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Anxiety-dominant concordance across sleep and clinical burden in cerebral small vessel disease: a robust summary-level analysis

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ABSTRACT

Sleep complaints, affective symptoms, somatic distress, and cognitive inefficiency frequently coexist in cerebral small vessel disease (CSVD). Their simultaneous occurrence makes a single statistically significant association difficult to interpret because large unadjusted differences may represent shared symptom variance rather than an independent sleep correlate. We examined whether one clinical domain remained concordant across three complementary evidential axes. Numerical summaries from 30 adults with CSVD and 35 controls, including sleep-defined subgroups of 14 and 16 participants with CSVD, were analysed. Conventional group comparisons, Spearman associations, and multivariable linear regression were retained. Added analyses comprised small-sample-corrected Hedges effect estimates with 95% confidence intervals, a signed three-axis concordance coefficient combining disease separation, sleep-stratified separation, and adjusted standardized association, and 20,000-replicate Monte Carlo stability analyses under Gaussian and Student-$t(5)$ sampling. Higher standardized estimates were oriented toward greater clinical burden. Somatization showed the largest CSVD–control displacement ($g = 1.21$, 95% CI 0.68–1.74), followed by global sleep burden ($g = 0.94$, 0.43–1.45), anxiety ($g = 0.87$, 0.36–1.37), global symptom burden ($g = 0.83$, 0.33–1.34), and cognitive disadvantage ($g = 0.71$, 0.21–1.20). Within CSVD, anxiety produced the largest separation between participants above and below the sleep threshold ($g = 1.05$, 0.30–1.80). Depression ($g = 0.93$, 0.19–1.67) and global symptoms ($g = 0.83$, 0.10–1.56) were also prominent. The adjusted model assigned independent positive coefficients to anxiety ($\beta = 0.428$, $p = 0.017$) and sex ($\beta = 0.418$, $p = 0.015$), while the global symptom coefficient approached zero. Anxiety achieved the greatest three-axis concordance (0.73), exceeding depression (0.53); the global symptom coefficient was negative because its adjusted contribution vanished. The anxiety direction persisted in at least 99.6% of resamples. The study question is answered by an anxiety-dominant pattern: anxiety, rather than the broad symptom total, is the clinical domain that remains aligned with sleep burden across disease separation, sleep-defined subgroup separation, and simultaneous covariate control. Somatization best distinguishes CSVD from control status, but it does not supply the same adjusted evidence for sleep. Screening and prospective sleep assessment in CSVD should therefore distinguish general bodily distress from anxiety-specific arousal.

Keywords: cerebral small vessel disease; sleep; anxiety; somatization; cognitive vulnerability; Hedges g; Monte Carlo analysis

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1. INTRODUCTION

Cerebral small vessel disease (CSVD) denotes a heterogeneous group of pathological processes involving perforating arteries, arterioles, capillaries, venules, and the tissue compartments they sustain. The disorder is expressed on magnetic resonance imaging through recent small subcortical infarcts, lacunes, white-matter hyperintensities, cerebral microbleeds, enlarged perivascular spaces, and atrophy. Standardized neuroimaging terminology has improved communication across studies, yet imaging burden and lived clinical burden remain only partly coupled.[1–3] A patient can carry substantial white-matter injury without a dramatic focal neurological syndrome, while another can experience slowing, gait instability, fatigue, emotional dysregulation, or reduced daily efficiency before a conventional cognitive screen becomes strikingly abnormal. This disparity motivates clinical analyses that treat CSVD as a distributed brain disorder rather than as a collection of isolated lesions.[4–6]

The traditional clinical emphasis on stroke and dementia is justified by prognosis. White-matter hyperintensities predict incident stroke, dementia, and mortality, and total CSVD burden is associated with cognitive decline and loss of independence.[7–9] Nevertheless, the neurobehavioral expression of CSVD is broader than cognition alone. Depression, anxiety, apathy, somatic complaints, disturbed motivation, and sleep–wake complaints can affect adherence, rehabilitation, caregiver strain, and perceived disability. Frontal–subcortical disconnection offers a biologically plausible substrate because circuits linking prefrontal cortex, striatum, thalamus, limbic structures, and brainstem arousal systems traverse vulnerable white matter. Periventricular and deep lesions have been associated with distinct cognitive and psychiatric expressions, while lesion location may matter as much as aggregate lesion volume.[10–12] A narrow cognitive description can therefore underestimate clinically meaningful disease burden.

Sleep adds an especially difficult interpretive layer. Sleep disturbance can follow cerebrovascular injury, but it can also precede and potentially aggravate vascular dysfunction through intermittent hypoxia, sympathetic activation, endothelial stress, blood-pressure variability, inflammation, impaired metabolic clearance, and altered circadian regulation. Reviews of stroke populations support a bidirectional relationship between sleep–wake disorders and cerebrovascular outcomes.[13,14] Obstructive sleep apnoea is associated with stroke and with imaging features of small-vessel injury,[15,16] whereas non-respiratory sleep fragmentation has been linked to cognitive performance in CSVD.[17] Post-stroke insomnia is common, although prevalence estimates vary with timing, ascertainment, lesion features, and psychiatric comorbidity.[18] Population estimates in older Chinese adults similarly show substantial heterogeneity across sleep definitions and settings.[19] Thus, a global sleep questionnaire can capture several partially overlapping processes rather than a single pathophysiological state.

