CONEXIONES INVISIBLES: Explorando la Diabetes y la Enfermedad de Alzheimer.

DIABETES TIPO 3

Lucía Sáez González
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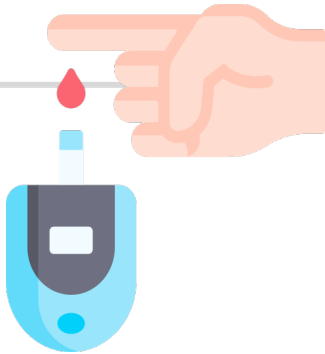
DIABETES



España

7.54%

90% DMT2

Año 2045: 1 de cada 8 adultos

783 millones de personas en el mundo

RESISTENCIA A INSULINA

DESTRUCCIÓN CÉLULAS ß

HIPERGLUCEMIA CRÓNICA

→ Polidipsia

→ Poliuria

→ Fatiga

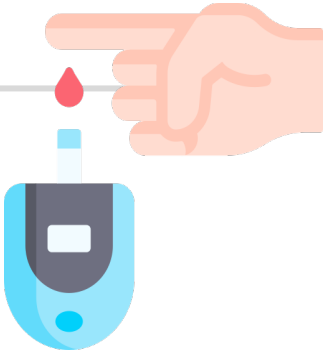
→ Hambre constante

→ Visión borrosa

→ Cetoacidosis diabética

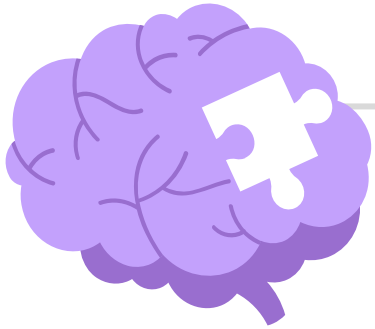
DIABETES

TIPO 2



- Asintomática
  - Desconocimiento del diagnóstico

  - Diagnóstico tardío → Complicaciones

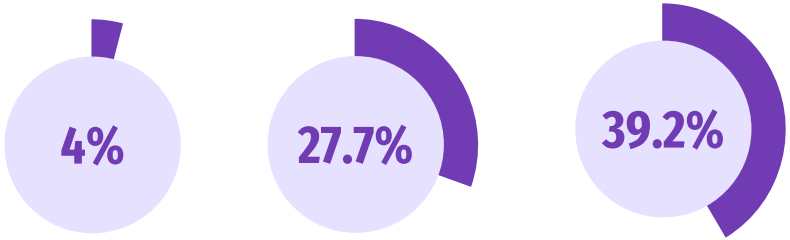


