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Original Article

Short-Term Memory Impairment in Different Ranges of Thyroid Stimulating Hormone in Patients with Subclinical Hypothyroidism

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Abstract

Introduction: Subclinical hypothyroidism (SCH) is one of the main causes of cognitive impairments. Despite being euthyroid or having Levothyroxine (LT-4), patients have memory impairments. The current study has investigated impairments in short-term memory in SCH across different ranges of thyroid-stimulating hormone (TSH).

Methods: This study included four groups: Group 1 Healthy individuals; Group 2 recently diagnosed patients with SCH (≥2.5mIU/L); Group 3: patients with elevated TSH levels ≥4.0mIU/L (having L-T4 treatment); and Group 4: euthyroids (TSH levels <4.0mIU/L), ongoing LT-4 treatment. The Cambridge Neuropsychological Test Automated Battery was administered, and delayed matching of the sample task was performed for short-term memory. (please add more details about statistical analysis, and all methods used for this study).

Results: Group 4 performed better than another two groups of patients, however group 3 showed better performance than group 2 (TSH levels ≥2.5mIU/L). Despite receiving LT-4, group 3 and 4 did not have better processing speed compared to newly diagnosed patients.

Conclusion: Patients who were receiving LT-4 treatment showed better performance in short-term memory function than those who were recently diagnosed with SCH.

Introduction

Subclinical hypothyroidism (SCH) occurs when levels of free thyroxine (fT4) fall within the normal reference values, yet the levels of thyroid-stimulating hormone (TSH) are elevated beyond the expected range.[1] It affects 3–15% of the adult population,[2] with higher prevalence associated with advancing age and female sex.[3] It has been recognized as a potentially treatable or reversible contributor to cognitive impairment. Consequently, thyroid profile tests are suggested in clinical measures as an essential element for the analysis of cognitive impairments.[4–7] Studies have documented that working memory (WM) is consistently the most affected cognitive domain in individuals with hypothyroidism.[8,9] WM serves as the "sketchbook of sensible thoughts" and functions as the platform where thoughts are manipulated and hold. It involves multiple processes that render task-relevant information accessible to more advanced cognitive functions like reasoning, decision-making, processing speed, and learning.[10]

WM, classified as Short-Term Memory (STM), which is required for remembering information characterized by its unpredictable fluctuations in both time and content.[11] Some studies suggest compelling evidence that the hypothyroid state results in notable alterations in both brain function and structure.[12–14] These alterations include decreased hippocampal volume and cerebral blood flow, particularly affecting regions involved in executive functions such as attention, short-term memory, and processing speed. Clinically, alterations such as emotional lability (slowness of thought process, lack of attention, apathy, rarely frank psychosis, and agitation); decrement in cognition (decline of general intelligence, memory, concentration) have been observed in the SCH population.[15] Patients frequently express complaints, including forgetfulness, impaired memory,[8,16,17] neuropsychological symptoms,[18–20] and other symptoms such as fatigue, weight gain, cold intolerance, and constipation.[21]

The potential improvements in memory function among patients undergoing levothyroxine (LT-4) treatment are often disregarded, despite some patients continuing to display deficits even after their TSH levels normalize, suggesting a lasting impact on cognitive function due to prior abnormal TSH levels.[17,22] Talaei et al., have also emphasized that individuals with TSH levels less

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Study Highlights

- Patients who were newly diagnosed with SCH with a TSH range of ≥ 2.5mIU/L had impaired short-term memory compared topatients who were receiving LT-4.
- The first study to indicate that euthyroid people who have been on the medication for 10 years or more have significantly better performance than those who have been on the prescription for 1 or more years.
- Our findings indicate a threshold of 2.5mIU/L for initiating LT-4. Hence, instead of a wait-and-watch approach to the process of neuropsychological symptoms, treatment may initiate priorly.

than 4.0mIU/L, in the absence of symptoms, are generally considered euthyroid.[23] However, if neuropsychological symptoms are present, the initiation of LT4 treatment may be justified at a lower TSH cut-off value, specifically 2.5 mIU/L.

