

Unraveling the role of neurotransmitters in stress buffering: A comparative study of individuals with strong and weak entrepreneurial intentions

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1. Introduction

Stress, caused by an imbalance between situational demands and coping resources (Agorastos and Chrousos, 2022; Ahmad et al., 2022), can negatively affect entrepreneurs' well-being and performance (Drnovšek and Slavec Gomezel, 2022; Lerman et al., 2021). The entrepreneurial context constantly exposes individuals to taxing situations: decision-making is time-sensitive (Lévesque and Stephan, 2020; Wood et al., 2021), occurs under high complexity (Fisher et al., 2020; Hmieleski and Cole, 2022), and involves substantial uncertainty (Bort et al., 2024; Uhl-Bien, 2021). These stressors can lead to harmful outcomes, including coronary heart disease (Kivimäki et al., 2012), psychological distress (Freeman et al., 2019), and poor physical health (Reid et al., 2018). Such effects may explain why many individuals exit entrepreneurial careers (Bernard and Dubard Barbosa, 2016; Corner et al., 2017).

Yet some entrepreneurs persist despite stress. Research suggests two explanations: some develop coping mechanisms over time (Nicolaou et al., 2008; Greene et al., 2014), while others who naturally experience less stress self-select into entrepreneurship (Bernard and Dubard Barbosa, 2016; Corner et al., 2017). Biological studies have found that genetic variables affect entrepreneurial intentions and entry (Nicolaou et al., 2008), and hormones like testosterone are positively associated with entrepreneurial entry (Greene et al., 2014). However, these studies do not explain the physiological mechanisms through which entrepreneurs cope with stress. Cortisol levels indicate perceived stress (Freeman et al., 2019; Koren and Korn, 2021), while dopamine regulates reward sensitivity during stressful situations (Wei et al., 2023; Ahmed et al., 2022). Although entrepreneurs have elevated stress markers (Donovan et al., 2022), we know little about how stress impacts the entrepreneurial mindset.

A substantial body of research outside of entrepreneurship has examined stress and psychological outcomes such as optimism (Arslan and Yildirim, 2021; Chang et al., 2000) and shown that pharmacological agents targeting dopaminergic and noradrenergic pathways can influence optimism (Eyding et al., 2010) and risk-taking (Rahman et al., 2006). However, these relationships have not been examined within the entrepreneurial context, where entrepreneurs face a distinctive combination of uncertainty, personal financial exposure, and identity-relevant challenges that may amplify or alter these mechanisms. Our study therefore tests whether the well-documented stress-buffering role of neurotransmitters operates differently depending on individuals' entrepreneurial intentions.

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We focus on two critical mindset characteristics: optimism (expecting positive outcomes despite uncertainty) and risk propensity (tendency to enter situations with unknown outcomes) (Greene et al., 2014; Donovan et al., 2022). Combined with entrepreneurial intentions, these characteristics drive entrepreneurial action (Sharma et al., 2021). We ask three research questions: (1) How does stress response impact optimism and risk propensity? (2) Why do some individuals buffer their mindsets from stress better than others? (3) Do entrepreneurial intentions affect individuals' stress-buffering capacity?

To address these questions, we build on reinforcement sensitivity theory (Corr, 2008; Gray, 1970) and test a model using a double-blind, placebo-controlled study. We used methylphenidate (MPH) to enhance dopaminergic activity and reboxetine (RBX) to enhance noradrenergic activity in 119 participants, then induced stress using decision-making tasks. A qualified nurse administered these agents under strict protocols, given potential risks including cardiac and psychiatric effects (Koren and Korn, 2021; Wei et al., 2023).

This study makes three contributions. First, we demonstrate how stress response negatively impacts critical entrepreneurial-mindset characteristics—optimism and risk propensity—extending research on why stress undermines entrepreneurial functioning (Ahmed et al., 2022; Rauch et al., 2018). Second, we show that enhanced dopaminergic and noradrenergic activity can buffer these negative effects, explaining heterogeneity in entrepreneurs' stress responses. Prior research has examined direct effects of neurochemicals on entrepreneurial behavior (Nicolaou et al., 2011; Rietveld et al., 2021); we extend this by exploring their moderating role. Third, we find that entrepreneurial intentions amplify this buffering effect, suggesting that intentions may interact with neurochemical processes to help preserve the mindset characteristics needed to enact them.

2. Theoretical framework and hypotheses

2.1. The cortisol stress response and Entrepreneurial Characteristics

From a psychological perspective, stress refers to a relationship between an individual and the environment appraised as potentially harmful or challenging (Lazarus and Folkman, 1984). This cognitive appraisal triggers physiological responses, including cortisol secretion (Dedovic et al., 2009). Cortisol is produced after acute stressors and is involved in chronic stress states (Kudielka et al., 2009). Salivary cortisol measurements, particularly the area under the curve (AUC), reliably capture stress response in both laboratory and daily life (Pruessner et al., 2003).