The psychological interpretation is equally complex. Anxiety may increase sleep latency, nocturnal vigilance, autonomic arousal, and attention to bodily sensations. Depression may shorten or lengthen sleep, reduce daytime activity, and alter the subjective appraisal of rest. Somatization can amplify awareness of discomfort and nocturnal interruption. Broad symptom inventories combine these domains and may appear strongly associated with sleep simply because they aggregate correlated complaints. Ecological momentary assessment has demonstrated close within-person coupling between mood and perceived sleep quality;[20] analogous relationships occur in Alzheimer disease and schizophrenia.[21] Obstructive sleep apnoea itself is associated with depressive symptoms and cognitive impairment,[22] which further complicates attribution when objective sleep physiology is unavailable.

Several strands of neuroimaging evidence suggest that this symptom coupling may have structural relevance. Community studies have related sleep complaints to silent CSVD markers,[23] while diffusion imaging has identified altered white-matter connectivity in insomnia.[24] In older adults, contemporaneous sleep quality has been associated with microstructural differences in widespread frontal–subcortical tracts.[25] These observations do not establish whether disturbed sleep causes white-matter injury, whether white-matter injury disrupts arousal and emotional regulation, or whether vascular and psychological factors influence both. They do, however, make it implausible to treat sleep, affect, and cognition as isolated clinical variables.

Assessment choices also influence the apparent clinical structure. The Pittsburgh Sleep Quality Index (PSQI) covers subjective quality, latency, duration, efficiency, disturbance, medication use, and daytime dysfunction, but its factor structure and screening performance vary across populations.[26,27] The Montreal Cognitive Assessment (MoCA) is sensitive to mild multidomain cognitive impairment and is commonly used in vascular populations.[28,29] The Beck inventories provide brief measures of depressive and anxiety symptoms,[30,31] and the Symptom Checklist-90 (SCL-90) samples a wide range of psychological complaints.[32] When these instruments are analysed together in a small cohort, correlated predictors can yield a large bivariate association but a negligible adjusted coefficient. Statistical significance from one test is therefore insufficient for deciding which domain deserves clinical priority.

Sex and educational exposure introduce additional heterogeneity. Women report insomnia and reduced sleep quality more frequently in many populations, with contributions from hormonal transitions, caregiving demands, stress exposure, mood symptoms, and ascertainment practices.[33,34] Educational experience can contribute to cognitive reserve and influence performance on screening instruments. If participants above a sleep

threshold also have fewer years of education, cognitive differences may reflect reserve, sleep, vascular injury, or their combination. A clinically useful analysis should preserve these covariates rather than interpret unadjusted symptom contrasts in isolation.

The present study asks a deliberately narrower and more discriminating question than whether CSVD is accompanied by worse sleep or more psychological symptoms. We ask which clinical domain shows aligned evidence across disease-related separation, sleep-related separation within CSVD, and adjusted association with PSQI. This question distinguishes a symptom that is merely characteristic of CSVD from one that is specifically informative about sleep burden after shared variance is considered. We retained the conventional tests because they preserve the direct clinical comparisons and familiar inferential scale. We then added small-sample-corrected standardized effects, a signed concordance calculation, and distributional stability analyses. The working hypothesis was that anxiety would show stronger cross-axis alignment than either depression or the broad SCL-90 total because hyperarousal is more directly connected to subjective sleep initiation and maintenance, whereas a broad total is more vulnerable to collinearity.

2. MATERIALS AND METHODS

This quantitative observational study used a published cohort comprising 30 adults with MRI-defined CSVD and 35 demographically comparable controls, together with the reported sleep stratification of the CSVD group into 14 participants with PSQI scores above 7 and 16 participants at or below that threshold. Group means, standard deviations, test statistics, bivariate correlations, and multivariable coefficients were transcribed from the three numerical tables and the correlation results in the attached article.[35] The clinical observations were collected at a neurology service in China between August and December 2020. No new participants were enrolled, no individual clinical record was accessed, and no unreported patient measurement was imputed.

The CSVD group was defined by compatible MRI features, including microbleeds, enlarged perivascular spaces, or recent small subcortical infarcts, in adults able to communicate and complete the assessments. Exclusions covered MRI contraindications, critical systemic illness, major alternative neurological disease, diagnosed Alzheimer disease or dementia, established psychiatric disorder, substance dependence, and major communication impairment. Controls were hospital support-service participants without major neurological or psychiatric illness, stroke, dementia, serious brain injury, or psychoactive substance use. The available summaries showed no conventional group difference in age, sex, education, or the demographic distribution used for the principal comparison.

The research question was operationalized across three axes. The disease axis quantified standardized differences between CSVD and controls. The sleep axis quantified differences between the two PSQI-defined CSVD groups. The adjusted axis used standardized regression coefficients for depression, anxiety, and global psychological symptoms entered concurrently with sex, age, and education. Concordance required a domain to point toward greater burden on all three axes. This requirement prevents a broad unadjusted contrast from being mistaken for domain-specific adjusted evidence.

