Does Tinnitus Affect the Cognitive Function?

Original Article

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ABSTRACT

Background: Tinnitus is defined as a subjective auditory phantom phenomenon in which patients hear internal sounds when there is no external source of acoustic stimuli. Tinnitus is a result of a chain of plastic changes which have an effect on the entire auditory system. The aim of this study is to assess the cognitive function in patients with chronic idiopathic tinnitus.

Methods: This case-control study included two groups: The control group (32 normal hearing individuals without tinnitus), the study group (32 normal hearing individuals with tinnitus). All individuals in the study had undergone full history taking, full otological examination, basic audiological evaluation, Arabic version of tinnitus handicap inventory (THI), Arabic version of Beck anxiety inventory (BAI), Arabic version of Montreal cognitive Assessment (MoCA) and electrophysiological tests (P300 and MMN).

Results: No significant differences were found between the two groups as regards age and sex distribution. Patients with tinnitus had statically significant delayed P300 latencies compared to the control group. No significant differences were found regarding P300 amplitude, MMN amplitude and latency between the studied groups. In the tinnitus group, there were significant positive correlations between THI scores and both BAI scores and P300 latencies (*P value* <0.05) and significant positive correlations between P300 latencies and BAI scores (correlation coefficient r=0.87, *P value* = 0.000) while significant negative correlations between P300 latencies and MoCA scores (correlation coefficient r=-0.78, *P value*= 0.000) were noted.

Conclusion: Tinnitus patients have impaired cognitive functions which are correlated to the severity of tinnitus and the degree of anxiety. The P300 test can be a useful test for objective evaluation of patients with tinnitus and to assess the cognitive function of tinnitus patients.

Key Words: Central auditory nervous system, cognitive function, MMN, P300, tinnitus.

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INTRODUCTION

Tinnitus is a subjective auditory phantom phenomenon in which patients hear internal sounds when there is no external source of acoustic stimuli[1]. Epidemiological studies in Europe and the USA indicate that about 10 to 15% of people experience tinnitus for an extended period of time. The prevalence of tinnitus is nearly equal among women and men, and it tends to increase significantly in individuals over the age of 65[2].

Tinnitus is a result of a chain of plastic changes which have an effect on the entire auditory system, which are triggered by destruction of the peripheral structures of the auditory system. Observations have shown reorganization of tonotopic maps in auditory cortical areas and an increase in neuronal activity[1].

Event related potentials (ERPs) are used to assess cognitive operations and attentional function that are linked to a mental or physical event[3], give quantitative data about tinnitus, help to determine objectively, signal processing changes in the brain caused by tinnitus and detecting the changes of electrical activity in the auditory pathway[4].

The P300 is extensively researched as an event-related potential component used to evaluate selective attention function[5]. It is triggered when a subject is required to differentiate the significant (target) stimulus from the non-significant (standard) stimuli[6]. The mismatch negativity (MMN) is defined as an auditory event-related potential which is generated in response to a deviant stimulus presented within a sequence of frequent stimuli. It likely represents the pre-attentive phases of sensory interpretation of auditory input[4].

Some researchers have indicated that some patients with tinnitus do not exhibit noticeable cognitive impairments; numerous other studies have revealed that individuals with severe tinnitus may experience significant cognitive deficits[7]. So, this study aimed to assess the cognitive function in individuals with chronic idiopathic tinnitus by

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utilizing the Montreal Cognitive Assessment (MoCA) as a subjective measure of cognitive ability, and P300 and MMN as objective tests to assess their selective attention and pre-attentive processes.

SUBJECTS AND METHODS

This case-control study was carried out in the audio-vestibular unit, ENT department, hospitals of Menoufia University in the duration from October 2022 to October 2023. Ethical approval from the hospital Committee was obtained [number: 19519ENT15] and a written consent was obtained from all subjects participating in the research. Subjects participating in this research were categorized into 2 groups: the control group which consisted of 32 normal subjects in the age range of 20-40 years old, with no otological or psychological complaints, and the study group (cases group) which consisted of 32 subjects fulfilled the following Inclusion criteria:

1. Subjects complaining of chronic idiopathic tinnitus (for at least 6 months).
2. All subjects have normal hearing threshold level.
3. The age range of 20-40 years old.

Exclusion criteria

1. Subjects with history of central nervous system disease.
2. Subjects with centrally acting medications.

All individuals in this research had been submitted to:

Full history taking, The Arabic version of Beck anxiety inventory (BAI)[8] was administered for assessment the severity of anxiety in tinnitus subjects. It is composed of 21 questions, according to the sum of all answers, the BAI score was classified into, no or very low anxiety (0-7), mild anxiety (8-15), moderate anxiety (16-25), and severe anxiety (26- 36).

