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Short-term blood pressure variability and brain functional network connectivity in older adults

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Consent for publication
Not applicable.

Availability of data and material
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Code availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Appendix A. Supplementary data
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Abstract

Background: Blood pressure variability is increasingly linked with cerebrovascular disease and Alzheimer's disease, independent of mean blood pressure levels. Elevated blood pressure variability is also associated with attenuated cerebrovascular reactivity, which may have implications for functional hyperemia underpinning brain network connectivity. It remains unclear whether blood pressure variability is related to functional network connectivity. We examined relationships between beat-to-beat blood pressure variability and functional connectivity in brain networks vulnerable to aging and Alzheimer's disease.

Methods: 53 community-dwelling older adults (mean [SD] age = 69.9 [7.5] years, 62.3% female) without history of dementia or clinical stroke underwent continuous blood pressure monitoring and resting state fMRI scan. Blood pressure variability was calculated as variability independent of mean. Functional connectivity was determined by resting state fMRI for several brain networks: default, salience, dorsal attention, fronto-parietal, and language. Multiple linear regression examined relationships between short-term blood pressure variability and functional network connectivity.

Results: Elevated short-term blood pressure variability was associated with lower functional connectivity in the default network (systolic: standardized ß = −0.30 [95% CI −0.59, −0.01], p = .04). There were no significant associations between blood pressure variability and connectivity in other functional networks or between mean blood pressure and functional connectivity in any network.

Discussion: Older adults with elevated short-term blood pressure variability exhibit lower resting state functional connectivity in the default network. Findings support the role of blood pressure variability in neurovascular dysfunction and Alzheimer's disease. Blood pressure variability may represent an understudied early vascular risk factor for neurovascular dysfunction relevant to Alzheimer's disease, with potential therapeutic implications.

Keywords

Blood pressure variability; Functional connectivity; Default network

1. Introduction

Fluctuations in blood pressure (BP) are increasingly recognized to carry important information about health beyond traditionally studied mean BP levels (Höcht, 2013; Kollias et al., 2017; Parati et al., 2013, 2018). A growing literature suggests elevated blood pressure variability (BPV) - whether measured over seconds, minutes, hours, days, weeks, months, or even years – independent of mean BP, is associated with cognitive (e.g., cognitive impairment and decline, risk for dementia) (de Heus et al., 2019, 2021; Gutteridge et al., 2023; Lattanzi et al., 2014a, 2014b, 2018, 2019; Nagai et al., 2014, 2015, 2017; Rouch et al.,

2020; Yoo et al., 2020), cardiovascular (e.g., stroke) (Höcht, 2013; Parati et al., 2013, 2018), and cerebrovascular (e.g., white matter hyperintensities, arteriolosclerosis) (Ma et al., 2021; Sible et al., 2021a; Tully et al., 2020) outcomes. One recent arterial spin labelling MRI study also found that older adults with higher BPV exhibited attenuated cerebrovascular reactivity in response to both hypercapnia and hypocapnia challenge (Sible et al., 2022a). Specifically, elevated BPV was associated with a diminished ability of the brain's blood vessels to dilate and constrict in response to stimuli, which may have implications for functional hyperemia underpinning brain network connectivity. Deficits in neurovascular coupling may be particularly important when affecting brain regions and networks critical for cognition and vulnerable to aging and Alzheimer's disease (AD), such as the medial temporal lobe (Iadecola, 2004; Jagust, 2018; Nation et al., 2019; Zlokovic, 2011) and default network (Greicius et al., 2003, 2004). Interestingly, several recent studies have linked higher BPV to neuroimaging markers of AD in key brain regions, including the medial temporal lobes, using structural MRI (e.g., gray matter atrophy) (Gutteridge et al., 2022; Ma et al., 2020b; Sible and Nation, 2021), arterial spin labelling MRI (e.g., cerebral perfusion decline and cerebral hypoperfusion) (Sible et al., 2021b, 2022b), and tau positron emission tomography (e.g., tau accumulation) (Sible and Nation, 2022a). However, few studies have used functional MRI to examine relationships between BPV and functional brain network connectivity. Although some evidence suggests more well-studied BP indices such as higher mean BP and hypertension status are associated with lower functional brain network connectivity (Carnevale et al., 2020; Feng et al., 2020; Gu et al., 2019; Shah et al., 2021), understanding the role of BPV in functional network connectivity may further bolster BPV as an emerging BP risk indicator associated with brain health outcomes beyond traditionally studied mean BP levels. To explore this possibility, we examined the relationship between short-term BPV and functional brain network connectivity in a sample of community-dwelling older adults. We hypothesized that higher BPV awould be associated with deficits in functional brain network connectivity.

