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Fondazione
TERESA CAMPLANI
Casa di Cura DOMUS SALUTIS

LA RIABILITAZIONE INTERDISCIPLINARE

della disabilità complessa
fra presente e futuro

Analogie e differenze nella diversa applicazione tecnologica diagnostica e terapeutica in riabilitazione neuro-fisiatrica

Giovanni B Frisoni
*University Hospitals and University of Geneva*

SOMMARIO

- Riabilitazione e traiettoria di malattia
- Traiettoria di malattia nella demenza, fra le demenze, nelle demenze
- Biomarcatori di traiettoria di malattia e riabilitazione
- Biomarcatori nella Riabilitazione e di precisione

LA MALATTIA CRONICA È UNA DEVIAZIONE DALLA TRAIETTORIA DELL'INVECCHIAMENTO NORMALE
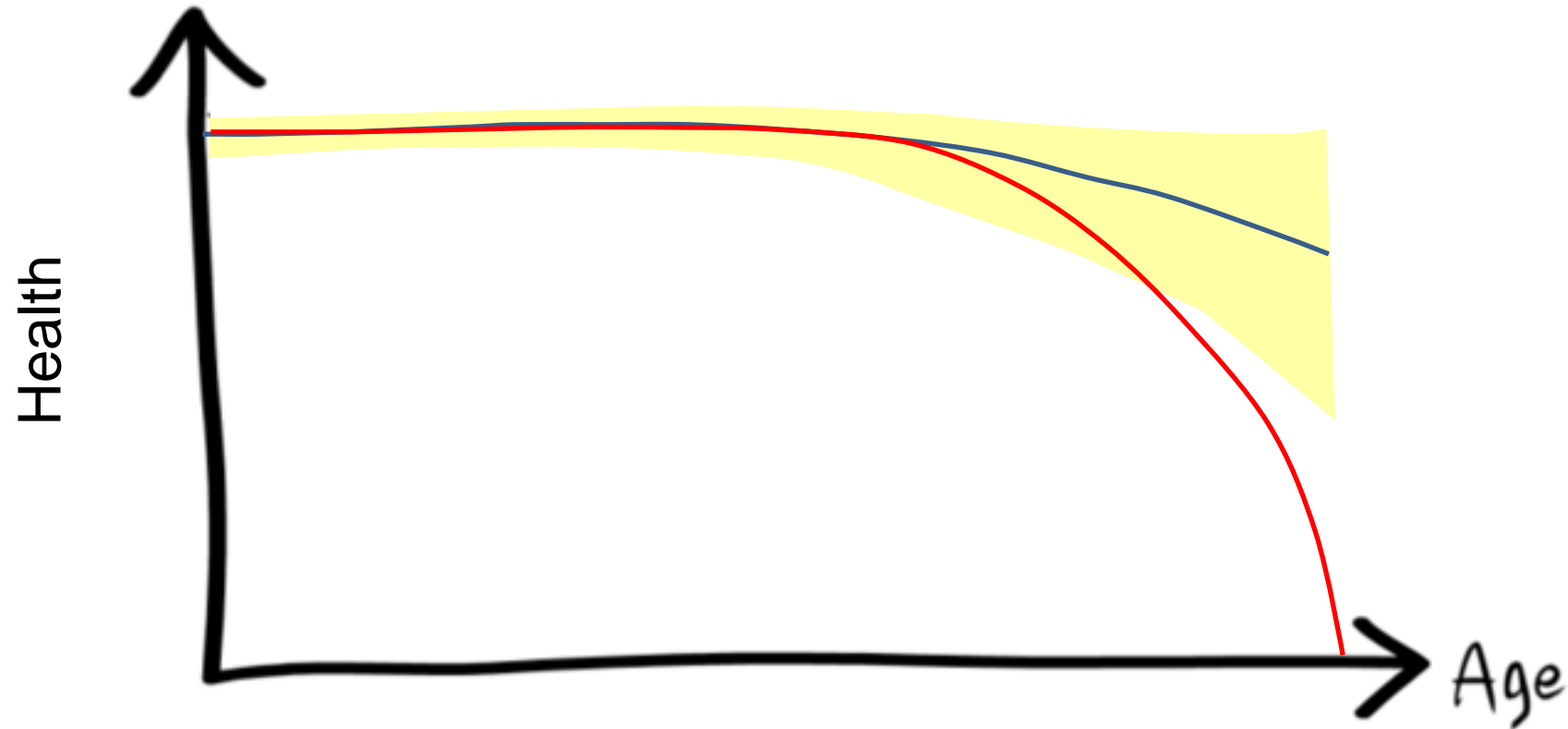
# LA TRAIETTORIA DELLA MALATTIA CRONICA È MULTI-DIMENSIONALE
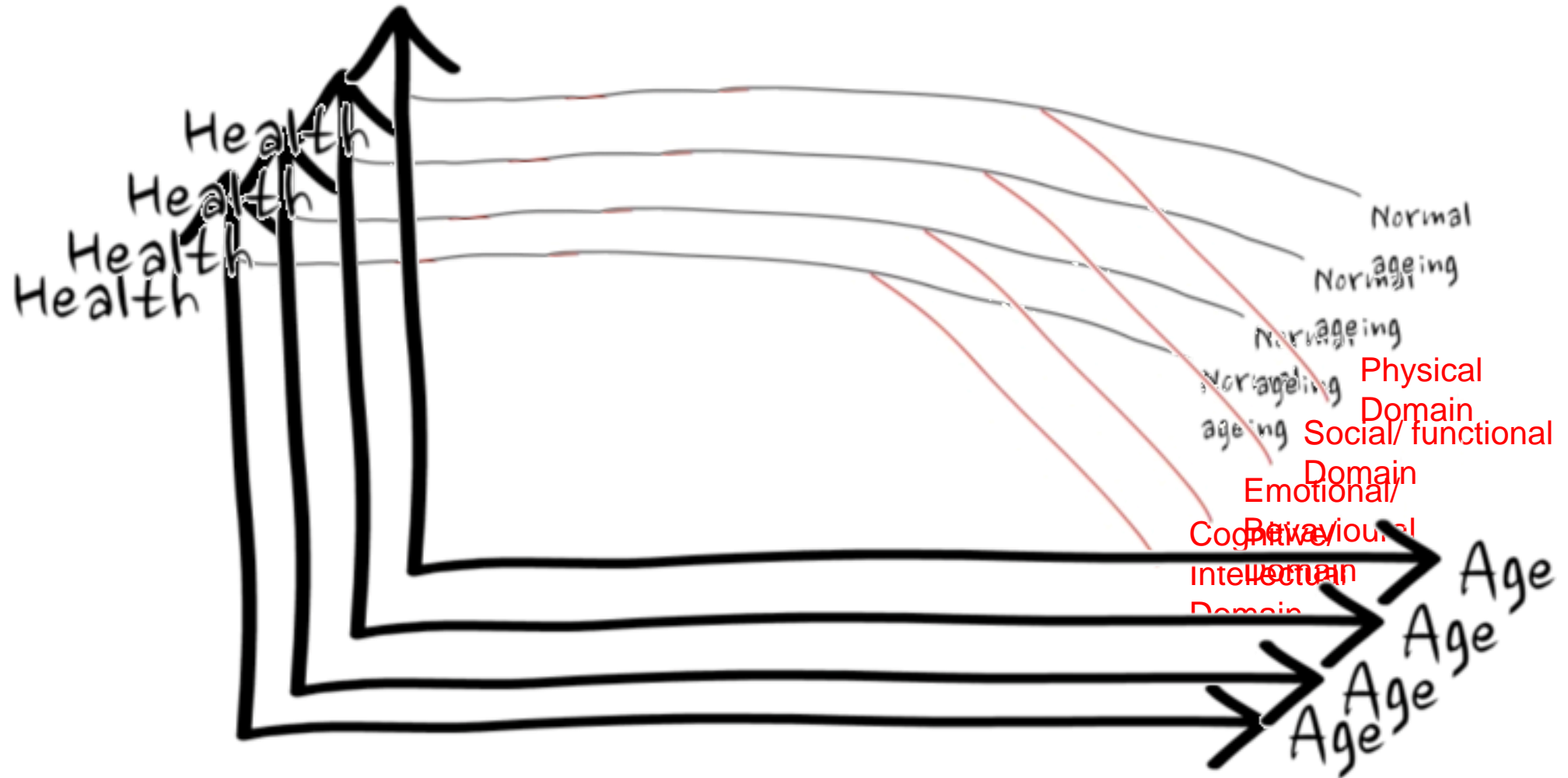
RIABILITAZIONE COME RIPRISTINO DELLA TRAIETTORIA

