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Hypnosis reshapes multilevel stress response and enhances executive performance in stressed medical students

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Abstract

Stress and anxiety impair executive function and degrade performance, yet rapid and scalable interventions remain limited. This controlled study tested whether a single personalized hypnosis session could enhance stress regulation and cognitive performance during negative memory recall in medical students. Forty-nine final-year students were assigned to hypnosis or a breath-focused attention condition (control arm) ([ClinicalTrials.gov: NCT06778109](https://clinicaltrials.gov/ct2/show/study/NCT06778109)). Executive function (Tower of London Revised), perceived stress and anxiety (VASs, VASa, PSS-10), were assessed before and after a repeated personal negative memory recall, while autonomic reactivity (heart rate, heart rate variability, electrodermal activity, skin conductance responses and percentage of time in sympathetic activation) before, during and after the repeated personal negative memory recall. Hypnosis yielded significantly greater improvements in executive functions (ANCOVA, $p < 0.05$, $d = 0.62$), reduced stress and anxiety, whereas stress increased in controls. Physiologically, hypnosis increased parasympathetic recovery (HRV), tonic sympathetic activity (EDA), while suppressing excessive phasic sympathetic surges (SCR/min) and reducing time spent in stress response. Bayesian analyses provided extreme evidence (Jeffreys' scale) for psychophysiological effects. Network analysis identified electrodermal activity as a central hub linking stress responses and executive functions. A logistic model accurately classified group membership. In leave-one-out cross-validation (LOOCV), the model retained strong performance (Accuracy=90%, AUC = 0.91, Brier score = 0.0796). These findings are consistent with a hypnosis-related shift toward an adaptive challenge-like autonomic profile, suggesting improved cognitive resilience and flexibility in high-pressure contexts.

Keywords: Executive function, TOL, hypnosis, stress management, HRV, EDA, medical students, Machine Learning

INTRODUCTION

Stress and anxiety are two related aspects of human functioning that impact performance, executive functions, emotional well-being, and overall quality of life¹⁻⁴. Medical doctors – especially those involved in invasive procedures, urgent and emergency care – often experience high levels of stress, making them prone to anxiety, burnout, and impaired decision-making⁵⁻⁸. Given the detrimental impact of these conditions on psychophysical health, growing interest has emerged in interventions aimed at modulating stress, anxiety, and cognitive functioning^{9,10}.

Medical students experience a progressive deterioration of mental health starting early in their training, and this condition frequently persists throughout medical school. Evidence indicates that this distress may contribute to substance abuse, relational problems, suicide risk, and even withdrawal from the profession¹¹. One psychological study reported that students often feel guilty if they do not dedicate their limited free time to studying; consequently, they perceive little opportunity for leisure activities or a healthy lifestyle¹². Overall, the excessive demands of medical education have been consistently reported as a threat to psychological well-being.

Another underestimated aspect of stress literacy concerns the tendency of medical students and future physicians to underestimate their own needs. Many cite heavy academic workload and demanding internships as major barriers to self-care. In response, targeted programs have been proposed, with pilot studies reporting improvements in sleep quality and stress levels¹³.

Stress literacy on medical doctor and related interventions are still in their infancy; however, several promising approaches have been proposed. Among these, mindfulness is one of the most frequently studied strategies. It has been shown to reduce perceived stress even when practiced over very brief periods¹⁴. However, long-term effects (≥ 1 month post-intervention) appeared inconsistent¹⁵, and a meta-analysis reported only small-to-moderate benefits¹⁶. Some studies documented reductions in burnout at 4-month follow-up¹⁷, and another systematic review found improvements in stress, psychological distress, perceived health and well-being; however, only perceived stress remained improved at follow-up¹⁸. A further meta-analysis focusing on medical

students and junior doctors concluded that the effectiveness of mindfulness in this population remains inconclusive¹⁹.

From a physiological perspective, heart rate variability (HRV) biofeedback has gained increasing interest, with robust effects reported on anxiety, depression and anger²⁰. In healthcare workers, pre-post studies²¹ have shown reductions in stress and anxiety and increases in HRV, though no meta-analysis has yet focused specifically on medical doctors. Despite the heterogeneity of available studies, cognitive and behavioral interventions overall appear promising in reducing stress and burnout in physician²².

There is also growing evidence for the impact of breathing techniques combined with cardiac biofeedback²³. These approaches have been shown to enhance performance in high-pressure simulated clinical scenarios, underscoring their relevance to executive functioning, an outcome that has received comparatively limited attention. Indeed, most research focuses either on stress perception or emotional burden, without assessing cognitive performance. This distinction is crucial, as subjective stress represents only one component of the problem, whereas impaired performance may directly affect patient safety.²⁴⁻²⁸ For this reason, it is essential to investigate the interaction between psychological, physiological and performance-based outcomes using multimodal data and multimodal levels of analysis. Understanding not only how individuals feel, but also how they function under stress -and how they perceive changes in performance²⁹ - may offer a more comprehensive picture of intervention efficacy.

Among the above-mentioned techniques, hypnosis has emerged as a promising intervention³⁰⁻³⁴.

Hypnosis can facilitate changes in perception, cognition, and emotional states by altering the way to respond to stressors. Hypnosis modulates autonomic functions, including heart rate (HR), HRV, electrodermal activity (EDA), and skin conductance responses (SCR/min), which are valid indicators of stress level and emotional regulation. RMSSD (a time-domain heart rate variability (HRV) metric), primarily reflecting a marker of parasympathetic nervous system activity³⁵, has been associated with greater resilience to stress and

better cognitive flexibility, while EDA has gained attention as a valuable sympathetic index to investigate the flight or fight system and to predict perceived stress³⁶.

The effects of hypnosis on stress and cognitive performance have been explored in several studies, although the underlying mechanisms are not yet fully understood^{37,38}. Hypnosis may increase the parasympathetic activity and reduce the sympathetic response to stress, lowering physiological markers such as HR and blood pressure^{39,40}. Additionally, hypnosis may enhance cognitive processing by improving focus, attention, and memory recall, possibly enhancing prefrontal cortex processes such as working memory, flexibility which are negatively impacted by acute stress⁴¹⁻⁴⁵.

Therefore, its potential to enhance cognitive performance, reduce stress and modulate negative memories could be particularly beneficial for high-pressure professionals, who need optimal cognitive functioning and stress regulation.

The aim of this study was to evaluate the effects of hypnosis in medical students, whose limited professional experience make them more prone to stress when managing adverse events.

Based on these assumptions, our hypothesis is that hypnosis, when appropriately administered, would: i) improve cognitive performance, evaluated using the revised Tower of London (TOL-R; primary outcome); ii) reduce perceived stress and anxiety (secondary outcomes); and iii) modulate physiological parameters, specifically HR modulation, increased HRV, and dissociation between tonic and phasic components of electrodermal activity (secondary outcomes)

(iv) Furthermore, we expected that physiological and subjective changes could accurately distinguish participants in the hypnosis (INT) and control groups (CTRL) using logistic regression and machine learning classification models.

We therefore expect that leave-one-out cross-validation (LOOCV), which provides a nearly unbiased estimate of generalization performance of logistic regression (and with a better generalization than k-fold cross validation on small samples⁴⁶), could support a physiological signature consistent with hypnosis. To test these hypotheses, medical students were exposed to a stressful condition by recalling a previously discussed negative personal

memory related to their medical training. Moreover, beyond classical statistics, the application of multimodal approaches (based on network analysis, Bayesian statistics and machine learning) could provide evidence to support our hypothesis, i.e., that hypnosis is an effective tool for executive function improvement and for stress and anxiety reduction in medical students, who face many and intense stressful situations.

MATERIALS AND METHODS

Participants

This study was conducted in Italy. Following the initial submission of the study, a CTRL group was included to strengthen the causal interpretation of the findings by accounting for non-specific effects such as repeated testing and time. Forty-nine healthy volunteers attending the final year of medical school at the University of Padua were prospectively enrolled between February 6 and October 1, 2025. Of these, 26 were assigned to the INT group (14 males [54%] and 12 females [46%], mean age 25 ± 2 years), and 23 to the CTRL group (12 males [52%] and 11 females [48%], mean age 25.6 ± 1.6 years). The study was conducted in accordance with the principles of Good Clinical Practice outlined in the Declaration of Helsinki. Participants enrolled in the present study have signed informed consent prior to participation. Subjects with cardiovascular diseases, psychiatric disorders, or any type of ongoing medication that could impact HR, sweating, or stress responses and prior experience with hypnosis were excluded.

This study was approved by the Ethical Committee of the Department of General Psychology, University of Padua (reference n. 3274/2019 on 05 November 2019, Chairwoman Professor A. Falco). This clinical study was registered at ClinicalTrials.gov (NCT06778109) on December 29 2024. As this study was not a randomized controlled trial, CONSORT guidelines were not applicable therefore it was written in accordance with the TREND statement reporting checklist (see **SDC1**).