The Arabic version of Montreal cognitive assessment (MoCA)[9] is a subjective method for assessment cognitive function; it is composed of 30 pointed tests conducted within 10 min. The sum of all answers was 30 points, a score of 26 or above was interpreted as normal and a score less than 26 was considered mild cognitive impairment (MCI).

The Arabic version of tinnitus handicapped inventory (THI)[10], which was used to assess the severity of tinnitus among the tinnitus group, which was composed of 25 questions, according to the sum of all answers, the THI score was divided into 5 grades., (Grade I) which reveals slight or no handicap (0-16), (Grade 2) which reveals mild handicap (18-36), (Grade 3) which reveals moderate handicap (38- 56), (Grade 4) which reveals severe handicap (58- 76) and (Grade 5) which reveals catastrophic handicap (78- 100).

General, neurological examination, otological examination, basic audiological evaluation which included pure tone audiometry (PTA), speech audiometry (using Inventis Piano), immittancemetry (using resonance 36 m),

P300 and MMN (using Neurosoft Ltd), MMN and P300 were recorded using the following electrode montage: four electrodes were positioned at Fz (active electrode), Fpz (ground electrode), M1 and M2 (right and left mastoid respectively) as reference electrodes. In MMN and P300 testing, 200 stimuli had been conducted monaurally at a stimulus intensity of 70 dBnHL with filter settings of (30 Hz) as a high pass filter and (1 Hz) as a low pass filter. The Mismatch Negativity (MMN) was recorded while the participants were in a relaxed seated position. The patients were directed to divert their focus away from the auditory stimuli. MMN was recorded using oddball paradigm, where two different tone burst stimuli been randomly represented. The standard stimulus frequency was (1000 Hz) which was presented 80% of the time, the deviant stimulus frequency was (1100 Hz) and was presented 20% of the time,

In P300 testing, the participants were directed to maintain a state of vigilance, focusing on an infrequent target stimulus (deviant stimulus) that was delivered randomly among standard frequent stimuli (oddball paradigm), and to respond by pressing a button. The standard stimuli (1000 Hz) had been presented 80% of the time while the deviant (2000 Hz) had been presented 20% of the time. The latency and amplitude of P300 and MMN waves were recorded for all the studied groups.

Statistical analysis

Data was collected and statistically analyzed by utilizing the statistical package of social science (SPSS) program (SPSS Inc., Chicago, IL, USA) Microsoft Windows (version 16). Comparing groups had been done using Chi-square-test($\chi 2$), Independent t test and Mann-whitney U test, which had been used to detect the significance of the difference among two independent means for parametric data. Pearson Correlation was done to determine the association between two variables. Significant test results were taken when *p- value* ($p < 0.05$).

RESULTS

The demographic characteristics of the studied groups are shown in (Table 1) with no statistically significant difference between both groups regarding age and sex distribution. All participants in both groups had normal hearing threshold, speech audiometry and immittancemetry results.

Table 1: Demographic data of the studied groups

Characteristics	Cases No.(32)	Controls No.(32)	Significance test	*P- value*
Age (mean± SD)	33.78±4.66	31.68±4.84	t=1.76	0.083
Sex:				
Males	14(43.8%)	15(46.9%)	$\chi 2$=0.66	0.802
Females	18(56.2%)	17(53.1%)		

No: number, SD: standard deviation, %: percentage, X2: Chi-square test,

t: student t test, p value: probability value (*significant difference p value <0.05)

The Arabic version of BAI revealed that 5 subjects in the tinnitus group (16%) had no anxiety, 10 subjects (31%) had mild anxiety, 6 subjects (19%) had moderate anxiety and 11 subjects (34%) had severe anxiety. In the control group, 11 (34%) of subjects had no anxiety.

The Arabic version of MoCA showed that, 21 subjects of the tinnitus group had within normal cognitive function while 11 subjects (34%) had mild cognitive impairment. In the control group, all subjects had within normal MoCA scores.

Results of The Arabic version of THI in the tinnitus group are demonstrated in (Figure 1).

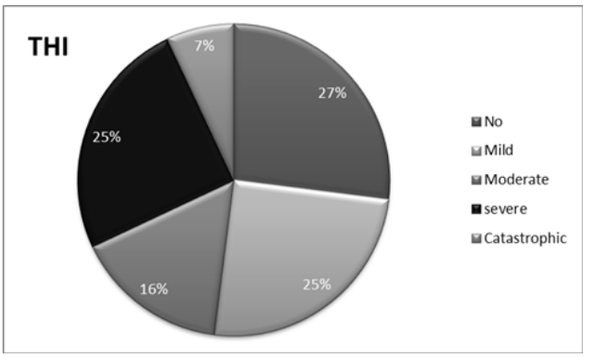

Fig. 1: Tinnitus handicap inventory results: (Grade 1) slight or no handicap, (Grade 2) mild handicap, (Grade 3) moderate handicap, (Grade 4) severe handicap and (Grade 5) catastrophic handicap.

