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Comparative Evaluation of Stress-Induced Brain Connectivity Changes in Pre-Eclamptic Versus Normotensive Women: Harnessing AI for Advanced Neuroimaging Data Analytics

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KEYWORDS

Artificial Intelligence. Brain Connectivity. Pre-eclampsia.

ABSTRACT:

Background: Artificial intelligence (AI) offers new opportunities for analyzing high-dimensional neuroimaging data to uncover subtle stress-related brain connectivity changes. This study applied AI-driven methods to compare stress-induced brain connectivity in pre-eclamptic versus normotensive women.

Aim: To evaluate stress-induced brain connectivity changes in pre-eclamptic versus normotensive women using AI-based neuroimaging data analytics.

Methods: A prospective comparative study was conducted on 80 participants (40 pre-eclamptic, 40 normotensive) recruited at a tertiary care center. Stress-induction paradigms were performed during fMRI acquisition, supplemented with diffusion tensor imaging. Connectivity matrices were analyzed using convolutional neural networks, graph neural networks, support vector machines, and autoencoders. Graph-theoretic measures (efficiency, modularity, clustering, hub disruption) were calculated. Model performance was validated using cross-validation, with interpretability provided through SHAP and attention mechanisms.

Results: Pre-eclamptic women exhibited significantly greater dynamic functional connectivity variance (0.87 ± 0.19 vs. 0.73 ± 0.17; $p=0.001$), higher temporal switching rates (3.90 ± 1.10 vs. 3.20 ± 0.90; $p=0.003$), and reduced network modularity (0.41 ± 0.07 vs. 0.45 ± 0.06; $p=0.005$). CNNs and GNNs identified more altered edges and higher anomaly scores in pre-eclampsia. AI-based biomarkers showed strong predictive accuracy with cross-validated AUC (0.88 vs. 0.82; $p<0.001$) and F1-score (0.81 vs. 0.72; $p<0.001$). SHAP analysis highlighted limbic edges as key discriminators.

Conclusion: AI models reliably identified stress-related brain network alterations in pre-eclamptic women, outperforming traditional measures. These findings validate the potential of AI-derived biomarkers for precision neuroimaging and early risk stratification in maternal brain health.

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INTRODUCTION

The advent of artificial intelligence (AI) in neuroimaging has revolutionized the way neuroscientists and clinicians conceptualize, process, and analyze brain connectivity, particularly under conditions of stress that perturb normal neurological dynamics. Traditional approaches to studying brain function in disorders like pre-eclampsia and in normotensive pregnant women have relied heavily on structural and functional imaging modalities such as MRI, fMRI, EEG, and diffusion tensor imaging (DTI), where the analytical burden rested largely on human interpretation or conventional statistical modeling. These conventional frameworks, while valuable, are constrained by their inability to capture high-dimensional, non-linear, and dynamic brain connectivity changes that arise in stress-induced states. AI, particularly through machine learning (ML), deep learning (DL), and graph-theoretic algorithms, offers transformative potential by enabling advanced pattern recognition, unsupervised clustering of latent features, and predictive modeling that can generalize across heterogeneous populations. In the context of pre-eclampsia-a pregnancy-specific hypertensive disorder that has neurological implications such as headaches, seizures, and potential long-term cognitive impact-the deployment of AI allows researchers to move beyond descriptive clinical comparisons and instead interrogate the underlying brain networks with unprecedented precision. [1]

Unlike purely clinical models that hinge on symptomatology, blood pressure readings, or biochemical markers, AI-driven neuroimaging analytics empower investigators to probe the subtle reconfiguration of neural circuits, the altered synchrony among cortical and subcortical regions, and the dynamic shifts in connectivity that define stress-related brain function. Furthermore, AI models trained on multi-modal neuroimaging data can integrate signals across fMRI time-series, EEG oscillatory patterns, and DTI-derived structural connectivity matrices to construct holistic signatures of brain adaptation or maladaptation under stress. [2]

These computational approaches not only facilitate group-wise comparisons between pre-eclamptic and normotensive women but also enable cross-validation through predictive modeling, where stress-induced connectivity patterns can serve as biomarkers of vulnerability or resilience. Importantly, by emphasizing AI over clinical dependencies, the study positions itself within the broader paradigm of computational neuroscience and digital medicine, where patient-specific phenotyping is no longer contingent on overt clinical manifestations but rather on latent neural signatures revealed through algorithmic exploration.[3]

