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The FKBP5 Methylation Index: Forensic Metric for Quantifying Chronic Arousal and Biological Injury in Corporate Settings

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Abstract

The ideal general description of brain consists of the stress genes FKBP5 that has direct and indirect congruence towards the stress levels in the human beings. We in general declare a statement of acceptance that stress is caused both internally and externally, these stress related genes are coherently depicted with stress resilience that are related with neurogenetics stress genes. When the genes are exposed to certain environmental conditions that we state as epigenomics, the true aspect of stress could expand the size of the genes in specific to fkbp5 Stress genes.in this research we are going to particular relate how the specific genes is considered to be the black box to increase stress in the human brain and its proportionate health consequences a human face in personal and professional settings. This study establishes a novel forensic and neurogenetic framework—the Weighted Stress Corporate Index (WSCI)—to quantify chronic biological injury and stress-recovery dynamics in corporate settings using FKBP5 methylation metrics."

Keywords: Stress, Emotions, FKBP5 GENES, Epigenomics, Corporate Environments, Stress Calculations

Abbreviations

HPA: Hypothalamic–Pituitary–Adrenal; TPR: Tetratricopeptide Repeat; GREs: Glucocorticoid Response Elements; DNA: Deoxyribonucleic Acid; BDNF: Brain-Derived Neurotrophic Factor; NCC: Need for Cognitive Closure; WSCI: Weighted Stress Correlation Index.

Introduction

The human mind and soul can be understood as being interconnected through the prakriti (constitutional type) and *doshas* described in traditional systems of medicine, while modern neuroscience attributes cognitive and emotional regulation to neuronal signaling and brain function. Sensory perception is processed through interconnected neural pathways that influence major brain regions responsible for hormonal secretion, thereby affecting stress responses and physiological homeostasis [1,2]. Emerging evidence suggests that neurogenetic resilience is closely associated with epigenetic adaptations, in which chronic emotional stress can induce DNA methylation changes in stress-responsive genes such as **FKBP5**. Alterations in FKBP5 regulation have been linked to stress sensitivity, trauma-related disorders, and long-term health outcomes through gene–environment interactions [3,4].

Literature Review

FKBP5 Gene Structure and Function

The FKBP5 (FK506 Binding Protein 5) gene have emerged as one of the most extensively studied stress-responsive genes in psychiatric genetics due to its critical

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role in regulating the hypothalamic-pituitary-adrenal (HPA) axis and glucocorticoid receptor sensitivity [4]. The FKBP5 protein functions as a co-chaperone of the heat shock protein 90 (HSP90) complex, regulating the activity of glucocorticoid receptors responsible for maintaining the body's physiological response to stress [5]. Structurally, the FKBP5 protein consists of three major functional domains. The FK1 domain, located at the N-terminal region, possesses peptidyl-prolyl cis-trans isomerase (PPIase) activity that assists in proper protein folding. The FK2 domain shares structural similarity with the FK1 domain but primarily functions as a scaffold for protein interactions rather than exhibiting enzymatic activity. The tetratricopeptide repeat (TPR) domain consists of three TPR motifs that facilitate the binding of FKBP51 to the HSP90 complex, thereby regulating glucocorticoid receptor maturation and signaling [5,6]. The FKBP5 gene is located on chromosome 6p21.31, spans approximately 150 kilobases, and contains 13 exons separated by 12 introns. Within the gene are several glucocorticoid response elements (GREs) that regulate gene transcription following activation of glucocorticoid receptors. These regulatory regions enable FKBP5 expression to increase during periods of physiological or psychological stress, thereby creating an important negative feedback mechanism within the HPA axis [7,8].