In addition, Hayashi et al. proposed ranges for TSH levels to categorize individuals as euthyroid or hypothyroid.[24] A range of 0.45-4.49 mIU/L indicates euthyroidism in asymptomatic individuals, while TSH values between 4.5-19.9 mIU/L, along with normal fT4 levels within the reference values (5.0 to 12.0 μg/dL), are considered SCH. Nevertheless, there is disagreement about the upper perimeter of the TSH reference values to be considered euthyroid. While several reviews[25,26] argue for an upper TSH limit between 4.5 and 5.0 mIU/L, certain authors[27] suggest dropping these values between 2.5 and 3.0 mIU/L.

The current study was designed to investigate deficits in short-term memory in patients with SCH across different ranges of TSH. Our decision to prioritize memory was based on previous studies,[22,28,29] which have shown that memory is particularly affected in individuals with hypothyroidism. Animal studies[30] have also consistently highlighted the significant impact of L-T4 on brain regions crucial for memory function. However, none of the previous studies have specifically focused on STM.

Therefore, we aimed to examine STM function in patients with SCH with raised TSH levels (≥ 4.0mIU/L) and euthyroid patients who were on LT-4 treatment with TSH levels < 4.0mIU/L, compared to those newly diagnosed with TSH ≥ 2.5mIU/L, and healthy controls. Also, we explore assessing whether patients undergoing LT-4 treatment show better performance in memory functions compared to healthy controls, taking into account the duration of medication.

Materials and Methods

Participants

Patients were recruited from Shri Guru Ramdas Hospital, Guru Nanak Dev University Health Center, and general practitioners in the city of Amritsar. A total of 136 participants were recruited, including 35 healthy individuals from the local community.

Study Design

This cross-sectional study was conducted between May 2022 and July 2023. The study procedure was approved by the Institutional Ethics Committee, Guru Nanak Dev University, Amritsar, with diary number 302/HG. The study is registered in the Clinical Trial Registry of India. All treating physicians gave their written informed consent before the start of patient recruitment. The study was conducted in harmony with the Declaration of Helsinki 2013. Written informed consent was taken from each subject of the study.

Selection Criteria

Inclusion criteria: Subjects aged 25-55 years; Mini-Mental State Examination (MMSE) score more than 24; Healthy individuals from the local community with no thyroid dysfunction; Diagnosed patients with SCH.

Exclusion criteria: Subjects with any other neurological disorders or any neuropsychiatric disorders; medical history of antidepressants or any other antipsychiatry drugs; history of dementia in family; any systemic diseases such as hypertension, diabetes mellitus, myocardial infarction; present history of any medication addiction.

Clinical Assessment

We interviewed the patients about their subjective symptoms, with particular emphasis on issues they associated with thyroid disease or believed were worsened by it. We also recorded coexisting medical conditions, any history of mental illness, and the use of medications for both psychiatric and non-psychiatric disorders. Each participant's thyroid profile was analyzed for biochemical signs. The medication history for ongoing treatment regimens included specific L-T4 dosages, as well as information regarding treatment duration, thyroid replacement history, and neuropsychological symptoms.

Thirty-four patients were referred for thyroid profiling after complaining of neuropsychological symptoms (e.g., fatigue, forgetfulness or memory impairment, insomnia, and depressive symptoms). After reviewing the test results, which showed TSH levels of ≥ 2.5 mIU/L, the clinicians concluded that the recently discovered patients had SCH. Along with 34 patients who were observed for hypothyroid symptoms and had elevated TSH levels, and who continued the LT-4, were recruited. Thirty-three euthyroid patients who visited the outpatient clinic for a follow-up examination. Prescription records from the clinical practices were reviewed to identify all euthyroid cases and patients with elevated TSH levels who were receiving LT-4 treatment. In addition, thirty-five healthy volunteers were recruited from the local community. They had normal thyroid function tests and were free of any symptoms of thyroid dysfunction.

The study categorizes the groups according to symptoms, medication history, and TSH values:

Group 1: Healthy individuals with no present or past

history of thyroid dysfunctions

Group 2: Newly diagnosed patients with SCH (TSH levels are equal to 2.5 mIU/L or higher)

Group 3: Patients with TSH levels of 4.0 mIU/L or higher who are currently on L-T4 treatment

Group 4: Patients with TSH levels less than 4.0mIU/L who are also on L-T4 treatment.

