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Under pressure: A systematic review of the association between blood pressure variability with depression and anxiety☆

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ABSTRACT

Blood pressure variability (BPV) impacts brain health by influencing brain structure and cerebrovascular pathologies, though the mechanisms are poorly understood. Changes in the cerebrovasculature may lead to late-onset depression, cognitive impairment, and dementia, however the relationship between BPV with depression and anxiety remains unclear, due to methodological differences and inconsistencies in past research. This review aims to clarify the association between BPV with depression and anxiety in adults to inform understandings of the mechanisms implicating BPV in cognitive health. A systematic search from inception through to January 2024 was performed on Embase, PubMed, PsycINFO, and Web of Science. Studies that assessed BPV quantified by beat-to-beat, 24-hour, or visit-to-visit were eligible if the standardised assessment of depression and/or anxiety were reported as a linear association, or mean differences across control and affect groups. A total of 14 articles reporting on 13 samples and $N = 5055$ persons met the inclusion criteria (median female proportion = 61 %, range 0 % - 76 %). A meta-analysis was not possible due to methodological heterogeneity in BPV measurements and metrics across studies. Mixed results were observed across depression studies with inconsistencies and variation in the direction, strength of association, and BPV metric. There was weak evidence from only three studies to support a linear association between systolic coefficient of variation and anxiety. Collectively, the findings contribute to understanding the association between BPV and brain health, suggesting that any relationship between BPV and brain structures critical for cognitive function are independent of depression and only modestly implicate anxiety.

1. Introduction

The relationship between blood pressure variability (BPV) and adverse health outcomes is a burgeoning area of research. BPV refers to the fluctuations in blood pressure readings quantified across beat-to-beat ([B2B] ultra-short term), ambulatory (short term) or visit-to-visit ([V2V] long term) measurements [1]. BPV has been studied in the context of cardiovascular diseases (CVDs) such as hypertension [2,3], incident stroke [4,5], stroke recurrence [6] and coronary heart disease [7], providing deeper insight into cardiovascular and autonomic function beyond average blood pressure (BP) measurements [8]. Emerging research indicates that BPV has broad implications for neurological health beyond stroke risk, with BPV implicated in brain morphology [9,10]. Specifically, BPV, independent of average BP, is associated with arterial stiffness [11], vascular remodelling [12], decreased cerebral perfusion [13,14] and cerebral small vessel disease [15]. The association between BPV with brain atrophy [16] and the progression of white matter lesions [17,18] and cerebral microbleeds [18] suggests that BPV is a broad risk factor for cerebrovascular disease. However, the association between BPV with dementia [19], Alzheimer's

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disease progression [20], and tau accumulation [21] raises the possibility that BPV is a consequence of cerebrovascular diseases and neurodegeneration. This highlights the importance of investigating other potential markers of brain health for their potential association with BPV.

Among early markers for poorer brain health, late onset depression is frequently associated with cerebrovascular changes in white matter tracts including white matter hyperintensities on magnetic resonance imaging (MRI) and cognitive impairment, especially in executive function [22]. One possibility is that changes to the cerebrovasculature contributes to the development of late onset depression and cognitive decline. There is strong evidence that elevated BPV is linked to the severity and progression of cerebrovascular diseases via pathways including micro-vascular cerebral arterial wall damage and changes to cerebral blood flow [22,23]. Such putative mechanisms may lead to psychomotor slowing and executive dysfunction in both late onset depression and prodromal or early-stage dementia [24]. Additionally, fluctuations in BPV might disrupt the central autonomic network, impacting emotional responses such as anxiety [25] and depression [26].

