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Blood transcriptomic overlap between major depressive disorder and experimental sleep restriction in a reanalysis of public microarray data

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Abstract

Background

Insomnia and depression are closely related, but evidence for a shared blood transcriptional signature depends on how the clinical groups and sleep responses are defined. We examined the consistency of transcriptomic overlap across sample inclusion rules and statistical models.

Methods

We reanalysed public microarray data from major depressive disorder (MDD; GSE98793) and experimental sleep restriction (GSE39445) using standard limma. Sleep responses were estimated from participant means and from repeated measurements with adjustment for sampling time and circadian phase. Signed Stouffer tests assessed combined associations; partial-conjunction tests required evidence in both phenotypes. A clinical-insomnia dataset was examined for confounding and excluded from validation.

Results

The sleep analysis included 21 participants with 185 paired measurements. In the 192-array MDD dataset, the contrast for MDD without generalized anxiety disorder identified 93 genes at a false discovery rate below 0.05, compared with 13 for pooled MDD. No gene met this threshold in the participant-mean sleep model, whereas 15 did in the time-and-phase model. Among 16180 common genes, the corresponding Stouffer analyses identified 134 and 617 associations with concordant directions. Neither analysis identified a significant partial-conjunction result; this remained the case across all 25 model combinations. Mean participant-level alignment was 0.0611 (95% bootstrap interval − 0.0174 to 0.1401; one-sided sign-flip P = 0.0737). The original 22-array MDD quality-control exclusion list could not be authenticated.

Conclusions

Apparent transcriptomic overlap was sensitive to the MDD contrast, sample inclusion and temporal modelling. These data did not establish a shared signature with support in both phenotypes after false discovery rate control. Limited power and unresolved historical quality control prevent interpreting this finding as evidence that shared biology is absent.

Background

Insomnia predicts subsequent depression [1]. Genetic studies also implicate pathways shared with psychiatric traits [2]. Blood gene-expression studies offer a complementary view of this relationship

because they measure transcriptional responses that may vary with clinical state and recent sleep. Whole-blood studies of major depressive disorder (MDD) have reported changes in immune-related expression [3], while experimental sleep restriction alters circadian rhythmicity and expression amplitude across the blood transcriptome [4]. These findings motivate a comparison of the two exposures, but they do not by themselves demonstrate a common transcriptional signature.

The available datasets differ in ways that affect this comparison. GSE98793 comprises people with MDD and controls, with generalized anxiety disorder (GAD) present in half of the MDD group [3]. GSE39445 repeatedly sampled healthy participants during extended wakefulness after restricted or sufficient sleep [4]. The sleep experiment therefore measures a response to an experimental exposure, not the phenotype of clinical insomnia. A further dataset, GSE208668, studied insomnia in older adults using peripheral blood mononuclear cells, but its case and control groups came from different parent studies [5]. The clinical exposures, tissues and sampling conditions cannot be treated as interchangeable.

Analytical choices introduce further uncertainty. Including GAD in the MDD model changes the clinical contrast, while averaging repeated sleep measurements removes information about sampling time and circadian phase. Sample eligibility also requires checking the deposited records against the original study reports. The source GSE98793 analysis excluded 22 arrays, and a subsequent reanalysis used the same exclusion count [3, 6]; the public series nevertheless contains all 192 arrays. A combined association test can then yield a significant result even when evidence comes predominantly from one dataset. Thus, a long list of combined associations need not imply convincing support in both phenotypes.

We reanalysed these public data to determine how consistently blood transcriptional changes in MDD align with experimental sleep restriction. We reconstructed sample eligibility, compared clinically distinct MDD contrasts, and evaluated participant-mean and temporal models of the sleep response. We also verified the differential-expression calculations against standard limma and distinguished exploratory combined associations from evidence requiring a non-null association in both datasets.

Methods

Study design and data sources

This secondary analysis used publicly available, de-identified, depositor-processed microarray matrices from the Gene Expression Omnibus (GEO) [7]. GSE98793 [8] and GSE39445 [9] were the primary datasets. GSE208668 [10] was used only to examine the consequences of confounding by parent study (Table 1). Source matrices were downloaded from official GEO endpoints on 8 September 2026 and matched the archived SHA-256 checksums. The analysis was not preregistered. Earlier results were known when the dated analysis specification was prepared; model choices were fixed after metadata inspection and before execution of the standard limma analyses. Sample size was determined by the available eligible observations.

The analyses began with the deposited expression matrices and did not repeat processing of raw CEL files. Supplementary methods and provenance checks are provided in Additional file 1. Executable code, source URLs and checksums, annotation and sample records are supplied in Additional file 2; main model designs and results are provided in Additional file 3. Additional file 4 contains sampling-time results; Additional files 5, 6 and 7 contain the cross-phenotype results for the complete, QC and renormalized MDD series, respectively. Pairing records and verification summaries are provided in Additional file 8.

