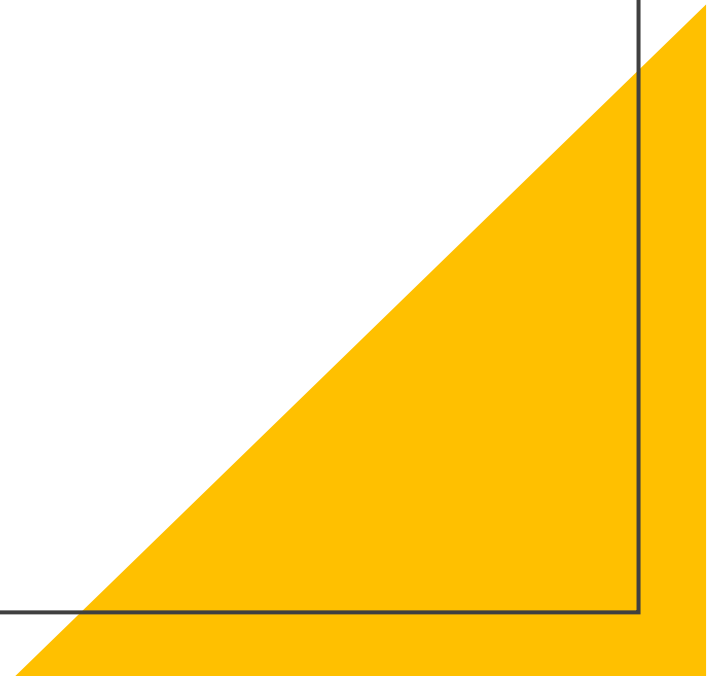




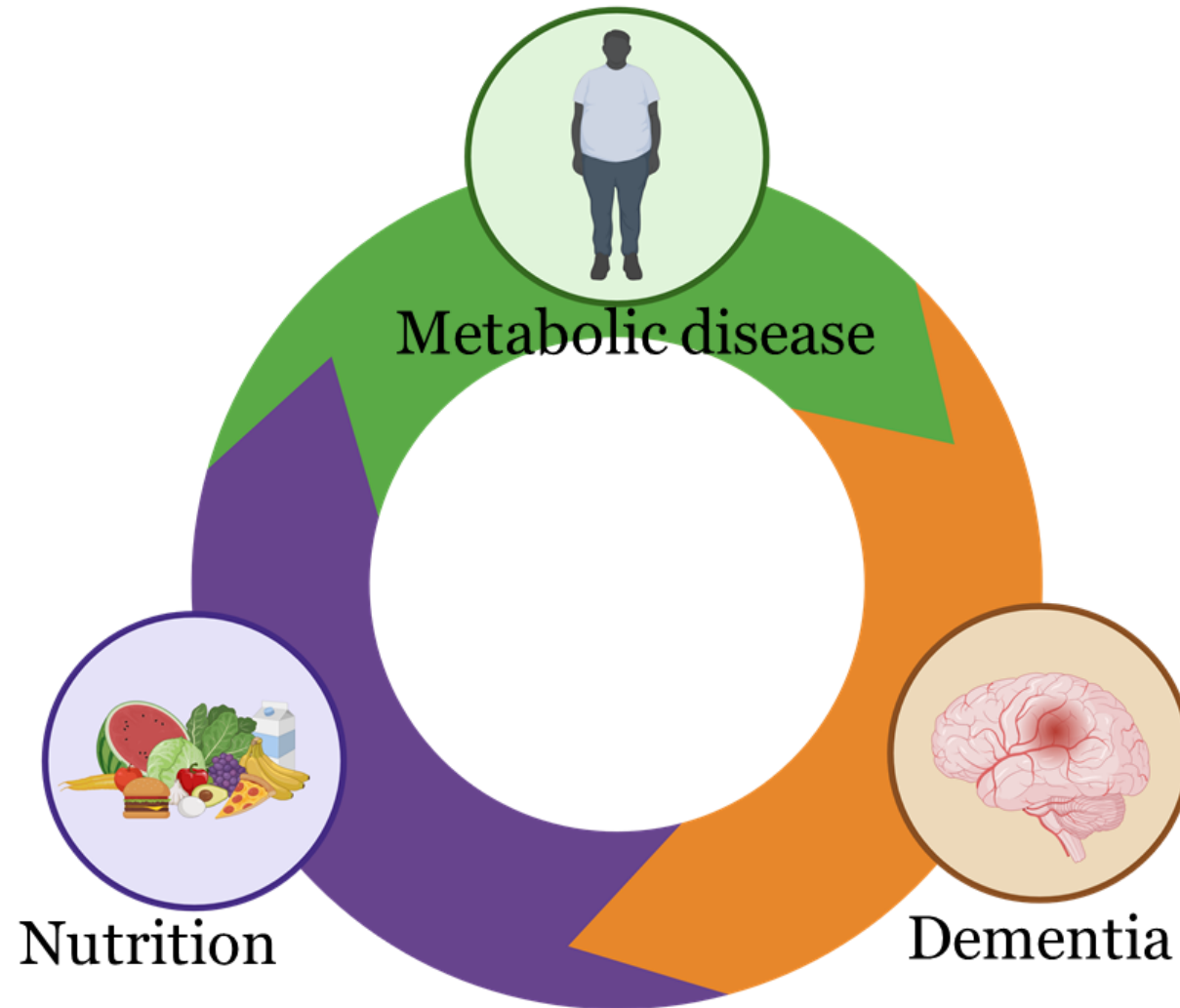
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Nutrizione , Sindromi Metaboliche e Demenza

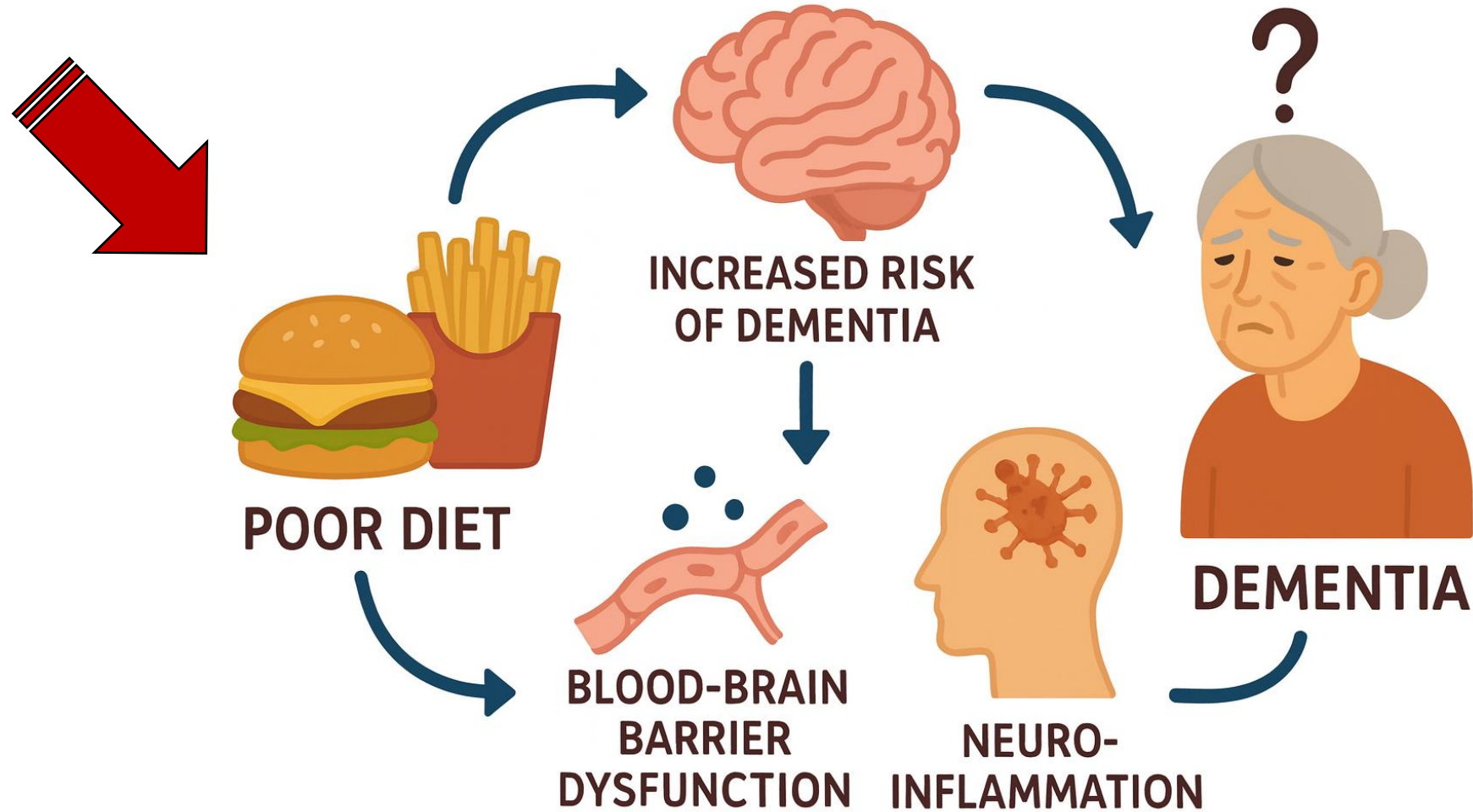
Prof Giuseppe Paolisso
Università Vanvitelli – Napoli



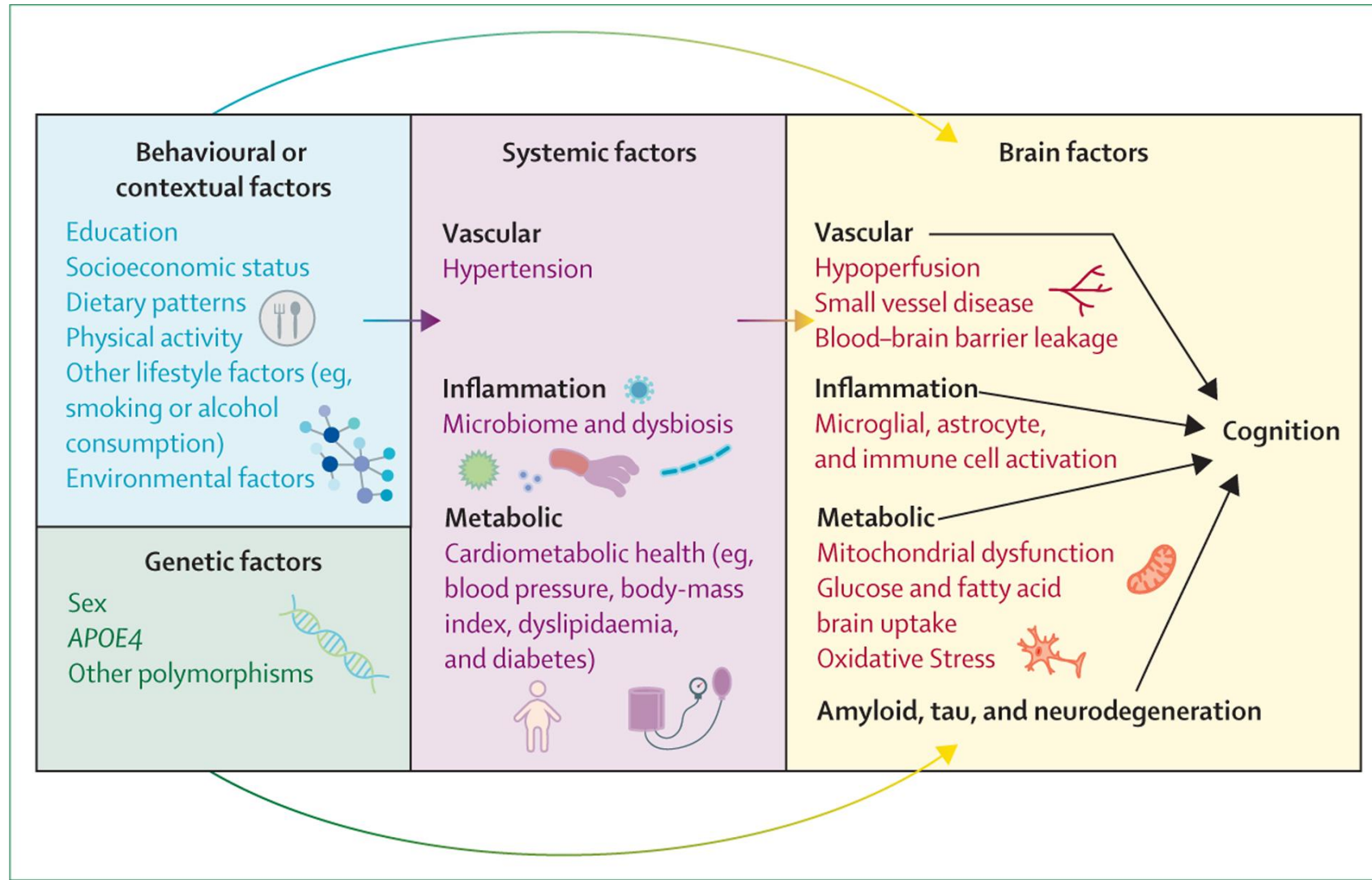
The interplay between metabolic diseases, nutrition and dementia



