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ORIGINAL ARTICLE

Investigating the Relationship Between Gut Microbiota and Stress Resilience in Adolescents: An Observational Approach

[1]Archana Amit Shah, [2]Gautam Saha

[1]Associate Professor, Department of Microbiology, Major SD Singh Medical College and Hospital, Farrukhabad, UP, India;
[2]Associate Professor, Department of Psychiatry, Major SD Singh Medical College and Hospital, Farrukhabad, UP, India

ABSTRACT:

Aim: This study aimed to investigate the relationship between gut microbiota composition and stress resilience in adolescents, focusing on microbial diversity, community composition, and specific taxa associated with psychological resilience. **Material and Methods:** An observational study was conducted with 100 adolescents aged 12–18 years. Stress resilience was assessed using validated scales (PSS and CD-RISC), while stool samples were collected for gut microbiota analysis. Microbial DNA was extracted, and the V3–V4 region of the 16S rRNA gene was sequenced using Illumina MiSeq. Alpha and beta diversity metrics were calculated, and Random Forest classifiers were employed to identify microbial taxa predictive of resilience levels. Statistical associations were assessed using ANOVA and Spearman's correlation. **Results:** High-resilience adolescents exhibited significantly greater microbial diversity (Shannon Index: 3.5 ± 0.8) and distinct microbial community compositions compared to lower-resilience groups ($p < 0.05$). Taxa such as *Bacteroides*, *Firmicutes*, and *Akkermansia* were more abundant in high-resilience participants. Correlation analysis revealed a positive association between alpha diversity metrics and resilience scores ($r = 0.42$, $p = 0.003$). The Random Forest model achieved high predictive performance (accuracy: 82%, AUC: 0.89), identifying key taxa associated with resilience. **Conclusion:** This study demonstrates a significant relationship between gut microbiota diversity and stress resilience in adolescents. Findings highlight the gut-brain axis's role in psychological resilience and suggest that targeting gut health through dietary or probiotic interventions could enhance adolescent mental well-being.

Keywords: Gut microbiota, stress resilience, adolescents, microbial diversity, gut-brain axis.

Corresponding author: Gautam Saha, Associate Professor, Department of Psychiatry, Major SD Singh Medical College and Hospital, Farrukhabad, UP, India

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INTRODUCTION

Stress resilience, the ability to adapt and thrive despite exposure to stressors, is a crucial factor influencing mental and physical health, particularly during adolescence. Adolescence is a developmental period marked by significant physiological, psychological, and social changes, making it a critical window for studying factors that influence stress resilience. Increasing evidence suggests that the gut microbiota, the complex community of microorganisms residing in the gastrointestinal tract, may play a pivotal role in modulating stress responses and contributing to resilience.[1]The gut microbiota is intricately linked to the brain through the gut-brain axis, a bidirectional communication network that involves neural, endocrine, and immune pathways. This axis allows the gut microbiota to influence brain function and behavior through mechanisms such as the production of neurotransmitters, modulation of the immune system, and regulation of the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis, a key component of the body's stress response system, can be directly impacted by microbial metabolites such as short-chain fatty acids (SCFAs) and tryptophan metabolites. These interactions suggest a potential role for gut microbiota in shaping individual differences in stress resilience.[2] Adolescents are uniquely positioned for research into gut microbiota and stress resilience due to the dynamic nature of their microbiota and stress regulation systems. During adolescence, the gut microbiota undergoes significant changes influenced by diet, lifestyle, and hormonal shifts. Simultaneously, the stress response system matures, with the HPA axis experiencing heightened reactivity during this period. These concurrent developments create a sensitive window during which the gut microbiota may exert profound effects on stress resilience.The relationship between gut microbiota and stress resilience is influenced by various factors, including diet, physical activity, and sleep. Diet is a major determinant of microbiota composition, with fiber-rich and nutrient-dense foods promoting microbial diversity and resilience. Physical activity has been shown to enhance microbiota richness and diversity, potentially contributing to better stress management. Sleep, while less directly studied in relation to microbiota, is also an important factor, as disrupted sleep patterns can alter microbial composition and exacerbate stress responses.[3] Despite the growing interest in the gut-brain axis, research specifically focusing on adolescents and their stress resilience is limited. Most existing studies have examined adults or animal models, leaving a gap in understanding the unique characteristics and needs of adolescents. Investigating the gut microbiota-stress resilience relationship in this age group could provide valuable insights into early interventions and strategies to promote mental health and well-being. For example, identifying specific microbial signatures associated with stress resilience could lead to personalized dietary or probiotic interventions aimed at enhancing mental health outcomes.[4,5] Stress resilience is assessed using validated psychological tools, while microbial analysis is performed using advanced sequencing techniques. This approach allows for a detailed characterization of the gut microbiota and its potential role in supporting mental resilience during adolescence.[6] Adolescence represents a critical period for understanding the interplay between gut microbiota and stress resilience. By investigating this relationship, the current study aims to provide a foundation for future research and intervention strategies that capitalize on the gut-brain connection to support adolescent mental health. The insights gained could have far-reaching implications for promoting resilience and well-being, not only during adolescence but across the lifespan.

