



EUSKAL
OSASUN
IKERKUNTZA

INVESTIGACIÓN
VASCA
EN SALUD

BASQUE
HEALTH
RESEARCH

AVANCES EN NEUROCIENCIAS Y SALUD MENTAL

M. MENDIBE
20-SEP-2023



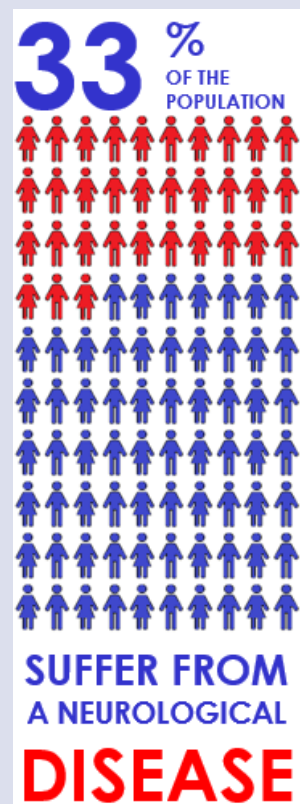
Osakidetza



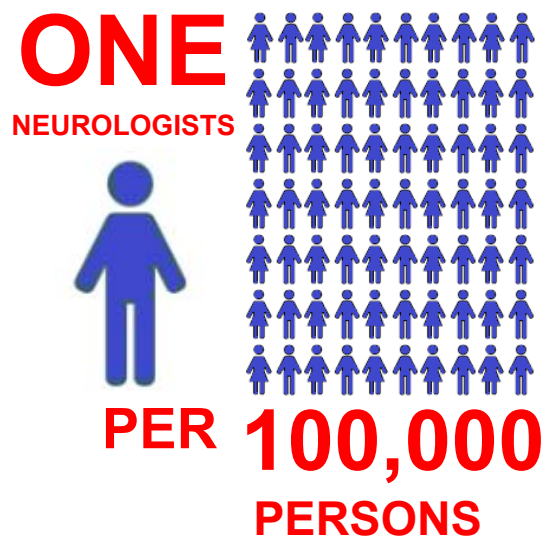
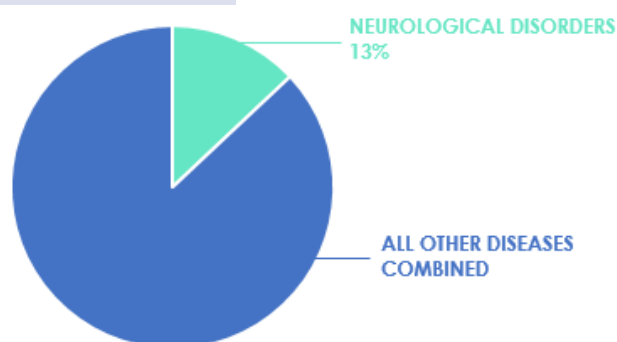
EUSKO JAURLARITZA
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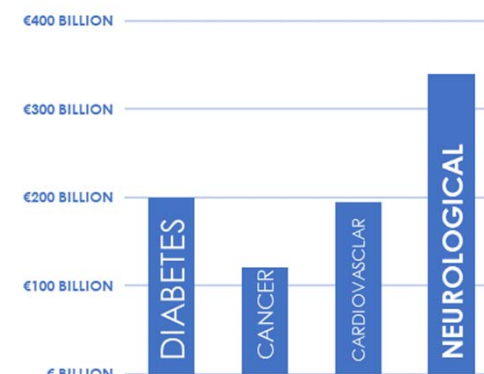
BURDEN OF MENTAL AND NEUROLOGICAL DISEASES



DISABILITY-ADJUSTED LIFE-YEARS (DALYS) PER YEAR

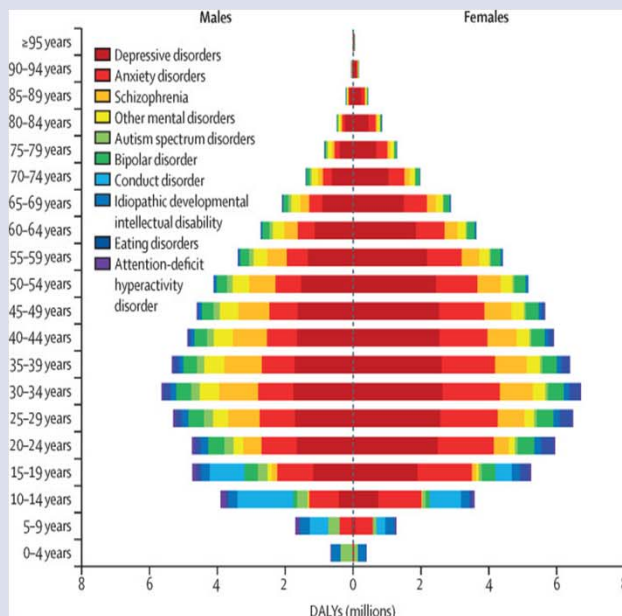


ANNUAL COST OF NCDs IN EUROPE PER YEAR



*GBD 2019 Mental Disorders Collaborators. Global, regional and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry. 2022 Feb;9(2): 137-150. doi: 10.1016/S2215-0366(21)00395-3. Epub 2022 Jan 10. PMID: 35026139; PMCID: PMC8776563





Lancet Psychiatry. 2022 Feb



EDITORIAL | VOLUME 22, ISSUE 8, P643, AUGUST 2023

Download Full Issue

Time to get serious about the Global Action Plan on dementia

The Lancet Neurology

Published: August, 2023 •

DOI: [https://doi.org/10.1016/S1474-4422\(23\)00248-X](https://doi.org/10.1016/S1474-4422(23)00248-X) •

CellPress
OPEN ACCESS

Cell
Review

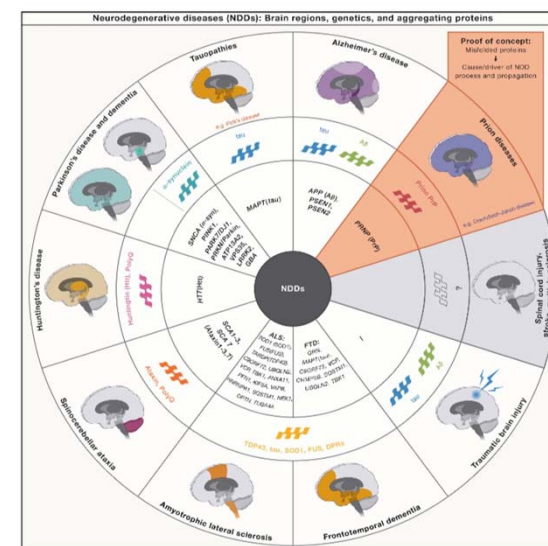
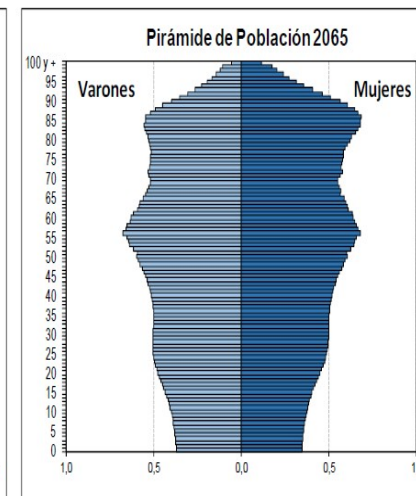
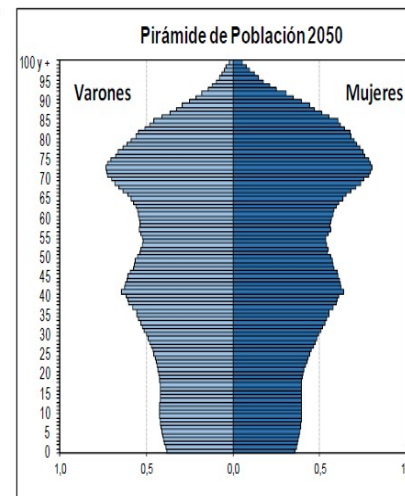
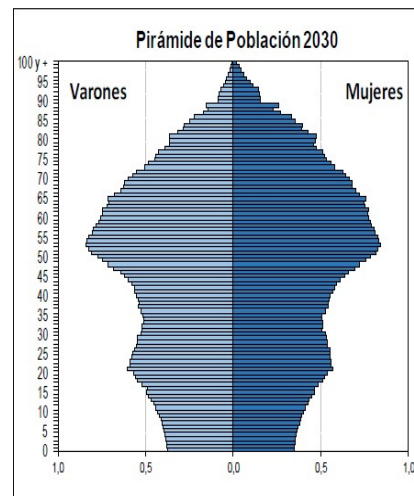
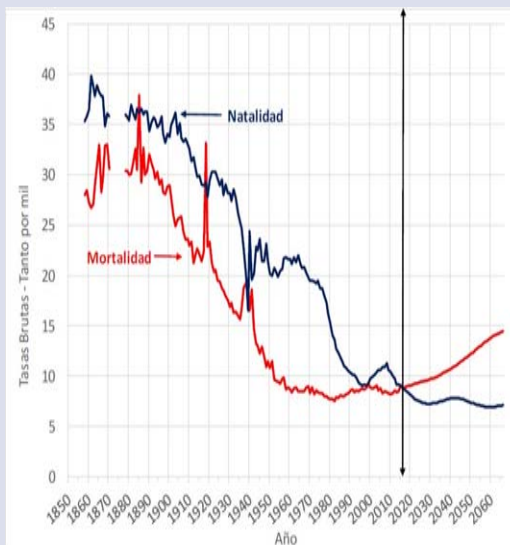