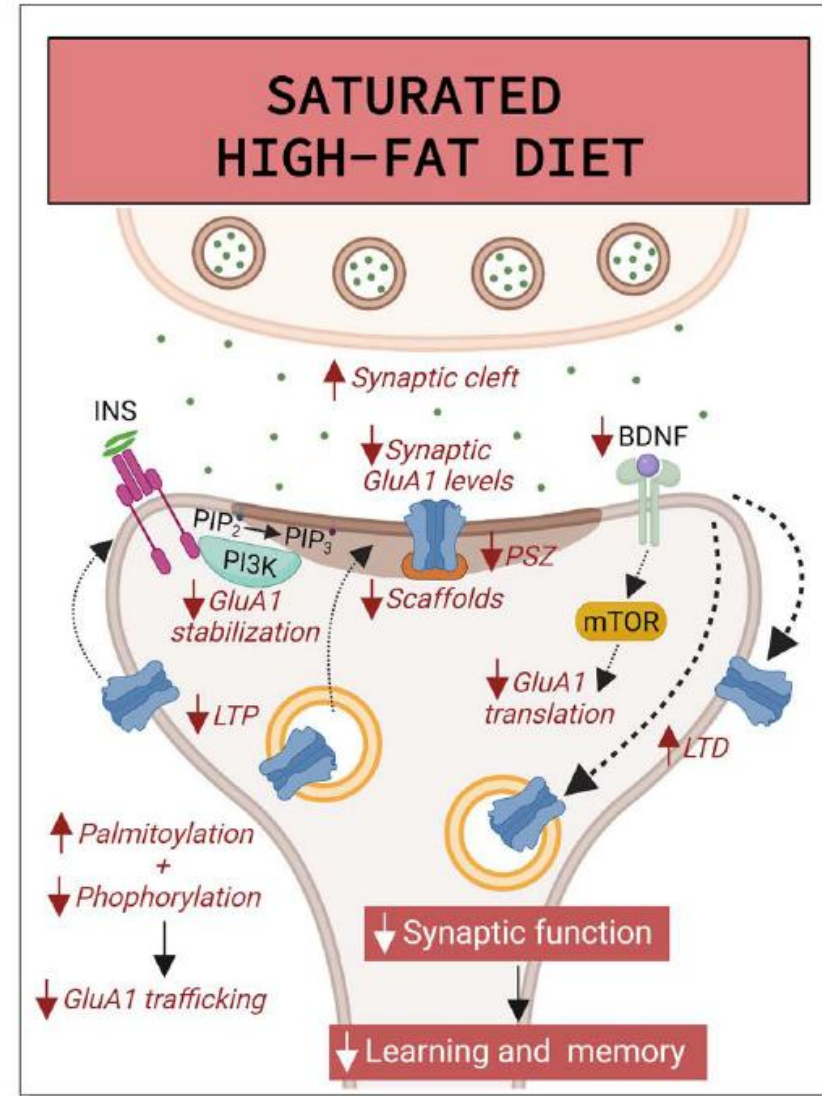
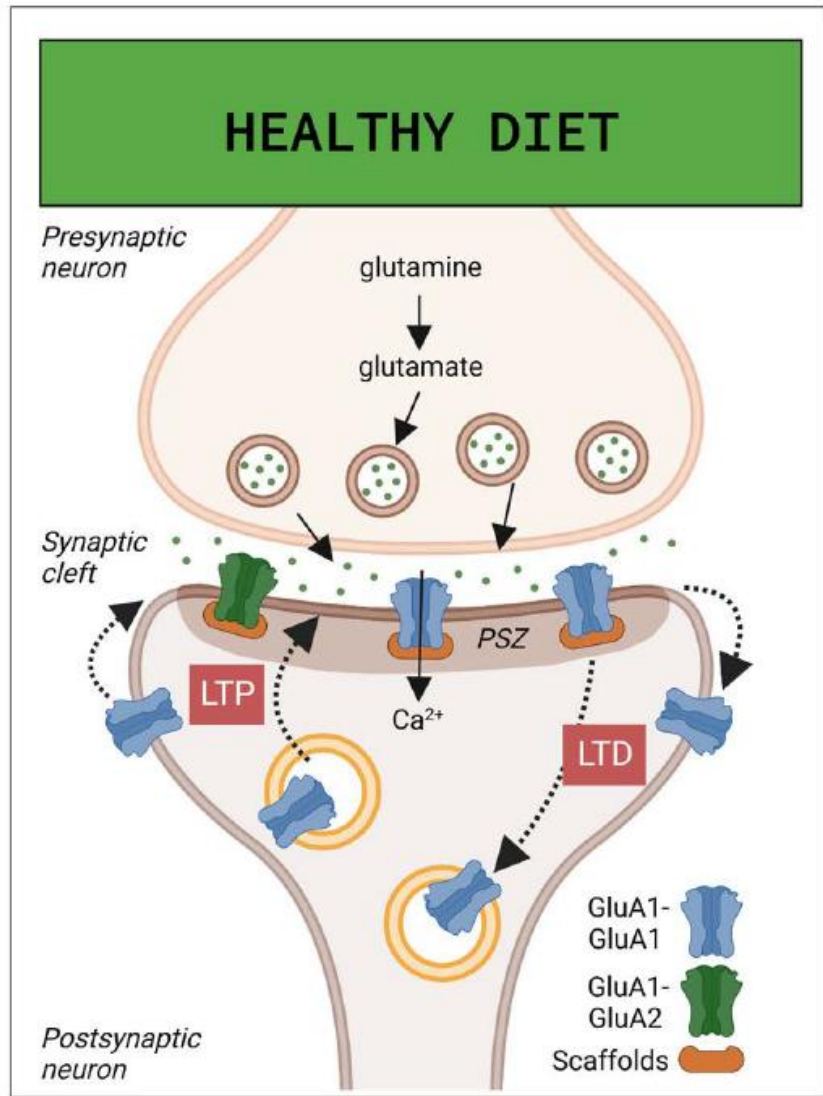
How Does Low-Quality Diet Contribute to Neurodegeneration and Dementia?



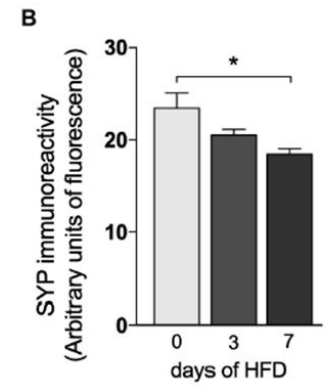
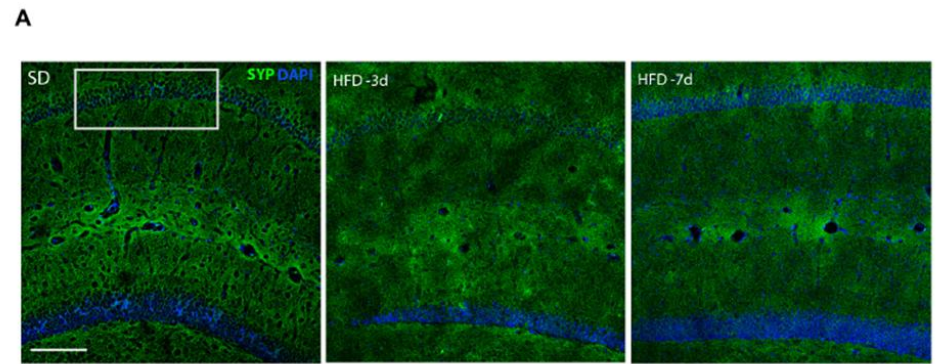
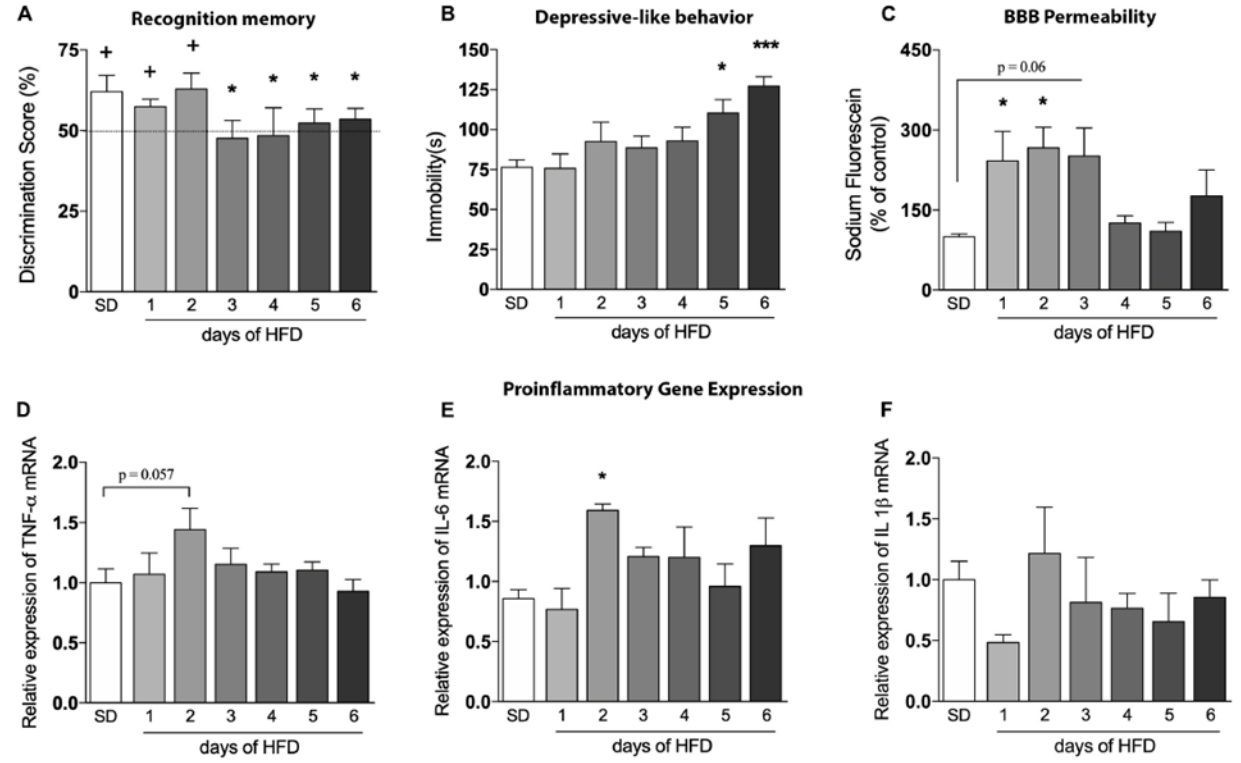
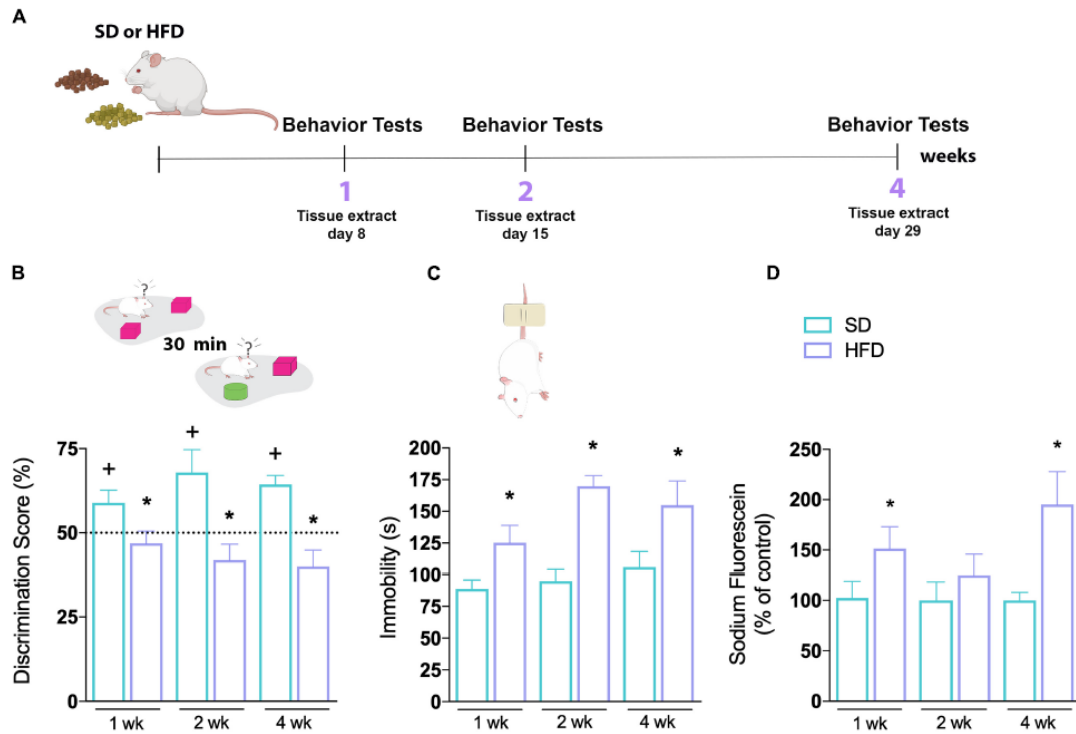
Biological pathways mediating the relationship of the diet with cognition