Measures

Cognitive performance, stress and anxiety were assessed with the following tests:

1) the Revised Tower of London (TOL-R) a standardized test of planning, problem solving, inhibitory control, and visuospatial working memory allowing to evaluate the cognitive performance with its prefrontal and fronto-parietal components⁴⁷⁻⁵⁰. The test consists of two boards with pegs and several beads with different colors. One board shows the goal arrangement of beads, and the other board is given to the examinee with the beads in a different configuration. The participant must alter the second board to match the first. The test consists of 30 problems with increasing difficulty, and the maximum score is 30 points.

2) the Visual Analog Scale for Anxiety (VASa)⁵¹; 3) the Visual Analog Scale for Stress to assess subjective stress levels⁵² were assessed through a digital scale (0-10 cm);

The Visual analogue scale questions are reported for clarity below:

“Please rate your current level of anxiety by marking a point on the line below.”

0 = no anxiety — 10 = extreme anxiety

“Please rate your current level of stress by marking a point on the line below.”

0 = no stress — 10 = extreme stress

4) The Perceived Stress Scale (PSS-10)^{53,54}

Perceived stress over the previous month was assessed using the 10-item Perceived Stress Scale (PSS-10). The PSS-10 is a widely used self-report measure evaluating the extent to which individuals perceive their lives as unpredictable, uncontrollable, and overloaded. Items are rated on a 5-point Likert scale (0 = “never” to 4 = “very often”), with higher scores indicating greater perceived stress. The scale shows good internal consistency (Cronbach’s α typically ranging from 0.78 to 0.91), satisfactory test-retest reliability, and well-established construct and convergent validity across populations.

5) At the end of the experimental session, all participants were explicitly asked to report how they felt compared to baseline, choosing among three options: “better”, “same”, or “worse.”

6) HIP test (Hypnotic Induction Profile):

All participants in the INT group underwent HIP after having completed all experimental procedures, and HIP was conducted as the final measurement of the study. The HIP allows to check hypnotic ability in less than 10 minutes, making it the scale with the best cost-benefit ratio in the high pace of the medical-surgical context⁵⁵. A 0-10 point Induction Score (IS) is obtained, where about 45-50% of individuals in the general population are classified as highly hypnotizable, 35-40% as medium hypnotizable and the remaining 15-20% as lows. The HIP has been validated⁵⁶ and significantly correlates with Stanford Scale^{57,58}.

The following physiological parameters were also recorded using the eSense Galvanometer (Mindfield Biofeedback): i) EDA, an indicator of stress-related sympathetic activity, SCR/min, percent (%) of time spent in skin conductance responses, in order to record the changes of electrical conduction in response to sympatho-cholinergic, stress-induced sweat secretions⁵⁹. After having visually inspected the raw data, artifacts were addressed by removing zero values and single-point deviations beyond ± 2 SD and tonic EDA was computed as the mean skin conductance level.

The Skin Conductance contains two components: the tonic, “static level” and the phasic, “fluctuating reactions”, and these components are usually designated as Skin Conductance Responses (SCR). While the “level” is represented well in the average of the measured values, the eSense Skin Response also measures the amount of SCR per minute. From 6-9 SCR/min starts an animated state. From 10 or even from 16 SCR/min, a level of stress or even high stress can be assumed⁶⁰. SCRs were identified through an automated stage.

Baseline Monitoring (“Listening State”) – The system continuously monitored the skin conductance signal during a neutral resting state to establish a provisional baseline.

Onset Detection – An SCR was triggered when either (a) a gradual rise in conductance persisted for ≥ 2 s, or (b) a sudden increase ≥ 0.5 μ S occurred relative to the baseline. If the signal decreased by > 0.1 μ S during this period, the detection was cancelled and baseline monitoring resumed.

Event Confirmation and Quantification – Once onset was confirmed, the first value was defined as the base level and the fluctuation amplitude was tracked to peak. SCRs were counted globally and within 1-min windows to derive indices such as SCR/min.

Recovery Phase – A SCR was considered complete when the signal declined by ≥ 50 % of the peak amplitude relative to baseline.

ii) HR and HRV.

Heart rate (HR) and parasympathetic activity were recorded using the HRV Camera App on a smartphone, which provides non-invasive measurements by detecting changes in blood volume pulse through photoplethysmography (PPG) via the camera lens. Participants, under supervision, were instructed to place a finger on the camera lens while physiological signals were recorded.

HR was expressed in beats per minute (bpm) and derived from the PPG signal using the HRV Camera App algorithms. Parasympathetic tone was estimated using the root mean square of successive differences (RMSSD) of inter-beat intervals, a time-domain HRV metric primarily reflecting vagal modulation^{35,61}. RMSSD was computed by calculating successive differences between consecutive normal-to-normal (NN) interbeat intervals (in milliseconds), squaring these differences, averaging them, and finally taking the square root of the mean^{62,63}.

The PPG method has been validated and shown to produce results comparable to traditional ECG-based measurements^{64,65}, and the HRV Camera App PPG quality has been tested against a PPG sensor (Shimmer3 GSR+) yielding good

accuracy, although not yet directly in comparison with ECG⁶⁶. As PPG recordings are known to be susceptible to motion and pressure artifacts⁶⁷, data were preprocessed by removing zero values and single-point deviations exceeding ± 2 SD, a commonly adopted threshold for identifying physiological recording noise.

Procedure and rationale

Figure 1 shows the design of the study. All participants in the INT group underwent HIP, PSS-10, VASa and VASs, TOL-R and measurement of physiological parameters (i.e., HR, HRV(RMSSD), EDA, SCR/min, %). The CTRL group comprised 23 participants. Participants in the breath-focused attention CTRL group underwent the same tests as the INT group, apart from HIP (all participants in the INT group underwent HIP after having completed all the experimental procedure; HIP was the last measurement of the study) and; hypnosis; was replaced by the breath-focused attention procedure matched in duration and structure to the INT condition. All participants were seated and supervised in a quiet room during the cognitive and physiological assessment. Then, each participant was exposed to a stress induction for 2 minutes (i.e., recalling a memory from a past negative medical education or academic experience), followed by an 8-minute session of hypnosis (or 8 minutes of breath-focused attention in the CTRL group), during which participants relived a previously discussed pleasant experience, such as sunbathing at the beach or relaxing under trees (for additional information about the stress induction, CTRL and INT procedures, see Supplementary Materials, **Appendix**). A few minutes later, a second stress induction was performed; the same negative memory was recalled once again for 2 minutes to check possible differences in stress-response after the intervention. After each step the physiological parameters were recorded, while TOL-R, VASa and VASs were retested at the end of the experimental session.

The stress induction procedure was designed to prioritize the elicitation of a meaningful stress response at the individual level rather than strict

standardization of the stressor itself. Psychological stress is inherently subjective and depends on individual appraisal⁶⁸; therefore, according to transactional models of stress and coping, individual differences in appraisal, personality, and available resources shape emotional and physiological responses, such that identical stressors may elicit markedly different responses across individuals, whereas different stimuli may result in comparable stress responses⁶⁹. Furthermore neuroendocrine and autonomic responses to standardized social stressors vary as a function of individuals' subjective appraisal of threat and perceived coping capacity⁷⁰ also to standardized stress laboratory stressors⁷¹. Accordingly, the procedure aimed to elicit functionally equivalent stress responses across individuals, with the subject's physiological and subjective response constituting the outcome of interest.

