ΕΠΙΣΤΗΜΟΝΙΚΗ ΗΜΕΡΙΔΑ

Εγκέφαλος και Νεφρός

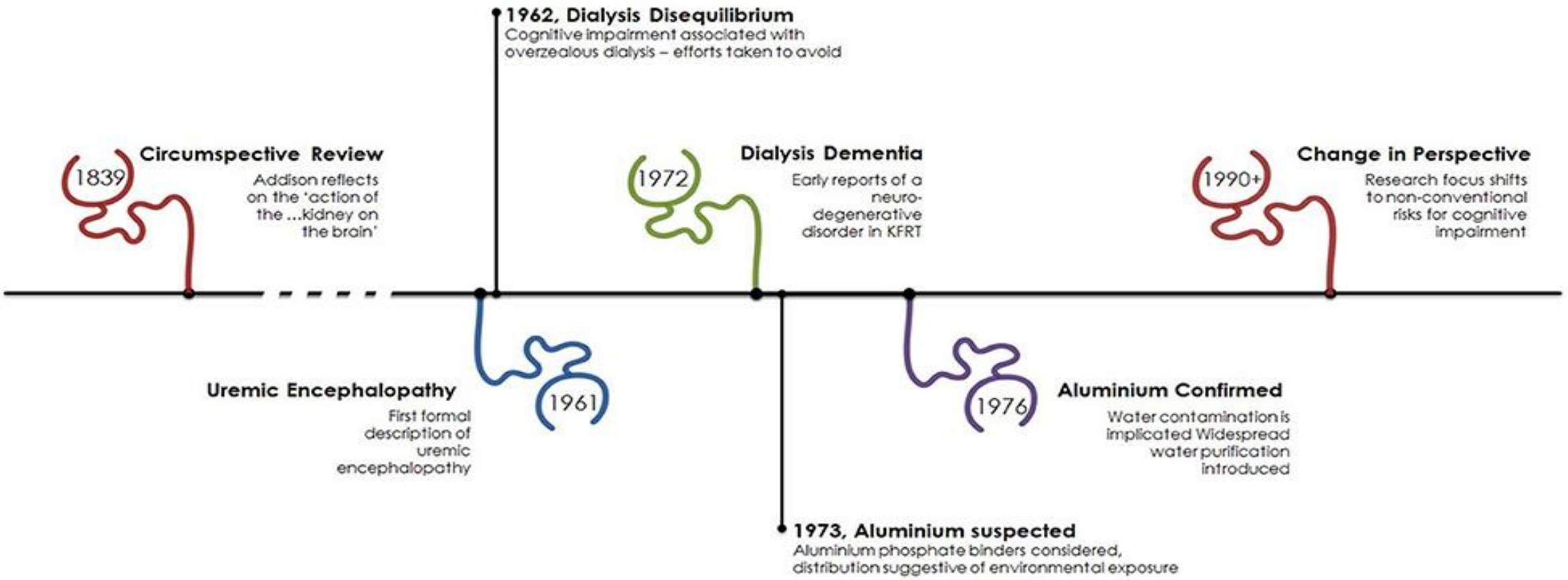
10-11 Νοεμβρίου 2023

Pandelidis Hotel, Θεσσαλονίκη

Γνωσιακή δυσλειτουργία στην προχωρημένη ΧΝΝ: Πρόληψη και θεραπευτικές στρατηγικές

Δέσποινα Καρασαββίδου
Νεφρολόγος

"Has Long Been Known..."—The History of Cognitive Impairment in Kidney Failure



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Ελληνική Νεφρολογία 2012; 24 (2): 118 - 126

Ανασκόπηση

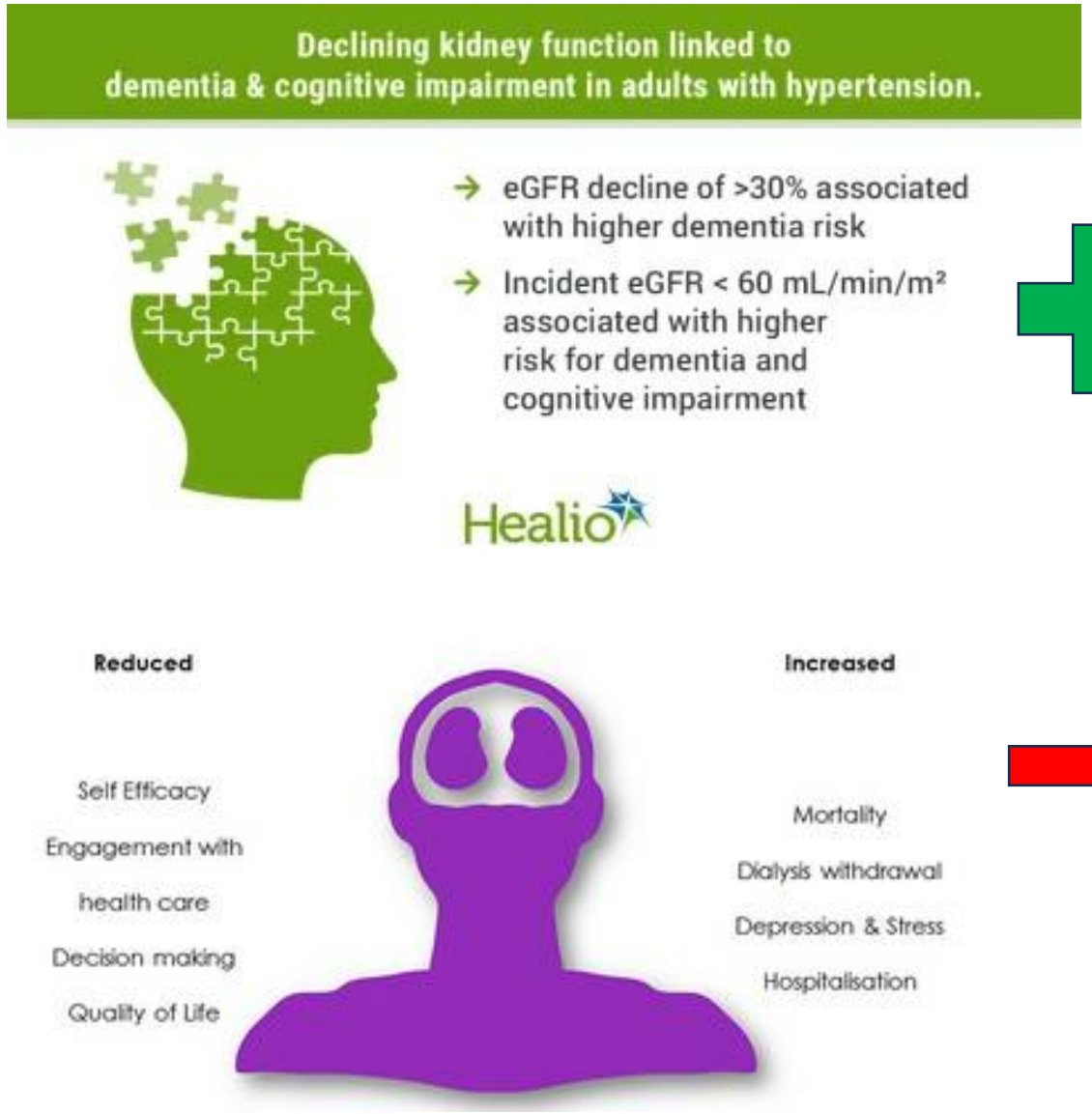
Η γνωστική δυσλειτουργία στη χρόνια νεφρική νόσο: ένας παράγοντας που παραμένει συχνά αδιάγνωστος

Δ. Καρασαββίδου[1]
Ρ.Γ. Καλαϊτζίδης[1]
Σ-Ε. Πελίδου[2]
Κ.Χ. Σιαμόπουλος[1]

Περίληψη

Οι ασθενείς με χρόνια νεφρική νόσο (ΧΝΝ) παρουσιάζουν συχνότερα νοητικές διαταραχές και έχουν πιθανότητα να υποστούν νοητική έκπτωση κατά 3.5 φορές περισσότερο σε σύγκριση με τα άτομα της ίδιας ηλικίας του γενικού πληθυσμού. Ωστόσο, μόλις την τελευταία δεκαετία έχει αναγνωριστεί αυτή η υψηλή επιβάρυνση της νοητικής λειτουργίας σε αυτούς τους ασθενείς. Πρόσφατα έχει περιγραφεί η σαφής αρνητική συσχέτιση του ρυθμού της σπειραματικής διήθησης με την γνωστική λειτουργία. Η γνωστική εξασθένιση εκδηλώνεται συνήθως ως αγγειακή άνοια και αναπτύσσεται είτε με τη μορφή της οξείας, είτε με τη μορφή της χρόνιας γνωστικής δυσλειτουργίας. Οι αιμοκαθαιρόμενοι ασθενείς διατρέχουν μεγαλύτερο κίνδυνο, λόγω της αυξημένης επίπτωσης που έχουν στα αγγειακά εγκεφαλικά επεισόδια, των πολλαπλών παραγόντων καρδιαγγειακού κινδύνου, καθώς επίσης και λόγω άλλων παραγόντων που σχετίζονται πιο ειδικά με τη νεφρική νόσο, όπως η ουραιμία, ο δευτεροπαθής υπερπαραθυροειδισμός και η αναιμία. Η παθοφυσιολογία της γνωστικής εξασθένισης δεν είναι πλήρως κατανοητή, ενώ πολλά α-

Η γνωστική δυσλειτουργία στην ΧΝΝ είναι ένας παράγοντας συχνά αδιάγνωστος παρά το γεγονός ότι κάθε νεφρολόγος αφιερώνει μέσο όρο 47 min στον ασθενή του (τρεις φορές την εβδομάδα επίσκεψη)



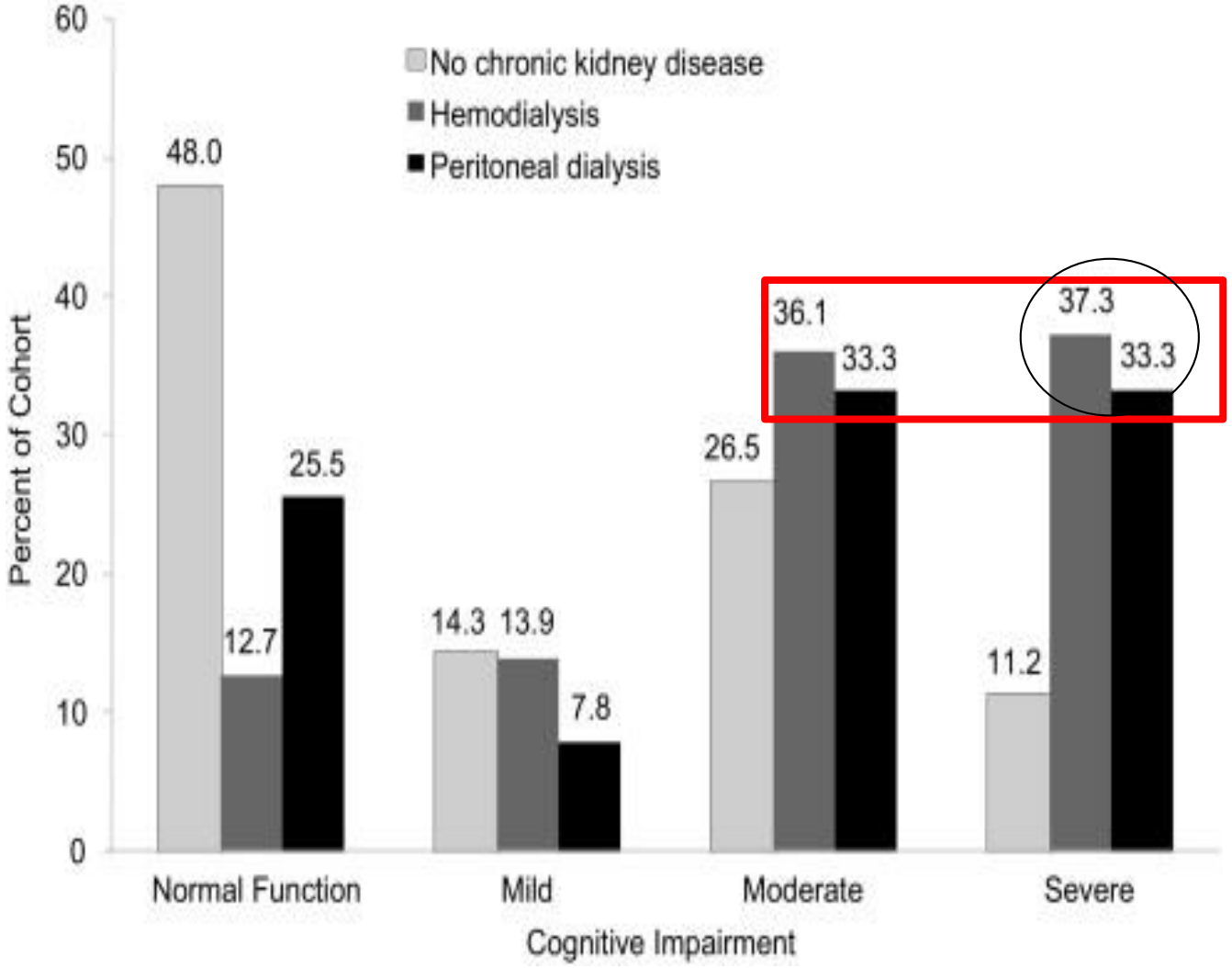
- ✓ Αυτό-φροντίδα, αυτάρκεια
- ✓ Λήψη αποφάσεων
- ✓ Συμμόρφωση σε ιατρικές οδηγίες-εκπαίδευση σε εξωνεφρική κάθαρση

- ✓ Αυξημένη νοσηλεία
- ✓ Θνητότητα
- ✓ Κατάθλιψη

Cognitive impairment in hemodialysis patients is common

A. M. Murray, D. E. Tupper, D. S. Knopman, D. T. Gilbertson, S. L. Pederson, S. Li, G. E. Smith, A. K. Hochhalter, A. J. Collins, R. L. Kane

First published July 24, 2006, DOI:
https://doi.org/10.1212/01.wnl.0000225182.15532.40



- Ο επιπολασμός της ΓΔ στην ΧΝΝ είναι από 10-40%
- Ενώ 50% των ασθενών σε αιμοκάθαρση έχουν γνωστική δυσλειτουργία

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

NEPHROLOGY - ORIGINAL PAPER

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

Ο κίνδυνος για ΓΔ αυξάνεται κατά 2.5 φορές με κάθε αλλαγή σταδίου

The main finding of the study was that in every CKD stage the risk of CO/DY increased more than twofold

Received: 24 September 2012 / Accepted: 12 April 2013

Journal of Nephrology (2022) 35:931–942
https://doi.org/10.1007/s40620-021-01170-3

ORIGINAL ARTICLE

Assessment of cognitive impairment and related risk factors in hemodialysis patients

Hristos Karakizlis[1,2] · Katharina Bohl[3] · Jannis Ziemek[4] · Richard Dodel[3,4] · Joachim Hoyer[1]

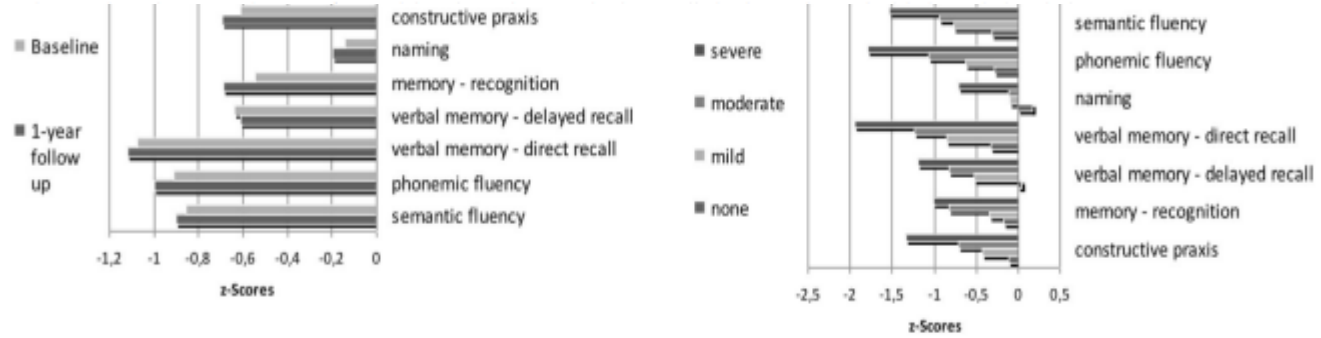
Received: 7 July 2021 / Accepted: 17 September 2021 / Published online: 16 October 2021

Abstract

Background Cognitive impairment in hemodialysis patients has been acknowledged over the last years and has been reported in up to 80% of patients. Older age, high prevalence of cardiovascular risk factors, such as stroke and transient ischemic attack, uremia, and multiple metabolic disturbances represent the most common factors for cognitive impairment in hemodialysis patients.

Methods We conducted a prospective cohort study on 408 patients from 10 hemodialysis centers in the regional government district of Middle Hesse (Germany). Patients underwent a neuropsychological test battery consisting of five tests, in addition to a phonemic fluency test, to assess cognitive profile. The patients were classified as no cognitive impairment or mildly-, moderately- or severely-impaired cognitive function, depending on the degree of impairment and number of domains where the deficit was determined. We analyzed the cognitive profile and the change in performance over time in hemodialysis patients based on their cognitive status at baseline vs. 1-year follow-up.

Results Of 479 eligible patients, 408 completed all tests at baseline. Only 25% (n = 102) of the patients had no cognitive impairment. Fourteen per cent (n = 57), 36.5% (n = 149), and 24.5% (n = 100) of patients showed mild, moderate, and severe impairment, respectively. In patients with cognitive impairment, all cognitive domains were affected, and impairment was significantly associated with depression and education. The most impaired cognitive performance was immediate memory recall, and the best performance was found in naming ability. No significant change was observed after 1-year follow up in any domain.



Nephrol Dial Transplant (2020) 35: 10–17
doi: 10.1093/ndt/gfz051
Advance Access publication 9 April 2019

Mild cognitive impairment and kidney disease: clinical aspects

Davide Viggiano [1,*], Carsten A. Wagner [2,*], Peter J. Blankestijn[3], Annette Bruchfeld[4], Danilo Fliser[5], Denis Fouque[6], Sebastian Frische[7], Loreto Gesualdo[8], Eugenio Gutiérrez[9], Dimitrios Goumenos[10], Ewout J. Hoorn[11], Kai-Uwe Eckardt[12], Samuel Knauß[13], Maximilian König[12], Jolanta Malyszko[14], Ziad Massy[15], Dorothea Nitsch[16], Francesco Pesce[8], Ivan Rychlík[17], Maria Jose Soler[18], Goce Spasovski[19], Kathryn I. Stevens[20], Francesco Trepiccione[1,21], Christoph Wanner[22], Andrzej Wiecek[23], Carmine Zoccali[24], Robert Unwin[25,26,†] and Giovambattista Capasso [1,21,†]

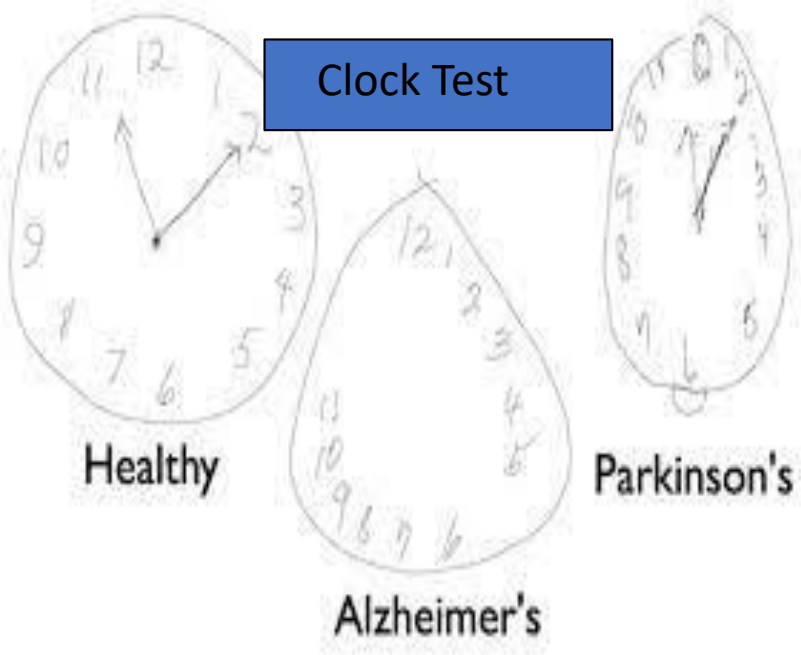
Table 1. Prevalence of MCI and dementia in different populations

Population	Prevalence of MCI (%)	Prevalence of dementia (%)	References
Healthy subjects	7–26	13	[41–43]
Early CKD (Stage 3)	14	Unknown	[39, 44]
Late CKD (Stage 4 and 5)	16–38	Unknown	[45, 46]
Haemodialysis	26–60	15–36	[47, 48, 51]
Peritoneal dialysis	35	3.9–31	[42, 49, 51]
Transplantation	(Only studies comparing pre–post transplant scores)	22	[50]

Table 2. Morphological, functional and pathogenetic features of MCI-CKD

Feature	MCI general population	MCI-CKD	References
Pathogenesis	Unknown	Uraemic (neuro)toxins	
Tractography	Lower connectivity of the basal nucleus	Internal capsule demyelination	[74, 75, 77]
MRI	Reduced amygdala and hippocampus grey matter	Deep white matter demyelination	[58, 70, 73, 76, 78, 80]
EEG	Altered cortical synchronization at alpha frequencies	Altered cortical synchronization at delta frequencies	[67–69]
Animal models	Cortical atrophy, damage to the cholinergic system	Normal neural architecture	[81–83]

Clock Test



MoCA

MONTREAL CO 004

ΟΝΟΜΑ: Α. Π. ΗΜΕΡΟΜΗΝΙΑ: 6/2/2017

ΗΛΙΚΙΑ: 45 Αρρεν

ΟΠΤΙΚΟΧΩΡΙΚΕΣ/ΕΚΤΕΛΕΣΤΙΚΕΣ (3 βαθμοί) — Κύκλος [+] Αριθμοί [+] Δείκτες [−] — 3/5

ΚΑΤΟΝΟΜΑΣΙΑ — 2/3

ΜΝΗΜΗ Διαβάστε τη λίστα με τις λέξεις, το υποκείμενο χρέιει να τις επαναλάβει. Κάντε 2 δοκιμές και μια καθυστερημένη ανάκληση μετά από 5 λεπτά.

