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Review Article

COGNITIVE DYSFUNCTION IN SUBCLINICAL HYPOTHYROIDISM USING AUDITORY P300 EVOKED POTENTIALS-SYSTEMATIC REVIEW AND META-ANALYSIS

KRISHNAMURTHY SOUNDARIYA[1], REENAA MOHAN[2], JENIFER FLORENCE MARY[3], DEEPIKA VELUSAMI[1]*

[1]Department of Physiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India. [2]Department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India. [3]Department of Community Medicine, Mahatma Gandhi Medical College and Research Institute, SBV (Deemed to be University), Puducherry, India.
***Corresponding author: Deepika Velusami; Email: deepy843@gmail.com**

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ABSTRACT

Subclinical hypothyroidism, an early and mild form of hypothyroidism rarely presents with clinical manifestations. Literature search has revealed conflicting results on cognitive dysfunction in subclinical hypothyroidism. While the majority of studies used neuropsychiatric tests for cognitive assessment, we aimed to study the cognitive function in subclinical hypothyroidism using evoked potentials "P300." The data sources used were Google Scholar, PubMed, MEDLINE, and Cochrane which were rigorously searched until March 2024. The meta-analysis includes all published studies that used P300 evoked potential to assess cognitive performance in subclinical hypothyroidism. A specified checklist supervised the data extraction process. Using RevMan 5 software, mean P300 at Cz values were aggregated from the chosen trials. The differences in P300 at Cz between normal and subclinical hypothyroidism were evaluated. Data analyses were conducted till March 2023. The current meta-analysis was done using 4 studies with 156 subjects with subclinical hypothyroidism and 182 apparently healthy subjects showed a significant increase in P300 latency in subclinical hypothyroidism (mean difference (MD)=21.65, 95% confidence interval [CI] 0.37–42.92, p<0.00001) at Cz. There was a significant decrease in P300 amplitude in subclinical hypothyroidism compared to healthy subjects at Cz (MD=−0.31, 95% CI −1.08 −0.47, p<0.33). Our study results suggest that subclinical hypothyroidism is associated with cognitive dysfunction as evidenced by the prolongation of the P300 latency. However, there is a need for analysis of more prospective cohort studies.

Keywords: Subclinical hypothyroidism, P300, Cognition, Evoked potentials.

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INTRODUCTION

Thyroid disorders are considered one of the most common endocrine disorders [1]. In the broad spectrum of thyroid disorders falls subclinical hypothyroidism, an early and mild form of hypothyroidism which rarely presents with clinical manifestations and is often diagnosed in routine health checks [2]. Subclinical hypothyroidism is biochemically defined with normal free thyroxine levels, but an elevated level of thyroid-stimulating hormone (TSH). A population-based study found that the incidence of subclinical hypothyroidism to be around 10.25% with a higher prevalence rate in women [3]. Subclinical hypothyroidism has a faster development rate to overt hypothyroidism [4].

While neuropsychiatric dysfunction is considered common in overt hypothyroidism [5,6], literature search revealed inconclusive results with cognitive assessment in subclinical hypothyroidism [7]. Studies on cognitive dysfunction in subclinical hypothyroidism have predominantly used screening tools like mini-mental state examination (MMSE) and other psychometric tests [8]. These cognitive assessment tests are not free of limitations [9]. Auditory P300 event-related potentials offer a non-invasive means of assessing the cognitive function of an individual [10]. Prolonged P300 latency is considered a sign of cognitive impairment [11].

There is a scarcity of data on the assessment of cognitive function in subclinical hypothyroidism using auditory P300 event-related potentials. Hence, the current meta-analysis aimed to evaluate the role of auditory P300-related potential in the assessment of cognitive dysfunction in subclinical hypothyroidism.

METHODS

Prospectively, the protocol of the study was filed in PROSPERO (Reg. No. CRD42024515755) and completed using "preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines" [12].