Comparison between BAI and MoCA scores among the studied groups are demonstrated in (Table 2). There were statistically significant differences as regards BAI and MoCA scores between both groups.

Table 2: BAI and MoCA Scores among the Studied Groups

Characteristics	Cases No.(32)	Controls No.(32)	Significance test	*P-value*
BAI Score (mean± SD)	19.84±12.03	11.50±7.90	t=3.27	0.002*
MoCA Score (mean± SD)	25.56±2.53	26.78±1.51	t=-2.33	0.023*

BAI: Beck Anxiety Inventory MoCA: Montreal Cognitive Assessment

The amplitudes and latencies of P300 and MMN waves are demonstrated in (Table 3). Tinnitus subjects had statistically significant delayed P300 latencies with no statistically significant difference as regards P300 amplitudes, MMN latencies, and amplitudes between both groups.

In the tinnitus group, there were significant positive correlations between THI scores and both BAI scores and P300 latencies, and a significant negative correlation between THI scores and MoCA scores as demonstrated in (Table 4). While no statistically significant correlations between THI scores and MMN latency, amplitude, and P300 amplitude were noted in tinnitus patients (Pearson correlation, ($p > 0.05$).

Table 3: P300 and MMN absolute latencies and amplitudes in the studied groups

Characteristics	Cases No.(32)	Controls No.(32)	Significance test	*P- value*
P300 Latency (mean± SD)	323.03±47.24	288.41±20.88	Z=3.12	0.002*
P300 Amplitude (mean± SD)	6.82±4.00	7.02±6.01	Z=-0.90	0.368
MMN Latency (mean± SD)	232.64±21.94	229.86±21.96	t=0.50	0.614
MMN Amplitude (mean± SD)	3.93±2.02	6.17±6.96	Z=-0.80	0.420

MMN: mismatch negativity, no: number, SD: standard deviation, t: student t test, *p value:* probability value (*significant difference *p value* <0.05)

Table 4: Correlation between THI score with BAI Score, MoCA, and P300 Latency in tinnitus patients

Correlation between THI score with:	Correlation coefficient (r)	*P value*
BAI Score	0.88	0.000*
MoCA Score	- 0.80	0.000*
P300 Latency	0.93	0.000*

*significant difference *p value* <0.05

There were significant positive correlations between P300 latencies and BAI scores (correlation coefficient r = 0.87, *P value* = 0.000) and significant negative correlations between P300 latencies and MoCA scores (correlation coefficient r = -0.78, *P value* = 0.000).

DISCUSSION

Tavanai and Mohammadkhani reported that tinnitus significantly impairs cognitive function, leading to a decrease in the cognitive capacity needed to carry out conscious, voluntary, and mentally demanding duties. Also, performance of the control and tinnitus groups was often similar in activities with minimal demands. However, when faced with challenging conditions, a difference in performance between the control and tinnitus groups was observed[11].

The cognitive resource depletion hypothesis suggests that when tinnitus subjects focus on their tinnitus, their resources of cognition get occupied. Consequently, the capacity to concentrate on other activities will be a demanding circumstance, resulting in reduced performance when other demanding jobs require controlled processes[12], so when tinnitus patients undergo the oddball paradigm (As P300 and MMN), this creates a challenging task for the tinnitus subject to focus on the rare stimulus which can effect on the amplitude and the latency of the waves[13]. Another consideration is that the acoustic signals

presented to these subjects are affected by the masking effect of tinnitus[14]. So, this research studied the impact of tinnitus on cognitive function in patients experiencing chronic idiopathic tinnitus, in comparison to normal subjects through challenging conditions in P300 and MMN responses.

As there are neither objective measures nor biomarkers for diagnosis of tinnitus, tinnitus severity can be assessed using specific self-reported questionnaires, which can facilitate collecting data about the impact of tinnitus on personal and social life[15]. In the current study, about two-thirds of tinnitus patients had different degrees of handicapping according to the Arabic version of THI. Tinnitus patients may have emotional distress, cognitive impairment, automatic arousal, and functional incompetence[16].