	ΠΡΟΣΩΠΟ	ΒΕΛΟΥΔΟ	ΕΚΚΛΗΣΙΑ	ΜΑΡΓΑΡΙΤΑ	ΚΟΚΚΙΝΟ
ΔΟΚΙΜΗ 1					
ΔΟΚΙΜΗ 2					

ΠΡΟΣΟΧΗ Διαβάστε τη λίστα των ψηφίων(1 ψηφίο/δευτ) Το υποκείμενο θα επαναλάβει με την ίδια σειρά τα εξής: [✓] 2 1 8 5 4 — 2/2

Το υποκείμενο θα επαναλάβει με την ανάποδη σειρά τα εξής: [✓] 7 4 2

Διαβάστε τον κατάλογο των γραμμάτων Το υποκείμενο θα χτυπά το χέρι στο τραπέζι κάθε φορά που ακούει το γράμμα Α Λε δίνονται βαθμοί εάν >2 λάθη [ ] — 1/1

Δυαδοχική αφαίρεση ανά 7, ξεκινώντας από το 100 [✓] 93 [✓] 86 [✓] 79 [✓] 72 [✓] 65 — 3/3

4-5 σωστές αφαιρέσεις: 3 βαθ , 2-3 σωστές: 2 βαθ , 1 σωστή: 1 βαθ , 0 σωστές: 0 βαθ

ΓΛΩΣΣΑ Επαναλάβετε: Το μόνο που ξέρω είναι ότι ο Γιάννης είναι αυτός που θα βοηθήσει σήμερα. [✓] — 2/2

Η γάτα κρυβόταν πάντα κάτω από τον καναπέ όταν βρίσκονταν σκυλιά μέσα στο δωμάτιο

Ροή/ Πείτε όσες γρηγορότερες λέξεις μπορείτε, σε ένα λεπτό, που να αρχίζουν από Χ [17] (Ν ≥ 11 λέξεις) — 0/1

χαρτί, δόντι, χέρι, χιονάνθρωπος, χέρι, χαρά, χαρτί, χειρουργός

ΑΦΑΙΡΕΤΙΚΗ ΣΚΕΨΗ Ομοιότητα μεταξύ π.χ. μπανάνα- πορτοκάλι – φρούτο [✓] τύπνο-τσεκούρι [✓] ρολόι- χάρακας — 1/2

ΚΑΘΥΣΤΕΡΗΜΕΝΗ ΑΝΑΚΛΗΣΗ	ανάκληση λέξεων ΧΩΡΙΣ ΒΟΗΘΕΙΑ	ΠΡΟΣΩΠΟ [ ]	ΒΕΛΟΥΔΟ [ ]	ΕΚΚΛΗΣΙΑ [✓]	ΜΑΡΓΑΡΙΤΑ [✓]	ΚΟΚΚΙΝΟ [ ]	βαθμοί μόνο για ανάκληση χωρίς βοήθεια
Προαιρετικό	βοήθημα κατηγορίας						3/5
	βοήθημα πολλαπλής επιλογής	✓				—	

ΠΡΟΣΑΝΑΤΟΛΙΣΜΟΣ [✓] ημ/μηνία [✓] μήνας [✓] έτος [✓] ημέρα [✓] τόπος [✓] πόλη — 4/6

Φυσιολογική επίδοση ≥ 26

Προσθέστε έναν βαθμό αν ≤ 12 έτη εκπαίδευσης

ΣΥΝΟΛΟ 18/30

MMSE

ΟΝΟΜΑΤΕΠΩΝΥΜΟ : ΗΜΕΡΟΜΗΝΙΑ : / /

MINI-MENTAL STATE EXAMINATION
Σύντομη Εξέταση της Νοητικής Κατάστασης

01. Προσανατολισμός

Ποιά είναι η ημερομηνία; Τσεκάρετε τις σωστές απαντήσεις	Ημέρα	Ημερ/νία ημέρας	Μήνας	Έτος	Εποχή

Που βρισκόμαστε; Τσεκάρετε τις σωστές απαντήσεις	Όνομα ή διεύθυνση	Όροφος	Πόλη	Νομός	Χώρα

02. Εγχάραξη

Θα ονομάσω τρία αντικείμενα. Όταν τελειώσω, θα σας ζητήσω να τα επαναλάβετε. Να θυμάστε ποια είναι γιατί θα σας ξαναρωτήσω σε λίγο. Τσεκάρετε τα αντικείμενα που είναι σωστά με την ΠΡΩΤΗ προσπάθεια, εάν γίνει κάποιο λάθος στην πρώτη προσπάθεια, επαναλάβετε όλα τα ονόματα έως όπου ο ασθενής τα μάθει και τα τρία.	Αριθ. Επαναλήψεων	Μπάλα	Σημαία	Δέντρο

03. Προσοχή και ικανότητα υπολογισμών

		Καταγραφή απάντησης	Σωστό
Αφαίρεση	Τώρα θα ήθελα να αφαιρέσετε το 7 από το 100. Από αυτόν τον αριθμό αφαιρέστε άλλα 7. Συνεχίστε τις αφαιρέσεις κατά 7, μέχρι να σας πω να σταματήσετε. Καταχωρήστε ως σωστή μία απάντηση κάθε φορά που η διαφορά είναι 7, ακόμη κι αν η προηγούμενη απάντηση είναι λάθος.	93	
		86	
		79	
		72	
		65	
Απόδοση λέξης	Συλλαβίστε τη λέξη "πέτρα" ανάποδα ("ΑΡΤΕΠ") Καταχωρίστε ως σωστό μόνον εαν τα γράμματα είναι με την σωστή σειρά		

Και οι δύο δοκιμές πρέπει να ολοκληρωθούν. Η τελική βαθμολόγηση (σωστές απαντήσεις) για αυτήν την ενότητα είναι η ΥΨΗΛΟΤΕΡΗ εκ των δύο (Αφαίρεση ή Απόδοση λέξης)

04. Ανάκληση

Ποιά είναι τα τρία αντικείμενα που σας ζήτησα να θυμάστε;	Μπάλα	Σημαία	Δέντρο

05. Γλώσσα

Ονομασία	Δείξτε δύο αντικείμενα (ρολόι, μολύβι) και ρωτήστε "Πως ονομάζεται αυτό το αντικείμενο;"	Ρολόι	
		Μολύβι	
Επανάληψη	Πρόκειται να πω κάτι και θα ήθελα να το επαναλάβετε μετά από εμένα: "Όχι αν, και ή αλλά" (Επιτρέπεται μία επανάληψη)		
Εντολές	Δώστε καθαρές οδηγίες με την πρώτη. "Θα σας δώσω ένα κομμάτι χαρτιού. Πάρτε το χαρτί με το δεξί σας χέρι, διπλώστε το στη μέση και ακουμπήστε το στο πάτωμα". Αφού δώσετε στον ασθενή το χαρτί, επαναλάβετε την ενταλή. Βαθμολογήστε ως σωστό, εάν οι εργασίες έγιναν με την σωστή σειρά.	Δεξί χέρι	
		Δίπλωμα	
		Στο πάτωμα	
Ανάγνωση	Δείξτε την κάρτα που γράφει "Κλείστε τα μάτια σας" και ζητήστε από τον ασθενή να ακολουθήσει την οδηγία.		
Γραφή	Υποδείξτε στον ασθενή το τέλος της σελίδας σχεδίου (επόμενη σελίδα) και ζητήστε του να γράψει μία οποιαδήποτε ολοκληρωμένη πρόταση. Κατόπιν ζητήστε από τον ασθενή να σας πει τι έγραψε. Η ορθογραφία και η γραμματική δεν είναι σημαντικά. Η πρόταση θα πρέπει να έχει ένα υποκείμενο (ή αυτό να υπονοείται) και ένα ρήμα.		
Αντιγραφή	Υποδείξτε στον ασθενή την επόμενη σελίδα και πείτε "Αντιγράψτε αυτό το σχέδιο". Κάθε πεντάγωνο, θα πρέπει να έχει 5 πλευρές και 5 καθαρές γωνίες και η τομή τους να σχηματίζει ένα ρόμβο.		

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Cognitive disorders in patients with chronic kidney disease: specificities of clinical assessment

Marion Pépin[1,2], Ana Carina Ferreira [3,4], Mustafa Arici[5], Maie Bachman[6], Michelangela Barbieri[7], Inga Arune Bumblyte[8], Sol Carriazo [9], Pilar Delgado[10], Liliana Garneata[11], Konstantinos Giannakou[12], Olivier Godefroy[13], Tomasz Grodzicki [14], Aleksandra Klimkowicz-Mrowiec[14], Justina Kurganaite [8], Sophie Liabeuf [15,16], Carmen Antonia Mocanu[11], Giuseppe Paolisso[7,17], Goce Spasovski[18], Evgueniy Stefanov Vazelov[19], Davide Viggiano[20], Carmine Zoccali [21,22], Ziad A. Massy[1,23] and Andrzej Więcek[24]; the CONNECT Action (Cognitive Decline in Nephro-Neurology European Cooperative Target)

Global cognition			
MMSE	30-point test (orientation, attention and calculation, memory, language and visuospatial abilities)	Screening of global CI	Yes
MoCA	30-point test (visuospatial abilities, executive functions, memory, attention, language, abstract reasoning and orientation)	Screening of global CI (including executive functions)	Yes
CDT	Non-verbal test. The patient is asked to draw a clock face and mark the hours and then draw the hands to indicate a particular time	Executive functions, visuospatial and visuoconstructional functioning	Yes
Language			
Boston Naming Test	Name objects shown in 60 black-and-white line drawings. Items are ordered according to their ability to be named, which is correlated with their frequency	Confrontation naming	Yes
Visuospatial and constructive abilities			
Cancellation test	Lines, circles, letters bells or stars are drawn in random positions on a sheet of paper (A4) and presented to patient, who is asked to cancel or cross out the target	Visual neglect, response inhibition, motor perseveration and attention	Yes
Judgement of line orientation	30-item test in which the patient is asked to match two angled lines to a set of 11 lines that are arranged in a semicircle and separated 18 degrees from each other	Visuospatial perception	Yes
Rey–Osterrieth complex figure test (copying)	Patient is asked to copy a complex geometrical figure	Complex visuospatial constructional ability	Yes
Wechsler Adult Intelligence Scale (WAIS) block design	Timed subtest of the WAIS. Identical blocks with surfaces of solid red, surfaces of solid white and surfaces that are half-red and half-white are presented to the patient. The patient is asked, using an increasing number of blocks, to	Visuospatial and organizational abilities and processing speed	Yes

Screening of Cognitive Impairment in the Dialysis Population: A Scoping Review

Aye San[a] Balaji Hiremagalur[a] Wendy Muircroft[b] Laurie Grealish[a, c]

[a]Gold Coast Health, Southport, QLD, [b]Southern Adelaide Palliative Service, Adelaide, SA, and [c]Menzies Health Institute Queensland and School of Nursing and Midwifery, Griffith University, Southport, QLD, Australia

Reference (first author) and country of study	Study groups	Sample			Exclusion criteria of interest				Screening tools	Prevalence based on screening test	Assessment timing
		size	age, years	gender, M/F	advanced dementia	cerebro-vascular disease	psychiatric disease	lack of language fluency			
Harciarek [21], 2012, Poland	HD C	49 30	47.9±12.01 47.23±10.21	27/22 22/8	E	E	E	E	MMSE	MMSE HD: baseline: 28.57±0.98; 1st follow-up: 28.59±0.99; 2nd follow-up: 28.56±0.96	24 h after the last dialysis
Huang [22], 2008, Taiwan	HD	147	group I: 68±8.46; group II: 57.51±12.64	61/86	NR	NR	NR	NR	MMSE	MMSE scores NR	shortly before dialysis session
Isshiki [23], 2014, Japan	PD C	18 60	67.5±6.9 71.5±8.3	12/6 28/32	NR	E	NR	NR	MMSE	MMSE 27 or more: 14 (78%); 24–26: 3 (17%); 25 or less: 1 (5%)	not applicable
Jung [24], 2013, South Korea	HD PD C	29 27 12	55.8±8.7 52.4±11.6 44.7±10.7	13/16 14/13 11/1	E	NR	E	NR	MMSE	MMSE <24: HD: 7 (24.1%); PD: 3 (11.1%)	off dialysis, minimum 1 h from last dialysis treatment
Kalaitzidis [25], 2013, Greece	HBP CKD I, II CKD III CKD IV HD PD	96[b] 160[b]	53±1.51 50.2±11.8 63.1±9.4 64.1±12.2 60.4±13.8 58.6±15.7	62/35[b] 15/4[b] 20/9[b] 33/14[b] 17/14[b] 20/13[b]	NR	E	E	NR	MMSE	NR	on HD patients before dialysis session middle of the week
Kalirao [26], 2011, USA	PD HD C	51 338 101	57.5±14.8 71.2±9.5 68.5±9.6	34/17 183/155 44/57	NE	NE	E	E	3MS	3MS raw scores: PD: range 93–100, SD 6.7; HD: range 83–100, SD 8.6; C: range 94.3–100, SD 5.7	during off-dialysis time, with an interval of at least 2 h from the time of last dialysis
Kang [27], 2012, USA	HD PD CKD	70 17 82	52.6±14.6	110/59	E	E	E	NR	3MS	3MS: total: 91.7±7.4; SDB: 90.5±7.9; non-SDB: 92.8±6.8	HD: morning of a non-dialysis day at home
Kato [28], 2012, Japan	HD CKD C	57 26 17	69.4±3.8 66.6±14.7 66.6±4.1	29/28 18/8 5/12	NR	NR	NR	NR	MMSE	HD: 27.4±2.4; CKD: 25.8±2.4; C: 28±2	NR
Kitaguchi [29], 2011, Japan	HD	37	68.9±4.1	16/21	NR	NR	NR	NR	MMSE	MMSE 27.1±2.4	NR
Kobayashi [30], 2014, Japan	HD	54	67.8±11.3	33/21	NR	E	NR	NR	MMSE	MMSE 28 or more: 34 (63%); 25–27: 13 (24%); 24 or less: 7 (13%)	NR
Kutlay [31], 2001, Turkey	HD	84	mean: 42	47/37	NR	NE	NE	NR	MMSE	mild impairment (MMSE 18–23): 18 (21%); moderate to severe impairment (MMSE <18): 9 (11%)	at various times: before, during, after, and at intervals; immediate beginning and termination of dialysis avoided
Leinau [32], 2009, USA	HD	109	61±10	71/38	NE	NR	NR	E	MMSE	CI reported to be present in 41 (38%); breakup of the scores not provided	midweek, after the dialysis treatment was underway

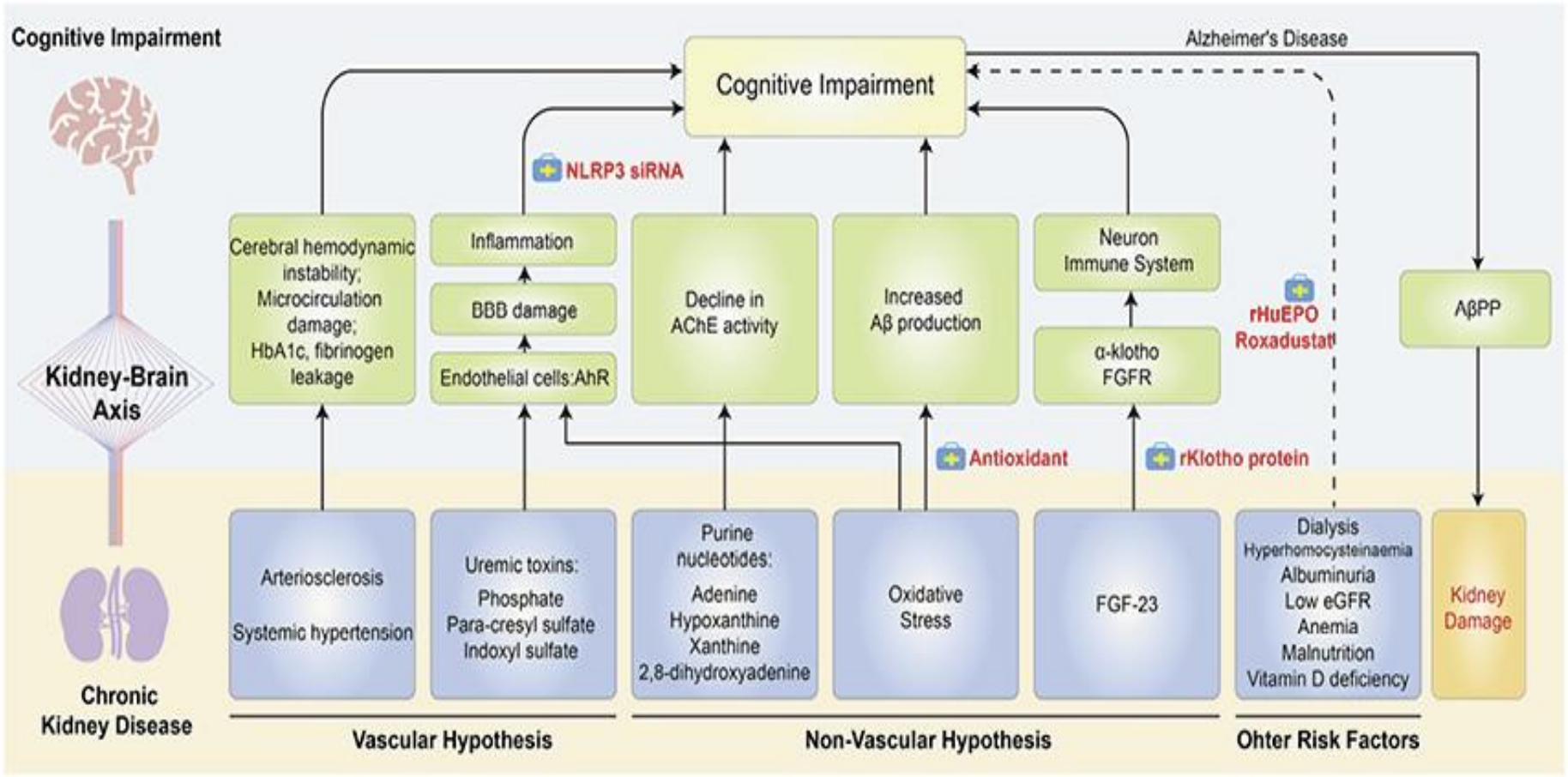
ΕΠΙΣΤΗΜΟΝΙΚΗ ΗΜΕΡΙΔΑ

Εγκέφαλος και Νεφρός

10-11 Νοεμβρίου 2023

Pandelidis Hotel, Θεσσαλονίκη

Πως ο νεφρός επηρεάζει τον εγκέφαλο;



Οι ασθενείς με ΧΝΝ μπορούν να οδηγηθούν σε γνωστική δυσλειτουργία
1.Αγγειακή υπόθεση (συστηματική ΑΥ, αθηρωμάτωση και ουραιμικές τοξίνες)
2.Μη αγγειακή υπόθεση (νουκελοτίδια πουρίνης, οξειδωτικό στρες,FG23)
3.Παράγοντες στην αιμοκάθαρση, αναιμία, λευκωματουρία και έλλειψη VitD

SAGE-Hindawi Access to Research
Cardiology Research and Practice
Volume 2011, Article ID 306189, 5 pages
doi:10.4061/2011/306189

Review Article

Clinical Interaction between Brain and Kidney in Small Vessel Disease

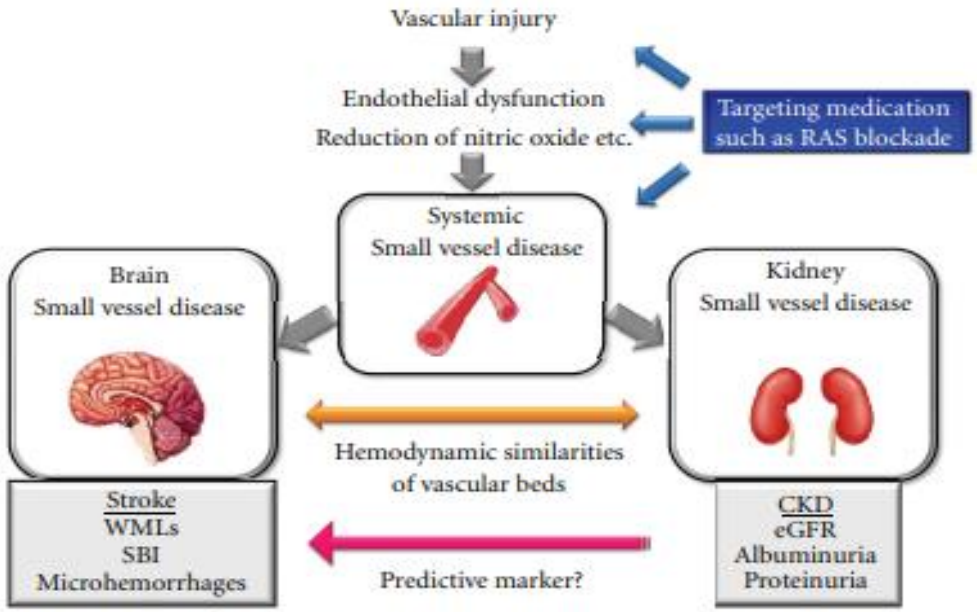
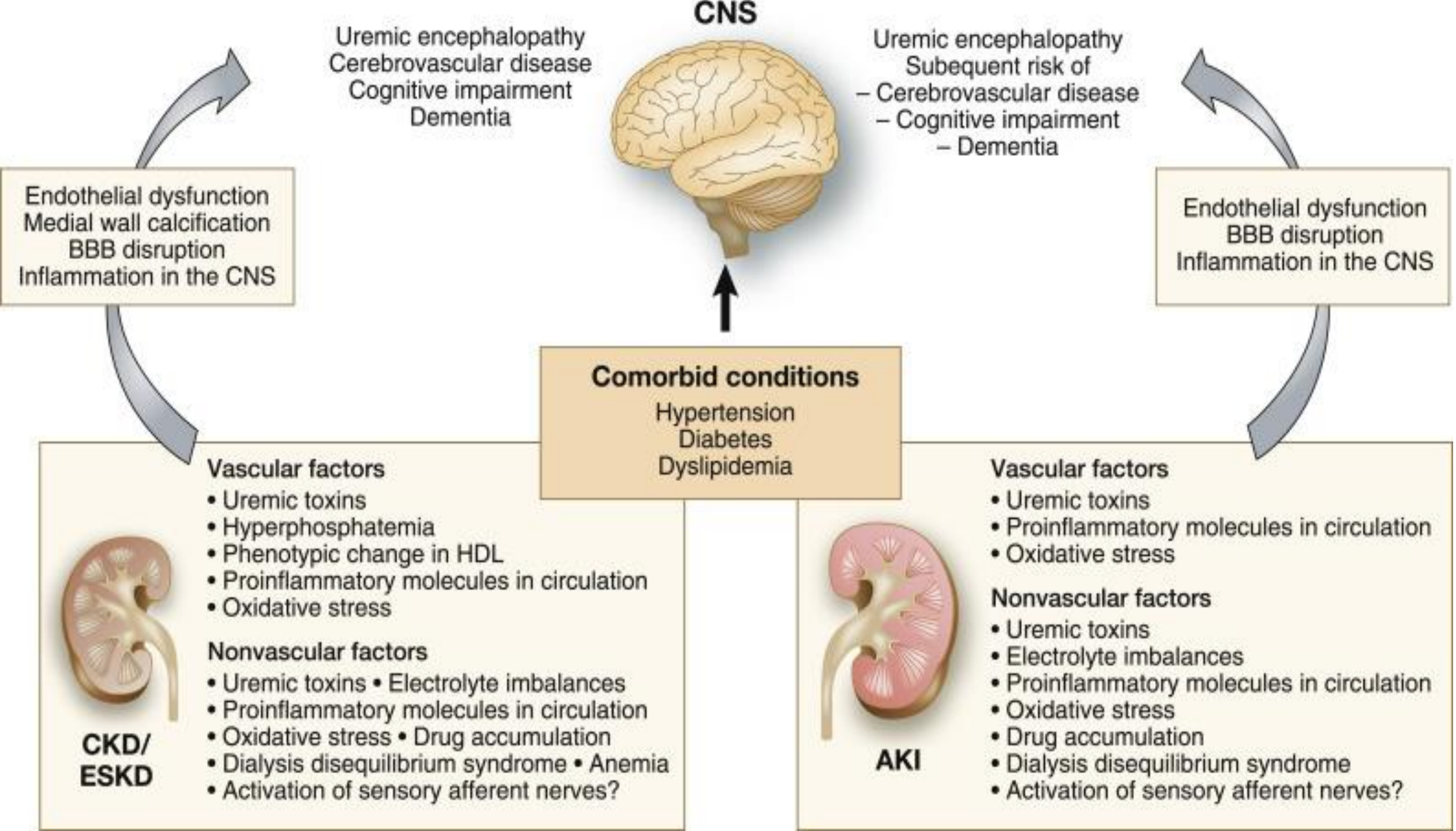
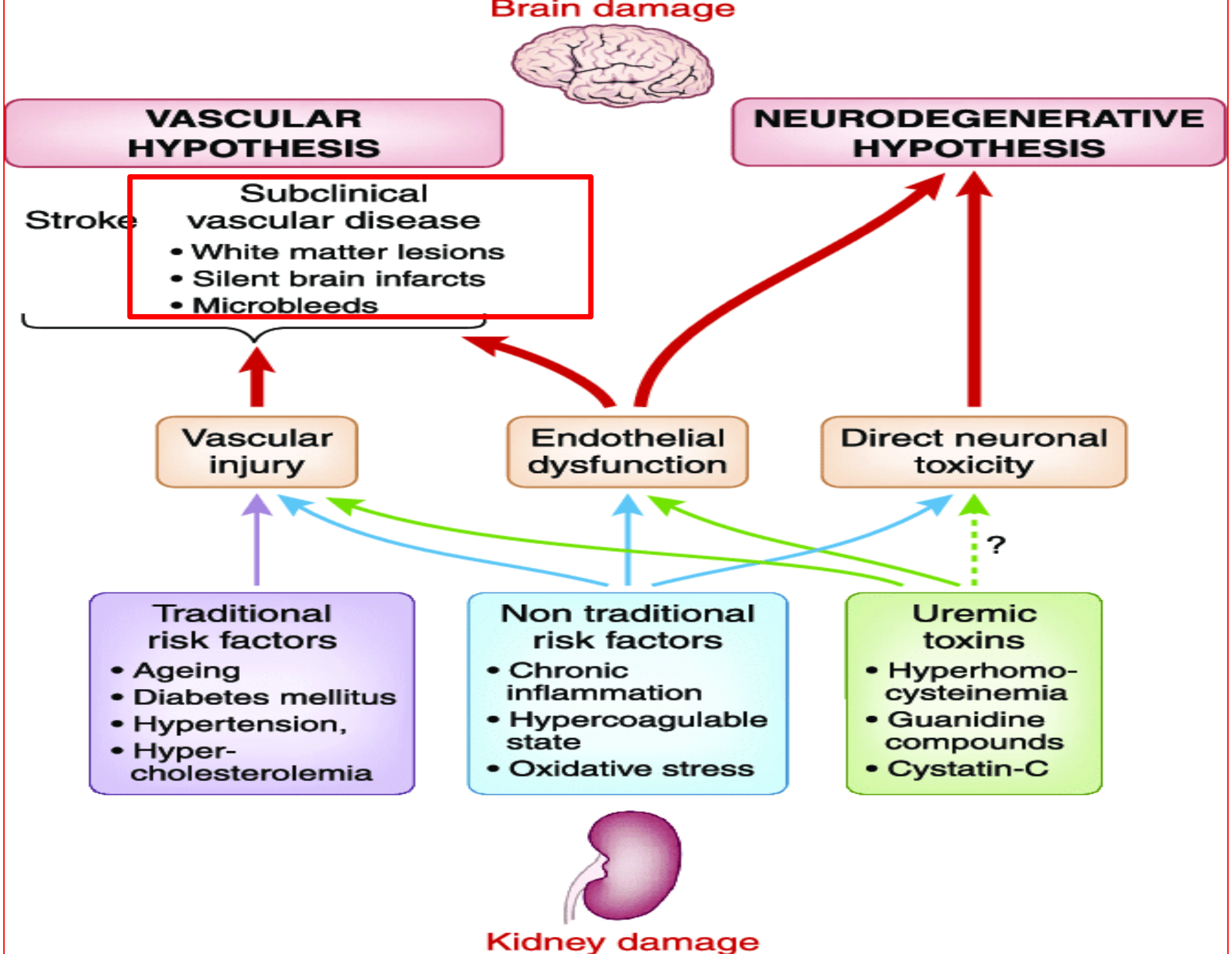


FIGURE 1: Schematic representation of cerebrorenal connection. RAS: renin-angiotensin system, CKD: chronic kidney disease, eGFR: estimated glomerular filtration rate, WMLs: white matter lesions, and SBI: silent brain infarction.

Η απώλεια της αγγειακής αυτορρύθμισης έχει αποτέλεσμα τις αιμοδυναμικής αλλαγές στον νεφρό (πρωτεινουρία) και στον εγκέφαλο (νόσος των μικρών αγγείων, μικροέμφρακτα και γνωστική δυσλειτουργία)


CNS
Uremic encephalopathy
Cerebrovascular disease
Cognitive impairment
Dementia
Uremic encephalopathy
Subequent risk of
– Cerebrovascular disease
– Cognitive impairment
– Dementia
Endothelial dysfunction
Medial wall calcification
BBB disruption
Inflammation in the CNS
Endothelial dysfunction
BBB disruption
Inflammation in the CNS
Comorbid conditions
Hypertension
Diabetes
Dyslipidemia
Vascular factors
• Uremic toxins
• Hyperphosphatemia
• Phenotypic change in HDL
• Proinflammatory molecules in circulation
• Oxidative stress
Nonvascular factors
• Uremic toxins • Electrolyte imbalances
• Proinflammatory molecules in circulation
• Oxidative stress • Drug accumulation
• Dialysis disequilibrium syndrome • Anemia
• Activation of sensory afferent nerves?
CKD/
ESKD
Vascular factors
• Uremic toxins
• Proinflammatory molecules in circulation
• Oxidative stress
Nonvascular factors
• Uremic toxins
• Electrolyte imbalances
• Proinflammatory molecules in circulation
• Oxidative stress
• Drug accumulation
• Dialysis disequilibrium syndrome
• Activation of sensory afferent nerves?
AKI


Brain damage
VASCULAR HYPOTHESIS
NEURODEGENERATIVE HYPOTHESIS
Stroke
Subclinical vascular disease
• White matter lesions
• Silent brain infarcts
• Microbleeds
Vascular injury
Endothelial dysfunction
Direct neuronal toxicity
?
Traditional risk factors
• Ageing
• Diabetes mellitus
• Hypertension,
• Hyper-cholesterolemia
Non traditional risk factors
• Chronic inflammation
• Hypercoagulable state
• Oxidative stress
Uremic toxins
• Hyperhomo-cysteinemia
• Guanidine compounds
• Cystatin-C
Kidney damage

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VOL. 73, NO. 25, 2019

THE PRESENT AND FUTURE

JACC SCIENTIFIC EXPERT PANEL

Vascular Cognitive Impairment and Dementia

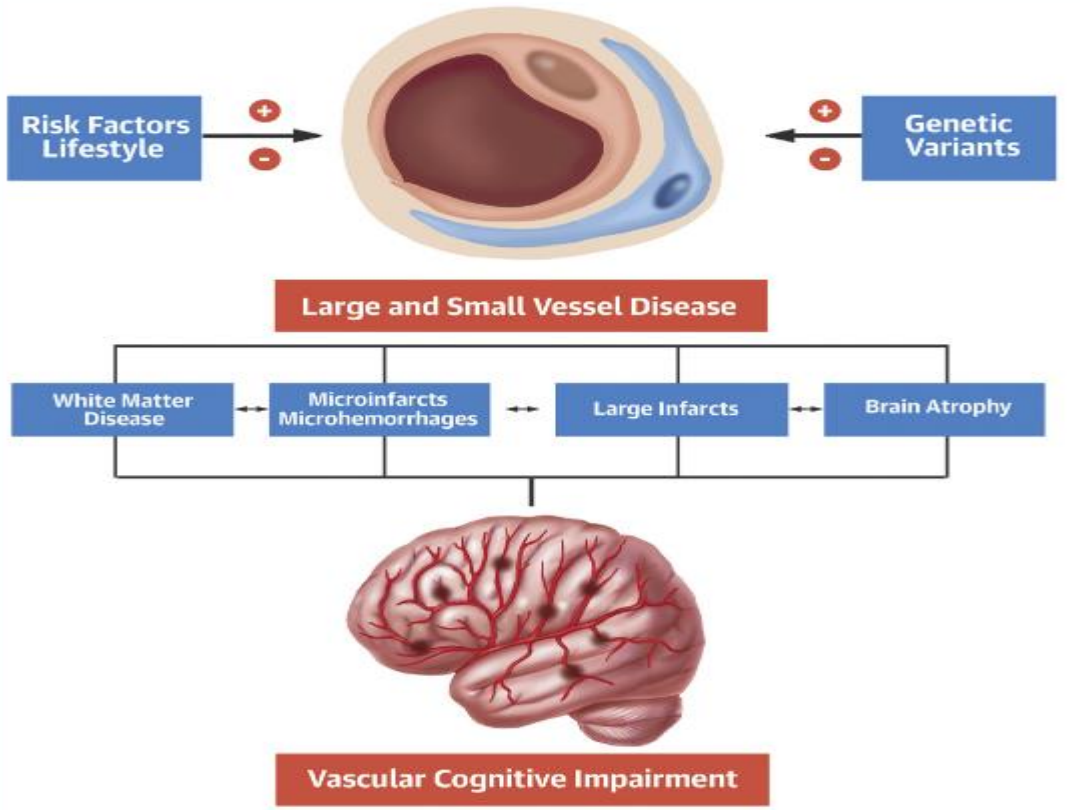
JACC Scientific Expert Panel

Costantino Iadecola, MD,[a] Marco Duering, MD,[b] Vladimir Hachinski, MD,[c] Anne Joutel, MD, PhD,[d] Sarah T. Pendlebury, PhD,[e] Julie A. Schneider, MD,[f] Martin Dichgans, MD[b,g,h]

TABLE 1 VICCCS Guidelines for VaD

- Clinical, neuropsychological, and imaging examination should follow the National Institute of Neurological Disorders–Canadian Stroke Network guidelines. Core domains for cognitive assessment should include executive function, attention, memory, language, and visuospatial function.
- Definition of major VCI (VaD): clinically significant deficits of sufficient severity in at least 1 cognitive domain (deficits may be present in multiple domains) and severe disruption to IADLs/ADLs (independent of the motor/sensory sequelae of the vascular event).
- Patients given a diagnosis of major VCI (VaD) are subcategorized according to the underlying pathology as appropriate (Figure 1).
- The terms "probable" and "possible" are used to define the available evidence.
- MRI is a "gold-standard" requirement for a clinical diagnosis of VCI. Probable mild VCI or probable major VCI (VaD) is the appropriate diagnostic category if computed tomography imaging is the only means of imaging available.
- Post-stroke dementia is defined by an immediate and/or delayed cognitive decline that begins within 6 months after a stroke and that does not reverse.
- Exclusions from diagnosis: drug/alcohol abuse/dependence within the last 3 months of first recognition of impairment or delirium.

CENTRAL ILLUSTRATION Vascular Cognitive Impairment and Dementia



Iadecola, C. et al. J Am Coll Cardiol. 2019;73(25):3326–44.

Risk factors and lifestyle, as well as genetic variants, can either promote (+) or stave off (−) damage to large and small cerebral blood vessels, which, in turn, leads to neuropathological changes that result in vascular cognitive impairment.

Nephrol Dial Transplant (2021) 37: ii4–ii12
doi: 10.1093/ndt/gfab216

Acidosis, cognitive dysfunction and motor impairments in patients with kidney disease

Review

Acidosis, cognitive dysfunction and motor impairments in patients with kidney disease

Background

CKD has recently been associated with cognitive dysfunction, and advanced CKD patients often have reduced motor function

$\downarrow HCO_3^-$

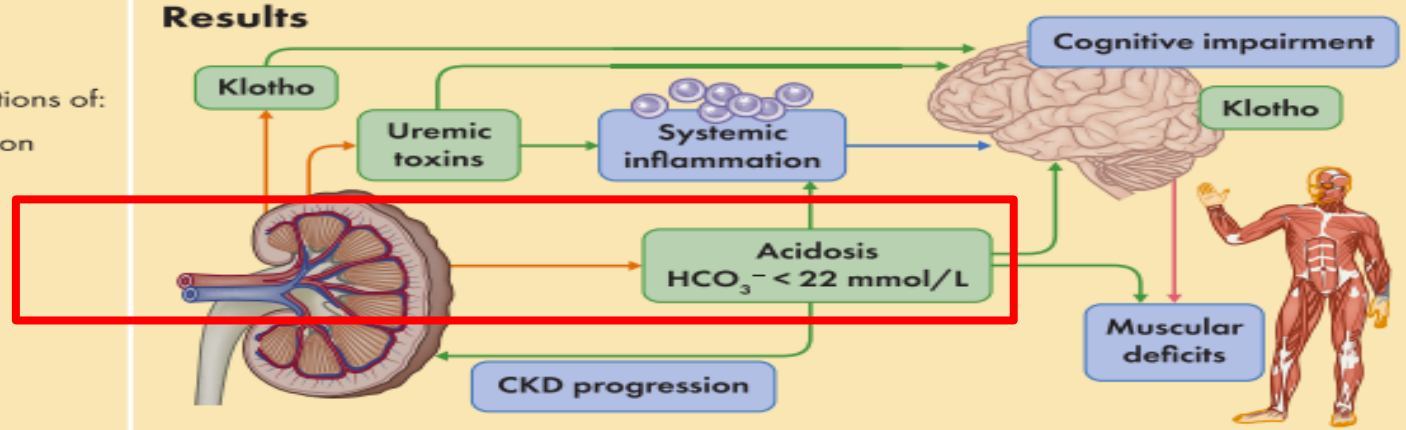
Recent data point towards the possibility that metabolic acidosis is one modifiable contributor to cognitive dysfunction

Methods

Literature search PubMed for combinations of:

- Cognitive dysfunction
- Brain function
- Motor function
- pH
- Acidosis
- CKD
- AKI

Results



Conclusion

CKD and acidosis are associated with forms of cognitive dysfunction. Further studies are required to test for causality, mechanisms, and therapies.

NEPHROLOGY DIALYSIS TRANSPLANTATION

Imenez Silva P.H., et al. NDT (2021)
@NDTSocial

- However, limited data show that patients with CKD 2 and normal serum [HCO_3^-] (eubicarbonatemia) manifest H^+ retention, and base administration ameliorates CKD progression.

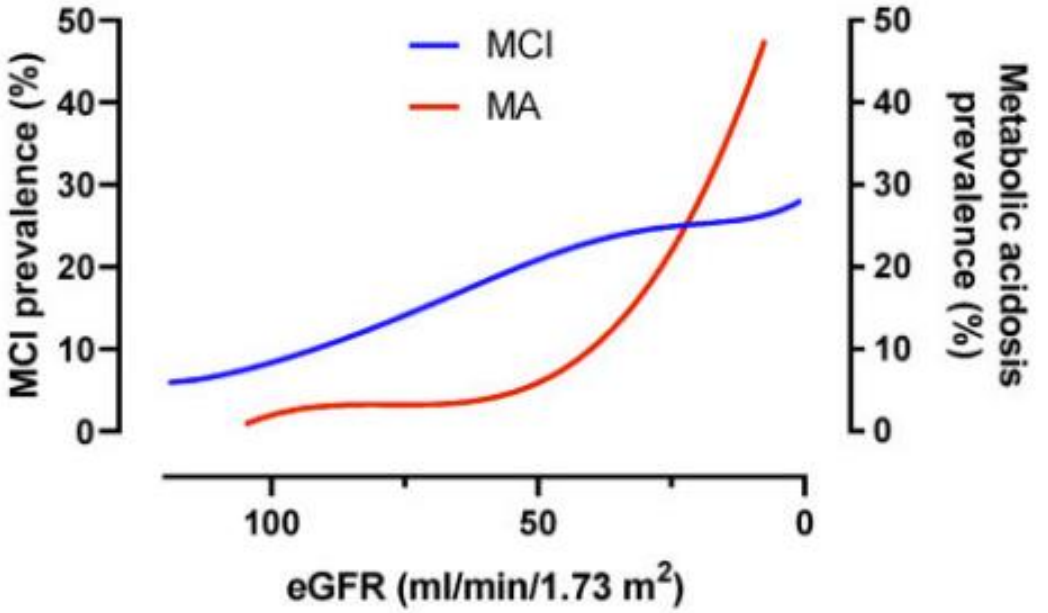


FIGURE 1: Prevalence of MCI and metabolic acidosis (MA) in patients with reduced kidney function. The prevalence of MCI and MA as a function of eGFR is estimated from several studies that reported the prevalence of MCI or MA in patients with reduced kidney function [1, 3, 5, 7, 8]. Cross-sectional studies analysing the prevalence of both clinical entities in the same cohort of patients have not been reported to date.

Blood-brain barrier perturbations by uremic toxins: Key contributors in chronic kidney disease-induced neurological disorders?

Quentin Faucher [a,*], Thomas K van der Made [a], Elizabeth De Lange [b], Rosalinde Masereeuw [a]

[a] Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Universiteitsweg 99, 3584 CG Utrecht, the Netherlands
[b] Predictive Pharmacology group, Division of Systems Pharmacology and Pharmacy, Leiden Academic Centre for Drug Research, the Netherlands

- Ο αιματοεγκεφαλικός φραγμός είναι κυτταρικός φραγμός που περιορίζει την είσοδο ουσιών στον εγκέφαλο

- Η αυξημένη έκθεση του εγκεφάλου σε ουραιμικές τοξίνες οδηγούν σε διαταραχή του φραγμού η ρήξη αυτού →

Νευρολογικές διαταραχές

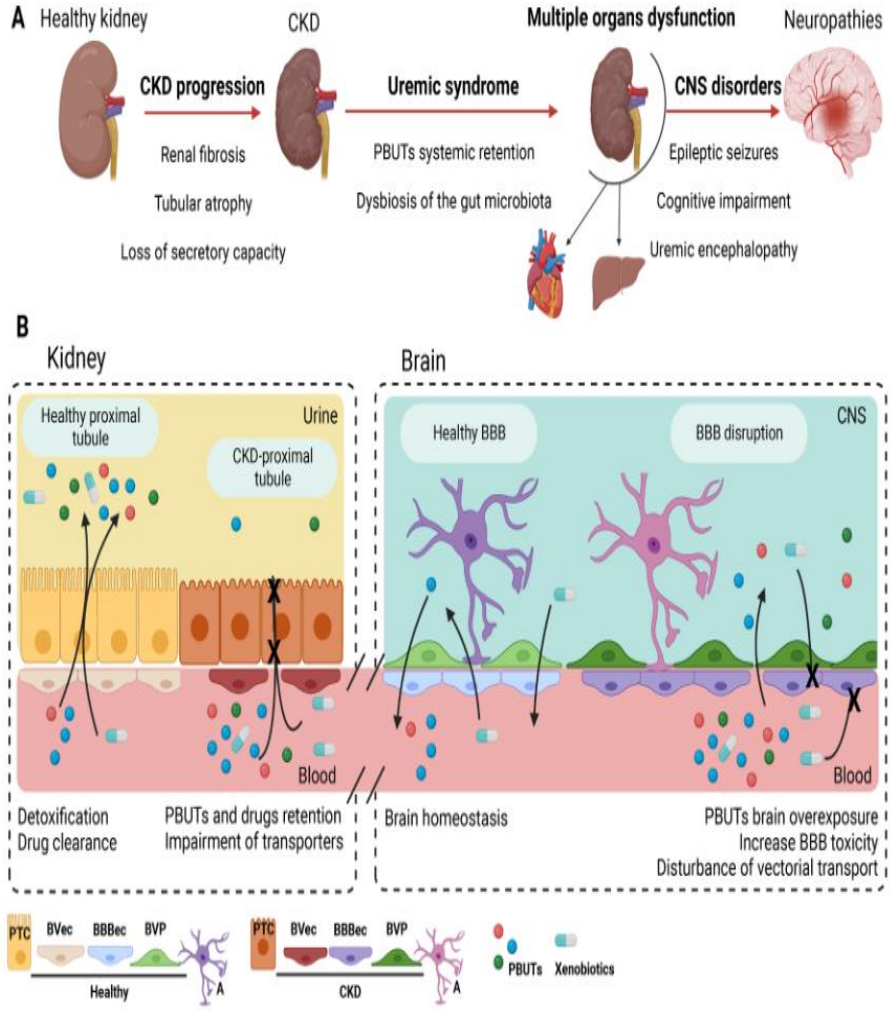


Fig. 1. Kidney-brain crosstalk and putative consequences in CKD-induced neurological complications at the (A) anatomical and (B) cellular level of tubular and blood-brain barrier. A, astrocytes; BBBec, blood-brain barrier endothelial cell; BVec, blood vessel endothelial cell; BVP, blood vessel pericyte; CKD, chronic kidney disease; CNS, central nervous system; PBUTs, protein-bound uremic toxins; PTC, proximal tubular cell. Illustration created with BioRender.com.

toxins

MDPI

Review

The Impact of Uremic Toxins on Cerebrovascular and Cognitive Disorders

Η αύξηση του Θεϊκού ινδοξυλίου στην ΧΝΝ συνδέεται άμεσα με την εγκεφαλική βλάβη μέσω οξειδωτικού στρες και εναπόθεση αμυλοειδούς

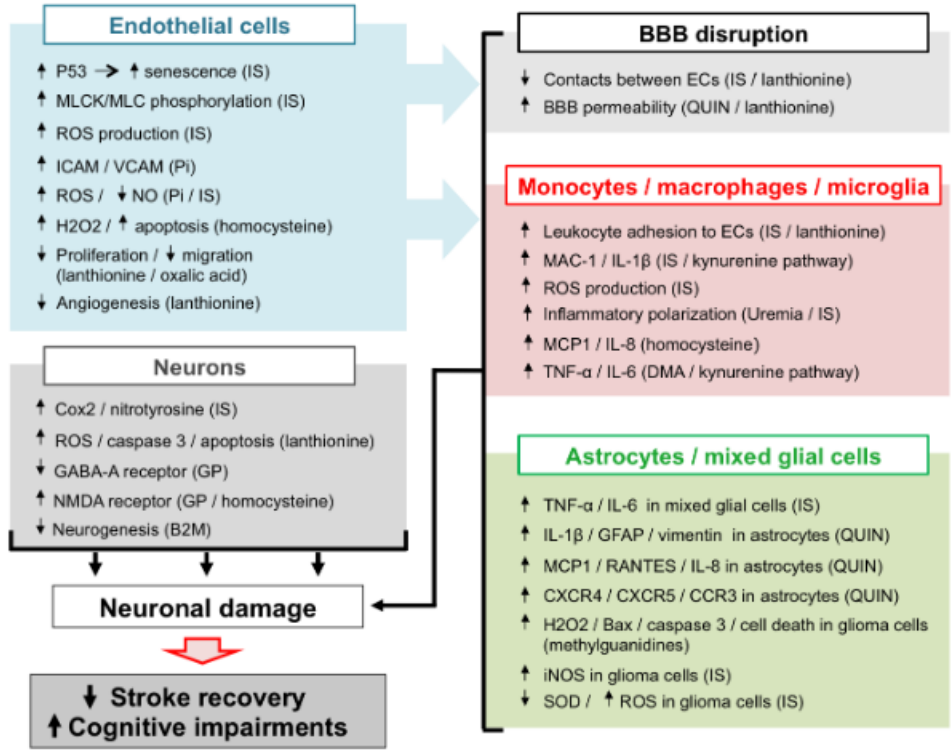


Figure 2. Impact of uremic toxins on neurological damage: a mechanistic view based on a review of the recent literature. B2M: β-2-microglobulin, BBB: blood-brain barrier, DMA: dimethylarginines, ECs: endothelial cells, GFAP: glial fibrillary acidic protein, GP: guanidino compounds, iNOS: inducible nitric oxide synthase, IS: indoxyl sulfate, MLCK: myosin light chain kinase, MLC: myosin light chain, NO: nitric oxide, Pi: inorganic phosphate, QUIN: quinolinic acid, ROS: reactive oxygen species, SOD: superoxide dismutase. ICAM: intercellular adhesion molecule, VCAM: vascular cell adhesion molecule, GABA-A: γ-aminobutyric acid receptor A, NMDA: *n*-methyl-*d*-aspartic acid, MCP1: Monocyte chemoattractant protein 1, MAC-1: macrophage-1 antigen, TNF-α: tumour necrosis factor, CXCR4: C-X-C chemokine receptor type 4, CXCR5: C-X-C chemokine receptor type 5, CCR3: C-C chemokine receptor type 3, RANTES: Regulated on Activation, Normal T Expressed and Secreted

Review

Diabetes, Albuminuria and the Kidney—Brain Axis

Published: 27 May 2021

Diana Maria Ariton [1], Joan Jiménez-Balado [1,2], Olga Maisterra [1], Francesc Pujadas [1], María José Soler [3] and Pilar Delgado [1,*]

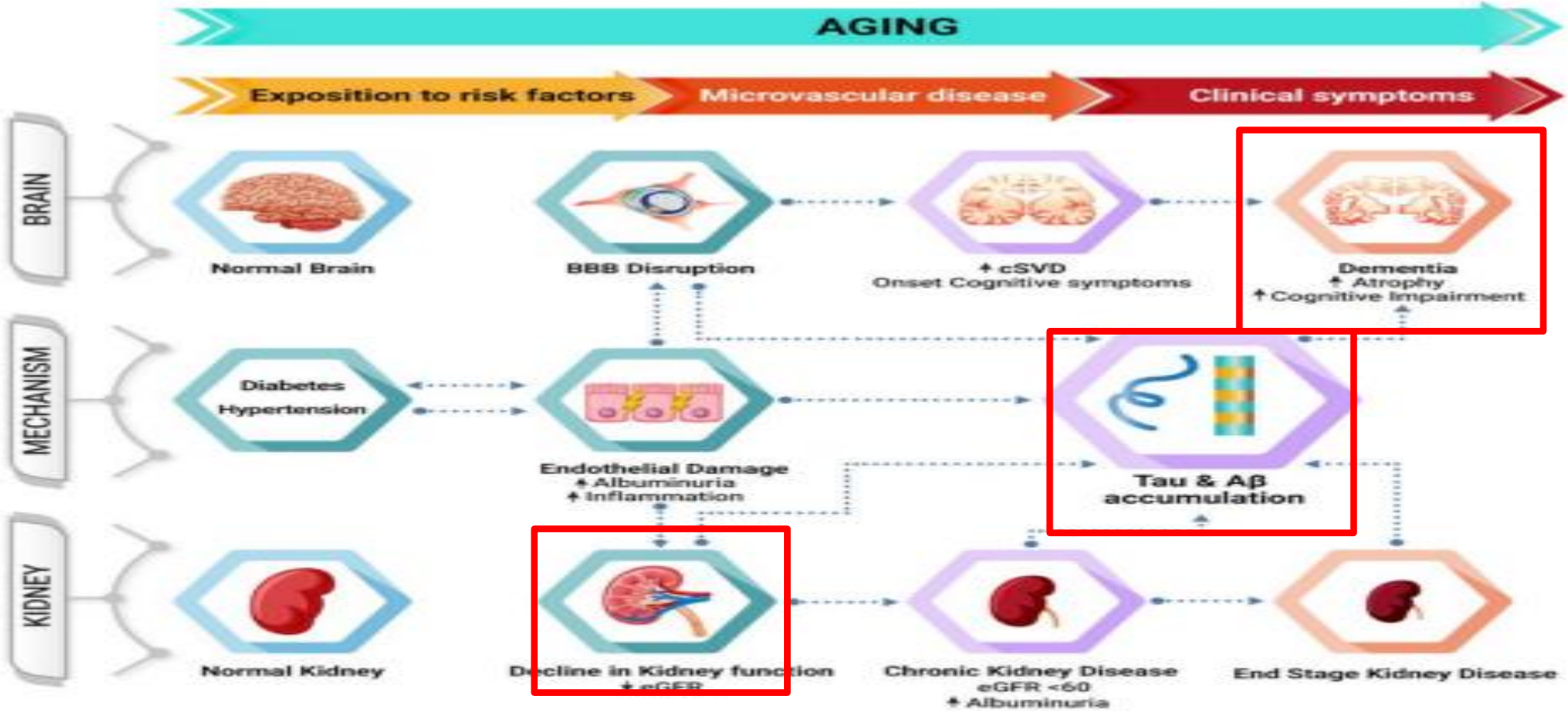


Figure 1. Schematic representation of the potential mechanisms linking albuminuria and cognitive impairment. Chronic exposure to risk factors during mid-life triggers endothelial damage, manifesting as increased albuminuria and leading to BBB disruption and decreased eGFR, which ultimately result in increased cerebrovascular burden and CKD. Additionally, decreased kidney function might compromise the systemic clearance of Aβ, increasing the likelihood of dementia during the later stages of the disease.Key: AD, Alzheimer's disease; BBB, blood–brain barrier; CKD, chronic kidney disease; cSVD, cerebral small vessel disease; and eGFR, estimated glomerular filtration rate.

Nephrol Dial Transplant (2021) 37: ii55–ii62
doi: 10.1093/ndt/gfab261

Albuminuria as a risk factor for mild cognitive impairment and dementia—what is the evidence?

Boris Bikbov [1], Maria José Soler [2], Vesna Pešić[3], Giovambattista Capasso[4,5], Robert Unwin [6], Matthias Endres[7], Giuseppe Remuzzi[1], Norberto Perico[1], Ron Gansevoort[8], Francesco Mattace-Raso[9], Annette Bruchfeld [10], Andreja Figurek[11] and Gaye Hafez [12]; the CONNECT Action (Cognitive Decline in Nephro-Neurology European Cooperative Target)

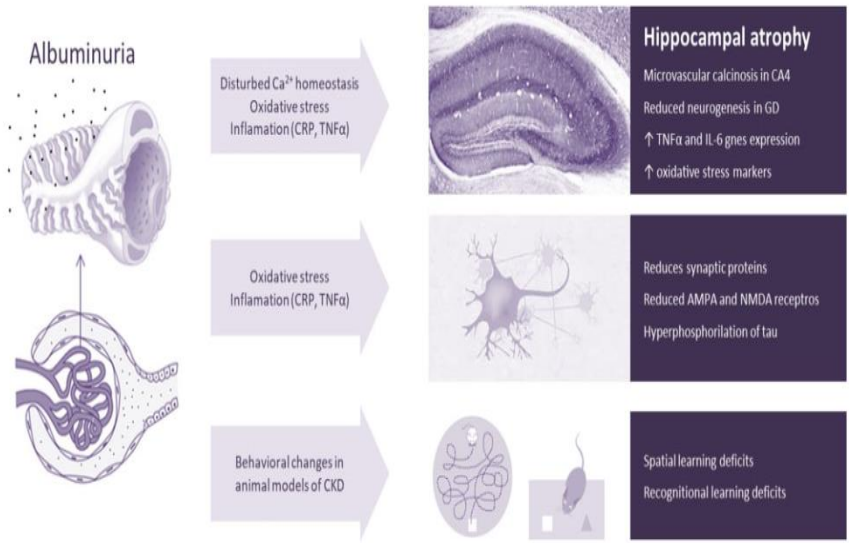


FIGURE 1: Hippocampal structural and functional changes in animal models of kidney disease. GD, gyrus dentatus.

Review Article

Albuminuria as a risk factor for mild cognitive impairment and dementia – what is the evidence?

Synopsis

This review summarizes the available evidence on increased albuminuria in the development of mild cognitive impairment (MCI) or dementia, points to existing gaps in our knowledge, and suggests actions to overcome them.

Clinical data

Epidemiological studies were conducted in different populations

They demonstrated that the presence of **increased albuminuria is associated with a higher relative risk of MCI or dementia** both in cross-sectional analyses and in studies with long-term follow-up

Pathophysiology

Underlying pathophysiological mechanisms of albuminuria's effect are still under investigation

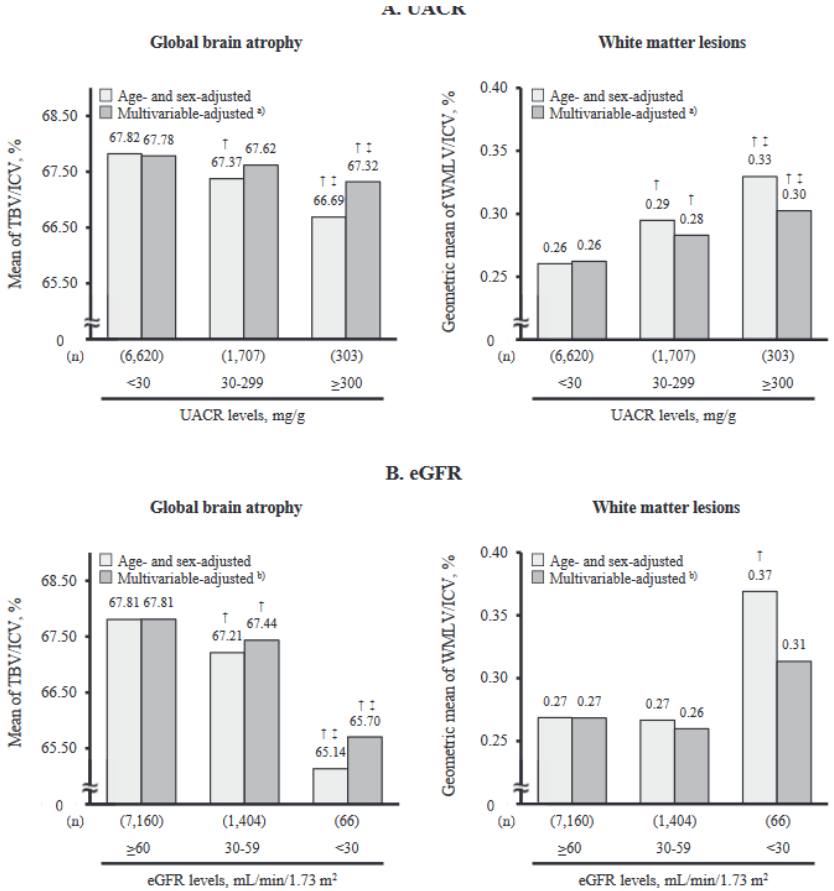
Available experimental data indicate that elevated albuminuria and low GFR are associated with **significant neuroanatomical declines in hippocampal function and gray matter volume**

Controversies and proposals

We propose 10 recommendations for further clinical studies on relationship between albuminuria and MCI or dementia that would resolve the major questions about a causal relationship and the effectiveness of interventions targeting albuminuria per se to prevent cognitive decline.

NEPHROLOGY DIALYSIS TRANSPLANTATION

Bikbov, B. et al. NDT (2021)
@NDTSocial



CKD, Brain Atrophy, and White Matter Lesion Volume: The Japan Prospective Studies Collaboration for Aging and Dementia

Kenji Maki, Tomoyuki Ohara, Jun Hata, Mao Shibata, Naoki Hirabayashi, Takanori Honda, Satoko Sakata, Yoshihiko Furuta, Masato Akiyama, Keisuke Yamasaki, Yasuko Tatewaki, Yasuyuki Taki, Takanari Kitazono, Tatsuya Mikami, Tetsuya Maeda, Kenjiro Ono, Masaru Mimura, Kenji Nakashima, Jun-ichi Iga, Minoru Takebayashi, and Toshiharu Ninomiya; on behalf of the Japan Prospective Studies Collaboration for Aging and Dementia (JPSC-AD) study group

Rationale & Objective: Chronic kidney disease, defined by albuminuria and/or reduced estimated glomerular filtration rate (eGFR), has been reported to be associated with brain atrophy and/or higher white matter lesion volume (WMLV), but there are few large-scale population-based studies assessing this issue. This study aimed to examine the associations between the urinary albumin-creatinine ratio (UACR) and eGFR levels and brain atrophy and WMLV in a large-scale community-dwelling older population of Japanese.

Study Design: Population-based cross-sectional study.

Setting & Participants: A total of 8,630 dementia-free community-dwelling Japanese aged greater than or equal to 65 years underwent brain magnetic resonance imaging scanning and screening examination of health status in 2016-2018.

Exposures: UACR and eGFR levels.

Outcomes: The total brain volume (TBV)-to-intracranial volume (ICV) ratio (TBV/ICV), the regional brain volume-to-TBV ratio, and the WMLV-to-ICV ratio (WMLV/ICV).

Analytical Approach: The associations of UACR and eGFR levels with the TBV/ICV, the regional brain volume-to-TBV ratio, and the WMLV/ICV were assessed by using an analysis of covariance.

Results: Higher UACR levels were significantly associated with lower TBV/ICV and higher geometric mean values of the WMLV/ICV (*P* for trend = 0.009 and <0.001, respectively). Lower eGFR levels were significantly associated with lower TBV/ICV, but not clearly associated with WMLV/ICV. In addition, higher UACR levels, but not lower eGFR, were significantly associated with lower temporal cortex volume-to-TBV ratio and lower hippocampal volume-to-TBV ratio.

Limitations: Cross-sectional study, misclassification of UACR or eGFR levels, generalizability to other ethnicities and younger populations, and residual confounding factors.

Conclusions: The present study demonstrated that higher UACR was associated with brain atrophy, especially in the temporal cortex and hippocampus, and with increased WMLV. These findings suggest that chronic kidney disease is involved in the progression of morphologic brain changes associated with cognitive impairment.

Visual Abstract included

Complete author and article information provided before references.

Correspondence to T. Ohara (ohara.tomoyuki.287@m.kyushu-u.ac.jp)

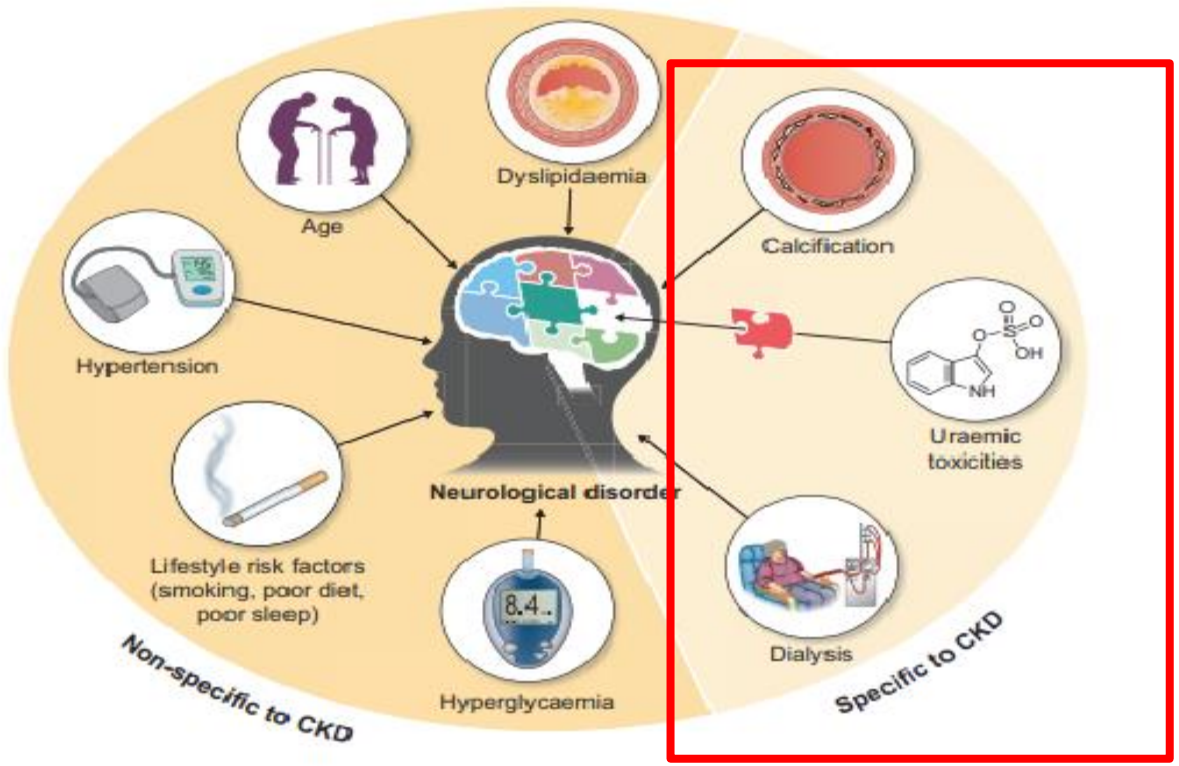
Kidney Med. 5(3):100593. Published online December 23, 2022.

doi: 10.1016/j.xkme.2022.100593

Nephrol Dial Transplant (2021) 37: ii33–i44
doi: 10.1093/ndt/gfab223

Chronic kidney disease and neurological disorders: are uraemic toxins the missing piece of the puzzle?

Sophie Liabeuf [1,2], Marion Pepin[3,4], Casper F.M. Franssen[5], Davide Viggiano[6], Sol Carriazo [7], Ron T. Gansevoort[5], Loreto Gesualdo[8], Gaye Hafez [9], Jolanta Malyszko[10], Christopher Mayer[11], Dorothea Nitsch[12], Alberto Ortiz [7], Vesna Pešić[13], Andrzej Wiecek[14] and Ziad A. Massy[3,15]; the CONNECT Action (Cognitive Decline in Nephro-Neurology European Cooperative Target)

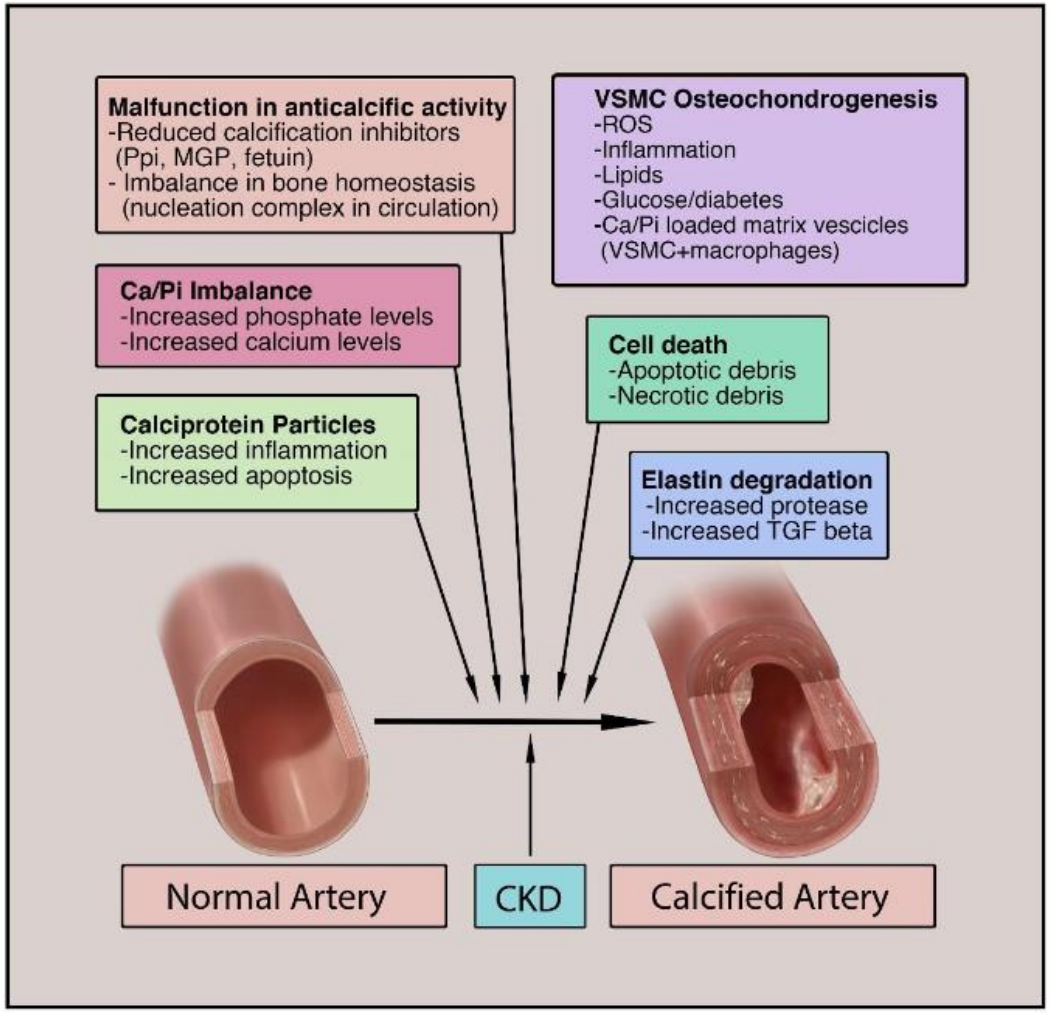


IGURE 1: The complicated puzzle of risk factors associated with neurological disorders in patients with CKD. Along with traditional ırdiovascular risk factors (such as diabetes, hypertension and dyslipidaemia), non-traditional risk factors related to kidney damage (such s uraemic toxicities) may predispose patients with CKD to neurological disorders.

Review

Vascular Calcification in Chronic Kidney Disease: Diversity in the Vessel Wall

Prabhatchandra Dube *,†, Armelle DeRiso †, Mitra Patel, Dhanushya Battepati, Bella Khatib-Shahidi, Himani Sharma, Rajesh Gupta, Deepak Malhotra, Lance Dworkin, Steven Haller and David Kennedy *



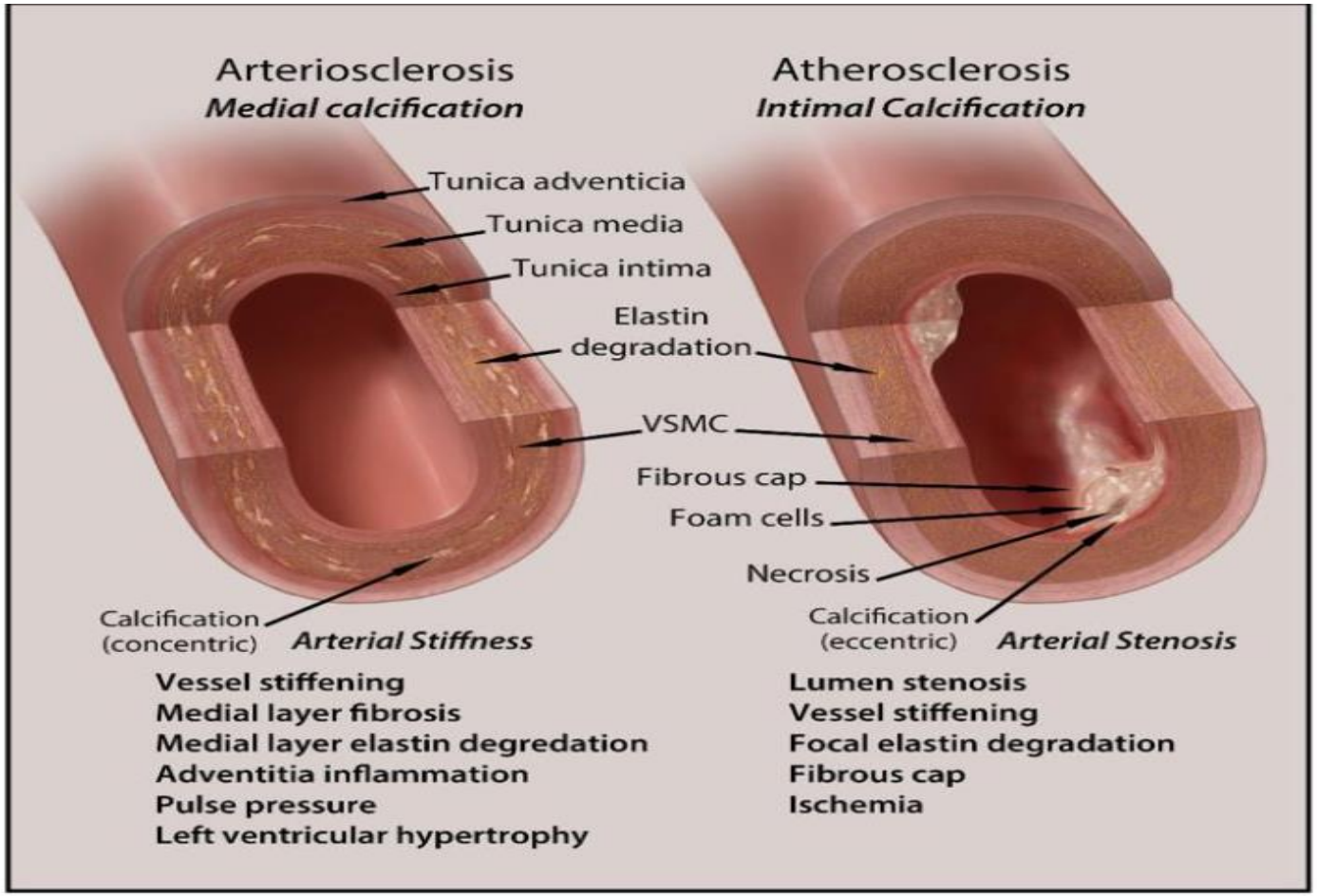


Figure 2. Schematic representation of intimal and medial calcification and their related pathologies.

DOI: 10.1111/jch.13350

ORIGINAL PAPER

WILEY

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]

TABLE 3 Multivariate analysis of the study

Parameters	In/Out	R^2 increment%	Beta coeff.	Lower CI	Upper CI	*P* value
Dependent variable MMSE						
Age	In	9.7	−0.102	−0.142	−0.062	<0.001
Education	In	58.1	7.159	6.137	8.354	<0.001
cf-PWV	In	1.0	−0.209	−0.409	−0.010	0.040
Ht	In	1.2	0.139	0.022	0.257	0.020
GFR-MDRD	Out		-	-	-	-
R^2 = 0.700						
(a) Dependent variable MMSE without age and aPP						
Education	In	57.9	8.031	6.891	9.171	<0.001
Ht	In	4.5	0.174	0.037	0.311	0.014
cf-PWV	In	1.5	−0.233	−0.446	−0.019	0.029
GFR-MDRD	In	1.1	0.020	0.001	0.039	0.032
R^2 = 0.650						
(b) Dependent variable MMSE without age and cf-PWV						
Education	In	58	7.949	6.776	9.123	<0.001
aPP	In	1.1	−0.043	−0.081	−0.005	0.026
LDL	In	1.3	0.012	0.001	0.023	0.035
Statin	In	1.5	−1.375	−2.622	−0.129	0.031
GFR-MDRD	In	4.3	0.018	0.001	0.037	0.050
R^2 = 0.663						
Dependent variable Clock-test						

American Heart Association.

Arterial Stiffness and Cognition Among Adults: A Systematic Review and Meta-Analysis of Observational and Longitudinal Studies

Celia Alvarez-Bueno, PhD; Pedro G. Cunha, MD, PhD; Vicente Martinez-Vizcaino, MD, PhD; Diana P. Pozuelo-Carrascosa, PhD; Maria Eugenia Visier-Alfonso, MSc; Estela Jimenez-Lopez, PhD; Ivan Cavero-Redondo, PhD

Global cognition	
Elias et al., 2009 [27]	-0.07 (-0.27, 0.12) 8.42
Fukuhara et al., 2006 [28]	-0.32 (-0.59, -0.04) 6.24
Hanon et al., 2005 [30]	-0.18 (-0.41, 0.04) 7.54
Karasavvidou et al., 2018 [31]	-0.17 (-0.49, 0.15) 5.27
Kim et al., 2009 [32]	-0.82 (-1.03, -0.61) 7.97
Lamballais et al., 2018 [34]	-0.13 (-0.18, -0.07) 12.49
Lee et al., 2014 [35]	-0.22 (-0.61, 0.17) 4.08
Lim et al., 2016 [13]	-0.10 (-0.33, 0.12) 7.54
Muela et al., 2018 [37]	-0.28 (-0.62, 0.05) 4.98
Palta et al., 2019 [40]	-0.11 (-0.18, -0.03) 12.06
Ryu et al., 2017 [43]	-0.49 (-0.85, -0.14) 4.63
Singer et al., 2013 [45]	-0.04 (-0.26, 0.18) 7.68
Zhong et al., 2014 [50]	-0.08 (-0.19, 0.03) 11.10
Subtotal (I-squared = 75.9%) (Q-Cochrane = 49.81, p =	-0.21 (-0.30, -0.11) 100.00

Conclusions

In conclusion, this systematic review and meta-analysis reveals a negative association between arterial stiffness, measured using PWV, and cognition, specifically executive function, memory, and global cognition. This association seems to be independent of sex, age, blood pressure levels, and PWV measurement characteristics. Separate analyses of longitudinal studies support the negative association between arterial stiffness and cognitive function found in cross-sectional studies. Our results accumulate evidence supporting that PWV assessment could be a useful tool to identify individuals at high risk of cognitive decline or early stages of cognitive decline, to implement interventions aimed at slowing the progression to dementia.

JAMA | Original Investigation

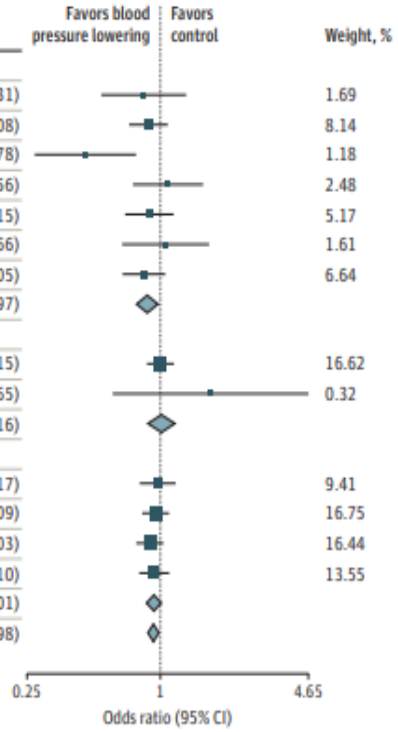
Association of Blood Pressure Lowering With Incident Dementia or Cognitive Impairment
A Systematic Review and Meta-analysis

Diarmaid Hughes, MB, BEng; Conor Judge, MB, BEng; Robert Murphy, MB; Elaine Loughlin, MB; Maria Costello, MB; William Whiteley, PhD; Jackie Bosch, PhD; Martin J. O'Donnell, PhD; Michelle Canavan, PhD

JAMA. 2020;323(19):1934-1944. doi:10.1001/jama.2020.4249

Figure 1. Association of Blood Pressure Lowering With Dementia or Cognitive Impairment

Study	Participants with dementia or cognitive impairment/total No.		Absolute risk reduction (95% CI), %	Odds ratio (95% CI)
	Blood pressure lowering group	Control group		
Dementia (criterion-referenced)				
SHEP,[22] 1994	37/2365	44/2371	0.29 (-0.45 to 1.03)	0.84 (0.54 to 1.31)
PROGRESS,[23] 2003	193/3051	217/3054	0.78 (-0.48 to 2.04)	0.88 (0.72 to 1.08)
Syst-Eur,[5] 2002	21/1485	43/1417	1.62 (0.54 to 2.70)	0.46 (0.27 to 0.78)
SCOPE,[24] 2003	62/2477	57/2460	-0.19 (-1.04 to 0.67)	1.08 (0.75 to 1.56)
HYVET-COG,[6] 2008	126/1687	137/1649	0.84 (-0.99 to 2.67)	0.89 (0.69 to 1.15)
ADVANCE,[25] 2009	39/5569	37/5571	-0.04 (-0.34 to 0.27)	1.05 (0.67 to 1.66)
SPRINT MIND,[12] 2019	149/4278	176/4285	0.62 (-0.18 to 1.43)	0.84 (0.67 to 1.05)
Random-effects model for subgroup (Q_6 = 7.92; P = .24; I^2 = 0.0%)				0.87 (0.78 to 0.97)
Dementia (clinical-based)				
PRoFESS,[26] 2008	408/8624	409/8646	0.00 (-0.63 to 0.63)	1.00 (0.87 to 1.15)
HOPE-3,[13] 2019	10/811	6/815	-0.50 (-1.46 to 0.46)	1.68 (0.61 to 4.65)
Random-effects model for subgroup (Q_1 = 0.99; P = .32; I^2 = 0.0%)				1.01 (0.88 to 1.16)
Dementia and mild cognitive impairment (composite)				
TRANSCEND,[7] 2011[a]	239/2694	245/2689	0.24 (-1.29 to 1.77)	0.97 (0.81 to 1.17)
ON TARGET (Dual),[7] 2011[a]	618/7807	326/3932.5	0.37 (-0.68 to 1.42)	0.95 (0.83 to 1.09)
ON TARGET (ARB),[7] 2011[a]	584/7797	326/3932.5	0.80 (-0.24 to 1.84)	0.90 (0.78 to 1.03)
SPS3,[27] 2014[a]	506/1323	535/1345	1.53 (-2.17 to 5.23)	0.94 (0.80 to 1.10)
Random-effects model for subgroup (Q_3 = 0.57; P = .90; I^2 = 0.0%)				0.93 (0.87 to 1.01)
Test for overall effect: z = -2.50; P = .01 Heterogeneity: τ^2 = 0.00; χ^2 = 12.14; P = .43; I^2 = 0.0%			0.39 (0.09 to 0.68)	0.93 (0.88 to 0.98)

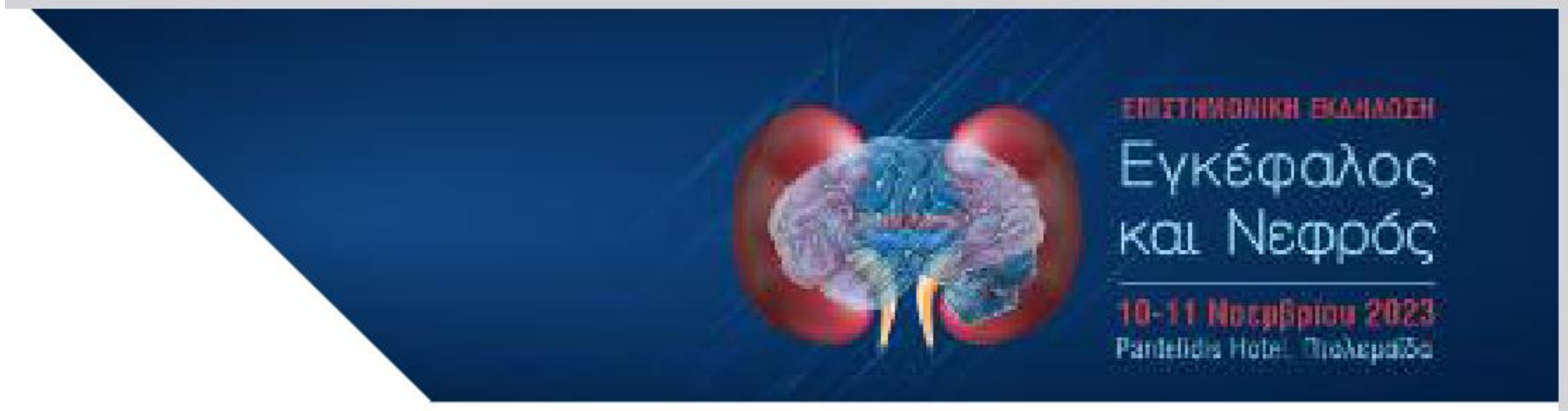


The squares and bars represent the mean values and 95% CIs of the effect sizes and the area of the squares reflects the weight of the studies. Diamonds represent the combined effects and the vertical dotted line represents the line of no association.

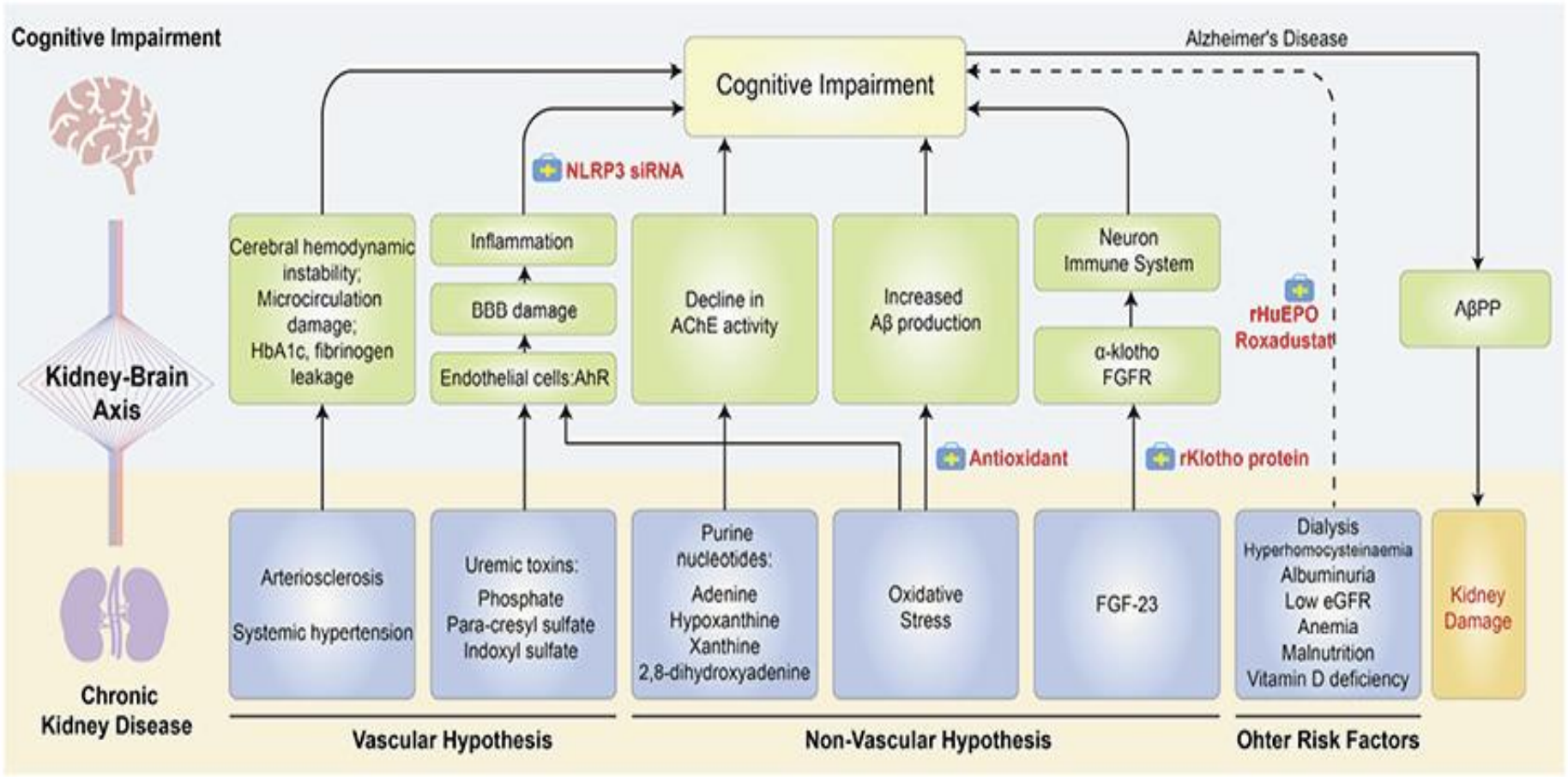
[a] Composite of dementia and cognitive impairment.

DOES TREATING HYPERTENSION REDUCE THE RISK OF COGNITIVE IMPAIRMENT?

Η υπέρταση μπορεί να οδηγήσει σε γνωστικό κίνδυνο εως 50% ενώ η χρήση αντιυπερτασικών φαρμάκων μπορεί να οδηγήσει σε μείωση του γνωστικού κινδύνου και της άνοιας έως 11%



Μη αγγειακή υπόθεση



Οι ασθενείς με ΧΝΝ μπορούν να οδηγηθούν σε γνωστική δυσλειτουργία είτε μέσω της
1.Αγγειακής υπόθεσης(συστηματική ΑΥ, αθηρωμάτωση και ουραιμικές τοξίνες)
2.Μη αγγειακή υπόθεση (νουκελοτίδια πουρίνης, οξειδωτικό στρες,FG23),Μεταβολικοί παράγοντες
3.Παράγοντες στην αιμοκάθαρση, αναιμία, λευκωματουρία και έλλειψη VitD

The Influence of Serum Uric Acid on the Brain and Cognitive Dysfunction

Natasa R. Mijailovic[1], Katarina Vesic[2] and Milica M. Borovcanin[3]*

[1] Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia, [2] Department of Neurology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia, [3] Department of Psychiatry, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

Uric acid is commonly known for its bad reputation. However, it has been shown that uric acid may be actively involved in neurotoxicity and/or neuroprotection. These effects could be caused by oxidative stress or inflammatory processes localized in the central nervous system, but also by other somatic diseases or systemic conditions. Our interest was to summarize and link the current data on the possible role of uric acid in cognitive functioning. We also focused on the two putative molecular mechanisms related to the pathological effects of uric acid—oxidative stress and inflammatory processes. The hippocampus is a prominent anatomic localization included in expressing uric acid's potential impact on cognitive functioning. In neurodegenerative and mental disorders, uric acid could be involved in a variety of ways in etiopathogenesis and clinical presentation. Hyperuricemia is non-specifically observed more frequently in the general population and after various somatic illnesses. There is increasing evidence to support the hypothesis that hyperuricemia may be beneficial for cognitive functioning because of its antioxidant effects but may also be a potential risk factor for cognitive dysfunction, in part because of increased inflammatory activity. In this context, gender specificities must also be considered.

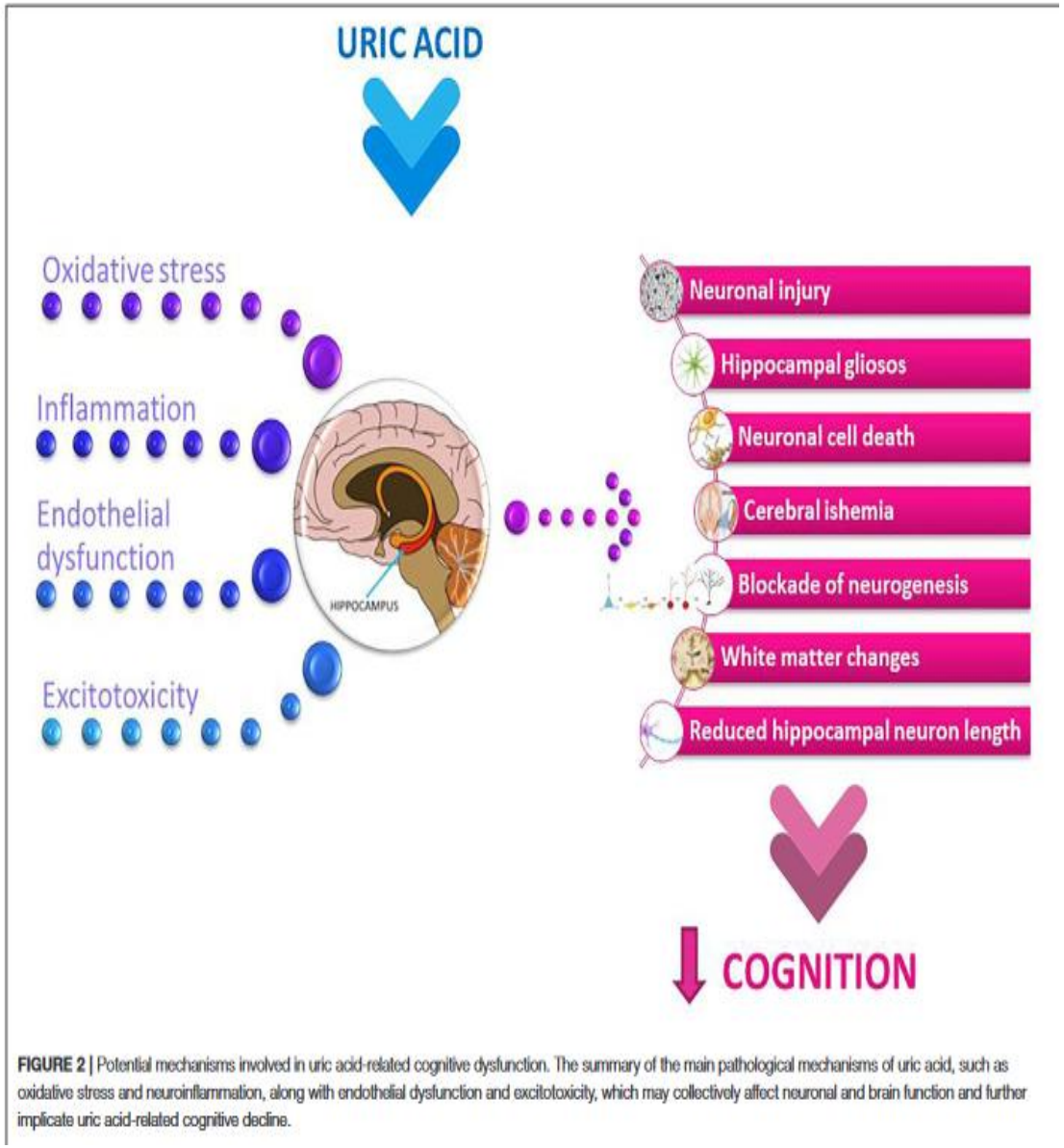


FIGURE 2 | Potential mechanisms involved in uric acid-related cognitive dysfunction. The summary of the main pathological mechanisms of uric acid, such as oxidative stress and neuroinflammation, along with endothelial dysfunction and excitotoxicity, which may collectively affect neuronal and brain function and further implicate uric acid-related cognitive decline.