The entrepreneurial mindset combines skills, including cognitive style, alertness, and coping abilities that enable adaptation to changing environments (Haynie et al., 2010). Critical to this mindset are optimism and risk propensity (Greene et al., 2014; Kuratko et al., 2021). Optimism—a form of positive affect leading individuals to expect positive outcomes even without a rational basis (Hmieleski and Baron, 2009)—is crucial for entrepreneurs striving toward goals despite uncertain markets (Lowe and Ziedonis, 2006), reentering markets after failure (Hayward et al., 2010), and maintaining well-being (Fisher et al., 2020). Highly optimistic individuals attribute negative events to external, situational causes, reducing grief from failure and maintaining motivation (Jenkins et al., 2014).

Risk propensity—the tendency to enter or avoid situations with unknown outcomes (Donovan et al., 2022)—is associated with entrepreneurial entry (Antoncic et al., 2016), alertness to new ideas (Cui et al., 2016), and venture performance (de Carolis et al., 2009). Combining these characteristics captures aspects of the entrepreneurial mindset across time: optimism is future-oriented (Carver et al., 2010), while risk propensity is present-oriented (Jochemczyk et al., 2017).

The cortisol stress response may impact these characteristics. Stress undermines optimism by promoting negative interpretations of ambiguous situations (Neta et al., 2017) and increasing susceptibility to negative information while blunting responses to unexpected rewards (Garrett et al., 2018; Ironside et al., 2018). Stress may reduce risk propensity by increasing risk aversion; individuals under stress overestimate risk probability and take more cautious approaches (Cahlíková and Cingl, 2017; Wang et al., 2021).

Hypothesis 1. The greater an individual's cortisol stress response, the lower their (a) optimism and (b) risk propensity.

2.2. Neurochemistry buffering the effect of stress

When individuals face threats, cortisol reaches the brain and interacts with neural structures, affecting information processing, memory, and behavior (James et al., 2023; Kim et al., 2015). The brain regions most closely associated with stress response are dopaminergic and noradrenergic pathways. Dopamine and noradrenaline—neurotransmitters involved in cell communication (Edwards, 2007)—play essential roles in scanning and detecting stressful and rewarding events (Goldstein, 2003).

Reinforcement sensitivity theory (Corr, 2008) provides a framework linking biology, behavior, and cognition. Two main mechanisms are relevant: the behavioral activation system (BAS), activated by reward expectancy and associated with dopaminergic neurons (Chau et al., 2018), drives approach behavior. Individuals with high BAS sensitivity have a greater desire for rewards and are more proactive (Geenen et al., 2016). The behavioral inhibition system (BIS), responsible for avoidance in uncertain situations (McNaughton and Corr, 2004), is associated with noradrenergic activity (Morilak et al., 2005). Higher BIS sensitivity produces a more intense physiological stress response (Espinoza Oyarte et al., 2021).

Therefore, while cortisol may decrease optimism and risk propensity, dopamine and noradrenaline may dampen this impact. Dopamine enhances reward sensitivity and positive affect (Sharot et al., 2012a), while noradrenaline modulates attention during stress (Ross and Van Bockstaele, 2020). Higher levels of these neurochemicals may counteract cortisol's negative cognitive effects.

Hypothesis 2. The negative relationship between an individual's cortisol stress response and optimism is less negative for those higher in (a) dopaminergic activity and (b) noradrenergic activity than those lower in these neurochemicals.

Hypothesis 3. The negative relationship between an individual's cortisol stress response and risk propensity is less negative for those higher in (a) dopaminergic activity and (b) noradrenergic activity than those lower in these neurochemicals.

2.3. Entrepreneurial intentions and buffering stress

Entrepreneurial intentions—the cognitive state preceding business startup decisions (Krueger et al., 2017)—may amplify neurochemical buffering effects. Strong intentions help explain self-selection into entrepreneurship (Fisher et al., 2020), engagement in entrepreneurial activities (Cui et al., 2021), and persistence in the face of obstacles (Caliendo et al., 2020).

Biological models highlight how entrepreneurial intentions emerge from neural processes affecting cognition and behavior (Sharma et al., 2021). It is important to note that entrepreneurial intentions are fundamentally a cognitive construct capturing an individual's planned career orientation (Krueger et al., 2017), and we do not claim that intentions directly measure biological differences. However, given the substantial overlap between those with strong intentions and those who enter entrepreneurship, and given evidence that certain genetic attributes are associated with entrepreneurial entry, it is plausible that some of these attributes are more prevalent among those with strong intentions. Two attributes are relevant. First, entrepreneurs have more or stronger dopamine receptor genes (Nicolaou et al., 2011; Krammer and Gören, 2021), making their brain systems more sensitive to dopamine (Rádosi et al., 2021). Second, entrepreneurs differ in monoamine oxidase (MAO) capability—the enzyme that breaks down dopamine and noradrenaline (Frydman et al., 2011a). Lower MAO means slower clearance, giving neurotransmitters longer to affect the brain (Zhong et al., 2009).