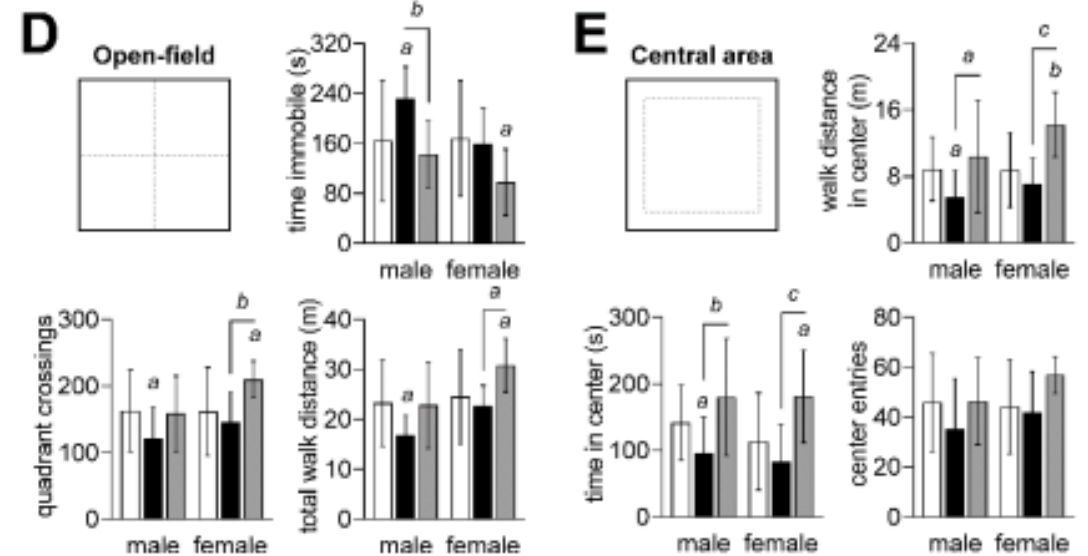
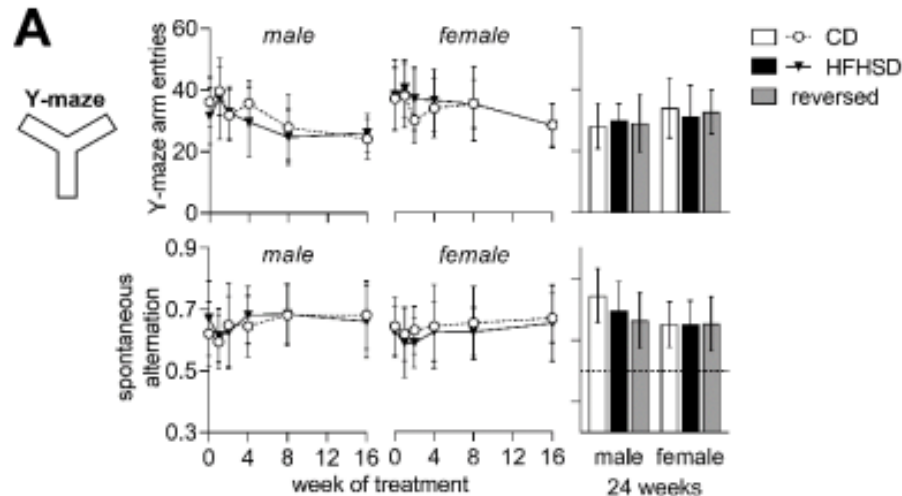
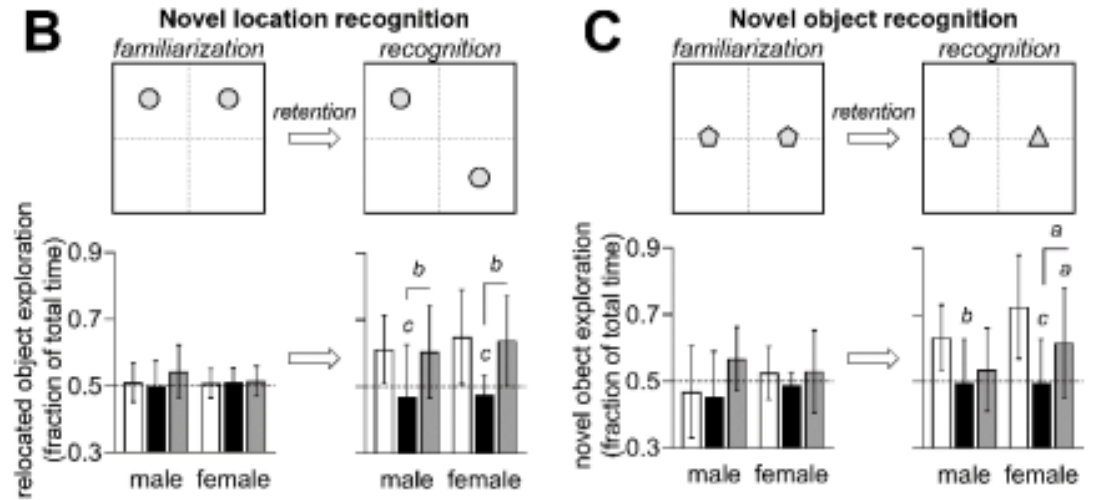
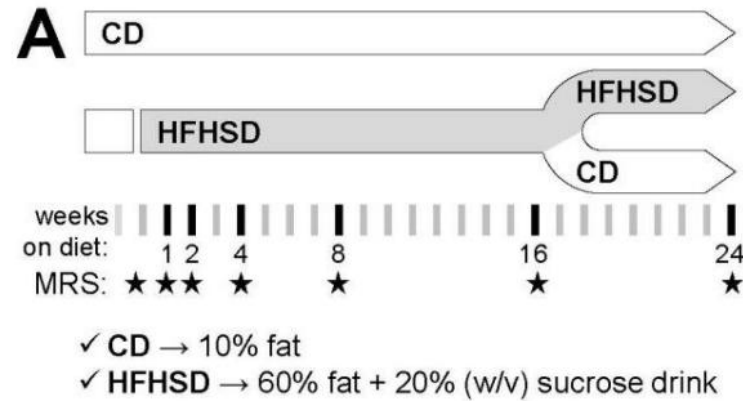
Why a high-fat diet can harm your memory?



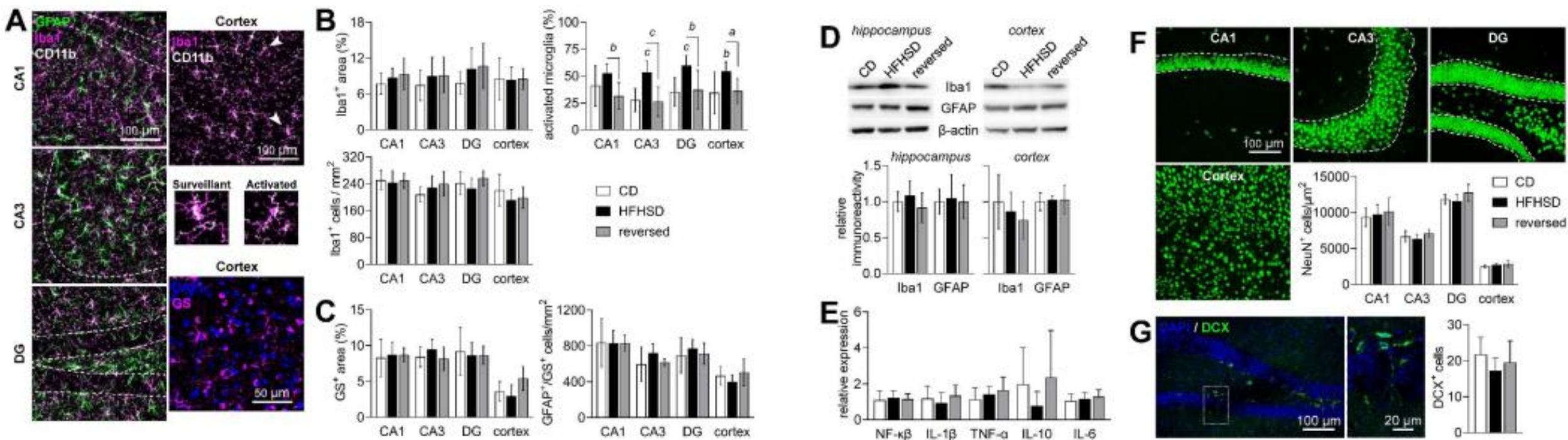
Hippocampal dysfunction in high-fat-diet mice



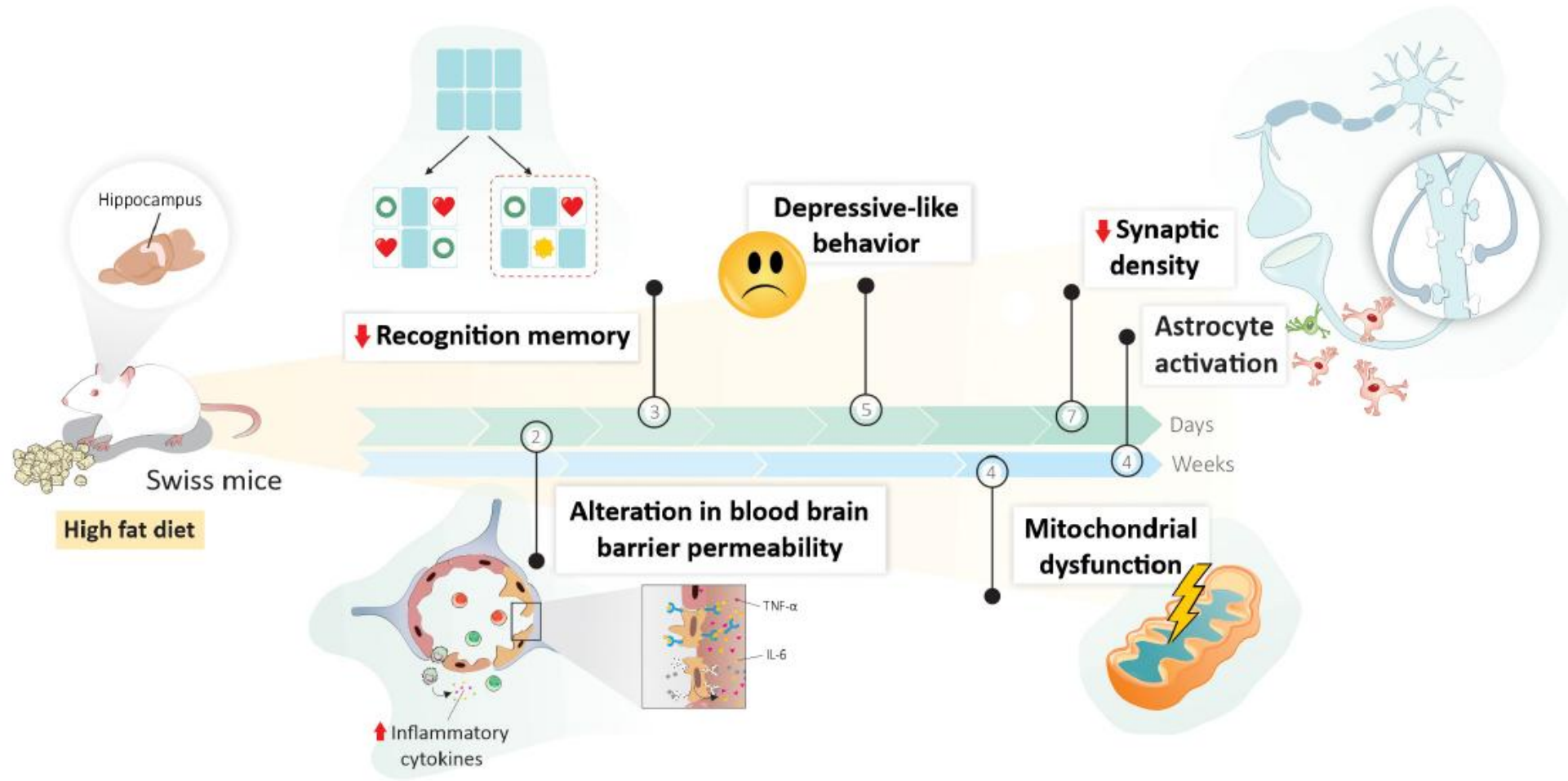
Memory impairment induced by HFHSD(high-fat and high-sucrose diet) exposure