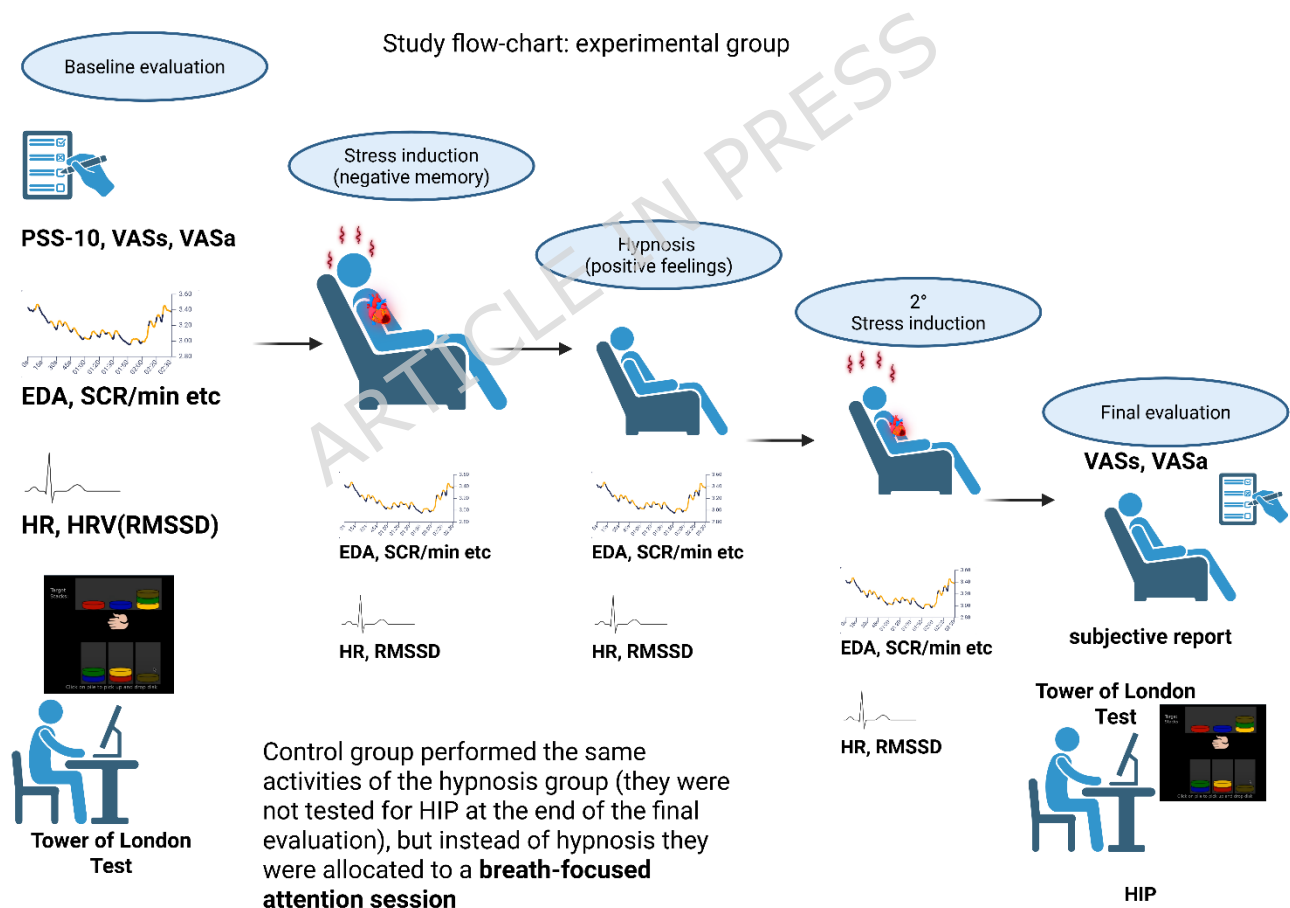


Figure 1-Study flow-chart. | BioRender

Abbreviations: TOL-R, Tower of London-Revised; VASa, Visual Analog Scale for Anxiety; VAS, Visual Analog Scale for Stress; EDA, Electrodermal Activity; SCR, skin conductance response; min, minute; HR, Heart Rate; HRV(RMSSD),

Heart Rate Variability; PSS-10, Perceived Stress Scale- 10 Item Version. Created in BioRender. Science Suite Inc. dba BioRender ("BioRender") has granted CC BY open access license permission to use this Completed Graphic in accordance with BioRender's Terms of Service and Academic License Terms ("License Terms"), Queirolo, L. (2026).

Statistical analysis and network analysis

According to an a priori power analysis, a minimum sample size of 19 participants was estimated to be sufficient to detect a within-subject pre-post difference in executive function in the experimental (INT) group, assuming a statistical power of 0.80, an expected effect size of 0.60, and a significance level of $\alpha = 0.05$. To account for potential dropouts or missing data, 26 participants were recruited for the INT group. The inclusion of a CTRL group was decided subsequently, and therefore no separate a priori power calculation was conducted for between-group comparisons

Continuous data were presented as mean \pm standard deviation (SD), when normally distributed, or as the median when non-normally distributed. The Shapiro-Wilk test was used to assess normality. Categorical data were summarized using absolute and relative frequencies. To compare paired data, the Paired t-test or Wilcoxon matched-pairs test was applied. To compare unpaired data, Unpaired t-test or Welch's t-test depending on variance. Pearson's or Spearman's coefficient were calculated to evaluate associations between variables. Normality, normality of residuals and homoscedasticity of variance (Levene's test or Bartlett's test) were checked before fitting ANOVA models. A repeated measures ANOVA was used to determine any significant difference in terms of physiological data (i.e., EDA, HR, RMSSD etc, defined as dependent variable) across four different conditions ("baseline", "stress induction", "hypnosis," "repeated stress induction"). For any violations of the parametric ANOVA assumptions, Friedman's ANOVA was performed. Sphericity was evaluated with Mauchly's test and corrected if necessary with Huynh-Feldt. Bonferroni correction was applied for post-hoc analysis. To

assess difference between the INT and the CTRL group, after having verified that assumptions of linearity, residuals normality, homogeneity of variances and Homogeneity of regression slopes were respected by including the group \times covariate interaction term in the models, we mitigated practice/learning effects and baseline imbalance, through ANCOVA. In the case of TOL-R we used the post-intervention Tower of London (TOL-R) score as the dependent variable, group (hypnosis vs breath-focused attention) as the fixed factor, and baseline TOL-R (Pre) as a covariate: $TOL-R \text{ Post} \sim \text{Group} + TOL-R \text{ Pre}$. This approach increases precision and reduces bias by adjusting for individual starting levels. The same ANCOVA framework was also applied to VAS stress and anxiety outcomes, with post-intervention scores as dependent variables and corresponding baseline values as covariates, to evaluate treatment effects after adjustment for baseline levels.

A Bayesian analysis was conducted to evaluate the relative evidence provided by the data for competing hypotheses concerning the observed effects on TOL-R performance, VAS-rated anxiety and stress, electrodermal activity (EDA), and other physiological parameters. In case of non-normality a Bayesian rank-based bootstrap have been implemented. The Bayes Factor (BF_{10}) was used to quantify the extent to which the observed data were more likely under the alternative hypothesis—postulating systematic changes associated with hypnosis in executive functioning, physiological responses, and subjective measures of stress, anxiety, and perceived wellbeing—than under the null hypothesis, which assumes that the observed effects are attributable to random variation. The strength of the evidence in favor of one hypothesis over the other was interpreted according to Jeffreys' scale⁷². Specifically, BF_{10} values between 1 and 3 were considered anecdotal evidence, values between 3 and 10 moderate evidence, values between 10 and 30 and between 30 and 100 strong and very strong evidence, respectively, and values greater than 100 were interpreted as extreme evidence in favor of the alternative hypothesis.

Finally, a two-step dimensionality reduction approach was employed to identify a parsimonious set of variables maximizing explainable variance in performance while preserving informative inter-variable relationships,

reducing redundancy. Specifically, in the first step, variables were retained if they exhibited at least five moderate-to-strong significant correlations ($r \geq 0.3$) with other variables in the dataset (using the appropriate correlation coefficients based on data distribution). This ensures that the selected variables are meaningfully embedded within the overall structure. Then, the Kaiser-Meyer-Olkin (KMO), measure of sampling adequacy, was applied to assess the suitability of the selected subset for multivariate analysis. Variables with individual measure of sampling adequacy for single variable (MSA) lower than 0.5 were excluded, overall all the selected variables must show at least an $MSA > 0.8$. To construct the network, a stricter correlation threshold ($r \geq 0.4$) was used to define edges in a weighted adjacency matrix serving as the basis for a spectral graph representation. Network topology was then evaluated using standard graph-theoretical metrics, including number of nodes and edges, average path length, network diameter, density, betweenness centrality, and closeness centrality. These measures were used to assess the integration and efficiency of information flow across physiological and cognitive domains.

Machine Learning analysis

A secondary aim of the study was to determine whether physiological and subjective changes could reliably distinguish participants in the INT group from those in the CTRL condition. Rather than adopting a purely data-driven variable selection strategy, we selected a parsimonious set of predictors based on theoretical and empirical considerations. Predictor selection was defined prior to model estimation, after data collection, but was not preregistered, as the inclusion of the control group and related analysis were not part of the original preregistered study design. Specifically, the model included $\Delta RMSSD$ (change in RMSSD between stress conditions), ΔSCR (change in skin conductance responses between stress conditions), ΔVAS stress (change in perceived stress), and post-intervention VAS stress scores.

These variables were chosen because hypnosis has been shown to influence autonomic flexibility (HRV)⁷³, phasic sympathetic activity⁷⁴, and perceived stress, making them conceptually plausible discriminators of group

membership. Predictor selection was defined prior to model estimation and was independent of model fit optimization, in order to limit model complexity and avoid redundancy among highly correlated predictors, which could inflate variance inflation factors and lead to unstable coefficient estimates given the moderate sample size. Accordingly, among subjective measures, VAS stress was selected as a more general index, whereas VAS anxiety was not included to prevent multicollinearity.

Group membership was classified using logistic regression. To assess the robustness and generalizability of the classification at the individual level, leave-one-out cross-validation (LOOCV) was applied. LOOCV was not intended to optimize classification accuracy, but rather to provide a conservative estimate of out-of-sample performance by evaluating how well the model classified previously unseen participants.