Thus, while cortisol response may be similar across individuals, effects on cognition may differ. In those with stronger entrepreneurial intentions, higher dopamine and noradrenaline may increase positive information recall (Harmer et al., 2004) and decrease susceptibility to negative beliefs about the future (Sharot et al., 2012b), counteracting cortisol's effects on optimism. Low MAO is also linked to greater financial risk-taking (Frydman et al., 2011b).

Hypothesis 4. The buffering effect of (a) dopaminergic activity and (b) noradrenergic activity on the relationship between the stress response and optimism is greater for individuals with stronger entrepreneurial intentions than for those with weaker entrepreneurial intentions.

Hypothesis 5. The buffering effect of (a) dopaminergic activity and (b) noradrenergic activity on the relationship between the stress response and risk propensity is greater for individuals with stronger entrepreneurial intentions than for those with weaker entrepreneurial intentions (Fig. 1).

3. Methods

3.1. Sample and design

We recruited 120 university students from local universities by promoting the study to entrepreneurship and management classes and the general student population. We excluded one individual from the analysis for invalid responses on the risk-propensity scale (similarly rating regular and reversed items), leaving $n = 119$. We recruited individuals varying in entrepreneurial intentions: some from entrepreneurship programs actively working on venture ideas; others from the general student population. Students were homogeneous in age, marital status, and educational background, and lacked prior entrepreneurial experience, reducing potential confounds (Klimas et al., 2021).

The Ethics Committee of the Canton of Zurich approved the study, consistent with the Declaration of Helsinki. Participants

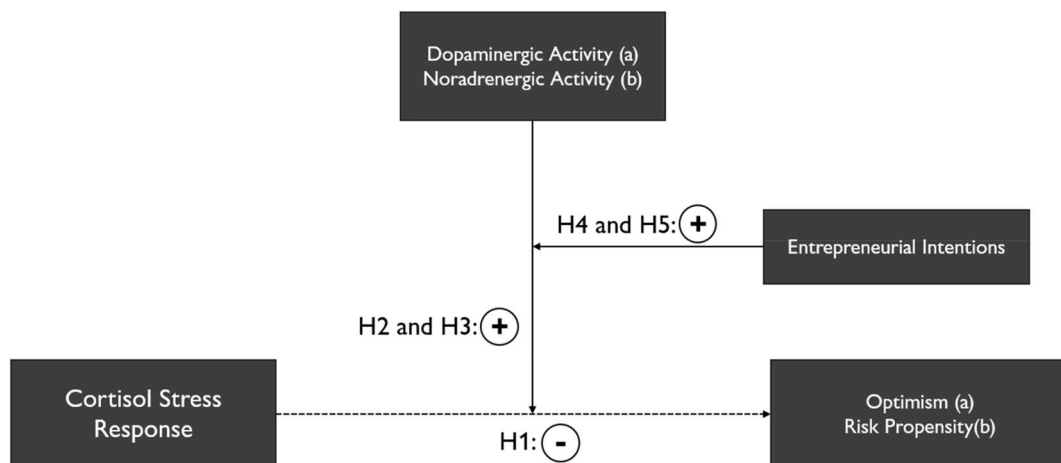


Fig. 1. Hypothesis framework.

provided informed written consent. A professional electrocardiogram screened participants, excluding those with present or past medical and psychiatric disorders, and a professional cardiologist conducted medical examinations. A qualified nurse administered doses within clinical ranges (20–40 mg MPH; 4–12 mg RBX) and remained present throughout. A medical doctor was on standby, and participants received a 24-h emergency number.

Using a double-blind, placebo-controlled, between-subjects design, we randomly assigned participants to one of three experimental groups: (1) placebo ($n = 39$), (2) MPH (35 mg, Ritalin, $n = 40$), or (3) RBX (8 mg, Edronax, $n = 40$).