Eligibility criteria

The PICO concept was followed to include the study participants. Population (adults of both gender with age ranging from 12 to 60 years with subclinical hypothyroidism); intervention/exposure (auditory event-related potential P300); control (health adults of the same age group as above); outcomes (cognitive dysfunction evident with prolonged latency P300).

Studies

Cross-sectional and case–control studies were included.

Search methodology

Literature retrieval was carried out electronically. A complete and systematic review of studies till March 2024 was undertaken with medical subject headings (MeSH), from multiple databases like PubMed, MEDLINE, Google Scholar, and Cochrane. The MeSH terms employed were cognitive dysfunction, hypothyroidism, subclinical, evoked potentials, auditory, P300, event-related potentials (ERP), electrophysiology, and thyroid function tests using Boolean operators such as AND and OR. The results of the search were entered in Rayyan, an online application employed for systematic review and articles were selected [13]. Two-stage screening approach was employed to select the studies. The literature search was done by three separate writers (DV, KS, and RM) conducted. Three authors (DV, KS, and RM) independently screened abstracts and completed texts to pick papers that met our review's inclusion criteria. Any conflicts or discordances that arose throughout the study were handled by consensus with the fourth author (JF).

The appropriate research features were collected from the included studies by the first and co-authors based on the outcome measure.

Data were extracted by means of the planned checklist and included the author's information, year of publication, sample size, study type, participant age, TSH, and P300 latency in subclinical hypothyroid and control subjects. The data were fed into RevMan 5.4 [14] and the third author (RM) carefully examined the data input for accuracy by comparing it to the data supplied. The selected articles are represented in Table 1.

Outcome of the study

The study's outcome measure was an assessment of cognitive impairment using auditory P300 latency and amplitude.

Quality assessment

The risk of bias in the included studies was evaluated using the Joanna Briggs Institute critical appraisal checklist [15], as summarized in Table 2.

Statistical analysis

A quantitative meta-analysis of binomial data was performed using RevMan 5.4 software [14]. Given the heterogeneity among studies, a logistic-normal random-effects model was applied. Study-specific and overall pooled prevalence estimates were reported with 95% confidence intervals (CIs). Heterogeneity was evaluated using the I^2 statistic, with values above 50% or a $p<0.05$ indicating substantial heterogeneity. Subgroup analyses were conducted to explore sources of heterogeneity and assess potential confounders. Forest plots were used to visually display individual study estimates and pooled results, both overall and within subgroups. Publication bias was assessed using funnel plots, and asymmetry in the plots was tested using Egger's regression. To test the robustness of the findings, sensitivity analyses were also conducted.

RESULTS

Study selection and characteristics

Initially, 59 studies were collected from the database. After the duplicates were removed, 40 studies were examined. Four of the studies satisfied the inclusive criteria and eventually included in the analyses [16-19]. The PRISMA flowchart for research selection is shown in Fig. 1.

Characteristics of the reviewed literature

The selected article's information up to March 2024 is shown in Table 1. The research designs fell into two categories: Analytical cross-sectional (two studies) [16,17] and case–control studies (two studies) [18,19].

Main findings

Meta-analysis of four comparative studies with cognitive dysfunction among subclinical hypothyroidism and healthy individuals in terms of ERP P300 Latency (C_z), involving 156 subjects with subclinical hypothyroidism and 182 subjects who appeared healthy, found a significant effect in favor of the subclinical hypothyroidism group. Table 3 shows a mean difference (MD) of 21.65 (95% CI 0.37–42.92, $p<0.00001$). The Q statistic reached statistical significance ($p=0.05$), indicating substantial heterogeneity, as reflected by a high I^2 value of 97%.

A meta-analysis of three eligible studies comparing cognitive dysfunction between individuals with subclinical hypothyroidism and healthy controls, based on ERP P300 latency (PZ), included 81 participants with subclinical hypothyroidism and 90 healthy controls. The analysis revealed a significant overall effect in favor of the subclinical hypothyroidism group (MD=28.95, 95% CI: 20.00–37.91, $p=0.24$), as shown in Table 4. In addition, a significant Q statistic ($p<0.00001$) suggested the presence of heterogeneity ($I^2=30\%$).

