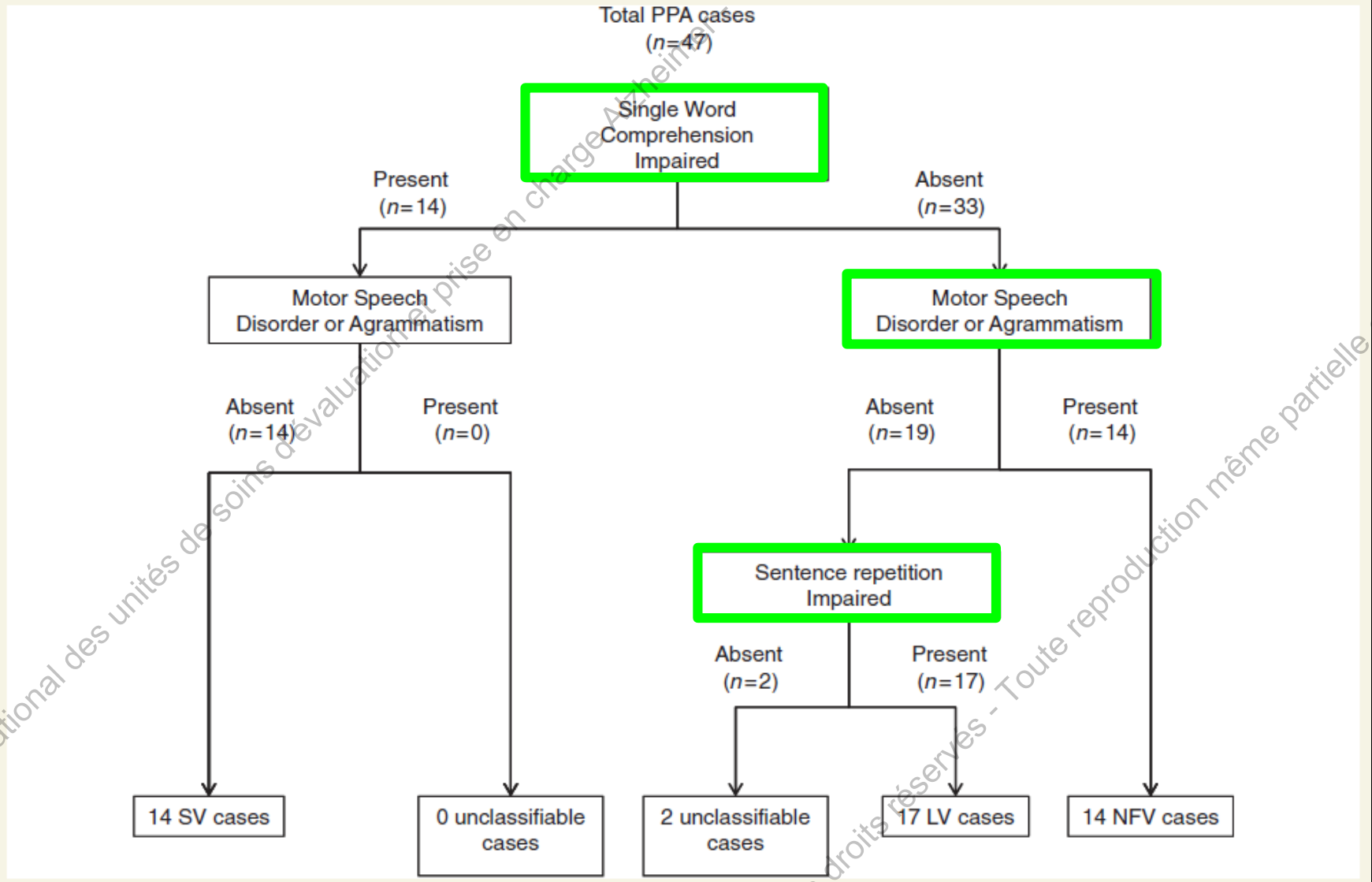


Figure 2 Algorithm for diagnosing PPA cases based on four key clinical features. 'Present' represents a rating of definite or severe on PALS. NFV = non-fluent variant; LV = logopenic variant; SV = semantic variant.