- [Rehabilitation (neuropsychology)](), therapy to regain or improve neurocognitive function that has been lost or diminished
- [Rehabilitation (wildlife)](), treatment of injured wildlife so they can be returned to the wild
- [Drug rehabilitation](), medical or psychotherapeutic treatment for dependency on substances such as alcohol and drugs
- [Occupational rehabilitation](), therapy to return injured workers to an appropriate level of work activity
- [Physical medicine and rehabilitation](), a branch of medicine that aims to enhance and restore functional ability to those with physical impairments or disabilities
- [Psychiatric rehabilitation](), a branch of psychiatry dealing with restoration of mental health and life skills after mental illness
- [Vision rehabilitation](), rehabilitation to improve vision or low vision
- [Vocational rehabilitation](), process which enables persons with impairments or disabilities to maintain or return to employment or occupation

source: wikipedia.org

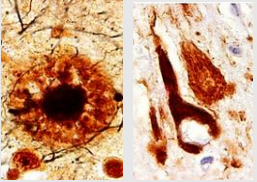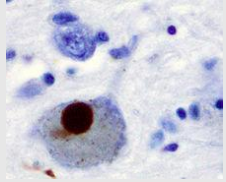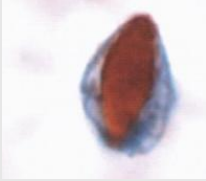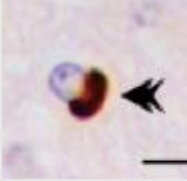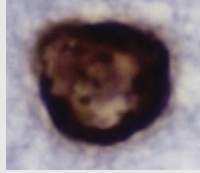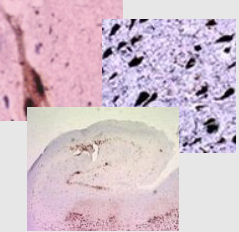# RIABILITAZIONE COME RIPRISTINO DELLA TRAIETTORIA
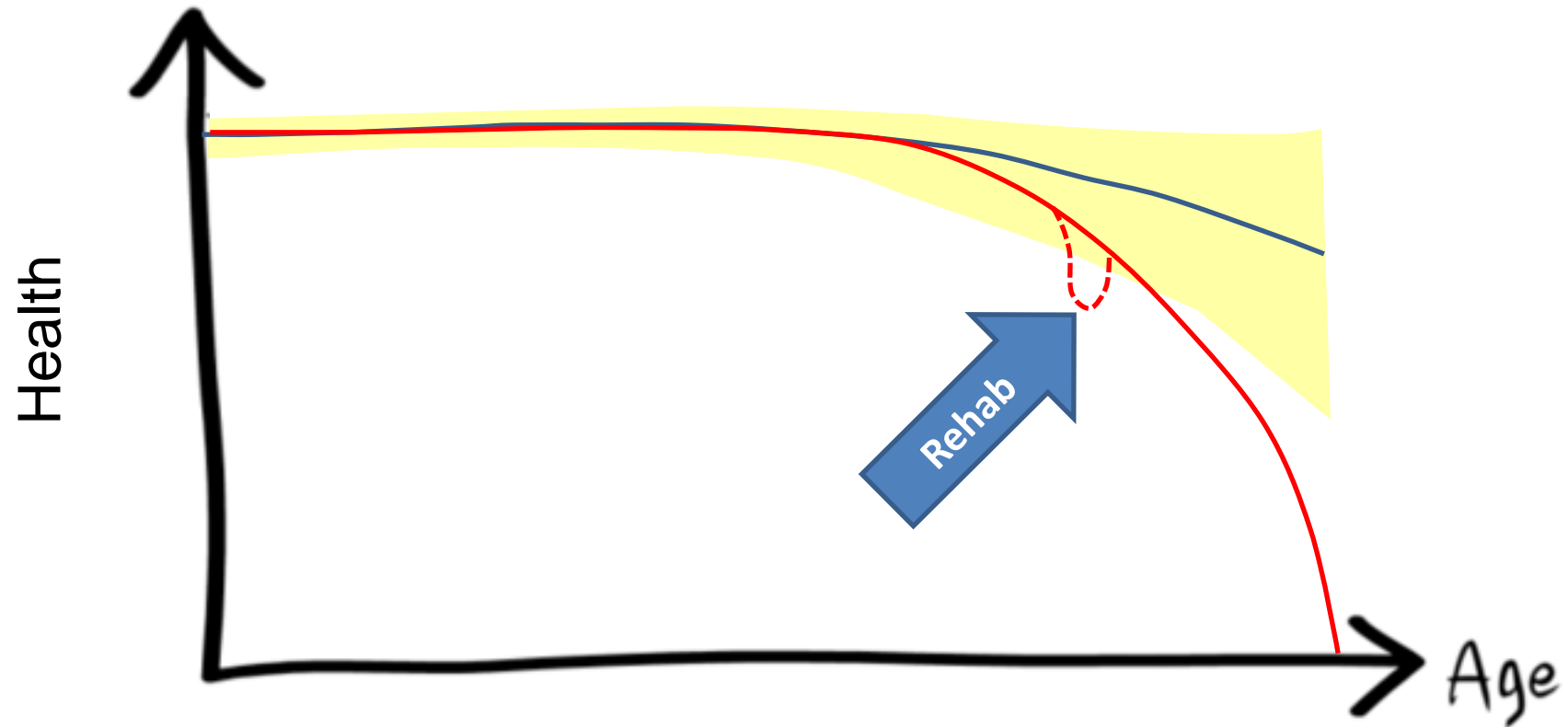
LE TRAIETTORIE MULTIDIMENSIONALI SONO MALATTIA-SPECIFICHE: L'ESEMPIO DELLE ATTIVITÀ DELLA VITA QUOTIDIANA NELLA DEMENZA DI ALZHEIMER
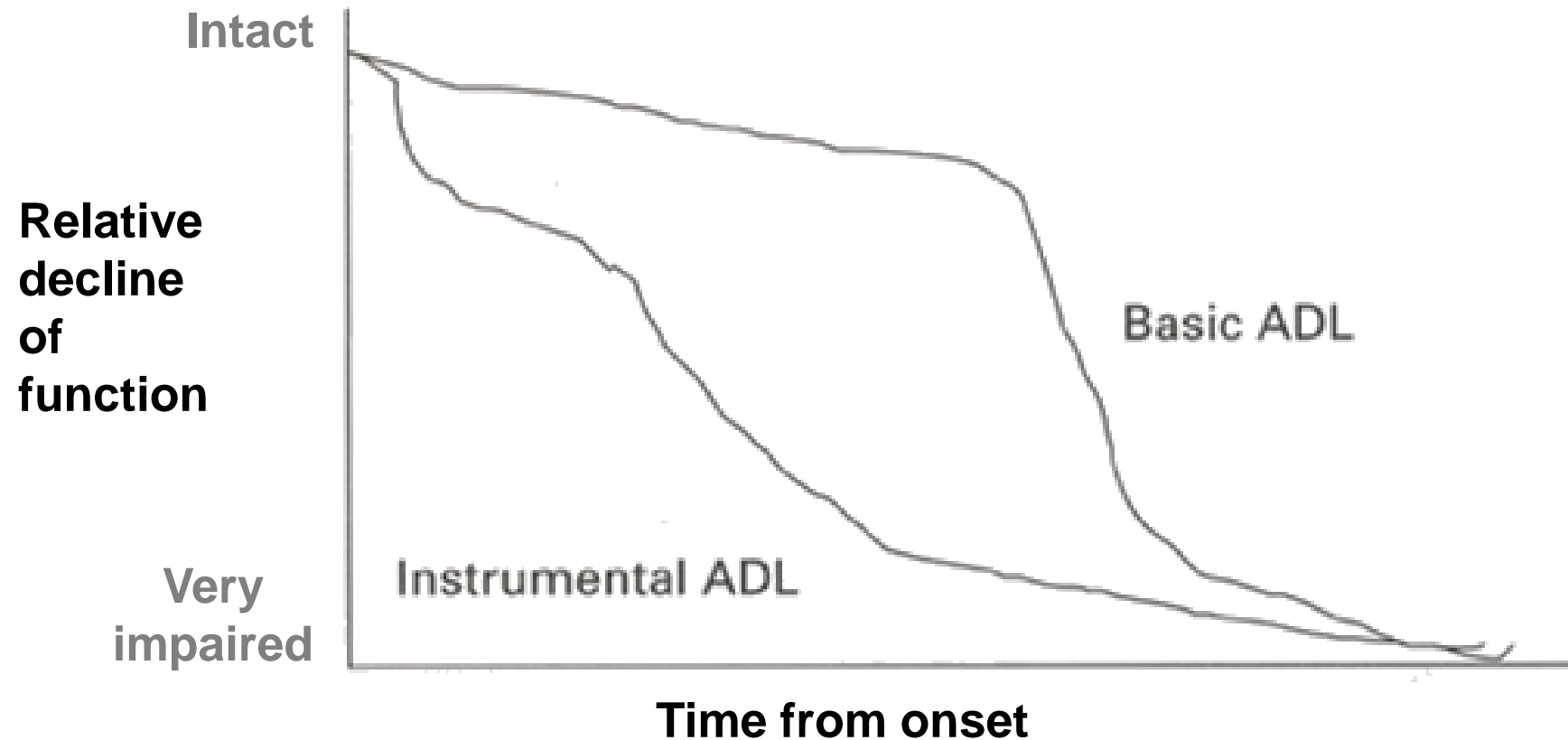
NELLE DEMENZE, LE TRAIETTORIE SONO DETERMINATE DALLE PROTEINOPATIE

