

Evaluating cognitive function in patients with differentiated thyroid cancer who experienced short-term hypothyroidism by levothyroxine withdrawal using Montreal Cognitive Assessment-Philippines (MoCA-P) tool

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Abstract

Background & Objective: Although there are numerous data studying cognitive dysfunction on hypothyroidism in general, there are limited researches that venture on short-term hypothyroidism. This study aimed to determine the cognitive function of patients with differentiated thyroid cancer (DTC) who experienced short-term hypothyroidism. **Methods:** This was a prospective study done in a tertiary hospital in Manila that enrolled 16 DTC patients either for radioactive iodine (RAI) therapy or thyroid cancer monitoring, who were followed at baseline before levothyroxine (LT4) withdrawal, during hypothyroid state and post-LT4 treatment. MoCA-P tool was used to objectively assess cognition while HADS-P tool was used to detect anxiety and depression. Mean scores were calculated for each time point and analyzed using paired T-test. **Results:** There was a decrease in the mean MoCA-P score from baseline to hypothyroid state (25.22 to 22.97, $p=0.032$) with improvement post-LT4 treatment (22.97 to 24.93, $p=0.004$). Older age was associated with decrease in MoCA-P scores ($p=0.04$). Total HADS-P scores were nonsignificant. Visuospatial (3.86 to 3.43, $p=0.014$) and attention (4.86 to 4.36, p value 0.021) domains declined with hypothyroidism, with reversal of visuospatial function post-LT4 treatment.

Conclusion: There is a significant alteration in cognition during short-term hypothyroidism that generally improves with LT4 treatment. It is important to educate patients on specific cognitive domains that can be affected to ensure occupational safety.

Keywords: Cognitive function, short term hypothyroidism, differentiated thyroid cancer, Montreal Cognitive Assessment, MoCA-P, HADS-P, anxiety, depression

INTRODUCTION

Thyroid cancer is the most common malignancy of the endocrine system.¹ The usual management for thyroid cancers is total thyroidectomy followed by radioactive iodine (RAI) ablation of remnant thyroid cells, then suppressive maintenance dose of levothyroxine (LT4) and lastly, thyroid cancer monitoring. In the Philippines, most of the patients for remnant ablation and thyroid cancer monitoring are subjected to hypothyroidism by LT4 withdrawal as the other alternative, recombinant human Thyroid stimulating hormone

(rhTSH) stimulation, is rather costly. Thus, patients have to undergo at least 3-6 weeks of “short-term” hypothyroidism.

In general, during a period of overt hypothyroidism, about 66-90% of patients manifest cognitive dysfunction characterized by slowed mentation, poor concentration and decreased short term memory.² Memory retrieval, learning, verbal fluency, and motor speed are also often particularly impaired.³ Other patients experience anxiety and depression and are associated with a decreased quality of life.⁴

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The pathogenesis of cognitive dysfunction in hypothyroidism is still unknown but some studies show a decrease in cerebral blood flow and decreased cerebral oxygen and glucose metabolism seen in single photon emission computed tomography (SPECT) and positron emission tomography (PET) scans.^{5,6} Animal studies suggest that hypothyroidism can produce alterations in the synaptic plasticity of neural pathways mediated by the dorsal hippocampus, which is an important area for many higher cognitive functions.⁷

The data on reversibility of cognitive dysfunction with LT4 treatment are varied. There are several studies that showed complete reversibility⁸⁻¹⁰ while some studies showed partial reversibility and even sparse data suggested irreversibility^{9,11,12} and the factors that affect reversibility are not yet known. Whether or not there is a correlation with the degree or the duration of hypothyroidism also needs to be clarified. Most of the available studies in the literature did not specifically define any duration of hypothyroidism in their population. A lot of these studies included patients that they received or recruited already in an overt hypothyroid state thus the duration of hypothyroidism was not completely defined. In addition, these studies used a battery of different neuropsychological tests which would further contribute to the varied results. The authors believed that these variables may be addressed by enrolling fairly uniform duration and degree of hypothyroidism using a single and sensitive instrument. The data on short-term hypothyroidism are also very scarce, thus this study was proposed. Moreover, using a more sensitive scale such as Montreal Cognitive Assessment Philippines (MoCA-P) tool which was adapted for use for Filipinos, would offer an advantage for proper assessment of cognitive function in our population.

This study aimed to determine the cognitive function of patients with differentiated thyroid cancer (DTC) who experienced short-term hypothyroidism by LT4 withdrawal using MoCA-P tool. Specifically, this study aimed to:

1. Describe the demographic profile of patients who underwent short-term hypothyroidism;
2. Determine if demographic and/or medical factors (including anxiety and depression) were associated with the cognitive outcome of patients;
3. Determine the overall cognitive function at baseline, during state of hypothyroidism, and after resumption of euthyroid state using MoCA-P tool; and lastly,
4. Determine the effect of short-term

hypothyroidism on the specific cognitive domains of the MoCA-P.