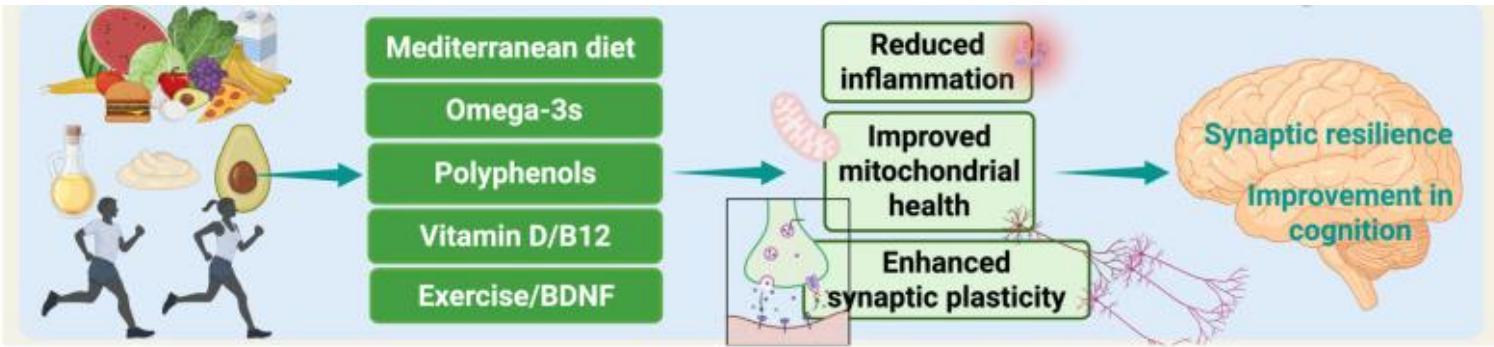
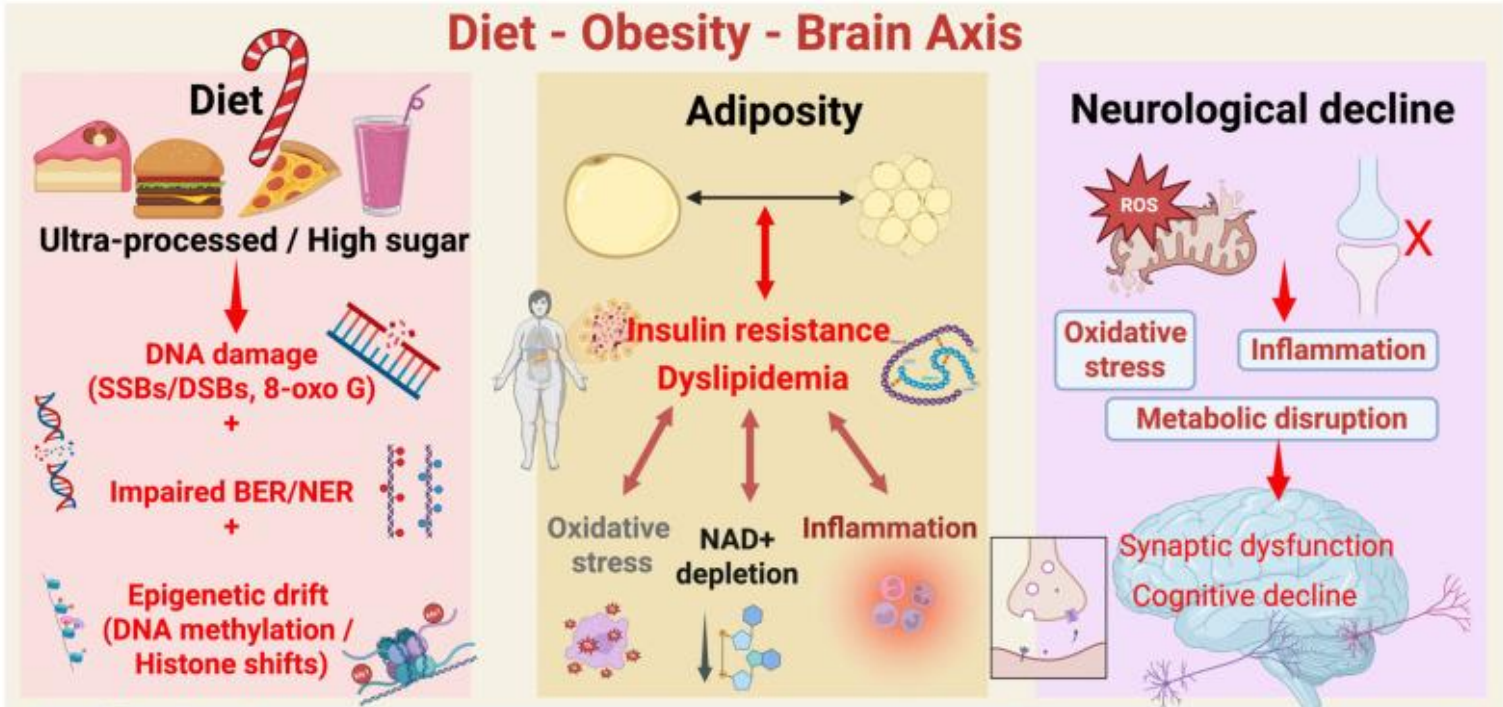
Neuroinflammation and neurodegeneration analysis in the hippocampus and cortex



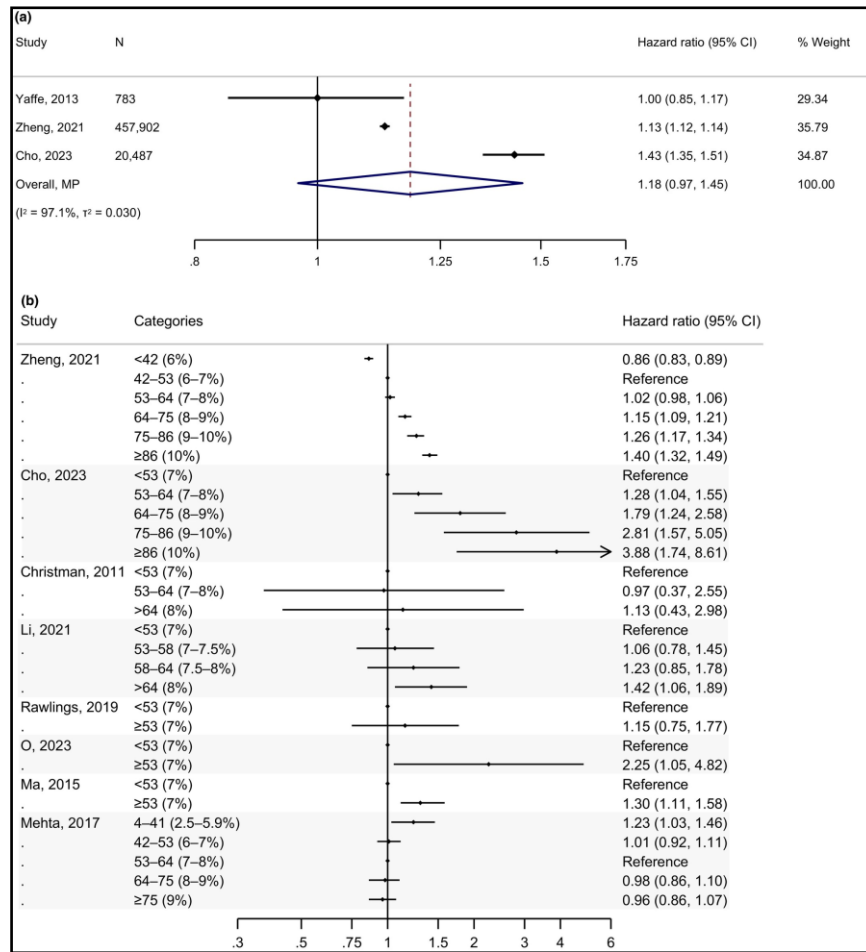
Short-term high-fat diet disrupts memory and brain integrity



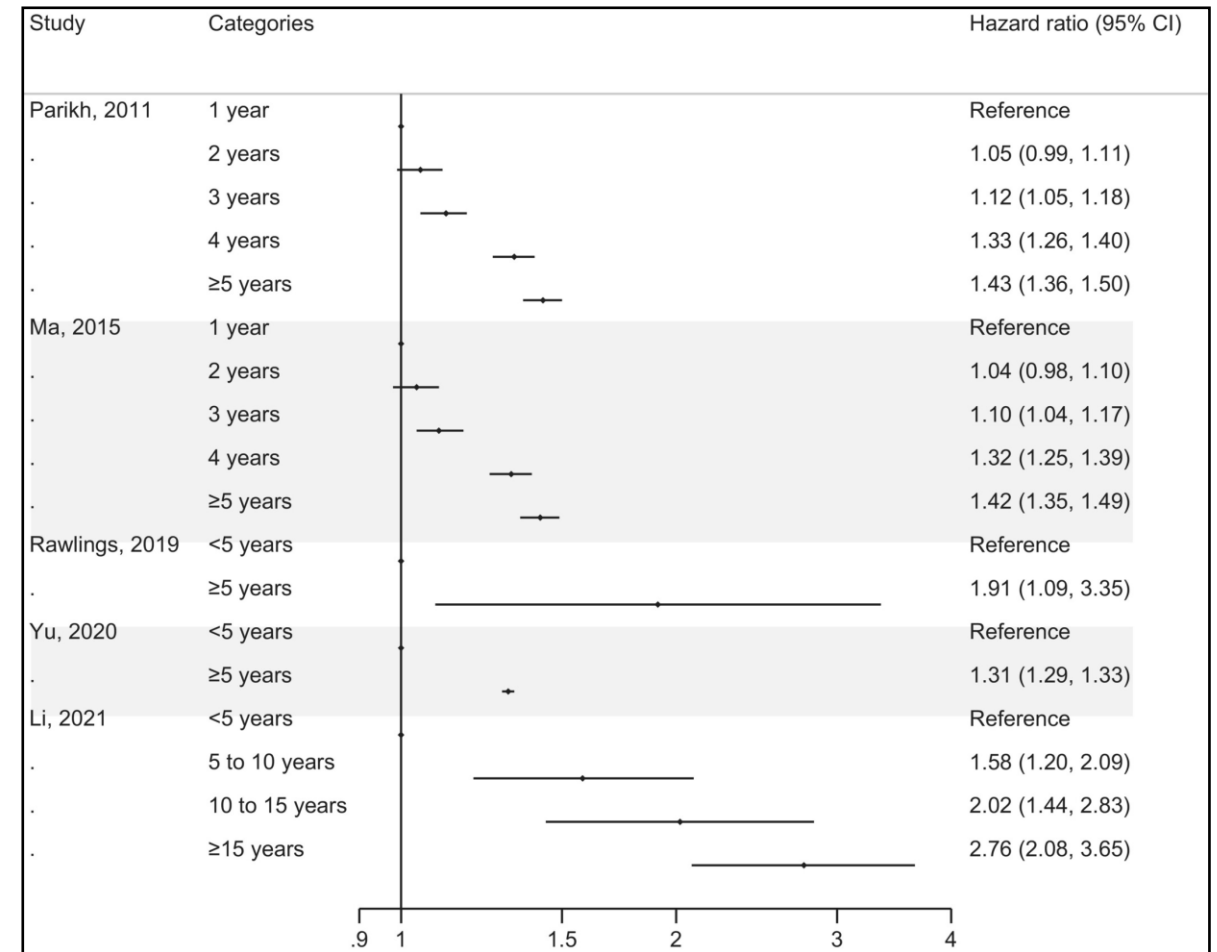
Diet quality modulates adiposity, systemic metabolism, and brain aging



Associations of glycaemia-related risk factors with dementia and cognitive decline in individuals with type 2 diabetes