Leyton et al, 2011

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

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 visuoperceptive 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 $A\beta_{1-42}$ 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

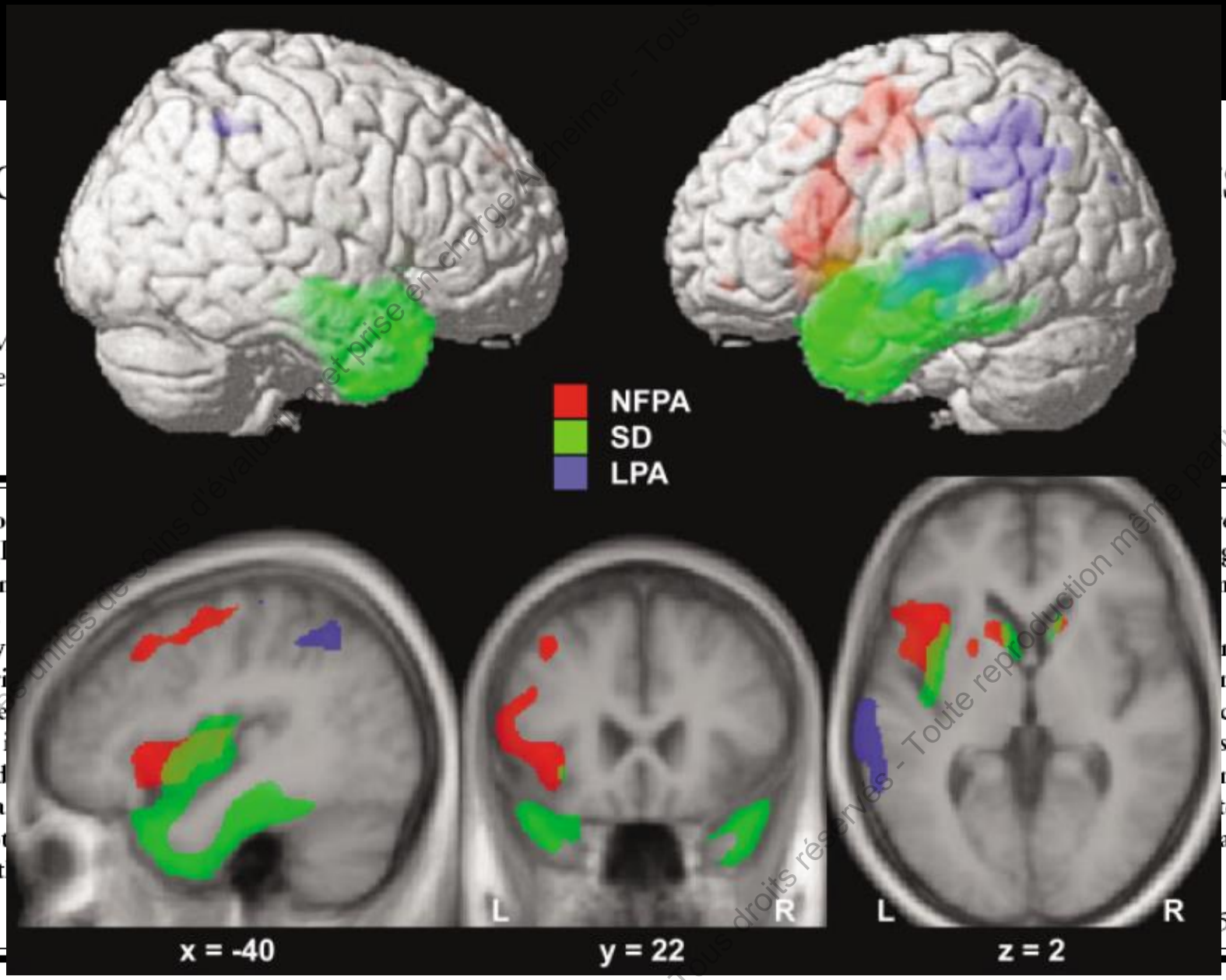
- Sudden onset
- Early and prevalent episodic memory disorders

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).