This AI-centric perspective aligns with the current trajectory of precision medicine, where high-dimensional imaging data are harnessed to derive individualized risk profiles, predictive trajectories, and intervention targets. Moreover, explainable AI (XAI) techniques-such as saliency maps, SHAP values, and attention-based neural networks-offer interpretability that bridges the gap between computational complexity and neuroscientific meaning, ensuring that derived insights are not only accurate but also biologically relevant. In sum, the comparative evaluation of stress-induced brain connectivity changes in pre-eclamptic versus normotensive women through AI-driven analytics reframes the research question away from a purely clinical inquiry and toward a data-centric exploration of how stress reshapes neural networks in pregnancy.[4]

Such work underscores the dual utility of AI: first, as a methodological scaffold for handling high-dimensional neuroimaging datasets with robustness and scalability; and second, as a discovery tool for unveiling mechanistic insights into stress-neural interactions that remain hidden to human observation. Ultimately, by integrating advanced computational models with real-world neuroimaging data, the study contributes to a deeper, algorithmically grounded understanding of maternal brain health in pregnancy, setting the stage for predictive, preventive, and personalized approaches to neurological care in obstetric populations.[5]

Aim

To evaluate stress-induced brain connectivity changes in pre-eclamptic versus normotensive women using AI-based neuroimaging data analytics.

Objectives

1. To apply AI-driven algorithms for the detection and quantification of stress-related brain connectivity patterns in pre-eclamptic and normotensive women.

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2. To compare and characterize alterations in brain network topology between the two groups using advanced computational models.
3. To validate AI-derived connectivity biomarkers as potential predictors of stress adaptation in pregnancy.

MATERIAL AND METHODOLOGY

Source of Data

The study utilized neuroimaging data obtained from women diagnosed with pre-eclampsia and normotensive pregnant women, recruited from a tertiary care center's obstetric and radiology departments.

Study Design

A prospective, observational, comparative study was conducted, focusing on advanced AI-driven analysis of stress-induced neuroimaging connectivity changes.

Study Location

The study was carried out in collaboration between the Department of Obstetrics & Gynecology and the Department of Radiodiagnosis and Neuroimaging, at a tertiary care teaching hospital equipped with MRI and computational AI laboratory facilities.

Study Duration

The study was conducted over a period of 24 months, including patient recruitment, imaging acquisition, AI model training, data analysis, and interpretation.

Sample Size

A total of 80 participants were included, consisting of 40 pre-eclamptic women and 40 age-matched normotensive pregnant women.

Inclusion Criteria

- Pregnant women aged 20–40 years.
- Gestational age between 28–36 weeks.
- Group 1: Women diagnosed with pre-eclampsia based on standard diagnostic criteria.
- Group 2: Normotensive pregnant women without medical complications.

Exclusion Criteria

- History of neurological or psychiatric disorders.
- Pre-existing chronic hypertension or diabetes mellitus.
- Contraindications to MRI (e.g., metallic implants, claustrophobia).
- Women on psychotropic or neuroactive medications.

Procedure and Methodology

Participants underwent standardized stress-induction protocols (validated psychological stress paradigms administered during fMRI acquisition). Functional MRI (fMRI) sequences were acquired at rest and under stress conditions. Additional imaging included diffusion tensor imaging (DTI) for structural connectivity assessment. Raw neuroimaging data were preprocessed using open-source platforms (SPM, FSL) and converted into time-series and connectivity matrices. AI models-specifically convolutional neural networks (CNNs), recurrent neural networks (RNNs), and graph neural networks (GNNs)-were trained to detect alterations in connectivity patterns. Feature extraction emphasized functional connectivity strength, network topology metrics (clustering coefficient, path length, modularity), and dynamic reconfiguration indices. Unsupervised learning algorithms (k-means, autoencoders) identified latent subgroups, while supervised models (random forest, support vector machines, deep neural networks) classified stress-induced connectivity states between pre-eclamptic and normotensive cohorts.

Sample Processing

Neuroimaging data were anonymized and stored in DICOM format, converted into NIfTI files for analysis. Preprocessing steps included motion correction, temporal filtering, spatial normalization, and artifact removal. Connectivity matrices were derived by correlating BOLD signals across defined brain regions (using automated anatomical labeling templates). DTI tractography provided complementary structural connectivity data.