3.2. Procedure

All participants arrived at the laboratory at 9:00 a.m., controlling for exogenous effects and potential daily variations in drug responses. After baseline measures, participants received their assigned condition under double-blind conditions. Following drug absorption (~90 min for both agents), participants completed a battery of decision-making tasks designed to induce stress: (1) a value and salience task, (2) a digit-span memory task, (3) a multiple price list task, (4) a salience to threat task, (5) an adaptive risk task, and (6) an effort-discounting task. Similar decision-making tasks have been shown to evoke psychophysiological stress responses (Agren et al., 2019; Studer and Clark, 2011). We collected salivary cortisol at three time points (baseline, before the first task block, and after the first task block) to calculate cortisol AUC (Pruessner et al., 2003). During the session, we drew a blood sample to capture participants' drug responses based on plasma concentrations. Post-stress measures assessed optimism and risk propensity. At the end of the experiment, participants waited 30 min to ensure no drug-related side effects before receiving compensation (30 CHF [approximately, USD 38] per hour plus a performance-based bonus) Fig. 2.

3.3. Measures

Cortisol AUC. We measured salivary cortisol using a commercially available chemiluminescence immunoassay with high sensitivity (IBL International, Hamburg, Germany). Samples were frozen immediately after collection and kept frozen until analysis. A lab professional centrifuged the saliva at 3,000 rpm for 5 min. The intra- and interassay coefficients for cortisol were below 6% and 10%, respectively. We determined each participant's cortisol stress response by calculating the cortisol AUC for all three time points (Pruessner et al., 2003).

Optimism. We assessed optimism using the Self-Efficacy-Optimism-Pessimism Questionnaire developed by Scholler et al. (1999). On a scale from 1 (not true) to 4 (true), individuals rated their optimism about the future and whether they always saw the positive side of life. We calculated the mean of the items' scores ($\alpha = 0.73$).

Risk Propensity. We measured risk propensity using the six-item questionnaire developed by Zhao et al. (2005). Participants indicated agreement on a 5-point Likert scale (1 = disagree completely to 5 = agree completely). We averaged the six items ($\alpha = 0.60$).

Entrepreneurial Intentions. We measured entrepreneurial intentions using the Entrepreneurial Intention Questionnaire (Liñán and Chen, 2009). The instrument contains six statements written in the first person describing plans or behaviors about entrepreneurship (e.g., "My professional goal is ...", "I have the firm intention to ..."). Respondents rated the extent to which each statement applied on a scale of 1 (total disagreement) to 7 (total agreement). Sum scores produced an entrepreneurial-intentions score for each individual.

Dopamine and Noradrenaline. In our primary analyses, we used binary dummy variables indicating the presence (1) or absence (0) of MPH and RBX treatment. We acknowledge that this dichotomous operationalization does not capture individual variation in drug response, and that both influence multiple neurochemical pathways beyond their primary targets. MPH primarily inhibits dopamine reuptake but also affects noradrenaline transporters (Heal and Pierce, 2006), while RBX primarily inhibits noradrenaline reuptake (Millan et al., 2001). Consequently, the observed effects may partially reflect changes in attention, arousal, or cognitive effort rather than purely specific neurotransmitter mechanisms. To address concerns about individual differences in drug response, we conducted robustness checks replacing the dummy variables with continuous measures of blood plasma levels of MPH and RBX, which account for

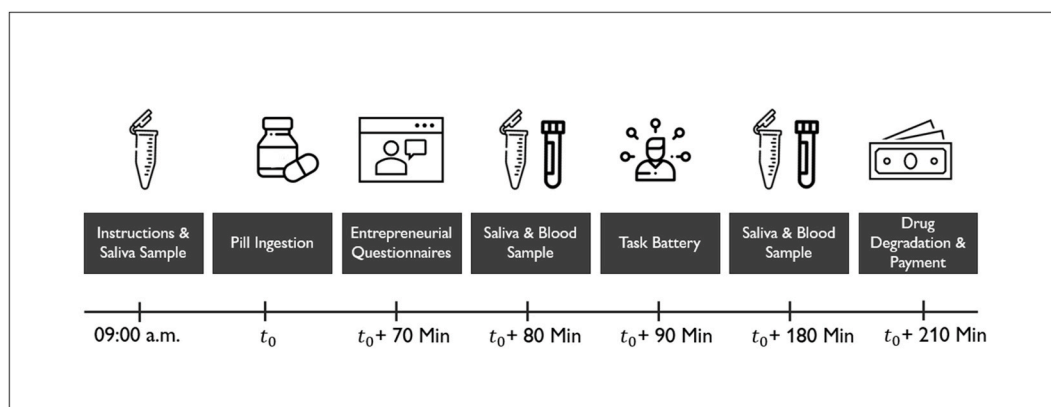


Fig. 2. Experimental design.

individual variation in drug absorption and metabolism.

Controls. We included age and gender (1 = woman, 0 = man) as controls since risk propensity decreases with age (Hincapié, 2020) and women's risk preferences differ from men's (Charness and Gneezy, 2012).