A meta-analysis of three eligible comparative studies examining cognitive dysfunction in subclinical hypothyroidism versus healthy individuals, based on ERP P300 amplitude (Cz), included 135 participants with subclinical hypothyroidism and 135 healthy controls. The analysis demonstrated a significant overall effect favoring the

Table 1: Selected articles for review

S. No.	Author details	Year	Name of the Journal	Study design	Population	Sample size		TSH		P300 Cz	
						SH (n)	Control (n)	SH (Mean±SD)	Control (Mean±SD)	SCH (Mean±SD)	Control (Mean±SD)
1.	Sharma *et al.*	2014	Journal of natural science, biology and medicine	Cross sectional	Adults <50 years	75	75	8.98±2.55	1.25±0.55	283.14±19.97	281.84±9.76
2.	Mahaur *et al.*	2016	MAMC journal of medical sciences	Case control	Only females	30	30	12.04±10.09	3.01±0.44	333.07±27.96	307.17±12.65
3.	Sivakumar and Rekha	2016	Indian Journal of basic and applied medical research	Cross sectional comparative study	Only women 25–40 years	30	30	11.22±2.42	2.59±1.05	291.64	328.51
4.	Paladugu *et al.*	2015	Indian Journal of Endocrinology and Metabolism	Case control	12–45 years	21	33	12.3±2.4	2.4±1.1	319.33±30	296.41±34

SH: Subclinical hypothyroidism; TSH: Thyroid-stimulating hormone. (n) represents sample size. Data is represented as mean±SD (standard deviation)

Table 2: Risk of bias analysis

S. No.	Analytical cross-sectional studies	Mahaur *et al.* 2016				Sivakumar and Rekha, 2016			
		Y	N	UC	NA	Y	N	UC	NA
1	Were the inclusion criteria for the sample explicitly stated?								
2	Did the study provide a detailed description of the participants and the research setting?								
3	Was the method of assessing exposure both accurate and consistent?								
4	Were standardized and objective methods used to determine the condition of interest?								
5	Did the study identify any potential confounding variables?								
6	Were specific approaches outlined to address the impact of confounding factors?								
7	Were the outcome measures applied with accuracy and consistency?								
8	Was the statistical analysis suitable for the study design and objectives?								
Case–control studies		**Sharma *et al.* 2014**				**Paladugu *et al.* 2015**			
		Y	N	UC	NA	Y	N	UC	NA
1	Were the case and control groups comparable aside from the presence or absence of the condition under study?								
2	Was matching between cases and controls conducted appropriately?								
3	Were consistent criteria applied to define both cases and controls?								
4	Was the exposure assessed using standardized, valid, and reliable methods?								
5	Was exposure information collected in the same manner for both groups?								
6	Did the study identify potential confounding variables?								
7	Were clear methods described for managing the effects of confounding factors?								
8	Were the outcomes evaluated using consistent, valid, and reliable measures across both groups?								
9	Was the duration of exposure sufficient to capture relevant effects?								
10	Was the statistical analysis methodologically appropriate for the study design?								

Y: Yes; N: No; UC: Unclear; NA: Not applicable, Y (Green color); Yes, N (White color): No, UC (yellow color): Unclear, NA (Grey color): Not Applicable

