



Polymodal nociceptors and neurofibrillary tangles: changes in adult cognition in the cohort study of gerontological linguistics. Senile dementias between progeria (HGPS) and atypical etiopathogenesis

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Abstract

The Italian and Romance Philology is certainly the area of evaluation development from which to begin the design of academic paths, already in place although still in a fragmented measure, in the contemporary world in order to form, in terms of experimental medical pedagogy, the resources and integrative activities of the learners to the medical humanities, in agreement with the major surveys that find the World Health Organization as a source, on binding issues such as the management, from the clinical point of view and from the point of view of neo-humanistic contemplation, of the narrative in medicine as to states of pathological vitiated by the dissolution of linguistic circuits or in cases of amusia. It is therefore possible to start the shared design of new courses of study in compliance with Ministerial Decree 6/2019, with concrete results in terms of strengthening and effectiveness of clinical skills, transferred to humanists, and linguistic-communicative skills strengthened in clinicians in collaboration in teams with exemplum princeps cardio pulmonary resuscitation to recognize the physiological or pathological nature of heart sounds, internists, cerebellars. Therapeutic writing can become a useful tool in the dialogical involvement between doctor-patient and encourage the communication of therapeutic strategies and care plans to which the patient is required to adhere. From the Franciscus Medievalis, adverse inventor contra medicum, endorsed by the argumentaria, Ubi tres medici, atheist duo, borrowed from the Historia Naturalis of Pliny the Elder, in the aftermath of the sizing of the Levantine contagioni where Mi Dons Laura fell into periculum in 1348, to the so-called Marciano Code, the main medical and pharmacotropic prescriptions in protection of public health, are preserved not without gaps and Fermani Pamela, Study pain, ancient recipe books and ethics of care in linguistic conversation in narrative medicine interpolations, in the Libraries and Universities of the Venetian and Ravenna area, originating in truth from Latin and Provençal manuscripts. The interdisciplinary nature that is located between literature and medicine, in the branches of the Right to Health with the object of promotion and prevention the first, the management and treatment in pathologies the second, in the health and academic ecosystem, equally regarding before the arts and sciences, is widely commented in statistical terms by about 3,000 publications listed in the main international platforms devoted to diglossia or bilingualism.

Keywords: *Dementia, Gerontology, Tübingen Psychiatric Convention, Neurofibrillary Tangles, Progeria, Tau Protein, Alpha Synuclein Protein*

1. Introduction- **Definitional issues, differential analysis, cognitive and metacognitive functions in physiological and pathological senescence-longevity.**

The test apparatus and psychometric batteries titled Mini Mental State of Examination (MMSE) or Clock Drawing Test, Cornell Scale is a screening test equal to thirty questions, aimed at sifting the domains in the intellectual faculties relating to prose memory, language, Movement, Re-enactment, Perception, Praxia, adopted in clinical practice with the aim of determining the neuro-cognitive efficiency gradient in the gerontological patient as a foundation in order to discern the multiform dementias (Lewy Body, Vascular, Frontotemporal, Alzheimer-Perusini).

In the natural history of dementia which takes its name from the theorist Alois Alzheimer, the onset occurs through the diagnosis of an isolated cognitive disorder with mild cognitive impairment (Mild Cognitive Impairment), figured in the criteria contemplated in the Statistical Manual of Mental Disorders.

The alteration concerns only one cognitive domain, preserving the activities of daily life. With reference to the neuropsychological and behavioral aspects of Alzheimer's-type dementia, the innovation of scientific research in the value chain of the pathology that differs from the physiological course of aging traced back to physiology, with regard to the strategies for taking charge and treatment of the disorder in the prodromal phases in which the disease has not yet manifested itself; the frontier of clinical care giving consists of pharmacological treatments formed by biomarkers of etiopathogenesis: neuropsychological tests, tests on liquor (tau protein and tau / Beta protein), genetic test (ApoE4), EEG, volumetric magnetic resonance, FDG-PET SCAN.

In light of the palliation demonstrated by cholinesterase inhibitor drugs or molecular memantine drugs, administered for the acute or moderate symptomatic phase of the disease with little significant benefit aimed at slowing the pathological course, it is necessary to go back to the etiopathogenesis with the chemical reactors that make trigger the accumulation of tau and beta amyloid proteins.

