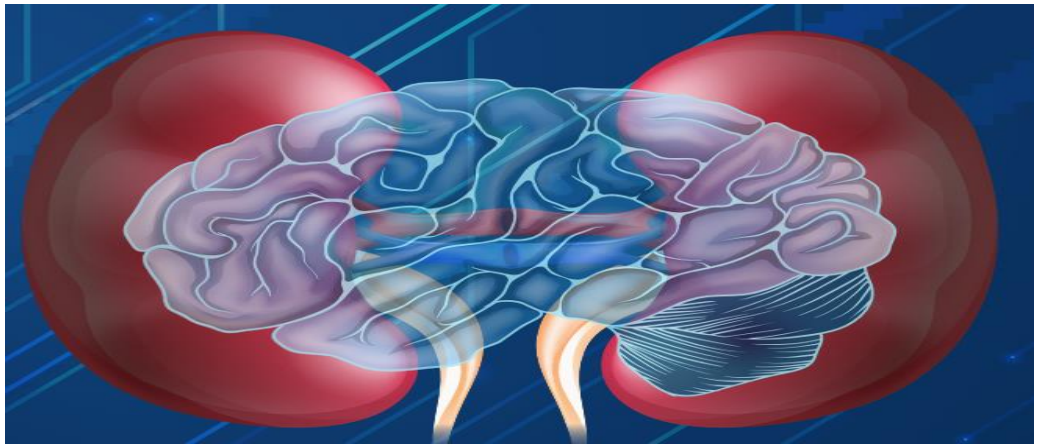


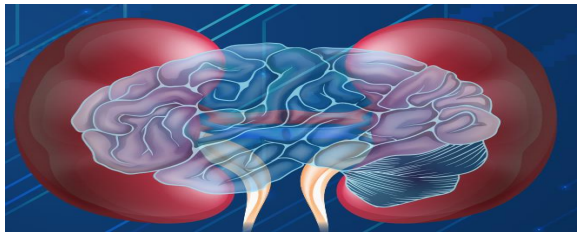
ΕΓΚΕΦΑΛΟΣ ΚΑΙ ΥΠΕΡΤΑΣΗ: ΠΑΘΟΦΥΣΙΟΛΟΓΙΚΟΙ ΜΗΧΑΝΙΣΜΟΙ

Ο ρόλος της υπέρτασης στην γνωσιακή λειτουργία

Ρ. Καλαϊτζίδης

ΣΑββΑΤΟ 11 ΝΟΕΜβΡΙΟΥ 2023

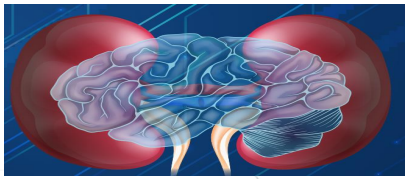
Disclosures



Consultant Advisory Board : Astra Zeneca, MEN,ARINI Boehringer Ingelheim, GSK

Speaker's Bureau: ELPEN, Astra Zeneca , MENARINI ,Boehringer Ingelheim , GSK, ASTELLAS

Ο ρόλος της υπέρτασης στην γνωσιακή λειτουργία



What did the guidelines suggest

Η υπέρταση οδηγεί σε γνωστική δυσλειτουργία

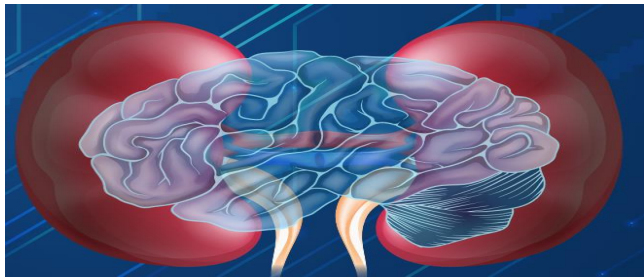
Η υπέρταση οδηγεί σε αρτηριακή σκληρία που προκαλεί γνωστική δυσλειτουργία

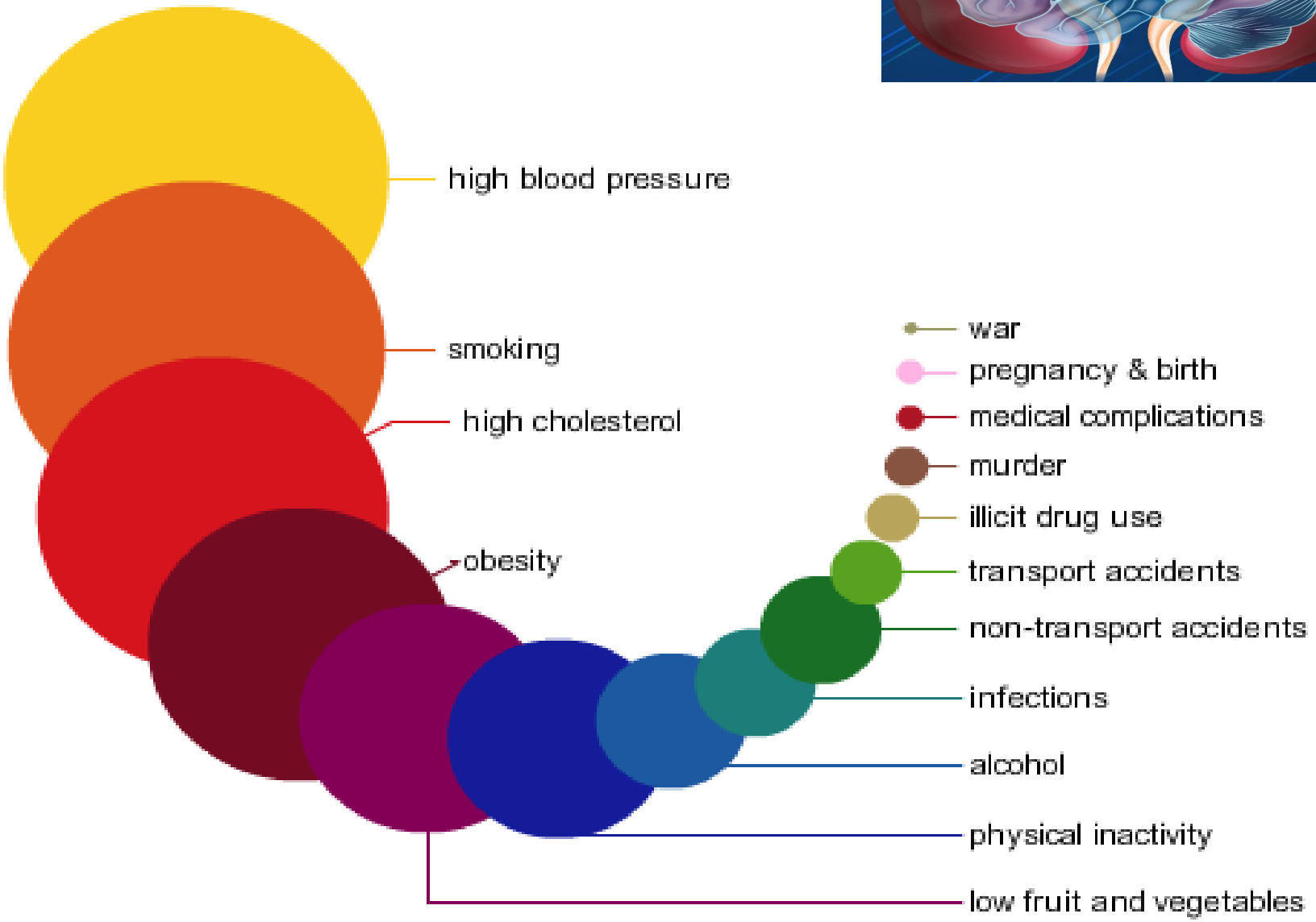
Pathophysiologic mechanisms

Ο έλεγχος της ΑΠ βελτιώνει την γνωστική δυσλειτουργία?

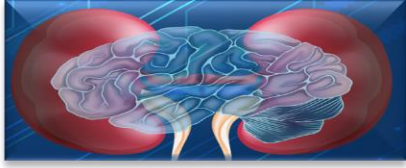
Συμπεράσματα

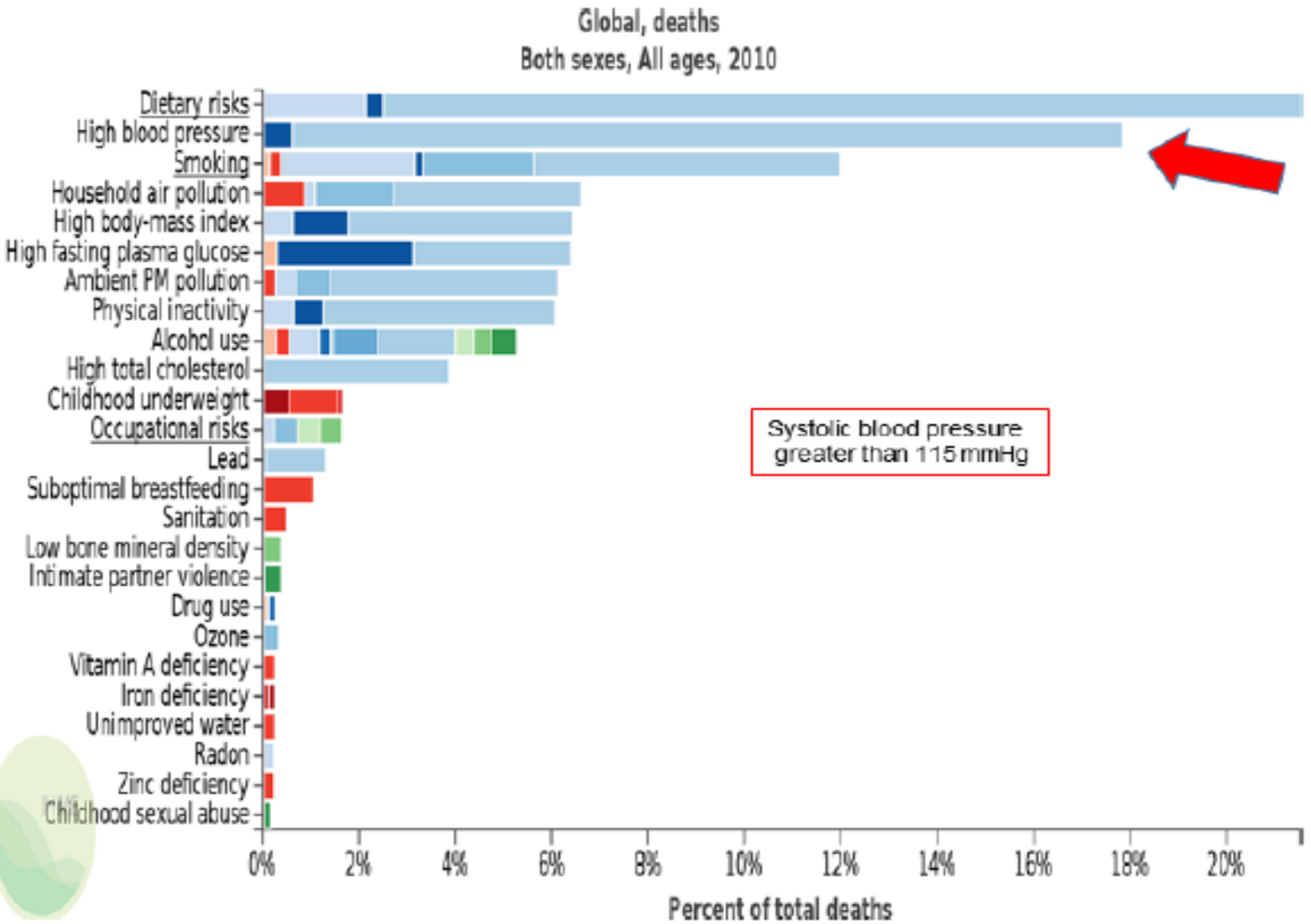
Risks leading to death in perspective



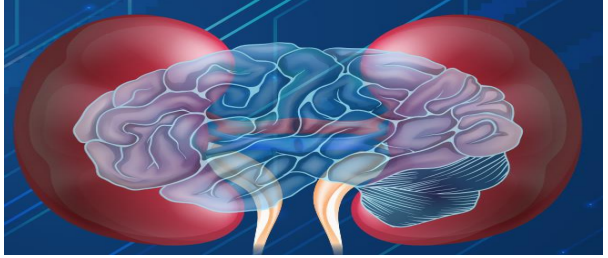


Increased blood pressure (red arrow) is the second leading risk attributed **to 17.8% of global deaths.**





J Clin Hypertens (Greenwich). 2015:1–3



Cognitive impairment
is comparatively **less considered** to be an adverse effect of hypertension

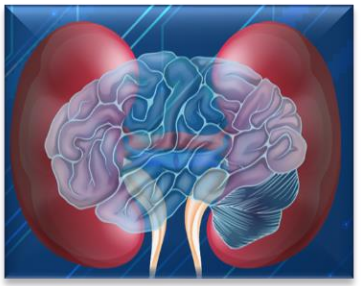
What did the guidelines suggest?

Whelton PK, et al.
2017 High Blood Pressure Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

WRITING COMMITTEE MEMBERS
Paul K. Whelton, MB, MD, MSc, FAHA, *Chair*
Robert M. Carey, MD, FAHA, *Vice Chair*



When the rate of cognitive decline (not dementia) has been a trial outcome

7 clinical trials of BP-lowering therapy have been completed,

and **2 of these have shown benefit**

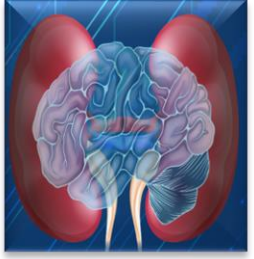
.S11.3-4–S11.3-6,S11.3-19–S11.3-22

Whelton PK, et al.
2017 High Blood Pressure Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

WRITING COMMITTEE MEMBERS
Paul K. Whelton, MB, MD, MSc, FAHA, *Chair*
Robert M. Carey, MD, FAHA, *Vice Chair*



Hypertension is also the primary risk factor **for small-vessel ischemic disease and cortical white matter abnormalities**.S11.3-12–

Vascular disease and its risk factors are implicated in a large proportion of patients with **dementia,** including those with **Alzheimer's dementi** a.S11.3-9–S11.3-

Dementia is a leading cause of mortality and placement into nursing homes and assisted living facilities, affecting >46 million individuals globally and 5 million persons in the United States, a number that is expected to **double** by 2050.S11.3-7

Whelton PK, et al.
2017 High Blood Pressure Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

WRITING COMMITTEE MEMBERS
Paul K. Whelton, MB, MD, MSc, FAHA, *Chair*
Robert M. Carey, MD, FAHA, *Vice Chair*

Most **observational studies** have suggested that better control of SBP **may reduce** Alzheimer's disease and other dementias

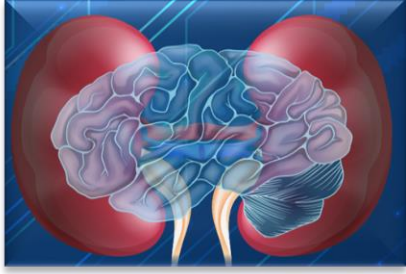
The evidence is stronger for BP lowering in **middle age** than in older adults.

Whelton PK, et al.
2017 High Blood Pressure Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

WRITING COMMITTEE MEMBERS
Paul K. Whelton, MB, MD, MSc, FAHA, *Chair*
Robert M. Carey, MD, FAHA, *Vice Chair*



11.3. Cognitive Decline and Dementia

Recommendation for Prevention of Cognitive Decline and Dementia

References that support the recommendation are summarized in Online Data Supplement 56.

COR	LOE	Recommendation
IIa	B-R	1. In adults with hypertension, BP lowering is reasonable to prevent cognitive decline and dementia.[S11.3-1–S11.3-6]

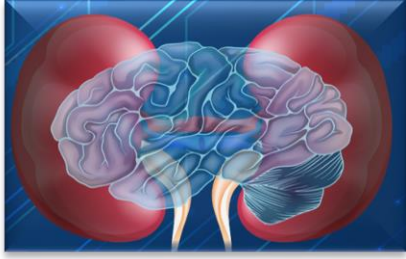
2023 ESH Guidelines for the management of arterial hypertension

Hypertension in **midlife** predicts

- **Cognitive decline**
- **Alzheimer's disease**
- **Vascular dementia**

in older patients [1267,1268].

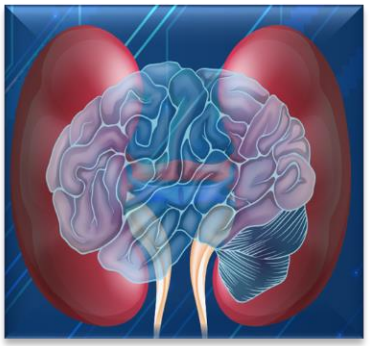
2023 ESH Guidelines for the management of arterial hypertension



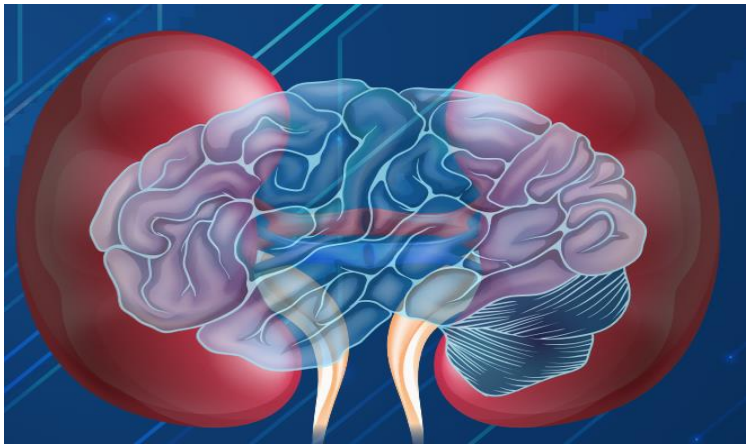
The effects of antihypertensive drug class in late life to prevent cognitive impairment, however, remain unclear.

Medication class may **be less relevant** if the SBP is not adequately controlled

2023 ESH Guidelines for the management of arterial hypertension

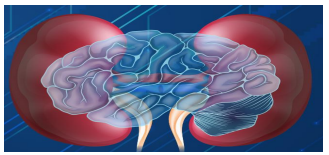


Several studies have shown that strict BP control, i.e. SBP <130 mmHg, reduces the progression of cerebral white matter lesions and the decrease in global cognitive performance [470,1275,1276].