3.4. Analysis

We estimated all models using robust linear regression via the `rlm` function from the MASS package in R (Venables and Ripley, 2002), which employs M-estimation with Huber's weighting function. This approach iteratively reweights observations to reduce the influence of outliers, providing coefficient estimates that are more resistant to violations of normality and heteroscedasticity than ordinary least squares (OLS). We report robust standard errors and, as a measure of model fit, we calculate a pseudo- R^2 defined as one minus the ratio of the weighted residual sum of squares from the fitted model to the weighted total sum of squares from the intercept-only model (see table notes for Tables 2 and 3). Model 1 tested controls; Model 2 added main effects; Model 3 added two-way interactions (H2-H3); Model 4 added three-way interactions (H4-H5). An analogous model sequence (Models 5–8) was estimated for risk propensity.

4. Results

Table 1 presents descriptive statistics and correlations. Most participants were men (55%) with an average age of 22.05 years ($SD = 2.68$). More than 80% had only graduated from high school, 17% had a bachelor's degree, and 3% had earned a master's degree. To validate our measure of entrepreneurial intentions, we compared scores between students in management or entrepreneurship classes ($n = 53$, $M = 12.23$, $SD = 3.58$) and individuals from other classes ($n = 67$, $M = 6.26$, $SD = 2.39$), revealing a significant difference ($t = -10.326$, $p < 0.001$). Optimism had a positive relationship with risk propensity ($r = 0.26$, $p = 0.014$).

H1: Stress and Entrepreneurial Characteristics. Table 2 presents the results. In Model 2, the cortisol stress response had a significant negative effect on optimism ($\beta = -0.04$, $p = 0.018$), supporting H1a. The effect on risk propensity showed that higher noradrenergic activity buffered the negative effect ($\beta = 0.38$, $p = 0.018$), providing support for the stress-risk propensity relationship.

H2-H3: Neurochemical Buffering. Model 2 demonstrated that the interaction between cortisol stress response and high dopaminergic activity ($\beta = 0.06$, $p = 0.018$) and noradrenergic activity ($\beta = 0.05$, $p = 0.036$) had significant positive effects on optimism. These findings support H2a and H2b, indicating that higher dopaminergic and noradrenergic activity made the negative relationship between cortisol stress response and optimism less negative. For risk propensity, noradrenergic activity buffered cortisol's negative effect ($\beta = 0.38$, $p = 0.018$), making the relationship between cortisol stress response and risk propensity less negative, supporting H3b. However, dopaminergic activity did not significantly buffer the cortisol-risk propensity relationship, so H3a was not supported (Fig. 3).

H4-H5: Entrepreneurial Intentions Moderating Buffering. In Model 4, we found a significant three-way interaction effect of dopaminergic activity, cortisol stress response, and entrepreneurial intentions on optimism ($\beta = 0.01$, $p < 0.05$), as well as a marginally significant three-way interaction effect of noradrenergic activity, cortisol stress response, and entrepreneurial intentions on optimism ($\beta = 0.01$, $p < 0.10$). These findings support H4a and marginally support H4b, indicating that dopaminergic and noradrenergic activity have greater buffering effects on the stress-optimism relationship in individuals with stronger entrepreneurial intentions. Model 7 shows a marginally significant positive interaction effect of noradrenergic activity and cortisol stress response on risk propensity ($\beta = 0.27$, $p < 0.057$), providing marginal support for H5b. H5a was not supported.

Robustness Checks. To control for differences in subject-specific drug responses, we replaced treatment dummy variables with blood plasma levels of MPH and RBX (Table 3). Results aligned with the main findings: significant positive interaction effects of blood plasma levels of both MPH ($\beta = 0.0005$, $p < 0.10$) and RBX ($\beta = 0.0001$, $p < 0.05$) with cortisol stress response in explaining optimism, and a significant positive interaction between blood plasma RBX ($\beta = 0.0007$, $p < 0.05$) and cortisol stress response in explaining risk propensity.

5. Discussion

This study provides experimental evidence suggesting that pharmacologically enhanced dopaminergic and noradrenergic activity can buffer stress effects on the entrepreneurial mindset. Three key findings emerge.

First, cortisol stress response reduces optimism and risk propensity, extending research on entrepreneurial stress (Ahmed et al., 2022; Rauch et al., 2018) by identifying specific mindset characteristics affected. Optimism is linked to opportunity recognition and market reentry after failure (Lowe and Ziedonis, 2006; Hayward et al., 2010), while risk propensity is associated with entrepreneurial entry (Antoncic et al., 2016) and alertness to new ideas (Cui et al., 2016). By showing that stress undermines these characteristics, our findings identify one cognitive pathway through which stress may translate into reduced entrepreneurial activity—decreased expectations of positive outcomes (McCann and Folta, 2012) coupled with increased risk aversion (Hilmerston and Papaioannou, 2015) may decrease alertness and entrepreneurial entry.