Table 1
Datasets and eligible samples

Dataset	Deposited data	Analytical role
GSE98793 / MDD	192 whole-blood arrays: 128 cases, 64 controls	All 192 in the deposited-series analysis; 183 after independent QC. Historical cohort not authenticated.
GSE39445 / sleep restriction	438 whole-blood arrays from 26 participants	21 participants with 185 eligible nominal-time pairs.
GSE208668 / insomnia diagnostic	42 PBMC arrays: 17 cases, 25 controls	Confounded by parent study; excluded from synthesis and validation.

MDD, major depressive disorder; PBMC, peripheral blood mononuclear cell; QC, quality control. The historical 170-sample MDD cohort could not be reconstructed from authenticated sample exclusions.

MDD sample eligibility and clinical contrasts

GSE98793 contains 128 MDD cases and 64 controls; 64 cases had GAD. The original study reported excluding 22 arrays, leaving 113 cases and 57 controls [3]. We searched the source publications, supplements, public repository records and archived project materials for the corresponding sample identities. The public code accompanying the Cole reanalysis [6, 11] refers to a separate sample-selection file, which was unavailable. A previously archived 22-array reconstruction was based partly on matching the published group counts and could not authenticate the original exclusions. It was not used in the present models. The primary analysis therefore describes the complete deposited series, and its results should not be interpreted as a reproduction of the original 170-sample analytic cohort.

We fitted expression as a function of MDD, GAD, age, sex and batch. Because GAD occurred only among MDD cases, the MDD coefficient estimates the contrast between MDD without GAD and controls, while the other cases contribute information to model fitting. We refer to this as the non-GAD MDD contrast. A second model omitted GAD to estimate the pooled-MDD contrast. Age was continuous; sex and batch were entered as indicator variables.

An independent quality-control (QC) sensitivity analysis used all 54675 processed probes without reference to diagnosis. For each array, we calculated the sum of its mean absolute distances from the

other arrays and the Kolmogorov–Smirnov distance between its expression distribution and the pooled empirical distribution. Values above the upper Tukey hinge plus 1.5 interquartile ranges were flagged. Both MDD models were refitted after excluding the union of these flags. We also refitted the non-GAD model after quantile renormalization of the retained probes, before gene aggregation. These diagnostics assess sensitivity to processed-expression outliers; they do not recover the historical raw-array QC decisions. Additional file 1 describes the supplementary reconstruction of the generic arrayQualityMetrics diagnostics.

Expression processing and differential expression

Each dataset was processed separately. Probe-to-gene annotation used GPL570, GPL15331 and the GPL10904 ORF field for the MDD, experimental-sleep and clinical-insomnia datasets, respectively. Probes without gene symbols or with delimiter-marked ambiguous assignments were excluded. Multiple unambiguous probes assigned to the same symbol were collapsed to their within-sample median. Genes with any non-finite value were excluded. Annotation tables and derived mappings were retained with the analysis files.

Differential expression was estimated using R 4.3.3 and limma 3.58.1 [12]. We used lmFit followed by eBayes with trend = FALSE and robust = FALSE. Benjamini–Hochberg adjustment [13] was applied across all eligible genes within each testing family; the significance threshold was a false discovery rate (FDR) below 0.05. For the MDD, participant-mean sleep and adjusted clinical-insomnia designs, we compared coefficients, moderated t statistics, P values, adjusted P values and significant-gene membership with a recovered custom implementation using identical inputs. This comparison evaluated numerical agreement independently of sample eligibility and model interpretation.

Sleep sample reconstruction and participant means

GSE39445 contains 438 arrays from 26 participants. GEO characteristics were parsed within each sample because their positions differed across metadata records. Both deposited title formats were accepted when identifying participants and conditions. We checked the uniqueness of each participant–condition–sampling-index combination and the completeness of recorded hours awake and circadian phase. Details of title parsing and sample identities are provided in Additional file 1 and Fig. 1.

Restricted-sleep (SR) and sufficient-sleep (SE) samples were paired within participant at the same nominal sampling index. All 189 resulting pairs had identical recorded hours awake within each pair. Participants needed at least five pairs to enter the analysis. We averaged SR-minus-SE expression differences within each eligible participant and fitted an intercept-only limma model to these independent participant means. This approach gives each participant equal weight and estimates the average response over that participant’s available sampling times.

For a diagnostic comparison, we repeated the analysis after restricting titles to those with the prefix used by most samples. This restriction excluded otherwise valid records and was not considered an eligible primary analysis. It was retained to quantify the effect of the historical sample-selection rule.