Statistical Methods

Statistical analysis was conducted using both conventional and AI-driven methods. Group comparisons were made using independent t-tests or Mann–Whitney U tests for continuous variables and chi-square tests for categorical variables. For connectivity

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data, graph-theoretic measures were compared using multivariate analysis of variance (MANOVA). Machine learning model performance was evaluated using accuracy, precision, recall, F1-score, and area under the ROC curve (AUC). Cross-validation (10-fold) ensured model generalizability. Feature importance was assessed using SHAP and attention-based interpretability methods. Statistical significance was set at $p < 0.05$.

Data Collection

Demographic and clinical details (age, gestational age, blood pressure, parity) were recorded at baseline. Imaging datasets were collected under standardized protocols and stored in secure servers. Stress-induced brain connectivity data were extracted, processed, and analyzed using AI pipelines. All data were de-identified before computational analysis to maintain confidentiality.

OBSERVATION AND RESULTS

Table 1: AI-Centric Stress-Induced Connectivity (n=80)

Variable	Pre-eclamptic (n=40)	Normotensive (n=40)	Test of significance	95% CI	p-value
Dynamic FC variance (stress) (a.u.)	0.87 ± 0.19	0.73 ± 0.17	t (77.1)=3.47	0.06 to 0.22	0.001
Mean stress FC strength (Fisher-z)	0.22 ± 0.11	0.15 ± 0.09	t(75.1)=3.11	0.03 to 0.11	0.003
Temporal switching rate (states/min)	3.90 ± 1.10	3.20 ± 0.90	t(75.1)=3.11	0.25 to 1.15	0.003
CNN stress-activation score (0–1)	0.68 ± 0.13	0.59 ± 0.12	t(77.5)=3.22	0.03 to 0.15	0.002
Autoencoder reconstruction error	0.09 ± 0.04	0.07 ± 0.03	t(73.5)=3.05	0.01 to 0.04	0.003
AI cluster: Hyper-reactive network (yes)	19 (47.5%)	12 (30.0%)	$\chi^2(1)=2.67$	–3.5% to 38.5%	0.102
Significant edge alterations ≥50 (yes)	14 (35.0%)	8 (20.0%)	$\chi^2(1)=2.32$	–4.3% to 34.3%	0.128

Table 1 highlights the fundamental alterations in stress-related brain connectivity between pre-eclamptic and normotensive women as quantified through AI-based feature extraction. Pre-eclamptic participants demonstrated significantly higher dynamic functional connectivity (FC) variance (0.87 ± 0.19 vs. 0.73 ± 0.17; p=0.001) and mean stress FC strength (0.22 ± 0.11 vs. 0.15 ± 0.09; p=0.003), indicating more variable and robust neural coupling under stress. The temporal switching rate of connectivity states was also elevated (3.90 ± 1.10 vs. 3.20 ± 0.90; p=0.003), suggesting rapid reconfiguration of networks. Deep learning–derived measures, such as the CNN stress-activation score, were significantly higher in pre-eclamptic women (0.68 ± 0.13 vs. 0.59 ± 0.12; p=0.002), while autoencoder reconstruction error was greater (0.09 ± 0.04 vs. 0.07 ± 0.03; p=0.003), reflecting more challenging model fitting due to atypical patterns. Although categorical indicators such as hyper-reactive AI clusters (47.5% vs. 30%) and significant edge alterations ≥50 (35% vs. 20%) trended toward higher prevalence in pre-eclampsia, these did not reach statistical significance.

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Table 2: AI Detection & Quantification (n=80)

Variable	Pre-eclamptic (n=40)	Normotensive (n=40)	Test of significance	95% CI	p-value
CNN-detected altered edges (count)	58.20 ± 14.70	46.90 ± 12.40	t(75.8)=3.72	5.24 to 17.36	<0.001
GNN anomaly score (a.u.)	1.37 ± 0.42	1.09 ± 0.35	t(75.5)=3.24	0.11 to 0.45	0.002
SVM decision margin (abs)	0.71 ± 0.21	0.58 ± 0.18	t(76.2)=2.97	0.04 to 0.22	0.004
Attention-weighted stress index	1.82 ± 0.49	1.51 ± 0.44	t(77.1)=2.98	0.10 to 0.52	0.004
Latent subgroup (A) assigned	21 (52.5%)	13 (32.5%)	$\chi^2(1)$=3.41	–1.2% to 41.2%	0.065
Detection probability ≥0.80	24 (60.0%)	17 (42.5%)	$\chi^2(1)$=2.53	–4.1% to 39.1%	0.112

Table 2 presents the outputs of AI-driven detection and quantification algorithms applied to stress-related neuroimaging data. Pre-eclamptic women exhibited a significantly higher number of CNN-detected altered edges (58.20 ± 14.70 vs. 46.90 ± 12.40; p<0.001), pointing to extensive connectivity disruptions. Similarly, the graph neural network (GNN) anomaly score (1.37 ± 0.42 vs. 1.09 ± 0.35; p=0.002) and support vector machine (SVM) decision margin (0.71 ± 0.21 vs. 0.58 ± 0.18; p=0.004) were elevated, reinforcing the discriminative capacity of AI classifiers. The attention-weighted stress index, derived from explainable AI layers, was also significantly higher in pre-eclampsia (1.82 ± 0.49 vs. 1.51 ± 0.44; p=0.004), indicating greater AI-predicted stress reactivity. Although not statistically significant, higher proportions of pre-eclamptic women were allocated to a distinct latent subgroup A (52.5% vs. 32.5%) and reached detection probability ≥0.80 (60% vs. 42.5%).

Table 3: Network Topology via Graph Modeling (n=80)

Variable	Pre-eclamptic (n=40)	Normotensive (n=40)	Test of significance	95% CI	p-value
Global efficiency (Eglob)	0.29 ± 0.03	0.27 ± 0.03	t(77.3)=2.34	0.00 to 0.03	0.022
Characteristic path length (L)	2.41 ± 0.28	2.56 ± 0.26	t(77.6)=–2.48	–0.27 to –0.03	0.015
Modularity (Q)	0.41 ± 0.07	0.45 ± 0.06	t(77.3)=–2.86	–0.07 to –0.01	0.005
Clustering coefficient (C)	0.36 ± 0.05	0.33 ± 0.05	t(77.7)=2.30	0.00 to 0.05	0.024
Small-worldness (σ)	1.81 ± 0.24	1.72 ± 0.22	t(77.4)=1.75	–0.01 to 0.19	0.084
Hub disruption index (κ)	–0.06 ± 0.08	–0.02 ± 0.07	t(77.4)=–2.45	–0.08 to –0.01	0.017

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Connector-hub loss (yes)	11 (27.5%)	6 (15.0%)	$\chi^2(1)$=1.91	–5.2% to 30.2%	0.167

Table 3 focuses on graph-theoretic measures of brain network topology, analyzed through AI-enabled modeling. Pre-eclamptic participants demonstrated significantly higher global efficiency (0.29 ± 0.03 vs. 0.27 ± 0.03; p=0.022), suggesting improved parallel information transfer under stress, but paradoxically also exhibited a shorter characteristic path length (2.41 ± 0.28 vs. 2.56 ± 0.26; p=0.015), reflecting altered integration strategies. Interestingly, modularity was significantly lower in pre-eclamptic women (0.41 ± 0.07 vs. 0.45 ± 0.06; p=0.005), indicating less segregated networks. Meanwhile, the clustering coefficient was elevated (0.36 ± 0.05 vs. 0.33 ± 0.05; p=0.024), pointing to denser local clustering. Although small-worldness (1.81 vs. 1.72) showed a trend (p=0.084), the hub disruption index was significantly more negative (–0.06 ± 0.08 vs. –0.02 ± 0.07; p=0.017), signaling impaired hub stability. Loss of connector hubs was more frequent in pre-eclampsia (27.5% vs. 15%), though not statistically significant.

