

## The Effects of Pythagorean Self-Awareness Intervention on Patients with Panic Disorder: A Randomized Controlled Trial

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### Abstract

**Introduction:** Panic Disorder constitutes one of the most common anxiety disorders, and is characterized by recurrent, unexpected panic attacks accompanied by multiple psychophysiological symptoms. Previous studies examining the effects of cognitive-behavioral interventions and other stress management techniques have yielded mixed findings.

**Materials and Methods:** This randomized controlled study aimed to evaluate the effects of the Pythagorean Self-Awareness Intervention (PSAI), a novel, non-pharmaceutical, stress management technique, on symptom severity, quality of life, emotional and cognitive characteristics, lifestyle factors, and stress-related biological markers in patients with panic disorder. Standardized questionnaires were administered at baseline and 8 weeks after the intervention to assess quality of life, perceived stress, depression, health locus of control, and anxiety. Sleep quality, lifestyle parameters, and hair cortisol concentrations were also evaluated.

**Results:** A total of 60 patients were randomly assigned to either the intervention group (n=30), which participated in the 8-week PSAI program, or the control group (n=30). Participants in the PSAI group demonstrated significant improvements across most outcomes. Large effect sizes (> 0.5) were observed for internal locus of control, perceived stress, and cortisol levels. Improvements were also found in secondary outcomes.

**Keywords:** Panic disorder; Generalized anxiety disorder; Panic attacks, Pythagorean Self-Awareness intervention; PSAI; Cognitive intervention; Quality of life; Stress; stress management; Hair cortisol

### Introduction

Panic Disorder (PD) is one of the most prevalent mental disorders. In clinical practice, however, it rarely presents in isolation and is frequently comorbid with other conditions, most commonly generalized anxiety disorder (GAD). GAD and PD are among the most common mental disorders in the United States and can have a detrimental impact on patient's quality of life by disrupting essential daily functioning [1]. PD is associated with impaired social functioning [2], an increased risk of suicide attempts [3], and substance use, including drug and alcohol misuse [4]. The disorder typically develops during late adolescence or early adulthood and is rare before the age of fourteen [5]. Epidemiological data indicate that PD affects between 1.7% and 4.7% of adults and adolescents worldwide [6].

Panic attacks represent the core clinical manifestation of PD and may also occur in the context of other psychiatric conditions, including anxiety

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disorders [5]. Increasing scientific interest has focused on the interplay between the behavioral and neurobiological dimensions of PD. From a neurobiological perspective, the stress system appears to function differently in panic disorder compared to other stress-related conditions. Stress represents a fundamental mechanism for maintaining homeostasis, which is continuously challenged by internal and external stressors [7,8]. Cortisol, a key biomarker of stress, reflects hypothalamic–pituitary–adrenal (HPA) axis activity, and its measurement may indicate dysregulation of this system [9].

Specifically, a study using the Trier Social Stress Test in patients with PD without comorbid depression or psychotropic medication reported a blunted cortisol response compared to healthy controls [10]. Similarly, another study found no significant change in cortisol levels in patients with PD during exposure to stressful stimuli, suggesting a lack of HPA axis hyperactivation [11]. One possible explanation is that the HPA axis in PD may exhibit chronic baseline activation, resulting in reduced responsiveness to acute stressors. This diminished physiological reactivity may reflect an altered biological stress response.

Three main treatment approaches are commonly used in the management of PD [12]. Among them, psychotherapy—particularly cognitive-behavioral therapy (CBT)—has demonstrated the most enduring effects [13]. Additionally, lifestyle modifications, including balanced nutrition, regular physical activity, and reduced consumption of stimulants such as caffeine, alcohol, and nicotine, may influence arousal regulation in individuals with PD [14].

The Pythagorean Self-Awareness Intervention (PSAI) has been proposed to offer a more holistic approach. PSAI is a stress management technique that integrates structured daily lifestyle modifications with cognitive practice. In recent years, it has been experimentally implemented in clinical settings, with patients across various conditions reporting both physical and psychological improvements following the intervention [15].

Taking all the foregoing into account, the primary goal of the present study was to evaluate the effects of PSAI on lifestyle factors and symptomatology in patients with PD. Secondary aims included the assessment of stress and depressive symptoms, emotional state, daily lifestyle patterns, locus of control, sleep quality, information processing speed, visuospatial memory, and verbal learning and memory. We hypothesized that PSAI would lead to improvements in PD symptoms, lifestyle behaviors, and emotional and cognitive functioning.