ALZHEIMER

60% casos de demencia

MÁS COMÚN EN MUJERES

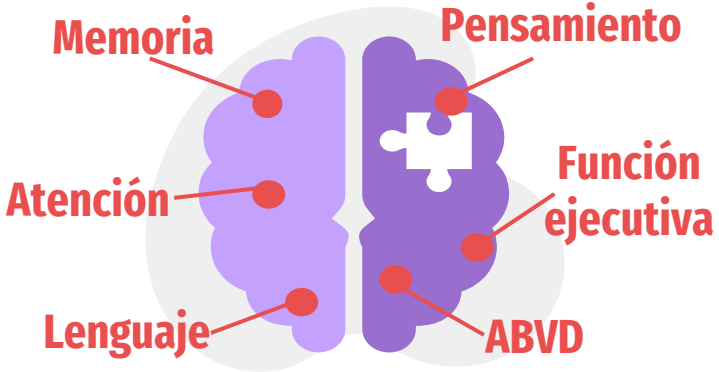
España



De 65—75 años | Mayores de 85 | Mayores de 90

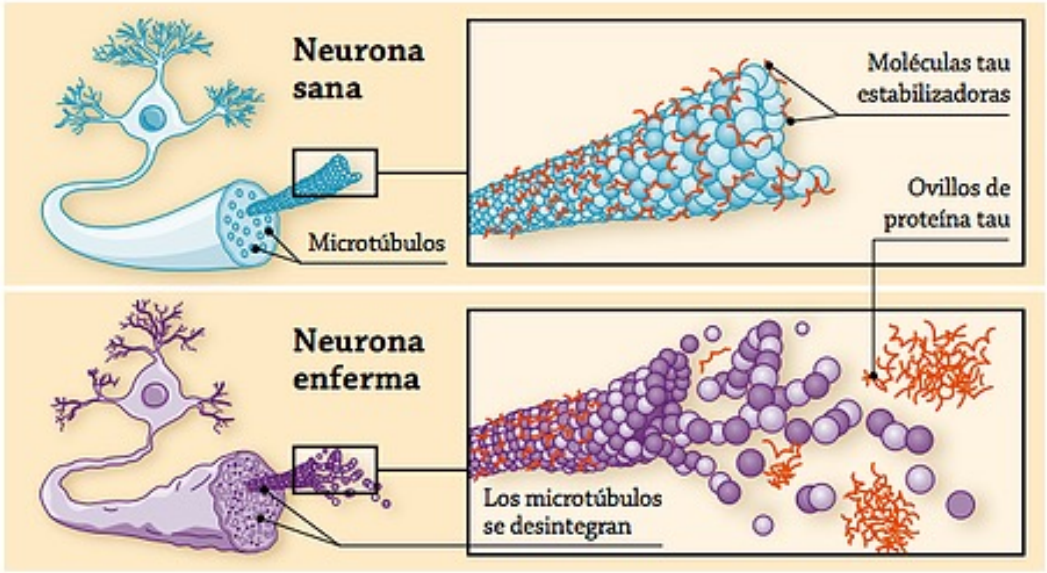
NEURODEGENERACIÓN

- Péptidos ß-amiloide → PLACAS SENILES
- Hiperfosforilación Proteínas Tau → OVILLOS NEUROFIBRILARES

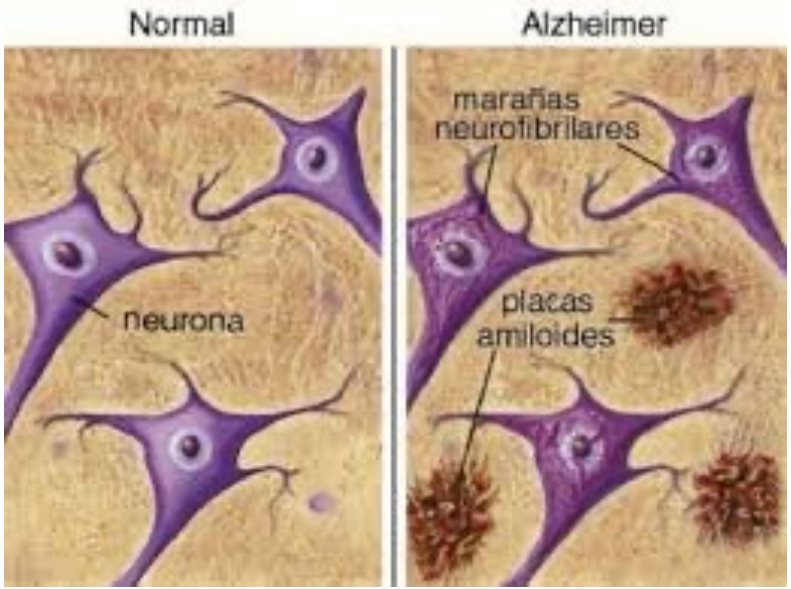


FISIOPATOLOGÍA DEL ALZHEIMER

OVILLOS NEUROFIBRILARES de proteína Tau



PLACAS SENILES de ß-Amiloide



DIABETES TIPO 3

¿NUEVA ENFERMEDAD?
Steen *et al.*, 2005

Journal of Alzheimer's Disease 7 (2005) 63–80
IOS Press

Impaired insulin and insulin-like growth factor expression and signaling mechanisms in Alzheimer's disease – is this type 3 diabetes?