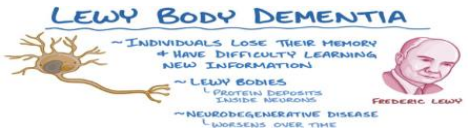


Impact of Hypertension on Cognition

Cognitive domains and disorders associated with hypertension

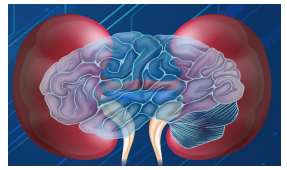


- Characteristic cognitive dysfunction domains
  - Greater impact on frontal lobe executive function
    - Goal formation
    - Abstract thinking
    - Initiating
    - Planning
    - Organizing
    - Sequencing
  - Performed better on memory tests
    - Impairments in recall
    - Relatively intact recognition
    - Benefit from cues
    - Mild forgetfulness
- Cognitive disorders (the strength of the association is in the order listed)
  - Vascular dementia
  - Alzheimer disease
  - Dementia with Lewy body



J Yeungnam Med Sci 2023;40(3):225-232

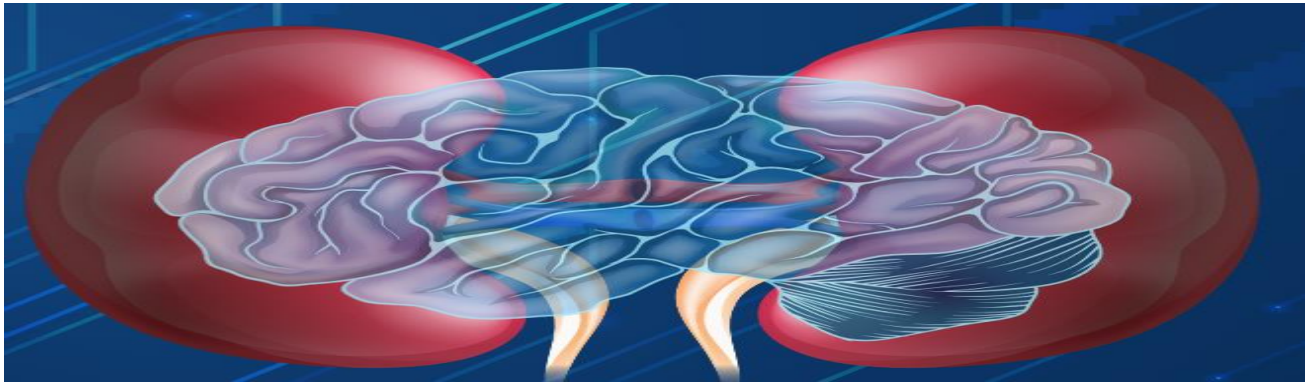
Impact of Hypertension on Cognition



Cognitive decline (worsening of cognitive function over years to decades, steeper than expected because of age alone) [Γνωστική εξασθένηση]

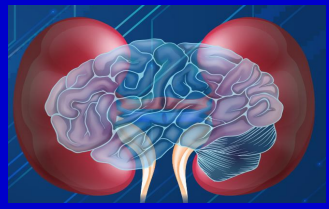
Mild cognitive impairment (MCI; reduced function in memory, thinking, and other cognitive domains but not impacting daily fun tioning) [Ήπια γνωστική εξασθένηση]

Dementia (impairments in cognition, including memory and other cognitive domains, but with adverse impacts on daily functioning) [Άνοια]



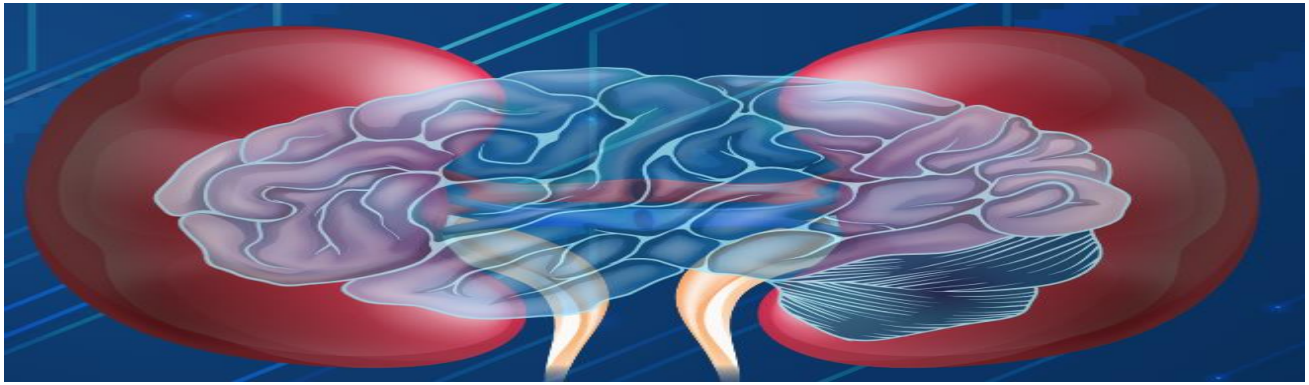
Hypertension a risk factor for adverse cognitive outcomes

Hypertension is clearly associated with



- Steeper cognitive decline [απότομη]
- Poor cognitive performance [Κακή γνωστική απόδοση]
- Incident **mild cognitive impairment**
- **Dementia**

J Yeungnam Med Sci 2023;40(3):225-232



CLINICAL TRIALS

Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial

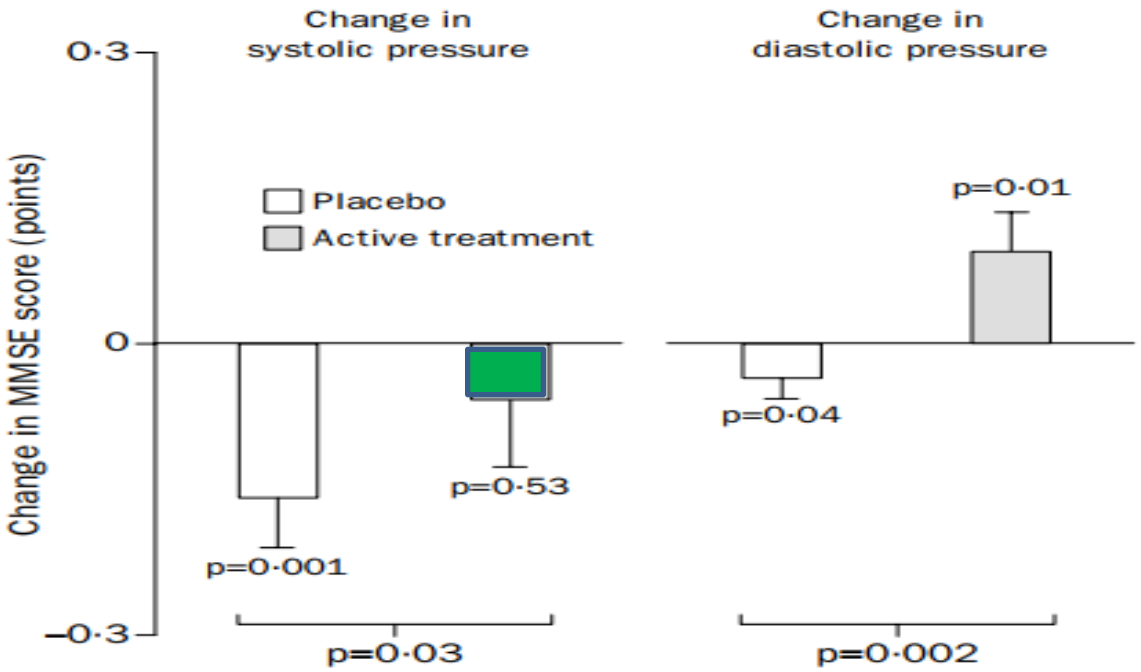


Figure 3: **Changes in MMSE score associated with mean decrease in systolic and diastolic blood pressure in placebo and active treatment groups**
Association sizes adjusted for sex, age, educational level, previous cardiovascular complications, antihypertensive treatment before enrolment, smoking, and alcohol consumption at randomisation.

In elderly patients with isolated systolic hypertension, active treatment starting with the dihydropyridine calcium-channel blocker nitrendipine halved the rate of dementia from 7·7 to 3·8 cases per 1000 patient-years.

In elderly people with isolated systolic hypertension, antihypertensive treatment was associated with a lower incidence of dementia.

Lancet 1998; 352: *1347–5*

Cognitive decline in individuals with high blood pressure: A longitudinal study in the elderly

Tzourio, Christophe MD, PhD; Dufouil, Carole PhD; Ducimetiere, Pierre PhD; Alperovitch, Annick MD, MSc; for the EVA Study Group

Blood pressure status at baseline*	n	Cognitive decline† %	Cognitive decline† Adjusted odds ratio‡ (95% CI)
Men			
Normal blood pressure	393	7.6	1§
High blood pressure	80	18.8	2.6 (1.2–5.7)
Women			
Normal blood pressure	623	7.2	1§
High blood pressure	53	15.2	2.9 (1.3–7.0)
Both sexes			
Normal blood pressure	1,016	7.4	1§
High blood pressure	133	17.3	2.8 (1.6–5.0)

* High blood pressure was defined as systolic BP ≥ 160 mm Hg

The risk of cognitive decliine was 4.3 (95% CI, 2.1 to 8.8) in those without antihypertensive therapy and 1.9 (95% CI, 0.8 to 4.4) in those being treated

ne

NeurologyIssue: Volume 53(9), 10 December 1999, pp 1948-1952

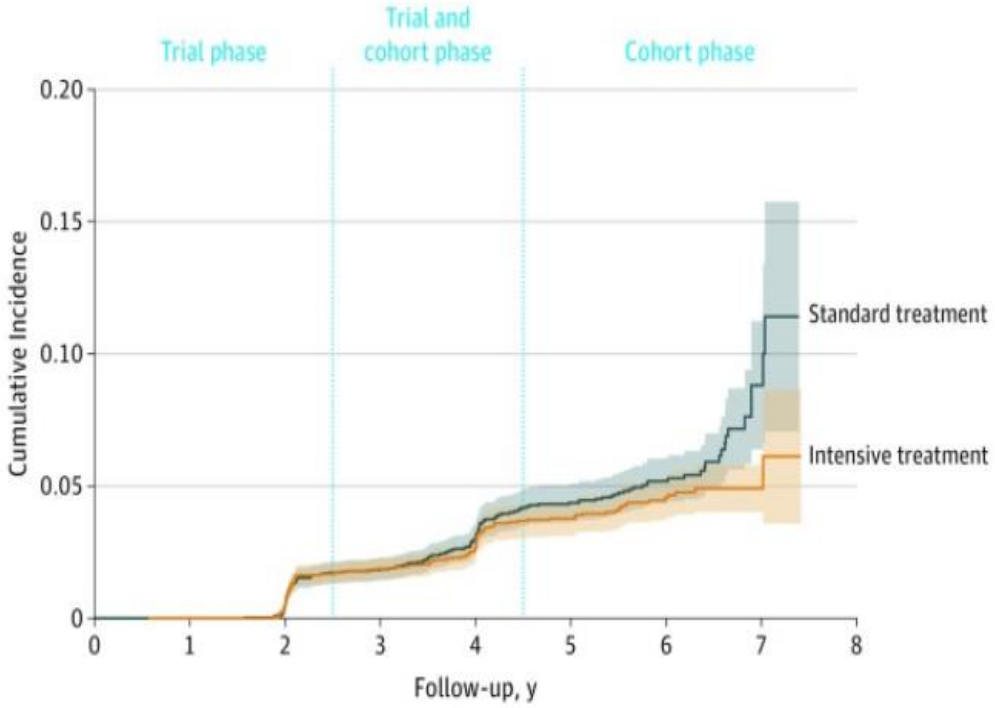
Antihypertensive medication use and risk of cognitive impairment

The Honolulu-Asia Aging Study

Επίπεδα Αρτηριακής Πίεσης

Analyses from the **Honolulu Asia Aging Study** (HAAS) have estimated that **27% of dementia cases** may be attributed to **midlife SBP >-120 mm** Hg among inadequately treated men

Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia



No. at risk

Standard treatment	4285	4282	4168	3886	2829	2107	989	87	0
Intensive treatment	4278	4277	4171	3917	2893	2189	1027	93	0

Among ambulatory adults with hypertension, treating to a systolic blood pressure goal of less than 120 mm Hg compared with a goal of less than 140 mm Hg **DID NOT RESULT IN A SIGNIFICANT REDUCTION IN THE RISK OF PROBABLE DEMENTIA.** Because of early study termination and fewer than expected cases of dementia, the study may have been underpowered for this end point.

Median follow-up time was **5.14 years** (interquartile range, 3.91-6.00) for the intensive treatment group and **5.07 years** (interquartile range, 3.87-5.98) for the standard treatment group.
For group comparison of incidence, hazard ratio, 0.83; 95% CI, 0.67-1.04; *P*=.10

JAMA. 2019 Feb 12; 321(6): 553–561

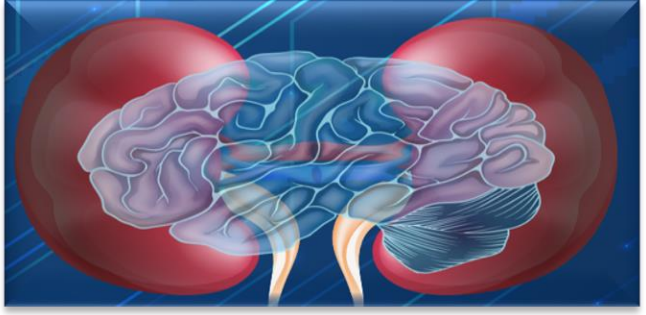
Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia

Incidence of Probable Dementia and Mild Cognitive Impairment by Treatment Group

Outcomes	Treatment Group				Hazard Ratio (95% CI)[a]	*P* Value
	Intensive		Standard			
	No. With Outcome/Person-Years	Cases per 1000 Person-Years	No. With Outcome/Person-Years	Cases per 1000 Person-Years		
Probable dementia	149/20 569	7.2	176/20 378	8.6	0.83 (0.67-1.04)	.10
Mild cognitive impairment[b]	287/19 690	14.6	353/19 281	18.3	0.81 (0.69-0.95)	.007
Composite of mild cognitive impairment or probable dementia	402/19 873	20.2	469/19 488	24.1	0.85 (0.74-0.97)	.01

Median follow-up time was 5.14 years (interquartile range, 3.91-6.00) for the intensive treatment group and 5.07 years (interquartile range, 3.87-5.98) for the standard treatment group.
For group comparison of incidence, hazard ratio, 0.83; 95% CI, 0.67-1.04; *P*=.10

JAMA. 2019 Feb 12; 321(6): 553–561



Have been suggested a U-shaped relationship between BP and cognition ?

Isolated studies of older adults

RESEARCH ARTICLES | DECEMBER 15 2000

Blood Pressure and Risk of Dementia: Results from the Rotterdam Study and the Gothenburg H-70 Study

In an analysis including data from the **Rotterdam study and the Göteborg H-70 study**, hypertension in old age appeared protective:

•

Elderly adults had an inverse association between BP and dementia, with a reduced relative risk for dementia of 0.93 (95% CI, 0.88–0.99) **per 10 mmHg higher SBP**

This association was confined to subjects who used anthypertensive medication.

Dement Geriatr Cogn Disord. 2001;12:33–39. doi: 10.1159/000051233

The Effect of Age on the Association Between Blood Pressure and Cognitive Function Later in Life

High BP was associated with greater risk of cognitive impairment in persons younger than 75
but with better cognitive function in older persons

Lower BP might lead to hypoperfusion
and thus *worse* cognitive outcomes in older persons

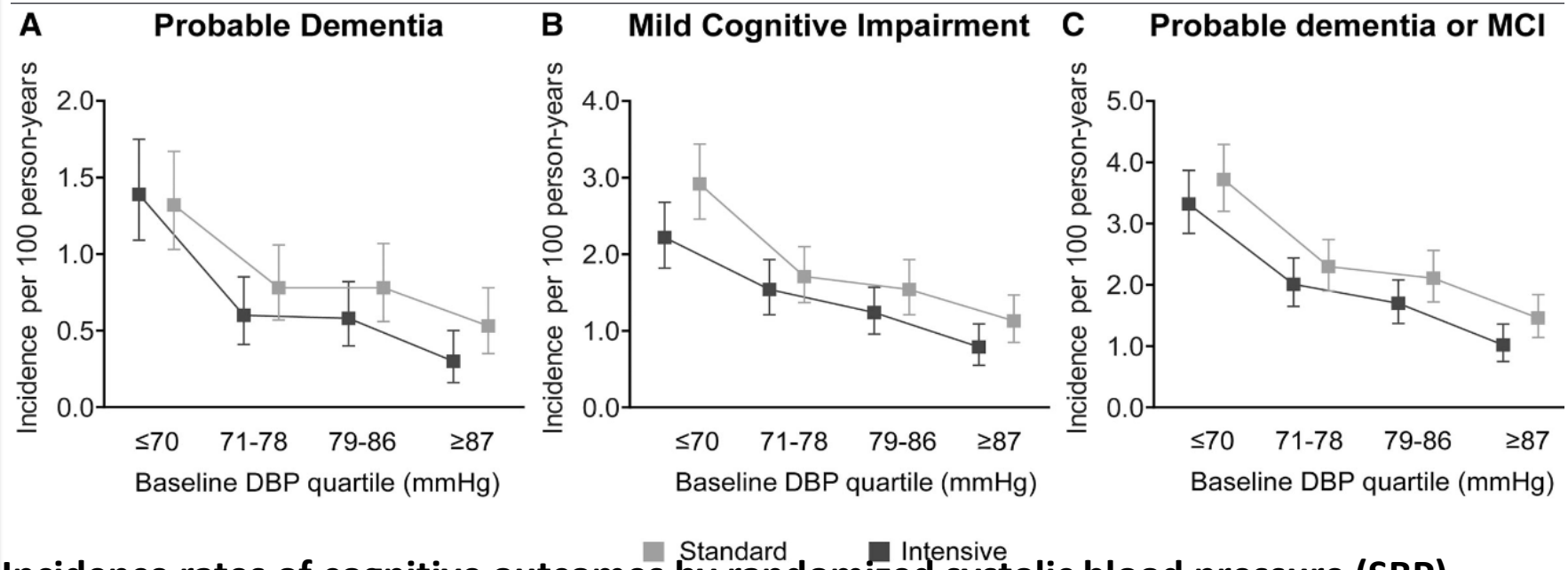
https://doi.org/10.1111/j.1532-5415.2009.02264.x

Ο ρόλος της Διαστολικής ΑΠ στην γνωστική λειτουργία

ORIGINAL ARTICLE

Diastolic Blood Pressure and Intensive Blood Pressure Control on Cognitive Outcomes: Insights From the SPRINT MIND Trial

Chao Jiang *, Sitong Li *, Yufeng Wang, Yiwei Lai, Yu Bai, Manlin Zhao, Liu He, Yu Kong, Xueyuan Guo, Songnan Li, Nian Liu, Chenxi Jiang, Ribo Tang, Caihua Sang, Deyong Long, Xin Du, Jianzeng Dong, Craig S. Anderson, and Changsheng Ma



Incidence rates of cognitive outcomes by randomized systolic blood pressure (SBP) intervention and baseline diastolic blood pressure (DBP) quartile.