Figure 2. Characteristic aggregating proteins, genes linked to and affected brain regions in NDDs



Plan Global OMS - Objetivos 2025
Demencias-Prioridad Salud Pública



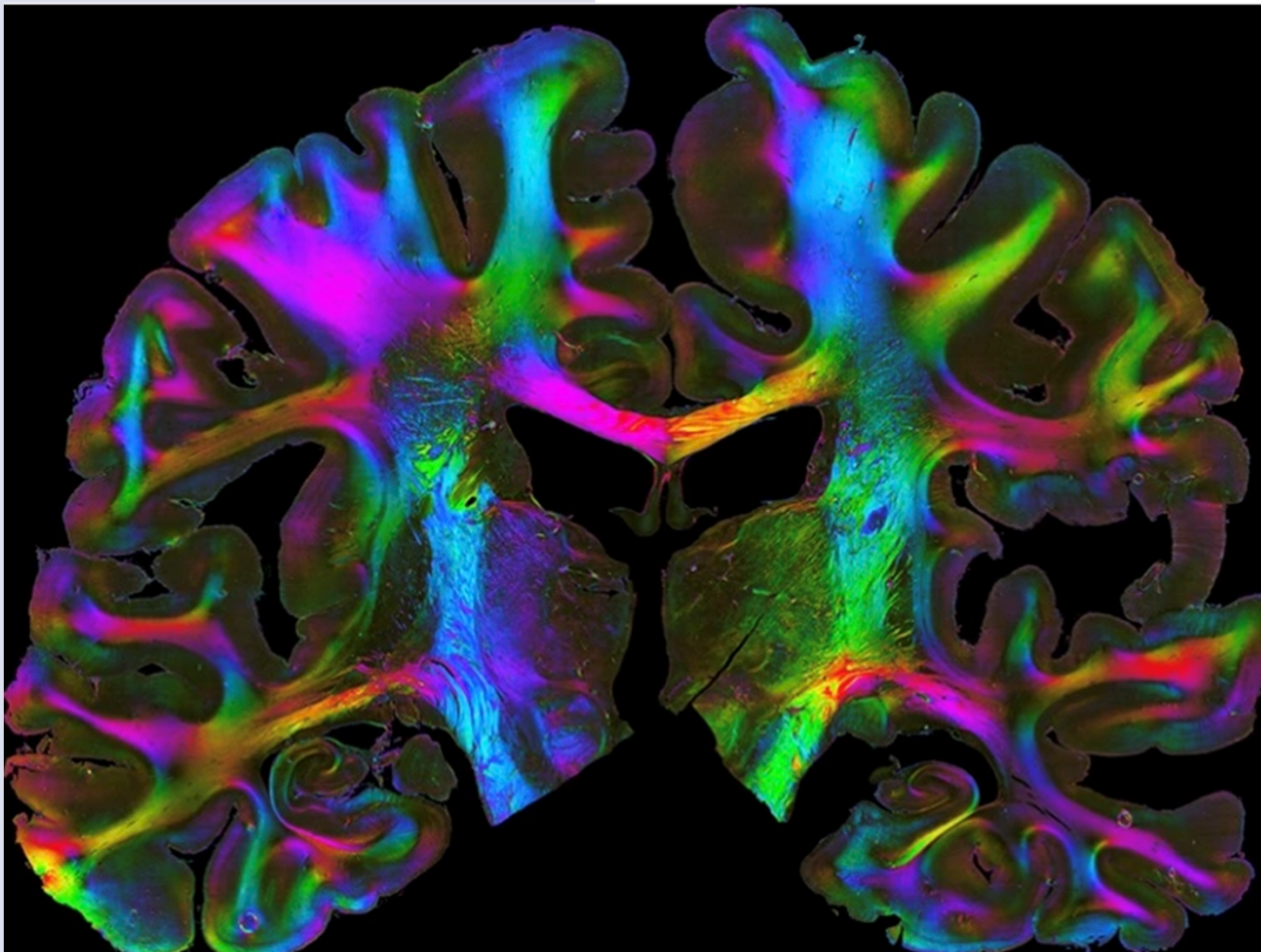


Fuente: INE, Censos de Población y Proyecciones de Población (www.ine.es)

3

- ✓ Euskadi con la máxima calificación otorgada por la Comisión Europea, por el **abordaje integral del envejecimiento activo y saludable a lo largo de la vida basado en la innovación.**