Eric Steen, Benjamin M. Terry, Enrique J. Rivera, Jennifer L. Cannon, Thomas R. Neely, Rose Tavares, X. Julia Xu, Jack R. Wands and Suzanne M. de la Monte *
From the Departments of Pathology and Medicine, Rhode Island Hospital and Brown Medical School, Providence, RI, USA

Abstract. The neurodegeneration that occurs in sporadic Alzheimer's disease (AD) is consistently associated with a number of characteristic histopathological, molecular, and biochemical abnormalities, including cell loss, abundant neurofibrillary tangles and dystrophic neurites, amyloid-β deposits, increased activation of pro-death genes and signaling pathways, impaired energy metabolism/mitochondrial function, and evidence of chronic oxidative stress. The general inability to convincingly link these phenomena has resulted in the emergence and propagation of various heavily debated theories that focus on the role of one particular element in the pathogenesis of all other abnormalities. However, the accumulating evidence that reduced glucose utilization and deficient energy metabolism occur early in the course of disease, suggests a role for impaired insulin signaling in the pathogenesis of AD. The present work demonstrates extensive abnormalities in insulin and insulin-like growth factorm typer I and II (IGF-I and IGF-II) signaling mechanisms in brains with AD, and shows that while each of the corresponding growth factors is normally made in central nervous system (CNS) neurons, the expression levels are markedly reduced in AD. These abnormalities were associated with reduced levels of insulin receptor substrate (IRS) mRNA, *tau* mRNA, IRS-associated phosphotidylinositol 3-kinase, and phospho-Akt (activated), and increased glycogen synthase kinase-3β activity and amyloid precursor protein mRNA expression. The strikingly reduced CNS expression of genes encoding insulin, IGF-I, and IGF-II, as well as the insulin and IGF-I receptors, suggests that AD may represent a neuro-endocrine disorder that resembles, yet is distinct from diabetes mellitus. Therefore, we propose the term, "Type 3 Diabetes" to reflect this newly identified pathogenic mechanism of neurodegeneration.

Keywords: Diabetes, insulin signaling, insulin gene expression, central nervous system, Alzheimer's disease, glycogen synthase kinase, growth factor receptors, real time RT-PCR

DIABETES TIPO 3

¿NUEVA ENFERMEDAD?

Steen *et al.*, 2005

Anormalidades en los mecanismos de señalización de la insulina y los IGF en los cerebros con EA

