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Increased Psychological Symptoms and Autonomic Arousal in Patients with Subclinical Hypothyroidism: A Case–Control Study

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Abstract: (1) Background: Subclinical hypothyroidism (SHT) is a condition that has been a subject of controversy in the literature due to its association with psychological and psychiatric symptoms as well as autonomic imbalances. To gain a better understanding of the effects of SHT on patients, a research study has been undertaken to investigate the presence of psychological symptoms and autonomic imbalances in a group of individuals diagnosed with SHT. (2) Methods: In this case–control study, 50 patients diagnosed with SHT who accessed the Department of Endocrinology of the University of Pisa were consecutively recruited. Psychological symptoms were measured through the Crown–Crisp Experiential Index (CCEI), whereas autonomic imbalance was described using the Psychophysiological Stress Profile (PSP), with simultaneous recording of the following psychophysiological parameters: Surface Electromyogram (sEMG), Skin Conductance Level (SCL), heart rate (HR), and peripheral temperature (PT). The patients' values were compared to those of 50 healthy control subjects. (3) Results: The comparison between groups highlighted significant differences in the CCEI and PSP. In particular, patients reported higher rates of psychological symptoms (anxiety, depression, somatic complaints, and hysteria behavior). Significantly higher levels of autonomic arousal were also recorded. More specifically, the sEMG, SCL, HR, and PT values were different between the two groups. (4) Conclusions: The study has confirmed the presence of autonomic hyperarousal in patients diagnosed with subclinical hypothyroidism. This is likely due to the body's attempt to compensate for a general lack of energy by accelerating the autonomic activity. The findings also underline the significance of a comprehensive assessment approach that takes into account various dimensions such as psychological and psychophysical well-being. Such an approach helps in evaluating the impact of subclinical diseases on overall health and well-being.

Keywords: subclinical hypothyroidism; psychophysiology; arousal; anxiety; depression

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1. Introduction

Subclinical hypothyroidism (SHT) is a condition that affects a significant number of adults (the prevalence rate falls between 3 and 10%) [1]. It occurs when the thyroid gland does not produce enough thyroid hormones, resulting in high levels of thyrotropin (TSH) and normal levels of free thyroxine (FT4). This condition can be caused by various factors, such as autoimmune disorders, iodine deficiency, or certain medications. Though SHT does not show any significant symptoms in the early stages, it can progress to overt hypothyroidism if untreated [1]. Therefore, it is essential to diagnose and treat SHT as soon as possible to prevent the progression of the condition and the development of severe symptoms. Hypothyroidism has a slow onset, and symptoms may not be noticeable until the condition has progressed significantly. In light of these assumptions, early diagnosis and treatment are vital to prevent complications [2,3].

Hypothyroidism can adversely affect various organ systems in the body, including the cardiovascular ones, leading to serious health issues [3]. Furthermore, hypothyroidism can also impair cognitive functions [4], which can hinder the brain's ability to support higher functions due to inadequate energy consumption [5]. Thyroid hormones play a vital role in the adult brain, and it is widely accepted that clinical hypothyroidism can lead to psychological [6,7] and psychiatric symptoms [8–10], as well as autonomic imbalance [11].

It is important to note that hypothyroidism can even simulate depressive syndromes or forms of dementia due to severe concentration deficits [12–14] and emotional disorders, such as dysphoria, anxiety, and restlessness [15]. Research suggests that these symptoms may stem from various underlying factors [16]. SHT shares certain symptoms of depression, including fatigue, low mood, weight gain, and decreased concentration [15]. This similarity may lead to confusion and mistakenly suggest an increased likelihood of depression in individuals with SHT [16,17]. Hypothyroid patients may even experience typical symptoms of major depressive episodes, including a depressed mood, a lack of interest and pleasure, apathy, tiredness, and increased fatigue [18,19]. Mood changes may also include a gradual augmentation in dysphoric reactions and irritability, leading to poorer interpersonal and social functioning [8]. In summary, numerous studies in the literature support the existence of a relationship between the efficiency of thyroid function and cognitive and emotional states [8,20].