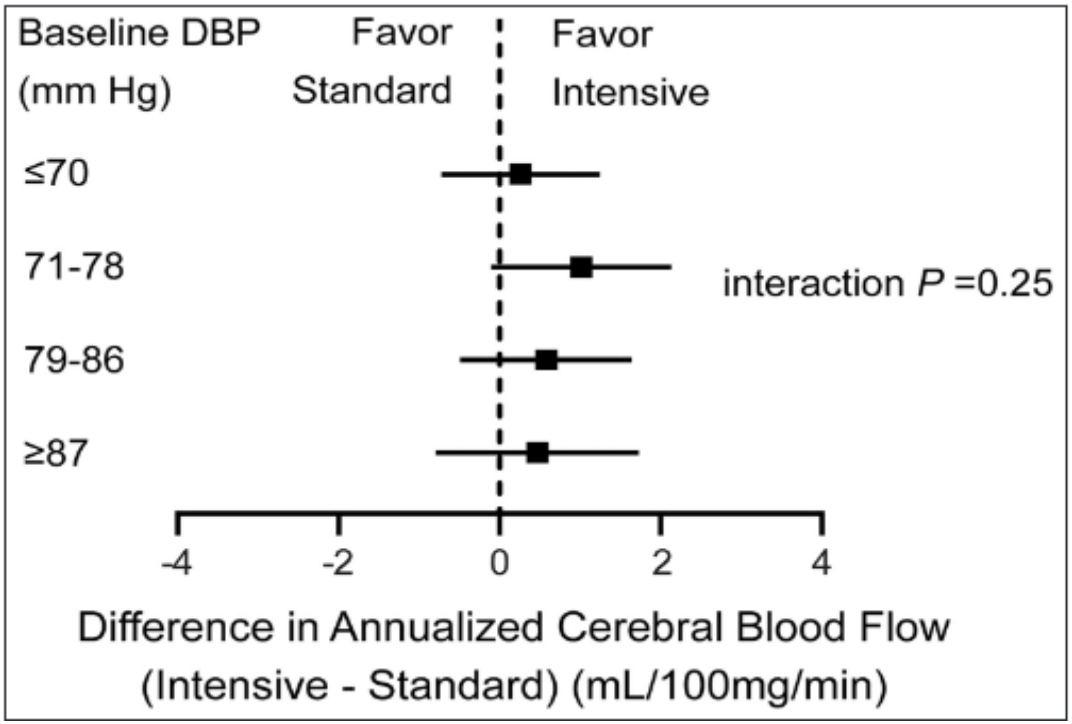
Conclusions: I ntensive BP control **DID NOT APPEAR TO HAVE** a detrimental effect on cognitive outcomes and cerebral perfusion in patients with low baseline DBP.

Hypertension Volume 80, Issue 3, March 2023; Pages 580-589

ORIGINAL ARTICLE

Diastolic Blood Pressure and Intensive Blood Pressure Control on Cognitive Outcomes: Insights From the SPRINT MIND Trial

Chao Jiang *, Sitong Li *, Yufeng Wang, Yiwei Lai, Yu Bai, Manlin Zhao, Liu He, Yu Kong, Xueyuan Guo, Songnan Li, Nian Liu, Chenxi Jiang, Ribo Tang, Caihua Sang, Deyong Long, Xin Du, Jianzeng Dong, Craig S. Anderson, and Changsheng Ma



In this **post hoc analysis** of the SPRINT MIND study, patients with lower DBP had a higher incidence of dementia or MCI. Nevertheless, **intensive BP control did not appear to have a detrimental effect** on cognitive function and cerebral perfusion. Low DBP level should not be an obstacle to intensive BP control from the perspective of brain health.

Effect of systolic blood pressure intervention on annualized CHANGE IN CEREBRAL BLOOD flow by baseline diastolic blood pressure (DBP) quartile.

HypertensionVolume 80, Issue 3, March 2023; Pages 580-589

Age-Dependent Risk
Midlife Versus Late Life

Hypertension's impact on late-life cognitive outcomes appears the greatest when considered in middle age

Midlife Versus Late Life

Midlife hypertension and 20-year cognitive change: The Atherosclerosis Risk in Communities Neurocognitive Study

Additional adjusted 20-year cognitive change for the association of visit 2 (1990–1992) with recommended treatmen t

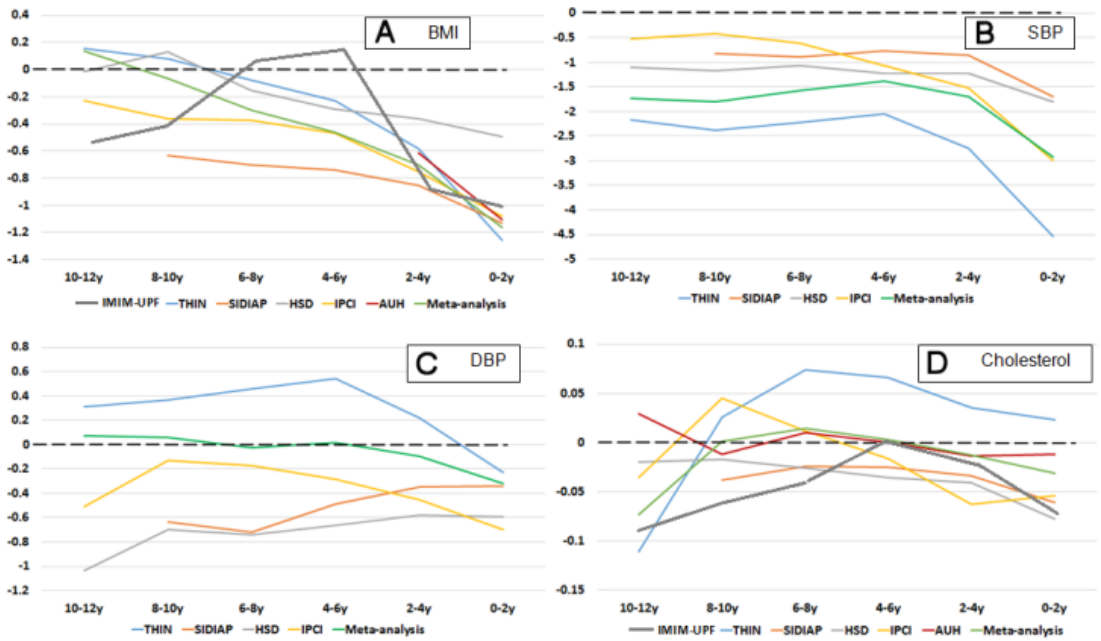
	Cognitive Change (95% CI)	
	HTN Treatment Not Indicated[a]	HTN Treatment Indicated[b]
All Participants[c]		
	(n=8,165)	(n=5,311)
Global *z* score	0 (reference)	**−0.044 (−0.085, −0.003)**
DWRT *z* score	0 (reference)	−0.008 (−0.074, 0.058)
DSST *z* score	0 (reference)	**−0.064 (−0.093, −0.035)**
WFT *z* score	0 (reference)	**−0.042 (−0.079, −0.005)**
DWRT raw score, No. of words	0 (reference)	−0.012 (−0.112, 0.088)
DSST raw score, No. of symbols	0 (reference)	**−0.909 (−1.319, −0.498)**
WFT raw score, No. of words	0 (reference)	**−0.520 (−0.982, −0.058)**

Midlife hypertension a**nd elevated midlife BUT NOT LATE-LIFE SYSTOLIC BP was associated with more cognitive decline** during the 20 years of the study. Greater decline is found with higher midlife BP in whites than in African Americans

JAMA Neurol. 2014 October 1; 71(10): 1218–1227

BMJ Open

Vascular and metabolic risk factor differences prior to dementia diagnosis: a multidatabase case–control study using European electronic health records



Mid-life SBP is a risk factor for dementia incidence 10–20 years later

LOWER SBP IN CASES AT THE TIME OF DIAGNOSIS

BMI, SBP and total cholesterol levels were lower overall in cases with dementia than controls and the difference was most marked closest to the point of diagnosis.

. BMJ Open 2020;10:e038753. doi:10.1136/

Studies using IMAGING surrogates for cognitive or dementia status

Also support
the importance **of midlife** hypertension

High Blood Pressure and Cerebral White Matter Lesion Progression in the General Population

Benjamin F.J. Verhaaren, Meike W. Vernooij, Renske de Boer, Albert Hofman, Wiro J. Niessen, Aad van der Lugt, M. Arfan Ikram

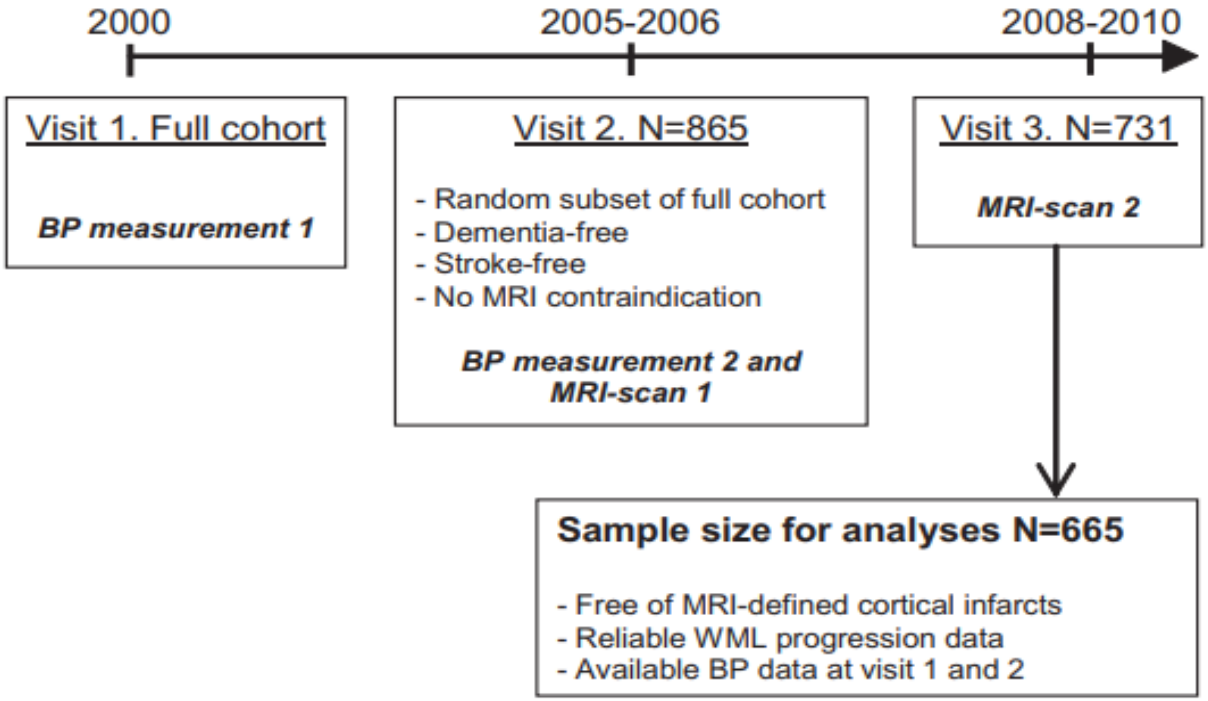


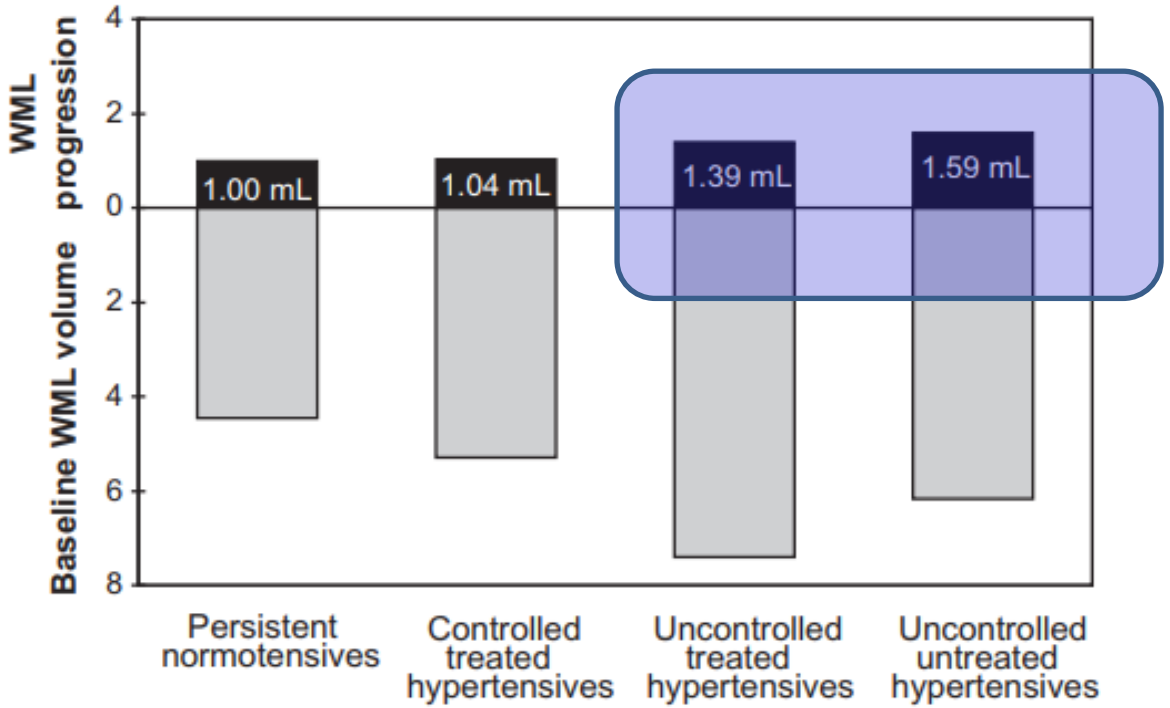
Figure 1. Schematic overview of the study design. BP indicates blood pressure; and WML, white matter lesion.

High blood pressure to precede **cerebral white matter lesions** and implies that hypertension treatment could reduce WML progression in the general population.

***Hypertension*. 2013;61:1354-1359**

High Blood Pressure and Cerebral White Matter Lesion Progression in the General Population

Benjamin F.J. Verhaaren, Meike W. Vernooij, Renske de Boer, Albert Hofman, Wiro J. Niessen, Aad van der Lugt, M. Arfan Ikram



Hypertension treatment and white matter lesion (WML) progression.

High blood pressure to precede cerebral white matter lesions and implies that hypertension treatment could reduce WML progression in the general population.

***Hypertension*. 2013;61:1354-1359**

Association of midlife blood pressure to late-life cognitive decline and brain morphology

- In the National Heart, Lung, and Blood Institute Twin Study,
  - **midlife SBP was associated**
  - with not only more white matter hyperintensities in later life but also
- **SMALLER BRAIN PARENCHYMAL VOLUMES**

Swan GE, DeCarli C, Miller BL, Reed T, Wolf PA, Jack LM, Carmelli D. Association of midlife blood pressure to late-life cognitive decline and brain morphology. *Neurology*. 1998;51:986–99

Hypertension Is Related to Cognitive Impairment

A 20-Year Follow-up of 999 Men

Lena Kilander, Håkan Nyman, Merike Boberg, Lennart Hansson, Hans Lithell

TABLE 3. Determinants of Low Cognitive Performance: Cross-sectional Data at Age 70 Years

	Cognitive Function			Logistic Regression	
Characteristic	Normal (n=743)	Low (n=186)	P^1	OR (95% CI)	P^2
24-h DBP, mm Hg	76 (8)	78 (8)	.0002	1.45 (1.20–1.75)	.0001
fP-Glucose, mmol/L	5.7 (1.4)	6.0 (1.8)	.034	1.13 (0.94–1.37)	.188
fP-Insulin, mU/L	12.7 (8.2)	13.3 (9.2)	.984	0.87 (0.69–1.09)	.223
M/I	5.2 (2.5)	4.8 (2.6)	.155	1.00 (0.77–1.29)	.983
fS-Triglycerides, mmol/L	1.39 (0.71)	1.57 (1.04)	.271	0.99 (0.79–1.23)	.911
BMI, kg/m^2	26.1 (3.2)	26.9 (3.9)	.089	1.12 (0.89–1.41)	.346
HDL cholesterol, mmol/L	1.30 (0.34)	1.25 (0.37)	.232	0.90 (0.72–1.13)	.349
Antihypertensive treatment, %	32.6	33.3	.775	0.64 (0.42–0.98)	.0418
Age, y	72.3	72.8		1.35 (1.14–1.58)	.0003
Education, L/M/H	46/35/19%	81/15/4%		0.42 (0.27–0.65)	.0001
Occupation, L/M/H	35/42/23%	66/30/4%		0.57 (0.39–0.83)	.0038

InUppsala, Sweden, using ambulatory BP monitoring, **nondipping circadian BP patterns** and persistently high 24-hour BP (at70 years of age)

- was associated **with worse cognitive performance**

Kilander L, Nyman H, Boberg M, Hansson L, Lithell H. Hypertensionis related to cognitive impairment: a 20-year follow-up of 999 men.*Hypertension*. 1998;31:780–786.

Pulse pressure is associated with early brain atrophy and cognitive decline: modifying effects of APOE4

Regression results for baseline pulse pressure predicting cognition at 5-7 year follow-up and annualized change in cognition, as well as interactions with the APOE-ε4 carrier status and blood pressure group.

A Time 2 Performance	Pulse Pressure (mm Hg) Main Effects		Blood pressure group * Interaction	APOE-ε4 status Interaction
	Beta (SE)	*P*	*P*	*P*
LM-delayed	-0.0018 (0.013)	0.89	0.08	0.48
VR-delayed	-0.018 (0.011)	0.10	0.74	0.09
Similarities	0.0017 (0.011)	0.88	0.60	0.16
Trails A **	-0.0017 (0.0012)	0.17	0.68	0.22
Trails B-A **	-0.0015 (0.00068)	0.02	0.25	0.66
BNT **	0.0021 (0.0022)	0.34	0.36	0.42
HVOT **	-0.0021 (0.0018)	0.25	0.63	0.26
B				
Time 2-1 Performance	**Beta (SE)**	***P***	***P***	***P***
LM-delayed	-0.00085 (0.0020)	0.67	0.11	0.49
VR-delayed	-0.00045 (0.0017)	0.79	0.82	0.78
Similarities	-0.0010 (0.0018)	0.57	0.43	0.18
Trails A	-0.000014 (0.00011)	0.89	0.69	0.68
Trails B-A	-0.00098 (0.00045)	0.03	0.65	0.30

PULSE PRESSURE was associated with cognitive decline among apolipoprotein E)-ε4 carriers in the Framingham Offspring Study.

. *Alzheimer Dis Assoc Disord*. 2016;30:210–215.

Association of visit-to-visit variability in blood pressure with cognitive function in old age: prospective cohort study

Table 2| **Cognitive function in thirds of visit-to-visit blood pressure variability. Values are means (standard errors) unless stated otherwise**

Variables	Third of visit-to-visit blood pressure variability			P value
	Low (n=1820)	Middle (n=1821)	High (n=1820)	
Systolic blood pressure				
Range of SD (mm Hg)	0.7-12.2	12.3-16.2	16.3-64.4	—
Stroop test score (seconds)	68.46 (0.79)	68.75 (0.79)	71.54 (0.82)	<0.001
Letter-digit coding test score (digits coded)	22.40 (0.19)	21.82 (0.19)	21.24 (0.19)	<0.001
Picture-word learning test (pictures remembered):				
Immediate recall score	9.37 (0.05)	9.28 (0.05)	9.10 (0.05)	<0.001
Delayed recall score	10.00 (0.07)	9.89 (0.07)	9.70 (0.08)	0.001
Diastolic blood pressure				
Range of SD (mm Hg)	0-6.5	6.6-8.5	8.6-33.1	—
Stroop test score (seconds)	68.28 (0.79)	68.89 (0.79)	71.34 (0.80)	<0.001
Letter-digit coding test score (digits coded)	22.35 (0.19)	21.93 (0.19)	21.27 (0.19)	<0.001
Picture-word learning test (pictures remembered):				
Immediate recall score	9.41 (0.05)	9.22 (0.05)	9.13 (0.05)	<0.001
Delayed recall score	10.01 (0.07)	9.88 (0.07)	9.74 (0.07)	0.001

- BP variability has also been described in several studies as an important risk factor for reduced cognitive function.