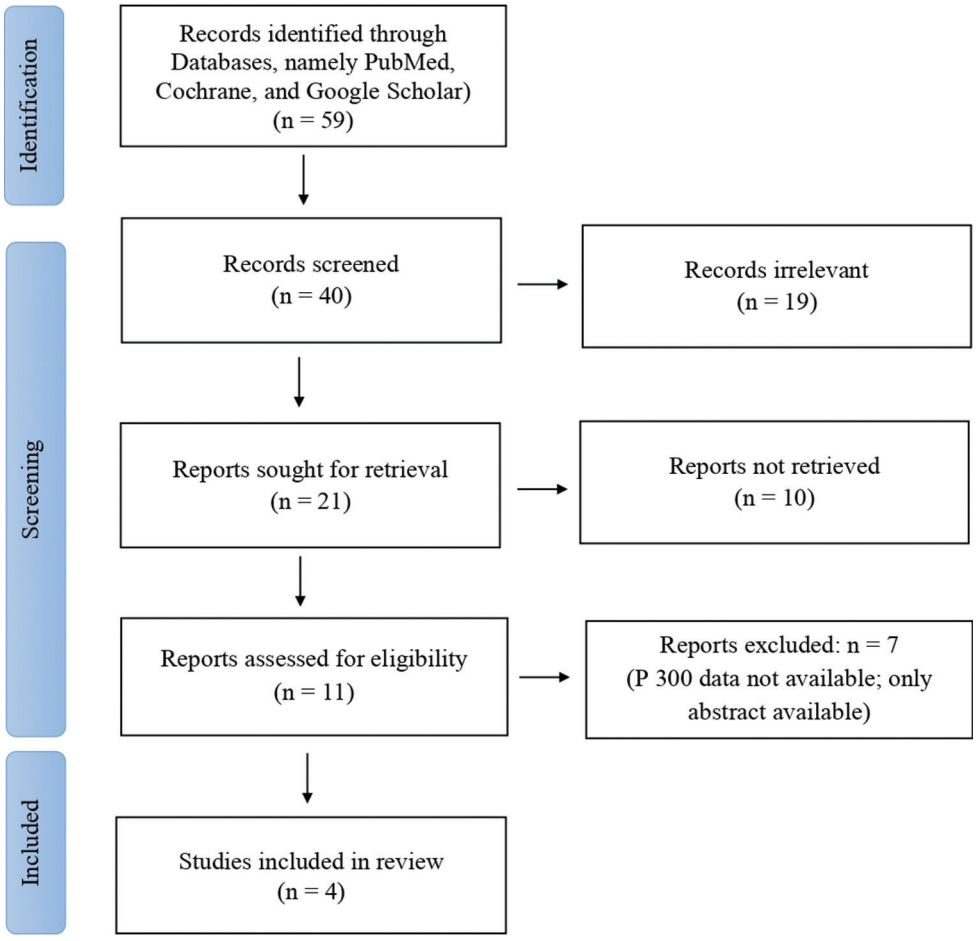

Fig. 1: Preferred reporting items for systematic reviews and meta-analysis flow-chart

Table 3: Forest plot data for auditory P300 in subclinical hypothyroidism

Study	SCH		Total (SCH)	Control		Total (control)	Weight (%)	Mean difference (95% CI)
	Mean	SD		Mean	SD			
Mahaur *et al*. 2016	333.07	27.96	30	307.17	12.65	30	24.9	25.90 (14.92, 36.88)
Paladugu *et al*. 2015	319.33	30	33	296.41	13.44	33	22.7	22.92 (5.62, 40.22)
Sharma *et al*. 2014	283.14	19.97	75	281.84	9.76	75	26.2	1.30 (−3.73, 6.33)
Sivakumar and Rekha, 2016	328.51	8	30	291.64	12	30	26.2	36.87 (31.71, 42.03)

SCH: Subclinical hypothyroidism. Results are expressed as mean±SD (standard deviation). Overall Statistics: Total (SCH): 156, Total (Control): 168, Overall mean difference (IV, Random, 95% CI): 21.65 (0.37, 42.92), Test for overall effect: Z=1.99 (p=0.05) Heterogeneity: Tau^2=442.30, Chi^2=95.26, df=3 (p<0.00001, I^2=97% Test for subgroup differences: Not applicable