While elevated BPV has been implicated in structural and functional cerebrovascular changes that could potentially influence mood disorders, it remains unclear whether mood and BPV are directly related. Confounding variables that influence both mood and BPV include cardiovascular health and lifestyle risk factors [27]. There is also selection biases related to the age groups and comorbidities within prior observational studies making it difficult to infer a direct causal link between BPV and mood disorders. Current literature is limited by various constraints, including methodological differences in BPV measurement type such as beat-to-beat (B2B), ambulatory blood pressure monitoring (ABPM) and V2V [28], as well as disparities in effect size measures (e.g. correlation, regression and mean difference) and BPV metrics (e.g. coefficient of variation [CoV], standard deviation [SD]) [1]. Additionally, B2B depression studies have primarily included younger participants with lower cerebrovascular disease and dementia risk compared to older adults [29,30]. As research suggests that depression is linked to an increased risk of cerebrovascular disease [31] and dementia [24,32,33], studies primarily focusing on children and young healthy populations with low cerebrovascular disease and dementia risk may not fully capture the potential longer-term impacts of BPV on affective states. A 2020 systematic review explored the relationship between different affective states with BPV [34]. A limitation of the previous review is that studies relating to nocturnal dipping patterns and orthostatic challenge were included which is discrepant from modern understandings of what constitutes BPV [35]. Additionally, the previous review [34] included studies with small sample sizes, adolescents, and a broad inclusion criterion encompassing non-disorders states such as hostility as well as bi-polar disorder, resulting in heterogeneity across studies. The lack of data synthesis for BPV metrics and separate affective disorders further magnified methodological heterogeneity, underscoring the need for clarity on the putative association between BPV and affect. The present systematic review extends beyond the previous review, by synthesizing BPV studies pertaining to depression and anxiety. By reconciling past limitations, this review aims to clarify whether BPV is associated with depression and anxiety in adults, thereby informing whether BPV's role in brain health encompasses the common affective states that are observed in the prodromal stages of dementia [32,36].

2. Method

2.1. Search strategy

This systematic review adhered to the guidelines outlined in the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) [37] and was pre-registered on PROSPERO (CRD42022312904). A literature search was performed on the 8th January 2024, using the following databases from inception: Embase, PsycINFO, PubMed, and Web of Science. The search strategy comprised of a combination of keywords associated with BPV, anxiety and depression (Supplementary Table S1).

2.2. Inclusion criteria

Population and exposure: Studies were required to have a study population of human participants aged 18 years or older with clinical depression and/or anxiety using standardised clinical interviews or validated questionnaires and were derived from samples without significant chronic disease other than cardiovascular disease or hypertension.

Outcomes: BPV quantified using a standardised and valid device (e.g. OMRON M4 or Task Force Monitor) from systolic and/or diastolic BP readings, reported as a known BPV metric (either CoV, or SD, or average real variability [ARV]) quantified over any time frame, characterised as B2B, ambulatory blood pressure measurement (ABPM) over 24 h, or V2V between assessments, including home BP monitoring. Studies were required to provide effect sizes from the *r* or *d* family, including correlations, standardised regression coefficients or differences in mean values, to be included in the review. Effect sizes reported as odds ratios or hazard ratios for risk of depression or anxiety attributable to BPV were ineligible.

2.3. Exclusion criteria

Ineligible studies were published in a language other than English, the case sample consisted of less than 10 persons, the sample comprised of nonhuman sample population, the sampled included children or adolescents <18 years old, experimental designs reporting on response to postural change or orthostatic challenge or an antihypertensive medication or other drug trial or CO_2 reactivity or laboratory induced stress or sadness, were focussed on serious mental illnesses such as bipolar disorder or schizophrenia, or were derived solely from populations with dementia or other neurodegenerative disease, or were a review article, letter or editorial or case study.

2.4. Study selection

Abstracts and titles were independently screened for eligibility by a single reviewer (Y.L) in Covidence (Covidence, 2021). Following the initial screening, full texts of relevant articles were assessed against the inclusion criteria by two reviewers (Y.L and P.J.T). Any discrepancies were resolved through discussion and consultation with a third author (S.C). The reference lists of eligible articles were also searched and all papers that met the criteria were within the systematic review. The study selection process is illustrated in the PRISMA flow diagram (Fig. 1).

2.5. Data extraction

All data were extracted by one author (Y.L), which was verified and cross-checked by a second author (P.J.T). Discrepancies were discussed until consensus was achieved. The data extracted from the included studies were study identification details (first author, publication year, country of testing), study design, characteristics of the study sample (derived from outpatients or community, number of participants, gender distribution, mean age), relevant effect sizes, BPV metric (CoV, SD, or average real variability), and type of depression or anxiety measure. Data extraction for studies reporting standard mean differences encompassed both the experimental and comparator groups.