Dubois et al 2014


NFPA
SD
LPA
L
R
L
R
x = -40
y = 22
z = 2

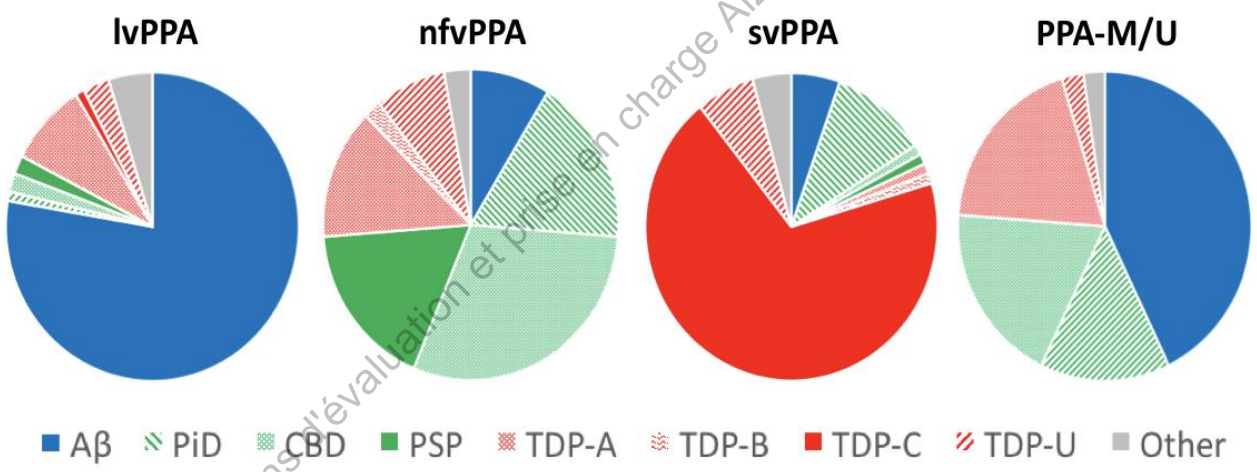
Prevalence of amyloid-β pathology in distinct variants of primary progressive aphasia

David Bergeron[1], Gil D. Rabinovici[2], Maria-Luisa Gorno-Tempini[2], William Seeley[2], Bruce L. Miller[2], Yolande Pijnenburg[3], Wiesje van der Flier[3], Bart van Berckel, Philip Scheltens[3], Colin Groot[3], Jonathan Rohrer[4], Jason Warren[4], Jonathan Schott[4], Nick Fox[4], Raquel Sanchez-Valle[5], Oriol Grau-Rivera[5], Ellen Gelpi[5], John Hodges[6], Christian Leyton[6], Olivier Piguet[6], Marsel Mesulam[7], Leila Koric[8], Kristensen Nora[8], Jérémie Pariente[9], Bradford Dickerson[10], Ian Mackenzie[11], Robin Hsiung[11], Serge Belliard[12], David Wolk[13], Murray Grossman[13], Matthew Jones[14], Jennifer Harris[14], Julie Snowden[14], Chrem-Mendez Patricio[15], Ismael Calandri[15], Alejandra Amengual[15], Eloi Magnin[16], Roberto Santangelo[17], Vincent Deramecourt[18], Florence Pasquier[18], Niklas Mattsson[19], Christer Nilsson[19], Julia Keith[20], Mario Masellis[20], Sandra Black[20], Jordi Matías-Guiu[21], Maria Cabrera-Martin[21], Claire Paquet[22], Julien Dumuirger[22], Marc Teichmann[23], Christopher Rowe[24], Victor Villemagne[24], Rik Vandenberghe[25], Elias Granadillo[26], Mario Mendez[26], Philip Meyer[27], Lars Frings[27], Marie Sarazin[28], Bruno Dubois[28], Sang Won Seo[29], Timo Grimmer[30], Kristian Steen Frederiksen[31], Pas

	lvPPA (n=425)	nfvPPA (n=319)	svPPA (n=370)	PPA-M/U (n=68)	All PPA (n=1182)
Age, mean (SD), y	67.9 (7.9)[b]	69.0 (8.4)[d]	65.7 (7.7)	70.3 (7.6)	67.5 (8.1)
Age, median (range), y	68 (40-94)[b*]	69 (45-90)[d*]	65 (44-86)	71 (52-83)	68 (40-94)
Age groups, No. (%), y					
<50	1 (0)	3 (1)	3 (1)	0 (0)	7 (1)
50-59	68 (17)	33 (11)	69 (21)	7 (11)	177 (16)
60-69	161 (39)	115 (40)	166 (50)	19 (30)	461 (42)
70-79	155 (38)	114 (39)	85 (25)	31 (48)	385 (35)
80+	25 (6)	24 (8)	12 (4)	7 (11)	68 (6)
Sex (% female)	48.9	46.8	53.2	38.2	49.0
Education, mean (SD), y	14.0 (5.3)	13.9 (4.1)	14.0 (4.1)	14.0 (4.0)	13.9 (4.6)
MMSE score, mean (SD)	21.0 (6.2)	24.0[c] (5.7)	23.1[e] (6.3)	20.9 (5.7)	22.4 (6.2)
Handedness (% non-right handed)	8.2	4.8	9.9	13.0	8.2
ApoE4 carrier/noncarrier (%ApoE4+)	67/91 (42.4)[a,b]	26/101 (20.5)	39/110 (26.2)	16/26 (38.1)	148/328 (31.1)
Modality % PET/CSF/Autopsy	36[b]/50[a]/23	35/37/37[c,d]	28/50[f]/27	4/40/62	31/46/30