Table 4: Forest plot data for P300 latency comparison

Study	SCH		Total (SCH)	Control		Total (Control)	Weight (%)	Mean Difference (95% CI)
	Mean	SD		Mean	SD			
Mahaur *et al*. 2016	336.93	34.84	30	308.34	10.48	30	33.1	28.59 (15.57, 41.61)
Paladugu *et al*. 2015	316.42	27	33	297.9	23	33	24.1	18.52 (2.39, 34.65)
Sivakumar and Rekha, 2016	336.89	14	27	301.8	25	30	42.9	35.09 (24.41, 45.77)

SCH: Subclinical hypothyroidism. Results are expressed as mean±SD (standard deviation). Total (SCH): 81, Total (Control): 90, overall mean difference (IV, Random, 95% CI): 28.95 (20.00, 37.91), Test for overall effect: Z=6.34 (p<0.00001), Heterogeneity: Tau^2=18.98, Chi^2=2.85, df=2 (p=0.24), I^2=30%, Test for subgroup differences: Not applicable

Table 5: Forest plot data for P300 amplitude comparison

Study	SCH		Total (SCH)	Control		Total (Control)	Weight (%)	Mean difference (95% CI)
	Mean	SD		Mean	SD			
Mahaur *et al*. 2016	9.25	6.12	30	7.98	2.91	30	9.8	1.27 (−1.15, 3.69)
Sharma *et al*. 2014	6.91	3.75	75	7.18	1.85	75	53.6	−0.27 (−1.22, 0.68)
Sivakumar and Rekha, 2016	7.532	2.395	30	8.316	2.304	30	36.6	−0.78 (−1.97, 0.41)

SCH: Subclinical hypothyroidism. Results are expressed as mean±SD (standard deviation). Total (SCH): 135, Total (Control): 135, Overall MD (IV, Random, 95% CI): −0.31 (−1.08, 0.47), Test for overall effect: Z=0.78 (p=0.44), Heterogeneity: Tau^2=0.06, Chi^2=2.25, df=2 (p=0.33), I^2=11%, Test for subgroup differences: Not applicable

control group (MD=−0.31, 95% CI: −1.08–−0.47, p<0.33), as shown in Table 5. A significant Q statistic (p=0.44) indicated the presence of heterogeneity (I^2=11%).

DISCUSSION

The present study aimed to identify the role of auditory P300 event-related potential in the identification of cognitive dysfunction in subclinical hypothyroidism. It has totally involved four studies including 338 study participants involving 156 subjects with subclinical hypothyroidism and 182 apparently healthy individuals. No randomized controlled trials were identified in our literature search.

In this study, we found a large increase in the latency of auditory P300 ERP s at both Cz and Pz, as well as a significant drop in P300 amplitude in individuals with subclinical hypothyroidism. Among the analyzed four studies, three studies showed a prolonged increase in the latency of the P300 [16,17,19]. Similar results were observed by Dejanovic *et al.* in individuals with subclinical hypothyroidism and suggested auditory P300 as a sensitive indicator for identifying subtle cognitive dysfunction in individuals with hypothyroidism [20]. Kocaaslan Atli *et al*. evaluated cognitive performance in children with subclinical hypothyroidism and showed that implicit alterations in cognitive functions not represented by neuropsychiatric tests can be identified by auditory P300 ERPs [21]. However, Sharma *et al.* did not record a significant difference in the latency of P300 between controls and subclinical hypothyroid individuals [18]. This inconsistency may be attributed to methodological variability, differences in study populations, or the degree of thyroid dysfunction among participants. In addition, subtle confounding variables such as undiagnosed vitamin B12 deficiency, anemia, or depression could influence P300 outcomes in these individuals [22].

The P300 ERP reflects cognitive functions including attention allocation and working memory. Its delay in latency may be an early biomarker for mild cognitive impairment (MCI). Reduced amplitude, although less consistent, may indicate diminished neural reserve or reduced allocation of cognitive resources [23,24]. Studies in other populations such as MCI and Alzheimer's disease also support the use of P300 as a neurophysiological marker of early cognitive decline [25,26].