The goal to aim for also by means of new generation molecular innovations concerns the improvement of lifestyles in the union with the evolution of treatment and the rhythm of the neurodegeneration process typical of apoptosis mechanisms, autophagy determined by the ATG gene or necrosis cell phone.

The residual cognitive reserve is crucial to ensure the execution of multiple activities in late-onset cognitive impairment, particularly evident in the control groups between twin couples, although they diverge in traits from the factors that allow to differentiate the imbricated vascular risk in vascular dementia.

The mechanism underlying the pathogenesis of Alzheimer's dementia in the context of the antitheses concerning intergenerational transmissibility is between 3 and 5 percentage points of probability. The chromosome 14, mutated in the loci induces the distortion of the essential enzyme in the gamma secretase process, presenilin 1-2 through the scissor synthesis of the active beta amyloid protein, generating the distal and proximal break in the insoluble protein L fragment, therefore, an aggregate that explains the protein accumulation in the cell, origin of the toxicity of the amyloid peptide that leads to the disease.

The phosphorylation of the tau protein in neurofibrillary tangles makes the study of mutated proteins relevant with targeted therapeutic techniques to defend the population from dementias linked to the geography of the population afferent to the ever widening range of demographic aging. The electrical-dynamic conduction moves acetylcholine, C₇H₁₆NO₂, a neurotransmitter of aminergic bundles that acts as a chemical mediator of nerve transmission in the synaptic wall, like a key that fits in a patch; well the receptor is able to activate the adjacent cell, therefore, facilitates the functioning of the Central Nervous System.

In Alzheimer's dementia there is a significant reduction in the quantity of synapses, particularly

marked, under the septal nucleus, in the basal nucleus of Meynert due to the lack of activation of the cortex. With the exception of sporadic forms of senile degeneration and those that define a nosographic picture of progeria with autosomal dominant and recessive transmission, 95% of dementias are age-related, which can be contained in the morbidity gradient by means of pharmacological therapy of the active neuroleptic class.

The extracerebral beta amyloid protein binds to the cerebral cortex in the CSF, an etymological figure for rock water, in smaller quantities than normal. The breakdown of the neuron contains the protein tau, the phosphorylated tau measured in pg / ml, the protein 14-3-3, insoluble and aggregable with absolute values higher than the quotient determined on the basis of the Erlangen score, determining parameters for the staging of dementia appealed in the nomen of the neuropathologist Alois Alzheimer in the category of the Psychiatric Convention of Tübingen (1906).

Alzheimer's disease is widely recognizable by virtue of the progressive degenerative course that begins with a slow and insidious onset for the patient, caused by the disabling effects determined by the assimilation of plaques derived from the filtration deficit of specific proteins (Tau protein and Beta Amyloid). The quantitative-qualitative research accepts the thesis according to which the progeroid syndrome, driven by a of molecular alarm, classes of RNA without coding, in vulnerable chronic patients due to other clinical diarthrotic conditions, which inhibits the natural tissue regeneration capacity of the cells, inevitably leading to growth arrest due to telomerase reduction.

1.1 Literature review - Linguistic Corpus of the Alzheimer's gerontological patient

From the observation of data obtained from a corpus of patients treated by the national network IRCCS-HUMANITAS, the use of *Words* as a reflection of the *Langue's own faculty*, measurable in the quantum of *Rey's Words*, changes significantly in the Alzheimer's worsening gerontological patient. Among the suggestive general linguistic correlates, the region located in the temporal lobe, therefore, delegated to the defense of the brain tissue, shows general cognitive deficit that progressively overwhelms all cognitive functions one by one (Working memory-semantic-episodic, logical reasoning, semantic production, executive functions, attention, visual-spatial skills, understanding of language). The patient manifests progressive difficulties in the *word retrieval process*, compensates with compensatory strategies for the planning and production of verbal language often through *empty speech*, gradually confining himself to the temple of silence with the final result being muted.

Degenerative pathology alters the link between infinite and indefinable emotions, endowed with a multisystemic structure and corresponding to gnoseological processes that culminate in the formulation of judgments based on indices of agency and real or imaginary symbolization. Apparently elusive emotions are collected and analyzed by the *Linguistics of Emotions*, considered the linguistic representation of emotions through the analysis of prosodic and lexical traits that usefully inform about the cognitive condition of the interlocutor with whom a conversation is established (the alternation of emotions, the speed of speech, the semantic fluency, the incongruent periphrases, the proof of naming, the bidialectalism, the deviation as a formal impact of psychic thought).