2.1. Clinical measures

Depressive symptoms were measured with the 13-item Beck Depression Inventory, and anxiety with the 21-item Beck Anxiety Inventory. Both instruments use ordered response categories in which higher totals indicate greater symptom severity. Multidomain psychological burden was assessed with the SCL-90 total and six reported subscales: somatization, obsessive–compulsive symptoms, interpersonal sensitivity, hostility, phobic anxiety, and paranoid ideation. Sleep during the preceding month was assessed with the PSQI. Its seven component areas are summed to a global score from 0 to 21, with higher values indicating greater sleep-related burden. The categorical sleep comparison used a threshold greater than 7. Global cognition was assessed with the MoCA, scored to a maximum of 30 with an education correction for participants with no more than 12 years of schooling.

The term “clinical burden” has a precise directional meaning in the analyses. Higher depression, anxiety, PSQI, SCL-90, and SCL-90 subscale scores indicate greater burden. Lower MoCA and fewer years of education were sign-reversed so that positive standardized estimates consistently denote disadvantage. This orientation permits direct visual comparison without asserting that instruments measure the same construct.

2.2. Conventional statistical analyses

Categorical group differences were assessed with chi-square tests. Continuous variables were screened for distributional form and compared with independent-samples t tests when the normality assumption was considered acceptable; Mann–Whitney tests were used otherwise. The conventional report included Cohen d for t-test contrasts and Freeman theta for Mann–Whitney contrasts. Within CSVD, Spearman coefficients described the association of PSQI with depression, anxiety, and global psychological symptoms. A multiple linear regression used PSQI as the dependent variable and sex, age, education, depression, anxiety, and SCL-90 total as simultaneous predictors. All tests were two-sided with $\alpha = 0.05$.

These analyses were retained because each addresses a distinct question. Group tests estimate whether observed samples differ; rank correlations assess monotonic pairwise relationships; regression estimates the partial contribution of a predictor while holding the others constant. Their coexistence is important here because the broad SCL-90 total correlates strongly with PSQI but con-

tributes almost no unique coefficient when anxiety and depression enter the same model.

2.3. Small-sample-corrected standardized effects

To place all continuous contrasts on a common scale, Hedges g was calculated from the reported means, standard deviations, and group sizes. For groups 1 and 0, the pooled standard deviation was

$$s_p = \sqrt{\frac{(n_1-1)s_1^2 + (n_0-1)s_0^2}{n_1+n_0-2}}, \tag{1}$$

and the standardized mean difference was corrected for small-sample bias using

$$g = J\frac{\bar{x}_1 - \bar{x}_0}{s_p}, \qquad J = 1 - \frac{3}{4(n_1+n_0-2)-1}. \tag{2}$$

The sampling variance used the conventional independent-group approximation, and 95% confidence intervals were formed as $g \pm 1.96\,SE(g)$. These intervals quantify precision around standardized mean separation; they do not correct for multiplicity and should not be read as dichotomous discovery labels. The principal value of g is comparative magnitude, particularly when one instrument has a 0–21 range and another has a much larger range.

The disease contrast included depression, anxiety, PSQI, cognition, the SCL-90 total, and six SCL-90 subscales. The sleep-defined contrast excluded PSQI because that variable created the groups; education was retained to expose the reserve difference. Estimates were oriented toward adverse status as described above. Reporting both magnitude and uncertainty avoids relying solely on p values, which are especially unstable with 14 and 16 participants in the sleep-defined groups.

2.4. Three-axis concordance coefficient

Depression, anxiety, and global psychological symptoms were available on all three axes. For domain j, the signed concordance coefficient was

$$C_j = \operatorname{sgn}(g_{D,j}g_{S,j}\beta_j)\,|g_{D,j}g_{S,j}\beta_j|^{1/3}, \tag{3}$$

where g_D is the adverse-oriented CSVD–control effect, g_S is the adverse-oriented sleep-group effect within CSVD, and β is the standardized coefficient from the simultaneous PSQI regression. The geometric mean was chosen because a near-zero value on any axis should sharply reduce concordance. An arithmetic average could remain large despite absence of adjusted evidence. A positive C_j indicates alignment across all three axes; a negative value indicates that the adjusted coefficient reverses the unadjusted direction.

This coefficient is not presented as a validated clinical score and has no diagnostic threshold. It is a transparent synthesis of three already interpretable quantities. Its purpose is to distinguish cross-axis consistency from simple effect size. A domain can strongly distinguish CSVD from controls yet receive a low concordance value if it does not separate sleep groups or if its adjusted coefficient disappears.

2.5. Monte Carlo stability analysis

Distributional stability was evaluated with 20,000 replicates for each endpoint and contrast. For the Gaussian condition, observations were generated from distributions parameterized by each reported mean and standard deviation at the exact group sizes. For the heavy-tailed condition, values were generated from Student-t distributions with five degrees of freedom, scaled to preserve the reported variance. Hedges g was recalculated in each replicate, and the proportion retaining the adverse direction was recorded. A result close to 1 indicates that the observed direction is unlikely to be overturned by sampling variation under the stated distribution; a value near 0.5 indicates weak directional stability.

The heavy-tailed condition was included because several symptom totals were not normally distributed and small samples are sensitive to extreme observations. The analysis deliberately evaluates direction rather than an exact replicated p value. It does not reconstruct correlations among endpoints, because their covariance matrix was unavailable. Each endpoint is therefore assessed independently, and conclusions concern the stability of univariate contrasts rather than a synthetic patient-level multivariate distribution.