Higher visit-to-visit variability in blood pressure independent of average blood pressure was associated with impaired cognitive function in old age.

BMJ. 2013;347:f4600. doi: 10.1136/bmj.f4600

Patients with

HYPERTENSION AND CKD

Risk factors for cognitive dysfunction in CKD and hypertensive subjects

Rigas G. Kalaitzidis · Despina Karasavvidou · Athina Tatsioni · Olga Balafa · Kosmas Pappas · Giorgos Spanos · Sigkliti-Henrietta Pelidou · Kostas C. Siamopoulos

Table 3 Multivariate analysis of non-dialysis population

Cognitive tests	Factor	OR (95 % CI)	*p*
MMSE	Stages	2.46 (1.81–3.34)	<0.001
	Age (years)	1.06 (1.02–1.09)	0.001
	DM	4.27 (1.88–9.75)	0.001
	PTH	1.01 (1.00–1.01)	0.010
Clock test	Stages	1.92 (1.23–2.99)	0.004
	Age (years)	1.07 (1.03–1.11)	0.001
	DM	4.48 (1.86–10.83)	0.001
	PTH	1.92 (1.23–2.99)	0.004
IADL	Stages	1.75 (1.26–2.45)	0.001
	Age (years)	1.11 (1.05–1.16)	0.000
	DM	7.64 (3.12–18.73)	0.000
	UTPR	1.00 (1.00–1.00)	0.047

Int Urol Nephrol 2013, DOI 10.1007/s11255-013-0450-y

Ο ρόλος της υπέρτασης στην γνωσιακή λειτουργία

What did the guidelines suggest

Η υπέρταση οδηγεί σε γνωστική δυσλειτουργία

Η υπέρταση οδηγεί σε αρτηριακή σκληρία που προκαλεί γνωστική δυσλειτουργία

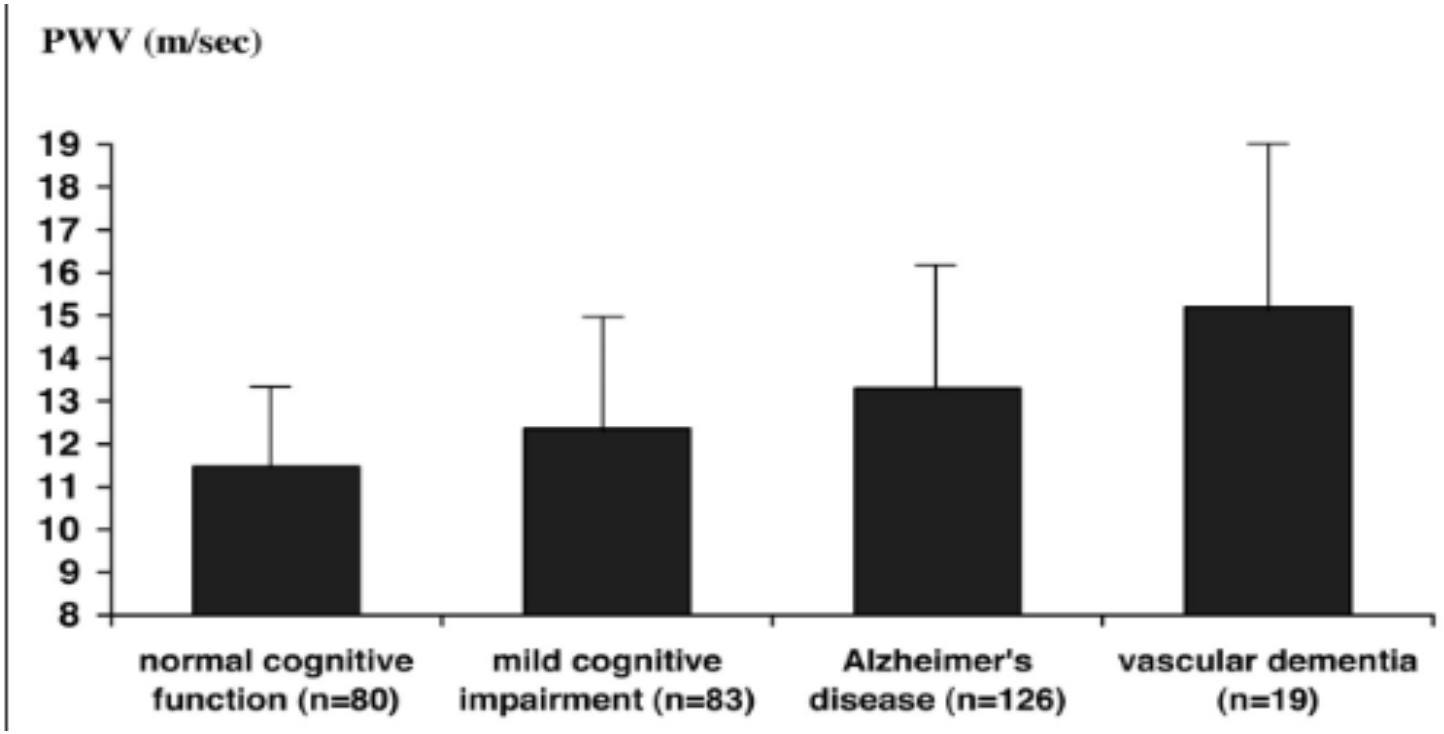
Pathophysiologic mechanisms

Ο έλεγχος της ΑΠ βελτιώνει την γνωστική δυσλειτουργία?

Συμπεράσματα

ORIGINAL CONTRIBUTIONS

Relationship Between Arterial Stiffness and Cognitive Function in Elderly



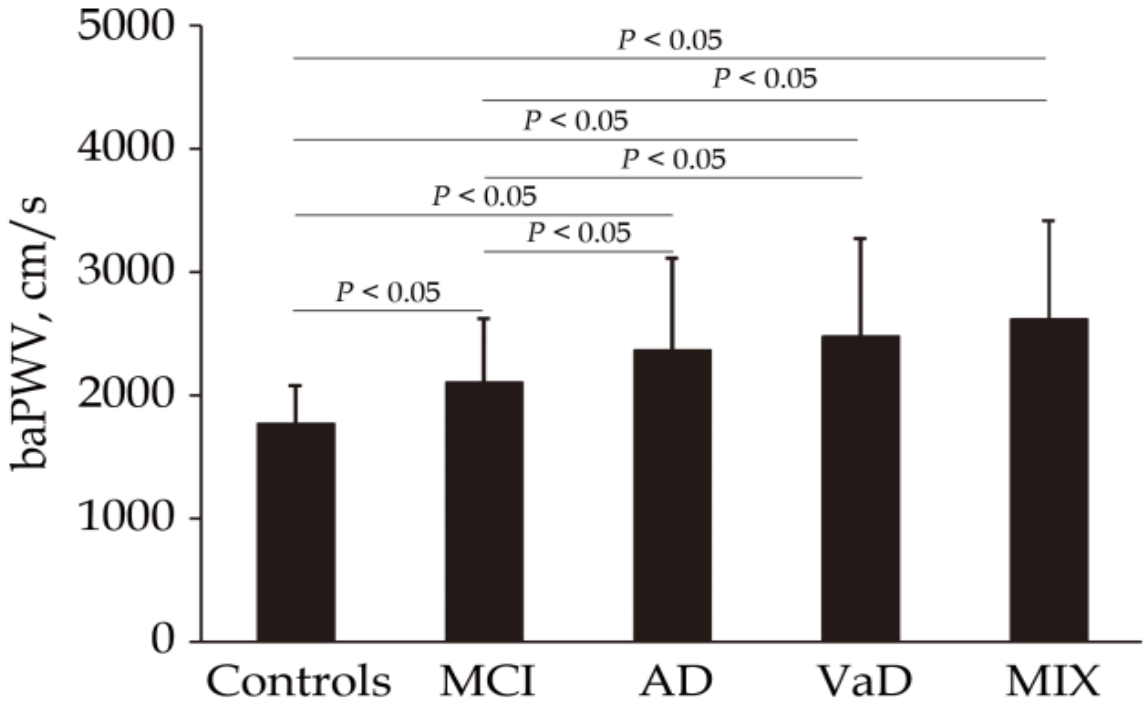
Relationship between PWV and cognitive status (normal cognitive function

Our results showed a relationship between arterial stiffness and cognitive impairment, suggesting that functional changes of the arterial system could be involved in the onset of dementia (VaD or AD types)

•. 2005 Oct;36(10):2193-7

Journal of Geriatric Cardiology | JGC
RESEARCH ARTICLE
J Geriatr Cardiol 2022; 19(8): 594–602

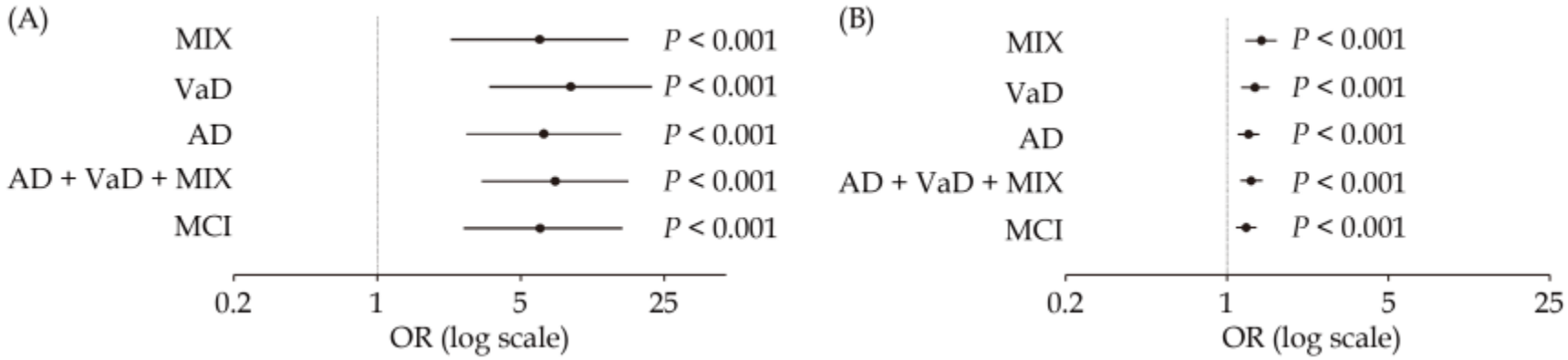
Relationship between arterial stiffness and cognitive function in outpatients with dementia and mild cognitive impairment compared with community residents without dementia



The baPWV values of Controls, MCI, AD, VaD and MIX patients.
AD: Alzheimer's disease; MCI: mild cognitive impairment; MIX: mixed dementia; VaD: vascular dementia

Journal of Geriatric Cardiology | JGC
RESEARCH ARTICLE
J Geriatr Cardiol 2022; 19(8): 594–602

Relationship between arterial stiffness and cognitive function in outpatients with dementia and mild cognitive impairment compared with community residents without dementia



the baPWV value to predict the presence of dementia.

The ORs are expressed as higher baPWV value (A) and per 1 m/s increase (B) in baPWV after adjustment for age gender, diabetes mellitus, hyperlipidemia, hypertension and smoking status

Albuminuria as a marker of arterial stiffness in chronic kidney disease patients

Rigas G Kalaitzidis, Despina P Karasavvidou, Athina Tatsioni, Kosmas Pappas, Giorgos Katatsis, Angelos Liontos, Moses S Elisaf

Table 4 Multivariate linear regression analysis of the parameters associated with the absolute values of pulse wave velocity

Covariates	β	*t*	β (95%CI)	*P* value
UAlb	1.038	2.638	0.257-1.820	< 0.010
pSBP	0.028	2.149	0.002-0.053	< 0.034
Ht	0.171	3.319	0.069-0.273	< 0.001

pSBP: Peripheral systolic blood pressure; Ht: Haematocrit.

World J Nephrol 205 July 6; 4(3): 00-00

Arterial damage and cognitive decline in chronic kidney disease patients

Despina Karasavvidou MD, PhD[1] | Pierre Boutouyrie MD[2] | Rigas Kalaitzidis MD[3] | Hakim Kettab MD[2] | Kosmas Pappas MD[3] | Dimitrios Stagikas MD[3] | Nikolaos Antonakis PhD[1] | Dimitrios Tsalikakis PhD[2] | Moses Elisaf MD[3] | Stephane Laurent MD[4]

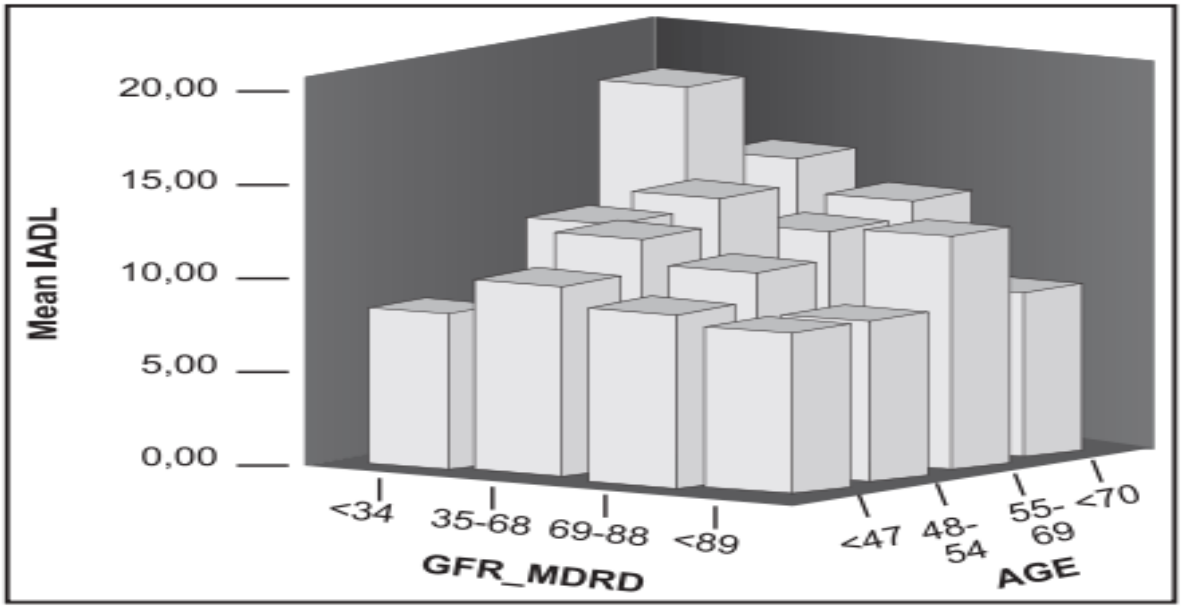
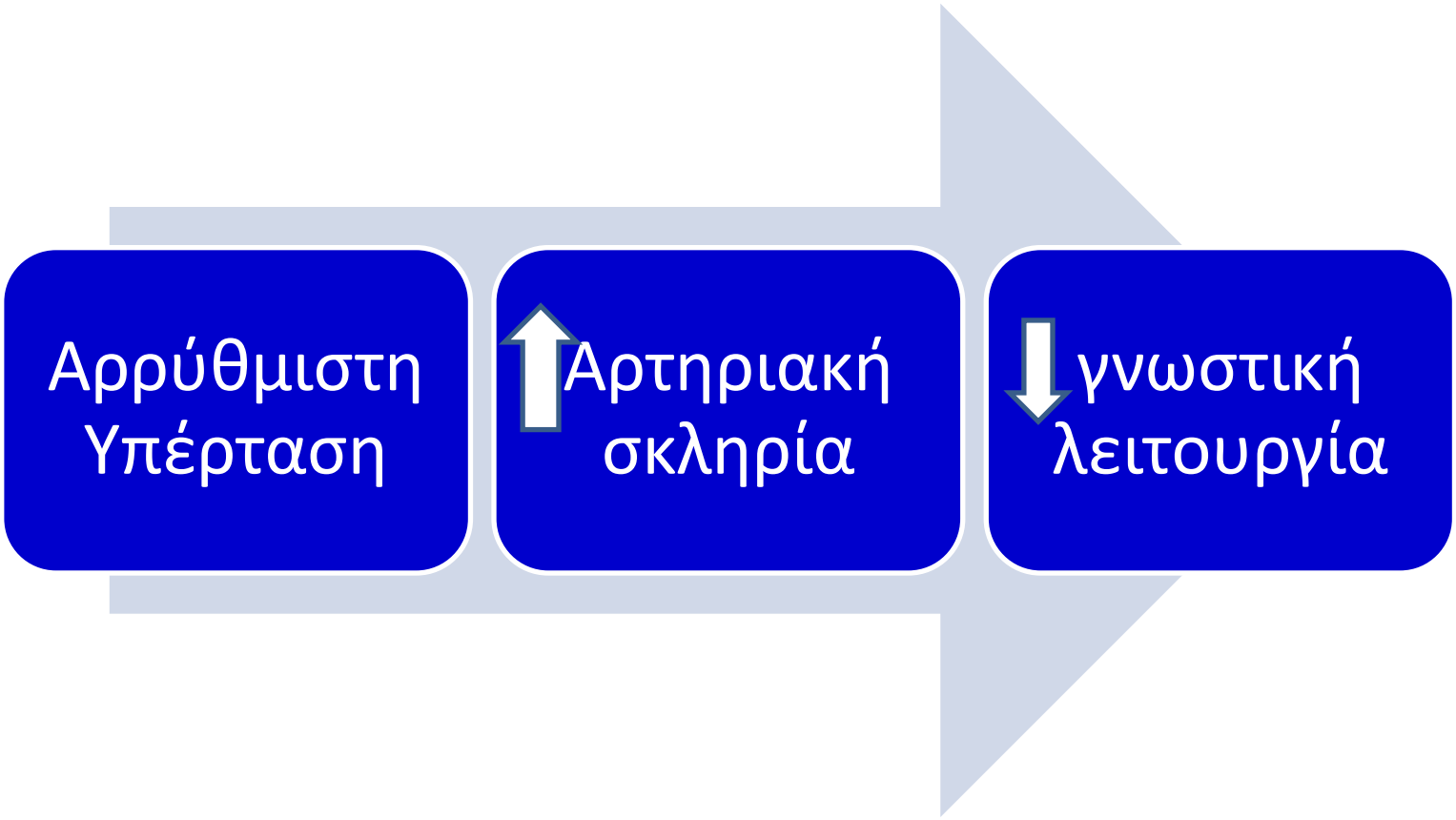


FIGURE 2 3D plot showing the interaction of IADL, GFR-MDRD, and age. IADL, Instrumental activity of daily living; GFR-MDRD, glomerular filtration rate -modification of diet in renal disease

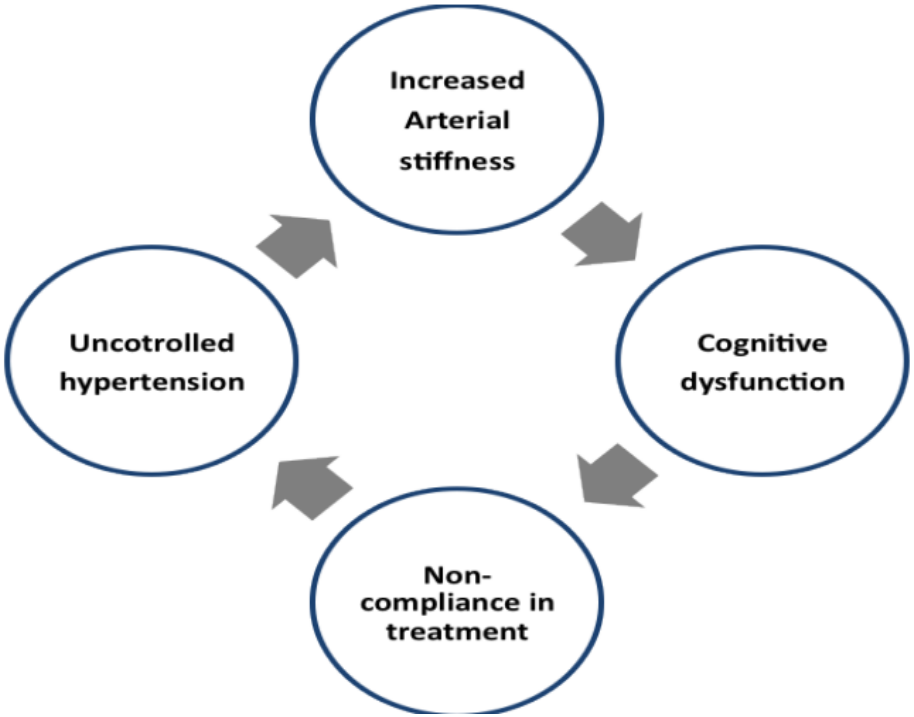
In CKD patients cognitive function was profoundly altered in parallel with the severity of CKD. High levels **of arterial stiffness indices**, either directly measured as cf-PWV or indirectly estimated as **aortic PP**, were correlated with MMSE, an index of cognitive decline.