Relationships between serum Klotho concentrations and cognitive performance among older chronic kidney disease patients with albuminuria in NHANES 2011–2014

Jialing Zhang[1] and Aihua Zhang[1,2]*

[1]Department of Nephrology, Xuanwu Hospital, Capital Medical University, Beijing, China, [2]The National Clinical Research Center for Geriatric Disease, Xuanwu Hospital, Capital Medical University, Beijing, China

Background: The potential relationship between Klotho and cognitive function is limited and controversial. This study aimed to quantify the association of Klotho and cognitive impairment in chronic kidney disease (CKD) patients with albuminuria.

Methods: Serum Klotho was measured by enzyme–linked immunosorbent assay. Patients with urine albumin to creatinine ratio (UACR) > 30mg/g from the National Health and Nutrition Survey (NHANES) 2011–2014 were divided into 4 groups according to the quartile of Klotho. Cognitive function was examined using the Consortium to Establish a Registry for Alzheimer's Disease (CERAD), Digit Symbol Substitution Test (DSST), and Animal Fluency Test. The relationship between Klotho and cognitive function was analyzed by multivariable regression and subgroup analysis.

Resutts: Among 368 CKD patients with albuminuria, we found that Klotho was negatively associated with creatinine, and positively associated with hemoglobin, and estimated glomerular filtration rate. No significant linear relationship was showed between Klotho (as a continuous variable) and cognitive function. When regarded Klotho as a category variable, patients in the quartile 3 group were at a better cognitive performance for CEARD–word learning subset and DSST, especially in the CKD patients with 30 mg/g < UACR <300 mg/g, but not in participants with UACR > 300 mg/g.

Conclusions: The increased Klotho was associated with an increased cognitive function in CKD patients with microalbuminuria. Further studies are needed to demonstrate whether Klotho may be a beneficial biomarker of cognitive health and neurodegeneration.

toxins

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Review

Klotho/FGF23 and Wnt Signaling as Important Players in the Comorbidities Associated with Chronic Kidney Disease

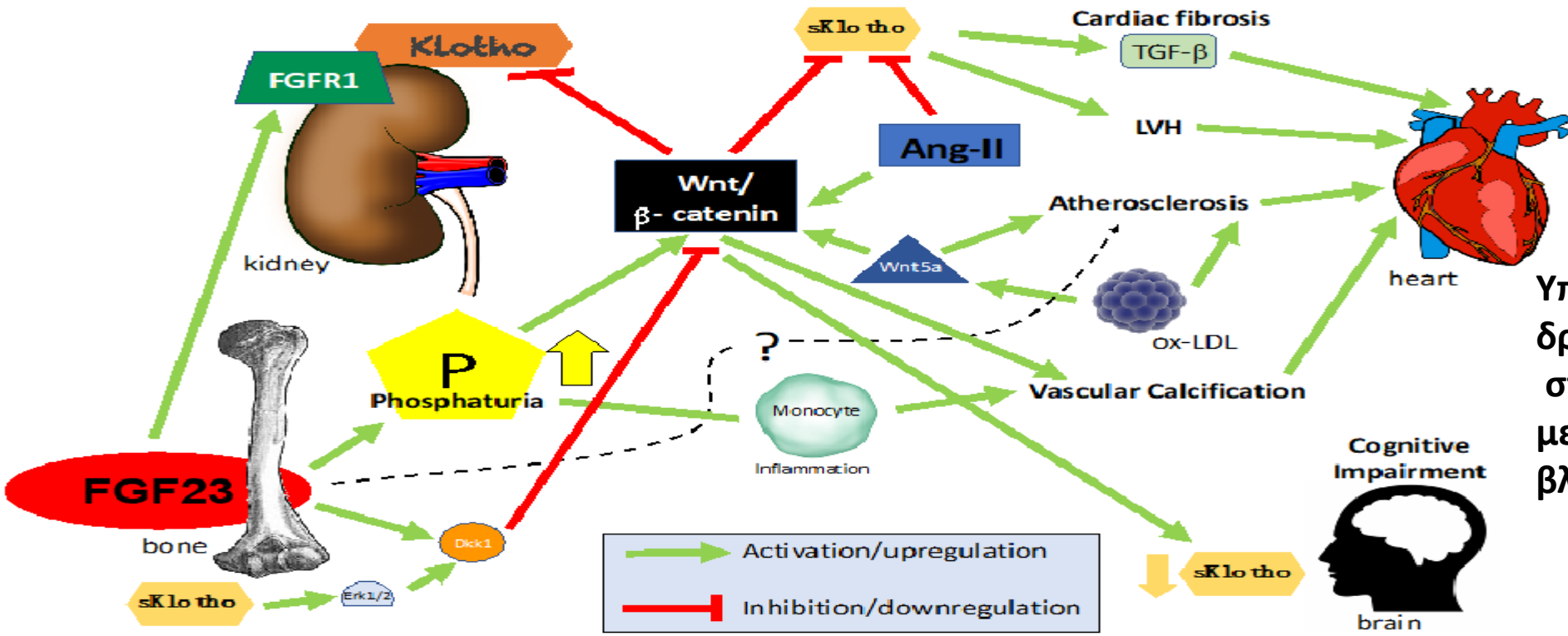
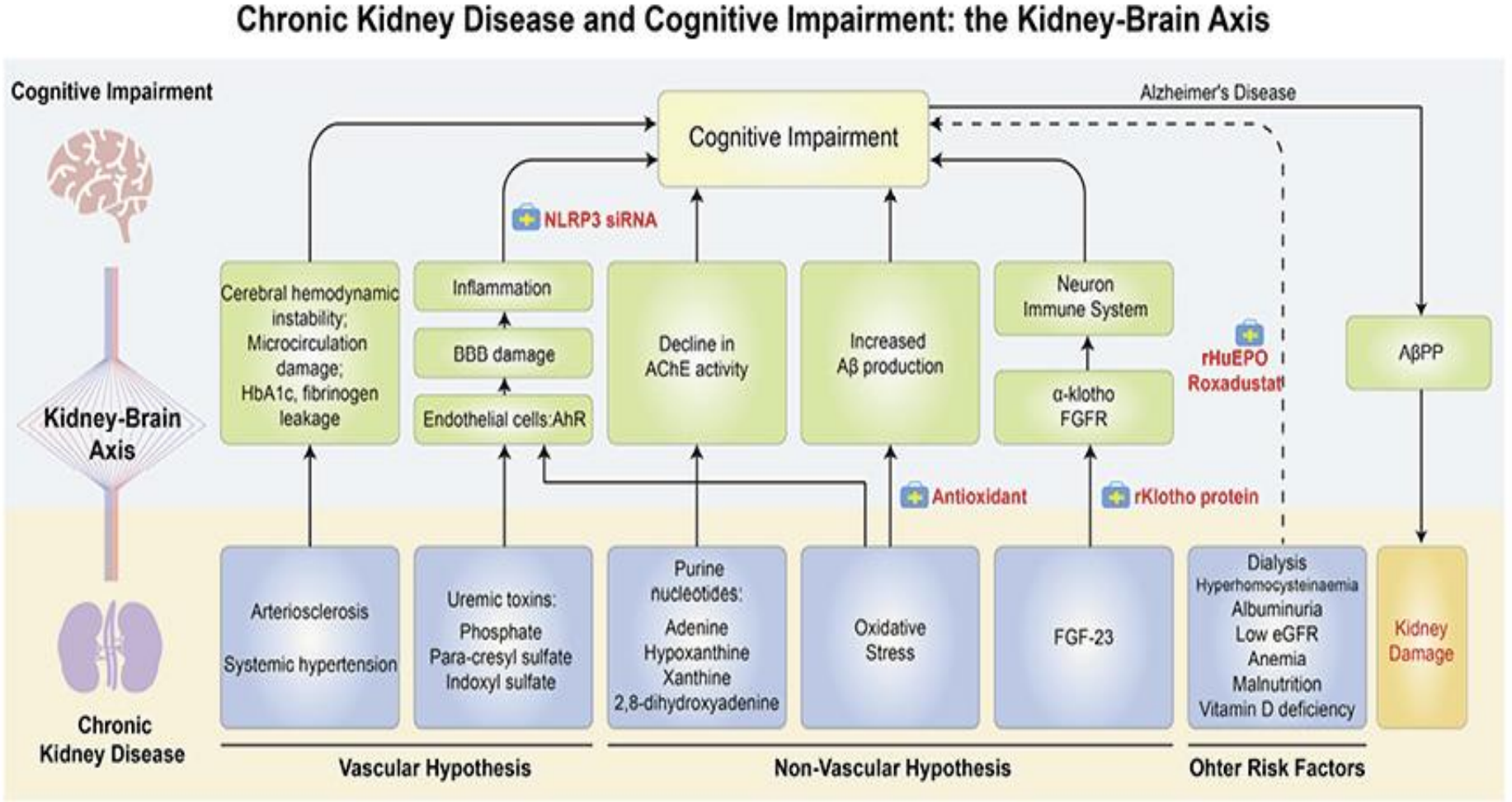


Figure 2. Schematic representation of FGF23/Klotho interactions with the Wnt/β-catenin pathway in the bone, kidney, and heart.

Υπάρχουν ενδείξεις ότι η FGF23 δρα απευθείας στην λειτουργία του ιππόκαμπού με αποτέλεσμα την εγκεφαλική βλάβη



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3.Παράγοντες στην αιμοκάθαρση, αναιμία, και έλλειψη VitD

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Environmental Research and Public Health

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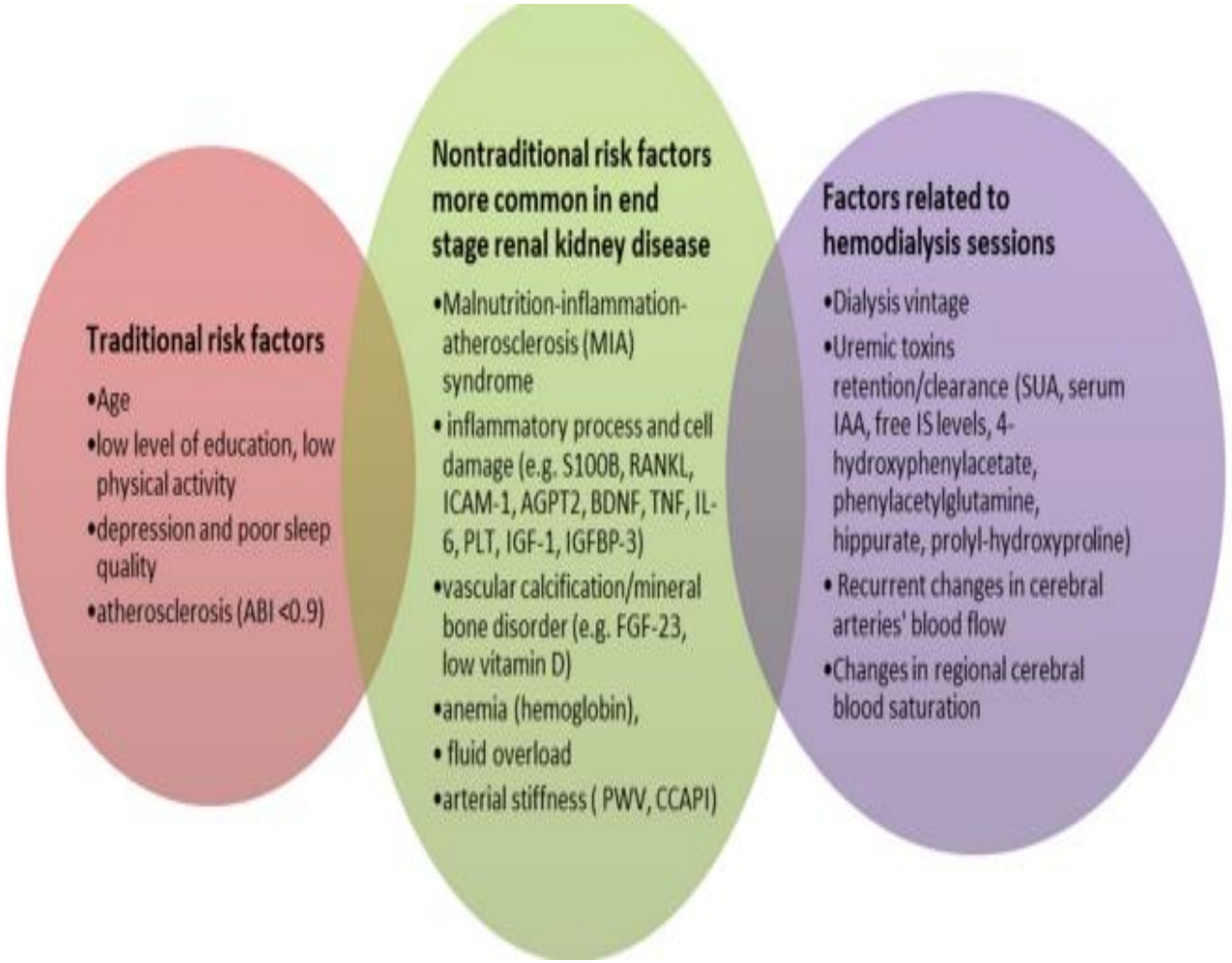
Review

Cognitive Impairment in End Stage Renal Disease Patients Undergoing Hemodialysis: Markers and Risk Factors

Piotr Olczyk, Mariusz Kusztal *, Tomasz Gołębiowski, Krzysztof Letachowicz and Magdalena Krajewska

Published: 18 February 2022

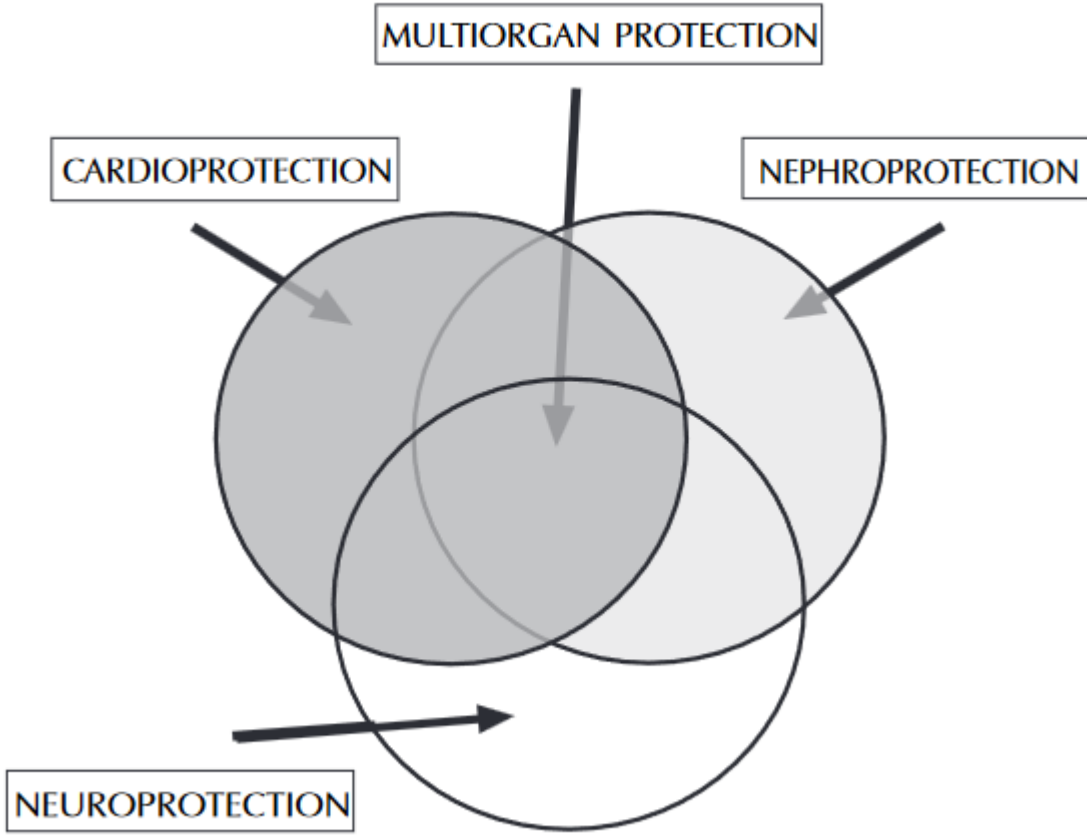


ΝΕΥΡΟΠΡΟΣΤΑΣΙΑ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ ΧΝΝ

ΝΕΦΡΟΠΡΟΣΤΑΣΙΑ

ΝΕΥΡΟΠΡΟΣΤΑΣΙΑ

Υπάρχουν φαρμακευτικές παρεμβάσεις?



nutrients

Review

Role of Vitamin D in Cognitive Function in Chronic Kidney Disease

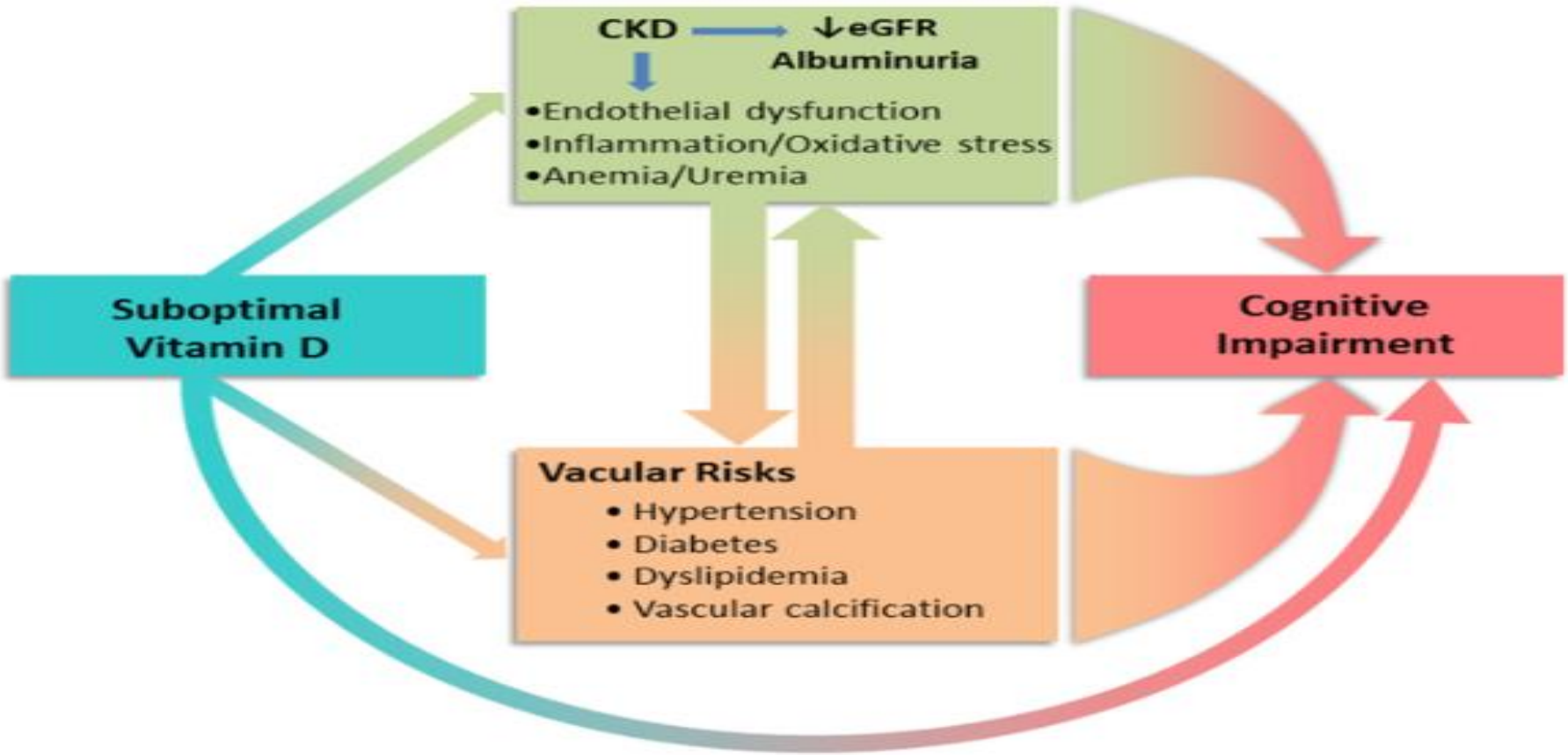
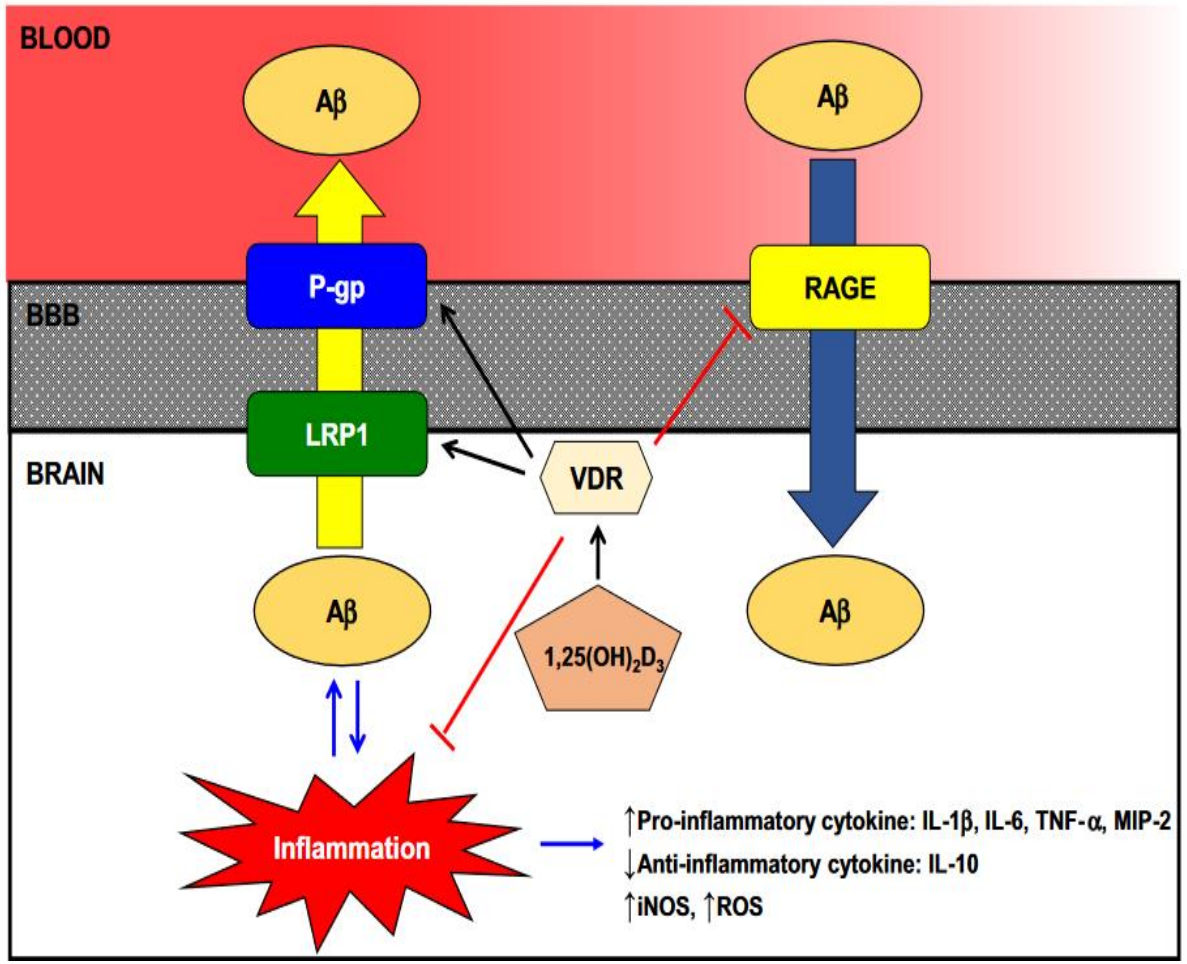
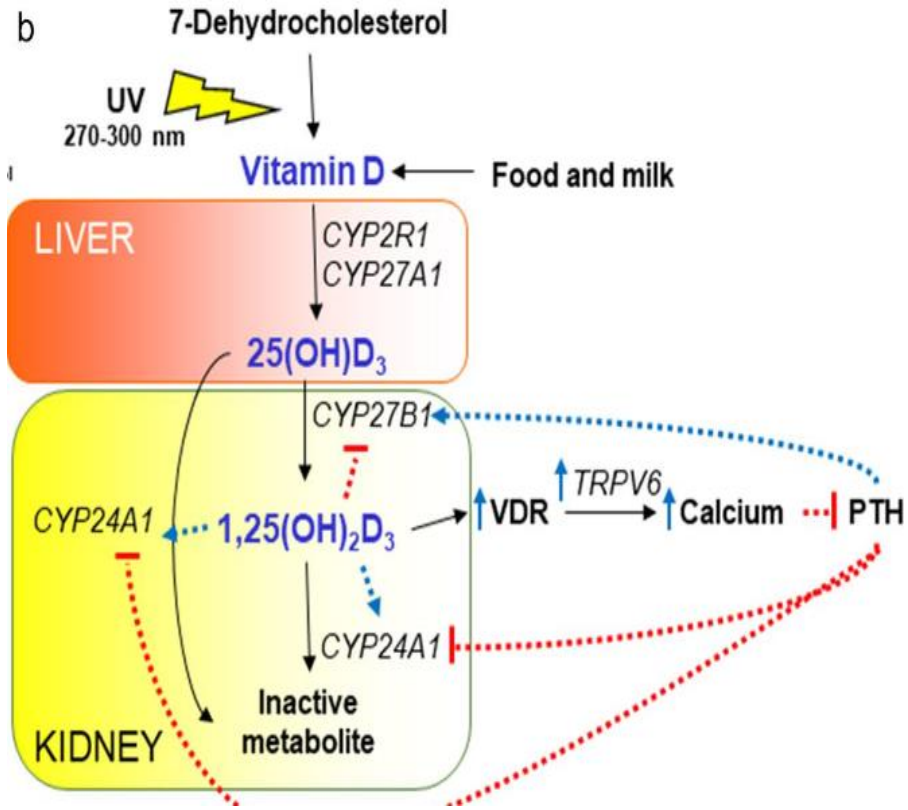