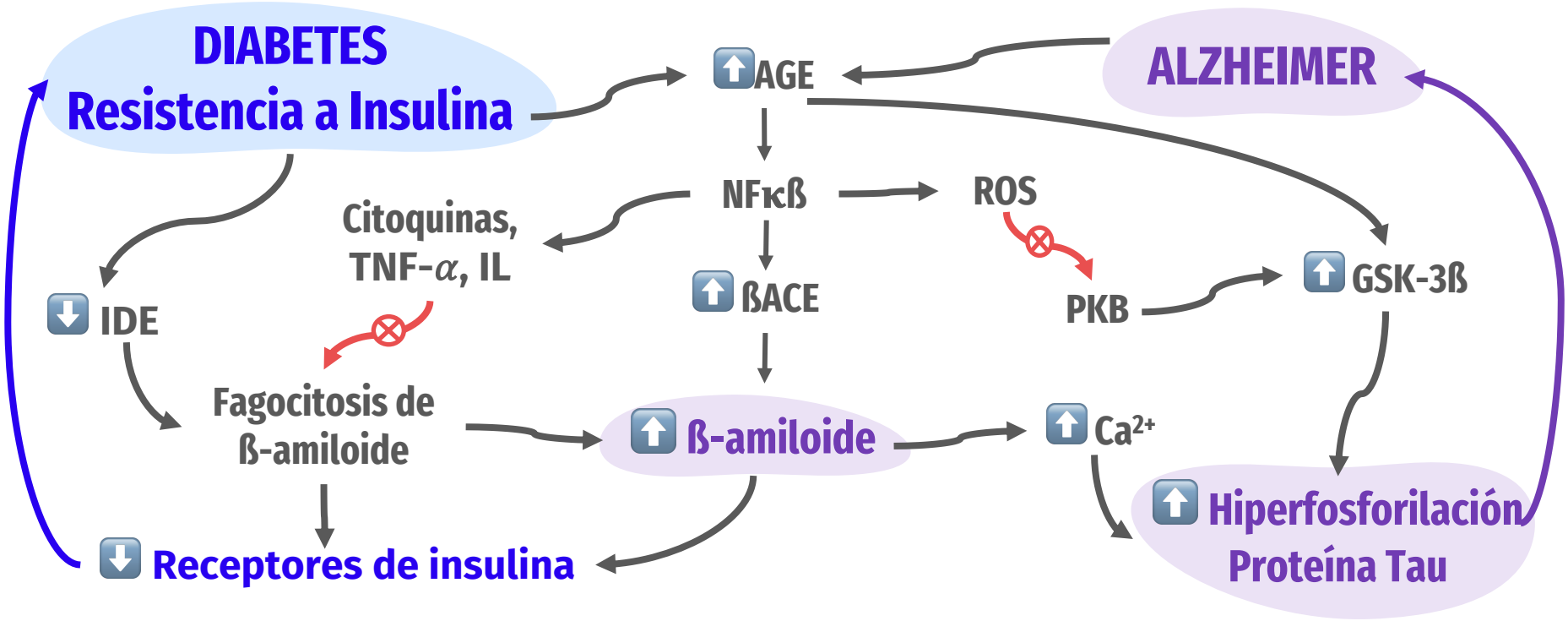
Abstract. The neurodegeneration that occurs in sporadic Alzheimer's disease (AD) is consistently associated with a number of characteristic histopathological, molecular, and biochemical abnormalities, including cell loss, abundant neurofibrillary tangles and dystrophic neurites, amyloid-β deposits, increased activation of pro-death genes and signaling pathways, impaired energy metabolism/mitochondrial function, and evidence of chronic oxidative stress. The general inability to convincingly link these phenomena has resulted in the emergence and propagation of various heavily debated theories that focus on the role of one particular element in the pathogenesis of all other abnormalities. However, the accumulating evidence that reduced glucose utilization and deficient energy metabolism occur early in the course of disease, suggests a role for impaired insulin signaling in the pathogenesis of AD. The present work demonstrates extensive abnormalities in insulin and insulin-like growth factorm typer I and II (IGF-I and IGF-II) signaling mechanisms in brains with AD, and shows that while each of the corresponding growth factors is normally made in central nervous system (CNS) neurons, the expression levels are markedly reduced in AD. These abnormalities were associated with reduced levels of insulin receptor substrate (IRS) mRNA, *tau* mRNA, IRS-associated phosphotidylinositol 3-kinase, and phospho-Akt (activated), and increased glycogen synthase kinase-3β activity and amyloid precursor protein mRNA expression. The strikingly reduced CNS expression of genes encoding insulin, IGF-I, and IGF-II, as well as the insulin and IGF-I receptors, suggests that AD may represent a neuro-endocrine disorder that resembles, yet is distinct from diabetes mellitus. Therefore, we propose the term, "Type 3 Diabetes" to reflect this newly identified pathogenic mechanism of neurodegeneration.