Sampling time and circadian phase

Matching nominal sampling indices did not ensure matching circadian phase. Of the 189 nominal-time pairs, 72 had identical phases and 117 had an SR phase three hours below the SE phase. We therefore fitted a repeated-measures model to the eligible paired differences, with ten sampling-index indicators and two phase covariates: the SR-minus-SE differences in the sine and cosine of circadian phase, assuming a 24-hour period. limma duplicateCorrelation estimated a consensus within-participant correlation, which was supplied to lmFit. The contrast of interest was the equally weighted mean of the ten sampling-index coefficients. Nine contrasts against the first index jointly tested heterogeneity over sampling time.

This model assumes an additive harmonic phase effect and a common within-participant correlation structure across genes. Its adjustment and weighting differ from those of the participant-mean model. Gene-wise results at each sampling index were also retained, with FDR adjustment within each time-specific family. These exploratory results were not corrected across all ten time families and were not used to select a preferred sampling time.

Two SE records for AF0182 reported the same phase despite different sampling indices. We retained the deposited values in the main time model and repeated it after omitting AF0182. A separate exact-phase analysis excluded the two ambiguous SE records, paired the remaining SR and SE samples by participant and recorded phase, and applied the same minimum-five-pair rule before averaging within participant. Phase matching does not also ensure equal hours awake; the resulting estimate addresses a different conditional comparison.

Combined associations and evidence in both phenotypes

The common gene universe comprised 16180 genes measured in both primary datasets. For each gene, two-sided P values and effect directions were converted to signed normal scores. Equal-weight Stouffer combination used $z = (z_{MDD} + z_{sleep})/\sqrt{2}$. We obtained a two-sided normal P value and applied Benjamini–Hochberg adjustment across the entire common universe before retaining genes with concordant effect directions. This test assesses combined evidence and can be significant when one dataset contributes most of that evidence.

We separately tested the partial-conjunction hypothesis [14], using max(PMDD, Psleep) as the gene-wise P value, followed by Benjamini–Hochberg adjustment across the same universe and the concordant-direction criterion. This procedure requires support for an association in both datasets. Because MDD and experimental sleep restriction are distinct exposures, it does not constitute replication of one clinical

phenotype. Five MDD definitions were crossed with five sleep definitions, including the diagnostic title restriction, to yield 25 model combinations. FDR control applied within each combination; these analyses were not treated as independent replications or pooled into a confirmatory discovery family.

Participant alignment and the clinical insomnia comparison

For each eligible sleep participant, we calculated the Spearman correlation between the complete mean sleep-response vector and the non-GAD MDD effect vector across common genes. The mean correlation was tested using 10000 whole-participant sign flips, with seed 20260724 and the plus-one Monte Carlo correction. A percentile 95% interval was obtained from 10000 participant bootstrap samples using seed 20260908. Resampling at participant level preserves dependence among genes within each vector. Both summaries condition on the observed MDD vector and do not incorporate uncertainty in its estimation. The sign-flip test was one-sided for positive alignment.

For GSE208668, we fitted models with insomnia status alone and with additional adjustment for age, sex, race, body mass index and depression history. Case status was fully confounded with parent study [5], so these models could not identify an insomnia effect separately from study-related differences. The dataset was excluded from cross-phenotype synthesis and external validation. Previously archived perturbation-query results were not used to infer treatment candidates from the current gene lists; no new perturbational screen was performed.

Computational assistance

OpenAI Codex assisted with source retrieval, metadata parsing, code development and checking, figure preparation and manuscript drafting. Statistical analyses were executed using the software described above, and expression values came from the public matrices. The authors remain responsible for the analyses, interpretation and manuscript.

Results

Eligible samples and numerical agreement

After annotation and completeness checks, 20848 genes were available in GSE98793, 19541 in GSE39445 and 33209 in GSE208668. In the sleep dataset, 22 participants had at least one nominal-time pair. AF0112 contributed four pairs and did not meet the eligibility threshold; AF0033 contributed seven and was retained. The participant-mean and main temporal analyses consequently included 21 participants with 185 pairs, ranging from six to ten pairs per participant (Table 1).

Eleven sleep arrays lacked the title prefix used by most samples (Fig. 1). Restricting eligibility to prefixed titles reduced the analysis to 20 participants and 173 pairs and reproduced the archived 52-gene Stouffer result. The recovered older code accepted both title formats; the separate script associated with

the later reported result could not be recovered. The diagnostic restriction therefore explains how the earlier counts can arise, but does not identify the operation actually performed by the unavailable script (Additional file 1).

Standard limma and the recovered custom implementation agreed to numerical precision on identical inputs. Across the three compared designs, the largest absolute difference was 1.43×10^{-14} for coefficients and 7.41×10^{-13} for moderated t statistics. Significant-gene membership was identical.