Figure 2. Suboptimal vitamin D status directly and indirectly contributes to the development and progression of cognitive impairment. Studies have demonstrated an association of hypovitaminosis D and diseases that raise vascular risks [85]. Endothelial dysfunction and inflammatory/uremic milieu in CKD act not only as a consequence of CKD but also through promoting vascular risk factors contributing the CKD progression.

g. 5 VDR regulation of
ceptors governing the influx
RAGE) and efflux (LRP1 and
-gp) of $A\beta_{1-40}$ and $A\beta_{1-42}$
eptides in brain; other benefits
f the VDR include anti-inflam-
atory activities and lowering
f reactive oxygen species





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Review

Phosphate in the Context of Cognitive Impairment and Other Neurological Disorders Occurrence in Chronic Kidney Disease

Merita Rroji [1,*], Andreja Figurek [2,3], Davide Viggiano [4,5], Giovambattista Capasso [4,5] and Goce Spasovski [6]

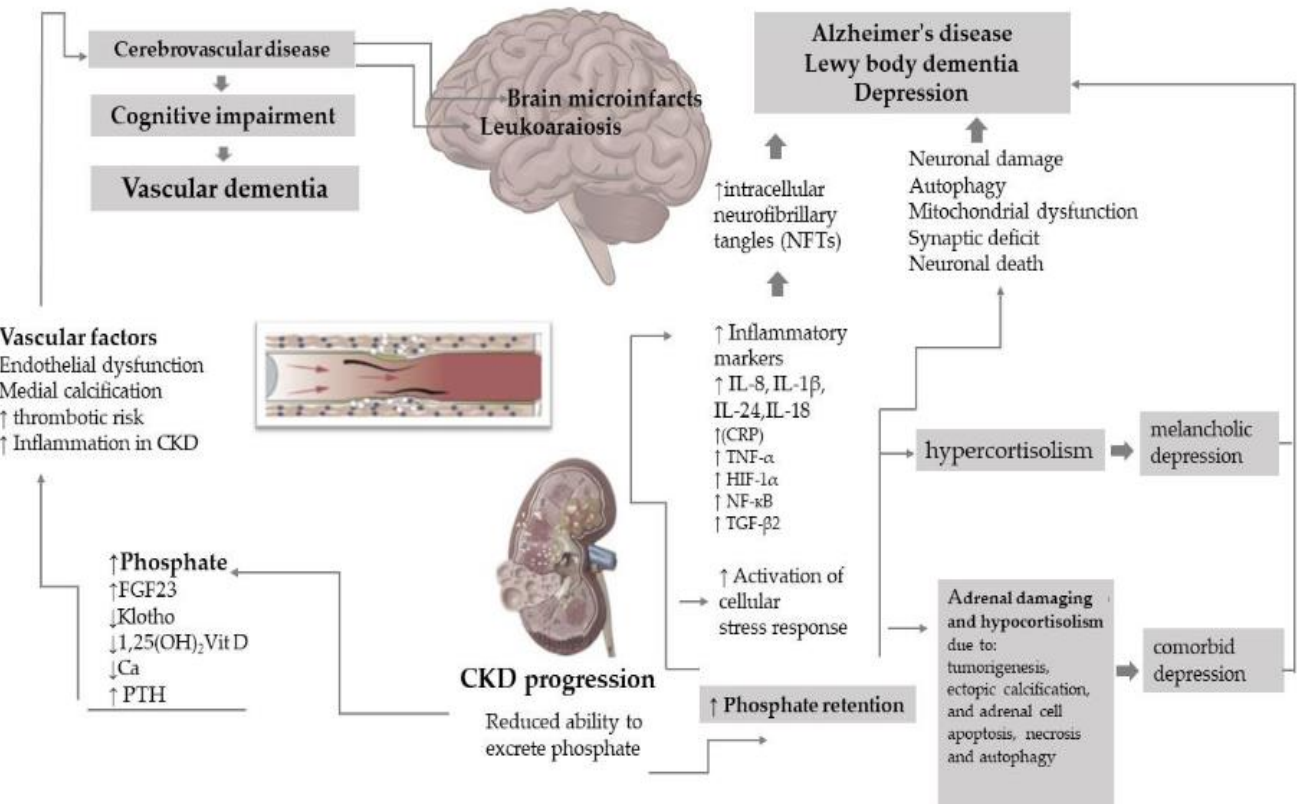


Table 1. CKD–MBD biomarkers, role in bone metabolism, vascular calcification, brain, and neurocognitive function.

CKD-MBD Biomarkers	Role in Bone Metabolism	Vascular Calcification	Brain and Neurocognitive Function
PTH	Key mediator of bone turnover Regulates P and Ca homeostasis	Complex paracrine and systemic effect Promotes VC Impairs endothelial function	Endothelial dysfunction Arterial stiffness ↑Ca→ neuronal signaling disruption, frontal-subcortical dementia, atrophy in hippocampus ↑PTH→significantly decreased gray matter volume (GMV) Impair executive function memory impairment
Vit D	Key role in Ca, P homeostasis Depletion promote sHPTH and osteitis fibrosis cystica	Biphasic curve of Vit D on calcification	↓Vit D→ impairs contractile function of vessels ↓Vit D→ may lead to disruption of calcium homeostasis in neurons, thus causing neuronal aging and neurodegeneration vulnerability ↓Vit D→↑Amyloid β deposition and tau protein tangles in the brain ↓Vit D→↑inflammation, ↑oxidative stress, endothelial dysfunction
Klotho	Acts as a Wnt-inhibitor Modify bone metabolism	Inhibitor of VC Klotho deficiency→ impair endothelial function	Klotho deficiency →impairment of vascular cell senescence, →impairment of brain immune system, →impairment of central nervous system
FGF23	Posphaturic hormone acts through α-klotho	Is not clear if it has a direct effect on VC	↑FGF23 not directly connected with cognitive impairment ↑FGF23→↓Vit D ↑FGF23→↑inflammation

Review

Neuroprotective Effect of SGLT2 Inhibitors

Table 1. Comparison of pleiotropic effects of Sotagliflozin, Canagliflozin, Dapagliflozin, Empagliflozin, Ertugliflozin.

	Sotagliflozin	Canagliflozin	Dapagliflozin	Empagliflozin	Ertugliflozin
SGLT2 Selectivity over SGLT1	20 fold [28]	250 fold [28]	1200 fold [28]	2500 fold [28]	2500 fold [28]
Brain/Serum Ratio	n/a	0.3	0.3	0.5	n/a
AChE Inhibition	K_i 5.6μM [29]	The most potent, even called a dual inhibitor K_i 0.13 μM [29]	K_i 25.02μM [29]	K_i 0.177μM [30]	K_i 31.69μM [29]
BDNF Increase	n/a	n/a	n/a	Yes [31]	n/a
Anti-epileptic Potential	n/a	n/a	Yes [32]	n/a	n/a
CIMT Regression	n/a	n/a	Yes [33]	Yes [34]	n/a
Anti-inflammatory	n/a	Yes [35]	Yes [36]	Yes [37]	No | n/a [38]
Blood-brain Barrier Protection	n/a	n/a	n/a	Yes [37]	n/a

Neuroprotective Effect of SGLT2 Inhibitors. Molecules 2021, 26, 7213

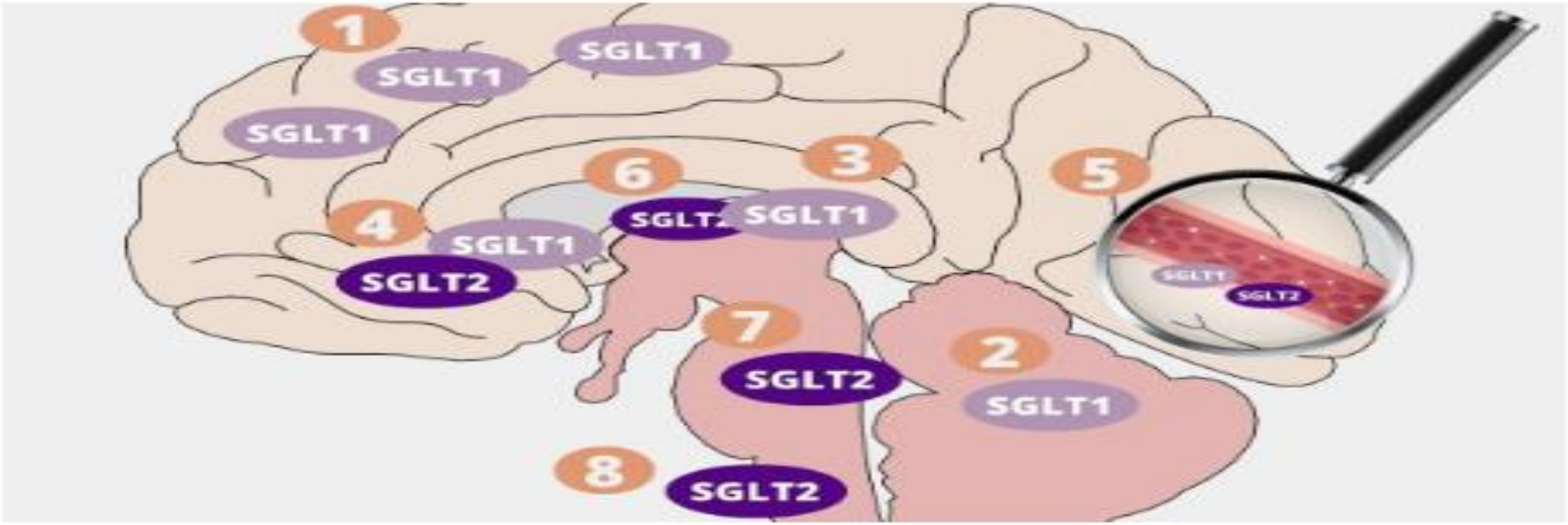


Figure 1. Distribution of SGLT1 and SGLT2 receptors in the Central Nervous System: 1. Pyramidal cells of brain cortex; 2. Purkinje cerebellum cells; 3. Hippocampus pyramidal and granular cells; 4. Hypothalamus; 5. Microvessels; 6. Amygdala; 7. Periaqueductal grey; 8. Dorsomedial medulla—nucleus of the solitary tract (NTS).

SGLT2 inhibitors are not fully selective for SGLT2 co-receptors, and they also affect SGLT1 to various extents (Table 1). Sotagliflozin has the most affinity to SGLT1 receptors. It is even called a "dual SGLT1/SGLT2 inhibitor", however, it is the newest Flozin, and it is not yet used in diabetic patients on a large scale [12]. Among commonly used SGLT2 inhibitors, Canagliflozin has the greatest potential for inhibiting SGLT1 receptors. In contrast, Empagliflozin and Ertugliflozin are the most selective for SGLT2 and have the lowest potential for interaction with SGLT1 [27]. Therefore, theoretically, to obtain the neuroprotective effect associated with SGLT1 inhibition in diabetic patients, Sotagliflozin and Canagliflozin should be preferred over Dapagliflozin, Empagliflozin, and Ertugliflozin.

Erythropoietin as a Neuroprotective Molecule: An Overview of Its Therapeutic Potential in Neurodegenerative Diseases

Federica Rey[1], Alice Balsari[1], Toniella Giallongo[1], Sara Ottolenghi[2], Anna M. Di Giulio[1,3], Michele Samaja[2], and Stephana Carelli[1,3]

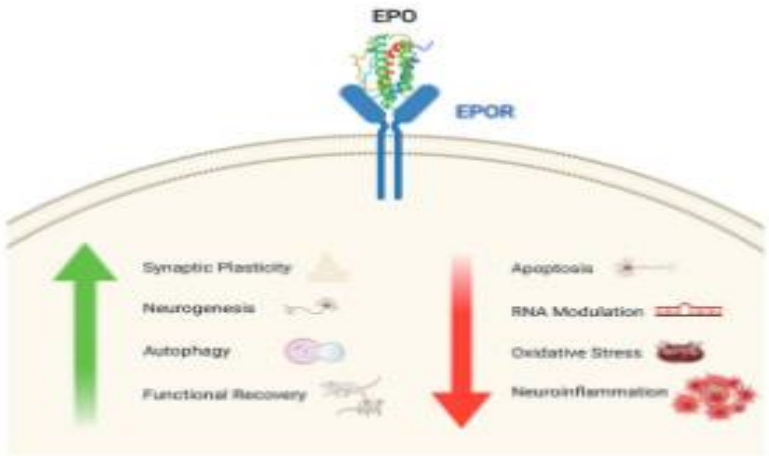


Figure 2. Neurotrophic role of EPO's binding with EPOR. In the CNS, EPO's binding to its receptor leads to an increase in neuroprotective actions (synaptic plasticity, neurogenesis, autophagy) with an overall functional recovery in animal models. Conversely, the binding leads to a decrease in apoptosis, expression of miRNAs regulating the apoptotic process, oxidative stress, and neuroinflammation. Made in ©BioRender—biorender.com
EPO = erythropoietin; EPOR = erythropoietin receptor.

Table 1. Summary of the Studies Describing EPO's Neurotrophic Effect in Neurodegenerative Diseases.

Pathology	Description	References
Parkinson's disease		
In vitro	EPO increases cell viability altering the Bax/Bcl-2 ratio in PC12 cells intoxicated with MPP+, modulates the autophagy process in rotenone-treated SH-SY5Y cells, activates the PI3K/Akt/FoxO3a pathway, and modulates neuroinflammation.	Wu et al., 2007; Maiese et al., 2012; Bond and Rex, 2014; Jia et al., 2014; Jang et al., 2016
In vivo	EPO restores TH levels and reduces the expression of early proinflammatory cytokines and microglia markers.	Qi et al., 2014; Erbas et al., 2015; Carelli et al., 2016a, 2017b, 2018
Clinical trials	EPO has positive effects on nonmotor symptoms, such as pain, apathy, and sexual difficulty.	Pedroso et al., 2012; Jang et al., 2014
Alzheimer's disease		
In vitro	EPO is used to block the apoptotic pathway and protects from Aβ toxicity, increases antioxidant mechanisms, and has a neurotrophic function in primary hippocampal neuron through BDNF's expression.	Viviani et al., 2005; Li et al., 2008; Ma et al., 2009; Shang et al., 2011, 2012; Esmaeili Tazangi et al., 2015
In vivo	EPO decreases tau hyper phosphorylation, reduces neuroinflammation and oxidative stress, increases neurogenesis, improves cognitive results in AD mice models, and improves synaptic plasticity but no effect on anxiety and spontaneous activity.	Lee et al., 2012; Armand-Ugón et al., 2015; Li et al., 2015; Samy et al., 2016; Hernández et al., 2017; Rodríguez Cruz et al., 2017
Clinical trials	EPO improves neuropsychological test scoring in chronic kidney disease and ameliorates AD patient's daily living.	Kumagai et al., 2018; Vinothkumar et al., 2018
Amyotrophic lateral sclerosis		
In vitro	EPO prevents apoptotic neuronal changes and decreases the levels of the SOD1 aggregates.	Nagańska et al., 2010; Cho et al., 2011
In vivo	EPO administration delays symptoms, preserves motor symptoms, and modulates the neuroinflammatory response, but results are controversial with regard to the life span.	Grignaschi et al., 2007; Grunfeld et al., 2007; Koh et al., 2007; Noh et al., 2014
Clinical trials	EPO administration has no adverse effects	Lauria et al., 2009; Kim et al., 2014
Spinal cord injury		
In vivo	EPO administration leads to a partial recovery of motor function, prevents the secondary injury through anti-inflammatory and neuroprotective actions, increases TH-positive fibers of lumbosacral cord of treated mice, reduces the production of proinflammatory cytokines, and induces neurogenesis increasing BDNF activity.	Gorio et al., 2002, 2005; Rees et al., 2010; Mofidi et al., 2011; Simon et al., 2011; Cerri et al., 2012; Carelli et al., 2014, 2015, 2017b
Clinical trials	EPO's effect was not efficiently evaluated.	Costa et al., 2015
Brain ischemia		
In vitro	EPO acts on neurogenesis, is involved in apoptotic and cellular recovery, and activates antiapoptotic genes.	Ruscher et al., 1998; Dirnagl et al., 1999; Suzuki et al., 2001; Marti, 2004
In vivo	EPO administration is involved in neuroprotection.	Shingo et al., 2001; Sanchez et al., 2009
Clinical trials	EPO reduces infarct size.	Tsai et al., 2015; Yao et al., 2017
Brain hypoxia and hyperoxia		
In vivo	EPO ameliorates the metabolic stress and induces neuroprotection in chronic hypoxia.	Chung et al., 2015; Fantacci et al., 2006
Clinical trials	EPO treatment in newborns with hypoxic-ischemic encephalopathy improves neurological outcomes.	Zhu et al., 2009

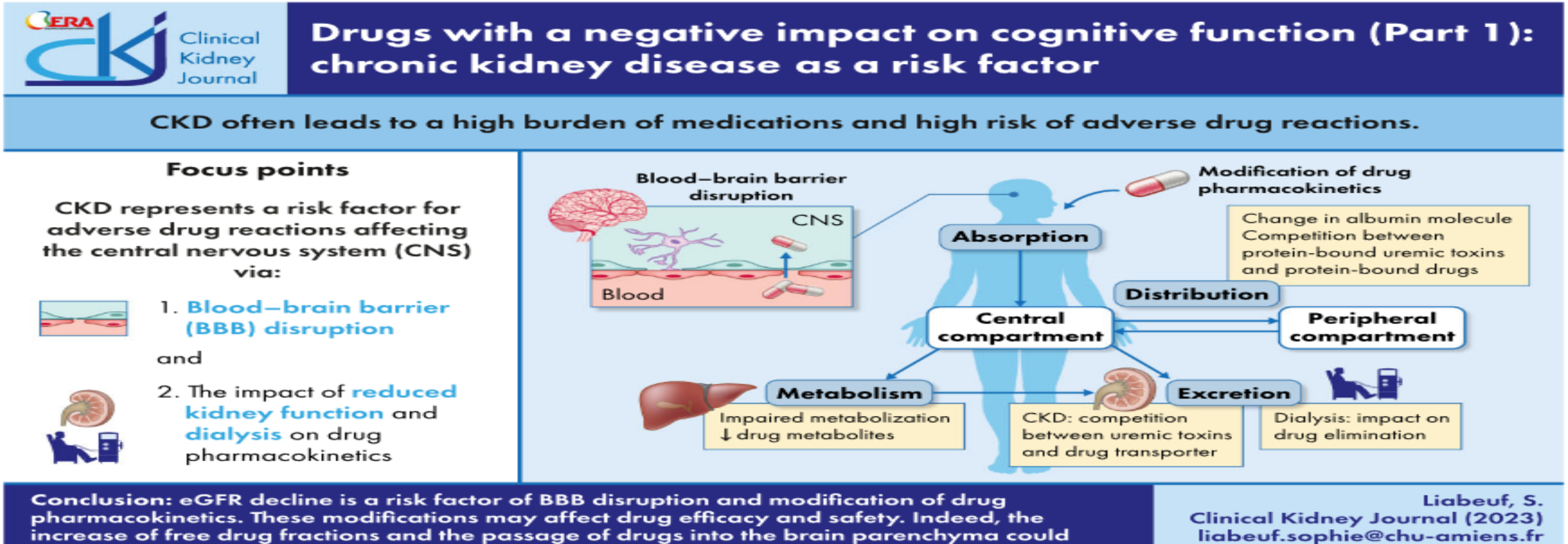
Note. EPO = erythropoietin; MPP+ = 1-methyl-4-phenylpyridinium; PI3K = phosphatidylinositol 3-kinase; TH = tyrosine hydroxylase; BDNF = brain-derived neurotrophic factor; AD = Alzheimer's disease; SOD1 = superoxide dismutase.