Nature Vol 620 24 August. 2023

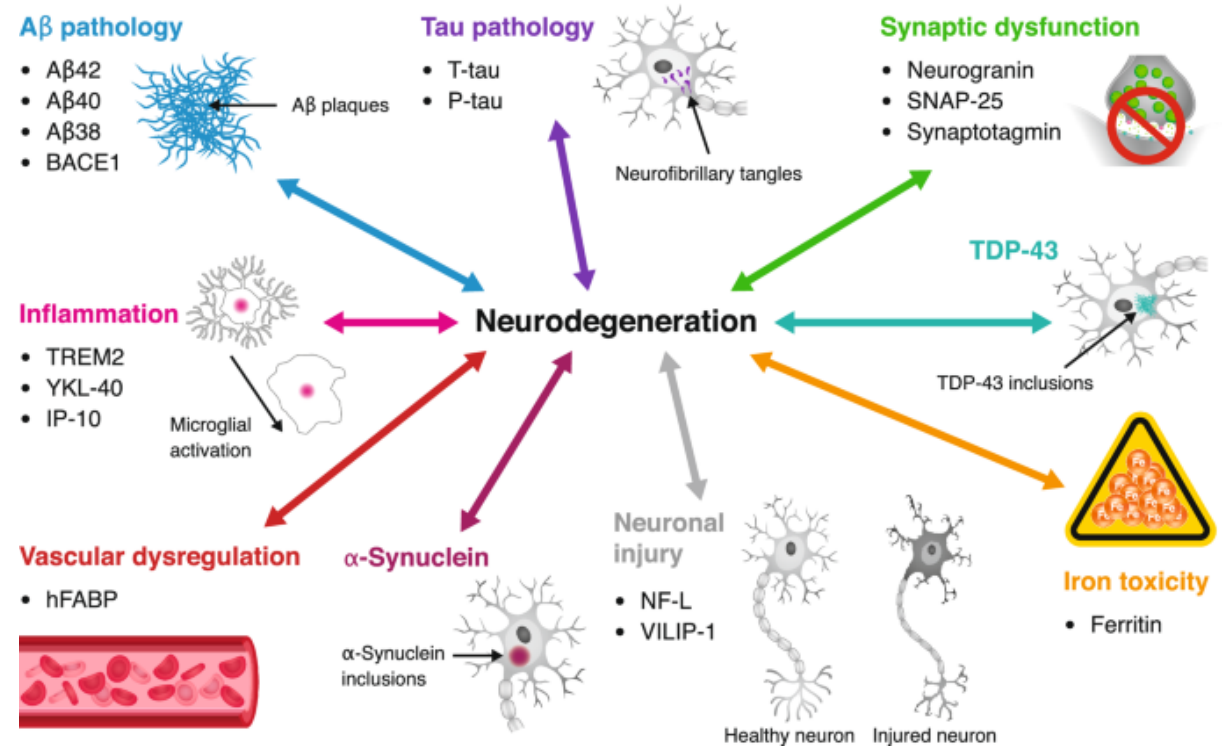
bto

1. BIOMARCADORES
2. ETIOPATOGENIA
3. ENSAYOS NUEVOS FARMACOS
4. PREVENCIÓN DE FACTORES MODIFICABLES
5. NEUROTECNOLOGÍA

7

1

+ DETECCIÓN PRECOZ Y BIOMARCADORES



1

+ DETECCIÓN PRECOZ Y BIOMARCADORES

Zetterberg and Blennow *Molecular Neurodegeneration* (2021) 16:10
<https://doi.org/10.1186/s13024-021-00430-x>

Molecular Neurodegeneration

REVIEW

Open Access

Moving fluid biomarkers for Alzheimer's disease from research tools to routine clinical diagnostics

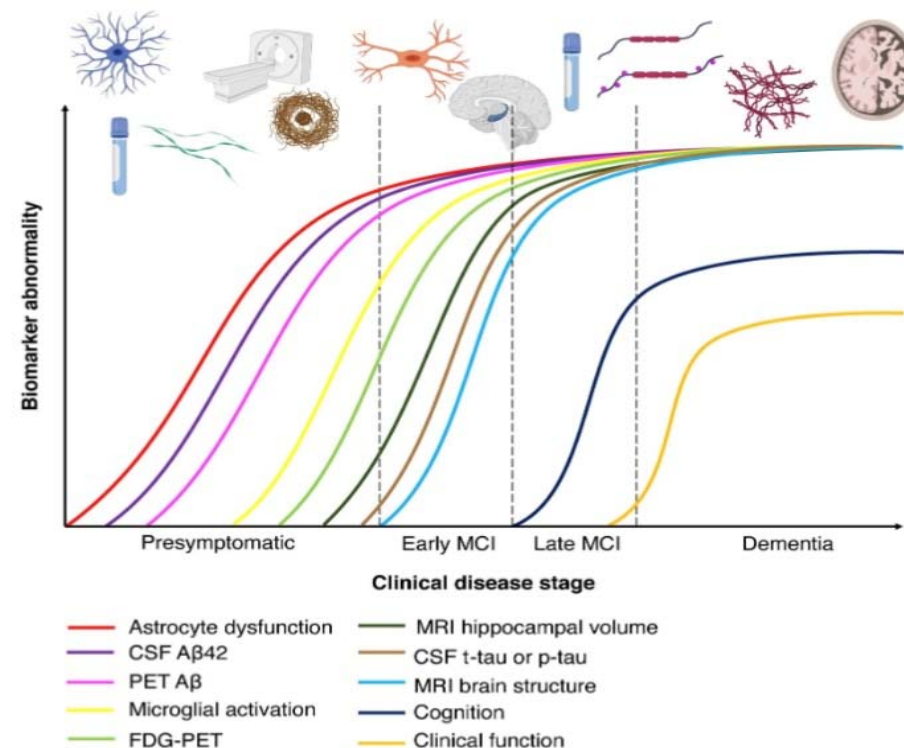
Henrik Zetterberg^{1,2,3,4*} and Kaj Blennow^{1,2*}



Abstract

Four fluid-based biomarkers have been developed into diagnostic tests for Alzheimer's disease (AD) pathology: the ratio of 42 to 40 amino acid-long amyloid β , a marker of plaque pathology; total-tau and phosphorylated tau, markers of AD-related changes in tau metabolism and secretion; and neurofilament light, a marker of neurodegeneration. When measured in cerebrospinal fluid, these biomarkers can be used in clinical practice to support a diagnosis of mild cognitive impairment or dementia due to AD. Recently, technological breakthroughs have made it possible to measure them in standard blood samples as well. Here, we give an updated account of the current state of the fluid-based AD biomarker research field. We discuss how the new blood tests may be used in research and clinical practice, and what role they may play in relation to more established diagnostic tests, such as CSF biomarkers and amyloid and tau positron emission tomography, to facilitate the effective implementation of future disease-modifying therapies.

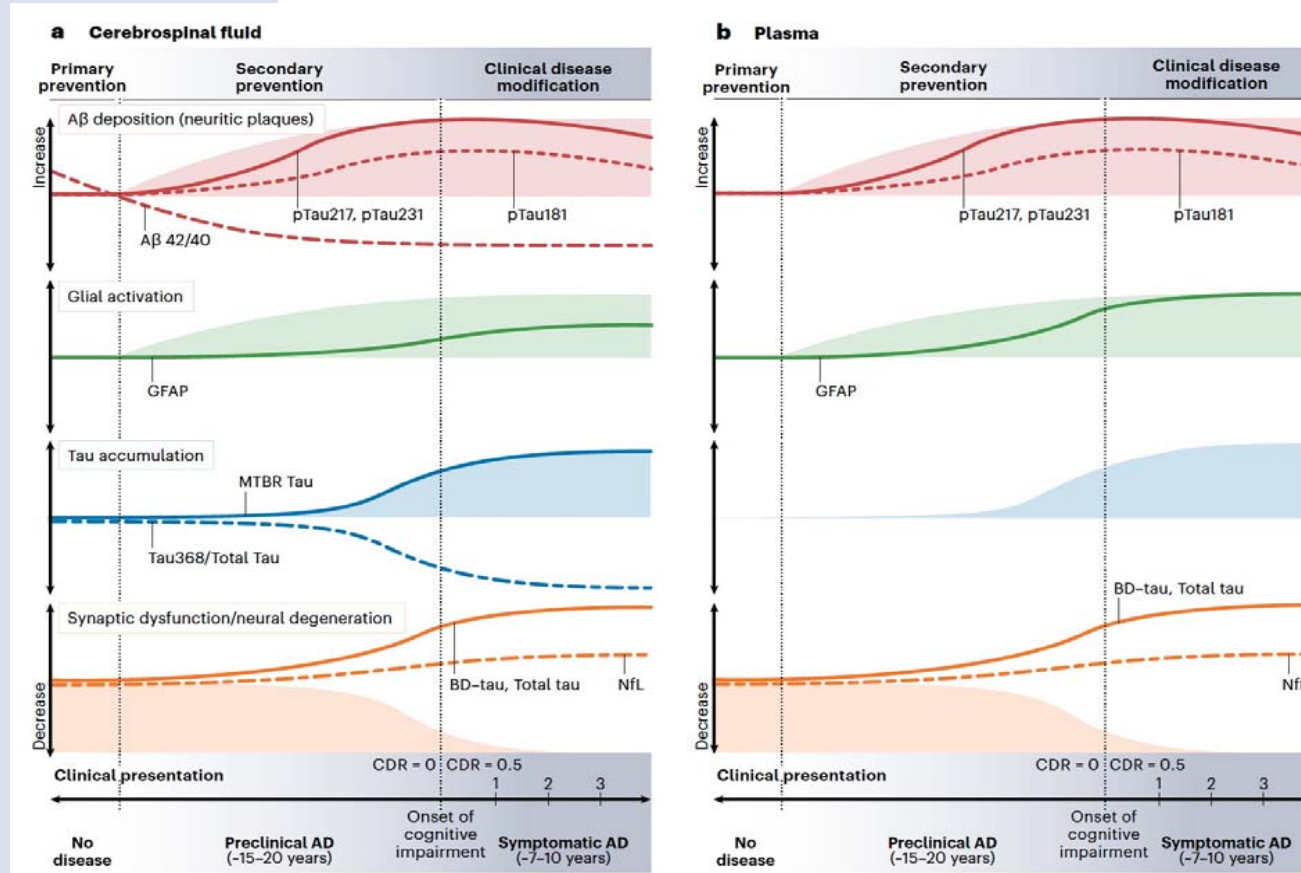
Keywords: CSF, Plasma, Biomarkers, Alzheimer's disease, Research, Clinical diagnostics