Table 4: Validation of AI-Derived Biomarkers (n=80)

Variable	**Pre-eclamptic (n=40)**	**Normotensive (n=40)**	**Test of significance**	**95% CI**	**p-value**
Cross-validated AUC (0–1)	0.88 ± 0.04	0.82 ± 0.05	t(76.8)=5.30	0.04 to 0.08	<0.001
F1-score (0–1)	0.81 ± 0.09	0.72 ± 0.10	t(77.1)=4.23	0.05 to 0.13	<0.001
Brier score (0–1, lower better)	0.14 ± 0.04	0.18 ± 0.04	t(77.6)=–3.85	–0.05 to –0.02	<0.001
Calibration slope	1.08 ± 0.21	0.93 ± 0.19	t(77.2)=3.35	0.06 to 0.24	0.001
Mean |SHAP| for limbic edges	0.03 ± 0.01	0.02 ± 0.01	t(76.9)=3.15	0.00 to 0.01	0.002
Biomarker-positive (thresholded)	23 (57.5%)	14 (35.0%)	$\chi^2(1)$=4.29	1.2% to 43.8%	0.038
Logit OR per SD (biomarker)*	1.62 ± 0.35	1.28 ± 0.31	t(76.9)=4.60	0.19 to 0.49	<0.001

Table 4 evaluates the robustness of AI-derived biomarkers as predictive tools for stress adaptation. The cross-validated AUC was significantly higher for pre-eclamptic women (0.88 ± 0.04 vs. 0.82 ± 0.05; p<0.001), showing superior classification performance. Similarly, F1-scores were higher (0.81 ± 0.09 vs. 0.72 ± 0.10; p<0.001), indicating balanced improvements in precision and recall. Pre-eclamptic models had significantly better calibration with lower Brier scores (0.14 ± 0.04 vs. 0.18 ± 0.04; p<0.001) and higher calibration slope values (1.08 ± 0.21 vs. 0.93 ± 0.19; p=0.001), reinforcing predictive reliability. Importantly, explainable AI analyses showed higher mean SHAP values for limbic edges (0.03 ± 0.01 vs. 0.02 ± 0.01; p=0.002), pinpointing stress-relevant connectivity biomarkers. A greater proportion of pre-eclamptic participants were classified as biomarker-positive (57.5% vs. 35%; p=0.038), and the logit odds ratio per SD change in biomarker scores was markedly elevated (1.62 ± 0.35 vs. 1.28 ± 0.31; p<0.001).

DISCUSSION

Table 1 - AI-centric stress-induced connectivity: It shows consistently higher dynamic FC variance, mean stress FC strength, and state-switching rates in the pre-

eclamptic group, alongside elevated CNN stress-activation scores and greater autoencoder reconstruction error. Methodologically, this pattern dovetails with core tenets of dynamic functional connectivity (dFC): under perturbation (here, stress), networks exhibit transient reconfigurations and greater dispersion of connectivity states. Xodo S *et al.*(2023)[6] reviewed how dFC captures rapid re-organizations that conventional static FC averages can obscure; higher variance and more frequent state transitions in pre-eclamptic cohort are a textbook signature of such reconfiguration dynamics.

The elevated CNN stress-activation score indicates the presence of discriminative micro-patterns within stress-epoch time-series or derived FC maps-precisely the sort of high-dimensional motifs that convolutional filters are designed to detect in medical images and spatiotemporal maps. This aligns with the broader literature demonstrating CNNs' superiority at extracting hierarchical representations from neuroimaging data. Jena MK *et al.*(2020)[7]

Importantly, greater autoencoder reconstruction error in pre-eclampsia echoes the logic of unsupervised anomaly detection: when a model trained on common/typical patterns is confronted with atypical inputs, reconstruction errors rise. Similar strategies have identified deviant brain patterns in other contexts using deep autoencoders, supporting interpretation that stress-epoch signals in pre-eclamptic brains deviate from normative manifolds. Hogan C *et al.*(2022)[8]

Although two categorical signals-"hyper-reactive AI cluster" and "≥50 edge alterations"-trend higher without crossing significance, their directions are consistent with the continuous metrics and with the expectation that stress accentuates transient hyperconnectivity/hypoconnectivity episodes in susceptible networks. This pattern is conceptually consonant with network neuroscience views that perturbed systems express *both* increased volatility and altered coordination across mesoscale communities. Wang Z *et al.*(2021)[9]

Table 2 - AI detection & quantification: The significant lift in CNN-detected altered edges, GNN anomaly scores, SVM margins, and attention-weighted stress indices demonstrates that multiple algorithmic families converge on the same conclusion: stress-epoch connectomes from pre-eclamptic participants contain more detectable, separable, and attention-worthy features. CNN counts of altered edges match the deep-learning literature's observation that convolutional pipelines reliably surface subtle, spatially structured deviations. Abad C *et al.*(2024)[10]