2. Methods

2.1. Participants

Study participants were recruited from ongoing studies of aging at the University of California Irvine (UCI) and from the local Orange County communities via flyers, word-of-mouth, and community outreach events. The present study investigated functional brain network connectivity and BPV data collected as part of the larger parent projects on aging as previously described (Kapoor et al., 2021, 2022; Sible et al., 2022a, 2022b, 2022c; Yew et al., 2022). Inclusion criteria for the parent studies and the present study required participants to be age 55–90 years and living independently in the community. Exclusionary criteria for the parent studies and the present study included: history of dementia, stroke, traumatic brain injury, learning disability, or other major systemic, psychiatric, or neurological disorder known to affect the central nervous system. Participants underwent baseline neuropsychological testing including the Mattis Dementia Rating Scale – 2 (DRS-2) (Griffiths et al., 2011) and age-adjusted total scaled scores were calculated as a measure of global cognitive function to screen for dementia. Participants with DRS-2 scores ≤126 (established cut-off score to rule out major neurocognitive impairment (Griffiths et al.,

2011)) were excluded from the study. The study was approved by the Institutional Review Board at UCI and all participants provided their written informed consent.

2.2. Measures

2.2.1. Functional MRI assessment—Participants underwent 3 T brain MRI (Siemens® MAGNETOM Prisma). T1-weighted magnetization prepared rapid gradient-echo (MP-RAGE) sequence for high resolution anatomical images was collected (TR = 2300 ms; TE = 2.98 ms; TI = 900 ms; slice thickness = 1.20 mm; flip angle = 9°; field of view = 256 mm). Participants also underwent resting state fMRI (rsfMRI) using the following scan parameters, as previously described (Jang et al., 2021): TR = 3000 ms; TE = 30 ms; flip angle = 80°; voxel size = 3.3 × 3.3 × 3.3 mm; matrix = 64 × 64; field of view = 212 mm; number of slices = 48; slice order = interleaved; number of time points (scans) = 140 contiguous echo-planar imaging (EPI); scan duration = 7 min 11 s. Participants were asked to lie still with their eyes open. Images were preprocessed according to the CONN Toolbox (Whitfield-Gabrieli and Nieto-Castanon, 2012) default processing pipeline, which includes the following steps: 1) realignment to the first scan and unwarp 2) center to (0,0,0) coordinates 3) slice-timing correction 4) outlier detection 5) direct segmentation and normalization to 2 mm isotropic MNI template 6) center to (0,0,0) coordinates 7) segmentation and normalization to MNI template 8) smoothing (spatial convolution with 6 mm full-width half-maximum Gaussian kernel). Further removal of confounding signals was completed through nuisance regression. Regressors include: 12 motion parameters (6 [3 rotation and 3 translation] obtained from step 1 in preprocessing [realignment] and their first-order derivatives); 10 white matter and 5 cerebral spinal fluid principal components (derived from white matter and cerebral spinal fluid masks using an anatomical component-based noise correction strategy [aComCor]); outlier volumes (identified in step 4 of preprocessing). Also, the following steps were included: temporal band-pass filtering (0.008 – 0.09 Hz); linear detrending. rsfMRI scans were excluded if the number of valid scans was less than 50% of the total number of scans (e.g., <70/140 scans). This resulted in the exclusion of 6 rsfMRI scans.

CONN provides region-of-interests (ROIs) (“network ROIs”) based on their findings from analyzing the connectivity maps of 497 participants in the Human Connectome Project (HCP), using independent component analysis. ROI-to-ROI connectivity metric within each network represents average connectivity (Fisher’s z-transformed correlation coefficients) between all pairs of ROIs specified within the network. We determined functional connectivity for several brain networks relevant to aging and AD (Greicius et al., 2003; Köbe et al., 2020), including default (medial prefrontal cortex, lateral parietal cortex, precuneus), salience (anterior cingulate cortex, anterior insula cortex, rostral prefrontal cortex, supramarginal gyrus), dorsal attention (frontal eye field, intraparietal sulcus), fronto-parietal (lateral prefrontal cortex, posterior parietal cortex), and language (inferior frontal gyrus, posterior superior temporal gyrus).