Alterations in the thyroid gland have a significant impact on the autonomic nervous system (ANS) [21]. According to some studies, hypothyroid patients experience a decrease in vagal modulation, leading to a withdrawal of the sympathetic system [22,23], while others have demonstrated that the sympathetic system exhibits greater activity in the autonomic cardiovascular system [11,24]. A study conducted on a rat model [17] revealed that all depression-like behaviors can be accompanied by a subtle hyperactivity of the hypothalamic–pituitary–adrenal axis in subclinical hypothyroidism. Furthermore, some autonomic functions, such as those modulated by the cardiovascular system, may also be affected [11]. Some authors described a marked sympathetic arousal due to an increase in cardiac activity [11,23] or a reduced compensation by the parasympathetic system due to vagal tone [25,26]. Other authors [27] noted that there is a decrease in sympathetic activity only in conditions of hypothyroidism with a TSH > 10 mIU/L.

The literature surrounding the psychophysiology of patients with SHT is full of controversies that have not yet been resolved. However, the available evidence suggests that hypothyroidism can cause changes in autonomic function, particularly in the cardiovascular system.

As a result, this study aims to evaluate psychological symptoms and autonomic arousal in patients diagnosed with SHT. The hypothesis is that the group of patients with SHT will exhibit higher levels of anxiety and depression. Moreover, the study expects to detect a general hyperarousal of the ANS, which can be documented by increased levels of psychophysiological parameters, such as muscle tension, skin conductance, peripheral temperature, and heart rate. The study will utilize a psychological test and a psychophysiological assessment to evaluate the psychological symptoms and the level of autonomic arousal among patients with SHT. The results of this study are expected to provide valuable insights into the relationship between thyroid alterations, autonomic function, and psychological symptoms, which can facilitate the development of effective treatment strategies for patients with SHT.

2. Materials and Methods

2.1. Participants and Procedure

In this case–control study, the researchers analyzed data from 50 patients diagnosed with SHT who accessed the Department of Endocrinology of the University of Pisa (Italy) in the period between 1998 and 2016. Additionally, 50 healthy and age-comparable subjects were recruited. The criteria for inclusion in the study were age > 18 years old; completion of informed consent; and no history of psychiatric and neurological syndromes (e.g., pre-

vious head trauma, epilepsy, etc.) or physical diseases (i.e., sensory disturbances of sight and hearing) that might have limited the administration of the tests. Lastly, people with clinically relevant endocrinological syndromes (i.e., hormonal alterations (high prolactin, low estradiol/testosterone levels), amenorrhea, diabetes, menopause, hypertension, etc.) were excluded, as well as people who had taken psychotropic drugs with rebound effects on the ANS in the last three months (i.e., oral contraceptives, tricyclic antidepressants, antipsychotics, norepinephrine–dopamine reuptake inhibitors such as bupropion, serotonin modulators, such as mirtazapine and trazodone, serotonin–norepinephrine reuptake inhibitors, such as venlafaxine and duloxetine, etc.).

The administration of the multidimensional assessment took place at the time of access to the service, after confirmation of the medical diagnosis of SHT. For this reason, the patients were not yet undergoing pharmacological treatment with levothyroxine.

The researchers explained the purpose of the study and the instruments that would be administered to them without specifying the single scales, so as not to nullify their face validity. Once the assessment was conducted, participants were offered the option to book an appointment with a licensed clinical psychologist to possibly receive an exhaustive commentary and ask questions.

All procedures were conducted following the Declaration of Helsinki and its later advancements, according to the Research involving Human Participants policy. Participants' anonymity was preserved, and the data obtained were used solely for scientific purposes. All participants gave their consent for the results derived from their data to be published.

2.2. Measures

During the multidimensional assessment, the following instruments were utilized.

The Crown–Crisp Experiential Index (CCEI; Italian version) [28] is a widely used questionnaire that is designed to assess the emotional distress and psychological well-being of an individual. The questionnaire consists of 48 items that are grouped into six different scales, each of which evaluates a specific aspect of mental health. The six scales of the CCEI are Free Floating Anxiety (FFA), Phobic Anxiety (PHO), depression (DEP), hysteroid behavior (HYS), obsessive traits (OBS), and somatic complaints (SOM). The FFA scale assesses the level of anxiety that is not related to any specific object or situation. The PHO scale evaluates the level of anxiety that is associated with specific phobias or fears. The DEP scale assesses the level of depression. The HYS scale evaluates the level of attention-seeking and dramatic behavior. The OBS scale assesses the level of obsessive–compulsive behavior. Lastly, the SOM scale evaluates the level of physical symptoms that are not related to any underlying medical condition. Previous research [29] has suggested that a clinical cut-off point of $\geq$6 is a clinically significant threshold. This means that a score of 6 or above on any of the six scales of the CCEI may indicate the presence of a clinically significant mental health issue and may require further evaluation and treatment.