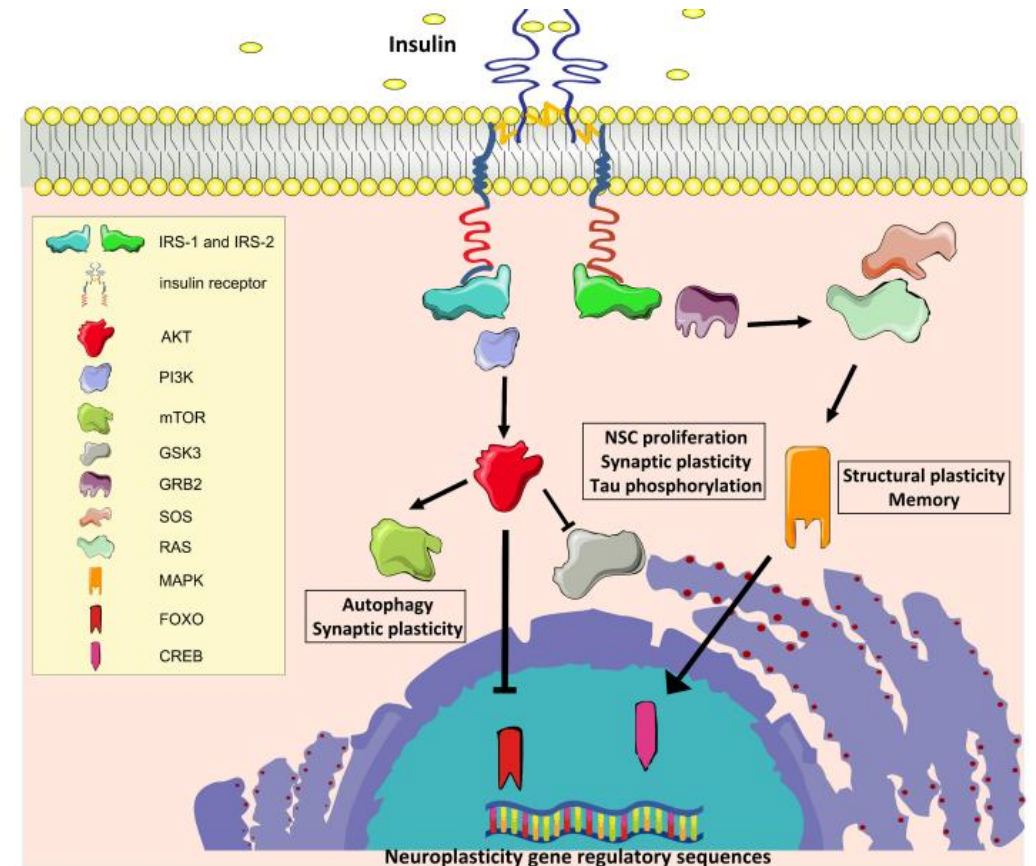
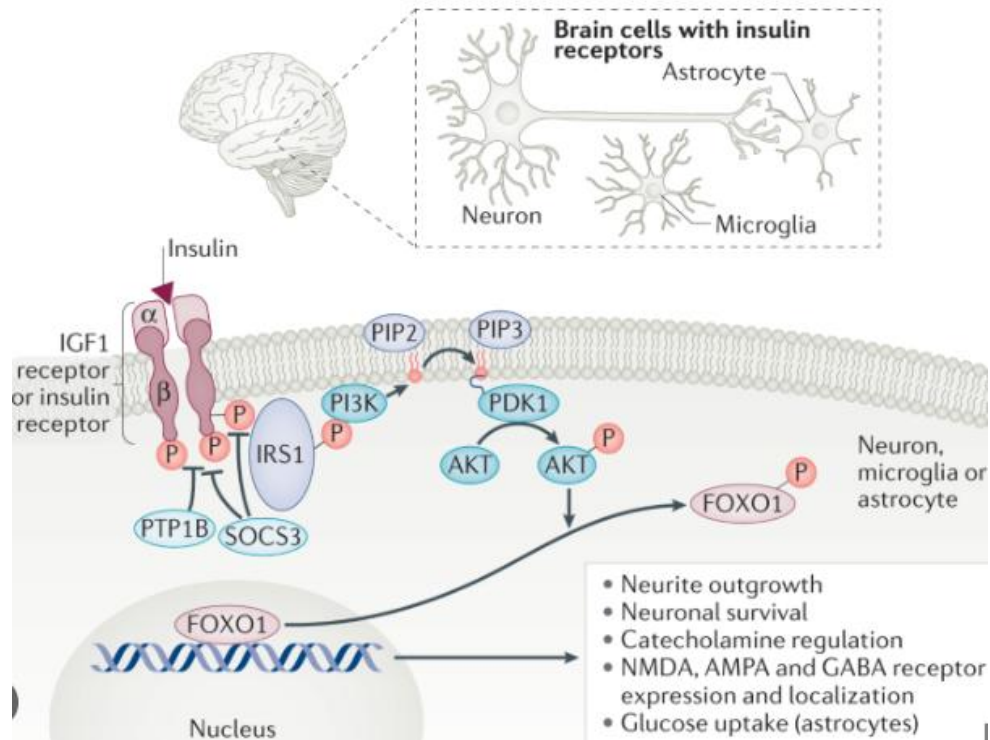
Association of HbA1c levels with incident dementia in people with type 2 diabetes. (a) Meta-analysis of studies assessing HbA1c as a continuous variable. (b) Summary of studies assessing HbA1c as a categorical variable.



Association of diabetes duration and incident dementia in people with type 2 diabetes.

Insulin Resistance in the Brain

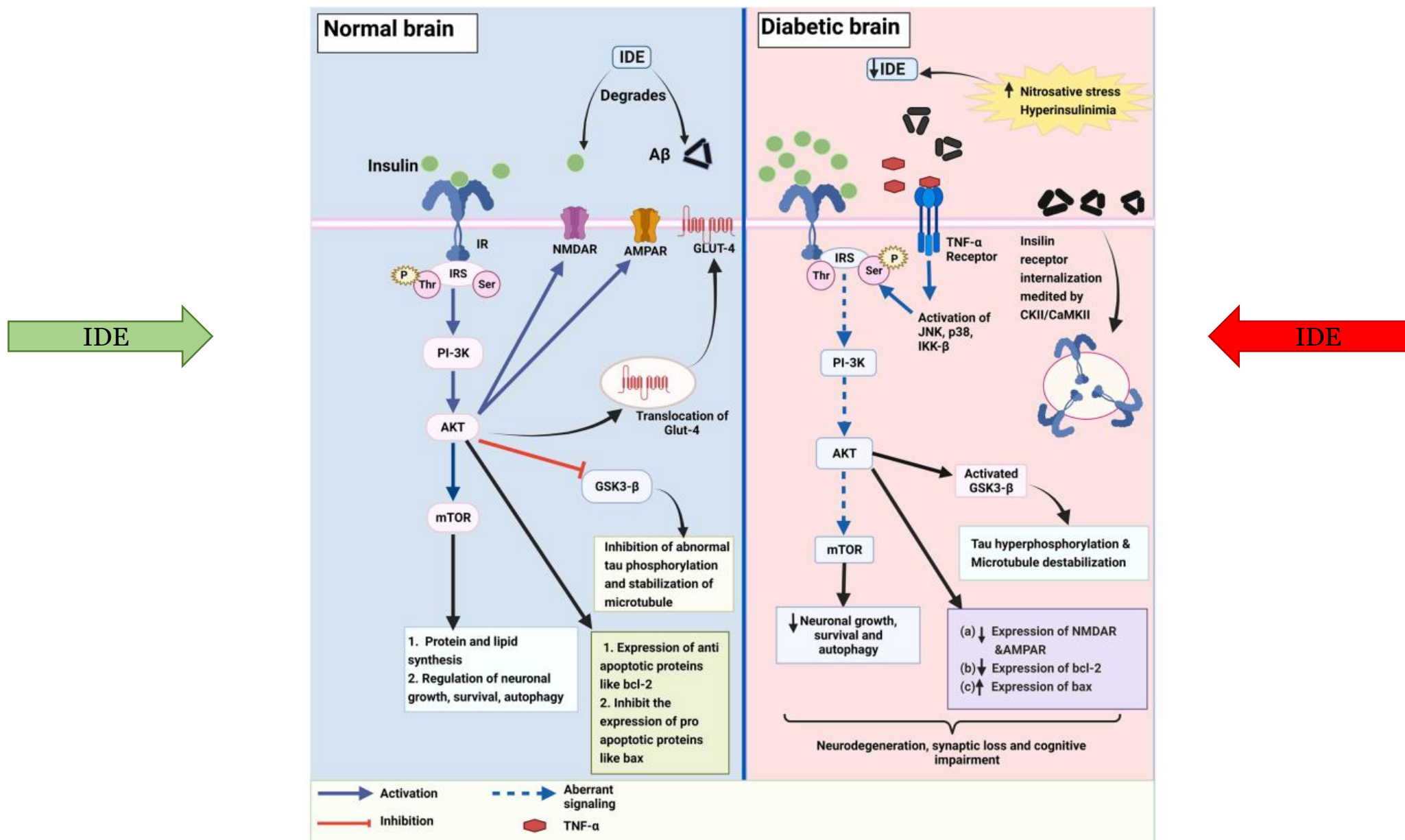
- Brain insulin resistance impairs synaptic function and learning.
- Linked to cognitive decline, Alzheimer's disease, and neuroinflammation.
- Affects hippocampus, cortex, and cerebrovascular function.



Mechanisms of action and pharmacological effects of anti-diabetic drugs exhibiting neuroprotection in preclinical studies

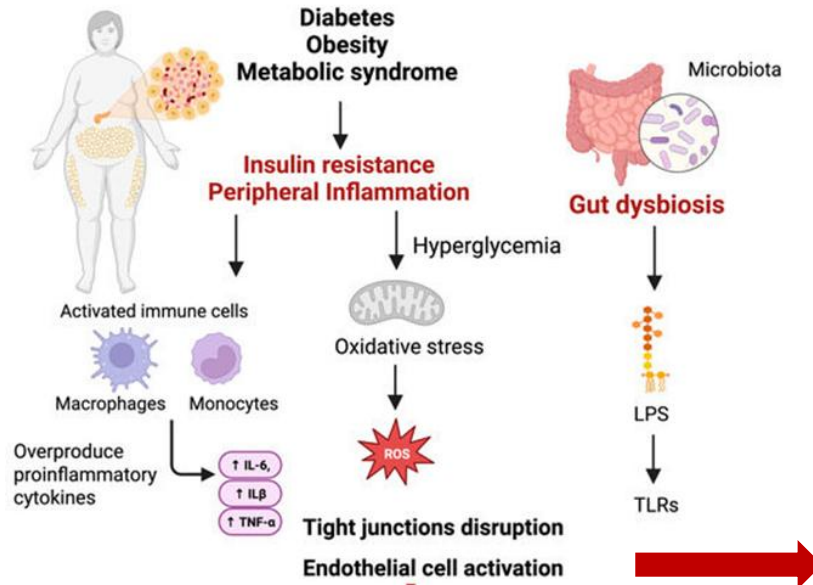
Classification	Drugs	Mechanisms of Action	Pharmacological Effects	References
Insulin	Intranasal insulin	<ul style="list-style-type: none"> - Decrease amyloidogenesis - Decrease neurofibrillary tangles formation - Decrease microglial overactivation 	<ul style="list-style-type: none"> - Reduced cognitive impairment 	[86,87,88,89,90,91,92]
Insulin Sensitizer	Metformin	<ul style="list-style-type: none"> - Decrease amyloidogenesis (contradictive) - Increase Aβ clearance - Decrease neurofibrillary tangles formation - Decrease microglial overactivation - Increase neuronal survival - Reduce mitochondria dysfunctions 	<ul style="list-style-type: none"> - Reduced cognitive impairment - Reduced Aβ plaques - Reduced neuroinflammation 	[94,95,96,97,98]
	Thiazolidinediones - Rosiglitazone - Pioglitazone	<ul style="list-style-type: none"> - Decrease amyloidogenesis - Increase Aβ clearance - Decrease neurofibrillary tangles formation - Preserve endothelial functions 	<ul style="list-style-type: none"> - Reduced cognitive impairment - Improved endothelial function 	[103,104,105,106,107]
Insulin secretagogues	Glucagon-like peptide-1 - Exendin-4 - Liraglutide	<ul style="list-style-type: none"> - Decrease amyloidogenesis - Increase Aβ clearance - Decrease neurofibrillary tangles formation - Preserve endothelial functions 	<ul style="list-style-type: none"> - Reduced cognitive impairment - Reduced neuronal loss - Reduced vascular damage 	[110,111,112,113,114]
	Sulfonylurea - Glibenclamide	<ul style="list-style-type: none"> - Decrease microglial overactivation 	<ul style="list-style-type: none"> - Reduced memory impairment - Reduced neuroinflammation - Reduced depression and anxiety-related symptoms 	[116,117,118]
Other anti-diabetics	Sodium-glucose cotransporter-2 - Dapagliflozin - Empagliflozin - Canagliflozin	<ul style="list-style-type: none"> - Increase neuronal survival - Increase autophagy 	<ul style="list-style-type: none"> - Reduced cognitive impairment 	[120,122]
	Amylin analogs - Pramlintide	<ul style="list-style-type: none"> - Increase Aβ clearance 	<ul style="list-style-type: none"> - Reduced cognitive impairment - Reduced Aβ plaques - Reduced neuroinflammation 	[125,126]

Neuronal insulin signaling in normal brain vs diabetic brain

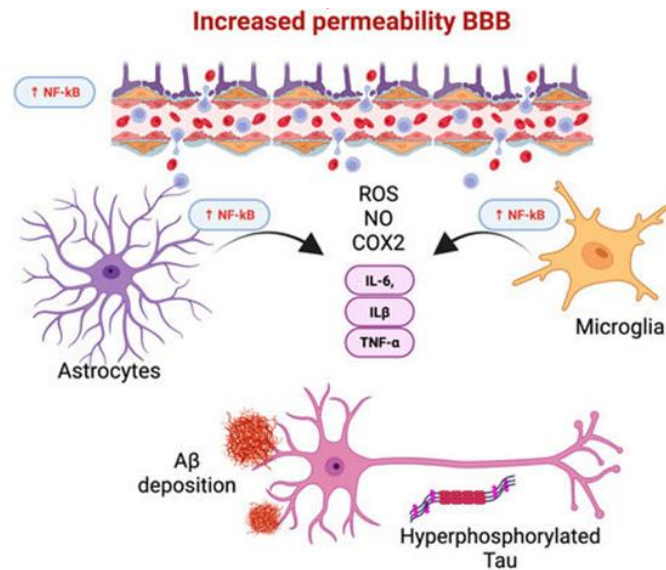


What is the link between metabolic syndrome and dementia?