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1

+ DETECCIÓN PRECOZ Y BIOMARCADORES



10

+ DETECCIÓN PRECOZ Y BIOMARCADORES

Moorfields
Eye Hospital 
NHS Foundation Trust

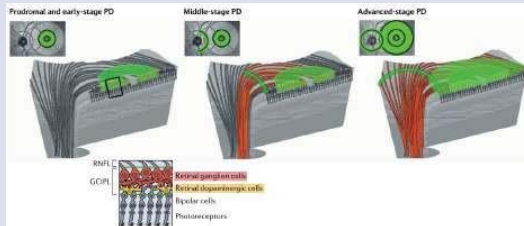


Review > Nat Rev Neurol. 2022 Apr;18(4):203-220. doi: 10.1038/s41582-022-00618-9.

Epub 2022 Feb 17.

Multimodal brain and retinal imaging of dopaminergic degeneration in Parkinson disease

Jee-Young Lee ^{1 2}, Antonio Martin-Bastida ³, Ane Murueta-Goyena ⁴, Iñigo Gabilondo ^{4 5}, Nicolás Cuenca ⁶, Paola Piccini ⁷, Beomseok Jeon ^{8 9}



> Neurology. 2023 Aug 21;101:2121/WNL.0000000000207727. doi: 10.1212/WNL.0000000000207727. Online ahead of print.

Retinal Optical Coherence Tomography Features Associated With Incident and Prevalent Parkinson Disease

Siegfried Karl Wagner ^{1 2}, David Romero-Bascones ^{2 3}, Mario Cortina-Borja ⁴, Dominic J Williamson ^{5 2 6}, Robbert R Struyven ^{5 2 6}, Yukun Zhou ^{5 2 6}, Salil Patel ⁷, Rimona S Weil ⁸, Chrystallina A Antoniadou ⁷, Eric J Topol ⁹, Edward Korot ^{2 3 10}, Paul J Foster ^{5 2}, Konstantinos Balaskas ^{5 2}, Unai Ayala ³, Maitane Barrenechea ³, Iñigo Gabilondo ^{11 12}, Anthony Hv Schapira ¹³, Anthony P Khawaja ^{5 2}, Praveen J Patel ^{5 2}, Jugnoo S Rathi ^{5 2 4 14 15}, Alastair K Denniston ^{2 16 17 18}, Axel Petzold ^{5 2 19}, Pearse Andrew Keane ^{5 2}; for UK Biobank Eye & Vision Consortium

Review > Front Neurol. 2017 May 24;8:206. doi: 10.3389/fneur.2017.00206. eCollection 2017.

The Retina in Multiple System Atrophy: Systematic Review and Meta-Analysis

Carlos E Mendoza-Santesteban ¹, Iñigo Gabilondo ², Jose Alberto Palma ¹, Lucy Norcliffe-Kaufmann ¹, Horacio Kaufmann ¹

IMSVISUAL

International Multiple Sclerosis Visual System Consortium

APOSTEL 2.0 Recommendations for Reporting Quantitative Optical Coherence Tomography Studies

Aykut Aynul, MD,* Andrés Cruz-Herranz, MD, PhD,* Orhan Aktas, MD, Laura J. Balcer, MD, Lisanne Balk, PhD, Piero Barboni, MD, Augusto Azuara Blanco, MD, Peter A. Calabresi, MD, Fiona Costello, MD, Bernardo Sanchez-Dalmau, MD, PhD, Della Cabrera DeBuc, PhD, Nicolas Felgen, MD, Robert F. Finger, MD, PhD, Jette Laurrup Frederiksen, MD, DMSci, Elliot Frohman, MD, Teresa Frohman, MD, David Garway-Heath, MD, Iñigo Gabilondo, MD, PhD, Jennifer S. Graves, MD, PhD, MAS, Ari J. Green, MD, Hans-Peter Hartung, MD, FRCP, Joachim Havla, MD, Frank G. Holz, MD, Jaime Imitola, MD, Rachel Kenney, MPhil, Alexander Klitsch, PhD, Benjamin Knier, MD, Thomas Korn, MD, Scott Kolbe, MD, Julia Kramer, MD, Wolf A. Lagrèze, MD, Letizia Leocani, MD, PhD, Oliver Maier, MD, Elena H. Martinez-Lapiscina, MD, Sven Meuth, MD, Olivier Outteryck, MD, Friedemann Paul, MD, Axel Petzold, MD, PhD, FRCP, Gorm Pihl-Jensen, MD, Jana Litvova Preiningerova, MD, PhD, Gema Rebollo, MD, PhD, Marius Ringelstein, MD, Shiv Saluja, MD, Sven Schippling, MD, Joel S. Schuman, MD, Robert C. Sergott, MD, Ahmed Tooty, MD, Pablo Villoslada, MD, Sebastian Wolf, MD, E. Ann Yeh, MD, Patrick Yu-Wai-Man, PhD, FRCOphth, FRCPath, Hanna G. Zimmermann, PhD, Alexander U. Brandt, MD,† and Philipp Albrecht, MD†

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Dr. Albrecht
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Neurology® 2021;97:68-79. doi:10.1212/WNL.0000000000001215

> Neurol Neuroimmunol Neuroinflamm. 2018 Mar 13;5(3):e449. doi: 10.1212/NXI.0000000000000449. eCollection 2018 May.

Multicenter reliability of semiautomatic retinal layer segmentation using OCT

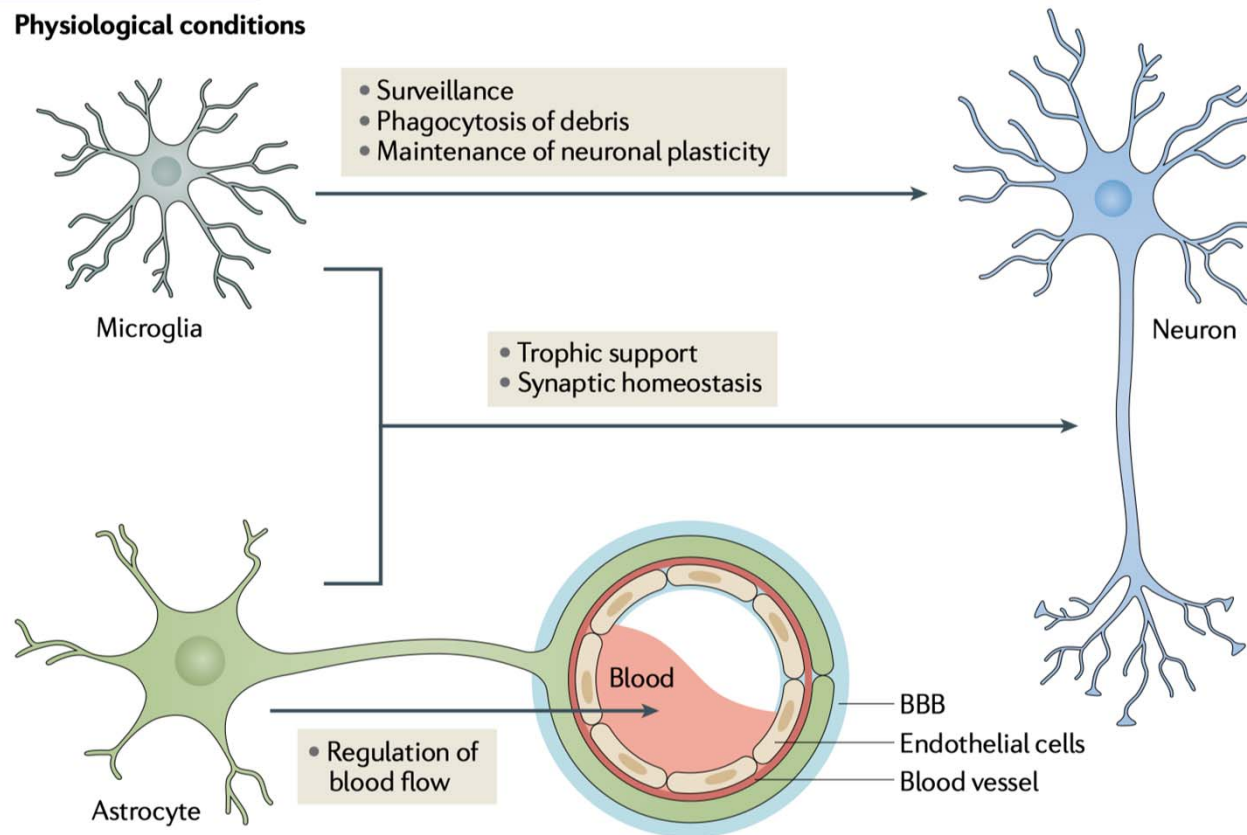
Timm Oberwahrenbrock ¹, Ghislaine L Traber ¹, Sebastian Lukas ¹, Iñigo Gabilondo ¹, Rachel Nolan ¹, Christopher Songster ¹, Lisanne Balk ¹, Axel Petzold ¹, Friedemann Paul ¹, Pablo Villoslada ¹, Alexander U Brandt ¹, Ari J Green ¹, Sven Schippling ¹

