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A Machine-Learning Approach to Modeling Cognitive Flexibility, Stress Reactivity, and Executive Function in Clinical Populations

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1. Round 1

1.1. Reviewer 1

Reviewer:

The introduction demonstrates impressive breadth of literature on cognitive flexibility, stress, and psychopathology, but it is somewhat overloaded with disparate clinical and psychosocial examples; tightening this section around a clearer conceptual through-line (e.g., a brief, systematic argument that culminates in the precise modeling gap) and formulating explicit, testable hypotheses (e.g., about the primacy of TMT B–A and cortisol reactivity) would substantially enhance focus and coherence.

The methodology is generally solid and well-described, with appropriate use of validated cognitive tests, a social-evaluative stress paradigm, and modern ML techniques (Random Forest, SVM, XGBoost with SHAP); nonetheless, the paper lacks crucial details on sample composition and control variables—especially exact group sizes, comorbidity patterns, psychotropic medication status, and potential confounders such as time-of-day for cortisol collection, menstrual cycle phase, and use of substances like caffeine or nicotine—which limits interpretability and reproducibility.

The manuscript's translational emphasis—linking cognitive flexibility and stress-system dysregulation to intervention paradigms such as CBT, ACT, neurofeedback, and neuromodulation—is laudable, yet this section would benefit from a more critical and selective integration: rather than listing numerous intervention studies across disparate populations, the authors could highlight a few paradigms most directly aligned with their measured constructs and clarify how their specific ML-derived patterns (e.g., non-linear cortisol effects) might meaningfully inform treatment personalization beyond what is already known.

Authors revised and uploaded the document.

1.2. Reviewer 2

Reviewer:

The data-processing and machine-learning pipeline is broadly appropriate (MICE imputation, feature standardization, cross-validated hyperparameter tuning, and a hold-out test set), yet several key technical aspects require clarification, including how class imbalance was handled (if at all), whether any feature selection or regularization strategies were used to mitigate overfitting given the relatively modest N versus feature space, and whether multiclass classification (across MDD, GAD, PTSD, HC) was attempted in addition to the binary clinical vs. healthy distinction stated as the primary aim.

The results convincingly demonstrate group differences in executive-function performance and stress reactivity, and they support the centrality of cognitive flexibility and aberrant cortisol/HRV dynamics; however, the reporting is incomplete in the current form—many exact statistics (ANOVA F values, p-values, effect sizes such as η^2 or Cohen's d) and per-group descriptive data are not consistently presented in the text, and the authors should ensure that all tables provide full numerical information accompanied by effect sizes, confidence intervals, and clear labeling of variables.

The machine-learning performance section is promising, particularly the use of SHAP to interpret the XGBoost model and link feature importance to theoretical constructs, but the claims of "excellent" classification remain difficult to evaluate without full performance metrics (AUC-ROC with confidence intervals, accuracy, precision, recall, F1, and ideally calibration indices such as Brier score or calibration plots) and without a clear description of how misclassifications were distributed across diagnostic categories, which would be especially relevant to any translational inference about clinical utility.

The discussion effectively situates the findings within a transdiagnostic framework and articulates plausible clinical implications, but at times it overreaches in causal language and in the strength of claims about treatment targets; the authors should more clearly distinguish between correlational associations (e.g., cognitive inflexibility as a classifier of current clinical status) and causal mechanisms or modifiable risk factors, and they should temper statements that imply direct prescriptive guidance for interventions based on cross-sectional, observational data.

Authors revised and uploaded the document.

2. Revised

Editor's decision after revisions: Accepted.
Editor in Chief's decision: Accepted.

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