The emotions classified within unique and unrepeatable emotional maps with complexity, are very important for the purpose of knowing one's own living environment.

Therefore, the taxonomy of universal emotions (Atlas of Emotions, 156 primary and secondary emotions) was created in the Enlightenment period by the scientist Charles Darwin, creator and collector of 1,830 questionnaires, administered by missionary explorers around the world in order to detect exogenous emotional expressions and endogenous as a result of the evolution supported by the impulses of indigenous peoples. In truth, emotions are born in the family culture through encounters

that are worth a lifetime; in other words, as clearly intuited in Freudian psychoanalysis in the modular mind during extended childhood (in the 3-6 year range), we inherit preferential styles through interaction, assimilation and simulation (the complementarity between parental love, romantic love, fear-happiness contrarities) that give shape and dimension to the emotional-sentimental structure that will accompany us throughout the journey of life, activating the sympathetic attack-escape system through the activation of catecholamines, father and mother of behaviors that express the interpersonal communicative function of emotions to ourselves in the interaction with and from other speakers becoming light.

The main models of emotionality, classic and contemporary, are adjective as follows: peripheral, central, attentional, innatist, appraisal and evolutionary (respectively attributed to James and Lange, Cannon and Bard, Darwin, Tomkins, Izard, Ekman and Friesen).

Well, the worsening in the gerontological patient thus considered in pathology with about 600,000 patients suffering from Alzheimer's dementia (Istat data) reverberates with emotional linguistic correlates, in particular as regards the lines of reasoning typical of recognition tasks such as reading, with difficulty in verbal communication of understanding and producing structured periods in function blocks, albeit in different proportions. Emotional disturbances in the gerontological age are observed in patients with Alzheimer's dementia in the inhibition-apathy dyad as a reaction to read sentences or to emotionally connoted stimulations with associated bodily reactions. The emotions often aroused in the initial stages of the disease in distinguishing between genders are expressed through a marked reluctance to the thematization of emotions that emerges in the substrate in the verbal level as if to signal a precise prosodic detachment typical of the negation of the at least syndromic condition in which the patient finds himself.

The analysis sample that is sent for neuropsychological evaluation is composed of 20 patients and 18 follow-up patients, called in the clinical setting to describe a vignette in order to induce the semi-spontaneous interview and record it through annotations and segments with multilevel extension .XML the product of speech equal to about 42,000 tokens, acquired given the degenerative character of the disease in different stages. Determined in the attempt to contain and preserve the patient's quality of life as much as possible, the doctor-patient relationship in the narrative turns out to be crucial for the purpose of collaboration and education for coexistence with the disease. The sample of analysis from which the Corpus of the Alzheimer's gerontological patient (CPGA) arises is composed of two control-patient pairs for each gender, analyzed around the risk factors contemplated in the socio-demographic variables with the methodology of longitudinal and individual case studies.

In comparing the parameters present in both linguistic and clinical literature with the statistics of the field of analysis, it is possible to obtain comprehensive and informative macro-linguistic data of the narrative plane around the conversations, on the congruence of the primary classification stylized by Ekman around the paraverbal and mimic expressions. The degree of education together with the chronological age in the aforementioned sample shows by quantification an opinion certainly counterintuitively shared by the scientific community or related to a recovery of the sensory faculties that if in the initial stages of third age it undergoes a significant collapse due to its dependence on the major / lower degree of literacy, subsequently by means of occupational therapies and conservative training preserves the residual share of cognitive functions with the recovery of an even positive sign in terms of valence and arousal.

The patient follows the description of images, harbingers of stimulating emotional responses, like projective techniques (among the major ones: Rorschach Inkblot Test, Hand Test, Draw-A-Person Test, Thematic Apperception Test, Washington University Sentence Completion Test, Luscher Color Test, Projective puppet play), applied to the clinical context, opposed as much as practiced in terms of efficacy in empirical prediction, is required to affirm the presence or absence of the single emotion

aroused by the image, such as to allow evaluation with the suffrage of pre-existing statistical tools and taxonomies.