## Materials and Methods

### Study design and participants

This pilot randomized controlled trial was conducted at

the Mental Health Center of Peristeri, a department of the Psychiatric Hospital of Attica, Greece, between December 2018 and November 2019. The study protocol was approved by the School of Medicine of the National and Kapodistrian University of Athens (Protocol n.1718038002/30-07-2018) and was conducted in accordance with the Declaration of Helsinki. Participants were informed about the study objectives and procedures by the research team and were enrolled only after providing written informed consent. The inclusion criteria were: (a) age between 18 and 65 years, (b) a diagnosis of PD according to DSM-5 criteria confirmed by a psychiatrist, and (c) fluency in the Greek language (reading, speaking, and writing).

### Randomization

Participants were randomly allocated to one of two groups: the Pythagorean Self-Awareness Intervention (PSAI) group or the control group, which received treatment as usual (TAU). Randomization was performed using a computer-generated random sequence created with an online randomization tool (Sealed Envelope Ltd., <https://www.sealedenvelope.com/simple-randomiser/v1/lists>). The study employed a non-blinded design, as both participants and researchers were aware of group allocation.

### Measurements

#### Sociodemographic Characteristics

Participants provided information regarding gender, age, marital status, parity, educational level, income satisfaction, smoking status, body mass index (BMI), and receipt of medical treatment for PD symptoms during the eight months preceding the intervention.

#### Questionnaires

A battery of self-report questionnaires was administered at baseline and after completion of the intervention.

**Beck Depression Inventory-II (BDI-II):** The BDI-II is a 21-item self-report instrument assessing the severity of depressive symptoms. Each item is rated on a 4-point scale (0–3), yielding a total score ranging from 0 to 63. A total score  $\geq 17$  indicates the presence of clinically significant depressive symptoms [16,17]. The instrument has been validated in the Greek population [18].

**Healthy Lifestyle and Personal Control Questionnaire (HLPCQ):** The HLPCQ consists of 26 items assessing dietary habits, harm avoidance related to unhealthy behaviors, daily routine, physical activity, and psychosocial balance [19]. Items are rated on a 4-point Likert scale (1 = never/rarely to 4 = always), with higher scores indicating healthier lifestyle behaviors.

**Depression-Anxiety-Stress Scale-21 (DASS-21):** The DASS-21 includes three 7-item subscales measuring

depression, anxiety, and stress. Items are rated on a 4-point Likert scale. The instrument assesses emotional distress rather than providing a formal clinical diagnosis. Higher scores indicate greater symptom severity [20]. This scale has been validated in the Greek language [21].

**Positive and Negative Affect Schedule (PANAS):** The PANAS assesses two dimensions of affect: positive and negative affect. It consists of two 10-item subscales, with items rated on a 5-point Likert scale (1 = very slightly or not at all to 5 = extremely), reflecting the extent to which respondents experienced each emotion during the past week [22].

**Pittsburgh Sleep Quality Index (PSQI):** The PSQI evaluates sleep quality over the past month. It includes 19 items forming seven component scores: sleep quality, latency, duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Global scores range from 0 to 21, with higher scores indicating poorer sleep quality. A total score >5 indicates poor sleep quality [23]. The Greek version has been validated [24].

**Perceived Stress Scale (PSS):** The 14-item PSS measures the degree to which situations in one's life are appraised as stressful over the past month [25]. Higher scores indicate greater perceived stress. The instrument has been validated in Greek populations [26].

**Health Locus of Control (HLC):** The HLC is an 11-item Likert-type scale comprising six external and five internal locus of control items, rated from 1 (strongly disagree) to 6 (strongly agree). It assesses whether individuals attribute control over their health to internal factors or to external influences such as chance, fate, or other people [27].

**Brief International Assessment of Cognition for Multiple Sclerosis (BICAMS):** Cognitive functioning was assessed using the BICAMS battery, which includes: the Symbol Digit Modalities Test (SDMT) assessing information processing speed, the California Verbal Learning Test-II (CVLT-II) assessing verbal learning and memory, and the Brief Visuospatial Memory Test-Revised (BVM-T-R) assessing visuospatial memory. Lower scores indicate poorer cognitive performance. Established cut-off scores have been proposed to identify clinically significant cognitive impairment [28,29].