Neurocognitive Assessment

The participants had to meet the conditions of being cognitively alert and possessing a state of good general health in order to meet the credentials for participation in the neurocognitive assessment. The Mini-Mental State Examination (MMSE) was employed to estimate the global cognitive status. It has a maximum score of 30 points. The classification of cognitive impairment severity is delineated into three categories: severe cognitive impairment corresponds to scores ranging from 0 to 17, mild cognitive impairment is denoted by scores between 18 and 23, and no cognitive impairment is indicated by scores falling within the range of 24 to 30. (Ong et al., 2016). Participants with scores of 24 or above were considered eligible for enrollment in the study. Hamilton Depression Rating Scale (HDRS), a special tool for assessing depressive symptoms, was used. The scale comprises 17 items (8 items valued on a 5-point scale, where 0-4 points were given according to the symptoms present, and 9 items valued on a 3-point scale from 0-2).[31] The interpretation of the total scores is as follows: 0 - 7 stands for an ordinary temperament or mood. 8 to 13 scores stand for mild depression present, 14 to 18 scores stand for moderate type of depression, 19 - 22 for severe form of depression, and scores more than 23 for actual severe type of depression.

The socioeconomic grade of the participants was addressed with the modified scale of Kuppuswamy[32], with scores ranging from 3 to 29, which is used to categorize families into five groups: 1. Upper class (I); 2. upper middle class (II); 3. lower middle class (III); 4. upper lower class (IV); 5. lower socioeconomic class (V). This classification is considered according to the occupation and educational level of the family's head and their total income per month. The educational level of each participant was recorded according to the following categories: Level 1 (left education before the age of 16), Level 2 (left education at the age of 16), Level 3 (left education at the age of 17–18), Level 4 (Bachelor's degree or correspondent), Level 5 (Master's degree or correspondent), and Level 6 (PhD or correspondent).

All study participants underwent the Delayed Matching to Sample (DMS) test, a component of the computerized neuropsychological test for visual STM from the Cambridge Neuropsychological Test Automated Battery (CANTAB). Participants were seated at a comfortable height and given the CANTAB-I pad (Cambridge Cognition Ltd, 2012) to perform the DMS task and record responses via the touchscreen interface.

The DMS task was a 4-choice recognition test of non-verbal patterns, consisting of 20 different trials. The participants had "to select, among four different choice patterns, the one that matches a complex visual pattern presented" (i.e., the target stimulus). The outcome variables were recorded:

1. DMS Percent Correct (all delays): The percentage of assessed trials, holding a delay during which the participants chose the accurate box on their first box choice. It is calculated across all assessed trials holding a delay.
2. DMS Percent Correct (simultaneous): The percentage of assessed trials where the target and response stimuli were offered simultaneously, during which the participants chose the accurate box on their first box choice. It is calculated across all assessed trials, holding the instantaneous demonstration of stimuli.
3. DMS Percent Correct (0 seconds delay): The percentage of assessed trials holding a 0-second delay during which the participants chose the accurate box on their first box choice. It is calculated across all assessed trials, holding a 0-second delay.
4. DMS Percent Correct (4 seconds delay): The percentage of assessed trials holding a 4-second delay during which the subject chose the accurate box on their first box choice. It is calculated across all assessed trials, holding a 4-second delay.
5. DMS Percent Correct (12-seconds delay): The percentage of assessed trials holding a 12-second delay during which the participant chose the accurate box on their first box choice. It is calculated across all assessed trials containing a 12-second delay.
6. DMS Mean Correct Latency: The mean latency among the demonstration of the response stimuli options and the participants picking the accurate box on their first attempt. It is calculated across all accurately assessed trials simultaneously and across all delays.