1.2 Research questions - Qualitative-quantitative methodologies in expressiveness and theming for typed unit shifts.

Given the semi-automatic classification of primary emotions and accompanied by the theory of expression and thematization of emotions, in the patients examined as to the limits of this collection of mnestic data, the possibility of making adequate distinctions in terms of the context from which they come is absent. The patients themselves, as it is not yet possible to propose an analysis free of dialectalisms which, if on the one hand denoted the preservation of real native language systems, on the other hand make the sample linguistically partially spurious. Considered so much in the kaleidoscope of emotions referred to the Alzheimer's patient, there is homogeneity between genders in the gaiety-wonder gradient of the sample selected in the onset of the disease, including the angry mood when the patient faces the disorientation dictated by the diagnosis of degenerative disease. In patients belonging to the control group, the loss of inhibition, especially noticeable in behavioral behavior typical of the advanced stages of the disease, in the follow-up control group the disappearance of the sense of impotence and annihilation is noted with an average of 53% in gender female and 43% among male patients, who in truth may also suffer from the lack of affectivity to externalize the emotions that the Victorian or Lancasterian patriarchal culture educated them, a drastic reduction of happiness equal to ¼ in the sampled controls, the feeling of fear, weakly attested in 1%, and on the same gradient non-physiological sadness, impact of the disease, is recognized in 13% of the controls.

In qualitative analysis, respect for the dialogic shift (following types: emotionally neutral or with theming of emotions and / or named, narrated for events full of emotional value, shifts with expression of emotions with the use of positive, negative, metaphorical terms, coexistence and of expressiveness and thematization of the emotions aroused by the interview) is the unit of measurement of the binomial thematization of emotions and appropriate expressive restitution mediated by the strategy of the cartoon to induce the interview by free association. For each patient in the total of the twenty patients studied, an exhaustive apparatus was observed and inventoried, made possible by virtue of a project that involved the research group on spoken communication within the Italian Linguistics Society, to which appropriately combine, demonstrating the character of innovation introduced in high schools of excellence, students and students of the Human Science curriculum with enhancement in Neuroscience, sent to the IRCCS research center closest to the place of residence in constant pandemic in the paper-based ways provided by the enlightened legislator, to involve each other in a generational dialogue in the logic of the construction of generational passages and value substitutes in all the appreciable globality.

Well, a first patient in recalling the memory of the glorious past, full of satisfactions, begins to stumble until the speech stops completely. It appears in all its evidence that amusia and silence are linked to the specific situation of deterioration, so great as to make the situation experienced in the past, drawn from long-term memory, fruitless, while the ability to thematization is unequivocally fully satisfactory.

stuck a few times while before I mean <a> I taught, I know <aa> I got the ehm + the degree in <nn> in English

I always went well, always the <mm> full marks and <ee> I I had a lot of satisfaction I have to tell the truth

we took him when he was six months old so we really raised him from <eh> from <ehm> little little </repetition>

In the control group we find examples of a whole anecdote reported to the patient's daily life drawn from perfectly preserved and still vivid memories such as the disengaged hobby of television, the day spent in the family because often in the terminal phases after multiple episodes of falls the gerontological patient becomes institutionalized in structures and as such the ruminant thought returns to relive as a film whole unrepeatable therefore special experience of life.

When I worked I was <o> huge I was the core head of Enel and I had five <dialectalism> workers with a desk as big as this one.

But I live alone <o> in my time when I lived with <n> my family because then my wife left to Parma with <n> the children and this was <uun> nice picture of watching TV, the united family that no longer exists today.

I went once when I was younger I went to Germany I went to Russia to Milan I went from there then passing over the years so it was no longer possible to travel.

In the group of patients, regardless of gender and age group, there is a tendency to thematize their health condition or events from their past. Patients use the same control strategies in a quantitatively comparable way. In the specific group of controls, especially on the part of female patients, there is a tendency to thematize references to the synchronic situation with respect to the time of the recordings with references to the recent Covidian in the perceived often pervasive in patients in a condition of fragility. Among the gender differences it is possible to observe mainly among male patients the tendency as much as possible from the damage caused by the disease to the syntactic denomination of the headwords, while the female patient often resorts to the use of figurative, metaphorical languages full of references and details of herself. The narration of connoted events or the description of emotional states aroused by questions from the drive content represent the prevailing strategies, thus showing the usefulness of methodological analysis in the context of expression and thematization of emotions, ultimately allowing to overcome taxonomies emotions that are often inadequate due to decontextualization.