2.2.2. BP assessment—BP was collected continuously from participants’ right arm using a Biopac® MRI-compatible BP monitoring device during a 5-min period of rest in the scanner, approximately 35 min before the rsfMRI scan, as previously described (Sible et al.,

2022a, 2022b, 2022c). Briefly, data were processed offline using a custom pipeline scripted in AcqKnowledge®, which includes removal of outliers ± 3 SD from the mean (Sible et al., 2022a, 2022b, 2022c; Sturm et al., 2018). We calculated intraindividual BPV as variation independent of mean (VIM), a newer index of BPV that is uncorrelated with mean BP levels and has been used in several recent biomarker studies (de Heus et al., 2019; Rothwell et al., 2010b; Rouch et al., 2020; Sible et al., 2021b, 2022b; Sible and Nation, 2020). A bivariate correlation between VIM and mean BP confirmed that VIM was not significantly correlated with mean BP levels (systolic: $r = .05$, $p = .72$; diastolic: $r = 0.08$, $p = .56$). VIM was calculated as: VIM = standard deviation (SD)/mean^x, where the power x was derived from non-linear curve fitting of BP SD against average BP using the nls package in R Project, as previously described (Rothwell et al., 2010b; Sible et al., 2021a, 2021b, 2022b; Sible and Nation, 2020). We also calculated the SD and coefficient of variation (CV [100 x SD/mean]) of BPV, as well as the mean BP across the scan.

2.2.3. Other measurements—Blood samples from venipuncture were used to determine AD genetic risk gene apolipoprotein (APOE) e4 carrier status (≥1 APOE e4 allele), as previously described (Kapoor et al., 2021; Sible et al., 2022c). Participants also underwent T2-FLAIR MRI sequence (TR = 10,000 ms; TE = 91 ms; T1 = 2500 ms; slice thickness = 5.0 mm; flip angle = 150°; field of view = 220 mm) to determine white matter lesion burden, as described elsewhere (Sible et al., 2022a, 2022b). One rater blinded to other study measures determined the severity of white matter lesions using the established Fazekas scoring scale (Fazekas et al., 1987) (0–3). Participants were categorized as taking antihypertensive medication (all classes) vs not taking antihypertensive medication. The following cardiovascular risk factors and health behaviors were determined from clinical interview: history of smoking, history of diabetes, history of hyperlipidemia, current alcohol use.

3. Statistical analysis

Multiple linear regression models examined the relationship between BPV (independent predictor) and functional connectivity in each of the networks separately (dependent outcomes).

To streamline results, systolic BPV findings are reported in the main text while diastolic BPV findings are reported in the Supplementary Materials. We also investigated associations between mean BP and functional connectivity to compare with potential findings with BPV. Sensitivity analyses controlled for 1) antihypertensive medication use, 2) race/ethnicity, 3) Fazekas score, 4) APOE e4 carrier status, 5) history of smoking, 6) history of diabetes, 7) history of hyperlipidemia, 8) current alcohol use (see Supplementary Tables 2–3). BPV models controlled for age, sex, and mean BP while mean BP models controlled for age and sex. Multiple comparison corrections using the False Discovery Rate (FDR) method (Benjamini and Hochberg, 1995) was set at $p < .05$. All analyses were 2-sided with significance set at $p < .05$ and were carried out in R (R Core Team, 2020).

4. Results

90 participants were enrolled in the ongoing studies of aging at the time of analysis. Of those, 10 participants did not have rsfMRI data available and 23 participants did not have BPV data available. Of those that did, 53 participants had both valid rsfMRI and valid BPV data available. Therefore, a total of 53 participants were included in the present investigation (Supplementary Fig. 1). The present study investigated BPV and rsfMRI data that were collected as part of ongoing studies of aging with myriad outcomes. Therefore, the sample size of the present analysis was calculated a posteriori of overall study data collection. Based on a post hoc power analysis to detect moderate-to-large effect sizes using G*Power (α = 0.05, 3 covariates, total sample size), achieved power was 91.6%.