Statistical Analysis

Comparison between groups for demographic and clinical data of all the participants was described using descriptive statistics. A non-parametric Kruskal-Wallis's test was executed in the comparisons between groups. Next, the Dunn test was performed for post hoc pairwise multiple comparisons for significant differences with the Bonferroni correction to examine the differences in the key parameter DMSML (reaction latency) score among the healthy control and the other three groups of patients. Further, we divided Group 4 (euthyroid – on LT-4) into two groups. Group 4a (ongoing LT-4 for 1 or more than one year), and group 4b (ongoing LT-4 for 10 or more than 10 years). DMSML scores were taken into account to examine whether the duration of LT-4 medication influences the performance of STM in SCH with the lessening of TSH levels. A linear regression model was performed for the key parameters of the DMS task, wherein confounding aspects such as age, level of education, and socioeconomic status were included as

independent variables to determine whether these factors influence the results. A statistical analysis was performed using SPSS 27.0 version (IBM SPSS Statistics, [IBM Corp., Armonk, NY. USA]). Additionally, sample size was determined by G* Power (3.1.9.2) with ρ1 (proportion of cognitive impairment in individuals with SCH = 0.36) and ρ2 (proportion of cognitive impairment in healthy individuals = 0.14).[33] The values set for α (absolute error) and β were 0.05 and 0.90.

Results

Clinical characteristics and demographics of the study participants are described with descriptive values, as mentioned in Table 1. A total of 136 participants were included in the study, consisting of 101 patients with SCH and 35 normal healthy individuals. The majority of participants (59.6%) had an undergraduate or corresponding level of education, whereas the socioeconomic status of 78.7% participants was upper middle class. The between-group comparison of DMS task variables was statistically significant ($P < 0.05$), as shown in Table 2. A Kruskal-Wallis test revealed a strong indication of a difference ($P < 0.05$) between the mean rank values of at least one pair of study groups. Further, Dunn's pairwise test was executed for all six pairs of groups. There was a strong indication ($P < 0.05$ with adjusted Bonferroni correction) of a difference between the groups of healthy controls and patients with elevated TSH who were on LT-4 treatment. The median DMS mean correct latency score for the healthy controls was 52.49, compared to 77.97 in patients with elevated TSH (>4.0 mIU/L). The comparison of percent correct scores at 0, 4, and 12 seconds of delay in choosing the correct box to complete the DMS task shows significant differences, as shown in Figure 1. All 3 patient groups had low performance as compared to the control group. In group 2, there is

Table 1. Descriptive analysis of characteristics of the participants of DMS task

Variable	Group 1 N = 35	Group 2 N = 34	Group 3 N = 34	Group 4 N = 33
Age (years)	36.37 ± 9.62	36.79 ± 8.88	38.76 ± 10.76	38.93 ± 9.66
Gender	M = 6; F = 29	M = 4; F = 30	M = 2; F = 32	M = 2; F = 31
Level of education	3.82 ± 0.74	3.61 ± 0.65	3.61 ± 1.07	3.42 ± 0.86
Socioeconomic status	20.80 ± 3.30	20.17 ± 3.01	20.11 ± 4.88	18.75 ± 4.75
MMSE	29.4 ± 0.73	29.32 ± 1.96	27.85 ± 2.03	27.30 ± 2.45
HDRS	1.82 ± 1.48	4.61 ± 3.69	4.61 ± 3.34	3.03 ± 2.31
TSH (mIU/L)	1.58 ± 0.48	3.97 ± 1.39	13.02 ± 20.55	2.45 ± 0.96
T3 (pmol/L)	1.48 ± 1.44	1.17 ± 0.59	1.05 ± 0.56	1.09 ± 0.49
Free T4 index (ug/dl)	7.74 ± 2.44	8.35 ± 1.71	8.93 ± 1.63	8.99 ± 1.51
Duration of LT-4 medication (years)	-	-	4.62 ± 3.79	3.85 ± 4.0
Neuropsychological and other clinical symptoms				
Fatigue	52.77%	73.72%	89.30%	57.14%
Weight Gain	16.5%	34.1%	67.8%	11.4%
Insomnia	22.2%	42.4%	59.3%	48.5%
Depressive symptoms	13.8%	80.9%	71.8%	57.1%
Memory loss	08.0%	78.78%	87.2%	42.8%
Cold intolerance	0.5%	29.2%	39.2%	25.7%
Dry skin	11.1%	22.2%	40.3%	30.4%
Hearing loss	4.5%	18.3%	47.7%	10.9%