2.6. Reproducibility and ethical considerations

All calculations and figures were produced in Python using NumPy, pandas, SciPy-compatible formulae, and Matplotlib. A fixed random seed was used, and the complete script accompanies the manuscript. Numerical outputs are stored as comma-separated files. Because the work used non-identifiable published summaries and involved no participant contact, additional ethics review was not required for the present computation. The clinical cohort had written consent procedures described by its investigators.

3. RESULTS

3.1. Cohort profile and conventional findings

The analytic population comprised 65 adults: 30 with CSVD and 35 controls. The CSVD group had a mean age of 64.63 years (SD 7.58), compared with 61.49 years (SD 4.83) in controls. Men accounted for 20 of 30 participants with CSVD and 15 of 35 controls. Mean educational exposure was 7.18 and 6.27 years, respectively. The conventional comparisons identified higher depression, anxiety, PSQI, SCL-90 total, somatization, and obsessive–compulsive scores in CSVD, together with lower MoCA performance. Interpersonal sensitivity, hostility, phobic

anxiety, and paranoid ideation did not reach the conventional significance threshold.

Within CSVD, 14 of 30 participants exceeded the PSQI threshold. The two sleep-defined groups were similar in age, and the sex distribution difference did not reach $p < 0.05$. Participants above the threshold had fewer years of education, higher depression and anxiety scores, and a higher SCL-90 total. The mean MoCA difference was 1.5 points in the adverse direction but was imprecise. Table 1 condenses the measurements that anchor the principal analyses.

The profile shows why significance alone is an incomplete guide. Anxiety differs by only four raw points between CSVD and controls but has a large standardized effect because control variability is narrow. Depression has a visibly skew-compatible pattern: the mean is higher in CSVD, yet its standard deviation exceeds the mean. The sleep-defined comparison also reveals an educational difference of approximately three years, making covariate adjustment essential for interpreting cognitive performance.

3.2. Standardized disease-linked displacement

Small-sample correction yielded a structured disease profile rather than a uniform elevation of every symptom. Somatization produced the largest CSVD–control effect ($g = 1.21$, 95% CI 0.68–1.74). Global sleep burden followed ($g = 0.94$, 0.43–1.45), then anxiety ($g = 0.87$, 0.36–1.37), SCL-90 total ($g = 0.83$, 0.33–1.34), and adverse-oriented MoCA performance ($g = 0.71$, 0.21–1.20). Depression was moderate ($g = 0.52$), whereas interpersonal sensitivity and paranoid ideation were small and imprecise.

The left-hand distribution in Figure 1 shows that bodily distress and sleep burden discriminate disease status more strongly than the narrowly affective depression score. This ordering is clinically important: it cautions against describing the CSVD phenotype as principally depressive. Anxiety and global symptom burden are prominent, but somatic complaints occupy the leading disease-linked position. The cognitive effect remains substantial despite heterogeneity in education, supporting the presence of clinically relevant cognitive disadvantage while leaving its mechanism unresolved.

3.3. Sleep-linked displacement within CSVD

The ordering changed when analysis was restricted to participants with CSVD. Anxiety became the largest sleep-linked effect ($g = 1.05$, 95% CI 0.30–1.80), followed by depression ($g = 0.93$, 0.19–1.67), global symptoms ($g = 0.83$, 0.10–1.56), phobic anxiety ($g = 0.80$, 0.08–1.53), and reduced educational exposure ($g = 0.78$, 0.05–1.51). Somatization remained positive ($g = 0.61$) but was no longer dominant. Cognition showed a smaller adverse-oriented estimate ($g = 0.34$, -0.38 to 1.06), with an interval spanning no difference.

The right-hand distribution in Figure 1 therefore answers a different question from the disease contrast. Somatization distinguishes CSVD from control status, whereas anxiety distinguishes the higher-PSQI subgroup within CSVD. The contrast between panels also reveals that an attribute can be disease-linked without being the principal sleep-linked attribute. The wide intervals reflect the 14-versus-16 subgroup sizes and argue for attention to effect ordering and replication rather than binary declarations.

A direct comparison of the most clinically informative estimates appears in Table 2. The directions are aligned for anxiety, depression, global symptoms, somatization, phobic anxiety, and cognition, but the magnitudes differ. Anxiety is the only domain among the top disease effects that also occupies the leading position within CSVD.

The paired presentation prevents overextension of the strongest single result. Somatization has convincing disease separation but weaker sleep separation, whereas phobic anxiety has modest disease separation and stronger sleep separation. Global symptoms are large in both unadjusted contrasts, yet the regression results below show that this apparent consistency is not independent of its affective components. Anxiety alone combines large effects on both contrasts with an independent adjusted coefficient.

3.4. Directional stability under alternative sampling distributions

The Monte Carlo analysis showed that the leading contrasts were not dependent on Gaussian tails. For the CSVD–control comparison, the adverse direction persisted in at least 99.9% of resamples for anxiety and global symptoms, 100% for somatization to the displayed precision, and 99.7% for cognitive disadvantage. Depression retained its direction in at least 97.8%. Small disease contrasts were less stable: interpersonal sensitivity had a minimum probability of 84.3%, and paranoid ideation 80.3%.