In the current study, subjects in the tinnitus group had variable degrees of anxiety according to the Arabic version of BAI. Pinto *et al*. stated that; there is a strong relationship between tinnitus severity and anxiety disorders. Anxiety usually occurs with tinnitus, reduces the patient's tolerance to tinnitus, and frequently exaggerates the functional handicap of tinnitus patients, which causes an increase in symptoms. Liability to anxiety could be genetic or may be caused by overlapping neurobiological pathways which cause the progression of both tinnitus and anxiety[17].

In the current study, there were statistically significant longer P300 latencies in the study group compared to the control group. This result is in agreement with the studies of Wang *et al*. and Majhi *et al*. who found a significant increase in P300 latencies in subjects with tinnitus compared to normal subjects[7, 18].

Latency and amplitude are the two basic neurophysiological measures of P300 for cognitive function evaluation. Latency can be used as a reliable measure of information processing speed in the brain. Delayed latency indicates that the duration of information processing is prolonged. Conversely, decreased peak amplitude represented a disturbance in the functioning of some central generators, leading to disruption in the processing of information in the cortex. Only one of the parameters is sufficient for the diagnosis of cognitive dysfunction[19].

No statistically significant difference between the 2 groups regarding P300 amplitudes was noted in the current study. Didoné *et al*. stated that P300 amplitude is thought to be of limited clinical value in P300 assessment[20]. These results are in accordance with the findings of Mannarelli *et al*., Wang *et al*., and Najafi and Rouzbahani who reported that there was a non-significant difference regarding P300 amplitude between both the tinnitus and control groups[1,7,21].

Some studies suggested that alternations in non-auditory central tinnitus generators including the limbic system and the prefrontal cortex, which also control top-down mechanisms of cognition, are thought to have an important role in attention, sensations and emotions resources regulation[22]. Because the limbic system, particularly the hippocampus, has been suggested to play an important role in P300 wave creation and modification, this could explain the abnormal findings in P300 results in patients with tinnitus[11].

The Montreal Cognitive Assessment scores revealed lower scores in tinnitus subjects than in normal controls, with significant differences between both groups. Magnetic resonance imaging (MRI) studies revealed that patients with tinnitus manifest an increase in the gray matter within the frontal cortex, anterior cingulate, and auditory thalamus, while there is a decrease in the gray matter within the superior frontal cortex and the ventromedial prefrontal cortex[23]. Those neuroanatomical modulations have a distinct function in both cognitive impairments associated with tinnitus and emotional disorders[7].

Positive correlations between P300 latencies, THI scores, and BAI scores were reported in the current study, in addition to a significant negative correlation between THI scores and MoCA scores, which means that the degree of cognitive affection is related to the severity of tinnitus and anxiety levels. These findings are in agreement with Dağ *et al*. and Lee *et al*.[24,25]. 67% of patients in this study had within normal cognitive function, which may be explained by the low anxiety level in those patients. Shakarami *et al*. reported that the absence of cognitive function impairment in some tinnitus patients may be attributed to the mildness of their tinnitus, as well as the low level of annoyance and loudness related to it. Also, in individuals with low tinnitus levels reduced conscious perception of the condition results in decreased attention and intervention of tinnitus on cognition[26].

MMN responses were analyzed in the current study which revealed no statistically significant difference regarding MMN absolute latency and amplitude between the studied groups. Also, no statistically significant correlations were found between (THI scores, BAI scores, MoCA scores) and MMN latency, amplitude in the studied patients. Mahmoudian *et al*. and Sendesen *et al*. reported significantly smaller MMN amplitude in the tinnitus subjects in comparison to healthy controls, with no statistically significant difference as regards MMN absolute latency among the studied groups. According to our study findings, MMN features revealed no differences among subjects with tinnitus and subjects without tinnitus, which may suggest that our tinnitus patients did not exhibit any changes in the pre-attentive processing stage, or may be due to using a small sample size. Therefore, it is recommended in future research to apply a larger sample size[4,27].

The effect of tinnitus on cognitive function was assessed in this study which revealed significant differences

between both the control and tinnitus groups regarding P300 latency and MoCA scores, which denote cognitive impairment in tinnitus patients. However, no differences between the studied groups were reported in the MMN test. This suggests that the measurement of the P300 value can be utilized to evaluate the cognitive function in subjects with tinnitus.

Finally, cognitive function should be assessed in tinnitus patients for early detection and subsequent rehabilitation with follow-up of the progression of the patient's condition. The lack of radiological functional assessment of the brain is one of the limitations of this study, in addition to the small sample size. Also, the lack of psychophysical tests assessing the central auditory functions, especially memory and attention, is considered one of this study's limitations.