**Hair cortisol concentration:** Hair cortisol concentration was measured as an objective biomarker of long-term endogenous cortisol exposure. Hair samples were collected at baseline and one month after completion of the intervention. A small hair strand was cut from the posterior vertex of the scalp as close to the scalp as possible. Samples were secured on paper and stored at room temperature until analysis. Hair grows at an average rate of approximately 1 cm per

month; therefore, the 1-cm segment proximal to the scalp reflects cortisol secretion during the preceding month, while subsequent segments reflect earlier periods [31]. Laboratory analyses were conducted at the Unit of Clinical and Translational Research in Endocrinology, First Department of Pediatrics, School of Medicine, National and Kapodistrian University of Athens (Choremeio Research Laboratory, Athens, Greece). The analytical procedure has been described previously [30].

### Pythagorean Self Awareness Intervention (PSAI)

The intervention group participated in the Pythagorean Self-Awareness Intervention (PSAI) stress management program, delivered over eight weekly sessions. The first session focused on addressing individual patient needs and clarifying any questions regarding the program. Baseline measurements, including hair sampling and questionnaire administration, were also performed. Additionally, participants were instructed in diaphragmatic breathing as a relaxation technique.

The second session was conducted in a group format and provided education on stress symptoms and their relationship to PD. Participants were also advised on lifestyle modifications, including regular physical activity, adherence to the Mediterranean diet, establishing a structured daily routine, and obtaining sufficient high-quality sleep. Pedometers were provided, with a recommended daily step goal of 10,000, consistent with NHS guidelines.

The PSAI technique was introduced during the third session. Participants were instructed to practice the technique twice daily—once in the morning and once before bedtime—for approximately 30 minutes per session. Each practice was performed in a quiet, comfortable location following five minutes of diaphragmatic breathing. During the evening session, participants were guided to review all daily activities, interactions, and issues related to diet, physical exercise, interpersonal relationships, and emotions. They were asked to observe themselves from a "third-person" perspective, maintaining emotional detachment, to gain a deeper understanding of stressful experiences and their personal responses.

As part of the self-reflective process, participants were instructed to ask themselves three questions: (1) "What did I do wrong?" (2) "What did I do correctly?" and (3) "What did I omit that I ought to have done?" This daily review was structured according to the lifestyle and moral principles outlined in Pythagoras' *Golden Verses* ([http://en.wikipedia.org/wiki/The\\_golden\\_verses\\_of\\_Pythagoras](http://en.wikipedia.org/wiki/The_golden_verses_of_Pythagoras)). Participants were then encouraged to reward or reprimand themselves based on their reflections and to set goals for the following day aimed at rectifying any identified shortcomings. This cognitive restructuring process enables individuals to serve

as objective evaluators of their own behavior, promoting self-awareness and self-regulation. A detailed description of the PSAI technique has been previously provided by Charalampopoulou et al. [32].

### Data analysis

Data are presented as frequencies and percentages (N, %) for categorical variables and as mean ± standard deviation (SD) for continuous variables. Differences between categorical variables were assessed using Pearson’s chi-square test. The same test was used to evaluate differences between the intervention and control groups in hair cortisol change (post-intervention minus baseline). Normality of continuous variables was assessed prior to analysis. For variables that did not meet the assumption of normality, the non-parametric Mann–Whitney U test was used to compare baseline values, post-intervention measurements, and

change scores (post-intervention minus baseline) between groups. Within-group differences were assessed using the Wilcoxon signed-rank test. Effect sizes were calculated for each outcome, with values <0.3 considered small, 0.3–0.5 moderate, and >0.5 large. Statistical significance was set at  $p < 0.05$  for all analyses. Analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) [33].

### Results

The study sample initially included 60 patients, with 30 participants allocated to the intervention group and 30 to the control group. Basic sociodemographic characteristics and group comparisons for the PSAI and control groups are presented in Table 1. Participants in the intervention group were significantly older, and a higher proportion of individuals in the PSAI group had children and were taking medication.

**Abbreviations:** PSAI: Pythagorean Self-Awareness Intervention, SD: standard deviation, SDI: special disabilities individuals, BMI: Body Mass Index.

**Table 1:** Baseline sociodemographic characteristics for PSAI and control group.

	PSAI Group N=30	Control Group N=30	p value	Total N=60
<b>Gender</b>				
• Females	22 (73.30)	16 (53.30)	0.18	38(63.00)
• Males	14 (46.70)	14 (46.70)		22 (36.70)
<b>Age (mean +/-SD)</b>	45.20 (10.50) 45 (14.00)	38.10 (11.60) 35 (23.50)	0.016	41.56 (11.57) 10.00 (19.00)
<b>Marital Status</b>				
• Married	10 (33.30)	17 (56.70)	0.119	27 (45.00)
• Single	20 (66.70)	13 (43.30)		33 (55.00)
<b>Cohabitation</b>				
• Yes	27 (90.00)	23 (76.70)	0.299	50 (83.30)
• No	3 (10.00)	7 (23.30)		10 (16.70)
<b>Children</b>				
• Yes	22 (73.30)	11 (36.70)	0.009	35 (55.00)
• No	8 (27.00)	19 (63.30)		27 (45.00)
<b>Care of S.D.I.</b>				
• Yes	1 (3.40)	4 (13.30)	0.353	5 (8.50)
• No	28 (96.60)	26 (86.70)		54 (91.50)
<b>Educational level</b>				
• sec./High School	26 (86.70)	19 (63.30)	0.074	45 (75.00)
• Higher Education/Master/Ph. D	4 (13.30)	11 (36.70)		15 (25.00)
<b>Job Satisfaction</b>				
• not at all	7 (23.30)	6 (20.0)	0.495	13 (21.70)
• a little	11 (36.70)	8 (26.70)		19 (31.70)
• rather-very much	12 (40.00)	16 (53.30)		28 (46.60)
<b>Smoking</b>				
• Yes	11 (37.00)	9 (30.00)	0.784	20 (33.30)
• No	19 (63.30)	21(70.00)		40 (67.00)
<b>Medication</b>				
• Yes	17 (60.70)	9 (30.00)	0.037	26 (45.00)
• No	11 (39.30)	21 (70.00)		32 (55.20)
<b>BMI (mean +/- SD)</b>	25.22 (5.16) 24.21 (7.09)	25.59 (5.93) 24.34 (4.69)	0.994	25.40 (5.51) 24.27 (5.72)

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Table 2 presents baseline measures for cognitive function, healthy lifestyle, personal control, hair cortisol concentration, and psychological outcomes across the intervention and control groups. Mann -Whitney U tests revealed statistically significant between-group differences in shape recall ( $p = 0.02$ ), hair cortisol concentration ( $p = 0.04$ ), dietary harm avoidance ( $p = 0.02$ ), daily routine ( $p = 0.003$ ), social and mental balance ( $p = 0.03$ ), and overall HLPCQ score ( $p = 0.03$ ).

Significant group differences were also observed in Health Locus of Control subscales and stress-related measures. Specifically, participants in the intervention group scored higher on internal locus of control ( $p < 0.001$ ) and powerful others ( $p = 0.04$ ) subscales, lower on external locus of control ( $p = 0.04$ ) and perceived stress ( $p < 0.001$ ), and higher on stress ( $p = 0.04$ ) compared with the control group.

**Abbreviations:** PSAI: Pythagorean, Self-Awareness Intervention, SD: standard deviation, SDMT: Symbol Digit Modalities Test, CVLT: California Verbal Learning Test, BVMT-R: Brief Visuospatial Memory Test-Revised, HCC: Hair Cortisol Concentration, HLPCQ: Healthy Lifestyle and Personal Control Questionnaire, HLCPOW: Health Locus of Control Powerful, PANAS: Positive and Negative Affect Schedule, PSS: Perceived Stress Schedule, DASS: Depression, Anxiety and Stress Scale, BDI: Beck' Depression Inventory, PSQI: Pittsburg Sleep Quality Index

**Table 2:** Between groups cognitive capability, healthy lifestyle, personal control, hair cortisol concentration and psychological function baseline measurement.

	PSAI Group N= 30	Control Group N= 30	p-value	Total Mean (SD), Median (IQR)
<b>Symbols SDMT</b> (mean +/- SD)	43.30(11.72)	48.07(13.30)	0.164	45.70(12.66)
	42.00(17.25)	47.00(20.00)		44.00(20.0)
<b>Word Recall CVLT-II</b> (mean +/- SD)	62.03(10.65)	62.37(12.33)	0.79	62.20(11.43)
	62.00(16.75)	63.00(17.75)		62.50(17.50)
<b>Shape Recall BVMT-R</b> (mean +/- SD)	23.17(7.80)	19.07(5.84)	0.021	21.12(7.14)
	24.00(12.50)	20.00(9.00)		22.00(9.50)
<b>HCC</b> (mean +/- SD)	11.96(9.44)	6.74(6.24)	0.044	9.36(8.36)
	8.16(9.66)	6.83(4.57)		7.28(18.00)
<b>Dietary Health Choices HLPCQ</b> (mean +/- SD)	15.20(5.69)	14.53(3.13)	0.888	14.87(4.57)
	15.00(10.25)	15.50(4.25)		15.00(5.00)
<b>Dietary Harm Avoidance HLPCQ</b> (mean +/- SD)	8.66(2.40)	7.63(2.25)	0.026	8.14(2.37)
	9.00(3.50)	7.00(2.00)		8.00(2.00)
<b>Daily Routine HLPCQ</b> (mean +/- SD)	18.58(4.93)	14.60(4.03)	0.003	16.56(4.89)
	18.00(6.00)	16.00(6.00)		16.00(6.00)
<b>Organized Physical Exercise HLPCQ</b> (mean +/- SD)	4.40(1.97)	3.66 (1.34)	0.182	4.03(1.72)
	4.00(4.00)	4.00(3.00)		4.00(3.00)
<b>Social and Mental Balance HLPCQ</b> (mean +/- SD)	10.86(2.94)	9.20(2.20)	0.029	10.03(2.71)
	11.00(5.00)	9.00(3.00)		10.00(4.00)
<b>HLPCQ Total</b> (mean +/- SD)	58.00(12.57)	49.63(9.32)	0.03	53.67(11.70)
	55.00(21.00)	51.50(10.00)		53.00(12.25)
<b>INTRENAL</b> (mean +/- SD)	22.03(4.87)	16.80(3.01)	<0.0001	19.42(4.81)
	21.00(7.25)	16.50(5.00)		18.50(6.00)
<b>EXTERNAL</b> (mean +/- SD)	18.13(5.69)	21.46(5.38)	0.042	19.80(5.75)
	18.50(6.50)	23.00(10.00)		19.50(8.75)
<b>POWERFULOTHERS</b> (mean +/- SD)	21.70(5.15)	24.43(4.97)	0.043	23.07(5.20)
	22.00(8.25)	25.00(8.25)		23.50(8.00)
<b>Positive Affect PANAS</b> (mean +/- SD)	32.60(4.51)	30.23(4.64)	0.057	31.42(4.69)
	32.50(6.25)	29.50(7.00)		32.00(13.00)
<b>Negative Affect PANAS</b> (mean +/- SD)	33.23(6.51)	31.20(4.99)	0.155	32.22(5.85)
	34.50(10.00)	30.50(7.50)		31.00(7.00)

<b>Perceived Stress PSS</b> (mean +/- SD)	34.80 (6.77)	41.87 (3.63)	<0.0001	38.33 (6.46)
	35.00 (8.75)	41.50 (4.50)		40.00 (8.75)
<b>Stress DASS</b> (mean +/- SD)	22.73(11.17)	16.93(8.58)	0.039	19.83(10.30)
	22.00(16.50)	16.00(12.00)		18.00(13.50)
<b>Depression DASS</b> (mean +/- SD)	20.93(11.91)	17.26(7.86)	0.342	19.10(10.18)
	18.00(17.00)	17.00(9.00)		18.00(12.00)
<b>Anxiety DASS</b> (mean +/- SD)	21.06(11.81)	18.26(6.61)	0.436	19.67(9.60)
	18.00(15.00)	18.00(10.50)		18.00(14.00)
<b>Depression BDI</b> (mean +/- SD)	24.23(12.19)	21.90(7.62)	0.662	23.07(10.15)
	22.00(10.75)	22.0(11.00)		22.00(11.75)
<b>Quality of Sleep PSQI</b> (mean +/- SD)	9.21(3.14)	10.00(2.55)	0.374	9.60(2.87)
	9.00(5.00)	9.00(3.75)		9.00(4.50)

Participants in the PSAI group demonstrated significant improvements across most outcome measures. Between-group pre-post comparisons revealed significant effects in cognitive, lifestyle, psychological, and biological outcomes, including:

**Cognitive function:** Symbol Digit Modalities Test (SDMT;  $p = 0.01$ ), Word Recall CVLT-II ( $p = 0.005$ )

**Biological measure:** Hair cortisol concentration ( $p < 0.001$ )

**Healthy lifestyle (HLPCQ):** Dietary health choices, dietary harm avoidance, daily routine, organized physical exercise, social and mental balance, and total HLPCQ score (all  $p < 0.001$ )

**Abbreviations:** PSAI: Pythagorean, Self-Awareness Intervention, SD: standard deviation, SDMT: Symbol Digit Modalities Test, CVLT: California Verbal Learning Test, BVMT-R: Brief Visuospatial Memory Test-Revised,

**HCC:** Hair Cortisol Concentration, HLPCQ: Healthy Lifestyle and Personal Control Questionnaire, HLCPOW: Health Locus of Control Powerful, PANAS: Positive and Negative Affect Schedule, PSS: Perceived Stress Schedule, DASS: Depression, Anxiety and Stress Scale, BDI: Beck's Depression Inventory, PSQI: Pittsburgh Sleep Quality Index

**Health locus of control (HLC):** Internal ( $p < 0.001$ ), external ( $p < 0.001$ ), powerful others (HLC-POW;  $p < 0.001$ )

**Affect (PANAS):** Positive and negative affect (both  $p < 0.001$ )

**Stress and psychological symptoms:** Perceived stress (PSS), stress, depression, and anxiety (DASS-21; all  $p < 0.001$ )

**Sleep quality:** PSQI total score ( $p < 0.001$ )

These findings indicate that the PSAI intervention led to broad improvements in cognitive performance, lifestyle behaviors, emotional regulation, perceived stress, and biological stress markers.

**Table 3:** Comparisons of outcomes' differences across study groups

	PSAI Group N=30	Control Group N=30	p value	Effect Size	Total Mean (SD), Median (IQR)
<b>ΔSymbols SDMT</b> (mean +/- SD)	7.36(8.66)	2.20(9.17)	0.01	0.111	4.78(9.22)
	9.00(9.25)	1.00(7.50)			5.00(10.75)
<b>ΔWord Recall CVLT-II</b> (mean +/- SD)	8.03(10.79)	-1.20(13.18)	0.005	0.132	3.42(12.82)
	9.50(14.50)	1.50(19.50)			3.50(14.25)
<b>ΔShape Recall BVMT-R</b> (mean +/- SD)	3.26(6.99)	3.66(6.21)	0.846	0.001	3.47(6.57)
	4.00(4.50)	3.00(6.50)			4.00(6.00)
<b>ΔHCC</b> (mean +/- SD)	6.23(5.77)	0.30(1.39)	<0.0001	0.298	3.27(5.13)
	6.50(8.00)	0.00(0.00)			0.00(6.75)
<b>ΔDietary Health Choices HLPCQ</b> (mean +/- SD)	3.82(3.71)	0.26(2.18)	<0.0001	0.44	2.02(3.50)
	4.00(5.00)	0.00(0.00)			1.00(4.00)