A Psychophysiological Stress Profile (PSP) [30] was implemented. During the experiment, patients were requested to sit in a comfortable chair with their eyes closed and remain still and relaxed for 10 min in total. The room temperature was maintained between 19 and 21 °C. Following a 4 min preparation period, a psychophysiological recording lasting 6 min was conducted. The PSP allows for the measurement of parameters related to a stress response. The influence of mental stress on different physiological functions is corroborated. In particular, the biomarkers frequently used are blood pressure, heart rate, temperature, and skin conductance, as well as muscle tension, as they are considered indicators of stress as well as possible links between psychosocial stress and various physical health outcomes [30]. Thus, the following parameters were continuously registered: (1) Surface Frontal Electromyography (sEMG), where the electrical potential was detected through two active electrodes placed 1 cm over the two eyebrows on the same line of the pupils and one reference electrode placed at the center of the front (2 cm of distance between poles); (2) Skin Conductance Level (SCL) (also called Electrodermal Activity—EDA—or Galvanic Skin Response—GSR), where a very low intensity electrical direct current was attained by

means of two electrodes placed on the first and second finger of the non-dominant hand; (3) heart rate (HR), which consists of the detection of the electrical potential of cardiac muscle by the classic bipolar shunt for the electrocardiogram (ECG); and (4) peripheral temperature (PT); the peripheral body temperature was recorded with a thermistor with a device placed on the thenar eminence of the non-dominant hand. EMG and HR parameters were detected by employing surface disposable electrodes with 0.5 mm active surfaces. For the SCL, two gold-plated electrodes were employed. For the PT, a very sensitive electronic thermometer (capable of evaluating fluctuations in temperature of less than 0.1 °C) was utilized. The employed technology device was the "psycholab VD 13" by SATEM, Rome (Italy), connected utilizing an infrared cable with a PC. Finally, all the data were detected and processed by PC soft VD 13SV VERSION 5.0 Works program software by SATEM, Rome (Italy).

As part of the diagnostic process, the levels of thyroid hormones in the body were measured. This involved collecting basal readings of TSH (thyroid-stimulating hormone) and both total and free T3 (triiodothyronine) and T4 (thyroxine). To execute this test, a blood sample was required to be taken. The purpose of this testing was to determine the functioning of the thyroid gland and document the thyroid imbalances in the body.

2.3. Statistical Analysis

The statistical analyses were performed using SPSS (Version 28.0.1.0; IBM Corp., Armonk, NY, USA). To obtain descriptive statistics, we calculated the mean (M) and standard deviation (SD). We also conducted tests for Skewness and Kurtosis and the Kolmogorov–Smirnov test to determine the normality of the distribution. To ensure that the conditions for the conduction of parametric statistics were met, we carried out tests on the differences between patients and controls on sociodemographic factors, such as gender and age, thyroid hormones, and clinical characteristics, including psychological symptoms and psychophysiological parameters. We used the Chi-square Test and Independent Samples *T* Test to calculate these differences. By using these tests, we aimed to obtain a detailed understanding of the differences between the two groups in terms of various characteristics.

3. Results

Both the patients and the controls were similar regarding their sociodemographic characteristics, such as age and gender. However, when it comes to thyroid hormonal dosages, there were significant differences between the two samples, particularly in terms of the levels of TSH. The patients had considerably higher levels of TSH compared to the controls, which could indicate an underlying thyroid disorder or dysfunction (Table 1).

Table 1. Comparisons of sociodemographic and clinical characteristics between the patient group and the control group.