Second, enhanced dopaminergic and noradrenergic activity buffers these negative effects, offering one explanation for heterogeneity in entrepreneurs' stress responses. While a broader literature has established these relationships in general populations (Eyding et al., 2010; Rahman et al., 2006), our study demonstrates that these buffering effects operate in the entrepreneurial context. Building on associations between dopamine genes and entrepreneurial tendency (Nicolaou et al., 2011; Rietveld et al., 2021), we show that MPH treatment buffered optimism from stress, while RBX treatment buffered both optimism and risk propensity. Because both

Table 1

Descriptive statistics and correlations.

	Mean	SD	Min	Max	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Optimism	2.32	0.54	1	3	1.00													
2. Risk Propensity	17.75	3.29	10	27	0.26**	1.00												
3. Entrepreneurial Intentions	16.53	9.52	6	42	0.05	0.04	1.00											
4. Cortisol Stress Response	14.21	6.74	4.33	38.16	−0.01	−0.04	0.1	1.00										
5. Age (Years)	22.05	2.68	18	35	−0.06	0.08	−0.1	−0.03	1.00									
6. Gender (1 = Woman, 0 = Man)	0.45	0.50	0	1	0.01	−0.18*	−0.05	−0.26***	−0.15	1.00								
7. Weight (kg)	70.01	5.37	60	80	0.05	0.13	0.01	0.02	0.23**	−0.38***	1.00							
8. Education: High School Graduate	0.80	0.40	0	1	0.21**	0.04	0.17*	0.09	−0.61***	−0.01	−0.05	1.00						
9. Education: Bachelor's	0.17	0.38	0	1	−0.17*	0.01	−0.13	−0.03	0.40***	0.00	0.03	−0.89***	1.00					
10. Education: Master's	0.03	0.18	0.00	1.00	−0.11	−0.13	−0.12	−0.12	0.52***	0.02	0.05	−0.37***	−0.08	1.00				
11. Marital Status (1 = No, 2 = Yes)	1.03	0.16	1.00	2.00	0.11	−0.02	0.12	0.15	0.14	0.07	−0.1	0.08	−0.07	−0.03	1.00			
12. Placebo (0 = No, 1 = Yes)	0.33	0.47	0.00	1.00	−0.08	0.07	−0.11	−0.35***	0.13	0.02	0.10	−0.1	0.02	0.17*	−0.11	1.00		
13. Dopamine (0 = No, 1 = Yes)	0.34	0.47	0.00	1.00	0.12	0.00	0	−0.15	0.01	0.08	0.01	−0.04	0.06	−0.03	0.00	−0.50***	1.00	
14. Noradrenaline (0 = No, 1 = Yes)	0.34	0.47	0.00	1.00	−0.05	−0.06	0.11	0.50***	−0.14	−0.1	−0.1	0.14	−0.08	−0.13	0.11	−0.50***	−0.51***	1.00

Note. * $p < .10$, ** $p < .05$, *** $p < .01$.

Table 2
Results of the pharmaceutical manipulations on optimism and risk propensity.

	Optimism				Risk Propensity			
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8
Dopamine (1 = Yes, 0 = No)	0.20 (0.132)	−0.49 (0.310)	−0.41 (0.310)	0.84 (0.707)	−0.15 (0.947)	−1.32 (2.129)	−1.01 (1.922)	−0.37 (5.078)
Noradrenaline (1 = Yes, 0 = No)	0.06 (0.154)	−0.55 (0.347)	−0.46 (0.356)	0.45 (0.789)	−0.72 (1.081)	−6.16*** (2.331)	−4.07* (2.155)	−4.60 (5.328)
Cortisol Stress Response	−0.00 (0.010)	−0.04** (0.019)	−0.04* (0.019)	0.04 (0.047)	−0.01 (0.065)	−0.24 (0.135)	−0.21* (0.122)	−0.32 (0.361)
Gender (Woman = 1, Man = 0)	−0.03 (0.113)	−0.03 (0.107)	0.03 (0.112)	−0.00 (0.116)	−1.14 (0.811)	−1.32 (0.755)	−0.20 (0.702)	−0.14 (0.757)
Age	−0.01 (0.020)	−0.02 (0.019)	−0.00 (0.022)	0.00 (0.023)	0.09 (0.165)	−0.04 (0.159)	0.06 (0.143)	0.06 (0.154)
Dopamine * Cortisol Stress Response		0.06** (0.024)	0.05** (0.024)	−0.06 (0.059)		0.13 (0.166)	0.11 (0.149)	0.11 (0.420)
Noradrenaline * Cortisol Stress Response		0.05** (0.023)	0.04* (0.023)	−0.05 (0.056)		0.38** (0.158)	0.27* (0.144)	0.28 (0.410)
Ent. Intentions			0.01 (0.006)	0.05* (0.029)			0.17*** (0.674)	0.10 (0.203)
Dopamine * Ent. Intentions				−0.07* (0.039)				−0.05 (0.260)
Noradrenaline * Ent. Intentions				−0.05 (0.043)				0.04 (0.267)
Entrepreneurial Intentions * Cortisol Stress Response				−0.01* (0.003)				0.01 (0.018)
Dopamine * Ent. Intentions * Cortisol Stress Response				0.01** (0.003)				0.00 (0.021)
Noradrenaline * Ent. Intentions * Cortisol Stress Response				0.01* (0.003)				−0.00 (0.020)
Number of Individuals	112	112	108	108	90	90	89	89
Pseudo-R ² values (adjusted R ²)	.01 (−.03)	.07 (.01)	.14 (.05)	.17 (.02)	.04 (−.02)	.10 (.02)	.27 (.20)	.26 (.14)