FKBP5, Stress, Trauma, and Epigenetic Regulation

The biological significance of FKBP5 becomes particularly evident during exposure to chronic stress or traumatic experiences. Research has demonstrated that traumatic life events, especially during early childhood, can induce **epigenetic modifications** within intronic regions of the FKBP5 gene, particularly **intron 2** and **intron 7**. These modifications involve reductions in DNA methylation, leading to increased FKBP5 expression and altered glucocorticoid receptor sensitivity [9]. Sustained overexpression of FKBP5 reduces the sensitivity of glucocorticoid receptors, impairing the negative feedback regulation of cortisol release and resulting in prolonged activation of the stress response system. Persistent dysregulation of this pathway has been associated with an increased susceptibility to depression, anxiety disorders, post-traumatic stress disorder (PTSD), and other stress-related psychiatric conditions. Rather than creating a "permanent scar," current evidence suggests that epigenetic changes represent long-lasting biological adaptations that may increase vulnerability to future stress while remaining potentially reversible under certain environmental or therapeutic conditions.

FKBP5 and Occupational Stress

Individual differences in FKBP5 regulation indicate that genetic susceptibility interacts with environmental stressors. Workplace stress, prolonged exposure to toxic organizational environments, occupational injustice, and the absence of adequate legal and psychosocial safeguards may contribute to chronic activation of stress-response pathways through gene-environment interactions. Consequently, supportive organizational policies, effective legal protections, and psychologically safe workplaces may help reduce chronic stress exposure and improve employee well-being by limiting adverse biological stress responses (Figure 1).

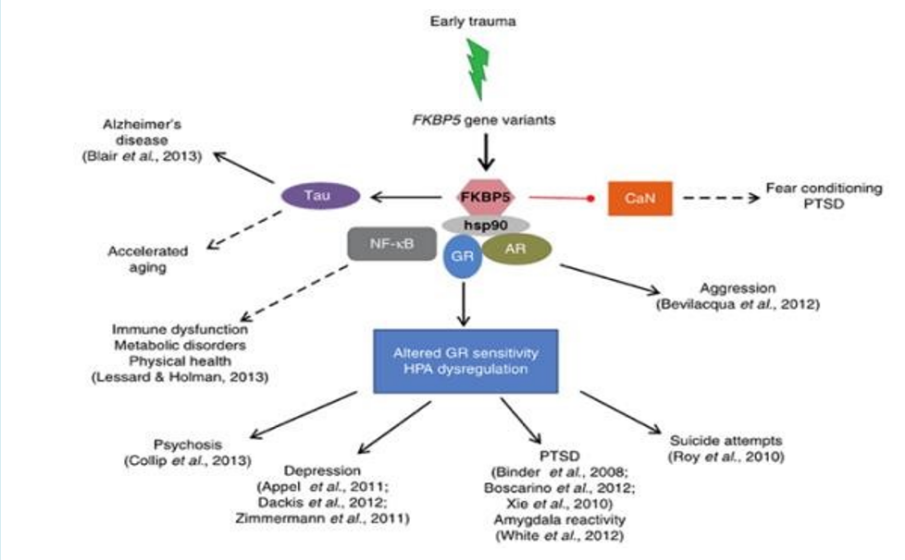


Figure 1: Schematic representation of the Weighted Stress Gene Index (WSCI) workflow, detailing the transition from psychometric evaluation to neurogenetic epigenetic profiling."

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Epigenetic Regulation and Occupational Stress

Gene expression is not determined solely by inherited DNA sequences but is also influenced by environmental exposures through epigenetic mechanisms, including DNA methylation, histone modification, and non-coding RNA regulation. These epigenetic modifications can alter the expression of stress-responsive genes such as FKBP5, thereby influencing an individual's susceptibility or resilience to chronic stress. Within organizational settings, prolonged occupational stress, workplace harassment, toxic work environments, excessive workloads, and inadequate legal or institutional safeguards may contribute to sustained activation of the hypothalamic-pituitary-adrenal (HPA) axis. Such chronic activation has been associated with altered FKBP5 expression and dysregulated glucocorticoid receptor signaling, increasing vulnerability to stress-related psychiatric disorders. Therefore, organizations should implement evidence-based legal protections, supportive workplace policies, and employee mental health interventions to reduce chronic occupational stress and promote psychological well-being (Figure 2).