Variable	Patients Group (n = 50)	Control Group (n = 50)	*t* or χ^2	*p*
Age, *M* (*SD*)	23.90 (5.20)	28.10 (8.40)	t (99) = 7.65	n.s.
Sex, *N* (%)			χ^2 (1, *N* = 99) = 0.55	n.s.
Male	17 (34%)	22 (44%)		
Female	33 (66%)	28 (56%)		
Marital status, *N* (%)			χ^2 (2, *N* = 99) = 2.18	n.s.
Married/cohabitant	12 (24%)	16 (32%)		
Unmarried	38 (76%)	32 (64%)		
Separated/divorced	0 (0%)	2 (4%)		
Education Level, *N* (%)			χ^2 (2, *N* = 99) = 3.33	n.s.
Middle school graduation	5 (10%)	13 (26%)		
High school graduation	30 (60%)	25 (50%)		
University	15 (30%)	12 (24%)		

Table 1. *Cont.*

Variable	Patients Group (n = 50)	Control Group (n = 50)	*t* or χ^2	*p*
Current Occupation, *N* (%)			χ^2 (2, *N* = 99) = 9.25	n.s.
Student	35 (70%)	28 (56%)		
Employed	15 (30%)	20 (40%)		
Unemployed/retired	0 (0%)	2 (4%)		
Thyroid Hormonal Dosages				
TSH (mg/μL)	9.50 (5.70)	1.90 (2.20)	1.92	<0.001
TT3 (ng/dL)	12.80 (2.50)	13.10 (4.70)	−0.08	n.s.
TT4 (μg/dL)	6.90 (1.40)	8.20 (3.30)	−0.55	n.s.
FT3 (pg/mL)	3.10 (0.70)	4.20 (3.10)	−0.58	n.s.
FT4 (pg/mL)	6.20 (1.60)	8.90 (4.90)	−0.83	n.s.

The patients diagnosed with SHT suffer from a variety of psychological symptoms that are significantly more severe in comparison with the control group. These symptoms include increased levels of anxiety, somatization, depression, and hysteria (Figure 1).

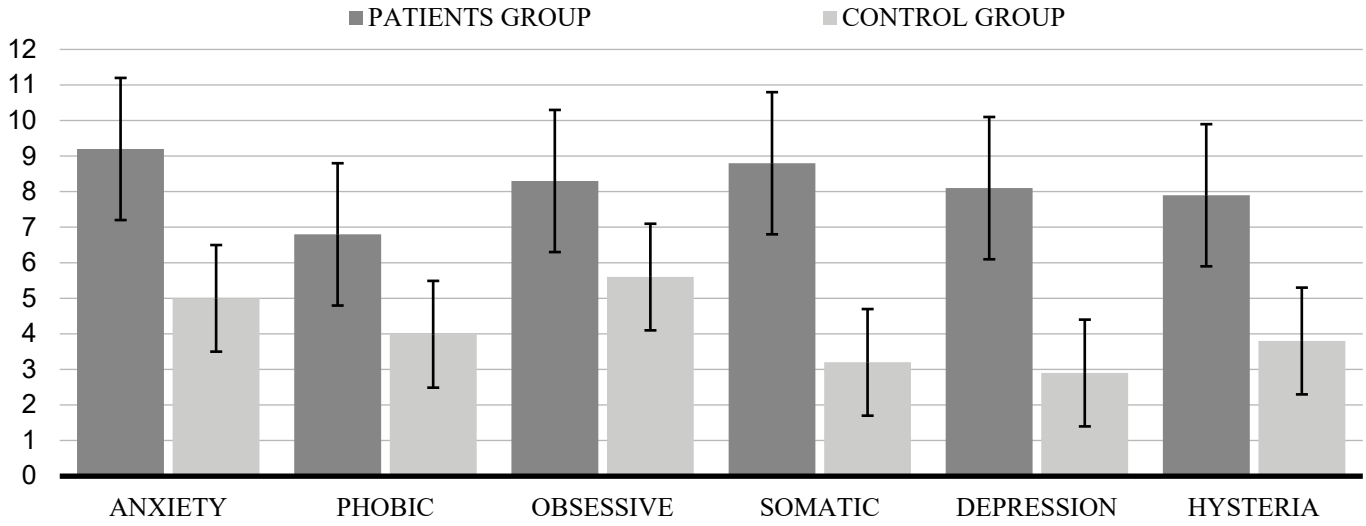

Figure 1. Comparison between patients and controls on the subscales of the Crown–Crisp Experiential Index.