METHODS

This study was conducted at the University of Santo Tomas Hospital, a tertiary hospital in Manila, Philippines from September 2019 to February 2020 (6 months) after approval by the institutional research ethics committee. This was a prospective study design which enrolled patients with DTC who underwent short-term hypothyroidism by LT4 withdrawal either for RAI or for thyroid cancer monitoring.

The inclusion criteria included all patients diagnosed with DTC who underwent total thyroidectomy and for LT4 withdrawal for RAI therapy or for thyroid cancer monitoring. Exclusion criteria were as follows: 1. With history of documented cerebrovascular disease (infarct or hemorrhage); 2. With known diagnosis of dementia or other neurodegenerative disease or taking any medication for said condition; 3. With medications that may interfere with cognitive functioning; 4. With known diagnosis of brain metastases of any source or malignancy; 5. With known psychiatric illness or taking any antipsychotic or antidepressants; 6. With severe language, writing, visual and hearing impairment or disability such that he or she is not able to carry out required tasks; and 7. Patients whose primary language is not Filipino. Sample size was not computed for this study due to the lack of prevalence of cognitive dysfunction among DTC patients experiencing short-term hypothyroidism. Convenience or purposive sampling was done instead.

Recruitment process was through a screening interview by endocrinology fellows at the outpatient department, inpatient, and in private clinics. Patients who fulfilled the inclusion and exclusion criteria were personally invited by the researcher to participate in the study. The patients were asked to sign a consent form prior to enrollment. Consent forms were likewise signed by private attending physicians for private patients who decided to enroll in the study. All recruited patients were required to take the MoCA-P tool at 3 points in time within the study duration. Participants were allowed to withdraw from the study anytime. Those who failed to follow up within 30 days of the expected follow up time were terminated.

Each of the patient was requested for laboratory exam for serum TSH and took the MoCA-P

testing at 3 points in time within the specified study duration: baseline (within a week prior to Total thyroidectomy or a week prior to LT4 withdrawal for thyroid cancer monitoring), during hypothyroid state (at least 3 weeks of LT4 withdrawal up to 6 weeks and patient fulfilling a TSH of more than 20 uIU/ml) and upon follow up after at least 4 weeks of LT4 treatment with documented repeat TSH within the normal limits or at goal. The MoCA-P testing was conducted by the researcher after training on proper MoCA-P tool assessment with a neurologist. The patients were not given any feedback of their performances until after the third part of the examination. A Hospital Anxiety and Depression scale-Pilipino version (HADS-P) was also extracted from patients at all time points to check for anxiety and/or depression as possible confounding factors for cognitive evaluation.

The MoCA tool is a widely used tool for detecting cognitive impairment and is noted to be a more sensitive tool than the commonly used MMSE.¹³ This was recently validated for use for Filipinos in 2013 and the translated version is called MoCA-P (Supplementary Figure 1). This tool was used to measure objectively the cognitive function in this study.

The MoCA-P tool is composed of 8 domains namely visuospatial and executive functioning, naming, memory, attention, language, abstraction, delayed recall and orientation. Considering that naming is a function of the domain of language, this will be considered as part of the latter. Each domain has corresponding points as follows:

1. Visuospatial/executive function- 5 points: This consists of trail making test (1 point), copying a cube (1 point) and clock drawing test (3 points)
2. Animal naming- 3 points: This includes naming a lion, an owl, and a camel.
3. Attention- 6 points: Patient was asked to repeat 5 numbers (2,1,8,5,4) in the same order as they were verbalized by the examiner (1 point); Patient was asked to repeat another set of 3 numbers (7,4,2) in reverse order as they were verbalized by the examiner (1 point); Patient was also asked to tap the table or a surface whenever letter "A" is being spoken, out of a series of letters as follows: FBACMNAAJKLBAFAKDEAAAJAMO FAAB (1 point); Lastly, patient was asked to calculate by subtracting 7 continually from 100 and to subsequent answers (3 points)
4. Language- 3 points: Patient was asked to repeat following statements:

"Ang alam ko lang, si Juan ang siyang tutulong ngayong araw." (1 point);

"Ang pusa ay nagtatago sa ilalim ng upuan kapag nasa kuwarto ang aso" (1point); Patient was asked to enumerate at least 11 words that start with the letter "B". (1 point)

5. Abstraction- 2 points: Patient was asked to answer what's the similarity of the following: Tren and Bisekleta (1 point); Timbangan and ruler (1 point)
6. Delayed Recall- 5 points: Patient was asked to recall previously mentioned words by the examiner (mukha asul, simbahan, rosas, seda). One point for each word recalled.
7. Orientation- 6 points: Patient was asked the date, month, year, day, place and town. (1 point for each correct answer.)