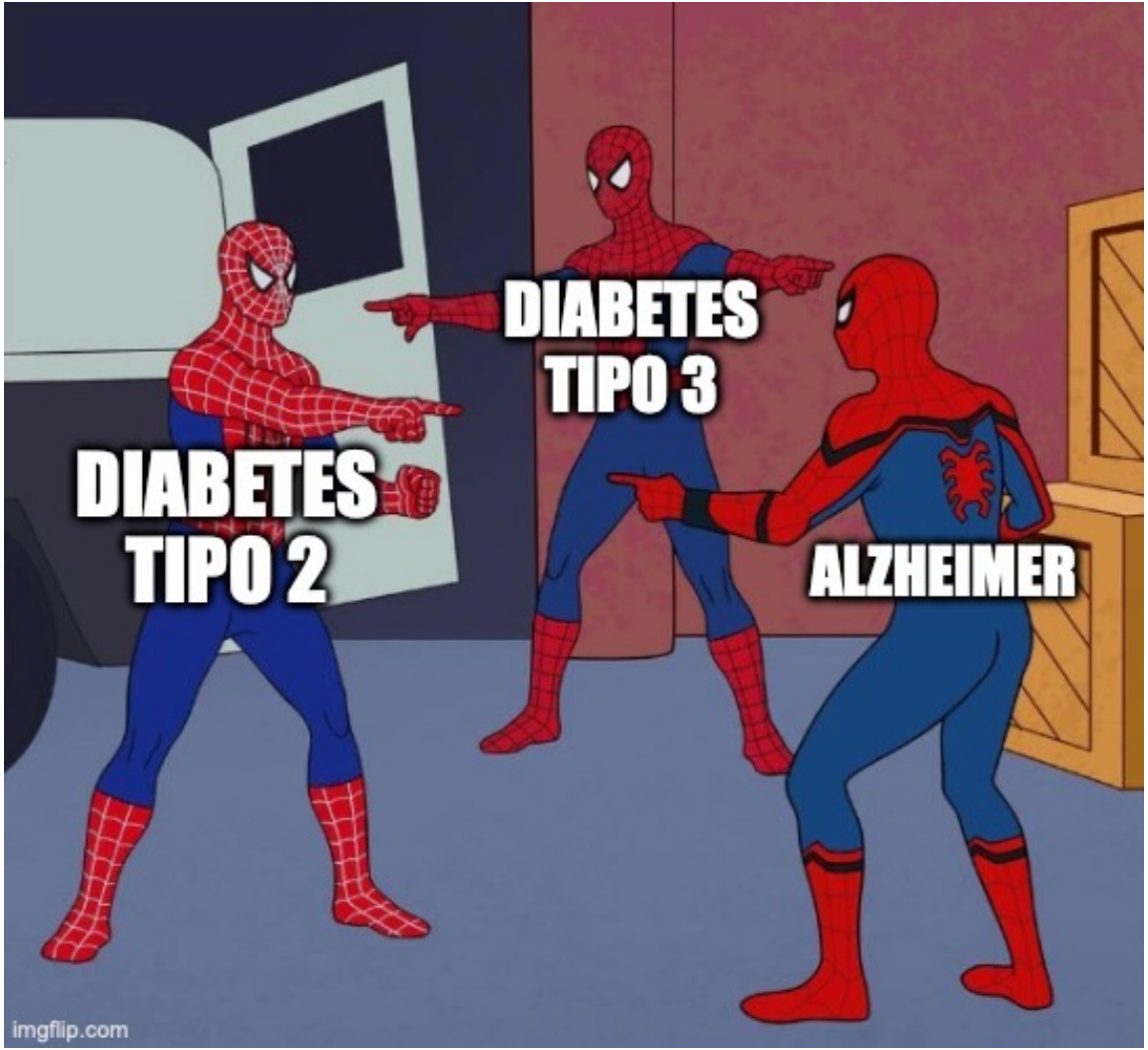
DIABETES TIPO 3

Mecanismos fisiopatológicos comunes entre DIABETES y ALZHEIMER

DIABETES TIPO 3

Mecanismos fisiopatológicos comunes




DIABETES
TIPO 2
DIABETES
TIPO 3
ALZHEIMER
imgflip.com

Alzheimer como enfermedad metabólica: DIABETES TIPO 3

CONEXIÓN DM2 + EA = DIABETES TIPO 3

Genética
Edad/Sexo

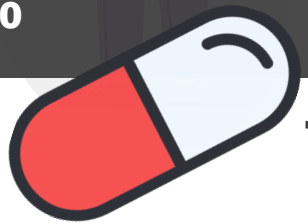
Ejercicio físico
Alimentación

DIABETES

Pérdida de memoria
Razonamiento impedido
Dificultades en el aprendizaje
Desorientación

ALZHEIMER

- Disfunción endotelial
- Isquemias
- Neuroinflamación
- Estrés oxidativo
- Déficit de insulina
- Resistencia a Insulina
- Agregados de ßA



PREVENCIÓN
(Dieta, Hábitos saludables...)