Figure 2. Autopsy results

A



B

Variant	Amyloid-β		FTLD Tau			TDP-43				Other
	Primary	Co-morbid	PiD	CBD	PSP	TDP-A	TDP-B	TDP-C	TDP-U	
lvPPA (n=97)	74	5	1	2	2	9	-	1	3	CJD, DLB (3), VaD
nfvPPA (n=103)	9	9	18	31	18	14	2	-	8	CJD, DLB (2)
svPPA (n=93)	5	4	10	1	1	1	1	64	6	AGD, DLB, GGT (2)
PPA-M/U (n=42)	18	4	6	8	-	8	-	-	1	DLB
Total (n=335)	106	22	35	42	21	32	3	65	18	AGD, CJD (2), GGT (2), DLB (6), VaD

A: Pie charts showing the respective prevalence of amyloid, tau, TDP and other pathologies in PPA; detailed data shown in B below.
Abbreviations: AGD: argyrophilic grain disease; CBD: corticobasal degeneration; CJD: Creutzfeld-Jackob disease; DLB: dementia with Lewy bodies; GGT: globular glial tauopathy; lvPPA: logopenic variant PPA; nfvPPA: non-fluent variant of PPA; PiD: Pick's disease; PPA-M/U: mixed/unclassifiable PPA; PSP: progressive supranuclear palsy; svPPA: semantic variant of PPA; TDP: TAR DNA-binding protein 43; TDP-U: TDP unclassified; VaD: vascular dementia

GRÉMOTs

Batterie d'évaluation des troubles du langage dans les maladies neurodégénératives

Sous la direction de
Catherine Bézy,
Antoine Renard,
Jérémie Pariente

Logiciel inclus
PC + Mac

Groupe de Réflexion sur les Évaluations COgnitives

GRECO

de boeck supérieur

1. Le trouble du langage est la plainte principale du patient

2. Le trouble du langage n’est pas au centre de la plainte du patient

	Expression	Compréhension
Orale	Dénomination noms/visage Répétition Informativité Fluences/Fluidité	Mots isolés Phrase Implicite
Ecrite	Dénomination Copie narration	Ordre simples ordres complexes

GRÉMOTs

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de boeck supérieur

Journal of Alzheimer's Disease 50 (2016) 687–698
DOI 10.3233/JAD-150408
IOS Press

Pauses During Autobiographical Discourse Reflect Episodic Memory Processes in Early Alzheimer's Disease

Aurélie Pistono[a,b,c,*], Mélanie Jucla[c], Emmanuel J. Barbeau[d], Laure Saint-Aubert[e], Béatrice Lemesle[f], Benjamin Calvet[g], Barbara Köpke[c], Michèle Puel[a,b,f] and Jérémie Pariente[a,b,f]

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[f] *Neurology Department, Neuroscience Centre, Toulouse University Hospital, Toulouse, France*