CKJ REVIEW

Drugs with a negative impact on cognitive function (Part 1): chronic kidney disease as a risk factor

Sophie Liabeuf[1,2], Vesna Pešić[3], Goce Spasovski[4], Romaldas Maciulaitis[5,6], Mickaël Bobot[7], Ana Farinha[8], Carsten A. Wagner[9], Robert J. Unwin[10], Giovambattista Capasso[11,12], Inga Arune Bumblyte[5] and Gaye Hafez[13]; on behalf of CONNECT Action (Cognitive Decline in Nephro-Neurology

GRAPHICAL ABSTRACT



Nephrol Dial Transplant (2021) 36: 385–386
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Advance Access publication 9 September 2020

Drug prescription in patients with chronic kidney disea a true challenge

Sophie Liabeuf[1,2] and Maurice Laville[3,4]

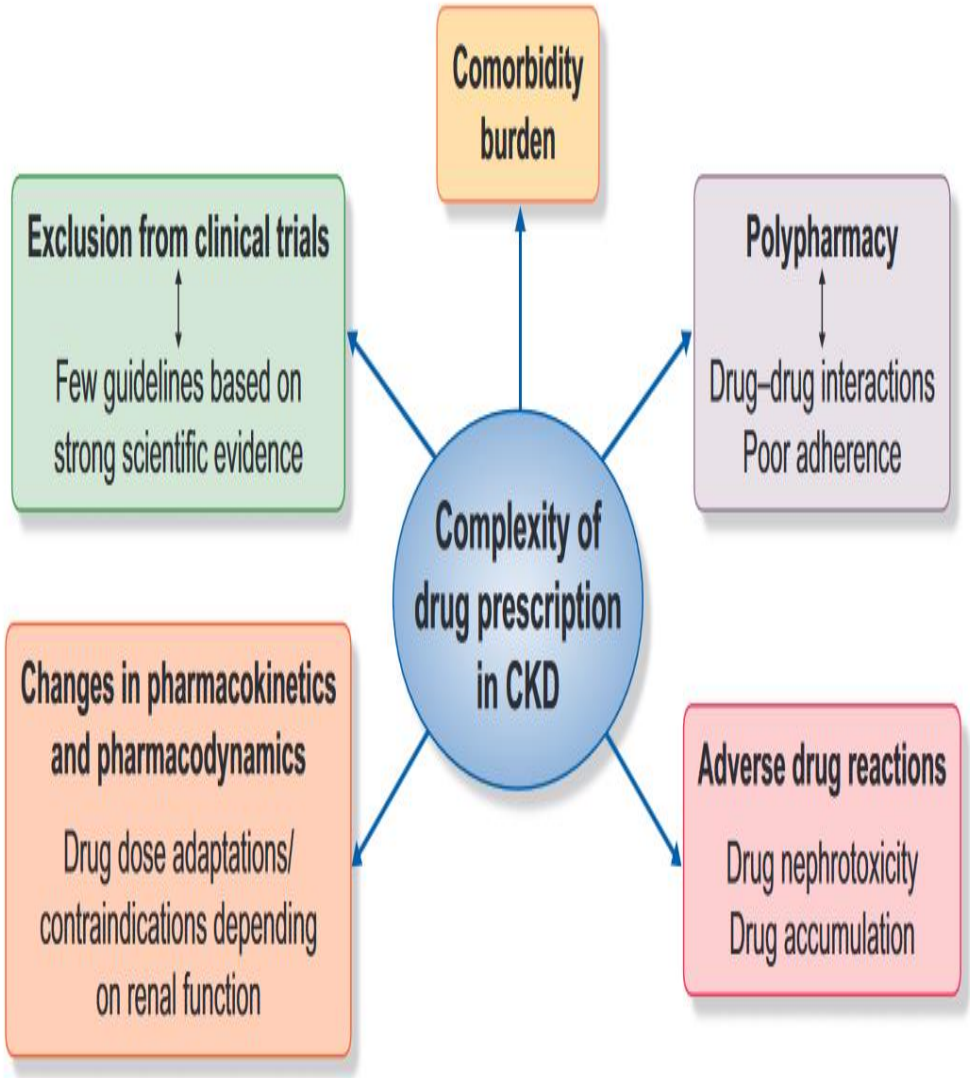


FIGURE 1: Factors accounting for the complexity of drug prescription in patients with CKD.

CKJ REVIEW

Drugs with a negative impact on cognitive functions (Part 2): drug classes to consider while prescribing in CKD patients

Gaye Hafez [1], Jolanta Malyszko [2], Aleksandra Golenia [3], Aleksandra Klimkowicz-Mrowiec [4], Ana Carina Ferreira [5,6], Mustafa Arıcı [7], Annette Bruchfeld [8,9], Dorothea Nitsch [10], Ziad A. Massy [11,12], Marion Pépin [12,13], Giovambattista Capasso [14,15], Laila-Yasmin Mani [16,*] and Sophie Liabeuf [17,18,*]; on behalf of CONNECT Action (Cognitive Decline in Nephro-Neurology European Cooperative Target)

Clinical Kidney Journal

Drugs with a negative impact on cognitive functions (Part 2): drug classes to consider while prescribing in CKD patients

A better understanding of risk factors associated with cognitive impairment could lead to new avenues to prevent further cognitive impairment in CKD patients. Adverse drug reactions affecting the central nervous system (CNS) could represent a modifiable risk factor as these may be prevented by re-evaluating patients' drug prescription.

Cognitive functions:

- Social functioning
- Language
- Visual functioning
- Learning and memory
- Complex attention
- Executive function
- Orientation
- Visuospatial

Adverse drug reactions on CNS:

- Sedation
- Decreased performance skills
- Cognitive impairment
- Neuroexcitatory effects
- Hallucination
- Delirium

Conclusion: CKD patients are frequently treated with drugs that are commonly recognized as at risk of cognitive impairment in the general population such as opioids, psychotropics, antibiotics, antivirals, and drugs with anticholinergic properties, suggesting that more

Hafez, G., et al.
Clinical Kidney Journal (2023)
gaye.hafez@altinbas.edu.tr

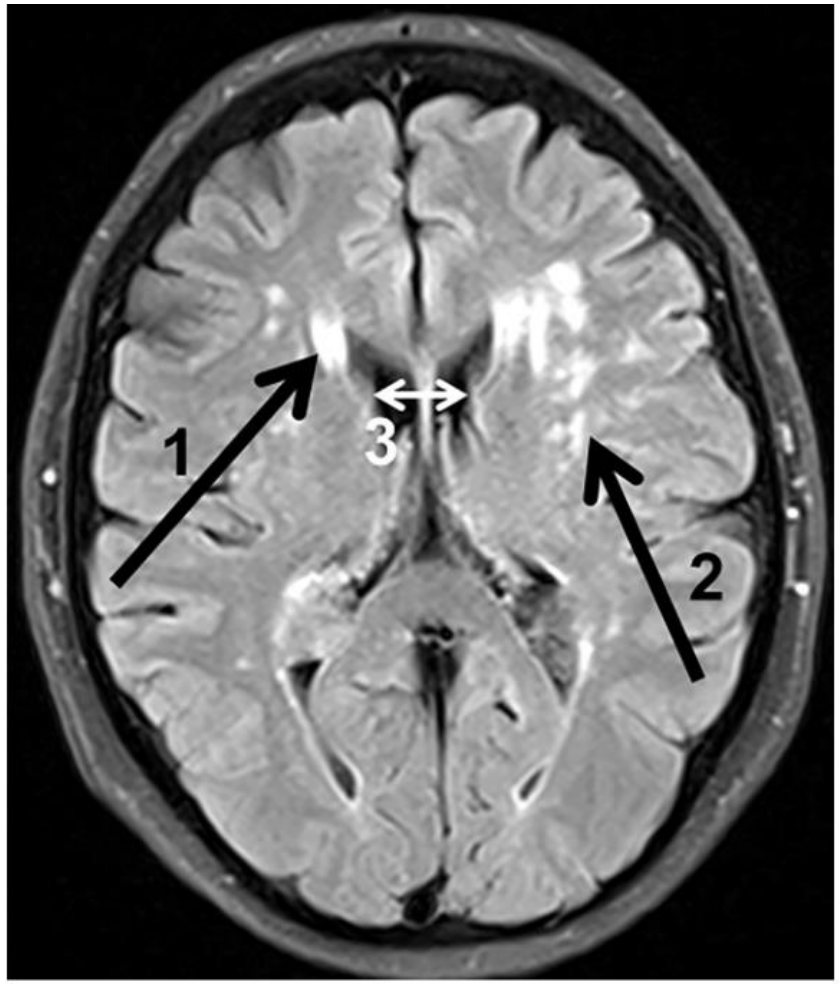


Fig 2. Exemplary illustration of magnetic resonance imaging parameters. This exemplary FLAIR image displays the assessed MRI values periventricular hyperintensities (PVH, arrow 1), white matter hyperintensities (WMH, arrow 2) and ventricular widths at the level of the caudate nucleus (VWCN, arrow 3) in a 54 year old female patient 11 years after kidney transplantation.

RESEARCH ARTICLE

Brain function and metabolism in patients with long-term tacrolimus therapy after kidney transplantation in comparison to patients after liver transplantation

Henning Pflugrad[1,2☯*], Patrick Nösel[3☯], Xiaoqi Ding[3], Birte Schmitz[3], Heinrich Lanfermann[3], Hannelore Barg-Hock[4], Jürgen Klempnauer[2,4], Mario Schiffer[2,5¤‡], Karin Weissenborn[1,2‡]

Farragher *et al. Systematic Reviews* (2020) 9:58
https://doi.org/10.1186/s13643-020-01320-x

Systematic Reviews

PROTOCOL Open Access

Cognitive interventions for adults with chronic kidney disease: protocol for a scoping review

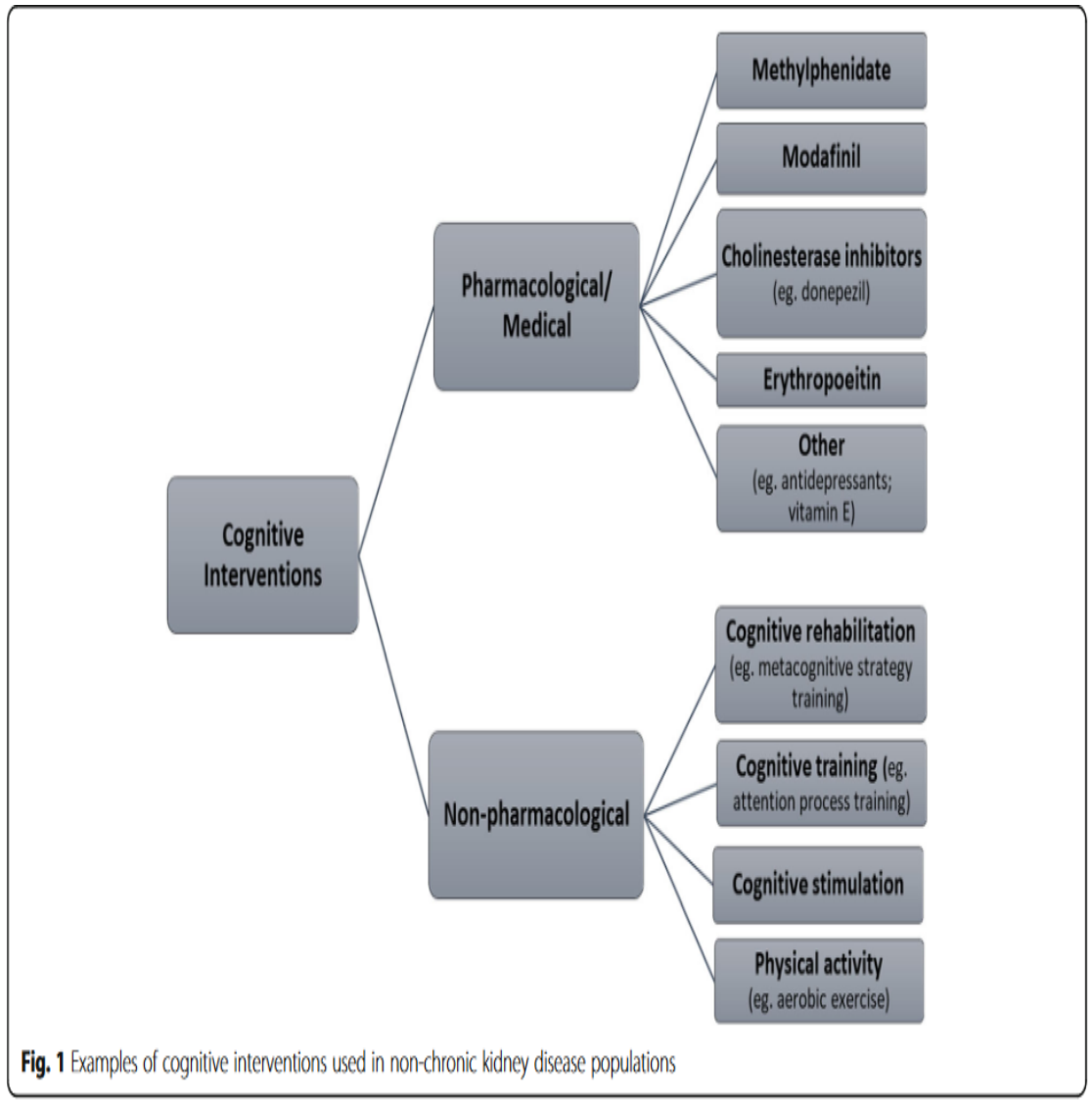
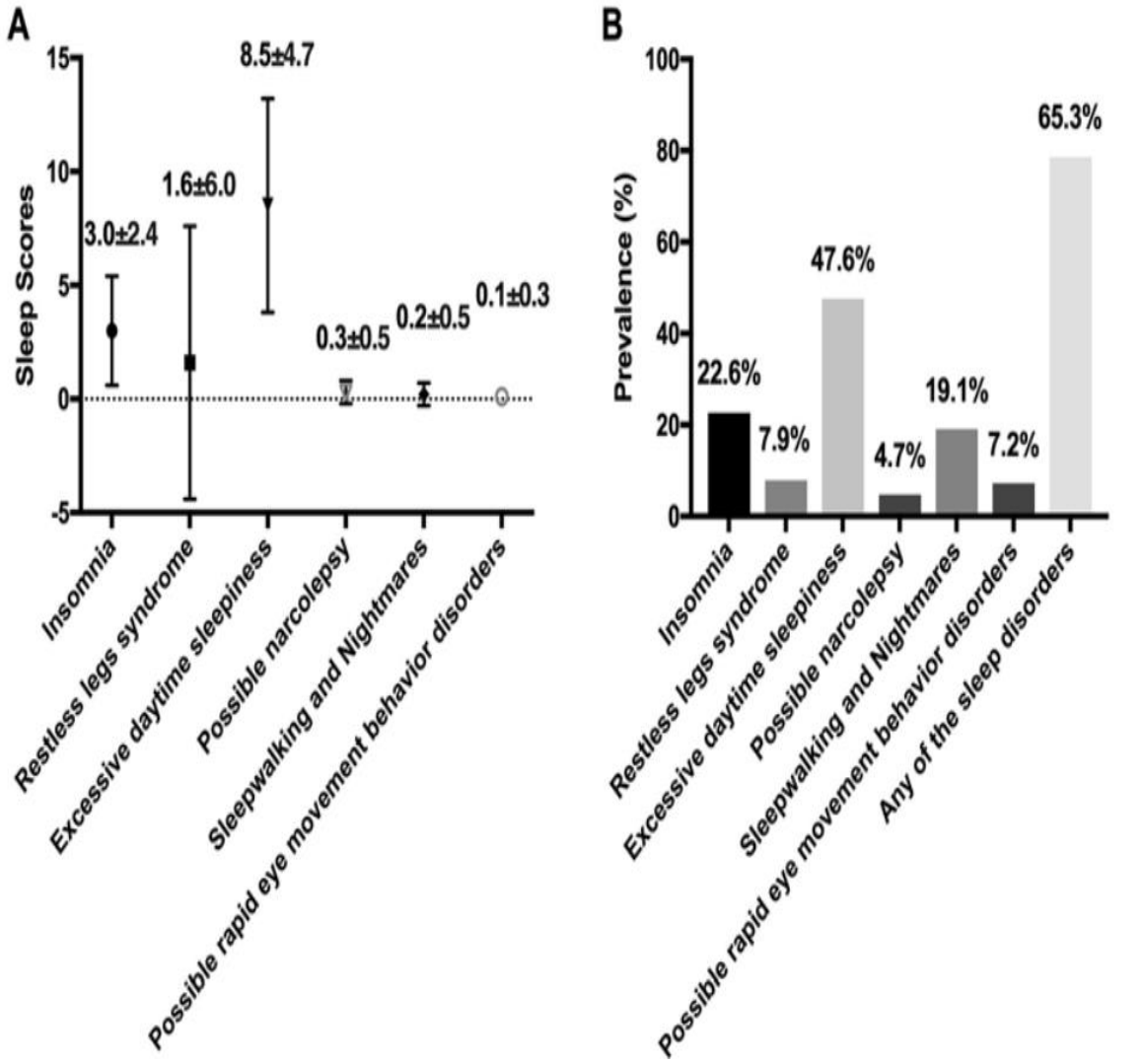


Fig. 1 Examples of cognitive interventions used in non-chronic kidney disease populations



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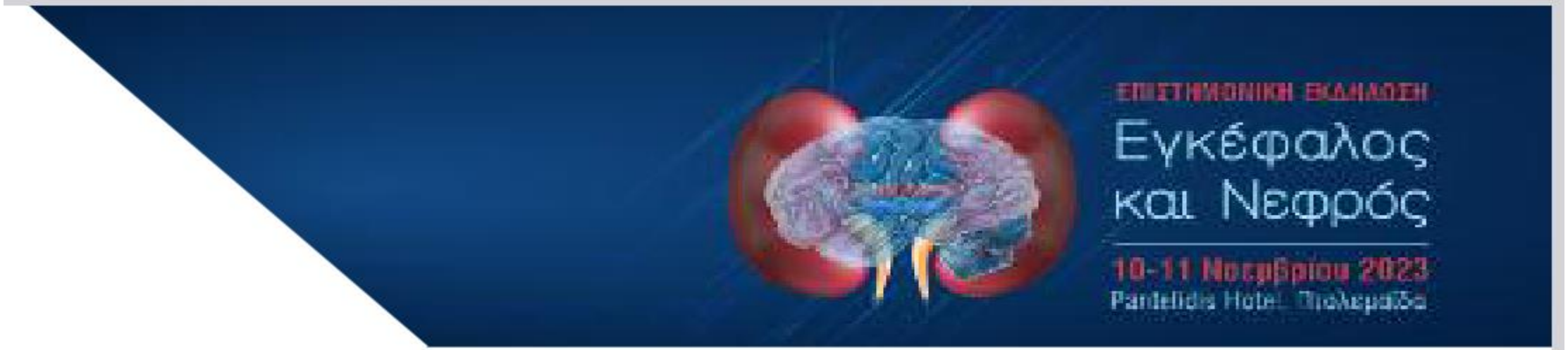
Research Article

Sleep Disorders and Cognitive Impairment in Peritoneal Dialysis: A Multicenter Prospective Cohort Study

- Οι διαταραχές ύπνου αποτελούν παράγοντα γνωστικής δυσλειτουργίας

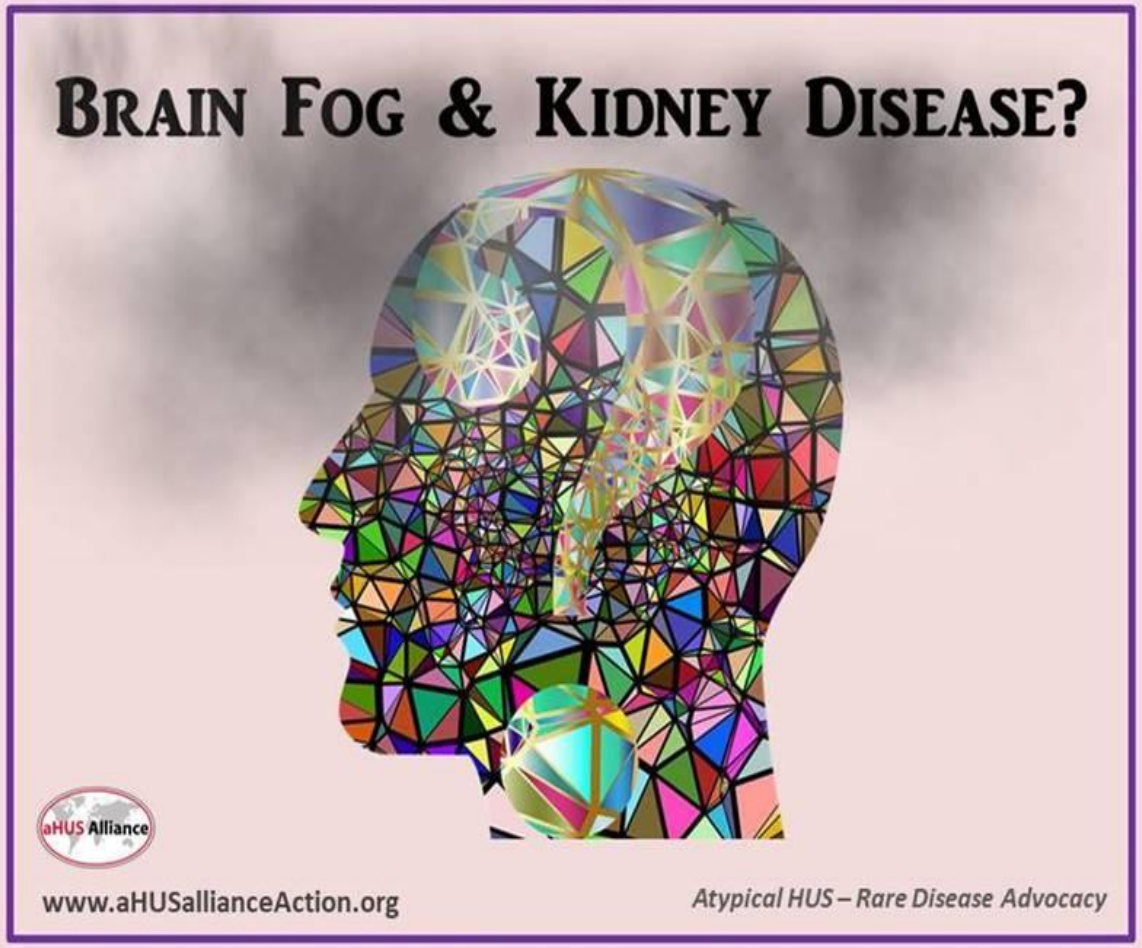


Συμπεράσματα

Η γνωσιακή δυσλειτουργία στην ΧΝΝ είναι υποτιμημένη, υποαναγνωρισμένη αλλά αποτελεί συχνό κλινικό πρόβλημα

Νευροπροστατευτικοί παράγοντες(ερυθροποιητίνη,Vit. D) μπορεί να επιβραδύνουν/αποτρέψουν την γνωσιακή δυσλειτουργία

Προγνωστικός δείκτης της γνωσιακής δυσλειτουργίας φαίνεται να αποτελεί η αυξημένη ΑΣ και η παρουσία λευκωματουρίας



KIDNEY AND BRAIN HEALTH

ΕΥΧΑΡΙΣΤΩ