2.6. Data synthesis

Due to heterogeneity in BPV measures (B2B, ABP, V2V), BPV metrics

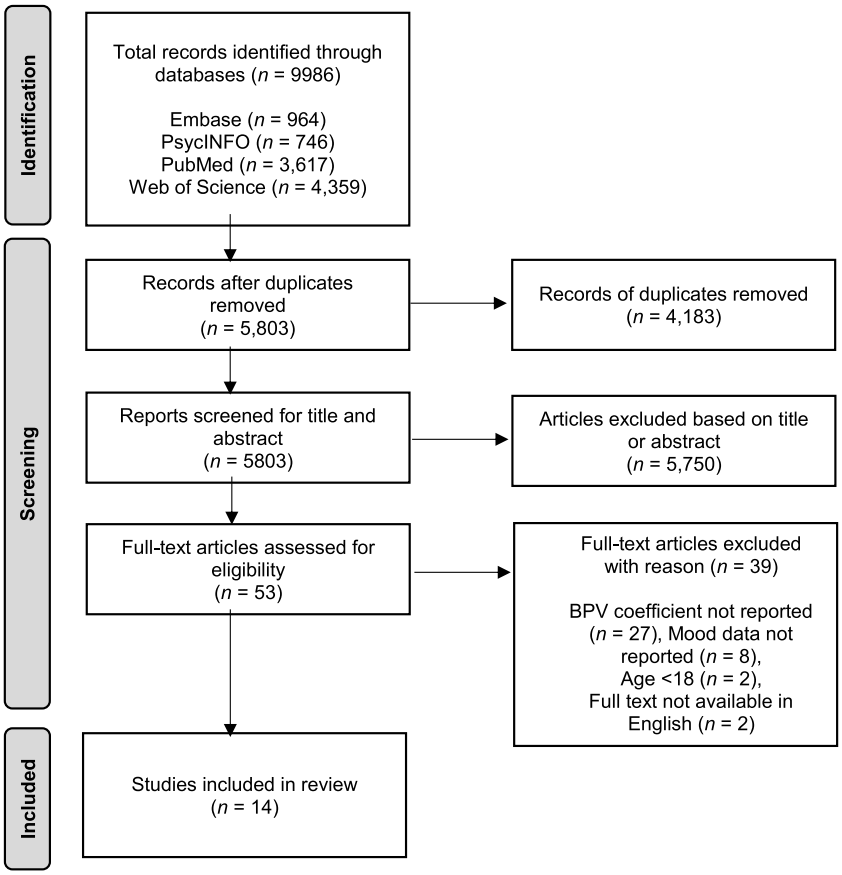

Fig. 1. PRISMA flow diagram illustrating the article selection and screening process.

(SD, CoV, ARV), and effect sizes (correlation, regression and mean difference), the included studies are synthesized qualitatively and a meta-analysis was not performed. Data on BPV outcomes were synthesised by categorising studies by depression and anxiety separately, the reported outcomes sub-divided as linear associations or mean differences, and stratified by B2B, ABPM, and V2V.

2.7. Quality assessment

In evaluating the quality of included studies, each study underwent an independent appraisal by authors (Y.L and P.J.T) using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies. The checklist consists of eight items: identifying inclusion/exclusion criteria, specifying study sample, measuring exposure, measuring condition, identifying, and addressing confounding factors, measuring outcomes, and appropriate statistical analysis. Each criterion was rated using a three-point scale (Yes/No/Unclear), which indicated whether the criterion is sufficiently addressed in the study under assessment. All conflicts were resolved by discussion.