The tool is composed of a total of 30 points. Score of less than 21 signifies cognitive impairment.

Hospital Anxiety and Depression Scale Pilipino or HADS-P (Supplementary Figure 2) is a 14-item, self-administered rating scale with independent subscales for evaluation of anxiety and depression. This is the validated Filipino version of HADS in which a cut off score of 11 optimally provides acceptable sensitivity and specificity for the presence of anxiety and/or depression.¹⁴ Current data or studies are conflicting whether anxiety and/or depression have direct effect on cognitive performance thus was assessed in this study.^{4,16}

Data were analyzed using IBM Statistical Package for the Social Sciences V26. The mean scores for TSH, MoCA-P, HADS-P total score, HADS-P *depression*, HADS-P *anxiety*, and different cognitive domains were calculated for each time frame (baseline, hypothyroid state, post LT4 treatment). TSH values of >100 uIU/ml were tabulated as 100 uIU/ml. A paired T-test was used to compare the mean baseline scores with mean scores during period of hypothyroidism; mean scores during period of hypothyroidism with mean scores post-LT4 treatment; and lastly, baseline mean scores with mean scores post-LT4 treatment with documented normal or at goal TSH. A mean MoCA-P score of less than 21 would be considered as having impaired cognition while a HADS-P Total score of ≥ 11 would signify anxiety and/or depression. Similarly, mean scores were also calculated for each cognitive domain and scores at baseline to scores during hypothyroid state, scores during hypothyroid state to scores after LT4 treatment and finally scores at baseline and after LT4 treatment, were also compared using

paired T-test. A *p* score of <0.05 was considered significant.

RESULTS

Of 26 eligible patients who consented to participate, 7 failed to follow up at the required time (incomplete data), 1 got pregnant, 1 patient refused RAI treatment due to financial constraint, and 1 was subsequently diagnosed with poorly differentiated thyroid cancer. Thus, 16 patients were ultimately included in the study. Table 1 shows the baseline characteristics of study participants. Fourteen were females (87.5%) and 2 were males (12.5%), with mean age of 44 ± 1.27 years old (range: 22 to 67). All of these patients have stage 1 papillary thyroid cancer. Six patients (37.5%) were for RAI therapy (post total thyroidectomy, first time hypothyroid) while 10 patients (62.5%) underwent LT4 withdrawal for thyroid cancer monitoring. Most of the patients are well educated with mean number of years of education of 12.8 years, with 50% of the participants currently working. Six of the patients have comorbidities such as hypertension, impaired fasting glucose and dyslipidemia controlled with maintenance medications. Only 1 patient had a history of smoking while 3 had occasional alcoholic beverage use.

To analyze whether certain demographic characteristics were associated with a decrease in MoCA-P score, the patient population was divided into two groups as shown in Table 2. During the period of hypothyroidism, 9 out of the 16 patients had MoCA-P score lesser than their baseline value while the other 7 patients scored either the same or slightly above their baseline. Comparing the 2 groups, it is noted that older age was significantly associated with a decrease in MoCA-P score while there was no noted difference in terms of gender, the duration of short-term hypothyroidism, and the number of years of education. On the other hand, an unchanged/slightly increased MoCA-P score was noted to be more associated with first time hypothyroidism, and working population but *p* value for these was not significant.

The patients underwent assessment of MoCA-P and HADS-P at 3 time points: baseline, hypothyroid and post-LT4 treatment as shown in Table 3. At baseline, all patients were euthyroid with mean TSH level of 1.8 ulu/ml. The mean MoCA-P score was 25.22 which is an acceptable level of cognitive function for Filipinos while the mean baseline HADS-P score was 10.22 which is also considered normal mood variation. After a mean duration of hypothyroidism of 4.6 weeks (range: 3 to 6), there was a significant increase

Table 1: Baseline demographics of study participants

Characteristics/Parameter	n = 16
Sex	
Female, number (%)	14 (87.5%)
Male, number (%)	2 (12.5%)
Age, mean age in years +/- SD, range	44±1.27 (22-67)
Type of Thyroid Cancer	
Papillary, number (%)	16 (100%)
Others (Follicular), number (%)	0
Stage of thyroid cancer	
Stage 1 number (%)	16 (100%)
Stage 2 and 3	0
Patient on LT4 withdrawal for RAI, number (%)	6 (37.5%)
Patient on LT4 withdrawal for thyroid cancer monitoring, number (%)	10 (62.5%)
Duration of hypothyroidism, mean in weeks, range	4.6 (3-6)
Education (# of years), mean, range	12.8 (12-13)
Working, number (%)	8 (50%)
Patients with comorbidities, number (%)	6 (37.5%)
Smoker, number (%)	1 (6.25%)
Alcohol drinker, number (%)	3 (18.75%)

Table 2. Patient characteristics according to MoCA-P score

	Decreased MoCA-P score (n=9)	Same/Increased MoCA-P score (n=7)	P- Value
Age, mean age in years +/- SD	48±0.52	41	0.047
Female Sex, number (%)	8 (88.88%)	6 (85.7%)	0.342
Patients on LT4 withdrawal for RAI (1st time hypothyroid), number (%)	3 (33.33%)	3 (42.8%)	0.072
Duration of hypothyroidism, mean in weeks	4.28	4.78	0.089
Years of education, mean	12.67 years	13 years	0.459
Working population, number (%)	4 (44.44%)	4 (57.1%)	0.072
Independent T-test			

in the mean TSH level to 83.32 ($p = <0.001$) associated with a significant decrease in the cognitive function with mean MoCA-P score of 22.97 ($p = 0.032$). There was no significant change noted with HADS-P total score but ironically, there was a trend towards improvement in the

depression score from 3.84 to 2.98 ($p = 0.05$). In addition, patients were less anxious during this period. This may imply that anxiety and depression may not play a role in cognitive dysfunction during the period of hypothyroidism. After treatment with LT4 therapy, there was significant improvement of

Table 3. Mean TSH, MoCA-P and HADS-P scores at 3 time points**3a. Baseline and Hypothyroid state**

	Baseline	Hypothyroid	P value
TSH (uIu/ml)	1.80	83.32	<0.001
MoCA-P	25.22	22.97	0.032
HADS-P Total	10.22	10.31	0.098
HADS-P Depression	3.84	2.98	0.050
HADS-P Anxiety	6.38	5.82	0.245

Paired T-test

3b. Hypothyroid state to Post LT4 treatment

	Hypothyroid State	Post LT4 treatment	P value
TSH	83.32	1.63	<0.001
MoCA-P	22.97	24.93	0.004
HADS-P Total	10.31	10.13	0.115
HADS-P Depression	2.98	4.12	0.042
HADS-P Anxiety	5.82	4.74	0.218

Paired T-test

3c. Baseline and Post LT4 treatment

	Baseline	Post LT4 treatment	P value
TSH	1.80	1.63	0.534
MoCA-P	25.22	24.93	0.212
HADS-P Total	10.22	10.13	0.192
HADS-P Depression	3.84	4.12	0.246
HADS-P Anxiety	6.38	4.74	0.072

Paired T-test

mean MoCA-P score to 24.93 ($p = 0.004$) while there was no significant change in mean HADS-P total score. Mean MoCA-P and HADS-P scores did not vary significantly when their baseline scores were compared to their scores post-LT4 treatment.

For the different cognitive domains (as shown in Table 4) during period of hypothyroidism, there was a significant decrease in the visuospatial/executive function with mean score of 3.43 from 3.86 ($p = 0.014$). The same was observed with the attention domain which decreased to 4.36 from 4.86 ($p = 0.021$). There was also a mean decrease in the language domain although this

was not statistically significant. No significant change was noted in the short-term memory, naming, abstraction and orientation domains at this time. After treatment with LT4 therapy, there was significant improvement in visuospatial/executive function ($p = 0.027$). There was also improvement in the attention domain although the result was not significant ($p = 0.121$). This may imply partial reversibility or it may require longer time for attention to completely recover. Surprisingly, there was a significant improvement in the score of delayed recall (memory domain) even without prior significant change during the period of hypothyroidism. This could be attributed

Table 4. Cognitive domains mean scores at 3 time points

4a. Baseline to Hypothyroid state

	Baseline	Hypothyroid	<i>P value</i>
Visuospatial/Executive	3.86	3.43	0.014
Naming	2.86	3.00	0.085
Attention	4.86	4.36	0.021
Language	2.00	1.71	0.202
Abstraction	2.00	2.00	0.500
Memory/Delayed Recall	2.43	2.43	0.500
Orientation	6.00	5.93	0.168

Paired T-test

4b. Hypothyroid to Post LT4 treatment

	Hypothyroid	Post LT4 treatment	<i>P value</i>
Visuospatial/Executive	3.43	3.90	0.027
Naming	3.00	2.91	0.84
Attention	4.36	4.81	0.121
Language	1.71	1.82	0.345
Abstraction	2.00	2.00	0.500
Memory/Delayed Recall	2.43	3.58	0.015
Orientation	5.93	5.98	0.184

Paired T-test

4c. Baseline and Post LT4 treatment

	Baseline	Post LT4 treatment	<i>P value</i>
Visuospatial/Executive	3.86	3.90	0.298
Naming	2.86	2.91	0.5
Attention	4.86	4.81	0.399
Language	2.00	1.82	0.297
Abstraction	2.00	2.00	0.500
Memory/Delayed Recall	2.43	3.58	0.059
Orientation	6.00	5.98	0.485

Paired T-test

to practice effect or maybe a probable enhancing effect of LT4 on memory. Cognitive domain scores did not vary significantly when their baseline scores were compared to their scores post-LT4 treatment except for a noticeable trend towards improvement on memory domain.

DISCUSSION

Adequate thyroid function is essential for cognition. Any derangement has been shown in many studies to cause various cognitive impairments which may decrease the overall function and quality of life of a patient.²⁻⁴ Although there are numerous data studying cognitive dysfunction on hypothyroidism in general^{8-12,15}, there are only a few or very limited researches that venture on this specific subset of population that undergoes short-term hypothyroidism.^{4,16-18} Moreover, very few data in the literature studied Filipino population thus this study was conducted.

A review article by Begin *et al.* in 2008 tabulated studies conducted on the effect of clinical hypothyroidism on global cognition and other specific cognitive domains and their reversibility with LT4 treatment.¹⁵ All of the studies showed alteration in global cognition during state of hypothyroidism but showed opposing results with LT4 treatment. In particular, Capet *et al.*⁸ who recruited 30 hypothyroid patients at the OPD comparing them to 30 normal controls and assessing them at 2 time points (during state of hypothyroidism and after hypothyroidism has been cured) using MMSE showed improvement in global cognition while Osterweil *et al.*⁹ which investigated on 54 hypothyroid patients with varying severity (30 overt, 14 mild) using similar methodology did not show improvement with LT4 treatment. Our study, on the other hand, showed that short-term hypothyroidism causes a significant level of cognitive impairment that generally returns to baseline level after treatment with LT4 which is comparable to the study by Capet *et al.* In addition, this decrease, although statistically significant, does not reach severe levels of impairment (MoCA-P score of less than 21) thus the current practice of inducing short-term hypothyroidism in DTC patients is acceptable.

As observed in many studies, cognitive decline in this study was also evident with older population, highlighting the role of normal aging process in the pathophysiology of cognitive decline.^{8,15} The number of exposures to several hypothyroidism episodes was also analyzed in this study. The authors initially hypothesized that there would be a difference in MoCA-P score

between patients experiencing first time short-term hypothyroidism (for RAI post thyroidectomy) and multiple times short-term hypothyroidism (thyroid cancer monitoring) but results did not show any statistical significance. This would imply that short-term hypothyroidism does not appear to have a “stacking effect” producing a cumulative damage when repeatedly done over time. Further research is recommended as there is scarcity of data regarding this topic. In terms of duration of hypothyroidism, as long as the patient is exposed to short-term hypothyroidism for at least 4 weeks, this can already result to a significant decrease in general cognition which may require safety and occupational considerations. The level of education in this study did not matter significantly. What mattered was the ability of being able to maintain normal cognitive function with an active “thinking” status as evidenced by a normal or greater MoCA-P score in the working population.

Anxiety and depression are common conditions in patients with cancer in general and may be aggravated during period of hypothyroidism which may influence cognitive performance.⁴ In our study, these factors were not found to influence cognition. During period of short-term hypothyroidism, even with a significantly increased serum TSH level, there was a trend towards improvement of depression and anxiety scores. This is comparable to the study done by Tagay *et al.*¹⁶ which did not show worsening of anxiety and depression during overt hypothyroidism. In contrast, the study by Badihian *et al.*⁴ showed significant occurrence of both anxiety and depression during the hypothyroid state using the same HADS tool. The difference in the result of these studies may either be due to methodology or the instrument used for extracting depression or anxiety or may be influenced by the frequent follow up/counseling that was done as part of extracting this psychological assessment which may have alleviated anxiety and depression in the process.