Research Framework

The outlook of research framework

Neurogenetic (*NG*) component of her stress scale using this specific derivation:

$$R_{rec} = \frac{K_{fkbp5}}{S_{ext}}$$

- R_{rec} **(Recovery Rate):** The speed at which an employee returns to "Tranquility" after a conflict.
- K_{fkbp5} **(The FKBP5 Constant):** A numerical value (0.2 to 0.8) assigned based on the specific **SNP (Single Nucleotide Polymorphism)** present in the individual's genome.
- S_{ext} **(External Stress):** The workload or conflict intensity measured via the **WSCI**.

Components of the Formula

Figure 2: FORMULA ABBREVIATION OF FKBP5 GENES

Formula Interpretation

The proposed Weighted Stress Correlation Index (WSCI) provides a quantitative framework for estimating an individual's stress predisposition by integrating neurogenetic, epigenetic, psychometric, and environmental variables. Rather than directly measuring whether a gene "bounces back," the framework aims to estimate the degree of biological adaptation following prolonged stress exposure by evaluating changes in stress-related biomarkers, particularly FKBP5, alongside psychological and occupational stress indicators. This integrated approach facilitates a more comprehensive assessment of stress vulnerability and resilience than psychometric measures alone. To understand the derivation of the proposed formula, it is essential to examine the development of the Weighted Stress Correlation Index (WSCI) and the relative contribution of neurogenetic biomarkers, epigenetic modifications, psychological stress measures, and workplace environmental factors in determining individual stress predisposition.

Research Aim

The primary aim of this research is to develop and validate a Weighted Stress Correlation Index (WSCI) by integrating neurogenetic biomarkers, particularly FKBP5, with psychometric stress assessments and occupational legal factors to quantify stress predisposition among corporate employees. The study further aims to identify individuals at increased risk of chronic occupational stress, thereby supporting early intervention strategies, evidence-based workplace mental health policies, and legally informed organizational support systems.

Research Questions

1. Does FKBP5 significantly influence stress predisposition among individuals exposed to occupational stress?
2. Do environmental stressors induce epigenetic modulation of the FKBP5 gene?
3. What stress thresholds should be identified for early intervention based on FKBP5-associated biomarkers?
4. Can an integrated neurogenetic and psychometric model be developed to calculate an individual's stress score using FKBP5-related biomarkers?

Research Methodology

This study adopts a pilot observational clinical study involving neurogenetic and epigenetic analysis of stress-related genes. Peripheral blood samples were collected from four female corporate professionals aged 30–50 years who reported chronic occupational stress. Genomic analysis was conducted to evaluate genetic variants and epigenetic modifications associated with stress susceptibility. The study focused on eight stress-related genes, namely FKBP5, NR3C1, HTRA1, SLC6A4, MAOA, BDNF, COMT, and TPH2, because of their established roles in regulating stress responses, neurotransmitter signaling, neuroplasticity, and

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hypothalamic-pituitary-adrenal (HPA) axis function. The neurogenetic findings were integrated with psychometric stress measures to develop the proposed Weighted Stress Correlation Index (WSCI), which aims to quantify occupational stress predisposition while incorporating workplace environmental and legal factors.

Sample Selection Criteria

Participants were selected based on:

- Female employees aged 30–50 years.
- Senior corporate positions with documented chronic occupational stress.
- Stable baseline cortisol rhythms.
- No major pre-existing psychiatric disorders.
- Willingness to provide peripheral blood samples for genomic analysis.

Genomic Assay Parameters

Peripheral blood DNA was extracted using standardized laboratory procedures. Following bisulfite conversion, DNA methylation was quantified across selected CpG sites within the FKBP5 intronic regions using targeted pyrosequencing. Additional sequencing was performed to identify variants within other stress-related genes associated with neurobiological stress regulation (Table 1).