MATERIAL AND METHODS

This study employed an observational design to explore the relationship between gut microbiota composition and stress resilience in adolescents. A total of 100 participants were recruited through a combination of school-based invitations, community outreach, and social media advertisements. The study included 100 adolescents aged 12–18 years. Inclusion criteria were: (1) self-reported good general health, (2) no chronic gastrointestinal or psychiatric conditions, and (3) no use of antibiotics or probiotics within the last three months. Participants with significant comorbidities or who failed to complete study procedures were excluded.

Data Collection

1. **Demographic and Lifestyle Data**: Participants completed a detailed questionnaire to collect information on age, sex, dietary habits, physical activity, and sleep patterns.
2. **Stress Resilience Assessment**: Stress resilience was measured using the validated **Perceived Stress Scale (PSS)** and **Connor-Davidson Resilience Scale (CD-RISC)**. Both tools were administered during an in-person visit.
3. **Biological Sample Collection**: Stool samples were collected from participants in sterile containers and stored at −80°C until analysis. Samples were collected within 48 hours of the stress resilience assessment to ensure temporal alignment between psychological and microbiota data.

Gut Microbiota Analysis

DNA was extracted from stool samples using the **Qiagen PowerSoil Pro Kit** following the manufacturer's protocol. The V3–V4 region of the bacterial 16S rRNA gene was amplified and sequenced using an **Illumina MiSeq platform**. Sequencing data were processed with the **QIIME2 pipeline**, including quality filtering, demultiplexing, and taxonomic classification using the SILVA database.

Statistical Analysis

Alpha diversity metrics, including the Shannon index and observed species, were used to assess within-sample microbial diversity, while beta diversity, reflecting inter-sample variability, was analyzed using principal coordinates analysis (PCoA) based on Bray-Curtis distances. To explore associations between microbiota composition and stress resilience scores, Spearman's correlation was employed, with significant relationships identified using a false discovery rate (FDR)-adjusted p-value threshold of < 0.05. Additionally, Random Forest classifiers were utilized to identify microbial taxa predictive of high or low stress resilience, with model performance rigorously evaluated through cross-validation.

RESULTS

Table 1: Demographic and Lifestyle Characteristics of Participants

The participants' average age was 15.2 years, with a balanced sex distribution (48% male and 52% female). Body Mass Index (BMI) was comparable across groups with no statistically significant differences ($p = 0.075$). Physical activity levels, measured in hours per week, showed a significant association with stress resilience ($p = 0.045$), suggesting that higher physical activity may be linked to greater resilience. Diet quality scores also differed significantly ($p = 0.023$), indicating better dietary patterns among higher resilience groups. Sleep duration did not show a statistically significant association ($p = 0.112$), suggesting no major differences in sleep patterns among the groups.

Table 2: Alpha Diversity Metrics by Stress Resilience Groups

Alpha diversity metrics, including the Shannon Index, Observed Species, Chao1 Index, and Simpson Index, were all significantly associated with stress resilience. High resilience groups exhibited the highest microbial diversity, with a Shannon Index of 3.5 ± 0.8 and an observed species count of 210 ± 45 ($p = 0.009$). The Chao1 and Simpson indices also followed a similar trend, indicating greater richness and evenness of gut microbiota in the high-resilience group. These findings suggest that stress resilience is positively correlated with a more diverse gut microbiota.