Abbreviations: M-Male; F-Female; MMSE-Mini Mental State Examination; HDRS- Hamilton Depression Rating Scale; TSH- Thyroid Stimulating Hormone; T3-thyroxine; T4-Triiodothyronine; Group 1 = Healthy controls; Group 2 = Newly diagnosed cases; Group 3 = Patients with elevated TSH (on going-LT-4); Group 4 = Euthyroid (currently on LT-4)

Table 2. Between group comparison of Delayed matching sample (DMS) task parameters

Parameters	Group 1 (n = 35) Mean rank	Group 2 (n = 34) Mean rank	Group 3 (n = 34) Mean rank	Group 4 (n = 33) Mean rank	*P* value
DMSPCAD	90.21	62.22	60.65	60.03	0.002*
DMSPCS	78.00	65.44	57.07	73.35	0.027*
DMSPC0	73.01	49.43	64.93	59.12	0.037*
DMSPC4	79.33	58.12	56.59	47.48	0.003*
DMSPC12	72.26	60.35	52.94	62.25	0.142
DMSML	52.49	70.91	77.97	73.24	0.039*

Abbreviations: DMS-Delayed matching sample; DMSPCAD-DMS Percent correct (all delays); DMSPCS-DMS Percent correct (simultaneous); DMSPC0-DMS Percent correct (0 seconds delay); DMSPC4- DMS Percent (4 seconds delay); DMSPC12- DMS Percent correct (12 seconds delay); DMSML- DMS Mean correct latency; Group 1 = Healthy controls; Group 2 = Newly diagnosed cases; Group 3 = Patients with elevated TSH (on going-LT-4); Group 4 = Euthyroid (currently on LT-4) *statistically significant ($P = < 0.05$)

no difference at 0 and 4-second delays. Group 3 shows low performance at 12 seconds delay as compared to all groups. Group 3 and 4 performed better at a 0-second delay than group 2. Results of between group comparison of response latency values to explore whether the duration of LT-4 medication affects the performance of DMS task show a noteworthy trend in DMS mean latency scores; the 4b group performed significantly better as compared to Group 1 as shown in Figure 2, which indicates an enhancement in short-term memory function along with the reduction in TSH levels in patients who were on LT-4 for a decade or more. The outcomes of the model of linear regression analysis, as shown in Table 3, indicate that the level of education has a significant impact on the dependent variables.

Figure 1 shows the comparison of percent correct scores at 0,4,12 seconds delay to choose the correct box to complete the DMS task. Groups 2, 3, and 4 had low performance as compared to Group 1. In group 2, there is no difference at 0 and 4-seconds delays. Group 3 shows low performance at 12 seconds delay as compared to all groups. Group 3 and 4 performed better at a 0-second delay than group 2.

Figure 2 shows, the between group comparison of response latency scores to explore if duration of LT-4 treatment affects the performance in DMS task. Group 4b performed significantly better as compared to Group 1, indicating an enhancement in short-term memory function along with the reduction in TSH levels in patients who were on LT-4 for a decade or more.

Discussion

The examination of short-term memory within the SCH population remains an unexplored area within current literature. This study was the first to focus on screening of short-term memory function in this patient population.

In our clinical observations, patients with SCH undergoing LT-4 treatment can be broadly categorized

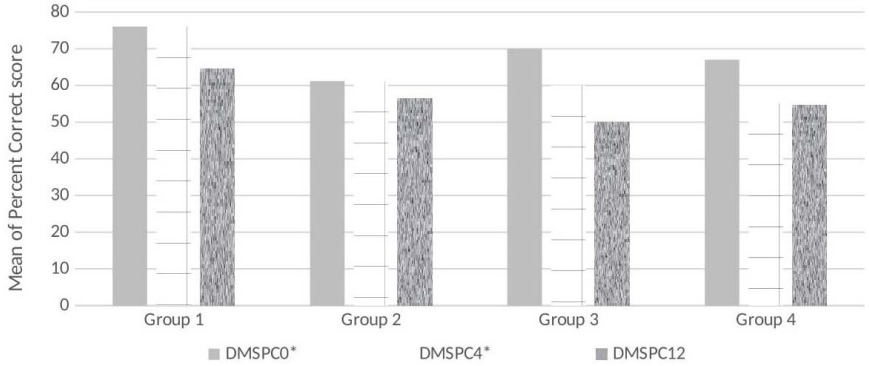

Figure 1. Comparison of percent correct scores at 0,4,12 seconds delay to choose the correct box to complete the DMS task
Abbreviations: DMS: Delayed matching sample; DMSPC0-DMS Percent correct (0 seconds delay); DMSPC4-DMS Percent correct (4 seconds delay); DMSPC12- DMS (12 seconds delay); Group 1 – Controls; Group 2 – Healthy controls; Group 3– Patients with elevated TSH (on going-LT-4); Group 4– Euthyroid (currently on LT-4); * statistically significant (p≤0.05)