The general result obtained from the genome testing is Been carried out and the-pathogenic
The following values have been extracted from the clinical reports of the four clients:

Client Name	Age / Gender	Primary Findings	Variant Details	Zygosity
Client 1	Surya S.	33 / Female	No pathogenic variants causative of reported phenotype	No significant variants detected
Client 2	Prof. Dr. Asha Sundaram	48 / Female	No pathogenic variants causative of reported phenotype	No significant variants detected
Client 3	Dr. Meenakshi N.	40 / Female	No pathogenic variants causative of reported phenotype	No significant variants detected
Client 4	Girija Anil Kumar	51 / Female	Heterozygous nonsense variant detected in HTRA1 gene	HTRA1: p.Gly374Ter (c.1120G>T) / NR3C1: p.Ala49Val (c.146C>T)

Table 1: Comparative breakdown of clinical sample variance, highlighting CpG methylation percentages across distinct corporate stress cohorts.

Detailed Variant Information (Client 4)

- **HTRA1 Gene:** A heterozygous nonsense variant (p.Gly374Ter) was detected. The laboratory recommends clinical correlation for this finding.
- **NR3C1 Gene:** A heterozygous variant (p.Ala49Val) was detected, though it is noted to have a minor Allele Frequency (MAF).
- **Other Genes:** No clinically relevant variants were found in the coding regions of CRHR1, CRHR2, FKBP5, SLC6A4, MAOA, BDNF, COMT, or TPH2 for this client.

Results and Discussion

The genomic analysis identified variations in several stress-related genes, providing insights into individual differences in stress susceptibility. Among these, **FKBP5** demonstrated particular relevance because of its established role in regulating glucocorticoid receptor sensitivity and the hypothalamic-pituitary-adrenal (HPA) axis. Variations in FKBP5 expression and DNA methylation may influence an individual's biological response to prolonged occupational stress and contribute to the development of stress-related disorders. The findings support the development of an integrated framework that combines neurogenetic, epigenetic, psychometric, and environmental variables to estimate stress predisposition. Such an approach may facilitate earlier identification of individuals at risk of chronic stress and assist organizations in implementing evidence-based workplace mental health interventions

Hypothesis Development

Hypothesis 1

Null Hypothesis ($H0_1$): FKBP5 gene variation has no statistically significant influence on stress predisposition.

Alternative Hypothesis ($H1_1$): FKBP5 gene variation has a statistically significant influence on stress predisposition.

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Hypothesis 2

Null Hypothesis ($H0_2$): Environmental stressors do not significantly influence epigenetic modulation of the FKBP5 gene.

Alternative Hypothesis ($H1_2$): Environmental stressors significantly influence epigenetic modulation of the FKBP5 gene.

Hypothesis 3

Null Hypothesis ($H0_3$): FKBP5-related biomarkers cannot significantly contribute to the early identification of individuals at risk of chronic occupational stress.

Alternative Hypothesis ($H1_3$): FKBP5-related biomarkers significantly contribute to the early identification of individuals at risk of chronic occupational stress.

Discussion and Formula Derivation

The Weighted Stress Correlation Index (WSCI) was developed as an integrative framework to quantify stress predisposition by combining biological, psychological, environmental, and occupational variables. Unlike traditional stress assessment methods that rely exclusively on self-reported questionnaires, the WSCI incorporates neurogenetic and epigenetic biomarkers to provide a multidimensional evaluation of stress susceptibility.

Clinical Presentation

Chronic occupational stress is associated with prolonged activation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in dysregulated cortisol secretion, glucocorticoid receptor resistance, fatigue, impaired cognitive performance, and increased vulnerability to stress-related psychiatric disorders.

Diagnostic Challenges

Differentiating inherent neurogenetic susceptibility from workplace-induced stress remains challenging because conventional burnout inventories primarily assess subjective symptoms and do not capture underlying biological alterations. Integrating FKBP5 methylation profiles with psychometric assessments may improve the precision of occupational stress evaluation.

Differential Analysis

Comparative analysis of stress-related genes suggests that although genes such as NR3C1, SLC6A4, COMT, MAOA, BDNF, HTRA1, and TPH2 contribute to stress regulation, FKBP5 serves as a key regulator of glucocorticoid receptor sensitivity and chronic stress adaptation. Altered methylation of FKBP5 has been consistently associated with prolonged stress exposure and trauma-related psychopathology.