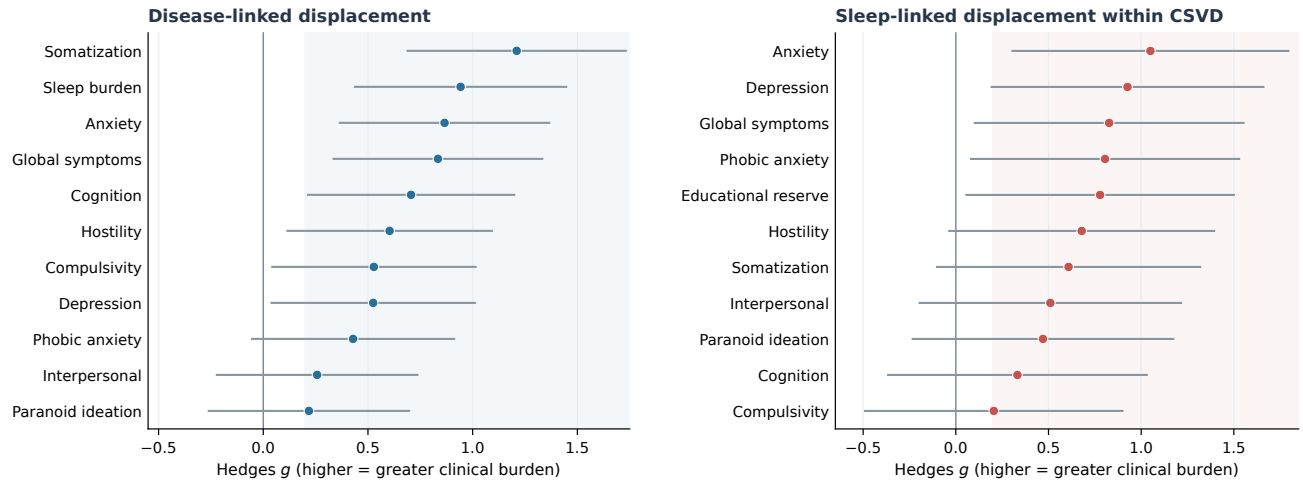
Within CSVD, the adverse anxiety direction persisted in at least 99.6% of resamples, depression in 99.2%, global symptoms in 98.6%, phobic anxiety in 98.1%, and reduced educational exposure in 98.5%. Cognitive disadvantage retained its direction in 82.6%, and obsessive–compulsive symptoms in 72.0%. Heavy tails modestly reduced certainty for several endpoints but did not alter the ordering of the strongest affective signals.

The effect plane in Figure 2 separates three clinical patterns. Somatization lies furthest along the disease axis but only midway along the sleep axis. Anxiety occupies the upper-right region, indicating large effects in both comparisons. Cognitive disadvantage lies to the right but relatively low, indicating clearer disease separation than sleep-related separation. The heatmap adds distributional information: the leading affective results remain dark across Gaussian and heavy-tailed conditions, whereas the paler cells for compulsivity and cognition in

Table 1. Cohort profile and principal clinical measurements.

Measure	CSVD $n = 30$	Control $n = 35$	High PSQI $n = 14$	Lower PSQI $n = 16$
Age, years	64.63 (7.58)	61.49 (4.83)	65.50 (5.29)	63.88 (9.25)
Education, years	7.18 (4.01)	6.27 (3.50)	5.57 (3.72)	8.59 (3.83)
Depression	2.60 (3.94)	1.03 (1.71)	4.43 (5.16)	1.00 (1.10)
Anxiety	27.17 (6.10)	23.17 (2.63)	30.29 (7.51)	24.44 (2.45)
PSQI	8.20 (4.03)	4.91 (2.85)	—	—
MoCA	19.80 (4.38)	22.49 (3.15)	19.00 (4.06)	20.50 (4.66)
SCL-90 total	66.17 (11.11)	58.23 (7.66)	70.86 (13.26)	62.06 (6.90)
Somatization	17.97 (3.42)	14.31 (2.56)	19.07 (3.36)	17.00 (3.27)

Values are mean (standard deviation). Higher PSQI denotes scores greater than 7. PSQI, Pittsburgh Sleep Quality Index; MoCA, Montreal Cognitive Assessment; SCL-90, Symptom Checklist-90.



(a) CSVD versus controls.