In addition, when measuring the psychophysiological parameters of the patients in a resting condition, significant differences were found in all of the values. This indicates that patients with SHT have a different physiological response to stress compared to non-SHT individuals. These findings are detailed in Table 2.

Table 2. Comparisons of clinical features between the patient group and the control group.

	Patients Group (n = 50)		Control Group (n = 50)		*t* Test	*p*
	M	SD	M	SD		
Crown–Crisp Experiential Index						
Anxiety	9.20	2.40	5.00	3.20	7.40	<0.001
Phobic	6.80	4.10	3.99	2.20	5.53	n.s.
Obsessive	8.30	2.20	5.60	3.10	1.02	n.s.
Somatic	8.80	1.70	3.20	1.80	3.20	<0.001
Depression	8.10	1.90	2.90	1.10	3.47	<0.001
Hysteria	7.90	3.20	3.80	2.30	1.49	<0.001

Table 2. *Cont.*

	Patients Group (n = 50)		Control Group (n = 50)		*t* Test	*p*
	M	**SD**	**M**	**SD**		
Psychophysiological Assessment						
Surface Electromiography	4.60	1.20	2.20	1.60	1.71	<0.001
Skin Conductance	11.90	3.60	4.60	2.50	2.39	<0.001
Heart Rate	84.60	11.40	74.10	8.10	1.08	<0.001
Peripheral Temperature	29.90	2.20	34.00	2.90	−1.61	<0.001

4. Discussion

In this study, the aim was to compare two groups—one consisting of patients with subclinical hypothyroidism and the other comprising age-matched control subjects. The researchers observed significant differences between the two groups, not only in terms of hormone dosage values but also in terms of psychophysiological values and psychological symptoms. The researchers found higher levels of anxiety, somatization, depression, and hysteria in the patient group as compared to the control group. Although these somatic symptoms can be explained by their recent medical diagnoses, the presence of anxiety, depression, and hysteria manifested as mental suffering for the patients. Moreover, the average values of anxiety and depression in the patient group exceeded the clinical cut-off of six, indicating the severity of these symptoms. It is worth noting that this is the first time that significant symptoms of anxiety and depression have been detected in a group of patients with subclinical hypothyroidism. Although these findings are in line with previous research [8,19,31], there are also studies where elevated psychological symptoms were observed only in full-blown hypothyroidism [4,32,33].

The symptoms of anxiety and depression reported by patients with SHT may correspond to the cognitive dimension and self-reported manifestation of autonomic arousal detected in the sample of patients with SHT. The ANS is the part of the nervous system that controls the involuntary functions of the body, such as heart rate, blood pressure, and digestion. The patient groups had higher levels of all psychophysiological parameters, including HR levels, compared to the controls. It is worth noting that the expected decrease in HR commonly seen in clinical hypothyroidism [21,23,24,26] was not observed in our SHT patient group. In clinical hypothyroidism, bradycardia, diastolic hypertension, or hypotension may occur due to reduced cardiac output [31]. Notwithstanding, some studies have already described sympathetic arousal due to increased cardiac activity (i.e., higher HR levels) or reduced compensation by the parasympathetic system [11,23] and vagal tone [25,26]. Other authors [27] attested to a decrease in sympathetic activity in conditions of hypothyroidism where the thyroid-stimulating hormone (TSH) exceeds a value of 10. These findings suggested that higher sympathetic arousal (i.e., higher HR levels) would be associated with SHT, whereas reduced cardiac activity would correlate with clinical hypothyroidism. Based on these assumptions, our data would be consistent.

There is a growing body of research suggesting that the cardiovascular system can be significantly affected by changes in thyroid hormone levels. Specifically, several studies found that patients with hypothyroidism may experience pre-hypertension, characterized by higher systolic blood pressure levels [11]. For instance, a study conducted by a group of researchers reported significant differences in systolic blood pressure levels between patients with hypothyroidism, with lower FT3 levels being associated with higher systolic and diastolic blood pressure levels [11]. Similarly, a study conducted by Galetta et al. showed that patients with SHT had higher systolic blood pressure levels and were pre-hypertensive [26]. The mechanisms underlying the autonomic alterations in thyroid disorders are complex and multifactorial. These mechanisms include an increase in thyrotropin-releasing hormone (TRH), which has a direct sympathetic activation effect on the heart, an elevated level of plasma adrenaline, and a decrease in receptor or post-receptor

sensitization. Furthermore, the metabolic effects of decreased thyroid hormones can lead to higher protein deposition in the extracellular space, resulting in water accumulation in the myocardial wall and fibrosis in the ventricular wall, all of which lead to augmented regional inhomogeneity of the ventricular repolarization. On top of this, adverse effects on circulating lipids, the swelling of vascular smooth muscle cells, and an impairment of endothelial function were suggested [11]. These effects can contribute to an increased risk of cardiovascular disease and may play a role in the development of hypertension in patients with thyroid disorders. Overall, these findings suggest that thyroid hormone levels may play a crucial role in regulating blood pressure and maintaining cardiovascular health. Further research is needed to better understand the complex interactions between thyroid hormone levels and cardiovascular function, as well as to develop targeted interventions that can help mitigate the risks associated with thyroid disorders.

Our unexpected results revealed that all psychophysiological parameters connected to ANS arousal were elevated, not just cardiac parameters. These data support the hypothesis that there may be a compensatory mechanism in the ANS. These findings suggested that the general lack of energy caused by SHT would be compensated and integrated with an increase in autonomic activity, particularly during the initial phase of endocrine dysfunction [11]. This suggests that the ANS may play a role in the pathophysiology of SHT and may be involved in the development of anxiety and depression in patients with SHT. These findings may have implications for the diagnosis and management of SHT, as well as for the treatment of anxiety and depression in this patient population.

Our study provided valuable insights into the autonomic changes and psychological distress experienced by patients with SHT. However, it is fundamental to acknowledge the limitations of our work. First, the inclusion criteria period was very long. Therefore, the impact of the sociopolitical and economic context, which affects the emotional well-being of the population, cannot be underestimated. Confirmation through further research with larger sample sizes (during a 1- or 2-year recruitment) is needed. By increasing the sample size, more sophisticated statistical analyses can be carried out to establish the relationship between endocrine imbalances (i.e., thyroid hormones), autonomic arousal (i.e., psychophysiological parameters), and psychological symptoms (i.e., anxiety and depression). Moreover, it is crucial to note that our study was cross-sectional, which means that we cannot establish the causality of the observed relationships between different variables. For instance, high levels of anxiety or depression may be simply reactions to stressful situations, such as receiving a medical diagnosis. In agreement with the reactivity hypothesis, somatic disorders or somato-psychic reactions can be a common occurrence in people with organic diseases that significantly impact their quality of life [34,35]. However, due to the nature of our study, we were unable to delve into a detailed interpretation of this phenomenon, and, therefore, further investigation is required to establish the predisposing, precipitating, and chronicizing role of emotional experiences in patients with SHT. Lastly, future studies should better discriminate between hormonal, psychophysiological, and anxiety–depressive aspects. First of all, the present study did not take into account other hormones (i.e., prolactin and estradiol, in the follicular phase) in addition to TSH, FT3, and FT4 values. Nonetheless, the analysis of anxious–depressive symptoms should be used to better analyze truly pathological cases, for instance, by calculating the prevalence of cases of clinical significance and avoiding involving euthymic SHT patients. A more useful comparison group would be a sample of euthyroid patients with a mild but different organic diagnosis, although having analyzed the psychological and psychophysiological aspects of people with SHT at the time of diagnosis should reflect to a lesser extent the psychological adaptation/reactivity to the diagnosis.

This study has certain limitations, but its findings have significant implications for clinical practice. The research highlights the importance of conducting extensive clinical and psychological analyses in medical contexts. As reported by the World Health Organization (WHO) [36], healthcare providers should consider treating patients for both their physical and psychological symptoms to ensure overall well-being. In clinical settings, it is

also crucial to identify the underlying organic causes of psychological symptoms, such as anxiety and depression. For instance, full-blown hypothyroidism can lead to anxiety-like symptoms, including tension, agitation, and confusion [16,37], as well as depressive-like symptoms, like asthenia, apathy, and increased fatigue [15,19]. Nonetheless, these symptoms might be mistakenly diagnosed as a depressive disorder with a purely psychogenic origin. This misdiagnosis can lead to the implementation of pharmacological interventions, which can further affect the autonomic nervous system. For instance, antidepressants can trigger autonomic arousal. On the other hand, anxiolytics can cause inhibitory effects [33]. Therefore, it is essential to conduct in-depth clinical–psychological analyses to accurately diagnose and treat patients with psychological symptoms.

Assessing psychological symptoms and autonomic arousal in individuals with physical conditions, such as SHT, can provide valuable insights into underlying alterations. Such multidimensional assessment programs can help in the early diagnosis of SHT by detecting and preventing the worsening of psychological symptoms and psychophysiological alterations associated with full-blown hypothyroidism. The functional neuroimaging findings support the existence of cognitive and affective changes associated with SHT. However, the reversibility of these phenomena with therapy was also observed [11,24–26]. These findings led to the suggestion that even patients with subclinical hypothyroidism may be outside the range of normal thyroid function and should be treated [11,24–26]. The physical symptoms of SHT could directly benefit from pharmacological intervention with levothyroxine [31,38], as could the psychological symptoms (cognitive, emotional, and behavioral) and physiological arousal indirectly. In situations where secondary mental disorders may arise, incorporating the expertise of a mental health specialist as part of a multidisciplinary intervention is recommended. The treatment approach would be tailored to the unique needs of the individual, which may include addressing issues such as illness anxiety, rumination, avoidant behavior, and low self-esteem. This collaborative approach ensures that the individual receives comprehensive care and support, which is critical in promoting optimal mental health outcomes. However, it is necessary to prioritize large-scale randomized trials to determine the optimal approach for treating individuals with subclinical thyroid disease [39,40]. This will help in identifying the most effective treatment options for such patients and ensure better treatment outcomes. Overall, a multidimensional assessment of psychological symptoms and autonomic arousal appears to be a valid and inexpensive methodology to better understand the alterations that accompany physical conditions such as SHT.

5. Conclusions

This study aimed to investigate the occurrence of psychological symptoms and autonomic imbalance in patients with SHT. Researchers have been contradicting each other on whether patients with SHT exhibit symptoms of anxiety or depression as well as autonomic changes. However, our study supports previous findings, as our group of patients with SHT reported higher levels of anxiety and depression, as well as hysteroid behavior, compared to healthy controls. We also detected an increase in sympathetic activity, not only by observing the psychophysiological parameters of the heartbeat but also by examining other parameters, such as skin conductance, peripheral temperature, and muscle tension. This is the first time an autonomic alteration has been observed in multiple parameters connected to a higher level of arousal of the ANS and not solely in cardiac function. Our findings emphasize the importance of investigating psychological symptoms and psychophysiological parameters in patients with SHT to help treat both their mental and physical health.

Our study has revealed crucial insights into the management of SHT patients. We found that it is of substantial importance to recognize and address both the physical symptoms of the condition as well as associated mental health concerns. Specifically, anxiety, depression, and autonomic changes were identified as common psychological symptoms in SHT patients that require attention. By taking a comprehensive approach that addresses both the physical and psychological symptoms of SHT, clinicians can develop

a more effective treatment plan. This can lead to substantial improvements in a patient's overall quality of life and better management of their condition. By treating the underlying psychological symptoms, patients may experience reduced stress levels, improved coping mechanisms, and a more positive outlook on their condition. These findings shed light on the need for a multidisciplinary approach to treating SHT patients, involving both medical and mental health professionals. By working together, healthcare providers can ensure that patients receive the care they need to manage their condition's physical and psychological aspects.

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Institutional Review Board Statement: The study was conducted under the recommendations of the local ethics committee at the Hospital of Pisa. In Italy, until 2018, no ethical approval was required for studies of an observational nature since they were not defined as medical/clinical research, according to Italian law No–11/2003. The study was conducted before 2018 and included non-clinical surveys that used non-invasive measures. Furthermore, this study complies with the Declaration of Helsinki and Italian privacy law (Legislative decree No. 196/2003). No treatments or false feedback were given, and no potentially harmful evaluation methods were used. Participation was voluntary, and participants could drop out at any time without any negative consequences. All data were stored only by using an anonymous ID for each participant.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent was obtained from the patients to publish this paper.

Data Availability Statement: The data presented in this study are available upon reasonable request from the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

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