ALZHEIMER	CORPS LEVY ET PARKINSON	DÉMENCE FRONTO-TEMPORALE ET SCLÉROSE LATÉRALE AMYOTROPH.			OTHERS NON ALZHEIMER
Plaques séniles Amas neuro-fibrillaires	Corps de Lewy	Inclusions intra-nucléaires	Amas cytoplasm. ubiquitine+	Amas cytoplasmiques et nucléaires	Argiroph. grain disease, PART, sclérose hipp.
β-amyloïde tau	α-synucléine	tau	TDP43	FUS	tau, TDP-43, others

DIMENSIONI DELLA STORIA NATURALE COLPITE NELLE DIVERSE DEMENZE

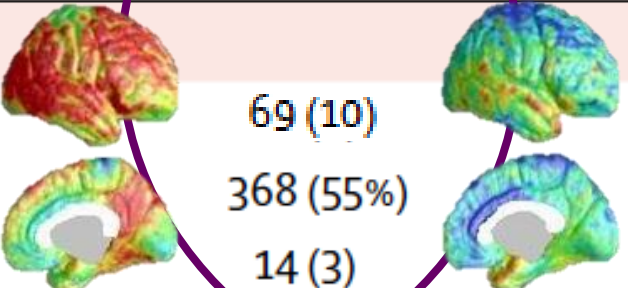|	Alzheimer's Disease	Dementia with Lewy Bodies	FrontoTemporal Dementia	Subcortical Vascular Dementia
Cognition	Memory (Late Onset) Neocortical (Early Onset)	Reasoning Constructional apraxia	Reasoning	Slowing of thought
ADL	Cognition-dependent activities: finance, medicines, telephone, public transport.	Motor-dependent activites: walking, deglutition	Instrumental Activities of Daily Living are lost due to lack of interest	Motor-dependent activites: walking, deglutition
Behaviour	Secondary (theft) delusions, reactive irritability	Visual hallucinations, delusions, Capgras	Loss of social graces Disinhibition	Apathy
Neuro	---	REM sleep behaviour disturbance	---	Early incontinence, gait disturbance, pyramidal signs, deglutition
Response to AChEIs	Improvement + of cognition	Improvement +++ of cognition and behavior Severe toxicity of neuroleptics	Worsening of cognitive performance	No beneficial effect Only adverse effects

PROGRESSIONE DIFFERENZIALE IN MALATTIA DI ALZHEIMER A ESORDIO PRECOCE E TARDIVO
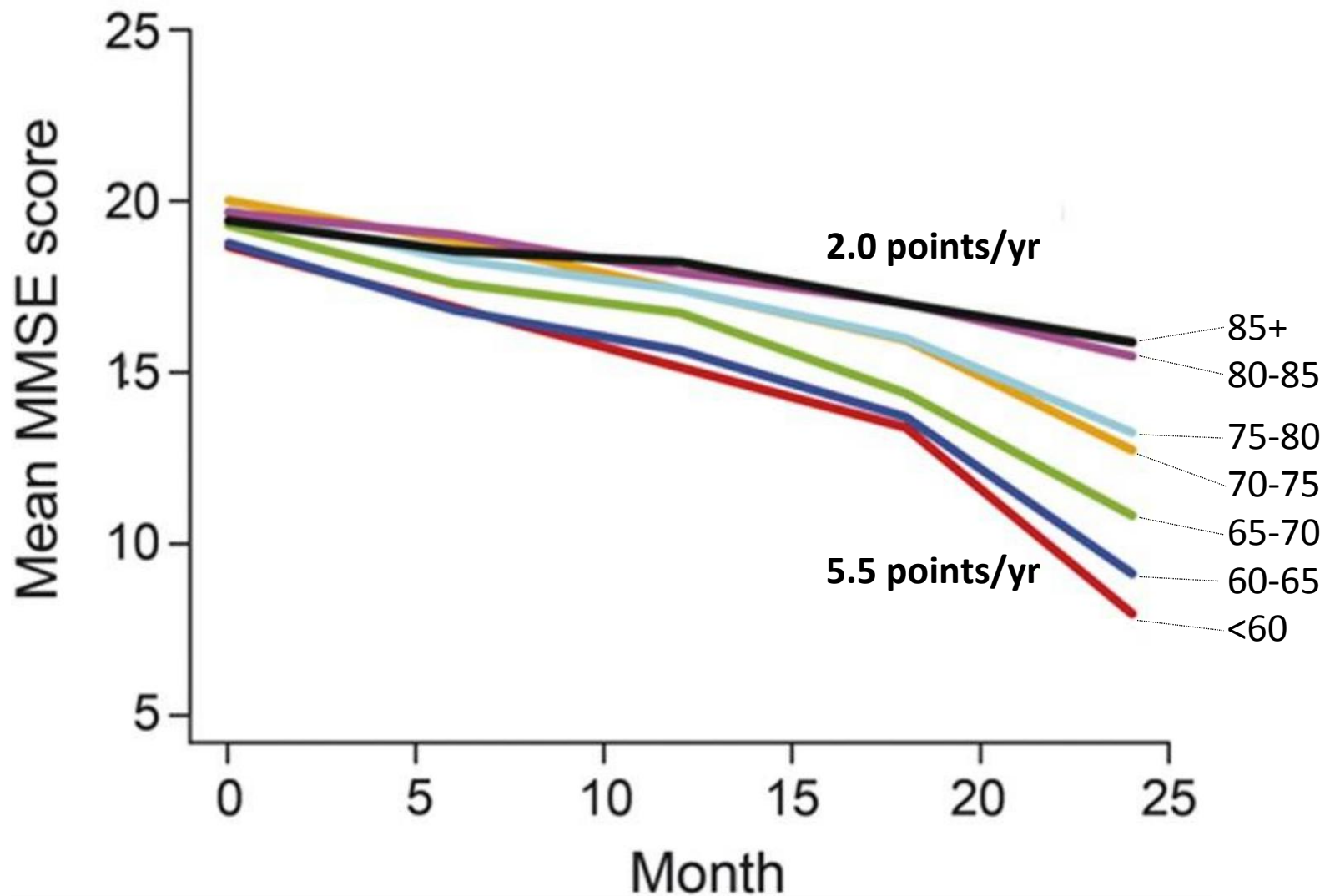
PROGRESSIONE DIFFERENZIALE IN MALATTIA DI ALZHEIMER A ESORDIO PRECOCE E TARDIVO

Murray et al., Lancet Neurology 2011	Hippocampal sparing AD (n=97) (neocortical)	Typical AD (n=665)	Limbic-predominant AD (n=127)
Demographic characteristics			
Age at onset (years)	63 (10)	69 (10)	76 (7)
Women	36 (37%)	368 (55%)	87 (69%)
Education (years)	15 (3)	14 (3)	14 (3)

Younger
Predominantly neocortical

Older
Predominantly limbic

Aphasia apraxia agnosia
ApoE ε4 negative

Amnesia
ApoE ε4 positive

Frisoni et al., Brain 2007

AMILOIDOSI CEREBRALE È BIOMARCATORE DI PROGRESSIONE DIFFERENZIALE IN DEMENZA CON CORPI DI LEVY

Abdelnour et al., Mov Disord 2016; 31: 1203–08

AMILOIDOSI CEREBRALE È BIOMARCATORE DI PROGRESSIONE DIFFERENZIALE IN DEMENZA CON CORPI DI LEVY

Abdelnour et al., Mov Disord 2016; 31: 1203–08
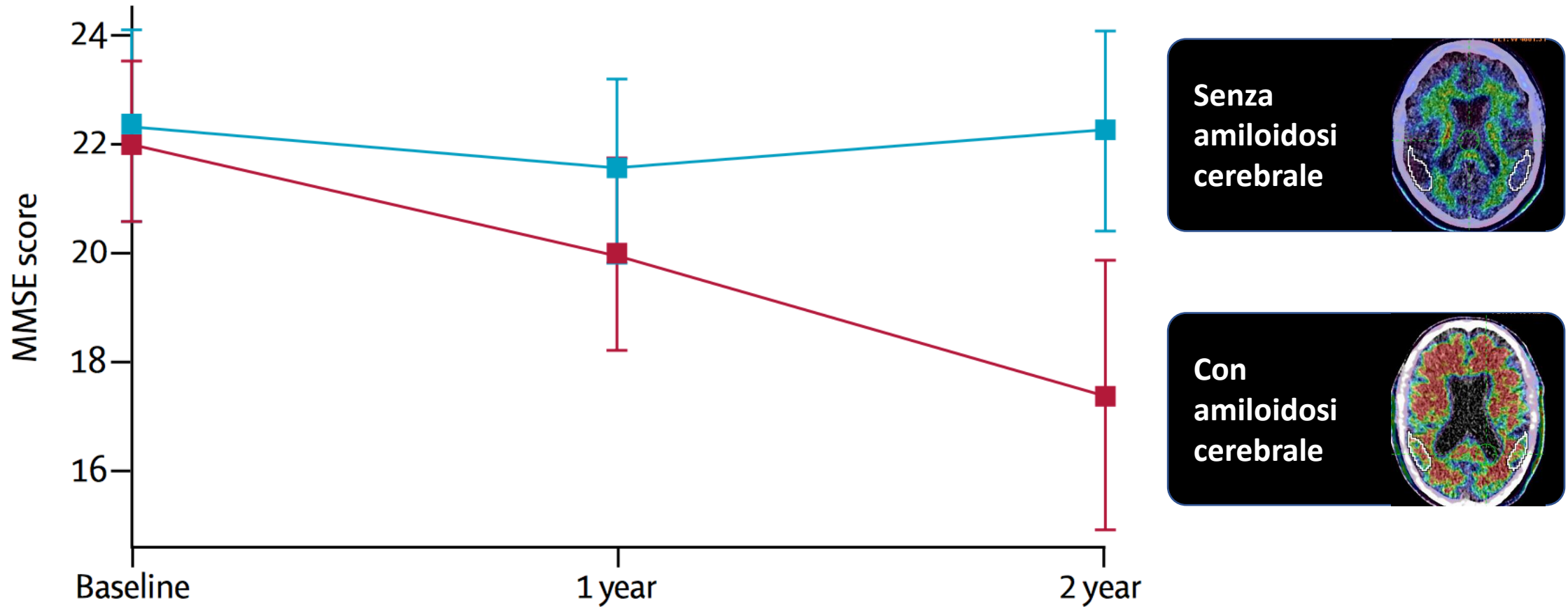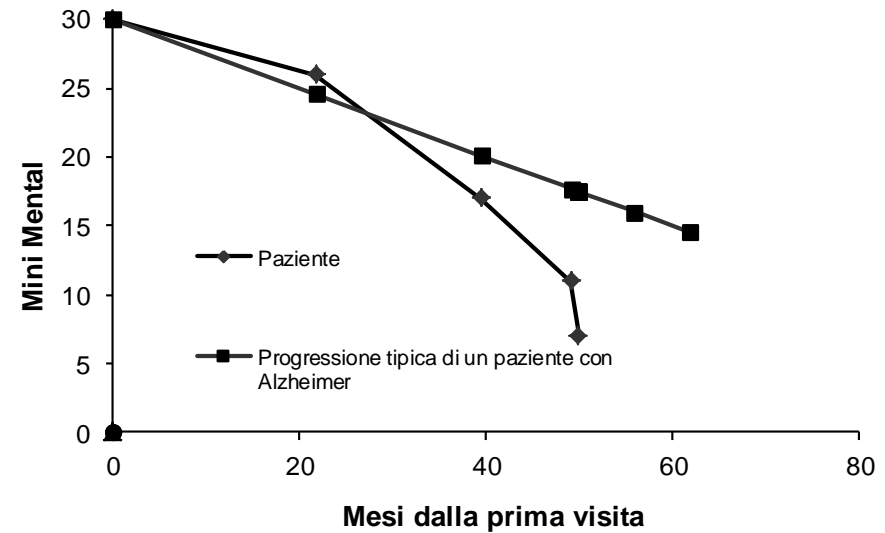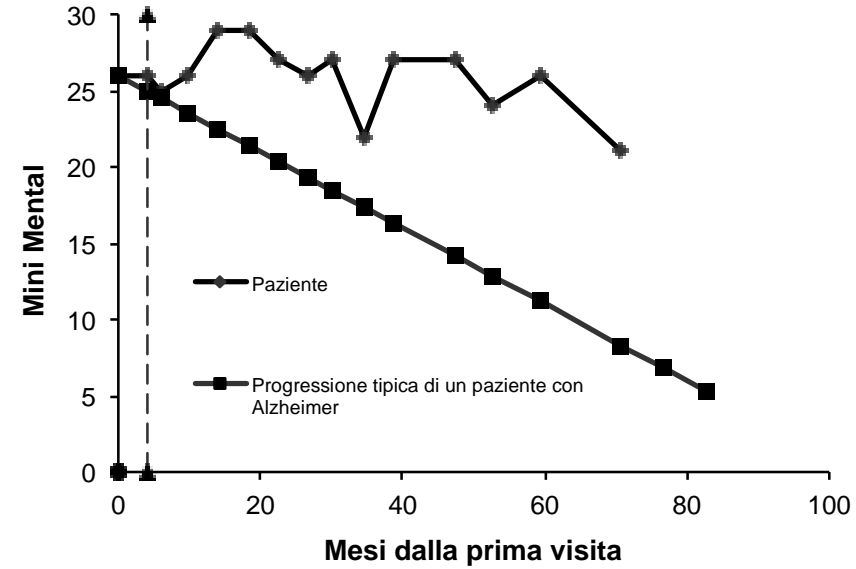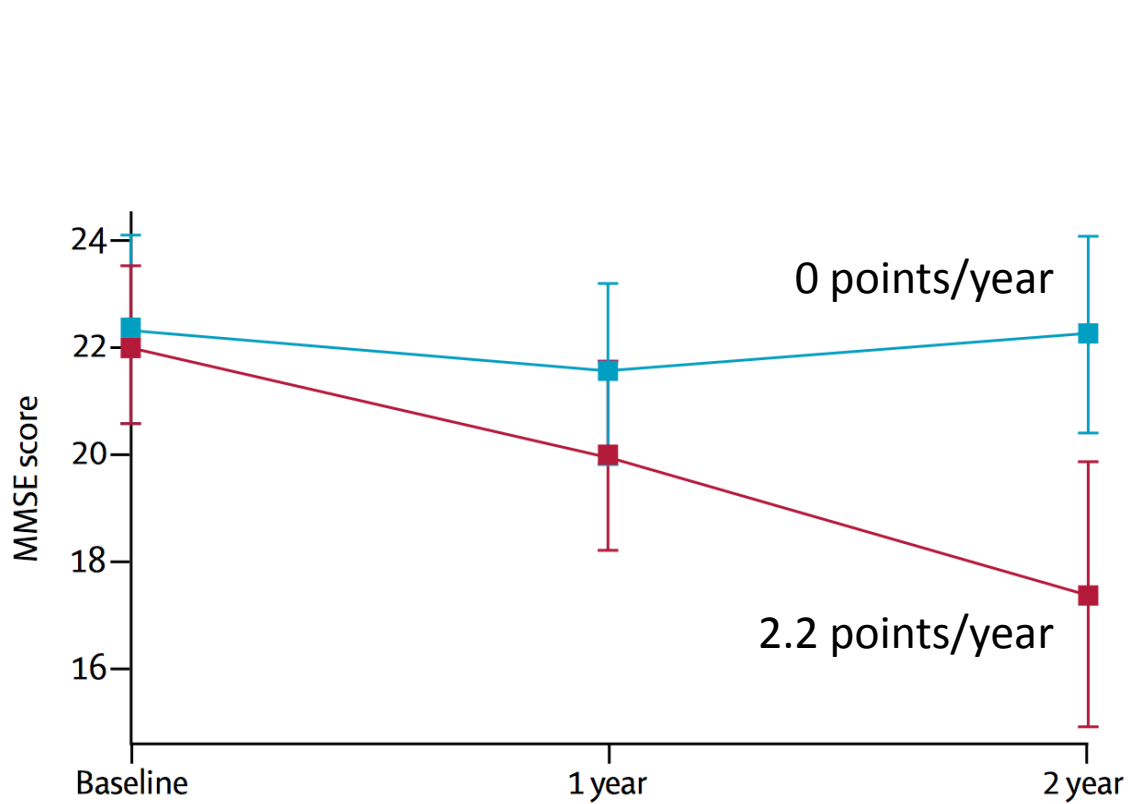
BIOMARCATORI DI RISPOSTA AGLI INTERVENTI RIABILITATIVI

Guerini, Bellelli, et al., JAGS 2004
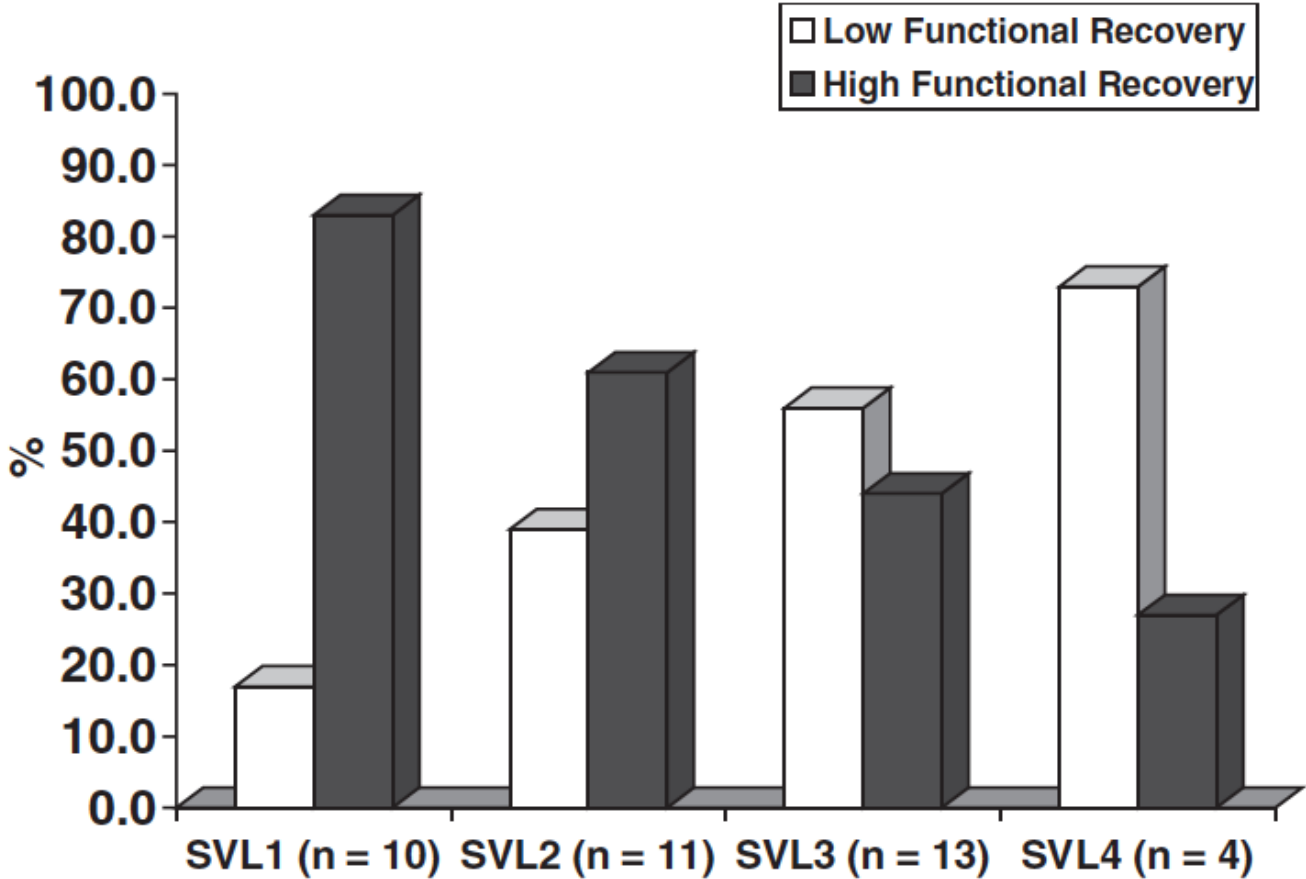
Studying the GMB ecosystem with PCA
AD patients with extreme ("typical") GMB composition
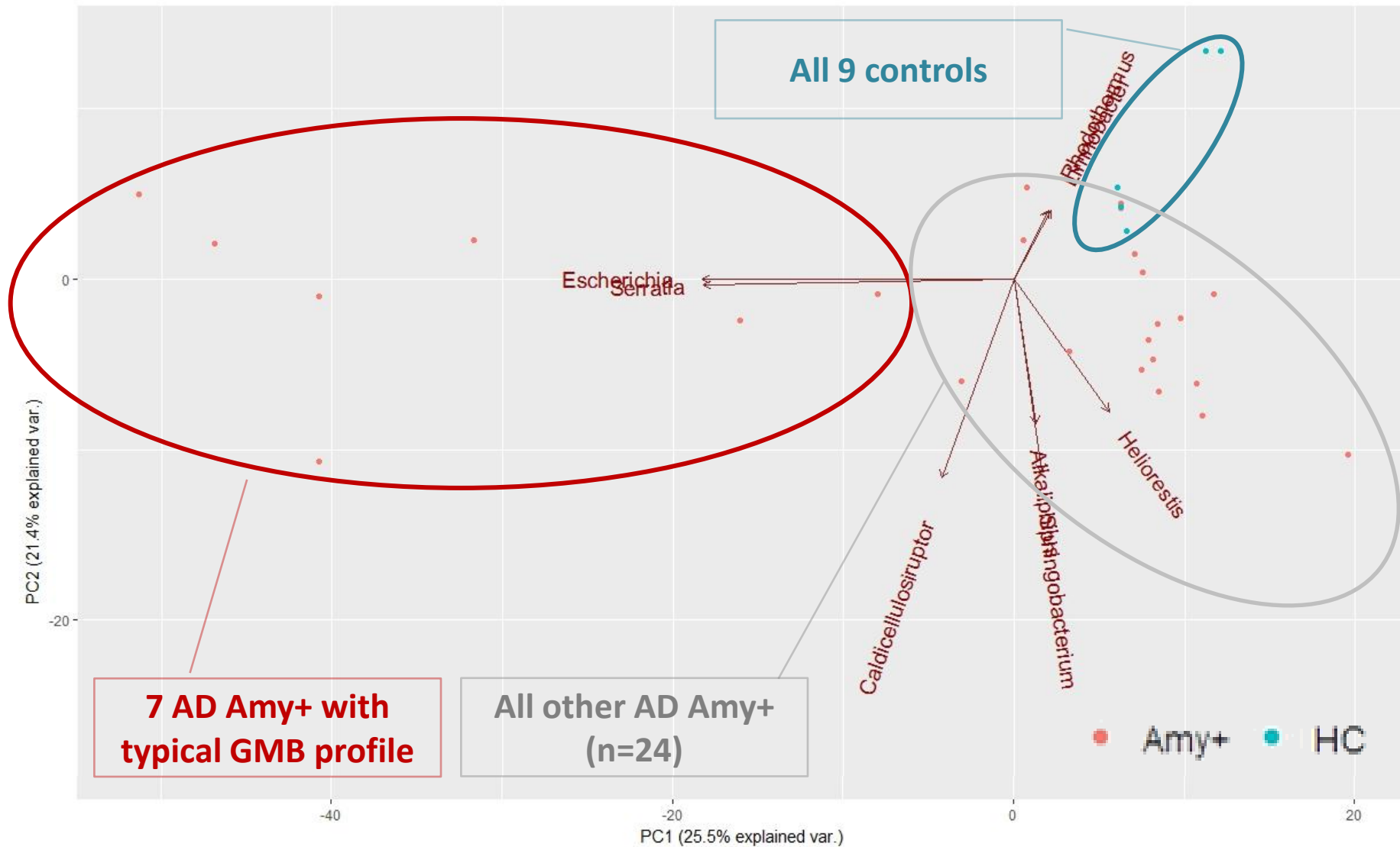
AD patients with extreme ("typical") GMB composition
Sociodemographic features

	Amy- controls (n=9)	Amy+ AD patients		P-value (K-W)
		Typical GMB profile (n=7)	Atypical GMB profile (n=24)	
Age, mean (SD)	68.4 (6.5)	69.2 (7.8)	69.8 (5.7)	n.s.
Female, No. (%)	6 (67)	3 (43)	11 (46)	n.s.
Education, mean (SD)	10.0 (5.6)	9.1 (4.9)	8.8 (4.3)	n.s.
MMSE	27.1 (1.6)	21.5 (4.1)	21.0 (4.9)	.002

AD patients with extreme ("typical") GMB composition
Clinical features

|	Amy-controls (n=9)	Amy+ AD patients		
		Typical GMB profile (n=7)	Atypical GMB profile (n=24)	P-value (M-W)
Cognitive performance				
ADAScog	7.2 (2.2)	19.1 (8.2)	17.7 (7.6)	n.s.
Logical memory	12.4 (1.8)	4.5 (2.5)	7.6 (4.2)	.094
Rey Auditory Verbal Learning Test	9.2 (2.3)	1.5 (1.2)	4.0 (3.0)	.039
Trail Making Test A	19 (14)	46 (30)	78 (108)	n.s.
Trail Making Test B	62 (64)	242 (114)	141 (85)	n.s.
Function and Behaviour				
Basic ADL, mean	-	.00 (.00)	.13 (.45)	n.s.
Functional Assessment Questionnaire	-	6.4 (3.6)	9.0 (6.0)	n.s.
NeuroPsychiatric Inventory	-	1.4 (3.4)	9.0 (10.6)	.014
Risk factors, No (%)				
Hypertension	1 (11)	3 (43)	12 (50)	n.s.
Diabetes	1 (11)	1 (14)	3 (12)	n.s.
Cardiovascular disease	2 (22)	1 (14)	4 (17)	n.s.
Hypercholesterolemia	5 (56)	3 (43)	13 (54)	n.s.
Ictus	1 (11)	0	2 (8)	n.s.
Multinfartual encephalopathy	0	0	2 (8)	n.s.
Drugs, No (%)				
AChEI	-	6 (86)	16 (70)	n.s.
Memantine	-	1 (14)	2 (9)	n.s.
Antidepressant/ hypnotic/ anxiolytic	-	2 (29)	11 (48)	n.s.
Antipsychotic	-	0	2 (9)	n.s.
Cognitive supplements*, No (%)	-	2 (29)	6 (26)	n.s.