In the LOOCV procedure, the model was iteratively trained on data from all participants except one, who served as the test instance. Each iteration was fully independent, with the model retrained on the remaining N-1 participants, ensuring that all predictions were strictly out-of-sample. Predicted probabilities from all iterations were aggregated to compute overall accuracy, sensitivity, specificity, area under the ROC curve (AUC), Brier score, and 95% confidence intervals. This approach maximizes data use under small-sample constraints while reducing optimistic bias and false-positive classification

RESULTS

TOL-R, VAS anxiety, VAS stress, PSS-10

At baseline, stress levels in the INT group were predominantly moderate (73%), with 15.4% reporting low stress and 11.5% high stress; baseline PSS-10 (INT=18.58± SD=6.159 vs CTRL=16.48± SD=4.3), VASs (INT=4.019± SD=2.385 vs CTRL=3.37± SD=2.664), VASa (INT=4.827± SD=2.782 vs CTRL=4.348 ± SD=2.424) and TOL-R (INT=19.9± SD=5.01 vs CTRL=18.96 ± SD=4.781) scores did not differ between groups at baseline evaluation.

Following the intervention, the INT group showed a significant improvement in TOL-R (TOL-R: pre $19.9 \pm \text{SD}=5.01$ vs post $24.3 \pm \text{SD}=3.58$, $p<0.001$, **Figure 2A**), accompanied by a marked reduction in subjective stress (VASs: $4.83 \pm \text{SD}=2.78$ vs $2.73 \pm \text{SD}=2.20$, $p<0.001$, $\text{BF}_{10}=23,017$, **Figure 2B**) and anxiety (VASa: $4.02 \pm \text{SD}=2.39$ vs $2.31 \pm \text{SD}=2.05$, $p<0.001$, $\text{BF}_{10}=35,952$, **Figure 2C**), further data are reported on **SDC 2 and SDC 4 in Supplementary Material**).

The CTRL group also showed improved TOL-R scores (18.96 ± 5.27 vs 21.87 ± 5.16 , $p<0.001$), but no reduction in anxiety and a significant increase in stress ($p<0.05$).

ANCOVA on post-intervention TOL-R, controlling for baseline performance, revealed a significant group effect favoring INT ($F(1,46)=4.62$, $p<0.05$, $\eta^2=0.038$, Cohen's $d=0.62$), with baseline TOL-R strongly predicting post-scores. Given the non-normality of data a Bayesian rank-based bootstrap estimated the probability of superiority in the INT group as $\text{PS} = 0.65$ (posterior mean = 0.65, 95% Credible intervals [0.47, 0.80]). The posterior probability for the directional hypothesis $\text{INT} > \text{CTRL}$ ($\text{PS} > 0.5$) was 0.954, indicating a 95.4% probability that the population effect favors the INT group. This corresponds to posterior odds of 20.6:1 in favor of $\text{INT} > \text{CTRL}$ (under equal prior odds) and could be interpreted as a strong evidence in Jeffreys' scale notation (**see Supplementary Data and Code**). ANCOVA with post-intervention VASs as the dependent variable and baseline VASa as covariate showed that the group effect remained highly significant after adjustment ($F = 40.36$, $p < 1 \times 10^{-7}$, $\eta^2 = 0.25$), confirming that the intervention effect is not explained by baseline differences the same applied for VASs ($F(1,46) = 22.45$, $p = 2.1 \times 10^{-5}$, $\eta^2 = 0.12$). Bayesian analyses of ΔVAS confirmed extreme evidence for stress ($\text{BF}_{10}=52,360$, $d=1.67$) and anxiety reduction ($\text{BF}_{10}=700$, $d=0.75$) in the INT group in comparison to the CTRL group HIP score ranges were 7 ± 2.56 , with all profiles ('low', 'medium', 'high') well represented, but the relationship between hypnotic ability and results was not significant (see **SDC 3**). 25 out of 26 participants reporting feeling better and one unchanged ($\chi^2 = 40.91$, $p < 0.001$). Contrasting this result with group CTRL, 18 referred

feeling worse and 5 no differences, but none feeling better ($\chi^2 = 22.5$, $df=2$, $p<0.001$).

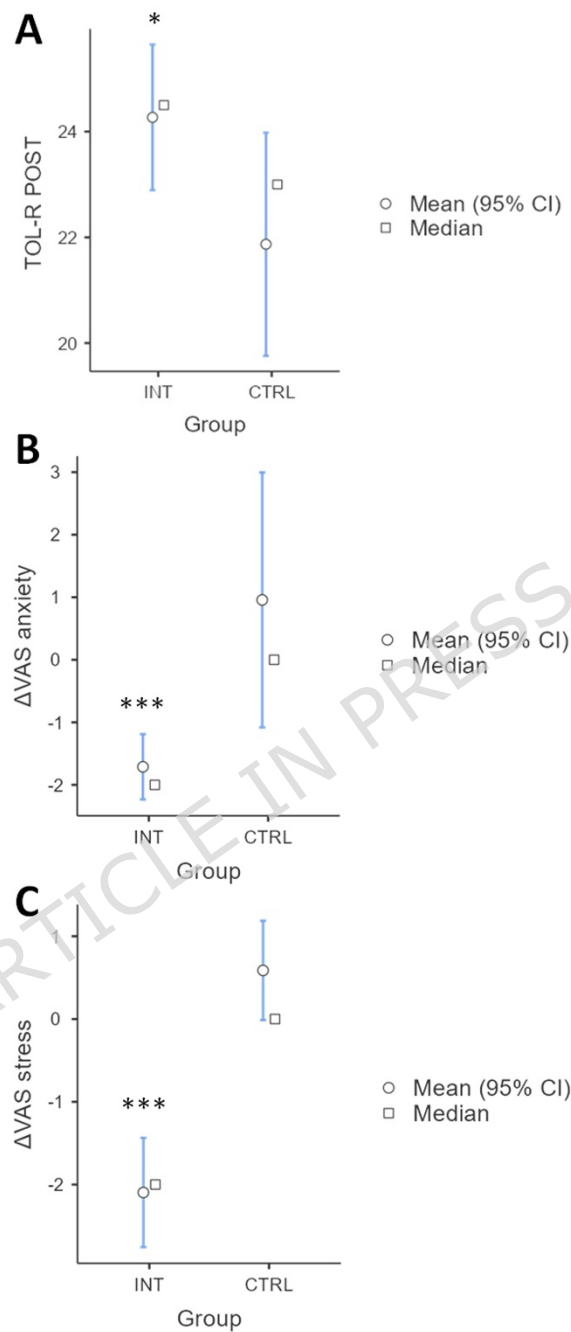


Figure 2-Cognitive performance, stress and anxiety before and after hypnosis.

A. TOL-R POST Group Experimental vs Group Control; **B.** Δ VAS for stress (VASs); **C.** Δ VAS for anxiety (VASa).

Abbreviations: TOL-R, Tower of London-Revised; VASa, Visual Analog Scale for Anxiety; VASs, Visual Analog Scale for Stress, *: p-value < 0.05, **: p-value < 0.01, *** p-value < 0.001. CTRL=control group, INT=Hypnosis group

EDA, SCR and % of time in skin conductance response

Figure 3A shows condition-dependent variability in EDA. In the INT group, Friedman's repeated-measures ANOVA was significant ($\chi^2 = 22.3$, $df = 3$, $p < 0.001$). Bonferroni-adjusted post-hoc tests indicated lower EDA at rest and significant increases during hypnosis and the second stress induction (both $p < 0.001$ vs baseline), as well as differences between the first and second stress inductions ($p < 0.001$). Additional details are reported in **SDC 2**.

SCR/min and % time in skin conductance response also varied in the INT group (**Figure 3B-C**), with significant Friedman's tests for SCR/min ($\chi^2 = 23.9$, $df = 3$, $p < 0.001$) and % time in SCR ($\chi^2 = 24.0$, $df = 3$, $p < 0.001$). Post-hoc comparisons showed that SCR/min increased from baseline and Stress-1 to hypnosis, then decreased from hypnosis to Stress-2, and further declined between Stress-1 and Stress-2 (all $p < 0.001$).

In the CTRL group (**Figure 3A**), repeated-measures ANOVA on EDA revealed a condition effect ($F=3.92$, $df=3$, $p=0.012$), with Bonferroni-corrected post-hoc tests showing an increase from breathing to Stress-2 ($p=0.013$). No significant condition effects were observed for SCR/min or % time in SCR (**Figure 3B-C**).

Between-group analyses showed significant condition-related differences in EDA (Friedman's ANOVA: $\chi^2=24.45$, $p<0.001$). Welch's t-tests indicated higher EDA in the INT group compared to CTRL during the intervention ($t=2.09$, $df=44.74$, $p<0.05$) and Stress-2 ($p=0.02$). For % time in SCR, Friedman's ANOVA was significant ($\chi^2=13.58$, $p<0.001$), with a between-

group difference at Stress-2, where CTRL showed a higher percentage of time in SCR than the INT group ($p=0.04$). Between-group SCR analyses indicated a decrease in the INT group at Stress-2 according to Tukey's test, but not after Bonferroni correction.

