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## Integrative analysis of gut microbiome and multimodal stress responses: Unveiling the interplay between biological, cognitive, and physical factors for early stress detection

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Early detection of stress is crucial to preventing decline in performance, mental and physical health problems, and improving overall well-being. Four stress trials (heat, muscle exertion, sleep deprivation, and psychosocial stress) were conducted to assess the impact of stress on interrelationships between biological, cognitive, and physical states.

This study is unique in its approach, aiming to elucidate the specific relationships between gut microbiome, health habits, psychological, cognitive, physiological, and physical aspects. An integrative analytical pipeline was employed, starting with unsupervised machine learning for variable reduction, followed by Redundancy Analysis (RDA) and supervised machine learning to determine which traits explain the most variance in the full omics datasets. Structural Equation Modelling (SEM) was then utilised to explore causal relationships between these traits and the gut microbiome.

In this research, the gut microbiome has been proven to be linked to sex, hormones, sleep duration, alcohol consumption, viral infection, workload, and physical and cognitive assessment. These factors had a significant impact on the gut microbiome, which indirectly contributes to stress levels. This approach offered new perspectives to complement traditional statistical analyses, such as differential expression and has served as a preliminary step before these analyses.

These findings have significant implications, emphasising the importance of integrating diverse data types to comprehensively understand stress and performance. This approach could advance early detection of stress while predicting and improving performance.

**Keywords**: Anthropologic Health Habits, Microbiome, Injury Prediction, Military, Performance, Random Forest, Principal Component Analysis, Structural Equation Modelling (SEM), Predictive Analytics.