Included participants were mean (SD) 69.9 (7.5) years old, 62.3% female, 75.5% non-Hispanic White, and had mean (SD) 17.0 (2.1) years of education. Demographic information is reported in Table 1. Mean (SD) systolic BP was 130.1 (15.9 SD) mmHg and mean (SD) systolic BPV was 3.7 (2.2 SD) mmHg for BPV SD, 2.8 (1.6 SD) mmHg for BPV CV, and 2.5 (1.2 SD) mmHg for BPV VIM.

4.1. BPV

As summarized in Table 2 and shown in Fig. 1, elevated systolic BPV was associated with lower functional connectivity in the default network (VIM: ß = −0.30 [95% CI −0.59, −0.01], $p = 0.04$). There were no significant associations between systolic BPV and functional connectivity in the salience, dorsal attention, fronto-parietal, or language networks (p's = 0.10 – 0.43). Consistent findings were observed with diastolic BPV (Supplementary Table 1). BPV findings did not survive after FDR-correction (p's = 0.20 – 0.46).

4.2. Mean BP

As reported in Table 3, mean systolic BP or diastolic BP was not significantly related to functional connectivity in any brain network (p's = .61 – 0.99).

4.3. Sensitivity analyses

Associations remained significant in sensitivity analyses controlling for race/ethnicity, Fazekas score, APOE e4 carrier status, history of smoking, history of diabetes, history of hyperlipidemia, and current alcohol use (see Supplementary Tables 2–3). However, findings were no longer significant when controlling for antihypertensive medication use (systolic p's = 0.06 – 0.07; diastolic p's = 0.06 – 0.07).

5. Discussion

Findings suggest older adults with elevated short-term BPV exhibit lower functional brain connectivity, specifically in the default network that is highly vulnerable to AD (Greicius et al., 2003, 2004). Prior work has used structural MRI (Gutteridge et al., 2022; Ma et al., 2020b; Sible and Nation, 2021), arterial spin labelling MRI (Sible et al., 2021b, 2022b), and positron emission tomography (Sible and Nation, 2022a) to characterize associations

between BPV and neuroimaging markers of AD. The present investigation adds to this work by using rsfMRI to explore relationships with functional connectivity in brain networks relevant to aging and AD. Together these studies support the possibility that elevated BPV may be related to early neuroimaging markers of vascular and neuronal dysfunction in AD.

In addition to growing evidence that BPV may be related to AD brain changes (Ma et al., 2020b, 2021; Sible et al., 2021b, 2022b; Sible and Nation, 2021, 2022a), several studies report strong links between BPV and cerebrovascular disease (Ma et al., 2020a, 2021; Sible et al., 2021a; Tully et al., 2020). BPV can be understood in the context of BP homeostasis (Parati et al., 2020), or the flexible responses of cardiovascular control mechanisms to changes in physiological demands and environmental conditions to ensure stable organ perfusion (Meng et al., 2019). It has been hypothesized that chronic BP surging may have a “tsunami effect” (Saji et al., 2016) on cerebral arterial walls and promote microvascular damage – beyond the effects of mean BP levels (Tully et al., 2020). Alterations in microvascular integrity, such as a leaky blood brain barrier, could have effects on neurovascular unit functioning and neural milieu (Iadecola, 2004; Zlokovic, 2011). Consistently, higher BPV was recently associated with attenuated cerebrovascular reactivity (Lattanzi et al., 2023; Sible et al., 2022a), an index of neurovascular functioning in response to vasoactive stimuli relevant to prodromal cerebrovascular disease (Liu et al., 2019). It is therefore interesting that in the current investigation, elevated BPV was related to lower functional connectivity – even at rest - which represents the strength of connection between hubs of active neurons at baseline. Since active neurons require a supply of increased local blood flow, our findings raise the possibility that higher BPV may also be associated with impaired neurovascular response to local basal neuronal activity. Large fluctuations in BP, therefore, could disrupt cerebrovascular functioning at a global level (e.g., cerebrovascular reactivity) and at a local network level (e.g., functional connectivity). Importantly, we examined functional network connectivity at rest, but it is possible that the observed associations could be amplified when examining connectivity during cognitively demanding tasks that require a dynamic and coordinated neurovascular response. Additionally, deficits in the neurovascular response – both for basal activity and in response to stimuli – may be exacerbated by arterial stiffness (Gutteridge et al., 2023). Due to the cross-sectional study design, we were not able to infer the directionality of these relationships.