Bayesian and effect-size contrasts indicated that Δ EDA (intervention-baseline) strongly favored the INT group, reflecting increased tonic electrodermal activity ($BF_{10} = 40$; $t = -3.32$, $p < 0.001$; $d = 0.95$), while Δ SCR (Stress-2-intervention) showed a decisive reduction in phasic sympathetic activity compared with CTRL ($BF_{10} = 473$; $t = 4.30$, $p < 0.001$; $d = 1.23$)

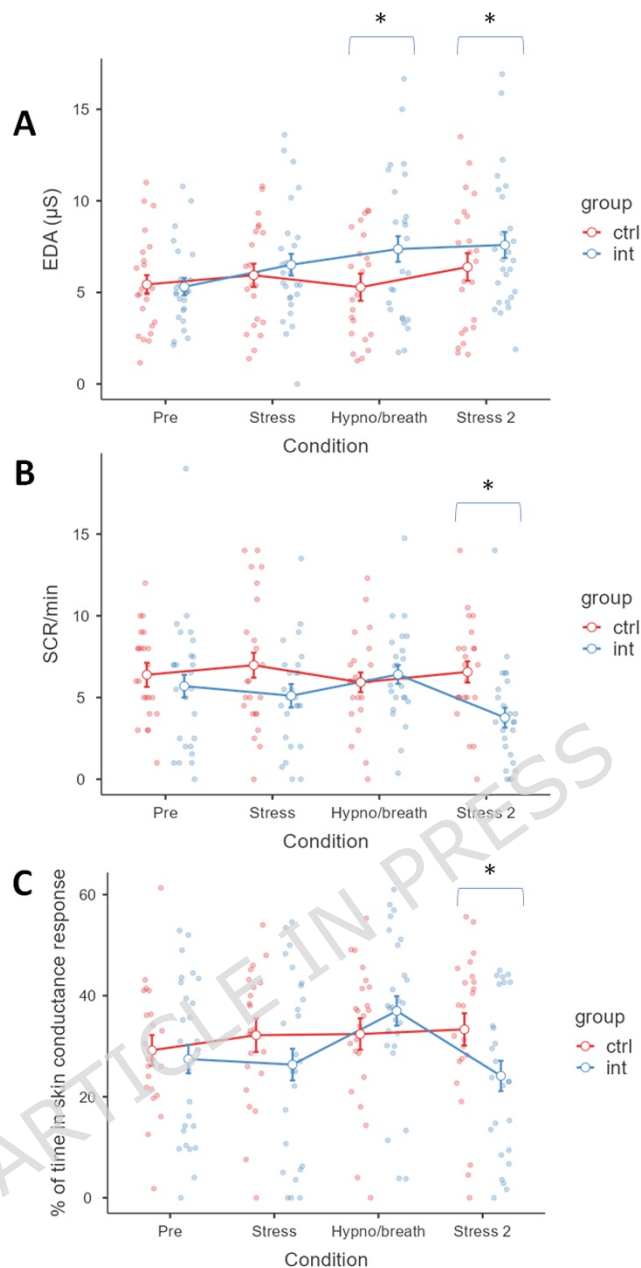


Figure 3-Physiological parameters at different time-points.

A. EDA; **B.** SCR/min; **C.** % of time spent in skin conductance response.

Abbreviations: μS , microsiemens; EDA, Electrodermal Activity; SCR, skin conductance response; %, percent; min, minute. CTRL=control group, INT=Hypnosis group. *: p-value < 0.05, **: p-value < 0.01, *** p-value < 0.001, *shown in the figure referred solely to the between INT and CTRL group analysis.

HR and RMSSD

In the INT group, HR significantly decreased between the first and second stress inductions, ($p = 0.007$, Bonferroni-corrected; **Figure 4A**). Similarly, RMSSD significantly varied across conditions ($\chi^2 = 14.1$, $df = 3$, $p = 0.0028$), with a marked increase between the first and second stress induction ($p < 0.001$, Bonferroni-corrected; **Figure 4B**).

A repeated-measures ANOVA (after Mauchly's test of sphericity, Huynh-Feldt correction and Bonferroni post-hoc adjustment) confirmed a main effect in the INT group of condition on HR ($F = 4.9$, $df = 3$, $SS = 427$, $p < 0.01$). Bayesian paired-sample comparisons further supported this finding, showing substantial evidence for HR reduction between the two stress phases ($BF_{10} = 11$, $error < 0.001$), and extreme evidence (Jeffreys' scale) for increased RMSSD ($BF_{10} = 100$, $error < 0.001$).

In contrast, the breath-focused attention CTRL group displayed on RMSSD an opposite physiological trend. Friedman's ANOVA showed a decrease in RMSSD from baseline to the second stress induction ($\chi^2 = 8.97$, $df = 3$, $p = 0.03$), confirmed by a post-hoc analysis (from 39.96 to 29.26 ms, $p < 0.05$, Bonferroni-corrected) see **Figure 4B**. Repeated-measures ANOVA on HR ($F = 4.66$, $df = 3$, $p = 0.005$) indicated an increase from rest to first stress administration ($p < 0.05$, Bonferroni corrected) and a decrease from 1st to 2nd stress induction ($p < 0.05$, Bonferroni corrected).

When both groups were analyzed together, a significant Condition \times Group interaction emerged for RMSSD ($F = 5.342$, $df = 3$, $p = 0.0016$). Specifically, during the second stress induction, RMSSD remained higher in the INT group ($M = 41.77$ ms) compared to CTRL ($M = 29.26$ ms; $t = 2.332$, $df = 47$, $p = 0.02$; Mean Difference = -12.51 ms), while HR did not significantly differ between groups. Comparing the adaptive Δ RMSSD between groups across both stress inductions yielded extremely decisive evidence (Jeffreys' scale) in favor of an increased RMSSD in the INT group difference ($BF_{10} = 792.9$, $error$

< 0.001). The frequentist test was consistent, $t(47) = 5.85$, $p < 0.001$, with a large effect size (Cohen's $d = 1.28$).

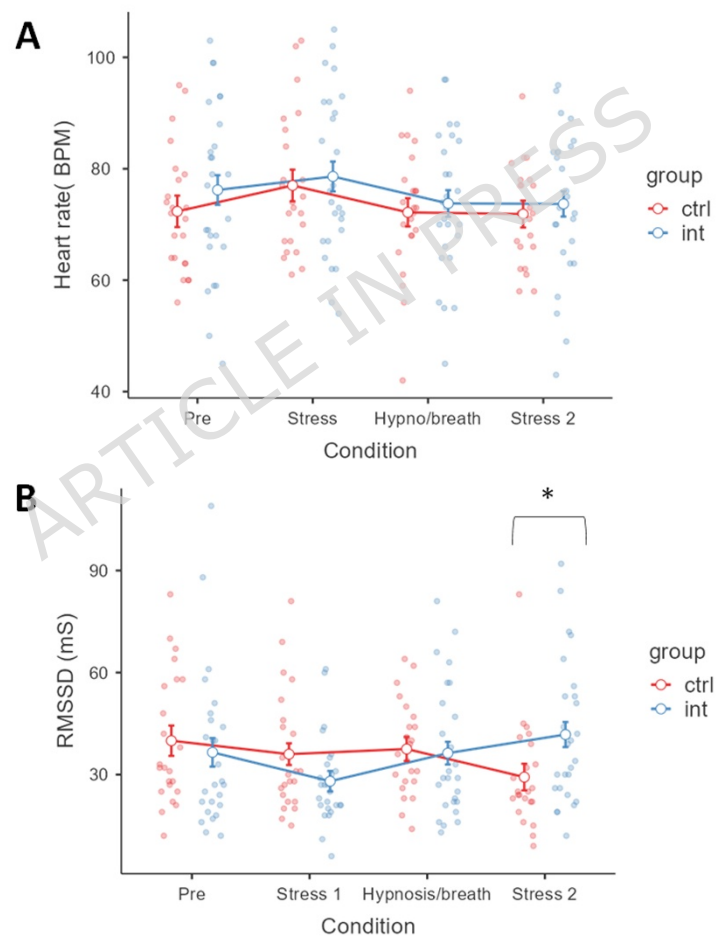


Figure 4-Additional physiological parameters at different time-points.