CONCLUSION

According to this study, P300 and MMN have been used as objective tests to assess cognitive function in subjects with chronic idiopathic tinnitus. The findings of our study indicate that tinnitus patients exhibit a considerably greater delay in P300 latency compared to normal controls. The cognitive function and the degree of anxiety were correlated to the severity of tinnitus.

Further large scaled studies are recommended to assess the effect of tinnitus on cognitive function and central auditory function. The routine screening and management of anxiety among tinnitus patients is highly recommended to improve their quality of life.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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Appendix

Table (A.1): The Arabic version of THI:

استبيان حول اعاقة طنين الاذن

استبيان رقم.....: التاريخ:.....

ان الهدف من هذا الاستبيان هو تحديد المشاكل التي يتسبب بها طنين الاذن لديك. اختر "نعم" او "احيانا" او "كلا" لكل سؤال في المكان المناسب. نرجو منك ألا تتخطى اي سؤال. Xعبر وضع علامة

١. هل يصعب عليك التركيز بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٢. هل يؤثر مستوى الطنين على سمعك للناس؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٣. هل تشعر بالغضب بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٤. هل تشعر بالارتباك بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٥. هل تشعر باليأس بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٦. هل تشكو كثيرا للناس حواليك من الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٧. هل تعاني من صعوبة بالغفو ليلا" بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٨. هل تشعر انه ليس بإمكانك الهروب من الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٩. هل يحد الطنين من قدرتك على الأستمتاع بالانشطة الأجتماعية مثل الخروج لتناول العشاء أو الذهاب ألى السينما؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٠. هل تشعر بالاحباط نتيجة الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١١. هل تشعر بأن لديك مرض خطير بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٢. هل يصعب عليك الاستمتاع بالحياة نتيجة الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٣. هل يتداخل الطنين مع عملك او مسؤولياتك المنزلية؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٤. هل تشعر غالبا انك سريع الانفعال بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٥. هل تصعب عليك القراءة بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٦. هل يجعلك الطنين مستاء؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٧. هل يسبب الطنين توتر في علاقاتك مع بقية أفراد عائلتك وأصدقائك؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٨. هل تجد انه من الصعب عليك تركيز انتباهك على امور اخرى بعيدا عن الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
١٩. هل تشعر انه ليس لديك اي سيطرة على الطنين ؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٢٠. هل تشعر غالبا" بالتعب بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٢١. هل تشعر بالكآبة بسبب الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٢٢. هل يدفعك الطنين الى القلق؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٢٣. هل تشعر بأن ك لم تعد قادر على التعايش مع الطنين؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٢٤. هل يسوء الطنين تحت الضغط؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)
٢٥. هل يشعرك الطنين بعدم الأمان؟	☐ نعم (4)	☐ أحيانا (2)	☐ كلا (0)

Appendix

Table (A.2): The Arabic version of BAI:

قائمة بيك للقلق BAI

يوجد بالأسفل قائمة من أعراض القلق، برجاء القراءة بحرص و وضع دائرة حول درجة إزعاج العرض لك إذا كنت قد عانيت من ذلك العرض خلال الشهر الماضي بما فيه اليوم.

أعراض القلق	لا تزعجني أبدا	تزعجني قليلا	تزعجني باعتدال و لكن أستطيع تحملها	تزعجني كثيرا و لا أستطيع تحملها
التنميل	٠	١	٢	٣
الإحساس بالحرارة	٠	١	٢	٣
رعشة في الساقين (اهتزاز الأرجل)	٠	١	٢	٣
عدم القدرة علي الاسترخاء	٠	١	٢	٣
الخوف من أن يحدث الأسوأ	٠	١	٢	٣
الإحساس بالدوخة (الإغماء الخفيف)	٠	١	٢	٣
رفرفة ف القلب	٠	١	٢	٣
عدم الاستقرار أو الثبات	٠	١	٢	٣
الرعب (الخوف الشديد)	٠	١	٢	٣
التوتر	٠	١	٢	٣
الإحساس بالاختناق	٠	١	٢	٣
ارتعاش اليدين	٠	١	٢	٣
الشعور بالاهتزاز (الرعشة)	٠	١	٢	٣
الخوف من فقد السيطرة	٠	١	٢	٣
صعوبة التنفس	٠	١	٢	٣
الخوف من الموت	٠	١	٢	٣
الفزع (الخوف)	٠	١	٢	٣
سوء الهضم	٠	١	٢	٣
الإغماء	٠	١	٢	٣
تدفق الدم إلي الوجه	٠	١	٢	٣
العرق (دون أن يكون الجو حارا)	٠	١	٢	٣
المجموع				

Appendix

Figure (A.1): The Arabic version of MoCA: