TURUN YLIOPISTO

Association between blood pressure and cognitive function in older adults

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Abstract

Background: Hypertension has been associated with cognitive decline, but the longitudinal relationship between different blood pressure measures and specific cognitive domains remains incompletely understood. The aim of this study is to examine changes in cognitive function over a 10-year follow-up period and to assess whether office blood pressure (BP), ambulatory blood pressure (ABP), and nocturnal dipping are associated with cognitive function and its changes over time.

Methods: Participants from the FIREA study underwent cognitive testing at baseline and follow-up using a computerized standardized cognitive test battery. Cognitive domains included memory and learning, reaction time, sustained attention and working memory. Hypertension status was determined using office BP, ABP and nocturnal dipping measures, and changes in cognitive function were compared between BP groups.

Results: During the 10-year follow-up period memory and learning improved while reaction time and sustained attention declined. There was also some indication of improvement in working memory. At baseline, dippers had better sustained attention than non-dippers. No statistically significant differences in cognitive function changes were observed between the BP groups, although indicatively non-dippers had a faster decline in sustained attention.

Conclusions: Changes in cognitive function over the follow-up period were mostly independent of hypertension status. The findings suggest that different cognitive domains change differently over time, with some aspects of cognitive function remaining well preserved until older age.

Keywords: cognition, cognitive function, blood pressure, nocturnal dipping

Sisällysluettelo

1 Introduction

Cognitive impairment and dementia are major burdens on today's healthcare system. The prevalence of dementia for those aged ≥ 60 years varies from 5%-7% in most world regions.[1] In addition, the overall global prevalence of mild cognitive impairment for those aged > 50 years is 19.7%, concerning nearly a fifth of the world's older adults.[2] These numbers are only expected to increase in the future, because of population aging. It is estimated that the number of people suffering from dementia would almost double every 20 years, resulting in 115.4 million dementia patients worldwide in 2050.[1] As there still is no curing treatment for dementia, and with AD and vascular dementia being the most common diseases behind it, it is important to study the possible risk factors causing these diseases. Primary prevention of dementia could then be done by treating these known factors.

Hypertension is one of the most common health conditions globally, affecting approximately 1.4 billion adults aged 30-79 years worldwide, and has been consistently linked with cognitive impairment and dementia.[3,4] Hypertension is particularly associated with vascular dementia, but also Alzheimer's disease (AD) dementia, as these diseases share overlapping pathophysiological mechanisms.[5] Chronic hypertension can lead to structural and functional changes in cerebral blood vessels, including arterial stiffness, endothelial dysfunction and disruption of the blood-brain barrier. These changes may contribute to reduced cerebral blood flow, microinfarcts and accumulation of neurotoxic proteins, all of which are connected to cognitive decline and the development of dementia.[4,5]

Elevated arterial blood pressure in mid-life is known to be a significant risk factor for later-life cognitive disorders.[6] Therefore, diagnosing and treating hypertension is recommended to prevent later cognitive impairment and dementia.[7] However, there hasn't been a consensus on the optimal BP levels to maintain cognitive function, as also low blood pressure can be a risk factor for cognitive decline and dementia in older adults.[4] In addition to BP levels, blood pressure variability (BPV), abnormal dipping patterns and blood vessel stiffness have been associated with brain health and risks of dementia.[4,8,9]

Cognitive function refers to an individual’s ability to process information, including domains such as memory, learning, attention, language, executive function, problem solving and decision making. Although gradual changes in cognitive function are part of normal aging, a significant decline in them may indicate pathological conditions such as mild cognitive impairment or dementia. Maintaining cognitive function is therefore important in preserving independence and quality of life in aging populations, further emphasizing the importance of identifying and managing risk factors such as hypertension.

The aim of this thesis is to examine how different blood pressure indicators are associated with cognitive function in older adults. This topic is especially important because of the increasing prevalence of both hypertension and cognitive impairment in ageing populations. Previous research suggests that vascular and cardiovascular factors contribute significantly to age-related cognitive decline. However, the underlying associations remain insufficiently understood. By examining the relationship between blood pressure indicators and cognitive function, this thesis intends to contribute to a better understanding of potential risk factors for cognitive decline and to support the development of strategies to prevent cognitive impairment in later life.

2 Objectives

The aim of this study is to examine the associations between office and ambulatory blood pressure (BP) and 10-year changes in cognitive function in older adults. The purpose is not to make cause-effective conclusions, but to rather tentatively evaluate the possibility of using blood pressure as a predictor for later cognitive function. The possible associations will be evaluated by conducting a literature review and analyzing data from the Finnish Retirement and Aging study.

3 Literature review

There are several studies that have examined the associations between blood pressure and cognitive function in older adults. Some of them only measure office blood pressure, but others also measure ambulatory blood pressure (ABP) and blood pressure variability (BPV). Here I will separately assess the relations between office BP and cognitive function, and on the other hand ABP and cognitive function. All the selected studies are published between the years 2008 and 2024.

3.1 Mechanisms underlying the relationship between hypertension and cognitive function

Hypertension contributes to neuronal damage and cognitive decline through several interrelated mechanisms. Chronic high blood pressure plays a role in atherosclerosis and arteriolosclerosis of the cerebral blood vessels, which are significant risk factors of cerebral infarcts, and therefore can cause cognitive decline and dementia. In addition, hypertension disturbs cerebral autoregulation, which can lead to chronic cerebral hypoperfusion.[4]

Moreover, hypertension is strongly associated with various cerebrovascular pathologies, such as small vessel disease, lacunar infarcts, microhaemorrhages, and white matter lesions, each of which have been linked to declined cognitive function.[4,5] High BPV has likewise been associated with strokes and cerebral small vessel disease, offering another mechanism that may underlie cognitive impairment.[8] Hypertension has also been associated with neuroinflammation and pathophysiologies of AD, for example increased tau phosphorylation and beta-amyloid accumulation.[4]

3.2 Office BP and cognitive function

Previous studies of the association between office BP and cognitive function are presented in Table 1. Five of the seven studies reported that higher SBP was associated with reduced cognitive function.[10–14] These five studies included both cross-sectional and longitudinal studies. However, one cross-sectional study found an association between lower SBP and worse everyday problem-solving ability.[15] Moreover, DBP didn’t seem to be related to cognitive function as significantly as

SBP.[10,11,13] Still, one cross-sectional study reported that lower DBP was related to worse executive functioning and processing speed.[15]

One longitudinal study examined the long-term effect of BP on cognitive function and found that elevated SBP in early midlife was associated with reduced performance in Trail Making Test part B (TMT B), but no other associations were found between early midlife SBP and later life cognitive function.[16] TMT B primarily measures executive functions such as effective problem solving and working memory.[17]

Previous studies have reported associations between office BP and cognitive function, but the study populations, follow-up times and cognitive assessment have varied markedly across the studies, including the longitudinal studies. In one of the longitudinal studies the follow-up period was only five years, the average educational level of the participants was low (10±5 years) and the fallout of especially the older participants probably affected the results significantly.[13] In one of the longitudinal studies the participants were only women.[14] One of the longitudinal studies had a long follow-up period (25 years), but the measurement of cognitive function was only performed during the follow-up, so the changes in cognitive function could not be evaluated.[16] Current evidence in this topic is limited by the lack of detailed assessments of specific cognitive functions, insufficient follow-up duration and limited sensitivity of cognitive outcome measures. Therefore, further research addressing these limitations is needed.

Table 1. Summary of studies reporting on office blood pressure and cognitive function

Author (year)	N (% Males)	Population characteristics	Age [mean ± SD (range), years]	Blood pressure measurement	Cognitive function measurement	Main results
Cross-sectional studies						
Chen et al. (2024)[10]	5158 (41.5)	Unselected Chinese adult population	50.9 ± 15.6 (18-96)	SBP, DBP	MMSE, impaired cognitive function diagnosed by a score of <24 points	Higher SBP, but not DBP, was associated with impaired cognitive function.
Tarraf et al. (2017)[11]	9019 (45.3)	Middle-aged and older Hispanics/Latinos	56.5 (45-74)	SBP, DBP	DSS, B-SEVLT, WF, SIS	Higher SBP was associated with lower cognitive function.
Yeung et al. (2011)[15]	74 (0)	Women ≥50 years old from Vancouver, Canada	66.20 ± 8.44 (51-91)	SBP, DBP	Parts of D-KEFS, MMSE, DSC, CVLT-II, EPS test	Lower SBP was associated with worse everyday problem-solving ability. Lower DBP was related to worse executive functioning and processing speed.
Knecht et al. (2008)[12]	377 (45.4)	Non-demented and non-depressed community-dwelling individuals from Muenster, Germany	64 ± 6.62 (44-82)	SBP	Neurological test battery including domains of memory, attention and executive functions, and intellectual functions	SBP was inversely related to cognitive function.

Table 1 continues on the next page.

Author (year)	N (% Males)	Population characteristics	Age [mean ± SD (range), years]	Blood pressure measurement	Cognitive function measurement	Main results
Longitudinal studies						
Sun et al. (2021)[13]	1215 (40)	Stroke-free individuals from a racially and ethnically diverse Northern Manhattan population	71 ± 9, follow-up time 5 years	SBP, DBP	Neuropsychological test battery with domains of episodic memory, executive function, processing speed/VMI, and semantic memory/word fluency	SBP, but not DBP, was negatively associated with cognitive function, both cross-sectionally and longitudinally.
Yasar et al. (2011)[14]	336 (0)	Community dwelling 70–80-year-old women in eastern Baltimore, U.S.	74.1 (70-80), follow-up time 9 years	SBP	MMSE, TMT, HVLT-R	Elevated SBP increases the risk for late-life cognitive impairment in older non-demented women.
Walle-Hansen et al. (2023)[16]	2424 (51)	Individuals born in 1950 living in Akershus, Norway	63.9 ± 0.6 (62-65), follow-up time 25 years	SBP	MoCA, Delayed recall trial, TMT B	Elevated SBP in early midlife was associated with reduced capacity in TMT B, but no other associations were found between SBP and cognitive function.

SBP – systolic blood pressure, DBP – diastolic blood pressure, MMSE – mini-mental state examination, DSS – Digit symbol substitution, B-SEVLT – the Brief-Spanish English Verbal learning test, WF – word fluency, SIS – the Six-Item Screener, D-KEFS – Delis-Kaplan Executive Function System, DSC – Wechsler Adult Intelligence Scale-III Digit Symbol Coding task, CVLT-II – California Verbal Learning Test-2, EPS – Everyday Problem Solving, TMT – Trail Making Test, HVLT-R – Hopkins Verbal Learning Test-Revised, MoCA – Montreal Cognitive Assessment

3.3 Ambulatory BP and cognitive function

ABP predicts cardiovascular risk better than office BP since it isn't affected by the white coat effect and has more measuring data from different times of the day. The findings between ABP and cognitive function are mostly similar in these chosen studies. The studies included are summarized in Table 2.

Four of these studies, which included both cross-sectional and longitudinal studies, found that increased systolic BPV was related to lower cognitive function in older adults.[18–21] In addition, three of the cross-sectional studies examined nocturnal dipping, which compares mean nighttime BP with mean daytime BP.[22–24] Two of these studies examining nocturnal dipping found that greater nighttime systolic dipping was related to better cognitive function.[22,24] In one of these studies, also smaller nocturnal DBP dipping or reverse dipping was associated with poorer cognitive performance.[22] On the other hand, one study didn't find a relationship between being nondipper and having low cognitive function.[23]

Increased SBP, but not DBP, levels and variability were mostly related to poorer cognitive function. Moreover, one cross-sectional study discovered that higher 24-hour DBP was connected to cognitive decline.[24] There was inability to identify the optimal level of BP. One cross-sectional study did however state that tension regulation was associated with higher scores in cognitive testing.[23]

Previous studies have reported associations between ambulatory BP and cognitive function, but there are several methodological limitations in many of these studies, including the longitudinal studies. In two cross-sectional and one longitudinal study cognitive assessment was restricted to the mini-mental state examination (MMSE) or standardized mini-mental test (sMMT), which is a narrow measure of global cognition.[18,23,25] In all of the three longitudinal studies the follow-up time was four years, and none of these studies examined the association of nocturnal BP dipping and cognitive function.[20,25,26] Therefore, there remains a need for longitudinal studies with comprehensive cognitive assessments, longer follow-up periods and evaluation of nocturnal BP dipping to clarify its role in cognitive decline.

Table 2. Summary of studies reporting on ambulatory blood pressure and cognitive function

Author (year)	N (% Males)	Population characteristics	Age [mean ± SD (range), years]	Blood pressure measurement	Cognitive function measurement	Main results
Cross-sectional studies						
Yıldırım et al. (2020)[27]	435 (38.4)	Hypertensive patients >65 years in Istanbul, Turkey	males 74.9 ± 8.3, females 76.1 ± 8.6	24-h BP levels, daytime BP, nighttime BP, 24-h BPV, daytime BPV, nighttime BPV	sMMT	Increased BPV was associated with poorer cognitive functions. Most important factor affecting the sMMT scores was 24-h systolic BPV.
Paganini-Hill et al. (2019)[22]	121 (37)	≥90-year-old individuals from California, U.S.	93.2 ± 0.3 (90-102)	24-h BP levels, daytime BP, nighttime BP, 24-h BPV, daytime BPV, nighttime BPV, nighttime dipping	Neuropsychological test battery including domains of language, recent memory, executive function, visual-spatial ability, attention/working memory, and global cognition	Smaller nocturnal dipping (both SBP and DBP) or reverse dipping was associated with poorer cognitive functions.
Kececi Savan et al. (2016)[28]	91 (23.1)	Essential hypertensive patients >60 years old, admitted to outpatient clinics of Cerrahpasa Medical Faculty, Turkey	males 72.5 ± 8.1, females 71.7 ± 7.7	24-h BP levels, daytime BP, nighttime BP, nighttime dipping	sMMT	No relationship was found between being nondipper and low cognitive function. Tension regulation was associated with higher scores in the sMMT.
Conway et al. (2015)[24]	319 (34)	Independently living adults in San Diego, U.S.	72 ± 7	24-h BP levels, wake BP, sleep BP, 24-h BPV, wake BPV, sleep BPV, nighttime systolic dipping	MoCA, Hopkins Verbal Learning Test-Revised, Trail-Making Test, Boston Naming Test (Short Form), Digit Symbol Substitution Test, Stroop Color-Word Test	Higher 24-hour DBP and greater nighttime systolic dipping were associated with improved cognitive function.

Table 2 continues on the next page.

Longitudinal studies						

Author (year)	N (% Males)	Population characteristics	Age [mean ± SD (range), years]	Blood pressure measurement	Cognitive function measurement	Main results
Melgarejo et al. (2024)[26]	437 (33.2)	Dementia-free residents of Macaibo, Venezuela who are ≥55 years old	65.2 ± 7.1, median follow-up time 4 years	24-h BP levels, BPV	3 memory domains from SRT, MMSE	Higher 24-h, daytime, and nighttime SBP and DBP variability, but not BP level, was associated with cognitive decline.
Yu et al. (2022)[20]	1398 (46.0)	Participants from the Korean Genome and Epidemiology Study	59.7 ± 6.7 (49-79), follow-up time 4 years	Daytime BP, nighttime BP, daytime BPV, nighttime BPV	Neuropsychological test battery including story recall test, visual reproduction, verbal fluency, trail making tests, Digit Symbol-coding, and Korean-Color Word Stroop Test	Increased night systolic BPV, rather than night mean BP or daytime BPV, was associated with cognitive decline.
Yamaguchi et al. (2014)[25]	210 (44.8)	Elderly residents of Yamagata, Japan	70.9 ± 0.9, follow-up time 4 years	24-h BP levels, daytime BP, nighttime BP, 24-h BPV	MMSE	Higher systolic BPV predicted cognitive decline.

BP – blood pressure, BPV – blood pressure variability, SRT – Selective Reminding Test, MMSE – mini-mental state examination, sMMT – standardized mini-mental test, MoCA – Montreal Cognitive Assessment

4 Methods

4.1 Participants and study design

The participants of this study are part of the Finnish Retirement and Aging (FIREA) cohort study.[29] The FIREA study was established in the University of Turku in 2013. Its main objectives are to examine the changes in lifestyle, health and functioning in older workers during and after the transition to retirement. The FIREA study population consists of public sector workers whose estimated retirement date was between 2014 and 2019 (n=10 629). In the first phase of the FIREA study, participants were asked to fill in a questionnaire annually before and after the transition to retirement, altogether four times. In total, 6783 participants responded to at least one survey by December 2018.

The FIREA clinical substudy was initiated in 2015. The participants who were Finnish-speaking questionnaire responders who lived in Southwest Finland and whose estimated retirement date was between 2017 and 2019 were invited to the substudy (n=773). Of these people, 290 consented to participate in a yearly clinical examination. For the current study information from baseline and 70-year follow-up visit are used.

4.2 Measurements of blood pressure

Office blood pressure was measured by the study nurse during the clinical study visits, using a digital BP measurement device (Microlife WatchBP Office Central, Microlife AG, Widnau, Switzerland).[30] Participants were asked to sit for five minutes before the BP measurement. The measurement cuff was placed in the participant's arm one minute before the measurement. The brachial BP was measured simultaneously from both arms and twice, with a one-minute break between measurements. In office BP measurements, hypertension was defined when systolic BP was ≥ 140 mmHg, diastolic BP ≥ 90 mmHg or if the participant used antihypertensive medication.

Ambulatory blood pressure was measured using the Microlife WatchBP O3 Monitor (Microlife AG, Widnau, Switzerland).[31] The participants were asked to take the ambulatory BP measurement on a work day, for 24 hours. The BP measurement was

taken from the participant's nondominant hand. One minute before every measurement, the device gave a signal that the participant should stop walking, sit down and relax their arm, if they were able to. If the measurement was unsuccessful, it would be repeated, until it was successful. Participants' BP was measured every 30 minutes, for 24 hours. The participants were asked to report times of waking up and going to bed, which were used to calculate the average awake and asleep blood pressures. Hypertension in ambulatory blood pressure measurements was defined as average SBP ≥ 130 mmHg, average DBP ≥ 80 mmHg or the use of antihypertensive medication. Nocturnal BP dipping percentage was calculated [1-(asleep BP/awake BP)]x100. Nondipping was defined as the nocturnal BP dropping less than 10%.[32]

4.3 Measurement of cognitive function

Cognitive function was assessed with different neuropsychological tests. The tests included a computerized neuropsychological test battery, which included five different tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB®). The tests were performed during the clinical study visits and supervised by the study nurse.

CANTAB® is a standardized and computerized test battery to assess cognitive function. It includes many tests that evaluate different domains of cognitive function, including learning and memory, attention and psychomotor speed, executive function, and emotion and social cognition. The tests are completed on a touchscreen computer tablet. The individual tests can be selected to form a set of tests that evaluate the subdomains wanted in each research or clinical trial.

In this study, the following tests from CANTAB® were used to assess various domains of cognitive function: (1) reaction time (RTI), (2) rapid visual information (RVP) for sustained attention and information processing, (3) paired associates learning (PAL) for memory and learning, and (4) spatial working memory (SWM) for working memory. These tests formed a whole that could be used to evaluate the participant's cognitive function from many different cognitive subdomains.

4.4 Measurements of covariates

Age, sex and occupational status data was obtained from the registers of the pension insurance institute for the municipal sector in Finland. Occupational status was categorized by occupational title into clerical/support, professional/executive and administrative. The study nurse asked the participants' current medication including possible antihypertensive medication on each study visit. Body mass index (BMI) was calculated from the participant's measured weight and height by dividing the weight with the squared height (kg/m^2).

The rest of the covariates were acquired from the questionnaire that the participants were asked to fill. The participants reported their physical activity with their estimate of metabolic equivalent of task (MET) hours. Chronic diseases diagnosed by a doctor, such as depression, were also asked in the questionnaire.

4.5 Statistical analysis

The characteristics of study participants were displayed as means and standard deviations for continuous variables, and numbers of participants and percentages for categorical variables.

To estimate the mean levels of each cognitive domain at baseline and at follow-up, separately for groups with no hypertension and hypertension, we used linear regression analyses with generalized estimating equation (GEE). Interaction term hypertension*time was included to examine the differences in changes between the groups. The analyses were adjusted for age, sex, occupational status, depression, physical activity and BMI.

All statistical analyses were conducted using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

5 Results

5.1 The characteristics of study participants

The characteristics of study participants in the beginning of the study, separately for participants of office BP (n=285) and ABP measurements (n=210), are presented in Table 3. The mean age of the participants for both office BP and ABP measurements was 62.4 years. The majority of participants were women, 82.8% in office BP measurements and 83.3% in ABP measurements. Most of the participants also had hypertension, 60.0% in office BP measurements and 58.1% in ABP measurements.

Table 3. Characteristics of the study participants

	Office BP (n=285)		Ambulatory BP (n=210)	
	Mean	SD	Mean	SD
Age	62.4	1.0	62.4	1.0
BMI	26.0	4.0	26.3	4.1
Physical activity (MET-h/week)	28.5	21.7	28.7	22.0
	N	%	N	%
Sex				
Male	49	17.2	35	16.7
Female	236	82.8	175	83.3
Occupational position				
Administrative	100	35.1	79	37.6
Professional/executive	97	34.0	76	36.2
Clerical/support	88	30.9	55	26.2
Depression	42	15.8	37	18.9
Hypertension*	170	60.0	122	58.1

*Office BP based hypertension: SBP ≥ 140 mmHg, DBP ≥ 90 mmHg or use of antihypertensive medication. Ambulatory BP based hypertension: avarage SBP ≥ 130 mmHg, average DBP ≥ 80 mmHg or use of antihypertensive medication.

5.2 Office BP and cognitive function

The mean cognitive test scores at baseline, at follow-up and their difference by office BP groups are shown in Table 4. At baseline, no difference among those with and without hypertension were observed in any of the cognitive tests. There was a statistically significant improvement in memory and learning from baseline to follow-up in both hypertension and non-hypertension groups, but the change did not differ

between the groups (Figure 1). On the other hand, there was a statistically significant decrease in reaction time test results in both groups, but it was similar in both groups. In working memory test scores, there was only a statistically significant improvement in the hypertension group. No difference within and between hypertension groups was observed for sustained attention test.