Table 3: Beta Diversity Analysis (Bray-Curtis Distances) by Stress Resilience Groups

Beta diversity analysis revealed distinct clustering of microbiota composition among stress resilience groups, as evidenced by significant differences in principal coordinates (PC1, PC2, and PC3). The high-resilience group showed greater variance explained by PC1 (35.2%) compared to moderate (29.6%) and low resilience groups (25.3%) ($p = 0.021$). These results indicate that microbiota composition varies significantly with resilience levels, suggesting that specific microbial communities may be associated with higher resilience.

Table 4: Significant Microbial Taxa Across Stress Resilience Groups

Specific microbial taxa, including *Bacteroides*, *Firmicutes*, *Akkermansia*, and *Lactobacillus*, were significantly more abundant in the high-resilience group compared to moderate and low-resilience groups. For instance, *Bacteroides* had a relative abundance of 35.2% ± 5.4 in the high-resilience group, compared to 25.3% ± 5.1 in the low-resilience group ($p = 0.008$). Similarly, *Firmicutes* and *Akkermansia* were more prevalent in the high-resilience group ($p = 0.021$ and $p = 0.047$, respectively). These findings suggest that specific taxa may play a role in stress resilience mechanisms.

Table 5: Correlation Between Alpha Diversity and Stress Resilience Scores

Positive correlations were observed between alpha diversity metrics and stress resilience scores. The Shannon Index showed the strongest correlation ($r = 0.42$, $p = 0.003$), followed by the Chao1 Index ($r = 0.40$, $p = 0.005$), Observed Species ($r = 0.38$, $p = 0.008$), and Simpson Index ($r = 0.35$, $p = 0.014$). These results reinforce the notion that greater microbial diversity is associated with higher stress resilience, with adjusted R^2 values ranging from 0.24 to 0.34, indicating moderate predictive strength.

Table 6: Random Forest Model Performance

The Random Forest model demonstrated strong predictive performance, achieving an accuracy of 82%, precision of 85%, recall of 80%, and an AUC of 0.89. Feature importance analysis identified *Bacteroides* (0.35), *Firmicutes* (0.28), and *Akkermansia* (0.22) as the top three taxa contributing to the prediction of stress resilience. The cross-validation score of 81.5% ± 2.3% indicates the robustness of the model in identifying microbial predictors of stress resilience.

Table 1. Demographic and Lifestyle Characteristics of Participants

Characteristic	Mean ± SD or % (n)	p-value
Age (years)	15.2 ± 1.8	N/A
Sex (Male/Female)	48% (48)/52% (52)	0.321
Body Mass Index (BMI) (kg/m²)	21.3 ± 2.8	0.075
Physical Activity (hours/week)	3.8 ± 1.5	0.045*
Sleep Duration (hours/night)	7.6 ± 1.2	0.112
Diet Quality Score	72.5 ± 10.3	0.023*

Table 2. Alpha Diversity Metrics by Stress Resilience Groups

Stress Resilience Group	Shannon Index (Mean ± SD)	Observed Species (Mean ± SD)	Chao1 Index (Mean ± SD)	Simpson Index (Mean ± SD)	p-value
High Resilience	3.5 ± 0.8	210 ± 45	230 ± 50	0.85 ± 0.05	0.009*
Moderate Resilience	3.2 ± 0.7	195 ± 40	215 ± 48	0.78 ± 0.06	0.037*
Low Resilience	2.8 ± 0.6	180 ± 35	200 ± 42	0.72 ± 0.07	N/A

Table 3. Beta Diversity Analysis (Bray-Curtis Distances) by Stress Resilience Groups

Stress Resilience Group	PC1 (Mean ± SD)	PC2 (Mean ± SD)	PC3 (Mean ± SD)	Variance Explained (%)	p-value
High Resilience	0.45 ± 0.12	0.32 ± 0.15	0.28 ± 0.10	35.2	0.021*
Moderate Resilience	0.38 ± 0.10	0.28 ± 0.12	0.26 ± 0.09	29.6	0.034*
Low Resilience	0.30 ± 0.09	0.25 ± 0.10	0.22 ± 0.08	25.3	N/A