There are many studies that explored on specific cognitive domains. The study by Capet *et al.* and Osterweil *et al.* did not only delve on global cognition but also used other neuropsychological tools to explore attention, memory, language and visuospatial domains. In the study by Capet *et al.*, there was noted significant alteration in all of these domains during state of hypothyroidism except for language domain. Improvement was noted in all of these domains except for language domain which remained to be unaffected after 6 months of LT4 treatment.⁸ On the other hand,

Osterweil *et al.* showed alteration in all of these domains with improvement only on memory and attention domain after 5 months of LT4 treatment.⁹ Miller *et al.*¹⁰ recruited 14 hypothyroid patients compared with 10 normal control in a prospective study which tested cognition at 2 time points, hypothyroid state and 3 months after LT4 treatment. They specifically studied memory domain which showed reversibility after LT4 treatment. Wekking *et al.*¹¹ recruited 141 hypothyroid patients on adequate LT4 replacement and assessed their cognitive function compared to results to reference values according to Dutch Clinical Neuropsychiatric practice. They noted poor performance on various domains especially on complex attention task and verbal memory tests. Their study concluded that neurocognitive functioning may not be completely restored in patients with hypothyroidism despite LT4 therapy. Lastly, Mennemeier *et al.*¹² noted in a single patient alteration on memory, and visuospatial abilities with improvement of visuospatial abilities while memory did not improve even after 6 months of LT4 treatment, which contrasts with the study by Miller *et al.*

As for the result of our study, short-term hypothyroidism affected primarily visuospatial/executive function, and attention domains, which usually show reversibility or improvement after LT4 treatment.^{8,15} A local study done by Go *et al.*¹⁸ examined hypothyroid patients and the reversibility of specific cognitive domains using LT4 and it showed that orientation and attention recovered first after 2 weeks followed by memory, calculation, reasoning and language at 4 weeks. Munte *et al.*¹⁷ also demonstrated improvement of attention domain after 2-3 months of Levothyroxine treatment. Although the attention domain in our study showed improvement, the result was not significant such that in contrast to the study by Go *et al.* and Munte *et al.*, attention domain may not completely reverse after 4 weeks of hypothyroidism and may require longer time. The result of our study is similar to the study by Miller *et al.*¹⁰ which also did not show significant improvement of attention domain even after 3 months of Levothyroxine treatment, which the authors attributed to the shorter duration of treatment and observation. This finding is further supported by the results of studies by Capet *et al.*, and Osterweil *et al.* which showed reversibility of the attention domain after a longer time at around 5-6 months.^{8,9} A fascinating finding in this study was the result on memory domain. There was noted absence of short-term memory impairment

during short-term hypothyroid state, which was not observed in most of the studies reviewed.^{8-12,17} This may suggest that a shorter duration of hypothyroidism may not be enough to induce irreversible damage from the memory area of the brain. Interestingly, even without prior decline in memory, there was noted significant improvement post-LT4 treatment. A similar observation was noted in the study by Schraml *et al.*¹⁹ where scores were notably higher in LT4 treated individuals than in control. Would this signify an enhancing effect of LT4 to memory? A study in animals suggested that there is an augmentative effect of thyroxine on cognitive function such as enhanced memory by an increased cholinergic activity in the frontal cortex and hippocampus.²⁰ However the exact mechanism is still unknown. Perhaps, a more plausible explanation for this would be the possibility of a practice/learning effect which can happen when using the same tool at least twice at a short time interval.

There were several limitations that may have affected the results of this study. First was the sample size which was small. A greater population would be recommended to better represent population and to have more reliable results. Second was the possibility of practice/learning effect for using the same tool thrice in a monthly interval as mentioned. This may be avoided by using an alternate MoCA tool however this is currently not available in the Philippines. Third, tests that can more comprehensively examine the presence of depression and anxiety in this type of population should be considered in future researches.

Putting into practice the results of this study, it is advisable that patients who undergo short-term hypothyroidism should be well-educated on its possible alterations in the general cognition and be informed of some expectations with performance involving affected cognitive domains which could in turn affect their activities of daily living and quality of life.⁴ Visuospatial/executive domain is used when we try to estimate distances between one object from another and one tries to manipulate objects in our mind to plan for their position/arrangement before actually doing it. This can be applied to activities such as parking a car or demonstrating and teaching procedures and in planning and organizing occasion and events. However, these limitations may be expected to recover after the patient also recovers from the state of hypothyroidism. Attention domain, on the other hand, was found to be not readily reversible after a month of LT4 therapy. This is usually

used in activities that highly demand attention. Examples are work-related conversations in call centers, driving, operating heavy equipment and machineries, calculation, teaching and many more.¹⁷ Patients may be assigned temporarily to a less attention demanding tasks and may resume once attention has improved. Lastly, physicians taking care of these patients should continue to provide support through psychological or emotional counseling whenever necessary.