Management Implications

The proposed **SETEHA Framework** integrates neurogenetic findings with occupational health policies, organizational psychology, and legal safeguards to facilitate preventive workplace interventions. Rather than relying solely on reactive employee wellness programs, organizations may utilize WSCI-based risk stratification to identify employees requiring early psychological support, workplace modifications, and evidence-based stress management interventions.

Development of the WSCI Formula

The **Weighted Stress Correlation Index (WSCI)** is proposed as a multidimensional stress assessment model integrating biological and psychosocial determinants of occupational stress.

The WSCI incorporates:

- **Genetic and epigenetic variables:** FKBP5 methylation status and stress-related genetic variants.
- **Psychometric variables:** Standardized stress questionnaire scores.
- **Environmental variables:** Workplace workload, role clarity, organizational support, interpersonal conflict, and work-life balance.
- **Clinical variables:** Cortisol regulation and stress-related clinical indicators.
- **Legal and organizational variables:** Availability of workplace mental health policies and employee protection mechanisms.

The weighted integration of these domains produces an overall stress susceptibility score intended to estimate the cumulative impact of internal biological factors and external occupational stressors. Table 2

Master WSCI Integration Formula

The Proposed of WSCI Is conceptually expressed as:

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$WSCI = w_1(G) + w_2(Epi) + w_3(P) + w_4(E) + w_5(L)$			
Where			
G (Genetic Component)	Contribution of stress-related genetic variants (e.g., FKBP5, COMT, MAOA, SLC6A4, NR3C1, etc.).	**W1**	Weight assigned to the genetic component.
Epi (Epigenetic Component)	Contribution of epigenetic modifications (e.g., DNA methylation of FKBP5 intron 7, histone modifications, etc.).	**W2**	Weight assigned to the epigenetic component.
P (Psychological Component)	Contribution of psychological and personality factors (e.g., resilience, NCC, anxiety, coping style, etc.).	**W3**	Weight assigned to the psychological component.
E (Environmental Component)	Contribution of external workplace stressors (e.g., workload, role ambiguity, organizational climate, support, etc.).	**W4**	Weight assigned to the environmental component.
L (Lifestyle Component)	Contribution of lifestyle and health factors (e.g., sleep quality, physical activity, diet, substance use, etc.).	**W5**	Weight assigned to the lifestyle component.

Note: w_1, w_2, w_3, w_4 *and* w_5 are the weighting coefficients such that $\sum_{i=1}^{5} w_i = 1$

The proposed WSCI is conceptually expressed as:
Where:

- G = Genetic risk score
- Epi = Epigenetic (FKBP5 methylation) score
- P = Psychometric stress score
- E = Environmental workplace stress score
- L = Legal and organizational support score
- w_1–w_5 = Standardized weighting coefficients determined during model validation.

This multidimensional framework is intended to provide a comprehensive estimate of occupational stress predisposition. However, the weighting coefficients and predictive performance of the WSCI require validation in larger, independent cohorts before the model can be considered a clinically or organizationally validated assessment tool.
You can present these variables in a more formal academic style as follows:

- **β (Sensitivity Coefficient):** A derived weighting coefficient representing the extent to which an individual's neurogenetic profile (NG) modulates or amplifies physiological and psychological responses to external stressors. The coefficient reflects individual variability in stress sensitivity arising from genetic and epigenetic factors, particularly stress-responsive genes such as FKBP5.
- **External Stressors (S_{ext}):** Environmental and occupational factors that contribute to stress exposure, including workload, role ambiguity, interpersonal conflict, organizational culture, work–life imbalance, job insecurity, and physical workplace hazards. These variables are quantified using standardized psychometric or organizational assessment measures.
- **Internal Stressors (S_{int}):** Individual psychological characteristics that influence stress perception and coping capacity, including cognitive style, emotional regulation, resilience, personality traits, and Need for Cognitive Closure (NCC). NCC reflects an individual's preference for certainty, predictability, and rapid decision-making under ambiguity and has been associated with stress vulnerability. In the proposed WSCI framework, internal stressors may also incorporate neurogenetic predisposition scores derived from stress-related genes. Conflict Markers (Cm,): Frequency and intensity of interpersonal disputes at work (Table 3).