J Clin Hypertens. 2018;1–9


Αρρύθμιστη Υπέρταση
Αρτηριακή σκληρία
γνωστική λειτουργία

Arterial Stiffness, Cognitive Dysfunction, and Adherence to Antihypertensive Agents. Is there a Link to Hypertensive Patients?

Rigas G Kalaitzidis[1,*], Thalia Panagiotopoulou[2], Dimitrios Stagikas[2], Kosmas Pappas[2], Olga Balafa[1] and Moses S Elisaf[2]



Relationship between uncontrolled hypertension, arterial stiffness, cognitive dysfunction and noncompliance with treatment

Adherence to Treatment, Arterial Stiffness and Cognitive Function in Irbesartan-Treated Newly Diagnosed Hypertensive Patients

Rigas G. Kalaitzidis[1,*], Olga Balafa[1], Evangelia Dounousi[1], Dimitrios Stagikas[1] and Vasilios Tsimihodimos[1]

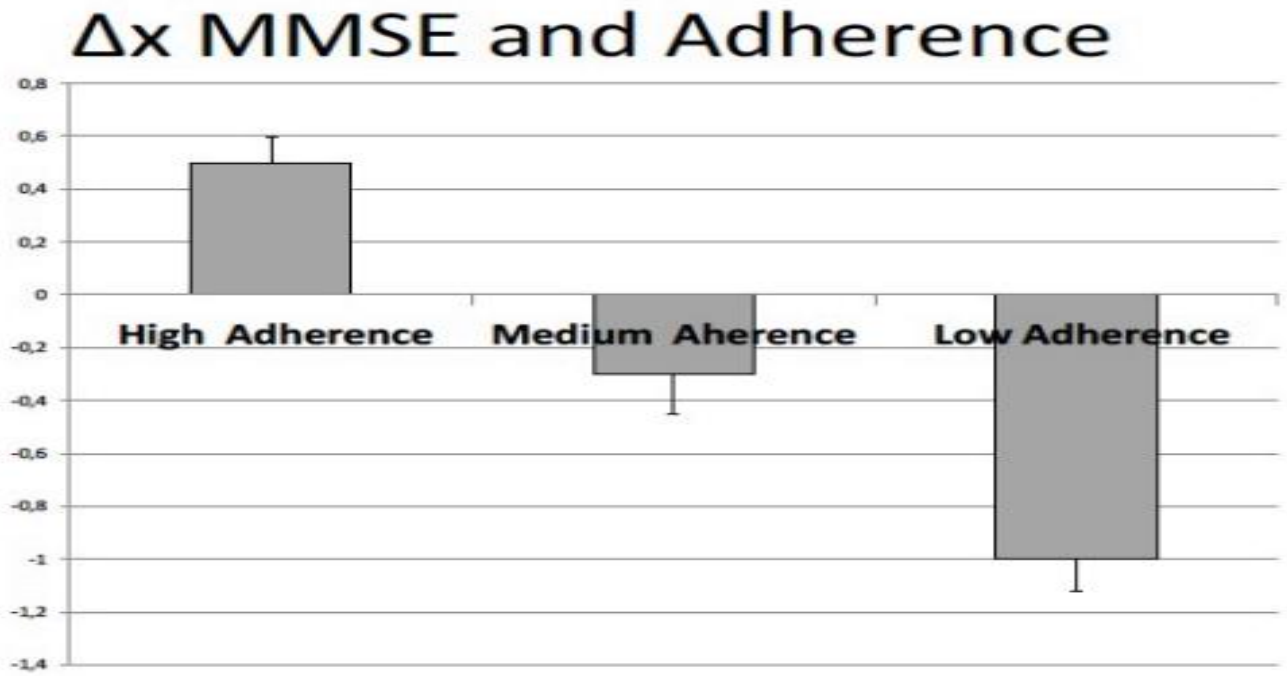
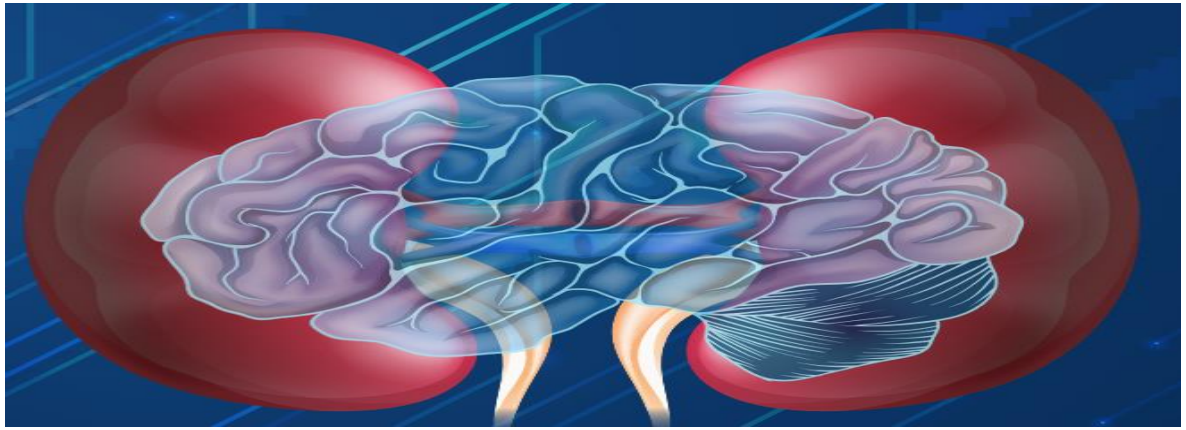


Fig. (1). MMSE and Adherence. MMSE test: Mini Mental State Examination test, Δx: Change in MMSE test before and after the treatment with irbesartan.



PATHOPHYSIOLOGIC MECHANISMS

Small vessel disease of the brain

The small vessels of the brain are unique as their cells receive continuous high-volume flow throughout systole and diastole against VERY LOW VASCULAR RESISTANCE.

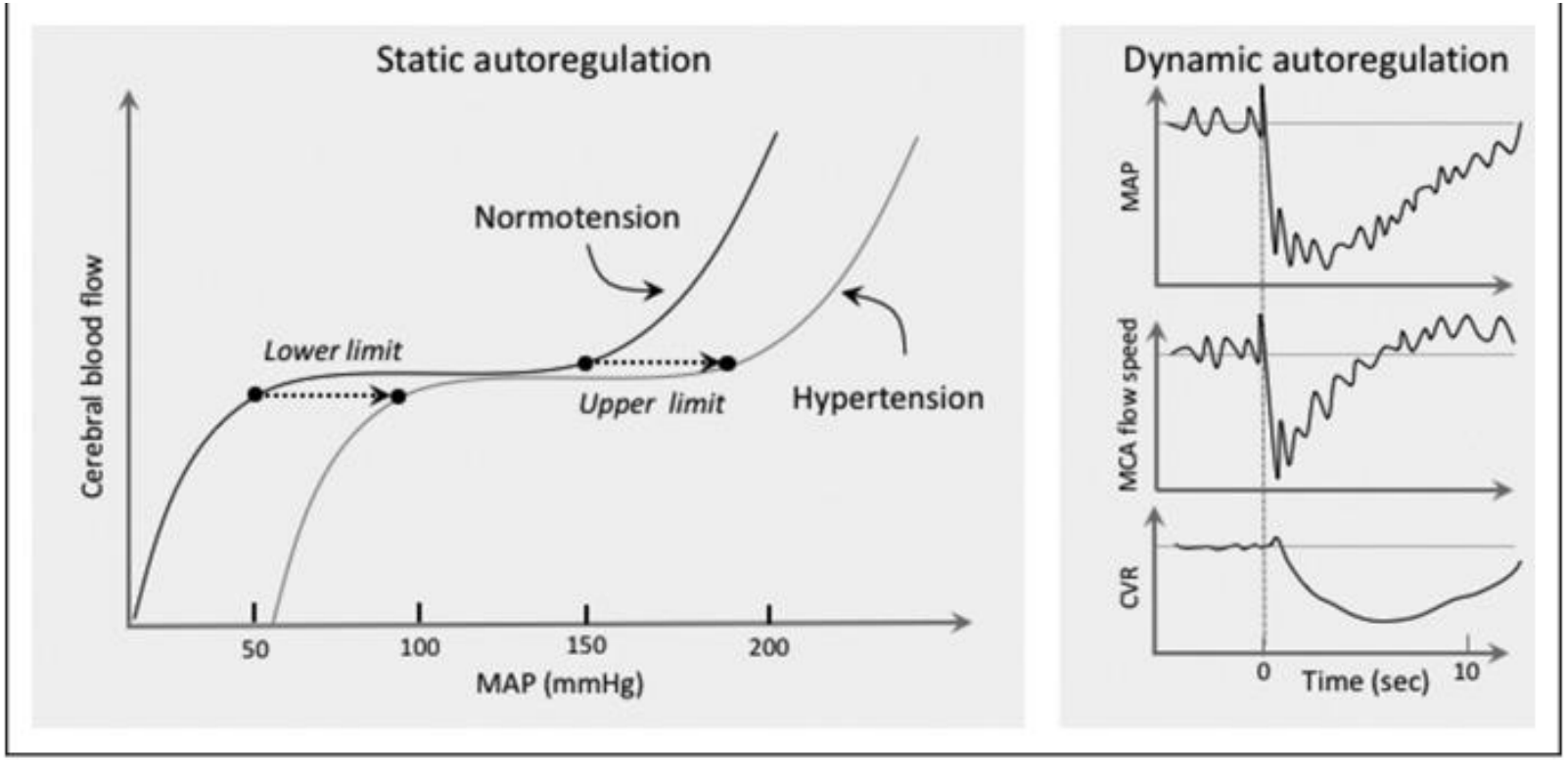
Given the particular anatomy and physiology of small vessel circulation, **brain tissue are susceptible to the microvascular insults** in response to aging and exposure to vascular risk factors

Are more prone to developing what is commonly referred as SVD

Stroke. (2009) 40:e322–30. doi: 10.1161/STROKEAHA.108.54 2266

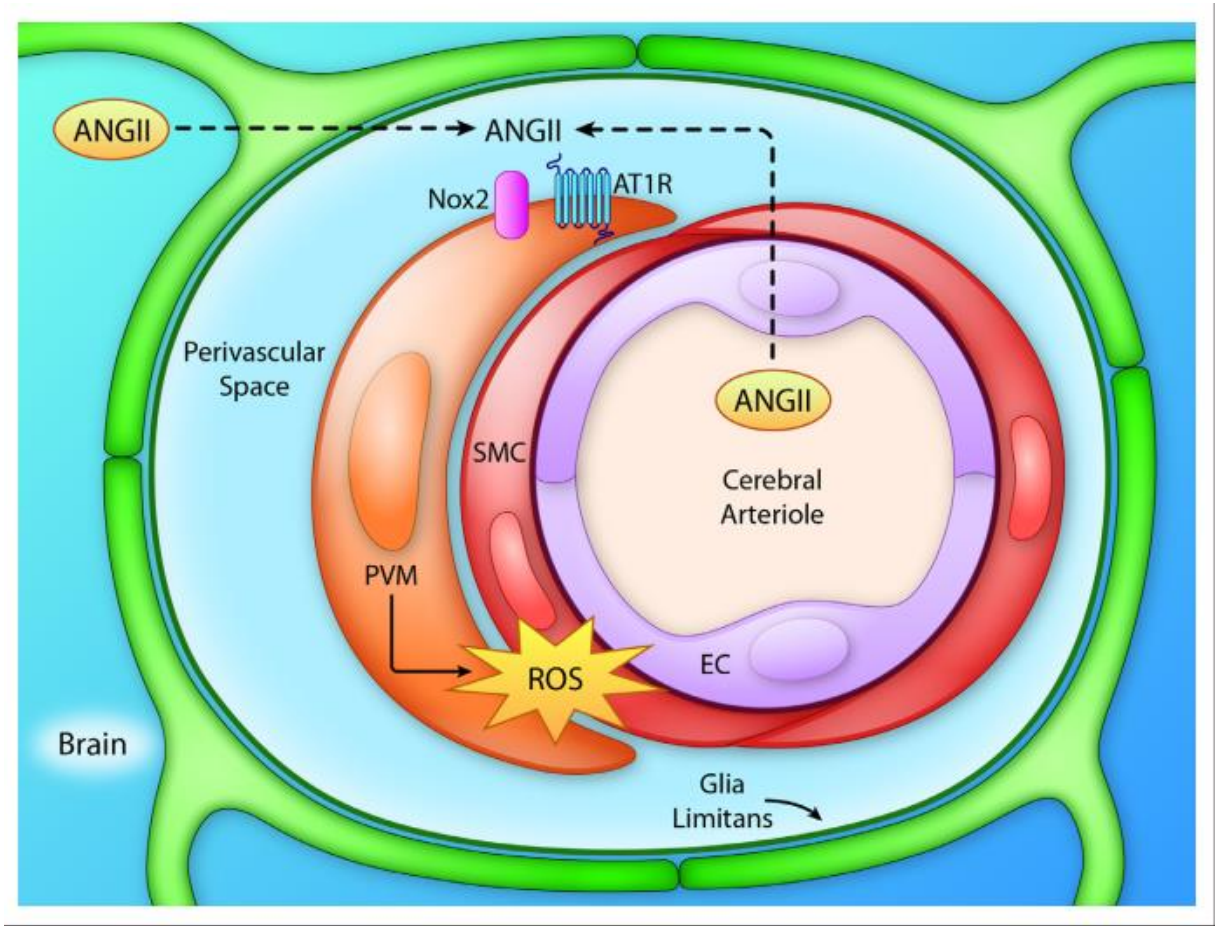
Cardiol Res Pract 2011: 306189, 2011)]

Cerebrovascular autoregulation and hypertension



Circ Res. 2019;124:1025-1044

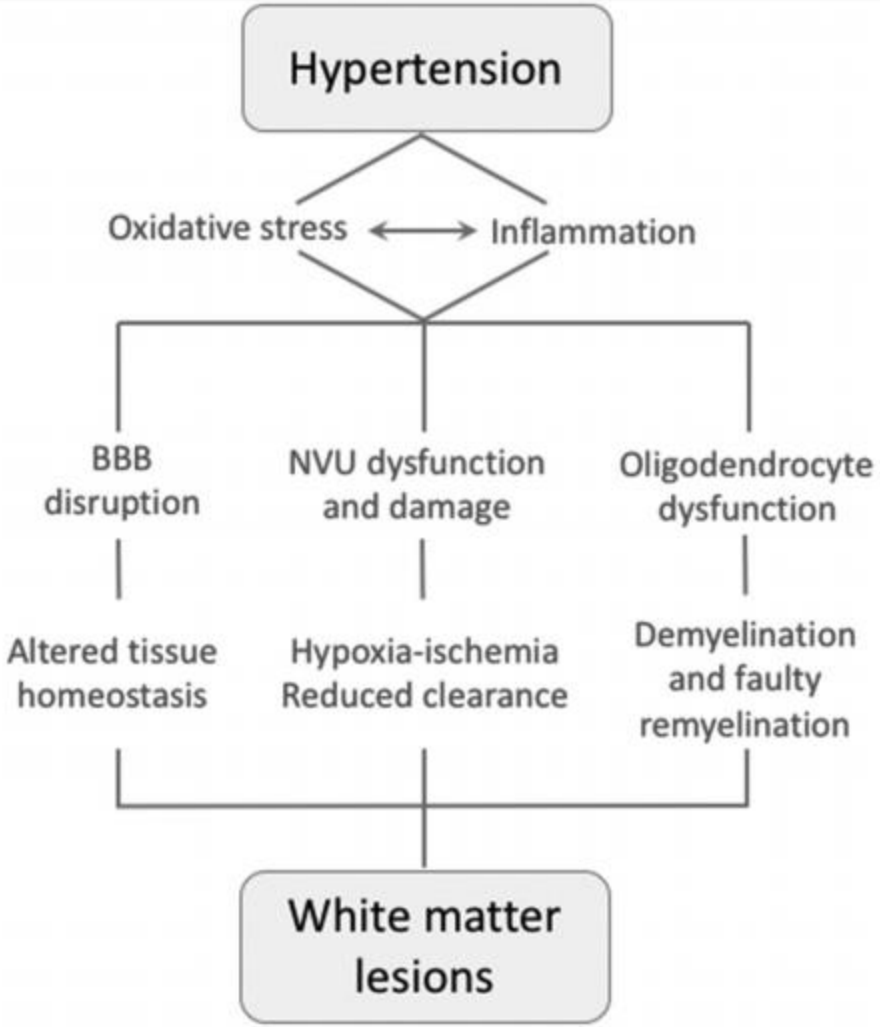
Putative mechanisms of neurovascular dysfunction in slow-pressor Ang II ,hypertension, BPH mice and deoxycorticosterone acetate+salt hypertension.