2. Method - Sample - Participants

The study's sample is derived from a corpus of patients treated by the national network IRCCS-HUMANITAS-SLI Speaking Group.

The core analysis sample designated for neuropsychological evaluation consists of 20 patients and 18 follow-up patients. Specifically, the Corpus of the Alzheimer's gerontological patient (CPGA) was constructed using two control-patient pairs for each gender. The participants were analyzed utilizing a methodology of longitudinal and individual case studies centered around risk factors contemplated in socio-demographic variables. Relevant demographic characteristics considered in the study include chronological age and degree of education. According to the linguistic analysis sample statistics, participants' ages ranged from 71 to 81 years, and their years of formal education ranged from 5 to 17 years old.

2.1 Instrument(s)

The study utilized standard psychometric batteries for initial cognitive screening, including the Mini Mental State of Examination (MMSE), the Clock Drawing Test, and the Cornell Scale. These batteries consist of thirty questions aimed at evaluating multiple intellectual domains such as prose memory, language, movement, perception, and praxia to determine the neuro-cognitive efficiency gradient. For the core linguistic investigation, the primary instrument was a visual "vignette" (a picture or cartoon) acting as a projective technique. Similar to the Rorschach Inkblot Test or Thematic Apperception Test, this image was used to stimulate emotional responses and induce free association.

Neurological evaluations were supported by clinical tools including neuropsychological tests, liquid tests for tau and beta-amyloid proteins, genetic testing (ApoE4), EEG, volumetric magnetic resonance, and FDG-PET scans.

3. Data collection and analysis

Patients in the clinical setting were asked to describe the provided vignette to induce a semi-spontaneous interview. These verbal interactions were recorded, annotated, and segmented using a multilevel .XML extension. The resulting linguistic corpus produced a speech volume of approximately 42,000 tokens. Data collection was uniquely supported by high school students from a Human Science curriculum (enhanced with Neuroscience), who engaged with patients through paper-based dialogic methods during the pandemic.

3.1 Data Analysis

The study employed qualitative-quantitative methodologies to examine the expressiveness and thematization of emotions. The linguistic corpus was analyzed to quantify the usage of words (measured as the quantum of Rey's Words) as a reflection of cognitive faculty. The qualitative unit of measurement was the "dialogic shift," which categorized speech turns into types: emotionally neutral, thematization of emotions, narration of emotionally valued events, and the use of positive, negative, or metaphorical terms.

Computational Processing: A computational tool, validated by a team of annotators, was utilized to process the gerontological patient language corpus. Quantitative linguistic metrics, such as the Token-Type Ratio (TTR) for both the interview and vignette phases, were extracted to measure semantic fluency and structural degradation. The analysis successfully identified that approximately 85.9% of the linguistic occurrences were mixed forms borrowed from regional Italian

4. Results

An important linguistic principle can be dictated by the theory of expression and thematization of emotions through sealing even in the patient who, due to softening, tends to dissolve the circuit of words and to recode with the sustainable support of stimulation the use of lexical elements emotionally connotations, like the use of interjections, metaphors, circumlocutions.

In the strict alternative, the themed emotion is conveyed on an informative level in the utterance or turn to speak, through the conceptual denomination or through the description of the emotional states narrated starting from an event with a strong emotional connotation (apathy and aggression are progressively replaced in the shifts short speech from positive spectrum emotions such as tenderness and joy) in line with established uses in assessment practice for multidimensional geriatric assessment.

The computational tool is validated by a team of annotators in order, fully achieved, to create a corpora of the language of the gerontological patient, full of mixed forms, borrowed from regional Italian equal to about 85.9% of occurrences.

Emotions that are not only binary as demonstrated in the literature can be classified on the basis of the level of neurophysiological activation, as regards the positive or negative value to which the emotion is associated, to aspects of amazement expressed on a continuum resulting compatible from refined technologies that through images PMN, high-definition PET allow clinicians to identify the degree of progression of the disease, commensurate with the stratification in the brain regions of precox, intermediate, late accumulation of neuropathological molecules such as the beta amyloid protein in an inversely proportional ratio to the tau protein present in the cerebrospinal fluid, corresponding to progressive cognitive impairment and organ atrophy.