Note. Standard errors in parenthesis. *p < .10, **p < .05, ***p < .01.

Table 3
Results of the pharmaceutical manipulations optimism and risk propensity (robustness checks).

	Optimism		Risk Propensity	
	Model 1	Model 2	Model 3	Model 4
Blood Plasma MPH	0.0026 (0.0021)	−0.0040 (0.0044)	0.0046 (0.0131)	0.0242 (0.0281)
Blood Plasma RBX	0.0001 (0.0003)	−0.0013 (0.0007)	−0.0002 (0.0019)	−0.0114** (0.0045)
Dopamine (1 = Yes, 0 = No)				
Noradrenaline (1 = Yes, 0 = No)				
Cortisol Stress Response	−0.0012 (0.0104)	−0.0292* (0.0154)	−0.0029 (0.0663)	−0.1377 (0.1032)
Blood Plasma MPH * Cortisol Stress Response		0.0005* (0.0003)		−0.0012 (0.0018)
Blood Plasma RBX * Cortisol Stress Response		0.0001** (0.0000)		0.0007** (0.0003)
Gender (Woman = 1, Man = 0)	−0.0369 (0.1227)	−0.0178 (0.1118)	−0.9214 (0.8062)	−1.0449 (0.7460)
Age	−0.0078 (0.0217)	−0.0130 (0.0200)	0.1858 (0.1649)	0.0597 (0.1564)
Number of Individuals	110	110	88	88
Pseudo-R ² values (adjusted R ²)	.01 (−.03)	.06 (−.00)	.03 (−.02)	.12 (.05)

Note. Standard errors in parentheses. *p < .10, **p < .05, ***p < .01.

compounds influence multiple neurochemical pathways (Heal and Pierce, 2006; Millan et al., 2001), the observed effects may partly reflect broader changes in attention, arousal, or cognitive processing rather than solely specific neurotransmitter mechanisms (Ucbasaran et al., 2013; Zunino et al., 2022).

Third, entrepreneurial intentions amplify buffering effects, consistent with the possibility that individuals predisposed toward entrepreneurship may have neurochemical profiles more responsive to stress-buffering properties. However, intentions are a cognitive construct (Krueger et al., 2017), and the amplifying role may also operate through motivational mechanisms that interact with pharmacological effects. This complements observations that individuals with stronger intentions persist longer facing obstacles