3. Results

3.1. Study selection and characteristics

A total of 9986 articles were obtained through the database search, title and abstracts were screened for 5803 articles, resulting in 53 articles selected for full-text review. Among these, 39 were excluded (Table S2), leaving 14 articles included in the systematic review, reporting on 13 unique study samples [38–51]. The included studies were published between 2003 and 2022. Geographically, three studies were conducted in the USA, two in Germany, one each in Finland, Italy, Japan, Malaysia, Poland, Taiwan and Turkey, while data from a French cohort study was reported in two separate articles. Eleven studies were cross-sectional in design and two were longitudinal studies. The cumulative sample was $N = 5055$ (median sample $n = 135$), and sample sizes ranged from 25 to 2297 participants. The proportion of female gender ranged from 0 % to 76 %. Effect sizes were most commonly regression/correlation studies (6 studies), five compared groups with standardized mean differences, and three reported both mean differences and correlations. Six studies utilised B2B, while five involved ABPM and the other three utilized V2V data to quantify BPV. Regarding mental health, 11 studies investigated depression and seven examined anxiety, with four studies addressing both depression and anxiety. Seven studies examining depression reported regression/correlational statistics, while six studies reported differences in mean BPV between a depressed and non-depressed group. For anxiety, five studies reported correlational values, while three studies reported mean differences between an anxiety and non-anxiety group (Table 1).

3.2. Study quality

Most criteria related to study eligibility in the JBI checklist were met by >70 % of the response (Table S4). All included studies used valid and reliable measures for both exposure (JBI item 3) and outcome variables (JBI item 7), as well as appropriate statistical analysis techniques (JBI item 8). Some studies displayed moderate methodological quality overall, with issues observed in specifying inclusion/exclusion criteria (JBI item 1) and addressing confounding variables (JBI Item 5).

3.3. Linear association between BPV and depression

A total of seven studies reported a linear association between BPV

Table 1
Comparative overview of studies on BPV, depression and anxiety.

Author	Country	Study Design	Group	N (Women %)	Mean age ± SD	Effect size	BPV Measure	Mood		Mood instrument
								Depression	Anxiety	
Davydov et al. (2007)	USA	Cross sectional	Clinical, Community	248 (61)	36.2 ± 10.9	SMD	B2B	Yes	No	HAMD
Imaizumi et al. (2016)	JPN	Cross sectional	Outpatient	85 (62)	79.2 ± 5.9	SMD, r	ABP	Yes	No	SRQD
Koklu et al. (2022)	TUR	Cross sectional	Outpatient	88 (43)	45.7 ± 15.1	SMD, r	ABP	No	Yes	BAI
Lin et al. (2020)	TWN	Longitudinal	Outpatient	1112 (0)	32	β	V2V	Yes	Yes	BSRS
Sanchez-Gonzalez et al. (2015)	USA	Cross sectional	Community	43 (53)	26 ± 1.0	SMD	B2B	No	Yes	STAI
Schulz et al. (2010)	GER	Cross sectional	Clinical, Community	114 (68)	30 ± 9.0	SMD	B2B	Yes	No	HAMD, BDI
Schumann et al. (2017)	GER	Cross sectional	Inpatient	58 (72)	38.8 ± 12.2	SMD	B2B	Yes	No	HAMD, BDI
Scuteri et al. (2008)	ITA	Cross sectional	Inpatient	135 (76)	78 ± 6.0	SMD, β	ABP	Yes	No	GDS
Shahimi et al. (2022)	MYS	Cross sectional	Community	25 (68)	70.88 ± 7.2	r	B2B	Yes	Yes	DASS21
Sible et al. (2022)	USA	Cross sectional	Clinical	505 (40)	77.7 ± 6.5	β	V2V	Yes	No	GDS
Symonides et al. (2014)	POL	Cross sectional	Outpatient	195 (46)	45.4 ± 15.9	r	ABP	Yes	Yes	CECS
Three-City - (2017)	FRA	Longitudinal	Community	1454 (59)	78.5 ± 3.8	β	V2V	Yes	Yes	MINI
Three-City - (2018)	FRA	Longitudinal	Community	2297 (61)	72	SMD	V2V	Yes	Yes	MINI + CESD
Virtanen et al. (2003)	FIN	Cross sectional	Community	150 (53)	NR	β	B2B	No	Yes	BSI