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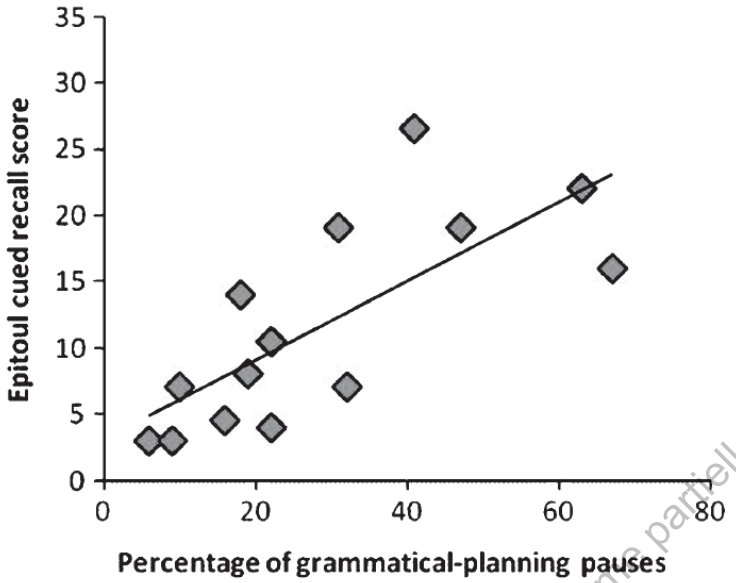

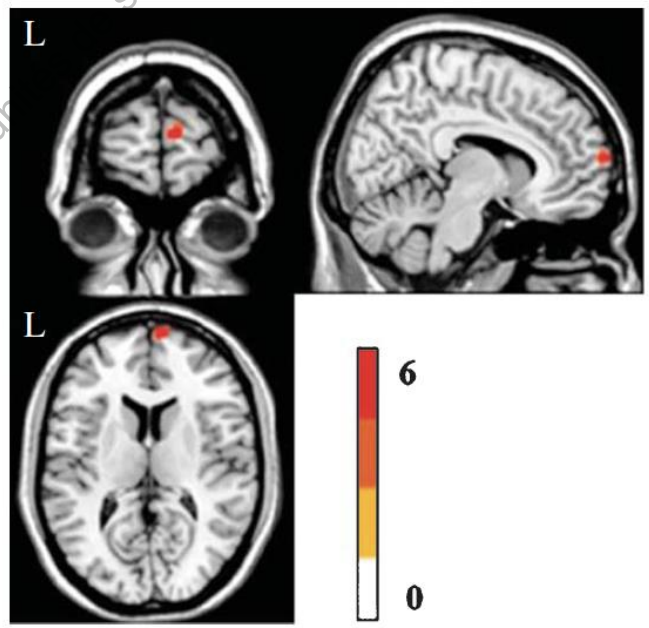

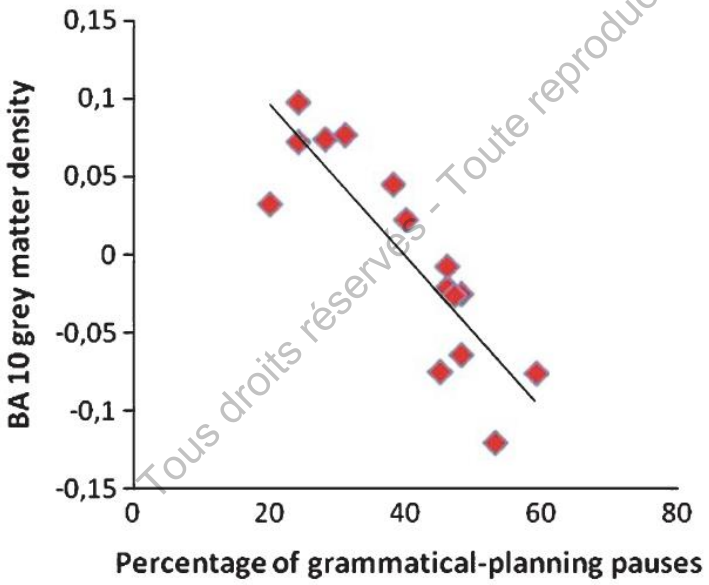

Des interrogations persistent !

PLOS ONE

RESEARCH ARTICLE

Childhood Learning Disabilities and Atypical Dementia: A Retrospective Chart Review

Alon Seifan[1]*, Stephanie Assuras[6☯], Edward D. Huey[2,3,4☯], Jesse Mez[5☯], Angeliki Tsapanou[4☯], Elise Caccappolo[6☯]

1 Department of Neurology Weill Cornell Medical College, New York, New York, United States of America, **2** Department of Neurology Columbia University, New York, New York, United States of America, **3** Gertrude H. Sergievsky Center, Columbia University, New York, New York, United States of America, **4** Cognitive neuroscience division, Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University, New York, New York, United States of America, **5** Department of Neurology, Boston University School of Medicine, Boston, Massachusetts, United States of America, **6** Department of Neuropsychology, Columbia University, New York, New York, United States of America