<b>ΔDietary Harm Avoidance HLPCQ</b> (mean +/- SD)	7.44(5.73)	0.73(3.16)	0.004	0.311	4.03(5.69)
	9.00(9.50)	0.00(0.25)			1.00(9.00)
<b>ΔDaily Routine HLPCQ</b> (mean +/- SD)	1.76(2.58)	0.36(1.21)	<0.0001	0.143	1.07(2.12)
	2.00(4.00)	0.00(0.00)			0.00(2.00)
<b>ΔOrganized Physical Exercise HLPCQ</b> (mean +/- SD)	4.60(3.94)	0.43(1.16)	<0.0001	0.353	2.52(3.57)
	5.00(5.50)	0.00(1.00)			1.00(5.00)
<b>ΔSocial and Mental Balance HLPCQ</b> (mean +/- SD)	24.14(18.36)	2.10(7.75)	<0.0001	0.242	12.74(17.71)
	30.50(31.75)	0.00(1.25)			1.50(31.50)
<b>ΔHLPCQ Total</b> (mean +/- SD)	8.63(6.61)	0.00(0.00)	<0.0001	0.644	4.32(6.36)
	9.00(9.50)	0.00(0.00)			0.00(9.00)
<b>ΔINTRENAL</b> (mean +/- SD)	-5.90(7.16)	-0.10(0.54)	<0.0001	0.439	-3.00(5.83)
	-7.00(9.25)	0.00(0.00)			0.00(7.50)
<b>ΔEXTERNAL</b> (mean +/- SD)	-6.26(6.18)	-0.16(0.64)	<0.0001	0.327	-3.22(5.34)
	-7.00(10.25)	0.00(0.00)			0.00(7.00)
<b>ΔPOWERFULOTHERS HLCPOW</b> (mean +/- SD)	5.31(7.40)	0.50(3.07)	0.001	0.192	2.86(6.09)
	6.00(9.50)	0.00(0.25)			0.00(8.00)
<b>ΔPositive Affect PANAS</b> (mean +/- SD)	-11.56(9.54)	-2.40(4.91)	<0.0001	0.249	-6.98(8.83)
	-11.50(15.00)	-0.50(3.00)			-3.00(13.00)
<b>ΔNegative Affect PANAS</b> (mean +/- SD)	-22.3 (11.07)	0.00 (.000)	<0.0001	0.747	-11.15 (13.66)
	-22.5 (16.00)	0.00 (0.00)			0.00 (22.75)
<b>ΔPerceived Stress PSS</b> (mean +/-SD)	-13.03(10.48)	-1.60(6.33)	<0.0001	0.287	-7.22(10.31)
	-14.00(13.00)	0.00(0.50)			-2.00(14.00)
<b>ΔStress DASS</b> (mean +/- SD)	-12.64(11.14)	-1.86(6.69)	<0.0001	0.305	-7.16(10.58)
	-14.00(13.00)	0.00(0.00)			0.00(14.00)
<b>ΔDepression DASS</b> (mean +/- SD)	-14.86(12.67)	-1.65(6.14)	<0.0001	0.328	-8.37(11.96)
	-13.00(19.50)	0.00(0.00)			-2.00(16.00)
<b>ΔAnxiety DASS</b> (mean +/- SD)	-14.26(14.55)	-2.00(4.67)	<0.0001	0.306	-8.13(12.37)
	-15.00(16.25)	0.00(2.25)			-3.00(15.00)
<b>ΔDepression BDI</b> (mean +/- SD)	-2.41(3.15)	-0.21(0.96)	<0.0001	0.219	-1.33(2.57)
	-2.00(4.00)	0.00(0.00)			0.00(2.50)
<b>ΔQuality of Sleep PSQI</b> (mean +/- SD)	-5.90(7.14)	-0.10(0.54)	<0.0001	0.437	-3.00(5.81)
	-7.00(9.22)	0.00(0.00)			0.00(7.50)

Table 4 shows that participants in the intervention group demonstrated a marked reduction in hair cortisol concentration, whereas those in the control group exhibited

a significant increase over the same period. These results are consistent with previous findings on hair cortisol levels in patients with PD.

**Table 4:** Comparisons of hair cortisol changes between study groups.

Hair cortisol change	Intervention group N (%)	Control group N (%)	Total N (%)
Amelioration*	21 (70)	1 (3, 3)	22 (36, 7)
Stagnation/DETERIORATION*	9 (30)	29 (96, 7)	38 (63, 3)

## Discussion

The present study aimed to examine the effectiveness of the Pythagorean Self-Awareness Intervention (PSAI), a cognitive-based stress management technique, in individuals diagnosed with panic disorder (PD). PSAI has previously demonstrated mental and cognitive benefits in patients with multiple sclerosis [34], obesity [35], insomnia [36], breast cancer [32], and moderate cognitive impairment [37]. For example, Simos et al. [35] reported that PSAI led to significant reductions in hair cortisol concentration, perceived stress, body mass index, and emotional and external eating behaviors. This is the first study to demonstrate multiple benefits of PSAI in patients with PD.

Overall, our findings support the hypothesis that PSAI improves psychological outcomes (depression, stress, anxiety), lifestyle control, health locus of control, sleep quality, and hair cortisol concentrations in PD patients. Strong effect sizes were observed for stress, perceived stress, depression, and anxiety symptoms. These results align with prior research highlighting the efficacy of cognitive-behavioral therapy (CBT) and other stress management interventions in PD. A recent meta-analysis of 41 randomized controlled trials found that CBT significantly improved anxiety and disorder-specific symptoms in PD patients, although its effects on depressive symptoms were negligible [38]. Small to moderate effect sizes were reported for anxiety (Hedges'  $g = 0.29$ ) and disorder-specific symptoms (Hedges'  $g = 0.56$ ), while depressive symptom effects were minimal. Interestingly, CBT appeared more efficacious for other anxiety disorders, such as generalized anxiety disorder and obsessive-compulsive disorder, including depressive symptoms.