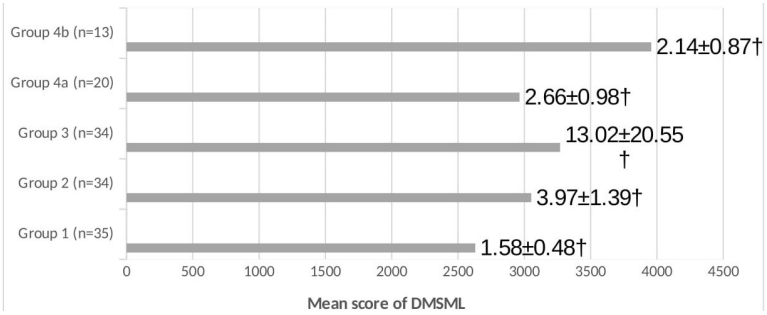

Figure 2. Between group comparison of response latency scores to explore if duration of LT-4 treatment affects the performance in DMS task
Abbreviations: † Thyroid stimulating hormone (TSH) mean and standard deviation; DMSML- Delayed matching sample mean latency; *statistically significant (p≤0.005); Group 1- Healthy Controls, Group 2- Newly diagnosed cases, Group 3- Patients with elevated TSH (ongoing LT-4), Group 4a – Euthyroid (currently on LT-4 for 1 or more than one year), Group 4b – Euthyroid-asymptomatic (currently on LT-4 for 10 or more years).

Table 3. Regression linear model analysis for cofounding factors (n=136)

Key variables of DMS task	Age		Socioeconomic Status		Level of education	
	F	*P* value	F	*P* value	F	*P* value
DMSPCAD	0.66	0.41	3.96	0.04*	10.43	0.002*
DMSPCS	1.36	0.24	0.47	0.49	2.10	0.14
DMSML	1.63	0.20	1.06	0.30	3.65	0.05*

Abbreviations: DMS-Delayed matching sample; DMSPCAD-DMS Percent correct (all delays); DMSPCS-DMS Percent correct (simultaneous); DMSML- DMS Mean correct latency; *statistically significant (*P*=≤0.05).

into three groups. Firstly, some have recently been diagnosed. Secondly, there is a subset of patients who have received a diagnosis but exhibit poor adherence to prescribed dosages, resulting in inadequately controlled TSH levels. Lastly, we have patients who demonstrate compliance with medication regimens and maintain regular follow-up appointments with clinicians to ensure their TSH levels remain within the normal range. Given this clinical context, it was considered appropriate to establish a classification system comprising three categories for patients diagnosed with SCH.

In order to uphold standardized testing protocols, we utilized a computerized battery of tests featuring touchscreen technology. The CANTAB-DMS task was administered to evaluate short-term memory. The DMS task, which is vital for memorizing information that varies erratically in time and/or in content, such as when diverse stimuli direct the criterion response on changed trials, so the cue that must be recalled diverges from trial to trial. Our results suggest significant impairment in short-term memory among the SCH patient groups when compared to the healthy controls, with statistical significance observed at a *P*-value of ≤ 0.05. DMS percent correct simultaneous score was higher in Group 4 (euthyroid group but on LT-4) as compared to Groups 2 and 3. This indicates better performance in visual short-term memory in the euthyroid group than in newly diagnosed and patients with elevated TSH levels. It is consistent with the study[34] conducted on animal model reported that thyroidectomized adult rats exhibited notable deterioration in cognitive function, impacting both types of memory (short and long-term memory), as assessed by the test named "radial arm water maze". However, cognition deficits were significantly mitigated following T4 treatment. Another study[35] documented that the administration of T4 notably enhanced the cognitive performance of euthyroid rats in the water maze memory task. Further, the authors mentioned that these enhancements were markedly correlated with a substantial surge in cholinergic movement in the frontal cerebral cortex and the hippocampus. In addition, interestingly, euthyroid patients, 13 out of 33, who had been using LT-4 for 10 years or longer, had a higher percentage of correct scores in the DMS task than controls, whereas those who had been taking medication for one or two years had lower scores. Thus, the relationship between LT-4 and the hippocampus in the brain may explain why short-term memory has improved after decades of treatment.