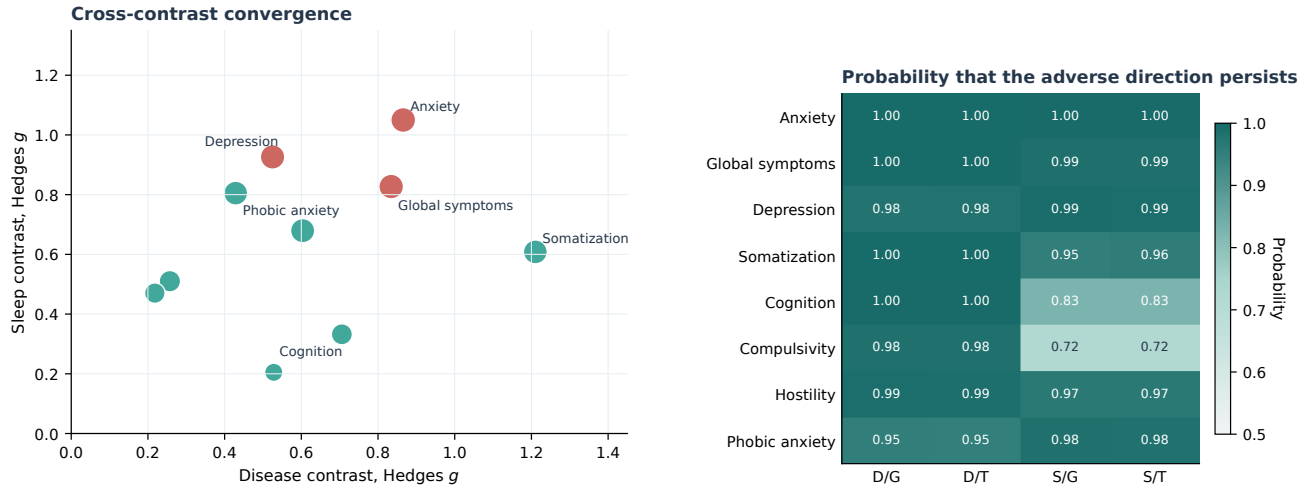
(b) Sleep-defined CSVD groups.

Figure 1. Standardized clinical displacement.

Table 2. Small-sample-corrected effects for selected domains.

Domain	CSVD versus control, g (95% CI)	High versus lower PSQI, g (95% CI)
Anxiety	0.87 (0.36, 1.37)	1.05 (0.30, 1.80)
Depression	0.52 (0.04, 1.01)	0.93 (0.19, 1.67)
Global symptoms	0.83 (0.33, 1.34)	0.83 (0.10, 1.56)
Somatization	1.21 (0.68, 1.74)	0.61 (−0.11, 1.34)
Phobic anxiety	0.42 (−0.06, 0.90)	0.80 (0.08, 1.53)
Cognitive disadvantage	0.71 (0.21, 1.20)	0.34 (−0.38, 1.06)

Positive values indicate greater burden in CSVD or in the higher-PSQI subgroup. Cognitive scores were sign-reversed. Confidence intervals are unadjusted for multiplicity.



(a) Cross-contrast effect plane.

(b) Direction probabilities.

Figure 2. Cross-contrast convergence and sampling stability.

the sleep comparison expose greater sensitivity to sampling variation.

The probabilities in Table 3 are sensitivity quantities, not frequencies observed in patients and not posterior probabilities of a clinical hypothesis. Their role is comparative. Anxiety, depression, global symptoms, and somatization retain their adverse directions under both distributional forms, while the sleep-linked cognitive and compulsivity contrasts are fragile enough that a modestly different sample could plausibly change their direction.

3.5. Adjusted associations and three-axis concordance

The conventional bivariate analysis found positive correlations between PSQI and depression ($r = 0.542$), anxiety ($r = 0.492$), and SCL-90 total ($r = 0.636$), all with $p < 0.001$. These correlations indicate substantial pairwise coupling but do not identify unique contributions. In the simultaneous regression, sex had an unstandardized coefficient of 3.510 PSQI points (95% CI 0.743–6.278; $\beta = 0.418$, $p = 0.015$), and anxiety had a coefficient of 0.283 PSQI points per BAI point (0.055–0.511; $\beta = 0.428$, $p = 0.017$). Age, education, depression, and global symptoms were not independently associated at $p < 0.05$. The model had adjusted $R^2 = 0.438$.

The coefficient display in Figure 3 makes the scale distinction explicit. Sex is a categorical contrast and therefore has a larger unstandardized coefficient than the continuous symptom predictors; standardized coefficients are required for cross-predictor comparison. The concordance strips show that anxiety remains positive and comparatively large on disease, sleep, and adjusted axes. Depression remains positive but attenuates after adjustment. The SCL-90 total is large on both unadjusted axes but falls just below zero in the simultaneous model, consistent with shared variance rather than a protective interpretation.

The decisive comparison in Table 4 is between anxiety and global symptoms. Both had large unadjusted effects, and the global total had the stronger bivariate correlation with PSQI. Once both affective inventories and covariates were entered, anxiety retained an independent positive coefficient while the global total did not. The concordance calculation penalizes this loss of unique information, producing 0.73 for anxiety, 0.53 for depression, and -0.18 for global symptoms. The negative sign reflects the slightly negative adjusted coefficient and should be interpreted as absence of domain-specific adjusted evidence, not as a clinically beneficial association.