Interestingly, associations were observed only in the default network, a system known to decline in the context of advancing AD (Greicius et al., 2004; Mevel et al., 2011). This finding is consistent with prior work suggesting particular links between BPV and brain changes in AD-prone regions, such as the medial temporal lobe (Gutteridge et al., 2022; Ma et al., 2020b; Sible et al., 2021b, 2022b; Sible and Nation, 2021, 2022a). It could be that repeated BP dipping/surging may alter pulse wave dynamics, including pushing the pulse wave deeper into the brain parenchyma, the effects of which may be greater in already vulnerable regions/networks (Nagai et al., 2017). Prior work suggests that vascular burden may impair functional connectivity, especially in networks susceptible to AD (Köbe et al., 2020). Specifically, individuals with more well-studied vascular risk factors (e.g., hypertension, dyslipidemia, obesity) have been shown to exhibit lower default network functional connectivity (Köbe et al., 2020). Together with our current findings with BPV, these studies highlight the vulnerability of default network structures’

cerebrovascular integrity. However, in our study, mean BP was not significantly associated with functional connectivity in any network, underscoring the unique role BPV may play in functional cerebrovascular health. The dissociation of findings with BPV vs mean BP in the current study and several others (de Heus et al., 2021; Tully et al., 2020) support the growing hypothesis that controlling the variability in BP levels may require antihypertensive treatment approaches that are distinct from current strategies aimed at managing mean BP levels. Some evidence suggests that certain classes of antihypertensive agents are able to lower both the mean and variability in BP levels better than others (Rothwell et al., 2010a; Webb et al., 2010), with potential implications for cerebrovascular health and cognitive function (Mahinrad et al., 2023). Importantly, recent studies suggest that even in adults with strictly controlled mean BP levels, higher BPV is associated with cognitive decline (Sible and Nation, 2022b) and increased risk for mild cognitive impairment and dementia (de Havenon et al., 2021; Guo et al., 2023). The current investigation was not adequately powered to examine antihypertensive treatment effects on functional connectivity, but future work in this area is needed and has the potential to update BP control guidelines for older adults. Nevertheless, both BPV elevation and attenuated default network functional connectivity have independently been shown to emerge before the onset of major neurocognitive symptoms of AD (Chhatwal et al., 2013; Sible and Nation, 2020). These findings suggest early changes in vascular and neuronal functioning associated with high BPV may have synergetic contributions to cognitive decline that could be intervened on with existing antihypertensive medications. Our study was cross-sectional and observational, but future longitudinal and/or interventional studies are needed to further appreciate the directionality of growing links between BPV and brain health outcomes, and potentially inform treatment decisions. Even small changes in BP control (Barnes and Yaffe, 2011; Yaffe, 2019), including taking any BP medication (Ding et al., 2020), has the potential to reduce dementia risk.

The present investigation provides new information on the relationship between short-term BPV and functional brain network connectivity. By utilizing rsfMRI, we were able to examine how BPV may be related to local cerebrovascular response in canonical brain networks. In addition to recent work linking higher BPV to attenuated cerebrovascular reactivity (Sible et al., 2022a), the current findings support the hypothesis that elevated short-term BPV may also be related to functional hyperemia underpinning brain connectivity in networks with known vulnerability to AD. Consistent with prior BPV work using other neuroimaging modalities (Ma et al., 2020b; Sible et al., 2021b, 2022a, 2022b; Sible and Nation, 2021, 2022a), study findings provide additional evidence that potentially modifiable BPV may be a newer aspect of BP control linked with vascular and neuronal brain changes relevant to aging and AD. The present study has several limitations. First, the sample size is relatively small and replication of the findings in larger cohorts is warranted. Relatedly, the limited sample size precluded our ability to examine potential interaction effects with antihypertensive treatment, APOE e4 carrier status, and other medical/demographic variables. Additionally, study participants were without major neurocognitive impairment and understanding the relationship between BPV and functional connectivity in samples with varied cognitive abilities is needed. The majority of participants had relatively minimal cerebrovascular risk (e.g., 75.5% had Fazekas scores