MDD results across clinical contrasts and QC definitions

In the complete 192-array series, 93 genes met FDR < 0.05 for the non-GAD MDD contrast and 13 for pooled MDD (Table 2). The independent processed-expression diagnostics flagged nine arrays, comprising seven cases and two controls. Removing them left 121 cases and 62 controls; the corresponding significant-gene counts were 118 and four. Quantile renormalization of the retained probes yielded 111 genes in the non-GAD contrast.

The supplementary reconstruction of the generic arrayQualityMetrics diagnostics flagged the same nine arrays (Additional file 1, Figure S1). These flags do not authenticate the original 22 exclusions. Results for the source study's 113-case/57-control cohort therefore remain unresolved.

Sleep results under alternative temporal models

No gene met FDR < 0.05 in the participant-mean sleep analysis; the smallest adjusted P value was 0.3238. The time-and-phase model identified 15 genes, with a minimum adjusted P value of 0.0001296 and a consensus within-participant correlation of 0.1499 (Fig. 2). Omitting AF0182 retained 20 participants and 179 pairs and increased the significant-gene count to 50. Exact-phase averaging retained 20 participants and 166 pairs and identified no significant gene (Table 2). The omnibus test of heterogeneity across sampling indices identified no gene at FDR < 0.05; its smallest adjusted P value was 0.2529.

Table 2
Differential expression across the main models

Dataset / model	Observations / people	Genes tested	FDR < 0.05
MDD: all 192, non-GAD contrast	192 / 192	20848	93
MDD: all 192, pooled contrast	192 / 192	20848	13
MDD: independent QC, non-GAD	183 / 183	20848	118
MDD: independent QC, pooled	183 / 183	20848	4
MDD: independent QC + renormalization	183 / 183	20848	111
Sleep: participant means	21 / 21	19541	0
Sleep: time and phase model	185 pairs / 21	19541	15
Sleep: time model omitting AF0182	179 pairs / 20	19541	50
Sleep: exact-phase participant means	20 / 20; 166 pairs	19541	0
Clinical-insomnia diagnostic: adjusted	42 / 42	33209	17441

Significance was defined as Benjamini–Hochberg FDR < 0.05 within each complete gene universe. Non-GAD denotes the contrast between MDD without generalized anxiety disorder and controls. Repeated pairs do not represent independent participants.

Associations across phenotypes and participant alignment

For the non-GAD MDD contrast and participant-mean sleep response, 9896 of 16180 common genes had concordant effect directions (61.2%). Stouffer synthesis identified 134 associations at FDR < 0.05, comprising 70 positive and 64 negative effects. Of these genes, 41 were also significant in the MDD analysis and none in the participant-mean sleep analysis. Using the time-and-phase sleep model increased the Stouffer count to 617; 61 were significant in MDD and 13 in sleep restriction. Neither combination produced a significant partial-conjunction result (Table 3).

The corresponding pooled-MDD combinations yielded 16 and 198 Stouffer associations. With the non-GAD contrast, omitting AF0182 from the temporal model yielded 898 associations, while exact-phase averaging yielded 484. Across all 25 model combinations, Stouffer counts ranged from seven to 981, whereas every partial-conjunction count was zero (Fig. 3). Complete gene-level estimates for all combinations are included in the accompanying results files.

Mean participant-level Spearman alignment was 0.0611, with a 95% bootstrap interval of − 0.0174 to 0.1401 and a one-sided sign-flip P value of 0.0737. Individual correlations ranged from − 0.2535 to 0.3784 (Fig. 3).

Table 3
Combined associations using the contrast for MDD without GAD

Sleep model	Stouffer associations	Significant in MDD	Significant in sleep	Partial conjunction
Participant means	134	41	0	0
Time and phase model	617	61	13	0
Time model, omit AF0182	898	62	35	0
Exact-phase participant means	484	65	0	0
Title restriction (diagnostic)	52	26	0	0

All combined tests use BH FDR < 0.05 over 16180 common genes. Component-study significance uses each complete within-study gene universe. The title restriction excludes otherwise eligible samples and is retained only as a diagnostic comparison.

Clinical insomnia and confounding by parent study

In GSE208668, the adjusted model identified 17441 of 33209 genes at FDR < 0.05 (52.5%), compared with 17194 in the status-only model. Their effect vectors were almost identical in rank, with a descriptive Spearman correlation of 0.9985. This broad separation persisted after adjustment for measured covariates, but insomnia status remained inseparable from parent study. These findings were not used as evidence of external validation.

Discussion

This reanalysis found that apparent blood transcriptomic overlap between MDD and experimental sleep restriction depended substantially on the clinical contrast and the model used to summarise repeated sleep measurements. The participant-mean and time-and-phase analyses yielded 134 and 617 concordant Stouffer associations, respectively. Neither established FDR-controlled evidence in both phenotypes, and this result was consistent across the full set of model comparisons. Participant-level alignment was modest, varied between individuals and had a bootstrap interval that included zero. The data therefore support a cautious interpretation of combined gene lists rather than a validated shared transcriptional signature.

The distinction between combined evidence and evidence in each phenotype is central to this interpretation. Stouffer synthesis aggregates signed evidence against a global null; a strong association in MDD can contribute to a significant combined result when the sleep evidence is weak. In the participant-mean analysis, none of the 134 selected genes was significant in sleep restriction on its own. Partial-conjunction testing addressed the more demanding question of whether both datasets supported

a non-null association. Its uniformly non-significant results limit claims of a shared signature, but do not demonstrate that MDD and sleep loss have no common biology. The sleep analysis included only 21 participants, and gene-level FDR control imposes a substantial power requirement.

Temporal modelling changed the sleep findings without resolving that uncertainty. Averaging within participant estimates a response over the available sampling times and gives equal weight to participants. The repeated-measures model uses the temporal structure of the experiment and adjusts for a harmonic phase contribution, but relies on assumptions about additivity and within-participant correlation. The increase from 15 to 50 significant genes after omitting one participant with ambiguous phase records illustrates the sensitivity of this estimate. A larger discovery count is not sufficient grounds for preferring a model. The original sleep experiment examined rhythmicity and expression amplitude within a richer temporal design [4]; the absence of significant genes in a reduced participant-mean comparison does not contradict all of those findings.

The MDD results also depend on the clinical question. Adjustment for GAD estimates the contrast between MDD without GAD and controls, rather than the average contrast for all people with MDD. The counts of 93 and 13 significant genes in the complete series should therefore be read as results for different estimands, not as competing estimates of one effect. The underlying samples and covariance structure are shared, but the contrasts need not describe the same clinical population. This distinction is relevant when comparing expression studies with different comorbidity profiles.

Historical QC remains an unresolved limitation. The complete public series contains arrays excluded from the source analysis, and neither the recovered author code nor the archived reconstruction authenticated the original sample list [3, 6, 11]. The independent diagnostics identified nine arrays and allowed sensitivity analyses, but they used processed expression values and cannot reproduce raw-array QC. Agreement between an archived reconstruction and the published exclusion counts was insufficient because the reconstruction explicitly used those counts during selection. Accordingly, the present results describe the deposited series and the specified sensitivity subsets. Their applicability to the original 170-sample cohort has not been established.

Sample reconstruction presents a separate reproducibility issue. Accepting both deposited title formats retained eligible sleep observations and changed the combined association count. A restriction to the more common title prefix reproduced the archived sample and gene counts, showing that a metadata rule alone can materially alter the result. However, the exact later script remained unavailable. The evidence supports sensitivity to that restriction, not a definitive claim about which line of the original code produced the discrepancy. The close agreement between standard limma and the recovered older implementation establishes numerical consistency on identical inputs; it does not settle the historical sample-selection question.

Biological and design differences further restrict interpretation. Bulk-blood expression can reflect cell composition, medication, smoking, inflammation and collection conditions, several of which could not be reconstructed adequately from these records. Experimental sleep restriction in healthy participants is

not a direct model of chronic insomnia in people with depression. Whole blood and peripheral blood mononuclear cells also differ in composition. In the clinical-insomnia dataset, complete confounding by parent study prevented separation of insomnia status from study-related effects, regardless of measured-covariate adjustment. An independent, clinically characterised cohort with comparable tissue and sampling procedures is needed before the present associations can be interpreted as a shared clinical signature.

The analysis was not preregistered, and earlier findings were known when the reanalysis was planned. The model comparisons should consequently be regarded as structured sensitivity analyses rather than independent confirmatory tests. FDR correction was applied within each prespecified testing family, not across every model and sampling-time comparison. Participant resampling preserved gene dependence, but the resulting interval and sign-flip test conditioned on the observed MDD effect vector. They do not include uncertainty in estimating that vector. These limitations are relevant even though the deposited inputs, model code and numerical results are reproducible.

The findings do not provide a sufficient basis for selecting therapeutic compounds. Connectivity Map compares expression signatures with profiles generated by experimental perturbations [15]. L1000FWD provides a complementary interface for exploring such profiles [16]. The reproducibility of these approaches depends on the input signature and the cellular context [17]. Archived results for an earlier gene list cannot be transferred to the larger lists generated here, and a connectivity score is not evidence of clinical efficacy. Further work should first establish the relevant clinical contrast, specify the temporal model prospectively and test it in an independent cohort. Any subsequent perturbation analysis would then require a justified input signature and appropriate biological validation.

Conclusions

Blood transcriptomic overlap between MDD and experimental sleep restriction was sensitive to sample inclusion, comorbidity adjustment and temporal modelling. Although exploratory combined tests identified concordant associations, no model established FDR-controlled support in both phenotypes. The current data therefore do not validate a shared blood signature or support therapeutic inference. Limited sample size, model sensitivity and unresolved historical MDD quality control leave the extent of shared biology uncertain.