bto

2

+ MECANISMOS ETIOPATOGÉNICOS

a Physiological conditions



12

Neuroinflammation and microglial activation in Alzheimer disease: where do we go from here?

Fangda Leng and Paul Edison  

Abstract | Alzheimer disease (AD) is the most common form of neurodegenerative disease, estimated to contribute 60–70% of all cases of dementia worldwide. According to the prevailing amyloid cascade hypothesis, amyloid- β ($A\beta$) deposition in the brain is the initiating event in AD, although evidence is accumulating that this hypothesis is insufficient to explain many aspects of AD pathogenesis. The discovery of increased levels of inflammatory markers in patients with AD and the identification of AD risk genes associated with innate immune functions suggest that neuroinflammation has a prominent role in the pathogenesis of AD. In this Review, we discuss the interrelationships between neuroinflammation and amyloid and tau pathologies as well as the effect of neuroinflammation on the disease trajectory in AD. We specifically focus on microglia as major players in neuroinflammation and discuss the spatial and temporal variations in microglial phenotypes that are observed under different conditions. We also consider how these cells could be modulated as a therapeutic strategy for AD.


<https://doi.org/10.1093/brain/awab366>

BRAIN 2022; 145; 17–26 | 17

BRAIN
REVIEW ARTICLE



The role of astrocytes in prion-like mechanisms of neurodegeneration

Phillip Smethurst,^{1,2} Hannah Franklin,^{1,2,†} Benjamin E. Clarke,^{1,2,†} Katie Sidle¹ and
 Rickie Patani^{1,2}

[†]These authors contributed equally to this work.

Accumulating evidence suggests that **neurodegenerative diseases are not merely neuronal in nature but comprise multicellular involvement**, with **astrocytes emerging as key players**. The pathomechanisms of several neurodegenerative diseases involve the deposition of misfolded protein aggregates in neurons that have characteristic prion-like behaviours such as template-directed seeding, intercellular propagation, distinct conformational strains and protein-mediated toxicity. The role of astrocytes in dealing with these pathological prion-like protein aggregates and whether their responses either protect from or conspire with the disease process is currently unclear. Here we review the existing literature implicating astrocytes in multiple neurodegenerative proteinopathies with a focus on prion-like behaviour in this context.



Astrocytes display cell autonomous and diverse early reactive states in familial amyotrophic lateral sclerosis

Doaa M. Taha,^{1,2,3,†} Benjamin E. Clarke,^{1,2,†} Claire E. Hall,^{1,2} Giulia E. Tyzack,^{1,2} Oliver J. Ziff,^{1,2} Linda Greensmith,¹ Bernadett Kalmar,¹ Mhoriam Ahmed,¹ Aftab Alam,⁴ Eric P. Thelin,⁴ Nuria Marco Garcia,⁴ Adel Helmy,⁴ Christopher R. Sibley^{5,6,7,8} and Rickie Patani^{1,2}

[†]These authors contributed equally to this work.

Amyotrophic lateral sclerosis is a rapidly progressive and fatal disease. Although astrocytes are increasingly recognized contributors to the underlying pathogenesis, the cellular autonomy and uniformity of astrocyte reactive transformation in different genetic forms of amyotrophic lateral sclerosis remain unresolved.

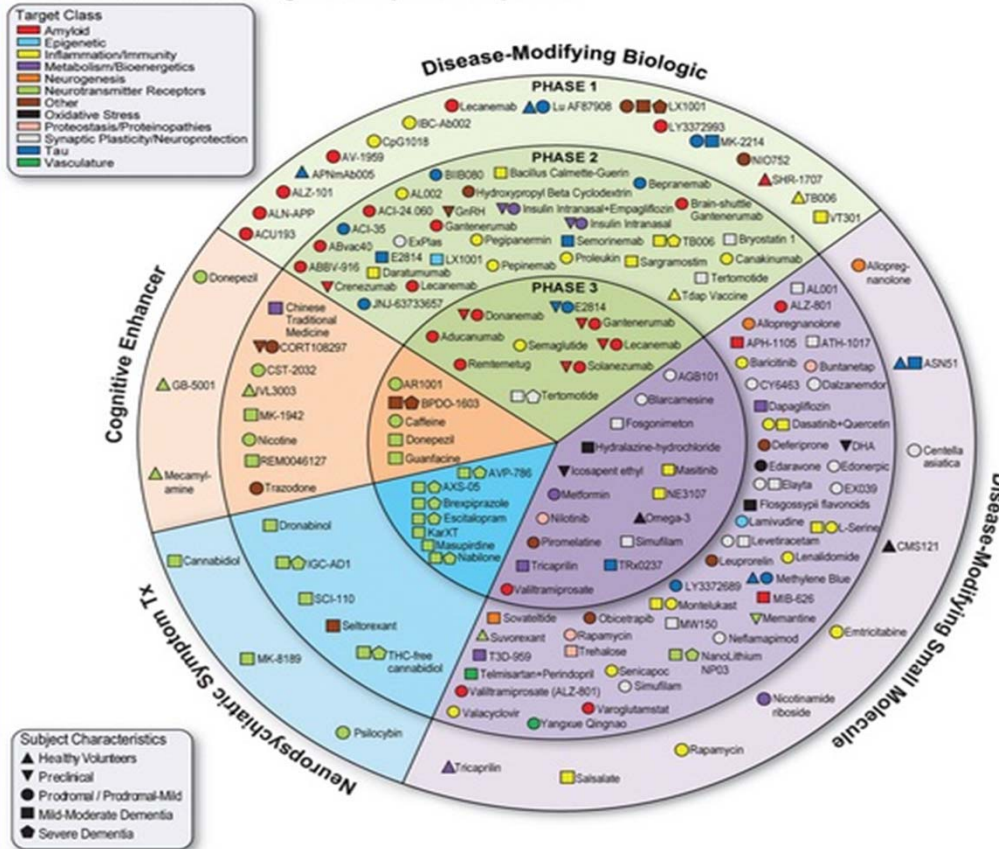
Here we systematically examine these issues by using highly enriched and human induced pluripotent stem cell-derived astrocytes from patients with VCP and SOD1 mutations.