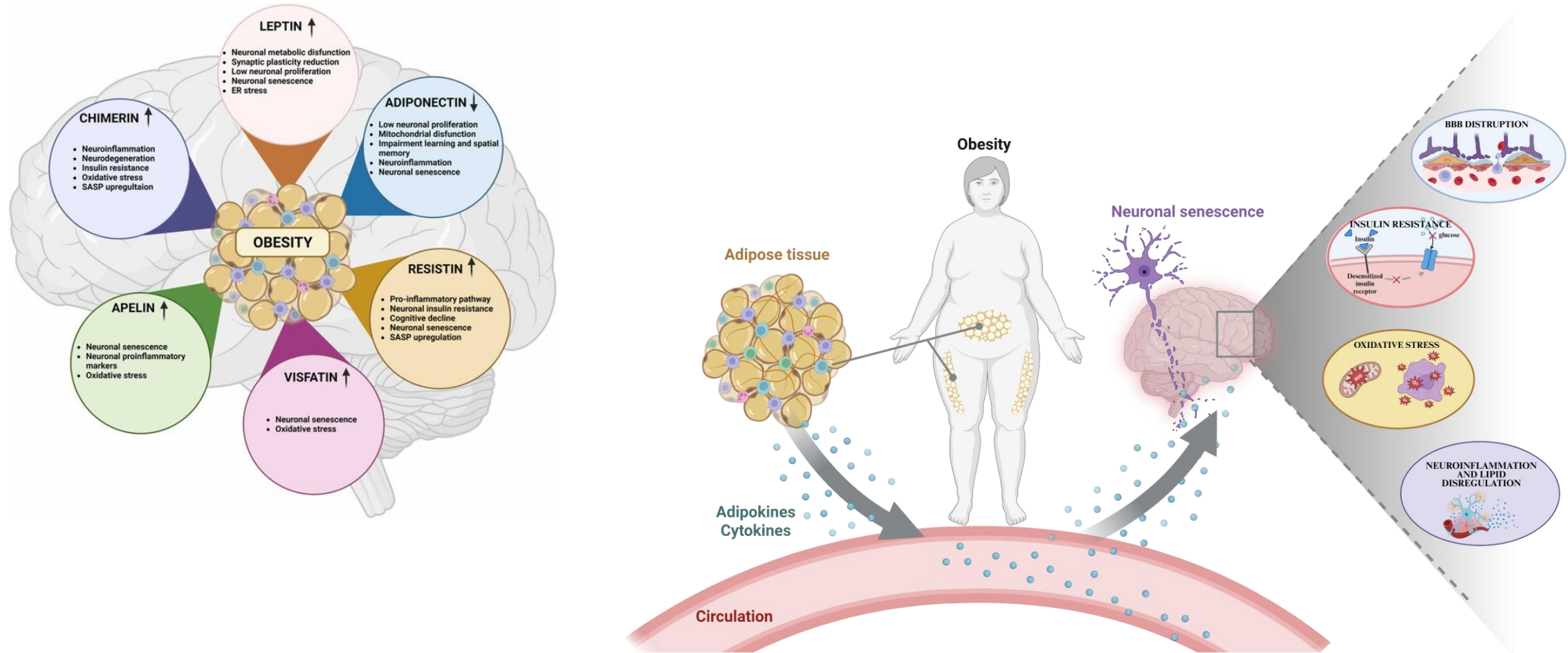
Molecular Mechanisms



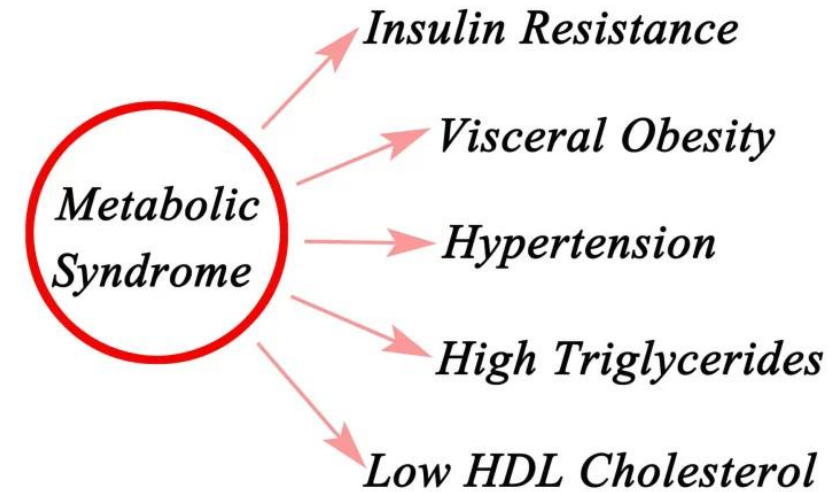
- ➔ • Insulin resistance affects amyloid- β and tau pathways
- ➔ • Chronic inflammation activates microglia and accelerates neurodegeneration
- ➔ • Oxidative stress and mitochondrial dysfunction damage neurons



Cytokines released by adipose tissue in obese patients induce neuronal senescence

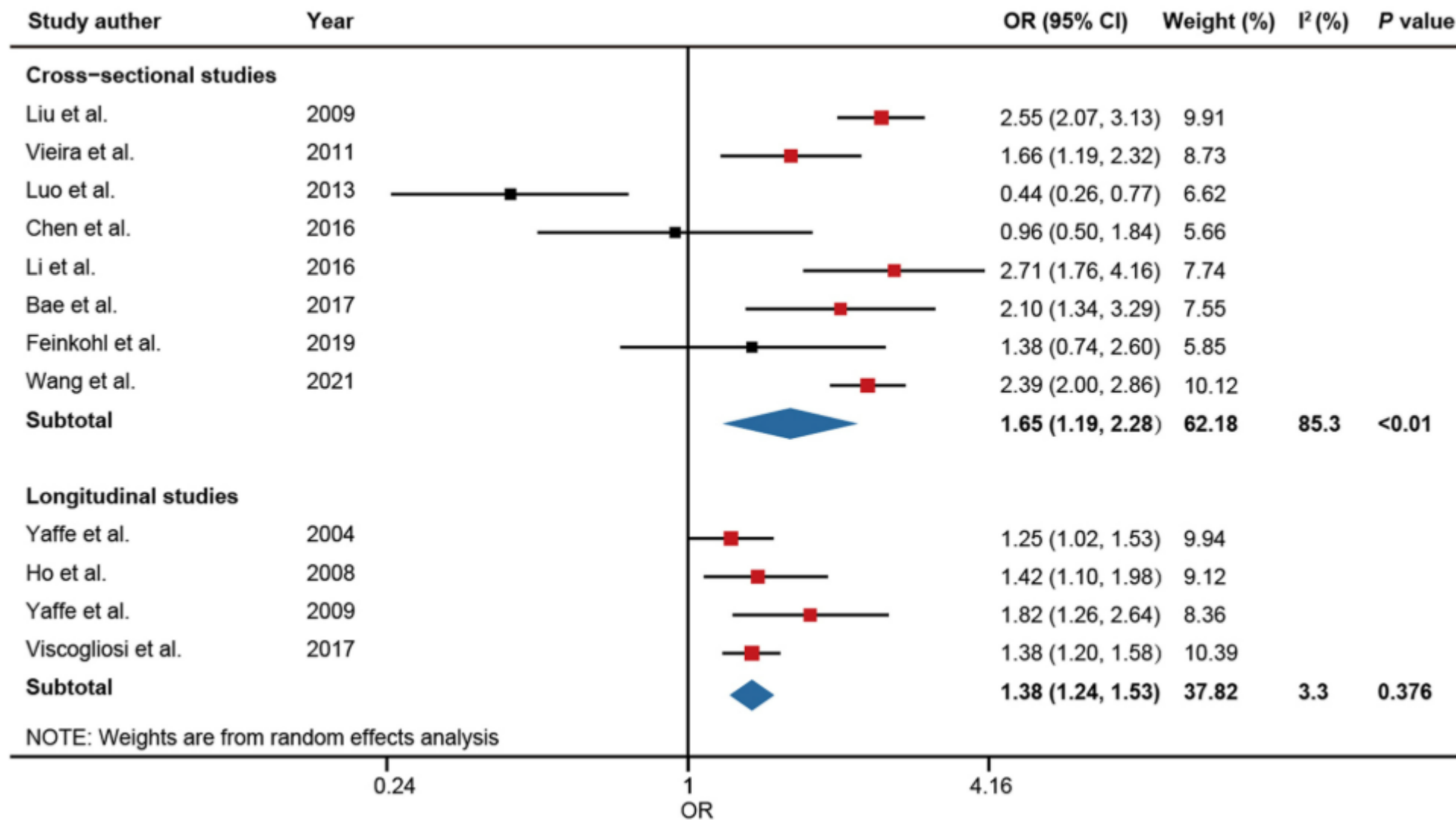


Metabolic syndrome

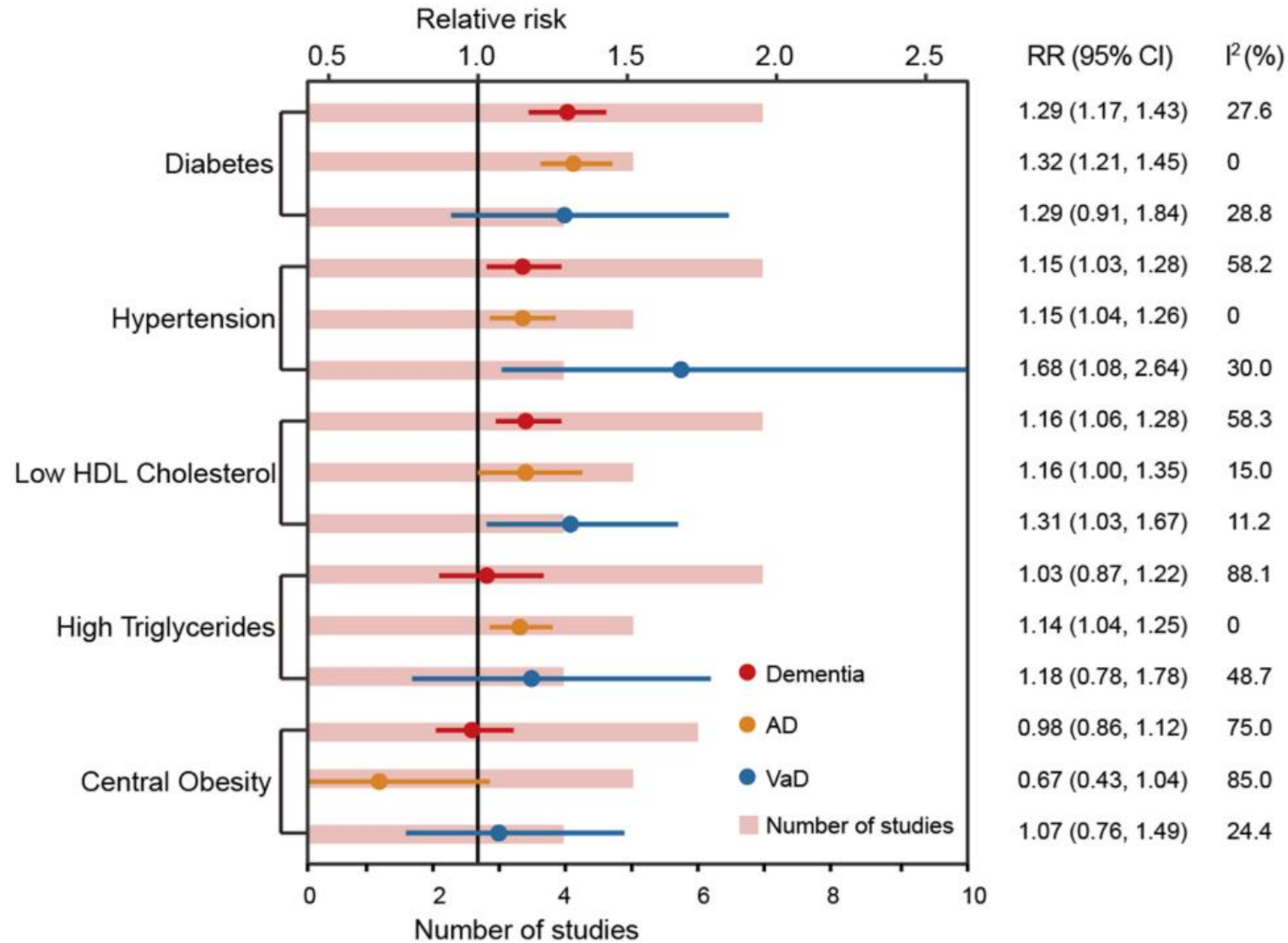


Metabolic syndrome is a combination of risk factor abdominal obesity, high blood pressure, high blood sugar, high triglycerides, and low HDL that together increase the risk of diabetes, heart disease, and dementia.