Previously, several studies have found a link between subclinical hypothyroidism and cognitive impairment. However psychometric tests like MMSE were used for assessing cognitive impairment. A study by Pasqualetti *et al.* and his colleagues identified a relationship between subclinical hypothyroidism and cognitive impairment only in individuals <70 years of age which they attribute to the over diagnosis of subclinical hypothyroidism in the elderly [8]. Another systematic review by Rieben *et al.* and his colleagues revealed no significant association between subclinical hypothyroidism and cognitive dysfunction. They have pooled the results of eleven prospective cohorts [27]. Similar results were observed by Pyun *et al.* [28].

The results reveal a probable cognitive impairment in people with subclinical hypothyroidism, as shown by the delayed latency of P300. The results may contribute to planning strategies for the management of subclinical hypothyroidism. Paladugu *et al.* observed a significant improvement in the P300 values in subclinical hypothyroidism after intervention [19]. In addition, Hebbar *et al*. emphasized the critical role of early detection and intervention in subclinical hypothyroidism, especially during pregnancy, to avert long-term negative consequences [29]. Similar findings by Correia *et al*. advocate for early screening of cognitive impairment since there is evidence

for specific defects in hippocampal memory in overt and subclinical hypothyroidism [30].

While our study strengthens the argument for using auditory P300 as a diagnostic adjunct in detecting early cognitive dysfunction in SCH, it is not without limitations. The included studies had varying methodologies, heterogeneous populations, and lacked longitudinal follow-up. Furthermore, comorbid conditions such as depression, which itself affects ERP parameters, were not uniformly controlled across studies [31]. Larger, well-designed prospective studies and randomized trials are needed to confirm the utility of P300 in clinical practice.

Future research should also examine the potential use of P300 latency as a treatment monitoring tool in SCH, especially in asymptomatic or borderline cases where a decision to treat may be uncertain. Integrating auditory P300 into cognitive assessment batteries could enhance the sensitivity of early cognitive dysfunction diagnosis, especially when used in combination with thyroid function monitoring and psychological evaluation [32,33].

Our meta-analysis tried to explore the role of auditory P300 in identifying subtle cognitive dysfunction in subclinical hypothyroidism, which is a major strength of the study among several meta-analysis which have pooled the results of cognitive dysfunction in subclinical hypothyroidism identified by neuropsychiatric tests. However, our study is not free of limitations. The pooled data reflect the results of only four studies. Hence, analysis of prospective cohort studies with adequate sample size may reflect the real impact of subclinical hypothyroidism on cognitive function.

CONCLUSION

Our meta-analysis found that patients with subclinical hypothyroidism have prolonged latency and less amplitude of auditory P300 event-related potentials, characterizing a possible cognitive dysfunction. These results may guide in planning the early management of subclinical hypothyroidism.

ETHICAL APPROVAL

There is no ethical issue.

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AUTHOR'S CONTRIBUTION

KS conceived and designed the study, conducted research, collected and organized the data RM, JF, and DV are involved in selecting the articles and analysis and data interpretation. KS wrote the initial draft and DV finalized the draft and provided logistic support. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

CONFLICT OF INTEREST

We have no conflict of interest to declare.