AD patients with extreme ("typical") GMB composition
Cytokine expression
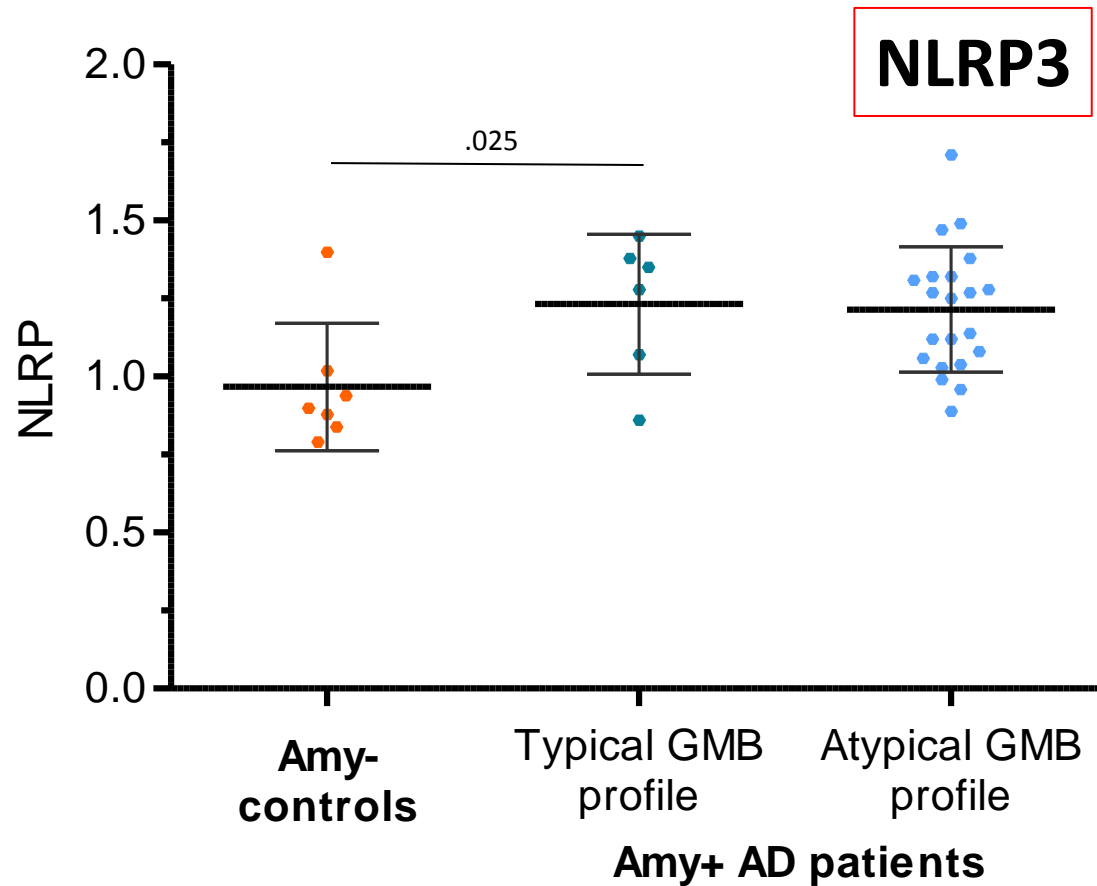
AD patients with extreme ("typical") GMB composition
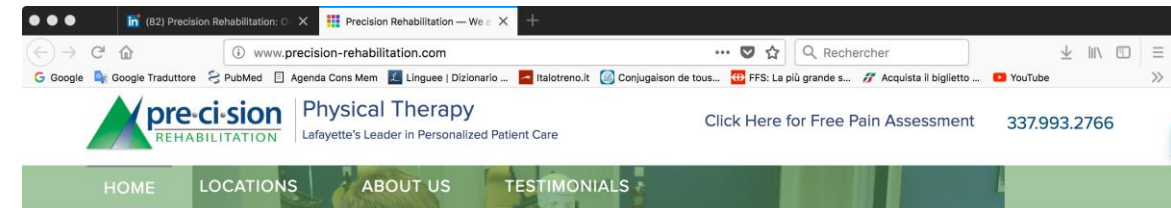Bacterial Lipopolysaccharide in the serum
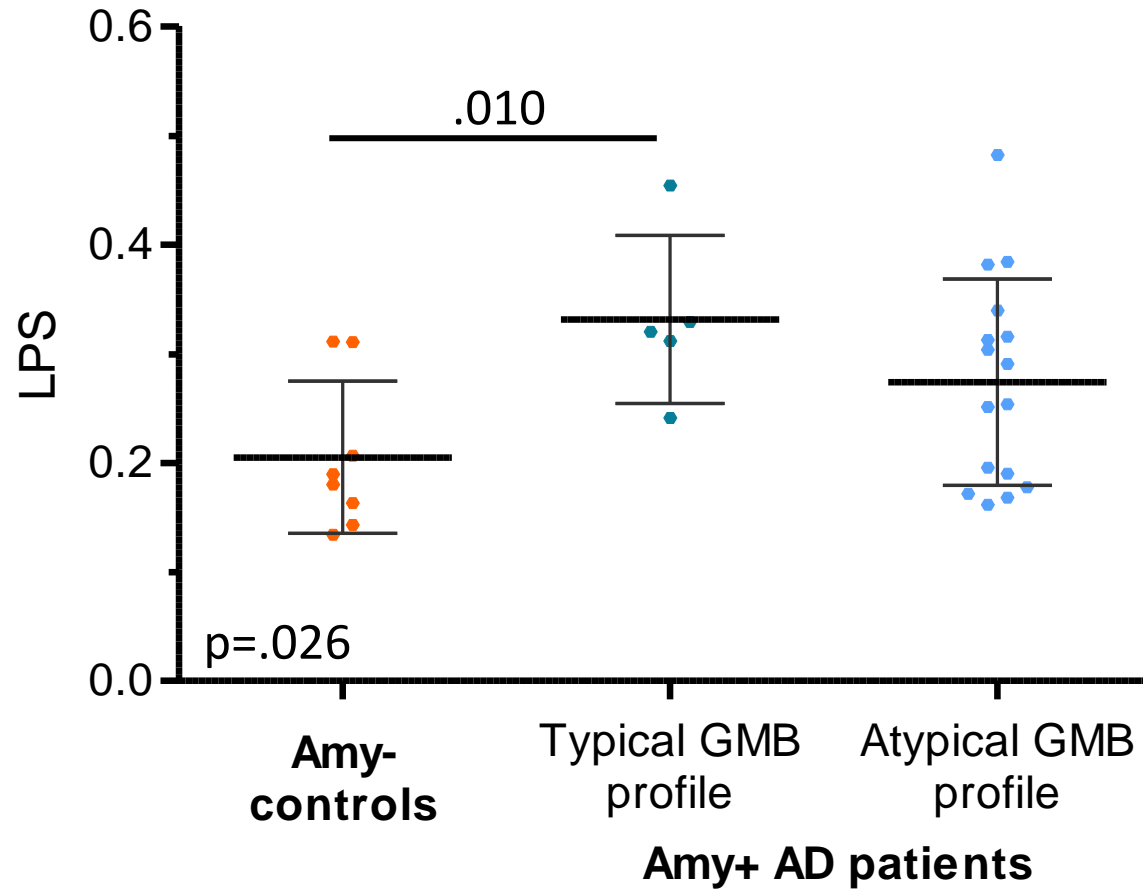
PRECISION REHABILITATION

CONCLUSIONI

- La ricostruzione della traiettoria multi-dimensionale di un paziente è essenziale per diagnosi, prognosi, risposta alla terapia farmacologica, risposta agli interventi riabilitativi
- I biomarcatori molecolari e strutturali di danno cerebrale permettono una ricostruzione fine e personalizzata della traiettoria di malattia (medicina di precisione)
- Biomarcatori periferici di pratica rilevazione possono e potranno essere utili nella pratica clinica del riabilitatore

IRCCS FATEBENEFRATELLI BRESCIA

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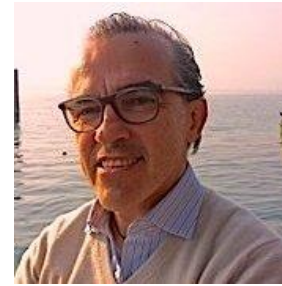Valentina Zonca

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RICOSTRUZIONE DELLA TRAIETTORIA E RIABILITAZIONE: UN CASO CLINICO

MONSIEUR F.B., 61 ANS

- Consulté en 2012 pour « évaluation de troubles mnésiques suite à un surmenage professionnel ».

- Patient originaire de Sion, boulanger-pâtissier, ensuite policier pendant 22 ans, responsable d'une équipe de 9 personnes, toujours parfaitement adapté. Marié depuis 1988, il a un fils né en 1990.