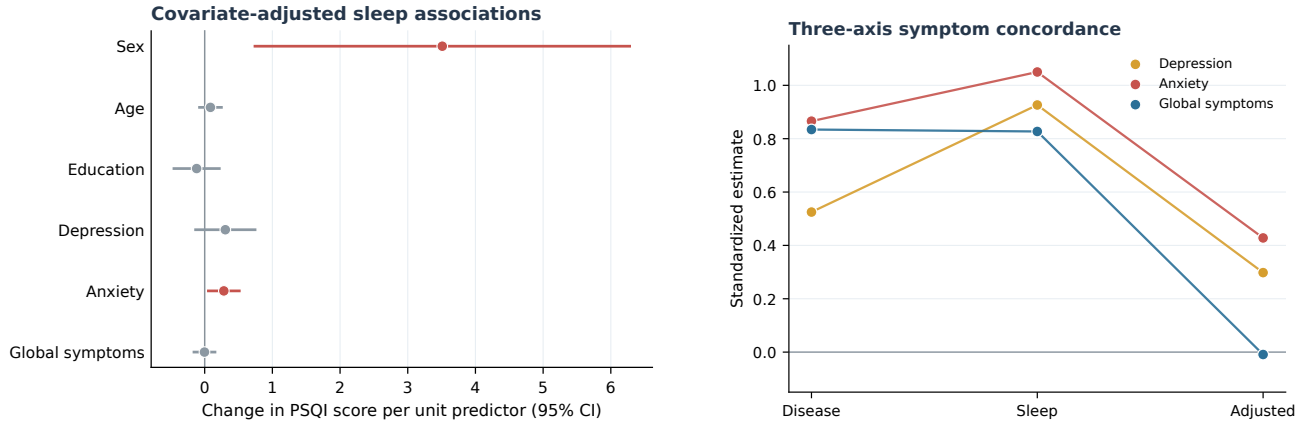
4. DISCUSSION

The study asked which clinical domain retains a stable relationship with sleep burden across disease status, sleep stratification within CSVD, and simultaneous adjustment. The answer is anxiety. Somatization most strongly distinguishes CSVD from controls, and the broad symptom total is prominent in unadjusted comparisons, but neither supplies the same three-axis alignment. Anxiety shows a large disease effect, the largest sleep-defined effect, an independently positive regression coefficient, the highest concordance coefficient, and near-complete directional stability under both Gaussian and heavy-tailed sampling. This is a more specific conclusion than stating that psychological symptoms and sleep are associated.

The distinction between disease discrimination and sleep discrimination deserves emphasis. Somatization had a standardized disease effect exceeding 1.2, which is large relative to most other domains. Cerebrovascular patients may experience dizziness, fatigue, pain, autonomic sensations, reduced mobility, medication effects, and heightened monitoring of bodily function. These experiences can elevate somatic symptom scores without identifying the mechanism of sleep disturbance. The within-CSVD effect for somatization remained positive

Table 3. Minimum probability of retaining the adverse direction.

Domain	CSVD versus control	High versus lower PSQI
Anxiety	0.999	0.996
Depression	0.978	0.992
Global symptoms	1.000	0.986
Somatization	1.000	0.953
Phobic anxiety	0.952	0.981
Cognitive disadvantage	0.997	0.826
Compulsivity	0.984	0.720



(a) Adjusted coefficients.

(b) Standardized alignment.

Figure 3. Adjusted sleep associations and symptom concordance.

Table 4. Adjusted model and three-axis concordance.

Predictor/domain	B	95% CI	β	p	C_j
Sex	3.510	0.743, 6.278	0.418	0.015	—
Age	0.085	−0.076, 0.247	0.161	0.285	—
Education	−0.119	−0.454, 0.216	−0.119	0.469	—
Depression	0.305	−0.134, 0.744	0.298	0.165	0.53
Anxiety	0.283	0.055, 0.511	0.428	0.017	0.73
Global symptoms	−0.003	−0.158, 0.152	−0.009	0.966	−0.18

The dependent variable is PSQI. C_j combines the disease effect, sleep-group effect, and standardized adjusted coefficient; it is computed only for domains represented on all three axes.

but was smaller and less precise. Clinically, a high somatization score may signal substantial overall burden, whereas an elevated anxiety score may be more informative about the sleep–arousal interface.

Anxiety is biologically and phenomenologically compatible with that interface. Cognitive worry, anticipatory threat, sympathetic activation, and selective attention to internal cues can prolong sleep latency and increase perceived nocturnal disruption. Repeated sleep loss can in turn weaken emotion regulation, intensify threat appraisal, and increase daytime bodily vigilance. Frontostriatal and limbic connections affected by small-vessel injury participate in both emotional control and arousal regulation. The present findings cannot determine the direction of causation, yet they show that anxiety remains informative after accounting for depression, global symptom burden, sex, age, and education. This persistence is consistent with an anxiety-specific component beyond undifferentiated distress.

The broad SCL-90 total illustrates why bivariate magnitude and adjusted contribution must be separated. It had the strongest reported Spearman association with PSQI and large standardized group effects. In the simultaneous model, however, its coefficient was essentially zero. Because the total includes somatic, obsessive, interpersonal, hostile, phobic, and paranoid content, it overlaps with anxiety and depression both conceptually and statistically. Multicollinearity can widen intervals and change coefficient signs, especially in a sample of 30. The near-zero adjusted coefficient does not negate the clinical burden represented by the SCL-90. It means that the total adds little sleep-specific information after the affective scores are known.

Depression occupied an intermediate position. Its disease effect was moderate, its sleep-defined effect was large, and its adjusted standardized coefficient remained positive but imprecise. Several explanations are plausible. The 13-item inventory had a low mean and marked dispersion, leaving the contrast sensitive to a small number of elevated scores. Depressive symptoms also share variance with anxiety and sleep questionnaire items. Fatigue, reduced activity, concentration difficulty, and altered sleep can contribute to both depressive and PSQI totals. Larger cohorts with item-level analysis could separate cognitive-affective depression from somatic and sleep-related items, reducing criterion overlap.