Circulating or brain Ang II reaches AT1R (angiotensin type-1 receptor) in perivascular macrophage (PVM)wherein it activates NOX2 leading the vascular oxidative stress and neurovascular dysfunction. AT1R and Nox2 are also present in other vascular cells, butthey do not seem to play a primary role in these hypertension models.

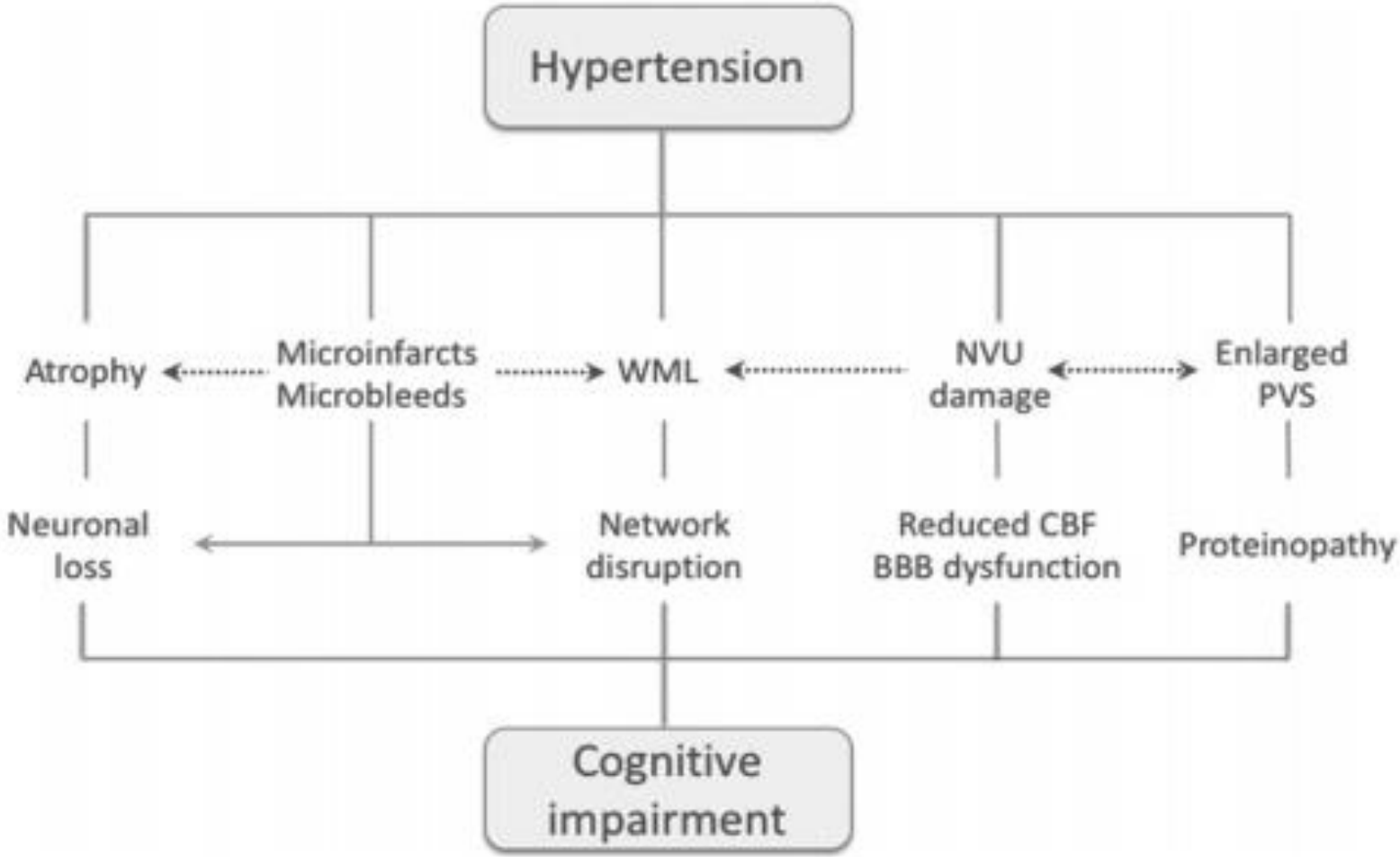
***Circ Res*. 2019;124:1025-1044**

Potential mechanisms of white matter (WM) damage by hypertension



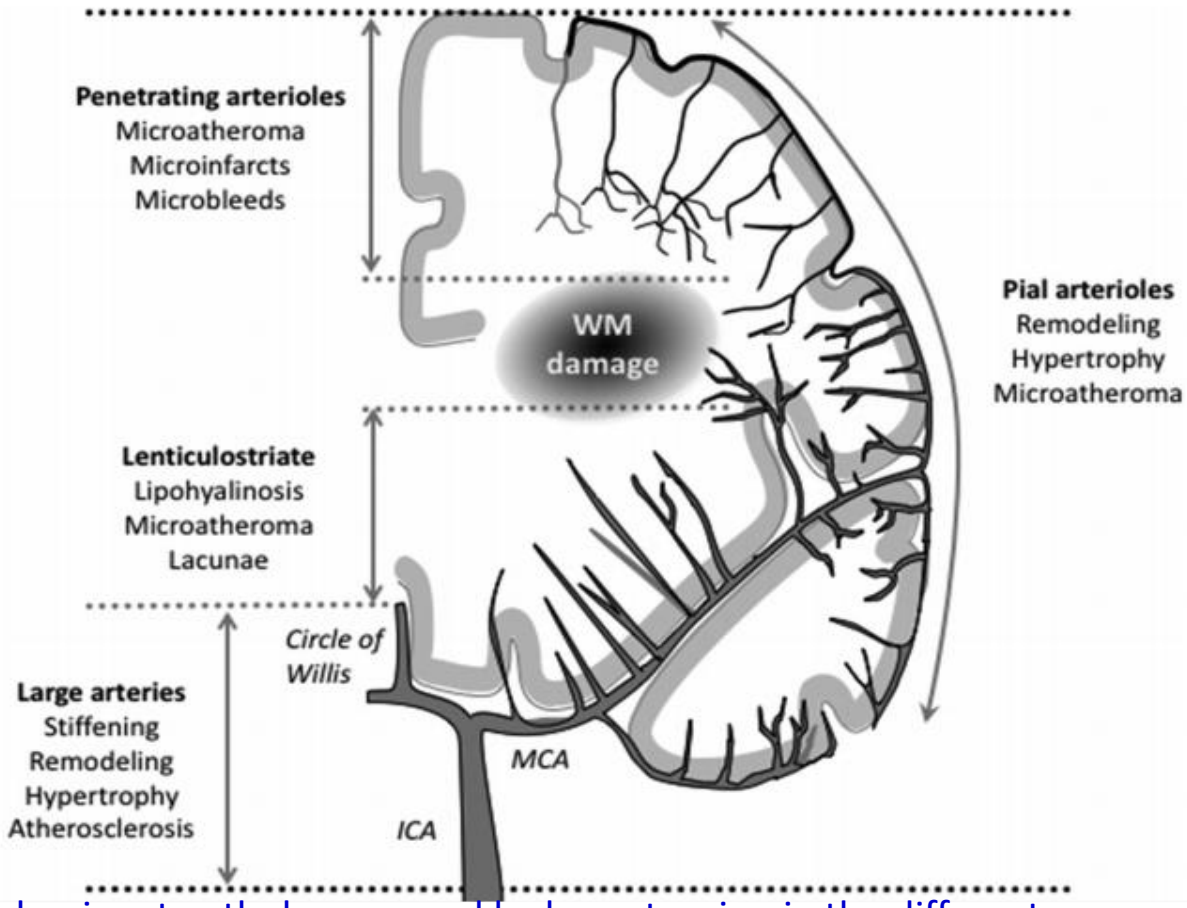
***Circ Res*. 2019;124:1025-1044**

Brain lesions produced by hypertension that underlie cognitive impairment



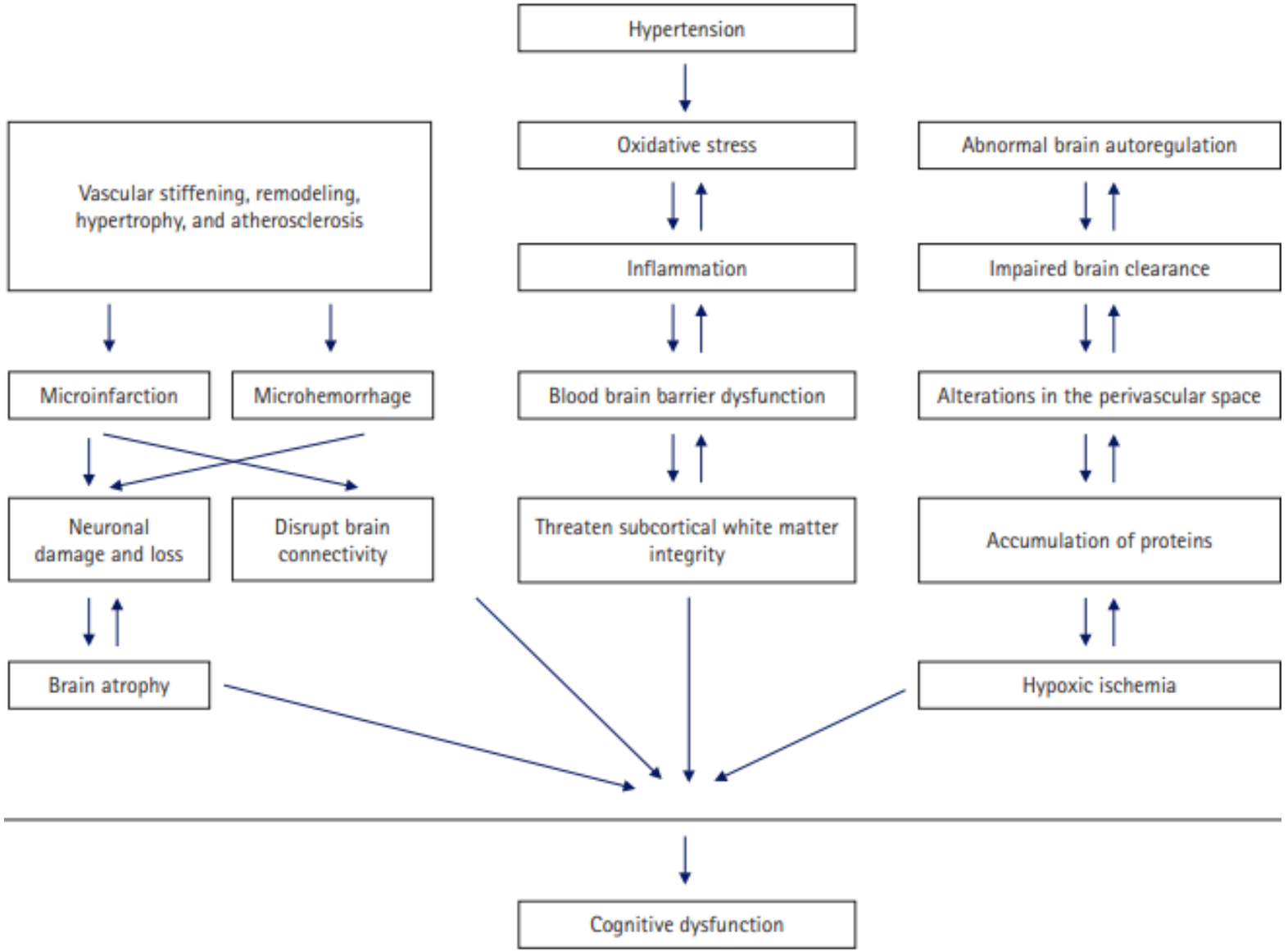
Circ Res. 2019;124:1025-1044

Cerebrovascular anatomy and segmental pathology induced by hypertension



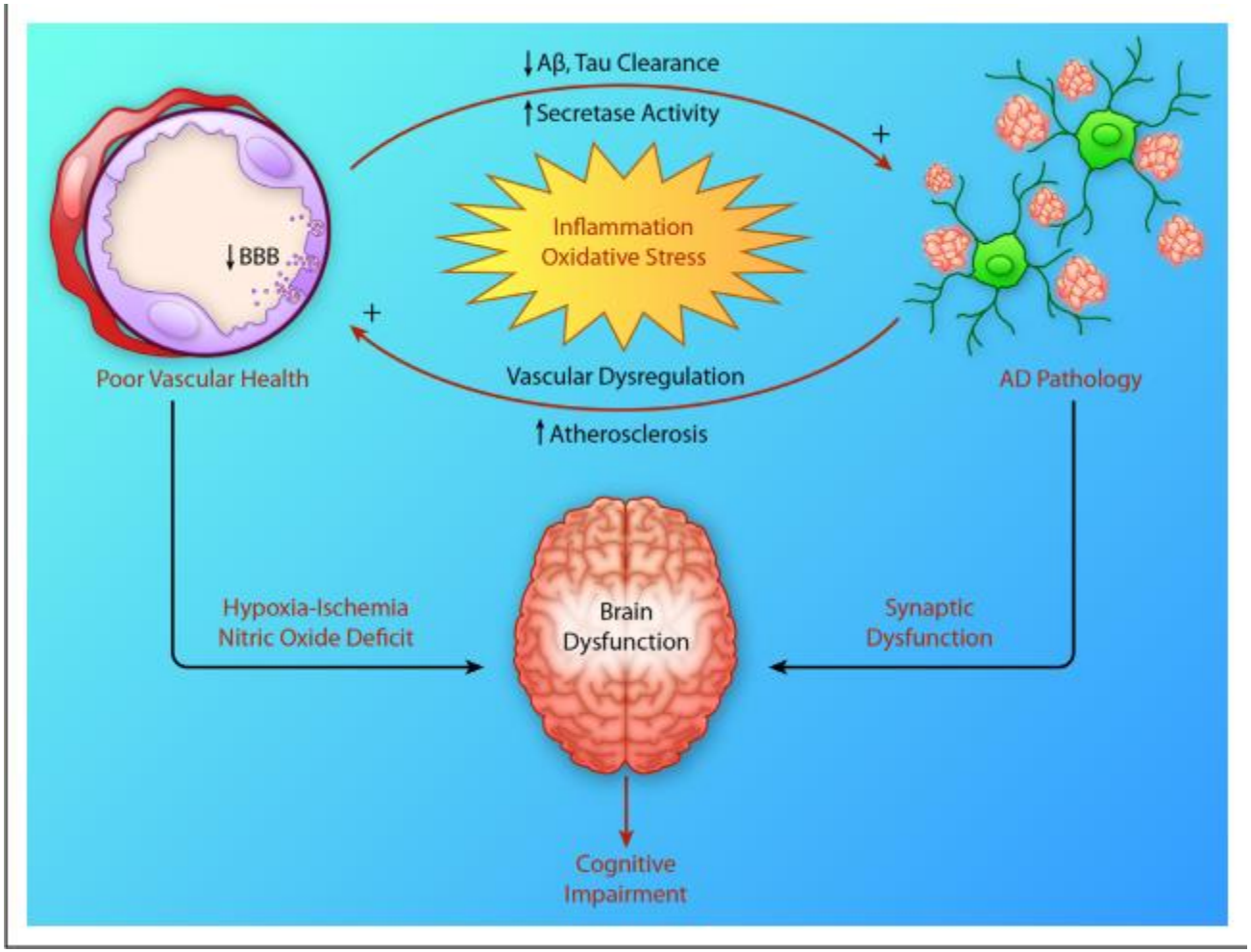
The predominant pathology caused by hypertension in the different segment of the cerebrovascular tree is indicated. Because of its precarious blood supply **from terminal arterioles** particularly vulnerable to hypertensive damage, the subcortical WM is highly likely to be harmed by hypoxia-ischemia. ICA indicates internal carotid artery; and MCA, middle cerebral artery.

***Circ Res*. 2019;124:1025-1044**



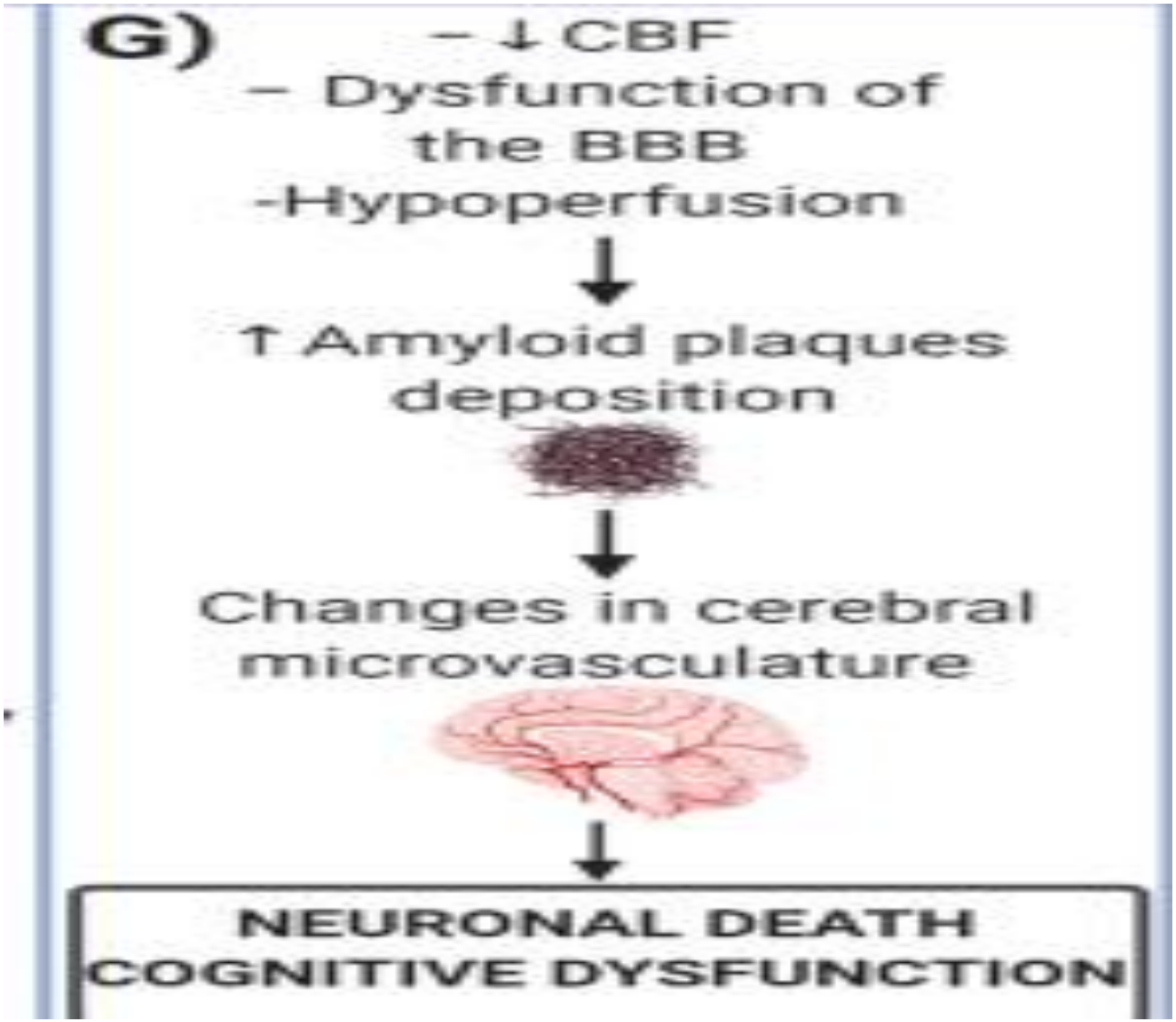
J Yeungnam Med Sci 2023;40(3):225-232

Potential mechanisms underlying the relationship between hypertension and **Alzheimer disease**