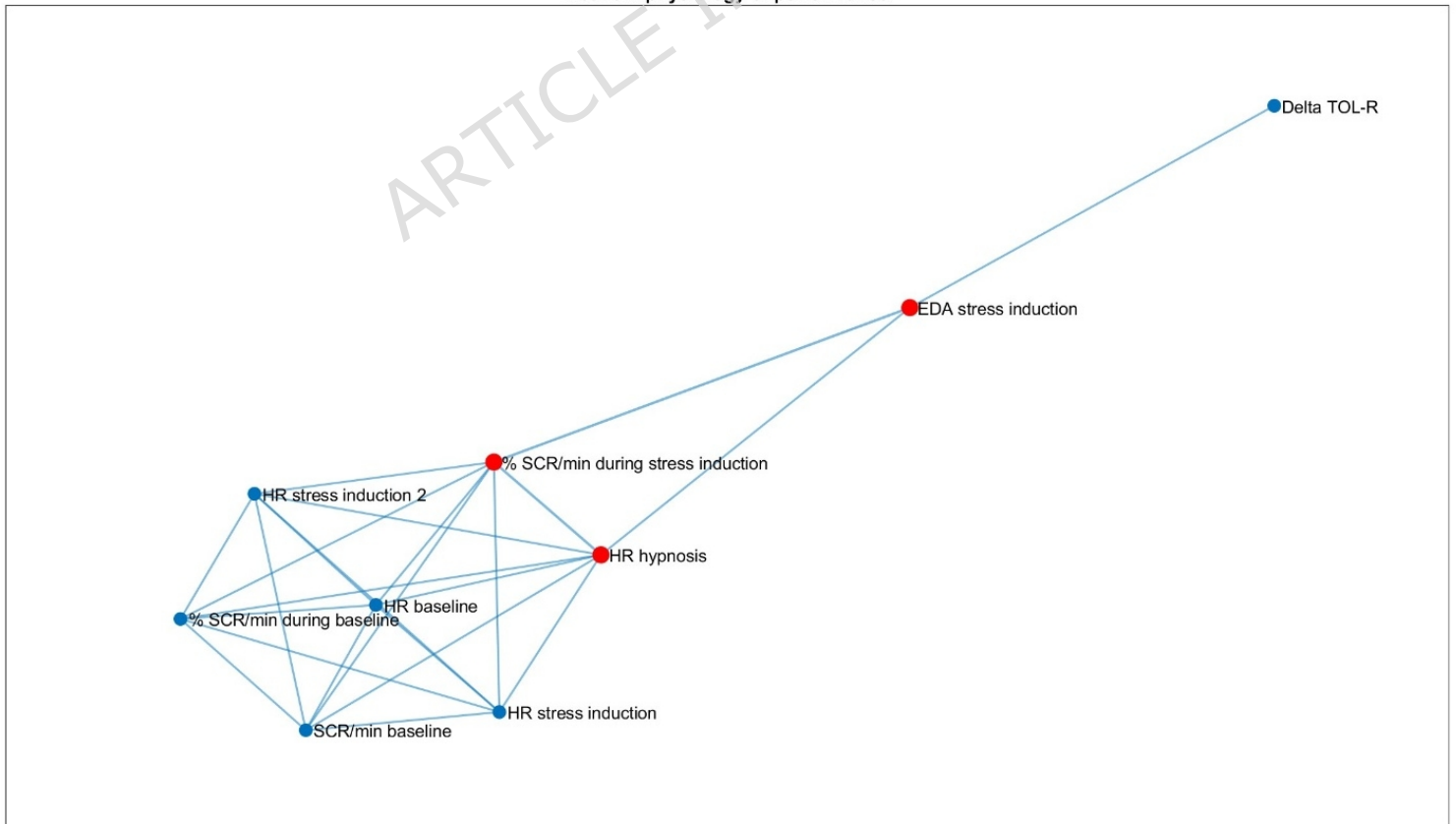
A. HR; **B.** RMSSD.

Abbreviations: HR, Heart Rate; BPM (Beats per Minute), RMSSD, measure reflecting parasympathetic tone; ms, milliseconds. CTRL=control group, INT=Hypnosis group. *: p-value < 0.05, **: p-value < 0.01, *** p-value < 0.001, *shown in the figure referred solely to the between INT and CTRL group analysis.

Network physiology of performance.

For network analysis in the INT group (see **Supplementary Data and Code**), nine variables met criteria of showing at least five moderate-to-strong correlations with other parameters and a KMO > 0.8 (overall KMO = 0.826), as shown in **Figure 5**. After applying a 0.5 correlation threshold, the spectral matrix for network analysis was constructed, and a well-connected structure,

Network physiology of performance



based on 9 nodes and 33 edges, was found, forming a single connected component. Specifically, the network showed high efficiency, with an average path length of 1.31 and a diameter of 3. Moreover, the network displayed a moderate density, highlighting a robust association between physiological and cognitive performance. Three nodes (highlighted in red in the figure) showed high betweenness centrality: EDA during stress induction, HR during hypnosis, and SCR/min during stress induction. Specifically, these three parameters are bridges/hubs playing a critical mediating role. Closeness centrality of HR during hypnosis and % of time in skin conductance response during stress induction, suggested that these nodes are central in accessing the whole network quickly.

Figure 5 - Network physiology of performance.

Network analysis across four time-points: at baseline, during stress induction (recalling negative memory), during hypnosis, and during the second stress induction (recalling for the second time the same negative memory). The following variables were included: HR at baseline, during stress induction, during hypnosis and during the second (2) stress induction; SCR/min at baseline; percent: %SCR/min at baseline and during stress induction; EDA during stress induction; and Δ TOL-R, defined as the difference between TOL-R after hypnosis and before hypnosis. Specifically, three red nodes, which are 'EDA during stress induction', '%SCR/min during stress induction' and 'HR during hypnosis', show high betweenness centrality. EDA at stress induction acts as a hub linking physiological activity to performance improvements (Δ TOL-R). The %SCR/min during stress induction and HR during hypnosis facilitate integration across different time-points, enabling efficient access to system-wide resources.

Abbreviations: TOL-R, Tower of London-Revised; EDA, Electrodermal Activity; HR, Heart Rate; %SCR/min, percentage of skin conductance response per minute, SCR/min number of Skin Conductance Responses per minute.

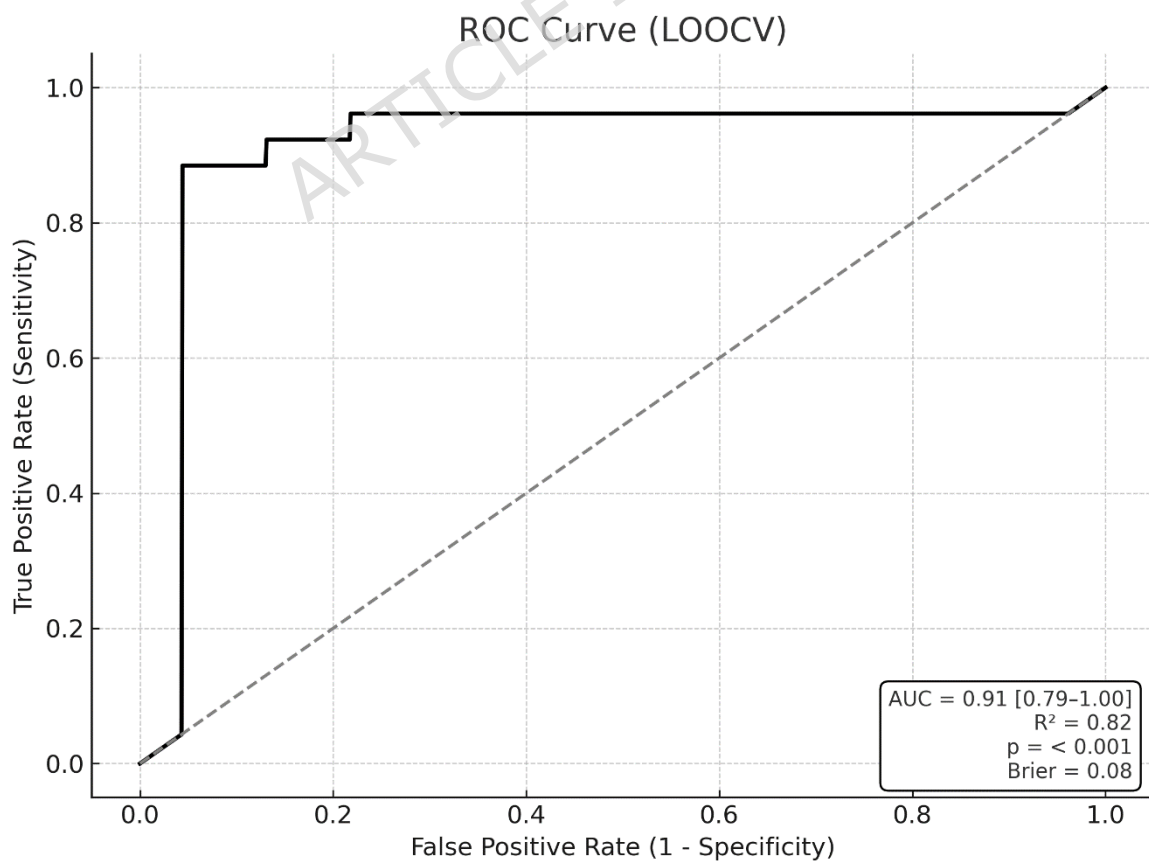
Machine Learning

Figure 6 -ROC Curve leave-one-out cross-validated (LOOCV)

ROC curve for the logistic regression model evaluated using leave-one-out cross-validation (LOOCV).

For visualization purposes only, the extreme ends of the ROC curve were smoothed. The classifier achieved excellent discrimination between the INT and CTRL groups (AUC = 0.91, 95% CI = 0.79–1.00, $p < 0.001$; McFadden's $R^2 = 0.82$). Visually, the ROC curve rises steeply toward the top-left corner, indicating high sensitivity with a low false-positive rate. The p-value reported and McFadden's R^2 referred to the multivariable logistic regression whose AUC has been validated through LOOCV. The curve remains well above the diagonal line representing chance-level performance. The low Brier score (0.08) further indicates good calibration of the predicted probabilities.