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REFERENCES

1. Vanderpump MP. Epidemiology of thyroid disorders. In: Luster M, Duntas LH, Wartofsky L, editors. The Thyroid and its Diseases: A Comprehensive Guide for the Clinician. Cham: Springer International Publishing; 2019. p. 75-85. doi: 10.1007/978-3-319-72102-6_6
2. Behera BP, Sen RK. A study on the prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus in a tertiary centre in a tribal population of eastern India. Int J Pharm Pharm Sci. 2023;15(6):29-34. doi: 10.22159/ijpps.2023v15i6.48019
3. Kumar S, Gupta RC. Prevalence of subclinical hypothyroidism in general adult population of Northern India. J Med Sci Clin Res. 2020;8(3):595-597. doi: 10.18535/jmscr/v8i3.103
4. Raza SA, Mahmood N. Subclinical hypothyroidism: Controversies to consensus. Indian J Endocrinol Metab. 2013 Dec;17(Suppl 3):S636-S642. doi: 10.4103/2230-8210.123555, PMID 24910826
5. Samuels MH. Psychiatric and cognitive manifestations of hypothyroidism. Curr Opin Endocrinol Diabetes Obes. 2014;21(5):377-383. doi: 10.1097/MED.0000000000000089, PMID 25122491
6. Ye Y, Wang Y, Li S, Guo J, Ding L, Liu M. Association of hypothyroidism and the risk of cognitive dysfunction: A meta-analysis. J Clin Med. 2022;11(22):6726. doi: 10.3390/jcm11226726, PMID 36431204
7. Akintola AA, Jansen SW, Van Bodegom D, Van Der Grond J, Westendorp RG, De Craen AJ, *et al*. Subclinical hypothyroidism and cognitive function in people over 60 years: A systematic review and meta-analysis. Front Aging Neurosci. 2015;7:150. doi: 10.3389/fnagi.2015.00150, PMID 26321946
8. Pasqualetti G, Pagano G, Rengo G, Ferrara N, Monzani F. Subclinical hypothyroidism and cognitive impairment: Systematic review and meta-analysis. J Clin Endocrinol Metab. 2015;100(11):4240-4248. doi: 10.1210/jc.2015-2046, PMID 26305618
9. Devenney E, Hodges JR. The mini-mental state examination: Pitfalls and limitations. Pract Neurol. 2017;17(1):79-80. doi: 10.1136/practneurol-2016-001520, PMID 27903765
10. Sur S, Sinha VK. Event-related potential: An overview. Ind Psychiatry J. 2009;18(1):70-73. doi: 10.4103/0972-6748.57865, PMID 21234168
11. Demirayak P, Kıyı İ, İşbitiren YÖ, Yener G. Cognitive load associates prolonged P300 latency during target stimulus processing in individuals with mild cognitive impairment. Sci Rep. 2023;13(1):15956. doi: 10.1038/s41598-023-43132-8, PMID 37743392
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al*. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71, PMID 33782057
13. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210. doi: 10.1186/s13643-016-0384-4, PMID 27919275
14. RevMan 5. Available from: https://training.cochrane.org/online-learning/core-software/revman/revman-5-download [Last accessed on 2024 Feb 20]
15. Santos WM, Secoli SR, Püschel VA. The Joanna Briggs institute approach for systematic reviews. Rev Lat Am Enfermagem. 2018;26:e3074. doi: 10.1590/1518-8345.2885.3074, PMID 30462787
16. Mahaur R, Mahajan AS, Jain AK, Singh T, Dhanwal DK, Gupta M. Role of event-related potentials in evaluation of cognitive function in subclinical hypothyroid patients. MAMC J Med Sci. 2016;2(1):43-47. doi: 10.4103/2394-7438.174838
17. Sivakumar S, Rekha A. Evaluation of cognitive function in subclinical hypothyroidism. Indian J Basic Appl Med Res. 2016;6(1):336-342.
18. Sharma K, Behera JK, Sood S, Rajput R, Satpal, Praveen P. Study of cognitive functions in newly diagnosed cases of subclinical and clinical hypothyroidism. J Nat Sci Biol Med. 2014;5(1):63-66. doi: 10.4103/0976-9668.127290, PMID 24678200
19. Paladugu S, Hanmayyagari BR, Kudugunti N, Reddy R, Sahay R, Ramesh J. Improvement in subclinical cognitive dysfunction with thyroxine therapy in hypothyroidism: A study from tertiary care center. Indian J Endocrinol Metab. 2015;19(6):829-833. doi: 10.4103/2230-8210.167547, PMID 26693436
20. Dejanovic M, Ivetić V, Nestorović V, Milanović Z, Biševac B, Miletić M, *et al*. P300 event related potential application to cognitive status assessment of the patients with subclinical hypothyroidism. Prax Med. 2015;44(2):97-102. doi: 10.5937/pramed1502097D
21. Kocaaslan Atli S, Olgaç Dündar N, Bayazit O, Evirgen Esin N, Erdoğan U, Çatli G, *et al*. Auditory event-related potentials demonstrate early cognitive impairment in children with subclinical hypothyroidism. J Pediatr Endocrinol Metab. 2019;32(7):689-697. doi: 10.1515/jpem-2018-0463, PMID 31194683
22. Tu MC, Lo CP, Chen CY. Vitamin B12 deficiency: Cognitive impairment and neuroimaging correlates. Neuropsychiatry (Lond). 2016;6(6):303-307.
23. Polich J. Updating P300: An integrative theory of P3a and P3b. Clin Neurophysiol. 2007;118(10):2128-2148. doi: 10.1016/j.