The cognitive findings were directionally coherent but less specific to sleep. CSVD participants had a sizeable adverse MoCA effect relative to controls, compatible with the established contribution of small-vessel injury to vascular cognitive impairment.[36] Within CSVD, the sleep-defined cognitive effect was smaller and uncertain. Educational exposure differed by approximately three years between the sleep groups, and the MoCA itself includes an education correction that may not fully remove reserve-related differences. Consequently, the available evidence supports cognitive disadvantage in CSVD but does not show that subjective sleep burden is its principal determinant in this cohort. Objective sleep measures, domain-specific cognitive tasks, and formal reserve indicators would be needed to resolve the pathway.

The sex coefficient was comparable in standardized magnitude to the anxiety coefficient. Its direction cannot be independently decoded from the coefficient table because the binary coding convention was not supplied with the numerical summaries. More broadly, sex differences in reported sleep can reflect menopausal transition, mood prevalence, social stress, caregiving, sleep-disordered breathing phenotype, medication, and reporting behavior. The small number of women in the CSVD group also makes the coefficient vulnerable to sampling variation. A future study should pre-specify coding and interaction analyses, measure reproductive and hormonal status where appropriate, document caregiving and socioeconomic stress, and assess respiratory sleep disorders. The present result identifies effect modification and confounding questions rather than a sex-specific treatment rule.

The stability analysis strengthens some conclusions while exposing others. Anxiety, depression, global symptoms, and somatization retained adverse directions even when data were generated from a heavy-tailed distribution with the observed variance and group sizes. This does not prove external reproducibility, because the simulation is anchored to one cohort. It does show that the leading directions are not mathematical artifacts of assuming Gaussian tails. By contrast, the within-CSVD cognitive and compulsivity effects were much less stable. These differences support a graded interpretation: anxiety is a high-priority replication target, whereas cognitive sleep separation requires more evidence before a confident claim.

Clinical application should remain proportionate to the evidence. A brief anxiety assessment may improve interpretation when a person with CSVD reports disturbed sleep, particularly if the broad symptom inventory is elevated. The result does not imply that anxiety is the sole cause of disturbed sleep or that treating anxiety will necessarily alter vascular outcomes. Respiratory disorders, restless legs, nocturia, pain, medication effects, circadian disruption, depression, and environmental factors remain relevant. The practical implication is diagnostic differentiation: anxiety-specific arousal should be assessed rather than absorbed into a single global distress total.

Research design can improve substantially on the present evidence. Prospective cohorts should combine repeated PSQI assessment with actigraphy, sleep diaries, and respiratory screening. MRI characterization should follow standardized definitions and include total CSVD burden, regional white-matter hyperintensity volume, lacunes, microbleeds, perivascular spaces, and diffusion-based integrity measures. Repeated anxiety and depression assessments would permit temporal ordering and

within-person analysis. Domain-specific cognitive testing should emphasize processing speed, executive control, and attention, which are often more sensitive to CSVD than global memory measures. Such a design could test whether anxiety precedes sleep deterioration, follows it, or modifies the association between sleep physiology and cognitive change.

The present analysis also clarifies the role of effect sizes in small clinical studies. A conventional p value answers whether a statistic is unusual under a null model, but it does not express the comparative prominence of somatization, anxiety, and cognition. Hedges g placed these domains on a common scale and corrected the upward bias of Cohen d in small samples. The cross-contrast plane then showed how prominence changes with the clinical question. This layered approach avoids declaring one universal symptom hierarchy when the hierarchy depends on whether the target is disease status or sleep burden.

The concordance coefficient supplies a further safeguard against selective emphasis. If only the disease contrast were considered, somatization would dominate. If only the bivariate sleep correlation were considered, the broad SCL-90 total would dominate. If only the adjusted model were considered, anxiety and sex would dominate without showing whether anxiety also differentiates disease and sleep subgroups. Requiring alignment across three axes identifies a clinically coherent signal while retaining the meaning of each component. The coefficient should nevertheless be tested in independent datasets before any predictive use.

Several aspects of the literature support the need for this distinction. CSVD is a dynamic whole-brain disorder whose clinical manifestations emerge from interacting vascular, tissue, and network processes.[4,37] Sleep supports memory, immune regulation, metabolic balance, and neural plasticity;[38] its disturbance can both reflect and influence neurological disease. Community evidence links CSVD burden, frailty, and sleep,[39] yet broad self-report measures do not isolate physiology. Cognitive training studies show that vascular cognitive impairment retains modifiable functional capacity,[40] but an intervention chosen from a cross-sectional symptom association may miss the active mechanism. Anxiety-specific assessment is therefore a tractable next step, not a substitute for mechanistic sleep measurement.

5. CONCLUSION

The paper's research question concerns cross-axis persistence, not the mere coexistence of sleep and psychological symptoms in CSVD. Anxiety provides the clearest answer. It combines a large CSVD–control effect, the largest sleep-defined effect within CSVD, an independent adjusted association with PSQI, the highest three-axis concordance coefficient, and at least 99.6% directional stability under the tested sampling distributions. Somatization is the strongest discriminator of disease status, but it is less specifically connected to the sleep contrast; the broad SCL-90 total is substantial before adjustment but adds negligible unique information once affective symptoms are entered. The evidence therefore supports anxiety-specific assessment alongside sleep evaluation in CSVD, while prospective multimodal measurement is required before causal or therapeutic conclusions are justified.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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