Amongst the patient groups, in newly diagnosed patients, the reaction latency score was lower in (Group 2 with mean TSH of 3.97 ± 1.39 mIU/L) as compared to patients who were suboptimal dosage or noncompliant(Group 3 with a mean TSH 13.02 ± 20.55 mIU/L) and euthyroid (Group 4 with a mean TSH value of 2.45 ± 0.96 mIU/L), indicating a quicker processing speed and memory retrieval, in terms of visual matching skill and visual STM, in patients who were newly diagnosed than euthyroid and patients with elevated TSH levels. This seems to be counterintuitive, as euthyroid patients should have had a better processing speed. It is possible that the cuneus in the occipital area of the brain, which is involved in visual processing,[36] and a sensitive target area in SCH, with a reduced blood supply,[37,38] recovers very slowly or perhaps does not recover once affected in SCH. It is also possible that the interval between diagnosis and initiation of medication may affect the function of this region. Although this was beyond the scope of the present study, it could be explored in future studies using fMRI. Haji et al[38] reported that, in patients with Alzheimer's disease, cerebral blood flow in the cuneus, among other regions, was reduced in patients with coexisting SCH (mean TSH: 17.9 ± 23.9 mIU/L), but not in patients with normal thyroid function (mean TSH: 1.7 ± 1.1 mIU/L).

The comparisons of the delay intervals in the performance of DMS tasks revealed significant differences. All three patient groups had lower intervals, indicating slower recall at 0,4,12 seconds delay compared to the control group. This shows that these values were impaired in all three patient groups. However, in euthyroid patients and patients with elevated TSH levels, the zero-second delay intervals were higher than in newly diagnosed patients, suggesting that short-term memory function was impaired in these patients. Further, newly diagnosed patients (group 2) had a lower interval than patients with SCH who were on LT-4 treatment. Literature suggests a reciprocal directive of thyroid hormones and the GABAergic system.[39,40] γ-Aminobutyric acid (GABA), the foremost inhibitory type of neurotransmitter in the brain, plays important roles in controlling mood or behavior and cognition.[41] Liu et al[42] reported that it rises to a normal level after L-T4 treatment and that memory impairments in euthyroid patients are alleviated at the same time.

Limitations

The cross-sectional study design may create selection bias in the study population, limiting the capacity to demonstrate a clear link between DMS task characteristics and TSH values. Furthermore, the absence of follow-up for patients is a key factor. This constraint may affect the results' generalisability. Whether or not patients with SCH require early treatment is an ongoing and fundamental issue. Our research suggests that early treatment with LT-4 is crucial. This is also supported by Zhu et al,[29] who recommend initiating early LT-4 treatment due to impaired memory, specifically in frontal executive function, in untreated SCH. However, our study indicates that a threshold of 2.5 mIU/L can be used to initiate LT-4.

Conclusion

This study provides valuable insights into the distinct short-term memory deficits observed in individuals with SCH across different TSH levels, as well as the potential cognitive benefits associated with LT-4 treatment. Further well-designed randomized controlled trials, supplemented by longitudinal follow-up studies, are needed to enhance our understanding of the pathogenesis and natural

progression of short-term memory impairments in SCH. Moreover, such studies are essential for evaluating the efficacy of LT-4 in improving these memory functions.

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Competing Interests
Authors declare no conflict of interest.

Ethical Approval
The present study's procedure was permitted by Institutional Ethics Committee, Guru Nanak Dev University, Amritsar, registered with diary number (302/HG). Each subject recruited in the study has signed the informed consent before the data collection started. Information regarding the samples was confidential and personal details of the participants were not disclosed.

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