clinph.2007.04.019, PMID 17573239
24. Snyder E, Hillyard SA. Long-latency evoked potentials to irrelevant, deviant stimuli. Behav Biol. 1976;16(3):319-331. doi: 10.1016/s0091-6773(76)91447-4, PMID 1275853
25. Bennys K, Portet F, Touchon J, Rondouin G. Diagnostic value of event-related evoked potentials N200 and P300 subcomponents in early diagnosis of Alzheimer's disease and mild cognitive impairment. J Clin Neurophysiol. 2007 Oct;24(5):405-412. doi: 10.1097/WNP.0b013e31815068d5, PMID 17912065
26. Han SH, Jeong HB, Park KY, Shin HW, Youn YC, Kim S. P300 latency changes in patients with mild cognitive impairment after taking choline alphoscerate; a preliminary study. eNeurologicalSci. 2018 Apr 12;11:5-8. doi: 10.1016/j.ensci.2018.04.004, PMID 29928709
27. Rieben C, Segna D, Da Costa BR, Collet TH, Chaker L, Aubert CE, *et al*. Subclinical thyroid dysfunction and the risk of cognitive decline: A meta-analysis of prospective cohort studies. J Clin Endocrinol Metab. 2016;101(12):4945-4954. doi: 10.1210/jc.2016-2129, PMID 27689250
28. Pyun JM, Park YH, Kim S. Subclinical hypothyroidism and cognitive impairment. J Alzheimers Dis. 2022;88(2):757-762. doi: 10.3233/JAD-220302, PMID 35694927
29. Hebbar H, Kumar S, Amin S, Doizode S. Subclinical hypothyroidism in pregnancy; is there a need for pharmacological intervention. Int J Pharm Pharm Sci. 2017;9(3):186-191. doi: 10.22159/ijpps.2017v9i3.16542
30. Correia N, Mullally S, Cooke G, Tun TK, Phelan N, Feeney J, *et al*. Evidence for a specific defect in hippocampal memory in overt and subclinical hypothyroidism. J Clin Endocrinol Metab. 2009 Oct;94(10):3789-397. doi: 10.1210/jc.2008-2702, PMID 19584178
31. Miranda EC, Pinheiro MM, Pereira LD, Iorio MC. Correlation of the P300 evoked potential in depressive and cognitive aspects of aging. Braz J Otorhinolaryngol. 2012 Oct;78(5):83-89. doi: 10.5935/1808-8694.20120013, PMID 23108825
32. Pavarini SC, Brigola AG, Luchesi BM, Souza ÉN, Rossetti ES, Fraga FJ, *et al*. On the use of the P300 as a tool for cognitive processing assessment in healthy aging: A review. Dement Neuropsychol. 2018 Jan-Mar;12(1):1-11. doi: 10.1590/1980-57642018dn12-010001, PMID 29682227
33. Eslami-Amirabadi M, Sajjadi SA. The relation between thyroid dysregulation and impaired cognition/behaviour: An integrative review. J Neuroendocrinol. 2021 Mar;33(3):e12948. doi: 10.1111/jne.12948, PMID 33655583