- Personnalité très stable, pas d'épisodes anxieux ni dépressifs pour le passé.

- Bonne santé physique, il est sous Aspirine cardio, Crestor, Co-aprovel.

- Plainte spontanée : confus, ralenti, moins performant, occasionnels oublis, très stressé sur son lieu de travail pour « surmenage professionnel » (arrêt de travail pendant une semaine).

- Parfaitement autonome dans toutes les activités de la vie courante.

Monsieur F.B., 57 ans

Bilan cognitif

Hospital Anxiety and Depression scale
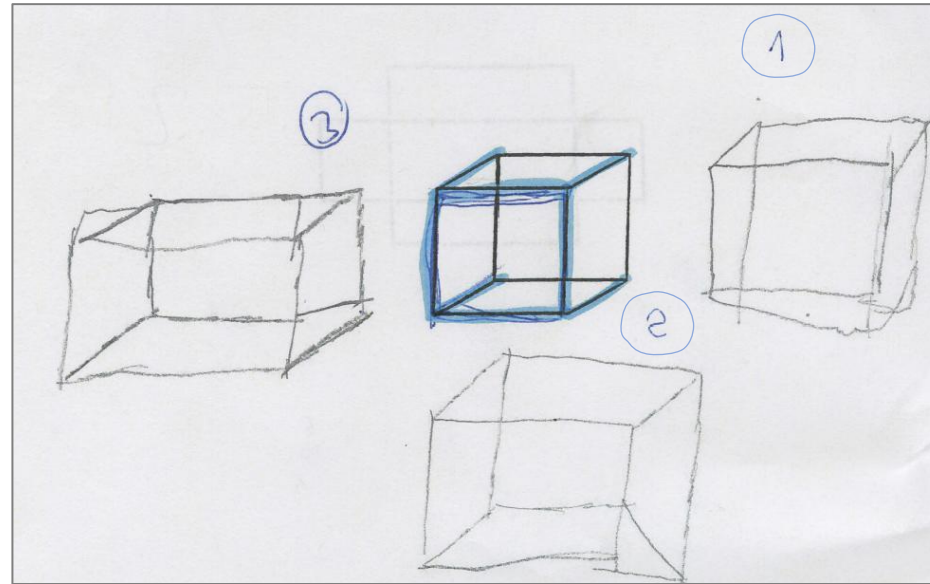State-Trait Anxiety Inventory (STAI)
Perceived Stress Scale (PSS)
Copie de figures géométriques (CERAD)
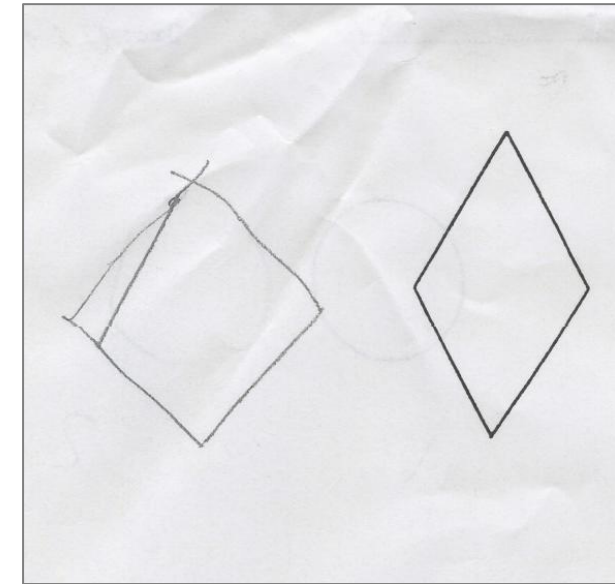Digit ordering task
California Verbal Learning Test
Trail Making Test
Fluence de mots

Copie d'un cube (3 essais)

Copie d'un rhombe

Interprétation de l'examen neuropsychologique : évaluation neuropsychologique limitée par l'anxiété... performances déficitaires en mémoire épisodique verbale, en mémoire de travail et en attention... dissociation entre l'observation clinique et la situation de tests durant laquelle l'anxiété majeure du patient parasite l'évaluation et l'amène à perdre ses moyens, rendant les résultats psychométriques délicats à interpréter.
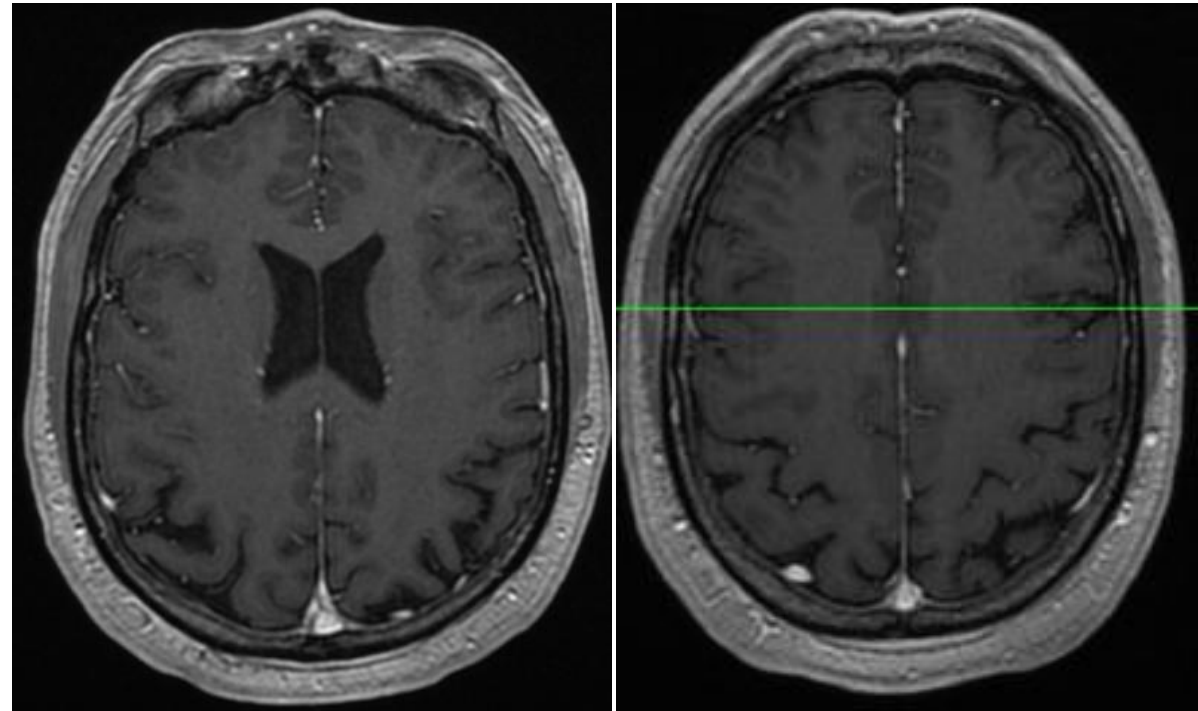
L'ANXIÉTÉ ET LES PERFORMANCES COGNITIVES: UN CAS CLINIQUE

MONSIEUR F.B., 57 ANS

RÉSULTATS DE NEUROIMAGERIE

IRM cérébrale (mai 2011) : données dans les limites de la norme en dehors de très discrètes anomalies de signal de la substance blanche à l'étage sus-tentoriel d'origine ischémique.

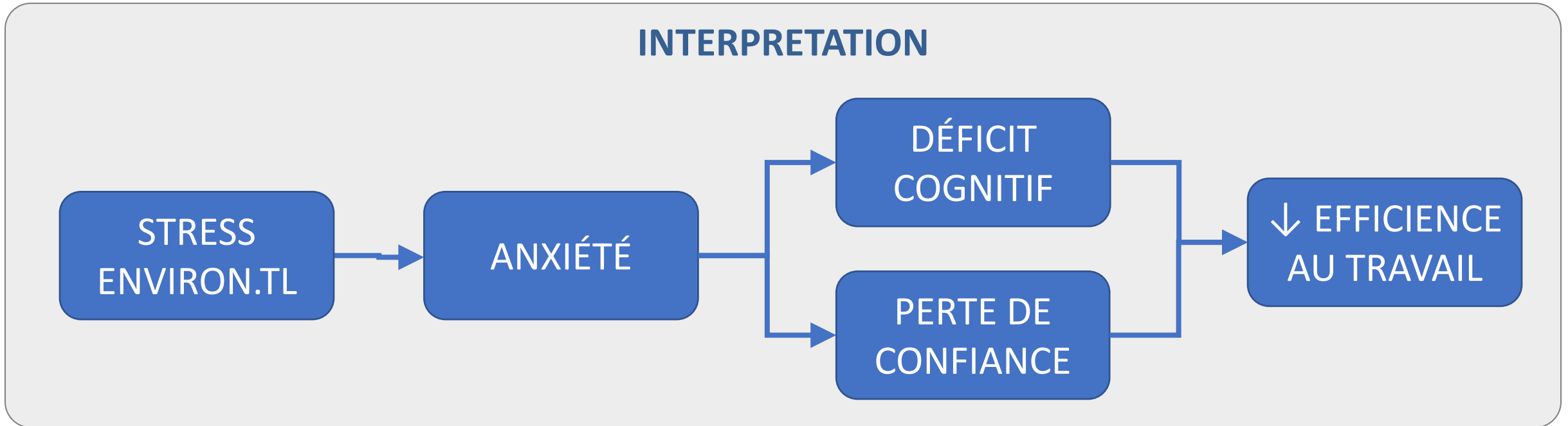# L'ANXIÉTÉ ET LES PERFORMANCES COGNITIVES: UN CAS CLINIQUE

MONSIEUR F.B., 57 ANS

Diagnostic: « problématique anxieuse et manque de confiance en ses capacités cognitives dans le contexte d'un burn-out professionnel »