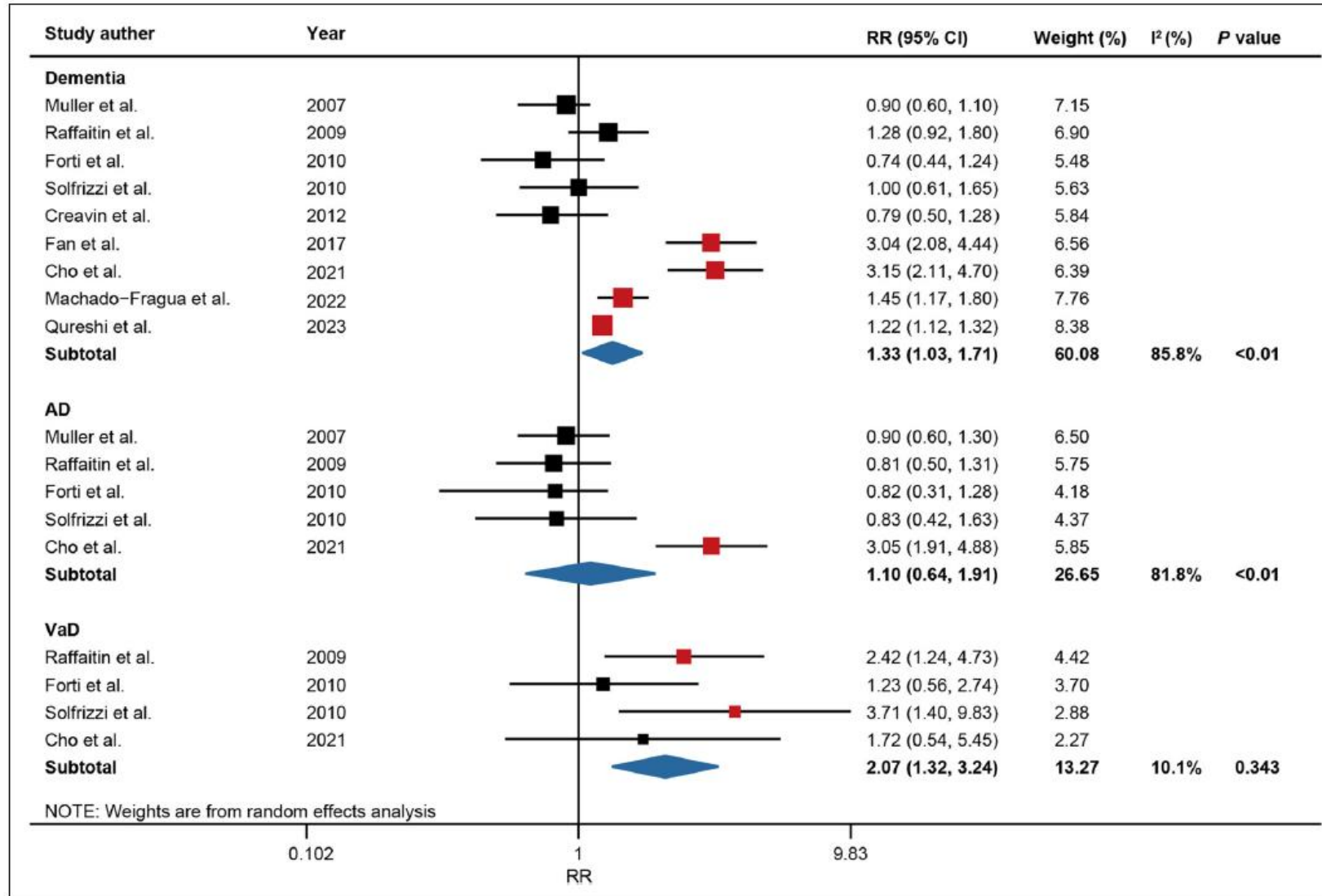
Meta-analysis of associations between MetS and cognitive impairment in longitudinal studies and cross-sectional studies.



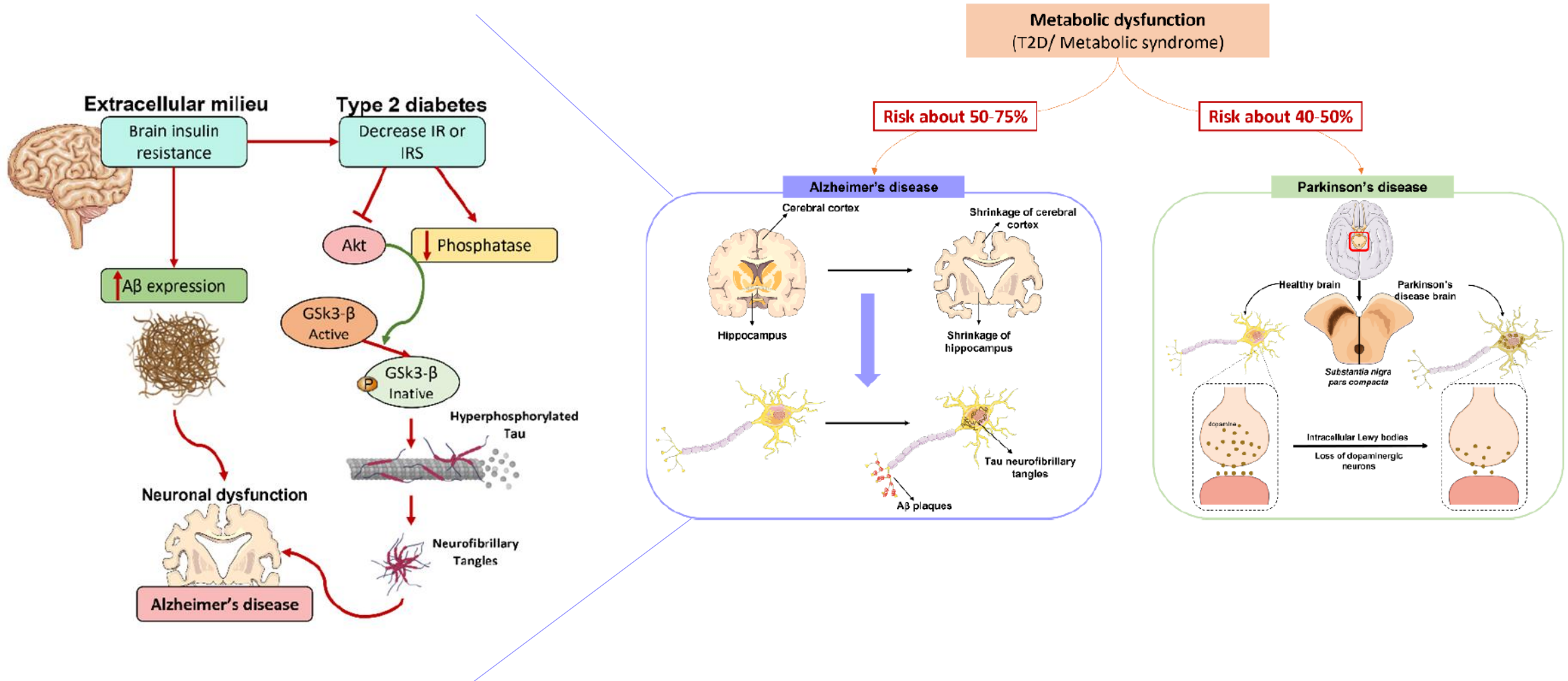
Associations between five components of MetS and the risk of dementia



Meta-analysis of associations of MetS with dementia.



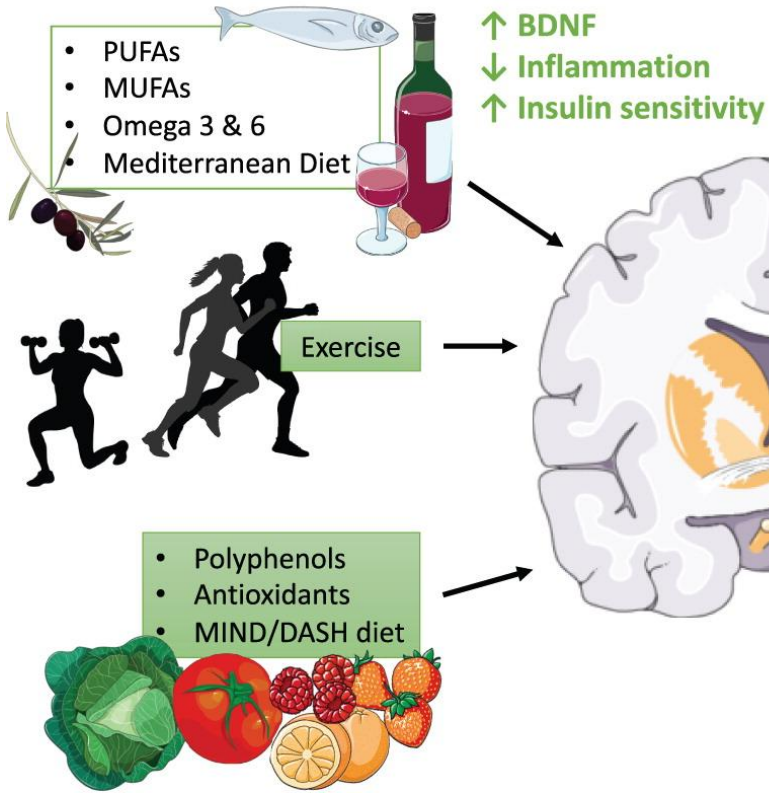
Metabolic syndrome increases the risk of developing Alzheimer's and Parkinson's diseases



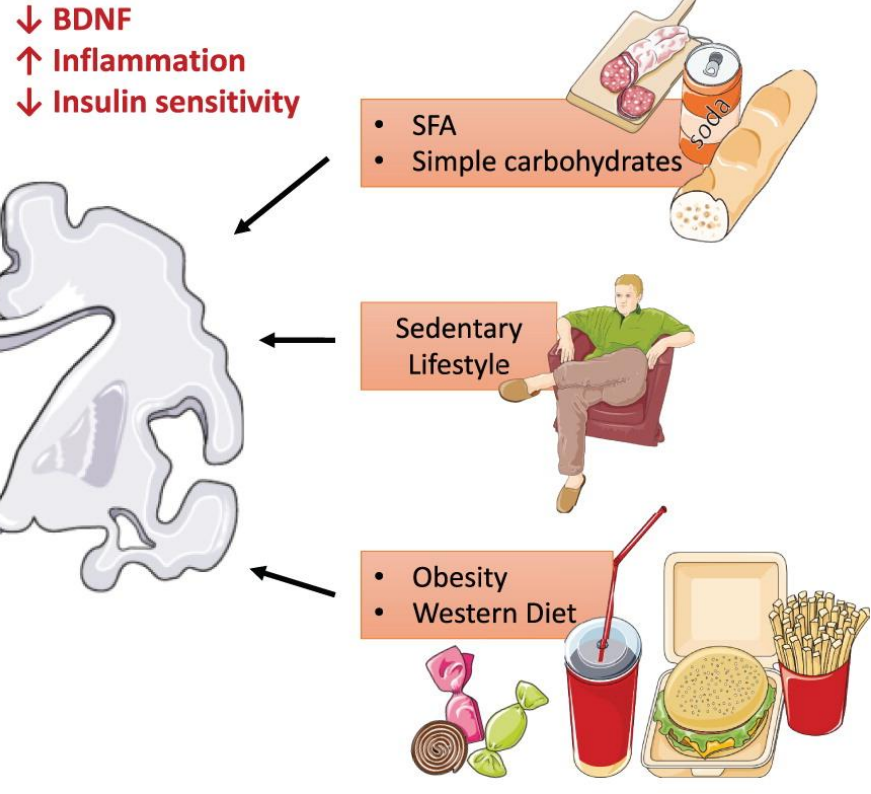
How dietary interventions improve cognitive health in Metabolic Syndrome?

Syndrome?