Abbreviations

BH
Benjamini–Hochberg
FDR
false discovery rate
GAD
generalized anxiety disorder

GEO
Gene Expression Omnibus
MDD
major depressive disorder
PBMC
peripheral blood mononuclear cell
QC
quality control
SE
sufficient sleep
SR
restricted sleep.

Declarations

Ethics approval and consent to participate

The Ethics Committee of the First Affiliated Hospital of Guangzhou University of Chinese Medicine granted an exemption from ethical review for this secondary analysis of publicly available, de-identified expression data. This study was conducted in accordance with the Declaration of Helsinki. No participants were recruited, contacted or re-identified, and no intervention was undertaken by the present authors. The source studies reported their ethics approval and informed-consent procedures [3,4,5].

Consent for publication

Not applicable. The manuscript contains no identifiable personal information.

Availability of data and materials

The source expression datasets are publicly available in GEO under accessions GSE98793 [8], GSE39445 [9] and GSE208668 [10]. Derived data supporting the conclusions are included in this article and its additional files. The supplementary files provide executable analysis code, official source URLs and checksums, annotation and sample records, model specifications, complete gene-level results and provenance evidence. The historical GSE98793 exclusion input and the exact script associated with the earlier archived result remain unavailable; these are not required to execute the present deposited-matrix analyses.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LH conceived and designed the study, coordinated the research, interpreted the findings and drafted the manuscript. CM contributed to the analytical methodology, developed the analysis code and performed the statistical analyses. SZ curated the public datasets, processed the data and assessed data quality. YZ contributed to the external dataset analysis and interpretation of cross-study findings. HL prepared the figures and tables and checked the analytical results. XL contributed to the study design, provided scientific supervision and critically revised the manuscript. All authors reviewed and approved the final manuscript and agreed to its submission to BMC Psychiatry.