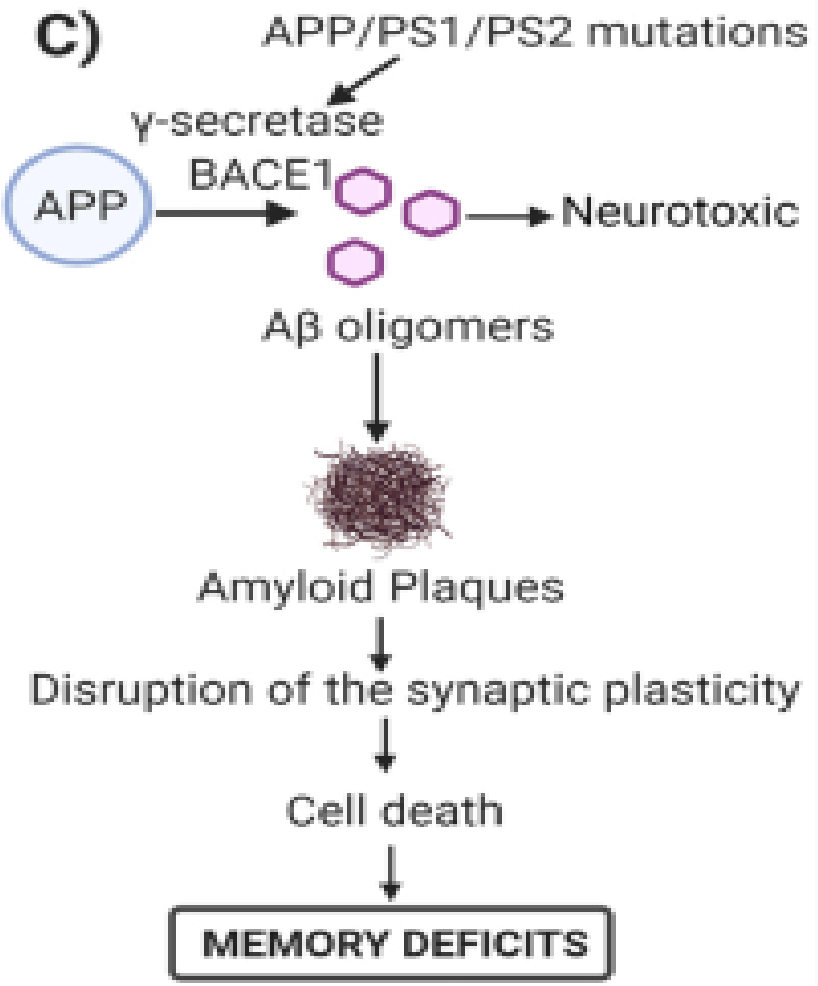


***Circ Res*. 2019;124:1025-1044**

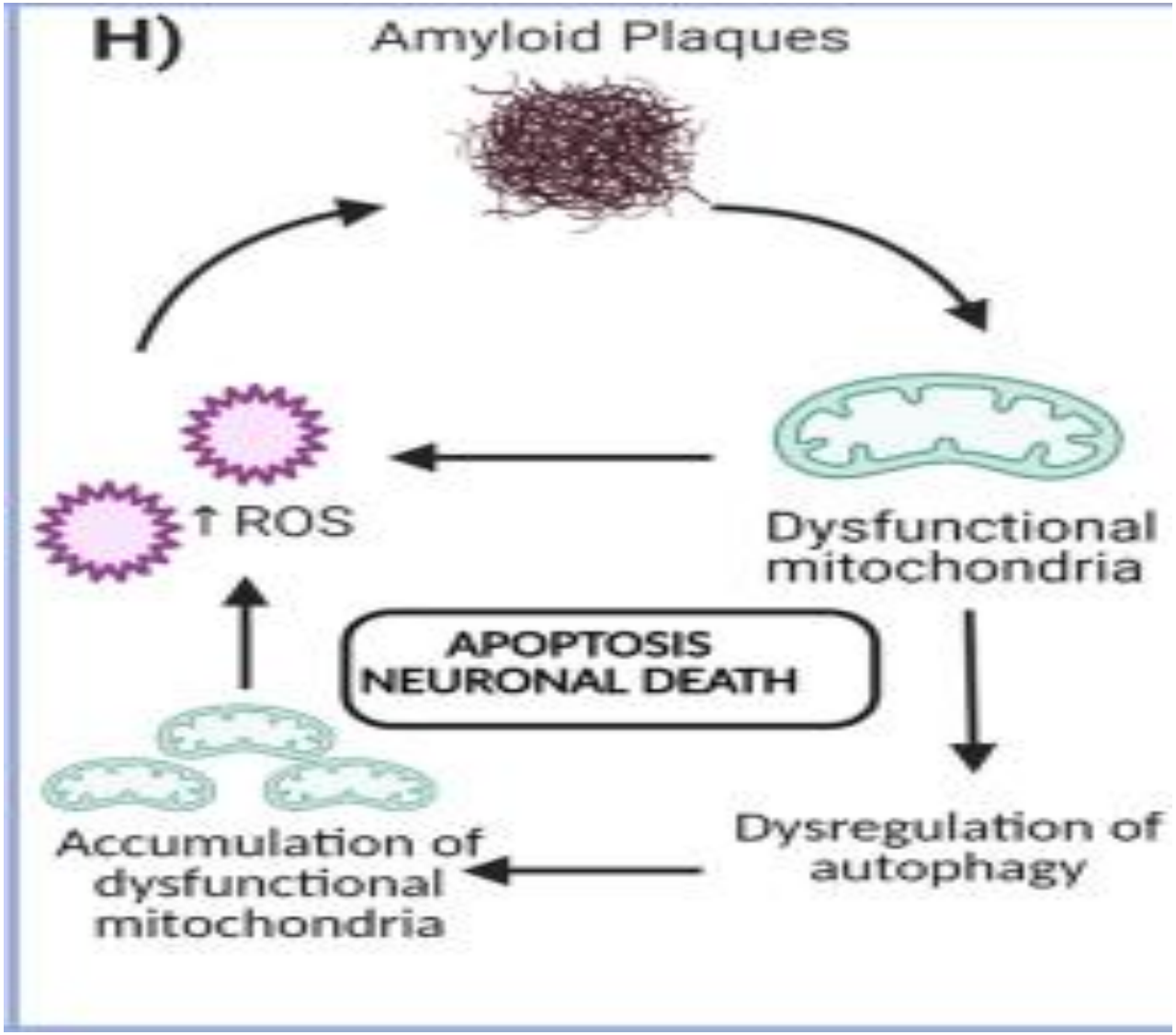
Vascular hypothesis



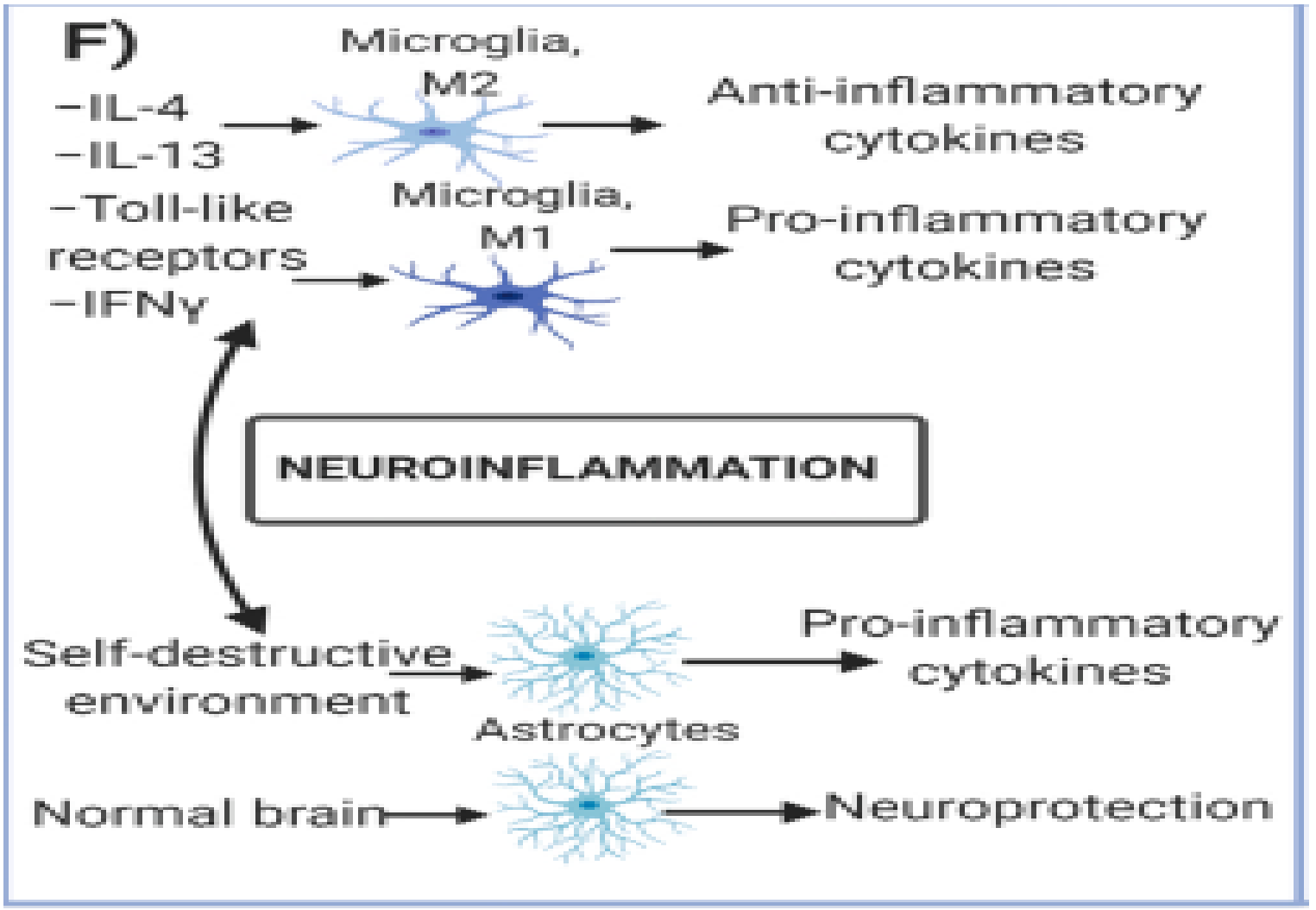
Amyloid hypothesis;



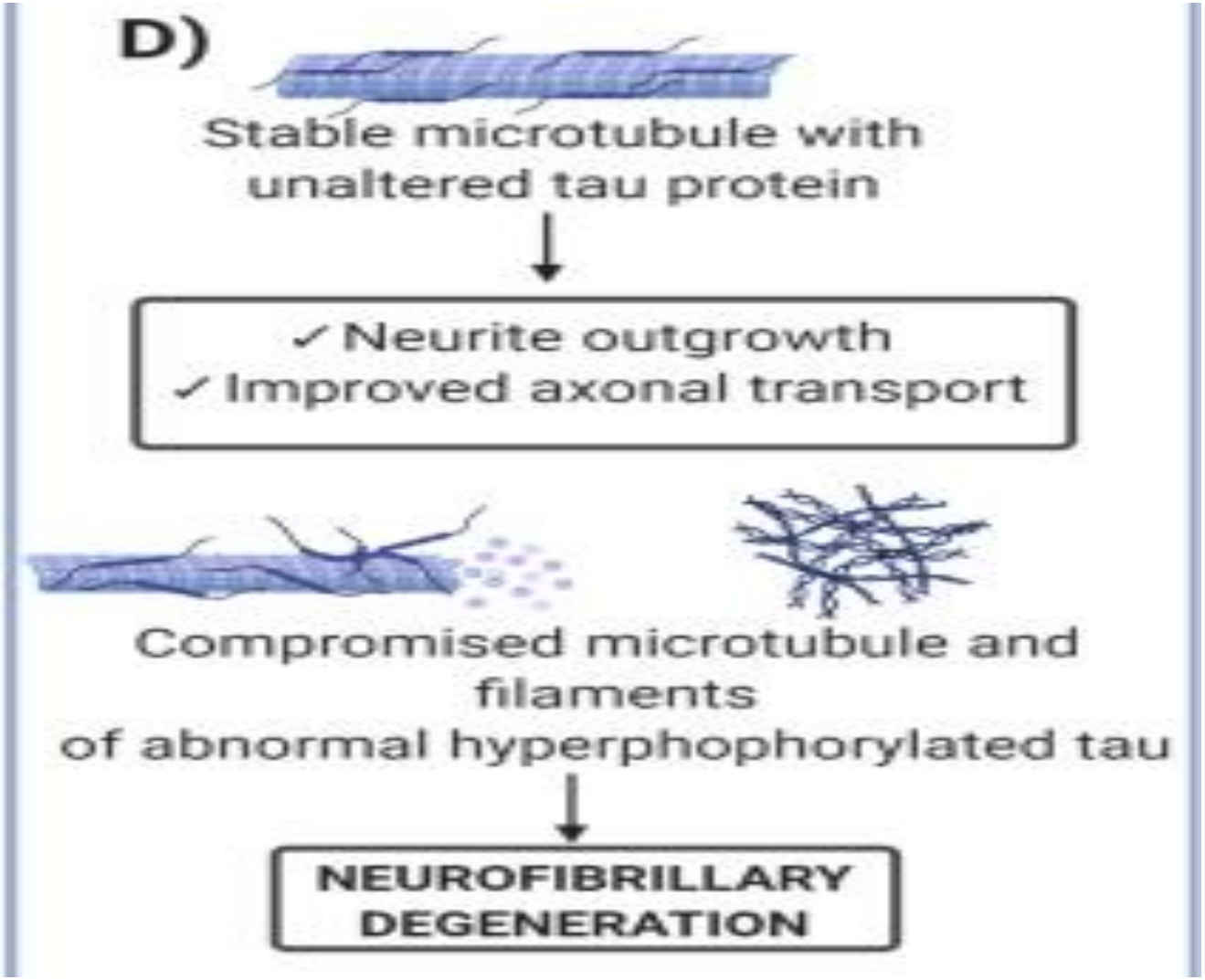
H) Mitochondrial hypothesis.



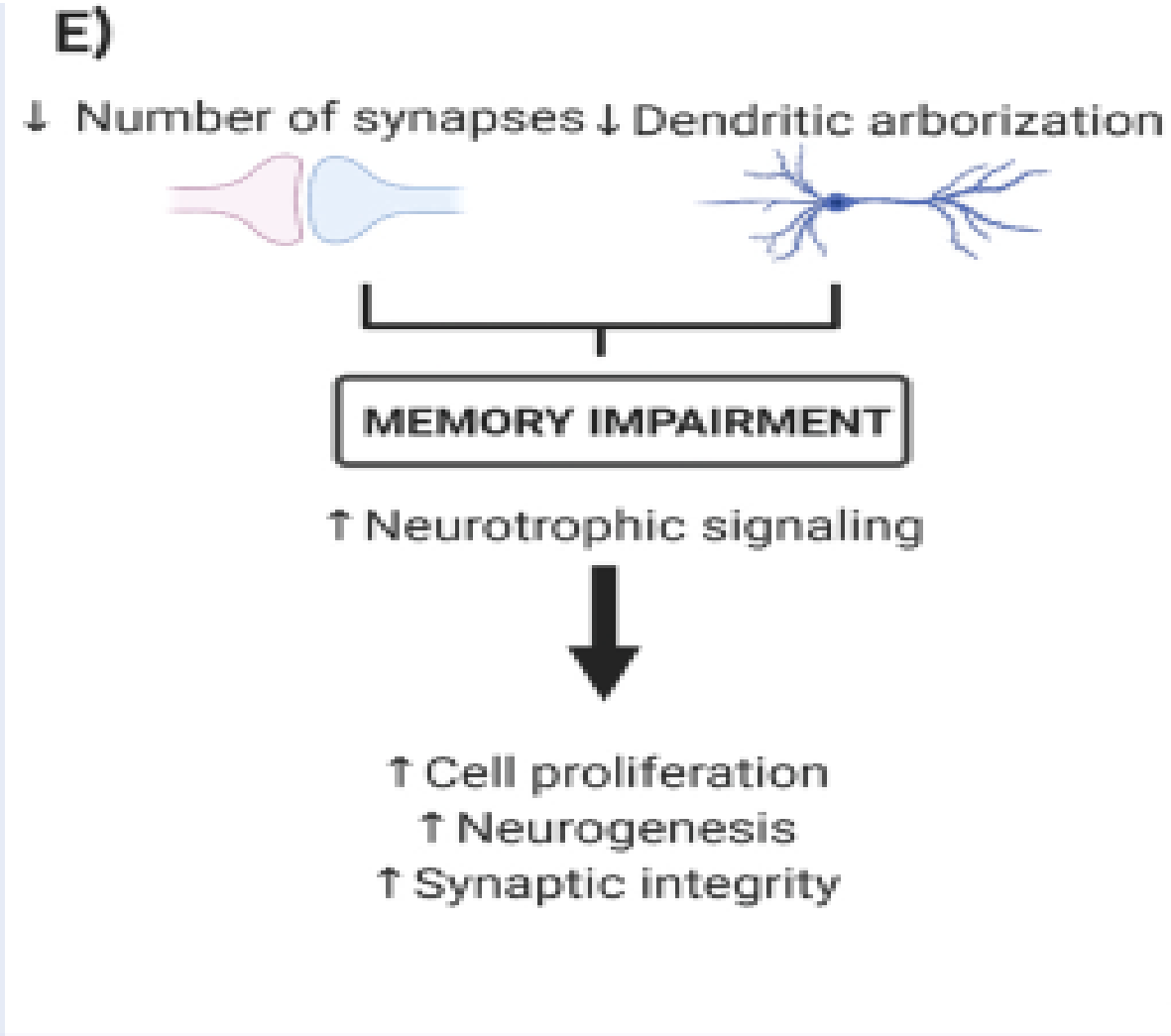
Neuroinflammation hypothesis;