In conclusion, there is a significant decrease in the cognitive function with short-term hypothyroidism that mostly improves and reverses with LT4 therapy. Older age is more associated with decreased cognition while anxiety and depression did not show any significant influence. Cognitive domains affected were visuospatial/executive and attention domains which also improved with treatment while there was no noted effect on memory and other cognitive domains.

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DISCLOSURE

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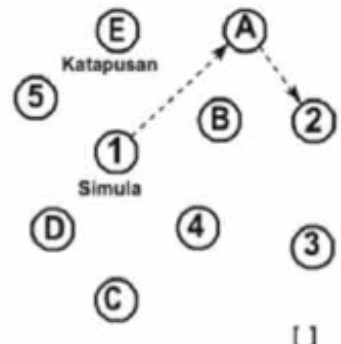
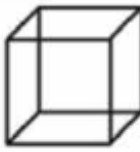


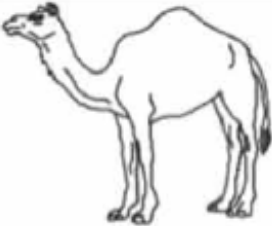
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Supplementary Figure 1. Montreal Cognitive Assessment-Philippines (MoCA-P) tool

NAME : _____
 Education : _____
 Sex : _____ Date of birth : _____
 DATE : _____

MONTREAL COGNITIVE ASSESSMENT - PHILIPPINES (MOCA-P)							POINTS
VISUOSPATIAL / EXECUTIVE							___/5
		Kopyahin Gumuhit ng orasan (Sampung minuto makalipas ng alas onse) (3 points)				[] HUGIS [] NUMERO [] KAMAY	
NAMING							___/3
						[] [] []	
MEMORY							No points
Basahin ang mga nakasulat na salita. Dapat maulit ng subject ang mga ito. Basahin ng pangalawang beses kahit ito ay naulit nang pang-una.							
1st trial	MUKHA	ASUL	SIMBAHAN	ROSAS	SEDA		
2nd trial							
ATTENTION							___/2
Dapat ulitin ng subject ang mga numero ayon sa pagkakabigkas [] 2 1 8 5 4 Basahin ang mga numero.(Numero/segundo) Dapat ulitin ng subject ang mga numero ng pabaliklad [] 7 4 2							
Basahin ang mga letra. Dapat tumapik ang subject sa mesa sa bawat bigkas ng letra 'A'. Walang puntos kapag dalawa ang mali. [] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B							___/1
Bawasan ng 7 ang 100 [] 93 [] 86 [] 79 [] 72 [] 65 4 o 5 na tamang sagot=3 puntos; 2 o 3 tama=2 puntos; 1 tama=1 puntos; 0 tama=0 puntos							___/3
LANGUAGE							___/2
Ulitin: Ang alam ko lang, si Juan ang siyang tutulong ngayong araw. [] Ang pusa ay nagtatago sa ilalim ng upuan kapag nasa kuwarto ang aso. []							
Fluency / Sabihin sa akin sa loob ng 1 minute ang mga salitang Filipino na nagsisimula sa letrang B. [] _____ (N ≥ 11 salita)							___/1
ABSTRACTION							___/2
Halimbawa: Pagkakarpareho ng orange at saging = prutas [] tren - bisikleta [] timbangan - ruler							
DELAYED RECALL							___/5
Dapat matandaan ang mga salita ng walang tulong.							
	MUKHA	ASUL	SIMBAHAN	ROSAS	SEDA	Bigyan ng puntos ang mga salitang natandaan ng walang tulong.	
Optional							
Category cue							
Multiple choice cue							
ORIENTATION							___/6
[] Petsa [] Buwan [] Taon [] Araw [] Lugar [] Lungsod							
© Z.Nasreddine MD Version 7.1 www.mocatest.org Normal ≥26 / 30							
TOTAL						___/30	
Philippine Version: 25 August 2011 Adapted by Dominguez JC and the Dementia Study Group Administered by: _____							
Add 1 point if ≤ 12 yr edu							

Supplementary Figure 2. The Hospital Anxiety and Depression Scale in Filipino version (HADS-P)

The Hospital Anxiety and Depression Scale in Filipino version (HADS-P)

Mga Direksyon sa Pagsagot:

Alam ng mga doktor na may mahahalagang papel ang damdamin natin sa maraming sakit. Kung alam ng iyang doktor ang inyong nararamdaman, mas matutulungan niya kayo. Ang palatanungang ito ay ginawa para tulungan ka ng inyong doktor na malaman ang inyong nararamdaman. Basahin ang bawat tanong at i-tsek ang kahon ang katugmang sagot na pinakamalapit sa inyong nararamdaman sa nakaraang lingga. Huwag masyadong magtagal sa pagsagot, ang inyong unang reaksyon ay mas malamang na tama kaysa mas matagal na pinag-isipang sagot.