Healthy Brain



Alzheimer's Disease



Exercise and dietary influences on brain health and Alzheimer's disease risk. Exercise and components of the Mediterranean diet have beneficial effects on the brain that result in increased BDNF, reduced inflammation, and increased insulin sensitivity. Conversely, a sedentary lifestyle and components of the Western diet increase the risk of Alzheimer's disease through reductions in BDNF, increased inflammation, and reduced insulin sensitivity.

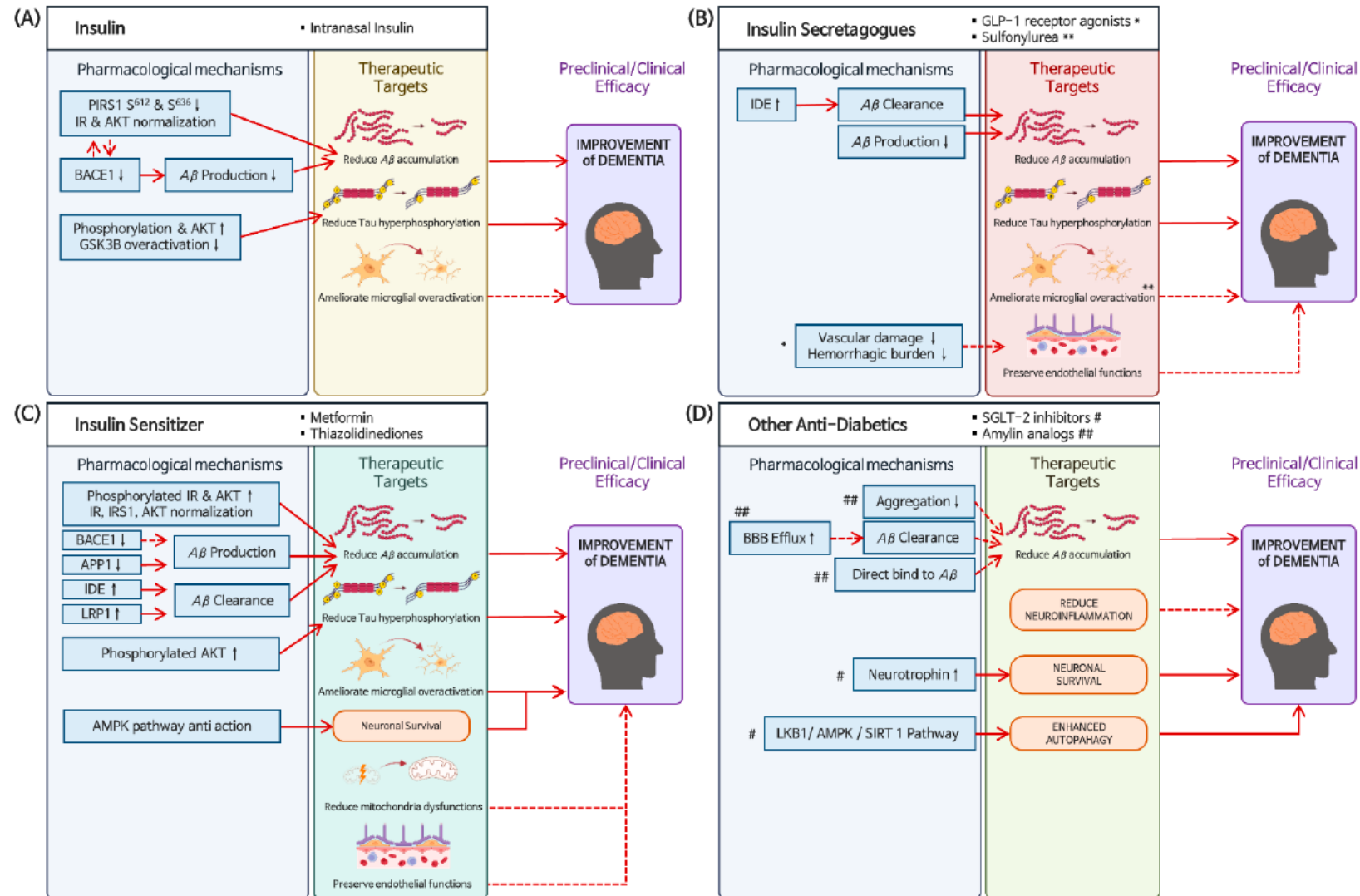
Nutrient classification, recommendations, and effect on cognition and Alzheimer's disease (AD) pathology

Table 1. Nutrient classification, recommendations, and effect on cognition and Alzheimer's disease (AD) pathology.

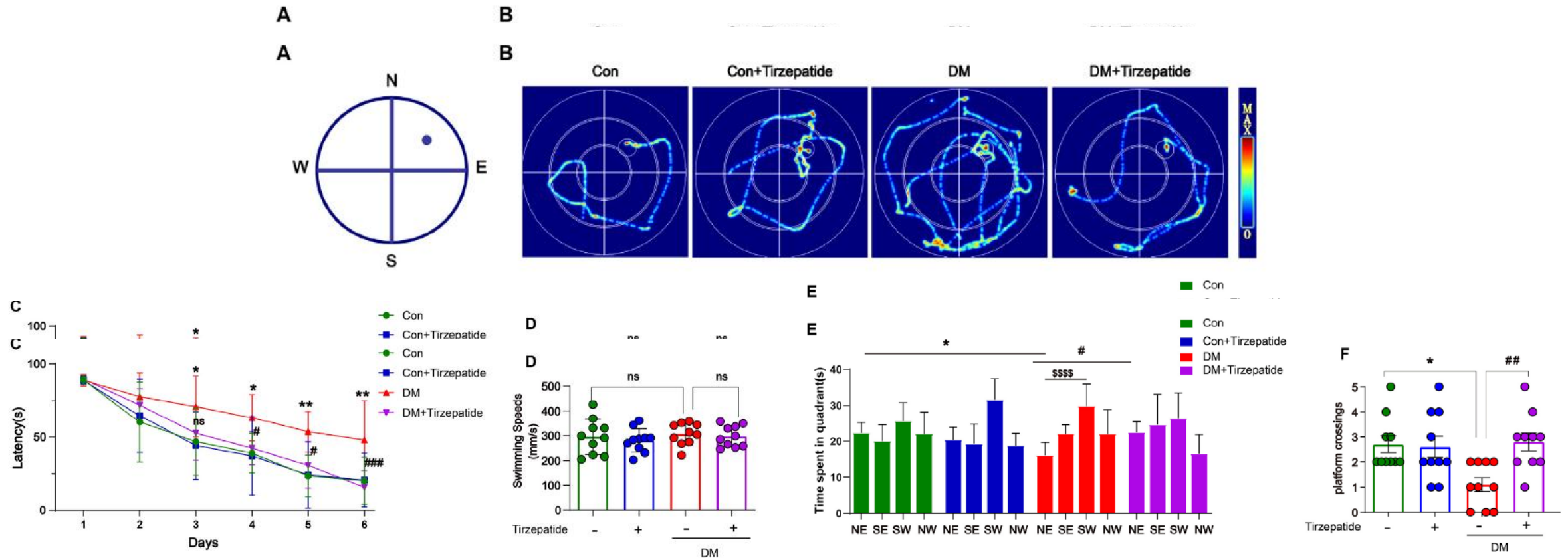
Nutrient (subclassification)	Food type	Recommendation	Effect on cognition and AD pathology
Fats			
SFA	Fatty meat (e.g., beef, lamb, dark chicken, pork), full-fat dairy products (e.g., butter, cheese, and ice cream), and oils (e.g., coconut and palm oil)	↓ Consumption	↓ Cognition ↑ Brain <i>BACE1</i> activity (Kalmijn et al. 2004; MacPherson et al. 2015)
PUFA			
Omega-3	Fish (e.g., salmon, tuna, trout, mackerel, and herring), oils (e.g., flaxseed, and canola oil), and nuts/seeds (e.g., flaxseeds, chia seeds, and walnuts)	↑ Consumption	↑ Cognition, ↓ AD progression (Avallone et al. 2019) ↓ Aβ production/aggregation (Avallone et al. 2019; Hossain et al. 2009)
Omega-6	Red meats, corn, safflower	↓ Consumption; aim for 2:1 omega-3:6 ratio	↑ Cognition if the ratio is 2:1
Carbohydrates			
Simple	Soft drinks, candy, table sugar, brown sugar, and fructose, glucose and sucrose additives	↓ Consumption	Simple carbohydrates impair cognition and increase risk of AD (Cao et al. 2007; Chong et al. 2019)
Complex	Brown and wild rice, whole wheat breads, quinoa, potatoes, corn, and legumes	↑ Consumption	
Polyphenols			
NA	Fruits (e.g., dark and citrus berries), vegetables (e.g., leafy greens, beans), tea/coffee, red wine, olive oil, and dark chocolate	↑ Consumption	↑ Cognition ↓ Neuroinflammation ↓ Aβ and tau (Hagan et al. 2016)
Anti-oxidants			
NA	Olive oil, fruits, vegetables, nuts, coffee/tea, red wine, and dark chocolate	↑ Consumption	↓ Neuronal damage ↓ AD progression ↓ Oxidative stress ↓ Aβ production/aggregation (Devore et al. 2012)

Note: ↑, increase; ↓, decrease; Aβ, amyloid-beta; *BACE1*, β-secretase 1; NA, not applicable (no subclassification); PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids.

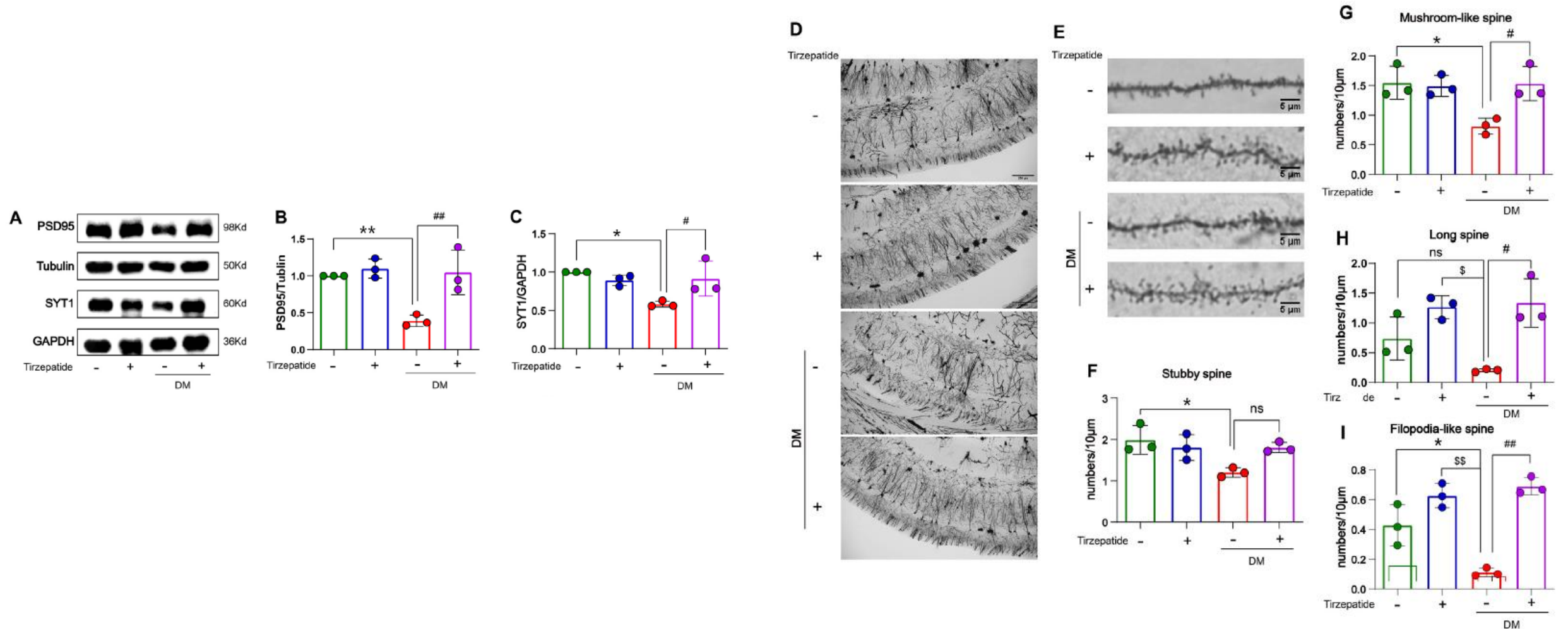
Neuroprotective effects of antidiabetic drugs: evidence from clinical trials and observational studies



Tirzepatide ameliorated DM-induced Spatial learning memory impairment



Tirzepatide affected synaptophysin proteins and dendritic spines in diabetic rats.



Conclusioni

- La dieta ad alti contenuti di Grassi Saturi provoca delle alterazioni molecolari che facilitano il declino cognitivo
- La Sindrome Metabolica come tale e i suoi componenti sono fattori associati
- La terapia antidiabetica (GLP1 RA) sembra avere una qualche utilità nel controllo del deficit cognitivo



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