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Figures

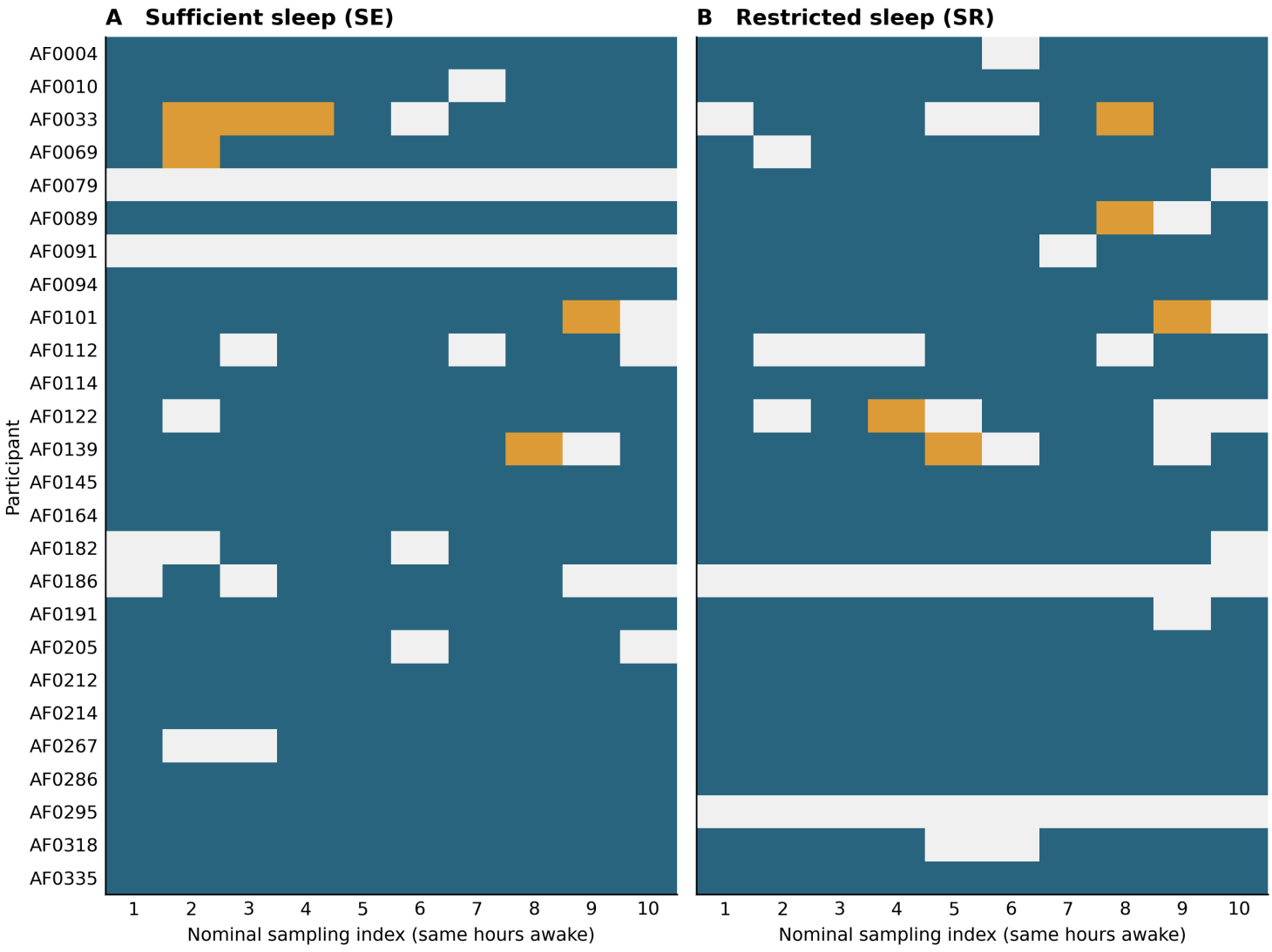


Figure 1

Reconstruction of the experimental sleep samples. All 438 deposited arrays are shown by participant, condition and nominal sampling index. Amber cells identify the 11 arrays whose titles lack the Subject_ prefix. These records were retained in the primary analysis. Grey cells indicate that no array was deposited for the corresponding combination. The diagram displays deposited samples before pairing and the minimum-five-pair eligibility criterion were applied.

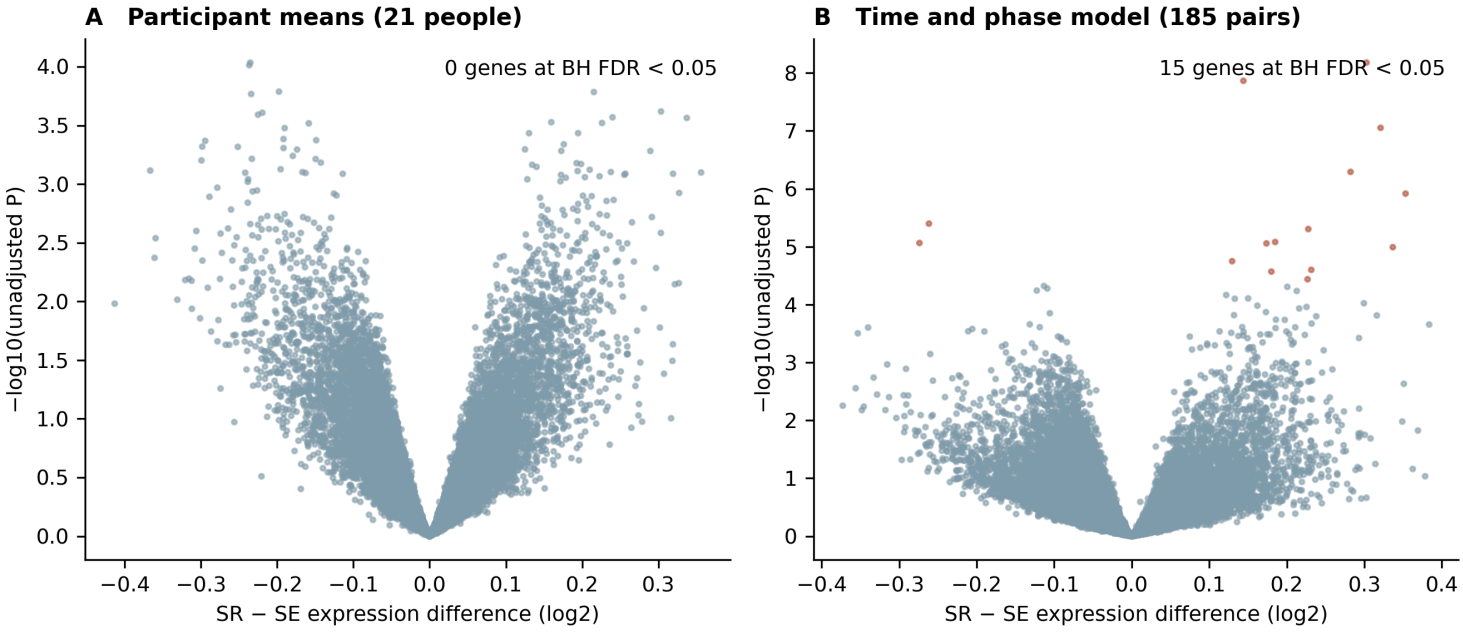


Figure 2

Differential expression under two sleep response models. The left panel shows the participant-mean analysis of 21 SR-minus-SE response vectors. The right panel shows the repeated-measures analysis of 185 paired differences with sampling-index and circadian-phase covariates. Red points denote genes meeting within-model BH FDR < 0.05. The vertical scales differ between panels. The discovery counts describe different estimators and should not be used alone to select a preferred model.