A multivariable logistic regression model fitted on the full dataset showed extremely high apparent discrimination between the INT and CTRL groups (deviance = 12.15; AIC = 22.15; BIC = 31.61; McFadden's $R^2 = 0.82$; omnibus likelihood-ratio test: $\chi^2 = 55.9$, $p < 0.001$), with an apparent accuracy of 0.96 and AUC = 0.99 (confusion matrix: TN = 25, FP = 1, FN = 1, TP = 22; N = 49; see Supplementary Data and Code). Given the limited sample size, this performance was considered potentially optimistic. Therefore, cross-validated performance was evaluated to reduce overfitting and optimistic bias (Figure 6).

Under leave-one-out cross-validation (LOOCV), classification accuracy was 0.90, sensitivity 0.885, specificity 0.913, and AUC = 0.91 (confusion matrix: TN = 21, FP = 2, FN = 3, TP = 23; N = 49; ROC curve shown in Figure 6), indicating robust discrimination while accounting for overfitting.

Changes in perceived stress (Δ VAS stress), post-intervention VAS stress, changes in heart rate variability (Δ RMSSD), and changes in skin conductance response (Δ SCR) emerged as strong discriminative predictors between the CTRL and INT groups (**see Supplementary Data and Code**).

DISCUSSION

Stress interventions are rarely evaluated across cognition, autonomic dynamics and subjective state within the same perturbation framework. The combined use, like in the present study, of frequentist statistics, Bayesian inference, network topology and predictive classification offered by Machine learning is exceptionally rare in existing stress-regulation research. Meta-analyses of established stress-regulation approaches including mindfulness^{75,76}, CBT⁷⁷ and HRV biofeedback⁷⁸ typically report modest to large improvements ($d \approx 0.2-0.8$). In contrast, in the present protocol we observed convergent modulation across cognition, autonomic regulation and perceived stress. Effect sizes were substantial across all domains: subjective outcomes ($d = 0.67$ for Δ VASa; $d = 1.67$ for Δ VASs), autonomic indices ($d = 0.95$ for Δ EDA; $d = 1.23$ for Δ SCR; $d = 1.28$ for Δ RMSSD), and cognitive performance (TOL-R, $d = 0.62$). Beyond statistical magnitude, the present study was specifically designed to test whether a single-session hypnotic protocol could enhance cognitive control, autonomic regulation and perceived stress during a stress induction.

Our results suggest that a single hypnosis session in hypnosis-naïve medical students in their final years of training was associated with significant improvements in executive function, and with reductions in both subjective and physical indices of stress and anxiety. The analysis showed the relevance of RMSSD, HR, EDA, SCR and % of time spent in stress responses as core hubs for performance under stress induction and hypnosis. Bayesian statistics and robust network analysis highlighted EDA during stress induction as key biomarker connecting stress responses and cognitive performance, while Δ RMSSD, Δ SCR and Δ VAS stress as the most important features in discriminating possible biomarkers of the treatment.

These findings align with the existing literature, which has consistently shown that high levels of stress and anxiety negatively impact executive functioning and mental well-being^{1-4,6-8,79,80}. Chronic stress has been linked to cognitive impairment, emotional exhaustion, burnout and even suicidal ideation among physicians and trainees^{2,5,7}, with interventions range from mindfulness to cognitive-behavioral therapy^{9,10,80}. Within this context, hypnosis has emerged

as a promising but understudied tool. Previous studies and meta-analyses have reported on the efficacy of hypnosis in reducing anxiety and stress^{31-33,81}, and improving resilience and well-being among healthcare workers as well as autonomic nervous system equilibrium^{37,73}. Physiological correlates of stress - such as HR, RMSSD, EDA, and SCR - are well-established markers of autonomic nervous system activity and emotional regulation^{36,36,61,82-86}, but, to our knowledge, no studies have been published on their combined modulation by hypnosis.

1) Executive Function

Regarding **Aim 1**, the intervention produced effects exceeding the a priori expectations. While the power analysis was based on an anticipated medium effect (Cohen's $d = 0.60$), the observed effect reached $d = 1.40$ in the within INT group analysis. A Bayesian factor of 1.85×10^5 provided decisive evidence according to Jeffreys' interpretative scale. This improvement could be partially explained by a task repetition and a learning effect, therefore between group analysis was conducted. The effect size was medium to large ($d = 0.62$), furthermore a Bayesian rank-based analysis yielded posterior odds of approximately 20:1 in favor of INT > CTRL under equal prior odds, indicating strong directional evidence for a treatment effect. This pattern suggests that while practice effects likely contributed to performance improvements in both groups, hypnosis accounted for an additional and substantial gain beyond learning alone.

Our TOL-R findings indicate improvements in planning and working memory, cognitive functions that are typically associated with rostralateral and dorsolateral prefrontal cortex activity^{47,50}. Although TOL-R performance can be considered a behavioral proxy of prefrontal executive engagement^{47,48,50}, and hypnosis could modulate these areas^{87,88}, we did not include neural measures in this study. Therefore, any interpretation that hypnosis directly impacts prefrontal circuitry in TOL-R should be regarded as hypothetical and tested in future neuroimaging studies.

The increased executive performance in the absence of a negative predictive value for low hypnotizability in our study may be explained by the easy hypnotic task and its tailoring according to participant's previous experience, probably doable by most people and able to improve individual executive functions within the limits of his/her hypnotic ability. This aligns with the increasing evidence that appropriate hypnotic suggestions may improve working-memory capacity even in patients with acquired brain injury regardless of hypnotizability⁸⁹.

In sum, our results (i) provide statistical evidence for a medium-to-large treatment effect on executive function, (ii) challenge the view that such effects depend solely on hypnotizability, and (iii) support the effectiveness of individualized hypnosis in enhancing executive function regardless of suggestibility.

These findings could be translated into concrete applications in domains such as clinical decision fatigue⁹⁰ and mental stress management. Enhanced executive functioning through hypnosis [and all the related psychological and physiological changes see **Discussion 2) and 3)**] may directly mitigate cognitive fatigue, which is known to contribute to sub-optimal diagnostic performance⁹¹ under time pressure⁹² – an everyday challenge faced by medical professionals, irrespective of their hypnotizability.

2) Anxiety, stress, wellbeing and Hypnotic profile

Similar effects were observed for **Aim 2**, i.e., the improvement of self-reported stress, anxiety (Bayes Factors > 20,000) and wellbeing – with 25 out of 26 participants reporting feeling better and one unchanged ($\chi^2 = 40.91$, $p < 0.001$). Contrasting this result with group CTRL, 18 referred feeling worse (a fact paralleled by Δ VAS stress), 5 no differences, but none feeling better ($\chi^2 = 22.5$, $df=2$, $p < 0.001$ compared to the assumption that feeling better, feeling

worse and equal would have shared the same probability, see **Supplementary materials and code** for further data on Bayesian analysis). Within-group analysis in the CTRL condition confirmed an increase in perceived stress levels; when VAS stress changes between groups (VAS post-VAS pre) were compared, an extreme Δ VAS post Bayesian analysis of more than 55,000 was found.

In Bayesian terms, this corresponds to $\sim 55,000:1$ odds in favor of the intervention effect –a level of evidence rarely observed in psychophysiological studies. These results exceeded previous studies and confirm the promising effects of hypnosis in medical students' wellbeing and stress modulation. In addition, we explored whether hypnotizability would modulate the observed effects. Unlike other studies emphasizing the relevance of hypnotic ability^{87,93,94}, we unexpectedly found no correlation, contributing to the ongoing debate on hypnosis as trait or state. The lack of correlation with hypnotic ability depends on two main factors: a) the administered hypnotic session was personalized and included a very easy task, doable for most people; b) though high hypnotizable subjects may show better results, relevant effect may be obtained by 85-90% of general population⁹⁴, while other studies have questioned the relevance of hypnotic suggestibility in clinical contexts⁹⁵. In this regard, a dynamic interaction between trait and state seems to be more reasonable^{96,97}, where high hypnotizability is relevant for the most difficult hypnotic tasks, like analgesia or gag reflex control⁹⁶. Accordingly, behavioral attempts to improve hypnotizability have provided inconsistent results, while the neuromodulation of the left dorsolateral prefrontal cortex (L-DLPFC) by transcranial brain stimulation can transiently enhance hypnotizability by strengthening L-DLPFC-dACC (dorsal Anterior Cingulate Cortex) connectivity⁹⁸. Overall, hypnotic responsiveness depends on several factors besides suggestibility, emphasizing the value of tailoring interventions according to subject's experience and needs^{38,97,99,100}. Our personalized hypnosis, using individually crafted suggestions rather than standard scripts, was an easy task, probably feasible for most people, aligning interventions with the individual's inner world.

Although speculative, aligning hypnotic suggestions with the individual's subjective inner experience may functionally resemble a transient modulation

of prefrontal control processes, potentially analogous to L-DLPFC neuromodulation.

Furthermore on a neuropsychological standpoint, it may reflect the dynamic interaction between central executive, salience, and default mode networks¹⁰¹. Further research should clarify the link between hypnotizability and outcome, since hypnotizability scales are based on the concept of suggestibility, a *leitmotif* in the history of hypnosis still remaining questionable over one century from its introduction^{101,102}.