ABP, ambulatory blood pressure; B2B, beat-to-beat; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; β, beta coefficient; BSI, Brief Symptom Inventory; BSRS, Brief Symptom Rating Scale; CECS, Courtauld Emotional Control Scale; CESD, Centre for Epidemiological Studies – Depression; DASS21, Depression, Anxiety, and Stress Scale; GDS, Geriatric Depression Scale; HAMD, Hamilton Rating Scale for Depression; MINI, Mini International Neuropsychiatric Interview; NR, not reported; r, correlation coefficient; SMD, standardised mean difference; SRQD, Self-Rating Questionnaire for Depression; STAI, State-Trait Anxiety Inventory; V2V, visit-to-visit;.

with depression symptom severity (Table 2). Of these, only one study used B2B measurements to evaluate BPV, while three used ABPM and three conducted V2V assessments. All reported systolic BPV, while five also reported diastolic BPV. Three studies reported correlation coefficients, while others reported beta-coefficients. Among the seven studies, it was generally observed that systolic and diastolic BPV was infrequently associated with depression, with four studies not reporting significant associations across B2B [42], ABPM [38,44], and V2V [40]. Significant effect sizes in systolic BPV were found in only two studies, and these were each in different directions. Scuteri et al. [41] found a significant negative association between CoV of systolic BPV and depression scores (β = −0.20), indicating higher systolic BPV was associated with lower depression severity. In contrast, the Three-City study [51] found a positive association for systolic BPV and

Table 2
Linear Associations between BPV, depression and anxiety.

Author (Year)	N (Female%)	BPV measure	Systolic			Diastolic		
			SD (CI)	CoV (CI)	ARV (CI)	SD (CI)	CoV (CI)	ARV (CI)
Depression								
Shahimi et al. (2022)	25 (68)	B2B	$r = 0.02$ (0.01 – 0.03)	$r = 0.04$ (0.03 – 0.05)	$r = 0.01$ (0.00 – 0.02)	$r = 0.17$ (0.16 – 0.18)	$r = 0.15$ (0.14 – 0.16)	$r = 0.07$ (0.06 – 0.08)
Imaizumi et al. (2016)	85 (62)	ABP	$r = 0.13$ (0.12 – 0.14)	$r = 0.18$ (0.17 – 0.19)	–	–	–	–
Scuteri et al. (2008)	135 (64)	ABP	–	β = −0.20*	–	–	–	–
Symonides et al. (2014)	195 (46)	ABP	$r = 0.15$ (0.15 – 0.15)	–	–	$r = 0.11$ (0.11 – 0.11)	–	–
Lin et al. (2020)	1112 (0)	V2V	β = −0.01	–	β = 0.0	β =0.00	–	β = 0.00
Sible et al. (2022)	505 (40)	V2V	–	β = 0.11	–	–	β = 0.16*	–
Three-City - (2017)	1454 (59)	V2V	β = 0.01	β = 0.11	–	β = 0.01	β = −0.01	–
Anxiety								
Shahimi et al. (2022)	25 (68)	B2B	$r = -0.32$ (−0.33 – −0.31)	$r = -0.39$* (−0.40 - −0.38)	$r = -0.05$ (0.04 – 0.06)	$r = -0.23$ (−0.24 - −0.22)	$r = -0.40$* (−0.41 - −0.39)	$r = -0.04$ (−0.05 - −0.03)
Virtanen et al. (2003)	150 (53)	B2B	–	β = 0.25*	–	–	–	–
Koklu et al. (2022)	88 (43)	ABP	$r = 0.32$* (0.31 – 0.33)	$r = 0.35$* (0.34 – 0.36)	–	–	–	–
Symonides et al. (2014)	195 (46)	ABP	$r = 0.15$* (0.15 – 0.15)	–	–	$r = 0.11$ (0.11 – 0.11)	–	–
Lin et al. (2020)	1112 (0)	V2V	β = −0.01	–	β = 0.00	β = 0.00	–	β = 0.00
Three-City - (2017)	1454 (59)	V2V	β = 0.10	β = 0.25*	–	β = 0.09	β = 0.04	–

ABP, ambulatory blood pressure; ARV, real average variability; β, beta coefficient; B2B, beat-to-beat; BPV, blood pressure variability; CI, 95 % Confidence Intervals; CoV, coefficient of variation; N, sample size; r, Pearson's correlation coefficient; SD, standard deviation; V2V, visit-to-visit.
* Statistical significance <0.05.

depression scores (β = 0.11). Significant effect sizes in diastolic BPV were reported in one study (β = 0.16) [43], and indicated that increased diastolic BPV was associated with higher depression scores.