We show that VCP mutant astrocytes undergo cell-autonomous reactive transformation characterized by increased expression of **complement component 3 (C3)** in addition to several characteristic gene expression changes. We then demonstrate that isochronic SOD1 mutant astrocytes also undergo a cell-autonomous reactive transformation, but that this is molecularly distinct from VCP mutant astrocytes. This is shown through transcriptome-wide analyses, identifying divergent gene expression profiles and activation of different key transcription factors in SOD1 and VCP mutant human induced pluripotent stem cell-derived astrocytes. Finally, we show functional differences in the basal cytokine secretome between VCP and SOD1 mutant human induced pluripotent stem cell-derived astrocytes.

Our data therefore reveal that reactive transformation can occur cell autonomously in human amyotrophic lateral sclerosis astrocytes and with a striking degree of early molecular and functional heterogeneity when comparing different disease-causing mutations. These insights may be important when considering astrocyte reactivity as a putative therapeutic target in familial amyotrophic lateral sclerosis.

+ ENSAYOS CLÍNICOS

2023 Alzheimer's Drug Development Pipeline



3

+ ENSAYOS CLÍNICOS

THE NEW ENGLAND JOURNAL OF MEDICINE

RESEARCH SUMMARY

Lecanemab in Early Alzheimer's Disease

van Dyck CH et al. DOI: 10.1056/NEJMoa2212948

CLINICAL PROBLEM

Some evidence suggests that amyloid removal slows the progression of Alzheimer's disease. Lecanemab, an anti-amyloid monoclonal antibody with high affinity for soluble amyloid protofibrils, is being tested in early Alzheimer's disease.

CLINICAL TRIAL

Design: A phase 3, multicenter, double-blind, randomized, placebo-controlled trial assessed the efficacy and safety of lecanemab in patients 50 to 90 years of age with early Alzheimer's disease.

Intervention: 1795 participants in North America, Europe, and Asia were assigned to receive intravenous lecanemab (10 mg per kilogram of body weight every 2 weeks) or placebo. The primary efficacy end point was the change in the score on the Clinical Dementia Rating–Sum of Boxes (CDR–SB) from baseline, with higher scores indicating greater impairment.

RESULTS

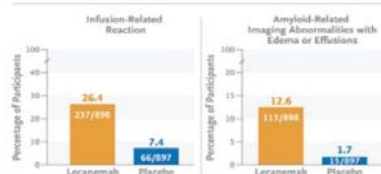
Efficacy: At 18 months, mean CDR–SB scores had worsened in both groups. The mean change in CDR–SB score was smaller (indicating less cognitive and functional decline) in the lecanemab group.

Safety: Overall incidences of adverse events were similar in the two groups. The most common adverse events in the lecanemab group included infusion-related reactions and amyloid-related imaging abnormalities with edema or effusions.

LIMITATIONS AND REMAINING QUESTIONS

- Longer-term follow-up is needed; an open-label extension study is ongoing.
- The trial was conducted during the Covid-19 pandemic and, as a result, faced challenges including missing data, missed doses, delayed assessments, and intercurrent illnesses.
- Occurrences of amyloid-related imaging abnormalities may have led to unblinding of participants and investigators.

Links: Full Article | NEJM Quick Take | Editorial



CONCLUSIONS

In patients with early Alzheimer's disease, lecanemab was associated with moderately less decline on measures of cognition and function than placebo over a period of 18 months.

Research

JAMA | Original Investigation

Donanemab in Early Symptomatic Alzheimer Disease The TRAILBLAZER-ALZ 2 Randomized Clinical Trial

John R. Sims, MD; Jennifer A. Zimmer, MD; Cynthia D. Evans, PhD; Ming Lu, MD, MS, MPH; Paul Ardayfio, PhD; JonDavid Sparks, PhD; Alette M. Wessels, PhD; Sergey Shcherbinin, PhD; Hong Wang, PhD; Emel Serap Monkul Nery, MD; Emily C. Collins, PhD; Paul Solomon, PhD; Stephen Salloway, MD; Liana G. Apostolova, MD; Oskar Hansson, MD, PhD; Craig Ritchie, MD, PhD; Dawn A. Brooks, PhD; Mark Mintun, MD; Daniel M. Skovronsky, MD, PhD; for the TRAILBLAZER-ALZ 2 Investigators



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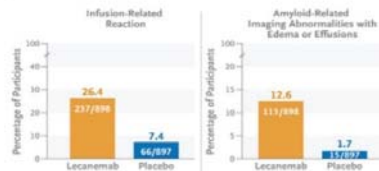
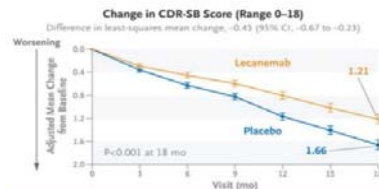
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Links: Full Article | NEJM Quick Take | Editorial

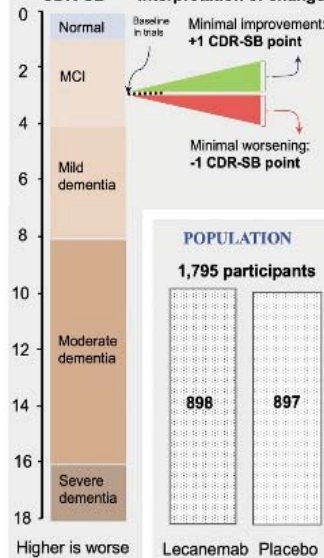


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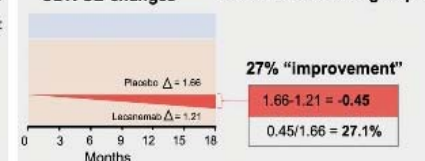
MEASUREMENT AND MEANING

CDR-SB Interpretation of change

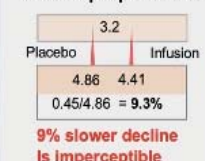


FINDINGS AND INTERPRETATIONS

CDR-SB changes Difference between groups



But can people notice?



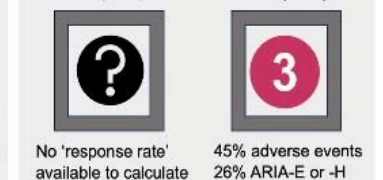
22,000 – 17,500 = 4,500 mm³
4,500/17,500 = 25.7%

26% (~ 1 teaspoon) less brain

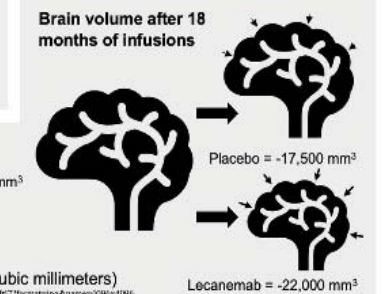
(Brain volume data in cubic millimeters)
<https://pubs.rsc.org/medRxiv/AlzDisXaAdh77foczarpgg&name=090x0906>

DATA TO ESTIMATE RISK/BENEFIT RATIO

Number needed to treat (NNT) Number needed to harm (NNH)