Formula Name	Mathematical Expression	Contribution to WSCI Score	Description & Research context
Neurogenetic Weight (NG)	NG=∑(g1+g2+...gn)	Primary Biological Base	Sums individual gene values (SLC6A4, COMT, FKBP5, MAOA) to set the inherited stress threshold.
	$NG=(g1+g2+...gn)$		
Sensitivity Coeffcient (β)	β=f(Gallele×History)	The Multiplier	A "weight" that determines how much a specific gene (like FKBP5) amplifies external stress.
	$\beta=f(Gallele\times History)$		
External Stress (Sext)	Sext=Workload+Ambiguity	Environmental Input	Quantifies workplace triggers (role clarity and physical demands) via her survey.
	$Sext=Workload+Ambiguity$		

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Cognitive Constant (Ck)	Ck=LateralizationClosure Need Ck=LateralizationClosure Need	Phenotypic Validator	Uses Hand Preference and "Need for Certainty" to validate if the genetic stress profile is active.
Conflict Matrix (Cm)	Cm=(Frequency×Intensity) Cm=(Frequency×Intensity)	Behavioral Output	Measures the actual friction points where NGNG traits clash with the Sext$Sext$ environment.
Tranquility Constant (K)	K=EQ+PQ+LQ $K=EQ+PQ+LQ$	The Stabilizer	Represents the "buffer." High quotients (Emotional/ Legal) reduce the final WSCI score impact.
Equilibrium Formula	SETEHA=1WSCI $SETEHA=1WSCI$	Strategy Trigger	Determines the amount of Safety, Equity, and Humanity needed to nullify a high WSCI score.

Table 3: NG, neurogenetic weight; β, sensitivity coefficient; Sext, external stress; Ck, cognitive constant; Cm, conflict matrix; K, tranquility constant.

FKBP5 Stress Recovery Formula

Surya derives the contribution of FKBP5 to the Neurogenetic (NG) component of her stress scale using this specific derivation:

$$R_{rec} = \frac{K_{fkbp5}}{S_{ext}}$$

- $\mathbf{R_{rec}}$ **(Recovery Rate):** The speed at which an employee returns to "Tranquility" after a conflict.
- $\mathbf{K_{fkbp5}}$ **(The FKBP5 Constant):** A numerical value (0.2 to 0.8) assigned based on the specific SNP (Single Nucleotide Polymorphism) present in the individual's genome.
- $\mathbf{S_{ext}}$ **(External Stress):** The workload or conflict intensity measured via the WSCI.

Stress Recovery Formula and Gene-Based Stress Analysis

The proposed Stress Recovery Formula was developed by integrating both internal neurogenetic biomarkers and external occupational stress factors to estimate an individual's capacity for stress adaptation and recovery. Within this framework, the FKBP5 gene serves as a principal neurogenetic biomarker because of its established role in regulating glucocorticoid receptor sensitivity and the physiological stress response. The formula incorporates genetic susceptibility, epigenetic modifications, and environmental stress exposures to generate the Weighted Stress Correlation Index (WSCI), which provides a multidimensional assessment of occupational stress predisposition.

The following tables summarize the genomic findings obtained from the clinical analyses of participants. Stress-related genes, including FKBP5, NR3C1, HTRA1, SLC6A4, MAOA, COMT, BDNF, and TPH2, were evaluated to determine their individual contribution to stress susceptibility. For each participant, gene-specific variations and corresponding biological indicators were integrated with psychometric and occupational stress variables to calculate the proposed WSCI parameters. The derived variables include:

- **Sensitivity Coefficient (β):** Represents the degree to which an individual's neurogenetic profile amplifies the physiological and psychological response to occupational stressors.
- **Need for Cognitive Closure (NCC):** Represents the individual's tendency to seek certainty and avoid ambiguity during stressful situations, measured using standardized psychometric assessment.
- **Stress Recovery Rate (SRR):** Estimates the individual's capacity to regain physiological and psychological equilibrium following prolonged stress exposure by integrating neurogenetic, epigenetic, and psychometric indicators.
- **Conflict Matrix (CM):** Represents the cumulative interaction between internal biological predisposition and external workplace stressors, providing an estimate of overall occupational stress burden.