3.4. Linear association between BPV and anxiety

Among the six included studies that reported a linear association between BPV and anxiety: two used B2B, two reported ABPM and two employed V2V assessments (Table 2). All studies examined the relationship between systolic BPV and anxiety, while four studies also reported diastolic BPV. Significant findings in systolic BPV were reported in five studies, three reported correlation coefficients ranging from a negative association ($r = -0.039$) to positive association ($r = 0.35$) [39,42,44] and two reported regression coefficients of β = 0.25 [45,51]. Four of the five studies reported a positive association between systolic BPV and anxiety scores, Virtanen et al. [45] and Symonides et al. [44] reported a significant positive association between the CoV of systolic BPV and anxiety scores (β = 0.25 and $r = 0.15$ respectively). Similarly, Koklu et al. [39] also reported a statistically significant increase in systolic BPV-SD ($r = 0.23$) and systolic BPV-CoV ($r = 0.35$) in individuals with high anxiety levels measured by the Beck Anxiety Inventory. In contrast, one study reported a negative correlation between CoV of systolic BPV and anxiety scores ($r = -0.39$) [42], with authors reporting similar findings between CoV of diastolic BPV and anxiety ($r = -0.40$). Only one study comprised of 1112 males did not report significant associations between systolic or diastolic BPV and anxiety [40].

3.5. Between depression group differences for bpv

Among the six studies included in this review that explored BPV between groups with high depression versus those with low or no depression (experimental versus control group), significant differences in systolic and diastolic BPV between experimental and control groups were observed in two studies. Both reported significantly higher systolic BPV in persons with depression by comparison to persons without depression [48,51], whereas only one study [48] found higher diastolic BPV in persons with depression. Otherwise, evidence for elevated BPV in persons with depression was not reported by four other studies [38,41,46,49] (Table 3).

3.6. Between anxiety group differences for BPV

Among the three studies that explored the mean difference of BPV between groups with high anxiety (experimental group) versus those with low or no anxiety (control group), only one study reported significant findings, while the other two did not. Sanchez-Gonzalez et al. [47] found a significant difference in systolic BPV with higher scores among individuals with anxiety than the control group. In contrast, the Three-City study [51] and Koklu et al. [39] did not find significant differences in either systolic or diastolic BPV between the anxious and non-anxious groups (Table 3).

4. Discussion

This systematic review does not support a consistent relationship between BPV with depression or anxiety. Unlike a previous review which broadly assessed bipolar disorder, mental illness, hostility, and BPV [34], this review focused specifically on uni-polar depression and anxiety in adult populations and contemporary conceptualisations of BPV. Our findings suggest that while there are sparse data supporting an association between BPV with depression and anxiety, the findings were generally inconsistent, in different directions and strength, and not uniform across the BPV metrics. Some evidence implicated systolic BPV in higher anxiety scores, however this was constrained largely to the CoV metric, whilst three studies reported a positive linear association, another reported a negative association. Consequently, the results from this systematic review provide insights into BPV's role in cognitive and cerebrovascular health. As research has previously demonstrated that BPV is associated with cognitive impairment, the findings of the current review tentatively suggest that the relationship between BPV and cognitive function is independent of depression, with only weak residual variance implicating anxiety.

The lack of a consistent association between BPV with common affective states prompts a deeper exploration into distinct cognitive mechanism and brain structures beyond those traditionally linked to cognitive function and dementia. BPV has been linked to cerebrovascular changes in brain structures critical for cognitive processing such as the prefrontal cortex and subcortical white matter [22,23]. The brain areas affected by depression and anxiety that are critical for mood

Table 3
Between group differences for BPV, depression and anxiety.