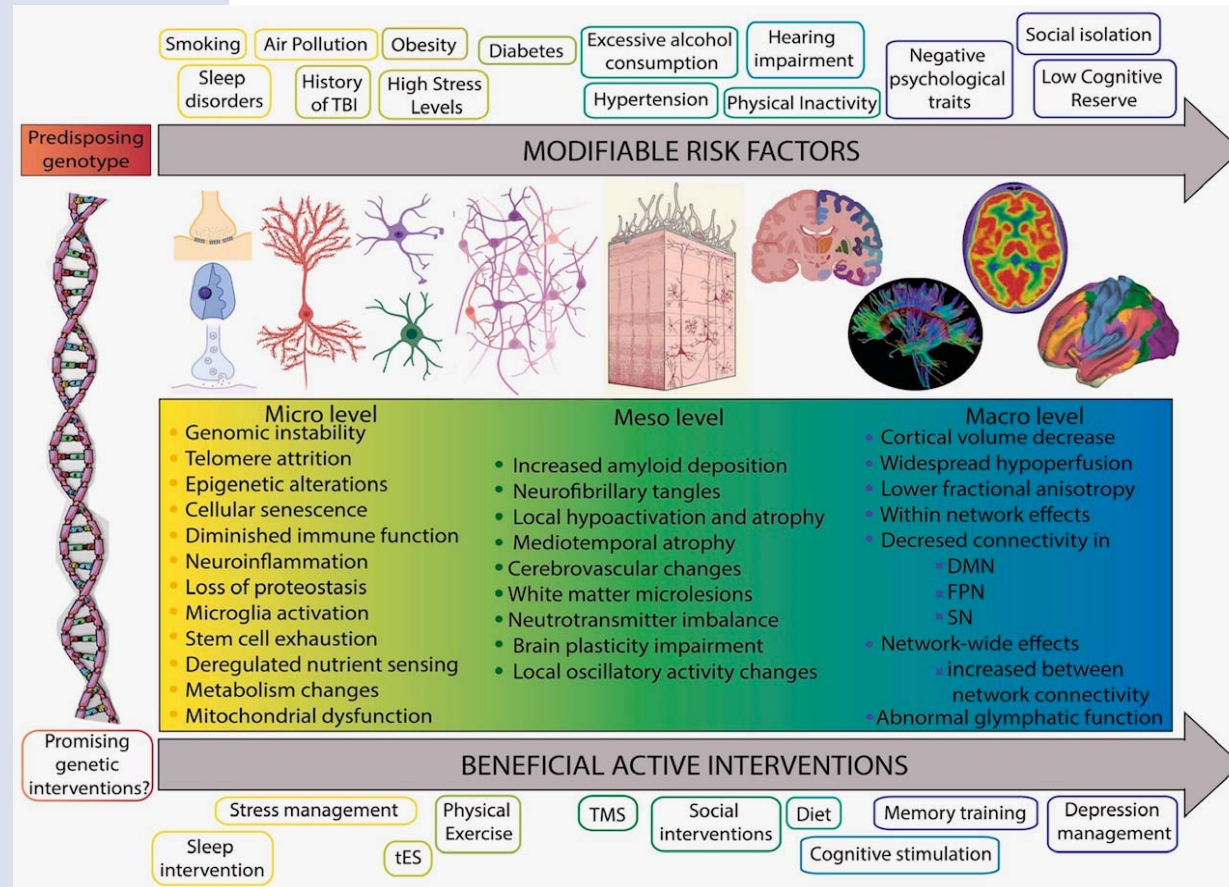


BRAIN VOLUME CHANGES



4

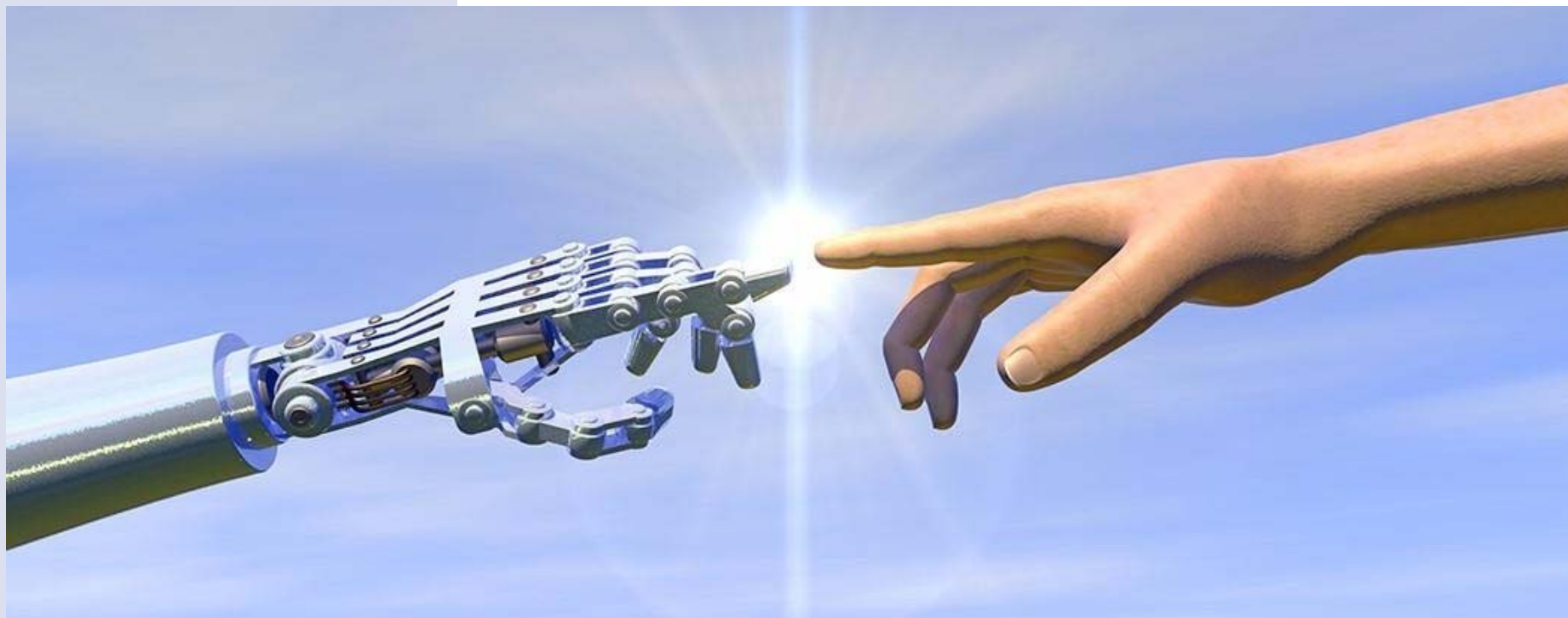
+ PREVENCIÓN



5

high-tech

+ NEUROTECNOLOGÍA



bto

high-touch



Osakidetza



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RevoluciónFUTURO
BIGDATA EVOLUCIÓN
VIRTUAL **DIGITAL**
INFINITUD NuevosRetos
Tecnología METAVERSO
INTELIGENCIAARTIFICIAL



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Top 10 new medical technologies 2022