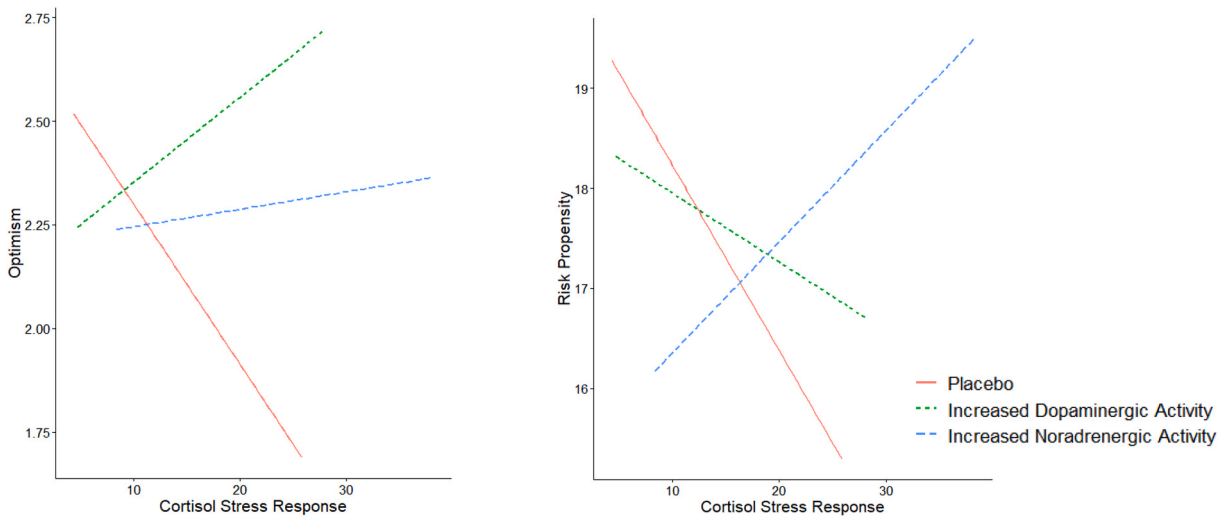


Fig. 3. The effect of increased dopaminergic and noradrenergic activity on optimism (left) and risk propensity (right).

(Caliendo et al., 2020), suggesting that enhanced neurotransmitter activity may help preserve entrepreneurial mindset benefits such as creativity (Phipps and Prieto, 2012) and adaptability (Nicolaou et al., 2008).

5.1. Practical implications

Our findings suggest that stress management interventions may benefit from understanding neurochemical heterogeneity. Rather than one-size-fits-all approaches, tailored strategies considering biological profiles may be more effective. Neurofeedback training (Vernon, 2005; Hellrung et al., 2022) could potentially help entrepreneurs noninvasively dampen stress effects on optimism and risk propensity, though we caution against pharmacological interventions outside clinical supervision (Koren and Korn, 2021; Wei et al., 2023).

5.2. Limitations and future research

Our student sample, while advantageous for ruling out experience confounds and survival bias, limits generalizability to established entrepreneurs. Future studies should replicate with practicing entrepreneurs. Additionally, while we classified MPH primarily as a dopamine reuptake inhibitor, it also affects the noradrenaline transporter to a lesser extent (Heal and Pierce, 2006). In contrast, RBX is primarily a noradrenaline reuptake inhibitor with little affinity for the dopamine transporter (Millan et al., 2001).

We did not include a serotonin reuptake inhibitor due to longer half-lives and the complexity of the serotonin system (Cools et al., 2008); future studies should investigate this pathway.

Regarding pharmacological interpretation, both MPH and RBX influence multiple neurochemical pathways and broader arousal systems (Heal and Pierce, 2006; Millan et al., 2001), so our results should be interpreted as reflecting enhanced dopaminergic and noradrenergic activity broadly rather than isolated neurotransmitter action. Our dichotomous treatment variable does not capture individual differences in drug response; robustness checks using continuous blood plasma levels partially address this, and the convergence across both specifications strengthens confidence. More broadly, confounding influences outside our model may contribute to the observed results given the complexity of stress physiology.

Furthermore, there has been debate regarding reboxetine's efficacy, with Eyding et al. (2010) finding less robust evidence than initially reported. Our study uses reboxetine as a pharmacological tool to enhance noradrenergic activity rather than as an antidepressant, and the doses administered (8 mg) produced measurable plasma levels, with convergence across binary and continuous analyses supporting a genuine pharmacological effect. Nevertheless, future replications should consider atomoxetine, which has a more established safety and efficacy profile (Elliott et al., 2020).

Regarding effect sizes, the doses used (35 mg MPH, 8 mg RBX) are within standard clinical ranges, likely producing effects at the upper range of natural neurotransmitter fluctuation. The observed interaction effects are modest (e.g., $\beta = 0.06$ for the dopamine-cortisol interaction on optimism), consistent with single-dose interventions in healthy participants. Caution is warranted in extrapolating from these laboratory-based effects to real-world entrepreneurial contexts where stress exposure can be chronic.

Finally, our outcomes are short-term psychological states measured in a laboratory among students without entrepreneurial experience, and the leap from laboratory cognition to real-world entrepreneurial behavior requires caution. Future longitudinal studies tracking individuals from pre-entrepreneurial intentions through actual venture creation would help bridge this gap.

6. Conclusions

This study provides experimental evidence that pharmacologically enhanced dopaminergic and noradrenergic activity can buffer stress effects on the entrepreneurial mindset and that entrepreneurial intentions amplify this buffering. While a broader literature has established these stress-buffering properties in general populations (Eyding et al., 2010; Rahman et al., 2006), our results offer initial evidence that these mechanisms operate specifically in the context of entrepreneurial mindset characteristics and are moderated by entrepreneurial intentions, reinforcing the importance of biological perspectives on entrepreneurship.

CRedit authorship contribution statement

Robert Schreiber: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **Dietmar Grichnik:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Dean A. Shepherd:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Formal analysis, Conceptualization. **Joakim Wincent:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Philippe N. Tobler:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization. **Geraldine Gvozdanovic:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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