The consultation of the data reported both in Ekman's Atlas of Emotions, the main

neuropsychological test systems, the statistical synthesis obtained from Allen's Atlas of the Human Brain on the genetic profiles of gerontological populations allow to identify, starting from an acute picture, in particular observable in the hippocampus of patients with dementia status and without degenerative pathology, the heterogeneity of the genetic heritage of a viral or genetic nature in the region where the white liquor is distributed, so as to lower the temperature of the inflammation, stabilize the epigenetics of telomeres, in the generally healthy gerontological patient from the Alzheimer's patient or atypical after having conducted a biological, neuropsychological, linguistic differential study that finds synthesis of progeric innatism in the lower quality of the RNA kit due to the loss of neurons transformed into fibrillar substance or into cells of the fibrotic glia in patients' Alzheimer's donors and high GDAP, others from healthy gerontological patients who show higher quality of their RNA kit, in detail the GABAergic interneurons (GAD1, GAD2) genes still forming new astrocytic neurons with recognized primary role in the formation of long-term memory capable to regenerate and save synaptic connections in the neurophysiological ecology of sleep to counteract the onset or phagocytosis of degenerative diseases of senile age by means of the blood-brain barrier in the central nervous system.

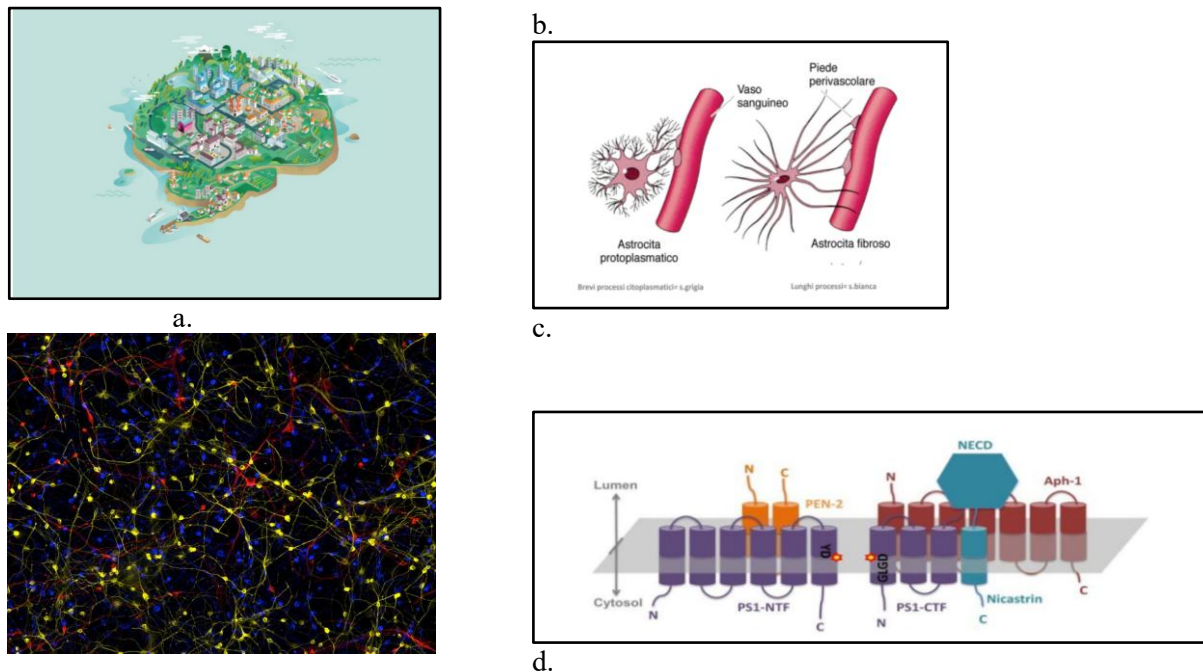
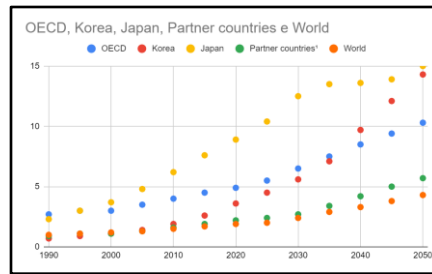
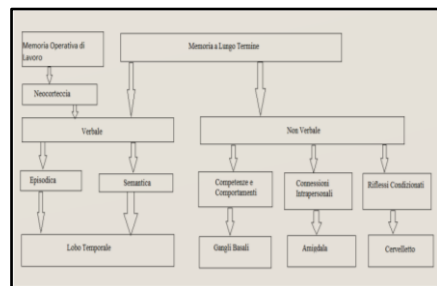