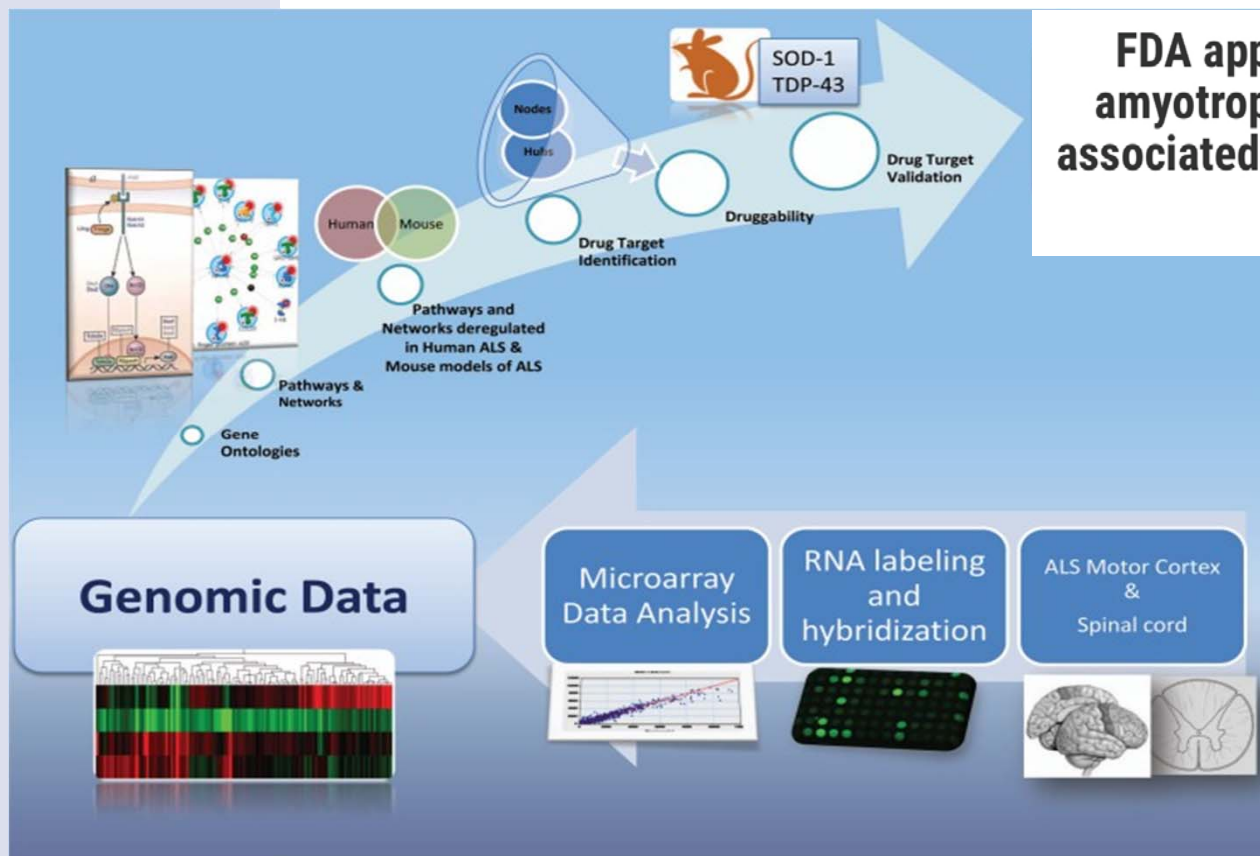


22

Hannah Burke, 14 de abril de 2022

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23



Qalsody safety and effectively. Aprobación: 2023



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Top 10 new medical technologies 2022



24

Hannah Burke, 14 de abril de 2022

Evaluating the effect and mechanism of upper limb motor function recovery induced by immersive virtual-reality-based rehabilitation for subacute stroke subjects: study protocol for a randomized controlled trial

Qianqian Huang^{1†}, Wei Wu^{1†}, Xiaolong Chen¹, Bo Wu^{1,2}, Longqiang Wu¹, Xiaoli Huang¹, Songhe Jiang^{1,3*} and Lejian Huang^{2,4*} 

Top 10 new medical technologies 2022

Artificial intelligence & robotics

26

Hannah Burke, 14 de abril de 2022

5

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Article | [Open Access](#) | [Published: 27 December 2022](#)

Multimodal and multidomain lesion network mapping enhances prediction of sensorimotor behavior in stroke patients

[Antonio Jimenez-Marin](#), [Nele De Bruyn](#), [Jolien Gooijers](#), [Alberto Llera](#), [Sarah Meyer](#), [Kaat Alaerts](#), [Geert Verheyden](#), [Stephan P. Swinnen](#) & [Jesus M. Cortes](#) 

[Scientific Reports](#) **12**, Article number: 22400 (2022) | [Cite this article](#)



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Journal of Neuropsychology / Volume 17, Issue 2 / p. 302-318

RESEARCH ARTICLE | [Open Access](#) |

One-year prediction of cognitive decline following cognitive-stimulation from real-world data

Borja Camino-Pontes ▾, Francisco Gonzalez-Lopez ▾, Gonzalo Santamaría-Gomez ▾, Antonio Javier Sutil-Jimenez ▾, Carolina Sastre-Barrios ▾, Iñigo Fernandez de Pierola ▾, Jesus M. Cortes ▾ ... See fewer authors ^



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Biological Psychiatry

A Journal of Psychiatric Neuroscience and Therapeutics

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The Neurogenetics of Functional Connectivity Alterations in Autism: Insights From Subtyping in 657 Individuals

[Javier Rasero](#)  ¹  • [Antonio Jimenez-Marin](#) ¹ • [Ibai Diez](#) • [Roberto Toro](#) • [Mazahir T. Hasan](#) • [Jesus M. Cortes](#) • [Show footnotes](#)

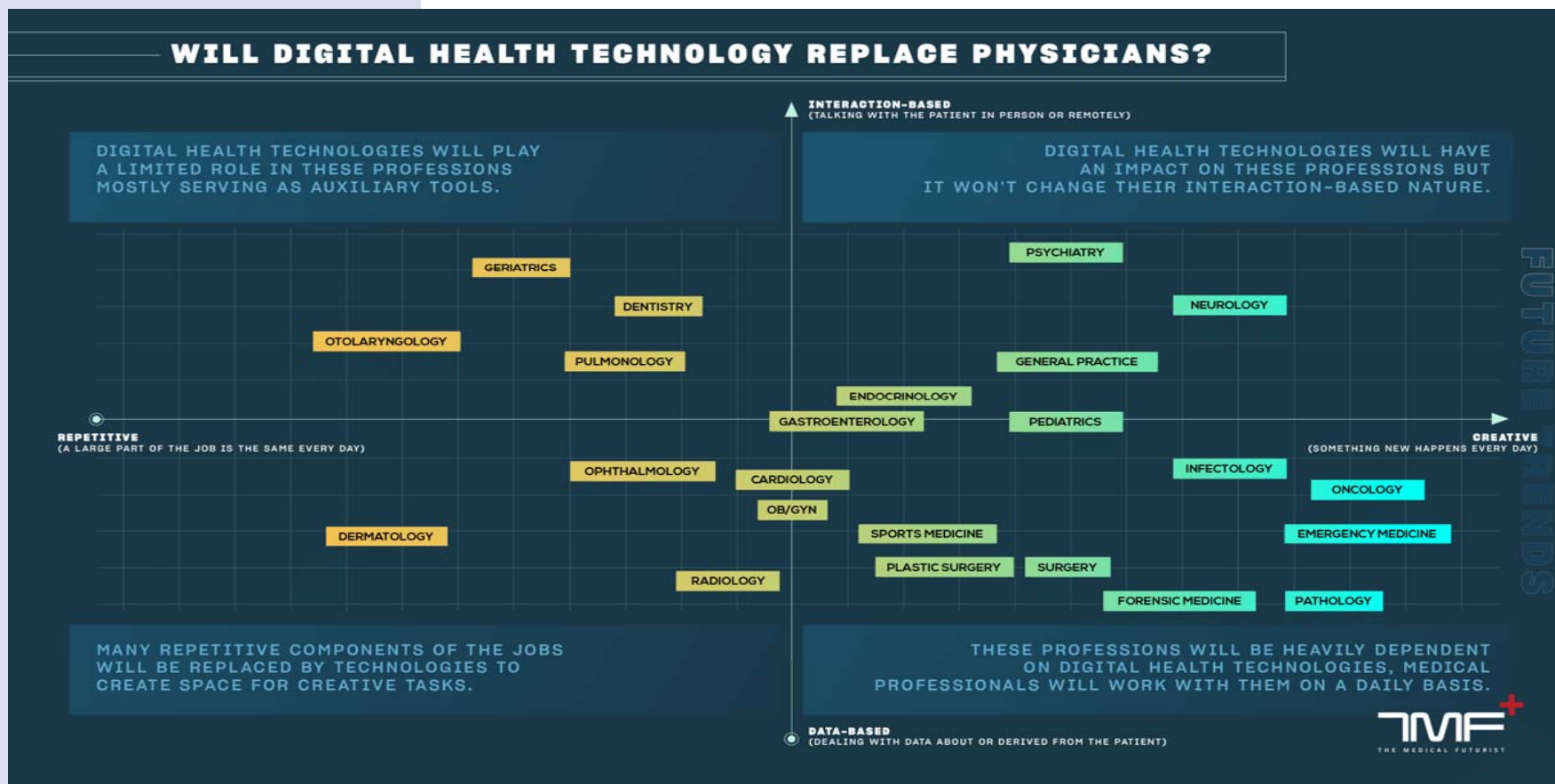
[Open Access](#) • Published: April 21, 2023 • DOI: <https://doi.org/10.1016/j.biopsych.2023.04.014>



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5

+ TECNOLOGÍA



30



bto


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GOBIERNO VASCO
OSASUN SAILA
DEPARTAMENTO DE SALUD

**ESKERRIK ASKO
MUCHAS GRACIAS
THANK YOU**