In the absence of prior evidence on PSAI in PD, discussion focuses on potential mediators of its observed effects. A key component of PSAI is self-awareness, defined as the ability to reflect on and identify stressful or distressing events, evaluate one's behaviors and emotions relative to personal internal standards, and develop objective self-consciousness through self-evaluation [39]. Self-awareness has been proposed to reduce perceived tension, worry, and nervousness while enhancing self-efficacy (confidence in one's ability to execute behaviors and manage specific situations) and self-control (ability to regulate thoughts, emotions, and behavior under stress) [40]. Accordingly, self-awareness may be a critical mechanism through which PSAI reduces psychological problems in PD patients.

Another important finding was the improvement in sleep quality among participants receiving PSAI. Sleep quality is known to affect daytime functioning [41], health outcomes [42], and overall quality of life [43], whereas poor sleep is often associated with elevated distress, anxiety, and psychiatric disorders [44]. In PD, sleep disturbances are common; Mellman and Uhde [45] reported that approximately 67% of PD patients experience regular insomnia. Consistently, PD patients exhibit poorer sleep quality on the Pittsburgh Sleep Quality Index (PSQI) compared to healthy controls [23,46]. Although CBT has been effective for sleep disturbances in primary insomnia [47], studies in PD have shown only weak [48] to modest [49] improvements in sleep quality. In contrast, the present study found that PSAI had a strong positive effect on sleep quality in PD patients.

A further important contribution of this study is the hair cortisol findings, which provide objective evidence of reduced physiological stress following the PSAI intervention. Hair cortisol concentration is considered a reliable biomarker of long-term hypothalamic-pituitary-adrenal (HPA) axis activity, reflecting cumulative cortisol secretion over weeks to months, unlike salivary or serum cortisol, which provide only momentary or short-term measurements. In the present study, participants in the PSAI group showed a significant decrease in hair cortisol levels post-intervention, approaching concentrations typically observed in healthy control populations. This suggests that PSAI may not only alleviate subjective stress but also modulate chronic physiological stress responses in PD patients. In contrast, prior studies evaluating the effects of cognitive-behavioral therapy (CBT) on cortisol levels in PD patients reported no significant changes [50,51]. This discrepancy may be largely explained by methodological differences. Most previous research relied on salivary or serum cortisol, which capture only acute fluctuations in cortisol and are highly sensitive to diurnal variation, temporary stressors, and participant compliance. Hair cortisol, on the other hand, provides a more stable measure of cumulative HPA axis activity, allowing for a more accurate assessment of the long-term effects of interventions on physiological stress. These findings highlight the potential of PSAI to produce sustained reductions in biological stress markers, offering an objective complement to the observed improvements in psychological and lifestyle outcomes.

Several limitations should be acknowledged. First, the sample size was relatively small, limiting the generalizability of the findings. Second, no follow-up assessment was conducted, preventing evaluation of the intervention's long-term effects. Third, recruiting participants with a primary

PD diagnosis without comorbidity is challenging, and some participants also met criteria for generalized anxiety disorder; however, PD was the dominant clinical presentation. Despite these limitations, PSAI appears to be a promising complementary intervention for PD, offering benefits across psychological, cognitive, lifestyle, and biological domains. While PSAI shares similarities with CBT, it incorporates a deeper philosophical reflection, potentially enhancing self-awareness and self-regulation.

## Conclusion

In conclusion, the Pythagorean Self-Awareness Intervention (PSAI) is a novel, non-pharmaceutical, and easily taught cognitive-based stress management program that demonstrates promising benefits for patients with panic disorder (PD). To our knowledge, this is the first study to show that PSAI can significantly improve multiple domains relevant to PD, including healthy lifestyle habits (such as nutrition and regular physical activity), sleep quality, biological stress markers (hair cortisol concentration), psychological stress, perceived stress, and anxiety symptoms. The intervention's holistic approach, combining daily routine adjustments with structured cognitive self-reflection, may contribute to its broad effects by enhancing self-awareness, self-regulation, and adaptive coping strategies. Future research should focus on conducting larger randomized controlled trials with more diverse and well-characterized patient populations, including participants with common comorbidities, to enhance generalizability. Comparative studies evaluating PSAI against other established interventions, such as cognitive-behavioral therapy, would provide further insight into its relative efficacy. Additionally, longitudinal follow-up assessments are warranted to determine the sustainability of PSAI's benefits over time and to evaluate its potential role as a complementary or adjunctive treatment in the long-term management of PD.

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