Conseils
- hygiène de vie (via l'alimentation, le sommeil, l'activité physique…) et implication dans des activités cognitives et sociales stimulantes
- suivi des facteurs de risque vasculaire
- effets néfastes du tabac
- prise en charge psychologique ciblée sur des techniques de gestion du stress

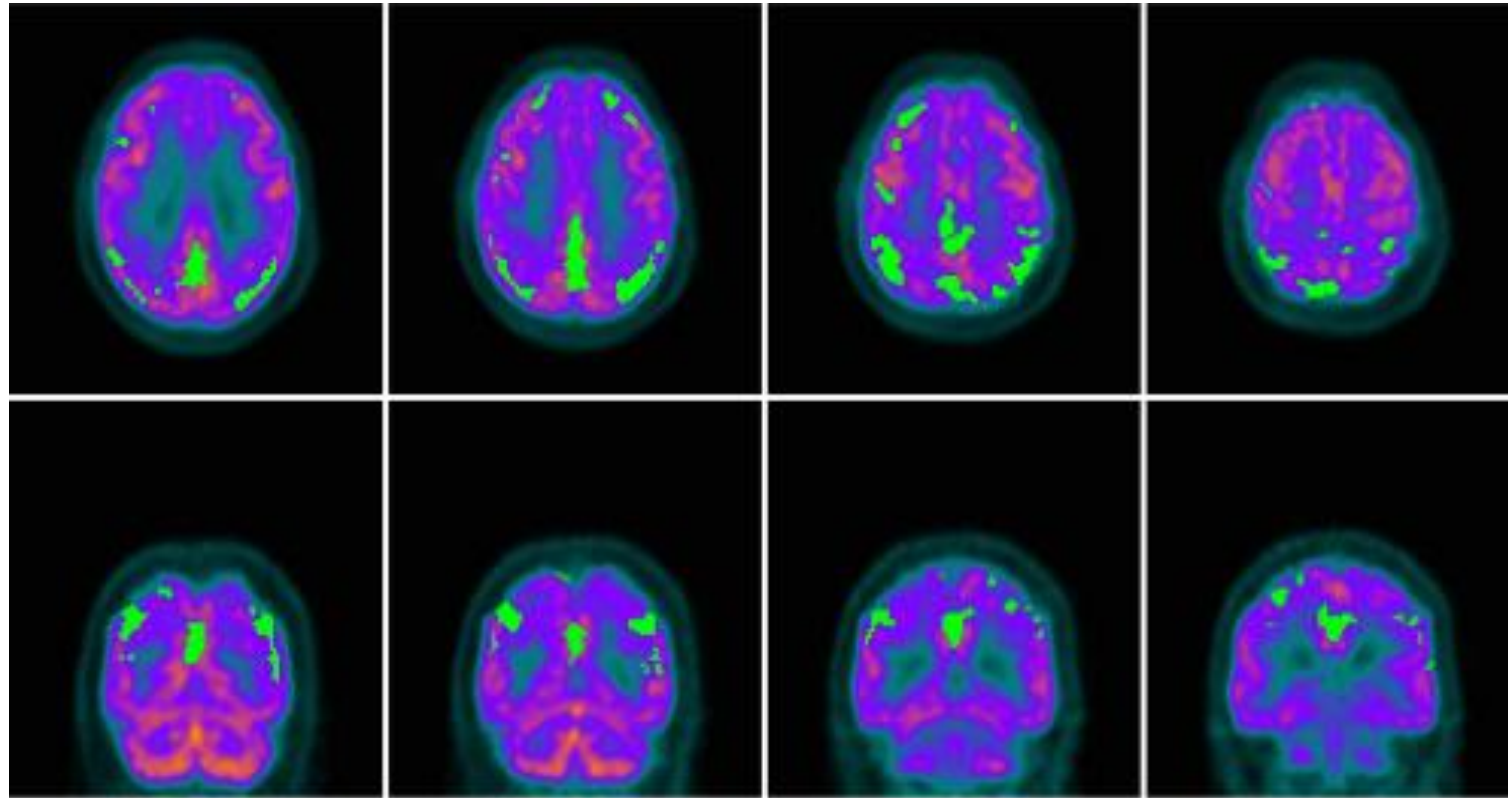# L'ANXIÉTÉ ET LES PERFORMANCES COGNITIVES: UN CAS CLINIQUE

L'ANXIÉTÉ ET LES PERFORMANCES COGNITIVES: UN CAS CLINIQUE
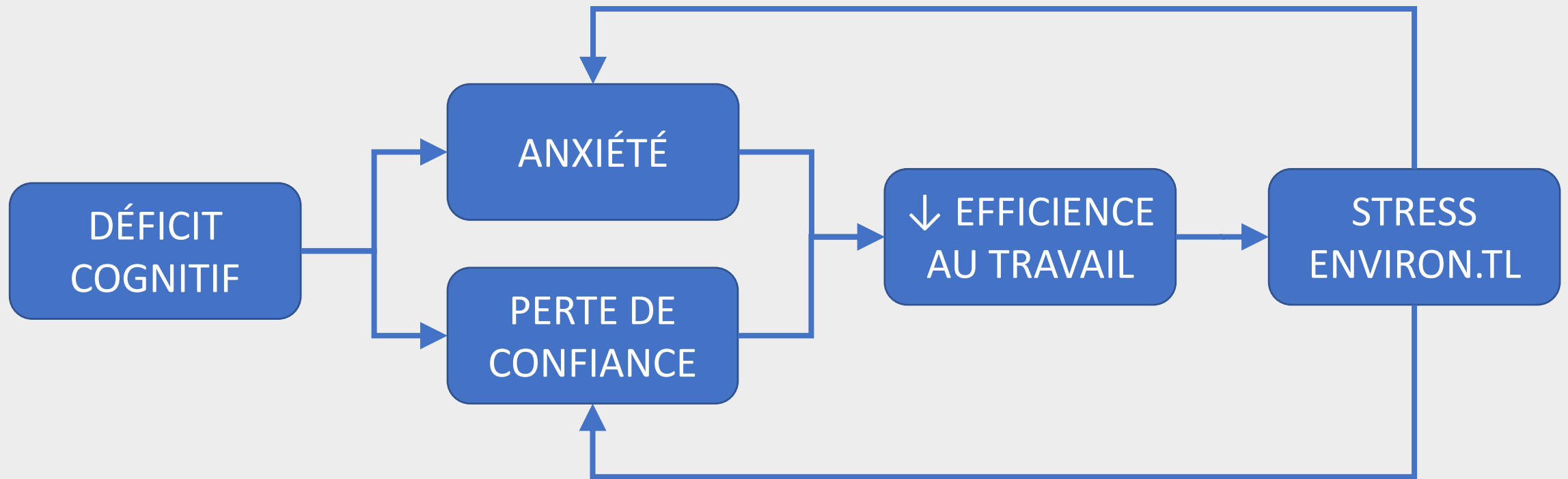
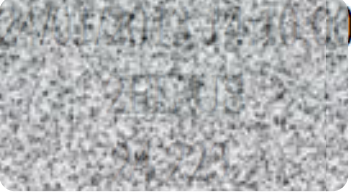# LE STRESS ET LES PERFORMANCES COGNITIVES: UN CAS CLINIQUE

Juin 2013:
Analyse du
métabolisme
corticale
par FDG PET

Computerised voxel-based analysis (BRASS) versus a reference template of cognitive normal adult and older persons (analysis by Valentina Garibotto)

LE STRESS ET LES PERFORMANCES COGNITIVES:
UN CAS CLINIQUE

Juin 2013:
Analyse des
biomarqueurs
dans le LCR
(Ab42, tau, p-tau)

voir sous MS-Excel				
Nombre de colonnes affichées :	Unité	Valeurs Réf./Seuil	LCR	LCR
glucose	mmol/l	2.8 - 4		4.0
protéines	g/l	0.15 - 0.45		0.40
protéine TAU	ng/l	< 360	594	
protéine Phospho-Tau	ng/l	< 60	81	
protéine AB42	ng/l	> 450	362	

(Analysis by Ilse Kern)

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