Fig.1a-bcd. Dementia Treatment and Stadiation's Disease, Union des associations France Alzheimer et maladies apparentées, 2020; Brain cells in the Alzheimer's patient. Salk Laboratory of Genetics; Function of astrocytes in the chemical composition of the interstitial fluid. The biological structure of Presenilin 1 and 2 imbricated in the development of Alzheimer's dementia.

Paese	Range 65-74			Range 75-84			Range < 85		
Belgium	4,4	4,1	4,8	11,1	10,4	12,3	11,0	10,0	7,8
Denmark	4,7	4,2	5,3	11,4	10,3	13,1	-	-	-
Finlandia	-	-	-	18,3	-	-	39,4	-	-
Francia	2,9	3,2	2,6	7,1	8,0	5,5	21,6	21,5	12,3
Germania	-	-	-	9,4	9,5	9,1	34,8	37,2	23,9
Italia	1,2	1,0	1,4	4,5	6,3	1,5	32,2	45,1	12,8
UK	1,4	1,1	1,7	6,4	7,7	5,1	19,9	24,4	13,5

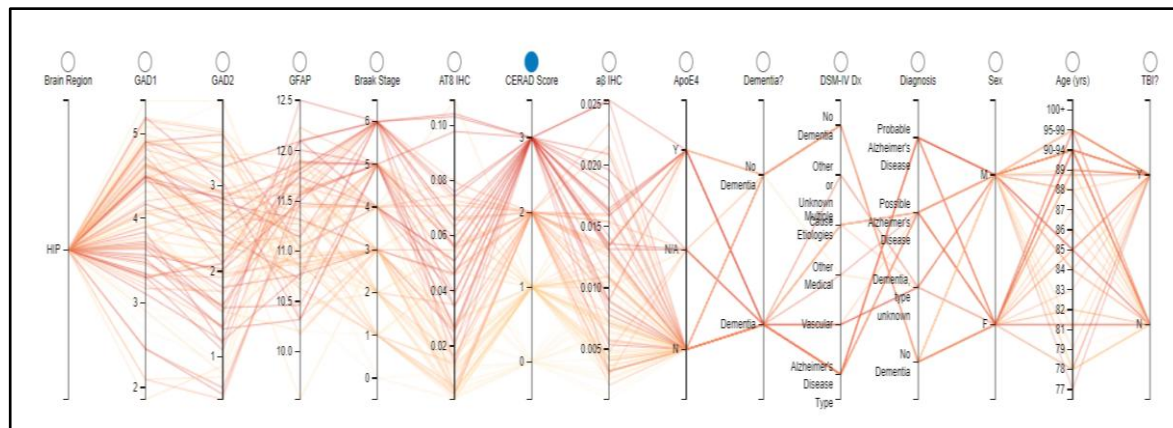


Tab. 1-2. Epidemiology of dementias in Europe. Prevalence of Alzheimer's dementia measured in percentage points in the main European countries (2012). Epidemiological projection on OECD 2020-2050 survey.



Soggetto età	Donne				Uomini			
	Cp01	Cp02	Fc01	Fc02	Ep01	Ep02	Gp01	Gp02
anni istruzione	81	71	75	73	76	75	75	77
token colloquio	13	13	13	13	17	17	5	8
type colloquio	418	598	322	534	1565	1497	674	485
token vignetta	199	280	148	224	437	476	324	223
type vignetta	368	255	237	288	308	687	194	190
TTR vignetta	169	129	120	129	149	246	93	105
TTR colloquio	0,47	0,46	0,45	0,41	0,28	0,32	0,48	0,46
	0,45	0,5	0,5	0,44	0,48	0,36	0,48	0,51

Tab. 2 ab. Neuronal plasticity: from the memorization process to Richard Atkinson and Richard Shiffrin's (1968) Memory and Cognition model; Statistics of the linguistic analysis sample.



Tab. 3. Quality of the RNA pool* in geriatric patients with Alzheimer's and non-Alzheimer's dementia in the TBI Study, Allen Reference Atlas.

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