Even more telling is the GNN anomaly score: by natively operating on graphs, GNNs encode topology (nodes/edges) and attributes in a single architecture, which recent surveys highlight as especially powerful for connectome-level inference. Higher GNN scores in pre-eclampsia align with reports that GNNs improve sensitivity to graph-level irregularities and community-boundary distortions in multimodal connectivity datasets. Zhang X *et al.*(2022)[11]

The attention-weighted stress index underscores that *explainable* deep models (attention mechanisms) are not just separating groups but also attributing importance to stress-responsive features-exactly the direction modern neuro-AI is moving toward (saliency/attention as first-class outputs rather than post-hoc add-ons).

Table 3 - Network topology via graph modeling: Graph-theoretic profile-higher global efficiency with shorter path length yet lower modularity and more negative hub-disruption index-maps neatly to a "re-tuned integration" phenotype: under stress, pre-eclamptic connectomes appear to transiently trade segregation (lower Q) for integration (higher Eglob), while disrupting the typical centrality structure of hubs. Network neuroscience has long emphasized that brain graphs balance segregation and integration; perturbations that push systems toward hyper-integration can carry costs, including hub instability and brittle small-world structure. Non-significant upward trend in small-worldness with significant hub-disruption fits that narrative. Mahdy ZA *et al.*(2022)[12]

Methodologically, these findings reinforce why topology-aware AI (e.g., GNNs) adds value beyond voxelwise or edgewise statistics: topology metrics summarize mesoscale organization shifts that linear tests might dilute, and GNNs can incorporate them natively (node/edge embeddings + message passing). Table 3 differences therefore provide a principled target space for graph-aware models noted in contemporary GNN/connectomics literature.

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Table 4 - Validation of AI-derived biomarkers: The higher AUC and F1, lower Brier score, and better calibration slopes in the pre-eclamptic group show that the features AI pipeline extracts during stress are not only separable but predictively reliable. That reliability is essential for moving from descriptive analytics to candidate biomarkers. The elevated mean |SHAP| for limbic edges strengthens interpretability: XAI methods like SHAP convert model discriminability into neurobiologically meaningful attributions, which is exactly the bridge regulators and translational teams expect for clinical-grade tools. García-Montero C *et al.*(2023)[13]

CONCLUSION

The present study demonstrates that artificial intelligence–driven neuroimaging analytics can successfully differentiate stress-induced brain connectivity changes between pre-eclamptic and normotensive women. By leveraging advanced models such as convolutional neural networks, graph neural networks, autoencoders, and explainable AI frameworks, we identified significant alterations in dynamic functional connectivity, network topology, and algorithm-detected biomarkers. Pre-eclamptic participants exhibited heightened variance in connectivity, increased switching rates, and more pronounced deviations in network modularity and hub stability. AI-based classification further validated these patterns, yielding high discriminative performance with robust calibration and interpretable features. These findings highlight the capacity of AI not only to detect subtle brain network disruptions but also to provide interpretable biomarkers of stress adaptation in pregnancy. Overall, the study underscores the promise of AI as a methodological tool for advancing precision neuroimaging, reducing reliance on clinical endpoints, and paving the way toward predictive, personalized maternal brain health assessment.

LIMITATIONS

1. **Sample size constraints**: Although the study included 80 participants, a larger cohort would strengthen the generalizability of the AI models and allow subgroup analyses (e.g., severity of pre-eclampsia).
2. **Cross-sectional design**: The study assessed stress-induced connectivity at a single time-point; longitudinal data could clarify temporal trajectories and predictive value of identified biomarkers.
3. **Data heterogeneity**: Despite standardized protocols, variability in imaging quality and stress-induction paradigms may have influenced AI model outputs.
4. **Model generalizability**: While cross-validation reduced overfitting, external validation on independent datasets is required before clinical translation.
5. **Interpretability challenges**: Although SHAP and attention-based methods were used, AI interpretability remains an evolving field, and neural attributions must be cautiously linked to biological mechanisms.
6. **Minimal clinical integration**: The study prioritized AI and neuroimaging analytics; however, integrating biochemical, cognitive, and obstetric outcomes could provide a more holistic picture of stress-related brain alterations.

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