Author (Year)	Total N	Case Group N (female%)	Control Group N (female%)	BPV Measure	BPV Coefficient	Systolic		Diastolic	
						Case Group M (SD)	Control M (SD)	Case Group M (SD)	Control M (SD)
Depression									
Davydov et al. (2007)	248	28 (60.7)	220	B2B	SD	8.8 (3.1)	8.3 (2.9)	–	–
Schulz et al. (2010)[a]	114	57 (68.4)	57 (68.4)	B2B	SD	6.8 (3.2)*	5.2 (2.9)*	5.6 (2.5)*	4.2 (3.4)*
Schumann et al. (2017)	58	29 (72.4)	29 (72.4)	B2B	SD	5.51 (2.36)	4.53 (2.12)	3.96 (1.71)	3.22 (1.38)
Imaizumi et al. (2016)	85	46 (68)	39 (68)	ABP	SD	23.3 (4.8)	21.5 (6.5)	–	–
Scuteri et al. (2008)	135	74 (84)	61 (66)	ABP	SD	13.3 (3.6)	13.9 (3.3)	9.8 (2.2)	10.0 (1.8)
Three-City - (2018) [b]	2297 (61)	105 (77.1)	2192 (60.6)	ABP	CoV	11.3 (2.4)*	8.9 (2.9)*	10.1 (4.2)	9.1 (3.6)
Anxiety									
Sanchez-Gonzalez et al. (2015)[c]	43	22 (55)	21 (52)	B2B	CoV	3.5 (0.3)*	1.5 (0.2)*	–	–
Koklu et al. (2022)[d]	72	30	42	ABP	SD	12.61 (3.24)	13.02 (3.96)	17.02 (5.04)	11.91 (4.21)
Three-City - (2017)	1454	84 (69)	1370 (59.1)	ABP	CoV	8.3 (2.5)	8.1 (2.9)	8.7 (3.7)	8.3 (3.6)

ABP, ambulatory blood pressure; B2B, beat-to-beat; BPV, blood pressure variability; CoV, coefficient of variation; IQR, interquartile range; N, population; S.E, standard error coefficient; SD, standard deviation; V2V, visit-to-visit.

* Statistical significance <0.05.

[a] normal-to-normal beat time series.

[b] Interquartile range reported.

[c] Standard Error reported.

[d] Moderate and Severe data combined for BAI case group.

regulation include the amygdala and hippocampus [25,52]. An association between longer-term BPV with lower hippocampal volume was recently observed in a narrative synthesis of six studies [9]. However, no consistent association between short-term BPV and hippocampal volume was found [9]. With >70 % of studies in the current review quantifying short-term BPV such as through B2B or ABPM, it is possible that there is a discrepant association between short- and long-term BPV with structural changes in amygdala and hippocampus, accounting for the lack of association between BPV and affective states here. It is also plausible that further imaging studies in frontotemporal dementia marked by behavioural and personality changes might elucidate associations between BPV and affect [53]. Further research into the impact of longer-term BPV on neurogenerative conditions could provide crucial insights into preventative and therapeutic interventions [24]. Exploring the practical applications, in clinical settings BPV monitoring could be integrated into routine assessments for early detection of cognitive decline or mood disorders [54] to significantly advance patient care. The finding that calcium channel blockers, an antihypertensive drug which reduces BPV more than other drugs, was associated with reduced depressive symptoms also highlights the potential for clinical relevance of BPV interventions to mood [55]. However, without further investigations on longer-term BPV and affect, in populations with and without dementia, it remains unclear if V2V measures of BPV over the longer term are relevant to depression and anxiety. This highlights the need for targeted research that can validate whether BPV is a potential biomarker for cognitive and mental health disorders.

While no consistent association was evident here between BPV and depression, the broad range of psychometric assessments utilised in the included studies may underestimate a potential association between BPV with somatic and affective depression subtypes. Differentiating between affective disorders and their subtypes is crucial as recent literature reveals differences in brain activity across major depression subtypes. Specifically, somatic depression involves increased activity in the brain's right inferior temporal gyrus, enhancing physical sensation perception, and decreased activity in the left hippocampus, impacting emotional regulation and memory, in contrast to non-somatic depression [56]. fMRI also reveals that somatic symptoms are linked to lower functional connectivity in key areas responsible for emotional processing and pain perception [57]. Given the putative link between BPV and brain morphology such as reduced hippocampal volume [9], it remains possible that BPV is associated with only a somatic or affective major depression but not both subtypes. Such a putative association would have been masked by the range of psychometric assessments here. This underscores the requisite need for further research with uniform measures of depression and anxiety that facilitate the investigation of subtypes. By identifying specific BPV patterns associated with subtypes of mood, healthcare providers could tailor treatment more effectively [56, 57], potentially improving patient outcomes.