Table 4. Office BP and cognitive function at baseline, follow-up and 10-year change

		Baseline	Follow-up	10-year change	
		Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	P-value*
Memory and learning	No hypertension	-0.13 (-0.34, 0.09)	0.98 (0.51, 1.44)	1.10 (0.59, 1.62)	0.61
	Hypertension	-0.24 (-0.43, -0.06)	0.77 (0.38, 1.16)	1.02 (0.55, 1.48)	
Reaction time	No hypertension	-0.04 (-0.18, 0.10)	-0.62 (-0.88, -0.36)	-0.58 (-0.91, -0.25)	0.56
	Hypertension	0.00 (-0.11, 0.11)	-0.64 (-0.86, -0.41)	-0.64 (-0.93, -0.34)	
Sustained attention	No hypertension	0.09 (-0.13, 0.30)	-0.52 (-1.19, 0.15)	-0.61 (-1.38, 0.17)	0.06
	Hypertension	0.11 (-0.10, 0.32)	-0.19 (-0.74, 0.36)	-0.30 (-1.01, 0.41)	
Working memory	No hypertension	0.08 (-0.09, 0.24)	0.22 (-0.15, 0.59)	0.14 (-0.33, 0.61)	0.09
	Hypertension	0.02 (-0.14, 0.18)	0.41 (0.14, 0.68)	0.39 (0.00, 0.77)	

*P-value indicates the comparison between hypertension groups in 10-year change

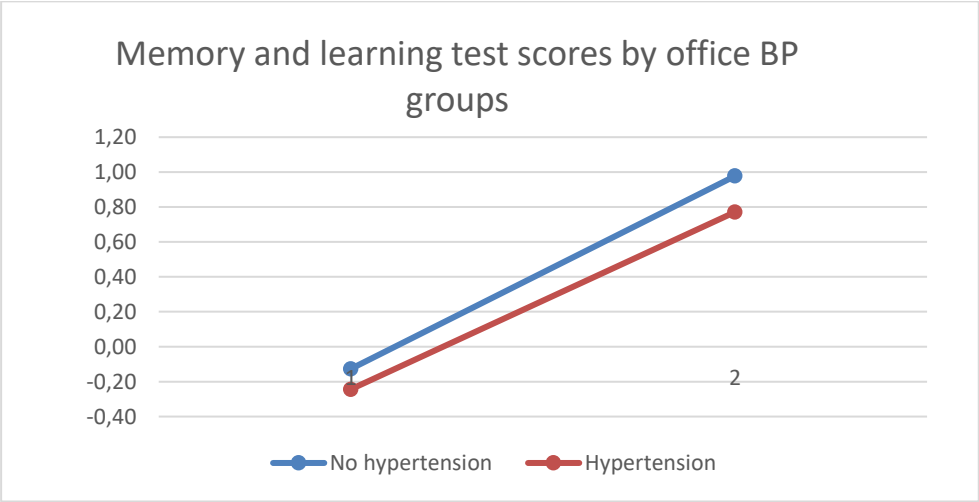

Figure 1. Memory and learning test scores by office BP groups at baseline and at follow-up

5.3 Ambulatory BP and cognitive function

The mean cognitive test scores by ambulatory BP groups at baseline, at follow-up and their difference are shown in Table 5. At baseline, there was indication of better scores in reaction time in the group with no hypertension compared to hypertension

group. No difference among those with and without hypertension were observed in any of the other cognitive domains. There was a statistically significant improvement in memory and learning as well as indicatively for working memory in both hypertension and non-hypertension groups. However, reaction time (Figure 2) and sustained attention test scores decreased in both groups. There were no statistically significant differences in any cognitive test score changes between the hypertension groups.

Table 5. Ambulatory BP and cognitive function at baseline, follow-up and 10-year change

		Baseline	Follow-up	10-year change	
		Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	P-value*
Memory and learning	No hypertension	-0.09 (-0.31, 0.14)	1.04 (0.60, 1.48)	1.13 (0.64, 1.62)	0.80
	Hypertension	-0.17 (-0.38, 0.03)	0.91 (0.55, 1.26)	1.08 (0.68, 1.48)	
Reaction time	No hypertension	0.04 (-0.09, 0.18)	-0.53 (-0.83, -0.23)	-0.57 (-0.94, -0.20)	0.46
	Hypertension	-0.07 (-0.21, 0.07)	-0.56 (-0.81, -0.31)	-0.49 (-0.83, -0.15)	
Sustained attention	No hypertension	0.15 (-0.04, 0.35)	-0.63 (-1.21, -0.05)	-0.78 (-1.39, -0.18)	0.25
	Hypertension	0.23 (0.04, 0.42)	-0.36 (-0.73, 0.00)	-0.59 (-1.04, -0.15)	
Working memory	No hypertension	0.04 (-0.12, 0.21)	0.47 (0.14, 0.80)	0.43 (-0.01, 0.86)	0.79
	Hypertension	-0.05 (-0.24, 0.14)	0.42 (0.08, 0.76)	0.47 (0.00, 0.93)	