≤1), which may limit generalizability of findings to samples with greater cerebrovascular burden. The study sample was comprised of largely non-Hispanic White individuals and studying cohorts with greater racial and ethnic diversity is essential for advancing our broader understanding of health disparities in vascular (CDC, 2021) and brain aging (Manly et al., 2022). Due to other sensor placements and MRI scan protocols, BP was collected from participants' right arm only. Some studies suggest measuring BP from both arms for improved accuracy of cardiovascular risk (Clark et al., 2012). Consistent with other recent studies on BPV and brain health (Sible et al., 2022a, 2022b, 2022c), we assessed BPV on a beat-to-beat scale using a device that has been validated with ultra-sensitive intra-arterial BP monitoring (Biopac, 2019; Gratz et al., 2017; Kwon et al., 2022). However, the BPV field is emerging and gold standards in methodology are not yet fully established (Parati et al., 2013, 2018). Nevertheless, several lines of evidence converge to suggest that higher BPV, whether measured over seconds to years, is robustly associated with poor brain health outcomes (de Heus et al., 2021; Ma et al., 2020a; Nagai et al., 2017; Tully et al., 2020).

6. Conclusions

Elevated short-term BPV, independent of mean BP, in older adults without major neurocognitive impairment is associated with lower functional connectivity specifically in the default network. Prior work links higher BPV with vascular and neuronal brain changes in AD and the current findings provide new evidence that higher short-term BPV may also be related to functional hyperemia relevant to aging and AD. BPV may be an understudied – and potentially modifiable – vascular risk factor associated with neurovascular dysfunction and AD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

Data will be made available on request.

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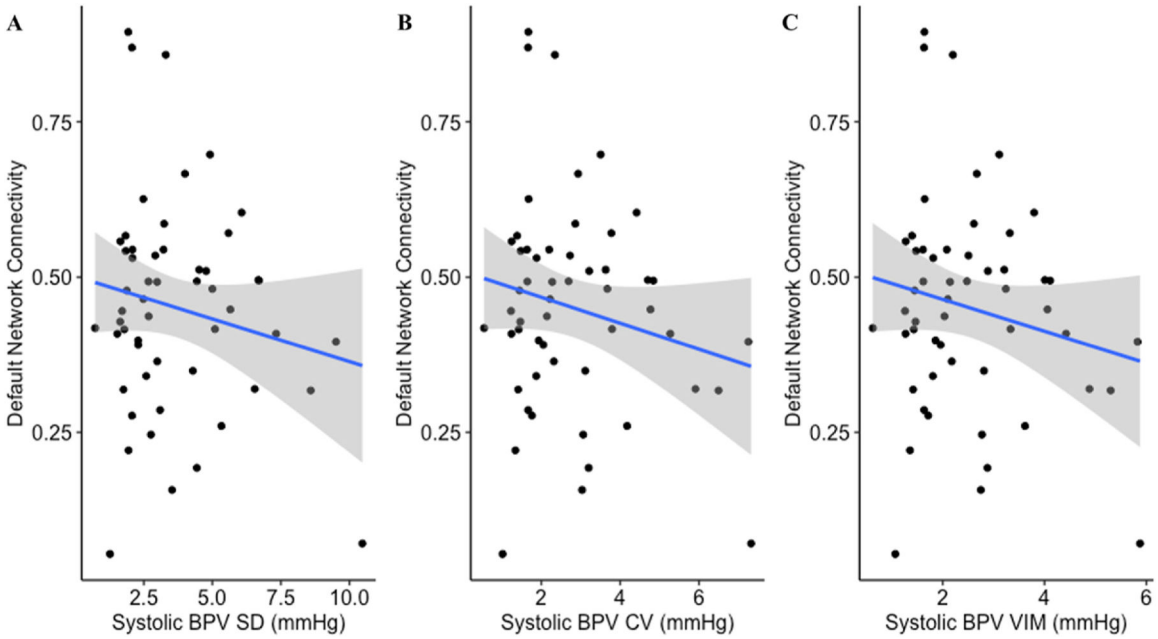

Fig. 1. Elevated systolic BPV is associated with lower functional connectivity in default network

Scatterplots display the relationship between default network functional connectivity and systolic BPV A) SD B) CV and C) VIM. 95% confidence intervals are shaded. Abbreviations: BPV = blood pressure variability; SD = standard deviation; CV = coefficient of variation; VIM = variation independent of mean.