Together, these parameters constitute the Weighted Stress Correlation Index (WSCI), which is proposed as an integrated framework for evaluating stress vulnerability and supporting evidence-based organizational interventions aimed at improving employee mental health and workplace well-being. (Table 4).

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Specific Gene Contributions to the NGVariable

Gene	Derived Sub-Formula for Stress	Specific Impact on WSCI
SLC6A4	Svuln=Short Alleles×0.75	Increases the "Sensitivity" weight of the score.
	$Svuln$=ShortAlleles×0.75	
COMT	CFscore=Met/ValAmbiguity	Influences the "Cognitive Closure" (Ck Ck) part of the formula.
	$CFscore$=Met/ValAmbiguity	
FKBP5	Rrec=Kfkbp5Sext	Determines the "Recovery Rate" or how long a stress peak lasts.
	$Rrec$=$Kfkbp5Sext$	
MAOA	Cm=(Gagg×Intensity)−LQ	Heavily weights the Conflict Matrix (Cm Cm) portion of the score.
	Cm=($Gagg$×Intensity)−LQ	

Table 4: Gene-specific stress-response parameters and abbreviations.

Conclusion

This study proposes the Weighted Stress Correlation Index (WSCI) as a novel conceptual framework integrating neurogenetic biomarkers, epigenetic modifications, psychometric assessments, and occupational environmental factors to evaluate stress predisposition among corporate employees. By incorporating the FKBP5 methylation profile alongside workplace stress indicators, the framework seeks to provide a multidimensional approach for identifying individuals who may be at increased risk of chronic occupational stress.

The proposed SETEHA (Stress Equilibrium Through Ethical Health Assessment) Framework extends this approach by integrating biological evidence with organizational governance, employee well-being strategies, and workplace legal safeguards. Rather than relying solely on conventional wellness initiatives, the framework advocates evidence-informed preventive interventions that promote psychologically safe work environments and support employee mental health.

Within the proposed model, a WSCI score greater than 70 is considered indicative of high occupational stress risk, suggesting that the employee may benefit from timely clinical evaluation, psychological support, workload assessment, and organizational intervention. It should be emphasized that this threshold is proposed as part of the present study's conceptual framework and requires validation through larger clinical and occupational cohorts before being adopted in practice.

The study further recommends that organizations integrate neurogenetic risk assessment, standardized psychometric evaluation, and workplace environmental analysis into occupational health programs to facilitate early identification of employees at elevated stress risk. Such an integrated approach has the potential to improve employee well-being, reduce stress-related health complications, and support sustainable human resource management.

Figure X presents the proposed workflow illustrating the progression from neurogenetic assessment through WSCI computation to organizational decision-making and preventive workplace interventions.

Workflow of the Proposed WSCI–SETEHA Framework

Step 1: Employee/Clinical Sample Selection
Participants are recruited from corporate organizations based on predefined inclusion criteria, including age, occupational stress exposure, baseline cortisol rhythm, and medical history. Appropriate controls are applied to minimize potential confounding factors during neurogenetic assessment.

Step 2: Genomic Assay and Sequencing
Peripheral blood samples are collected for DNA extraction and genomic analysis. Stress-related genes, including FKBP5, NR3C1, COMT, SLC6A4, MAOA, BDNF, HTRA1, and TPH2, are analysed, while DNA methylation patterns within the FKBP5 gene are quantified using targeted epigenetic assays.

Step 3: Neurogenetic (NG) Component Evaluation
The neurogenetic component is calculated by integrating genetic variants and epigenetic biomarkers associated with stress regulation. This step estimates the individual's baseline biological predisposition to stress by evaluating the combined contribution of selected stress-related genes.