*P-value indicates the comparison between hypertension groups in 10-year change

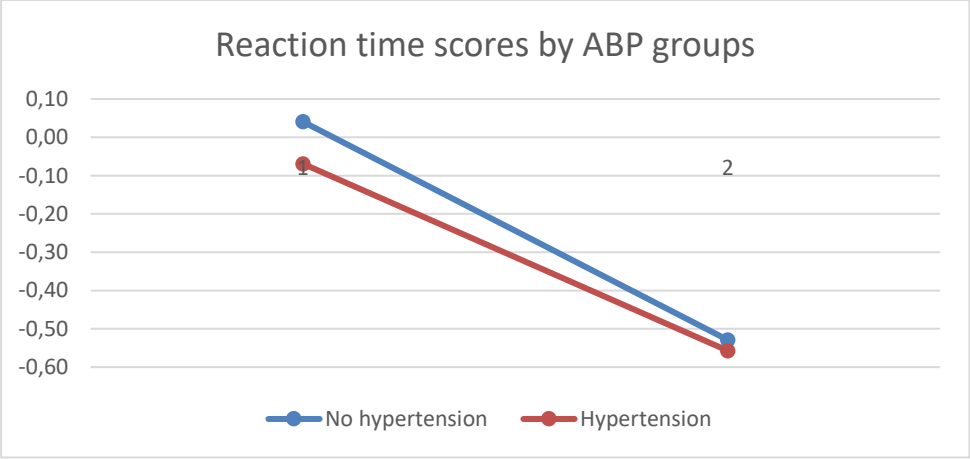

Figure 2. Reaction time scores by ABP groups at baseline and at follow-up

5.4 Nocturnal dipping and cognitive function

The average cognitive test results by dipping groups at baseline, at follow-up and their difference are shown in Table 6. At baseline, dippers had significantly better scores in the sustained attention test than non-dippers, but in other cognitive tests

there was no difference among the dipping groups. There was statistically significant decrease in reaction time and sustained attention scores (Figure 3) and a statistically significant improvement in memory and learning as well as indicatively for working memory in both dipper and non-dipper groups. There were no statistically significant differences in any cognitive test score changes between dipping groups, but there was borderline difference that non-dippers had a faster decline in sustained attention scores than dippers (Figure 3).

Table 6. Dipping and cognitive function at baseline, follow-up and 10-year change

		Baseline	Follow-up	10-year change	
		Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	P-value*
Memory and learning	Non-dippers	-0.13 (-0.61, 0.35)	1.02 (0.10, 1.94)	1.14 (0.33, 1.96)	0.89
	Dippers	-0.13 (-0.33, 0.06)	0.95 (0.60, 1.30)	1.08 (0.68, 1.49)	
Reaction time	Non-dippers	0.04 (-0.25, 0.32)	-0.61 (-0.87, -0.36)	-0.65 (-0.99, -0.31)	0.34
	Dippers	0.01 (-0.12, 0.14)	-0.54 (-0.78, -0.30)	-0.55 (-0.86, -0.24)	
Sustained attention	Non-dippers	-0.09 (-0.41, 0.23)	-1.31 (-2.18, -0.45)	-1.22 (-1.87, -0.57)	0.26
	Dippers	0.24 (0.11, 0.37)	-0.58 (-0.89, -0.26)	-0.81 (-1.13, -0.50)	
Working memory	Non-dippers	0.09 (-0.25, 0.43)	0.28 (-0.07, 0.64)	0.19 (-0.37, 0.76)	0.28
	Dippers	-0.01 (-0.18, 0.16)	0.44 (0.11, 0.77)	0.45 (0.00, 0.89)	