The detailed inclusion and exclusion criteria here ensuring only contemporary measures of BPV in adult populations generally free from major chronic diseases are key strengths that offer comprehensive insights regarding the current literature into BPV and affect. Distinguishing linear relationships from mean differences between groups allow researchers to better understand the heterogeneous nature of the extant research. However, a notable limitation is the heterogeneity of BPV measurement instruments used across studies, contributing to the variability in results and complicating the identification of consistent patterns. This variability, alongside the sparse homogeneous data, precluded the execution of a meta-analysis, resulting in a narrative review describing only trends. The paucity of eligible and comparable BPV studies highlights the need for more research aimed at understanding the association between BPV and affect. By comparison, previous reviews on brain health and BPV have included 18 studies pertaining to stroke [58], 27 concerning cerebral small vessel disease [10], 20 for other brain morphology [9], and 53 for dementia and cognition [54].

Given the inconsistent methodologies and findings across studies, future research and well-designed studies in the field of BPV and mood are crucial. More focus on longitudinal studies in future research is needed to establish whether there is a temporal relationship between BPV and mood, as current evidence heavily relies on cross-sectional and observational data. In future research, ideal studies should comprise of larger sample sizes, with extensive follow-up periods, regular BP measurements including 24-hour monitoring, and repeated standardised assessments of depression and anxiety. These studies will significantly contribute to filling the gap in V2V BPV research and also assist in revealing whether there is a causal association between BPV and mood, which is particularly crucial given the established link between longer-term BPV and structural changes in the brain [9]. Researchers should also attempt to control for confounding factors such as underlying health conditions, medications and demographic variables that may independently influence BPV and mood outcomes. Larger and more diverse cohorts are also needed to improve the generalisability of findings alongside comprehensive and validated mood assessments. Future investigations could also prioritise reporting more than one BPV metric (e.g. CoV, SD, ARV) at a minimum as well as defining both linear and between-group comparisons with mood. Such consistency in methods would help further our understanding of BPV's association with brain health and especially mood. Future research could also focus on observing the relationship between affect and BPV through longitudinal research with growth curve modelling or joint modelling the dynamic nature of BP fluctuations over time [59].

In conclusion, this review contributes to improving our understanding of the relationship between BPV and brain health. By employing a more standardized and rigorous examination approach than previous studies, the review provides critical insights to the relationship between BPV and brain health. It reveals a lack of consistent association between BPV with depression, and only modest evidence for a linear association between BPV and anxiety. The results highlight the methodological heterogeneity within data, emphasizing the necessity for more consistent research methodologies. Specifically, there is a need for further longitudinal studies focusing on V2V BPV to thoroughly investigate the potential temporal relationship with mental health and cognitive decline. Such research could significantly enhance our understanding of the mechanisms underlying neurodegeneration and inform the development of targeted interventions that could mitigate these effects. This review therefore not only enriches current understandings, but also shapes future research that could have profound implications for both clinical practice and public health strategies.

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CRediT authorship contribution statement

Yuvthi Lutchman: Conceptualization, Investigation, Methodology, Data curation, Writing – original draft, Writing – review & editing. **Rajiv Mahajan:** Writing – review & editing. **Suzanne M. Cosh:** Supervision, Resources, Writing – review & editing. **Katie Harris:** Writing – review & editing. **Christophe Tzourio:** Writing – review & editing. **Phillip J. Tully:** Conceptualization, Investigation, Methodology, Data curation, Resources, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Dr Mahajan has served on the advisory board of Abbott and Medtronic. The University of Adelaide reports receiving on behalf of Dr Mahajan lecture and/or consulting fees from Abbott, Bayer, Biotronik, Medtronic, and Pfizer. The University of Adelaide reports receiving on

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Supplementary materials

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