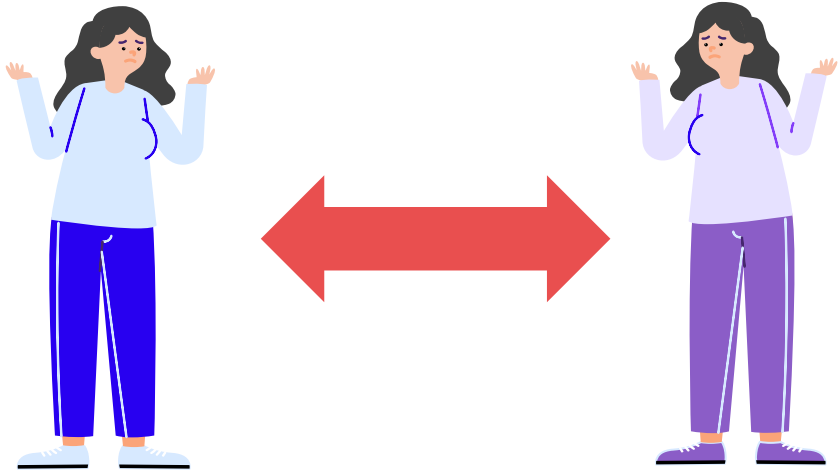
TRATAMIENTO
(Fármacos)

RELACIÓN DM2 + EA

NO EXISTE CRIBADO CRUZADO

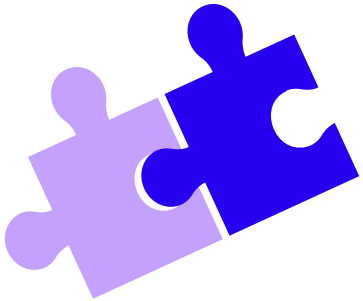
Diabéticos

CONTROL GLUCOSA
NO CONTROL DC



Alzheimer

CONTROL DC
NO CONTROL GLUCOSA



ESTUDIO DiAlz

RELACIÓN DM2 + EA

ESTUDIO DiAlz

Mayores de 65 años

20% Diabetes

4-11% Alzheimer

ESTUDIO OBSERVACIONAL

1ª fase: transversal

2ª fase: prospectivo

1ª fase	2ª fase
Primera entrevista	Segunda entrevista
PREVALENCIA DIABETES TIPO 3 Comparar grupos	Comparar grupos y observar diferencias

GRUPOS DE ESTUDIO

1. CONTROL **Sujetos sanos:** **- No Diabetes** **- No Deterioro cognitivo**	**2.** **- No Diabetes** **- Riesgo de Deterioro cognitivo**	**3.** **- No Diabetes** **- Enfermedad de Alzheimer**
4. **- Diabetes** **- No Deterioro cognitivo**	**5.** **Diabetes + Riesgo de deterioro cognitivo**	**6. DIABETES TIPO 3** **Diabetes + Alzheimer**

VARIABLES

Edad	Sexo	Estado Civil	Forma de convivencia familiar	Lugar de residencia (Rural/Urbano)	Relaciones sociales (OARS-MFAQ)
Nivel de estudios	Reserva Cognitiva (CRC)	COMORBILIDAD (Enfermedades crónicas)	Consumo de medicamentos (RUM)	Adherencia (Morisky-Green)	Independencia ABVD (Barthel)
Hábito tabáquico	Ingesta de Alcohol (ISCA)	Actividad Física (IPAQ)	Valoración dieta	Estado nutricional (MNA)	Grado de Hidratación (Osm. Orina)
Parámetros BQ (Analíticas)	Antropometría (IMC, %grasa, contornos...)	ESTADO COGNITIVO (Test)	DIABETES (Diagnóstico, fecha)	Glucemia basal (Cribado oportunista)	Control de glucemia (HbA1c)

RESULTADOS ESPERADOS Y CONCLUSIONES

1. Resistencia a la Insulina  Riesgo de DC y EA

Diabéticos 60% más riesgo de demencia

2. Conocer el efecto protector o de riesgo de las variables analizadas → Medidas higiénico-dietéticas

"Mens sana in corpore sano"

3. Antidiabéticos protectores contra el Alzheimer

MUCHAS GRACIAS
POR SU ATENCIÓN

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