Table 4. Significant Microbial Taxa Across Stress Resilience Groups

Taxa	High Resilience (Mean ± SD)	Moderate Resilience (Mean ± SD)	Low Resilience (Mean ± SD)	Relative Abundance (%)	p-value
Bacteroides	35.2 ± 5.4	30.8 ± 4.9	25.3 ± 5.1	18.2	0.008*
Firmicutes	40.1 ± 6.2	38.7 ± 5.9	34.8 ± 5.5	22.1	0.021*
Akkermansia	12.4 ± 3.5	10.2 ± 3.2	8.9 ± 2.8	7.3	0.047*
Lactobacillus	8.6 ± 2.4	7.5 ± 2.1	6.3 ± 1.8	4.5	0.032*

Table 5. Correlation Between Alpha Diversity and Stress Resilience Scores

Metric	Correlation Coefficient (r)	p-value	Adjusted R^2
Shannon Index	0.42	0.003*	0.34
Observed Species	0.38	0.008*	0.28
Chao1 Index	0.40	0.005*	0.31
Simpson Index	0.35	0.014*	0.24

Table 6. Random Forest Model Performance

Metric	Value	Feature Importance (Top 3 Taxa)
Accuracy	82%	*Bacteroides*: 0.35
Precision	85%	*Firmicutes*: 0.28
Recall	80%	*Akkermansia*: 0.22
AUC (Area Under Curve)	0.89	N/A
Cross-Validation Score	81.5% ± 2.3%	N/A

DISCUSSION

The significant association between physical activity and stress resilience aligns with findings by Hillman et al. (2014), who demonstrated that higher physical activity levels are linked to improved cognitive function and stress adaptability in adolescents.[7] Similarly, the diet quality scores reflecting better dietary habits among high-resilience individuals are supported by Logan and Jacka (2014), who reported that nutrient-rich diets enhance mental resilience by modulating inflammation and oxidative stress.[8] The lack of association between BMI and resilience in this study contrasts with findings by Davis et al. (2011), where BMI was inversely related to psychological health, possibly due to this study's focus on generally healthy adolescents.[9] The observed positive association between alpha diversity metrics and stress resilience is consistent with the work of Clarke et al. (2013), who found that individuals with greater microbial diversity exhibited lower levels of stress and anxiety.[10] The diversity indices such as Shannon and Chao1 highlight the richness and evenness of gut microbial communities, which have been linked to the production of metabolites like short-chain fatty acids (SCFAs) that influence brain-gut communication pathways. These findings reinforce the importance of microbial diversity as a marker of gut and mental health.Distinct clustering of microbiota composition across resilience groups in beta diversity analysis is supported by the study of Kelly et al. (2015), which showed that stress-induced changes in microbiota composition were associated with behavioral changes.[11] The significant differences in principal coordinates (PC1, PC2, and PC3) observed here mirror those findings, suggesting that specific microbial community structures are integral to stress resilience.The higher abundance of *Bacteroides*, *Firmicutes*, *Akkermansia*, and *Lactobacillus* in high-resilience individuals is consistent with findings by Cryan and Dinan (2012), who highlighted the role of these taxa in modulating stress responses through SCFA production and regulation of the hypothalamic-pituitary-adrenal (HPA) axis.[12] In particular, *Akkermansia* has been linked to gut barrier integrity, which is crucial for mitigating systemic inflammation—a factor in stress-related disorders.The correlation between higher alpha diversity metrics and resilience scores corroborates the findings of Ainsworth et al. (2012), who noted that diverse microbiota support metabolic flexibility and reduce the impact of environmental stressors. The strength of these correlations further supports the hypothesis that microbial diversity plays a protective role in psychological well-being.[13] The robust predictive performance of the Random Forest model in identifying microbial taxa associated with resilience aligns with the study by Dinan and Cryan (2013), which demonstrated the feasibility of using gut microbiota profiles as biomarkers for stress-related conditions.[14]The high accuracy (82%) and AUC (0.89) indicate that gut microbiota composition could be a reliable predictor of stress resilience, supporting the utility of machine learning in microbiome research.

CONCLUSION

This study highlights the significant relationship between gut microbiota composition and stress resilience in adolescents, demonstrating that higher microbial diversity and the presence of specific taxa are associated with greater resilience. The findings underscore the potential of the gut-brain axis as a target for interventions aimed at enhancing mental health and stress management. By identifying key microbial markers and their associations with resilience, this research provides a foundation for developing personalized strategies, such as dietary or probiotic interventions, to promote adolescent well-being.

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