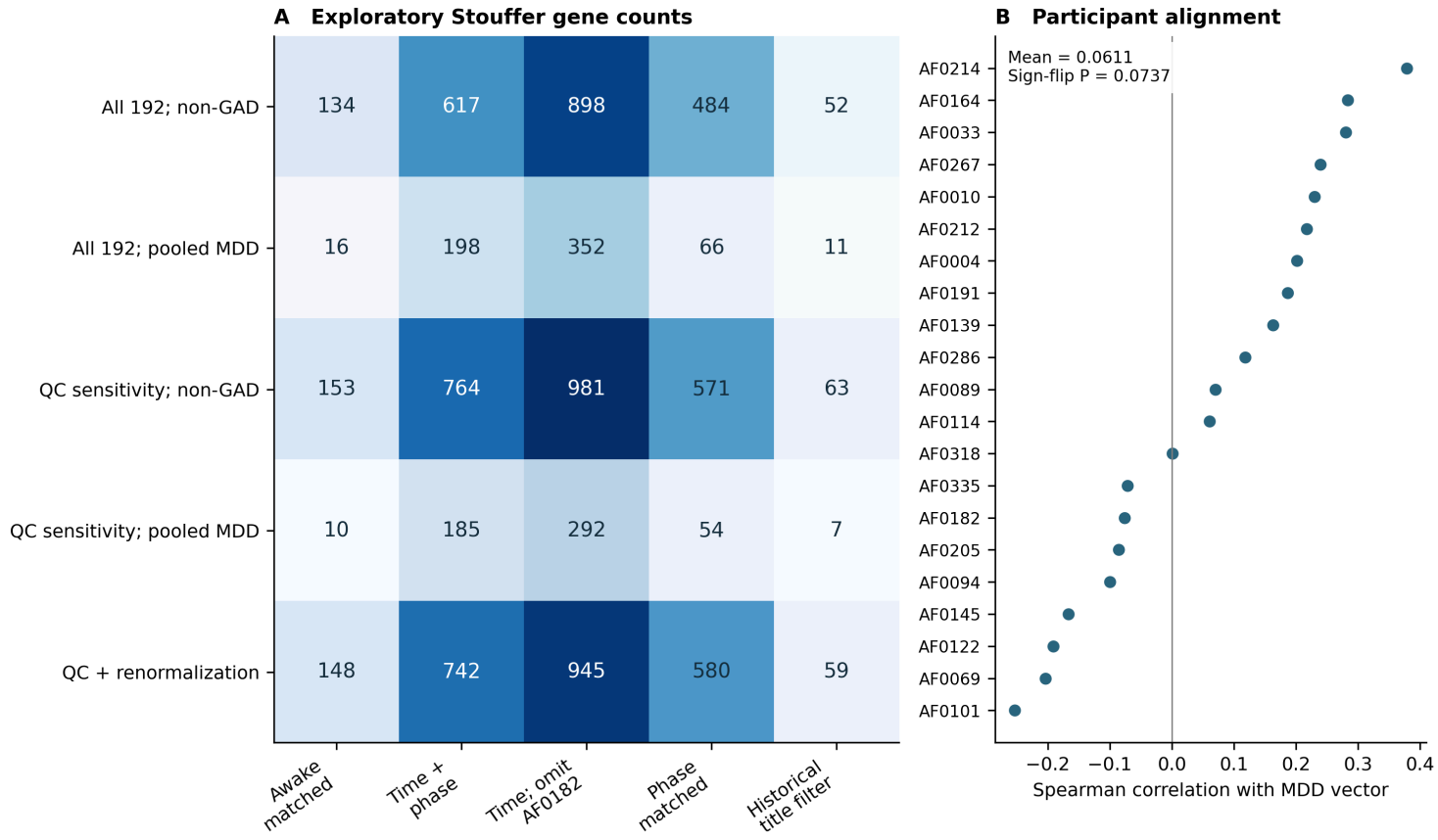


Figure 3

Sensitivity of combined associations and participant alignment. Panel A shows concordant Stouffer counts for five MDD and five sleep definitions (BH FDR < 0.05 over 16180 genes per combination). QC analyses exclude nine independently flagged arrays; the title-restriction diagnostic excludes valid sleep records. No partial-conjunction result was significant. Panel B shows participant-level Spearman correlations with the non-GAD MDD effect vector. The P value uses whole-participant sign flips; the bootstrap interval is reported in the text.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1SupplementaryMethods.docx
- Additionalfile8PairingQCandVerification.zip
- Additionalfile5SynthesisAllSamples.zip
- Additionalfile6SynthesisQCSubset.zip
- Additionalfile4SleepTimeResults.zip
- Additionalfile2CodeandSourceRecords.zip
- Additionalfile3MainModelResults.zip

- Additionalfile7SynthesisRenormalized.zip