☯ These authors contributed equally to this work.
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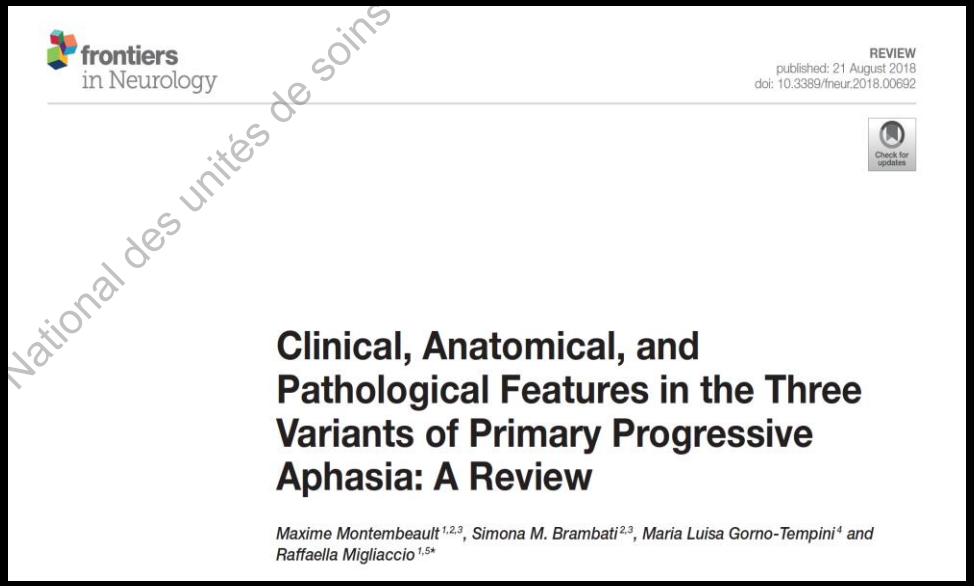
Merci de votre attention !



frontiers in Neurology

REVIEW
published: 21 August 2018
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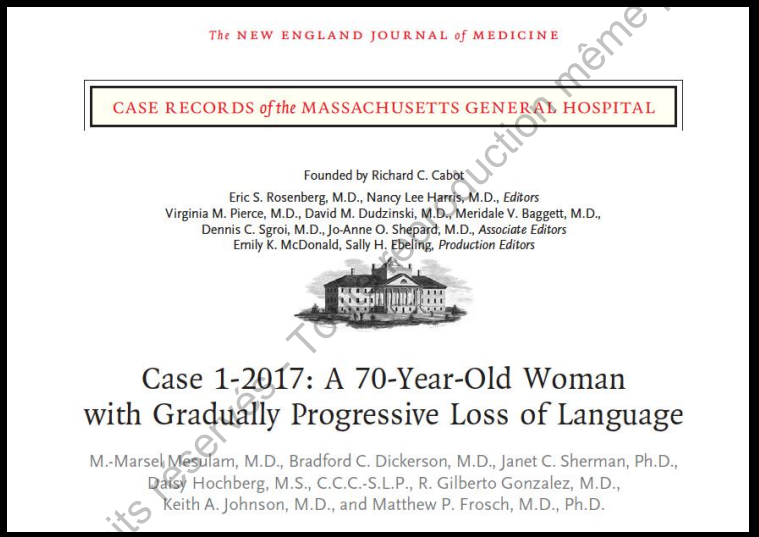
Check for updates

Clinical, Anatomical, and Pathological Features in the Three Variants of Primary Progressive Aphasia: A Review

Maxime Montembeault[1,2,3], Simona M. Brambati[2,3], Maria Luisa Gorno-Tempini[4] and Raffaella Migliaccio[1,5]



The NEW ENGLAND JOURNAL of MEDICINE

CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 1-2017: A 70-Year-Old Woman with Gradually Progressive Loss of Language

M.-Marsel Mesulam, M.D., Bradford C. Dickerson, M.D., Janet C. Sherman, Ph.D., Daisy Hochberg, M.S., C.C.C.-S.L.P., R. Gilberto Gonzalez, M.D., Keith A. Johnson, M.D., and Matthew P. Frosch, M.D., Ph.D.

N Engl J Med 2017;376:158-67.
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