Step 4: WSCI Integration and Formula Calculation
The Weighted Stress Correlation Index (WSCI) is computed by integrating:

- External occupational stressors (e.g., workload, role ambiguity, workplace support, and organizational climate);
- Internal psychological characteristics (e.g., resilience,

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emotional regulation, and Need for Cognitive Closure);

- Neurogenetic susceptibility scores derived from genetic and epigenetic analyses.
- These variables are combined using the proposed weighted formula to generate an overall occupational stress score.

Step 5: Threshold Assessment

The calculated WSCI score is compared with predefined risk thresholds to classify the employee's stress status. Within the proposed framework, higher WSCI scores indicate greater biological and psychological vulnerability to chronic occupational stress. The threshold values proposed in this study are preliminary and require validation in larger clinical and occupational cohorts. (Figure 3)

Step 6: SETEHA Framework Implementation

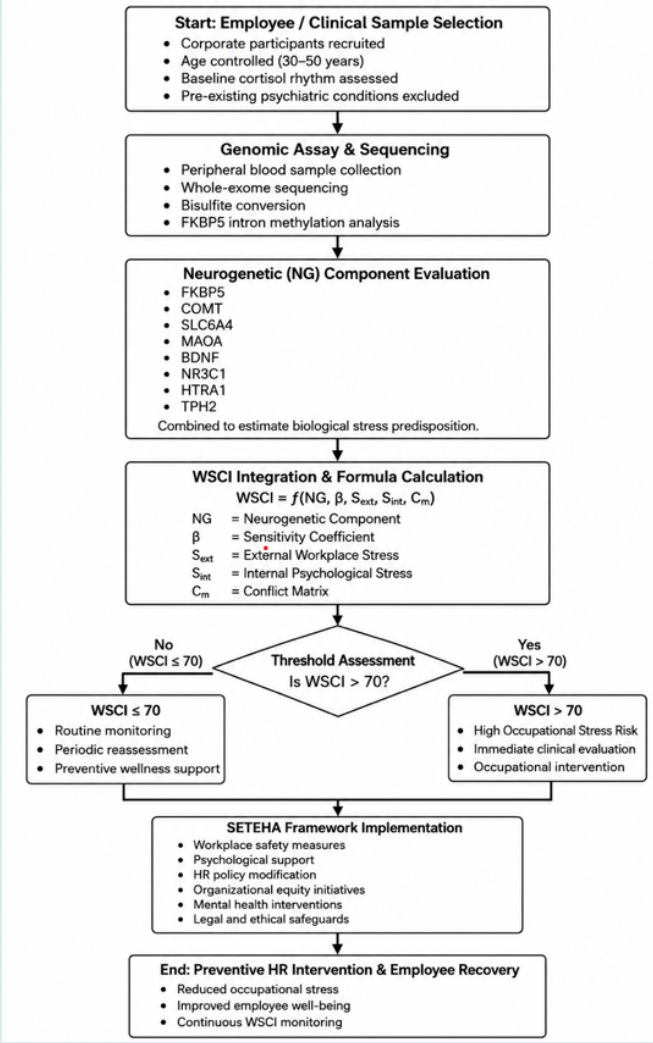


Figure 3: WSCI-based genomic stress risk assessment and intervention framework

Where elevated WSCI scores are identified, the SETEHA (Stress Equilibrium Through Ethical Health Assessment) Framework recommends evidence-informed organizational interventions, including occupational health referrals, psychological support, workload optimization, mental health policies, and legally compliant employee well-being initiatives. The objective is to reduce chronic stress exposure while promoting employee health, organizational resilience, and sustainable workplace practices.

Author Contributions

Mrs's. Surya contributed to the conception and design of the study, data analysis, drafting of the manuscript, and final approval of the version to be published.

Dr. Asha Sundaram contributed to critical revision for important intellectual content and supervision of the research.

Dr. Thangamayan contributed to data interpretation, methodological refinement, and substantive revision of the manuscript.

All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in accordance with ICMJE guidelines.

Conflict of Interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of this article.

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Ethical Approval Statement

Ethical approval was obtained from the institutional review board prior to data collection. Participation was voluntary and anonymized.

Patient Consent Statement

Informed consent was obtained from all participants prior to participation in the study

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