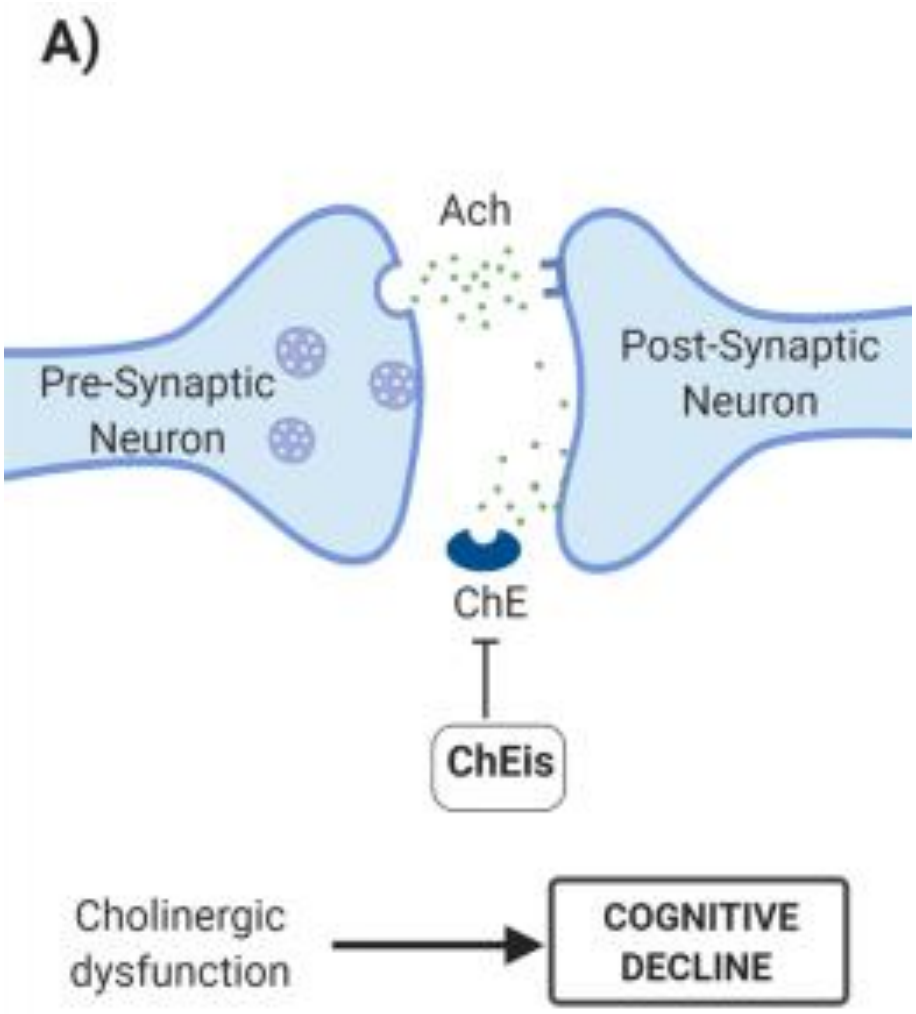
Tau hypothesis



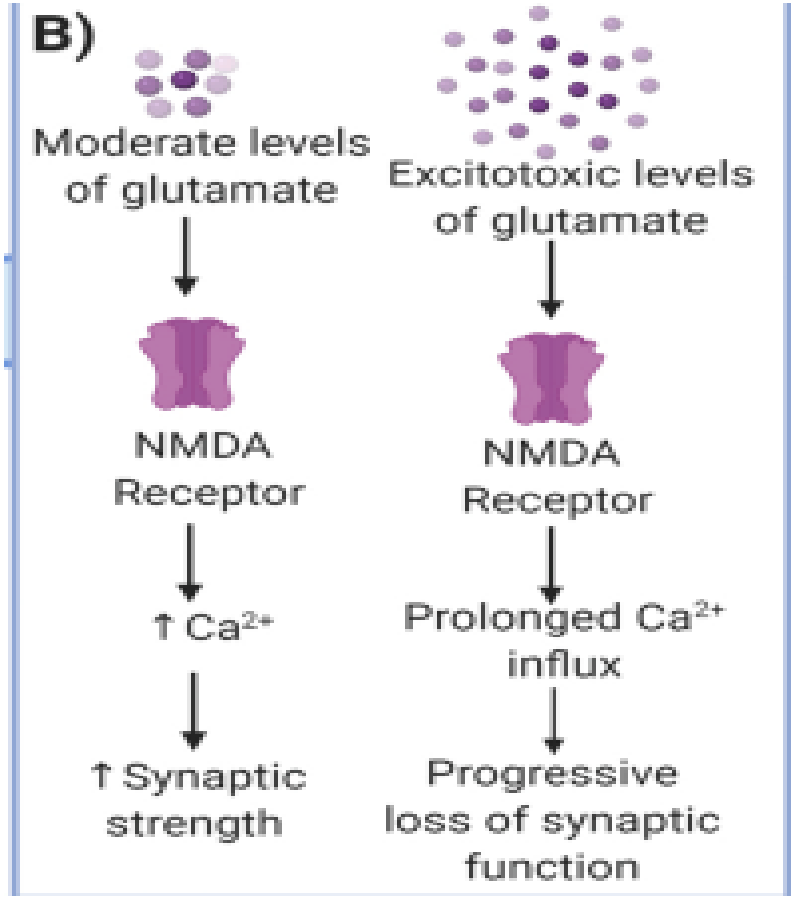
Synaptic dysfunction hypothesis;

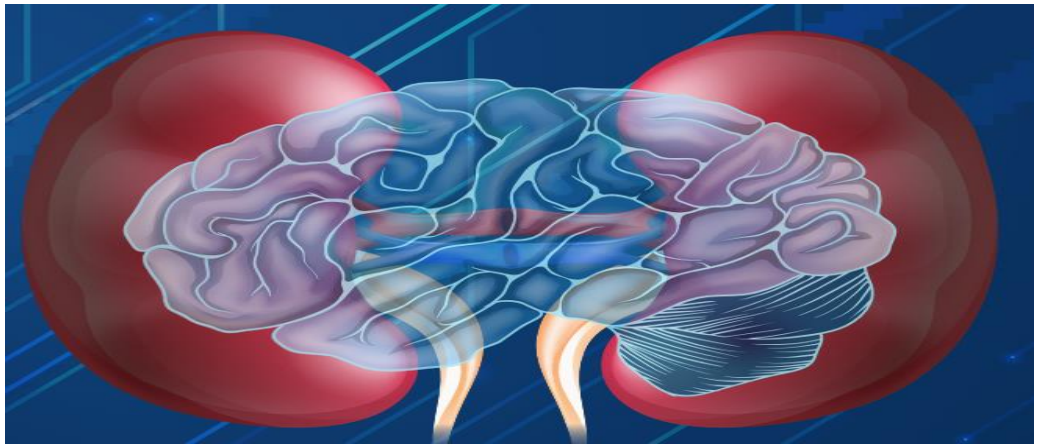


Cholinergic hypothesis;



Glutaminergic hypothesis;

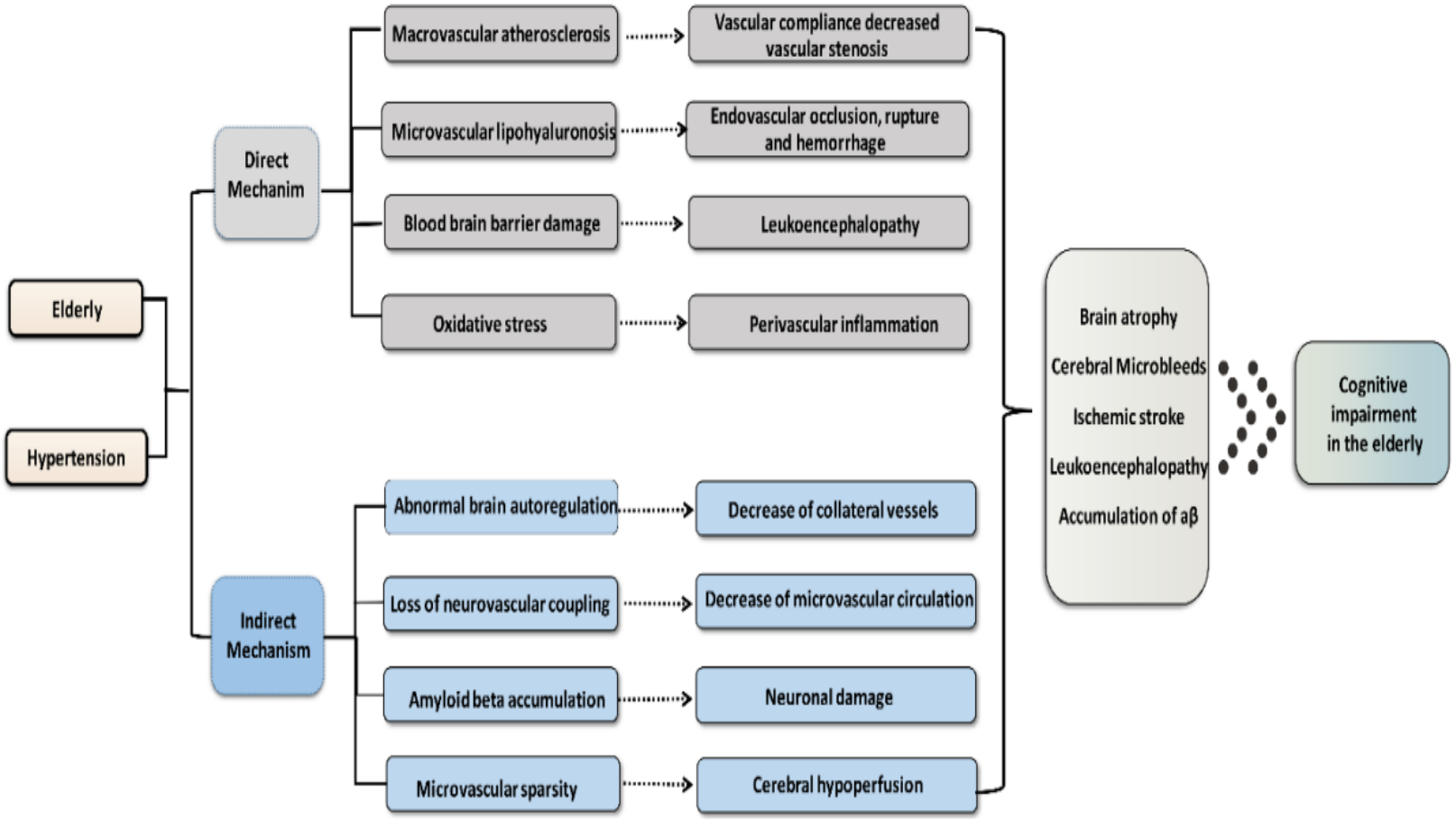




Ο έλεγχος της ΑΠ βελτιώνει την γνωστική δυσλειτουργία?

Effects of Antihypertensive Drugs on Cognitive Function in Elderly Patients with Hypertension: A Review

Wei Yang*, Hongyu Luo, Yixin Ma, Sicong Si, Huan Zhao



The underlying mechanism of cognitive impairment caused by hypertension in the elderly

Blood pressure-lowering treatment for preventing recurrent stroke, major vascular events, and dementia in patients with a history of stroke or transient ischaemic attack (Review)

Zonneveld TP, Richard E, Vergouwen MDI, Nederkoorn PJ, de Haan RJ, Roos YBWEM, Kruyt ND

Death by any cause	35,110 (8 RCTs)	⊕⊕⊕⊖ Moderate[a]	RR 0.98 (0.91 to 1.05)	Study population	
				79 per 1000	2 fewer per 1000 (7 fewer to 4 more)
Dementia	6671 (2 RCTs)	⊕⊕⊕⊕ High	RR 0.88 (0.73 to 1.06)	Study population	
				67 per 1000	8 fewer per 1000 (18 fewer to 4 more)

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

BPLDs: blood pressure-lowering drugs; **CI:** confidence interval; **HR**: hazard ratio; **RCT**: randomised controlled trial; **RR:** risk ratio.

Cochrane Database of Systematic Reviews
2018, Issue 7. Art. No.: CD007858

Reducing the Risk of Dementia
Efficacy of Long-Term Treatment of Hypertension

Rita Peila, PhD; Lon R. White, MD, MPH; Kamal Masaki, MD;
Helen Petrovitch, MD; Lenore J. Launer, PhD

Duration of Treatment With Antihypertensive Medications and Yearly Cognitive Function

	Midlife Hypertensives' Treatment History				
		Years			
	Never	0–5	5–12	>12	Normotensives
No.	121	171	138	342	414
Initial CASI score	83.05	82.86	82.56	83.03	81.58
CASI change/y	−1.46*‡	−1.22	−1.14†	−1.08	−1.01†

The untreated hypertensive group is the reference group for the analysis. **P* value <0.01 compared to a slope=0; †*P* value <0.05 compared to the reference group. The analysis was adjusted for age and age squared at baseline, education, *APOE* ε4 status, midlife (mean of exam 1, 2 and 3) and late-life (exam 4) blood pressure and smoking status.

The longer the duration of antihypertensive medication use, the significantly lower the risk for dementia

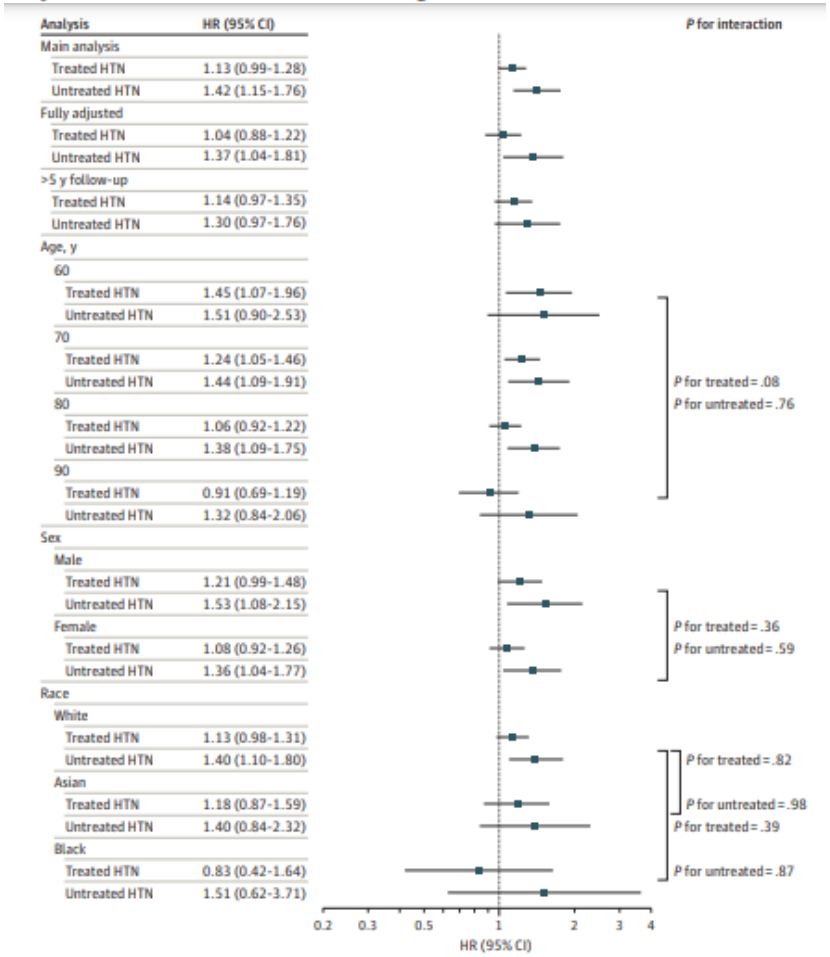
Results suggest that in hypertensive men, the duration of the antihypertensive treatment is associated with a reduced risk for dementia and cognitive decline

***Stroke*. 2006;37:1165-1170.**

Original Investigation | Geriatrics

Use of Antihypertensives, Blood Pressure, and Estimated Risk of Dementia in Late Life

An Individual Participant Data Meta-Analysis



Association of Hypertension (HTN) and Antihypertensive Status With the Risk of All-Cause Dementia

This individual patient data meta-analysis of longitudinal cohort studies found **that antihypertensive use was associated with decreased dementia risk** compared with individuals with untreated hypertension through all ages in late life. Individuals with treated hypertension had no increased risk of dementia compared with healthy controls.

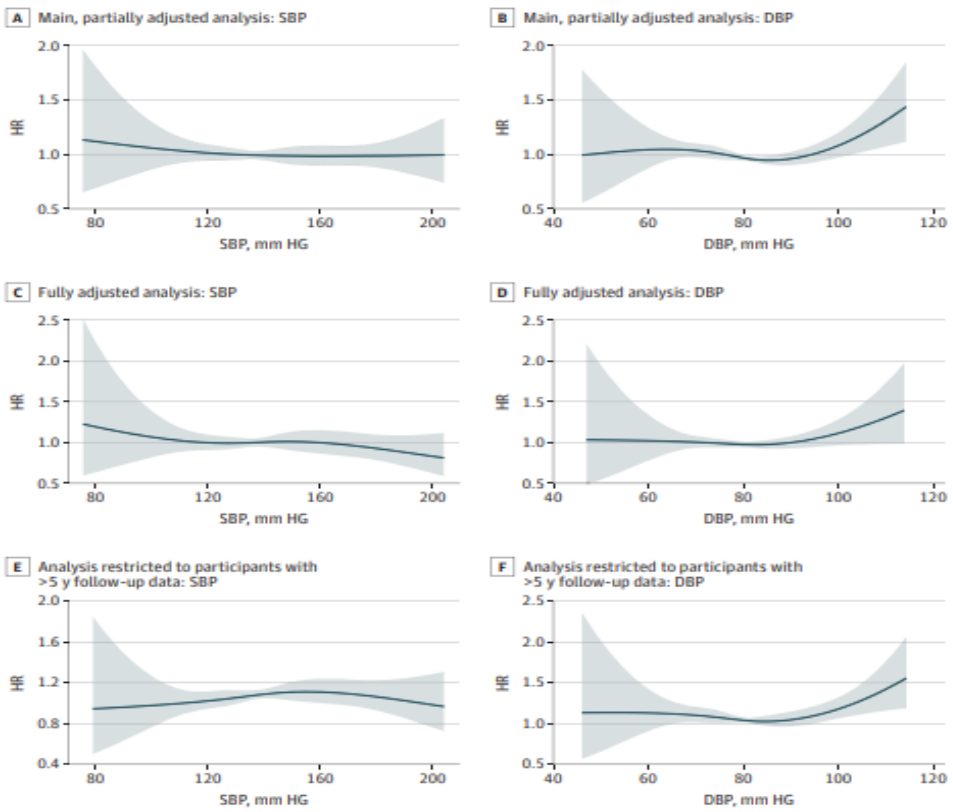
JAMA Network Open. 2023;6(9):e2333353

Original Investigation | Geriatrics

Use of Antihypertensives, Blood Pressure, and Estimated Risk of Dementia in Late Life

An Individual Participant Data Meta-Analysis

The Associations of Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) With Dementia Risk



A SINGLE MEASURE OF SBP OR DBP AT BASELINE HAD NO SIGNIFICANT ASSOCIATION with latelife dementia risk, and, corroborating extant hypertension guidelines,46 it seems that more than 1 measure is needed to inform treatment

JAMA Network Open. 2023;6(9):e2333353

Original Investigation | Geriatrics

Use of Antihypertensives, Blood Pressure, and Estimated Risk of Dementia in Late Life

An Individual Participant Data Meta-Analysis

Dementia risk reduction may be 1 of the multiple goals of antihypertensive treatment in late-life (eg, prevention of ischemic heart disease, chronic kidney disease).

This individual patient data meta-analysis of longitudinal cohort studies found that antihypertensive use was associated with decreased dementia risk compared with individuals with untreated hypertension through all ages in late life. Individuals with treated hypertension had no increased risk of dementia compared with healthy controls.

JAMA Network Open. 2023;6(9):e2333353


Ευχαριστώ