*P-value indicates the comparison between hypertension groups in 10-year change

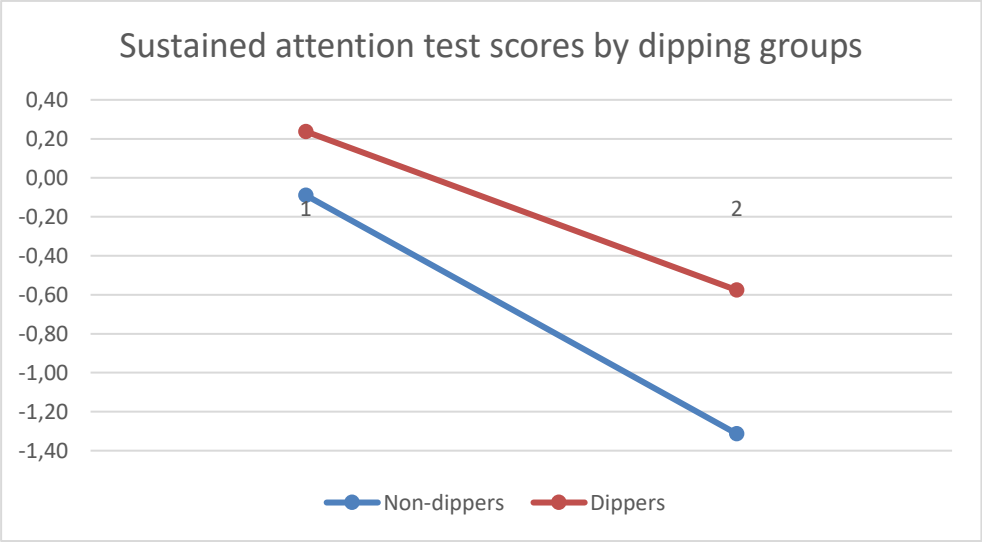

Figure 3. Sustained attention test scores by dipping groups at baseline and at follow-up

6 Discussion

In this study, we examined changes in multiple domains of cognitive function over a 10-year follow-up period. We also studied the associations between several blood pressure indicators and their cross-sectional and longitudinal associations with cognitive function. Memory and learning performance improved and reaction time scores declined over the follow-up period, both in participants with and without hypertension, regardless of whether hypertension status was defined by office BP, ABP or nocturnal dipping. In addition, sustained attention scores declined in both the ABP and dipping groups. There was a statistically significant improvement in working memory in the hypertension group defined by office BP, and there was borderline improvement in working memory in all other BP groups.

At baseline, the only statistically significant difference in cognitive function was observed between the dipping groups in the sustained attention test, with dippers performing better than non-dippers. No statistically significant differences were found between blood pressure groups in cognitive test score changes. However, there was some indication that sustained attention scores declined more rapidly among non-dippers than among dippers.

Another study using the FIREA cohort data examined changes in cognitive function during the transition to retirement, although with a considerably shorter follow-up period. That study reported improvements in memory and learning, working memory and sustained attention from the pre-retirement to post-retirement years, but no significant changes were observed in reaction time. In contrast, this study extended the follow-up period by several years, allowing the assessment of longer-term cognitive trajectories beyond the retirement transition. While reaction time remained stable during the retirement transition, our findings suggest a decline in reaction time performance over the 10-year follow-up period. However, improvements in memory and learning persisted over time and were consistent with those observed during the retirement transition.[33]

The finding that reaction time performance declined several years after, rather than during the retirement transition may suggest that cognitive demands and mentally stimulating tasks associated with working life help maintain processing speed. It was

also notable that performance in several cognitive domains continued to improve throughout the follow-up period. These findings suggest that cognitive function remains relatively well preserved among older adults, with many individuals maintaining good cognitive health well into their seventies.

Dippers demonstrated better sustained attention than non-dippers, which is consistent with previous cross-sectional studies reporting better cognitive performance among dippers than non-dippers.[22,24] Most studies examining the relationship between ABP and cognitive function have focused on BPV, with several reporting an association between higher BPV and cognitive decline.[18,20,25,26] BPV was not assessed in this study, limiting direct comparisons with these findings.

Comparison with the existing literature is further complicated by methodological differences. Previous studies, including studies with office BP and ABP measurements, have generally evaluated global cognitive function or broader cognitive outcomes, while this study examined specific cognitive domains separately. In addition, many studies have analyzed SBP and DBP independently and have reported that elevated SBP rather than DBP is associated with poorer cognitive performance.[10–14]

A major strength of this study is the longitudinal assessment of multiple cognitive domains using a comprehensive, computerized standardized test battery capable of detecting subtle changes in cognitive function. Furthermore, the study provides longitudinal data on the relationship between nocturnal dipping and cognitive function, an area that has received relatively limited attention in previous research. Additional strengths of this study include the extended 10-year follow-up period and the use of several hypertension indicators, including office BP, ABP and nocturnal dipping status.

The limitations of this study should also be acknowledged. The sample size was relatively small and consisted mostly of women and relatively healthy individuals who remained employed until retirement. Consequently, the findings may not be fully generalizable to the broader population. Cognitive decline may have been more prominent in a study population that was more representative of the general population, including individuals with poorer health and lower working ability. Additionally, although the 10-year follow-up period was relatively long, an even

longer follow-up period might have allowed more age-related cognitive changes. As the participants were mostly in their 70s during the follow-up, cognitive decline may have become more apparent at older ages.

In conclusion, reaction time and sustained attention declined, and memory and learning improved during the 10-year period. There was also some indication of improvement in working memory. These changes were mostly independent of hypertension status. The findings suggests that cognitive ageing is not uniform across cognitive domains and that several aspects of cognitive function remain well preserved among adults in their 70s. Further research with larger and more diverse study populations, more comprehensive assessments of cognitive function and the inclusion of BPV measures is needed to further clarify the relationship between blood pressure and cognitive function in older adults.

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