Isang sagot lamang ang i-tsek sa bawat tanong.

- | | |
|--|--|
| <p>A 1. Naliligalig at punong-puno na ako:
 <input type="checkbox"/> Mas madalas kaysa hindi
 <input type="checkbox"/> Madalas
 <input type="checkbox"/> Paminsan-minsan
 <input type="checkbox"/> Hinding-hindi</p> <p>D 2. Pakiramdam ko parang pinapabagal ako:
 <input type="checkbox"/> Halos lagi-lagi
 <input type="checkbox"/> Napakadalas
 <input type="checkbox"/> Minsan
 <input type="checkbox"/> Hinding-hindi</p> <p>D 3. Ikinasasaya ko pa rin ang mga bagay na dati ko nang ikinasasaya:
 <input type="checkbox"/> Katulad din ng dati
 <input type="checkbox"/> Konti lang
 <input type="checkbox"/> Halos hindi na
 <input type="checkbox"/> Halos hindi na</p> <p>A 4. Para akong natatakot na may nararamdamang nerbiyas:
 <input type="checkbox"/> Hinding-hindi
 <input type="checkbox"/> Paminsan-minsan
 <input type="checkbox"/> Medyo madalas
 <input type="checkbox"/> Madalas na madalas</p> <p>A 5. Para akong natatakot na may mangyayaring masama.
 <input type="checkbox"/> Lagi-lagi at medyo lang
 <input type="checkbox"/> Palagi pero di-gaanong malala
 <input type="checkbox"/> Konti, pero 'di ako nag-aalala ng nararapat
 <input type="checkbox"/> Hinding-hindi</p> <p>D 6. Nawalan na ako ng interes sa aking itsura.
 <input type="checkbox"/> Talaga
 <input type="checkbox"/> Hindi nangangalaga ng dapat
 <input type="checkbox"/> Pwedeng hindi ako mag-alaga
 <input type="checkbox"/> Pinapangalagaan ko pa rin ito katulad ng dati</p> <p>D 7. Kaya ko pang tumawa at mapansin ng nakakatuwang bahagi sa mga bagay-bagay:
 <input type="checkbox"/> Lagi-lagi tulad ng dati
 <input type="checkbox"/> Mas madalang na konti kaysa dati
 <input type="checkbox"/> Hindi na katulad ng dati</p> | <p><input type="checkbox"/> Hinding-hindi</p> <p>A 8. Hindi ako mapakali na parang gusto kong may pinagkakaabalahan:
 <input type="checkbox"/> Talagang Madalas
 <input type="checkbox"/> Medyo madalas
 <input type="checkbox"/> Di naman ganito
 <input type="checkbox"/> Hinding-hindi</p> <p>A 9. Pag-aalala ang nasa isip ko:
 <input type="checkbox"/> Madalas na madalas
 <input type="checkbox"/> Madalas
 <input type="checkbox"/> 'Di gaanong madalas
 <input type="checkbox"/> Konting-konti</p> <p>D 10. Masaya akong umaasa sa bagay-bagay.
 <input type="checkbox"/> Kasingdalas ng nakagawian ko
 <input type="checkbox"/> 'Di singdalas ng nakagawian ko
 <input type="checkbox"/> Mas madalang
 <input type="checkbox"/> Halos hindi na</p> <p>D 11. Masaya ang aking pakiramdam.
 <input type="checkbox"/> Hindi kailanman
 <input type="checkbox"/> Madalang
 <input type="checkbox"/> Paminsan-minsan
 <input type="checkbox"/> Kadalasan</p> <p>A 12. Bigla ako nakakaramdam ng pagkatakot.
 <input type="checkbox"/> Madalas na madalas
 <input type="checkbox"/> Medyo madalas
 <input type="checkbox"/> 'Di-gaanong madalas
 <input type="checkbox"/> Madalang na madalang</p> <p>A 13. Kaya kong umupo ng kumparTable at mag-relax.
 <input type="checkbox"/> Palagi
 <input type="checkbox"/> Madalas
 <input type="checkbox"/> Madalang
 <input type="checkbox"/> Hinding-hindi</p> <p>D 14. Kaya kong maaliw ng isang magan dang libro o programa sa radya/TV
 <input type="checkbox"/> Madalas
 <input type="checkbox"/> Paminsan-minsan
 <input type="checkbox"/> Madalang</p> |
|--|--|

Hinding-hindi

Pakitiyak lang kung nasagutan ninyo ang lahat ng tanong. Maraming salam at po!

PARA SA HOSPITAL: A _____ D _____