Table 1

Demographic information.

	Total sample (*N* = 53)
Age (years)	69.9 (7.5)
Sex (M/F)	20/33
Race (*n*, %)	
Asian	11 (20.8%)
Black	1 (1.9%)
White	40 (75.5%)
Other	1 (1.9%)
Ethnicity (*n*, %)	
Hispanic	2 (3.8%)
Non-Hispanic	51 (96.2%)
APOE e4 (*n*, % carrier)	30 (56.6%)
0 e4 alleles	23 (43.4%)
1 e4 allele	28 (52.8%)
2 e4 alleles	2 (3.8%)
Fazekas score (*n*, %)	
0	4 (7.6%)
1	36 (67.9%)
2	10 (18.9%)
3	3 (5.7%)
Education (years)	17.0 (2.1)
DRS-2 total (scaled score)[a]	12.2 (1.7)
Antihypertensive medication use (*n*, %)	21 (39.6%)
History of smoking (*n*, %)	19 (35.9%)
History of diabetes (*n*, %)	5 (9.4%)
History of hyperlipidemia (*n*, %)	23 (43.4%)
Current alcohol use (*n*, %)	32 (60.4%)
Systolic BP	
Mean	130.1 (15.9)
SD	3.7 (2.2)
CV	2.8 (1.6)
VIM	2.5 (1.2)
Diastolic BP	
Mean	78.1 (10.6)
SD	1.9 (1.1)
CV	2.4 (1.3)
VIM	1.8 (.9)
Functional connectivity[b]	
Default	.45 (.2)
Salience	.37 (.1)

	Total sample (*N* = 53)
Dorsal attention	.41 (.2)
Fronto-parietal	.57 (.1)
Language	.45 (.2)

Abbreviations: BP = blood pressure; BPV = blood pressure variability; M = male; F = female; SD = standard deviation; CV = coefficient of variation; VIM = variation independent of mean; DRS-2 = Dementia Rating Scale – second edition; APOE = apolipoprotein.

Mean (SD) reported unless otherwise indicated.

[a]DRS-2 total scaled scores are age-adjusted.

[b]ROI-to-ROI connectivity metric within each network represents average connectivity (Fisher's z-transformed correlation coefficients) between all pairs of ROIs specified within the network.

Table 2

Model estimates of systolic BPV predicting functional connectivity.

Systolic BPV						
	SD	***P*-value**	**CV**	**P-value**	**VIM**	***P*-value**
Network						
Default	**−.31 [−.60, −.01]**	**.04**	**−.31 [−.59, −.02]**	**.04**	**−.30 [−.59, −.01]**	**.04**
Salience	.26 [−.05, .57]	.10	.24 [−.06, .54]	.12	.24 [−.06, .54]	.12
Dorsal attention	−.13 [−.45, .19]	.43	−.12 [−.43, .20]	.46	−.13 [−.44, .18]	.41
Fronto-parietal	.18 [−.13, .48]	.25	.17 [−.13, .46]	.27	.16 [−.13, .46]	.27
Language	.24 [−.07, .54]	.12	.24 [−.05,.54]	.10	.24 [−.06, .54]	.11

Standardized beta (ß) and 95% confidence intervals shown unless otherwise indicated.

Bolded items indicate systolic BPV is significantly associated with functional connectivity in that network.

Models covaried for age, sex, and mean systolic BP.

Abbreviations: SD = standard deviation; CV = coefficient of variation; VIM = variation independent of mean; BPV = blood pressure variability.

Table 3

Model estimates of mean BP predicting functional connectivity.

Network	Systolic BP		Diastolic BP	
		P-value		*P*-value
Default	.06 [−.28, .39]	.73	.04 [−.30, .37]	.83
Salience	−.003 [−.34, .34]	.99	.09 [−.26, .43]	.61
Dorsal attention	.01 [−.34, .35]	.96	.05 [−.30, .40]	.78
Fronto-parietal	.06 [−.27, .40]	.70	−.04 [−.37, .30]	.82
Language	.05 [−.29, .39]	.77	.03 [−.31, .37]	.85

Standardized beta (ß) and 95% confidence intervals shown unless otherwise indicated.

Bolded items indicate mean BP is significantly associated with functional connectivity in that network.

Models covaried for age and sex.

Abbreviations: BP = blood pressure.