3) and 4) Physiological Indicators, Network Connectivity and Machine Learning

Regarding **Aim 3 is concerned**, hypnosis did not prevent physiological arousal but promoted more efficient resource mobilization. We observed increased tonic EDA, decreased SCR (phasic component of sympathetic activity), and reduced time in stress response states, particularly during the second stress induction, indicating an effective stress management. This pattern has previously been observed in studies reporting opposite shifts in EDA and SCR following hypnosis⁷⁴.

Comparing Δ SCR, Δ RMSSD, and Δ EDA between groups, a clear divergence in autonomic response patterns emerged between groups. Participants in the INT group showed a challenge-like pattern, characterized by increased sympathetic tonic activity, enhanced parasympathetic activation, and reduced sympathetic phasic responses. This combination suggests an adaptive mobilization of resources rather than a defensive reaction^{103,104}.

In contrast, the CTRL group exhibited a threat-like physiological profile, featured by: a) reduced parasympathetic between the stress inductions; b) increased tonic EDA from baseline breathing to the second stressor; c) no decrease in SCR and HR between the two stress phases. This autonomic pattern – together with increased VAS ratings of stress and decrease of perceived wellbeing – points toward a defensive, resource-conserving state rather than active coping.

At first glance, the increase in tonic EDA observed in the INT group may appear counterintuitive, as hypnosis is often associated with relaxation. However, hypnosis does not necessarily suppress autonomic arousal; rather, it may reorganize autonomic dynamics toward a more efficient and adaptive pattern. In the present study, increased tonic EDA co-occurred with decreased phasic sympathetic activity (SCR), increased parasympathetic modulation (RMSSD), reduced subjective stress, and improved executive performance.

One possible explanation is that hypnosis facilitated a more vivid, focused, and engaged processing of the recalled experience, thereby increasing tonic sympathetic activation while simultaneously reducing maladaptive stress reactivity. This pattern is consistent with a challenge-like physiological state, characterized by sustained resource mobilization and flexible autonomic regulation, rather than a defensive or threat-related response. Thus, increased EDA in this context likely reflects adaptive engagement rather than heightened distress.

Our results suggest that SCR is crucial for initiating an adaptive physiological mobilization of resources (as indicated by closeness centrality in the network and no change in the CTRL group), whereas EDA, the tonic component, is essential for sustaining the utilization of these resources over the long term (as reflected by improvements in TOL-R scores).

The initial decrease in parasympathetic activity during the first stress induction in both groups aligns with prior findings linking negative emotions to reduced parasympathetic tone¹⁰⁵, while higher parasympathetic activity correlates with lower rumination and anxiety, reflecting emotional regulation¹⁰⁶ and higher flexibility⁸². Elevated HR after stress indicates residual anxiety as well^{85,86}.

The HR decrease and RMSSD increase, alongside EDA and SCR modulation after hypnosis, aligns with biopsychosocial models of arousal regulation^{103,104,107}. Furthermore, in the INT group, the significant negative correlation between Δ EDA and Δ TOL-R ($r = -0.556$, $p = 0.03$, $df = 24$) suggests that participants showing more controlled increases in EDA also exhibited the greatest cognitive improvements. This supports the notion that a better

performance is driven by regulated resource mobilization rather than by arousal suppression, a fact in line with Bayesian models of energy allocation under cognitive load ¹⁰⁸.

The network analysis confirmed EDA during negative memory recall as a central node linking stress responses and executive function. Closeness centrality highlighted HR during hypnosis and SCR post-hypnosis as key connectors in emotional and cognitive regulation. Although RMSSD was excluded due to overlap with HR, combined HR, RMSSD, and EDA changes indicate improved autonomic regulation post-intervention. The position of EDA as a central node highlights the sympathetic system's role as a core mechanism in adaptive stress management, providing a novel, actionable target for stress intervention.

Overall, the classification results in the logistic regression and LOOCV validation reinforce and extend the inferential findings. The classifier was not intended for baseline prediction but to test whether a compact psychophysiological signature of the intervention exists; the autonomic markers (\downarrow SCR, \uparrow RMSSD) combined with subjective stress reduction (Δ VASs) provide convergent signals that reliably distinguish INT from CTRL with high accuracy and good probability calibration. Although exploratory, these results strengthen the plausibility of a specific hypnotic effect on stress-regulation mechanisms, support the development of more mature predictive and mechanistic models (e.g., SEM or dynamical approaches) to be tested in larger samples with independent validation and underline the relevance of investigate stress through a wide range of modalities¹⁰⁹ (avoiding simplistic interpretation).

These findings align with stress physiology, indicating a shift from threat to challenge states ¹⁰⁴. Strong to extreme Bayesian factors for HR, RMSSD and EDA as well for Δ before and after hypnosis further support that hypnosis may help reframe situations as manageable challenges, possibly by enhancing neural efficiency.

Limitations and Future Directions

While promising, this study has some limitations. Neuroimaging (e.g., fMRI, EEG) could clarify neural mechanisms¹¹⁰, particularly the involvement of the PFC, underlying hypnosis-related changes in the relationship between executive function and autonomic regulation. Another limitation is the monocentric nature of the study which may restrict generalizability. Although causal models such as structural equation modeling could theoretically clarify directional pathways among physiological, cognitive, and subjective variables, the sample size of this study was not sufficient for SEM. Future studies with larger samples may test such models explicitly. Longitudinal designs are also needed to assess the durability of effects on cognition and well-being. Additionally, exploring different hypnotic protocols, including self-hypnosis, could further define its potential for enhancing executive function, stress reduction, and resilience, supporting its integration into medical education and stress management programs. The participants' subjective choice of stressors during the recall of past negative medical education experiences, while representing a strength of the present study, should be complemented by standardized arousal and valence ratings in future research. In addition, the six-month temporal separation between the within-subject phase and the CTRL group assessment represents a potential time-related confound and should be considered when interpreting between-group comparisons. Finally, a further limitation concerns possible learning effects due to task repetition. Although this issue was mitigated using ANCOVA, future studies could further address it by increasing the interval between test and re-test assessments. Future studies should investigate the interaction between hypnotizability, motivation and task complexity. Furthermore, while focusing attention on an idea is an integral component of hypnosis, future studies should also include a control group exposed to positive memory recall without hypnosis to disentangle the specific effects of hypnotic induction from those of pleasant imagery. Given the magnitude of physiological and psychological outcomes, we strongly encourage integrating highly promising interventions¹¹¹⁻¹¹³ with hypnosis to enhance stress management in healthcare. It is very likely that hypnosis, together with other approaches such as biofeedback and meditation, may have synergistic effects, promoting improved well-being in both current and future medical doctors. Finally, a particularly interesting direction for

future research would be to explore the impact that we observed on executive functions and emotional regulation in various contexts such as during examinations²⁹, surgical procedures (where stress decreases performance¹¹⁴), high-pressure situations, and across different stages of expertise acquisition.

Conclusion

In the clinical setting, increasingly dominated by concerns about burnout, cognitive fatigue, and emotional distress, this study offers a scientifically grounded, non-invasive, scalable, rapid and promising intervention. Our findings support that a single personalized hypnosis session can enhance executive function, resilience, largely reduce stress and anxiety, and improve emotional regulation in medical students naïve to hypnosis, regardless of hypnotizability in this sample. EDA emerged as a key biomarker linking stress regulation with cognitive performance, supporting hypnosis as a scalable intervention for stress management. Changes in RMSSD, SCR, VAS Stress are biomarkers of hypnosis regulation and classified participants with excellent categorization. These results encourage further studies to better understand neural mechanisms and long-term effects, paving the way for integrating hypnosis into medical education and resilience training.

Author contributions:

All authors directly accessed and verified the underlying data reported in the manuscript and take full responsibility for its submission and content.

All have approved the final version for publication and agree to be accountable for all aspects of the work, ensuring that any questions related to its accuracy or integrity are appropriately investigated and resolved.

Substantial contributions to the conception or design of the work: **LQ**

Acquisition, analysis, or interpretation of data: **LQ, AB, CT, MO, EF**

Graph, Machine learning and Bayesian analysis: **LQ**

Drafting of the manuscript: **LQ, AB, EF**

Critical revision for important intellectual content: **LQ, AB, EF, GZ, ES, PN**

Data availability statement: Preprocessed datasets used for all statistical, network, and machine-learning analyses are available to ensure full computational reproducibility of the reported results. All materials are provided in a single compressed archive (ZIP), which includes: (i) preprocessed physiological and behavioral data underlying all analyses, (ii) analysis scripts for network analysis and machine-learning classification, and (iii) derived feature-level datasets used for the logistic regression and cross-validation procedures.

Statistical analyses conducted in the jamovi environment (including Bayesian analyses with the jsq module and effect size estimation with pamlj) can be fully reproduced using the provided datasets and the analysis specifications described in the Methods section, while the part elaborated in Python has been added as script.

Raw physiological recordings are not available; however, all results reported in the manuscript can be independently reproduced using the shared preprocessed data and materials. For further information regarding the datasets and materials, please contact the corresponding author luca.queirolo@unipd.it

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° These authors have contributed equally to the manuscript

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